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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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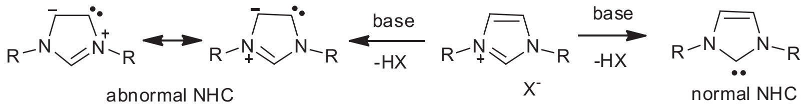


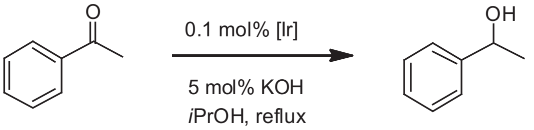
Scheme 1. Imidazole-based normal and abnormal NHCs.

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

Table 1
Screening of iridium catalysts[a]



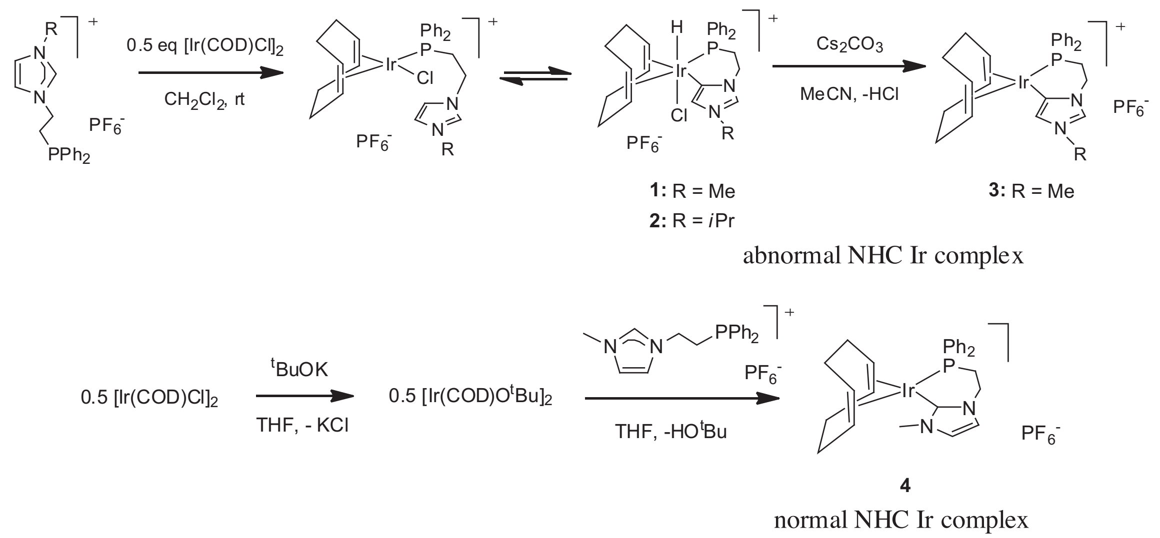
Entry	Catalyst	Time (h)	Yield[b] (%)
1	**1**	5	92
2	**2**	5	95(90[c])
3	**3**	5	94
4	**4**	5	26
5	**4**	12	28

[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.

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]