Fluorinated Ligands

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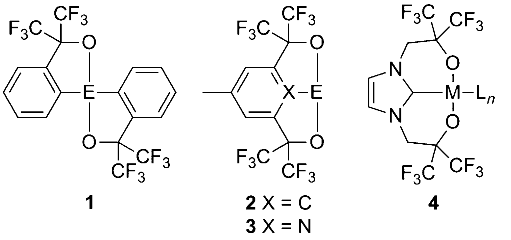
Synthesis and Complexes of Fluoroalkoxy Carbenes

Anthony J. Arduengo III, Joshua S. Dolphin, Gabriela Gurău, William J. Marshall, Joseph C. Nelson, Viacheslav A. Petrov, and Jason W. Runyon**

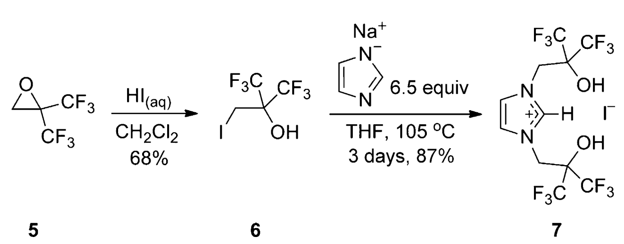
Building on the success of his hexafluorocumylalcohol-derived bidentate ligand **1** (Scheme 1), Martin and co-workers designed two versions of a tridentate ligand, **2** and **3**, which were used to explore the chemistry of main-group elements in unusual coordination environments.[1–4] The relatively electropositive equatorial substituent (C or N, respectively), the electronegative axial substituents ($R-C(CF_3)_2-O$), the formation of favorable five- and six-membered rings, and the Thorpe–Ingold effect all contribute to the efficacy of the Martin ligand.[5] The use of Martin-type ligands for d-block metals is limited, partially owing to the relatively poor aryl–metal bond.



Scheme 1. Bi- and tridentate Martin-type complexes **1**–**3** and a similar architecture, **4**, based on an imidazol-2-ylidene. E = main-group element, M = metal.

The abundance of adducts of hypervalent main-group elements with carbenes and of transition-metal–carbene complexes suggests that replacement of the central aryl group in the Martin-type structures **2** and **3** with an imidazol-2-ylidene (as in **4**) as the central binding moiety should provide a more suitable ligand for d-block metal complexes while taking advantage of all of the other attractive aspects of the Martin ligands.[6–9] A number of popular tridentate ligands already exist, but the architecture of **4** offers a remarkably robust structure.[10–19]

Introduction of an $CH_2C(CF_3)_2OH$ group on an azole is simplified by the availability of hexafluoroisobutylene oxide (**5**).[20–26] In an effort to avoid ring-opening polymerization of the epoxide, initial attempts to prepare the desired tridentate ligands involved the use of the iodohydrin **6** (derived from epoxide **5**) as an alkylating agent.[27] When a solution of sodium imidazolide in THF was heated at reflux with two equivalents of the iodohydrin over a period of days, the imidazolium salt **7** was formed (Scheme 2).



Scheme 2. Synthesis of bis(fluoroalcohol)-substituted imidazolium iodides.

The reaction can be carried out as a one-pot process or as two successive alkylation steps to form first the mono-substituted imidazole and eventually the desired imidazolium salt. The chemical shifts in **7** resemble those of other imidazolium salts ($\delta_H(C2{-}H) \approx 9$ ppm; $\delta_C(C2) \approx 140$ ppm).[28] The crystal packing of **7** (Figure 1) displays a hydrogen-bonded network of cations and anions. Hydrogen bonds are formed between the alcohol hydrogen atoms and the iodide, and a third hydrogen bond is formed between the

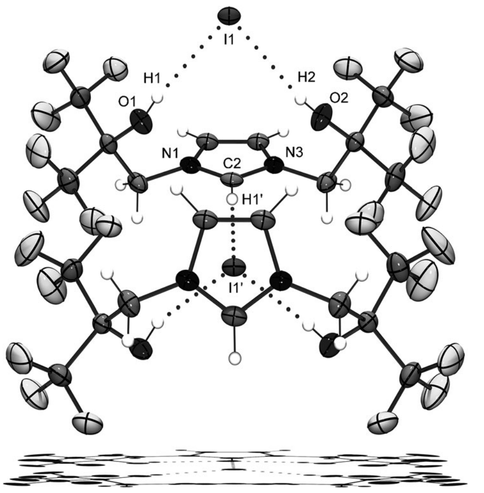


Figure 1. Diagram of the X-ray crystal structure of the imidazolium salt **7**. Thermal ellipsoids are drawn at the 50% probability level; hydrogen-bond distances [Å]: H1'–I1' 3.07, H1/H2–I1 2.75.

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[*] Prof. Dr. A. J. Arduengo III, J. S. Dolphin, Dr. G. Gurău, J. C. Nelson, Dr. J. W. Runyon
The University of Alabama, Department of Chemistry (USA)
E-mail: aj@ajarduengo.net
jwrunyon@crimson.ua.edu
Homepage: http://ajarduengo.net
W. J. Marshall, Dr. V. A. Petrov
DuPont Central Research and Development
Wilmington, DE 19880-0500 (USA)

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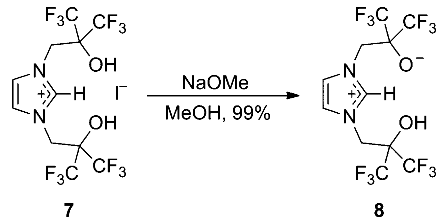
hydrogen atom at C2 (H1′) of another cation and the iodide. Electrostatic interactions between the imidazolium ions and iodide counterions are also evident ($r = 3.47$ Å).

The electron-withdrawing nature of the geminal CF_3 groups renders the alcohol hydrogen atoms more acidic than those on the azolium ring. These acidities are expected to be very different from those found in the tridentate bis(alkoxy) carbene ligands introduced by Arnold and coworkers.[29–34] The acidity and stability of the fluoroalkoxy carbene ligands reported herein offer distinct advantages over their nonfluorinated counterparts. Treatment of **7** with one equivalent of a base results in the deprotonation of an alcohol group to form the stable zwitterion **8** (Scheme 3). These fluoroalkoxy zwitterions are unique, because more basic alkoxides have been shown to attack the imidazolium carbon atom (C2).[33] The solubility of compound **8** in nonpolar organic solvents facilitates separation from the imidazolium salt.



Scheme 3. Synthesis of imidazolium fluoroalkoxides.

The growth of crystals of **8** under different solvent conditions resulted in different packing motifs. Both a chain of hydrogen-bonded molecules (Figure 2a) and hydrogen-bonded "dimers" could be obtained (Figure 2b). The hydrogen-bond distances lie in the range of 1.4–2.2 Å. This hydrogen bonding is quite dynamic, as illustrated by the two low-energy crystal motifs and rapid proton tautomerism in fluid solution (the ^{1}H NMR signals for the alcohol and imidazole C2–H hydrogen atoms are broad, whereas the methylene groups appear as a sharp singlet).

The iodohydrin-based synthetic approach to the tridentate ligand is practical. However, complications associated with an iodide counterion in subsequent reactions involving transition metals render this approach undesirable. It was reported that conditions of phase-transfer catalysis (PTC) were successful for the preparation of a pyrazole bearing a $CH_2C(CF_3)_2OH$ nitrogen substituent.[25b,26]. Therefore, the analogous azoles **9**, **13**, and **14** were prepared under PTC conditions (Scheme 4). These adducts were obtained by the treatment of imidazole or triazole with only one equivalent of epoxide **5**. Some over-alkylation occurred during the preparation of **9** and **13**. Thus, a mixture of mono- and bis-substituted azoles (zwitterion **8** or **15**) was obtained, whereby the monoalkylated species was isolated as the major product. Selective alkylation of 1,2,4-triazole proved difficult owing to the multiple nucleophilic centers on the triazole ring. The reaction of 1,2,4-triazole also competes with the oligomerization of epoxide **5**, which leads to a complex mixture. A minor (uncharacterized) symmetrical adduct was observed in the NMR spectra which may be the 4-substituted regioisomer. This compound may be the 4-substituted regioisomer. Adduct **13** could be isolated and was fully characterized (Figure 3); however, the product was obtained in low yield (10%). Although only one isomer was isolated, the existing data are not sufficient to make a conclusion regarding the regioselectivity of this reaction. In stark contrast to the reactivity of 1,2,4-triazole with **5**, the reaction of 1,2,3-triazole with **5** led to only one regioisomer, **14**. No evidence for bisalkylation was found, even when an excess of the epoxide **5** was used.

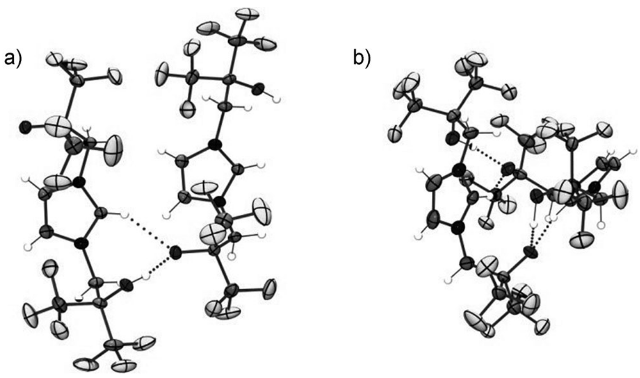
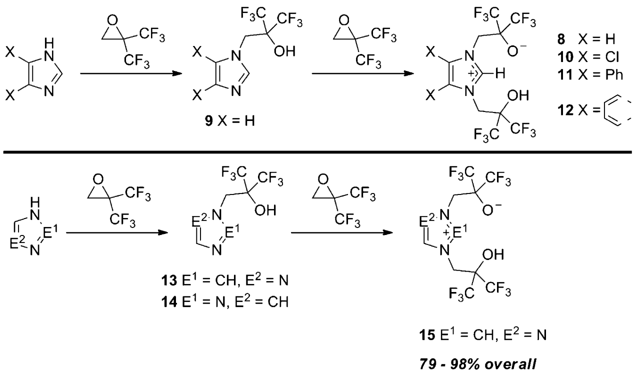


Figure 2. Packing motifs in **8**: a) linear hydrogen-bonding network; b) hydrogen-bonding "dimers". Thermal ellipsoids are drawn at the 50% probability level.



Scheme 4. Alkylation of azoles, including substituted azoles, with epoxide **5**.

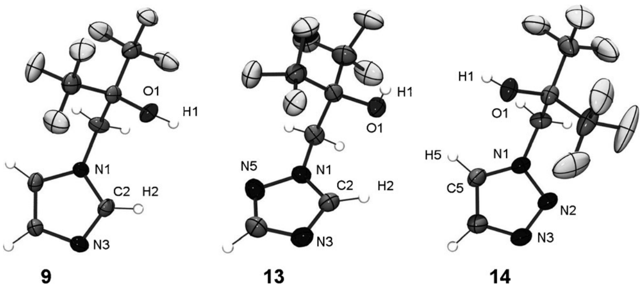


Figure 3. X-ray crystal structures of **9**, **13**, and **14** with thermal ellipsoids drawn at the 50% probability level.

X-ray single-crystal diffraction studies on **9**, **13**, and **14** (Figure 3) confirmed the substitution patterns of the azole rings and indicated that the preferred tautomeric structure is neutral (the proton lies on the oxygen atom), rather than a zwitterionic imidazolium alkoxide.

Since some bis-alkylation occurred in the preparation of monosubstituted azoles even under PTC conditions, it was envisioned that zwitterions **8**, **10**–**12**, and **15** could be obtained in a one-pot reaction without the isolation of an intermediate. Indeed, the addition of exactly two equivalents of epoxide **5** to the initial azoles led to the formation of zwitterions **8**, **10**–**12**, and **15** in good yields with none of the by-products found under PTC conditions. Alkylation occurred exclusively at the nitrogen atoms: no ethoxy ethers derived from oxygen alkylation were observed. In the case of 1,2,4-triazole, alkylation with two equivalents of epoxide **5** afforded only the 1,4-disubstituted isomer. An X-ray crystal structure of **15** (Figure 4) confirmed this substitution pattern and revealed the same hydrogen-bonding tendencies as observed for **8**.

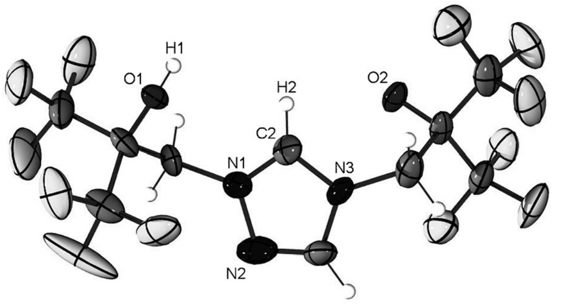
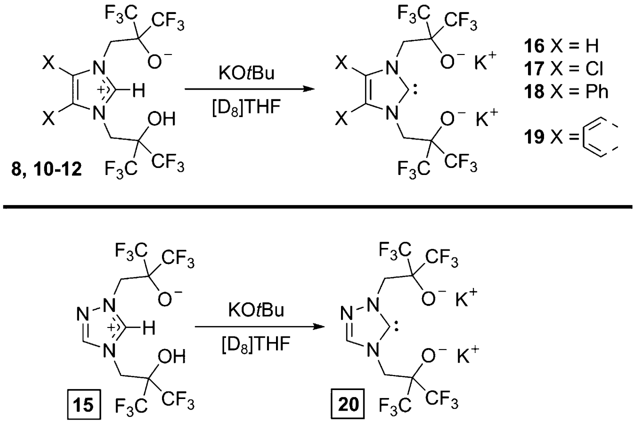


Figure 4. X-ray crystal structure of **15** with thermal ellipsoids drawn at the 50% probability level.

Two different methods were developed for the epoxide-ring-opening alkylation (the reactions were carried out in acetonitrile or toluene). Although some small specific advantages for particular substrates differentiate these two epoxide-based methods, both approaches provide the products in higher overall yields, involve fewer steps, offer broader scope for the synthesis of ligands, and enable simpler purification of the products than the iodohydrin-based method described above.

The treatment of zwitterions **8**, **10**–**12**, and **15** with two equivalents of a strong base generated the free bis(fluoroalkoxy) carbenes **16**–**20** (Scheme 5). The existence of transient carbenes was unambiguously confirmed in situ by ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy. Deprotonation with KO*t*Bu is rapid and complete within minutes. Spectroscopic evidence (multiple broad ^{19}F signals and broad methylene resonances in the ^{1}H NMR spectra) suggests that the alkoxy groups may form ionic aggregates with alkali-metal cations in solution.

The chemical shifts of the carbene carbon atom in **16**–**20** (Table 1) are in good agreement with those of other nonionic carbenes; this similarity suggests little or no carbene–potassium coordination.[35–37] Thus far it has not been possible to isolate single crystals of any of these anionic carbene ligands. Although the free carbenes are conveniently stable in solution for short periods, they decompose when left in solution over days.

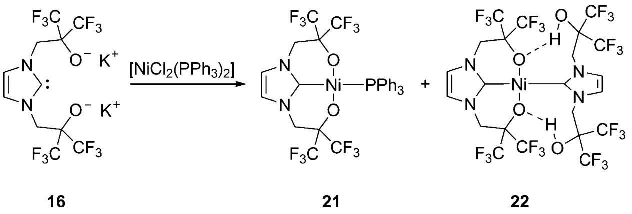


Scheme 5. Preparation of bis(fluoroalkoxy) carbenes.

Table 1: ^{13}C NMR chemical shifts of the C2 carbon atom of carbenes **16**–**20** in [D$_8$]THF.

Compound	δ_C [ppm]
16	218.34
17	220.25
18	219.27
19	229.75
20	212.76

Addition of the anionic fluoroalkoxy carbene **16** to [NiCl$_2$(PPh$_3$)$_2$] afforded the tridentate complex **21** and the bis(carbene) complex **22** (Scheme 6). The latter complex was isolated after workup on neutral alumina. In spite of the 1:1 stoichiometry and dropwise addition of the carbene to [NiCl$_2$(PPh$_3$)$_2$], both complexes were isolated from the reaction mixture in a ratio of 2:1 (**21**/**22**). The formation of this mixture of products results from a combination of factors, including solvent effects, the greater donor strength of C: relative to that of P:, a chelation effect, and differences in the ligand-dissociation kinetics of the nickel–phosphine adducts in solution. The different physical properties of **21** and **22** enable facile separation of these compounds.



Scheme 6. Synthesis of a tridentate nickel carbene complex **21** and a bis(carbene) nickel complex **22**.

The resonances of both the carbene carbon atom and the phosphorus atom in **21** ($\delta_C = 159.5$ ppm, $\delta_P = 6.03$ ppm) appear upfield in the corresponding NMR spectra relative to those of nonchelated carbene analogues ([IMesNiCl$_2$PPh$_3$]: $\delta_C = 165.3$ ppm, $\delta_P = 13.74$ ppm; IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene).[38] The methylene and trifluoromethyl groups of the ligand appear as singlets in the ^{1}H and ^{19}F NMR spectra, respectively. This latter observation suggests flexibility of the somewhat twisted geometry for a planar tridentate arrangement (see below).

An X-ray crystal structure of **21** (Figure 5) revealed the expected square-planar geometry around the nickel center. The formation of a 6,5,6 tricyclic fused ring system about a square-planar metal center slightly distorts the structure by twisting the imidazol-2-ylidene ring out of the O-Ni-O plane ($\phi_{\mathrm{twist}} = 13$–20°). This variability in solid-state torsions supports the observations from NMR spectroscopy in solution of a flexible and a conformationally dynamic process. The C–Ni and P–Ni bond lengths are typical of those in other nickel complexes despite this twisting; this similarity suggests that tridentate chelation does not substantially distort the carbene–nickel interaction.[38]

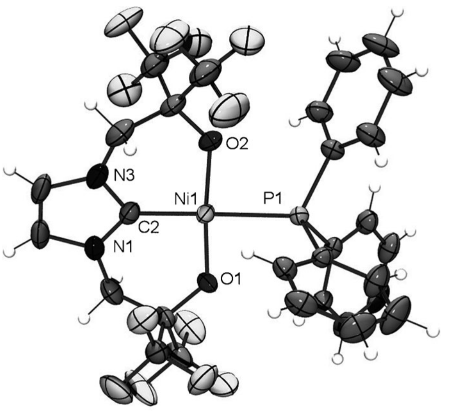


Figure 5. X-ray crystal structure of **21** with thermal ellipsoids drawn at the 50% probability level. Selected bond lengths [Å] and angles [°]: C2–Ni1 1.853, P1–Ni1 2.289, O1/O2–Ni1 1.83; N1-C2-N3 105.17, C2-Ni1-P1 172.51, O1-Ni1-O2 171.65.

The chelated and hydrogen-bonded carbene ligands in **22** give separate signals in the ^{1}H, ^{13}C, and ^{19}F NMR spectra, which suggests that their interconversion is slow on the NMR timescale. An X-ray crystal structure of **22** (Figure 6) showed that two alkoxy groups from one carbene ligand are bound to nickel, whereas two hydroxy groups from the other carbene ligand are hydrogen-bonded to the adjacent oxygen atoms. The two ligands adopt an antiplanar relationship to one another with a dihedral angle ranging from 83 to 93° as a result of the rotation of the dihydroxy carbene ligand to form hydrogen bonds that complete two distorted eight-membered rings through H-bonding. The bonds of the chelated ligand in **22** are elongated by 0.05 Å relative to those in complex **21**. The bond lengths and angles around the nickel center do not significantly deviate from those of other *trans*-bis(carbene) nickel complexes.[38–41]

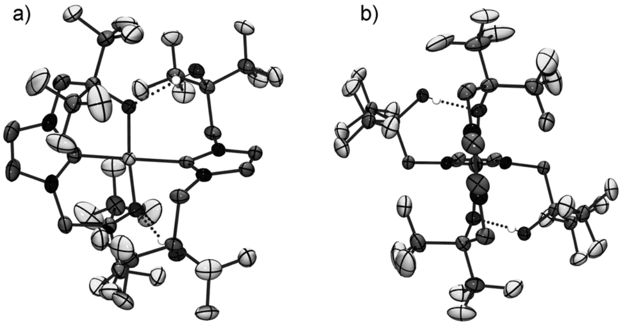


Figure 6. X-ray crystal structure of **22** with thermal ellipsoids drawn at the 50% probability level: a) side-on view; b) view down the axis of the chelated carbene. Non-hydroxy hydrogen atoms are omitted for clarity.

In conclusion, we have described a versatile new series of fluoroalkoxy tridentate carbene ligands. Studies of novel organometallic complexes of these ligands with a variety of metals, including Fe, Ta, Ti, Ru, and W, in various catalytic reactions will be reported subsequently.

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Keywords: carbenes · fluorinated ligands · imidazol-2-ylidenes · nitrogen heterocycles · tridentate ligands

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