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An insight into copper catalyzed allylation of alkyl zinc halides. Comparison of reactivity profiles for catalytic and stoichiometric alkylzinc–copper reagents

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ABSTRACT

The γ-selective allylation of catalytic and stoichiometric alkylzinc–cuprates have been kinetically studied. The reactivity profiles generated by allylation reactions of *n*-butylzinc chloride catalyzed by CuX compounds (X = I, Br, Cl, CN, SCN) and also catalyzed by *n*-butylzinc–copper reagents and di *n*-butylzinc–copper reagents were evaluated. Reactivity profiles for allylation of stoichiometric *n*-butylzinc–copper reagents and di *n*-butylzinc–copper reagents were also prepared. All CuX compounds have been screened for the preparation of Grignard reagent derived *n*-butylzinc–copper reagents and di *n*-butylzinc–copper reagents.

The evaluation of the profiles indicates that the active catalyst might be RCu(X)ZnCl and also to some degree, $R_2CuZnCl \cdot ZnClX$, which both could favor formation of γ-product. All data supports the reductive elimination of σ-allyl Cu (III) complex formed at vinylic terminal to give γ-allylated product with a quite slow isomerization to σ-allyl Cu (III) complex formed at allylic terminal to give α-allylated product. In the allylation mechanism of zinc cuprates, the role of counter ion, $ZnCl^+$ has been discussed.

1. Introduction

Transition metal catalyzed or mediated allytic alkylation is a highly useful synthetic methodology for C–C bond formation. [1–3] In recent years, controlling the regio- and stereochemistry of alkyl–allyl coupling using allylic substrates has received much attention. Several methods have been developed for regioselective allylation of alkyl Grignard [4–8] and alkylzinc reagents [9–11] under copper catalysis or stoichiometric cuprates derived from these reagents (Scheme 1) [12,13].

The regiochemistry in the copper catalyzed allylation of alkyl Grignard reagents is controlled by the structure of the Grignard reagent, the allylic substrate, copper catalyst and the solvent as well as reaction conditions. [14–21] It is commonly accepted that the reaction parameters governing formation of a dialkylcuprate as an intermediate give α-substitution whereas reaction conditions governing formation of an alkylcopper as an intermediate give γ-substitution predominantly [20,21]. In the light of the reported results, the regiochemical outcome of the allylation of stoichiometric alkylcopper and dialkylcuprate reagents are mainly consistent with those of copper catalyzed alkyl Grignard and – lithium reagents [22–27].

However, the regiochemistry in the uncatalyzed [24,28] and copper catalyzed allylation of alkylzinc halides and dialkylzincs was reported to be γ-selective [25,29–33]. Allylation of dialkyl zinc cuprates and alkyl cyanozinc cuprates was also reported to take place with high γ-selectivity [29,34–51].

The mechanism of copper catalyzed allylation of alkyl Grignard reagents and also dialkylcuprates derived from alkyllithium and Grignard reagents has been discussed in a number of reports. According to the mechanism proposed by Goering and co-workers [52–55] and confirmed by Backvall et al. [21] (Scheme 2), initial complexation of RCu(X)MgBr to the allylic double bond gives an alkene-Cu(I) complex **A** and an oxidative addition anti to the leaving group takes place at vinylic terminal. The σ-allyl-Cu(III) complex intermediate **B** thus formed can undergo reductive elimination to give γ-product or isomerize to the σ-allyl-Cu(III) complex intermediate **D** formed at allylic terminal, presumably via a π-allyl-Cu(III) complex intermediate **C**. Reductive elimination of **D** would give the α-product. The overall regiochemistry of the allylation is determined by the relative rates of elimination and isomerization of the complex **B**. If X group on cuprate is an electron withdrawing group (X = halide, CN), reductive elimination is fast relative to isomerization and γ-substitution is observed. In the case of X = alkyl group, isomerization predominates over reductive elimination and elimination of **D** gives α-substitution. Reductive elimination of σ-allyl-Cu(III) complexes **B** and **D** is stereospecific and occurs with retention of configuration.

Recently, Nakamura reported [56] a study showing that formation of α-product occurs directly from the π-allyl-Cu(III) complex intermediate **C** via an enyl [σ + π]-type transition state (Scheme 3, pathway a).

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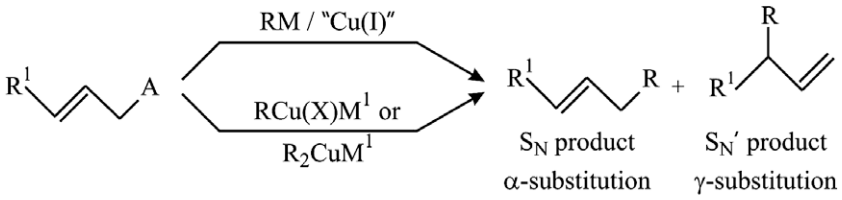
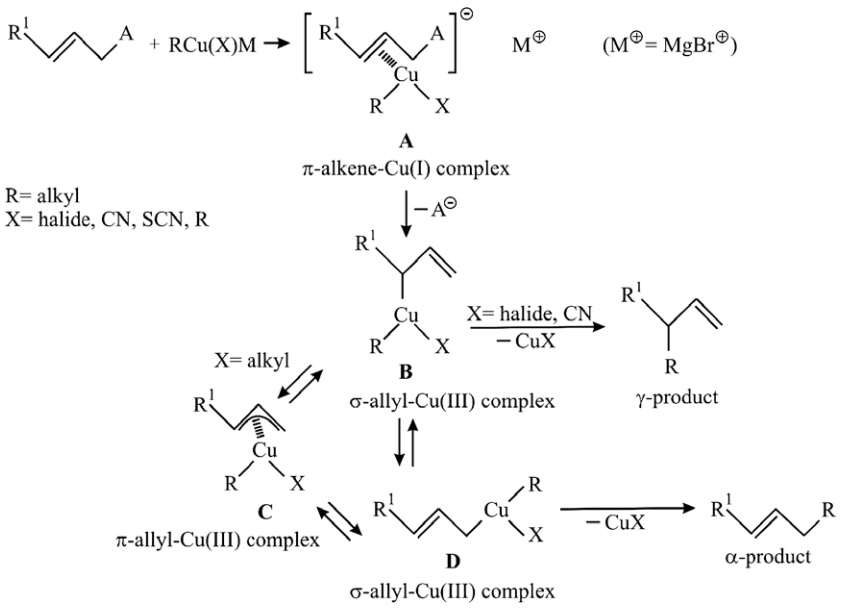


A: Leaving group, R: Alkyl, X: Halogen, CN
M: Li, MgBr, ZnCl, 1/2Zn, 1/3ZnMgBr, 1/3ZnLi
M^1: Li, MgBr, ZnCl

Scheme 1.



Scheme 2.

Nakamura also reported [56] that Lewis acid favors anti and γ-selective reaction. These reactions may occur directly via an enyl [σ + π]-type complex intermediate **E** without going through a π-allyl-Cu(III) complex intermediate **C** (Scheme 3, pathway b). Nakamura, recently used density functional calculations to study the origin of the contrasting regioselectivities in allylic substitution of MeCu(CN)Li and Me_2CuLi. [57] Bertz and Ogle have been able to prepare and characterize the first examples of both σ-allyl- and π-allyl-Cu(III) complexes and to study their reactions by using rapid injection NMR spectroscopy [58].

However, a mechanism for copper catalyzed allylation of dialkylzincs has been discussed only in one report [24].

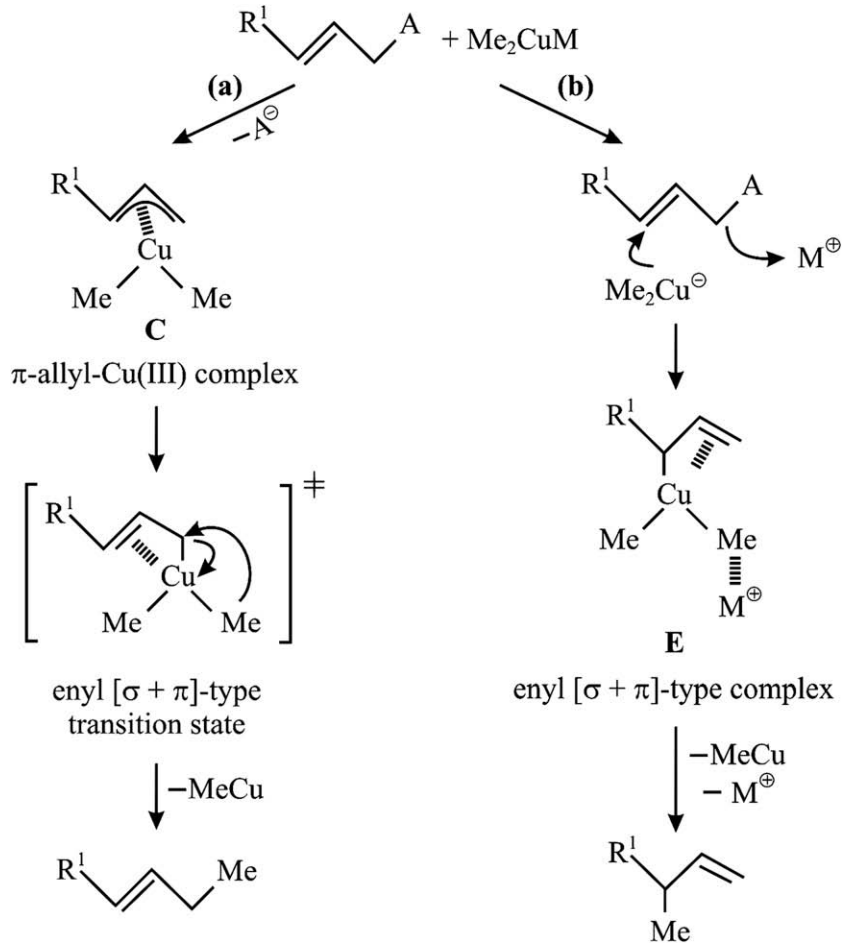
Our interest in controlling the regiochemistry of allylation of alkylmagnesium-copper reagents [59] and alkylzinc–copper reagents [60,61] by changing the reaction conditions prompted us to carry out a kinetic study for the mechanism of allylic coupling of alkylzinc–copper reagents. We evaluated reactivity profiles generated by allylation reactions of catalytic and stoichiometric mono- and di *n*-butylzinc–copper reagents prepared using various Cu(I) compounds.

Here we report our results on the alkylzinc–copper nucleophiles as active catalysts in the copper catalyzed γ-selective allylation of alkylzinc halides.

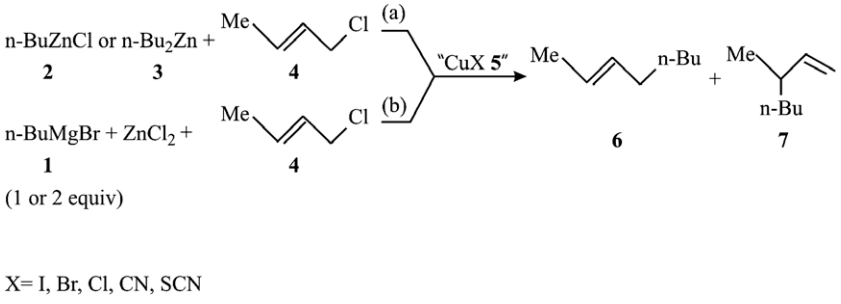
2. Results and discussion

In our long term investigation on the reactions of homo and mixed organozinc reagents, we found that the copper catalyzed allylation of *n*-butylmagnesium bromide **1** derived *n*-butylzinc chloride **2** and di *n*-butylzinc **3** with *E*-crotyl chloride **4** in THF, took place with an α:γ ratio not higher than 12:88 (Scheme 4, pathway a) [60]. We also observed that reaction temperature, addition mode of the allylic substrate, CuX catalyst and its concentration and N-donor and O-donor solvents such as TMEDA, HMPA and diglyme as cosolvents did not change the γ-regioselectivity. We also obtained similar results in the copper catalyzed allylation of organozinc reagents **2** and **3** prepared by in situ transmetallation of *n*-butylmagnesium bromide **1** (Scheme 4, pathway b). Stoichiometric *n*-butylcopper *n*-BuCu(X)ZnCl (**8**) and di *n*-butylcuprate *n*-Bu_2-CuZnCl (**9**) reagents prepared from *n*-butylzinc chloride (**2**) and CuX compounds **5** also gave γ-allylated products with an α:γ ratio of 10:90 in their reaction with *E*-crotyl chloride **4** in THF.

If we assume that the allylation of alkylzinc–copper reagents may take place according to the mainly accepted mechanism (Scheme 2, $M^+ = ZnCl^+$) proposed by Goering and co-workers [52–55] and Backvall et al. [21] for allylation of alkylmagnesium-copper reagents, then we should find support for the following points:



Scheme 3.

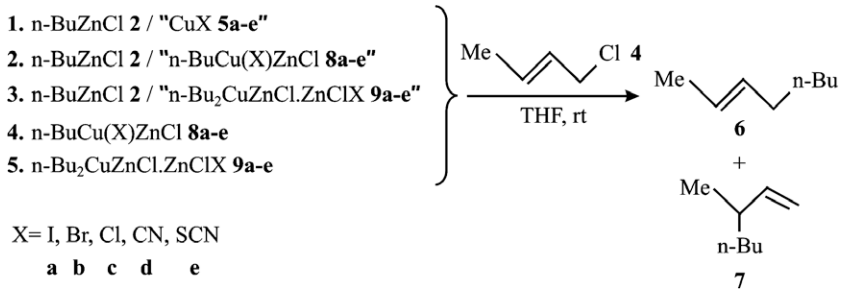


Scheme 4.

1. In the Cu catalyzed γ-allylation of alkylzinc reagents, reductive elimination seems to occur predominantly from σ-allyl-Cu(III) complex **B** rather than σ-allyl-Cu(III) complex **D**. Then, X group on the zinc cuprate seems to be mainly halide, CN or SCN rather than alkyl, or in other words RCu(X)ZnCl rather than $R_2CuZnCl$ seems to form as catalytic species.
2. However, stoichiometric alkylcopper-zinc reagents, i.e. not only RCu(X)ZnCl (X = halide, CN, SCN), but also $R_2CuZnCl$, which is expected to give α-allylated product, afford mainly γ-allylated products. This indicates that in the allylation of zinc cuprates, isomerization rate of σ-allyl-Cu(III) complex **B** to **D** does not predominate over reductive elimination even in the case of X = R on the contrary to the allylation of magnesium cuprates.
3. In the allylation of zinc cuprates, it may be probable that isomerization of complex **B** to **D** via **C** may not be slow compared to reductive elimination in the case of X = R; however complex **D** may not form and complex **C** is expected to give γ-allylated product in some way.

This study was undertaken to critically examine this assumption, i.e. in the Cu catalyzed allylation of alkylzinc reagents, cuprate nucleophile species seems to be $RCu(X)^-$ or R_2Cu^- which are both responsible for γ-substitution.

For this purpose, we carried out a kinetic study and we compared the reactivity profiles [62,63] for the allylation of *n*-butylzinc chloride, *n*-BuZnCl (**2**) with *E*-crotyl chloride (**4**) catalyzed by CuX



Scheme 5.

(**5**). We also prepared the reactivity profiles for allylation of stoichiometric *n*-butylcopper *n*-BuCu(X)ZnCl (**8**) and di *n*-butylcuprate *n*-Bu_2CuZnCl (**9**). In order to gain some insight into the catalytic species, we used these preformed *n*-butylcopper reagents **8** and **9** also as catalysts in the allylation of *n*-BuZnCl (**2**). The list of the reactions in the kinetic study are given in Scheme 5. CuX compounds (X = I, Br, Cl, CN, SCN) **5a–e** were used as catalysts in the allylation of *n*-butylzinc chloride (**2**) (Reactions **1a–e**). *n*-Butylzinc–copper reagents, i.e. *n*-BuCu(X)ZnCl (**8a–e**) and *n*-Bu_2CuZnCl · ZnClX (**9a–e**) were prepared using CuX compounds and used as catalysts (Reaction **2a–e** and Reaction **3a–e**, respectively) and as stoichiometric reagents to be allylated (Reaction **4a–e** and Reaction **5a–e**).

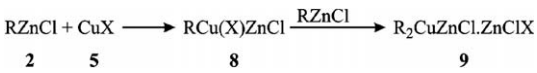
For reactivity profiles, the progress of allylation **reactions 1–5** was followed at room temperature in time. Instead of conversion-time profiles, we prepared γ-allylated product-time, [R-γ]-t profiles since the relative amount of γ-product, which is 80–90% in **reactions 1–5**, is almost constant during the reaction. The amount of γ-product was monitored by GC analysis. However, due to the heterogeneous reaction, the reproducibility for the GC analysis of samples taken from the reaction mixture containing the internal standard seemed low. So, a definite number of reactions were carried out in different flasks and each reaction was quenched at appropriate times. This method, although time consuming led to accurate and reproducible results in GC analysis. For catalytic reactions, 1.1 mmoles of *n*-BuZnCl (**2**) was allowed to react with 1 mmole of *E*-crotyl chloride (**4**) in the presence of 0.20 mmoles of CuX catalyst **5** in THF at room temperature. For stoichiometric reactions, 1.1 mmoles of *n*-BuCu(X)ZnCl (**8**) or *n*-Bu_2CuZnCl (**9**) was allowed to react with 1 mmole of *E*-crotyl chloride in THF at room temperature. The reactions are rather fast and according to the kinetic results, a reaction time of 60 min was chosen to guarantee complete allylation for all regents. The amount of γ-product values used in reactivity profiles are an average of at least three parallel reactions. The reactivity profiles for **reactions 1–5** were given in Fig. 1 and they were collected to compare the allylation reactivity of catalytic and stoichiometric *n*-butylzinc–copper reagents prepared using the same CuX compound. The reactivity profiles for the allylation of *n*-butylzinc–copper reagents prepared using CuI (**5a**), CuBr (**5b**), CuCl (**5c**), CuCN (**5d**) and CuSCN (**5e**) were given in Fig. 1a–e, respectively.

In the kinetic study we reasoned that one or more of the following results should be obtained from the comparison of the reactivity profiles:

(i) As *n*-BuCu(X)$^-$ is the catalytic alkylcopper intermediate which is assumed to be responsible for γ-substitution in the Cu catalyzed allylation of alkylzinc reagents according to Scheme 2, the reactivity profiles of **reaction 1** should be similar to those of **reaction 2** and possibly those of **reaction 4** for each CuX **a–e**.

(ii) A similarity between the profiles of **reaction 1** and **reaction 3** would reveal that the catalytic alkylcopper intermediate might be R_2Cu^- rather than RCu(X)$^-$. However, this result also indicates that R_2Cu^- undergoes to reductive elimination in order to give γ-substitution although it is expected to undergo isomerization and give α-substitution.

(iii) In the presence of excess *n*-BuZnCl (**2**), the catalyst *n*-BuCu(X)ZnCl (**8**) may not have time to undergo allylation **(reaction 2)**; but reacts faster with *n*-BuZnCl (**2**) to form *n*-Bu_2CuZnCl (**9**) as catalytic intermediate for allylation **(reaction 3)** (1). In this case the catalytic species in **reaction 2** and **reaction 3** are not different and the reactivity profiles for these reactions should be similar



(1)

(iv) An agreement is expected between the profiles of **reaction 3** and **5** since the active *n*-butylzinc–copper reagents to be allylated are same.

First, we compared the reactivity profiles for allylation **reactions 1a–5a, 1b–5b, 1c–5c, 1d–5d** and **1e–5e**. In Table 1, we gave a list of reactions which generate similar profiles.

Before evaluating the superimpossibility and similarity of the profiles, we also determined some numerical values for the catalytic efficiency of *n*-butylzinc–copper reagents at 20 mol% Cu(I) catalyst (**5**, **8** or **9**) loading in **reactions 1–3**, respectively. We used the kinetic data for this purpose. The determined values correspond to the ratio of the maximum% yield of γ-product to the reaction time (min) in which this yield was obtained (*y* values). We calculated this ratio for also stoichiometric *n*-butylzinc–copper reagents (*z* values) in order to make a comparison between their reactivities in **reactions 4** and **5**. *y* Values may be regarded as TOF values for allylation of catalytic *n*-butylzinc–copper reagents and we think that *y* and *z* values can be also used to get an idea for relative reactivity of catalytic and stoichiometric *n*-butylzinc–copper reagents. *y* Values were found to be 1.2–1.6 and *z* values were found to be 1.3–1.8, except 0.7 for the allylation of *n*-BuCu(CN)ZnCl (**4d**). The error on these values does not exceed 10%.

We also listed the allylation reactions of catalytic and stoichiometric *n*-butylzinc–copper reagents which have equal *y* and *z* values (Table 2).

As seen, the similarity of the reactivity profiles (given in Table 1) and the maximum γ-product yield to time ratios (*y* and *z* values) (given in Table 2) are mostly in agreement.

Below, the similarities and differences in the reactivity profiles of allylation **reactions 1–5** were evaluated for each CuX compound **5a–e** (X = I **a**, Br **b**, Cl **c**, CN **d**, SCN **e**).

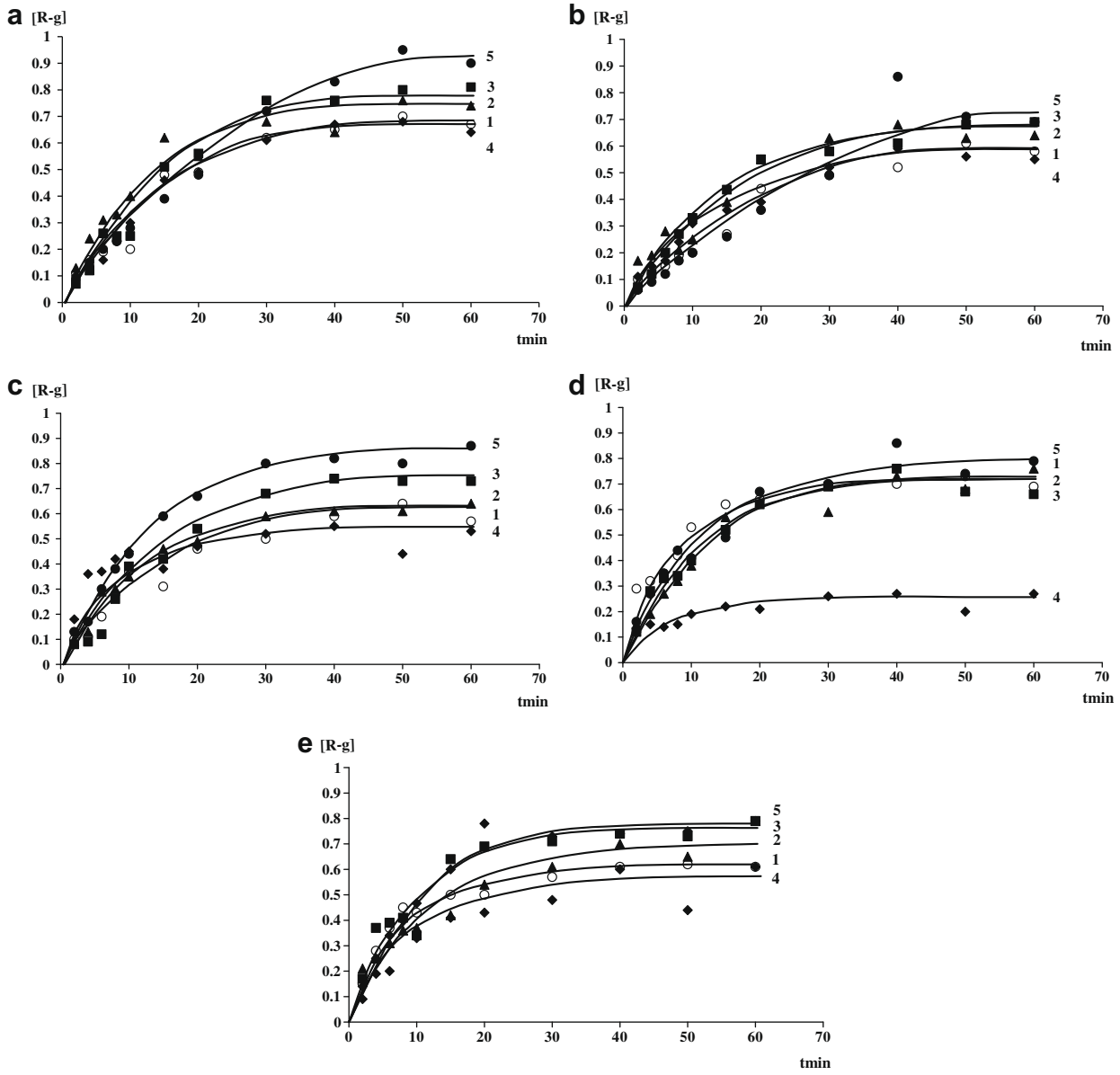


Fig. 1. Kinetic study (γ-allylated product-time curves) for the allylation reaction of catalytic and stoichiometric *n*-butylzinc–copper reagents with *E*-crotyl chloride in THF at room temperature. (The amount of γ-allylated product (mmol) is given versus time (min) in the allylation with 1 mmol of *E*-crotyl chloride **4**.) (The reagents for the profiles: 1. ○, 2. ▲, 3. ■, 4. ♦, 5. ●). The reagents to be allylated: 1. *n*-BuZnCl (**2**)/20 mol% CuX (**5**); 2. *n*-BuZnCl (**2**)/20 mol% *n*-BuCu(X)ZnCl (**8**); 3. *n*-BuZnCl (**2**)/20 mol% *n*-Bu_2CuZnCl · ZnClX (**9**); 4. *n*-BuCu(X)ZnCl (**8**); 5. *n*-Bu_2CuZnCl · ZnClX (**9a**). (a) Copper source is CuI (**5a**), (b) copper source is CuBr (**5b**), (c) copper source is CuCl (**5c**), (d) copper source is CuCN (**5d**), (e) copper source is CuSCN (**5e**).

*2.1. Reactions **1a–5a***

The profiles generated by allylation of *n*-BuZnCl (**2**) with the catalysis of *n*-BuCu(I)ZnCl (**8a**) and *n*-Bu_2CuZnCl (**9a**) **(reactions 2a and 3a,** respectively) are quite similar. This indicates that the same catalytic species are present in these reactions. However, the difference in the profile with the catalysis of CuI (**5a**) **(reaction 1a)** possibly originates from the difference in the ease of formation of the catalytic species, and this profile agrees well with the profile of the stoichiometric allylation of *n*-BuCu(I)ZnCl (**8a**) **(reaction 4a)**. This indicates that the active catalyst, formed from the precatalyst CuI (**5a**) is possibly *n*-BuCu(I)ZnCl (**8a)** species. Then, in **reaction 2a**, *n*-BuCu(I)ZnCl (**8a**) catalyst seems to react first with excess *n*-BuZnCl (**2**) to give *n*-Bu_2ZnCl (**9a**) as catalytic species rather than allylation. This explanation supports the observation of similar profiles in the allylation with **8a** and **9a** as catalysts (**reactions 2a and 3a**) but a different profile with CuI (**5a**) catalysis (**reaction 1a**). *y* Values also support the similarity of active catalysts in **reactions 2a and 3a** and may provide a support for formation of **8a** as active catalyst from precatalyst CuI in catalytic allylation.

*2.2. Reactions **1b–5b***

The results are in well accordance with the results outlined in Section 2.1.

*2.3. Reactions **1c–5c***

The superimpossible profiles obtained from the allylation of *n*-BuZnCl (**2**) with the catalysis of CuCl (**reaction 1c**) and *n*-BuCu(Cl)ZnCl (**8c**) **(reaction 2c)** indicates that the active catalyst is **8c**.

Table 1
Allylation reactions of catalytic[a] and stoichiometric *n*-butylzinc–copper reagents[b] which generate superimpossible and similar reactivity profiles (reactions are given in Scheme 5).

CuX	Reactions which generate superimposible (or similar) reactivity profiles
CuI (**5a**)	**2** and **3**[c]; **1** and **4**
CuBr (**5b**)	**2** and **3**; **1** and **4**
CuCl (**5c**)	**1** and **2**
CuCN (**5d**)	**1**, **2** and **3**
CuSCN (**5e**)	**1** and **4**[c]; **3** and **5**

[a] **Reactions 1, 2 and 3** were carried out by reacting *n*-BuZnCl (**2**) (1.1 mmoles) with *E*-crotyl chloride (**4**) (1 mmole) in the presence of CuX (**5**) (0.20 mmoles), *n*-BuCu(X)ZnCl (**8**) (0.20 mmoles) and *n*-Bu_2CuZnCl (**9**) (0.20 mmoles), respectively in THF at room temperature.
[b] **Reactions 4 and 5** were carried out by reacting *n*-BuCu(X)ZnCl (**8**) or *n*-Bu_2CuZnCl (**9**) (1.1 mmoles) with *E*-crotyl chloride (**4**) (1 mmole) in THF at room temperature.
[c] The profiles are not superimposible, but quite similar.

Table 2
Allylation reactions of catalytic and stoichiometric *n*-butylzinc–copper reagents which yield equal values for maximum γ-product yield to time ratios (*y*[a] and *z*[b] values) (reactions are given in Scheme 5).

CuX	Reactions which give equal *y*[a] and *z*[b] values[c]
CuI (**5a**)	**1** and **2**[c]; **2** and **3**; **1** and **4**
CuBr (**5b**)	**1** and **2**[c]; **2** and **3**; **1** and **4**
CuCl (**5c**)	**1** and **2**; **2** and **3**[c]; **1** and **4**[c]
CuCN (**5d**)	**1**, **2** and **3**; **1**, **2**, **3** and **5**[c]
CuSCN (**5e**)	**1** and **2**[c]; **2** and **3**[c]; **3** and **5**

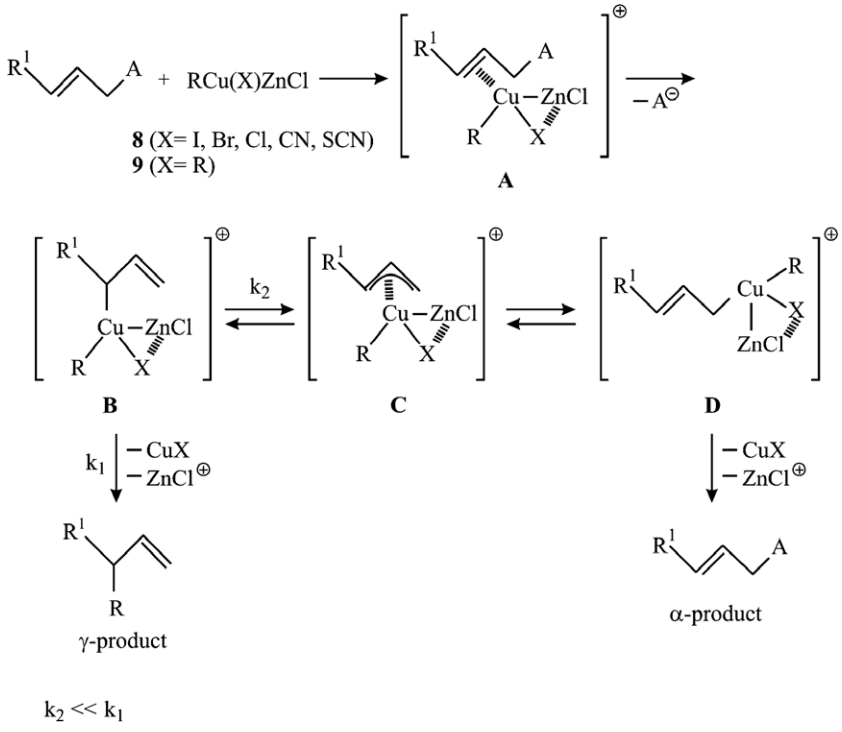
[a] *y* = (max. %yield of γ-product)/(reaction time, min.) for allylation of *n*-BuZnCl (**2**) in the presence of 20 mol% catalyst (CuX (**5**), *n*-BuCu(X)ZnCl (**8**) or *n*-Bu_2CuZnCl (**9**)).
[b] *z* = (max. %yield of γ-product)/(reaction time, min.) for allylation of *n*-BuCu(X)ZnCl (**8**) and *n*-Bu_2CuZnCl (**9**).
[c] The values are equal in the error limit of ±10%.

2.4. Reactions **1d–5d**

The profiles generated by allylation of *n*-BuZnCl (**2**) with the catalysis of CuCN (**5d**) (**reaction 1d**), *n*-BuCu(CN)ZnCl (**8d**) (**reaction 2d**) and also *n*-Bu_2Cu(CN)$(ZnCl)_2$ (**9d**) (**reaction 3d**) are superimpossible indicating that the active catalysts might be the same. A larger deviation of the profile generated by the stoichiometric allylation of *n*-BuCu(CN)ZnCl (**8d**) (**reaction 4d**) can also be accounted for by the different structure of the catalytic cuprate species. Then, we can conclude that the active catalyst might not be *n*-BuCu(CN)ZnCl (**8d**), but can be *n*-Bu_2Cu(CN)$(ZnCl)_2$ (**9d**). However, Nakamura and Yoshikai demonstrated [64,65] that reaction of 2 equiv. of RLi with 1 equiv. of CuCN does not give $R_2Cu(CN)Li_2$ (Lipshutz cuprates) and these higher cyanocuprates exist as R_2Cu-Li · LiCN (cyano-Gilman cuprates). Then the large discrepancy between the profiles generated by the allylation of stoichiometric cuprates, *n*-BuCu(CN)ZnCl (**8d**) (**reaction 4d**) and *n*-Bu_2Cu(CN)$(ZnCl)_2$ (**9d**) (**reaction 5d**) supports the view that CN group is not resting on copper in **9d** and **9d** may exist as *n*-Bu_2CuZnCl · ZnCl(CN) [16]. The equality of *y* values for catalytic allylation reactions (**reactions 1d, 2d and 3d**) to *z* value for stoichiometric allylation of *n*-Bu_2Cu(CN)$(ZnCl)_2$ reacting as *n*-Bu_2CuZnCl (**9d**) (**reaction 5d**) rather than *z* value for allylation of *n*-BuCu(CN)ZnCl (**reaction 4d**) also provides another support for formation of *n*-Bu_2CuZnCl type cuprate from CuCN (**reaction 3d**) rather than *n*-BuCu(CN)ZnCl (**reaction 2d**) as active catalyst.

2.5. Reactions **1e–5e**

The difference between the profiles obtained from the allylation of *n*-BuZnCl (**2**) with the catalysis of CuSCN (**5e**) **(reaction 1e)**, *n*-BuCu(SCN)ZnCl (**8e**) **(reaction 2e)** and *n*-Bu_2Cu(SCN)$(ZnCl)_2$ (**9e**) **(reactions 3d)** indicates the difference between the structure of active catalyst in each reaction. However, the similarity between the profiles generated by allylation of *n*-BuZnCl (**2**) with the catalysis of CuSCN (**5e**) (**reaction 1e**) and stoichiometric allylation of



Scheme 6.

n-BuCu(SCN)ZnCl (**8e**) **(reaction 4e)** may indicate the formation of **8e**, as catalytic species from precatalyst CuSCN (**5e**).

Earlier studies by Lipshutz on the use of CuSCN for the formation lithium cuprates [66] also showed that while CuI serves as a precursor to lower order cuprates R_2CuLi, CuSCN may actually be forming a higher order mixed species $R_2Cu(SCN)Li_2$.

The similarity between the profiles generated by allylation of *n*-BuZnCl (**2**) with the catalysis of **9e (reaction 3e)** and stoichiometric allylation of **9e (reaction 5e)** can be reasonably explained by the formation of a higher order mixed cuprate *n*-$Bu_2Cu(SCN)(ZnCl)_2$ (**9e**) from *n*-BuZnCl (**2**)/CuSCN (**5e**) and at least suggest that to some degree there are differences between CuCN- and CuSCN-derived higher order cuprates.

In summary, (i) the reactivity profiles generated by the allylation of *n*-BuZnCl (**2**) with the catalysis of CuX (**reaction 1**) are quite similar to those generated by the allylation of stoichiometric *n*-BuCu(X)ZnCl (**8**) (**reaction 4**) in the case of X = I, Br and SCN. In the case of X = Cl, the similarity of the profiles generated by the allylation of *n*-BuZnCl (**2**) with the catalysis of CuX (**reaction 1**) and with the catalysis of *n*-BuCu(X)ZnCl (**8**) (**reaction 2**) is observed. Then we can conclude that the active catalyst seems to be RCu(X)ZnCl (**8**) which would favor formation of γ-product.

(ii) The similarity of the profiles generated by the allylation of *n*-BuZnCl (**2**) with the catalysis of *n*-BuCu(X)ZnCl (**8**) (**reaction 2**) or *n*-$Bu_2CuZnCl$ (**9**) (**reaction 3**) in the case of X = I, Br and CN indicates that the active catalyst might be also *n*-$Bu_2CuZnCl$ (**8**) formed from the reaction of *n*-BuCu(X)ZnCl (**8**) with excess *n*-BuZnCl (**2**). Then, not only *n*-BuCu(X)ZnCl (**8**), but also *n*-$Bu_2CuZnCl$ (**9**) is expected to give γ-allylation.

(iii) However, in the case of X = CN, the dissimilarity of the profiles generated by the allylation of *n*-BuZnCl (**2**) with the catalysis of CuCN (**5d**) (**reaction 1**) or *n*-BuCu(CN)ZnCl (**8d**) (**reaction 2**) with the profile generated by the allylation of stoichiometric *n*-BuCu(CN)ZnCl (**reaction 4**) indicates that the active catalyst might be *n*-$Bu_2CuZnCl$.

According to these findings, our assumption that the allylation of alkylzinc–copper reagents takes place according to the mechanism outlined in Scheme 2 seems correct. We obtained all of the results that we expected from the reactivity profiles and we found support to propose the reductive elimination of σ-allyl-Cu(III) complex **B** to give γ-allylated product in the case of X = halide, CN, SCN or alkyl with a quite slow isomerization of complex **B** to complex **D** to give α-allylated product in the case of X = alkyl, e.g. $k_2 \ll k_1$. So, in the allylation of alkylzinc–copper reagents, the counter ion $ZnCl^+$ is expected to be responsible for much slower isomerization of complex **B** resulting in γ-allylation of both RCu(X)ZnCl and $R_2CuZnCl$ (Scheme 6). We may think that zinc cuprates possibly can not react as solvent separated ion pairs [64] due to the less polar character of Cu–ZnCl bond compared to Cu–MgBr bond. Then, $ZnCl^{\delta+}$, which is a strong Lewis acid can possibly decrease σ-donor character of R group, which is responsible for the isomerization of η^1-σ-allyl-Cu(III) complex **B** to η^3-π-allyl-Cu(III) complex **C**, but instead can give rise an easier reductive elimination of RCu similar to elimination of CuX.

We hope that results of our kinetic study on the allylation of catalytic and stoichiometric CuX (X = I, Br, Cl, CN, SCN) derived alkylzinc–cuprates contributes to a better understanding for the role of alkylzinc–copper nucleophiles as active catalyst in the γ-selective allylic coupling of alkylzinc halides.

3. Experimental

3.1. General

All reactions were carried out under a nitrogen atmosphere in oven dried glassware using standard syringe-septum cap techniques [67]. Quantitative GC analysis were performed on a Thermo Finnigan gas chromatograph equipped with a ZB-5 capillary column packed with phenyl-polysiloxane using internal standard technique. THF was distilled from sodium benzophenone dianion; *n*-butyl bromide and *E*-crotyl chloride were obtained commercially and purified using literature procedures. Mg turnings for Grignard reagents was used without purification. $ZnCl_2$ (Aldrich) was dried under reduced pressure and used as a THF solution prepared prior to use. CuI [68], CuBr [69], CuCl [69], CuCN [70] and CuSCN [68] were purified according to the published procedures. *n*-Butylmagnesium bromide *n*-BuMgBr (**1**) was prepared in THF according to standard procedure and its concentration was found by titration prior to use [71]. *n*-Butylzinc chloride, *n*-BuZnCl (**2**) was prepared by dropwise addition of 1 mol equiv. of *n*-BuMgBr (**1**) in THF to a solution of 1 mol equiv. of $ZnCl_2$ in THF at 0 °C and stirring at that temperature for 20 min. *n*-Butylcopper reagents, *n*-BuCu(X)ZnCl (X = I, Br, Cl, CN, SCN) **8a–e** and chlorozinc di *n*-butylcuprate reagents, *n*-$Bu_2CuZnCl \cdot ZnClX$ **9a–e** were prepared by addition of 1 mol equiv. of CuX to 1 mol or 2 mol equiv. of freshly prepared *n*-BuZnCl (**2**), respectively in THF at 0 °C and stirring at that temperature for 20 min [10,11,13].

3.2. Procedure for kinetic study of catalytic and stoichiometric allylation of n-butylzinc–copper reagents

CuX (X = I, Br, Cl, CN, SCN) (**5**) catalyzed allylation of *n*-BuZnCl **2** with *E*-crotyl chloride **4**.

In a flame-dried and two-necked flask equipped with septum caps and a stirring bar, *n*-BuZnCl **2** (1.1 mmol) was prepared from *n*-BuMgBr (**1**) (1.1 mmol in 1.1 ml of THF) and $ZnCl_2$ (1.1 mmol in 1.7 ml of THF) at 0 °C. CuX (**5**) (0.2 mmol) was added at 0 °C and *E*-crotyl chloride (**4**) (1 mmol, 0.1 ml) was added at room temperature. A number of reactions was carried out in different flasks and each reaction was stirred at room temperature for appropriate time, i.e. 2, 4, 6, 8, 10, 15, 20, 30, 40, 50 and 60 min. Each reaction was quenched with aqueous NH_4Cl solution. The aqueous phase was extracted with Et_2O. After evaporation of the solvent to a convenient volume, internal standard was added and aliquots were analyzed by GC.

In the reactions catalyzed by *n*-BuCu(X)ZnCl (**8**) and *n*-$Bu_2CuZnCl \cdot ZnClX$ (**9**) the same procedure was applied. Except, these reagents were firstly prepared before the reaction. *n*-BuCu(X)ZnCl (**8**) was prepared from *n*-BuZnCl (**2**) [0.2 mmol, prepared from *n*-BuMgBr (**1**) (0.2 mmol in 0.2 ml of THF) and $ZnCl_2$ (0.2 mmol in 0.3 ml of THF) at 0 °C] and CuX (0.2 mmol) at 0 °C. Secondly, *n*-BuZnCl **2** (1.1 mmol in 2.8 ml THF) was prepared at 0 °C and added to freshly prepared *n*-BuCu(X)ZnCl (**8**). *E*-Crotyl chloride (**4**) (1 mmol, 0.1 ml) was added at room temperature. For the preparation of *n*-$Bu_2CuZnCl \cdot ZnClX$ (**9**) as a catalyst, *n*-BuZnCl (**2**) (0.4 mmol in 1 ml of THF) and CuX (0.2 mmol) were used.

Allylation of *n*-BuCu(X)ZnCl (**8**) and *n*-$Bu_2CuZnCl \cdot ZnClX$ (**9**) with *E*-crotyl chloride (**4**).

n-BuCu(X)ZnCl (**8**) was prepared from *n*-BuZnCl (1.1 mmol in 2.8 ml of THF) and CuX (1.1 mmol) at 0 °C. *E*-Crotyl chloride (1 mmol, 0.1 ml) was added at room temperature. A number of reactions was carried out in different flasks and the same procedure was applied for kinetic study. For the preparation of *n*-$Bu_2CuZnCl \cdot ZnClX$ (**9**), *n*-BuZnCl (2.2 mmol in 5.6 ml of THF) and CuX (1.1 mmol) were used.

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References

[1] A. Meijere, F. Diederich (Eds.), Metal Catalyzed Cross Coupling Reactions, Wiley, 2004.
[2] M. Beller, C. Bolm (Eds.), Transition Metals for Organic Synthesis, 2nd ed., Wiley-VCH, Weinheim, 2004.
[3] B.H. Lipshutz, in: M. Schlosser (Ed.), Organometallics in Synthesis. A Manual, Wiley, Chichester, 2002.
[4] G.A. Silverman, P.A. Rakita (Eds.), Handbook of Grignard Reagents, Marcel Dekker, New York, 1996.
[5] A. Kar, N.P. Argada, Synthesis (2005) 2995.
[6] B.M. Trost, D.L. vanDrenken, Chem. Rev. 96 (1996) 395.
[7] B.H. Lipshutz, S. Sengupta, Org. React. 41 (1992) 135.
[8] R.M. Majid, Tetrahedron 36 (1980) 1901.
[9] Z. Rappoport, I. Marek (Eds.), The Chemistry of Organozinc Compounds, Wiley, Chichester, 2006.
[10] P. Knochel, P. Jones (Eds.), Organozinc Reagents. A Practical Approach, Oxford University Press, Oxford, 1999.
[11] E. Erdik, Organozinc Reagents in Organic Synthesis, CRC Press, New York, 1996.
[12] N. Krause (Ed.), Modern Organocopper Chemistry, Wiley-VCH, Weinheim, 2001.
[13] R.J.K. Taylor (Ed.), Organocopper Reagents. A Practical Approach, Oxford University Press, 1994.
[14] C.A. Falciola, K. Tissot-Crosset, A. Alexakis, Angew. Chem., Int. Ed. 45 (2006) 5995.
[15] T. Yamazaki, H. Umetani, T. Kitazume, Tetrahedron Lett. 38 (1997) 6705.
[16] E.S. Person, M. Kluveren, D.M. Grove, J.E. Backvall, Chem. Eur. J. 1 (1995) 351.
[17] A. Yanagisawa, N. Nobuyoshi, H. Yamamoto, Tetrahedron 50 (1994) 6017.
[18] A. Yanagisawa, N. Nomura, H. Yamamoto, Synlett (1993) 689.
[19] A. Yanagisawa, Y. Noritake, N. Nomura, H. Yamamoto, Synlett (1991) 251.
[20] H.L. Goering, T.L. Underiner, J. Org. Chem. 56 (1991) 2563. and earlier references cited therein.
[21] J.E. Backvall, M. Sellen, B. Grant, J. Am. Chem. Soc. 112 (1990) 6615. and earlier references cited therein.
[22] K.A. Woerpel, J.H. Smitrovich, J. Am. Chem. Soc. 120 (1998) 12988.
[23] V. Calo, V. Fiandanase, A. Nacci, A. Salimati, Tetrahedron 50 (1994) 7383. and earlier references cited therein.
[24] M. Arai, M. Kawasuji, E. Nakamura, Chem. Lett. (1993) 357.
[25] N. Fujii, Nakai, H. Habshita, H. Yohizawa, T. Ibuka, F. Garrido, A. Mann, Y. Chounan, Y. Yamamoto, Tetrahedron Lett. 34 (1993) 4227.
[26] T.L. Underiner, S.D. Paisley, J. Schmitter, L. Lesheski, H.L. Goering, J. Org. Chem. 54 (1989) 2370. and earlier references cited therein.
[27] T. Ibuka, M. Tanaka, S. Nishii, Y. Yamamoto, J. Am. Chem. Soc. 111 (1989) 4864.
[28] W. Tückmantel, K. Oshima, H. Nozaki, Chem. Ber. 119 (1986) 1581.
[29] E.-I. Nakamura, K. Sekiya, M. Arai, S. Aoki, J. Am. Chem. Soc. 111 (1989) 3091.
[30] K. Sekiya, E. Nakamura, Tetrahedron Lett. 29 (1988) 5155.
[31] D.J. Burton, L.G. Sprague, J. Org. Chem. 54 (1989) 613.
[32] H. Ochiai, Y. Tamaru, K. Tsubaki, Z-I. Yoshida, J. Org. Chem. 52 (1987) 4418.
[33] E.-I. Nakamura, S. Aoki, K. Sekiya, H. Oshima, I. Kuwojima, J. Am. Chem. Soc. 109 (1987) 8056.
[34] H. Stadtmüller, R. Lentz, C.E. Tucker, T. Stüdeman, W. Dörner, P. Knochel, J. Am. Chem. Soc. 115 (1993) 7027.
[35] P. Knochel, T.S. Chou, J. Jubert, D. Rajagopal, J. Org. Chem. 58 (1993) 588.
[36] S.A. Rao, T.S. Chou, F. Schipor, P. Knochel, Tetrahedron 48 (1992) 2025.
[37] S.A. Rao, P. Knochel, J. Am. Chem. Soc. 114 (1992) 7579.
[38] M.J. Dunn, R.F.W. Jackson, J. Chem. Soc., Chem. Commun. (1992) 319.
[39] Y. Yamamoto, Y. Chounan, M. Tanaka, I. Ibuka, J. Org. Chem. 57 (1992) 1024.
[40] H.P. Knoees, M.T. Furlong, M.J. Rozema, P. Knochel, J. Org. Chem. 56 (1991) 5974.
[41] P. Knochel, S.A. Rao, J. Am. Chem. Soc. 112 (1990) 6146.
[42] T.S. Chou, P. Knochel, J. Org. Chem. 55 (1990) 4791.
[43] C. Retherford, T.S. Chou, R.M. Shelkun, P. Knochel, Tetrahedron Lett. 31 (1990) 1833.
[44] S.A. Rao, C.E. Tucker, P. Knochel, Tetrahedron Lett. 31 (1990) 7575.
[45] H.G. Chen, J. Gage, S.D. Barrett, P. Knochel, Tetrahedron Lett. 31 (1990) 1829.
[46] P. Knochel, N. Jeong, M.J. Rozema, M.C.P. Yeh, J. Am. Chem. Soc. 111 (1989) 6474.
[47] T.N. Majid, M.C.P. Yeh, P. Knochel, Tetrahedron Lett. 30 (1989) 5069.
[48] P. Knochel, M.C.P. Yeh, S.C. Berk, J. Talbert, J. Org. Chem. 53 (1988) 2390.
[49] M.C.P. Yeh, P. Knochel, Tetrahedron Lett. 29 (1988) 2395.
[50] G. Courtois, L. Miginiac, J. Organomet. Chem. 133 (1987) 285.
[51] E.-I. Nakamura, K. Sekiya, H. Oshino, I. Kuwajima, J. Am. Chem. Soc. 109 (1987) 8056.
[52] T.L. Underiner, S.D. Paisley, J. Schmitter, L. Lesheski, H.L. Goering, J. Org. Chem. 54 (1989) 2369.
[53] C.C. Tseng, S.J. Yen, H.L. Goering, J. Org. Chem. 51 (1986) 2892.
[54] C.C. Tseng, S.D. Paisley, H.L. Goering, J. Org. Chem. 51 (1986) 2884.
[55] H.L. Goering, S.S. Kantner, E.P. Seitz Jr., J. Org. Chem. 50 (1985) 5495. and earlier references cited therein.
[56] M. Yamanaka, S. Kato, E.-I. Nakamura, J. Am. Chem. Soc. 126 (2004) 6287.
[57] N. Yoshiaki, S.-L. Zhang, E.-I. Nakamura, J. Am. Chem. Soc. 130 (2008) 12862.
[58] E.R. Bartholomew, S.H. Bertz, S. Cope, M. Murphy, C.A. Ogle, J Am. Chem. Soc. 130 (2008) 11244.
[59] E. Erdik, M. Koçoğlu, Tetrahedron Lett. 48 (2007) 4211.
[60] E. Erdik, M. Koçoğlu, Appl. Organomet. Chem. 20 (2006) 290.
[61] M. Koçoğlu, E. Erdik, in preparation.
[62] S.H. Bertz, A. Chopra, M. Eriksson, C.A. Ogle, P. Seagle, Chem. Eur. J. 5 (1999) 2680.
[63] T.Zs. Nagy, A. Csâmpai, A. Kotschy, Tetrahedron 61 (2005) 9767.
[64] E.-I. Nakamura, S. Mori, Angew. Chem., Int. Ed. 39 (2000) 3750.
[65] E.-I. Nakamura, N. Yoshikai, Bull. Chem. Soc. Jpn. 77 (2004) 1.
[66] B.H. Lipshutz, J.A. Kozlowski, R.S. Wilhelm, J. Org. Chem. 48 (1983) 546.
[67] J. Leonard, B. Lygo, G. Procter, Advanced Practical Organic Chemistry, Blackie, London, 1995.
[68] R.N. Keller, H.D. Wynocoff, Inorg. Synth. 2 (1946) 1.
[69] D.D. Perrin, W.L.F. Armarego, Purification of Laboratory Chemicals, Pergamon Press, Oxford, 1988.
[70] J. Barber, J. Chem. Soc. 1 (1943) 79.
[71] J.H. Watson, J.F. Eastham, J. Organomet. Chem. 9 (1967) 165.