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Simple Ligand Modifications as a Key to Playing with the Stability of Cu(I), Cu(II), and Cu(III) Organometallic Complexes

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Elusive Cu(III) organometallic complexes are extremely attractive intermediates in catalysis. Using a computational approach, we show that C−X activation by some Cu(I) complexes to yield Cu(III) intermediates is actually feasible, although ligands of appropriate structure must be used.

Understanding and possibly controlling the stability of Cu(III) organometallic complexes is an extremely important area in catalysis[1−5] because it would make available to the synthetic chemist one of the fundamental steps of organometallic catalysis, i.e., the activation of a R−X bond through its oxidative addition, $L_nM^{n+} + R-X \rightarrow L_nM^{(n+2)+}(R)(X)$, to the metal. This step is not very easy with first-row transition metals, and it is particularly difficult with Cu(I) complexes, despite the high industrial attractiveness for Cu because of its low toxicity and low cost.[6]

Scheme 1

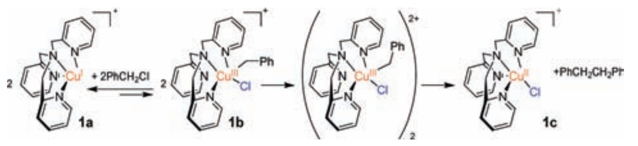
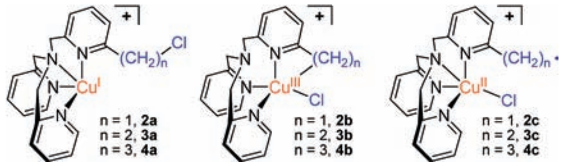


Chart 1



Recently, the existence of a Cu(III) organometallic complex has been suggested in the C−X (X = halogen) bond activation promoted by Cu(I) complexes containing (2-pyridyl)alkylamine-based ligands,[5] such as tris(2-pyridylmethyl)amine (TMPA) of **1a** in Scheme 1. In a first paper,[5] C−C bond formation according to eq 1 was investigated.[7]

$$2(\mathrm{TMPA})\mathrm{Cu}^{\mathrm{I}} + 2\mathrm{PhCH_2Cl} \rightarrow 2(\mathrm{TMPA})\mathrm{Cu}^{\mathrm{II}}\mathrm{Cl} + \mathrm{Ph(CH_2)_2Ph} \quad (1)$$

The key step of the proposed mechanism is the formation of an unstable copper(III) benzyl species, **1b** in Scheme 1, that possibly forms a dimer from which the C−C coupling step proceeds. Support to the real existence of the Cu(III) species **1b** was achieved through the design of a modified (2-pyridyl)alkylamine-based complex, **2a** of Chart 1, which could allow for an intramolecular C−Cl activation step. Indeed, also in this case experiments are consistent with a

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Table 1. Energy, in kcal/mol, of the Cu(III) and Cu(II) Species **1b**−**4b** and **1c**−**4c**, Relative to the Cu(I) Species **1a**−**4a**, Assumed as Zero Energy

	B3LYP			BLYP		
system	**a**, $\mathrm{Cu^{I}}$	**b**, $\mathrm{Cu^{III}}$	**c**, $\mathrm{Cu^{II}}$	**a**, $\mathrm{Cu^{I}}$	**b**, $\mathrm{Cu^{III}}$	**c**, $\mathrm{Cu^{II}}$
1	0	1.7	0.3	0	−1.7	6.2
2	0	24.9	−3.5	0	15.8	5.2
3	0	8.1	16.4	0	3.6	21.7
4	0	9.4	16.2	0	4.8	21.3

mechanism where the first step is the intramolecular activation of the C−Cl bond, to yield a somewhat unstable Cu(III) complex, **2b**, that further reacts.[5]

In order to investigate the stability and electronic structure of these elusive copper(III) alkyl species, we performed density functional theory calculations[8] on the closed-shell Cu(I) species **1a** and **2a** and Cu(III) species **1b** and **2b**. However, we immediately realized that the biradical Cu(II) species **2c** in the triplet electronic state should also be considered (vide infra). To our surprise, not only the relative stability but even the order of stability of the Cu(I), Cu(II), and Cu(III) species is highly dependent on the specific ligand used. For this reason, we extended our analysis to species **3** and **4** of Chart 1, which are strictly related to **2** but present a longer spacer between the Py ring and the C−Cl bond to be activated.

The relative stability of the closed-shell Cu(I) **1a**−**4a** and Cu(III) **1b**−**4b** species and of the open-shell triplet Cu(II) **1c**−**4c** species is reported in Table 1. Species **1c** is calculated as $\mathrm{(TMPA)Cu^{II}Cl + PhCH_2^{\bullet}}$.

Results clearly indicate that the Cu(III) complex **1b**, originating from the intermolecular activation of the C−Cl bond of $\mathrm{PhCH_2Cl}$ by the Cu(I) complex **1a**, is comparable in energy with separated **1a** + $\mathrm{PhCH_2Cl}$ whatever functional is considered. The structure of **1b** (see Figure 1) shows a well-formed Cu−benzyl bond. The natural population analysis (NPA) charge on the Cu atom of **1b** is 1.32, which is 1.04 greater than the NPA charge in **1a**, which supports the $\mathrm{Cu^{I} \rightarrow Cu^{III}}$ oxidation. The Cu(II) complex **1c** + free benzyl radical is instead of energy comparable to that of **1a** with the hybrid B3LYP functional, while it is of somewhat higher energy with the pure BLYP functional, which is expected because pure functionals usually stabilize the singlet electronic state. The remarkable stability of **1c** + free benzyl radical is clearly associated with the formation of the rather stable benzyl radical by transfer of a Cl atom from $\mathrm{PhCH_2Cl}$ to **1a**. In conclusion, our results support the reaction pathway proposed by Karlin et al. because the Cu(III) intermediate **1b** is of accessible energy. However, our results also indicate that the formation of Cu(II) species **1c** together with a free benzyl radical cannot be excluded, which could contribute to the complex reactivity of TMPA-based systems.[5]

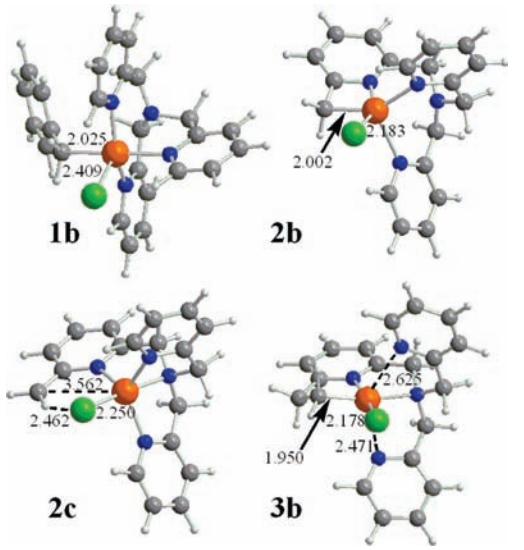

Figure 1. Geometry of the Cu(III) species **1b**−**3b** and of the Cu(II) species **2c**. Distances are in angstroms.

Differently, moving to the modified TMPA ligand **2**, it is clear that, despite a well-formed Cu−C bond, the Cu(III) species **2b** is remarkably less stable than the starting Cu(I) species **2a** whatever functional is used. The high instability of **2b** can be easily related to the high strain associated with the formation of a four-membered metallacyclobutane. Differently, the Cu(II) species **2c** remains quite close in energy to **2a**, and it is the species that should be formed after C−Cl activation. The structure of **2c** (see Figure 1) clearly indicates the absence of the Cu−C bond. The NPA charge on the metal, 1.08, is intermediate between those of the Cu(I) and Cu(III) species **1a** and **1b**, which further supports an oxidation state 2+ for Cu. These results, which are independent of the specific functional used, suggest that care should be used to extrapolate from the reactivity of the model complex **2a** the reactivity of the TMPA-based system **1a** and that the formation of the Cu(III) organometallic species **2b** is not very likely.

To propose model systems that might better represent the TMPA-based system and could avoid the complicacy of intermediates with three electronic states accessible, we investigated the model systems **3** and **4**. We reasoned that these structures should lead to Cu(III) species **3b** and **4b**, which present less strained five- and six-membered metallacycles, which should increase the stability of the Cu(III) intermediate. At the same time, the presence of a $-(\mathrm{CH_2})_n-$ ($n = 1, 2$) spacer between the Py ring and the $-\mathrm{CH_2Cl}$ group should lead to the formation of a rather unstable methylidene radical in **2c** or **3c**, which should decrease the stability of the Cu(II) intermediate.

Calculations on systems **3** and **4** clearly support this approach (see Figure 1). Indeed, the Cu(III) species **3b** and **4b** are roughly 5 kcal/mol only less stable than the starting Cu(I) species **3a** and **4a** (see Table 1), whereas the Cu(II)

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(8) The geometry optimizations have been performed with the *Gaussian03* package. The B3LYP functional together with the 6-31G(d) basis set on all atoms was used. The real nature of the minima was checked through frequency calculation. The energies reported in Table 1 have been obtained through single-point calculations on the 6-31G(d)/B3LYP geometries, using the 6-311G(d,p) basis sets and BLYP and B3LYP. The reported energies are free energies in solvent (acetonitrile) calculated with the polarizable continuum model. Although the two functionals give somewhat different relative stabilities between the various electronic states considered, the overall chemical behavior is the same, which reinforces our conclusions.

species **3c** and **4c** are far higher in energy.[10,11] Considering that intramolecular C−Cl activation is not entropy disfavored (which is instead the case in the intermolecular activation **1a** + $PhCH_2Cl$), our calculations suggest that the Cu(III) species **3b** and **4b** are maybe even more accessible that the Cu(III) species **1b**. Additionally, systems **3** and **4** clearly do not present the problem of competitive Cu(II) intermediates[9] and thus could be ideal candidates to gain insight on the complex reaction mechanism of C−X activation by Cu(I) complexes. As a final remark, the poor stability of the Cu(II) species **3c** and **4c** could be relieved by dimerization. However, before dimerization, the poorly stable **3c** and **4c** species should be formed in competition with the formation of the remarkably more stable **3b** and **4b** species, which seems a rather unlikely event.

In conclusion, our calculations evidenced that, as suggested by Karlin et al., the experimentally investigated system **1** presents a rather stable Cu(III) species. However, our calculations also indicated that the experimentally investigated system **2** is probably not the best model to gain insight into the chemistry of **1** because the assumed Cu(III) intermediate **2b** is of very high energy, while the rather stable Cu(II) intermediate **2c** could be formed. For these reasons, we propose systems **3** and **4** as more appropriate models to investigate C−X activation by Cu(I) complexes. In fact, according to our calculations, systems **3** and **4** seem to present the double benefit of rather accessible Cu(III) species, while the Cu(II) species is moved very high in energy.

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Supporting Information Available: Cartesian coordinates and drawings of all of the stationary points located, as well as additional computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Aromaticity calculations[11] on the phenyl group next to the CH_2Cl group confirm that **2c** is stabilized by delocalization of the benzyl-type radical because the harmonic oscillator model of aromaticity (HOMA) index of **2c** (0.761) is remarkably lower than those of **3c** and **4c** (0.935 and 0.927, respectively).

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