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Ligand Exchange in Mixed Organocuprate(I) π-Complexes

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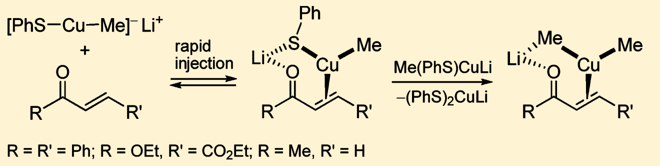
Supporting Information

ABSTRACT: π-Complexes of mixed organocuprate(I) reagents with α,β-unsaturated carbonyl compounds can undergo ligand exchange to give the corresponding homocuprate−olefin π-complexes. The mechanism of this metathesis, which has profound implications for synthetic applications, involves a second-order reaction of the mixed cuprate with the mixed cuprate−olefin π-complex.

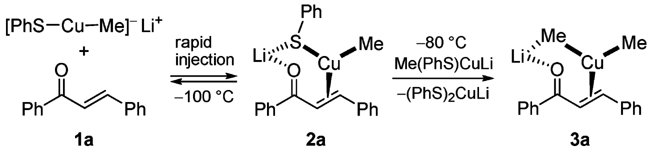


The current renaissance in organocopper chemistry is being led by mixed cuprates R(R′)CuLi and the related organocopper(I) compounds R(L)Cu, where R′ is an anionic "dummy" ligand (alkynyl, phenylthio, thienyl, etc.) and L is a neutral ligand (phosphine, thioether, pyridine, etc.).[1,2] Anionic or neutral, the auxiliary ligands R′ and L promote solubility and thus reactivity—with the prerequisite that they are not transferred to the substrate under ordinary conditions. These special organocopper reagents are critically important when the R group is valuable, since homocuprates R_2CuLi only transfer one of the R groups in most applications.

We have recently shown that several popular mixed cuprates exhibit a powerful orientation effect in π-complexes, where the auxiliary ligand R′ is oriented toward the carbonyl or other activating group.[3] This orientation places the transferred group R in close proximity to the usual site of addition. During the course of these studies, we noted that some of the mixed cuprate π-complexes tended to metathesize to the corresponding homocuprate complexes. Considering the importance of mixed cuprates in the burgeoning field of asymmetric induction,[1,2] we decided to investigate the ligand exchange phenomenon in more detail.

For kinetic studies we chose Posner's Me(PhS)CuLi,[4] since the precursor, PhSCu, is commercially available and the cuprate is free of LiI, which is present when mixed cuprates are prepared from CuI (vide infra). Organocuprates and their complexes are known to form aggregates with lithium halides,[5] which is a potential complicating factor for the kinetics. Chalcone (**1a**), diethyl fumarate (**1b**; DEF), and methyl vinyl ketone (**1c**; MVK) were chosen as substrates, since they are structurally diverse and give stable π-complexes with a range of mixed cuprates,[3] as well as the homocuprate, Me_2CuLi.[6,7]

Scheme 1. Formation and Metathesis of the Me(PhS)CuLi−Chalcone Complex 2a



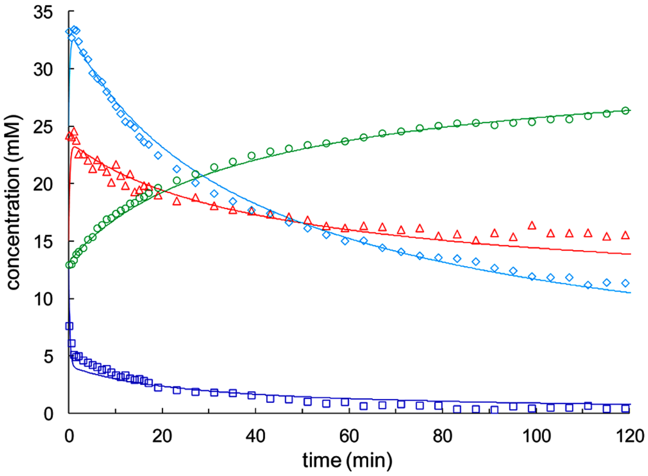


Figure 1. Conversion of Me(PhS)CuLi−chalcone complex **2a** (□) to Me_2CuLi−chalcone complex **3a** (○). Substrate (△) and mixed cuprate (◇) data are also plotted. The continuous curves are calculated by a least-squares method (see text).

For the kinetics measurements, the substrate (20−40 μmol) was dissolved in THF-d_8 and injected into a solution of the cuprate in THF-d_8/benzene-d_6 (7:1, 420 μL, 30 μmol) at −100 °C, using our usual rapid injection methodology (30−60 μL injection).[3,6,7] When equilibrium had been established, the temperature was increased rapidly to −80 °C, and after 2 min to allow for thermal equilibration and magnetic field shimming, single-pulse ^{1}H NMR spectra were collected. The reaction of **1a** with Me(PhS)CuLi is shown in Scheme 1, and the resulting concentration versus time curves are plotted in Figure 1.

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Chart 1 contains the basic kinetic scheme used to fit the data from all runs. For the reaction in Scheme 1, MC = Me(PhS)CuLi, Sub = **1a**, MC−Sub = **2a**, and HC−Sub = **3a**. The theoretical curves plotted in Figure 1 were calculated using Mathcad and a global least-squares program in which the initial concentrations were set and the values of k_1, k_{-1}, and k_2 were varied. Optimal values for the rate constants were $k_1 = 0.016$ min^{-1} mM^{-2}, $k_{-1} = 3.0$ min^{-1} mM^{-1} and $k_2 = 0.0035$ min^{-1} mM^{-2}.

Chart 1. Metathesis Mechanism for Mixed Cuprate Complexes

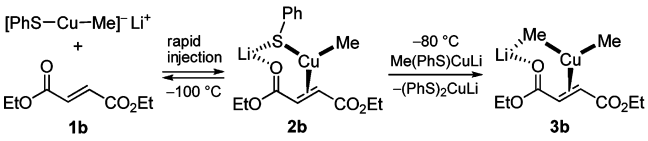
$$\text{MC} + \text{Sub} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{MC-Sub} \qquad (1)$$

$$\text{MC-Sub} + \text{MC} \xrightarrow{k_2} \text{HC-Sub} + \text{HC'} \qquad (2)$$

MC = mixed cuprate, RR'CuLi [e.g., Me(PhS)CuLi]
Sub = substrate [chalcone, diethyl fumarate, MVK]
HC = homocuprate 1 = R_2CuLi [e.g., Me_2CuLi]
HC' = homocuprate 2 = R'_2CuLi [e.g., $(PhS)_2CuLi$]

When the kinetics experiment was repeated with **1b** as the substrate (Scheme 2), the reaction was significantly slower, since DEF forms much "tighter" π-complexes than chalcone.[6] Complexes **2b** and **3b** each had major and minor species, which were integrated together. The data are plotted in Figure 2, and optimal values for the rate constants are $k_1 = 0.025$ min^{-1} mM^{-2}, $k_{-1} = 0.0040$ min^{-1} mM^{-1}, and $k_2 = 0.000\,90$ min^{-1} mM^{-2}, calculated using the global least-squares method.

Scheme 2. Formation and Metathesis of the Me(PhS)CuLi−DEF Complex 2b



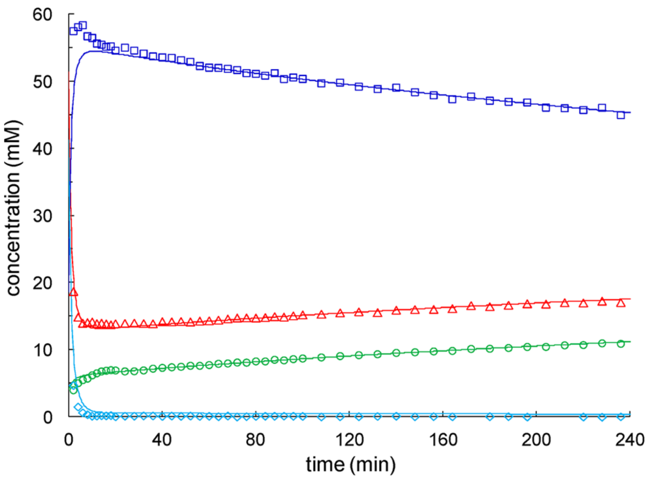
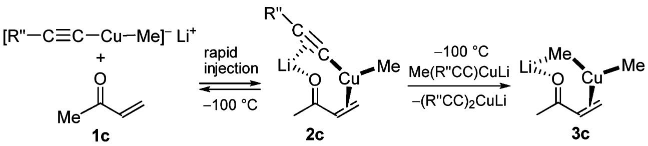


Figure 2. Conversion of Me(PhS)CuLi−DEF complex **2b** (□) to Me_2CuLi−DEF complex **3b** (○). Substrate (△) and mixed cuprate (◇) data are also plotted. The continuous curves are calculated by a least-squares method (see text).

The reaction of Me(PhS)CuLi with **1c** was too fast to get useful kinetic data; therefore, we looked for a less reactive mixed cuprate. The first mixed cuprate reagents were based on alkynes; however, they were much less reactive than the corresponding homocuprates, which is why there has been a great deal of subsequent research to find more reactive mixed cuprates.[2−4] We chose Corey's second-generation alkynylcuprate $CH_3(R''C{\equiv}C)CuLi$ ($R'' = CH_3O(CH_3)_2C$) for further study.[8]

The Corey cuprate was prepared from the corresponding alkynyllithium reagent and MeCu, derived from CuI.[8] When **1c** in THF-d_8 was injected as usual into a solution of Corey's cuprate in THF-d_8/benzene-d_6 at −100 °C, the product was complex **2c**, which underwent metathesis at this temperature to give the corresponding homocuprate complex **3c** (Scheme 3; N.B.: it was not necessary to warm the sample to −80 °C in this case). Figure 3 shows stacked ^{1}H NMR spectra for the reaction in Scheme 3.

Scheme 3. Formation and Metathesis of the Me(R″C≡C)CuLi−MVK Complex 2c



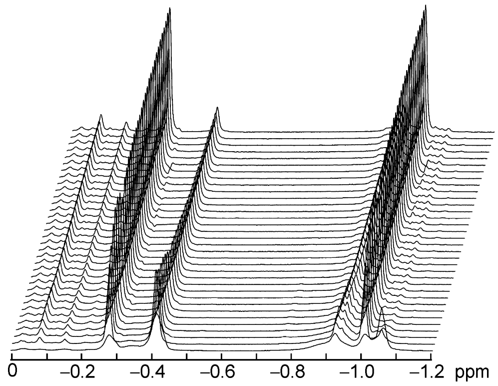


Figure 3. Stacked ^{1}H NMR spectra (Me−Cu region, 4 min apart) for the conversion of **2c** (−0.41 ppm) to **3c** (major, −0.27, −1.01 ppm; minor, −0.08, −0.94 ppm). Mixed cuprate appears at −1.06 ppm in the initial spectrum.

Only one mixed cuprate π-complex, **2c**, was observed; however, the presence of LiI gave rise to major complex **3c** and minor complex **3c**·LiI,[3,6] which were integrated together. The global least-squares fit gave $k_1 = 0.15$ min^{-1} mM^{-2}, $k_{-1} = 0.20$ min^{-1} mM^{-1}, and $k_2 = 0.030$ min^{-1} mM^{-2}. In this case the data were not quite as good as the previous two examples, owing to the usual complications observed with MVK.[3] Nevertheless, the kinetic data are consistent with the mechanism in Chart 1 and not an alternative mechanism involving two molecules of **2c**.

In summary, popular phenylthio and alkynyl mixed cuprates and typical α,β-unsaturated carbonyl compounds give π-complexes that undergo a facile ligand exchange reaction to generate the corresponding homocuprate π-complexes. The metathesis was more rapid with excess mixed cuprate, and it was arrested by excess substrate. Conditions that favor fast reductive elimination may serve to minimize this complication. In some applications the homocuprate complex may well be the key intermediate for subsequent product formation.

ASSOCIATED CONTENT

Supporting Information

Figures and a table giving typical spectra, raw data, and sample calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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