

Density Functional Studies on Kinetic Reactivity of "Higher Order" Lipshutz Cuprate in Addition Reaction to Acetylene

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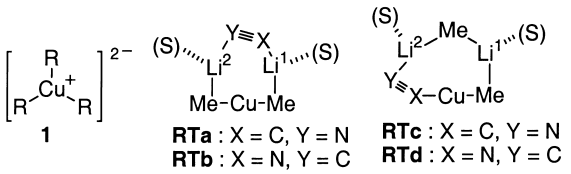
There is a frequently used organocuprate species that was introduced by Lipshutz and possesses a molecular structure written as $CuLi_2R_2(CN)$. This species was previously called "higher order cuprate", but is now considered to exist as an equilibrating mixture of various isomers of $R_2CuLi{\cdot}LiCN$ and $R(CN)CuLi{\cdot}LiR$, among which $R_2Cu^-{\cdot}Li_2CN^+$ is known to be dominant in solution. The present studies on the kinetic reactivity of these species in the addition reaction to acetylene suggest that the minor species $R(CN)CuLi{\cdot}LiR$ may be more reactive than the major species, thereby making it equally possible that addition reaction products may arise through both the major and the minor reactive species. The reason for the high reactivity of the minor species has been ascribed to the anisotropic and multi-coordination capability of the cyanide ligand to metals; such capability is not available for a halide or alkyl anion ligand.

The chemistry of nucleophilic organocopper reagents is full of mysteries, among which there is a story of "higher order cuprate".[1] This is an organocopper(I) reagent containing two alkyl anions and one cyanide anion (initially formulated as $R_2(CN)Cu^{2-}{\cdot}Li_2^{2+}$ by Lipshutz[2] and hence will be denoted as the Lipshutz reagent hereafter). It has been a subject of controversy since the insightful initial suggestion by Bertz.[3,4,5] The controversy[6] rested on a single point, that is, whether or not the cyanocuprate(I)$^{2-}$ species **1** exists (Chart 1). The current consensus based on a large number of structural studies[7] says that the cyanide anion is not attached to copper and the cuprate must be regarded as $R_2Cu^+{\cdot}Li_2CN^+$ (i.e., **RTa**). Cyanide anion is stable enough to remain as it is, while the alkyl anion (R^-) stabilizes itself through the formation of a covalent C–Cu bond. Various possible arrangements of R × 2, CN, and Li × 2 groups have been considered on the basis of experiments and theoretical calculations,[8] and these have led to the proposal of four series of structures **RTa-d**, among which the computationally most stable species **RTa** has often been assigned experimentally as the dominant species existing in solution.[3a,8a,c,d,9]



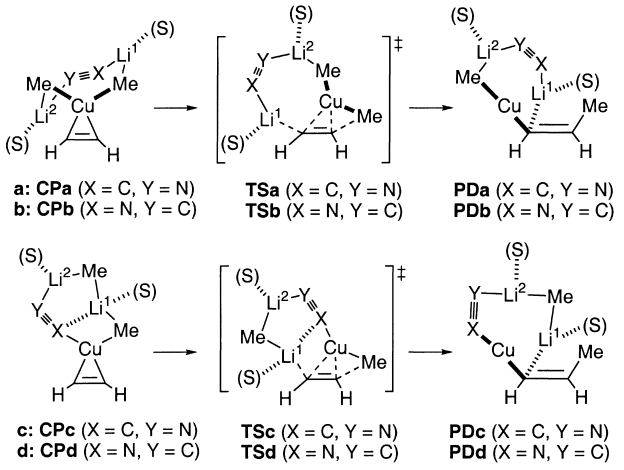
(Note that the carbon-lithium bonds are essentially electrostatic despite the use of single bond notation which might suggest covalent bonding. Carbon-copper bonds are essentially covalent.)

Chart 1. Models of cuprate structures.

In these previous studies, it was silently assumed that the dominant species **RTa** is responsible for the observed reactivities of the Lipshutz reagent. The importance of these structural studies notwithstanding, we considered it worthwhile to study the relative reactivities of the four series of cuprates **RTa-d**; that is, whether the thermodynamic stability of these four species is reflected in their kinetic reactivities. There are some experimental results that suggest some importance of **RTc** and **RTd**. For instance, the Lipshutz reagent is positive to the Michler's ketone and is quite basic (e.g., deprotonation predominating in the reaction with acetylene). We have carried out density functional studies (B3LYP) on the relative reactivities of **RTa-d** toward acetylene and found that the reactivity order may be different from the stability order, and that less stable cyanocopper species **RTc** or **RTd** may be as reactive as **RTa** and **RTb**. Together with a similar conclusion that we reported for the S_N2 reaction of these isomeric species,[10] the present study suggests that we must take into account the kinetic reactivities of minor intermediates when we consider the reactivity of the Lipshutz cuprate. The results endorse the necessity of theoretical calculations in the studies of organocopper reactions (and also other organometallic cluster reactions), since a minor species existing in a minute amount (hence experimentally unobservable) may easily be more reactive than the major one.

Theoretical Method

All calculations were performed with a GAUSSIAN 94 package.[11] The geometry optimization was performed at the B3LYP level with the basis set denoted as 631AS that consists of Ahlrichs-SVP all-electron basis set for the Cu atom and 6-31G(d) for the rest.[12] Equilibrium (local minima) and transition state structures have zero and one imaginary frequency,



Scheme 1.

respectively. It was shown by the intrinsic reaction coordinate (IRC) analysis followed by the geometry optimization that the stationary points, **CPa-TSa-PDa** and **CPc-TSc-PDc**, are connected smoothly along the reaction coordinate.

Results and Discussion

The nucleophilic reactivity of the isomeric cuprate reactants ($CuLi_2Me_2(CN)$; **RTa-d**) has been examined for their addition reaction to acetylene, which is a simple but useful model of nucleophilic addition reactions of cuprate species.[13] Note[14] that the important orbital interactions in the addition reaction of cuprate are different from those in the S_N2 substitution reaction studied previously for the Lipshutz reagent.[10] Two factors that contribute to the stability of **RTa** and **RTb** being larger than that of **RTc** and **RTd** are the presence of two Me–Cu(I) covalent bonds and the stabilization of the cyanide anion which coordinates to two lithium atoms.[8c] We modeled the reaction of **RTa-d** with acetylene along the pathway described previously for the homocuprates, $(Me_2CuLi)_2$ and $Me_2CuLi{\cdot}LiCl$,[13a] and obtained the cuprate/acetylene complex **CP**, the transition state of C–C bond formation **TS**, and the product **PD** (Scheme 1, Fig. 2). The reaction possess mechanistic features essentially the same as those previously found the reaction of $(Me_2CuLi)_2$ and $Me_2CuLi{\cdot}LiCl$.

For series **a** and **c**, we also examined the cuprates solvated with one Me_2O molecule on each lithium atom ($CuLi_2Me_2(CN)(Me_2O)_2$; **RT·S**) to obtain **CP·S** and **TS·S**. (In the following paragraphs, only the series **a** and **c** are discussed in details since those in the series **b** and **d** are essentially the same as those in **a** and **c**, respectively.)

The most interesting feature is the energetics summarized in Figs. 1a and b. Whereas the reaction of **RTa** and **RTb** goes through rather unstable acetylene complexes **CP** (as in the reaction of $Me_2CuLi{\cdot}LiCl$),[13a] **RTc** and **RTd** gain ca. 10-kcal/mol stabilization energy to form the stable Cu(III) complexes **CPc** and **CPd**. The activation energy of C–C bond formation (**CP** to **TS**) is similar in all four cases, and the relative energy of the four **TS**s is directly reflected in the relative energy of **CP**s. Solvation of the lithium atoms with ether molecules attenuates the difference betwen series a and c to make the energies of **TSa·S** and **TSb·S** nearly equal to each other (Fig. 1b). Upon consideration of solvent polarity (SCRF calculation with the Polarized Continuum model (PCM), $\varepsilon = 4.335$ for ether), the energy difference between **TSa·S** and **TSc·S** became as small as 0.9 kcal/mol.

One reason for the stabilization of series **c** upon complexation with acetylene can be found in the structures of **CPc** and **TSc** as compared with those of **CPa** and **TSa** (Fig. 2). An extra interaction exists between CN and Li^1 in **CPc** and **TSc**, which is not present in **CPa** and **TSa**. This electrostatic interaction between Li^1 and CN is strong and the coordination of a

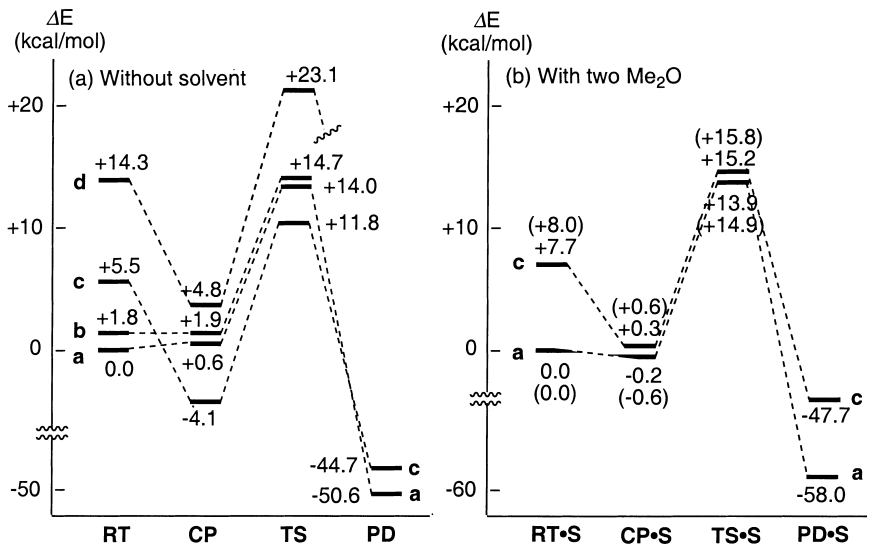


Fig. 1. Energetics (ΔE) of addition of (a) $Me_2CuLi{\cdot}LiCN$ (**RTa**), $Me_2CuLi{\cdot}LiNC$ (**RTb**), $MeCuCN{\cdot}LiMe$ (**RTc**) and $MeCuNC{\cdot}LiMe$ (**RTd**) to acetylene and (b) series **a** and **c** coordinated with two molecules of Me_2O on lithium atoms (B3LYP/631AS//B3LYP/631AS). The values in parentheses were obtained with the SCRF calculation.

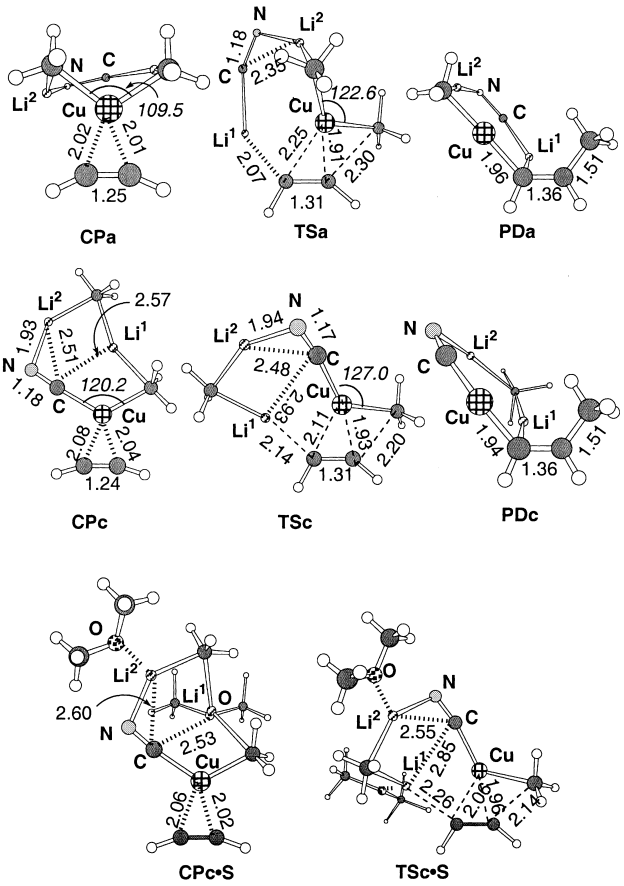
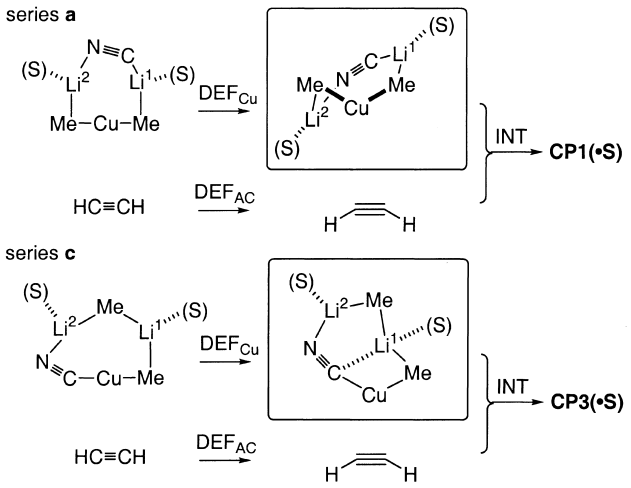


Fig. 2. Geometries of stationary points (**CP**, **TS**, and **PD**) in series **a** and **c** (B3LYP/631AS//B3LYP/631AS). Bond lengths are shown in Å and bond angles (in italic) in degrees.



series	DEF$_{AC}$	+ DEF$_{Cu}$	= DEF$_{total}$	INT	BE
a (S = none)	+11.7	+27.1	+38.8	-40.1	+0.6
c (S = none)	+5.7	+14.7	+20.4	-30.0	-9.6
a (S = Me_2O)	+14.8	+30.0	+44.8	-45.0	-0.2
c (S = Me_2O)	+7.2	+17.7	+24.9	-32.3	-7.4

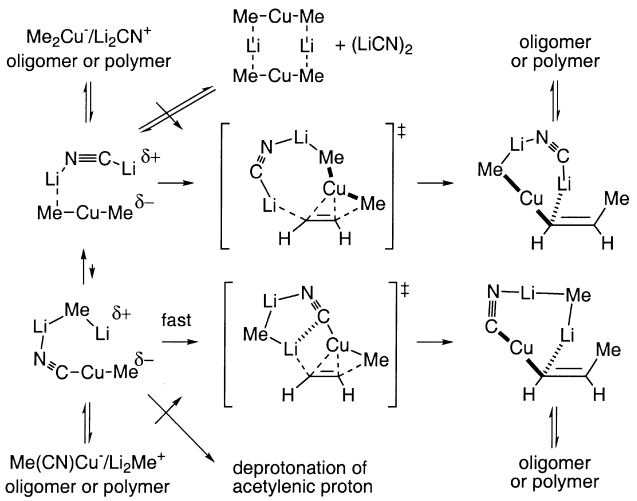
Fig. 3. Deformation (DEF) and interaction (INT) energies in kcal/mol for cuprate cluster and acetylene fragments in series **a** and **c**. BE = DEF$_{total}$ + INT (B3LYP/631AS// B3LYP/631AS)

Me_2O molecule to each of Li^1 and Li^2 does not change much either the energy (Fig. 1b) or the structure of **CPc** or **TSc** (Fig. 2).

In order to probe the origin of stabilization in series **c**, we separated **CP** into two fragments: acetylene (AC) and the cuprate cluster moieties (Cu), and evaluated the energies needed to deform the reactants (**RT**) into the **CP** geometry (denoted as DEF, DEF$_{total}$ = DEF$_{AC}$ + DEF$_{Cu}$). The binding energy (BE) upon formation **CP** from **RT** is expressed as a sum of DEF$_{total}$ and INT, where INT is the energy gained by interaction of the two deformed fragments.[15] The total deformation energy (DEF$_{total}$) in series **a** is +38.8 kcal/mol (Fig. 3), while DEF$_{total}$ in series **c** is as small as +20.4 kcal/mol. DEF$_{total}$ for the solvated model is 44.8 kcal/mol and +24.9 kcal/mol, respectively. Thus, in both the non-solvated and the solvated models, DEF$_{total}$ in series **c** is ca. 20 kcal/mol smaller than that in series **a**. On the other hand, INT in series **c** is only ca. 10–13 kcal/mol smaller than that in series **a**. The smaller DEF$_{total}$ in series **c** mainly comes from the smaller DEF$_{CU}$, which can be ascribed to the π-coordination of Li^1 and Li^2 to CN group in the deformed cuprate cluster moiety (vide supra). Thus, the stabilization upon formation of the cuprate/acetylene complex **CP** in series c originates largely from the smaller energy of deformation (DEF$_{CU}$) of the cuprate cluster (shown in the box of Fig. 3). In other words, the more extensive metal-CN coordination in series **c** compared to that in series **a** results in the global stabilization of series c upon complexation with acetylene (and hence also during C–C bond formation.)

The foregoing analysis indicates that the stabilization in series **c** originates from the poly coordination ability of CN anion. However, the different DEF$_{CU}$ could originate also from a difference in the energy required for bending the Me–Cu–Me bond in **CPa** and the NC–Cu–Me bond in **CPc**. In order to examine how much this energy may contribute to the overall deformation energy, we took the Me–Cu–Me^- and the NC–Cu–Me^- part structures and bent the C–Cu–C angle to 109.5° and 120.2° according to the angles found in **CPa** and **CPc**, respectively. The energy for the bending in Me–Cu–Me^- was 9 kcal/mol smaller than that in NC–Cu–Me^- (33.1 kcal/mol for Me–Cu–Me^-, 24.1 kcal/mol for NC–Cu–Me^-, B3LYP/631AS// B3LYP/631AS).[16] We therefore conclude that the large stabilization energy in series **c** upon interaction with acetylene is mainly due to smaller energy required for bending the NC–Cu–Me bond in **CPc**. The structural difference of the cuprate moiety in between **CPa** and **CPc** resides in the difference of the π-coordination between the CN moiety and the two lithium atoms.

In summary, we have examined the interaction of four structural isomers of $CuLi_2Me_2(CN)$ (**RTa-d**) with acetylene in the absence and in the presence of two Me_2O molecules (under the polarity of diethyl ether). We first confirmed the reported order of the thermodymic stability of these isomers, but found that a minor species such as **RTc** is more reactive than the major one **RTa**. The key is the anisotropic and strong complexation of cyanide anion to metal atoms that is not available for



Scheme 2.

halide (strong but isotropic) or alkyl (aniosotropic but weak) anionic ligands. Thus, the cuprate cluster in series **c** (or **d**) gains energy upon complexation with acetylene (that transforms the linear C–Cu–C geometry into a bent one). In the light of the presence of diverse equilibrium processes where various potentially reactive intermediates ranging from solvent-separated ion pairs to oligomeric lithium cuprate species coexist, we suggest feasible reaction pathways of the addition reaction of the Lipshutz cuprate as shown in Scheme 2. In our previous studies on the S_N2 alkylation reaction of the Lipshutz reagent,[10] we have presented a related proposal, based also on the metal coordination behavior peculiar to a cyanide anion, that the minor species may be as reactive as the major one. Note that there have been reported similar effects of anisotropic coordination in the chemistry of a mixed cuprate bearing a cyanide or acetylide ligand.[17]

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