# A Chemical Scale for Electron-transfer Ability of Methylcopper Reagents

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The ratio of methyl transfer (**2**) and reduction (**3**) products in the reaction of trimethoxycarbonylethylene **1** with methylcopper reagents MeCuLn varies with the copper species, and decreased in the following order: MeCu(CN)Li > MeCu > $Me_2Cu(CN)Li_2$ >> $Me_2CuLi$ > $Me_3CuLi_2$.

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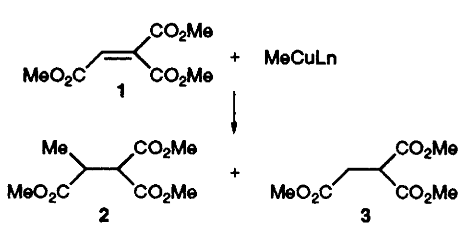
The popularity of organocopper complexes as reagents in organic synthesis[1] has brought forth numerous mechanistic investigations of both substitution and conjugate addition reactions.[2] Concerning conjugate addition, cuprate–olefin π-complexes have been detected by NMR spectroscopy[2a,c,d] and it is proposed that the complexes go on to form $Cu^{III}$ intermediates (nucleophilic addition process). In addition to this plausible and currently more accepted mechanism, an electron-transfer process from RCuLn to unsaturated substrates has been proposed frequently as the second mechanism.[3,4] Both processes may take place competitively. In the second mechanism, there must be a correlation between the electronic requirements of the organocopper reagents and the electronic demands of the enones and enoates.† The electron-accepting ability of the substrates can be elucidated from their polarographic one-electron reduction potentials.[3,4] Little is known, however, about the electron-donating ability of the reagents.[5]

We report here the order of electron-transfer ability for methylcopper reagents. Initially we attempted to measure the oxidation potential of copper reagents using physicochemical methods, but all trials resulted in failure due to their instability.[5] We have found that the reaction of trimethoxycarbonylethylene **1**[6] with methylcopper reagents is a suitable reaction to investigate the scale of the electron-donating ability of the organocopper reagents. The reaction gave a mixture of the methyl transfer (**2**) and reduction (**3**) products in high yields [eqn. (1)].‡ The **2**:**3** ratio-MeCuLn plots are shown in Fig. 1. The ratio of **2**:**3** decreased in the following order; $MeCu(CN)Li{\cdot}LiBr$ > $MeCu{\cdot}LiI{\cdot}LiBr$ > $Me_2Cu(CN)Li_2{\cdot}2LiBr$ >> $Me_2CuLi{\cdot}LiI{\cdot}2LiBr$ > $Me_3CuLi_2{\cdot}LiI{\cdot}3LiBr$.[7] It has been believed for a long time in organocopper chemistry, without concrete evidence, that a reduction product is produced *via* an electron-transfer process.



(1)

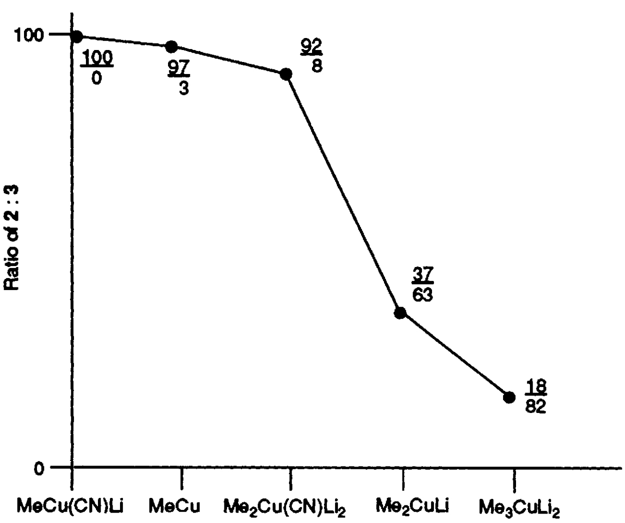
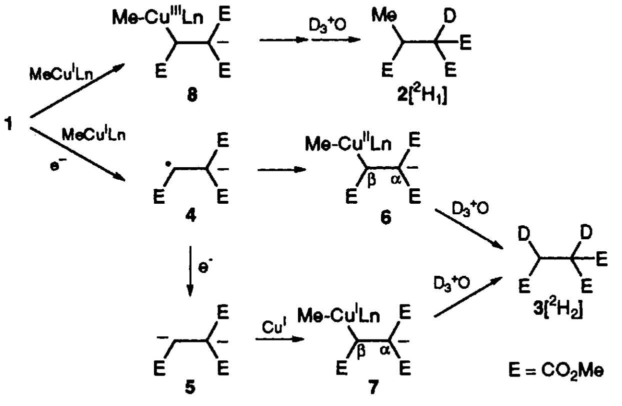


**Fig. 1** MeCuLn dependence on the ratio of **2**:**3**

The reactions of **1** with MeCuLn were quenched with $D_2O$–DCl, instead of $NH_4Cl$–$H_2O$.‡ The reduction product $3[^2H_2]$, obtained using any MeCuLn, contained two deuteriums at the α- and β-positions,[8] whereas one deuterium was incorporated into the α-position of the conjugate adduct $2[^2H_1]$. A possible reaction mechanism is shown in Scheme 1. Transfer of one electron from MeCuLn would produce the radical anion **4**, and further electron transfer would give the dianion **5**. These intermediates (**4** and **5**) may react with $MeCu^{I}Ln$ to afford the $Cu^{II}$ **6** and $Cu^{I}$ **7** species, respectively. It is not clear at present whether $3[^2H_2]$ was produced *via* **6** or *via* **7**. The ratio of **2**:**3** and deuterium content in **3** did not depend on the reaction time, suggesting that **6** (or **7**) would be stable at 0 °C.

The $^{13}C$ NMR spectrum of the stable intermediate, obtained from the addition of 2 equiv. $Me_3CuLi_2$ (2 equiv.) to $^{13}C$-enriched **1** ($EC^{*}H{=}CE_2$), is shown in Fig. 2. The intermediate was stable at 0 °C at least for 8 h, which gave $3[^2H_2]$ upon quenching with $D_3^{+}O$. A signal at δ 43.13 was assigned to the β-carbon of the intermediate. The β-carbon of



**Scheme 1** Nucleophilic addition *vs.* electron transfer process

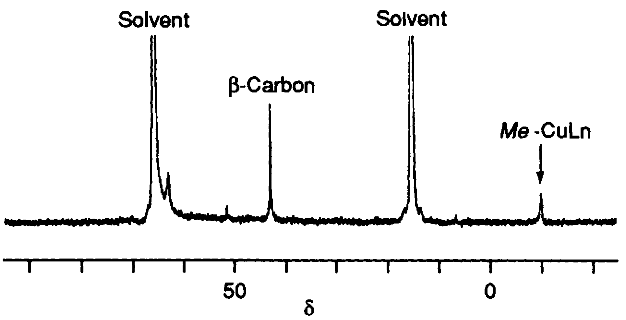


**Fig. 2** $^{13}C$ NMR spectra of the reaction of **1** ($^{13}C$-enriched) with $Me_3CuLi_2$ in diethyl ether at 0 °C

**3** appeared at δ 32.96 and that of **2** at δ 39.11. If the intermediate adopts a copper enolate form LnCuO-(MeO)C=C*HC$^-$E$_2$, instead of an α-cuprio ester structure, the β-carbon (C*) should appear at much lower field, *i.e. ca.* δ 150. The α-carbon of the intermediate was not observable because of non-$^{13}$C-enriched carbon.§ Furthermore, when a diethyl ether solution of this intermediate was kept under $O_2$ atmosphere, only trace amounts of **3** were detected and **2** was obtained exclusively; **2**:**3** > 99:1, and the total yield was 85%. This clearly indicates that the intermediate was oxidized to an unstable Cu$^{III}$ species with $O_2$, which instantaneously gave **2** *via* reductive elimination. Taken together, the stable intermediate is either Cu$^{II}$ **6** or Cu$^{I}$ **7** species and the Cu$^{III}$ intermediate **8** is very unstable. It is now clear that the reduction product **3** arises *via* an electron-transfer process whereas the adduct **2** is produced through the nucleophilic addition.

Consequently, the electron transfer ability of methylcopper reagents is in the following order; $Me_3CuLi_2 > Me_2CuLi >> Me_2Cu(CN)Li_2 > MeCu > MeCu(CN)Li$.[9] This chemical scale using the reaction of **1** may be applicable to other copper reagents. The order reported here will be useful for considering the mechanism of organocopper reactions and for designing organic synthesis *via* copper reagents.

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## Footnotes

† The correlation may also play an important role for controlling formation of the π-complexes in the first mechanism.

‡ To a diethyl ether solution of MeCuLn (2 mmol) cooled at −78 °C was added a diethyl ether solution of **1** (1 mmol). The mixture was stirred for 5 min at −78 °C and allowed to warm to 0 °C. After stirring for 1 h at 0 °C, the reaction was quenched by adding $NH_4Cl$ (aq.) solution. In addition to the two major products, small to trace amounts of the reductive coupling product of **1** $\{(MeO_2C)_2CH(MeO_2C)CH\}_2$ and the methoxy adduct $MeO(MeO_2C)CHCH(CO_2Me)_2$ were produced in some cases.

§ The β-carbon of the precursor of **2**[$^2H_1$], MeEC*HC$^-$E$_2$, was not observable in Fig. 2, presumably not only because it was produced as a minor product but also because a minus charge was located near the β-carbon.

## References

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5 The diastereoselectivity of the conjugate addition to certain enoates depends upon, to some extent, the electron-donating ability of organocopper reagents. Y. Yamamoto, Y. Chounan, S. Nishii, T. Ibuka and H. Kitahara, *J. Am. Chem. Soc.*, 1992, **114**, 7652.

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7 For example, the higher order reagent $Me_2Cu(CN)Li_2$ may be better represented as $Me_2CuLi{\cdot}LiCN$. S. H. Bertz, *J. Am. Chem. Soc.*, 1990, **112**, 4031; B. H. Lipshutz, S. Sharma and E. L. Ellsworth, *J. Am. Chem. Soc.*, 1990, **112**, 4032; S. H. Bertz, *J. Am. Chem. Soc.*, 1991, **113**, 5470; T. Stemmler, J. E. Penner-Hahn and P. Knochel, *J. Am. Chem. Soc.*, 1993, **115**, 348. We are not concerned about the exact structure, but watch the species as a reagent system. Methylcopper was prepared from CuI and MeLi which contained an equivalent amount of LiBr.

8 The deuterium at the α-position was exchanged significantly for hydrogen during work-up procedure, but the deuterium at the β-position was not exchanged. For the incorporation of two deuteriums, see N. Krause and G. Handke, *Tetrahedron Lett.*, 1991, **32**, 7229.

9 Although we depict the reagent, for simplification, in an ordinarily accepted formula, each reagent should be represented as its LiX including form (as shown above). Evidence for an electron-transfer process of substitution reactions has been obtained; S. H. Bertz, G. Dabbagh and A. M. Mujsce, *J. Am. Chem. Soc.*, 1991, **113**, 631.