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Preparation of σ- and π-Allylcopper(III) Intermediates in S_N2 and S_N2' Reactions of Organocuprate(I) Reagents with Allylic Substrates

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The reactions of organocopper(I) reagents with allylic substrates have been among their most valuable synthetic applications,[1] and consequently, they have been scrutinized from experimental[2] as well as theoretical[3] points of view. Nevertheless, the outcome is difficult to predict for each new case, as the partition between S_N2 and S_N2' products is a complex function of the experimental parameters. Both σ- and π-allylcopper(III) intermediates have been proposed, and a detailed understanding of their roles can only accelerate progress in this important area, for example, in the development of enantioselective reactions.

Copper(III) intermediates have been shown to play a central role in the conjugate addition[4] and S_N2 reactions[5–7] of organocopper(I) reagents. σ-Allyl Cu^I compounds are well-known,[8] but π-allyl Cu^I compounds appear to be unknown;[9] thus, the corresponding Cu^{III} complexes have theoretical as well as practical interest. We can now report that, by using rapid injection NMR spectroscopy (RI-NMR),[10,11] we have been able to prepare and characterize the first examples of both η^1 σ-allyl and η^3 π-allyl Cu^{III} complexes and to study their reactions.

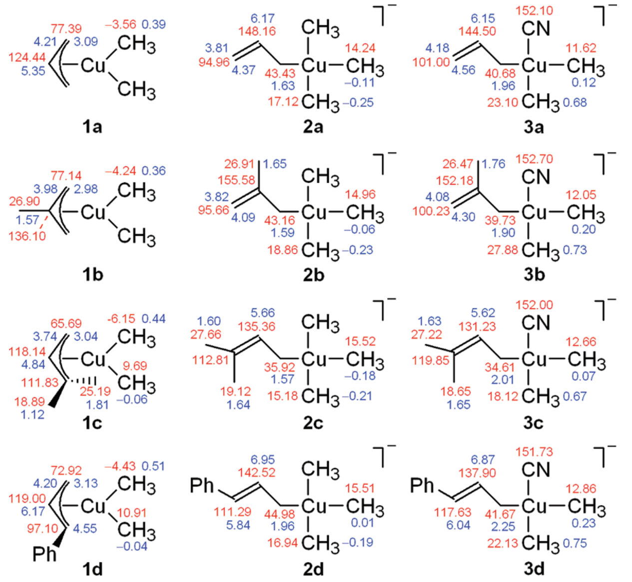
Prototypical π-allyl Cu^{III} complex, (η^3-allyl)dimethylcopper(III) **1a** (Chart 1), was prepared by injecting a solution of allyl chloride in THF-d_8 into a solution of iodo-Gilman reagent $Me_2CuLi{\cdot}LiI$ (**A**) in THF-d_8, spinning in the probe of an NMR spectrometer at −100 °C. A σ-allyl Cu^{III} species, lithium (η^1-allyl)trimethylcuprate(III) **2a**, also appeared rapidly (∼50% maximum yield, 0.1 h), but then disappeared by the time **1a** reached its maximum yield (∼80%, 0.5 h). Complex **1a** slowly decomposed to 1-butene.

Likewise, substituted π-allyl Cu^{III} compounds **1b**−**d** and σ-allyl Cu^{III} *ate* complexes **2b**−**d** were prepared from **A** and the corresponding allyl chlorides. As in reactions involving **A** and EtI,[5,6] the main side product with excess **A** was Ashby's cuprate, Me_3Cu_2Li;[12] otherwise it appeared to be MeCu(Cl)Li.

When the organocopper(I) reagent was $Me_2CuLi{\cdot}LiI/PBu_3$, the product was **2a** (>90%) and the side product was $MeCuPBu_3$. No **1a** was present: PBu_3 appears to inhibit the conversion of **2a** to **1a** by complexing MeCu (vide infra). No copper(III)−phosphine complex was observed, in contrast to the result with this reagent and EtI, where the product was *trans*-$EtMe_2Cu(PBu_3)$.[6]

Structures of the new compounds were assigned by using 1D and 2D NMR (see Supporting Information). Especially noteworthy are the ^{13}C NMR chemical shifts to higher shielding from TMS in **1a**−**d** (Chart 1). The ^{13}C NMR shifts for the methyl (−3.56 ppm) and allyl (77.39 ppm for C1/C3) groups in **1a** are similar to the corresponding values for π-complexes of **A** with α-enones.[10,13,14] The lack of a clear demarcation between NMR shifts for Cu^I and Cu^{III} compounds is not surprising, as Snyder has calculated that the charges on Cu in what are *formally* organocopper(III) complexes are actually ca. +1.[15]

Chart 1. New Compounds Prepared in This Study with NMR Chemical Shifts for ^{13}C (Red) and ^1H (Blue) in THF-d_8 at −100 °C (The Li^+ counterions in **2** and **3** have been omitted for clarity.)



Lithium *cis*-(η^1-allyl)cyanodimethylcuprate(III) **3a** was obtained in essentially quantitative yield (0.3 h) from allyl chloride and cyano-Gilman reagent $Me_2CuLi{\cdot}LiCN$ (**B**) in THF-d_8 at −100 °C. At longer times, minor amounts of **2a** appeared as Me replaced CN. Substituted cyano *ate* complexes **3b**−**d** were prepared analogously from **B** and the corresponding allyl chlorides. In contrast to the *cis*-cyano complexes formed here, *trans*-$EtMe_2Cu(CN)Li$ was formed in the reaction of **B** with EtI.[5]

Two-bond $^{13}C-^{13}C$ coupling constants ^2J across copper have been invaluable for structural studies of organocopper(I)[13,16] and organocopper(III) compounds.[4–6] In the case of labeled **1a**, (η^3-$^{13}CH_2CH^{13}CH_2$)($^{13}CH_3$)$_2$Cu,[17] a single two-bond coupling constant, $^2J = 9.7$ Hz,[13] was measured between C1/C3 of the π-allyl group and the carbon atoms of the (equivalent) methyl groups. Its magnitude lies between typical values for *cis* and *trans* two-bond couplings in square planar complexes of copper(III).[4–6] For example, in labeled **2a**, (η^1-$^{13}CH_2CH^{13}CH_2$)($^{13}CH_3$)$_3$CuLi,[17] the methylene−methyl *trans* coupling was $^2J = 34.2$ Hz, while the methylene−methyl *cis* coupling was too small to be resolved. The methyl−methyl *cis* coupling was $^2J = 2.3$ Hz.

In labeled **3a**, (η^1-$^{13}CH_2CH^{13}CH_2$)($^{13}CH_3$)$_2$Cu(^{13}CN)Li,[17] two-bond $^{13}C-^{13}C$ couplings between the cyano group and the methyl groups *cis* and *trans* to it were $^2J = 4.2$ and 38.0 Hz, respectively. The methylene−methyl *trans* coupling was $^2J = 31.1$ Hz. The rest of the *cis* couplings were not resolved.

Addition of allyl acetate to **A** in THF-d_8 at −100 °C gave a good yield (>90%) of **2a** (Scheme 1). In the absence of acetate or

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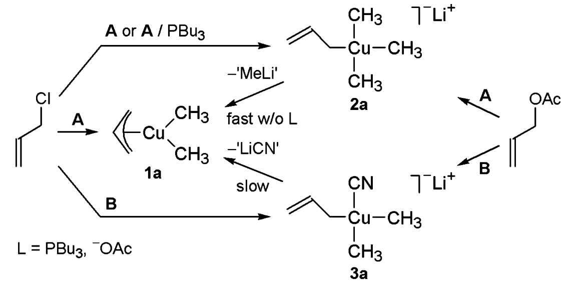
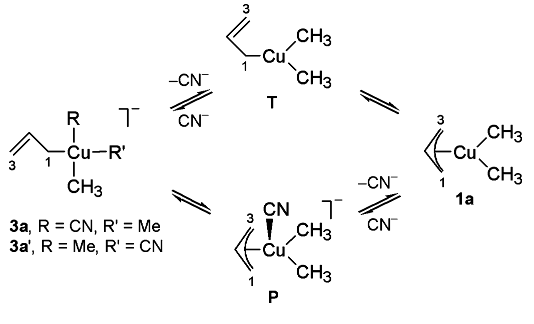
Scheme 1. Alternative Routes to Organocopper(III) Complexes



Scheme 2. Dissociative versus Associative Reaction Mechanisms (The Li$^+$ counterions are not shown for the sake of simplicity.)



PBu$_3$, methyl is rapidly removed from **2a**, perhaps by a soluble form of MeCu (e.g., Me$_3$Cu$_2$Li). Substituted *ate* complexes **2b**−**d** were prepared analogously from the corresponding allyl acetates.

Under the same conditions, allyl acetate and **B** gave an essentially quantitative yield of **3a**. Substituted *cis*-cyano complexes **3b**−**d** were prepared in good yields from **B** and the corresponding allyl acetates, although prenyl acetate required higher temperatures. Small amounts of π-allyl complexes **1** appeared at longer times or higher temperatures; presumably, **3** loses cyanide in a soluble form such as Li$_2$CN$^+$.[18]

Addition of either prenyl acetate or dimethylvinylcarbinol acetate to a solution of **B** in THF-d_8 at −60 °C yielded **3c** exclusively. Upon warming the reaction mixture to −40 °C, 2-methyl-2-pentene appeared as the only alkene.

In a related experiment, addition of allyl-1-d_1 acetate to **B** in THF-d_8 at −100 °C gave **3a**-d_1 in which the label was scrambled between C1 and C3.

Since **1a** and **3a** are 16-electron d^8 species, either dissociative or associative mechanisms can account for the results from **B** and allylic substrates (Scheme 2). The former involves a trigonal 14-electron species **T**[3,15] and the latter a pyramidal 18-electron one, **P**.[19,20] Allyl isomerization occurs when C3 in **3a** (or **T**) attaches to Cu to form a π-allyl moiety in **P** (or **1a**), and then C1 detaches.

In principle, **3a** can be formed via capture of cyanide by **1a** or via rearrangement of **3a′**, produced by the same concerted mechanism that yields *trans*-EtMe$_2$Cu(X)Li from Me$_2$CuLi·LiX and EtI.[5] The *trans* to *cis* isomerization is observed for some X, but not X = CN; hence, allyl must play a key role if **3a′** is involved. Rearrangement could occur by a mechanism analogous to one of those above. For example, coordination of the double bond in **3a′** gives a pyramidal intermediate with Me in the apical position (i.e., **P′**), which affords **3a** when this methyl group replaces the coordinated double bond *trans* to the cyano group.

Addition of cinnamyl chloride to **A** in THF-d_8 at −100 °C resulted in a mixture of **1d** and **2d** (1:2, 0.5 h; 1:1, 2 h; 2:1, 3.5 h). Upon warming to −90 °C (0.5 h), 90% of **2d** had been converted to **1d** and alkenes (1:3), 3-phenylbutene **4** (S$_N$2′ product) and (*E*)-1-phenylbutene **5** (S$_N$2 product, ca. 20:1 at −100 °C). Upon warming to −70 °C, **1d** decomposed at a significant rate to afford the final mixture of **4** and **5** (1:1, 1 h). The ratio of **4** to **5** from **1d** at −70 °C was 1:3.

The analogous reaction of cinnamyl chloride with **B** gave only **3d** at −100 °C. It slowly decomposed at −80 °C to **4** and **5** (1:14, 2 h), as a small amount (15% max) of π-allyl complex **1d** appeared.

Thus, in the reaction of **A** with cinnamyl chloride, the π-allyl Cu^{III} intermediate **1d** gave mainly S$_N$2 product, whereas the σ-allyl Cu^{III} intermediate **2d** gave mainly S$_N$2′ product. In contrast, σ-allyl Cu^{III} intermediate **3d** from **B** and cinnamyl chloride gave predominantly S$_N$2 product, which can be rationalized by the intermediacy of **1d**, as in the case of the S$_N$2 product from **A**.

In summary, we have confirmed the structures proposed for π-allyl Cu^{III} complexes by preparing the first examples. On the other hand, the *ate* structures that we have established for the first σ-allyl Cu^{III} complexes are novel, and they are crucial to understand the reactivity of allylic substrates with organocopper(I) reagents.

Finally, *cis*-cyano σ-allyl Cu^{III} intermediates are found in both the 1,4-addition reaction of **B**/TMSCl with 2-cyclohexenone[4] and the S$_N$2′ reaction of **B** with dimethylvinylcarbinol acetate; hence, the two types of conjugate addition are unified by a deep connection, which we conjecture to be π-allylcopper(III).

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Supporting Information Available: NMR spectra for compounds **1a**, **2a**, and **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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