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Iridium phosphine abnormal N-heterocyclic carbene complexes in catalytic hydrogen transfer reactions

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ABSTRACT

Several iridium complexes bearing chelating abnormal N-heterocyclic carbenes (NHCs) are shown to be active catalysts for transfer hydrogenation of ketones or enones, dehydrative C–C coupling between primary and secondary alcohols, and dehydrogenation of benzyl alcohol to benzyl benzoate. In the transfer hydrogenation of acetophenone, abnormal NHC complexes give higher activity than a normal analogue. Dehydrative C–C coupling reactions between primary and secondary alcohols result in β-alkylation of the secondary alcohols, using primary alcohols as the apparent alkylating reagents, and such reactions proceed with high yield and selectivity. These catalytic processes are known to involve metal-mediated temporary borrowing of hydrogen from alcohols and subsequent delivery of the hydrogen to C=C and /or C=O bonds.

In the past decade neutral carbon-centred ligands, especially N-heterocylic carbenes (NHCs), have found wide applications in organometallic chemistry and are actively competing with phosphine ligands.[1–3] As common and representative carbon-centred ligands, NHCs (typically imidazole-2-ylidenes) hold strong σ-donating but weak π-accepting characters, and they become highly popular in catalysis owing to their ability to stabilize transition metals in both high and low oxidation states and their labilizing effects to facilitate the rate-limiting steps.[4] NHC complexes have shown advantages in homogeneous catalysis, such as C–C coupling,[5] olefin metathesis reactions,[6] hydrogenation,[7] and hydroamination reactions.[8]

Imidazole-based 'abnormal' NHCs, first discovered by Crabtree and co-workers in the cycolmetalation of iridium(III) complexes,[9] are zwitterionic ligands obtained from the metalation of imidazoliums at the C4/5 position (Scheme 1). This relatively less common binding mode has been further extended to the complexes of other transition metals in both monodentate and chelation settings.[10,11] Furthermore, other non-conventional N-heterocyclic carbenes that are derived from pyridines, quinolines and pyrazolines have also been reported and reviewed.[10] Significantly, Bertrand and co-workers have described a strategy of isolating the first free abnormal carbene that is stable at room temperature.[12] Thus facile and controllable preparation of abnormal carbenes and their complexes should offer new opportunities in catalysis, by allowing access to a plethora of new highly active metal complexes.[13] Both experimental and theoretical data suggested that abnormal NHCs are even stronger electron-donor ligands than the normal ones.[14,15] Our recent work demonstrated that besides being strong σ-donors, abnormal NHCs can be strong π-acceptors, and the electronic effects of annulated abnormal NHCs can be even readily tuned by remote modification or by annulation.[15] This unique electronic effect could be partially responsible for the higher catalytic activity of abnormal NHC complexes of Pd, Rh, and Ru than the corresponding normal NHC analogues in catalytic transformations involving C–C coupling[16] and hydrogen transfer reactions via metal hydride intermediates (hydrogen-borrowing processes).[17,18]

To date most literature reports of abnormal NHC complexes have focused on their synthetic aspects, structures, and electronic effects. Catalytic applications of these complexes are still limited.[10,16–18] We now report that iridium abnormal NHC complexes can catalyse a series of reactions that feature hydrogen transfer, including transfer hydrogenation of ketones, dehydrative C–C coupling between primary and secondary alcohols, and dehydrogenation of benzyl alcohol.

We[19] and others[20] recently demonstrated the synthesis of a series of iridium(III) abnormal NHC hydride complexes (**1** and **2**) via highly selective oxidative addition of the C4/5-H bonds of phosphine-tethered imidazolium ions, which can be further converted to the corresponding Ir(I) complex (**3**) by base-promoted reductive

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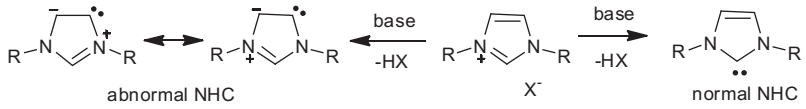


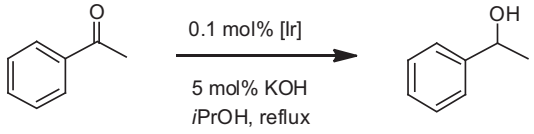
Scheme 1. Imidazole-based normal and abnormal NHCs.

elimination (Scheme 2). In comparison, normal NHC complex **4**[8a,19a] was obtainable from the reaction of the phosphine-tethered imidazolium ion and $[Ir(COD)(\mu\text{-O}t\text{Bu})]_2$ (Scheme 2).

Iridium complexes of normal imidazole[21] and pyridine-based NHCs[22] in chelation settings are known to be active catalysts for transfer hydrogenation reactions. It is important to compare the catalytic activity of iridium normal and abnormal carbene complexes. The reduction of acetophenone by *i*PrOH was used to screen the catalytic activity of complexes **1**–**4** in 0.1 mol % loading in the presence of a catalytic amount of KOH (Table 1). In all cases, the transfer hydrogenation proceeded smoothly and similar activities were obtained for complexes **1**, **2**, and **3**. The fact that complexes **1** and **3** gave essentially the same result likely suggests that the Ir(-III) hydride complex enters the catalytic cycle in the form of Ir(I) abnormal NHC since base-promoted reductive elimination of HCl is instantaneous and quantitative (Scheme 2). The steric bulk of the N-alkyl group has no significant effect, while the coordination mode of the carbene does in that normal carbene complex **4** gives only 26% yield in 5 h and 28% yield even after 12 h (Table 1, entries 4 and 5). We noted that higher catalytic activity of abnormal NHC complexes than the normal counterparts has been reported in some systems.[16–18]

Under the same conditions, other methyl aryl ketones containing electron-withdrawing or electron-donating groups could also be reduced to the corresponding alcohols in high isolated yield (79–95%) using complex **2** as a catalyst (Table 2, entries 1–10). The scope of the ketone substrate was further extended to α,β-unsaturated ketones and aldehydes, where chemoselectivity can be an issue.[23] Both C=C and C=O double bonds of enones are reduced with high yield and selectivity (Table 2, entries 13–18). It is obviously possible that transfer hydrogenation of enones could occur first to C=C then to C=O group. To further test whether the other stepwise sequence is possible, we then examined *trans*-PhCH=CHC(OH)Me, which can be cleanly hydrogenated under the same conditions (Table 2, entry 12). These results suggest that

Table 1
Screening of iridium catalysts[a]

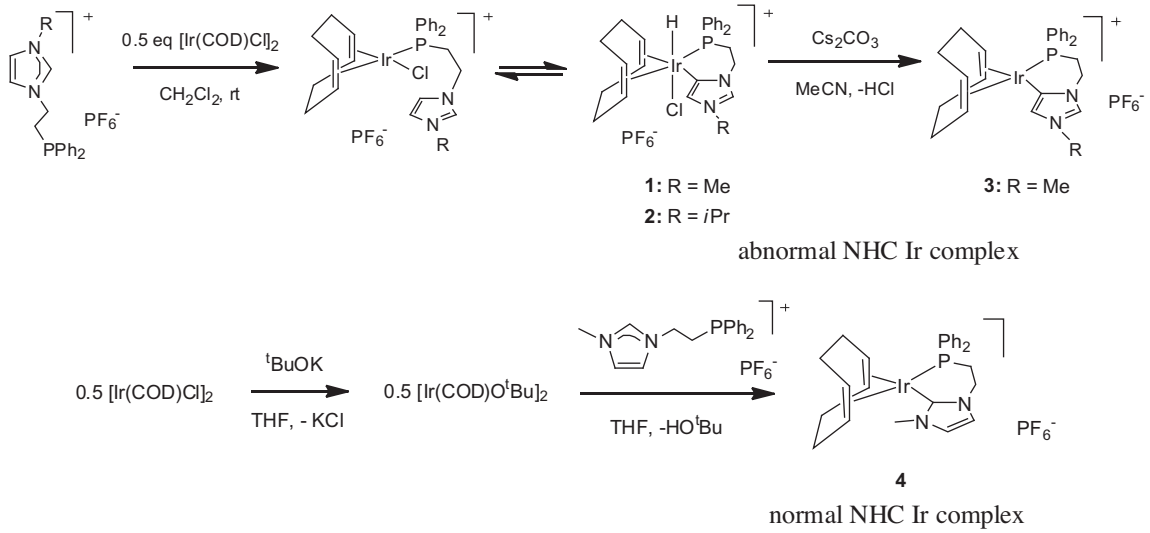


Entry	Catalyst	Time (h)	Yield[b] (%)
1	**1**	5	92
2	**2**	5	95(90[c])
3	**3**	5	94
4	**4**	5	26
5	**4**	12	28

[a] Reaction condition: acetophenone (1.0 mmol), KOH (0.05 mmol), and catalyst (0.001 mmol), *i*PrOH (3 mL), under nitrogen.
[b] NMR yield using 1,3,5-trimethoxybenzene as an internal standard.
[c] Isolated yield.

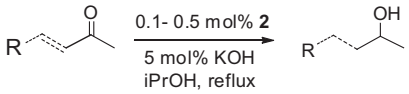
transfer hydrogenation here can follow either stepwise sequence. For cinnamaldehyde, only 61% 3-phenylpropan-1-ol was isolated although only one product was observed from crude ^{1}H NMR (Table 3, entry 14).

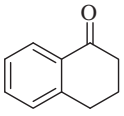
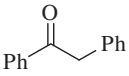
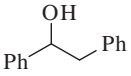
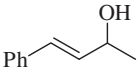
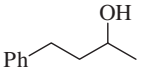
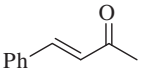
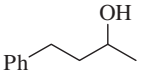
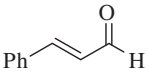
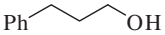
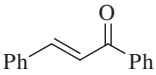
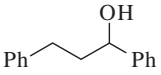
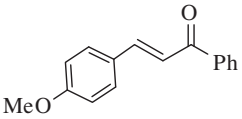
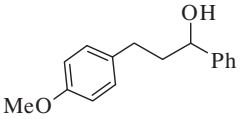
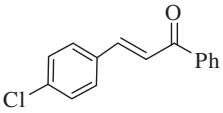
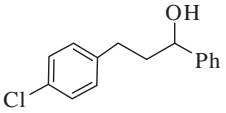
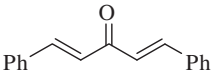
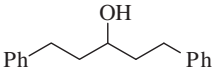
We further focused on the β-alkylation of secondary alcohols using primary alcohols (Table 3).[24] This catalytic reaction represents an environmentally friendly process for the synthesis of alcohols, and Ru[18,25,26] and Ir[23a] complexes have been reported for this transformation. This reaction is believed to involve transfer of hydrogen from both alcohols to the catalyst to give metal hydride species, a ketone, and an aldehyde. The latter two undergo aldol condensation, yielding an enone. The metal hydride intermediates further deliver hydrogen to the C=C and C=O bonds of the enone intermediate to eventually give the alcohol product.[23a] Since our iridium abnormal NHC complexes have been proved to be highly active catalyst for transfer hydrogenation of α,β-unsaturated



Scheme 2. Synthesis of iridium abnormal and normal N-heterocyclic carbenes.[19]

Table 2
Transfer hydrogenation of acetophenones and enones [a]



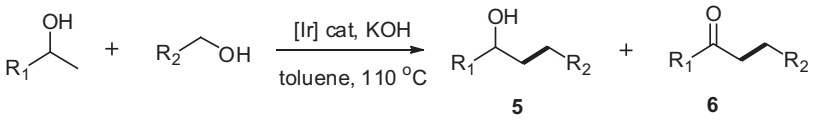
Entry	Substrates	Time	Product	Yield[b]
				
1	Ar = Ph	5		90
2	4-$MeOC_6H_4$	10		78
3	4-MeC_6H_4	6		91
4	4-FC_6H_4	4		95
5	4-ClC_6H_4	4		88
6	4-BrC_6H_4	3		97
7	3-BrC_6H_4	4		94
8	2-Napthyl	3		92
9	1-Napthyl	3		90
10		6		79
11		6		81
12		4		87
13		4		98
14		6		61
15		4		97
16		4		88
17		2		94
18		2		93

[a] Reaction conditions: 1 mmol of ketone, KOH (0.05 mmol), 0.1 mol % of catalyst **2** for entries 1–10 and 0.5 mol % of **2** for entries 11–19, *i*PrOH (3 mL).
[b] Isolated yield.

ketone, we reason that they should catalyse this C–C coupling reaction via this 'hydrogen-borrowing' mechanism.

The benzylation of 1-phenylethanol and benzyl alcohol was carried out in equimolar ratio. Complex **2** (1 mol %) was used as a catalyst in the presence of KOH (1 equiv) in toluene (110 °C, 2 h), leading to excellent activity and high selectivity in that the alcohol product was isolated in 92% yield without any ketone by-product (Table 3, entry 1). The more dosage of base (2 equiv KOH) has no significant effect on selectivity (entry 2), while prolonging reaction time (10 h) led to a small amount of ketone (entry 3), which indicates that the alcohol product may be further dehydrogenated under the catalytic conditions even without any sacrificial hydrogen acceptor. In this case, appropriate reaction time seems a key factor in controlling the selectivity. Furthermore, normal NHC Ir complex **4** showed less activity (88% yield) and selectivity (the ratio of **5** and **6** is 91: 9, entry 4) in the transformation. The coupling reactions between various secondary and primary alcohols are summarized (Table 3, entries 5–15). The coupling between simple benzyl alcohol and different 1-arylethanols bearing either electron-withdrawing or electron-donating groups gave the corresponding products in high yields. The reaction of 1-phenylethanol and primary aliphatic alcohols, such as 1-butanol or 2-phenylethanol, could also give the β-alkylated products. For most of the reactions, this process is very selective in the production of the alkylated alcohols,

Table 3
β-Alkylation of secondary alcohols using primary alcohols catalyzed by **2**[a]

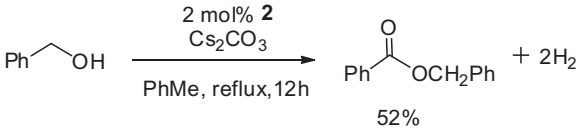


Entry	R_1	R_2	Time (h)	5:6 [b]	5[c] (%)
1	Ph	Ph	2	100:0	92
2[e]	Ph	Ph	2	100:0	94[d]
3	Ph	Ph	10	93:7	91[d]
4[f]	Ph	Ph	2	91:9	88[d]
5	4-$MeOC_6H_4$	Ph	1.5	87:13	61
6	4-MeC_6H_4	Ph	2	92:8	73
7	4-FC_6H_4	Ph	2	94:6	90
8	4-ClC_6H_4	Ph	1	96:4	81
9	4-BrC_6H_4	Ph	1.5	98:2	90
10	4-$CF_3C_6H_4$	Ph	2	93:7	84
11	3-BrC_6H_4	Ph	2	81:19	74
12	2-Naphthyl	Ph	1	95:5	84
13	1-Naphthyl	Ph	1	90:10	83
14	Ph	$PhCH_2$	1	88:12	68
15	Ph	*n*-Hexyl	2	85:15	61

[a] Reaction conditions: primary alcohols (2 mmol), secondary alcohols (2 mmol), KOH (2 mmol), catalyst **2** (0.02 mmol, 1 mol %) and toluene (1 mL), under nitrogen, 110 °C.
[b] Determined by ^1H NMR based on crude product.
[c] Isolated yield.
[d] NMR yield using 1,3,5-trimethoxybenzene as a standard.
[e] Two equivalents of KOH based on alcohol was used.
[f] Normal NHC complex **4** (1 mol %) as catalyst.

although in some cases a small amount of the corresponding ketones were obtained as by-products.

The presence of a small amount of ketone byproduct in the reactions given in Table 3 indicates that **2** might be applied as a dehydrogenation catalyst. Catalytic acceptorless dehydrogenation of alcohols has been reported,[24b,27,28] and primary alcohols can be dehydrogenated to esters with the release of two molecular hydrogens (Eq. 1).[27] We thus applied **2** as a catalyst for the dehydrogenation of benzyl alcohol. In all our experiments, essentially no benzaldehyde was obtained on the basis of ^1H NMR analysis. Benzyl benzoate was obtained as the major product together with dibenzyl ether. The formation of the latter is probably due to the Lewis acidic nature of complex **2**. Attempts to inhibit the formation of the dibenzyl ethyl by addition of water (1 equiv) failed to give any improved yield of benzyl benzoate. The best results were obtained using Cs_2CO_3 as a base and **2** (2 mol %) as a catalyst (toluene, reflux, 48 h), where the conversion is 87%, and the yield of benzyl benzoate and dibenzyl ether is 52% and 27%, respectively. Further improvement is necessary for this reaction, and neutral Ir(I) or Ir(III) catalysts with low Lewis acidity but high thermal stability are desirable.



(1)

In summary, several iridium complexes bearing chelating abnormal N-heterocyclic carbenes (NHCs) have been synthesized from the cyclometalation of phosphine-tethered imidazolium ions, and they are shown to be active catalysts for transfer hydrogenation of ketones or enones, dehydrative C–C coupling between primary and secondary alcohols, and dehydrogenation of benzyl alcohol. In the transfer hydrogenation of acetophenone, abnormal NHC complexes give higher activity than a normal analogue. Dehydrative C–C coupling reactions between primary and secondary alcohols result in β-alkylation of the secondary alcohols, using primary alcohols as the formal alkylating reagents, and such reactions proceed with high yield and selectivity. These catalytic processes are known to involve metal-mediated temporary borrowing of hydrogen from alcohols and subsequent delivery of the hydrogen to C=C and /or C=O bonds. For the acceptorless dehydrogenation of benzyl alcohol to benzyl benzoate, moderate yield and selectivity were obtained. Our results have confirmed that abnormal NHC complexes can be excellent choices in the design of active catalysts. Preparation of other non-conventional NHC complexes is in progress in our laboratory.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.08.058.

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