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Enabling Bifunctionality and Hemilability of N-Heteroaryl NHC Complexes

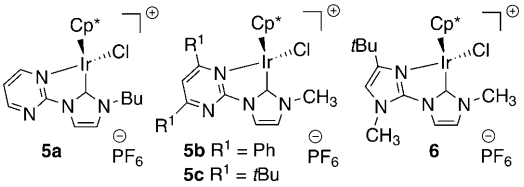
Zephen G. Specht,[a] Sara A. Cortes-Llamas,[a, d] Hai N. Tran,[a] Christoffel J. van Niekerk,[a] Khing T. Rancudo,[a] James A. Golen,[b] Curtis E. Moore,[b] Arnold L. Rheingold,[b] Tammy J. Dwyer,[c] and Douglas B. Grotjahn*[a]

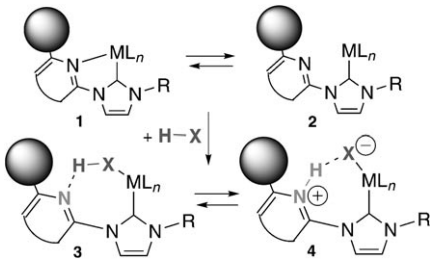
N-Heterocyclic carbene (NHC) complexes have been shown to be extremely versatile and stable catalysts for reactions as diverse as olefin metathesis, transfer hydrogenation, and C-C coupling reactions.[1] NHCs are attractive ligands due to their strong σ-donating ability, poor back bonding,[2a–h] and relative air, moisture, and thermal stability of their complexes.[2e,g,i]

Electronic and steric optimization of the properties of NHC-metal complexes is possible through NHC ligand design.[2g,j,k] Further improvement of catalyst performance through NHC functionalization[3] has been studied using a variety of pendant groups, including heterocycle, phosphine, amine, and imine donor functions. In many cases the added ligand creates a stable chelate or pincer, whereas in other cases a hemilabile system and its temporary ligand loss (as in **2**) favor catalysis.[4]

In contrast, this paper introduces a fundamentally different approach, where a substituent on an NHC ligand will act as a hydrogen bond acceptor (**3**) or base (**4**), which could facilitate catalysis (Scheme 1). Some recent studies on NHC metal complexes have raised the possibility of pendant nitrogen involvement,[5] though as far as we are aware, no direct evidence was presented in these studies.

In particular, for **5a**,[5b] decoordination of the pyrimidine (cf. **1**→**2**) would make a basic nitrogen available near the metal active site (cf. **2**→**3** or **4**). However, the NMR spectrum of **5a** was reported to remain sharp even at 110 °C,[5b] suggesting that decoordination and rotation about the pyrimidine–NHC bond is a process with a high activation barrier. Therefore, in order to fully realize the potential of NHC ligands with pendant heterocyclic bases their ability to chelate with a metal must be decreased (Scheme 1), and we hypothesized that this could be achieved by introducing a large substituent R^1. Here we report successful strategies toward achieving this aim, which should be of general application to NHC chemistry.





Scheme 1. Enabling chemistry of a pendant group.

Although many (pyridyl)-[6] and fewer (pyrimidyl)NHC complexes are known,[7] we were interested in probing more basic heterocycles; as far as we are aware, there are no other reports of imidazolyl(NHC) ligands. Syntheses[8] of (heteroaryl)NHC ligands start with coupling of sodium imidazolate with halogenated heterocycles **7** or **11** (Scheme 2). The pyrimidyl cases reacted at considerably lower temperature (110–140 °C)[8] than did **11**, reflecting the significant differences between the two aromatic systems. Transformation of **8** or **12** by methylation at the most reactive nitrogen and ion exchange gave **9c**-PF_6 or **13**-PF_6, which was converted to a silver carbene complex, and transmetalated to give **5c**, or **6** in high yields. The rhodium analog of **5c** (**5c**-Rh) was made for comparison of second- and third-row metals. All complexes were isolated as rather air-stable solids. For com-

[a] Z. G. Specht, Prof. S. A. Cortes-Llamas, H. N. Tran, C. J. van Niekerk, K. T. Rancudo, Prof. D. B. Grotjahn
Department of Chemistry and Biochemistry
San Diego State University
5500 Campanile Drive San Diego, CA 92182-1030 (USA)
Fax: (+1) 619-594-4634
E-mail: grotjahn@chemistry.sdsu.edu

[b] Prof. J. A. Golen, Dr. C. E. Moore, Prof. A. L. Rheingold
Department of Chemistry and Biochemistry
University of California at San Diego
La Jolla, CA 92093-0385 (USA)

[c] Prof. T. J. Dwyer
Department of Chemistry and Biochemistry
University of San Diego
San Diego, CA 92110 (USA)

[d] Prof. S. A. Cortes-Llamas
Fulbright Scholar on leave from Universidad de Guadalajara to SDSU.

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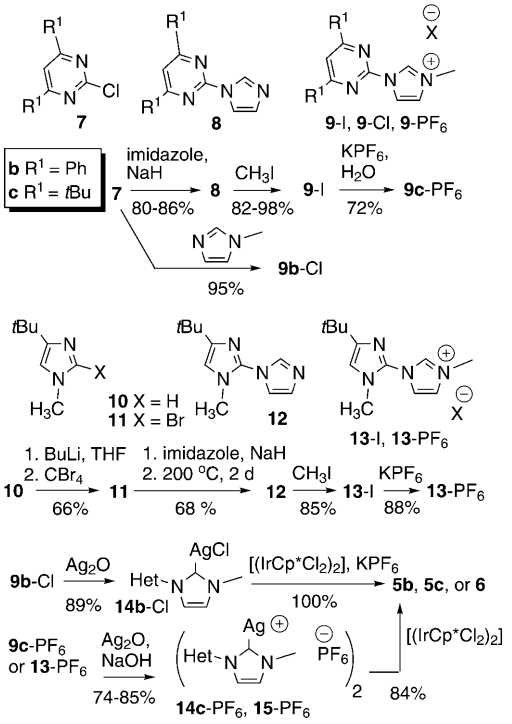


Scheme 2. Synthesis of new N-heteroaryl NHC complexes.

parisons, complex **5a** was made according to the literature.[5b]

Samples of each new species were analyzed by single-crystal X-ray diffraction, with key results shown in Table 1 and the structure of **5c** (Figure 1).[9] All complexes exhibited octahedral geometry about the metal, with consistent distortion imposed by the chelating (heteroaryl)NHC unit (C-Ir-N angles ca. 74.6–76.7°).

Table 1. Key bond lengths [Å] and angles [°][a] and activation energy of pyrimidyl ring flip (E_a [kcal mol^{-1}]).

	Ir–C	Ir–N	Sum	C-Ir-N	Torsion[b]	E_a
5a	2.044(7)	2.109(6)	4.153	76.7(3)	1.8	29.6±0.9
5b	1.996(3)	2.180(2)	4.176	76.5(1)	4.1	22.0±0.3
5c	1.990(7)	2.266(6)	4.256	75.4(3)	7.8	12.5±0.2
5c-Rh	1.998(2)	2.317(2)	4.315	74.60(9)	7.4	14.3±0.3
6	1.947(8)	2.200(6)	4.147	76.3(3)	0.2	NA[c]

[a] Literature X-ray data for **5a**.[5b] [b] Defined as (for example, looking at Figure 1) carbene C-N3-C-N1 (coordinating N) angle. [c] NA = not applicable.

Striking features of data in Table 1 are 1) progressive lengthening of the Ir–N bond as (heteroaryl) substitution becomes more sterically demanding, with a difference between **5a** and **5c**-Rh of 9%, 2) compensation for Ir–N lengthening by Ir–C contraction, and 3) shorter metal–chelate bonds for imidazolyl derivative **6** than pyrimidyl analogues with the same *tert*-butyl substitution (**5c** or **5c**-Rh). Moreover, Figure 1 shows how the pyrimidyl ring in **5c** is distorted from planarity by interaction of the *tert*-butyl group closest to the metal with the Cp*M fragment; in Supporting Information, Figure S3 of **5b** shows a similar interaction involving a phenyl ring.

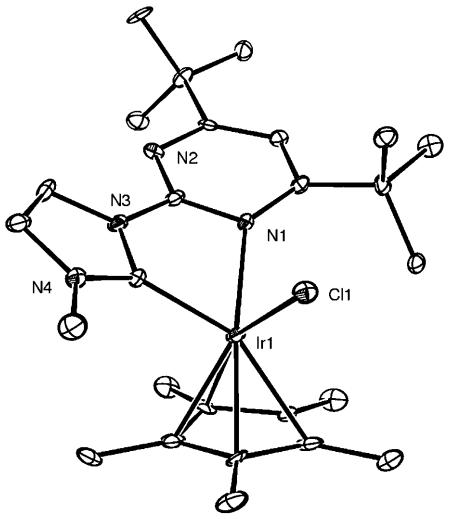
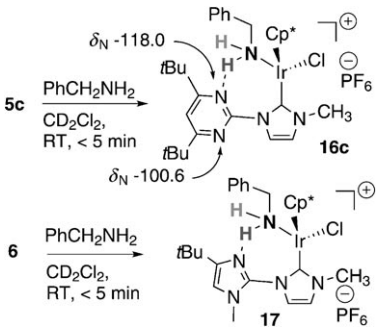


Figure 1. Molecular structure of the cation of **5c**.

The lability of the chelate in **5c** and **5c**-Rh suggested by solid-state data was confirmed by ^{1}H NMR spectra at 30°C showing a single broadened resonance for the two *tert*-butyl groups.

Quantification of ligand dynamics (last column in Table 1) was obtained by variable-temperature NMR experiments. The case of **5a** required EXSY in the range of 110-135°C, whereas for **5c** and **5c**-Rh line-shape analyses of ^{1}H NMR spectra between −40 and +30°C sufficed. The lowered activation energies clearly show the dramatic effects of phenyl or *tert*-butyl groups on the strength of the metal-nitrogen bond.

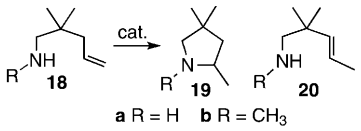
Preliminary results show that weakening the chelation has significant effects on ligand binding: benzylamine reacted with either **5c** or **6**, forming adducts **16c** and **17** quantitatively (Scheme 3). In contrast, **5a** remains completely intact. Distinctive features of **16c** and **17** include a four-spin system for the -CH_2NH_2 unit, with the two NH protons resonating at 6.63 and 4.17 ppm (**16c**), and 3.95 and 7.67 ppm (**17**). NMR spectroscopy was used successfully to examine hydro-



Scheme 3. Intramolecular hydrogen bonding of one benzylamine NH and pendant base as observed by ^{15}N NMR chemical shifts.

gen bonding. For **17**, as determined by ^{1}H-^{15}N gHMBC correlation on natural abundance material, an upfield ^{15}N chemical shift (by ca. 10 ppm) for the basic imidazolyl nitrogen (−135.3 ppm) relative to values seen for **13**-PF_6 and **15**-PF_6 (−125.3 and −121.2 ppm, respectively) may be considered useful spectroscopic evidence for the intramolecular hydrogen bonding shown.[8,10] For the pyrimidyl system of **16c** at 30 °C, a single set of ^{1}H and ^{13}C NMR peaks for the two *t*Bu groups suggest free rotation around the heteroaryl–NHC bond; moreover for the pyrimidyl nitrogen atom in the ^{1}H-^{15}N gHMBC spectrum a single peak at −108.5 ppm was seen. In contrast, at −90 °C, two nitrogen ^{1}H-^{15}N gHMBC crosspeaks were seen at −100.6 and −118.0 ppm, clearly showing an upfield shift of 17.4 ppm which is strong evidence[10] for hydrogen-bond acceptance by one pyrimidyl nitrogen.

Table 2. NMR yields [%] of **19** and **20** from catalyzed conversion of primary (**18a**) or secondary (**18b**) amines by cyclization or isomerization.[a]



	Catalyst	Substrate	Conditions[a]	1 h			24 h			72 h		
				18	**19**	**20**	**18**	**19**	**20**	**18**	**19**	**20**
1	[(IrCp*Cl_2)$_2$]	**18a**	A							72	0	26
2	**5c**[b]	**18a**	A				4	68	9	0	72	5
3	**5c**[b]	**18a**	B	57	29	4.4	0	75	3.4	0	64	0.4
4	**5c**	**18b**	B	2.9	89	2.0	3.0[c]	89[c]	2.0[c]			
5	**5c**-Rh	**18a**	A				9	0	82	3	0	94
6	**5b**	**18a**	A				87	0	9	69	10	18
7	**5a**	**18a**	A							98.5	0	1.5
8	**6**	**18a**	A				65	27	0	36	55	3
9	**6**	**18b**	B	37	62	3.9	3.8	86	4.4			

[a] Conditions A: **18a** (0.25 mmol) and catalyst (5 mol %; 2.5 mol % in the case of entry 1) in toluene (1.0 mL) at 100 °C. Yields shown are based ^{1}H NMR spectroscopy, averaging results from two separate runs, except for entry 1, using 1,3,5-trimethoxybenzene as an internal standard. No entry means yield not determined at that time. Conditions B: same quantities as in A, except reaction run in [D_8]THF and analyzed directly, and only one run was used. [b] In entries 2 and 3 yields of **19a** may be lower because of a dehydrogenation side reaction, forming an imine. [c] Data collected after 3 h, after which the reaction did not proceed further.

Catalyzed cyclization of aminoalkenes **18a** or **18b** to give **19a**,**b** (Table 2) was chosen as a test reaction because of ongoing and intense synthetic and mechanistic interest in alkene hydroamination.[11] Table 2 shows that **5c** is the most active of (heteroaryl)NHC catalysts examined, with **6** as the second most active. Looking at results from primary amine **18a**, among (pyrimidyl)NHC derivatives, increase in conversion of **18a** occurs on going from **5a**, which is virtually inactive (entry 7), to **5b**, which is about as active as [(IrCp*Cl_2)$_2$] (entries 6 and 1), to **5c**, which is much more active (entries 2 and 3). The effect of changing from toluene to THF as the solvent was minimal (entries 2 and 3). Intriguingly, congener **5c**-Rh (entry 5) gives isomerization exclusively as quickly as **5c** performs selective hydroamination, showing a dramatic role for the central metal in the course of the cyclization. Although our preliminary results have not resulted in a hydroamination catalyst significantly more active than recent impressive improvements in the state-of-the-art,[11a–e,q] nonetheless the fact that a completely inactive NHC-based system (**5a**) can be turned into a synthetically useful one constitutes a significant proof of concept. We also note that the consumption of the secondary amine substrate **18b** is at least 20 times faster than that of the primary amine (entry 4 versus entry 3), affording cyclized product in higher yield (89 %) using **5c**, which are differences consistent with results from other known rhodium and iridium based catalysts.[11b,i] Given the variety of mechanistic possibilities for hydroamination reactions[12] and their synthetic utility, further work on these reactions is underway.

In conclusion, increasing the steric bulk around the pendant nitrogen atom results in dramatic lengthening of the M–N bond as revealed by X-ray crystallography, dynamic NMR behavior, improved ligand binding, and catalysis of intramolecular hydroamination, a reaction of significant mechanistic and synthetic interest. The applications of these findings, which are expected to be applicable to a wide variety of NHC systems, are a subject of ongoing in work in these laboratories.

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Keywords: cyclization · iridium · N-heterocyclic carbenes · NMR spectroscopy · pendant base

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[12] For recent discussions, see references [11a] and [11b].

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