Communications to the Editor

Ligand Transfer Selectivity in the Conjugate Addition of a Mixed Organocuprate Bearing a Dummy Ligand

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Introduction of mixed organocuprates,[1] $R(X)Cu^-$, in which the X group acts as a nontransferable dummy ligand (Scheme 1), provided a breakthrough of the synthetic problem associated with homocuprates R_2Cu^- that can transfer only one of the two precious R ligands to the target electrophile (E^+, e.g., α,β-unsaturated carbonyl compound). A long accepted hypothesis[1a] has been that an X group forming a stronger Cu−X bond acts as a better dummy ligand (hence resists transfer). The selectivity of the ligand transfer has been considered to arise in the process of reductive elimination of a Cu(III) intermediate bearing three ligands, R, X, and E. While such a ligand coupling reaction is a fundamental process in organo transition metal chemistry, it has so far escaped detailed mechanistic analysis. We have carried out density functional studies[2] on the dummy ligand issue in mixed organocuprate chemistry, which has shown, contrary to the conventional hypothesis, that the transfer selectivity is controlled by the metal-coordination ability of the X group rather than the Cu−X bond strength.

Recent mechanistic studies indicated that the final and rate-determining stage of the conjugate addition[3] of organocuprate is the reductive elimination of a tetracoordinated Cu(III) open complex.[4,5] Models of such Cu(III) complexes (**CPxm, mx**) and the transition structures (**TSxm, mx**) are shown in Scheme 1 for the two isomeric pathways (XM: X bridges Li^1 and Cu, and Me as nucleophile; MX: vice versa) of the reaction of $Me(X)CuLi\cdot LiCl$ with acrolein.

If the reaction rate depends on only the nature of the Cu−X bond, consideration of the lithium moiety must be unimportant for the selective transfer. Thus, we first studied the reductive elimination reaction of the simplest model species[6] $Me_2(X)Cu^{III}\cdot Me_2O$ (**CPx**) lacking the cluster structure of lithium cuprates
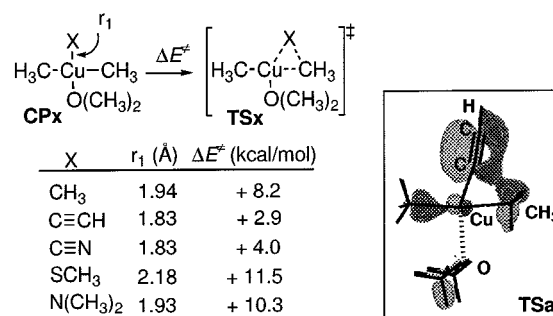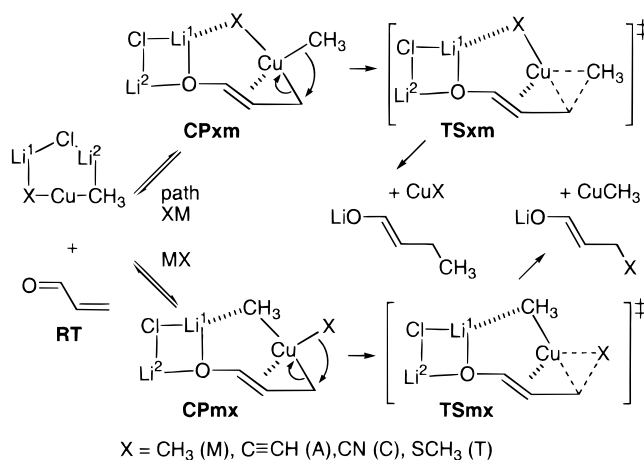

Figure 1. Reductive elimination of $Me_2(X)Cu^{III}\cdot Me_2O$. Localized Kohn−Sham orbital of **TSa** (X = ethynyl) is in the box, indicating π-orbital participation in the C−C bond forming process.

X	r_1 (Å)	$\Delta E^{\ddagger}$ (kcal/mol)
CH_3	1.94	+ 8.2
$C\equiv CH$	1.83	+ 2.9
$C\equiv N$	1.83	+ 4.0
SCH_3	2.18	+ 11.5
$N(CH_3)_2$	1.93	+ 10.3

Scheme 1

X = CH_3 (M), $C\equiv CH$ (A), CN (C), SCH_3 (T)

(Figure 1). The ethynyl (A), CN (C), NMe_2 (N), and SMe (T) groups were studied as models of alkynyl,[1a] CN,[1d] N(cyclohexyl)$_2$,[1g] and SPh^{1f} dummy ligands used in experiments, and were compared with the reference X = Me (M).

In agreement with the original concept of the ligand design,[1] the Cu^{III}−X bond length r_1 in CPx (Figure 1) is shorter (and expected to be stronger) for X = ethynyl and cyano than for X = Me.[7] In contrast, the activation energies ($\Delta E^{\ddagger}$) for X = ethynyl and cyano are equally much lower than that for X = Me (Table in Figure 1). The low $\Delta E^{\ddagger}$ value can be attributed to π-orbital participation during the 1,2-migration of the X group from Cu-(III) to the adjacent methyl group just as the one widely known in organic chemistry for the 1,2-migration of an sp or sp^2 group. In fact, participation of the carbon π-orbital of the ethynyl group was identified in the localized Kohn−Sham orbital (LMO)[8] of **TSa** (Figure 1). The relatively high energy barriers for X = SMe and NMe_2 may indeed be related to the Cu−X bond strength. Thus these simplest models for the rate determining step of conjugate addition do not necessarily account for the ligand transfer selectivity.

The whole cluster structure of lithium cuprate therefore seemed mandatory for probing the true role of the dummy ligands. To

(1) (a) Corey, E. J.; Beames, D. J. *J. Am. Chem. Soc.* **1972**, *94*, 7210−7211. (b) House, H. O.; Umen, M. J. *J. Org. Chem.* **1973**, *38*, 3893−3901. (c) Mandeville, W. H.; Whitesides, G. M. *J. Org. Chem.* **1974**, *39*, 400−405. (d) Gorlier, J. P.; Hamon, L.; Levisalles, J.; Wagnon, J. *J. Chem. Soc., Chem. Commun.* **1973**, 88. (e) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005−5038. (f) Posner, G. H.; Whitten, C. E.; Sterling, J. *J. Am. Chem. Soc.* **1973**, *95*, 7788−7797. (g) Bertz, S. H.; Dabbagh, G.; Villacorta, G. M. *J. Am. Chem. Soc.* **1982**, *104*, 5824−5826. (h) Bertz, S. H.; Eriksson, M.; Miao, G.; Snyder, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 10906−10907.

(2) The basis set denoted as 631A consists of Ahlrichs all-electron SVP basis set for the Cu atom and 6-31G(d) for the rest. For details of theoretical methods and chemical models of cuprate clusters, see: Nakamura, E.; Mori, S.; Nakamura, M.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4887−4899. Mori, S.; Nakamura, E. *J. Mol. Struct. (THEOCHEM)* **1999**, *461−462*, 167−175.

(3) Frantz, D. E.; Singleton, D. A.; Snyder, J. P. *J. Am. Chem. Soc.* **1997**, *119*, 3383−3384.

(4) (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.

(5) Mori, S.; Nakamura, E.; Morokuma, K. *J. Am. Chem. Soc.* **1998**, *120*, 8273−8274.

(6) (a) Snyder, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 11025−11026. (b) Dorigo, A. E.; Wanner, J.; Schleyer, P. v. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 476−478.
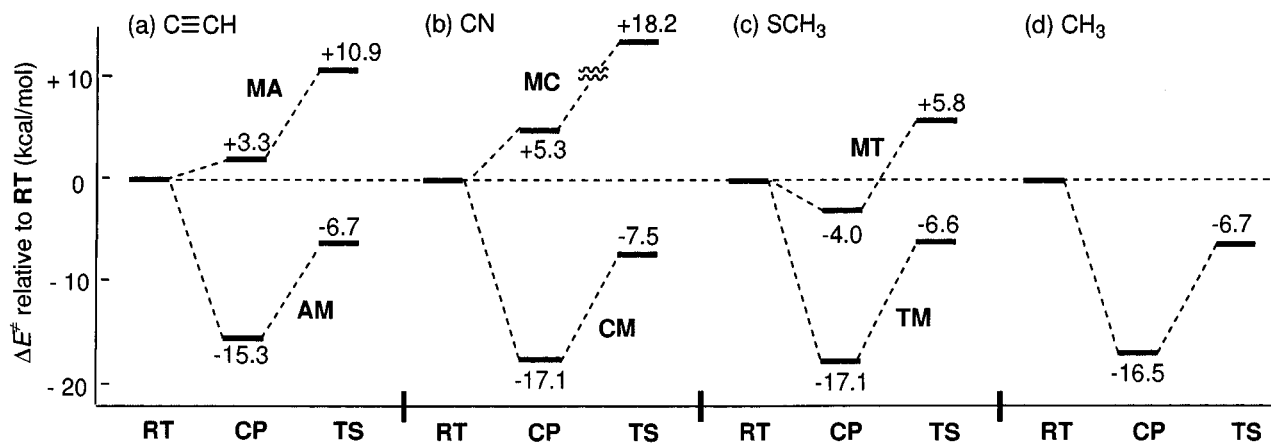
(7) The Cu(I)−X bond length in $Me-Cu-X^-$ shows the same trend (X = Me, 1.97 Å; ethynyl, 1.90 Å; cyano, 1.91 Å).

(8) (a) Boys, S. F. *Quantum Theory of Atoms, Molecules, and the Solid State*; Lowdin, P. O., Ed.; Academic Press: New York, 1968; pp 253−262. Haddon, R. C.; Williams, G. R. *J. Chem. Phys. Lett.* **1976**, *42*, 453−455. (b) Kohn, W.; Sham, L. *J. Phys. Rev.* **1965**, *140*, A1133−1138.

Figure 2. Energetics of conjugate addition of Me(X)CuLi·LiCl for X = CCH (a), CN (b), SCH₃ (c), and CH₃ (d) (B3LYP/631A//B3LYP/631A). The numbers are the energetics relative to **RT**. These energies are in kcal/mol.
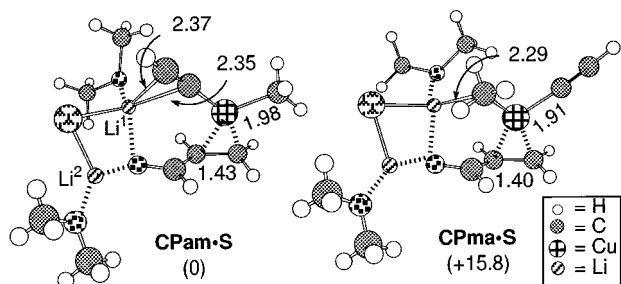

Figure 3. 3D structures of two isomeric open complexes between acrolein and Me(ethynyl)CuLi·LiCl bearing Me₂O on each lithium atom (B3LYP/631A). Bond lengths are in Å, and the relative energies (in parentheses) are in kcal/mol.

this end, the two pathways in Scheme 1 were optimized for X = ethynyl (A), cyano (C), and SMe (T), and the energetics are compared with the cases of X = Me (M) (Figure 2a−d). As exemplified by the solvent-coordinated open complexes **CPam·S** and **CPma·S** in Figure 3, the gross structures of **CPxm,mx** and **TSxm,mx** remained largely the same as the one obtained for X = Me.[4a]

The most intriguing feature of the energetics in Figure 2a−c is that the XM pathway (Me transfer) is overwhelmingly favored over the MX pathway (dummy transfer).[9] *In **CPxm**, the electron-rich X group acts as a good bridge between Cu(III) and Li¹ (cf. **CPam·S** in Figure 2). The methyl group becomes tetracoordinated and ready for reductive elimination through a pentacoordinated TS (cf. **TSxm** in Scheme 1).[10]* Note that the π-coordinated metal alkynyl structure such as the one in **CPam·S** (Figure 3) is

ubiquitous in crystals.[11] The thermodynamic stability of the Li−X coordination thus makes the XM pathway favored over the MX alternative. As shown in Figure 3, solvent coordination does not change much the energetics of the Me vs ethynyl pathway. In addition, the energy difference between the two pathways is so large that the relatively small difference of the activation energies of the reductive elimination process (**CP** to **TS**) does not affect the net ligand transfer selectivity.

In summary, we have found that the dummy X group must be able to simultaneously bind to Cu and Li atoms to be an effective nontransferable ligand and, by default, the less effective bridging ligand (viz. Me) is involved in the reductive elimination leading to C−C bond formation. The present results illustrate the pressing needs to understand the roles of polymetallic clusters in the design and analysis of organometallic reactions commonly used in the experimental laboratories.[12,13]

Supporting Information Available: Tables of Cartesian coordinates of **CPxm**, **CPmx**, **CPxm·S**, **CPmx·S**, **TSxm, TSmx, CPx,** and **TSx** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) The energy comparison is made here for **CPxm** and **CPmx**, which are in mobile equilibrium with each other. Therefore Curtin−Hammet boundary conditions are satisfied (see ref 4b), and one needs to consider only the energies of the **TS**s for the analysis of ligand transfer selectivity. The energy of the reactants serves only as a reference zero point.

(10) Such consideration also accounts for the low reactivities of bis(alkynyl) homocuprates in terms of the thermodynamic problem in dissociation of the Li−X bond in the starting cuprate cluster.

(11) (a) Goldfuss, B.; Schleyer, P. v. R.; Hampel, F. *J. Am. Chem. Soc.* **1997**. *119*, 1072. (b) Varga, V.; Mach, K.; Thewalt, H. U. *J. Organomet. Chem.* **1996**, *506*, 109. (c) Edwards, A. J.; Fallaize, A.; Raithby, P. R.; Rennie, M. A. A.; Steiner, A.; Verhorevoot, K. L.; Wright, D. S. *J. Chem. Soc., Dalton Trans.* **1996**, 133−137.

(12) Cf.: Hirai, A.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* accepted for publication. Nakamura, E.; Hirai, A.; Nakamura, M. *J. Am. Chem. Soc.* **1998**, *120*, 5844−5845. Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1993**, *115*, 11016−11017. Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 1789−1798. Mori, S.; Kim, B. H.; Nakamura, M.; Nakamura, E. *Chem. Lett.* **1997**, 1079−1080.

(13) 3D pictures and coordinates are available on http://www.chem.s.u-tokyo.ac.jp/∼common/Theo/Mix1/title.