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Synthesis, characterization and reactivity of copper(I) imidazole complexes based on a cavitand ligand design†

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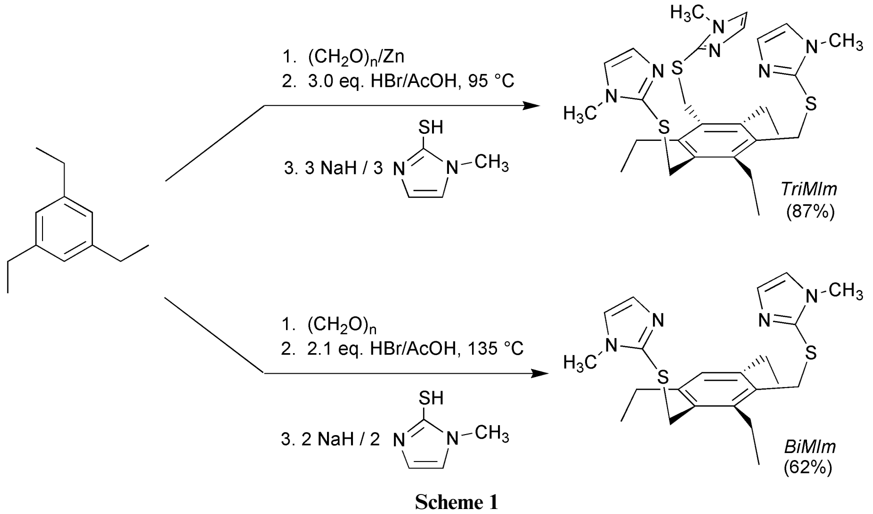
Two new cavitand-based imidazolyl ligands and their corresponding copper(I) complexes are reported; the tris(imidazole) complex is substitutionally inert while the bis(imidazole) complex readily reacts with CO, PMe$_3$, N$_3^-$ and SCN$^-$.

Preorganization of metal binding residues is an important thermodynamic advantage achieved by proteins that insures kinetically robust active site compositions. The entatic state is the classic and most extreme case in which the polypeptide fold fixes ligand positions resulting in a metal ligation sphere distorted from the thermodynamic ground state structure.[1] The consequence of the distortion is a reduced activation barrier to electron transfer or to a chemical transformation. Entatic-like structures are difficult to reproduce outside the protein matrix. Consequently, ligand preorganization remains a challenging goal for the synthetic chemist. Herein, we report our initial contribution to the area with the design, preparation and characterization of two new cavitand ligands preorganized to provide biologically representative imidazolyl donors for metal ion coordination. The crystallographically defined copper(I) derivatives exhibit markedly different reactivity with the potential donors CO, PMe$_3$, N$_3^-$ and SCN$^-$. Contemporary with these studies, several reports of calixarene-[2,3] and 1,3,5-trimethylbenzene-based[4] poly(imidazolyl) ligands have appeared.

Each ligand was prepared in good yield starting from 1,3,5-triethylbenzene and 3-methyl-1-imidazolyl-2-thione following the procedures outlined in Scheme 1.† Careful control of temperature during bromomethylation of 1,3,5-triethylbenzene allowed for clean formation of either the bis(bromomethyl) or tris(bromomethyl) intermediates required for ligand formation. X-Ray structure analysis of the tris(imidazolyl) TriMIm‡ confirmed that the free ligand adopts the expected *ababab* (*a* = above, *b* = below) conformation in which successive substituents reside on alternating faces above and below the hexasubstituted arene ring. The highly predisposed binding conformations of TriMIm and BiMIm are maintained in solution as supported by proton NMR analysis. Reaction of [Cu(CH$_3$CN)$_4$]BF$_4$ with TriMIm proceeded smoothly yielding [(TriMIm)Cu]BF$_4$ as an analytically pure, microcrystalline white solid. [(TriMIm)Cu]BF$_4$ has been characterized by X-ray diffraction, Fig. 1. TriMIm binds to the copper(I) ion to form a trigonal planar geometry with an average Cu–N distance of 2.00(1) Å and an average N–Cu–N angle of 119.5(1)°. The copper ion occupies a position above the center of the arene ring, Cu–arene centroid, 3.02 Å. The imidazolyl groups are canted in the same direction resulting in a propeller twist and a chirality of the cation. In solution there is a small barrier to equilibration of the two enantiomers which can be observed by variable temperature NMR studies, $\Delta G^{\ddagger} = 13$ kcal mol^{-1} ($T_{\text{coal}} \approx 285$ K). [(TriMIm)Cu]BF$_4$ exhibits a quasi-reversible oxidation in acetonitrile, $E_{1/2} = 355$ mV (*vs.* Fc/Fc$^+$), $\Delta E_p = 290$ mV, $I_{p,a}/I_{p,c} = 2.0$, consistent with formation of the copper(II) adduct. The lack of clean electrochemical reversibility highlights the structural change, to square planar, required to access Cu(II). Despite the observed electrochemical oxidation [(TriMIm)Cu]BF$_4$ does not react with O$_2$. Furthermore, it is inert to other small molecules such as CO, NO, or PR$_3$. Therefore we synthesized the bis(imidazole) analog with the goal of uncovering such reactivity.

Reaction of [Cu(CH$_3$CN)$_4$]BF$_4$ with BiMIm in methylene chloride afforded [(BiMIm)Cu(CH$_3$CN)]BF$_4$ as an analytically pure, white solid. [(BiMIm)Cu(CH$_3$CN)]BF$_4$ is soluble in most organic solvents and decomposes both in solution and in the solid state upon exposure to moist air. The coordination of acetonitrile was confirmed by FT-IR spectroscopy, ν_{CN} at



Scheme 1

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† Electronic supplementary information (ESI): complete synthetic details. See http://www.rsc.org/suppdata/dt/b1/b102480a/

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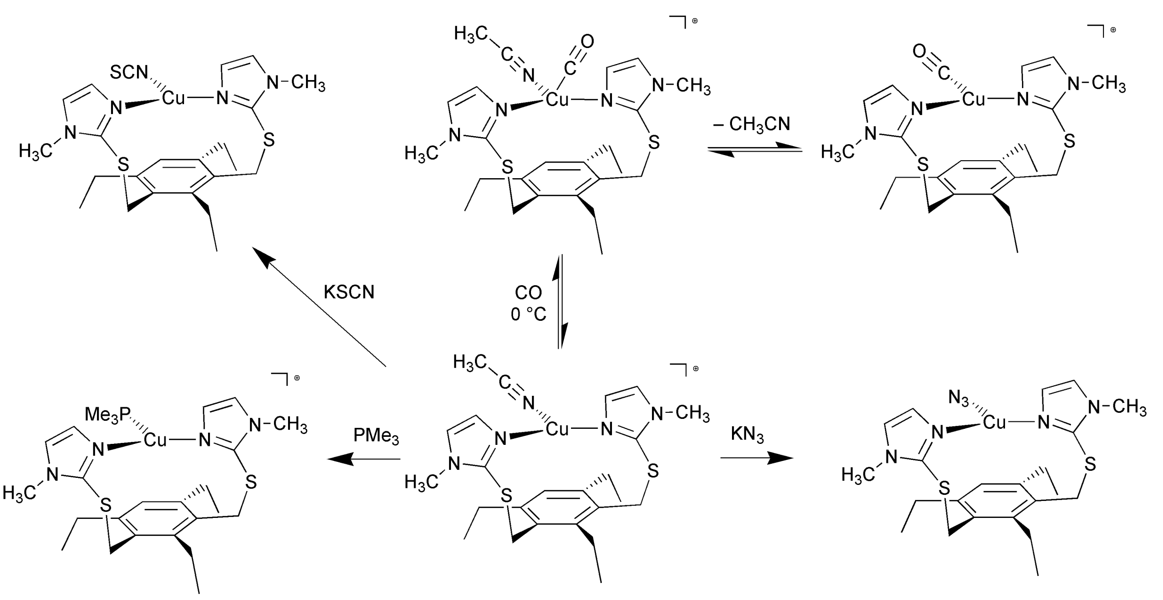

Scheme 2

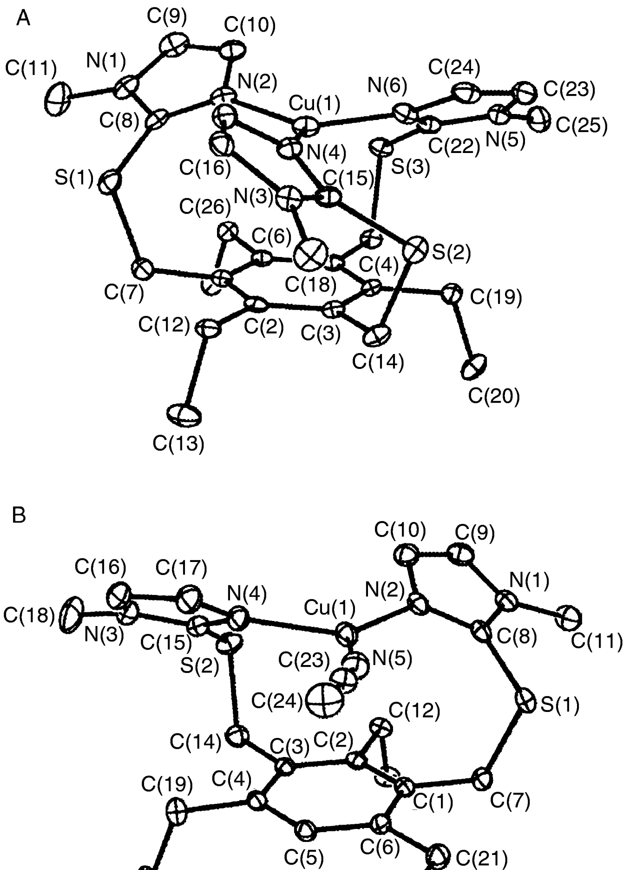

Fig. 1 Molecular structures of the cations of [(TriMIm)Cu]BF$_4$ (A) and [(BiMIm)Cu(CH$_3$CN)]BF$_4$ (B). Selected bond distances (Å) and bond angles (°) for [(TriMIm)Cu]BF$_4$: Cu(1)–N(2) 2.003(3), Cu(1)–N(4) 2.001(3), Cu(1)–N(6) 1.990(3); N(2)–Cu(1)–N(4) 119.4(1), N(2)–Cu(1)–N(6) 119.9(1), N(4)–Cu(1)–N(6) 119.1(1) and for [(BiMIm)Cu(CH$_3$CN)]BF$_4$: Cu(1)–N(2) 1.956(3), Cu(1)–N(4) 2.021(3), Cu(1)–N(5) 1.987(3); N(2)–Cu(1)–N(4) 126.2(1), N(2)–Cu(1)–N(5) 130.7(1), N(4)–Cu(1)–N(5) 101.2(1).

2267 cm^{-1}.[5] [(BiMIm)Cu(CH$_3$CN)]BF$_4$ has been characterized by X-ray diffraction, Fig. 1. The structure reveals the Cu(I) ion residing in a trigonal planar geometry with the BiMIm ligand bound *via* both imidazolyl groups, N2 and N4, with coordination completed by an acetonitrile molecule. The average Cu–N distance of 1.99(1) Å and average N–Cu–N angle of 119.1(1)° lie within the range of known three-coordinate Cu(I) complexes with nitrogen donors.[6] The coordination of acetonitrile provided an anticipated metal–solvent labile site for ligand substitution studies. [(BiMIm)Cu(CH$_3$CN)]BF$_4$ exhibits an irreversible oxidation in acetonitrile at high potential, E_a = 1050 mV, consistent with formation of the copper(II) adduct. That its oxidation is *ca.* >600 mV more positive than [(TriMIm)Cu]BF$_4$ indicates that the three imidazolyl donors of the latter greatly stabilize the Cu(II) oxidation state. This observation is well documented in blue copper protein sites, although the origin of the redox stabilization is attributed to peptide structural effects.[7]

Unlike the TriMIm analog, [(BiMIm)Cu(CH$_3$CN)]BF$_4$ reacts with a variety of donor ligands, as highlighted in Scheme 2. At −78 °C, [(BiMIm)Cu(CH$_3$CN)]BF$_4$ binds CO reversibly producing the three and four coordinate adducts as evidenced by the appearance of terminal ν_{CO} stretching bands in the FT-IR spectrum at 2073 cm^{-1} and 2108 cm^{-1}. The former band is assigned to a four coordinate complex, [(BiMIm)Cu(CH$_3$CN)(CO)]BF$_4$, whilst the latter is consistent with three coordinate [(BiMIm)-Cu(CO)]BF$_4$.[8,9] The bands are appropriately sensitive to isotopic substitution; under an atmosphere of ^{13}CO, two bands appear at 2026 cm^{-1} and 2061 cm^{-1}. Under these conditions the four coordinate complex was formed initially followed by conversion to the three coordinate species, ultimately yielding an equilibrium mixture of the two complexes. The reversible nature of CO binding was evidenced by the disappearance of the CO bands upon warming the solution to ambient temperature.

Reaction of [(BiMIm)Cu(CH$_3$CN)]BF$_4$ with PMe$_3$ in methylene chloride yielded [(BiMIm)Cu(PMe$_3$)]BF$_4$ as a white solid. PMe$_3$ coordination was indicated by the quartet resonance in the ^{31}P NMR spectrum, $^1J_{Cu-P}$, 800 Hz (^{63}Cu, I = 3/2). Although several copper(I)–PPh$_3$ complexes with nitrogen based ligands have been reported,[10] few of the analogous Cu(I)–PMe$_3$ compounds have been synthesized.[11]

Neutral thiocyanato and azido derivatives of [(BiMIm)-Cu(CH$_3$CN)]BF$_4$ were accessed *via* metathetical ligand exchange, Scheme 2. [(BiMIm)Cu(CH$_3$CN)]BF$_4$ reacted with KSCN in acetone resulting in isolation of [BiMIm]Cu(NCS). Coordination of SCN$^-$ was confirmed by a strong FT-IR absorption band at 2109 cm^{-1} assigned to the CN stretch of the thiocyanate ligand. No CH$_3$CN derived vibration was present. The assignment corresponds well with other reported Cu(I)–thiocyanate compounds.[12] The azido species, [BiMIm]Cu(N$_3$), was accessed similarly. The diagnostic asymmetric azide stretch occurs at 2041 cm^{-1}, again consistent with values reported for nitrogen ligated copper(I)–azido complexes.[13]

In summary, two new imidazolyl cavitand ligands and their corresponding copper(I) complexes have been prepared and structurally characterized. In [(TriMIm)Cu]BF_4, the ligand provides a trigonal array of donors that greatly stabilizes the copper(I) with respect to ligand substitution and oxidation. Removal of one imidazolyl substituent results in isolation of [(BiMIm)Cu(CH_3CN)]BF_4 in which the acetonitrile ligand is sufficiently labile to permit access to three coordinate derivatives with CO, PMe_3, N_3^- and SCN^- coordination. Curiously, [(BiMIm)Cu(CH_3CN)]BF_4 does not react with NO.

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Notes and references

‡ TriMIm = 1,3,5-tris(3-methyl-1-imidazolyl-2-thione)-2,4,6-triethylbenzene; BiMIm = 1,3-bis(3-methyl-1-imidazolyl-2-thione)-2,4,6-triethylbenzene.

Crystal data for [(TriMIm)Cu]BF_4·0.5CH_2Cl_2: $C_{27.5}H_{37}BClCuF_4N_6S_3$, $M = 733.61$, triclinic, $a = 8.4150(2)$ Å, $b = 12.8962(2)$ Å, $c = 15.3722(2)$ Å, $\alpha = 90.4394(6)°$, $\beta = 99.6345(5)°$, $\gamma = 93.8131(4)°$, $V = 1640.75(2)$ Å^3, $T = 173(2)$ K, space group $P\bar{1}$, $Z = 2$, μ(Mo-Kα) = 99.0 cm^{-1} ($\lambda = 0.71073$ Å), 9720 reflections measured, $R1 = 0.0561$.

Crystal data for [(BiMIm)Cu(CH_3CN)]BF_4: $C_{24}H_{33}BCuF_4N_5S_2$, $M = 606.02$, monoclinic, $a = 18.6841(2)$ Å, $b = 8.2017(2)$ Å, $c = 19.1047(2)$ Å, $\beta = 100.8733(3)°$, $V = 2875.07(6)$ Å^3, $T = 193(2)$ K, space group $P2_1/n$, $Z = 4$, μ(Mo-Kα) = 95.3 cm^{-1} ($\lambda = 0.71073$ Å), 11762 reflections measured, $R1 = 0.0514$. CCDC reference numbers 163539 and 163540. See http://www.rsc.org/suppdata/dt/b1/b102480a/ for crystallographic data in CIF or other electronic format.

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