

Mechanism of Addition of Organocuprates to Alkynyl Carbonyl Compounds. A Mechanistic Bridge between Carbocupration and Conjugate Addition

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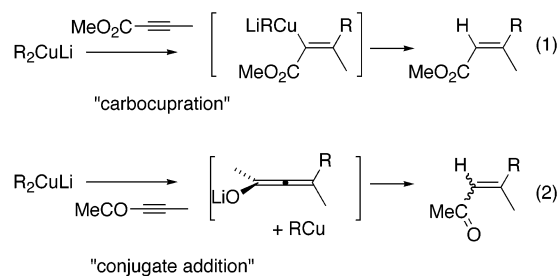
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The reaction pathway of the addition of a lithium dialkylcuprate to an alkynyl carbonyl compound was examined by the use of hybrid density functional calculations for $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ and two carbonyl substrates, 3-butyn-2-one and methyl propynoate. Both substrates react in essentially the same manner to give first a 1,2-carbocupration product. This α -cupriocarbonyl product is thermodynamically stable in the case of methyl propynoate. On the other hand, the α -cupriocarbonyl product obtained from 3-butyn-2-one is in equilibrium with the corresponding lithium allenolate with a low activation barrier. Comparison of the calculated IR frequencies of the putative products with those of the experimentally obtained product mixture suggested that the product of the ynone reaction is a mixture of an α -cuprioketone and an allenolate, which may be in mobile equilibrium with each other in solution.

After fifty years since the first report by Gilman,¹ lithium organocuprates (R_2CuLi) still play important roles in organic synthesis^{2,3} and serve as a useful source of mechanistic information about copper-catalyzed nucleophilic reactions.^{4,5} Conjugate addition to an α,β -unsaturated ketone (enone) represents the most useful and the most typical reaction of the cuprate, and the reaction results in 1,4-addition of R^- and Li^+ across the conjugated system. The product is generally assumed to be a lithium enolate, which may sometimes be (weakly) bonded to a copper(I) atom on the α -carbon atom.^{6,7} 1,2-Addition of a cuprate across an alkyne represents another important category of synthetic reactions for stereoselective synthesis of polysubstituted alkenes.⁸ The reaction generates an alkenyl copper

intermediate as the result of 1,2-addition of R^- and Cu^+ to the alkenyl moiety and, hence, has been known as “carbocupration”.



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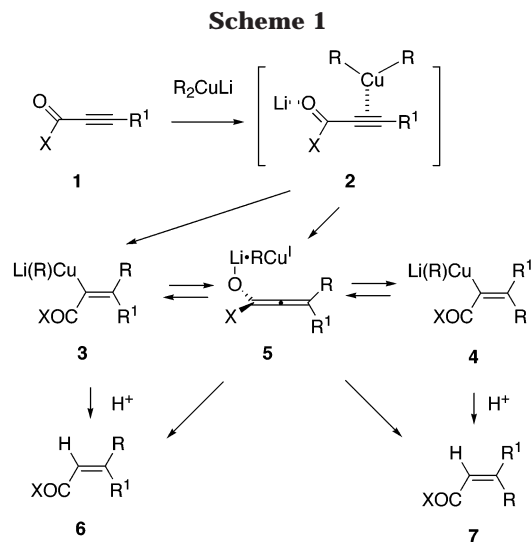
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For a long time, the mechanistic basis of the “carbocupration” reaction of simple alkynes has been considered to be solid (i.e., simple 1,2-carbometalation across the π -system); however, there has been some confusion as to the reactivities of alkynes bearing an electron-withdrawing substituent (eqs 1 and 2).⁹ A lithium organocuprate undergoes *syn* addition to an acetylenic ester (ynoate) at low temperature and gives stereoselectively an α -cuprio ester, which then gives an α,β -unsaturated ester upon protonation (eq 1, “carbocupra-

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tion").¹⁰ Recent NMR study on a few selected cases confirmed the formation of α -cuprio esters.¹¹ On the other hand, the same reaction with an acetylenic ketone (ynone) tends to produce a mixture of *E* and *Z* isomers of an α,β -unsaturated ketone, and hence the major product of the reaction is generally assumed to be an allenolate (eq 2, "conjugate addition").^{12,13} IR and NMR studies for some cases confirmed the formation of allenolates,^{11,14} which has been suggested to be a secondary product derived from the initial α -cuprio ketone product.¹⁴ A copper allenolate intermediate instead of the lithium allenolate has also been proposed.^{15,16}

This subtle issue of mechanistic dichotomy has been considered to be trivial and neglected. Nonetheless, a series of our recent theoretical studies on the cuprate mechanisms⁴ suggested that the dichotomy represents a useful mechanistic probe and therefore may provide an important link between "conjugate addition" and "carbocupration" reaction. Indeed, these two reactions have recently been shown to be mechanistically related in that both of them involve an "oxidative addition/reductive elimination" mechanism, i.e., a Cu(I)/Cu(III) mechanism.^{17,18} In this article, we will report the studies on the reaction pathways of ynone and ynoate reactions and demonstrate that the reactions of simple alkynes, electron-deficient alkynes, and electron-deficient alkenes take place essentially in the same manner.

From what we have learned by experiments and by theory, we can intuitively construct a reaction pathway for the ynone and ynoate reactions, which is shown as a simplified scheme in Scheme 1. The first intermediate

from **1** is likely the complex **2** (note the bent geometry of Me–Cu–Me, which is necessary for back-donation to the π -system and thus for the formation of the complex).¹⁹ According to the conventional wisdom, it will then proceed either to the vinylcopper intermediate **3** or to the allenolate **5**. The former will afford **6** upon protonation, while **5** will give a mixture of **6** and **7**.

We have compared the reaction pathways of an ynone (3-butyn-2-one; **1**, X = Me, R¹ = H) and an ynoate (methyl propynoate; **1**, X = MeO, R¹ = H) with those of acrolein, cyclohexenone, and acetylene either in the absence or in the presence of Me₂O molecules coordinated to metal atoms.^{17,34} The study indicated that the reaction of **1** first produces π -complex **2** and then α -cuprio carbonyl intermediate **3**. The latter undergoes isomerization either to stable allenolate **5** or further to stereoisomeric α -cuprio carbonyl intermediate **4**. In this article, we will show that the essence of this scheme is consistent both internally and with known experimental data, will add further details to the scheme, and will finally discuss the general considerations of cuprate addition reactions.

Theoretical Models and Methods

Among various models of organocopper reagents (MeCu, Me₂Cu⁺, Me₂CuLi, Me₂CuLi·LiCl, (Me₂CuLi)₂), the latter two behave similarly and can be taken as reasonable models of lithium cuprate in solution, as discussed in detail in our previous papers.^{4,17,18} In the present study, we have employed a Me₂CuLi·LiCl molecule as a less expensive model of (Me₂CuLi)₂, a species considered to be the true reactive

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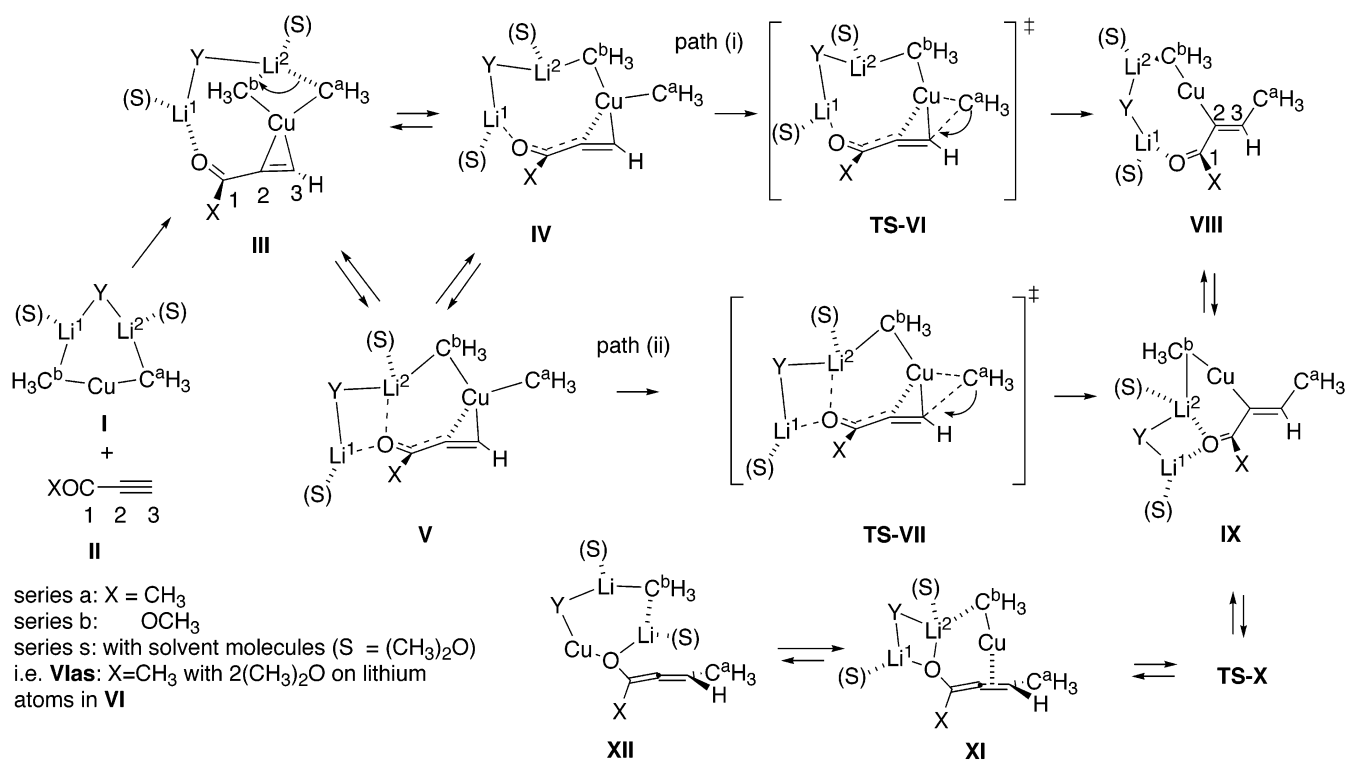
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Scheme 2



intermediate.^{18,20,21} 3-Butyn-2-one and methyl propynoate in their *s-trans* conformation were used as model substrates of alkynes. The effect of solvent coordination was evaluated for the reaction of 3-butyne-2-one by the use of Me₂O (and H₂O, data not shown) on lithium atoms, as well as by the use of the self-consistent reaction field (SCRf) method based on Onsager model ($\epsilon = 4.34$ for Et₂O, 20 °C)^{22,23} performed with full geometry optimization; the bulk polarity effects were small as in the previous studies¹⁸ and hence not discussed in the text. Solvent effects did not affect the overall pathway of the ynone reaction and therefore were not examined for methyl propynoate.

Throughout the present studies, Gaussian 94 and 98 programs²⁴ were used at the B3LYP hybrid functional²⁵ with the 631A protocol (the Ahlrichs all-electron SVP basis sets²⁶ for Cu atoms, and 6-31G(d) for the rest),²⁷ which we have previously shown to give reasonable structures and energies for the cuprate reactions.^{28–36} We found no biradical character in the complexes and the TSs (**Va**, **TS-VIa**, **TS-VIIa**, **IVb**, and **TS-VIb**) as studied at the UB3LYP/631A level.³⁷ Normal coordinate analysis (performed for all TSs) and natural charges³⁸ are calculated at the same level used for structural optimization unless noted otherwise, and confirmed that transition states have only one imaginary frequency and minima zero. A scale factor of 0.9614 for B3LYP/6-31G(d) frequencies was employed.³⁹ To confirm the connectivity of all stationary points, intrinsic reaction coordinate (IRC) analysis⁴⁰ at the B3LYP/631A level was performed near all TSs followed by further structural optimization to reach local minima next to each TS.

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Results and Discussion

Our previous studies on the carbocupration of acetylene^{17,28} and the conjugate addition to an enal¹⁸ and an enone^{31,34} revealed the mechanistic significance of electron donation from a copper atom to the substrate. On the basis of this knowledge and the previous experimental evidence for cuprate/ynone complexes,⁹ we started by exploring the mechanistic possibilities of the reaction of ynones and ynoates with special focus on the C–C bond forming stage. In Scheme 2 are listed all stationary points and pathways (i.e., not all these are involved in all reactions examined) found and examined in the present studies for reaction of Me₂CuLi–LiCl with an ynone (3-butyne-2-one, series “a”) and an ynoate (methyl propynoate, series “b”) as found in the present study.

In series “a” (X = CH₃), binding of the cuprate **I** with the ynone **IIa** produces a lithium/carbonyl and copper/acetylene “closed” complex **IIIa**. In the complex **IIIa**, an interaction between C^aH₃ and Li² is preserved. Isomerization among complexes **IIIa**, **IVa** (which does not exist in the absence of solvent molecules), and **Va** takes place by cluster-opening of the lithium organocuprate aggregate. In complexes **IVa** and **Va**, the C^aH₃–Li² bond is already cleaved, and C^bH₃ and Li² groups interact with each other. **IVa** does not have a Li²–O bond, whereas **Va** does. There are two paths, (i) and (ii), found in the C–C bond formation step leading to **IXa**. Along path (i), C–C bond formation from **IVa** occurs to give a vinylcopper intermediate **VIIIa** through **TS-VIa**, which may isomerize to another vinylcopper intermediate **IXa**. Along path ii this latter product can be reached directly via **Va** and **TS-VIIa** from **III**. The

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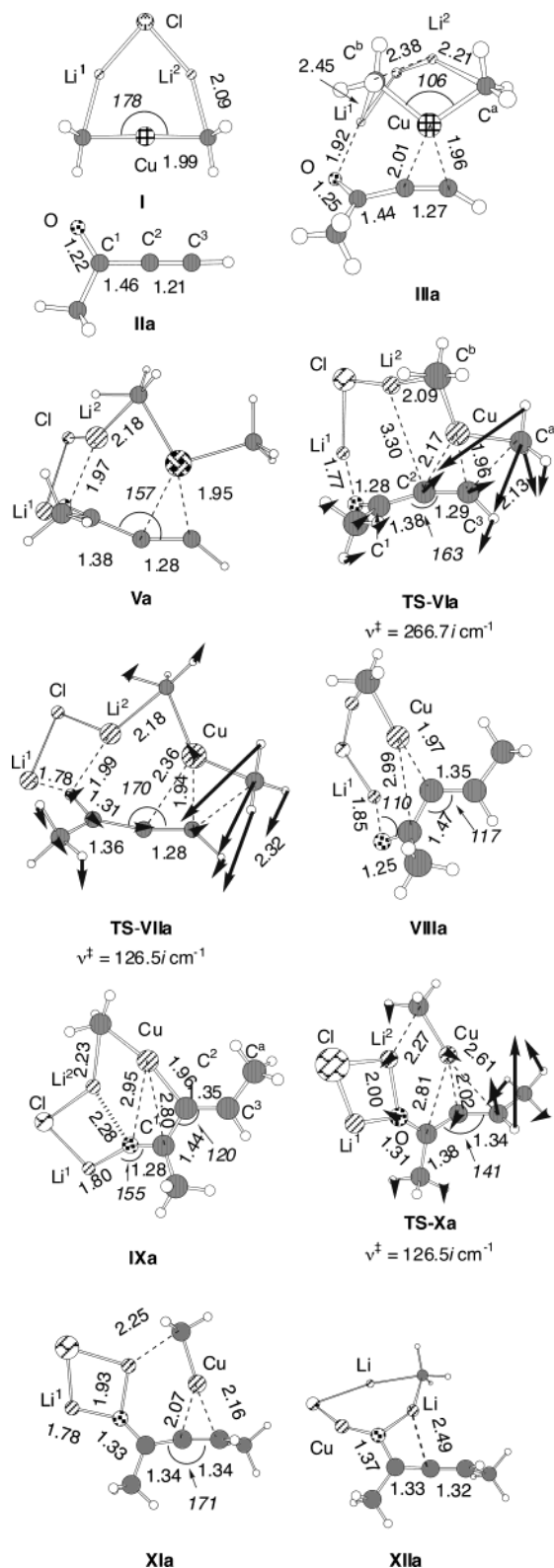


Figure 1. Intermediates and TSs in the reaction of $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ with 3-butyn-2-one (series "a"). Bond lengths are in angstroms and angles are in italics in degrees at the B3LYP/631A level. Arrows indicate imaginary vibration modes at TSs.

intermediate **IXa** exists in equilibrium with the lithium allenolate **XIa** via **TS-Xa** and may go further to another allenolate, **XIIa**.

In series "b" ($\text{X} = \text{OCH}_3$), complexation between **I** and **IIb** gives complex **IIIb** followed by cluster-opening,

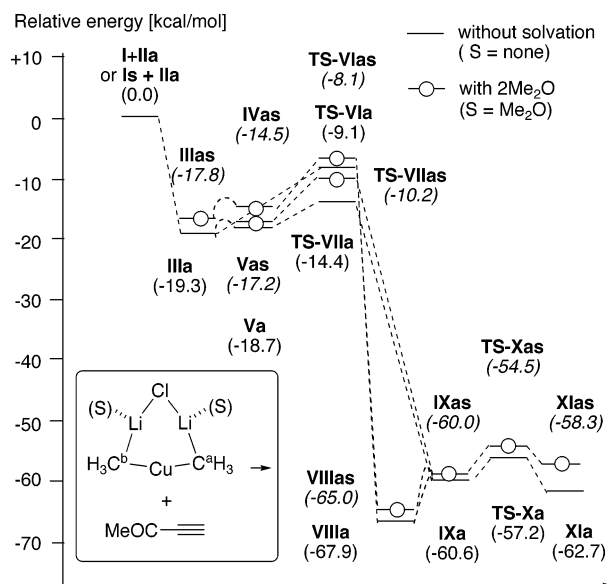


Figure 2. Energy profile in the reaction of $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ with 3-butyn-2-one (series "a" and "as") (B3LYP/631A). The numbers in plain type and in italic are energies in kcal/mol relative to reactants in the $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ and the $\text{Me}_2\text{CuLi}\cdot\text{LiCl}\cdot 2\text{Me}_2\text{O}$ reactions, respectively.

giving the complex **IVb**. We found only path (i) for the ynoate, and hence the complex **IIIb** was connected to the vinylcopper intermediate **IXb** only via path (i). The vinylcopper **IXb** is much more stable than the allenolates **XIb** and **XIIb** and, hence, expected to be the final product of the reaction.

1. Reaction of an ynone ($\text{X} = \text{CH}_3$, Scheme 2; series "a"). The 3D structures of the stationary points involved in the reaction are shown in Figure 1. Figure 2 depicts the energetics. Figure 3 shows the changes of energies (a), a geometric parameter (b), and natural charges (c) for representative stationary points obtained by the IRC analysis in the vicinity of the C–C bond forming step.

A. Solvent-Free Reaction Pathway. The initial interaction between the copper atom of the cuprate cluster **I** and the acetylene part of 3-butyn-2-one **IIa** produces a "closed" complex, **IIIa**. Our optimization of "open" complex **IVa** led to complex **IIIa**. The $\text{Me}-\text{Cu}-\text{Me}$ bond of the cuprate is significantly bent in these complexes so that the copper $3d_{xz}$ orbitals can mix with the methyl carbon $2s$ and $2p$ orbitals and become capable of donating electrons to the π^* orbitals of the acetylene.^{4,15,19} Two isomeric pathways, (i) and (ii), have been found, as shown in Scheme 2. Along path (i) (Scheme 2), the C–C bond formation occurs from **IIIa** via **TS-VIa**, to give an intermediate, **VIIIa**, which is a vinylcopper species. In the TS of the C–C bond formation **TS-VIa** (path (i)), the $\text{C}^2-\text{C}^1=\text{O}$ plane is almost perpendicular to the $\text{C}^1-\text{C}^2-\text{C}^3$ plane ($\angle\text{C}^3-\text{C}^2-\text{C}^1-\text{O} = -94^\circ$). In **VIIIa**, the $\text{C}^1-\text{C}^2-\text{C}^3$ moiety is bent ($\text{C}^1-\text{C}^2-\text{C}^3$ angle of 117°) and one lithium atom Li^1 interacts with the carbonyl oxygen. Interaction of the other lithium atom, Li^2 , with the carbonyl oxygen in **VIIIa** yields **IXa** (Scheme 2). Despite our efforts we could not find a transition state on the path from **VIIIa** to **IXa**; the TS is likely to have a structure similar to that of **IXa**, and the reverse barrier from **IXa** is anticipated to be very small. Toward the intermediate **IXa**, an alter-

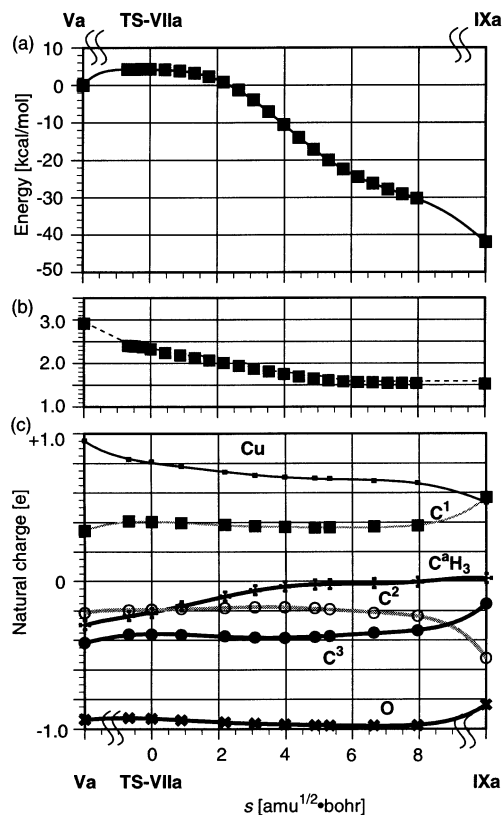


Figure 3. Stationary structures and representative points on the IRC near **TS-VIIa** (B3LYP/631A) in the reaction of $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ with 3-butyn-2-one (series “a”, step (ii)). Changes in (a) relative energy [kcal/mol], (b) $\text{C}^3\text{-C}^a$ bond length [Å], (c) natural charge of various atoms and groups along the reaction coordinate: dot, Cu; \times , O ; cross, C^aH_3 ; square, C^1 ; open circle, C^2 ; black circle, C^3 .

native path (ii) involving an open precursor complex **Va** through **TS-VIIa** was found. As shown in Figure 3b, along path (ii) the forming $\text{C}^3\text{-C}^a$ bond shrinks monotonically as the reaction proceeds from **Va** to another vinylcopper intermediate **IXa**.

B. Energetics of Solvent-Free Pathways. The energy profile of the solvent-free pathways is shown in Figure 2. The activation energy of the C-C bond formation along path (i) (**IIIa** \rightarrow **TS-VIa**) is quite low (10.2 kcal/mol), and that along path (ii) (**IIIa** \rightarrow **TS-VIIa**) is even lower, 4.9 kcal/mol. Double activation of the carbonyl oxygen by two lithium atoms in **TS-VIIa** makes the energy lower than **TS-VIa** by 5.3 kcal/mol. These activation energies are much lower than that of the reaction of simple acetylene (12.8 kcal/mol).¹⁷ The activation energy of isomerization from a vinylcopper to a lithium allenolate (**VIIIa** \rightarrow **TS-Xa** \rightarrow **XIa**) is quite small (3–10 kcal/mol). An isomeric copper allenolate species (**XIIa**, Figure 1)¹⁶ is 26.1 kcal/mol less stable than lithium allenolate **XIa**. In solution, aggregation of MeCu species may stabilize the lithium allenolate, as found by experiments.⁶

C. Changes in Electronic Charge. The natural population analysis of representative intermediates through path (ii) in the 3-butyn-2-one reaction (Figure 3c) indicates that electron density of the copper atom is already decreased in the Cu /ynone π -complex (with the positive charge of +0.48 in **I** and +0.95 in **Va**). During the C-C bond formation from **Va** to **IXa**, both the

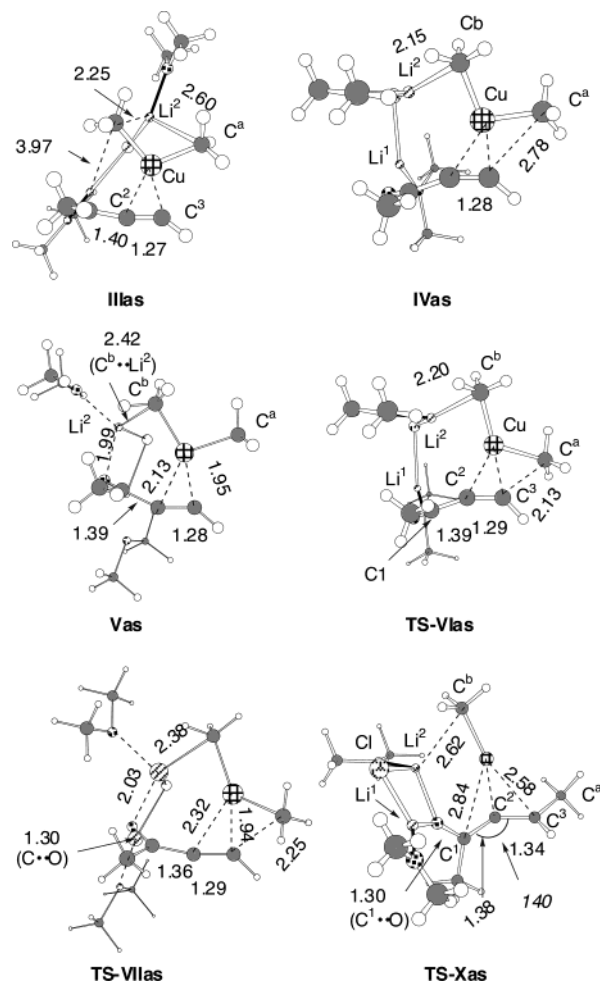


Figure 4. Representative intermediates and TSs in the reaction of $\text{Me}_2\text{CuLi}\cdot\text{LiCl}\cdot 2\text{Me}_2\text{O}$ with 3-butyn-2-one (series “as”). Bond lengths are in angstroms and angles are in italics in degrees at the B3LYP/631A level.

positive charge on the copper atom and the negative charge of the nucleophilic C^aH_3 decrease monotonically. Electronic charges of the carbonyl oxygen, C^2 , and C^3 do not change much except the final stage close to the formation of **IXa**. The charge changes suggest that back-donation from copper into an ynone occurs during the copper π -complex formation, which is followed by electron flow from the methyl group into copper and C^2 atoms during the C-C bond formation.

D. Explicit Solvent Effects in Series “a” (series “as”). Explicit solvent effects have already been found to be rather small in the conjugate addition of lithium organocuprates.^{18,34,41} Coordination of Me_2O molecule lengthens C-Li bonds, especially the $\text{C}^a\text{-Li}^2$ bond (2.21 Å in **IIIa** and 2.60 Å in **IIIas**). In addition to **IIIas**, “open” complexes, **IVas** and **VIas**, were found, in which the Li^2 atom is connected not to the C^aH_3 group but to the other methyl group, C^bH_3 . In **TS-Vas**, **TS-VIIas**, and **TS-Xas**, the $\text{C}^1\text{-C}^2\text{-C}^3\text{-Cu-C}^a\text{H}_3\text{-C}^b\text{H}_3$ part does not change very much with the solvent coordination (Figures 1 and 4). Structures of **IXa** and **XIa** are also similar in solvent-free and solvent-coordinated paths (data not shown). The energy profiles of solvent-coordinated paths (i) and (ii) in the present reaction

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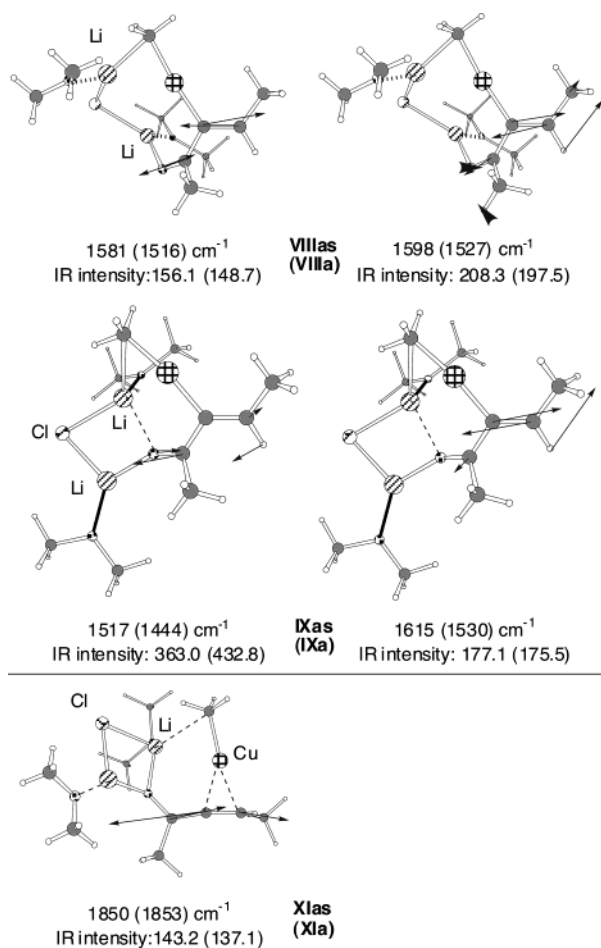


Figure 5. Representative vibrational modes (arrows) of harmonic frequencies of the intermediates in the reaction of 3-butyn-2-one with $\text{Me}_2\text{CuLi}\cdot\text{LiCl}\cdot 2\text{Me}_2\text{O}$ (B3LYP/631A). The data for the molecules without coordinated Me_2O molecules are shown in parentheses for comparison.

have also been found to be essentially the same as the solvent-free one except that a new “open” intermediate **IVas** was found between **IIIas** and **TS-VIas** (Figure 2). The activation energies of C–C bond formation on path (i) (from **IVas** to **TS-VIas**) and on path (ii) (from **Vas** to **TS-VIIas**) were found to be 6.4 kcal/mol (10.2 kcal/mol in the solvent-free case from **IIIa** to **TS-VIa**) and 7.0 kcal/mol (4.3 kcal/mol in the solvent-free case from **Va** to **TS-VIIa**), respectively. Note that energy difference between paths (i) and (ii) is made smaller by solvent coordination (5.3 kcal/mol in **TS-VIa** and **TS-VIIa** and 2.1 kcal/mol in **TS-VIas** and **TS-VIIas**). We expect that further solvent coordination may have less impact on the activation energy than the first coordination. Overall, explicit solvent coordination does not change geometries of stationary points very much except that of **IV**.

E. IR Spectroscopy. To obtain a link between the calculations and the experiments via IR spectroscopic properties, harmonic frequencies have been computed (Figure 5). The IR spectrum of the reaction mixture of the addition of Me_2CuLi to 4-phenyl-3-butyn-2-one at -80°C in THF was reported to exhibit bands at 1550 (weak), 1575 (weak), and 1600 cm^{-1} (strong), and protonation of the mixture gave stereoselectively the *syn*-addition product.¹⁴ These have been taken as evi-

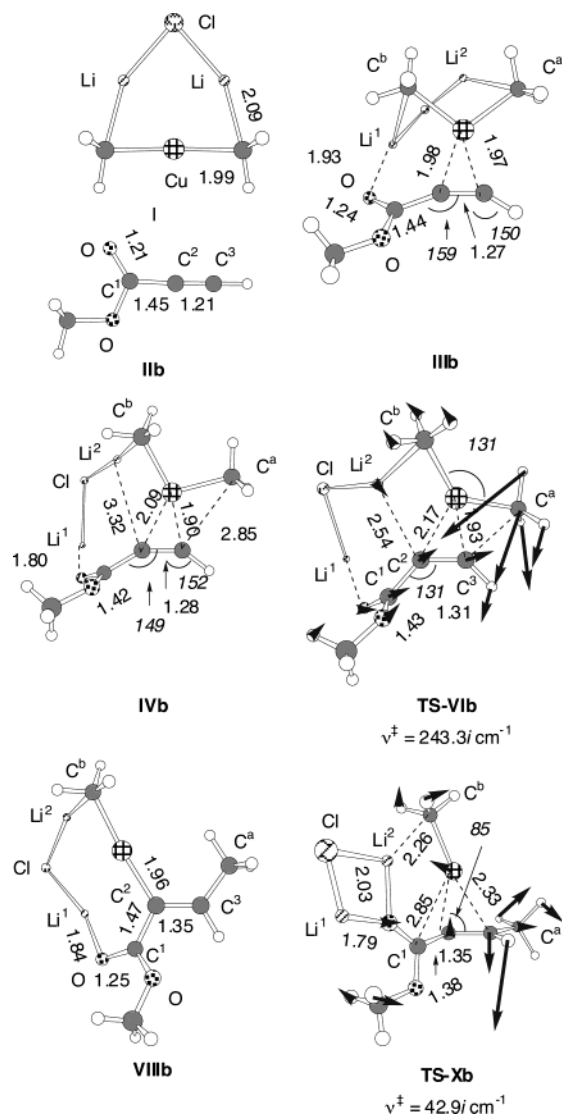


Figure 6. Intermediates and TSs in the reaction of $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ with methyl propynoate (series “b”). Bond lengths are in angstroms and angles are in italics in degrees at the B3LYP/631A level. Arrows indicate the imaginary vibrational modes.

dence for the *syn*-addition and the production of an α -cuprio ketone intermediate.

To identify the nature of the intermediate(s) that gave rise to these bands, IR calculations on various intermediates in our series “a” reaction (ynone model) were performed. The observed product is unlikely to be an allenolate; indeed, the IR band for allenolate **XIas** was calculated to be at 1850 cm^{-1} (strong $\text{C}^2\text{--C}^3\text{--C}^4$ asymmetric stretching band), and no bands were found in the 1600 cm^{-1} region. As for the α -cuprio ketone product, we found two isomers, more stable **VIIIas** and transient **IXas**, in the solution model reaction, whose harmonic frequencies associated with the carbonyl group are 1581 and 1598 cm^{-1} for **VIIIas** and 1517 and 1615 cm^{-1} for **IXas**. In these pairs of vibration, the $\text{C}=\text{O}$ stretching is coupled with the $\text{C}^2=\text{C}^3$ bond stretching and the $\text{C}^2\text{--C}^3\text{--C}^a$ bending (Figure 5). The data are insufficient for characterization of the conformation and aggregation states of the species under experimental conditions. Although the complexity of the molecules and the accuracy of the calculations do not allow exact

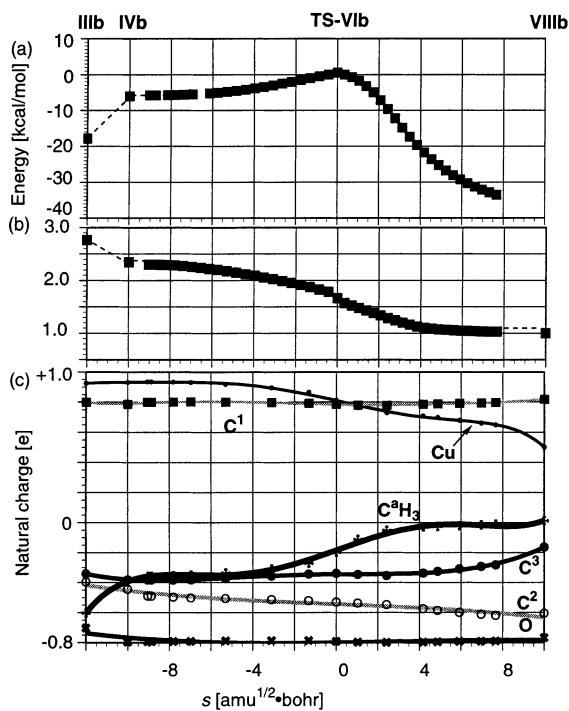


Figure 7. Representative points on the IRC near **TS-VIb** (B3LYP/631A) in the reaction of $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ with methyl propynoate (series "b"). (a) Energy changes [kcal/mol], (b) C^3-C^a bond length [Å], (c) natural charge of various atoms and groups along the reaction coordinate: dot, Cu; \times , O; cross, C^aH_3 ; square, C^1 ; open circle, C^2 ; black circle, C^3 .

identification of the experimental peaks, matching between the experimental and the computational data suggests that the major product in solution is most likely to be the α -cuprio enone of the general structure **3** in Scheme 1.

2. Reaction of an Ynoate ($X = \text{OCH}_3$, Scheme 2; series "b"). A. Reaction Pathway. The reaction pathway of methyl propynoate is similar to the ynone pathway except that **IVb** could be located in the solvent-free pathway and that **V**, **TS-VII**, and **IX** (see path (ii) in Scheme 2) could not be found along the pathway. 3D structures of reactants, intermediates, TSs, and products are shown in Figure 6. Figure 7 shows (a) the changes of energies, (b) geometric parameters, and (c) natural charges for representative stationary points obtained by the IRC analysis in the vicinity of the C–C bond forming step. Figure 8 shows the energetics. The activation energy of 6.6 kcal/mol for C–C bond formation (**IVb** \rightarrow **TS-VIb**) is comparable to that of 6.4 kcal/mol in the reaction of 3-butyn-2-one (Figure 4). The C^3-C^a bond length monotonically decreases from **IIIb** to **VIIIb** (Figure 7b).

Two types of complexes, copper/acetylene (**IIIb**) and lithium/carbonyl (**IVb**) π -complexes, are involved in the initial stage of the reaction (Figure 6). In the closed complex **IIIb**, C^a-Cu-C^b , $C^1-C^2-C^3$, and C^2-C^3-H are bent. In the open complex **IVb**, C^a is already detached from Li^2 . The complex **IVb** directly goes to the vinylcopper product **VIIIb** via the transition state of C–C bond formation **TS-VIb**. In **TS-VIb**, $C^1-C^2-C^3$ is bent to 131° (Figure 6). The C^1-C^2 bond length (1.43 Å) in **TS-VIb** is nearly the same as that in the starting material **IIb** (1.45 Å), whereas that in **TS-VIa** (1.38 Å) is shorter than that in the reactant (1.46 Å) (cf. Figure

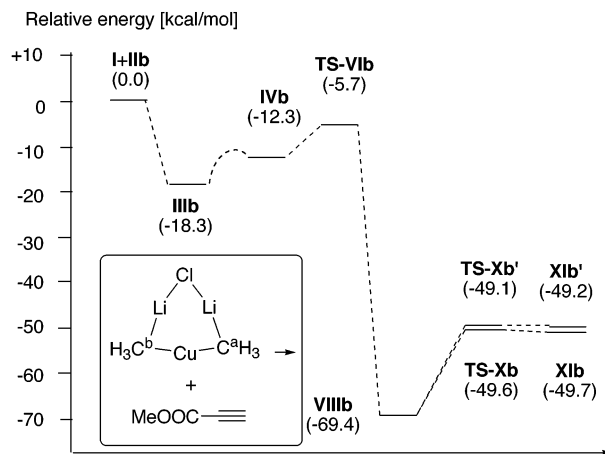


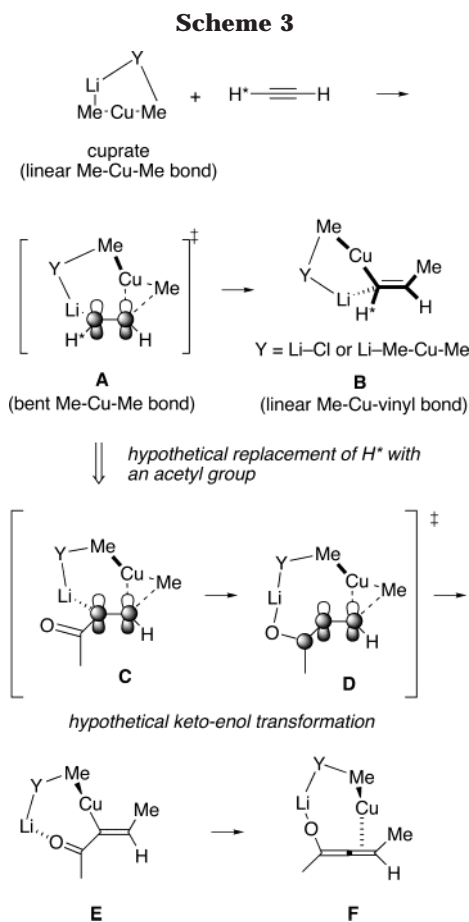
Figure 8. Energy profile in the reaction of methyl propynoate (series "b") with $\text{Me}_2\text{CuLi}\cdot\text{LiCl}$ (B3LYP/631A). Values below the name of the stationary structures refer to energies relative to reactants in kcal/mol.

1). **VIIIb** is 69.4 kcal/mol more stable in energy than the reactants (**I** and **IIb**) (Figure 8). In this reaction, we could not find a complex corresponding to **IXb** (Scheme 2) on the potential energy surface. The activation barrier of isomerization from α -cuprioester intermediate **VIIIb** to allenolate **XIb** or **XIb'** is very high (ca. 20 kcal/mol). **VIIIb** is much more stable than **XIb** or **XIb'**, by ca. 20 kcal/mol.

B. Changes in Electronic Charge. Figure 7c shows the change in the natural charge in the ynoate reaction. The profile of charge change is essentially the same as that for ynone, supporting the similarity between the ynone and the ynoate reactions. During the formation of the closed copper/ynoate π -complex, positive charge on copper of +0.48 in **I** increases to +0.92, and the negative charge of the carbonyl oxygen of -0.55 increases to -0.79. During the C–C bond formation, the negative charge on C^aH_3 decreases monotonically (on the reaction coordinate s between -2 and +4 $\text{amu}^{1/2}\cdot\text{bohr}$) and the positive charge on the copper atom decreases in agreement with the change of the formal oxidation state from Cu(III) to Cu(I).

Conclusions

We have determined for the first time the pathways of the reactions of lithium organocuprate(I) clusters with an α,β -acetylenic ketone and an ester. The reaction occurs through 1,2-addition of organocuprate(I) to the acetylenic carbons to give first a vinylcopper intermediate (α -cuprioenone or α -cuprioenoate).¹¹ The C–C bond formation process in both reactions occurs with a low activation energy (4–7 kcal/mol). On the basis of the previous experimental and the present theoretical studies, we conclude that the apparent difference of stereoselectivity between the ynone and the ynoate reactions (after protonation of the organometallic products) is due to the difference of the ease of isomerization of the α -vinylcopper intermediates **VIIIa** and **VIIIb** (cf. Scheme 2) rather than due to the fundamental mechanistic difference. In the ynone reaction, the activation energy for isomerization is ca. 6 kcal/mol and the resulting allenolate **XIa** is as stable as the vinylcopper intermediate. On the other hand, in the ynoate reaction, the activation energy of the isomerization is 20 kcal/mol and



the resulting allenolate **XIb** is 19.7 kcal/mol less stable than the vinylcopper species **VIIIb**, and hence the α -cuprio ester looks like a reasonable final product. Apparently, the enol preference in the keto/enol equilibrium is larger for ketones than for esters.

In addition, the present study established the connection between “carbocupration” and “conjugate addition”. This may be illustrated by the “metamorphosis” illustrated in Scheme 3. The structure **A** is the TS of the addition of a cuprate reagent ($\text{Me}_2\text{CuLi}\cdot\text{Y}$, $\text{X} = \text{Me}_2\text{CuLi}$ or lithium halide),¹⁷ where the bent cuprate is coordinated to the acetylenic π orbital in the plane of the paper, while the lithium atom is attached electrostatically to the π orbital perpendicular to the plane of the paper (backside). After **A**, intramolecular transmetalation between Li and Cu takes place to give the carbocupration product **B**. Assuming that we replace H^* in **A** with an acetyl group, we can draw a new TS, **C**, which represents a hypothetical TS of carbolithiation of an ynone. We can readily imagine that the lithium cation prefers the carbonyl oxygen to the vinylic carbon atom. Hence, **C** should isomerize to **D**, which is essentially identical with the TSs reported in the foregoing paragraphs (**TS-VIa**, **TS-VIIa**). Just as the TS **A** goes

to **B**, the TS **D** leads to the *syn*-1,2-carbocupration product **E**. In the reaction of an ynone, *E/Z*-isomerization of **E** to **F** takes place easily because of higher stability of the enolate form than the α -metallocarbonyl form of the ketone.

In conclusion, the crucial stage of the addition reaction of a lithium cuprate cluster ($\text{R}_2\text{CuLi}\cdot\text{LiX}$) to either an alkyne, an electron-deficient alkyne, or an electron-deficient alkene involves (1) bending of the cuprate $\text{R}-\text{Cu}-\text{R}$ bond to raise the energy of and expose the $3d_{xz}$ orbital, (2) back-donation from the $3d_{xz}$ orbital to the π^* orbital of the substrate,^{4,19} and (3) reductive elimination of the Cu(III) intermediate. *The initial intermediate, whether experimentally detectable or undetectable, is always the carbocupration product. However, depending on the stability of the resulting organocopper intermediate, diversion to the final experimentally detectable products occurs to give either a syn-carbometalation product or a conjugate addition product.* If the copper-carbon bond is strong as in eq 1 (alkyne and alkynyl ester), the product is the carbocupration product. If the bond is covalently weak enough, the copper-carbon bond is replaced by an electrostatically more favorable lithium-oxygen bond to form a lithium enolate (or allenolate in eq 2) (which may be still complexed with a Cu(I) residue in solution and maintains the memory of the stereochemistry of the *cis*-carbocupration).⁷ It has been suggested by Krause that the ease of the vinylcopper/allenolate equilibrium is affected by lithium solvation.^{11b} The present calculations (cf. Scheme 2) do indicate that this equilibrium accompanies significant change of the coordination state of the lithium atoms and hence corroborate the Krause observation.

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Supporting Information Available: Cartesian coordinates of stationary points. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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