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Palladium-catalyzed phosphorus–carbon bond formation: cross-coupling reactions of alkyl phosphinates with aryl, heteroaryl, alkenyl, benzylic, and allylic halides and triflates

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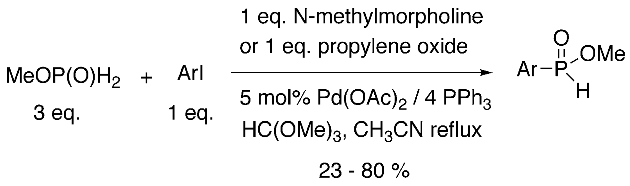
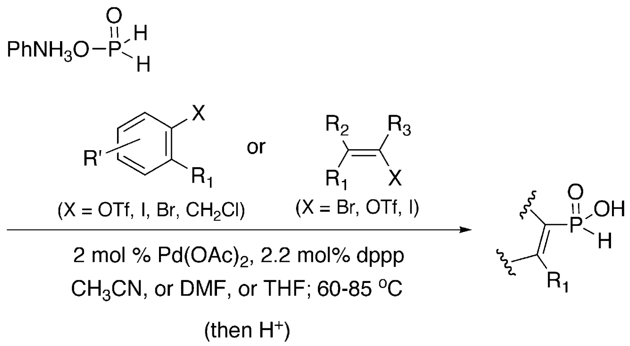
Abstract—The direct formation of H-arylphosphinates and related compounds can be accomplished using palladium catalysis. This full paper examines the scope and some mechanistic aspects of this phosphorus–carbon bond forming reaction. The reactions of alkenyl and allylic halides are also described for the first time. This novel cross-coupling provides a convenient access to a variety of substituted H-phosphinates.

1. Introduction

Cross-coupling reactions have become some of the most popular methods for the formation of carbon–heteroatom bonds.[1] Most notably, carbon bonds to nitrogen, oxygen, and sulfur are now commonly prepared using palladium catalysis, and to a lesser extent other transition metals such as copper and nickel. Buchwald, Hartwig, and others have been major contributors in this area.[1] The formation of carbon–phosphorus bonds via cross-coupling has also been examined.[2] In fact, the palladium-catalyzed cross-coupling of dialkyl phosphites $(RO)_2P(O)H$ with aryl- and alkenyl-halides was already described in the early eighties by Hirao and co-workers.[3] More recent reactions have focused mainly on the synthesis of phosphines and their derivatives.[2] However, the cross-coupling reactions of compounds containing two phosphorus–hydrogen bonds are much less common, because of the possibility for competing transfer hydrogenation with these substrates. For example, reductions of a variety of functional groups with hypophosphorous acid and its derivatives have been known and used preparatively for several decades.[4] Thus, it may not be surprising that the cross-coupling of hypophosphorous derivatives was not described until recently. In pioneering studies, Schwabacher was the first to report the palladium-catalyzed coupling of alkyl phosphinates $(ROP(O)H_2)$ with aryl iodides (Eq. 1).[5] A few years earlier, Holt reported one example of cross-coupling between triethylammnonium hypophosphite and a dienyl triflate, but the generality of this reaction was not established.[6]



(1)



(2)

In the context of studies aiming at the synthesis of functionalized H-phosphinates as intermediates in the preparation of biologically-active compounds, we recognized the need for developing the cross-coupling of hypophosphorous acid derivatives with various electrophiles. As a result, we have been involved in the study of hypophosphites and alkyl phosphinates as nucleophilic

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Keywords: Cross-coupling; Hypophosphorous; Alkoxysilane; Palladium.

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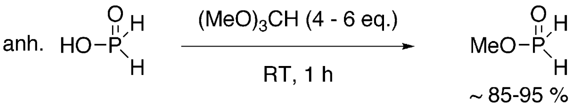
partners in palladium-catalyzed reactions. This work produced the remarkably general cross-coupling reaction of anilinium hypophosphite (AHP) with a variety of electrophilic partners, and this has been reported in two publications (Eq. 2).[7] More recently and based on our experience with AHP, we tackled the problem of preparing H-phosphinate esters directly from alkyl phosphinates and tried to significantly expand the scope of the Schwabacher coupling. This manuscript provides a full account of these studies, and follows up on our preliminary communication.[8] As mentioned above, Schwabacher developed the cross-coupling of methyl phosphinate,[5a] and later *tert*-butyl phosphinate,[5b] with aryl iodides. However, only reactive iodides were successfully employed, and the yields were generally moderate (ca. 50–60%), reaching 80% in the best case (4-iodotoluene). The cross-coupling of aryl bromides and triflates was unsuccessful.[5a] Aside from the competing transfer hydrogenation, a major problem was the rapid thermal decomposition of methyl phosphinate (complete decomposition in 1 h at 80 °C), which prevented the use of relatively unreactive electrophiles.[5a]

We have reported a novel synthesis of alkyl phosphinates, which is based on the esterification of hypophosphorous acid and some of its salts (ammonium and anilinium) with alkoxysilanes in a variety of solvents.[9] Under these conditions, the thermal decomposition of the alkyl phosphinates is surprisingly slow (less than 20% in 20 h at 80–110 °C in several different solvents).[9] We therefore, were in an excellent position to examine the cross-coupling reactions of alkyl phosphinates with a variety of electrophiles. In a proof of concept experiment, we reported the coupling of butyl phosphinate with iodobenzene in 80% isolated yield.[9] We have since investigated the palladium-catalyzed cross-coupling reactions of alkyl phosphinates in some detail, and those results are now discussed.

2. Results and discussion

2.1. Alkyl phosphinate preparation

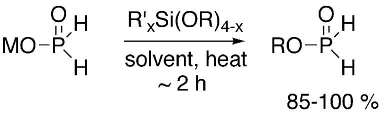
Schwabacher prepared methyl phosphinate using the Fitch method (Eq. 3),[10] and *tert*-butyl phosphinate was prepared in low yield (37%) through the transesterification of the methyl ester.[5b] The *tert*-butyl ester is only slightly more thermally stable than its methyl counterpart.[5b]



$$\text{anh. } \text{HO–P(=O)H}_2 \xrightarrow[\text{RT, 1 h}]{(\text{MeO})_3\text{CH (4 - 6 eq.)}} \text{MeO–P(=O)H}_2 \quad \text{~ 85-95 \%} \qquad (3)$$

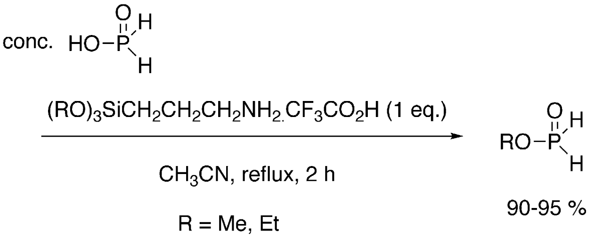
M = H, $PhNH_3$, NH_4

R = Me, Et, Bu, Allyl, Ph, Bn, *i*-Pr



$$\text{MO–P(=O)H}_2 \xrightarrow[\text{solvent, heat} \atop \text{~ 2 h}]{R'_x\text{Si(OR)}_{4-x}} \text{RO–P(=O)H}_2 \quad \text{85-100 \%} \qquad (4)$$

In contrast, we have reported a convenient and general alkyl phosphinate synthesis (Eq. 4), which proceeds in high yield in a wide variety of solvents and does not require anhydrous H_3PO_2.[9] The solutions of alkyl phosphinates are used directly in subsequent reaction, and the thermal stability profile of the esters is excellent. Stock solutions of alkyl phosphinates can also be employed because they are stable at room temperature under N_2 for well over a month (<10% decomposition). This unique preparative method allows us to examine reactions which were previously difficult or impossible. For cross-coupling, the thermal limitations would be eliminated, so that only transfer hydrogenation must be dealt with, even if it is still the major expected problem. We also reported a variation on our alkyl phosphinate synthesis (Eq. 5), which employs salts of aminosilicates, and allows the removal of the silicate byproducts at the end of the reactions by simple aqueous wash.[9]



$$\text{conc. HO–P(=O)H}_2 \xrightarrow[\text{CH}_3\text{CN, reflux, 2 h}]{(\text{RO})_3\text{SiCH}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{.CF}_3\text{CO}_2\text{H (1 eq.)}} \text{RO–P(=O)H}_2 \quad \text{90-95 \%}$$

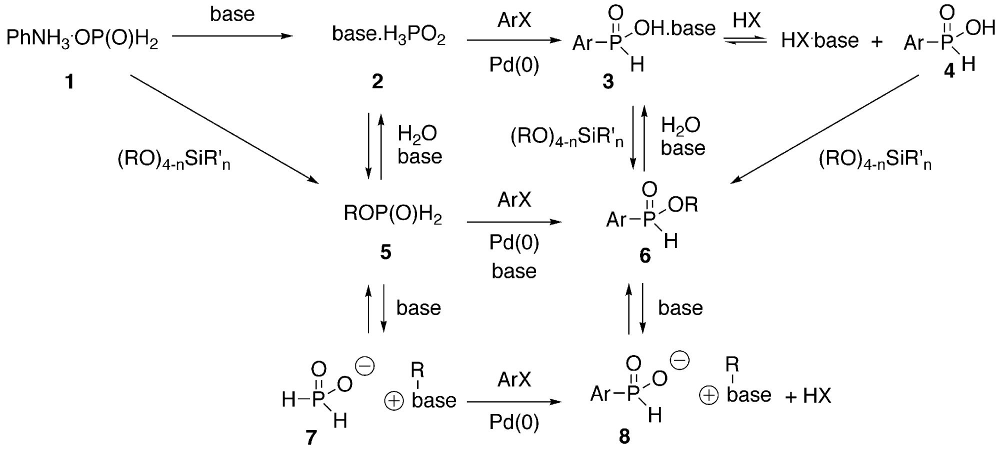
R = Me, Et

(5)

2.2. Cross-coupling reactions of aryl- and heteroaryl-halides or triflates

2.2.1. Mechanistic considerations. As expected, aryl iodides are the easiest substrates for cross-coupling with alkyl phosphinates because they are the most reactive toward palladium insertion into the C–I bond, so transfer hydrogenation is minimized as a competing side-reaction. With these substrates, the thermal decomposition of the alkyl phosphinate (prepared by the Fitch method, Eq. 3) is still not fast enough to cause the yield to drop below useful levels for the reactive substrates.[5a] However, electrophiles less reactive toward oxidative addition could not be employed in the Schwabacher coupling, and aryl bromides or triflates failed to give the desired products.[5a]

While our AHP-based cross-coupling (Eq. 2)[7] is successful on a wide range of electrophiles (including bromides and triflates), access to the H-phosphinate ester requires the separate esterification of the products. Our silicate-based esterification[11] and other methods[12] can be used to achieve this, but a direct one-step access to the ester is more desirable. This is especially true in the case of substrates containing basic functionalities, which cannot be esterified simply. We therefore investigated the direct coupling of alkyl phosphinates with aromatic and heteroaromatic electrophiles. The alkyl phosphinates were prepared according to Eq. 4; the electrophile, base, and palladium catalyst were subsequently added. As expected, aryl iodides reacted uneventfully to afford good yields of cross-coupled products, using Et_3N as the base. In fact, the cross-coupling still proceeds in high yield even without any added base. In this case, the alkyl phosphinate serves as HI scavenger and reduces the Pd(II) back to Pd(0). It also indicates that the coupling likely proceeds through the P(III) tautomer of the alkyl phosphinate, and that deprotonation of the phosphorus nucleophile is not necessary.



Scheme 1. Mechanistic pathways.

Unfortunately, electrophiles other than iodides were generally poor substrates. Initially, we found that DABCO worked better for those substrates using preformed alkyl phosphinates. However, we discovered that the presence of moisture in the batch of DABCO we employed appeared to be responsible for this success.[8] Indeed, Et_3N could be used in place of DABCO if 0.5–1 equiv water was added to it. This suggested a complex mechanism in which many pathways had to be considered.[8] Scheme 1 summarizes various reaction pathways. We reasoned that the role of water was to hydrolyze the preformed alkyl phosphinate to a hypophosphite salt (**5**→**3**, Scheme 1), which could then couple with the electrophile (**2**→**3**, Scheme 1 and Eq. 2), followed by in situ esterification of the product in the presence of the alkoxysilane (**3**→**6**, or **4**→**6**, Scheme 1). If that is true, then a one-pot cross-coupling procedure should take place without the need for any added water (path **1**→**2**→**3/4**→**6**, Scheme 1). This turned out to be correct, at least in practice: when anilinium hypophosphite, an alkoxysilane, anhydrous Et_3N or DABCO, and ArX were reacted in the presence of $Pd(OAc)_2$/dppp, good yields of H-phosphinate esters were obtained. The **1**→**2**→**3** sequence occurs during the AHP coupling (Eq. 2)[7a] and appears very general with respect to the ArX employed. Apparently, the direct coupling **5** to **6** only takes place when X = I (and in this case even in the absence of base). When water is present, hydrolysis of **5** leads to the rapid formation of salt **2**, which can then couple efficiently.

In order to better understand the mechanistic subtleties of this cross-coupling, a series of control experiments were conducted. The results are summarized in Table 1. The direct coupling of butyl phosphinate with iodobenzene occurs in good yield even in the absence of base (entry 1). As expected (see Eq. 2) the salt of H_3PO_2 with DABCO couples efficiently (entry 2), and variable amounts of compound **3** are observed in the ^{31}P NMR spectrum of the crude reaction mixtures in other runs. However, the esterification of isolated product **3** (prepared from H-phenylphosphinic acid and DABCO) into H-phosphinate ester **6** does not occur efficiently (entry 3).[11] This suggests that the hydrogen halide formed during the coupling step must play a key role, and we have previously established that acidity of H-arylphosphinate salt **3** is a key parameter in the esterification process.[11] Under anhydrous conditions with aryl bromides (which are less reactive than the iodides toward oxidative addition), no phosphinate ester is formed from butyl phosphinate (entry 4). Addition of water completely reverses this (entry 5). The failure of coupling **5**→**6** in the absence of water is likely due to ester dealkylation to form tetraalkyl ammonium hypophosphites **7** (entry 6) which are not capable of coupling (entry 7). When the P–C bond-forming step (cross-coupling) is slow, competing transfer hydrogenation[4] (Eq. 6) becomes significant or even dominant. For example, gas chromatographic analysis shows that the major product formed in entry 7 is naphthalene, whereas no P–C bond formation is observed. Salts **7** are also not esterified (entry 8). In the presence of water, hydrolysis of **5** is rapid even at room temperature, and leads to **2** (entry 9) which is then capable of undergoing coupling (entry 3). Entry 10 shows that the reverse reaction **2**→**5** is inefficient. In these pathways, H-phosphinate esters **6** are always much more stable than alkyl phosphinate **5** toward hydrolysis or nucleophilic dealkylation (entry 11 vs. entry 9). Finally, the one pot process delivers useful yields in the absence of water, as shown in entry 12.

$$\mathrm{ArX} + \mathrm{ROP(O)H_2} \xrightarrow{\mathrm{Pd(0)}} \mathrm{Ar{-}H} \qquad (6)$$

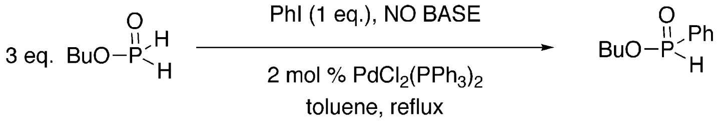
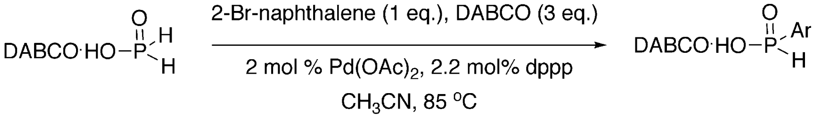
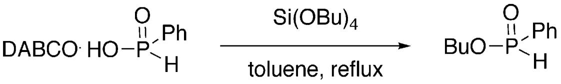
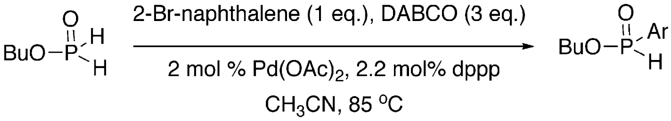
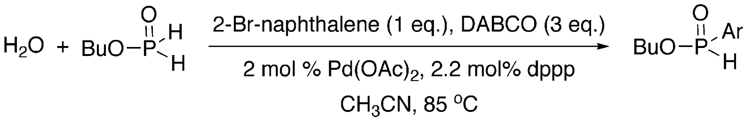
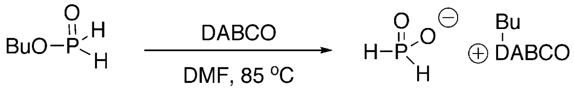
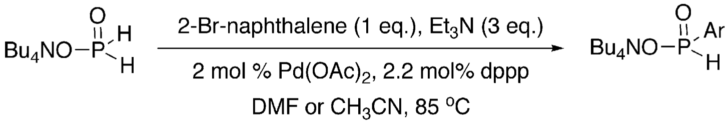
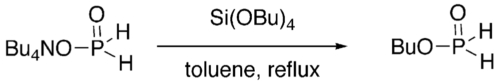
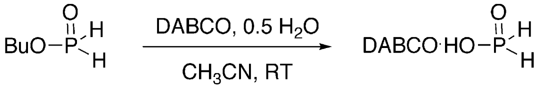
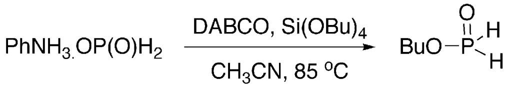
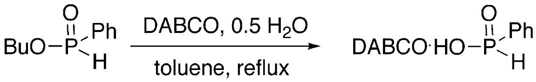
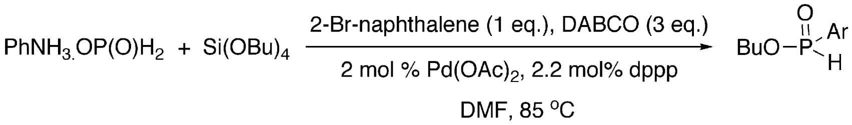
R = $PhNH_3$ **1**, baseH **2**, alkyl **5**, R'_4N **7**

The conclusion of these mechanistic studies is that the cross-coupling can take place in a one-pot process in the absence of water, and that the path must be **1**→**2**→**3**→**4**→**6**. An important consequence is that an asymmetric cross-coupling reaction (using a chiral ligand around palladium) is not likely to be successful with electrophiles other than iodides, since all the intermediates are achiral phosphinate salts, and since the esterification **4**→**6** should not be enantioselective because the chiral ligand is not involved in this step. In the case of aryl iodides, a direct coupling with the alkyl phosphinate is taking place and this is a minimum requirement to conserve potential chirality at the phosphorus atom. Initial experiments to achieve the asymmetric coupling of alkyl phosphinates with aryl iodides have however not been successful at this time.

2.2.2. Scope.

The one-pot process[8] which was developed as a result of the above mechanistic considerations was

Table 1. Control experiments related to the mechanistic pathways[a]

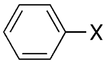
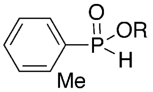
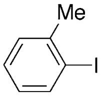
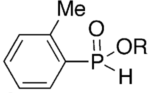
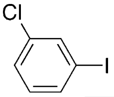
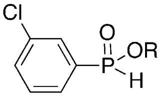
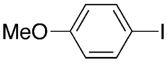
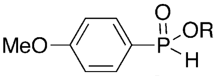
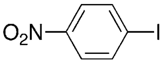
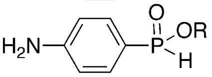
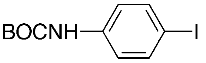
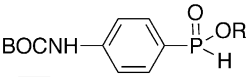
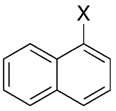
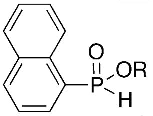
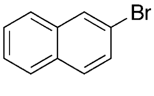
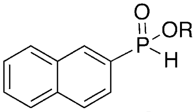
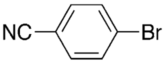
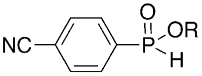
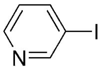
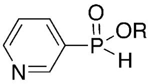
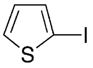
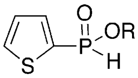
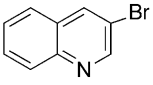
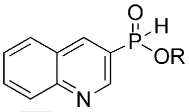
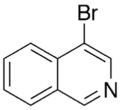
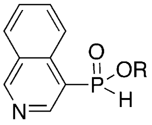
Entry	Reaction	Model for step	^{31}P NMR yield, %[b] reaction outcome
1		5→6	100%
2		2→3	100%
3		3→6	11%
4		5→6	no H-phosphinate ester
5		5→3 4→6	78%
6		5→7	65%
7		7→8	No cross-coupling product
8		7→5	No esterification
9		5→2	92%
10		2→5	17%
11		6→3	15%
12		1→6	74%

[a] See Scheme 1.

[b] NMR yields are determined by integrating all the signals in the spectrum.

subsequently tested on a variety of aromatic and heteroaromatic electrophiles. Some of these results are summarized in Table 2. In terms of ligand, PPh_3 is only satisfactory with aryl iodides (as in the Schwabacher coupling, see entry 1), while dppp is the most generally useful ligand. A similar trend was already noticed with the AHP cross-coupling of aryl electrophiles so this may not be surprising considering the postulated mechanism (Scheme 1). The H-phosphinate products were isolated in moderate to good yield. Several solvents can be employed, but acetonitrile appears to be the most generally useful. Although Et_3N can be used successfully (results not shown), DABCO was employed throughout because it gave better results (Table 2, Method B). Various substituted aryl iodides can be employed, including the sterically hindered 2-iodotoluene (entry 2) or the deactivated 4-iodoanisole (entry 4). Entry 5 shows an interesting example of cross-coupling/transfer hydrogenation where a nitroaromatic is also reduced to the corresponding aniline. It was not possible to find conditions where the nitro group remains completely intact. Aryl bromides and triflates could also be used (entries 7–9). However, unactivated bromobenzene does not react in high yield. This is probably due to a slower cross-coupling so that transfer hydrogenation (Eq. 6) becomes a major competing pathway. Indeed, deactivated bromoanisole does not give the H-arylphosphinate product. Heterocyclic substrates react successfully (entries 10–13). While the AHP coupling[7a] (Eq. 2) was successful with all the heterocycles

Table 2. Cross-coupling scope with (hetero)aromatic electrophiles

Entry	Electrophile	H-Phosphinate product	R	X	Method[a]	Isolated yield[b] %
1			Bu Et Et Et	I I I Br	A[c] B[d] C[c] B[d]	80 61 72 40[e]
2			Bu	—	B[c]	83
3			Bu	—	B[c]	63
4			Bu	—	B[c]	78
5			Bu	—	B[c]	53
6			Bu	—	B[c]	82
7			Me Bu	Br OTf	C[c] B[f]	100 80
8			Et Et Et	— — —	B[d] C[c] C[d]	69 88 74
9			Bu Et	— —	B[f] C[c]	51 92
10			Bu	—	B[c]	64
11			Bu	—	B[c]	36
12			Bu	—	B[f]	65
13			Bu	—	B[f]	78

[a] Method A: 3 equiv AHP, 3 equiv $(BuO)_4Si$, 3 equiv Et_3N, 2 mol% $Cl_2Pd(PPh_3)_2$; Method B: 3 equiv AHP, $(RO)_{4-n}SiR'_n$, 3 equiv DABCO, 2 mol% $Pd(OAc)_2$/dppp; Method C: 1.2 equiv AHP, 1.2 equiv $(RO)_3Si(CH_2)_3NH_2$, 2 mol% $Pd(OAc)_2$/dppp.

[b] Unless otherwise noted, yields are for isolated product which gave satisfactory spectral data (>95% purity).

[c] CH_3CN, reflux.

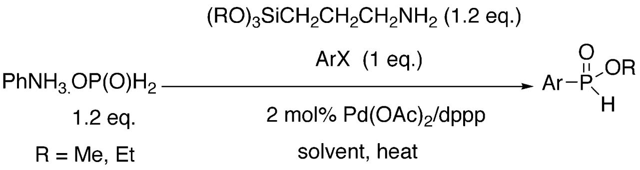
[d] Toluene, reflux.

[e] ^{31}P NMR yield.

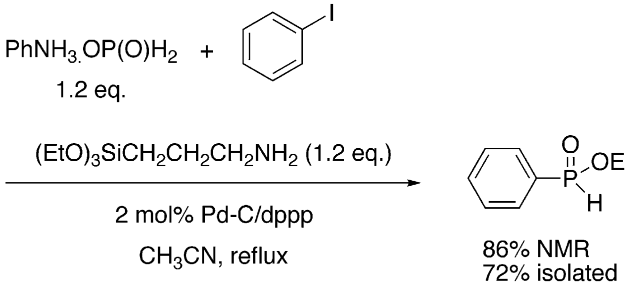
[f] DMF, 85 °C.

we tested, the nitrogen-containing ones would require either ion-exchange chromatography or a separate esterification step to access the corresponding H-heteroarylphosphinate ester. The silicate esterification[11] is also inefficient on those products, so different conditions (for example: PivCl + ROH) need to be employed.[12] Thus the present one-step cross-coupling of alkyl phosphinates is particularly useful for nitrogen-containing heterocycles.

2.2.3. Use of aminotrialkoxysilanes. Although the silicate by-products from the esterification of anilinum hypophosphite or H_3PO_2 can be removed during chromatography over silica gel (or in some cases by hexane/CH_3CN partitioning), a process in which these byproducts are removed by extraction has definite advantages. In Scheme 1, the three major species which are soluble in an organic solvent during an extractive work-up are the desired H-phosphinate esters **6**, the dialkyl phosphite $(RO)_2P(O)H$, and the silicates. In some cases, the dialkyl phosphite (which comes from the decomposition of the alkyl phosphinate) can be removed in vacuo. Therefore, if the silicates can be made water-soluble, one could hope to obtain the cross-coupling products in reasonably pure form after a simple aqueous work-up. In the past, we have shown that aminosilicate-derived byproducts can be removed easily and that aminosilicates can replace other silicates, both in the esterification of hypophosphorous acid (Eq. 5),[9] and of H-phosphinic acids,[11] as long as an equivalent of acid (usually trifluoroacetic acid, TFA) is also added. We have now found that aminotrialkoxysilanes can be used, not only as the esterifying agent, but also as the base for the palladium-catalyzed process, and that TFA is not needed (Eq. 7). Representative cross-couplings conducted with this system (method C) are shown in Table 2. It appears that the aminosilicate serves the dual purpose of esterification and of base in the palladium-catalyzed process. Of course, the use of the aminosilicate is not appropriate with nitrogen-containing heterocycles, since competing protonation of the heterocycles occurs and extraction is therefore problematic.



(7)



(8)

We also found that palladium on carbon can be used successfully with dppp as the ligand for this cross-coupling (Eq. 8). Thus the aminosilicate method provides a straightforward approach to the synthesis of various H-arylphosphinate esters.

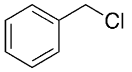
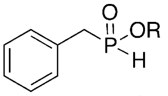
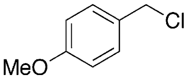
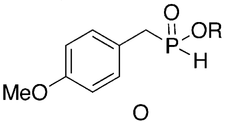
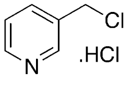
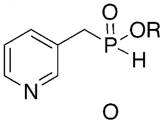
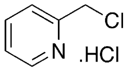
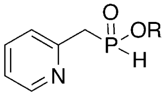
2.3. Cross-coupling of benzylic- and heterobenzylic chlorides

Benzylic and heterobenzylic chlorides can also be used as coupling partners (Table 3). However with these substrates, the best ligand is now dppf.[8] For the pyridine-containing substrates, an additional equivalent of base is also employed to deprotonate the commercially available hydrochlorides. The reason for the low isolated yields observed with the chloromethyl pyridines (entries 3 & 4) is somewhat unclear. Changing the base from Et_3N to i-Pr_2NEt does not improve the yield so that quaternarization with the electrophile is not a likely explanation. Some possible reasons for the observed yields include: (a) dealkylation of the ester by the base followed by inefficient re-esterification (see Section 2.2.1. and Scheme 1); and (b) the high polarity of the products and their facile hydrolysis during purification by chromatography. Additionally, in the case of entry 3, an unusual amount of disubstitution is also observed in the crude mixture (singlet, δ 49 ppm, $\sim$20%). Disubstitution generally does not take place to a significant extent ($<$5%) with other substrates. In spite of these limitations, the direct cross-coupling is probably the best synthetic method available currently to prepare these kinds of benzylic H-phosphinates. For example, Froestl et al. reported on the inability to prepare the product in entry 4 via esterification of the corresponding H-phosphinic acid.[13]

2.4. Cross-coupling of alkenyl halides

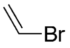
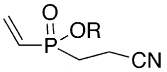
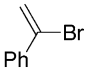
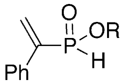
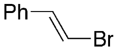
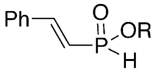
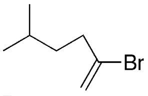
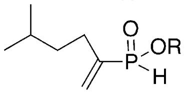
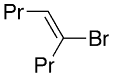
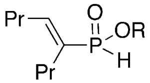
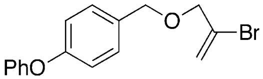
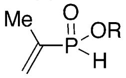
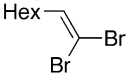
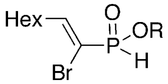
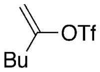
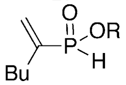
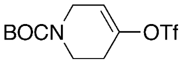
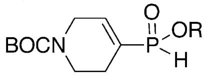
We have also investigated the cross-coupling of alkenyl halides and triflates. The results are summarized in Table 4. Alkenyl-H-phosphinates can be prepared by palladium-catalyzed hydrophosphinylation of alkynes with alkyl phosphinates.[14,15] However, the regiocontrol for the formation of linear versus the branched alkenyl-H-phosphinates isomers is generally about 3 to 1, even though the branched isomers can be obtained with high selectivity. Thus, the present cross-coupling allows access to a variety of alkenyl-substituted compounds with complete regio- and stereocontrol. Vinyl bromide couples in high yield ($\sim$80% NMR yield), but the isolated yield is low (ca. 40%) and the product could not be obtained in good purity. We attempted

Table 3. Cross-coupling scope with benzylic chlorides

Entry	Electrophile	H-Phosphinate product	R	Ligand	Isolated yield % (NMR yield %)
1			Bu	dppf dppp	88 (100) (21)
2			Bu	dppf	53 (65)
3			Bu	dppf	46 (60)
4			Bu	dppf	24 (38)

The yields reported are for isolated compounds with satisfactory spectral data ($\sim$95% purity). The yield in parentheses is determined by ^{31}P NMR. Conditions: 3 equiv AHP, 3 equiv, $(RO)_4Si$, DABCO 3 equiv (4 equiv for hydrochlorides), 2 mol% $Pd(OAc)_2$/dppf, CH_3CN, reflux.

Table 4. Cross-coupling scope with alkenyl electrophiles

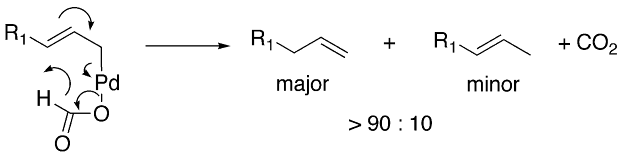
Entry	Electrophile	H-Phosphinate product	R	solvent	Method[a]	Isolated yield %
1			Et	CH_3CN	A	30
2			Bu	THF	B	79
3			Bu	THF	B	95
4			Bu	CH_3CN	B	63
5			Bu	CH_3CN	B	77
6			Bu	CH_3CN	B	57
7			Et	CH_3CN	A	48
8			Bu	CH_3CN	B	58
9			Bu	CH_3CN	B	95

[a] Method A: 2 equiv AHP, 2 equiv $(RO)_3Si(CH_2)_3NH_2$, 2 mol% $Pd(OAc)_2$/dppf [for entry 7, 3 equiv AHP + 3 equiv $(RO)_3Si(CH_2)_3NH_2$]; Method B: 3 equiv AHP, 2.1 equiv $(BuO)_4Si$, 1.0 equiv Et_3N, 2 mol% $Pd(OAc)_2$/dppp.

to use a tandem reaction to facilitate product isolation and purification, but the isolated yield remains low (Table 4, entry 1). With vinyl bromide, further optimization is therefore necessary. On the other hand, less polar coupling products can be obtained in satisfactory yields (Table 4, entries 2–5). The cross-coupling and simultaneous reduction (hydrogenolysis) of a substrate containing an allylic ether moiety was observed (entry 6). A 1,1-dibromoolefin was also studied, and in this case the reaction takes place stereospecifically to yield substitution of the bromine atom in the E-configuration (entry 7). Alkenyl triflates can also be coupled successfully (entries 8 and 9). This study is the first to show the successful cross-coupling of alkenyl electrophiles with alkyl phosphinates. This approach presents some advantages over our previously reported coupling with AHP since the products do not need to be esterified in a separate step.[7b]

2.5. Reactions of allylic electrophiles

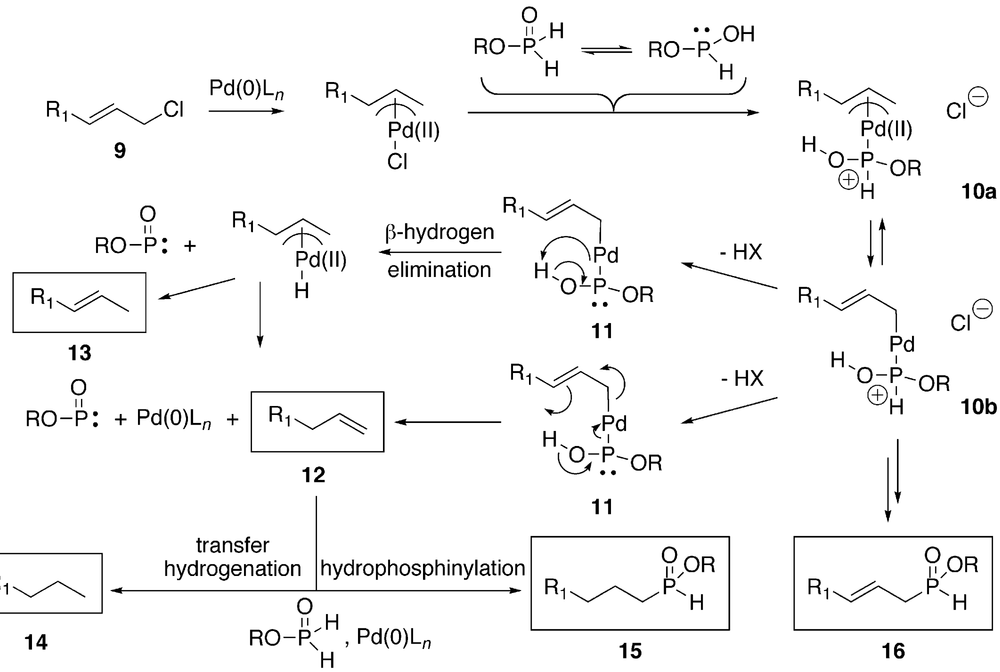
The cross-coupling of allylic substrates was examined next. In spite of much experimentation, a general and high yielding procedure was not found. Allylic H-phosphinic acids have been prepared using the Arbuzov-like reaction of $(TMSO)_2PH$ (BTSP), but disubstitution is usually a significant side reaction, and the handling of BTSP is problematic.[16] We have found that allylic H-phosphinate esters are best prepared from alkyl phosphinates via a direct nucleophilic displacement under basic conditions.[17] Nonetheless, some interesting results related to catalytic cross-coupling were collected, and these are discussed now.



(9)

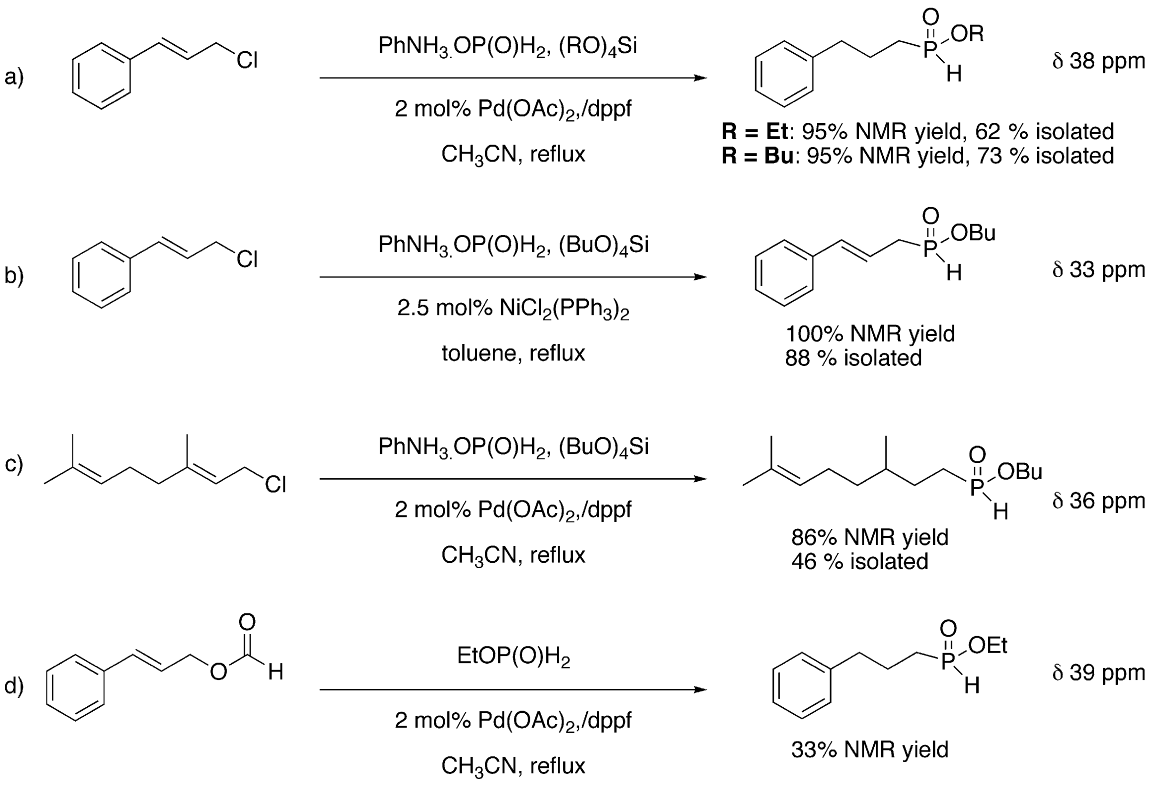
When allyl chloride or bromide was reacted under conditions similar to the ones developed for other electrophiles, no P–C bond formation could be detected. We reasoned that reduction might be taking place instead, in a manner similar to the formate-promoted reduction of allylic electrophiles (Eq. 9).[18] In an attempt at identifying the product of the reaction, we turned our attention to cinnamyl chloride which would give a higher boiling, more easily detected, reduction product. However, with cinnamyl chloride (**9**, $R_1 = Ph$), cross-coupling did take place rather efficiently. The product of the reaction proved to be butyl (3-phenylpropyl)-H-phosphinate (**15**, $R_1 = Ph$), and not the expected cinnamyl-H-phosphinate (**16**, $R_1 = Ph$).

A proposed mechanism to account for the formation of **15** is shown in Scheme 2. Since the reduction of allylic electrophiles is known to take place with formates (Eq. 9),[18] an analogous reductive pathway (**11** → **12**) could occur with the related H-phosphinates if proton transfer or β-hydrogen elimination are faster than reductive elimination from intermediates **10** or **11**. The product of reduction is then the corresponding terminal alkene (again a reaction well precedented with formates), at which point palladium-catalyzed addition[14] of excess alkyl phosphinate can take place (hydrophosphinylation, **12** → **15**). We have



Scheme 2. Mechanistic pathways with allylic electrophiles.

previously discovered the palladium-catalyzed hydrophosphinylation of alkenes, and have shown that it has broad scope and that various ligand (including PPh_3 and dppf) can be employed.[14] A similar reaction would explain the formation of compound **15** from **12**, and the failure of substrates which would give volatile alkenes **12** in the first step. In the reduction with formates (Eq. 9), the β-hydrogen elimination is considered unlikely because the least-substituted alkene always forms with very high regioselectivity.[18] In the case of alkyl phosphinates, regioisomeric alkene **13** could also form, but if it does, hydrophosphinylation of internal alkenes is known to be inefficient[14] and would not lead to any significant P–C bond formation. Experiments using gas chromatographic and ^{31}P NMR analyses were conducted to probe the mechanism further. Monitoring after 35 min, the cinnamyl chloride reaction



Scheme 3. Reactions of allylic electrophiles.

with palladium catalyst (Scheme 3a) reveals, clean and rapid formation of allylbenzene **12** (87%), complete consumption of cinnamyl chloride, and formation of some **15** (13%). No β-methylstyrene **13** can be detected, thus ruling out β-hydrogen elimination as the major pathway (Scheme 2). Evidently, the reductive isomerization (**9**→**12**) is efficient and analogous to formate reduction (Eq. 9). Over time, allylbenzene slowly disappears while product **15** forms (33 and 65%, respectively, after 2.5 h). After 8 h, **15** is formed in nearly quantitative yield (with no detectable **16**), and with only traces of allylbenzene **12** and propylbenzene **14** (1 and 2%, respectively) remaining. This shows that hydrophosphinylation[14] (**12**→**15**) occurs smoothly with negligible competing transfer hydrogenation (**12**→**14**).

Scheme 3 shows some results of the cross-coupling with allylic electrophiles. Interestingly, the use of a nickel catalyst (Scheme 3b) in toluene did give the expected cinnamyl product **16** with little competing reduction to **15** (**16:15** ratio = 95:5). This might be due to a more rapid reductive elimination (**10/11**→**16**) versus reductive isomerization (**11**→**12**) in the case of the nickel complex.[19] A GC/NMR monitoring experiment shows the slow disappearance of cinnamyl chloride and the appearance of **16** with only traces of allylbenzene or propylbenzene at any given time. Thus, unlike what was observed with the palladium catalyst formation of **16** takes place directly.

Geranyl chloride also reacted to form the reduced coupling product with $Pd(OAc)_2$/dppf as a catalyst (Scheme 3c). Cinnamyl formate (Scheme 3d) was also reacted under identical conditions with palladium catalysis, in an attempt at probing further our postulated mechanism for cinnamyl chloride. Although the yield is low, the detection of **15** but not **16** indicates that a reduction-hydrophosphinylation pathway is indeed reasonable.

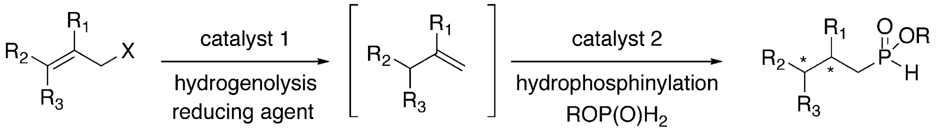
Even if the reactions described here are probably not very useful synthetically, the mechanistic implications are interesting. Alkyl phosphinates can react as formates to promote the hydrogenolysis of allylic compounds, and our independently discovered hydrophosphinylation reaction[14,15] appears to be operative under palladium catalysis. This suggests that a one-pot, two-step process where an allylic electrophile is first hydrogenolyzed,[18] then hydrophosphinylated[14] could be a useful approach to P–C bond formation (Scheme 4) by employing in tandem two known reactions. For example, reaction d in Scheme 3 could possibly be improved using AHP and catalytic Pd_2dba_3/PBu_3/xantphos. Furthermore, asymmetric versions of the first step have already been reported.[20] We are currently examining this puzzling possibility.

The different outcome observed with nickel suggests an avenue for research to develop the cross-coupling of allylic electrophiles, and this will be explored in the near future. However, the best synthetic approach to prepare allylic H-phosphinates from allylic halides remains the base-promoted direct alkylation of alkyl phosphinates in the absence of catalyst.[17,21] The situation is different with other allylic electrophiles (acetate, formate, carbonate) and would justify more work in this area.

3. Conclusions

The palladium-catalyzed cross-coupling reactions of alkyl phosphinates with various electrophiles has been studied, and some mechanistic insights have been provided. A one-pot process was developed which gives moderate to good yields of H-phosphinate esters. This includes a variation employing aminoalkoxysilanes to facilitate the work-up and isolation of the H-phosphinate ester products. The reactions of alkenyl and allylic electrophiles were examined for the first time. Alkenyl halides and triflates are good substrates for the cross-coupling, whereas allylic compounds apparently react in a reduction-hydrophosphinylation sequence. Fortunately, allylic H-phosphinates are accessible through other methods.[17,21] Although our previously reported AHP coupling has a broader scope,[7] the present one-step synthesis of H-phosphinate esters is still quite generally applicable, and is advantageous when H-phosphinic acids cannot be isolated or esterified easily.

The reactions described cover a broad scope of substrates beyond Schwabacher's aryl iodides,[5] and provide a novel access to H-phosphinate esters. Applications to the synthesis of biologically active organophosphorus compounds are in progress. Based on the postulated mechanism of the aryl coupling, the development of a catalytic desymmetrization of alkyl phosphinates for the preparation



X = Hal, O_2CH, OAc, OC(O)OR, OPh, NO_2

catalyst 1: $Cl_2Pd(PPh_3)_2$, Pd_2dba_3/Bu_3P, $Pd(PPh_3)_4$

reducing agent: HCO_2NH_4, $HCO_2H{\cdot}Et_3N$, PMHS, $ROP(O)H_2$

catalyst 2: Pd_2dba_3/xantphos, Pd_2dba_3/dppf

$ROP(O)H_2$: H_3PO_2, AHP, $AlkOP(O)H_2$

Scheme 4. Possible tandem process.

of P-chiral H-phosphinate esters poses significant challenges for substrates other than aryl iodides.

4. Experimental

General experimental procedures and the preparation of AHP and alkyl phosphinates have been described elsewhere.[7,9,14] The NMR yields are determined by integration of all the resonances in the ^{31}P NMR spectra. The yields determined by NMR are accurate within ~10% of the value indicated, and are reproducible. Some experiments with internal standards and gas chromatography also confirmed the validity of the method.[15] In several cases, the isolated yields are very close to the NMR yields. However, isolated yields are often significantly lower which mostly reflects the fact the H-phosphinic esters are typically difficult to purify, rather than some inaccuracy in NMR yield measurements. Chromatography is often complicated by the very polar nature of these compounds, and their relative ease of hydrolysis. Mass spectrometry was provided by the Washington University Mass Spectrometry Resource, an NIH Research Resource (Grant No. P41RR00954), or by the Mass Spectrometry Facility of the University of South Carolina. Experimental procedures for Table 2

4.1. Experimental procedures for Table 2

Table 2, Method A.[9] *Entry 1.* A solution of anilinium hypophosphite (0.952 g, 6 mmol) and tetrabutoxysilane (1.933 g, 6 mmol) in CH_3CN (12 mL) was refluxed for 2 h, under N_2. After cooling to rt, iodobenzene (0.25 mL, 2 mmol), anhydrous Et_3N (0.30 mL, 2 mmol), and $Cl_2Pd(PPh_3)_2$ (0.025 g, 0.04 mmol), were added successively. The reaction mixture was then refluxed for 5 h. At that point, the black mixture was concentrated under reduced pressure, and the residue partitioned between EtOAc and aq $KHSO_4$. The organic layer was washed successively with saturated aq $NaHCO_3$ (1×), and brine (1×). Drying, concentration, and purification by radial chromatography (4 mm thickness, hexane, EtOAc/hexane 1:1, v/v, EtOAc) afforded butyl phenylphosphinate (0.300 g, 80%).

Table 2 Method B. Entry 12. To a solution of 3-bromoquinoline (0.425 g, 2 mmol), $(BuO)_4Si$ (1.923 g, 6 mmol) in DMF (12 mL), were added anilinium hypophosphite (0.955 g, 6 mmol), 1,4-diazabicyclo[2.2.2]octane (0.676 g, 6 mmol), $Pd(OAc)_2$ (0.009 g, 0.04 mmol), 1,3-bis(diphenylphosphino)propane (0.018 g, 0.044 mmol). The resulting mixture was heated at 85 °C for 2 h. The reaction mixture was concentrated in vacuo, the residue was treated with brine (15 mL) and extracted with ethyl acetate (3×20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexane/EtOAc 7:3, v/v, EtOAc) afforded butyl quinolin-3-yl phosphinate. (0.322 g, 65% yield).

Table 2, Method C. Entry 8. To a suspension of anilinum hypophosphite (0.382 g, 2.4 mmol) and 3-aminopropyltriethoxysilane (0.531 g. 2.4 mmol) in CH_3CN (12 mL), was added 2-bromonaphthalene (0.414 g, 2 mmol), $Pd(OAc)_2$ (0.009 g, 0.040 mmol), and 1,3-bis(diphenylphosphino)propane (0.0182 g, 0.044 mmol). The reaction mixture was heated at reflux for 18 h. After cooling to rt, ^{31}P NMR analysis showed the product at 25.8 ppm (90%). The mixture was then diluted with EtOAc and washed successively with aq HCl (1 M). The aq phase was extracted with EtOAc (3×) and the combined organic fractions were washed with saturated aq $NaHCO_3$ (1×) and brine. Drying over $MgSO_4$ and concentration afforded ethyl 2-naphthylphosphinate (0.387 g, 88%).

4.2. Experimental procedures for Table 3

Entry 1. To a solution of benzyl chloride (0.253 g, 2 mmol), $(BuO)_4Si$ (1.923 g, 6 mmol) in CH_3CN (12 mL), were added anilinium hypophosphite (0.955 g, 6 mmol), 1,4-diazabicyclo[2.2.2]octane (0.676 g, 6 mmol), $Pd(OAc)_2$ (0.009 g, 0.04 mmol), 1,1′-bis(diphenylphosphino)ferrocene (0.0266 g, 0.048 mmol). The resulting mixture was heated at reflux for 1 h. The reaction mixture was concentrated in vacuo, the residue was treated with HCl (1 M, 15 mL) and extracted with ethyl acetate (3×20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexane/EtOAc 7:3, v/v, EtOAc) afforded butyl benzylphosphinate. (0.357 g, 78%) Note: for entries 3 & 4, the difference in workup was that brine was used instead of 1 M HCl above. For entry 4, 10 mmol AHP was used instead of 6 mmol.

4.3. Experimental procedures for Table 4

Table 4, Method A. Preparation of ethyl (vinyl-2-cyanoethyl)phosphinate (entry 1). A mixture of anilinum hypophosphite (0.955 g, 6 mmol), in CH_3CN (12 mL) was placed in a pressure tube. 3-Aminopropyltriethoxysilane (1.328 g, 6 mmol), vinyl bromide (1.0 M in CH_3CN, 3 mL, 3 mmol), $Pd(OAc)_2$ (0.0135 g, 0.06 mmol), and 1,1′-bis(diphenylphosphino)ferrocene (0.0400 g, 0.072 mmol) were then added in that order. The mixture was heated at 85 °C for 6 h. After cooling to rt, 1,8-diazabicyclo[5.4.0]undec-7-ene (0.90 mL, 6 mmol) and acrylonitrile (0.40 mL, 6 mmol) were added in the same reaction tube and the reaction was stirred overnight under nitrogen. After this time, ^{31}P NMR analysis showed the product at 38.3 ppm (72%). The mixture was then diluted with EtOAc and washed successively with aq HCl (1 M). The aq phase was then extracted with EtOAc (3×) and the combined organic fractions were washed with saturated aq $NaHCO_3$ (1×) and brine. Drying, concentration, and purification by radial chromatography (2 mm thickness, EtOAc to MeOH) afforded the product as a dark yellow oil (0.156 g, 30%).

4.4. Preparation of Ethyl (1-bromo-oct-1-enyl)-phosphinate (entry 7)

To a mixture of anilinum hypophosphite (0.955 g, 6 mmol) and 3-aminopropyltriethoxysilane (1.328 g. 6 mmol) in CH_3CN (12 mL), was added 1,1-dibromo-octene (0.540 g, 2 mmol), $Pd(OAc)_2$ (0.009 g, 0.040 mmol), and 1,1′-bis-(diphenylphosphino)ferrocene (0.0270 g, 0.048 mmol). The resulting mixture was heated at reflux for 7 h. The mixture was then diluted with EtOAc and washed successively with aq HCl (1 M). The aq phase was extracted with EtOAc (3×)

and the combined organic fractions were washed with saturated aq $NaHCO_3$ (1×) and brine. Drying, concentration, and purification by radial chromatography (2 mm thickness, hexanes/EtOAc 5:1, v/v, EtOAc) afforded the product as a light yellow oil (0.272 g, 48%).

Table 4, Method B. Entry 9. A mixture of anilinum hypophosphite (0.955 g, 6 mmol) and $(BuO)_4Si$ (1.346 g, 4.2 mmol) in CH_3CN (12 mL) was heated to reflux for 2 h under nitrogen and then cooled to rt. To the resulting mixture was added *tert*-butyl-1,2,3,6-tetrahydro-4-[(trifluoromethyl)sulfonyloxy]-pyridine-1-carboxylate (0.663 g, 2.0 mmol), anhydrous Et_3N (0.28 mL, 2.0 mmol), $Pd(OAc)_2$ (0.009 g, 0.04 mmol) and 1,3-bis(diphenylphosphino)propane (0.0182 g, 0.044 mmol). The reaction was then refluxed under nitrogen for 8 h. After cooling to rt, ^{31}P NMR analysis showed the product at 26.0 ppm (100%). The mixture was diluted with EtOAc and washed with aq $NaHSO_4$ (1 M). The resulting aqueous phase was extracted with EtOAc (3×) and the combined organic layers were washed with saturated aq $NaHCO_3$ (1×) and brine. Drying over $MgSO_4$ and concentration afforded the crude compound, which was purified by radial chromatography (2 mm thickness, hexanes/EtOAc 3:1, v/v, EtOAc). The product was obtained as a yellow oil (0.576 g, 95%).

4.5. Representative procedure for cross-coupling of allylic substrates

Palladium. Scheme 3a: A mixture of anilinum hypophosphite (0.955 g, 6 mmol) and $(BuO)_4Si$ (1.346 g, 4.2 mmol) in CH_3CN (12 mL) was heated to reflux for 2 h under nitrogen. After cooling to rt, cinnamyl chloride (0.280 mL, 2.0 mmol), $Pd(OAc)_2$ (0.009 g, 0.04 mmol), and 1,3-bis(diphenylphosphino)propane (0.0182 g, 0.044 mmol) were added to the reaction flask and the mixture was heated at reflux under nitrogen for 10 h. At this time, ^{31}P NMR analysis of the reaction mixture showed the product at 39.7 ppm (95%). The mixture was then diluted with EtOAc and washed with aq $NaHSO_4$ (1 M). The resulting aq phase was extracted with EtOAc (3×) and the combined organic fractions were washed with saturated aq $NaHCO_3$ (1×) and brine. Drying, concentration, and purification by radial chromatography (2 mm thickness, hexanes/EtOAc 5:1, v/v, EtOAc), afforded butyl (3-phenyl-propyl)phosphinate (0.351 g, 73%).

Nickel. Scheme 3b: A mixture of anilinum hypophosphite (0.955 g, 6 mmol) and $(BuO)_4Si$ (1.346 g, 4.2 mmol) in CH_3CN (12 mL) was heated to reflux for 2 h under nitrogen and cooled to rt. Cinnamyl chloride (0.280 mL, 2.0 mmol) and bis(triphenylphosphine)nickel (II) chloride (0.0327 g, 0.050 mmol) were then added to the reaction flask and the mixture was heated at reflux under nitrogen, for 8 h. ^{31}P NMR analysis of the reaction mixture showed the product at 37.1 ppm (100%). The reaction mixture was diluted with EtOAc and washed with aq $NaHSO_4$ (1 M). The resulting aqueous phase was extracted with EtOAc (3×) and the combined organic fractions were washed with saturated aq $NaHCO_3$ (1×) and brine. Drying, concentration, and purification by radial chromatography (2 mm thickness, hexanes/EtOAc 5:1, v/v, EtOAc) afforded a ∼95:5 mixture of butyl (3-phenyl-prop-2-enyl)phosphinate and butyl (3-phenyl-propyl)phosphinate (0.419 g, 88%).

4.5.1. Butyl phenylphosphinate (Table 2, entry 1). ^1H NMR ($CDCl_3$) δ 7.81 (d, $J=7$ Hz, 1H), 7.76 ($J=7$ Hz, 1H), 7.58 (d, $J=562$ Hz, 1H), 7.55–7.6 (m, 1H), 7.45–7.55 (m, 2H), 3.95–4.15 (m, 2H), 1.6–1.8 (m, 2H), 1.35–1.5 (m, 2H), 0.92 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 132.4 (d, $J_{PCCCC}=3$ Hz), 130.3 (d, $J_{PCCC}=12$ Hz), 129.4 (d, $J_{PC}=132$ Hz), 128.1 (d, $J_{PCC}=14$ Hz), 65.1 (d, $J_{POC}=7$ Hz), 31.8 ($J_{POCC}=6$ Hz), 18.2, 12.9; ^{31}P NMR ($CDCl_3$) δ 25.3 (dm, $J_{P\text{-}H}=563$ Hz).

4.5.2. Ethyl phenylphosphinate (Table 2, entry 1). ^1H NMR ($CDCl_3$) δ 7.81 (d, $J=14$ Hz, 1H), 7.79 (d, $J=14$ Hz, 1H), 7.60 (d, $J=563$ Hz, 1H), 7.55–7.60 (m, 1H), 7.50–7.55 (m, 2H), 4.15–4.20 (m, 2H), 1.39 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 133.1 (d, $J_{PCCCC}=3$ Hz), 130.9 (d, $J_{PCCC}=12$ Hz), 130.0 (d, $J_{PC}=132$ Hz), 128.8 (d, $J_{PCC}=14$ Hz), 62.0 (d, $J_{POC}=6$ Hz), 16.4 (d, $J_{POCC}=6$ Hz); ^{31}P NMR ($CDCl_3$) δ 25.7 (dm, $J_{P\text{-}H}=562$ Hz).

4.5.3. Butyl *o*-tolylphosphinate (Table 2, entry 2). ^1H NMR ($CDCl_3$) δ 7.82 (dd, $J=16$, 7 Hz, 1H), 7.64 (d, $J=555$ Hz, 1H), 7.40–7.50 (m, 1H), 7.25–7.35 (m, 2H), 4.05–4.15 (m, 2H), 2.57 (s, 3H), 1.65–1.80 (m, 2H), 1.35–1.50 (m, 2H), 0.93 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 141.1 (d, $J_{PCC}=11$ Hz), 132.9 (d, $J_{PCCCC}=7$ Hz), 131.9 (d, $J_{PCCC}=13$ Hz), 131.1 (d, $J_{PCCC}=12$ Hz), 128.1 (d, $J_{PC}=131$ Hz), 125.8 (d, $J_{PCC}=14$ Hz), 65.8 (d, $J_{POC}=7$ Hz), 32.4 (d, $J_{POCC}=7$ Hz), 19.9 (d, $J_{PCCC}=7$ Hz), 18.8, 13.6; ^{31}P NMR ($CDCl_3$) δ 26.9 (dm, $J_{P\text{-}H}=555$ Hz); HRMS (FAB) calcd for $C_{11}H_{17}O_2P$, $(M+Li)^+$ 219.1126, found 219.1122.

4.5.4. Butyl (3-chlorophenyl)phosphinate (Table 2, entry 3). ^1H NMR ($CDCl_3$) δ 7.77 (d, $J=14$ Hz, 1H), 7.65–7.70 (m, 1H), 7.58 (d, $J=570$ Hz, 1H), 7.55–7.60 (m, 1H), 7.45–7.50 (m, 1H), 4.05–4.15 (m, 2H), 1.70–1.75 (m, 2H), 1.40–1.50 (m, 2H), 0.94 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 135.2 (d, $J_{PCCC}=18$ Hz), 133.2 (d, $J_{PCCCC}=3$ Hz), 132.2 (d, $J_{PC}=130$ Hz), 130.9 (d, $J_{PCC}=13$ Hz), 130.3 (d, $J_{PCCC}=15$ Hz), 129.0 (d, $J_{PCC}=11$ Hz), 66.7 (d, $J_{POC}=7$ Hz), 32.4 (d, $J_{POCC}=6$ Hz), 18.8, 13.6; ^{31}P NMR ($CDCl_3$) δ 23.5 (dm, $J=570$ Hz); HRMS (FAB) calcd for $C_{10}H_{14}ClO_2P$, $(M+Li)^+$ 239.0580, found 239.0586.

4.5.5. Butyl (4-methoxyphenyl)phosphinate (Table 2, entry 4). ^1H NMR ($CDCl_3$) δ 7.70–7.75 (m, 2H), 7.55 (d, $J=561$ Hz, 1H), 7.00–7.05 (m, 2H), 4.05–4.10 (m, 2H), 3.85 (s, 3H), 1.65–1.75 (m, 2H), 1.40–1.45 (m, 2H), 0.93 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 163.4 (d, $J_{PCCCC}=3$ Hz), 133.0 (d, $J_{PCC}=13$ Hz), 121.1 (d, $J_{PC}=139$ Hz), 114.3 (d, $J_{PCCC}=15$ Hz), 65.4 (d, $J_{POC}=7$ Hz), 55.4, 32.5 (d, $J_{POCC}=6$ Hz), 18.8, 13.6; ^{31}P NMR ($CDCl_3$) δ 25.9 (dm, $J=561$ Hz); HRMS (FAB) calcd for $C_{11}H_{17}O_3P$, $(M+Li)^+$ 235.1075, found 235.1084.

4.5.6. Butyl (4-aminophenyl)phosphinate (Table 2, entry 5). ^1H NMR ($CDCl_3$) δ 7.55 (dd, $J=13$ Hz, $J=8$ Hz, 2H), 7.51 (d, $J=559$ Hz, 1H), 6.73 (dd, $J=9$, 3 Hz, 2H), 3.99–4.1 (m, 4H), 1.67–1.72 (m, 2H), 1.38–1.46 (m, 2H), 0.93 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 151.3

(d, $J_{\mathrm{PCCCCC}}=3$ Hz), 133.1 (d, $J_{\mathrm{PCC}}=13$ Hz, 2C), 117.4 (d, $J_{\mathrm{PC}}=142$ Hz), 114.5 (d, $J_{\mathrm{PCCC}}=15$ Hz, 2C), 65.4 (d, $J_{\mathrm{POC}}=6$ Hz), 32.7 (d. $J_{\mathrm{POCC}}=7$ Hz), 19.0, 13.8; ^{31}P NMR (CDCl$_3$) δ 27.1 (dm, $J=559$ Hz).

4.5.7. Butyl [(4-*tert*-butoxycarbonylamino)phenyl]phosphinate (Table 2, entry 6). ^{1}H NMR (CDCl$_3$) δ 7.86 (s, 1H), 7.70–7.75 (m, 2H), 7.60–7.65 (m, 2H), 7.56 (d, $J=564$ Hz), 4.05–4.10 (m, 2H), 1.65–1.75 (m, 2H), 1.50 (s, 9H), 1.35–1.45 (m, 2H), 0.92 (t, $J=7$ Hz); ^{13}C NMR (CDCl$_3$) δ 152.6, 143.6 (d, $J_{\mathrm{PCCCC}}=3$ Hz), 132.2 (d, $J_{\mathrm{PCC}}=13$ Hz), 123 (d, $J_{\mathrm{PC}}=138$ Hz), 118.0 (d, $J_{\mathrm{PCCC}}=14$ Hz), 80.9, 65.5 (d, $J_{\mathrm{POC}}=7$ Hz), 32.4 (d, $J_{\mathrm{POCC}}=6$ Hz), 28.3, 18.8, 13.6; ^{31}P NMR (CDCl$_3$) δ 26.1 (dm, $J=565$ Hz); HRMS (FAB) calcd for $C_{15}H_{24}NO_4P$, $(M+Li)^+$ 320.1603, found 320.1610.

4.5.8. Butyl 1-naphthylphosphinate (Table 2, entry 7). ^{1}H NMR (CDCl$_3$) δ 8.43 (d, $J=8$ Hz, 1H), 8.11 (dd, $J=7$, 1 Hz, 1H), 8.05 (dd, $J=7$, 4 Hz, 1H), 7.91 (d, $J=563$ Hz, 1H), 7.90 (d, $J=8$ Hz, 1H), 7.50–7.65 (m, 3H), 4.05–4.20 (m, 2H), 1.60–1.75 (m, 2H), 1.30–1.45 (m, 2H), 0.87 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl3) δ 134.1 (d, $J_{\mathrm{PCCCC}}=3$ Hz), 133.6 (d, $J_{\mathrm{PCC}}=10$ Hz), 132.7 (d, $J_{\mathrm{PCC}}=13$ Hz), 132.5, 129.2 (d, $J_{\mathrm{PCCC}}=2$ Hz), 128.0, 126.9, 126.2 (d, $J_{\mathrm{PC}}=129$ Hz), 125.0 (d, $J_{\mathrm{PCCCC}}=1$ Hz), 124.8 (d, $J_{\mathrm{PCCC}}=11$ Hz); ^{31}P NMR (CDCl$_3$) δ 27.1 (dm, $J=563$ Hz); HRMS (FAB) calcd for $C_{14}H_{17}O_2P$, $(M+Li)^+$ 255.1126, found 255.1138.

4.5.9. Ethyl 2-naphthylphosphinate (Table 2, entry 8). ^{1}H NMR (CDCl$_3$) δ 8.40 (d, $J=16$ Hz, 1H), 7.95–8.00 (m, 2H), 7.90 (d, $J=9$ Hz, 1H), 7.72 (d, $J=564$ Hz, 1H), 7.65–7.80 (m, 1H), 7.60–7.65 (m, 2H); 4.15–4.25 (m, 2H), 1.41 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 135.6 (d, $J_{\mathrm{PCCCC}}=3$ Hz), 133.7 (d, $J_{\mathrm{PCCC}}=12$ Hz), 132.6 (d, $J_{\mathrm{PCC}}=15$ Hz), 129.1 (d, $J_{\mathrm{PCCC}}=3$ Hz), 128.9, 128.8, 128.2, 127.1 (d, $J_{\mathrm{PC}}=132$ Hz), 127.4, 125.4 (d, $J_{\mathrm{PCC}}=12$ Hz), 62.3 (d, $J_{\mathrm{POC}}=6$ Hz), 16.7 (d, $J_{\mathrm{POCC}}=6$ Hz); ^{31}P NMR (CDCl$_3$) δ 25.8 (dm, $J=565$ Hz).

4.5.10. Butyl (4-cyanophenyl)phosphinate (Table 2, entry 9). ^{1}H NMR (CDCl$_3$) δ 7.90–8.00 (m, 2H), 7.80∼7.90 (m, 2H), 7.65 (d, $J=574$ Hz, 1H), 4.10–4.20 (m, 2H), 1.70–1.80 (m, 2H), 1.40–1.50 (m, 2H), 0.95 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 135.0 (d, $J_{\mathrm{PC}}=129$ Hz), 132.3 (d, $J_{\mathrm{PCCC}}=14$ Hz), 131.6 (d, $J_{\mathrm{PCC}}=12$ Hz), 117.7, 116.7 (d, $J_{\mathrm{PCCCC}}=3$ Hz), 66.5 (d, $J_{\mathrm{POC}}=7$ Hz), 32.4 (d, $J_{\mathrm{POCC}}=6$ Hz), 18.7, 13.5; ^{31}P NMR (CDCl$_3$) δ 22.5 (dm, $J=574$ Hz); HRMS (FAB) calcd for $C_{11}H_{14}NO_2P$, $(M+Li)^+$ 230.0922, found 230.0917.

4.5.11. Butyl 3-pyridinylphosphinate (Table 2, entry 10). ^{1}H NMR (CDCl$_3$) δ 8.98 (dm, $J=7$ Hz, 1H), 8.85 (m, 1H), 8.10–8.20 (m, 1H), 7.45–7.50 (m, 1H), 7.69 (d, $J=573$ Hz, 1H), 4.15–4.20 (m, 2H), 1.70–1.80 (m, 2H), 1.40–1.50 (m, 2H), 0.96 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl3) δ 153.7 (d, $J_{\mathrm{PCCNC}}=2$ Hz), 151.8 (d, $J_{\mathrm{PCC}}=14$ Hz), 139.0 (d, $J_{\mathrm{PCC}}=10$ Hz), 126.2 (d, $J_{\mathrm{PC}}=131$ Hz), 123.7 (d, $J_{\mathrm{PCCC}}=10$ Hz), 66.4 (d, $J_{\mathrm{POC}}=7$ Hz), 32.4 (d, $J_{\mathrm{POCC}}=7$ Hz), 18.8, 13.6; ^{31}P NMR (CDCl$_3$) δ 22.0 (dm, $J=573$ Hz).

4.5.12. Butyl 2-thienylphosphinate (Table 2, entry 11). ^{1}H NMR (CDCl$_3$) δ 7.75–7.80 (m, 1H), 7.70–7.75 (m, 1H), 7.72 (d, $J=593$ Hz, 1H), 7.25–7.30 (m, 1H), 4.10–4.20 (m, 2H), 1.70–1.80 (m, 2H), 1.40–1.50 (m, 2H), 0.95 (t, $J=8$ Hz, 3H); ^{13}C NMR (CDCl3) δ 136.7 (d, $J_{\mathrm{PCC}}=13$ Hz), 134.5 (d, $J_{\mathrm{PCSC}}=6$ Hz), 130.2 (d, $J_{\mathrm{PC}}=145$ Hz), 128.5 (d, $J_{\mathrm{PCCC}}=16$ Hz), 65.8 (d, $J_{\mathrm{POC}}=6$ Hz), 32.4 (d, $J_{\mathrm{POCC}}=7$ Hz), 18.8, 13.6; ^{31}P NMR (CDCl$_3$) δ 16.3 (dm, $J=593$ Hz); HRMS (FAB) calcd for $C_8H_{13}O_2PS$, $(M+Li)^+$ 211.0534, found 211.0531.

4.5.13. Butyl 3-quinolinylphosphinate (Table 2, entry 12). ^{1}H NMR (CDCl$_3$) δ 9.15 (dd, $J=5$, 2 Hz, 1H), 8.71 (d, $J=15$ Hz, 1H), 8.19 (d, $J=9$ Hz, 1H), 7.95 (d, $J=8$ Hz, 1H), 7.85–7.90 (m, 1H), 7.82 (d, $J=573$ Hz, 1H), 7.65–7.70 (m, 1H), 4.15–4.25 (m, 2H), 1.75–1.85 (m, 2H), 1.40–1.55 (m, 2H), 0.96 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 149.7, 149.6, 142.1 (d, $J_{\mathrm{PCC}}=10$ Hz), 132.3, 129.6, 128.8, 127.9, 126.7 (d, $J_{\mathrm{PCC}}=12$ Hz), 123.0 (d, $J_{\mathrm{PC}}=131$ Hz), 66.4 (d, $J_{\mathrm{POC}}=7$ Hz), 32.5 (d, $J_{\mathrm{POCC}}=6$ Hz), 18.8, 13.6; ^{31}P NMR (CDCl$_3$) δ 25.9 (dm, $J=561$ Hz); HRMS (FAB) calcd for $C_{13}H_{16}NO_2P$, $(M+Li)^+$ 256.1079, found 256.1072.

4.5.14. Butyl 4-isoquinolinylphosphinate (Table 2, entry 13). ^{1}H NMR (CDCl$_3$) δ 9.44 (d, $J=2$ Hz, 1H), 8.98 (d, $J=11$ Hz, 1H), 8.46 (d, $J=9$ Hz, 1H), 8.09 (d, $J=8$ Hz, 1H), 7.98 (d, $J=570$ Hz, 1H), 7.85–7.90 (m, 1H), 7.70–7.80 (m, 1H), 4.15–4.25 (m, 2H), 1.70–1.80 (m, 2H), 1.40–1.50 (m, 2H), 0.92 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 157.7 (d, $J_{\mathrm{PCCNC}}=9$ Hz), 147.8 (d, $J_{\mathrm{PCC}}=16$ Hz), 134.8 (d, $\mathrm{J}_{\mathrm{PCC}}=9$ Hz), 132.3, 128.8, 128.3, 128.0 (d, $J_{\mathrm{PCCC}}=8$ Hz), 124.2 (d, $J_{\mathrm{PCCC}}=6$ Hz), 119.9 (d, $J_{\mathrm{PC}}=121$ Hz), 66.3 (d, $J_{\mathrm{POC}}=6$ Hz), 32.4 (d, $J_{\mathrm{POCC}}=6$ Hz), 18.8, 13.5; ^{31}P NMR (CDCl$_3$) δ 24.3 (dm, $J=570$ Hz); HRMS (FAB) calcd for $C_{13}H_{16}NO_2P$, $(M+Li)^+$ 256.1079, found 256.1086.

4.5.15. Butyl benzylphosphinate (Table 3, entry 1).[22] ^{1}H NMR (CDCl$_3$) δ 7.20–7.35 (m, 5H), 7.03 (d, $J=544$ Hz, 1H), 3.90–4.10 (m, 2H), 3.19 (d, $J=18$ Hz, 2H), 1.55–1.65 (m, 2H), 1.25–1.40 (m, 2H), 0.89 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 129.9, 129.8 (d, $J_{\mathrm{PCCC}}=7$ Hz), 128.9 (d, $J_{\mathrm{PCCCC}}=3$ Hz), 127.7 (d, $J_{\mathrm{PCCCCC}}=4$ Hz), 66.4 (d, $J_{\mathrm{POC}}=7$ Hz), 37.0 (d, $J_{\mathrm{PC}}=89$ Hz), 32.3 (d, $J_{\mathrm{POCC}}=6$ Hz), 18.7, 13.5; ^{31}P NMR (CDCl$_3$) δ 37.9 (dm, $J=545$ Hz); HRMS (FAB) calcd for $C_{11}H_{17}O_2P$, $(M+Li)^+$ 219.1126, found 219.1125.

4.5.16. Butyl (4-methoxybenzyl)phosphinate (Table 3, entry 2). ^{1}H NMR (CDCl$_3$) δ 7.15 (dd, $J=9$ Hz, $J=3$ Hz, 2H), 7.0 (d, $J=542$ Hz, 1H), 6.87 (d, $J=8$ Hz, 2H), 3.9–4.15 (m, 2H), 3.8 (s, 3H), 3.14 (d, $J=18$ Hz, 2H), 1.58–1.68 (m, 2H), 1.28–1.42 (m, 2H), 0.91 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 159.0 (d, $J_{\mathrm{PCCCCC}}=4$ Hz), 131.0 (d, $J_{\mathrm{PCCC}}=6$ Hz, 2C), 121.8 (d, $J_{\mathrm{PCC}}=8$ Hz), 114.6 (d, $J_{\mathrm{PCCCC}}=3$ Hz, 2C), 66.7 (d, $J_{\mathrm{POC}}=7$ Hz), 55.5, 36.2 (d, $J_{\mathrm{PC}}=90$ Hz), 32.6 (d, $J_{\mathrm{POCC}}=6$ Hz), 18.9, 13.8; ^{31}P NMR (CDCl$_3$) δ 40.2 (dm, $J=542$ Hz); HRMS (EI$^+$) calcd for $C_{12}H_{19}O_3P$, $(M)^+$ 242.1072, found 242.1069.

4.5.17. Butyl (pyridin-3-yl-methyl)phosphinate (Table 3, entry 3). ^{1}H NMR (CDCl$_3$) δ 8.50–8.55 (m, 2H), 7.60–7.65 (m, 1H), 7.25–7.35 (m, 1H), 7.12 (d, $J=548$ Hz, 1H), 4.00–4.15 (m, 2H), 3.20 (d, $J=18$ Hz, 2H), 1.60–1.70 (m, 2H), 1.30–1.40 (m, 2H), 0.92 (t, $J=7$ Hz, 3H); ^{13}C NMR

(CDCl3) δ 150.6 (d, $J_{PCCC}=7$ Hz), 148.7 (d, $J_{PCCCNC}=4$ Hz), 137.3 (d, $J_{PCCC}=6$ Hz), 126.1 (d, $J_{PCC}=7$ Hz), 123.7, 66.8 (d, $J_{POC}=7$ Hz), 34.2 (d, $J_{PC}=89$ Hz), 32.3 (d, $J_{POCC}=6$ Hz), 18.7, 13.5; ^{31}P NMR ($CDCl_3$) δ 35.1, (dm, $J=547$ Hz); HRMS (FAB) calcd for $C_{10}H_{16}NO_2P$, $(M+Li)^+$ 220.1079, found 220.1131.

4.5.18. Butyl (pyridin-2-yl-methyl)phosphinate (Table 3, entry 4). ^{1}H NMR ($CDCl_3$) δ 7.20–7.25 (m, 2H), 7.19 (d, $J=548$ Hz, 1H), 6.75–6.85 (m, 1H), 6.69 (d, $J=8$ Hz, 1H), 4.05–4.20 (m, 2H), 3.57 (dm, $J=10$ Hz, 2H), 1.65–1.75 (m, 2H), 1.35–1.45 (m, 2H), 0.95 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 147.1 (d, $J_{PCC}=9$ Hz), 129.7, 119.2, 113.7, 113.5, 67.1 (d, $J_{POC}=7$ Hz), 42.8 (d, $J_{PC}=105$ Hz), 32.6 (d, $J_{POCC}=6$ Hz), 19.0, 13.8; ^{31}P NMR ($CDCl_3$) δ 33.3 (dm, $J=548$ Hz).

4.5.19. Ethyl (vinyl-2-cyanoethyl)phosphinate (Table 4, entry 1). ^{1}H NMR ($CDCl_3$) δ 6.03–6.5 (m, 3H), 3.96–4.16 (m, 2H), 2.6–2.71 (m, 2H), 2.0–2.2 (m, 2H), 1.35 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 138.4, 127.9 (d, $J_{PC}=121$ Hz), 118.6, 61.4 (d, $J_{POC}=6$ Hz), 29.9, 25.2 (d, $J_{PC}=101$ Hz), 16.7 (d, $J_{POCC}=6$ Hz); ^{31}P NMR ($CDCl_3$) δ 38.3 (s); HRMS (ES^+) calcd for $C_7H_{12}NO_2P$, $(M+H)^+$ 172.0527, found 172.0529.

4.5.20. Butyl (1-phenyl-vinyl)phosphinate (Table 4, entry 2).[14] ^{1}H NMR ($CDCl_3$) δ 7.35 (d, $J=563$ Hz, 1H), 7.48–7.52 (m, 2H), 7.35–7.38 (m, 3H), 6.27 (d, $J=46$ Hz, 1H), 6.21 (d, $J=25$ Hz, 1H), 4.01–4.08 (m, 2H), 1.6–1.66 (m, 2H), 1.3–1.58 (m, 2H), 0.88 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 141.7 (d, $J_{PC}=119$ Hz), 135.2 (d, $J_{PCC}=12$ Hz), 130.1 (d, $J_{PCC}=13$ Hz), 128.7 (3C), 127.0 (d, $J_{PCCC}=6$ Hz, 2C), 65.9 (d, $J_{POC}=7$ Hz), 32.3 (d, $J_{POCC}=6$ Hz), 18.7, 13.5; ^{31}P NMR ($CDCl_3$) δ 28.7 (dqt, $J=563$, 25, 8 Hz); HRMS (EI^+) calcd for $C_{12}H_{17}O_2P$, $(M)^+$ 224.0966, found 224.0967.

4.5.21. Butyl (*trans*-styryl)phosphinate (Table 4, entry 3).[23] ^{1}H NMR ($CDCl_3$) δ 7.33 (d, $J=560$ Hz, 1H), 7.3–7.58 (m, 5H), 6.4 (d, $J=18$ Hz, 1H), 6.37 (d, $J=22$ Hz, 1H), 4.06–4.15 (m, 2H), 1.67–1.75 (m, 2H), 1.4–1.48 (m, 2H), 0.95 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 149.7 (d, $J_{PCCC}=7$ Hz), 134.5 (d, $J_{PCC}=21$ Hz), 130.6, 129.0 (2C), 127.9 (2C), 116.3 (d, $J_{PC}=133$ Hz), 65.7 (d, $J_{POC}=6$ Hz), 32.5 (d, $J_{POCC}=6$ Hz), 18.8, 13.6; ^{31}P NMR ($CDCl_3$) δ 25.8 (dtt, $J=560$, 23, 8 Hz); HRMS (EI^+) calcd for $C_{12}H_{17}O_2P$, $(M)^+$ 224.0966, found 224.0963.

4.5.22. Butyl [1-(3-methyl-butyl)vinyl]phosphinate (Table 4, entry 4). ^{1}H NMR ($CDCl_3$) δ 7.1 (d, $J=547$ Hz, 1H), 5.94 (d, $J=25$ Hz, 1H), 5.84 (d, $J=49$ Hz, 1H), 3.95–4.1 (m, 2H), 2.2–2.35 (m, 2H), 1.5–1.7 (m, 3H), 1.35–1.44 (m, 4H), 0.85–0.95 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 142.5 (d, $J_{PC}=118$ Hz), 128.5 (d, $J_{PCC}=14$ Hz), 66.1 (d, $J_{POC}=7$ Hz), 37.2 (d, $J_{PCC}=5$ Hz), 32.7 (d, $J_{POCC}=6$ Hz), 28.7 (d, $J_{PCCC}=12$ Hz), 27.9, 22.6, 22.5, 19.0, 13.8; ^{31}P NMR ($CDCl_3$) δ 31.6 (dm, $J=547$ Hz).

4.5.23. Butyl (1-propyl-pent-1-enyl)phosphinate (Table 4, entry 5). ^{1}H NMR ($CDCl_3$) δ 6.98 (d, $J=542$ Hz, 1H), 6.37 (dt, $J=33$, 7 Hz, 1H), 3.88–4.0 (m, 2H), 2.0–2.2 (m, 4H), 1.55–1.63 (m, 2H), 1.3–1.45 (m, 6H), 0.87 (t, $J=7$ Hz, 9H); ^{13}C NMR ($CDCl_3$) δ 147.1 (d, $J_{PCC}=14$ Hz), 131.9 (d, $J_{PC}=124$ Hz), 65.7 (d, $J_{POC}=7$ Hz), 32.6 (d, $J_{POCC}=7$ Hz), 30.5 (d, $J_{PCC}=18$ Hz), 28.4 (d, $J_{PCCC}=12$ Hz), 22.6, 21.9, 18.9, 14.2, 13.9, 13.7; ^{31}P NMR ($CDCl_3$) δ 33.5 (dm, $J=542$ Hz); HRMS (EI^+) calcd for $C_{12}H_{25}O_2P$, $(M)^+$ 232.1592, found 232.1590.

4.5.24. Butyl (1-methyl-vinyl)phosphinate (Table 4, entry 6). ^{1}H NMR ($CDCl_3$) δ 7.09 (d, $J=549$ Hz, 1H), 5.79–6.0 (m, 2H), 3.97–4.14 (m, 2H), 1.96 (d, $J=14$ Hz, 3H), 1.62–1.75 (m, 2H), 1.35–1.5 (m, 2H), 0.95 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 129.8 (d, $J_{PCC}=14$ Hz), 66.0 (d, $J_{POC}=13$ Hz), 32.7 (d, $J_{POCC}=6$ Hz), 19.0, 17.1 (d, $J_{POCCC}=13$ Hz), 13.8; ^{31}P NMR ($CDCl_3$) δ 30.5 (dm, $J=549$ Hz).

4.5.25. Ethyl (1-bromo-oct-1-enyl)phosphinate (Table 4, entry 7). ^{1}H NMR ($CDCl_3$) δ 6.97 (d, $J=601$ Hz, 1H), 7.16–7.3 (m, 1H), 4.07–4.2 (m, 2H), 2.37 (qd, $J=7$, 3 Hz, 2H), 1.41–1.56 (m, 2H), 1.39 (t, $J=7$ Hz, 3H), 1.23–1.35 (m, 6H), 0.89 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 150.9 (d, $J_{PCC}=13$ Hz), 114.9 (d, $J_{PC}=136$ Hz), 62.4 (d, $J_{POC}=7$ Hz), 32.1 (d, $J_{PCCC}=11$ Hz), 31.7, 29.1, 27.6, 22.7, 16.5 (d, $J_{POCC}=7$ Hz), 14.3; ^{31}P NMR ($CDCl_3$) δ 20.9 (ddd, $J=602$, 14, 9 Hz); HRMS (ES^+) calcd for $C_{10}H_{20}BrO_2P$, $(M+H)^+$ 283.0463, found 283.0456.

4.5.26. Butyl (1-butyl-vinyl)phosphinate (Table 4, entry 8). ^{1}H NMR ($CDCl_3$) δ 7.13 (d, $J=547$ Hz, 1H), 5.97 (d, $J=25$ Hz, 1H), 5.86 (d, $J=44$ Hz, 1H), 4.0–4.16 (m, 2H), 2.15–2.3 (m, 2H), 1.1–2.06 (m, 8H), 0.9–0.97 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 142.0 (d, $J_{PC}=118$ Hz), 128.5 (d, $J_{PCC}=13$ Hz), 65.8 (d, $J_{POC}=7$ Hz), 32.4 (d, $J_{POCC}=6$ Hz), 30.4 (d, $J_{PCC}=12$ Hz), 30.0 (d, $J_{PCCC}=5$ Hz), 22.3, 18.8, 13.8, 13.6; ^{31}P NMR ($CDCl_3$) δ 30.9 (dm, $J=547$ Hz); HRMS (ES^+) calcd for $C_{10}H_{21}O_2P$, $(M+H)^+$ 205.1357, found 205.1360.

4.5.27. Butyl (1-carboxylic acid-*tert*-butyl ester-1,2,3,6-tetrahydro-pyridin-4-yl)phosphinate (Table 4, entry 9). ^{1}H NMR ($CDCl_3$) δ 7.07 (d, $J=552$ Hz, 1H), 6.62–6.75 (m, 1H), 4.0–4.13 (m, 4H), 3.45–3.6 (m, 2H), 2.2–2.4 (m, 2H), 1.64–1.74 (m, 2H), 1.47 (s, 9H), 1.36–1.48 (m, 2H), 0.95 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 154.7, 139.8 (d, $J_{PCC}=11$ Hz), 129.8 (d, $J_{PC}=56$ Hz), 80.4, 66.2 (d, $J_{POC}=7$ Hz), 43.7 (br), 39.4 (br), 32.6 (d, $J_{POCC}=6$ Hz), 28.6 (3C), 23.5 (d, $J_{PCC}=10$ Hz), 18.9, 13.8; ^{31}P NMR ($CDCl_3$) δ 25.99, 26.6 (dm, $J=552$ Hz); HRMS (EI^+) calcd for $C_{14}H_{26}NO_4P$, $(M)^+$ 303.1599, found 303.1601.

4.5.28. Butyl (3-phenyl-propyl)phosphinate (Scheme 3a, R = Bu). ^{1}H NMR ($CDCl_3$) δ 7.0 (d, $J=528$ Hz, 1H), 7.15–7.31 (m, 5H), 3.9–4.15 (m, 2H), 2.72 (t, $J=7$ Hz, 2H), 1.57–2.0 (m, 6H), 1.26–1.46 (m, 2H), 0.93 (t, $J=7$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 140.9, 128.7 (4C), 126.5, 66.3 (d, $J_{POC}=7$ Hz), 36.4 (d, $J_{PCC}=16$ Hz), 32.5 (d, $J_{POCC}=6$ Hz), 28.3 (d, $J_{PC}=94$ Hz), 22.6 (d, $J_{PCCC}=3$ Hz), 19.0, 13.8; ^{31}P NMR ($CDCl_3$) δ 39.9 (dm, $J=528$ Hz); HRMS (EI^+) calcd for $C_{13}H_{21}O_2P$, $(M)^+$ 240.1279, found 240.1275.

4.5.29. Ethyl (3-phenyl-propyl)phosphinate (Scheme 3a, R = Et). ^{1}H NMR ($CDCl_3$) δ 7.06 (d, $J=530$ Hz, 1H), 7.15–7.31 (m, 5H), 3.98–4.23 (m, 2H), 2.71 (t, $J=7$ Hz, 2H), 1.72–2.0 (m, 4H), 1.34 (t, $J=7$ Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 140.9, 128.74 (4C), 126.5, 62.6 (d, $J_{\mathrm{POC}}=7$ Hz), 36.5 (d, $J_{\mathrm{PCC}}=16$ Hz), 28.3 (d, $J_{\mathrm{PC}}=94$ Hz), 22.6 (d, $J_{\mathrm{PCCC}}=3$ Hz), 16.5 (d, $J_{\mathrm{POCC}}=6$ Hz); ^{31}P NMR (CDCl$_3$) δ 39.7 (d, $J=530$ Hz).

4.5.30. Butyl (3-phenyl-prop-2-enyl)phosphinate (Scheme 3b). ^{1}H NMR (CDCl$_3$) δ 7.06 (d, $J=543$ Hz, 1H), 7.23–7.38 (m, 5H), 6.06–6.17 (m, 1H), 6.55 (dd, $J=16$, 6 Hz, 1H), 4.0–4.2 (m, 2H), 2.82 (dd, $J=19$, 8 Hz, 2H), 1.65–1.74 (m, 2H), 1.36–1.48 (m, 2H), 0.94 (t, $J=7$ Hz, 3H); ^{13} C NMR (CDCl$_3$) δ 136.6, 136.1 (d, $J_{\mathrm{PCCC}}=14$ Hz), 128.7 (2C), 128.0, 126.4 (2C), 116.9 (d, $J_{\mathrm{PCC}}=10$ Hz), 66.5 (d, $J_{\mathrm{POC}}=7$ Hz), 34.7 (d, $J_{\mathrm{PC}}=90$ Hz), 32.6 (d, $J_{\mathrm{POCC}}=6$ Hz), 18.9, 13.8; ^{31}P NMR (CDCl$_3$) δ 37.1 (dt, $J=543$ Hz, $J=7$ Hz); HRMS (EI$^+$) calcd for $C_{13}H_{19}O_2P$, (M)$^+$ 238.1123, found 238.1126.

4.5.31. Butyl (3,7-dimethyl-oct-6-enyl)phosphinate (Scheme 3c). Mixture of stereoisomers: ^{1}H NMR (CDCl$_3$) δ 7.1 (d, $J=528$ Hz, 1H), 5.08 (t, $J=7$ Hz, 1H), 3.94–4.17 (m, 2H), 1.91–2.08 (m, 2H), 1.1–1.84 (m, 17H), 0.86–0.97 (m, 6H); ^{13}C NMR (CDCl$_3$) δ 131.7, 124.6, 66.3 (d, $J_{\mathrm{POC}}=7$ Hz), 65.7 (d, $J_{\mathrm{POC}}=6$ Hz), 36.6, 33.1 (d, $J_{\mathrm{PCCC}}=16$ Hz), 32.6 (d, $J_{\mathrm{POCC}}=6$ Hz), 27.5 (d, $J_{\mathrm{PCC}}=3$ Hz), 26.5 (d, $J_{\mathrm{PC}}=94$ Hz), 25.9, 25.5 19.0 (d, $J=6$ Hz), 17.8, 13.8, 13.7; ^{31}P NMR (CDCl$_3$) δ 41.35, 41.33 (d, $J=528$ Hz); HRMS (EI$^+$) calcd for $C_{14}H_{29}O_2P$, (M)$^+$ 260.1905, found 260.1904.

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Supplementary data

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