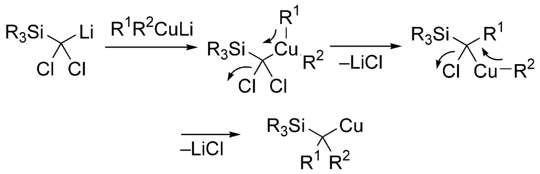
Organocuprates

Consecutive Double 1,2-Migration of Two Different Groups in Silyl(dichloromethyl)cuprates**

Junichi Kondo, Yuki Ito, Hiroshi Shinokubo, and Koichiro Oshima**

Organocuprates are among the most important classes of organometallic compounds that have a wide range of utility in organic synthesis.[1] There are several types of copper reagents, such as the classical Gilman cuprates, cyanocuprates, heterocuprates, and boron trifluoride complexes of alkylcopper compounds. Among them, cyano-Gilman cuprates prepared from copper cyanide and organolithium or organomagnesium reagents have been frequently employed in a number of reactions due to their high and reliable reactivity.[2] Here we report on the very different reactivity of cyanocuprates derived from organolithium and Grignard reagents.[3]

1,2-Migration of an alkyl group on the metal center in metal carbenoid reagents is a typical reaction of ate-type organometallic compounds.[4] This process has been successfully utilized in alkylation of α-haloalkylmetal compounds (metal = Zn, B, Al, Cu, Mn, etc.) and allows facile introduction of an alkyl group into organometallic reagents.[5] This process enables complex metal reagents to be prepared from relatively simple and easily accessible organometallic reagents. In this context, we expected that consecutive double migration of two different alkyl groups in α,α-dihaloalkylmetal compounds would afford a diversity of more complex organometallic reagents that can be easily manipulated (Scheme 1).



Scheme 1. Consecutive double alkylation of silyl(dichloromethyl)-cuprate.

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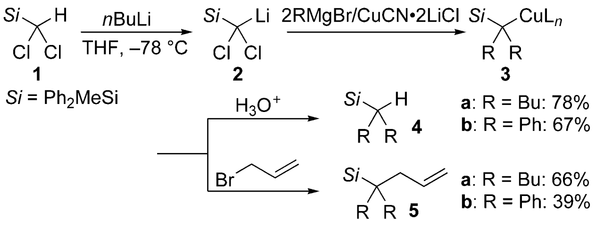
Addition of butyllithium to a solution of dichloromethyl(methyl)diphenylsilane (**1**)[6] in THF at −78 °C led to quantitative formation of silyl(dichloromethyl)lithium **2**, which was then treated with copper reagents derived from copper cyanide. As expected from Scheme 1, the copper reagent prepared by mixing butylmagnesium bromide with CuCN in a 2:1 ratio gave the dibutylated product **4a** by consecutive migration in good yield after aqueous workup (Scheme 2).[7] Using phenylmagnesium bromide instead of BuMgBr gave the diphenylated product **4b** in 67 % yield. Addition of allyl bromide before quenching resulted in trapping of the intermediate copper species to provide **5a**,**b**.[8]



Scheme 2. Dialkylation reaction of **1**.

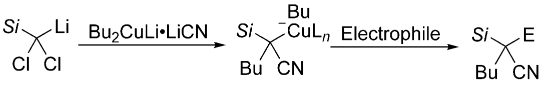
Surprisingly, the cyano-Gilman cuprate $Bu_2CuLi{\cdot}LiCN$ gave butylation/cyanation product **7a** in good yield without formation of dibutylated silane **4a** (Scheme 3).[9] The reaction with $s$$Bu_2CuLi{\cdot}CuCN$ furnished α-cyanosilane **7b** in 56 % yield. The intermediate copper species **6** reacted with a variety of electrophiles, such as allyl bromide, methyl iodide, acyl chlorides, and aldehydes (Table 1).[10] Reaction with aldehydes provided α,β-unsaturated nitriles by Peterson elimination of the initial adducts.[11]

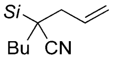
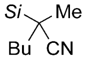
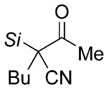
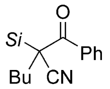
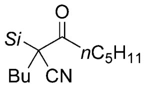
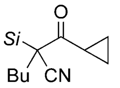
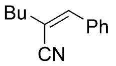
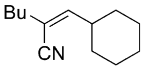
Alkylation/cyanation also occurred with the copper reagent derived from butylmagnesium bromide and CuCN in a 1:1 ratio (Scheme 4). However, the reactivity of the resulting copper species **8** in trapping reactions is very different from that of **6**. For example, treatment of **8** with allyl bromide gave none of the allylated product. On the basis of stoichiometry, the copper reagent is assumed to be an alkylcopper compound rather a cuprate. Hence, the reactivity of **8** is lower than that of the corresponding cuprate **6**.

In addition to alkylation/cyanation, consecutive butylation/phenylation was accomplished by sequential treatment of **2** with BuCu and PhMgBr (Scheme 5). The key here is the use of CuI not CuCN as the starting copper salt. Using CuCN instead of CuI led to a 1:1.1 mixture of **10** and **7a**, along with unidentified products. The intermediate copper compound **9** can be coupled with allyl bromide and acetyl chloride in moderate yield.

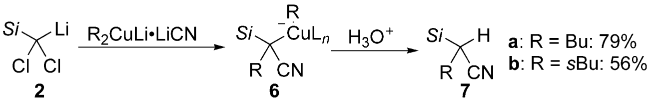
In conclusion, we have demonstrated very different reactivity between two types of cyanocuprates prepared from CuCN and Grignard or lithium reagents. Treatment of a silyl(dichloromethyl)lithium compound with the copper reagent prepared from 2 BuMgBr and CuCN gives the dibutylation product, whereas $Bu_2CuLi{\cdot}LiCN$ (cyano-Gilman cuprate) yields butylation/cyanation products. An EXAFS study indicated that these two cuprate reagents have

Table 1: Consecutive butylation/cyanation followed by C–C bond formation.[a]

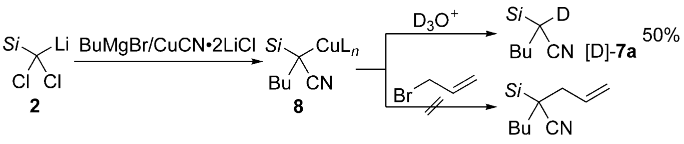


Entry	Electrophile	Product	Yield [%]
1	$CH_2{=}CHCH_2Br$		71
2	MeI		70
3	CH_3COCl		54
4	PhCOCl		57
5	$n$$C_5H_{11}COCl$		54
6	$c$$C_3H_7COCl$		48
7	PhCHO[b]		75 (Z/E => 99/1)
8	$c$$C_6H_{11}CHO$[b]		57 (Z/E = 55/45)

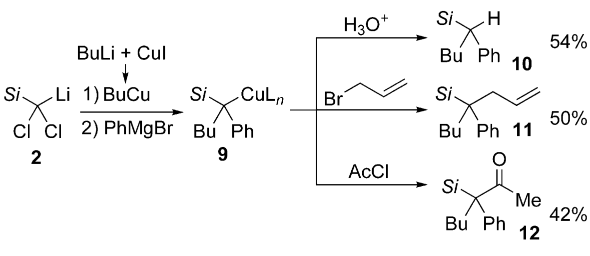
[a] Conditions: $Bu_2CuLi{\cdot}LiCN$ (1.1 equiv) and electrophile (2.0 equiv) were employed. Si = Ph_2MeSi. [b] $Bu_2CuLi{\cdot}LiCN$ (1.1 equiv), RCHO (3.0 equiv), and Me_3SiCl (4.5 equiv) were employed. Me_3SiCl was used as the Lewis acid.



Scheme 3. Alkylation/cyanation of **2**.



Scheme 4. Reaction of **2** with a cyanocuprate.



Scheme 5. Consecutive butylation/phenylation of **2**.

very different structures, which may be responsible for the differing reactivity of these species.[3]

Experimental Section

7a: *n*BuLi (0.31 mL, 1.6 M in hexane, 0.50 mmol) was added to a solution of **1** (141 mg, 0.50 mmol) in THF (5 mL) dropwise at −78 °C, and the mixture was stirred for 30 min. To the resulting solution at −78 °C, a solution of $n\mathrm{Bu_2CuLi \cdot LiCN}$, prepared by mixing *n*BuLi (0.78 mL, 1.6 M in hexane, 1.25 mmol) and $\mathrm{CuCN \cdot 2\,LiCl}$ (0.55 mL, 1.0 M in THF, 0.55 mmol) at 0 °C, was added. After 5 min, the mixture was allowed to warm gradually to 0 °C. The mixture was stirred for 1 h at 0 °C and then poured into dilute aqueous HCl. The mixture was extracted with ethyl acetate, and the organic layers were dried over anhydrous $\mathrm{Na_2SO_4}$. Concentration and purification gave 2-(methyldiphenylsilyl)hexanenitrile **7a** (116 mg, 0.39 mmol) in 79 % yield.

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Keywords: alkylation · C—C coupling · carbenoids · copper · cyanation

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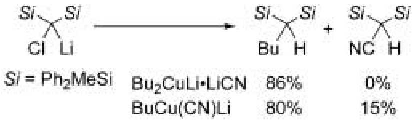
[9] We performed a preliminary experiment on the reaction of monochlorocuprate. Treatment of chlorodisilylmethyllithium with $\mathrm{Bu_2CuLi \cdot LiCN}$ or BuCu(CN)Li provided predominantly butylated product [Eq. (1)]. However, the order of migration of butyl and cyano groups in dichlorocuprates is not clearly elucidated and requires further investigation.



(1)

[10] The reaction with acetophenone resulted in a low yield of the desired α,β-unsaturated nitrile (14 %).

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