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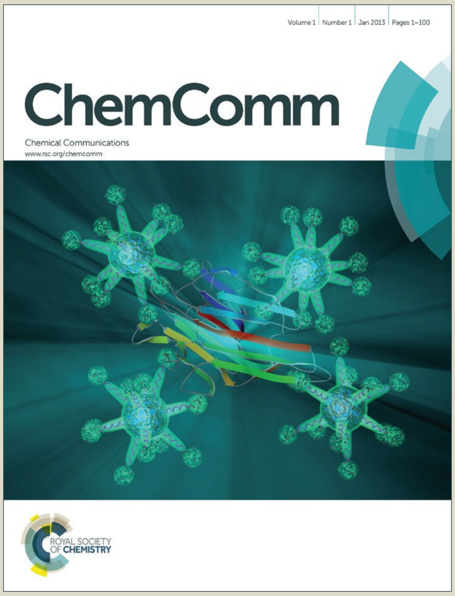

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ARTICLE TYPE

Nickel-Catalysed P–C Bond Formation via P–H/C–CN Cross Couplings

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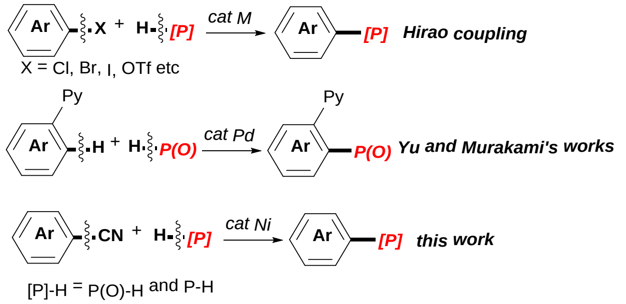
Nickel-catalysed P–H/C–CN cross couplings take place efficiently under mild reaction conditions affording the corresponding *sp*^{2}C–P bonds. This transformation provides a convenient method for the preparation of arylphosphines and arylphosphine oxides from the readily available P–H compounds and arylnitriles.

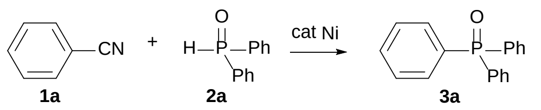
Arylphosphorus compounds have wide applications in material chemistry, organic synthesis and catalysis, thus the studies on their preparation have attracted much attention.[1] Conventional procedures use nucleophilic substitutions of the toxic phosphoryl halides with organolithiums or Grignard reagents; however the hazardous reaction conditions limited the application.[1,2] Since the palladium-mediated coupling reported by Hirao et al,[3] transition metal-catalysed cross couplings of aryl halides or counterparts with P–H compounds have been well established for the construction of *sp*^{2}C–P bonds (Scheme 1).[3,4] Arylphosphorus compounds can also be produced by the palladium-catalysed pyridine group-directed C–H/P(O)–H cross coupling (Scheme 1).[5] However, the preparation of phosphorus compounds via C–CN/P–H cross couplings has never been developed.[6]



Scheme 1 Synthesis of arylphosphorus compounds via transition metal-catalysed cross couplings.

Aryl nitriles are readily available chemicals which are widely used in organic synthesis. However, known functionalization of aryl nitriles via the cleavage of carbon–cyano bonds focused on carbon–carbon bonding formations that usually use noble metal catalysts and/or phosphine ligands.[7] Herein, we report an efficient synthesis of both arylphosphines and arylphosphine oxides from the readily available P–H compounds and aryl nitriles by using the P–H/C–CN direct cross coupling strategy (Scheme 1). This transformation proceeds smoothly with a simple Ni(COD)$_2$/8-hydroxyquinoline catalyst, providing an alternative protocol for the construction of *sp*^{2}C–P bonds under mild reaction conditions.

Table 1 Nickel-catalysed cross coupling of benzonitrile with diphenylphosphine oxides.[a]



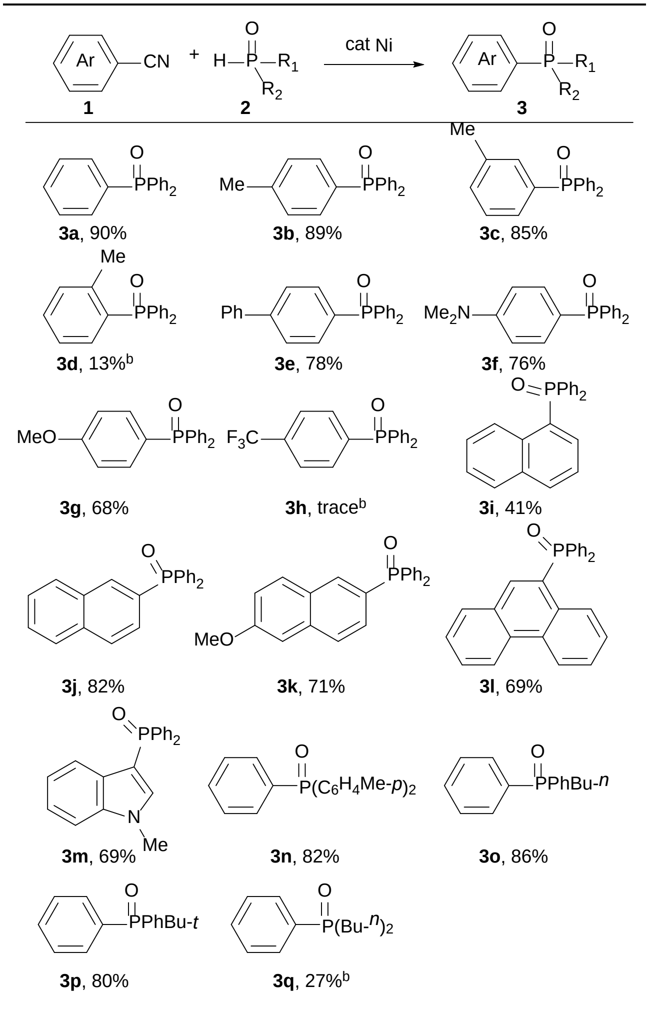
Entry	Cat Ni	Ligand	Base	Solvent	Temp	Yield(%)[b]
1	Ni(COD)2	dcype	K_2CO_3	dioxane	90 °C	trace
2	Ni(COD)2	dcype	LiOBu-*t*	dioxane	90 °C	18
3	Ni(COD)2	dcype	NaOBu-*t*	dioxane	90 °C	40
4	Ni(COD)2	dcype	KOBu-*t*	dioxane	90 °C	72
5	Ni(COD)2	dppm	KOBu-*t*	dioxane	90 °C	66
6	Ni(COD)2	dppp	KOBu-*t*	dioxane	90 °C	59
7	Ni(COD)2	Ph_3P	KOBu-*t*	dioxane	90 °C	70
8	Ni(COD)2	TMEDA	KOBu-*t*	dioxane	90 °C	65
9	Ni(COD)2	HQ	KOBu-*t*	dioxane	90 °C	89
10	Ni(COD)2	-	KOBu-*t*	dioxane	90 °C	80
11	-	HQ	KOBu-*t*	dioxane	90 °C	none
12	Ni(COD)2	HQ	KOBu-*t*	toluene	90 °C	75
13	Ni(COD)2	HQ	KOBu-*t*	DMF	90 °C	none
14	Ni(COD)2	HQ	KOBu-*t*	dioxane	110 °C	66
15	Ni(COD)2	HQ	KOBu-*t*	dioxane	70 °C	71
16[c]	Ni(COD)2	HQ	KOBu-*t*	dioxane	90 °C	94

[a] Reaction conditions: a mixture of benzonitrile **1a** (0.1 mmol), diphenylphosphine oxide **2a** (0.1 mmol), a nickel catalyst (0.01 mmol), a ligand (0.01 mmol), a base (0.2 mmol) and solvent (0.5 mL) in a 25 mL glass tube is heated at the indicated temperature for 16 h. HQ: 8-hydroxyquinoline. [b] ^{31}P NMR yield using methyldiphenylphosphine oxide as an internal standard. [c] 1.3 equiv **2a** was loaded.

This reaction was accidently found during the studies on the synthesis of arylphosphorus compounds using phenol derivatives and P(O)–H compounds by the nickel-catalysed P–H/C–O cross coupling.[8] It was found that 2-methoxynaphthalene reacted with diphenylphosphine oxide **1a** in the presence of 10 mol% Ni(COD)$_2$ and 2 equivs KOBu-*t* in benzonitrile at 90 °C for 16 h, could produce 81% yield of triphenylphosphine oxide via C–CN/P(O)–H cross coupling, while the expected product 2-naphthyldiphenylphosphine oxide by C–O/P(O)–H cross coupling was not detected at all. The cross coupling of benzonitrile with **2a** was further investigated and the results were compiled in Table 1. The use of a proper base is crucial for this reaction. The yield of the coupling product **3a** increased as a stronger base was employed and KOBu-*t* showed the best (entries

1-4). Phosphine ligands tested did not enhanced the reaction efficiency (entries 5-8), because in the absence of such a ligand, this cross coupling also proceeded to give **3a** in 80% yield (entry 10). However, when 8-hydroxyquinoline was employed as the ligand, the yield increased to 89% (entry 9). The yield further increased to 94% when 1.3 equiv of **2a** was used under similar reaction conditions (entry 16). Nickel complex is essential for this reaction, since no product was detected in the absence of a nickel catalyst (entry 11). As to the solvent, this cross coupling also took place in toluene, but hardly proceeded in DMF (entries 12 and 13). In addition, this reaction was sensitive to the reaction temperature (entries 14 and 15).

Table 2 Synthesis of arylphosphine oxides via nickel-catalysed P(O)–H/C–CN cross coupling.[a]

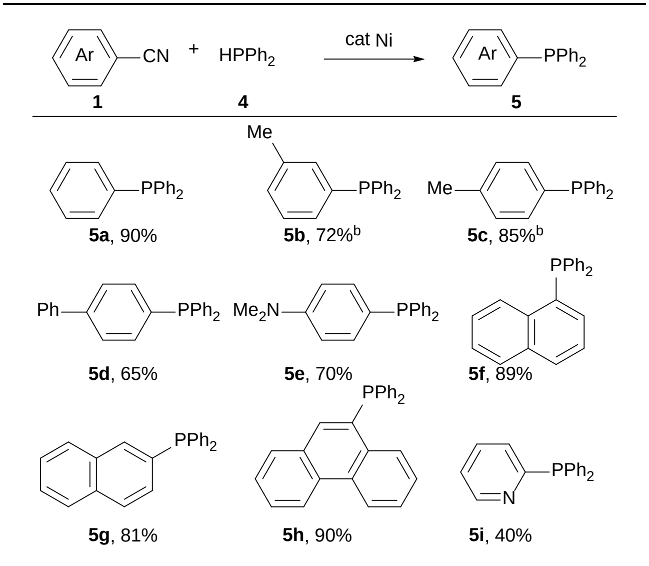


[a] Reaction conditions: nitrile **1** (0.2 mmol), P(O)–H compound **2** (0.26 mmol), Ni(COD)$_2$ (0.02 mmol), 8-hydroxyquinoline (0.02 mmol), KOBu-*t* (0.4 mmol), dioxane (1 mL), 25 mL glass tube, 90 ^{o}C, 16 h. Isolated yield. [b] ^{31}P NMR yield.

This P–H/C–CN cross coupling strategy is applicable to other substrates and a wide range of arylphosphine oxides are prepared under similar reaction conditions (Table 2). Thus, 3-methylbenzonitrile and 4-methylbenzonitrile coupled with diphenylphosphine oxide **2a** readily to yield the corresponding product **3b** and **3c** in 89% and 85% yield, respectively. However, with 2-methylbenzonitrile, only 13% of product was detected under similar reaction conditions, perhaps due to the steric hindrance of the substrate. Other substrates with electron-rich groups like phenyl, methoxy and amino group were readily phosphorylated to produce the expected products in high yields. However, when an electron-deficient 4-(trifluoromethyl)benzonitrile was used as the substrate, only a trace of **3h** was obtained. Though only 41% yield of **3i** was obtained from 1-napthylnitrile, 2-napthylnitriles served well in the present catalytic system and were converted to the corresponding coupling products in high yields. Worth noting is that cyanoindole was also successfully phosphorylated by using this nickel-catalysed P–H/C–CN cross coupling strategy.

As to the hydrogen phosphoryl compounds, other secondary phosphine oxides also acted as good coupling partners. For example, di(*p*-tolyl)phosphine oxide coupled with benzonitrile smoothly, furnishing the expected **3n** in 82% yield. A high yield of **3o** was also obtained from (*n*-Bu)PhP(O)H. The bulky (*t*-Bu)PhP(O)H also underwent P–H/C–CN cross coupling with **1a** to give **3p** in a high yield. The cross coupling of dibutylphosphine oxide with benzonitrile also took place to produce **3q** in 27% yield under similar reaction conditions.

Table 3 Synthesis of arylphosphines via nickel-catalysed P–H/C–CN cross coupling.[a]



[a] Reaction conditions: nitrile **1** (0.2 mmol), diphenylphosphine **4** (0.26 mmol), Ni(COD)$_2$ (0.02 mmol), 8-hydroxyquinoline (0.02 mmol), KOBu-*t* (0.4 mmol), dioxane (1 mL), 25 mL glass tube, 90 ^{o}C, 16 h. Isolated yield. [b] obtained as the corresponding phosphine oxides.

Interestingly, in addition to the above mentioned P(V) compounds, the highly coordinative P(III) secondary phosphines also served as the efficient coupling partner in this nickel-catalysed P–H/C–CN cross coupling reaction to produce the valuable P(III) phosphines. As shown in Table 3, benzonitrile coupled with diphenylphosphine **4** readily to produce the corresponding product **5a** in 90% yield. Other benzonitrile analogues bearing methyl or phenyl group also coupled with **4** and were converted to the expected phosphine **5** in high yields. Worth noting is that substrate with amino group served well in this catalytic system, yielding **5e** in 70% yield. Under similar reaction conditions, both 1-napthyl nitrile and 2-napthyl nitrile coupled with diphenylphosphine efficiently to produce the

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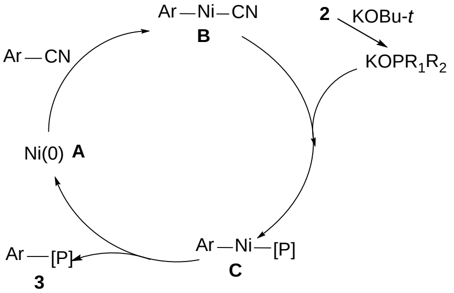
corresponding **5f** and **5g** in high yields. An high yield of arylphosphine **5h** was also obtained from the cross coupling of 9-cyanophenanthrene with **4** under similar reaction conditions. Picolinonitrile also underwent P–H/C–CN cross coupling to afford **5i** in 40% yield.



Scheme 2 A simplified mechanism for the nickel-catalysed P–H/C–CN cross coupling

A simplified catalytic cycle is outlined in Scheme 2 for this nickel-catalysed P–H/C–CN cross coupling of P–H compounds with aryl nitriles. The Ni(0) complex **A** oxidatively adds to the C–CN bonds to give **B**, which subsequently reacts with KOPR$_1$R$_2$, formed via the deprotonation of **2** by KOBu-*t*, to yield **C**.[9] Reductive elimination of **C** produces the corresponding arylphosphorus compounds and regenerates Ni(0) complex **A**. [9]

Conclusions

In summary, a Ni(COD)$_2$/8-hydroxyquinoline catalysed P–H/C–CN cross coupling reaction was reported that could efficiently construct sp^2C–P bonds. By using this new cross coupling reaction, both arylphosphines and arylphosphine oxides were produced from the readily available P–H compounds and aryl nitriles under mild reaction conditions.

Notes and references

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† Electronic Supplementary Information (ESI) available: [General information, experimental procedures, characterized data and copies of ^{1}H, ^{13}C and ^{31}P NMR spectra for products]. See DOI: 10.1039/b000000x/

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9 This KOR$_1$R$_2$ should coordinate to the nickel species **A**-**C**. The products derived from the CN group were not clearly determined at this stage. Although the formation of KCN was possible, it could not be detected from the reaction mixture (SI).