Facile C-N Bond Cleavage Promoted by Cuprous Oxide: Formation of C-C-Coupled Biimidazole from Its Methylene-Bridged Congener

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Summary: The methylenebis(N-alkylimidazolium) halides are converted to dialkylbiimidazoles by cuprous oxide with concurrent C-N bond cleavage and C-C bond formation. This unusual C-N bond cleavage is proposed to involve a Cu-(I)-NHC (N-heterocyclic carbene) complex. The reaction is unique, as it involves C-H bond activation, C-N bond cleavage, and C-C bond formation.

Carbon-nitrogen bond cleavage by transition-metal complexes has been the recent focus in organometallic chemistry.¹ Catalytic C–N bond cleavage by a Rh complex with a phosphine ligand² and model C–C coupling reactions catalyzed by Ru and Ni with organoborates via C–N bond cleavage are known.³ However, direct observation or isolation of a C–C-coupled biimidazole type product in metalcatalyzed coupling reactions is very rare.⁴ This is quite surprising, since transition-metal-catalyzed C–C coupling reactions have broad applications in organic synthesis and related disciplines.⁵ In addition, the C–C-coupled dialkylbiimidazoles are versatile ligands for deriving metal complexes with interesting structural, luminescent, and catalytic properties.⁶ These ligands exhibit different properties, and their commercial nonavailability demands that a synthetic method be devised.⁷ In our efforts to study the metalcatalyzed C–C coupling reactions, we have found that solid cuprous oxide can promote C–C coupling in methylenebis-(*N*-alkylimidazolium) halides through unusual C–N bond cleavage under ambient conditions. The reaction is unique, as it involves C–H bond activation, C–N bond cleavage, and C–C bond formation which are, to our knowledge, being reported for the first time.

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Treatment of L1 or L2 with Cu₂O in acetonitrile resulted in reactive, air-sensitive copper(I) complexes ([Cu₂(μ -Membim)₂](Cl)₂ (1), [Cu₂(μ -Bu-mbim)₂](Cl)₂ (2)) which on exposure to air were transformed to the copper(II) complexes Cu₂(Me₂biim)₂Cl₄ (3; 72%) and Cu₂(Bu₂biim)₂Cl₄ (4; 71% yield), respectively. These two copper(II) complexes were characterized by MALDI-MS, UV-vis spectroscopy, and elemental analysis, and the molecular structures of **3** and **4** (see Supporting Information) were confirmed by X-ray crystallography. The structures clearly show carbon–carboncoupled dialkylbiimidazoles (R₂-biim) through which the coppers are coordinated. The R₂-biim ligands were quantitatively extracted from the copper(II) complexes by simple treatment with ammonia (Scheme 1).

The obtained C–C-coupled product gave us a hint that the imidazolium C2 protons of L1/L2 were probably abstracted by basic cuprous oxide to produce initially a Cu(I) carbene species. Hence, we tried to analyze the cuprous products before exposure to air. As predicted, the successive formation of the copper(I)-carbene intermediate $[Cu_2(\mu-Bu$ $mbim)_2$ (Cl)₂ (2) in the case of L2/Cu₂O is indicated by an examination of the ¹H NMR spectra in Figure 1, which show the disappearance of C₂-imidazolium protons at 10.16 ppm upon coordination to Cu(I). The imidazole-ring protons appear at 7.59 and 7.47 ppm, bridging methylene appears at 6.5 ppm, and *n*-butyl protons appear at 4.05, 1.73, 1.19, and 0.81 ppm, respectively. The disappearance of bridging methylene at 6.5 ppm was clear when the C-C-coupled product L4 was formed. The ¹³C NMR spectrum of complex 2 shows a chemical shift at 177.18 ppm characteristic of carbenoid carbons bonded to Cu(I) (Figure S2, Supporting Information).

The use of cuprous oxide in copper-carbene chemistry is limited. So far, only two literature reports have been known to use Cu₂O as a base as well as a coordination center.⁸ The

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Figure 1. Comparative ¹H NMR spectra of L2, $[Cu_2(\mu-Bu-mbim)_2](Cl)_2$ (2), and C-C-coupled L4 in DMSO- d_6 (asterisks denote solvent and moisture peaks).



reaction failed to yield the C–C-coupled L3/L4 in the absence of a copper source. Also, $[Cu_2(\mu-Bu-mbim)_2](Cl)_2$ (2) is stable in solution compared to $[Cu_2(\mu-Me-mbim)_2](Cl)_2$ (1). The extreme air sensitivity of the cuprous carbene complex 1 prevents us from obtaining the NMR data, as it changes color to blue instantly. This difference implies that the steric hindrance might control the stability of the carbene intermediate.^{9a} Recently, a Cu(I)–NHC bearing an N-substituted bulky *tert*-butyl group has been isolated.^{9b}

To understand the fate of bridging methylene during C–N bond cleavage, we have synthesized phenylbis(3-methylimidazolium-1-yl)methane dichloride (L5) from α,α' -dichlorotoluene and 1-methylimidazole. Reaction of L5 with cuprous



oxide under identical reaction conditions (Scheme 2) afforded complex **3** along with benzaldehyde. The identity of benzaldehyde was confirmed by TLC, ¹H NMR, and GC-MS analyses. Alternatively, treatment of the formaldehyde produced in Scheme 1 with 2,4-dinitrophenylhydrazine led to its quantitative conversion to formaldehyde 2,4-dinitrophenylhydrazone and complex **3**.

Further, the yield of C–C-coupled product relies on methylenebis(*N*-methylimidazolium) halide sources. The reaction of Cu₂O with bromide and iodide salts ($\mathbf{L} \cdot \mathbf{2Br}$ or $\mathbf{L} \cdot \mathbf{2I}$ where **L** is methylenebis(*N*-methylimidazolium dication) afforded 42% and 15% of **L3**, respectively, along with an uncharacterizable material. It is also observed that the use of $\mathbf{L} \cdot \mathbf{2PF_6}$ with Cu₂O under identical reaction conditions did not afford the C–N-cleaved product, whereas **L1/L2** readily gives the C–N-cleaved products.

To substantiate the involvement of a Cu(I)-NHC complex during C-N bond cleavage, parallel synthesis of

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Figure 2. ORTEP plot (30% probability ellipsoids) of the dicationic part of $[Cu_2(\mu-Me-mbim)_2](PF_6)_2$ (5). Hydrogens are omitted for clarity. Selected interatomic distances (Å) and angles (deg) are as follows: Cu1-C8, 2.112(8); Cu2-C9, 2.083(8); Cu1-Cu2, 3.350; C8-Cu1-C8', 167.6(4); C9-Cu2-C9', 170.3(4).



 $[Cu_2(\mu-Me-mbim)_2](PF_6)_2$ (5) by an Ag transfer route¹⁰ was performed. Reaction of [Ag₂(µ-Me-mbim)₂](PF₆)₂ with cuprous iodide under an inert atmosphere afforded the copper-(I)-carbene complex 5, which was characterized by spectral analysis and single-crystal XRD (Figure 2). The complex was crystallized from an acetonitrile-acetone mixture and crystallizes in the orthorhombic system with the Pnma space group. The structure shows two copper centers separated at a distance of 3.350 Å. Each copper is bridged by a bis-Nheterocyclic carbene ligand with Cu-C distances of 2.083(8) and 2.112(8) Å. The copper atom adopts a slightly bent geometry (C-Cu-C = 170.3(4), $167.6(4)^{\circ}$), in comparison to the linear geometry (~180°) seen in many NHC-Cu(I) complexes.¹¹ The molecule has Cu-F interactions at 2.9 Å and intermolecular $C-H\cdots F$ interactions (see the packing diagram given by Figure S3 in the Supporting Information). The reaction of a 1:2 ratio of $[Cu_2(\mu-\text{Me-mbim})_2](PF_6)_2$ (5) and lithium chloride afforded complex 3 in 65% yield (Scheme 3).

The C–N bond cleavage of methylenebis(*N*-alkylimidazolium) halides was found to be linker dependent. The ethylene ($-CH_2CH_2-$)-bridged imidazolium salt, in contrast with the salt containing a single methylene bridge, failed to afford a C–C-coupled product, which strongly suggests



Figure 3. ORTEP plot (30% probability ellipsoids) of $Cu_2(Me_2-biim)_2Cl_4$ (3). Hydrogens are omitted for clarity. Selected interatomic distances (Å) and angles (deg) are as follows: Cu1-Cu2, 3.594; Cu1-N4, 1.981(2); Cu1-Cl3, 2.2456(5); Cu2-N3, 1.965(1); Cu2-Cl4, 2.2346(6); Cl4-Cu2-Cl4, 135.46(4); Cl3-Cu1-Cl3, 135.69(4); N3-Cu2-N3, 140.72(9); N4-Cu1-N4, 141.37(9).

that the active methylene acidic protons of $L \cdot 2X$ (X = anion) play a significant role during the course of the reaction. In the present study, this has been substantiated by the formation of aldehyde products. In general, palladium, rhodium, and ruthenium catalysts routinely used for the activation of C–H bonds are expensive.¹² The use of active metal catalysts that are cheaper and less exotic (e.g., copper, iron, and manganese) is clearly attractive.

The C-C-coupled copper(II) complexes Cu₂(Me₂biim)₂- Cl_4 (3) and $Cu_2(Bu_2biim)_2Cl_4$ (4) were characterized by single-crystal XRD. They exhibit similar structural and spectral features. As shown in Figure 3, complex 3 consists of two copper centers connected by two Me₂biim ligands with four terminal chloride ions. The ORTEP plot of complex 4 is shown in Figure S4 (Supporting Information). Me₂biim/ Bu₂biim acts as a bridging ligand rather than a bidentate chelate. Of special note, the alkyl substituent causes the two imidazole rings to be out of planarity to give an unfavorable bite angle suitable for bidentate chelation.¹³ The coppers are separated at a distance of 3.594 Å in 3 and 4. Each copper(II) adopts a highly distorted tetrahedral coordination with angles of 96.98(5), 97.66(5), 140.72(9), 141.37(9)° and 93.95(3), 95.87(5), 139.87(3), 144.60(7)° in 3 and 4, respectively, which deviate significantly from 109°.

The tetrahedral Cu(II)–Me₂biim complex **3** with unusual geometric distortion exhibits interesting luminescent behavior in solution.¹⁴ The UV–vis absorption spectrum of complex **3** in water shows electronic transitions at 210 (18666), 270 (1714), 390 (952), 580 (ε 5048 M⁻¹ cm⁻¹), and 880 nm due to π – π *, charge transfer, and d–d transitions, respectively. When the aqueous solution of complex **3** is excited at 580 nm, an emission band at 630 nm (Supporting Information) is observed. Such fluorescent behavior of L3 with Cd and Zn is known,^{6a} whereas this is the first report of copper(II) with L3. Its fluorescent behavior in the visible region is a promising feature to apply in materials.

In summary, we have observed an unprecedented C-N bond cleavage promoted by cuprous oxide in methylenebridged bis-imidazolium salts. The active methylene group is

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converted to formaldehyde during the C–N bond cleavage. The reaction works well in gram-scale synthesis. The reaction is proposed to involve a Cu(I)–carbene intermediate, as evidenced by ¹H NMR. The isolated $[Cu_2(\mu-Me-mbim)_2]$ - $(PF_6)_2$ complex **5** and its reaction with chloride anion further supports the involvement of a Cu(I)–NHC complex. The Cu(II) complexes **3** and **4** show promising fluorescent behavior and are the first examples of fluorescent Cu(II) complexes with R₂biim ligands. The novel Cu-mediated transformation leading to the formation of **3** and **4** involves a sequence of C–H bond activation, C–N bond cleavage, and C–C bond formation steps. The role of chloride anion, the reaction sequences, and the exact mechanism by which this unusual C–N bond cleavage occurs is currently under investigation. Acknowledgment. We acknowledge the National Science Council (Taiwan, ROC) and National Dong Hwa University for financial support. We sincerely thank Dr. Babu Varghese, Sophisticated Analytical Instruments Facility (SAIF), IIT Madras, India, for the structure solution of **5**.

Supporting Information Available: Text giving experimental details, figures giving ¹H and ¹³C NMR spectra of complex 2, an ORTEP plot of 4, the emission spectrum of 3, and a packing diagram of 5 showing the cooperative $C-H\cdots$ F interactions, and Table 1 and CIF files giving crystallographic data for 3–5. This material is available free of charge via the Internet at http:// pubs.acs.org. Crystal data are also available from the Cambridge Crystallographic Database as file numbers 714906, 714908, and 739121.