Electronically tunable *N*-heterocyclic carbene ligands: 1,3-diaryl *vs.* 4,5-diaryl substitution†

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The catalytic activity of iridium-mediated transfer hydrogenation is readily tuned by electronic variation of the ligated tetraaryl-*N*-heterocyclic carbene and the installation of electron donating groups on the *N*-aryl substituents is more important than on the *C*-aryl substituents for effecting catalytic enhancement.

Numerous research groups—notably those of Crabtree, Herrmann, and Nolan—have employed various methods for characterizing the electronic properties of *N*-heterocyclic carbenes (NHCs),[1–7] which are proven to be a privileged class of ancillary ligand in metal-mediated catalysis.[8–13] Prominent among these methods is the analysis of infrared carbonyl stretching frequencies in NHC–metal carbonyl species. Comparison of the IR carbonyl stretches in iridium carbonyl NHCs to Tolman electronic parameters, based on nickel carbonyl NHCs, has been achieved with a high degree of correlation. Most of these studies have been conducted on 1,3-disubstituted NHCs (nitrogen substitution), although a few 4,5-disubstituted NHCs (carbon substitution) have been investigated.[2,3,5,14–21] Nonetheless, we have a limited understanding of the influence that 4,5-disubstitution bears on the electronic and catalytic properties of NHCs compared to 1,3-disubstitution.[22] The prospect of holistic electronic tuning[23] of NHCs is alluring.

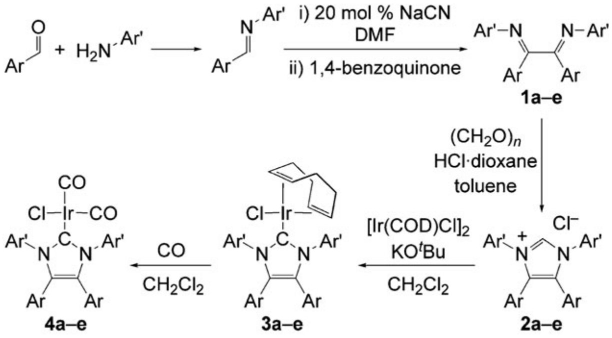
Recently, we published a strategy based on aldimine coupling for the facile access of 1,2,3,4-tetraaryldiimines, precursors to 1,3,4,5-tetrarylimidazolium salts.[24] Scheme 1 depicts our straightforward synthetic route from electronically prescribed benzaldehydes and anilines to 1,5-cyclooctadiene iridium NHC complexes (**3a–e**) or the corresponding carbonyl complexes (**4a–e**). Surprisingly, comparison of the average IR carbonyl stretch ($\nu_{CO}{}^{av}$) with those of over thirty literature Ir–NHC species indicated that the NCH ligands of **4a–e** are among the most electron-rich[25] developed so far; they also exhibited the widest range of electronic character for NHCs prepared *via* a single synthetic approach.[1–4,7,17]

A robust system for testing the viability of new Ir–NHC catalysts is the transfer hydrogenation of acetophenone.[21,26–30] For this reaction, complexes **3a–e** represent the most active mono-NHC iridium(I) catalysts known. Complexes **3a** and **3b** exhibited the highest turnover frequencies (1080 and 1240 h^{-1}, respectively) but are still less active than a few specialized bidentate-NHC iridium(III) catalysts tested by Crabtree and co-workers (TOF up to 50 000 h^{-1}).[29,31] Note that catalyst **3b** is 65% more active than **3c**, suggesting that electronic control at the 1,3 (nitrogen) positions is more effective than at the 4,5 (carbon) positions of the NHC.

Fig. 1 plots the $\log_{10}$ of the turnover frequency (in h^{-1}) of **3a–e** against the average carbonyl stretching frequency of the corresponding Ir carbonyl complexes **4a–e**. The linear relationship observed highlights the catalytic control that can be exerted *via* precise electronic tuning of the NHC ligand. Generally, electron donating groups (−OMe) enhance the catalytic activity compared to electron withdrawing groups (−F). While much less electron-rich and less active, the well-known IMesIr(COD)Cl catalyst has an activity in accord with the apparent linear trend.[2,32]

Analysis of the NMR spectra for the complexes **3a–e** can also be used as an electronic assessment. As the iridium metal gains electron density, the metal–alkene bond distances (of Ir–COD) decrease, the sp^2 C–H bond distances increase and therefore lose shielding, causing a downfield shift of the ^1H NMR peaks in the vinylic region. A linear relationship was found between the TOF (in h^{-1}) and the chemical shift (in ppm) of the 1,5-cyclooctadiene protons in the alkene bound *trans* to the carbene: $\text{TOF} = -14\,300\,(\delta) + 62\,600$ (with $R^2 = 0.852$).†

The complexes **3a–e** were also analyzed *via* Hammett correlations, a reasonable approach because the *para* substituents impact the electronics, but likely have a minimal steric effect.[4] We compared transfer hydrogenation rates for the 1,3-diaryl series **3a**, **3b**, and **3d** and the 4,5-diaryl series **3a**, **3c**, and **3e**. Fig. 2 illustrates that the correlations with σ_{meta} ($R^2 = 0.810, 0.993$) and σ_I ($R^2 = 0.619, 0.983$) were superior to that with σ_{para} ($R^2 = 0.506, 0.064$), indicating that inductive



	a	b	c	d	e
Ar'	$-C_6H_5$	$-p\text{-}C_6H_4OMe$	$-C_6H_5$	$-p\text{-}C_6H_4F$	$-C_6H_5$
Ar	$-C_6H_5$	$-C_6H_5$	$-p\text{-}C_6H_4OMe$	$-C_6H_5$	$-p\text{-}C_6H_4F$

Scheme 1 Synthesis of iridium carbonyl carbene complexes **4a–e**.

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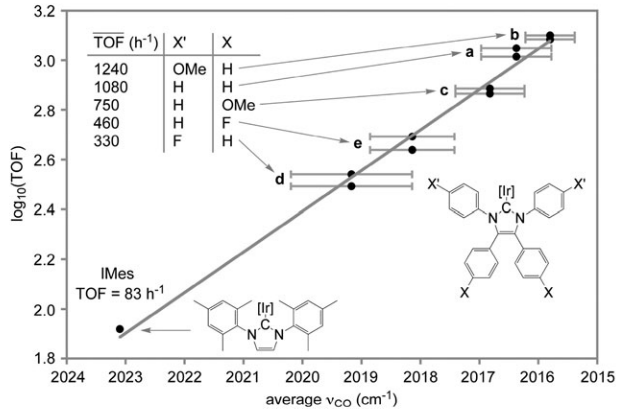

Fig. 1 Catalytic turnover by **3a–e** in the transfer hydrogenation of acetophenone with acetone. The $\log_{10}$ of the TOF (in h^{-1}) is linearly proportional to the average IR carbonyl stretch of the corresponding Ir carbonyl complexes **4a–e**. TOFs are determined by ^1H NMR at $t = 1$ hour for two reactions each; IMesIr(COD)Cl values are from ref. 2 and 32; error bars represent one standard deviation for 3 to 4 measurements of ν_{CO}.

effects are more important than resonance effects for this system. An explanation for this is that the aryl rings are not coplanar with the central heterocycle and resonance effects are correspondingly diminished, as suggested by X-ray crystallography of the cognate NHC–AgCl complexes **5a–e**.[24] The average dihedral angles for the 1,3-aryl rings are 68°, 73°, 60°, 75°, and 67°, while the average dihedral angles for the 4,5-aryl rings are 67°, 69°, 47°, 70°, and 68° for **5a–e**, respectively.

For the σ_{meta} and σ_I analyses, the slopes for the 1,3-diaryl series ($\rho = -1.65, -0.99$, respectively) are somewhat greater in magnitude than those for the 4,5-diaryl series ($\rho = -1.06, -0.73$, respectively). This suggests that substitution at the 1,3 positions of NHCs is more effective than substitution at the 4,5 positions for electronic tuning. However, this conclusion is not unequivocal since data sets were synthetically restricted and regression analyses for 1,3 substitution were modest ($R^2 = 0.810, 0.619$). Nonetheless, the negative ρ values validate a recent mechanistic proposal by Bi and co-workers[35] for the transfer hydrogenation of ketones: the rate-limiting step involves transfer of an iridium hydride to the carbonyl carbon of a pendant ketone and net loss of electron density at iridium as the transition state is approached.

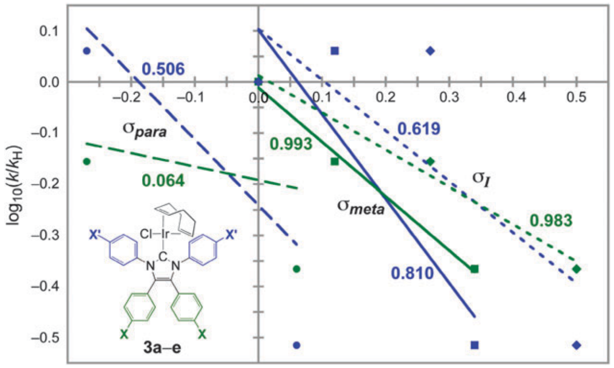

Fig. 2 Hammett plots for the transfer hydrogenation of acetophenone by **3a–e**. Rates are determined by ^1H NMR conversion at $t = 1.0$ hour (average of two reactions) and are plotted as $\log_{10}(k/k_H)$ *vs.* σ_{para} (circles), σ_{meta} (squares), or σ_I (diamonds).[33,34] All linear fits include the point at 0,0, R^2 values are given, blue = 1,3-diaryl X′, and green = 4,5-diaryl X.

Anomalously, catalyst **3b** proved to be the most active catalyst studied, despite its inductively withdrawing $-C_6H_4OMe$ aryl groups in the 1,3 positions. Perhaps the modest fits to σ_{meta} and σ_I ($R^2 = 0.810, 0.619$) indicate that resonance effects—and not inductive effects alone—have significance for substituents at the 1,3 positions. A *para*-methoxy group is a good π-donor *via* resonance and probably contributes some electron density this way to iridium, lowering the transition state energy.

Computational studies support the conclusion that electronic variation of the 1,3-*N*-aryl groups is more consequential than electronic variation of the 4,5-*C*-aryl groups. The free carbenes from structures **4a–e** were subjected to a density functional theory study at the B3LYP 6-31G* level. The carbene ground state structures were derived from the X-ray crystal structures of the corresponding NHC–AgCl complexes **5a–e**,[24] following removal of the AgCl portion. Fig. 3 shows the resulting electrostatic potential maps along with the calculated electrostatic charge at the carbene carbon. These results clearly indicate that electronic perturbation of the 4,5-*C*-aryl groups is minimally effective, whereas perturbation of the 1,3-*N*-aryl groups significantly changes the calculated charge on the 2-carbon of the heterocycle. Specifically, addition of *para* F substituents to the 1,3-*N*-aryl groups results in a decrease of 0.049 e^- while addition of *para*-methoxy substituents to the 1,3-*N*-aryl groups results in an increase of 0.023 e^- at the carbene carbon. Similar additions to the 4,5-*C*-aryl groups result in a minute change of 0.001 e^-.

In conclusion, we developed a series of five iridium COD 1,3,4,5-tetraaryl *N*-heterocyclic carbene complexes **3a–e**, all of which excel known 1,3-diaryl-NHC analogues for catalytic transfer hydrogenation of ketones. Electronic tuning was possible by variation of the *para*-C_6H_4X aryl groups in the 1,3 and 4,5 positions of the NHC. The catalytic turnover frequencies correlated strongly to the average ν_{CO} stretches found in the corresponding iridium carbonyl complexes **4a–e**. Hammett plots suggested that inductive effects are generally more important than resonance effects—probably a result of poor π overlap between the aryl groups and the heterocycle. Electronic variation of the 1,3-aryl groups seemed to have a noticeably greater effect on turnover frequency than variation of the 4,5-aryl groups. In general, electron σ-withdrawing methoxy and fluorine substituents hamper catalysis. The exception is complex **3b**, which appears to be the most active mono-NHC iridium-based transfer hydrogenation catalyst. Ostensibly, its *para*-C_6H_4OMe aryl groups in the 1,3 positions contribute electron density *via* resonance and assuage the loss of electron density at iridium during the rate-limiting transfer of hydride to a ligated ketone.

Indeed, the substituents of *N*-heterocyclic carbenes can be electronically tuned to optimize catalysis. With just a handful of catalysts, we have demonstrated the importance of substitution at all four positions of imidazolylidene NHCs and we believe that further optimization is certainly possible with this and other catalytic systems.

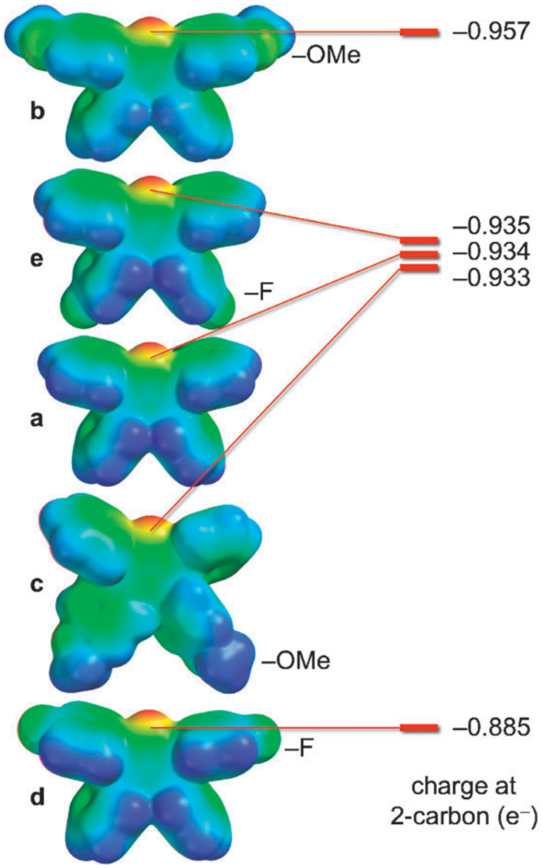

Fig. 3 Calculated (DFT B3LYP 6-31G*) electrostatic charge on the 2-carbon of the free carbenes excised from NHC–AgCl complexes **5a**–**e**.

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