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Evidence for Iron-Catalyzed α-Phosphinidene Elimination with Phenylphosphine

Justin K. Pagano,[a]‡ Brandon J. Ackley,[a] and Rory Waterman[a]*

Abstract: The ubiquitous half-sandwich iron complex $CpFe(CO)_2Me$ (Cp = η^5-C_5H_5) appears to be a catalyst for α-phosphinidene elimination from primary phosphines. Dehydrocoupling reactions provided initial insight into this unusual transformation, and trapping reactions with organic substrates gave products consistent with an α elimination mechanism, including a rare example of a three component reaction. The substrate scope of this reaction is consistent with generation of a triplet phosphinidene. In all, this study presents catalytic phosphinidene transfer to unsaturated organic substrates.

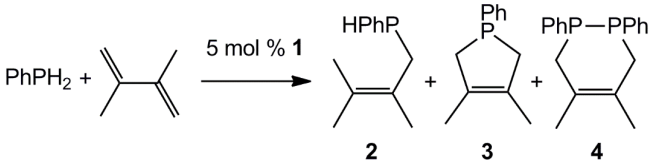
The catalytic formation of main-group bonds is of growing importance in the targeted synthesis of value-added molecules and materials.[1] Among the various elements, bond formation to phosphorus remains an ongoing field of study due to its increasing scarcity and importance in a variety of chemical disciplines.[1d, 1f, 2] An acutely underdeveloped reaction in main group bond formation is α elimination. Reported initially by Neale and Tilley in 2002, they identified that the dehydropolymerization of stannanes occurred via the formal de-insertion of a stannylene fragment from a group 4 stannyl intermediate. [3] The examples of bona fide α elimination were extended to antimony[4] and arsenic[5] in subsequent years, though a reasonable supposition for α-silylene elimination was reported by McIndoe and Rosenberg.[6] In all instances, the products from these catalytic reactions were homocoupled, either as polymers in the case of tin or as small molecules for antimony and arsenic. However, Neale and Tilley observed the *stoichiometric* trapping of a stannylene fragment during the thermal decomposition of $CpCp^*HfCl(SnMes_2H)$ in the presence of excess 2,3-dimethyl-1,3-butadiene, which gave 1,1-dimesityl-3,4-dimethylhydrostannole.[3a]

Trapping of low valent fragments is of deep synthetic importance. Returning to phosphorus, Mathey and coworkers isolated metal-stabilized 7-phosphanorbornadienes,[7] which initiated a decades-long adventure in organophosphine synthesis via phosphinidene trapping.[8] Recently, Bertrand and coworkers have shown stable singlet phosphinidenes to behave in an electrophilic manner.[9] Indeed, it is well established that phosphinidene fragments are readily trapped by dienes.[10] Despite advances from each Lammerstma and Cummins in easier-to-prepare phosphinidene precursors,[10c, 11] limitations remain—most notably that the method is not catalytic. Our objective has been to leverage hereto unknown α-phosphinidene elimination in the catalytic synthesis of organophosphines akin to stoichiometric PR transfer. Layfield and coworkers provided a critical advance in realizing this goal. In 2016, they reported the catalytic dehydrogenation of primary phosphines with trapping as phosphaalkenes in the presence of *N*-heterocyclic carbenes.[12]

Simple iron derivatives are attractive for this reaction. Ruiz and coworkers have shown that $Cp_2Fe_2(CO)_3(PR)$ (R = Mes, Mes*) and $CpFe(CO)_2(PHMes^*)$ are susceptible to apparent phosphinidene elimination under mild conditions; however, these putative phosphinidene intermediates were not successfully trapped.[13] With these results in mind, we hypothesized that $CpFe(CO)_2Me$ (**1**) would be a potential catalyst for α-phosphinidene elimination. Herein, we demonstrate that **1** is a catalyst for this reaction and subsequent catalytic trapping of these fragments with organic substrates is indeed possible. This system, however, does not exhibit a broad substrate scope, which we tentatively attribute to generation of a triplet phosphinidene.

Compound **1** is dehydrocoupling catalyst for primary and secondary phosphines (See SI for full details). For example, treatment of phenylphosphine with 10 mol % of **1** at 65 °C in a 1:9 benzene:Et_2O solution gave hydrogen and primarily $(PhPH)_2$ in approximately 45% conversion as observed by ^{31}P NMR spectroscopy.[14] Additionally, the two unusual products for dehydrocoupling catalysis, a triphosphine, $(PhPH)_2PPh$, and Ph_2PH, were observed in 6% and 1% conversion, respectively, by ^{31}P NMR spectroscopy.[1g][15] The reliable formation of $(PhPH)_2PPh$ is unknown in catalytic dehydrocoupling reactions of $PhPH_2$,[1g] and Ph_2PH was also observed in Layfield's recent report on catalytic phosphinidene transfer.[12] These two products, the triphosphine and diphenylphosphine, hint at α-phosphinidene elimination, which prompted attempts to trap such putative fragments with unsaturated substrates.

Treatment of equimolar 2,3-dimethyl-1,3-butadiene and phenylphosphine with 5 mol % of **1** in a 1:9 benzene:Et_2O solution at 65 °C for four hours gave secondary phosphine (**2**), dihydrophosphole (**3**), and tetrahydrodiphosphorin (**4**) products as a mixture in 18%, 53%, and 29% conversion, respectively (Scheme 1).



Scheme 1. All products from the reaction of phenylphosphine and 2,3-dimethyl-1,3-butadiene in the presence of 5 mol % of **1**. Reaction conditions: $PhPH_2$, 2 equiv. of 2,3-dimethyl-1,3-butadiene, and 0.05 equiv. of **1** at 65 °C for 4 h, but higher temperatures disfavor formation of **2**.

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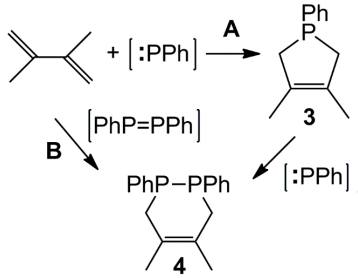
Products **3** and **4** are suggestive of phosphinidene trapping. However, the formation of a hydrophosphination product, **2**, avails the possibility that **3** results from ring closure of **2**, as **1** is a known hydrophosphination catalyst.[16] Monitoring the formation of these products by ^{31}P NMR spectroscopy does not reveal an apparent dependence of the formation of **3** on the concentration of **2** (Figure S-1). Additionally, results from two additional experiments eliminate a ring-closure pathway (i.e., **2** converted to **3**): 1) Isolated samples of **2**[2c] are not converted to **3** by **1** under catalytic conditions with or without added hydrogen, and 2) using phenylphosphine-d_2 as a substrate yields only D_2 and **2**-d_2 as observed by ^{2}H NMR spectroscopy, whereas a ring closure event would result in formation of HD and partial deuteration of **3** and **4**. Given that formation of **2** is independent of the other products, two pathways to form **4** appeared possible (Scheme 2). In pathway **A**, **4** is formed by the sequential trapping of phosphinidene equivalents, the first to give **3** followed by **3** reacting with an additional phosphinidene equivalent to give **4**. In pathway **B**, 1,2-diphenyldiphosphine, formed by the condensation of phosphinidene fragments, undergoes a [4+2] cycloaddition with 2,3-dimethyl-1,3-butadiene to give **4** directly. Two observations support pathway **A** over pathway **B**: 1) Monitoring these reactions by ^{31}P NMR spectroscopy reveals a decrease in the concentration of **3** as the concentration of **4** increases (Figure S-1), and 2) when additional $PhPH_2$ is added to a typical catalytic reaction that has reached completion (i.e., phosphine and diene substrates have been consumed), the concentration of **3** decreases with an increase in the concentration of **4**.

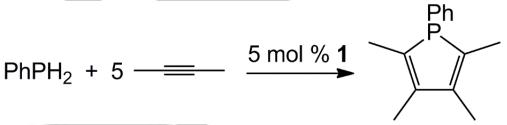


Scheme 2. Potential paths to tetrahydrodiphosphorin **4**. Path A is the sequential trapping of phosphinidene equivalents, and path B is the direct formation of **4** via a [4+2] cycloaddition with diphosphene. Observation of catalytic reactions and sequential addition of $PhPH_2$ support path A.

Formation of **3** and **4** do not appear to result from reaction of $(PPh)_5$ with 2,3-dimethyl-1,3-butadiene under these conditions, which is a known process in the melt or under UV photolysis conditions.[17] Indeed, reaction of $(PPh)_5$ with five equivalents of 2,3-dimethyl-1,3-butadiene in the presence of 10 mol % of **1** in a 1:9-benzene:Et_2O mixture at 65 °C gave only 11% conversion to **3** after 48 hours (i.e., >10x reaction time; see Supporting Information for details). In control reactions without **1**, formation of the cyclophosphines $(PPh)_x$ (x = 4, 6) are observed after 48 hours with no trapping or hydrophosphination products as determined by ^{31}P NMR spectroscopy.

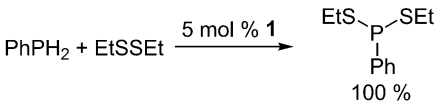
With the success of trapping reactions with 2,3-dimethyl-1,3-butadiene, more challenging substrates were attempted. Treatment of $PhPH_2$ with five equivalents of diphenylacetylene and 5 mol % of **1** afforded double hydrophosphination[16] of the alkyne in 42% conversion[2d] with trace amounts of 1,2,3,4,5-pentaphenylphosphole as measured by ^{31}P NMR spectroscopy.[10b] Formation of phosphole in greater than 10% were achieved by running the same reaction under 1 atm of hydrogen. This observation, while ineffective for synthesis, illustrates that there are tunable factors in developing this catalysis for synthesis.

In contrast, 2-butyne proved to be a more successful substrate. Reaction of $PhPH_2$ with five equivalents of 2-butyne and 5 mol % of **1** gave 2,3,4,5-tetramethyl-1-phenylphosphole in 53% conversion from starting $PhPH_2$, as identified by ^{31}P NMR spectroscopy (Scheme 3).[18] Competitive hydrophosphination was not observed under these reaction conditions. These alkyne examples indicate that there are substantial steric and electronic effects to be explored in this catalysis, and are rare examples of three-component reactions involving phosphinidene chemistry.[19]



Scheme 3. Reaction of phenylphosphine and 2-butyne with 5 mol % of **1**, which gives the 2,3,4,5-tetramethyl-1-phenylphosphole as the primary product (53% conversion by ^{31}P NMR spectroscopy). Reaction conditions: $PhPH_2$, 5 eq. 2-butyne, 0.05 eq. **1**, 65 °C, 2 h.

Diethyl disulfide also proved to be an effective trap under these reaction conditions. Treatment of a 1:9 benzene:Et_2O solution of $PhPH_2$ with equimolar $(SEt)_2$ and 5 mol % of **1** gave $PhP(SEt)_2$ in quantitative conversion after one hour as evidenced by ^{31}P NMR spectroscopy (Scheme 4). The use of diethyl disulfide as a trap for phosphinidenes is well established by Schmidt and coworkers.[20]



Scheme 4. Reaction of phenylphosphine and diethyl disulfide with 5 mol % of **1**. Reaction conditions: $PhPH_2$, EtSSEt, 0.05 eq. **1**, 65 °C, 1 h.

Further trapping reactions were largely unsuccessful. For example, reactions run in the presence of or utilizing *N*-methylimidazole as a solvent yielded no new phosphorus containing products as observed by ^{31}P NMR spectroscopy. This result indicates that involvement of a phosphenium (R_2P^+) fragment is not likely in this reaction. Furthermore, some previously reported phosphinidene traps were not successful. Simple ketones like acetone or benzophenone provide no trapping.[20] The similarity of the substrate scope to reactions reported by Schmidt is an initial indication that any phosphinidene intermediate is a triplet. The observation that singlet phosphinidenes are not readily trapped by alkynes or 2,3-dimethyl-1,3-butadiene further supports this supposition.[21] Thus, these results are consistent with the catalytic formation of triplet phosphinidenes as opposed to singlet phosphinidenes, and provide a potential avenue to develop this kind of group transfer catalysis.

Literature understanding of **1** and the observed reaction chemistry provide the basis for a working mechanistic hypothesis for this catalysis (Scheme 5). Activation of **1** would arise from migratory insertion of the methyl ligand,[22] rather than protonation, based on the relatively low acidity of these phosphine substrates[23] and prior study of protonolysis[24] and migratory insertion reactions at **1**.[25] This proposal is buttressed by the

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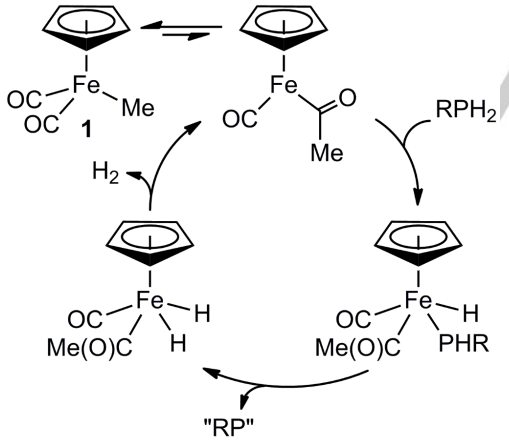
persistence of **1** at the end of catalysis. For example, catalytic reactions using **1**-d_3 result in nearly quantitative restoration of the pre-catalyst by ^{2}H NMR spectroscopy upon complete conversion of the substrates. Though it is a negative result, CD_3H was not observed in reactions using **1**-d_3 as a catalyst. Following migratory insertion, activation of phosphine substrate by P–H oxidative addition would give an iron(IV) intermediate that would engage in α-phosphinidene elimination, though the order of steps (PR transfer vs. H_2 evolution is unknown). It is also possible that a terminal iron phosphinidene derivative is formed. However, the transfer reactions herein are inconsistent with the PR-transfer reactivity of known terminal phosphinidene compounds,[26] though that area is sorely under-investigated. It is unclear that trapping with organic substrates need or need not involve interaction with the metal. Thus, we favor α elimination as a working hypothesis. The observed dehydrocoupling products including those of P–H insertion, P–P insertion, and condensation are consistent with other α-elimination reactions.[3-4] Current evidence prevents more than speculation at this point. Given the reactivity of :PPh,[17, 20] the lack of apparent reaction with solvent suggests high association with iron, consistent with theoretical analysis of α-stannylene elimination.[27] Reductive elimination of H_2 would close the cycle and is also consistent with the observation of H_2 in the dehydrocoupling and trapping reactions. Such a cycle is consistent with iron-based steps in Si–S coupling involving the retention of **1** and H_2 loss as proposed by Nakazawa.[28]

In conclusion, a rare example of what may catalytic α-phosphinidene elimination mediated by the ubiquitous iron complex **1** is reported. Phosphine dehydrocoupling reactions provided initial insight into this interesting reaction type, and catalytic trapping reactions were successful using 2,3-dimethyl-1,3-butadiene, internal alkynes, and diethyldisulfide, which are consistent with the reactivity expected for a putative triplet phosphinidene. Deuterium labelling studies, product distributions, and reaction studies further support the claim that this catalysis is based largely on the α-elimination of a triplet phosphinidene. Further work to expand the substrate scope of this reaction to a broader set of reagents, and investigation of the phosphinidene spin state are underway.



Scheme 5. Potential catalytic cycle for the liberation of phosphinidene fragments by **1** based on prior examples of E–H activation by **1** and related derivatives. The order of phosphinidene elimination versus H_2 loss is not known and may be reversed. Initial H_2 loss may promote formation of an iron-phosphinidene intermediate that available data can neither prove nor refute.

Acknowledgements

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Keywords: Phosphorus • Phosphinidene • Iron • Catalysis • Trapping

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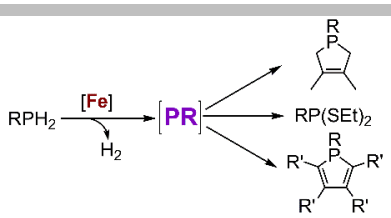
A simple iron compound can catalytically transfer a phosphinidene equivalent to a 2,3-dimethyl-1,3-butadiene, alkynes, and diethyl disulfide with loss of hydrogen. These phosphinidene transfer reactions and dehydrocoupling catalysis indicate α-phosphinidene elimination



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