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Complexation of Lewis Acid with Trialkylcopper(III): On the Origin of BF_3-Acceleration of Cuprate Conjugate Addition

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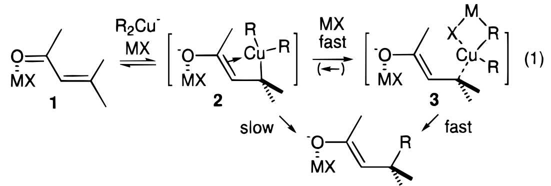
Shortly after the opening of the “Lewis acid age” with the Mukaiyama aldol reaction,[1] Yamamoto introduced a new concept in organocopper chemistry,[2,3] that is, a Lewis acid such as BF_3 dramatically increases the reaction rate and changes the selectivities of a conjugate addition reaction of an organocopper reagent. However, the origin of the BF_3 effects has thus far remained a mystery. Structural analysis of the BF_3-complexed reagent failed to account for the enhanced reactivities.[4] The Lewis acid activation of the carbonyl substrate (**1**) has been proposed as a reason for the acceleration. On the other hand, recent experimental[5] and theoretical[6] studies demonstrated that the rate-determining step of the conjugate addition is the last stage of the reaction,[7] which is the C−C bond formation via reductive elimination of a β-cuprio(III) enolate intermediate (cf. **2**).[6b] In this intermediate **2**, the Cu(III) center is stabilized by the enolate moiety that acts as a strong internal donor ligand. Therefore, it is now necessary to consider the possibility that a Lewis acid acts on this last step. There have been neither experimental nor theoretical studies on such interactions. We have carried out quantum mechanical studies (B3LYP and CCSD(T))[8] on the interaction of a Lewis acid (MX) with a model trialkylcopper(III) species **4**, and found that a Lewis acid forms a tight complex with the Cu(III) species (e.g., **10**) and promotes its reductive elimination reaction. We propose herein a new mechanistic possibility that BF_3 intercepts the β-cuprio(III) enolate intermediate **2** and accelerates C−C bond formation through a Lewis acid complex **3** (eq 1).



A T-shaped alkylcopper(III) species (e.g., **4**)[9−11] is a kinetically unstable[9a] Lewis acidic species, which can be stabilized through formation of a square planar Lewis acid/base complex such as $(CF_2H)_4Cu^-$ (**7**, crystal structure)[12] and $Me_3Cu·Me_2O$ (**5**, theoretical studies).[9] To probe systematically the additive effects, we examined the transformations shown in Scheme 1 for four categories of complexing agents; neutral donor (**5**; Me_2O, Me_2S, and Me_3P), anionic donor (**7**; Cl^-), cationic metal (**9**; Li^+), and neutral Lewis acid (**10**; $(LiCl)_2$ and BF_3).[13]

Comparison among neutral donors (Figure 1a) showed that a soft donor of higher affinity toward copper atom ($O < S \ll P$) causes better thermodynamic and kinetic stabilization of Me_3Cu(III). Thus, the activation energy of the reductive elimination of **5** via **6** almost doubled from 9.6 kcal/mol for Me_2O (9.1 kcal/mol at CCSD(T)/631A//B3LYP/631A) to 17.5 kcal/mol for PMe_3.

An anionic donor such as Cl^- forms a stable square planar coomplex **7**. The complex decomposes with a very high activation barrier (18.0 kcal/mol; 17.7 kcal/mol at CCSD(T)/631A//B3LYP/631A) (Figure 1a). In contrast, coordination of a cationic metal Li^+ on Me^3 in **4** induces reductive elimination to produce ethane without giving a discrete intermediate **9**.

Interaction of Lewis acids MX with **4** generated entirely different energy profiles (Figure 1b). Allowing $(LiCl)_2$ to interact with Me_3Cu, we located a stable complex **10** (**I** in Figure 2a), which undergoes facile reductive elimination via **11** with small activation energy (4.3 kcal/mol). BF_3 forms an even more thermodynamically stable but kinetically labile complex **10** (**III** in Figure 2b). The barriers of reductive elimination was only 2.2 kcal/mol (both at B3LYP/631A//B3LYP/631A and at CCSD(T)/631A//B3LYP/631A). In contrast to BF_3, Me_3SiCl acts as a very weak base (chlorine/Cu coordination with 3.9 kcal/mol, which is only $^1/_3$ of the stabilization energy with Me_2O: Figure 1a) and such a Me_3SiCl/Cu(III) interaction will have little impact on the reaction course of the conjugate addition.[14]

The Lewis acid complexation exerts significant effects on the coordination geometry of copper, and the magnitude of the effects depends on the nature of the Lewis acid as illustrated in Figure 2. Thus, $(LiCl)_2$ has relatively small effects, and the Me_3Cu moiety retains its original T-shape (Figure 2a), while BF_3 complexation changes the nature of the complex from $[(CuMe_3)(BF_3)]$ into $[(CuFMe_2)(BF_2Me)]$. Therefore, in **III**, the copper(III) center now bears a highly electronegative fluoride ligand, and the donative Me^3 ligand is (almost) removed through bonding to the boron atom (note the orientation of the hydrogen atoms in Me^3). The geometries of the TSs of reductive elimination (**II** and **IV**) already suggest the product structures (see Supporting Informaton); namely, from **II** will be formed ethane and a six-centered mixed cuprate cluster $MeCu·(LiCl)_2$, and, from **IV**, ethane and a $CuF·MeBF_2$ complex.

Ligand−ligand coupling (e.g., R−M(II)−R to R−R + M(0)) is a fundamental reaction in transition metal organometallic

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[1] Mukaiyama, T.; Banno, K.; Narasaka, K. *Chem. Lett.* **1973**, 1011.

[2] Maruyama, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1977**, *99*, 8068−8070.

[3] Smith, A. B., III.; Jerris, P. J. *J. Am. Chem. Soc.* **1981**, *103*, 194−195. Matsuzawa, S.; Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedron* **1989**, *45*, 349−362.

[4] Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 5869−5871.

[5] Frantz, D. E.; Singleton, D. A.; Snyder, J. P. *J. Am. Chem. Soc.* **1997**, *119*, 3383−3384.

[6] (a) Nakamura, E.; Mori, S.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4900−4910. (b) Mori, S.; Nakamura, E. *Chem. Eur. J.* **1999**, *5*, 1534−1543. (c) Nakamura, E.; Yamanaka, M. *J. Am. Chem. Soc.* **1999**, *121*, 8941−8942.

[7] Krauss, S. R.; Smith, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 141−148.

[8] All calculations were performed with GAUSSIAN 94 package, and details are described in Supporting Information. The geometry optimization was performed at the B3LYP level with the basis set denoted as 631A consisting of Ahlrichs-SVP all-electron basis set for the Cu atom and 6-31G(d) for the rest. Equilibrium (local minima) and transition-state structures have zero and one imaginary frequency, respectively. In some cases, the energies were evaluated at the CCSD(T) level. Electron population was calculated by natural population analysis, see: Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735.

[9] (a) Dorigo, A. E.; Wanner, J.; Schleyer, P. v. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 476−478. As reported, Me_3Cu(III) **4** (C_s symmetry assumed) has a very small negative eigenvalue. (b) Snyder, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 11025−11026.

[10] Bera, J. K.; Samuelson, A. G.; Chandrasekhar, J. *Organometallics* **1998**, *17*, 4136−4145.

[11] For Au(III) species, see: Komiya, S.; Albright, T. A.; Hoffmann, R.; Kochi, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 7255−7265. Komiya, S.; Albright, T. A.; Hoffmann, R.; Kochi, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 8440−8447.

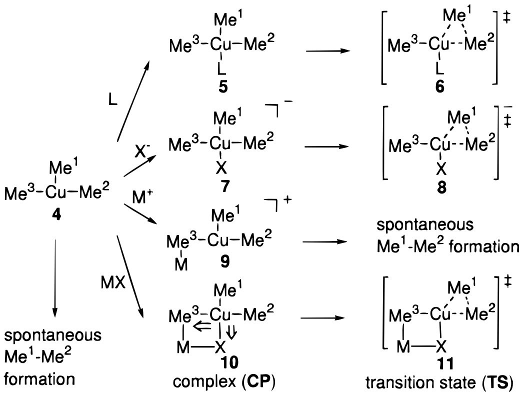
[12] Neumann, D.; Roy, T.; Tebbe, K.-F.; Crump, W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1482−1483. Eujen, R.; Hoge, B.; Brauer, D. J. *J. Organomet. Chem.* **1996**, *519*, 7−20.

[13] $MgCl_2$ and $ZnCl_2$ were also examined, and the results fell between the cases dicussed in the text. In ether, lithium halide exists as a four-centered dimer, and hence $(LiCl)_2$ is discussed in the text. The effect of Me_2O coordination was also examined for $(LiCl)_2$ (Supporting Information).

[14] For different interpretation of this magnitude of the stabilization energy, see: Bertz, S. H.; Miao, G.; Rossiter, B. E.; Snyder, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 11023−11024.

10.1021/ja993124o CCC: $19.00

Scheme 1. Effects of Additives on Reductive Elimination of $Me_3Cu(III)$*a*



[a] MeCu and ethane formed after **TS** are omitted. The arrows in **10** indicate electron polarization caused by M^+ complexation (cf. Figure 2).

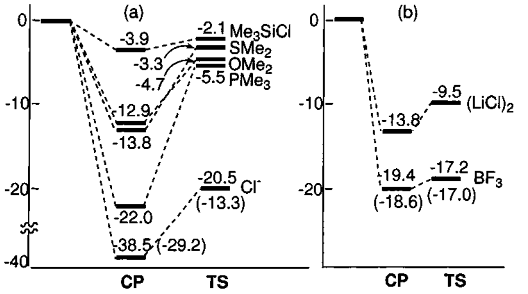


Figure 1. Energetics of complex formation (**CP**) and reductive elimination (**TS**) through interaction of $Me_3Cu(III)$ with (a) Lewis bases and (b) Lewis acids (B3LYP/631A). The values in parentheses were obtained with (a) B3LYP/Ahlrichs-SVP for Cu and 6-31+G(d) for the rest and (b) B3LYP/Ahlrichs-SVP for Cu and 6-311G(d,p) for the rest.

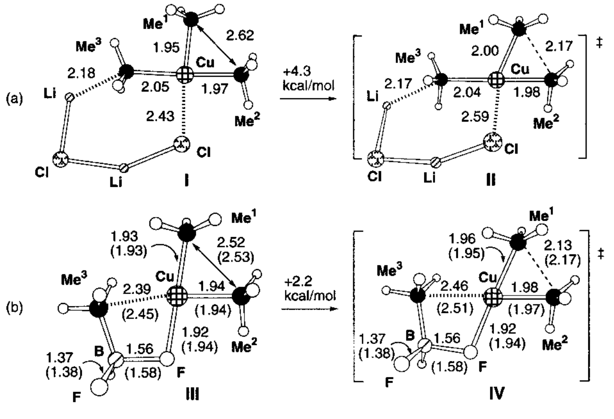


Figure 2. 3D structures of **CP** and **TS** of reductive elimination for (a) $Me_3Cu{\cdot}(LiCl)_2$ and (b) $Me_3Cu{\cdot}BF_3$. Bond lengths [Å] are at the B3LYP/631A level (those in parentheses are at the B3LYP/Ahlrichs-SVP for the Cu and 6-311G(d,p) for the rest.

chemistry. In this reaction, both the positive charge on the center metal and the negative charge on R decrease as the reactant goes toward the TS of reductive elimination. Thus, any outside influence on the reactant to assist such changes of electron population will accelerate the reductive elimination. Natural population analysis on the Me_3Cu/Lewis acid complexes indicated that a Lewis acid does assist such a change and hence lowers the activation energy of the reductive elimination.

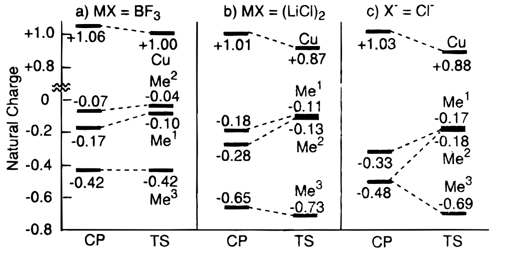
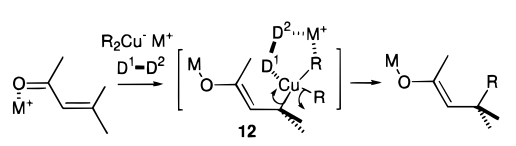


Figure 3. Natural population analysis of Me^1, Me^2, Me^3, and Cu in **CP** and **TS** for the complexes of MX or X^- with $Me_3Cu(III)$ (B3LYP/631A).

As shown in Figure 3a for the natural population of the Me^1, Me^2, Me^3, and Cu groups in the BF_3 complex, the charge distribution in **CP** is very similar to that in **TS**. This similarity agrees well with the very small energy difference between **CP** and **TS** (cf. Figure 1b). Thus, the BF_3 complexation makes the Me^3 group much more negative than the Me^1 and Me^2 groups (this non-equivalency has already been discussed for **III**), and the latter are almost as neutral in **CP** as in **TS**. As the result of the electron-withdrawing effects of BF_3, the BF_3 moiety in **CP** (i.e., **III**) has a charge of −0.40. Similarly, the electron populations in **CP** and **TS** are similar to each other in the $(LiCl)_2$ complex (Figure 3b). On the other hand, it is seen in Figure 2c that the conversion from **CP** to **TS** in the $Me_3(Cl)Cu^-$ complex necessitates a great deal of charge redistribution, and hence leads to a high activation energy (cf. Figure 1a).

In summary, the present studies have shown that a neutral Lewis acid MX thermodynamically stabilizes the $R_3Cu(III)$ species, while keeping it kinetically labile. The X^- moiety endows thermodynamic stability to the complex and serves as an "anchor" between R_3Cu and MX. Electrostatic effect of the M^+ moiety lowers the kinetic barrier toward reductive elimination and accelerates C−C bond formation.

This mechanism further suggests that a combination of M^+ and a ligand $D^1{-}D^2$, which bears a soft donor (D^1) and a hard donor moiety (D^2) directly connected to each other, may achieve better control of the reaction than a simple Lewis acid MX (eq 2). Thus, the soft donor D^1 (e.g., phosphorus) anchors the Cu(III) center, and the hard donor D^2 (e.g., nitrogen) secures M^+ in position suitable for coordination to the R group. If suitable chirality is installed on the ligand, the diastereomeric ternary complexes **12** will produce non-equal amounts of enatiomers of the conjugate adduct.[15,16]



(2)

Supporting Information Available: Structures of stationary points (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Such consideration may be in consonance with the spectacular success of the Feringa ligand: Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; Vries, A. H. M. de *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2621−2623.

(16) For 3D structures and coordinates, see: http://www.chem.s.u-tokyo.ac.jp/~common/Theo/BF3/title.