

Imidazo[1,5-a]pyridine: A Versatile Architecture for Stable N-Heterocyclic Carbenes

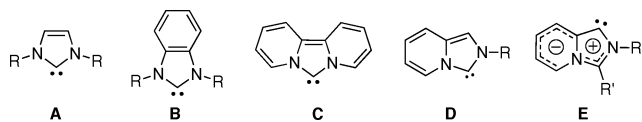
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N-Heterocyclic carbenes (NHCs) have emerged during the past decade as a new type of stable compounds^{1,2} and as a powerful class of C-ligands. The stabilizing properties by NHCs, expressed by strong metal carbene bonds and slow dissociation rates, have been key for the development of a number of applications in catalysis.³ To exploit further the potential of NHCs as C-ligands, it is necessary to provide additional tools for the tuning of their electronic properties, an aspect where the more developed trivalent phosphorus-based ligands (phosphanes, phosphites, phosphoramidites, etc.) offer much higher variability.

The construction of benzannulated derivatives is a very simple strategy to modify the properties of Arduengo's "original" imidazol-2-ylidenes **A**,¹ as was demonstrated in the benzimidazol series **B**.⁴ An interesting variation is the bipyridine-derived carbene **C**,⁵ but this rather unstable carbene was never used as a C-ligand for transition metals. We now wish to report on the use of the imidazo[1,5-a]pyridine skeleton for the synthesis of unprecedented carbenes **D** and the mesoionic structures **E**, containing a single bridgehead nitrogen, and the first transition-metal complexes derived therefrom.



A straightforward synthesis of alkyl derivatives **2a,b** was accomplished by alkylation of known **1**, carrying a methyl group at C(5) for an eventual kinetic protection of the target carbene **4** (Scheme 1, Table 1, entries 1 and 2). A second approach was designed from formamides **3c–f**, which were transformed into *N*-alkyl/aryl imidazo[1,5-a]pyridinium salts **2c–f** by POCl₃-mediated cyclization. Products were isolated either as chlorides [**2c**, **2d(Cl)**; entries 3 and 4] or as hexafluorophosphates [**2d(PF₆)**, **2e**, **2f**; entries 5–7] after anion exchange with KPF₆. This second route is more versatile, offering fewer restrictions in the nature of the N(2)R group and involving more accessible starting materials.

The stability of the free carbenes **4** proved to be strongly dependent on their steric environment. Thus, deprotonation of 5-unsubstituted **2c,f** by NaH/KO^tBu (cat.) in dry THF resulted in the formation of a complex mixture, presumed to arise from formation and decomposition of the desired carbene. In sharp contrast, deprotonation of 5-substituted azolium salts **2a,b,d,e** proceeded cleanly to afford free carbenes **4a,b,d,e** (Scheme 1). These products were found to be stable for long periods at room temperature and could be isolated as viscous oils or amorphous solids and characterized by ¹H and ¹³C NMR. The ¹³C resonance for C(3) of **4** ($\delta = 206\text{--}209$ ppm), slightly upfield with

Scheme 1

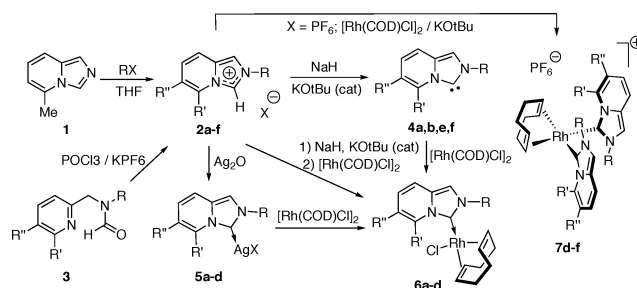


Table 1. Synthesis of Imidazo[1,5-a]pyridinium Salts **2a–f**

entry	educt	reagent	product	yield (%)
1	1	MeI	2a	97
2	1	BnBr	2b	94
3	3c	POCl ₃	2c	50
4	3d	POCl ₃	2d(Cl)	60
5	3d	POCl ₃ /KPF ₆	2d(PF₆)	58
6	3e	POCl ₃ /KPF ₆	2e	52
7	3f	POCl ₃ /KPF ₆	2f	48

respect to Arduengo's type **A** carbenes, confirmed their free carbene structure.

The properties of compounds **4** as C-ligands were investigated: RhImPy(COD)Cl (ImPy = Imidazo[1,5-a]pyridine-3-ylidene) complexes **6** were prepared by: (a) direct metalation of carbenes **6** with [Rh(COD)Cl]₂ (Scheme 1, Table 2, entries 2, 4, and 7) or (b) transmetalation of silver carbene complexes **5**, available from halides **2a–c** and **2d(Cl)** (entries 1, 3, 5, and 6). The single-crystal X-ray analyses of **6b** and **6d** (Figure 1) revealed distorted square-planar geometries (CRhCl 92.8° and 95.4°, respectively), and marked differences in NCRh angles (**6b**: 132.8° versus 123.5°; **6d**: 131.2° versus 124°), both attributed to steric repulsions. As in related structures,⁶ ¹H NMR studies indicated high configurational stability due to restricted rotation around the C(3)–Rh bond, even for C(5)-unsubstituted derivatives such as **6c**. Different behavior was observed when **2d(PF₆)**, **2e**, or **2f** (X = PF₆) were reacted with KO^tBu and [Rh(COD)Cl]₂: cationic 2:1 [Rh(ImPy)₂(COD)]⁺

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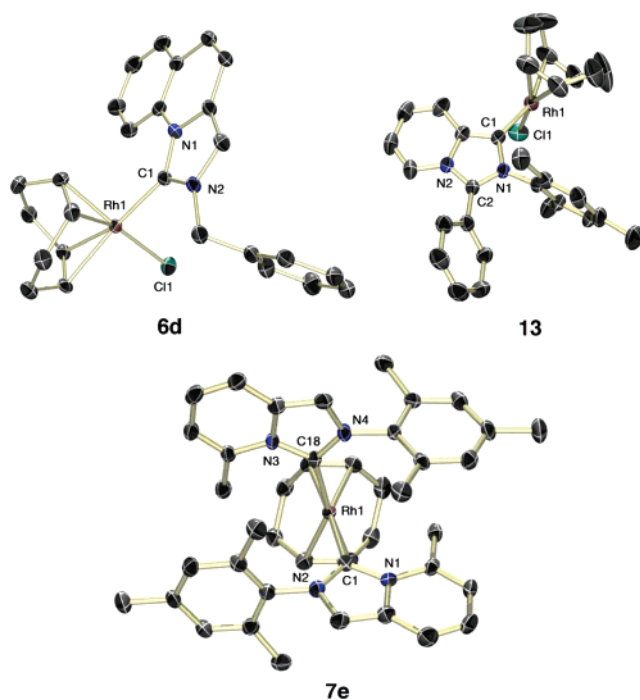
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Table 2. Synthesis of Silver and Rhodium Complexes **5**, **6**, and **7**

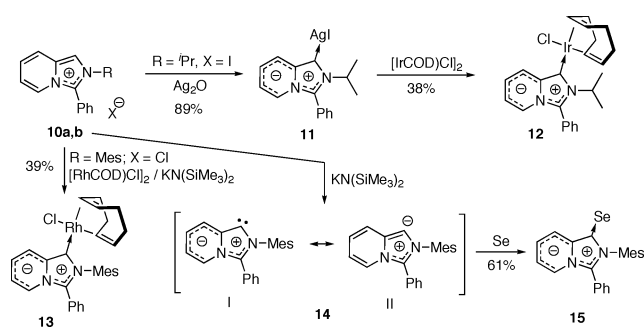
entry	starting material	X	5	yield (%)	6	yield (%)	7	yield (%) ^a
1	2a	I	5a	63	6a	91		
2	4a	—	—	—	6a	93		
3	2b	Br	5b	92	6b	96		
4	4b	—	—	—	6b	94		
5	2c	Cl	5c	98	6c	96		
6	2dCl	Cl	5d	96	6d	92		
8	2dPF₆	PF ₆ ⁻					7d	71 (82)
9	2e	PF ₆ ⁻					7e	72 (86)
10	2f	PF ₆ ⁻					7f	84 (93)

^a Yield of recrystallized product. In parentheses: yield before crystallization.

**Figure 1.** ORTEP drawings for Rh–ImPy complexes **6d**, **7e**, and **13**.

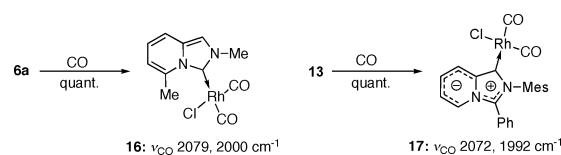
complexes **7d–f** were obtained, even though the Rh/carbene precursor ratio was 1:1 (Scheme 2). Good yields of compounds **7** were observed for reactions performed with the right 2:1 stoichiometry, even for bulky ligands such as **4d,e**. The structures of **7d–f** were also analyzed by X-ray diffraction (see **7e** in Figure 1). It is noteworthy that all these molecules exhibit C₂-symmetric geometry as a result of the “antiparallel” arrangement of the carbene ligands, necessary to avoid severe steric interactions. The ¹H and ¹³C NMR spectra recorded for the crude products confirmed the absence of the meso diastereomers that would result from a “parallel” arrangement of the ImPy ligands in **7**.

The structure of the imidazo[1,5-a]pyridinium salts suggests additional possibilities for the synthesis of unusual structures by deprotonation at C(1).⁷ To this aim, salt **10a** was reacted with Ag₂O to afford Ag complex **11** in 89% yield (Scheme 2). Transmetalation with [Rh(COD)Cl]₂ did not afford the expected Rh(I) complex, but the corresponding Ir(I) complex **12** was obtained in 38% yield by reaction with [Ir(COD)Cl]₂. In contrast, salt **10b**, reacted with [Rh(COD)Cl]₂ under Herrmann conditions⁸ to afford complex **13** in 39% yield. Additionally, “carbene” **14** was trapped by reaction with selenium to afford **15** in 61% yield. The X-ray structure of **13** (Figure 1) reveals a standard C(1)–Rh bond length of 204.3 pm, but a 138.8 pm C(1)–C(9) bond, longer than in **4** or **5** (135.1–135.9 pm). This fact and a higher degree of delocalization in the pyridine

Scheme 2

ring support a strong contribution of the mesoionic form **I**, as drawn in **11**, **12**, **13**, and **15**.

Finally, dicarbonyl Rh complexes **16** and **17** were prepared from **6a** and **13**, and their $\nu(\text{CO})$ stretching frequencies were used to evaluate the σ -donor ability of **4** and **14**. The results indicate that these carbenes are among the strongest σ -donors in the unsaturated series, but still weaker than the best known C-ligands.⁹



In conclusion, the imidazo[1,5-a]pyridine skeleton is a versatile platform for the synthesis of new types of free NHCs and their transition-metal complexes. The effect of electron-withdrawing or -donating groups in ImPy ligands, and the development of applications in catalysis, is currently the object of study in our laboratories.

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Supporting Information Available: Crystallographic data for **6b**, **6d**, **7d**, **7e**, **7f**, and **13**, and experimental procedures (CIF, PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) Arduengo, A. J.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361–363.
- (2) (a) Bourissou, D.; Guerret, O.; Gablaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39–91. (b) Alder, R. W. In *Carbene Chemistry: From Fleeting Intermediates to Powerful Reagents*; Bertrand, G., Ed.; Marcel Dekker: New York 2002; Chapter 5, pp 153–176.
- (3) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309.
- (4) Hahn, F. E.; Wittenbecher, L.; Boese, R.; Bläser, D. *Chem.–Eur. J.* **1999**, *5*, 1931–1935.
- (5) (a) Weiss, R.; Reichel, S.; Handke, M.; Hampel, F. *Angew. Chem., Int. Ed.* **1998**, *37*, 344–346. (b) Weiss, R.; Reichel, S. *Eur. J. Inorg. Chem.* **2000**, 1935–1939.
- (6) Chianese, A. R.; Li, X.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2003**, *22*, 1663.
- (7) For C4(5) carbenes, see: (a) Gründemann, S.; Kovacevic, A.; Albrecht, M.; Faller, J. W.; Crabtree, R. H. *Chem. Commun.* **2001**, 2274–2275. (b) Gründemann, S.; Kovacevic, A.; Albrecht, M.; Faller, J. W.; Crabtree, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 10473–10481. (c) Lebel, H.; Janes, M. K.; Charette, A. B.; Nolan, S. P. *J. Am. Chem. Soc.* **2004**, *126*, 5046–5047.
- (8) Köcher, C.; Herrmann, W. A. *J. Organomet. Chem.* **1997**, *532*, 261–265.
- (9) (a) Mayr, M.; Wurst, K.; Ongania, K.; Buchmeiser, M. R. *Chem.–Eur. J.* **2004**, *10*, 1256–1266. (b) Denk, K.; Sirsch, P.; Herrmann, W. A. *J. Organomet. Chem.* **2002**, *649*, 219–224. (c) Bazinet, P.; Yap, G. P. A.; Richeson, D. S. *J. Am. Chem. Soc.* **2003**, *125*, 13314–13315. (d) Lavallo, V.; Mafhouz, J.; Canac, Y.; Donnadiou, B.; Schoeller, W.; Bertrand, G. *J. Am. Chem. Soc.* **2004**, *126*, 8670–8671. (e) Herrmann, W. A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G. R. *J. Chem.–Eur. J.* **1996**, *2*, 772–780.

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