Green Chemistry

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DOI: 10.1039/C6GC03096C

Green Chemistry

ARTICLE

Efficient and recyclable Ir(I)-catalysts with involvement of π-acceptor phosphines for *N*-alkylation of aryl amines with alcohols

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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The mono-phosphines (**L1** and **L2**) and the diphosphines (**L3** and **L4**) with typical π-acceptor character were prepared and applied in Ir(I)-catalyzed *N*-alkylation of amines with alcohols. It was found that the π-acceptor character of the applied phosphines closely co-related to the catalytic efficiency of $[Ir(COD)Cl]_2$ complex for this green reaction. Compared to PPh_3 as the typical σ-donor (i.e. with the poor π-acceptor character), **L1-L4** all corresponded to the efficient *N*-alkylation of aniline to benzyl-aniline. While **L1-L4** coordinating to Ir(I)-catalyst, the consolidated Ir-P linkages due to π-backdonation could well protect the Ir-catalyst against deactivation, giving rise to the *N*-alkylation of aniline. On the other hand, the stabilized Ir-catalyst with the involvement of **L2** could be recycled successfully at least 4 runs in the ionic liquid of $[MePh_3P]Br$ without the detectable leaching of Ir and P elements in the organic products.

Introduction

Conventionally, *N*-alkyl-amines are prepared via nucleophilic substitution of amines with alkylating reagents such as alkyl halides [1]. Since reported by Grigg [2] and Watanabe [3] independently for the first time in the eighties, alkylation of amines with alcohols via homogeneous catalysis has emerged as an attractive alternative for the production of *N*-alkyl-amines, due to the advantages of avoided overalkylation, readily available alcohols to replace the toxic alkylating agents, and water as the only by-product [4]. Hence, this method represents a greener synthesis route for alkylated amines with high atom-economy [5]. A number of transition metal catalysts such as Ru/Ir-complexes have been exploited as the typical homogeneous catalysts for alkylation of amines with alcohols [6]. The overall transformation is based on a mechanism called "borrowing hydrogen" or "hydrogen (auto)transfer" [4,7]. In this "borrowing hydrogen" process, the oxidative dehydrogenation ($-H_2$) of alcohol is followed by the condensation of obtained aldehyde intermediate with amine to give imine intermediate. The latter was hydrogenated ($+H_2$) to generate alkylated amine. Comparatively, Ir-complexes have been found more reactive than Ru-complexes [5,8] with the supportive evidence by the DFT calculations [9]. It is also believed that the nature of the involved ligands plays the significant role in modulating the performance of the Ir(I,III)-complexes for "borrowing hydrogen" in this reaction. Hence, several kinds of ligands have been applied such as carbenes [4,10], phosphaalkenes [11], P,N-hemilabile ligands [12], and cyclopentadienyl derivatives (Cp*) [11b,13]. Since the π-acceptor character was basically required for the ligands like phosphaalkenes and Cp* in this reaction, the uses of phosphines with the typical σ-donor character were rarely successful. On the other hand, the recycling uses of the homogeneous Ir-catalysts applied in *N*-alkylation of amines with alcohols have never been reported

It is well known that the classical examples of P-containing ligands with π-acceptor character are phosphinites, phosphonites and phosphites [14]. Anyway, the lability of P-O bonds towards hydrolysis has limited their practical applications [15,16]. So, the phosphine fragments linked to the electron-withdrawing groups such as -F and $-CF_3$ with inert P-C linkages are always considered as the alternatives [17]. The objective of this work was to develop the typical phosphines with π-acceptor character and good stability to fulfill the efficient *N*-alkylation of amines with alcohols catalyzed by simple Ir(I)-complex of $[Ir(COD)Cl]_2$. In order to develop such phosphines, the electron-deficient groups of imidazolyl and imidazolium moieties were used to substitute one phenyl group (-Ph) in PPh_3. Then the obtained mono-phosphines (**L1** and **L2**) were definitely featured with π-acceptor character at different extent. For comparison, the corresponding diphosphines (**L3** and **L4**) were prepared in parallel (Scheme 1). On the other hand, the use of the ionic imidazolium-based phosphine (**L2**) with the RTIL solvent could fulfill the facile recovery and recyclability of the Ir(I)-catalyst, which had become an efficient

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Electronic Supplementary Information (ESI) available: the crystallographic data of CCDC-1515520 (**Ir-L1A**) and CCDC-1515519 (**Ir-L2**) can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. The Supplementary Information associated with this article can be found online. See DOI: 10.1039/x0xx00000x

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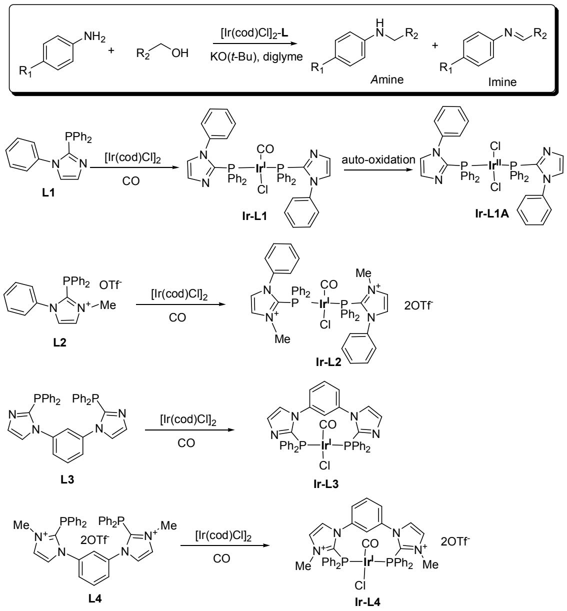
DOI: 10.1039/C6GC03096C

alternative to immobilize the homogeneous transition metal catalysts [18].



Scheme 1 The phosphines **(L1-L4)** with π-acceptor character and the corresponding Ir-complex catalyzed *N*-alkylation of aryl amines with alcohols

Results and discussion

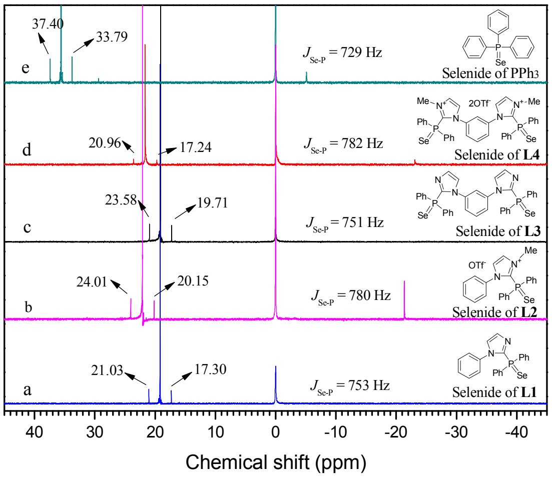


Fig. 1 ^{31}P NMR spectra of the selenides of **L1-L4** in comparison to that of PPh$_3$ (202 MHz): a) reacting elemental selenium with **L1** in CDCl$_3$ at 70 °C for 10 h; b) reacting elemental selenium with **L2** in CDCl$_3$ at 70 °C for 10 h; c) reacting elemental selenium with **L3** in CDCl$_3$ at 70 °C for 10 h; d) reacting elemental selenium with **L4** in DMSO-d_6 at 70 °C for 10 h; e) reacting elemental selenium with PPh$_3$ in CDCl$_3$ at 70 °C for 10 h [19, 20]

It has been claimed that an increase of $^1J_{^{31}\text{P}-^{77}\text{Se}}$ indicates an increase in the character of π-acceptor ability (i.e., less σ-donor character) of a phosphine [21-23]. The value of $^1J_{^{31}\text{P}-^{77}\text{Se}}$ for the phosphine fragments in **L1-L4** in comparison to PPh$_3$ is in an order of **L2** ($^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 780 Hz), **L4** ($^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 782 Hz) > **L1** ($^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 753 Hz), **L3** ($^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 751 Hz) > PPh$_3$ ($^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 729 Hz) (Fig. 1) [19,20]. Hence, it was indicated that **L1-L4** were definitely featured with stronger π-acceptor character (i.e. less σ-donor character) than PPh$_3$. Among them, the ionic **L2** and **L4** are the strongest π-acceptor phosphines with $^1J_{^{31}\text{P}-^{77}\text{Se}}$ of 782 Hz due to the most intensive electron-withdrawing effect from the positive-charged imidazoliums. It was also found that only the electronic effect rather than steric effect of the organic groups like imidazolyl or imidazolium would affect the π-acceptor character of the neighboured phosphino-fragments. Hence, nearly the same $^1J_{^{31}\text{P}-^{77}\text{Se}}$ of ~ 750 Hz was observed for **L1** and **L3** both tailed imidazolyl groups without discrimination to their steric skeleton. The same phenomenon was observed over the imidazolium-tailed **L2** and **L4** with $^1J_{^{31}\text{P}-^{77}\text{Se}}$ of ~ 780 Hz.

The influence of **L1-L4** and PPh$_3$ with different π-acceptor character on the catalytic performance of [Ir(COD)Cl]$_2$ was investigated in the model reaction of *N*-alkylation of aniline with benzyl alcohol. Firstly, the strong alkali of KO(*t*-Bu) after screening from Et$_3$N, NaHCO$_3$ and KOH corresponded to the best reaction rate, resulting in 100% aniline conversion and 90% selectivity to benzyl-aniline. The strong basicity of KO(*t*-Bu) did facilitate the condensation of aldehyde with alcohol to afford imine intermediate, as well as enhanced the nucleophilicity of –C=N to favor the subsequent hydrogenation of imine. Then under the selected conditions [P/Ir = 1 molar ratio, 4 h, 120 °C, KO(*t*-Bu) as an additive, diglyme as a solvent], the reaction data over the different phosphines (**L1-L4**) were given in Table 1. Obviously over [Ir(COD)Cl]$_2$ without the involvement of any ligand, only 70% conversion of aniline and 73% selectivity to benzyl-aniline were obtained (Entry 1). While the mono-phosphines with the enhanced π-acceptor character (**L1**, $^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 753 Hz; **L2**, $^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 780 Hz) were added, **L1** and **L2** based Ir-catalysts both resulted in much higher yields of benzyl-aniline (~ 90%; Entries 2 and 3). And the diphosphines of **L3** and **L4** (**L3**, $^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 751 Hz; **L4**, $^1J_{^{31}\text{P}-^{77}\text{Se}}$ = 782 Hz) also corresponded to the comparable yields under the same reaction conditions (Entries 4 and 5). While the reaction time was shortened to 2 h, the excellent yields of benzyl-aniline (~ 90%) were still obtained over **L1** and **L3** based Ir-catalysts (Entries 7 and 9), whereas **L2** and **L4** with the strongest π-acceptor character ($^1J_{^{31}\text{P}-^{77}\text{Se}}$ ~ 780 Hz) showed the relatively sluggish reaction rate (Entries 8 and 10). In contrast, over PPh$_3$-based Ir-catalyst, not only the conversion of aniline but also the selectivity to benzyl-aniline was universally lower than those over **L1-L4** (Entries 6 and 11). In addition, diglyme was indeed to be the best choice as a solvent after screening from *p*-xylene and anisole (or no solvent) (Entries 14-16), due to its high boiling point and high polarity to provide a homogenous catalytic process carried out at 120 °C in a heavy-walled safe glass reactor. The data in Table 1 all

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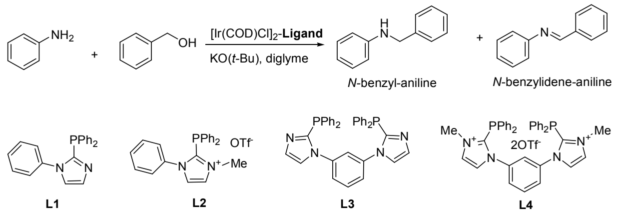
demonstrated the presence of *N*-benzylidene-aniline by-product, further confirming that *N*-alkylation of benzyl-aniline with benzyl alcohol underwent the formation of imine intermediate as found in many examples [4,7,9,10,11(b),13(c)].

It was noted that, as for **L1** (mono-phosphine) and **L3** (diphosphine), although they possessed the different coordination mode to Ir-center, nearly the same yields of benzyl-aniline (~90%) were obtained (Entries 2 and 4) only if they possessed the same π-acceptor character ($^1J_{^{31}P\text{-}^{77}Se}$ ~ 750 Hz). The similar situation was observe over **L2** (mono-phosphine) and **L4** (diphosphine) both with the same high π-acceptor ability ($^1J_{^{31}P\text{-}^{77}Se}$ ~ 780 Hz). The results indicated that only the π-acceptor character but not the chelation mode of the applied phosphines co-related to the catalytic efficiency of $[Ir(COD)Cl]_2$ precursor for *N*-alkylation. **L1-L4** with the higher π-acceptor character indeed corresponded to the more efficient transformation of aniline to benzyl-aniline in comparison to PPh_3 with the poor π-acceptor character ($^1J_{^{31}P\text{-}^{77}Se}$ = 729 Hz).

It was also found that when **Ir-L2** was used to replace the mixture of $[Ir(COD)Cl]_2$ and **L2** as the pre-catalyst, nearly the same conversion of aniline and selectivity to benzyl-aniline were obtained under the same conditions (Entries 12 *vs* 2 and 13). It was indicated the *in situ* formed Ir-complex ligated by **L2** exhibited the same activity as the as-synthesized **Ir-L2**.

Table 1 Ir-catalyzed *N*-alkylation of aniline with benzyl alcohol in presence of the different phosphines[a]



Entry	Ligand	Sol.	Conv. of aniline (%)[b]	Time (h)	Sel. (%)[b] Benzyl-aniline	*N*-Benzylidene-aniline
1	--	Diglyme	70	4	73	27
2	**L1**	Diglyme	100	4	92	8
3	**L2**	Diglyme	100	4	89	11
4	**L3**	Diglyme	100	4	96	4
5	**L4**	Diglyme	98	4	90	10
6	PPh_3	Diglyme	66	4	76	24
7	**L1**	diglyme	100	2	90	10
8	**L2**	Diglyme	60	2	93	7
9	**L3**	Diglyme	97	2	94	6
10	**L4**	Diglyme	56	2	89	11
11	PPh_3	Diglyme	44	2	73	27
12[c]	**Ir-L2**	Diglyme	99	4	90	10
13[d]	**L2**	Diglyme	98	4	89	11
14	**L1**	--	83	2	89	11
15	**L1**	*p*-Xylene	84	2	86	14
16	**L1**	Anisole	63	2	76	27

[a] $[Ir(COD)Cl]_2$ 0.025 mmol (Ir 1 mol %), mono-phosphine 0.05 mmol (**L1**, **L2**, and PPh_3), diphosphine 0.025 mmol (**L3** and **L**4), P/Ir = 1 (molar ratio), aniline 5.0 mmol, KO(*t*-Bu) 3.5 mmol, benzyl alcohol 7.5 mmol, solvent 2 mL, temperature 120 °C, time 4 h; [b] Determined by GC; [c] The complex of **Ir-L2** was used instead of the mixture of $[Ir(COD)Cl]_2$ (0.025 mmol) and **L2** (0.1 mmol); [d] P/Ir = 2 (molar ratio) ($[Ir(COD)Cl]_2$ 0.025 mmol, L2 0.1 mmol]).

The molecular structural information of the corresponding Ir-complexes ligated by **L1-L4** could help us further understand the importance of π-acceptor character of the phosphine in modulating the behaviour of Ir-complex. The Ir-complexes ligated by **L1** and **L2** (mono-phosphines) was successfully prepared in this work and the Ir-complexes ligated by **L3** and **L4** (diphosphines) had been obtained in our previous work [20] (Fig. 2). It was found that the complexation of **L1-L4** respectively to $[Ir(COD)Cl]_2$ dimer under CO atmosphere all afforded the corresponding Ir(I)-complexes (**Ir-L1**, **Ir-L2**, **Ir-L3** and **Ir-L4**). However, **Ir-L1** was irreversibly converted to **Ir-L1A** at the ambient temperature during the crystal growth in co-solvent of dichloromethane/diethyl ether. The latter was a paramagnetic complex in which Ir-centr was in +2 valence state without ^{31}P NMR signal.

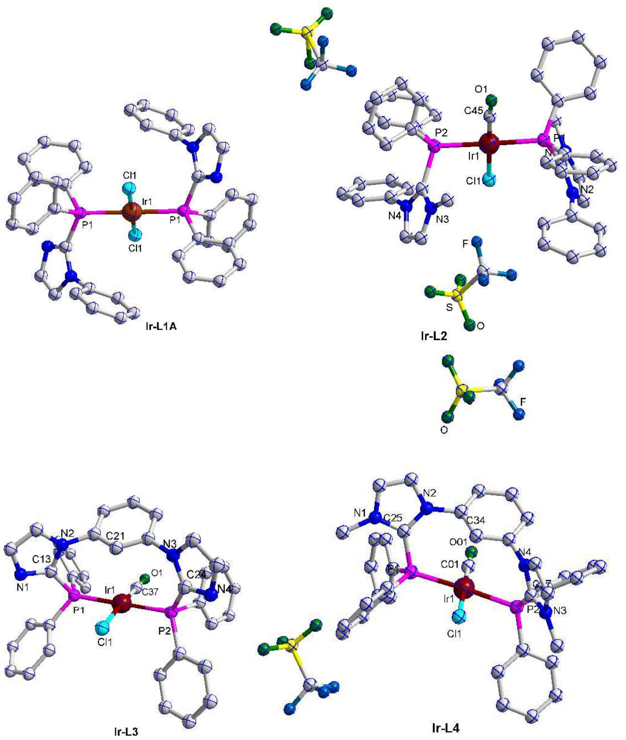


Fig. 2 The single crystal structures of **Ir-L1A**, **Ir-L2**, **Ir-L3** [20] and **Ir-L4** [20] (The hydrogen atoms and the solvent molecules were omitted for clarity)

Table 2 The selected bond distances and bond angles for Ir-complexes

Ir-complex	Selected bond length/Å Ir-P1	Ir-P2	Ir-Cl	Bond angle/° ∠P1-Ir-P2
Ir-L1A	2.328(8)	--	2.147(2)	180.00(-)
Ir-L2	2.319(2)	2.309(2)	2.344(2)	176.67(7)
Ir-L3[20]	2.317(1)	2.310(2)	2.384(1)	176.35(5)
Ir-L4[20]	2.291(1)	2.309(1)	2.374(1)	176.31(4)
$Ir(CO)(PPh_3)_2Cl$ [24]	2.330(1)	--	2.382(3)	180.00(-)

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DOI: 10.1039/C6GC03096C

These Ir(I)-complexes (**Ir-L1**, **Ir-L2**, **Ir-L3** and **Ir-L4**) were all in the typical square-planar geometry, in which Ir(I)($5d^8$)-center was coordinated by the two phosphine fragments in *trans*-position, one CO, and one Cl^- ion. In **L3** and **L4** as the diphosphines, the bulky bis(imidazolyl)-phenyl arms between the two phosphine fragments allowed them to develop P-Ir-P linkages in *trans*-position with bite angle of 176° (Table 2) [20]. Hence, **L1** and **L3** (or **L2** and **L4**) with the similar values of $^1J_{^{31}P-^{77}Se}$ corresponded to the similar product yields due to the same coordination ability and *trans*-coordinating mode to Ir-center (Table 1, Entries 2 and 4; Entries 3 and 5). However, as for **Ir-L3** and **Ir-L4**, the different π-acceptor character in **L3** ($^1J_{^{31}P-^{77}Se}$ = 751 Hz) and **L4** ($^1J_{^{31}P-^{77}Se}$ = 782 Hz) made the Ir-P bond strength quite different (Table 2). The Ir-P linkages in the analogues of **Ir-L2, Ir-L3** and **Ir-L4** [Ir-P, 2.291~2.319 Å] were universally shorter than that in $Ir(CO)(PPh_3)_2Cl$ [2.330(1) Å] [24], due to the stronger π-backdonation derived from the π-acceptor ligands. It was noted that, the stronger π-acceptor character was, the more intensive π-backdonation was observed with the indication of the shortened Ir-P bond length. For example, **L4** was the strongest π-acceptor ligand with $^1J_{^{31}P-^{77}Se}$ of 782 Hz, the corresponding Ir-P bond lengths in **Ir-L4** were shortest [Ir-P, 2.2913(11) and 2.3086(11) Å]. Consequently, the consolidated Ir-P linkages could well protect the Ir-catalyst against deactivation. However, the too stable Ir-P bond in **L4** (or **L2**) didn't favour the timely dissociation of the phosphine to make a vacancy for the accommodation of the substrate (alcohol), leading to the sluggish transformation of benzyl alcohol with aniline to benzyl-aniline (Table 1, Entries 8 and 10). Hence, over **L2** and **L4** able to develop the most stable Ir-P linkages, the prolonged reaction time of 4 h was enough to obtain the product (benzyl-aniline) yield up to ~90% (Table 1, Entries 3 and 5).

Although **L1** and **L2** exhibited dramatic promoting effect on the catalysis of Ir-complex towards *N*-alkylation of aniline with benzyl alcohol in diglyme, the separation and recycling uses of the involved Ir-P catalyst was still a bottleneck problem. Recently, many examples have shown that the ionic phosphines can be applied together with ionic liquid (IL) solvents as the efficient alternative to immobilize the transition metal catalysts for separation and recycling uses [18]. Herein, the ionic phosphine of **L2** also highlighted us to explore the separation and recycling of the Ir-P catalyst by using the IL solvent in place of diglyme. To demonstrate this issue, $[Ir(COD)Cl]_2$ and **L2** were applied with the IL of $[MePh_3P]Br$ (methyltriphenylphosphonium bromide) for *N*-alkylation of aniline (Table 3). It was found that the catalytic system of $[Ir(COD)Cl]_2$-**L2** could be recycled at least 4 runs without obvious deactivation. The ICP-AES analysis indicated that the leaching of Ir and P in the combined organic phase after 4 runs was non-detectable (below the detection limit of <0.1 μg/g). Anyway, in the fifth run the yield of benzyl-aniline dropped to 56% along with the precipitation of Ir-black, indicating the deactivation of Ir-catalyst. When the imidazolium-based RTIL of $[Bmim]BF_4$ or $[Bmim]PF_6$ was applied in place of $[MePh_3P]Br$ as the IL solvent, the *N*-alkylation was completely inhibited under the same reaction conditions, probably due to the complexation of Ir with $[Bmim]^+$ cation as the potential *NHC*-carbene ligand. Comparatively, the recycling experiment of $[Ir(COD)Cl]_2$ and **L1** in $[MePh_3P]Br$ was unsuccessful. Due to the serious leaching of Ir and P into the organic phase and the quick deactivation of the catalyst, the yield of benzyl-aniline dropped to 50% even in the 2nd run.

Table 3 Recycling uses of the catalytic system of $[Ir(COD)Cl]_2$-**L2** with the presence of the phosphonium-based IL of $[Ph_3MeP]Br$ for *N*-alkylation of aniline with benzyl alcohol [a]

Run	Ionic salt	Conv. (%)[b]	Sel.(%)[b]		Yield to benzyl-aniline (%)
			Benzyl-aniline	*N*-Benzyliden-aniline	
1st (Fresh)	$[MePh_3P]Br$	98	98	2	96
2nd	$[MePh_3P]Br$	97	97	3	94
3rd	$[MePh_3P]Br$	95	96	7	91
4th	$[MePh_3P]Br$	91	92	8	84
5th*	$[MePh_3P]Br$	82	68	32	56
Fresh	$[Bmim]BF_4$	<5	--	--	--
Fresh	$[Bmim]PF_6$	<5	--	--	--

[a] $[Ir(COD)Cl]_2$ 0.025 mmol (Ir 1 mol %), **L2** 0.05 mmol, $[MePh_3P]Br$ 5.6 mmol (2.0 g), aniline 5.0 mmol, benzyl alcohol 6.0 mmol, KO(*t*-Bu) 3.5 mmol, 4 h, 120 °C; [b] Determined by GC; * Ir-black precipitated upon reaction.

The generality of $[Ir(COD)Cl]_2$ with the involvement of **L1** for the *N*-alkylation of amines with several kinds of alcohols was examined in Table 4. It was found that the quite narrow scope of substrates was suitable for this reaction. Only aniline derivatives and benzyl alcohol derivatives could be applied to perform the corresponding *N*-alkylation. The similar phenomenon had been found in many examples [4, 11 and 25]. The electronic substituent groups such as $-OCH_3$, $-CH_3$, and -Cl at the *para*-position of benzyl alcohol barely influenced the yields of amine products (Entries 1-3). 2-Pyridinemethanol with the electron-with drawing group of pyridyl reacted efficiently with aniline to afford the desired product in 98% yield (Entry 4). Under the similar reaction conditions, Aniline derivatives with *p*-MeO, *p*-Me, and *p*-Cl substituents successfully reacted with benzyl alcohol to afford *N*-benzylated products in high yields without discrimination to the electronic-effect (Entries 5-7). However, the alkylation of phenethylamine with benzyl alcohol resulted in the formation of the imine [(*E*)-N-

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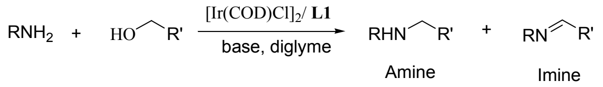
DOI: 10.1039/C6GC03096C

benzylidene(phenyl)methanamine] in 89% yield, indicating that the increased basicity of the imine without the super-conjugated structure badly depressed its subsequent hydrogenation to the targeted amine product (Entry 8).

Conclusions

While one -Ph group in PPh_3 was substituted by imidazolyl and imidazolium respectively, the resultant mono-phosphines of **L1** and **L2** were developed with the obviously enhanced π-acceptor character. For comparison, the corresponding diphosphines of **L3** with the similar π-acceptor character to **L1** ($^{1}J_{^{31}P\text{-}^{77}Se}$ ~ 750 Hz) and **L4** with the similar π-acceptor character to **L2** ($^{1}J_{^{31}P\text{-}^{77}Se}$ ~ 780 Hz) were prepared in parallel. It was found that the π-acceptor character of the applied phosphines co-related to the catalytic performance of $[Ir(COD)Cl]_2$ for *N*-alkylation. Compared to PPh_3 with the poor π-acceptor character ($^{1}J_{^{31}P\text{-}^{77}Se}$ =729 Hz), **L1-L4** all corresponded to the efficient *N*-alkylation of aniline to benzyl-aniline. While **L1-L4** as the π-acceptor phosphines were coordinated to Ir-center, the resultant consolidated Ir-P linkages due to π-backdonation could well protect the Ir-catalyst against deactivation, giving rise to the catalytic efficiency for *N*-alkylation of benzyl alcohol with aniline. On the other hand, the stabilized Ir-catalyst with the involvement of **L2** could be recycled successfully at least 4 runs in the IL of $[MePh_3P]Br$ without the detectable leaching of Ir and P elements in the organic products. The generality of $[Ir(COD)Cl]_2$-**L1** catalytic system was not improved herein. Only the narrow scope of the substrates such as aniline derivatives and benzyl alcohol derivatives was applicable for this type of *N*-alkylation.

Table 4 *N*-Alkylation of amines with alcohol catalyzed by $[Ir(COD)Cl]_2$ with the involvement of **L1**[a]



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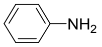
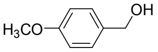
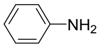
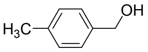
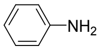
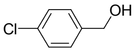
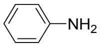
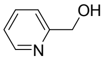
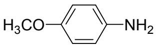
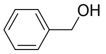
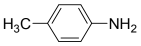
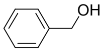
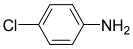
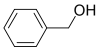
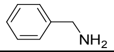
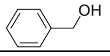
Entry	RNH₂	ROH	Time (h)	Conv. (%)[b]	Yield (%)[b]	
					Amine	Imine
1			4	95	87	8
2			4	99	90	9
3			4	100	89	11
4			4	100	98	2
5			6	100	77	23
6			6	100	92	8
7			6	100	89	11
8			6	99	10	89

[a] $[Ir(COD)Cl]_2$ 0.025 mmol (Ir 1 mol %), **L1** 0.05 mmol, aniline 5.0 mmol, alcohol 7.5, mmol, KO(*t*-Bu) 3.5 mmol, diglyme 2 mL, 120 °C; [b] Determined by GC.

Experimental

Reagents and analysis

All the reagents used in this work were purchased from Shanghai Aladdin Chemical Reagent Co. Ltd. and Acros China, and used as received. THF was purified by refluxing, and distilling from sodium which removes water, peroxides, inhibitors and other impurities. Dichloromethane was dried by CaH_2 and DMSO by anhydrous sodium sulphate. The ^{1}H and ^{31}P NMR spectra were recorded on a Bruker Avance 500 spectrometer. The ^{31}P NMR spectra were referenced to 85% H_3PO_4 sealed in a capillary tube as an internal standard. CHN-elemental analysis was performed on a Vario EL III Element Analyzer. Gas chromatography (GC) was performed on a SHIMADZU-2014 equipped with a DM-Wax capillary column (30 m × 0.25 mm × 0.25 μm).

Synthesis

L1-L4 were prepared according to the procedures reported by our group previously [19,20].

Complex Ir-L1

Under nitrogen atmosphere, a solution of $[Ir(COD)Cl]_2$ [dimer of dichloro(1,5-cyclooctadiene)iridium(I), 33.6 mg, 0.05 mmol] in dry CH_2Cl_2 (5 mL) was stirred vigorously at room temperature for ca. 10 min, and then the atmospheric CO (in a balloon) was introduced into the reaction mixture for 50 min. The obtained mixture was treated with a solution of L1 (32.8 mg, 0.1 mmol) in acetonitrile (5 mL) and stirred vigorously for

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5 h. Then diethyl ether was added to afford the yellow precipitates, which were collected after dryness under vacuum with the yield of 90 % (41.4 mg). ^{1}H NMR (500 MHz, δ, ppm, CD_3Cl_3): 7.71-7.75 (m, 8H, H_{Ph}), 7.40-7.43 (m, 4H, H_{imi}), 7.34-7.37 (m, 10H, H_{Ph}), 7.02-7.18 (m, 8H, H_{Ph}), 6.91-6.94 (m, 4H, H_{Ph}). ^{31}P NMR (202.4 MHz, δ, ppm, CD_3Cl_3): 12.06 (s, PPh_2). When the sample of **Ir-L1** was dissolved in co-solvent of dichloromethane/diethyl ether to grow crystals for several days, the obtained complex was found to be **Ir-L1A** upon the single crystal X-ray diffraction analysis, in which Ir-center was in +2 valence state which was coordinated by two Cl^- and two **L1**. Consistently, the ^{31}P NMR spectrum of **Ir-L1A** crystal was broadened to flatness due to the paramagnetic nature of Ir(II)-center.

Complex Ir-L2

Under nitrogen atmosphere, a solution of $[Ir(cod)Cl]_2$ (33.6 mg, 0.05 mmol) in dry CH_2Cl_2 (2 mL) was stirred vigorously at room temperature for 10 min. Then the atmospheric CO (in a balloon) was introduced into the reaction mixture for 50 min. Afterwards, the reaction mixture was treated with a solution of **L2** (49.2 mg, 0.1 mmol) in dry CH_2Cl_2 (3 mL). The resultant mixture was stirred for another 3.5 h and then n-hexane was added to precipitate the yellow solids. The yellow solids were collected after dryness under vacuum with the yield of 89 % (55.2 mg). The sample suitable for single crystal X-ray diffraction analysis was obtained by slow volatilization from acetonitrile. ^{1}H NMR (500 MHz, δ, ppm, CD_3OD): 8.08 (s, 2H, H_{imi}), 7.94-7.98 (m, 10H, H_{Ph}), 7.61-7.64 (m, 4H, H_{Ph}), 7.61-7.64 (m, 4H, H_{Ph}), 7.52-7.55 (m, 8H, H_{Ph}), 7.39-7.42 (s, 2H, H_{imi}), 7.35-7.37 (m, 4H, H_{Ph}), 7.22-7.26 (m, 4H, H_{Ph}), 3.32-3.34 (m, 6H, NCH_3). ^{31}P NMR (202.4 MHz, δ, ppm, CD_3OD): 27.73 (s, PPh_2).

Ir-L3 and **Ir-L4** were prepared according to the procedures reported by our group previously [20].

X-ray Crystallography

Intensity data were collected at 296 K for **Ir-L1A** and **Ir-L2** on a Bruker SMARTAPEX II diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data reduction included absorption corrections by the multi-scan method. The structures were solved by direct methods and refined by full matrix least-squares using SHELXS-97 (Sheldrick, 1990), with all non-hydrogen atoms refined anisotropically. Hydrogen atoms were added at their geometrically ideal positions and refined isotropically. The crystal data and refinement details are given in Table 5.

General procedures for *N*-alkylation of amines with alcohols

All reactions were carried out under nitrogen atmosphere by using mercury-free vacuum Schlenk line techniques. In a heavy-walled safe glass reactor charged with atmospheric N_2 were added diglyme (2.0 mL), $[Ir(COD)Cl]_2$ (0.025 mmol, 1.0 mol % Ir), the ligand (0.05 mmol), KO(*t*-Bu) (3.5 mmol), aniline (5.0 mmol), and benzyl alcohol (7.5 mmol) in sequential. The obtained mixture was stirred at 120 °C for 2~6 h in the sealed reactor. Upon completion, the reaction solution was analyzed by GC to determine the conversions (*n*-dodecane as internal standard) and the selectivities (normalization method). The retention time for the products of benzyl-aniline (amine) and N-benzylideneaniline (imine) in GC analysis were calibrated by the authentic samples which were commercially available. The temperature-programmed analysis for the samples was performed on GC-SHIMADZU-2014 with a flame ionization detector (FID). The analysis conditions were as follows: Injector temperature, 250 °C; Detector temperature, 250 °C; Initial oven temperature at 60 °C with retention time of 2 min and then rising up to 240 °C with a temperature ramp of 5 °C min^{-1}; Final oven temperature 240 °C with retention time of 25 min.

As for the recycling experiments, in a heavy-walled safe glass reactor charged with atmospheric N_2 were added $[Ph_3MeP]Br$ (5.3 mmol), $[Ir(COD)Cl]_2$ (0.025 mmol, 1.0 mol % Ir), **L2** (0.05 mmol), KO(*t*-Bu) (3.5 mmol), aniline (5.0 mmol), and benzyl alcohol (6.0 mmol) in sequential. The mixture was stirred at 120 °C for 4 h in the sealed reactor. Upon completion, the reaction solution was added with methanol (1.0 mL) and *n*-hexane (18 mL). Then the upper organic phase was decanted from the obtained biphasic reaction mixture, and the remaining IL phase was washed with *n*-hexane (3 mL × 3) to completely extract the reactants and products. The combined organic phase was analyzed by GC and ICP-AES. The IL residue after the removal of methanol under vacuum was reused for the next run.

Table 5 The crystal data and structure refinement for **Ir-L1A** and **Ir-L2**

	Ir-L1A	**Ir-L2**·2(CH_2Cl_2)
Empirical formula	$C_{42}H_{34}Cl_2Ir_1N_4P_2$	$C_{49}H_{44}Cl_5Ir_1N_4O_1P_2$ $\cdot 2(CF_3SO_3)\cdot 2(CH_2Cl_2)$
Formula weight	919.77	1410.39
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/n$	P-1
a (Å)	9.0997(3)	12.17337(7)
b (Å)	15.2322(5)	12.9667(7)
c (Å)	13.1977(5)	19.5210(11)
α (°)	90	93.601(2)
β (°)	93.1090(10)	96.085(2)
γ (°)	90	111.847(2)
V (Å^3)	1826.62(11)	2826.4 (3)
Z	2	2
d_{calc} (g cm^{-3})	1.672	1.657
μ (Mo-K$_\alpha$) (mm^{-1})	3.926	2.801
T (K)	296(2)	296(2)
λ (A)	0.71073	0.71073
Total reflections	20971	32873
Unique reflections (R_{int})	3209 (0.0233)	9892(0.0576)
R_1 [I>2σ(I)]	0.0222	0.0582
wR_2 (all data)	0.0522	0.1798
F(000)	910	1400
Goodness-of-fit on F^2	1.089	1.018

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Acknowledgements

This work was financially supported by the National Natural Science Foundation of China (Nos. 21673077, 21473058, and 21273077).

Notes and references

1 M. B. Smith and J. March, *Advanced Organic Chemistry, Wiley, New York*, 2001, **5**, 499.
2 R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit and N. Tongpenyai, *J. Chem. Soc. Chem. Commun.,* 1981, 611.
3 Y. Watanabe, Y. Tsuji, H. Ige, Y. Ohsugi and T. Ohta, *J. Org. Chem.,* 1984, **49**, 3359.
4 J. Li and P. G. Andersson, *Chem. Commun.*, 2013, **49**, 6131.
5 S. Imm, S. Bähn, L. Neubert, H. Neumann and M. Beller, *Angew. Chem. Int. Ed.*, 2010, **49**, 8126.
6 For reviews, see: (a) T. D. Nixon, M. K. Whittlesey and J. M. J. Williams, *Dalton Trans*., 2009, **5**, 753; (b) G. E. Dobereiner and R. H. Crabtree, *Chem. Rev.*, 2010, **110**, 681; (c) G. Guillena, D. J. Ramón and M. Yus, *Chem. Rev.*, 2010, **110**, 1611; (d) S. Bähn, S. Imm, L. Neubert, M. Zhang, H. Neumann and M. Beller, *ChemCatChem*, 2011, **3**, 1853.
7 (a) G. Guillena, D. J. Ramón and M. Yus, *Angew. Chem., Int. Ed.*, 2007, **46**, 2358; (b) S. Ruch, T. Irrgang and R. Kempe, *Chem. Eur. J.*, 2014, **20**, 1; (c) K-i. Fujita, Y Enoki, R Yamaguchi, *Tetrahedron*, 2008, **64**, 1943.
8 S. Agrawal, M. Lenormand and B. Martín-Matute, *Org. Lett.*, 2012, **14**, 1456.
9 (a)D. Balcells, A. Nova, E. Colt, D. Gnanamgari, R. H. Crabtree and O. Eisenstein, *Organometallics*, 2008, **27**, 2529; (b) P. Fristrap, M. Tursky and R. Madsen, *Org. Biomol. Chem.*, 2012, **10**, 2569.
10 Carbene: Q. Zou, C. Wang, J. Smith, D. Xue and J. Xiao, *Chem. Eur. J.* 2015, **21**, 9656.
11 Phosphaalkene: (a) Y. Chang, I. Tanigawa, H.-O. Taguchi, K. Takeuchi and F. Ozawa, *Eur. J. Inorg. Chem.*, 2016, **5**, 754; (b) Y. Chang, Y. Nakajima and F. Ozawa, *Organometallics,* 2013, **32**, 2210.
12 P,N-hemilabile ligand: (a) B. Blank, S. Michlik and R. Kempe, *Adv. Synth. Catal.*, 2009, **351**, 2903; (b) S. Michlik and R. Kempe, *Chem. Eur. J.*, 2010, **16**, 13193.
13 $[Cp^*Ir^{III}X_2]_2$ as precursor for *N*-alkylation of amines: (a) K.-i. Fujita, K. Yamamoto and R. Yamaguchi, *Org. Lett.*, 2002, **4**, 2691; (b) R. Kawahara, K.-i. Fujita and R. Yamaguchi, *J. Am. Chem. Soc.*, 2010, **132**, 15108; (c) R. Kawahara, K-i Fujita and R. Yamaguchi, *Adv. Synth. Catal.*, 2011, **353**, 1161; (d) M. Zhu, K.-i. Fujita and R. Yamaguchi, *Org. Lett.*, 2010, **12**, 1336; (e) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden and J. M. J. Williams, *Chem. Commun.,* 2010, **46**, 1541; (f) S. Agrawal, M. Lenormand and B. Martín-Matute, *Org. Lett.*, 2012, **14**, 1456; (g) C. Xu, L. Y. Goh and S. A. Pullarkat, *Organometallics*, 2011, **30**, 6499.
14 (a) N. Sakai, S. Mano, K. Nozaki and H. Takaya, *J. Am. Chem. Soc*., 1993, **115**, 7033; (b) Y. Yan, Y. Chi and X. Zhang, *Tetrahedron: Asymmetry.*, 2004, **15**, 2173.
15 (a) Y. Canac, N. Debono, L. Vendier and R. Chauvin, *Inorg. Chem.*, 2009, **48**, 5562; (b) H. Tricas, O. Diebolt and P. W. N. M. van Leeuwen, *J. Catal.*, 2013 **298**, 198.
16 P. W. N. M. van Leeuwen and J. M. Chadwick, *Homogeneous Catalysts: Activity-Stability- Deactivation, Wiley VCH, Weinheim*, 2012, **1**, 1.
17 (a) C. L. Pollock, G. C. Saunders, E. C. M. S. Smyth and V. I. Sorokin, *J. Fluor. Chem.*, 2008, **129**, 142; (b) M. L. Clarke, D. Ellis, K. L. Mason, A. G. Orpen, P. G. Pringle, R. L. Wingad, D. A. Zaher and R. T. Baker, *Dalton Trans.*, 2005, **7**, 1294; (c) S. Jeulin, S. D. D. Paule, V. Ratovelomanana-Vidal., J. P. Genêt, N. Champion and P. Dellis, *Angew. Chem., Int. Ed.*, 2004, **43**, 320.
18 (a) C. Huo and T. H. Chan, *Chem. Soc. Rev.*, 2010, **39**, 2977; (b) B. Ni and A. D. Headley, *Chem. Eur. J.*, 2010, **16**, 4426; (c) R. Šebesta, I. Kmentová and Š. Toma, Green Chem., 2008, **10**, 484; (d) W. Miao and T. H. Chan, *Acc. Chem. Res.*, 2006, **39**, 897; (e) J. Zhang, Y. Wang, X. Zhao and Y. Liu, *Eur. J. Inorg. Chem.*, 2014, **6,** 975; (f) H. You, Y. Wang, X. Zhao, S. Chen and Y. Liu, *Organometallics,* 2013, **32**, 2698; (g) S. Chen, Y. Wang, W. Yao, X. Zhao, G. VO-Thanh and Y. Liu, *J. Mol. Catal. A: Chem.*, 2013, **378**, 293.
19 Y. Li, P. Wang, H. Zhang, X. Zhao, Y. Lu, Z. Popović and Y. Liu, *J. Mol. Catal. A: Chem.*, 2015, **402,** 37.
20 H. Zhang, Y. Li, P. Wang, Y. Lu, X. Zhao and Y. Liu, *J. Mol. Catal. A: Chem.*, 2016, **411**, 337.
21 D. W. Allen and B. F. Taylor, *Dalton Trans*., 1982, 51.
22 A. Suárez, M. A. Méndez-Rojas and A. Pizzano, *Organometallics*, 2002, **21**, 4611.
23 B. Milde, D. Schaarschmidt, T. Rüffer and H. Lang, *Dalton Trans*., 2012, **41,** 5377.
24 M. R. Churchill, J. C. Fettinger, L. A. Buttrey, M. D. Barkan and J. S. Thompson *Organometallics,* 1988, **340**, 257.
25 (a) A. Bartoszewicz, R. Marcos, S. Sahoo, A. K. Inge, X. Zou and B. Martín-Matute, *Chem. Eur. J.*, 2012, **18**, 14510; (b) D. Wang, K. Zhao, C. Xu, H. Miao and Y. Ding, *ACS Catal.*, 2014, **4**, 3910.

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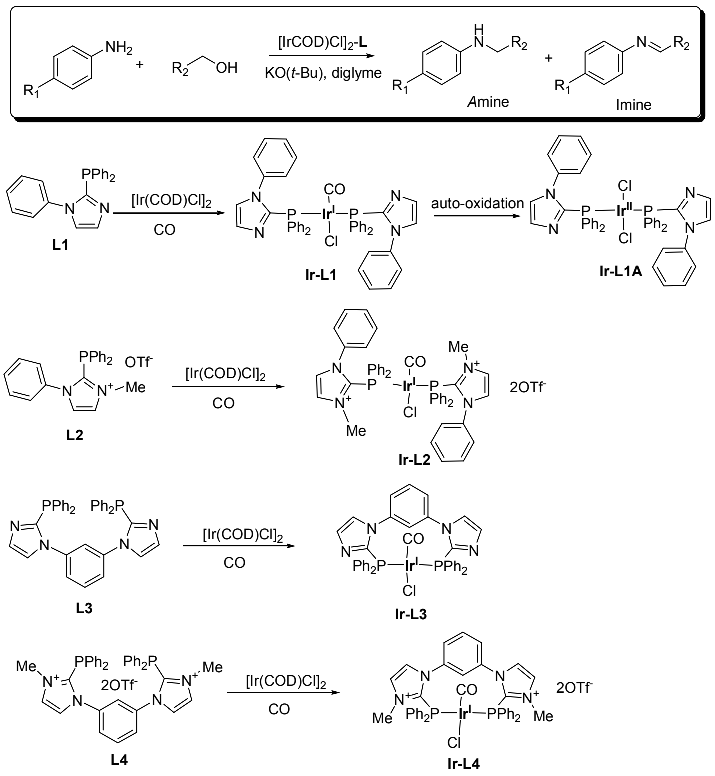
Graphical abstract



Efficient and recyclable Ir-catalyst with involvement of ionic π-acceptor phosphine in ionic liquid solvent for *N*-alkylation of amines with alcohols