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Decarbonylative C−P Bond Formation Using Aromatic Esters and Organophosphorus Compounds

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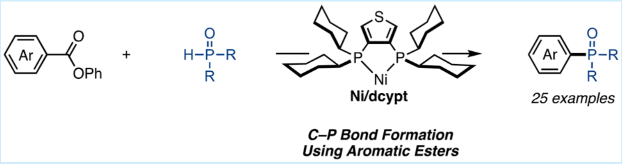
Supporting Information

ABSTRACT: Ni-catalyzed C−P bond formation was achieved using aromatic esters as unconventional aryl sources. The key to success was the use of a thiophene-based diphosphine ligand (dcypt). Several aromatic esters including heteroaromatics can be coupled with phosphine oxides and phosphates, providing aryl phosphorus compounds. The synthetic utility of the method was demonstrated by application of the present protocol to the sequential coupling reactions.



Phosphine-containing aromatic molecules have broad applications from the field of medicinal chemistry to materials chemistry, because of the strong influence of phosphorus groups on the physical, chemical, and biological properties of adjacent arenes. Furthermore, the high coordinating ability of the P atom to a metal center has been extensively exploited for the development of various transition-metal catalysts. Given these unique properties, it is not surprising that many synthetic methods have been developed for the formation of arene−phosphorus bonds.[1] Classically, the nucleophilic substitution of arylmetals with phosphine chlorides had been used for the synthesis of aromatic phosphorus compounds. As a catalytic method, the Hirao coupling of aryl halides and organophosphorus compounds by palladium catalysis is recognized (Figure 1A).[2] Along with the development of efficient metal catalysts, several synthetic methods for aryl phosphorus molecules have been reported using phenol derivatives,[3] arene diazoniums,[4] thiophenols,[5] aryl nitriles,[6] and arene itself[7] through inert bond activation.[8]

Recently, our group has focused on the transformation of aromatic esters through decarbonylation to construct C−C and C−O bonds by nickel and palladium catalysis.[9,10] Because aromatic esters are abundant, easy to prepare, and different as a chemical feedstock from haloarenes, coupling reactions using esters are attractive for the synthesis of substituted aromatic molecules. Furthermore, since ester moieties are usually stable under classic cross-coupling conditions such as the Suzuki−Miyaura coupling, aromatic esters can be orthogonally utilized as versatile building blocks for the synthesis of highly functionalized arenes. Among several reports on the cross-coupling of aromatic carboxylic acid derivatives,[11] the Szostak group recently developed a decarbonylative C−P bond-forming reaction of aromatic amides with phosphites under the influence of palladium and nickel catalysts (Figure 1B).[12] Similarly, Wang and co-workers reported an aryl phosphine synthesis through a catalytic decarbonylation of aroylphosphines.[13] We herein report a Ni-catalyzed decarbonylative cross-coupling of aromatic esters and organophosphorus compounds such as phosphine oxides and phosphates.

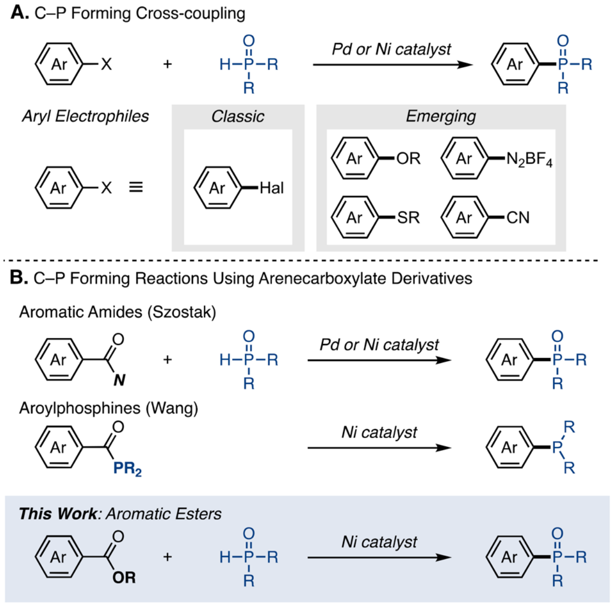


Figure 1. (A) Catalytic C−P forming cross-couplings. (B) C−P coupling using arenecarboxylate derivatives.

Our study commenced with a survey of appropriate catalytic conditions using phenyl isonicotinate (**1A**) and diphenyl phosphine oxide (**2a**) (Table 1). In order to avoid catalyst deactivation by coordination of **2a** to the metal, we focused on the use of robust ligands. To our delight, our in-house catalytic system using Ni(OAc)$_2$/dcypt (dcypt: 3,4-bis(dicyclohexylphosphino) thiophene)[14,15] showed high reactivity toward decarbonylative C−P bond formation (Table 1,

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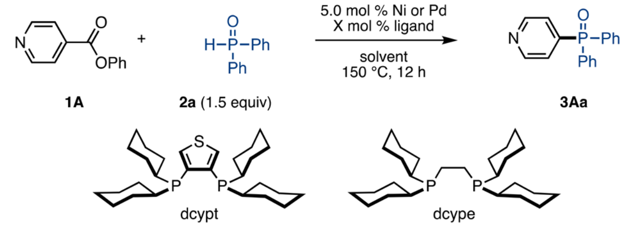
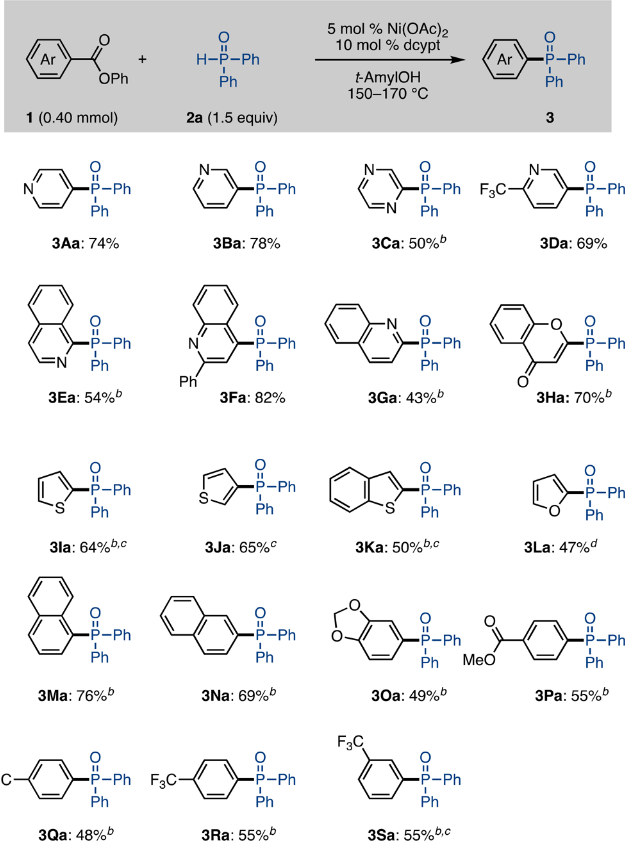
Table 1. Reaction Optimization[a]



entry	Ni or Pd	ligand	solvent	yield of 3Aa[b] (%)
1	Ni(OAc)$_2$	dcypt	*t*-AmylOH	74
2	Ni(OAc)$_2$	dcype	*t*-AmylOH	6
3	Ni(OAc)$_2$	dppe	*t*-AmylOH	9
4	Ni(OAc)$_2$	PCy$_3$·HBF$_4$[c,d]	*t*-AmylOH	0
5	Ni(OAc)$_2$	IPr·HCl[c,d]	*t*-AmylOH	0
6	Ni(OAc)$_2$	ICy·HBF$_4$[c,d]	*t*-AmylOH	0
7	Ni(OAc)$_2$	dcypt	*t*-BuOH	50
8	Ni(OAc)$_2$	dcypt	toluene	47
9	Ni(OAc)$_2$	dcypt	1,4-dioxane	65
10	Pd(OAc)$_2$	dcypt	*t*-AmylOH	0

[a] Conditions: **1A** (0.20 mmol), **2a** (1.5 equiv), Ni or Pd (5 mol %), ligand (10 mol %) in solvent (1.0 mL) at 150 °C, 12 h. [b] Yield was determined by GC analysis using *n*-decane as an internal standard after the treatment of crude material with H_2O_2. [c] 20 mol % of ligand was used. [d] NaO*t*-Bu (25 mol %) was added.

Scheme 1. Substrate Scope of Aromatic Esters 1[a]



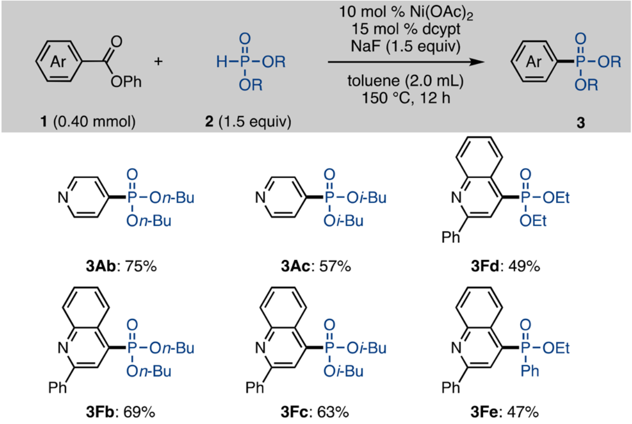
[a] Conditions: Ni(OAc)$_2$ (5 mol %), dcypt (10 mol %), **1** (0.40 mmol), **2a** (1.5 equiv), *t*-AmylOH (2.0 mL), 150 °C, 12 h. [b] 170 °C, 18 h. [c] NaF (1.5 equiv) was added. [d] HCO_2Na (1.5 equiv) was added and toluene (2.0 mL) was used instead of *t*-AmylOH.

entry 1). Other diphosphine ligands, such as dcype and dppe, significantly decreased the reaction yield (Table 1, entries 2 and 3). PCy$_3$[16] and *N*-heterocyclic carbene ligands,[17] which are effective for inert bond activation using nickel catalysis,[18] were completely ineffective (Table 1, entries 4 and 5. See the Supporting Information (SI) for details). Regarding the solvent effect, it was found that tertiary alcohols give good results (Table 1, entries 1 and 7). Nonpolar solvents such as toluene and 1,4-dioxane were found to be applicable, albeit in slightly lower yields (Table 1, entries 8 and 9). Palladium catalysis showed no reactivity in the C–P bond formation (Table 1, entry 10). It is noteworthy that this reaction proceeds without base, in contrast to Hirao-type coupling, which often requires a stoichiometric amount of base.

With optimized conditions (Table 1, entry 1) in hand, we investigated the substrate scope of this catalytic reaction (see Scheme 1). Various azinecarboxylates could be used in this reaction, as 4-pyridyl (**3Aa**), 3-pyridyl (**3Ba**), and pyrazinyl (**3Ca**) phosphine oxides were obtained in moderate to good yields. Unfortunately, 2-pyridyl substrates diminished the reaction yield (see the SI). Isoquinoline (**3Ea**) and quinoline (**3Fa** and **3Ga**) substrates also underwent the present reaction. Flavone derivative **3Ha** could be synthesized in a good yield. Five-membered heteroaromatics, such as thiophenes, benzothiophenes, and furans, were reactive, providing the corresponding heteroaryl phosphine oxides (**3Ia**–**3La**). In these cases, the addition of sodium formate and NaF improved the reaction yield, although their effect is still unclear. This reaction was also applicable to a range of benzoates (**3Ma**–**3Sa**). Regarding the effect of substituents, it was revealed that this reaction favors substrates bearing electron-withdrawing groups (see the SI). Although *ortho*-substituents diminished the reaction efficiency, *meta*- and *para*-substituted benzoates can couple with **2a** to give the corresponding aryl phosphines (**3Ra** and **3Sa**). Reactive functional groups such as acetal, alkyl esters, and cyano groups were compatible under these catalytic conditions.

Next, we investigated applicable phosphates (see Scheme 2). At first, we subjected phosphate **2b** to the reaction with **1A** under the optimized conditions; however, the reaction resulted in a poor yield. After reinvestigating the reaction conditions, we

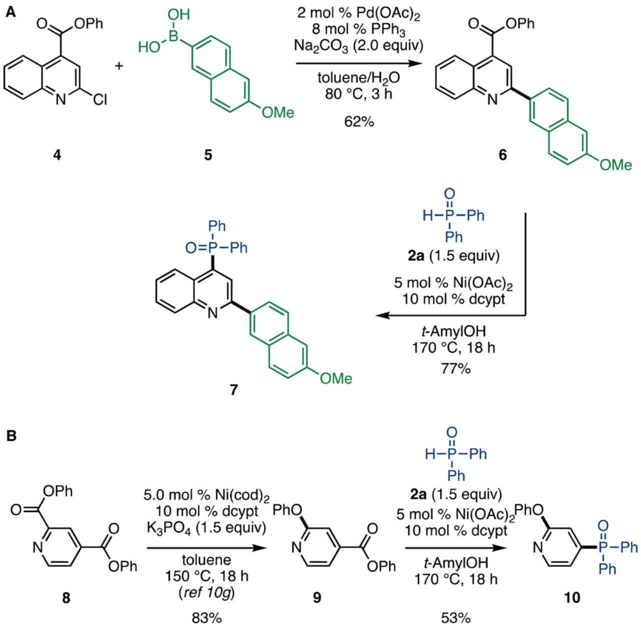
Scheme 2. Substrate Scope of Phosphates 2[a]



[a] Conditions: Ni(OAc)$_2$ (10 mol %), dcypt (15 mol %), **1** (0.40 mmol), **2** (1.5 equiv), NaF (1.5 equiv), toluene (2.0 mL), 150 °C, 12 h.

found that alternative conditions using NaF in toluene were effective for the reaction of alkyl phosphates (see the SI for details). Phosphinite **2e** was also coupled to generate the desired product **3Fe** in an acceptable yield.

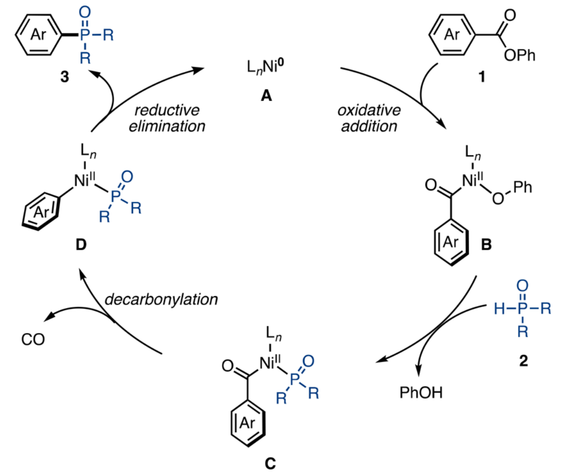
Scheme 3. Sequential Couplings



Since ester groups are generally intact under classic cross-coupling conditions, we conducted a sequential cross-coupling of **4** (Scheme 3). First, Suzuki–Miyaura coupling of **4** with **5** smoothly produced biaryl **6** without any decomposition of the phenyl ester moiety (Scheme 3A). The resulting aromatic ester **6** was subjected to the present C–P bond-forming reaction with **2a**, providing **7** in a good yield.[19] In another example, a sequential decarbonylative coupling was achieved in a site-selective manner (Scheme 3B). A previously reported decarbonylative etherification of **8**,[10g] followed by the present decarbonylative C–P bond formation, successfully generated **10** in a good yield.

Scheme 4 shows a plausible mechanism for this reaction.[20] We assume a Ni(0)/Ni(II) catalytic cycle as follows. First, oxidative addition of the C–O bond to Ni(0) generates a Ni(II) intermediate **B**. To this intermediate **B**, a phosphorus nucleophile effectuates a ligand exchange, followed by decarbonylation to form Ni(II) intermediate **D**. Finally, reductive elimination produces product **3** with regeneration of a Ni(0) species.[21]

Scheme 4. A Plausible Mechanism



In summary, we have developed a Ni-catalyzed C–P bond formation of aromatic esters and organophosphorus compounds such as phosphine oxides and phosphates. Intriguingly, only the use of dcypt as a ligand enabled this reaction. Sequential coupling reactions speak for the synthetic utility of not only the present reaction, but also of aromatic esters as an unconventional coupling partner. Further studies to expand the scope of ester-based coupling are ongoing in our group and will be reported in due course.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b00080.

Detailed experimental procedures, spectral data for all compounds, and ^{1}H, ^{13}C, and ^{31}P NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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(21) According to the fact that we never observed aroylphosphines during the reaction, we conclude that this reaction does not proceed through decarbonylation of in situ generated aroylphosphines, which is similar to reports by the Wang group (see the Supporting Information for details).