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The carbonyl group tuned electron-deficient phosphorus ligands and their application in Rhodium catalyzed arylation to aldehydes

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ABSTRACT

Acylphosphines, which could be efficiently prepared from acid chlorides and secondary phosphines, were developed as a type of carbonyl group tuned electron-deficient phosphorus ligand. They were found to be a kind of efficient ligand in Rhodium catalyzed arylation to aldehydes through accelerating the transmetalation process. Chiral acylphosphine ligands could be generated from carboxylic acids bearing the chiral framework correspondingly.

Transition metal catalyzed reactions are playing an essential role in modern organic synthesis. Numerous chemical transformations could be realized by number-limited transition metals, which were endowed by ligands with divers catalyzing ability through an electronic and sterically hindered effect on the metal center. Various ligands based on hetero atoms or coordinative functional groups have been designed and prepared with the development of organic synthesis methodology,[1] among which the phosphorus ligands have taken an essential place in homogenous catalysis and organometallic chemistry.[2] The electronic property of phosphorus ligands, which could be tuned by the adjacent functional group, would greatly affect the reactivity of the catalyst.[1e,3] Comparing to the electron-rich phosphorus ligands which would usually enhance catalysts' reactivity in hydrogenation and hydroformylation reactions, electron-deficient phosphorus ligands, such as DIFLUORPHOS developed by Jean-Pierre Genet and the phosphoramidite ligands by Feringa, have also been found to be good ligands in a broad range of reactions.[1e,3a,4] Except tuned by aryl groups adjacent to phosphorus atom, the electron-deficient phosphorus ligands are still much less developed with a new type of electron tuning group (Fig. 1).

Carbonyl group, a fundamental functional group, is an important electron withdrawing group which could efficiently reduce the electron density of its α-atoms. Acylphosphines or phosphomides (**L** in Scheme 1), in which the phosphine is adjacent to a carbonyl group, have been prepared as key intermediates for the synthesis of polymerization photoinitiators, acylphosphine oxides.[5] Comparing to the wide use in polymerization, their trivalent phosphine structure was much less regarded as a potential electron-deficient ligand in transition metal catalyzed reactions.[6] The character of the carbonyl group decreasing σ-donor and increasing π-acceptor abilities of phosphine ligands would be just essential to accelerate the transmetalation process,[3a] for example, in Rhodium catalyzed arylation of organoboronic reagents. Herein we would like to report a type of electron-deficient phosphorus ligand, acylphosphines, and their first successful application in Rhodium catalyzed arylation to aldehydes.[7]

The acylphosphines **L1**–**L5** could be efficiently prepared from commercial available acid chlorides **1** and secondary phosphines **2** in ethers as shown in Scheme 1.[6f,g] Only a few researches showed that the acylphosphines could form stable complexes through coordinating with transition metals, such as Ruthenium, Rhodium, and Iridium, and some of these complexes have tried to be used as ligands in the catalysts for organic reactions.[6] In our study, the pre-catalyst for arylation of organoboronic reagents, $[RhCl(coe)_2]_2$ (Chlorobis(cyclooctene)Rhodium(I)), was found to be able to undergo a ligand exchange with acylphosphines. By mixing benzoyldiphenylphosphine **L1** and $[RhCl(coe)_2]_2$, a fast coordination would be detected from the changing of chemical shifts on the ^{31}P NMR spectrum. Even with the Wilkinson's Catalyst, $RhCl(PPh_3)_3$, a ligand exchange on the Rhodium center could also take place very fast, which indicated the acylphosphines have successfully inherited the coordinative ability from traditional trivalent phosphines. Initial studies for the acylphosphines' application in Rhodium catalyzed arylation were carried out with the reaction

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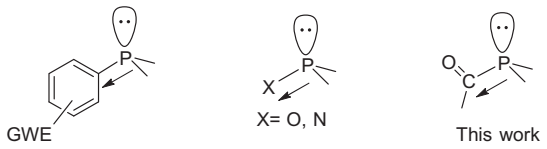
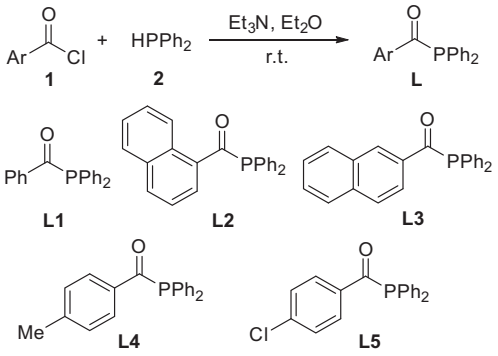


Figure 1. Electron-withdrawing groups on phosphorus ligands.

of benzaldehyde **3a**, 2.5 equiv of $PhB(OH)_2$ **4a,** and 2.5 equiv of base Na_2CO_3 in toluene/H_2O (1:1.5) in the presence of 0.5 mol % of [RhCl(coe)$_2$]$_2$ and 1 mol % of acylphosphine **L1**. After 24 h at room temperature, the reaction would afford the addition product **5a** in 65% yield (Table 1, entry 1), while the triphenylphosphine could only achieve 29% yield under the same conditions (Table 1, entry 3). This result indicated the acylphosphine **L1** performed as an electron-deficient phosphorus ligand and enhanced the reactivity of Rhodium catalyzed arylation by accelerating the transmetalation process.[3a]

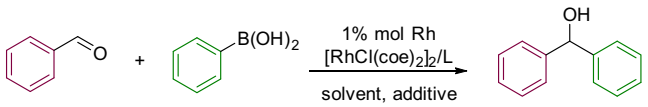
We investigated different bases as adducts in the addition to benzaldehyde **3a**, and found relatively weaker bases, such as Na_2CO_3 and KF, would give better yield than stronger bases (Table 1, entries 5–7), while a dramatical shift of yield, from 65% to 95%, was found when the ratio of toluene and water was optimized from 1:1.5 to 1:0.5 (Table 1, entry 8). Variations of solvent with water at this ratio were tested and toluene was found to be the best solvent of all, while dichloromethane could give a similar high yield but DME was found to draw down the yield greatly (Table 1, entries 9–11). Further optimization of reaction conditions showed that a slight heating of the reaction mixture to 60 °C would enhance reactivity and shorten the reacting time to 4 h with 99% yield (Table 1, entry 12) at a low catalyst loading (1 mol % Rh). Under this condition, the derivatives of the acylphosphines, **L2**–**L5**, were found to work as the ligands in this reaction as well (Table 1, entries 13–16), in which **L2** and **L5** showed a moderate to good reactivity. But not quite such an obvious electronic effect could be observed in the variation of the substitution on the benzoyl group, which may be due to the overwhelming electron-withdrawing effect of the carbonyl group comparing to the substances on the benzoyl group.

With the optimized reaction condition, the reactions of various arylboronic acids **4** and aldehydes **3** were tested, and the results are shown in Table 2. Several arylboronic acids reacting with benzaldehyde **3** would afford the desired product **5** in good to excellent yields (Table 2, entries 1–5). Sterically hindered arylboronic acids would give a relatively lower yield (Table 2, entry 6), while not quite such an obvious electronic effect was observed in some cases (Table 2, entries 7–9). As for the aldehydes **3**, most substituted benzaldehydes with arylboronic acid could afford the corresponding diarylmethanols in good to excellent yield, showing



Scheme 1. The synthesis of acylphosphines **L1**–**L5**.

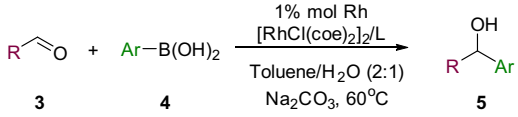
Table 1
Rhodium-acylphosphine catalyzed arylation to benzaldehyde[a]

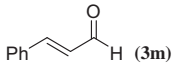


Entry	L.	Sol./ratio to H_2O	Add.	Temp (°C)	Yield[b] (%)
1	**L1**	Tol/1:1.5	Na_2CO_3	rt	65
2	No	Tol/1:1.5	Na_2CO_3	rt	N.R.[c]
3	**L1**	Tol/1:1.5	Na_2CO_3	rt	13[d]
4	PPh_3	Tol/1:1.5	Na_2CO_3	rt	29
5	**L1**	Tol (1:1.5)	KF	rt	60
6	**L1**	Tol (1:1.5)	KOH	rt	Trace
7	**L1**	Tol (1:1.5)	K_3PO_4	rt	11
8	**L1**	Tol (1:0.5)	Na_2CO_3	rt	95
9	**L1**	Diox/1:0.5	Na_2CO_3	rt	40
10	**L1**	DME/1:0.5	Na_2CO_3	rt	<5
11	**L1**	DCE/1:0.5	Na_2CO_3	rt	92
12	**L1**	Tol/1:0.5	Na_2CO_3	60	99
13	**L2**	Tol/1:0.5	Na_2CO_3	60	36
14	**L3**	Tol/1:0.5	Na_2CO_3	60	78
15	**L4**	Tol/1:0.5	Na_2CO_3	60	50
16	**L5**	Tol/1:0.5	Na_2CO_3	60	85

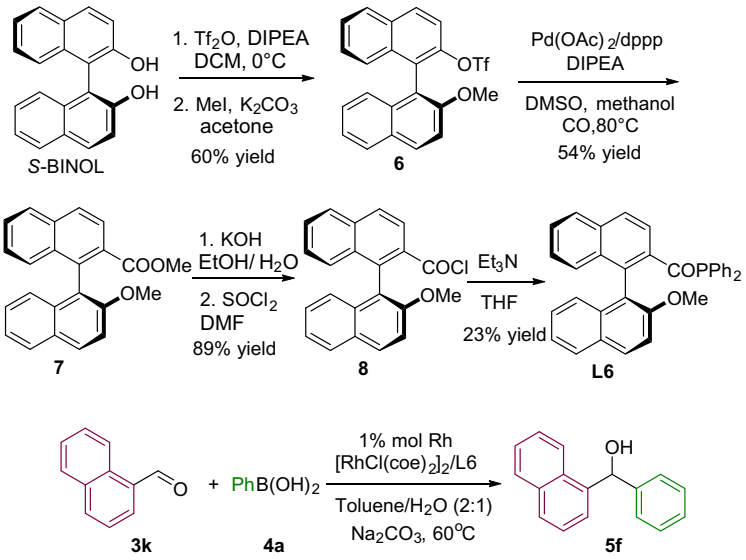
[a] Reaction condition unless otherwise noted: aldehyde (0.3 mmol, 1.0 equiv), phenylboronic acid (2.5 equiv), solvent (1 mL), base (2.5 equiv), 0.5 mol % of [RhCl(coe)$_2$]$_2$ and 1 mol % of acylphosphine **L1**.
[b] Isolated yield.
[c] No ligand employed.
[d] 2 mol % of acylphosphine **L1** was used.

Table 2
Rhodium-acylphosphine **L1** catalyzed arylation to aldehydes[a]



Entry	**3** (R=)	**4** (Ar=)	Yield[b] (%)
1	C_6H_5 (**3a**)	C_6H_5 (**4a**)	99 (**5a**)
2	C_6H_5 (**3a**)	4-MeC_6H_5 (**4b**)	95 (**5b**)[c]
3	C_6H_5 (**3a**)	3-MeC_6H_5 (**4c**)	82 (**5c**)[c]
4	C_6H_5 (**3a**)	2-MeC_6H_5 (**4d**)	73 (**5d**)
5	C_6H_5 (**3a**)	2-Naphthyl (**4e**)	96 (**5e**)[c]
6	C_6H_5 (**3a**)	1-Naphthyl (**4f**)	53 (**5f**)[c]
7	C_6H_5 (**3a**)	4-$CF_3C_6H_5$ (**4g**)	53 (**5g**)[c]
8	C_6H_5 (**3a**)	4-MeOC_6H_5 (**4h**)	31 (**5h**)
9	C_6H_5 (**3a**)	4-ClC_6H_5 (**4i**)	41 (**5i**)
10	4-MeOC_6H_5 (**3b**)	C_6H_5 (**4a**)	99 (**5h**)
11	4-MeC_6H_5 (**3c**)	C_6H_5 (**4a**)	74 (**5b**)
12	4-BrC_6H_5 (**3d**)	C_6H_5 (**4a**)	81 (**5j**)
13	4-ClC_6H_5 (**3e**)	C_6H_5 (**4a**)	85 (**5i**)
14	2-MeOC_6H_5 (**3g**)	C_6H_5 (**4a**)	68 (**5k**)
15	2-ClC_6H_5 (**3h**)	C_6H_5 (**4a**)	94 (**5l**)[d]
16	2-MeC_6H_5 (**3i**)	C_6H_5 (**4a**)	62 (**5d**)
17	2-Naphthyl (**3j**)	C_6H_5 (**4a**)	74 (**5e**)
18	1-Naphthyl (**3k**)	C_6H_5 (**4a**)	83 (**5f**)
19	*n*-C_4H_9 (**3l**)	C_6H_5 (**4a**)	64 (**5m**)
20	*n*-C_4H_9 (**3l**)	4-MeC_6H_5 (**4b**)	77 (**5n**)
21	*n*-C_4H_9 (**3l**)	3-MeC_6H_5 (**4c**)	62 (**5o**)
22	*n*-C_4H_9 (**3l**)	2-Naphthyl (**4e**)	73 (**5p**)
23	2-ClC_6H_5 (**3h**)	4-MeOC_6H_5 (**4h**)	85 (**5q**)[d]
24	 (**3m**)	C_6H_5 (**4a**)	50 (**5r**)

[a] Reaction condition unless otherwise noted: aldehyde (0.3 mmol, 1.0 equiv), phenylboronic acid (2.5 equiv), solvent (1 mL), base (2.5 equiv), 0.5 mol % of [RhCl(coe)$_2$]$_2$ and 1 mol % of acylphosphine **L1**, reactions were monitored by TLC.
[b] Isolated yield.
[c] 3 mol % of Rhodium catalyst was employed.
[d] 5 mol % of Rhodium catalyst was employed.



Scheme 2. Synthesis of a chiral acylphosphine **L6** and application as a chiral ligand in Rhodium catalyzed arylation to 1-naphthylaldehyde **3k**.

the sterical and electrical effect of substitution on benzaldehyde had a less affection on the reactivity (Table 2, entries 10–18, 23). For the less reactive aliphatic aldehydes, this condition with acylphosphine **L1** as the ligand for Rhodium catalyst could afford products **5m**–**5p** in good yield as well (Table 2, entries 19–22). In the presence of a potential 1,4-addition competition (Table 2, entry 24), the 1,2-addition would take place as the main reaction and afford the corresponding alcohol product **5r**, just as the selectivity of traditional phosphine ligands would have done.[8]

Acylphosphines could also be decorated into chiral ligands by connecting the phosphine with chiral carboxylic acid.[9] An acylphosphine ligand **L6** bearing axial chiral binaphthyl skeleton could be synthesized from (*S*)-BINOL generated acid chloride **8** and diphenylphosphine **2** as shown in Scheme 2.[10] In the Rhodium catalyzed arylation to 1-naphthylaldehyde **3k** with phenylboronic acid **4a**, the chiral acyphosphine **L6** performing as the chiral ligands for Rhodium could afford the product **5f** in a nearly quantitative yield, even much higher than **L6**, but unfortunately with a poor enantioselectivity. Though the enantioselectivity in the aldehyde addition is not satisfying, the chiral ligands' decoration and application in other asymmetric synthesis could be carried on in future.

Conclusion

In summary, we found the easily prepared acylphosphines could be successfully used as a new type of electron-deficient ligands in Rhodium catalyzed arylation to aldehydes. The experimental studies showed that the acylphosphine ligands have a good coordinative ability inherited from tradition trivalent phosphines and a positive ability of the accelerating transmetalation process tuned by the adjacent carbonyl group. The acylphosphines could be generated into chiral ligands based on (*S*)-BINOL framework. Studies of chiral acylphosphine ligands' decoration and application in asymmetric synthesis would be taken under investigation.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.08.076.

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