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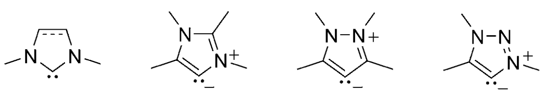
Stability and Electronic Properties of Imidazole-Based Mesoionic Carbenes

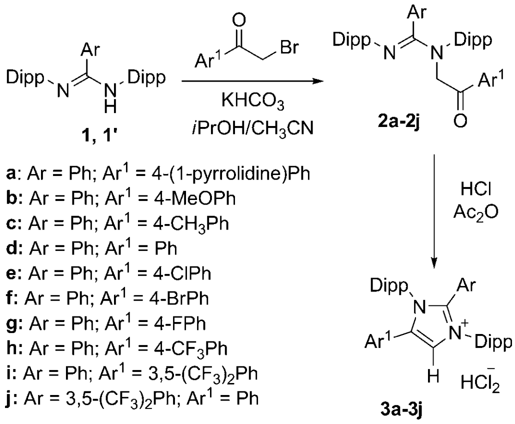
Gaël Ung and Guy Bertrand*[a]

During the last two decades, stable carbenes,[1,2] especially N-heterocyclic carbenes (NHCs) (**A**), have been widely used as ligand for transition-metal complexes.[3] Among their most appealing features is their strong σ-donor ability, which can be superior to that of very basic phosphines. Moreover, there are numerous synthetic routes towards NHCs,[4] which allows a significant tuning of their electronic properties.[5] As recently noted by Dröge and Glorius,[6] "understanding and tuning their distinct properties has been and will be key to the success for improving catalytic activity and other applications." Recently, a new family of stable carbenes has emerged. Named abnormal carbenes (aNHCs)[7] or mesoionic carbenes (MICs),[8] compounds **B**–**D**[9] exhibit stronger electron-donor properties than classical NHCs, and give rise to robust complexes.[2a,10] Here we report the first study of the influence of the substituents on the electronic properties of imidazol-5-ylidenes **B**.



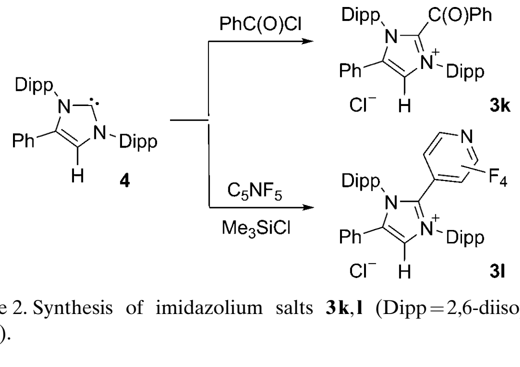
A **B** **C** **D**

To study the electronic influence of the substituent in the 4- position, we focused our studies on *para*-substituted phenyl groups, which preserve a comparable steric environment around the carbene center (Scheme 1). Derivatives **2a–i** were prepared by a slightly modified published procedure.[9a] Dehydrative cyclization of **2a–i** readily occurred by using a slight excess of concentrated hydrochloric acid in acetic anhydride, affording imidazolium salts **3a–i** in good to excellent yields (67–92 %).



Scheme 1. Synthesis of imidazolium salts **3a–j** (Dipp = 2,6-diisopropylphenyl); **1**: Ar = Ph, **1′**: Ar = 3,5-(CF$_3$)$_2$C$_6$H$_3$.

To extend our study to the influence of the substituent at the 2-position of MICs, imidazolium salts **3j–l** were prepared. Heterocycle **3j** was synthesized in moderate yield by using the same synthetic route as for **3a–i**, but starting from the 3,5-bis-CF$_3$-phenyl C-substituted amidine **1′** (Scheme 1). Since the amidines corresponding to imidazolium salts **3k**,**l** are difficult to prepare, we chose a different synthetic strategy, which involves the nucleophilicity of NHCs (Scheme 2). 4-Phenyl-substituted NHC **4**[11] was treated with benzoyl chloride, affording **3k** in 99 % yield. Similarly, addition of pentafluoropyridine, in the presence of trimethylchlorosilane, gave rise to imidazolium salt **3l** in 84 % yield.



Scheme 2. Synthesis of imidazolium salts **3k**,**l** (Dipp = 2,6-diisopropylphenyl).

Having in hand a variety of MIC precursors, the deprotonation reactions were carried out with excess potassium bis(trimethylsilyl)amide (KHMDS). We first studied the stability of free MICs **5a–l**. MIC **5a** cannot be isolated since it rearranges to compound **6** in a few minutes (Scheme 3). This product formally results from the deprotonation of an isopropyl substituent of the Dipp group by the carbene center

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[a] G. Ung, Prof. G. Bertrand
UCR-CNRS Joint Research Chemistry Laboratory (UMI 2957)
Department of Chemistry
University of California Riverside
Riverside, CA 92521-0403 (USA)
Fax: (+1) 951-827-2725
E-mail: guy.bertrand@ucr.edu
Homepage: http://research.chem.ucr.edu/groups/bertrand/guybertrandwebpage/

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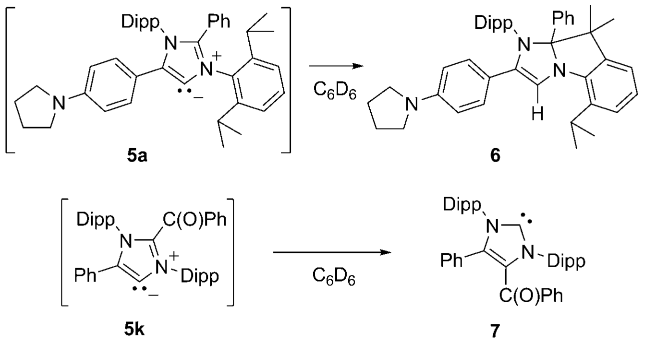

Scheme 3. Rearrangement of MICs **5a** and **5k** (Dipp = 2,6-diisopropylphenyl).

Table 1. Selected ^{13}C NMR data for carbenes **5** and Tolman electronic parameter (TEP) for complexes **8**.

	C-4 substituent	C-2 substituent	δ $C_{carbene}$ **5** [ppm]	δ C_{Ir} **8** [ppm]	TEP [cm^{-1}][a]
a	4-(C_4H_8N)Ph	Ph	N/A[b]	157.8	2036.5
b	4-MeOPh	Ph	200.2	159.7	2039.3
c	4-CH_3Ph	Ph	200.0	159.1	2038.3
d	Ph	Ph	201.9	159.6	2038.5
e	4-ClPh	Ph	201.3	160.0	2039.8
f	4-BrPh	Ph	202.9	160.3	2039.8
g	4-FPh	Ph	200.1	159.7	2040.5
h	4-CF_3Ph	Ph	204.1	161.3	2040.9
i	3,5-$(CF_3)_2$Ph	Ph	205.8	162.9	2043.0
j	Ph	3,5-$(CF_3)_2$Ph	202.9	161.5	2041.1
k	Ph	COPh	N/A[b]	164.8	2041.3
l	Ph	2,3,5,6-F_4-C_5N	N/A[b]	165.7	2041.4

[a] TEP [cm^{-1}] = 0.847 ν_{CO}^{av} + 336.[15] [b] Carbenes **5a**, **5k**, and **5l** could not be spectroscopically characterized.

followed by nucleophilic addition of the resulting benzyl anion to C-2. This rearrangement process has previously been reported when the C-4 substituent was an unsubstituted phenyl group (**5d**), but only under heating at 50 °C for two days.[9a] The significant rate enhancement observed for **5a** can readily be rationalized by the enhanced basicity of the carbene bearing the strong electron-donating pyrrolidine in the *para*-position of the aryl group on C-4. MICs **5b** and **5c**, also bearing electron-donating substituents, can be isolated and fully characterized by NMR spectroscopy, but decompose in a few hours in solution, as well as in the solid state, giving complex mixtures. MICs **5e**–**5i** and **5j**, bearing an electron-withdrawing group on the C-4 and C-2 aryl group, respectively, are stable both in solution and in the solid state. For example, no decomposition was observed for **5i** after a week in solution at room temperature. Not surprisingly, MIC **5k** cannot be spectroscopically observed since it spontaneously rearranges into its NHC isomer **7** (Scheme 3), as already observed for similar carbenes.[12] Lastly, **5l** also appears to be unstable, probably because of intermolecular reactions of the nucleophilic carbene with the electron-poor tetrafluoropyridino substituent.

The ^{13}C NMR spectra of MICs **5b**–**j** exhibit carbene carbon signals at approximately $\delta = 200$ ppm, with a rather consistent trend; electron-withdrawing substituents induce a small downfield shift (Table 1). By comparing **5i** and **5j**, it appears that the influence of the substituent at C-4 is stronger than that at C-2. The small effect on the ^{13}C chemical shift ($\Delta < 6$ ppm) is consistent with the minor chemical shift differences observed in C-4 substituted 1,2,3-triazol-5-ylidenes.[13] To better quantify the electronic effects of the C-4 and C-2 substituents, the corresponding iridium chloride *cis*-dicarbonyl complexes **8a**–**l** were prepared. Interestingly, even when the free MICs are not isolable, the corresponding [(MIC)IrCl(cod)] complexes can be synthesized in good yields by performing the deprotonation of imidazolium salts in the presence of half an equivalent of [{IrCl(cod)}$_2$]. Subsequent treatment with excess of carbon monoxide afforded [(MIC)IrCl(CO)$_2$] complexes **8a**–**l**, which were isolated in good yields (57–89 %; structure of **8g** is given in Figure 1).

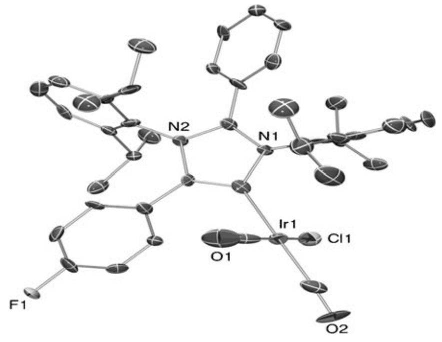

Figure 1. Molecular structure of **8g** in the solid state (ellipsoids are drawn in 50 % probability; hydrogen atoms are omitted for clarity).[14]

The Tolman electronic parameters (TEPs)[16] of complexes **8a**–**l** are given in Table 1. The observed values, ranging from 2036.5 cm^{-1} (**8a**) to 2043.0 cm^{-1} (**8i**), clearly indicate that all MICs **5a**–**l**, even those bearing electron-withdrawing groups, are significantly stronger electron donors than the classical NHC isomers (Figure 2). The TEP of complexes **8a**–**i** follows the expected trend, and the differences in the values

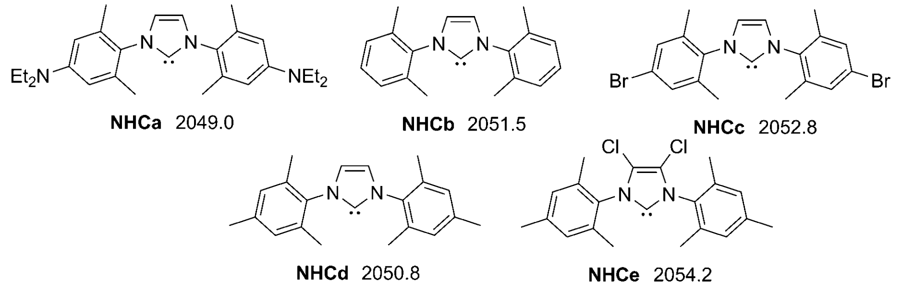

Figure 2. TEP values of selected NHCs

are comparable to those observed by varying the substituent at the two nitrogen atoms of NHCs, as exemplified by **NHCa–c**.[5g] Confirming the NMR data, the IR study shows that the influence of the C-2 substituent is much weaker than that of the C-4 one, which can be expected since the latter is in direct conjugation with the carbene center. However, note that in the case of NHCs, the substituents at C-4,5 have a significant influence on the TEP as evidenced by comparing **NHCd**[5g] and **NHCe**.[17,18]

In summary, we have successfully improved the synthesis of imidazole-based MICs, which allowed the placement of a series of electro-active substituents in close proximity to the carbene center. Electron-withdrawing groups stabilize MICs. Electron-donating substituents do not allow the isolation of the free carbenes, but the corresponding metal complexes can be prepared by performing the deprotonation of imidazolium salts in the presence of the metal fragment. According to the Tolman electronic parameters, MICs are stronger electron donors than NHCs, even when they bear electron-withdrawing substituents. The substituent at C-2 modestly affects the electronic properties of MICs, but the group in 4-position does allow a significant tuning, which will be of interest for the catalytic community.

Experimental Section

General information: All manipulations were performed under an atmosphere of dry argon using standard Schlenk or dry box techniques. Solvents were dried by standard methods and distilled under argon.

Synthesis of imidazolium salts 3a–j: A 93:7 2-propanol/acetonitrile solution of amidine **1** or **1′**, 2-bromo-1-arylethanone (1.1 equiv), and potassium bicarbonate (2.4 equiv) was heated under reflux for 5 h. Hot filtration, followed by slow evaporation of the solvent under reduced pressure induced the precipitation of products **2a–j**. HCl (37% in water, 2 mL) was added dropwise to a cold suspension (0°C) of **2a–j** in acetic anhydride (2.2 mL) under vigorous stirring. The mixture was warmed to room temperature and stirred overnight. Water was added until a white precipitate persists. The resulting suspension was extracted with dichloromethane. The combined organic layer were washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated under vacuum. The residue was stirred with diethyl ether (15 mL) for 45 min, and then filtered. The resulting solid was washed with diethyl ether to afford imidazolium salts **3a–j**.

Synthesis of imidazolium salts 3k,l: A solution of the electrophile in hexanes (0.5 mmol in 5 mL) was added to a solution of NHC **4** in hexanes at −78°C (0.5 mmol in 5 mL). The resulting suspension was stirred for 1 h at room temperature. The solid was allowed to decant. Filtration, followed by drying under vacuum afforded the desired imidazolium salts **3k**,**l**.

Synthesis of MICs 5b–j: THF (2 mL) was added to a solid mixture of imidazolium salts **3b–j** and potassium hexamethyldisilazide (2 equiv) at −78°C. The mixture was stirred 30 min at −78°C, and then warmed to room temperature and stirred 30 min. Evaporation of the solvent gave a solid residue, which was extracted with hexanes. Filtration and evaporation of the solvent afforded the free carbene. MIC **5b**,**c** were characterized by ^{1}H and ^{13}C spectroscopy but decomposed after a few hours in solution.

Synthesis of complexes 8b–j: THF (1.5 mL) was added to a solid mixture of MICs **5b–j** and chloro-(1,5-cyclooctadiene)iridium(I) dimer (0.5 equiv) at room temperature. The mixture was stirred overnight at room temperature. Evaporation of the solvent gave a solid residue, which was extracted with diethyl ether. Filtration and evaporation of the diethyl ether afforded a brown solid, which was dissolved in benzene. Then carbon monoxide was bubbled through the mixture for 45 min. The solvent was evaporated and the resulting solid was purified by column chromatography on silica gel (eluant hexanes/ethyl acetate). Crystallization in chloroform/hexanes afforded the desired complexes **5b–j** as yellow solids.

Synthesis of complexes 8a,k,l: THF (3 mL) was added to a solid mixture of imidazolium salts **3a**,**k**,**l**, potassium hexamethyldisilazide (2 equiv) and chloro-(1,5-cyclooctadiene)iridium(I) dimer (0.5 equiv) at −78°C. The mixture was stirred for 30 min at −78°C, and then warmed to room temperature and stirred overnight. Evaporation of the solvent gave a solid residue, which was extracted with diethyl ether. Filtration and evaporation of the diethyl ether afforded a brown solid, which was dissolved in benzene. The carbon monoxide was bubbled through the mixture for 45 min. The solvent was evaporated and the resulting solid was purified by column chromatography on silica gel (eluant hexanes/ethyl acetate). Crystallization in chloroform/hexanes afforded the desired complex as a yellow solid.

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Keywords: electronic effects · iridium · ligands · mesoionic carbenes

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