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## Iridium(III) Homo- and Heterogeneous Catalysed Hydrogen Borrowing C-N Bond Formation

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Pentamethylcyclodienyl iridium(III) complexes of bidentate carbene-triazole ligands were found to be excellent homogeneous catalysts for the hydrogen borrowing mediated coupling of alcohols with amines. The reactions are highly efficient, able to reach completion in under 6 h at 100 °C at low catalyst loadings of 0.5 mol%, and are environmentally benign, the only by-product is water. The Ir(III) catalysts promoted C-N bond formation across a range of alcohol and amine substrates, including biologically relevant motifs. Covalent attachment to a carbon black surface generated a well-defined "hybrid" heterogeneous catalyst which gave good conversion to products in the coupling reaction of aniline with benzyl alcohol, and could be recycled with no catalyst leeching. This represents the first report of a covalently linked heterogeneous iridium catalyst on carbon used for hydrogen borrowing. Turnover numbers (TON) for the heterogeneous were found to be significantly higher than the corresponding homogeneous reaction. To elucidate the homogeneous reaction mechanism, <sup>1</sup>H NMR studies inconjuction with deuteration experiments allowed a mechanism to be postulated.

## 1. Introduction

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Alkylated amines play an important role as intermediate building blocks in many organic synthesis reactions and as final products employed in pharmaceuticals, agrochemicals, fragrances, dyes, and other fine chemicals.<sup>1-3</sup> Numerous multistep bench-top reactions are available to synthesise Nsubstituted alkylamines, which include reactions of amines with alkyl halides,<sup>4-6</sup> electrophilic amination<sup>7-8</sup> and reductive alkylation routes.<sup>9-10</sup> However, these reactions tend to suffer from additional side reactions, tedious work-up, use of toxic reagents, and the formation of stoichiometric amounts of waste.<sup>11-12</sup> The alternative synthetic pathway of reacting alcohols with amines through "hydrogen borrowing" provides a promising route to create a more sustainable carbonnitrogen bond formation reaction.<sup>1, 13-20</sup> Inexpensive alcohols are widely available and as water is the sole by-product of this reaction, the ability to react amines with alcohols makes it an atom-economical and environmentally friendly synthetic method.21

Hydrogen borrowing facilitates C-N bond formation by using a catalyst to abstract or "borrow" hydrogen from the alcohol substrate, thereby oxidising the alcohol to form a more reactive carbonyl group, see Scheme 1.<sup>17</sup> This circumvents the

The carbonyl group, typically an aldehyde, then undergoes condensation with an amine to form an imine intermediate; this step yields water as the sole by-product. Hydrogenation of the imine intermediate by the metal hydride complex ([MH] or [MH<sub>2</sub>]) generates the *N*-alkylamine product and regenerates the catalyst.

mismatched reactivity of alcohol and amine coupling partners.



Scheme 1 General	mechanistic	pathway	to	react	amines	with	alcohols	using	the
hydrogen borrowing methodology.									

Investigations into homogeneous catalysed C-N bond transformations using hydrogen borrowing began as early as 1981 with Grigg *et al.*<sup>22</sup> and Watanabe *et al.*,<sup>23</sup> who used simple coordination complexes of Ru, Ir, and Rh as catalysts. Since then, a wide range of early and late transition metals have been explored as catalysts for these reactions including ruthenium,<sup>24-30</sup> iridium,<sup>31-40</sup> gold,<sup>41</sup> iron<sup>42</sup> and cobalt.<sup>43-44</sup> A recent Ru(II) example using an alanine-triazole ligand overcame a competing transfer hydrogen reaction in order to efficiently couple ketones with alcohols using hydrogen borrowing.<sup>45</sup> A bisbenzoxazolyl Ir(III) performed exceptionally well across a range of couplings involving amines, primary and secondary alcohols, and ketones.<sup>46</sup> A related bisbenzothienyl Ir(III) catalyst was also able to catalyse the cross-coupling of

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alcohol,<sup>47</sup> and primary alcohols with ketones.<sup>48</sup> Despite these reports, more active catalysts which work at low catalyst loadings (<0.5 mol%), lower temperatures ( $\leq$ 70 °C) and have shorter reaction times (<12 h) are needed.

Heterogeneous catalysis in the field of hydrogen borrowing reactions has also been explored for the reaction of alcohols with amines. Heterogeneous systems have a major advantage over homogeneous catalysts in that they can simplify the separation, purification, and recycling following catalytic processes and hence reduce operational consumption costs. The majority of heterogeneous catalysts investigated so far for hydrogen borrowing involves metal nanoparticles, oxides or hydroxides adsorbed or impregnated on inorganic materials such as metal oxides, zeolites, silica or alumina.14, 49-50 However, key disadvantages of these types of catalysts can include metal leaching and uncertain stability and recyclability. Comparatively, there have only been a few reports where isolated complexes immobilised on surfaces have been used as a heterogeneous catalyst for catalysed C-N bond formation reactions via hydrogen borrowing.<sup>51-54</sup> A key benefit of using isolated complexes immobilised on surfaces, so-called "hybrid catalysts", is that the active catalyst sites are well-defined, with easy catalyst optimisation (through ligand modification prior to surface immobilisation), and by being attached to a surface the catalyst is easily recycled.

Herein, we report how Ir(III) complexes of easily synthesised bidentate ligands, featuring carbene and triazole donors, function as catalysts for hydrogen borrowing. Separately, carbene<sup>55-57</sup> and triazole<sup>58-60</sup> ligands have proved highly effective as catalysts for a range of organic transformations. The combination of carbene and trizaole donors represents a great basis from which to tune reactivity.<sup>61-63</sup> The Ir(III) complexes reported here are exceptionally efficient catalysts for C-N bond formation between alcohols and amines, tolerating a wide substrate scope. In addition, we covalently attached an Ir(III) complex to a carbon surface and were able to affect the same catalysis reaction using the new hybrid catalyst with excellent recyclability. To elucidate the mechanism, the homogeneous reaction was followed by NMR spectroscopy and deuterium labelling studies, allowing us to postulate a mechanism.

## 2. Results and Discussion

## 2.1 Homogeneous Catalyst Synthesis

All bidentate carbene-triazole ligands **1a-f** were synthesised using a standard Cu(I) catalysed alkyne-azide cycloaddition reaction (CuAAC) between 1-propargyl-3-mesitylimidazolium bromide and a corresponding azide (Scheme 2).<sup>64</sup> The CuAAC reaction is ideal as it installs a second coordination (triazole) site and provides diversification allowing a series of carbene-triazole ligands containing various electron-withdrawing or electron-donating groups located on the aryl ring to be synthesised.

The bidentate carbene-triazole ligands **1a-f** were subsequently used to synthesise Ir(III) complexes **2a-f** 

containing a Cp\* (1,2,3,4,5-pentamethylcyclopentadiene) coligand and the weakly coordinating anion  $BAr_{4}^{F_{4}}$ (B(3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>)<sub>4</sub>) by following a modified literature procedure.<sup>63</sup> The imidazolium salts **1a-f** were complexed to Ir(III) using [IrCp\*Cl<sub>2</sub>]<sub>2</sub> via a silver(I) oxide transmetallation reaction in acetone. Counter-ion exchange of the crude metal complex with NaBAr<sub>4</sub><sup>F</sup> in dichloromethane yielded the complexes as bright yellow (**1a**, **1c** and **1e**), yellow-brown (**1d**), red-brown (**1b**) or light brown (**1f**) crystalline solids. The colours of the complexes were clearly a result of the substituents on the aryl group of the ligands, demonstrating potential for the substituents to tune catalysis reactivity.

All the ligands and Ir(III) complexes were stable in both the solid state and in solution and were fully characterised by NMR spectroscopy, mass spectrometry and elemental analysis, see ESI. The <sup>1</sup>H NMR spectra of all the complexes showed that the methylene protons of the CH<sub>2</sub> linking the imidazolium and the triazole donors as two AB doublets at significantly different chemical shifts, with a  $^{2}J$  of ~16 Hz, illustrating coordination to the metal centre, similar to previously reported complexes.<sup>65</sup> This difference in chemical shift is due to the diastereotopic nature of the protons caused by the chiral coordination around the metal centre, such that one of the protons is oriented towards the Cp\* ring and hence subjected to a strong ring current effect, while the other proton is oriented away from the Cp\* ring. In addition, the observation of pairs of resonances attributed to inequivalent ortho-CH<sub>3</sub> and meta-CH protons of the mesityl ring in the <sup>1</sup>H NMR spectra, as well as related exchange cross peaks observed in the <sup>1</sup>H-<sup>1</sup>H NOESY spectra, indicate restricted rotation around the N-C bond between the mesityl and carbene group on the NMR time scale. This hindered rotation was observed for all complexes 2a-f.



Single crystals of Ir(III) complexes **2a-f** suitable for single crystal X-ray diffraction analysis were grown by slow diffusion of hexane into a concentrated dichloromethane solution for complexes **2a**, **2c** and **2f** or by slow diffusion of hexane or cyclohexane into a concentrated toluene solution of **2b**, **2d** and **2e**. The solid-state structure of complex **2d** is shown in Figure 1. Structures of all other Ir(III) complexes and a summary of selected bond lengths and angles of complexes **2a-f** are given in the ESI. The solid-state structures of Ir(III)

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complexes all exhibit a piano-stool type octahedral conformation around the metal centre. In all cases, the 6membered metallacycle formed upon coordination of the bidentate carbene-triazolyl ligands to the metal centre adopts a distorted boat conformation. The four torsion angles centred on bend in the boat range from 42° to 46° and average to ~43° in Ir(III) complex 2d. The C-Ir-N bite angles are slightly smaller than those reported for analogous Ir(III) complexes containing bidentate carbene-triazole ligands,65 indicating that upon coordination to Ir(III), the bidentate carbene-triazole ligand 1 is forced into a highly strained conformation. The average Ir-C\* distances (C\* = centroid of the Cp\* ring) and the average Ir-N(triazole) bond lengths are similar to those reported for analogous Ir(III) complexes with bidentate carbene-triazole<sup>65</sup> and pyrazole-triazole ligands.<sup>66</sup> Although the Ir(III) metal centres of the various complexes were chelated with bidentate carbene-triazole ligands containing different substituents on the aryl ring, the selected bond lengths connected to the metal centre (Ir-C\*(centroid of Cp\*), Ir-C(carbene), Ir-N(triazole), Ir-Cl) were generally similar, see ESI Table S6 and Figures S8-S13. This is unsurprising as the aryl substituents are too remote to influence the conformation around the metal centre.



Figure 1 X-ray crystal structures of Ir(III) complex 2d featuring the *p*-CF<sub>3</sub> substituent, as viewed from (a) above the Ir(III) 6-membered metallocycle and (b) face-on to the Ir(III) metallocycle. Ellipsoids are shown at the 40% probability level, hydrogens and BAr<sub>4</sub> counterions have been omitted for clarity. Selected bond lengths (A) and angles (°): C1-Ir 2.058(7), N1-Ir 2.065(5), C\*-Ir 1.824, CI-Ir 2.404(2), C1-Ir-N1 82.9(2). CCDC 1529842.

## 2.2 Heterogeneous Catalyst Synthesis

The Ir(III) hybrid catalyst containing the bidentate carbenetriazole ligand was synthesised utilising a direct covalent attachment of the complex to a carbon surface.<sup>63</sup> Complex **2f** containing the *para*-amino substituent on the aryl ring was dissolved in a hydrochloric acid solution of nitromethane and sodium nitrite. Glassy carbon was allowed to stand in this solution for 24 h, whereas carbon black was stirred into the solution for the same amount of time. Subsequently, the glassy carbon was washed thoroughly and dried under a gentle stream of nitrogen to yield **2-GC**. The carbon black reaction was centrifuged, washed repeatedly with methanol and water, and then the carbon powder was dried under vacuum overnight to give **2-CB** as a black powder.

The Ir(III) hybrid catalysts were characterised using X-ray photoelectron spectroscopy (XPS), thermogravimetric analysis (TGA) and inductively coupled plasma mass spectrometry (ICP-MS). XPS can be used to analyse the elemental composition of the surfaces, therefore allowing a determination on whether the chemical structure of the complex is preserved when immobilised on the surface. The XPS spectra of **2-CB** is shown in Figure 2a and ESI Figure S1; selected binding energies related to N1s and Ir4f peaks and the atomic ratio of N:Ir are summarised in the ESI Table S1. The binding energy of N1s

representative of the nitrogen atoms on the ligand coordinated to the Ir metal centre appears at ca. 401-402 eV in both hybrid catalysts 2-CB and 2-GC. In the XPS spectra of both hybrid catalysts, a minor peak was observed within the N1s peak at about 399-400 eV, this peak is indicative of an azo bond (N=N). This is likely to originate from incomplete diazonium reaction of the aniline moiety of complex 2f to the carbon surface; this has been observed in many previous reports.<sup>67</sup> The binding energy of Ir4f representing the Ir(III) metal centre on the carbon surfaces appears at ca. 62-63 eV, in agreement with the binding energy of other reported Ir(III) metal complexes.<sup>68-69</sup> From the XPS data, the elemental ratio of nitrogens to iridiums on the surface was determined to be close to 5:1, which is consistent with the expected molecular structure, indicating that the Ir(III) complexes were immobilised onto the glassy carbon or carbon black surfaces as intact complexes.



Figure 2 a) XPS survey scan of 2-CB with selected narrow scans of N1s and Ir4f (dashed boxes). b) TGA analysis of 2-CB and unmodified carbon black.

Thermogravimetric analysis was also performed on **2-CB** to analyse the stability of the hybrid complex on carbon black. From the thermogram of **2-CB**, there is one distinct weight loss process from 100-542 °C (Figure 2b). This process accounts for 26.6% loss in weight due to the whole iridium complex from the carbon black surface. From this weight loss, the iridium content on the surface was calculated to be 7.2 wt.%. After 542 °C, the loss in weight of the sample is due to decomposition of the carbon black material. By ICP-MS, the quantitative amount of iridium on the carbon black surface in complex **2-CB** was determined to be 0.84 wt.%. The difference in calculated weight of Ir(III) as determined by TGA and ICP-MS is likely due to the fact that the total weight loss as observed by TGA can also be attributed to decomposition of impurities such as oxidised functional groups on the carbon surfaces.

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## 2.3 Homogeneous H<sub>2</sub> Borrowing Catalysis for C-N Bond Formation

The reaction of benzyl alcohol (3, 1.1 equiv.) and aniline (4, 1.0 equiv.) in air using the unsubstituted complex 2a (0.5 mol%) as a catalyst, was selected as a model reaction for optimisation studies. Initially, a solvent screen (toluene- $d_8$ , dioxane- $d_8$ , 1,1,2,2-tetrachloroethane- $d_2$  and dimethylsulfoxide- $d_6$  at 100 °C and tetrahydrofuran-d<sub>8</sub> at 60 °C) was conducted using KOH as the base. From this, toluene- $d_8$  was the found to be the best solvent for the reaction giving the highest conversion of 60% after 7 h. In order to improve the conversion of the model reaction further, the reaction was tested in toluene- $d_8$  using a series of different bases (KOH, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, CsCO<sub>3</sub>, KO<sup>t</sup>Bu, DABCO, Et<sub>3</sub>N, DIPEA). The use of KO<sup>t</sup>Bu as the base provided increased conversion to product 5a, reaching 80% in 6 h at 100 °C. No reaction was observed when using K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub> or Cs<sub>2</sub>CO<sub>3</sub>. The use of organic bases such as DABCO, Et<sub>3</sub>N or DIPEA provided less than 10% conversion to the desired product N-benzylaniline (5a). Certain catalysts reported in the literature require silver salt additives in order to function effectively.<sup>41, 46</sup> We screened various silver salt additives, such as AgOTf, AgOAc and AgBF<sub>4</sub>, however they all had negligible effect on the percent conversion observed for this reaction. Clearly our catalysts reported here do not require addition of silver salts to function effectively, and thus represent a greener catalysis system compared to other reported hydrogen borrowing catalysts. The reactions did not require the addition of molecular sieves to scavenge water.



Figure 3 Catalyst screen for C-N bond formation between benzyl alcohol and aniline via hydrogen borrowing. Reaction conditions: **3** 1.1 equiv., **4** 1.0 equiv., Ir(III) catalyst **2** (0.5 mol%), KO Bu 1.1 equiv., toluene-*d*<sub>8</sub>, 100 °C, 6 h.

Using the optimised reaction conditions of 0.5 mol% catalyst loading, KO<sup>t</sup>Bu as a base, toluene- $d_8$  solvent, reaction time of 6 h at 100 °C, the full series of Ir(III) complexes **2a-f** were assessed as catalysts for the reaction of benzyl alcohol (**3**) and aniline (**4**), see Figure 3. As expected the catalytic efficiency of each complexes varied depending on the electronic environment around the metal centre. Complex **2d**, containing an inductively electron-withdrawing *p*-CF<sub>3</sub> on the aryl ring of the ligand, catalysed the reaction with the highest conversion of 96% in 6 hours at 100 °C. The observed trend in catalytic efficiency of the Ir(III) complexes for the conversion of

**3** and **4** to **5a** was seen to be:  $p-CF_3$  (**2d**) >>  $m-CF_3$  (**2e**) >  $p-NO_2$ (**2b**) ~ p-H (**2a**) >  $p-CH_3$  (**2c**) >  $p-NH_2$  (**2f**). Overall, Ir(III) complexes from ligands containing the more electron-withdrawing groups (CF<sub>3</sub> or NO<sub>2</sub>) led to better conversions for the C-N bond formation than those with ligands containing more electron-donating groups (CH<sub>3</sub> or NH<sub>2</sub>) on the aryl ring.

As a control experiment, the catalytic activity of  $[IrCp^*Cl_2]_2$ , ligand **1d**, NaBAr<sup>F</sup><sub>4</sub> and KO<sup>t</sup>Bu was determined for the reaction of **3** and **4** after 6 h at 100 °C. Pleasingly, this *in situ* formed catalyst gave only 50% conversion to **5a**, compared against 96% conversion using catalyst **2d**. In the absence of ligand **1d**,  $[IrCp^*Cl_2]_2$ , NaBAr<sup>F</sup><sub>4</sub> and KO<sup>t</sup>Bu at 100 °C gave 70% conversion of **3** and **4** to **5a** after 15 h. This result is in alignment with the results reported by Fujita, whereby  $[IrCp^*Cl_2]_2$  in the presence of NaHCO<sub>3</sub> instead of KO<sup>t</sup>Bu gave 44% conversion to **5a**.<sup>34</sup>

There are few examples of hydrogen borrowing at temperatures lower than 100 °C. Complexes **2a** and **2d** were found to still catalyse this same reaction at a lower temperature of 60 °C for 24 hours. Whilst longer than our experiments at 100 °C, these reaction times are not longer than most literature reports. Complex **2d** gave a near identical conversion to **5a** of 96% after 24 h. Whilst complex **2a** achieved 63% conversion to **5a** after 24 h. These results further demonstrate that complex **2d** is a highly active catalyst for the C-N bond formation between benzyl alcohol and aniline, therefore it was used as the catalyst for subsequent substrate scope investigations.

To determine the substrate scope of this Ir(III) catalysed hydrogen borrowing reaction we separately varied both the alcohol and amine substrates, see Scheme 3. First, the alcohol partner was varied in the reaction with aniline (4). All reactions resulted in over 80% conversion to products 5b-5h after 6h at 100 °C. Methyl, methoxy, and bromide substituted benzyl rings were tolerated as were alkyl and cyclic alcohols. Secondly, the amine coupling partner was varied in the reaction with benzyl alcohol (3). Most reactions resulted in over 90% conversion after 6 h at 100 °C. Methyl and halogen substituents were well tolerated as were pyridyl and napthyl rings. The biologically relevant motifs of dibenzylaniline 5r and piperonyl aniline 5s gave excellent conversions. N-alkyated products 5c, 5e, 5i, 5l and 5s could also be obtained at the lower reaction temperature of 60  $\,^{\circ}\text{C}$  after 24 h; all gave near identical conversions to those reactions performed at 100 °C (yields in square brackets, Scheme 3).

To further our understanding of the efficiency of the Ir(III) catalytic reaction, benzyl alcohol (**3**) was reacted with different aniline substrates functionalised at the *para*-position in the presence of 0.5 mol% **2d** and KO<sup>t</sup>Bu in toluene- $d_8$  at 100 °C and the progress of each reaction was monitored at 0.5-1 hour intervals by <sup>1</sup>H NMR spectroscopy. All of the catalytic reactions showed unprecedented efficiency, reaching at least 80% conversions in less than 6 hours, see ESI Figure S2 and Table S2. The hydrogen borrowing C-N coupling of **2** with *p*-bromoaniline was the fastest reaction, reaching 96% conversion in only one hour. Whereas, the reaction of benzyl alcohol **3** with unsubstituted aniline **4** or *p*-toluidine required 6 h to achieve a good conversion. Thus, a clear improvement in

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reaction efficiency was observed when the functionalised aniline substrate contained an electron-withdrawing group compared to an electron-donating group.

In comparison to other reported Ir(III) catalysts used for hydrogen borrowing, our catalyst achieves similar conversions at half the catalyst loading in at least half the time, without addition of silver salts. Our homogeneous catalyst also can affect complete conversions at 60 °C, in comparison to 100 °C which is often reported, confirming that the Ir(III) catalyst **2d** offers a significant improvement over existing Ir(III) catalysts. Despite the higher activities resulting in shorter reaction times and reduced reaction temperatures for reactions involving primary alcohols, the catalysts reported here could not catalyse the hydrogen borrowing reaction between the secondary alcohol, 1-phenly ethanol, and aniline.



## Scheme 3. Substrate scope for the homogeneous Ir(III) catalysed hydrogen borrowing catalysed coupling of amines and alcohols. %Conversions were determined by 'H NMR spectroscopy. Isolated yields are given in parentheses (). %Conversions after 24 h at 60 °C are given in square brackets [].

## 2.4 Heterogeneous H<sub>2</sub> Borrowing Catalysis for C-N Bond Formation

Ir(III) heterogeneous catalyst **2-CB** was tested as a catalyst for the reaction of benzyl alcohol **3** with aniline **4**. At a catalyst loading of 0.01 mol%, **2-CB** gave 42% conversion to benzyl aniline after 24 h at 100 °C which equates to a turnover number (TON) of 4362. We recycled the heterogeneous catalyst over three reaction cycles (24 h at 100 °C), after each cycle the conversion was measured. It was found that each cycle gave close to 42% conversion, with only a slight decrease after the third cycle (37%), see Figure 4a. Despite not reaching complete conversion after 24 h, the Ir(III) heterogeneous catalyst performs well with high turnover numbers. The excellent recyclability was determined after each recycling step where the filtrate and washings were collected and analysed by ICP-MS to determine what, if any, loss of iridium from the carbon surface occurred. It was found that only 0.33% of total iridium content was lost after the three catalysis runs, Figure 4b and Table S3. This is significantly better than our findings with a related heterogeneous Rh catalyst which after an initial 12% loss of physisorbed rhodium gave a 3% total loss of rhodium after the second and third cycles.<sup>63</sup>

There are limited examples of heterogeneous catalysts used for hydrogen borrowing for the specific reaction between aniline and benzyl alcohol. A related Ir(III) complex on a silica support gave higher conversion but had to use a much higher catalyst loading, hence much lower TONs were obtained.<sup>53</sup> A Pd(II) catalyst on silica was able to produce a higher turnover as a result of a lower catalyst loading, though this required a longer reaction time.<sup>51</sup>



Figure 4 Heterogeneous recycling experiments using catalyst 2-CB for the reaction of benzyl alcohol 3 and aniline 4 at 100 °C for 24 h showing (a) % conversion after each catalysis cycle and (b) the % iridium remaining on the carbon black surface after each cycle. Reagents and conditions: 3 1.1 equiv., 4 1.0 equiv., Ir(III) catalyst 2-CB 0.01 mol%, KO'Bu 1.1 equiv., toluene- $d_s$ , 100 °C, 24 h.

## 3. Mechanistic Investigations

Although a precise mechanism for the C-N bond formation reaction of alcohols with amines *via* hydrogen borrowing using iridium catalysts has not yet been clarified, several theoretical studies using density functional theory (DFT) calculations have been reported recently.<sup>37, 67, 70-71</sup> From these DFT studies, the catalysed reaction of alcohols with amines has been demonstrated to be composed of three main multistep reactions: (1) metal catalysed oxidation of the alcohol, (2) nucleophilic addition of the amine to the aldehyde, and (3) metal catalysed reduction of the imine to the amine product. We conducted NMR spectroscopy based investigations in an attempt to probe the reaction mechanism. The results obtained allowed us to postulate a plausible mechanism. **3.1** NMR Hydride Investigations

## The first key step in the hydrogen borrowing reaction is the

oxidation of the alcohol substrate to an aldehyde. This is thought to proceed via  $\beta$ -hydride elimination from the alcohol upon coordination to the metal centre with the metal centre capturing the hydride. Therefore, we examined what

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substrates were necessary to generate an Ir(III) hydride complex and if a base was required. Iridium complex 2d was reacted with ca. 5 equivalents of benzyl alcohol (3) or aniline (4) in toluene- $d_8$  in separate NMR tubes and monitored by NMR spectroscopy. In both cases, no reaction was observed. Subsequently, ca. 5 equivalents of KO<sup>t</sup>Bu was added to both NMR tubes. No reaction was observed for the reaction mixture containing aniline (4). Whereas, upon addition of  $KO^{t}Bu$  to the NMR tube containing Ir(III) complex 2d and benzyl alcohol (3), a hydride species (broad resonance,  $\delta$  -13.3 ppm) was observed by <sup>1</sup>H NMR spectroscopy. A <sup>1</sup>H-<sup>13</sup>C HMBC experiment revealed a correlation between the hydride resonance and a carbon signal at  $\delta$  155.3 ppm which was attributed to the carbene carbon coordinated to the iridium metal centre (see Scheme 5 inset). This confirms that a hydride was bound to the Ir metal centre. Additionally, a sharp singlet resonance appears over time at  $\delta$  9.52 ppm, indicative of an aldehyde, possibly coordinated to the Ir(III) centre, complex I. Whilst the initial Ir(III) hydride complex forms quickly, the catalysed conversion of benzyl alcohol to benzaldehyde proceeds slowly.

To further confirm that an Ir(III) hydride complex was part of the catalytic cycle, an iridium hydride complex II was prepared and tested as a catalyst for this reaction. Complex 2d was reacted with sodium borohydride in methanol and Ir(III) hydride complex II was isolated as a pale yellow solid. Complex II was characterised by 1D and 2D NMR and mass spectrometry, see ESI. A <sup>1</sup>H-<sup>13</sup>C HMBC NMR experiment revealed a correlation between the hydride resonance at  $\delta$  -13.3 ppm and a  $^{13}\mathrm{C}$  resonance at  $\delta$  155.1 ppm, similar to that observed previously in the HMBC NMR experiment containing iridium complex **2d**, benzyl alcohol (**3**) and  $KO^{t}Bu$  in toluene- $d_{8}$ . The <sup>13</sup>C resonance at  $\delta$  155.1 ppm was identified as the carbene carbon resonance coordinated to the metal centre. Complex II was also used as a catalyst in place of complex 2d in the reaction of benzyl alcohol (3) and aniline (4) under the optimised conditions identified previously. This reaction reached a conversion to N-benzylaniline (5a) of 77%, which was lower compared to the 96% conversion observed when using 2d as catalyst. Despite the lower conversion, this result proves that Ir(III) hydride complex II is an intermediate during this reaction and that Cl<sup>-</sup> is required to achieve complete conversion, possibly by sequestering  $K^{+}$  from the base.

Iridium hydride complex II was proposed to activate the imine intermediate leading to hydride transfer to the imine. Diphenylmethanimine, was synthesised then reacted in an NMR tube with hydride complex II in toluene- $d_8$ . <sup>1</sup>H NMR analysis of this reaction did not present any evidence of the activation of the C=N double bond by the hydride complex II. Subsequently, addition of benzyl alcohol (**3**) to the reaction mixture containing complex II and diphenylmethanimine, showed no reaction. Upon addition of approximately stoichiometric amount of KO<sup>t</sup>Bu to the same reaction mixture and heating at 100 °C, the *N*-benzylaniline **5a** was observed. These results imply that hydride transfer from iridium hydride complex II to the imine is a slow process that requires base and alcohol in order to progress C-N bond formation.

3.2 NMR Deuteration Investigations

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From the hydride experiments, Ir(III) hydride complex II was proven to be an active catalytic intermediate, with the hydride most likely originating from the alcohol substrate. To determine that the hydride on complex II does not originate from the amine substrate, complex 2d was used to catalyse the reaction of benzyl alcohol (3) with deuterated aniline substrates 4- $d_5$  or 4- $d_7$  in non-deuterated toluene for 6 hours at 100 °C (Scheme 4a). The products were then isolated and analysed by <sup>1</sup>H NMR in toluene- $d_8$ , and <sup>2</sup>H NMR in toluene which showed that only deuterated product 5a- $d_5$  was formed; no deuteration of the NH or CH<sub>2</sub> moieties was observed.



Scheme 4 Deuteration NMR studies of the C-N bond formation reaction of benzyl alcohol (3) with deuterated aniline substrates (4) catalysed by complex 2d.

Complex 2d was next used as catalyst for the reaction of deuterated benzyl alcohols  $3-Cd_2$  and  $3-Od_1$  with aniline (4) in toluene for 6 hours at 100 °C (Scheme 4b). The products were isolated and analysed by <sup>1</sup>H NMR in toluene- $d_8$  and <sup>2</sup>H NMR in toluene. The reaction of benzyl alcohol- $d_2$  ( $3-Cd_2$ ) and aniline (4) gave a 1:1 mixture of *N*-benzyl aniline (5a), and the deuterated *N*-benzylaniline product ( $5a-Cd_1$ ) containing only one deuterium on the benzyl position. On the other hand, the reaction between benzyl alcohol-OD ( $3-Od_1$ ) and aniline (4) gave 5a as the major product ( $5a-Cd_1$ ) (for the relevant spectra, see ESI Figures S3 – S4).

For further confirmation that the hydride bound to the iridium metal in **II** derives from the benzylic CH<sub>2</sub> on the alcohol, complex **2d** was reacted in a series of NMR tube experiments with *ca*. 5 equivalents of deuterated benzyl alcohols **3-Cd<sub>2</sub>** or **3-Od<sub>1</sub>** and KO<sup>t</sup>Bu in toluene or toluene-*d*<sub>8</sub> (Scheme 4d, e). The <sup>1</sup>H NMR spectrum of benzyl alcohol-*d*<sub>2</sub> (**3-Cd**<sub>2</sub>) and complex **2d** displayed no hydride or aldehyde resonances (see SI, Figure S5). The <sup>2</sup>D NMR experiments for this reaction in non-deuterated toluene showed that the deuterated hydrogen resonances appear at  $\delta$  9.52 ppm, corresponding to the aldehyde proton of benzaldehyde. Whilst

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hydride complex II was expected to be formed during this NMR experiment, no deuterated hydride resonance was observed either in the <sup>2</sup>H NMR spectrum, likely because the resonance was too broad. The <sup>1</sup>H NMR spectrum from the reaction of benzyl alcohol-OD (**3-OD**) and Ir(III) complex **2d** in toluene-*d*<sub>8</sub> with KO<sup>t</sup>Bu (Scheme 5, inset) showed immediate formation of a hydride resonance at  $\delta$  -13.3 ppm as well as the distinctive aldehyde proton resonance at  $\delta$  9.57 ppm attributed to benzaldehyde. In the <sup>2</sup>D NMR spectra, no deuterated resonances were observed either in the hydride or aldehyde regions.

The combination of all the deuteration NMR studies provides clear experimental evidence that the hydride on iridium complex II must come from one of the benzylic  $CH_2$  protons during the oxidation of benzyl alcohol (3) to benzaldehyde and not from the OH of the benzyl alcohol or from the amine substrate. These results also demonstrate the lack of the reaction between alcohol and alcohol, or alcohol and aldehyde under a catalysed hydrogen borrowing reaction in the absence of amine substrate.

## 3.3 Base Requirement

We attempted to use catalytic quantities of KO<sup>5</sup>Bu (0.5 mol% or 10 mol%) in these reactions. However, this resulted in very poor yields of *N*-alkylated product. Using no base, the reaction did not proceed at all. It appears that a stoichiometric quantity of base is required to deprotonate all alcohol substrate present in order to drive the reaction forward. This finding is reinforced from our other experimental findings that most steps do not proceed without base present. This is potentially due to our catalyst only being able to accommodate one hydride. Literature reports usually describe metal catalysts with the ability to coordinate two hydrides or a metal complex that can deprotonate the alcohol substrate.<sup>25, 39</sup>

## 3.4 Proposed Mechanism

Based on our NMR studies and DFT studies reported in the literature,<sup>37, 67, 70-71</sup> a mechanism was proposed using our Ir(III) complex 2d to catalyse C-N bond formation between alcohols and amines via hydrogen borrowing (Scheme 5). In step A of the proposed mechanism, the Ir(III) complex exchanges a chloride for an alkoxide to produce an iridium alkoxide complex. Subsequent  $\beta$ -hydride elimination of a hydrogen from the benzylic CH<sub>2</sub> of the alkoxide in steps B and C yields an aldehyde and a hydride bound to the Ir(III) metal centre I. These steps are facilitated by partial de-coordination of the bidentate ligand, most likely via dissociation of the triazole donor from the metal centre. In the presence of an amine substrate, the release of the aldehyde in step D allows imine formation away from the metal centre in step E, and also releases a water molecule as the only by-product of this reaction. Imine intermediate III enters the catalytic cycle to form a complex with Ir(III) hydride complex II at step F, aided by partial decoordination of the bidentate ligand. The proximal orientation of the activated imine and hydride promotes the hydride transfer from the Ir metal centre to the imine in step G. An alkoxide then exchanges with the deprotonated amine which then picks up a proton from <sup>t</sup>BuOH to generate the N-

alkylated amine product in step H. The catalyst is then regenerated and the catalytic cycle continues. From our NMR studies, we postulated that steps F and G are reversible and highly favour the reverse reaction. It is only step H that is irreversible, hence driving the overall cycle toward *N*-alkylated product.



Scheme 5 Proposed mechanism of Ir(III) catalysed C-N bond formation reaction of alcohols with amines via hydrogen borrowing. Inset, hydride-carbene coupling observed in 'H-<sup>15</sup>C HMBC NMR.

Considering the lack of reactivity observed with secondary alcohols, one possible explanation is the inability of the catalyst to dehydrogenate the secondary alcohol to the corresponding ketone. This is could be due to the sterics around the active catalytic site which is contained within a pocket defined by a bulky carbene-triazole ligand in addition to the large Cp\* co-ligand.

## 4. Conclusions

Six new Ir(III) complexes 2a-f were synthesised from a set of ligands 1a-f based on a bidentate carbene-triazole motif. From this series of Ir(III) complexes, complex 2d, featuring a p-CF<sub>3</sub> substituent on the ligand, emerged as the most efficient catalyst for C-N bond formation reactions of alcohols with amines using hydrogen borrowing. Ir(III) complex 2d was found to be an excellent catalyst, catalysing reactions of a range of alcohol and amine substrates, and tolerating a range of functional group substituents on those substrates, including biologically relevant molecules. Catalyst 2d is selective for primary alcohols over secondary alcohols which did not react under these conditions. Reactions proceeded at a low catalyst loading of 0.5 mol% and reached completion between 1-6 hours at 100 °C, showing unprecedented efficiency to date compared to other similar Ir(III) complexes. Furthermore, Ir(III) catalyst 2d was just as efficient at catalysing the couplings of

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alcohols with amines at a lower temperature (60  $^{\circ}\mathrm{C})$  in 24  $^{\phantom{0}5}$  hours.

Heterogeneous Ir(III) carbene-triazole hybrid complexes covalently attached to carbon black and glassy carbon were synthesised and fully characterised by XPS, TGA and ICP-MS. For C-N bond formation between benzyl alcohol and aniline using hydrogen borrowing, the heterogeneous Ir(III) hybrid catalyst **2-CB** gave a moderate conversion to benzyl alcohol of 42% with a turnover number of 4363. Whilst the conversions were slightly lower compared to the homogenous catalysis, the turnover number achieved using the hybrid catalyst was significantly higher than that of the homogeneous catalysed reactions, which suggests that the hybrid complex was a more efficient catalyst. The excellent recyclability was confirmed by ICP-MS which showed that the total loss of iridium over three cycles was 0.33%, this is an order of magnitude better than our previously reported heterogeneous Rh catalyst.<sup>63</sup>

The mechanism of the C-N bond formation using hydrogen borrowing with catalyst **2d** was studied using deuterium labelling and NMR spectroscopy. To corroborate our proposed mechanism an intermediate hydride Ir(III) complex was observed and the source of the hydride was clearly identified as the benzyl hydrogens from the alcohol substrate. A 15 stoichiometric quantity of base is necessary for the reaction to reach complete conversion.

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Ir(III) complexes were found to be highly active catalysts for the hydrogen borrowing coupling of amines and alcohols.