

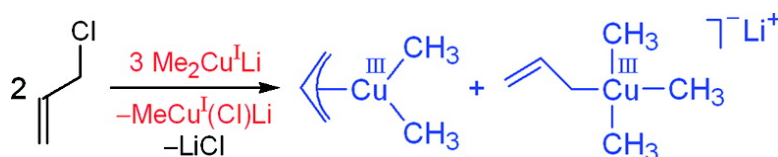
Communication

**Preparation of  $\pi$ - and  $\sigma$ -Allylcopper(III) Intermediates in  $S_N2$  and  $S_N2^{\#}$  Reactions of Organocuprate(I) Reagents with Allylic Substrates**

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## Preparation of $\sigma$ - and $\pi$ -Allylcopper(III) Intermediates in $S_N2$ and $S_N2'$ Reactions of Organocuprate(I) Reagents with Allylic Substrates

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The reactions of organocuprate(I) reagents with allylic substrates have been among their most valuable synthetic applications,<sup>1</sup> and consequently, they have been scrutinized from experimental<sup>2</sup> as well as theoretical<sup>3</sup> 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  $\sigma$ - and  $\pi$ -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<sup>4</sup> and  $S_N2$  reactions<sup>5–7</sup> of organocuprate(I) reagents.  $\sigma$ -Allyl Cu<sup>I</sup> compounds are well-known,<sup>8</sup> but  $\pi$ -allyl Cu<sup>I</sup> compounds appear to be unknown;<sup>9</sup> thus, the corresponding Cu<sup>III</sup> complexes have theoretical as well as practical interest. We can now report that, by using rapid injection NMR spectroscopy (RI-NMR),<sup>10,11</sup> we have been able to prepare and characterize the first examples of both  $\eta^1$   $\sigma$ -allyl and  $\eta^3$   $\pi$ -allyl Cu<sup>III</sup> complexes and to study their reactions.

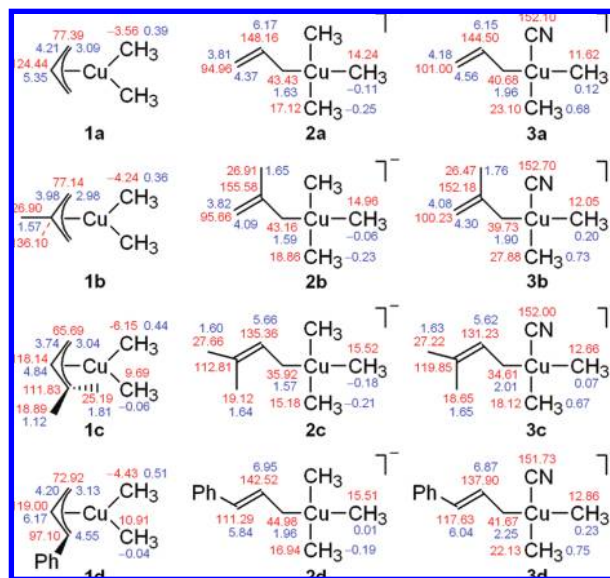
Prototypical  $\pi$ -allyl Cu<sup>III</sup> complex, ( $\eta^3$ -allyl)dimethylcopper(III) **1a** (Chart 1), was prepared by injecting a solution of allyl chloride in THF-*d*<sub>8</sub> into a solution of iodo-Gilman reagent Me<sub>2</sub>CuLi·LiI (**A**) in THF-*d*<sub>8</sub>, spinning in the probe of an NMR spectrometer at –100 °C. A  $\sigma$ -allyl Cu<sup>III</sup> species, lithium ( $\eta^1$ -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  $\pi$ -allyl Cu<sup>III</sup> compounds **1b–d** and  $\sigma$ -allyl Cu<sup>III</sup> *ate* complexes **2b–d** were prepared from **A** and the corresponding allyl chlorides. As in reactions involving **A** and EtI,<sup>5,6</sup> the main side product with excess **A** was Ashby's cuprate, Me<sub>3</sub>Cu<sub>2</sub>Li;<sup>12</sup> otherwise it appeared to be MeCu(Cl)Li.

When the organocuprate(I) reagent was Me<sub>2</sub>CuLi·LiI/PBu<sub>3</sub>, the product was **2a** (>90%) and the side product was MeCuPBu<sub>3</sub>. No **1a** was present: PBu<sub>3</sub> 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<sub>2</sub>Cu(PBu<sub>3</sub>).<sup>6</sup>

Structures of the new compounds were assigned by using 1D and 2D NMR (see Supporting Information). Especially noteworthy are the <sup>13</sup>C NMR chemical shifts to higher shielding from TMS in **1a–d** (Chart 1). The <sup>13</sup>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  $\pi$ -complexes of **A** with  $\alpha$ -enones.<sup>10,13,14</sup> The lack of a clear demarcation between NMR shifts for Cu<sup>I</sup> and Cu<sup>III</sup> compounds is not surprising, as Snyder has calculated that the charges on Cu in what are *formally* organocuprate(III) complexes are actually ca. +1.<sup>15</sup>

**Chart 1.** New Compounds Prepared in This Study with NMR Chemical Shifts for <sup>13</sup>C (Red) and <sup>1</sup>H (Blue) in THF-*d*<sub>8</sub> at –100 °C (The Li<sup>+</sup> counterions in **2** and **3** have been omitted for clarity.)



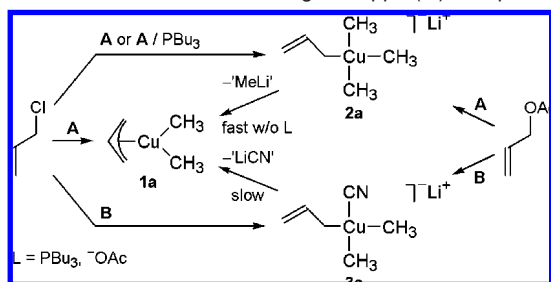
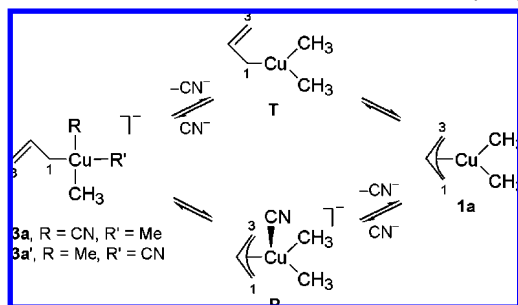
Lithium *cis*-( $\eta^1$ -allyl)cyanodimethylcuprate(III) **3a** was obtained in essentially quantitative yield (0.3 h) from allyl chloride and cyano-Gilman reagent Me<sub>2</sub>CuLi·LiCN (**B**) in THF-*d*<sub>8</sub> at –100 °C. At longer times, minor amounts of **2a** appeared as Me replaced CN. 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<sub>2</sub>Cu(CN)Li was formed in the reaction of **B** with EtI.<sup>5</sup>

Two-bond <sup>13</sup>C–<sup>13</sup>C coupling constants <sup>2</sup>*J* across copper have been invaluable for structural studies of organocuprate(I)<sup>13,16</sup> and organocuprate(III) compounds.<sup>4–6</sup> In the case of labeled **1a**, ( $\eta^3$ -<sup>13</sup>CH<sub>2</sub>CH<sup>13</sup>CH<sub>2</sub>)(<sup>13</sup>CH<sub>3</sub>)<sub>2</sub>Cu,<sup>17</sup> a single two-bond coupling constant, <sup>2</sup>*J* = 9.7 Hz,<sup>13</sup> was measured between C1/C3 of the  $\pi$ -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).<sup>4–6</sup> For example, in labeled **2a**, ( $\eta^1$ -<sup>13</sup>CH<sub>2</sub>CH<sup>13</sup>CH<sub>2</sub>)(<sup>13</sup>CH<sub>3</sub>)<sub>3</sub>CuLi,<sup>17</sup> the methylene–methyl *trans* coupling was <sup>2</sup>*J* = 34.2 Hz, while the methylene–methyl *cis* coupling was too small to be resolved. The methyl–methyl *cis* coupling was <sup>2</sup>*J* = 2.3 Hz.

In labeled **3a**, ( $\eta^1$ -<sup>13</sup>CH<sub>2</sub>CH<sup>13</sup>CH<sub>2</sub>)(<sup>13</sup>CH<sub>3</sub>)<sub>2</sub>Cu(<sup>13</sup>CN)Li,<sup>17</sup> two-bond <sup>13</sup>C–<sup>13</sup>C couplings between the cyano group and the methyl groups *cis* and *trans* to it were <sup>2</sup>*J* = 4.2 and 38.0 Hz, respectively. The methylene–methyl *trans* coupling was <sup>2</sup>*J* = 31.1 Hz. The rest of the *cis* couplings were not resolved.

Addition of allyl acetate to **A** in THF-*d*<sub>8</sub> 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  $\text{Li}^+$  counterions are not shown for the sake of simplicity.)

$\text{PBu}_3$ , methyl is rapidly removed from **2a**, perhaps by a soluble form of  $\text{MeCu}$  (e.g.,  $\text{Me}_3\text{Cu}_2\text{Li}$ ). 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  $\pi$ -allyl complexes **1** appeared at longer times or higher temperatures; presumably, **3** loses cyanide in a soluble form such as  $\text{Li}_2\text{CN}^+$ .<sup>18</sup>

Addition of either prenyl acetate or dimethylvinylcarbinol acetate to a solution of **B** in  $\text{THF-d}_8$  at  $-60^\circ\text{C}$  yielded **3c** exclusively. Upon warming the reaction mixture to  $-40^\circ\text{C}$ , 2-methyl-2-pentene appeared as the only alkene.

In a related experiment, addition of allyl-1- $d_1$  acetate to **B** in  $\text{THF-d}_8$  at  $-100^\circ\text{C}$  gave **3a-d** 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**<sup>3,15</sup> and the latter a pyramidal 18-electron one, **P**.<sup>19,20</sup> Allyl isomerization occurs when C3 in **3a** (or **T**) attaches to Cu to form a  $\pi$ -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*- $\text{EtMe}_2\text{Cu(X)Li}$  from  $\text{Me}_2\text{CuLi}\cdot\text{LiX}$  and  $\text{EtI}$ .<sup>5</sup> 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  $\text{THF-d}_8$  at  $-100^\circ\text{C}$  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  $-90^\circ\text{C}$  (0.5 h), 90% of **2d** had been converted to **1d** and alkenes (1:3), 3-phenylbutene **4** ( $\text{S}_{\text{N}}2'$  product) and (*E*)-1-phenylbutene **5** ( $\text{S}_{\text{N}}2$  product, ca. 20:1 at  $-100^\circ\text{C}$ ). Upon warming to  $-70^\circ\text{C}$ , **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  $-70^\circ\text{C}$  was 1:3.

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

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

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

Finally, *cis*-cyano  $\sigma$ -allyl  $\text{Cu}^{\text{III}}$  intermediates are found in both the 1,4-addition reaction of **B**/TMSCl with 2-cyclohexenone<sup>4</sup> and the  $\text{S}_{\text{N}}2'$  reaction of **B** with dimethylvinylcarbinol acetate; hence, the two types of conjugate addition are unified by a deep connection, which we conjecture to be  $\pi$ -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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