Direct Generation and Reactions of Sulfur-substituted Allylcopper Reagents by a Novel Reduction Reaction using Organocuprate

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Sulfur-substituted allylcopper species, generated by a novel reduction reaction of ketene dithioacetals bearing a chlorine atom at an allylic position using organocuprate, react with aldehyde, ketone, chlorotrimethylsilane, enone, oxirane and ester to afford the corresponding allylated products.

Much attention has been devoted to allylation reactions using allylmetals from the viewpoint of not only synthetic but also mechanistic chemistry.[1] Allylcopper species[2] have also been studied, and regio- and stereo-chemistries in these reactions depend on the structure of the allyl moiety. In such a context, heteroatom-substituted allylcopper species are interesting. For the generation of allylcopper reagents, two methods are known, one using transmetallation techniques[3] and the other based on direct metallation using low-valent copper species.[4] We report here a novel method for the generation of alkylthio-substituted allylcopper species, which draws out the reductive ability of the cuprate, eqn. (1).

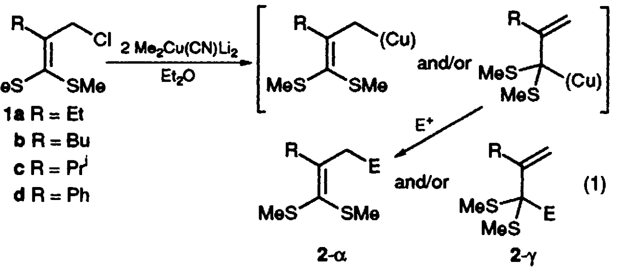
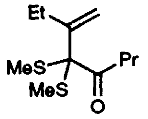
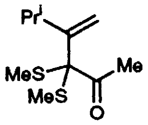


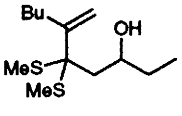
Table 1 Reaction of Allylcopper Species with Carbonyl Compounds[a]



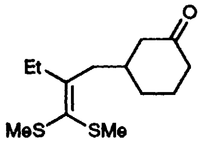
2f, 63%[a] (0/100)



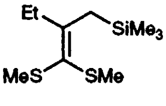
2g, 40%[a] (0/100)



2h, 45%[a] (0/100)



2i, 37%[b] (100/0)



2j, 83% (100/0)

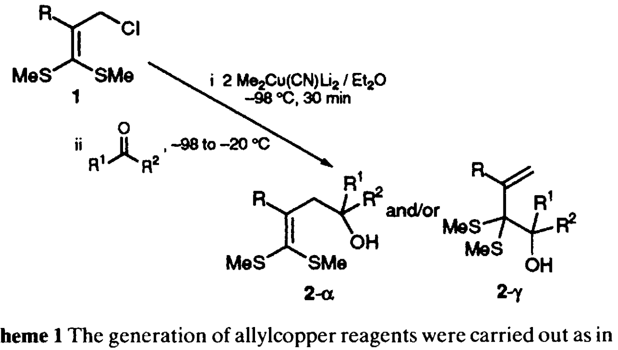
Substrate **1**	Carbonyl compound R^1	 R^2	Product	 Yield[b] (%)	 α/γ[c]
a: R = Et	Pr^i	H	**2a**	77	31/69
b: R = Bu	Bu^t	H	**2b**	47	83/17
c: R = Pr^i	Et	H	**2c**	83	23/77
	Ph	H	**2d**	57	50/50
d: R = Ph	Et	Et	**2e**	66	100/0

[a] To a solution of cuprate (0.8 mmol) in diethyl ether (4.0 ml) was added a solution of allyl chloride **1** (0.4 mmol) in diethyl ether (4.0 ml) by a syringe at −98 °C. After 30 min, carbonyl compound (1.6 mmol) was added and the mixture was allowed to rise in temperature to −20 °C over 3 h and the reaction was quenched with saturated NH_4Cl solution. [b] Isolated yield by chromatography on silica gel. [c] The ratio of isolated adduct **2**-α/**2**-γ.

We found that ketene dithioacetals bearing a chlorine atom at an allylic position† are cleanly reduced to generate the corresponding allylcopper reagents by treatment with dimethylcuprate (2 equiv.) derived from cuprous cyanide $[Me_2Cu(CN)Li_2]$.‡ Cuprates generally work as nucleophiles. However, this reaction displays a remarkable contrast to hitherto known reactions of cuprates[5] in a sense of highly chemoselective reduction (only metal–halogen exchange reaction occurs) toward substitution reactions,§[6] and is formally a new type of reaction for the generation of allylcopper species.

These allylcopper reagents were subjected to reaction with aldehydes and ketones and the corresponding adducts were obtained as an isomeric mixture (α- and γ-adduct). As can be seen in Table 1, steric bulkiness of a carbonyl compound tends to increase the ratio of α-isomer.

Electrophiles other than carbonyl compounds such as ester, oxirane, α,β-enone and chlorosilane also react with these allylcopper reagents and products are summarized in Scheme 1. Addition of methyllithium (1 equiv. more) to the reagent before the reaction with an electrophile increased the reactivity of this reagent.[4] Interestingly, esters and oxirane react to give allyl ketone (**2f**: ethyl butyrate with **1a**, **2g**: ethyl acetate with **1c**) and alkenol (**2h**: 1,2-epoxybutane with **1b**), respectively (γ-isomer). Enone also reacts in the presence of $BF_3{\cdot}OEt_2$ to give a 1,4-adduct (**2i**: 2-cyclohexenone with **1a**, α-isomer),[2,3] and by use of chlorotrimethylsilane as an electrophile, which is known as an activator of enone in conjugate addition of cuprates,[7] allylsilane (**2j**: with **1a**) was obtained selectively (α-isomer).



Scheme 1 The generation of allylcopper reagents were carried out as in the conditions shown in Table 1 and successive reactions with electrophiles were conducted at −78 °C for 1 h. The α/γ ratio of adduct was shown in parenthesis. [a] One more equiv. of methyllithium to a substrate **1** was added before introducing an electrophile and 4 equiv. of electrophile were used to a substrate. [b] 3 equiv. of electrophile to a substrate were used and $BF_3{\cdot}Et_2O$ (3.0 equiv. to substrate) were added after addition of enone.

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Footnotes

† These allyl chlorides were prepared by chlorination of the corresponding allyl alcohols[8] prior to use, and immediately subjected to the reaction with cuprate.

‡ In a typical example, to the solution of the cuprate in diethyl ether, prepared by adding a diethyl ether solution of methyllithium (1.15 mol dm^{-3}; 1.4 ml) to a suspension of CuCN (0.80 mmol) in Et_2O (4.0 ml) at −20 °C, was added a solution of the allyl chloride **1a** (0.40 mmol) in Et_2O (1.0 ml) by a syringe at −98 °C. The mixture was stirred for 30 min at the same temperature. Isobutyraldehyde (1.6 mmol) was added and the mixture was allowed to rise in temperature to −20 °C over 3 h. Addition of saturated NH_4Cl solution, ether extraction, drying, and evaporation of solvents gave a crude mixture. After purification by chromatography on silica gel (hexane/ethyl acetate = 20), **2a** was obtained in 77% yield. All new compounds were satisfactorily characterized by spectroscopic and elemental analyses.

§ The undesired reduction (metal–halogen exchange reaction) occurs as a side reaction in substitution reactions using a cuprate as a nucleophile. The cases in which only a reduction reaction proceeds are rare and the efficiencies (molar ratio of substrate to cuprates) are not so high.

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