1,4-Addition Reactions of Bis(iodozincio)methane with α,β-Unsaturated Ketones

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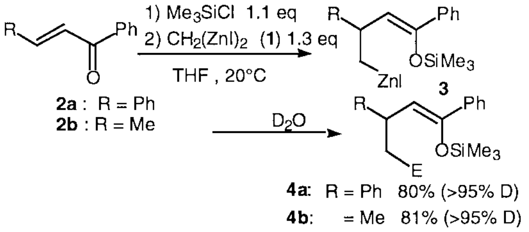
Received 31 May 1999

Abstract: A reaction of bis(iodozincio)methane with acyclic enones proceeded in 1,4-addition manner to afford zinc enolate of β-zinciomethylketone. In the case of the 1,4-addition reactions of bis(iodozincio)methane with 2-cyclohexen-1-one, an assistance by copper salt was necessary to complete the reaction.

Key words: zinc, 1,4-addition, dimetal, copper, enolate

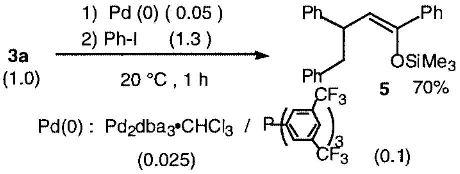
Reaction of *gem*-dimetallic reagents have attracted considerable attention as versatile reagents in organic synthesis.[1] Recently we reported the selective coupling reactions of *gem*-dizinc compound with organic halides;[2] 1,3-diketone synthesis,[2] and carbonyl olefination.[3] As other applications, we examined a reaction of *gem*-dizinc compound with α,β-unsaturated carbonyl compound to perform 1,4-addition. This reaction will afford zinc enolate of β-zinciomethylketone.

A reaction of bis(iodozincio)methane (**1**)[3] with α,β-unsaturated ketone **2a** was examined. The zinc enolate being formed *in situ* was trapped with an equimolar amount of chlorotrimethylsilane.[4] The procedure afforded a silyl enolate of organozinc compound **3a**.[5,6] A treatment of **3a** with D_2O gave **4a** in 80% yield. Following the same procedure for **2b**, the compound **4b** was obtained in 81 % yield (Scheme 1).

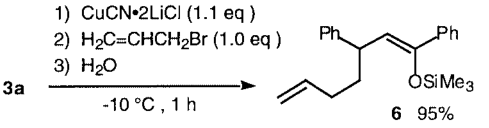


Scheme 1

The organozinc moiety in **3** was able to be reacted with organic halide as shown in Scheme 2. The zinc species **3a** was treated with iodobenzene in the presence of a palladium catalyst, Pd_2dba_3•$CHCl_3$ / $[3,5\text{-}(CF_3)_2C_6H_3]_3P$.[2] The reaction gave **5** in 70% yield. The copper salt mediated reaction of **3a** with allyl bromide gave the coupling product **6** in 95% yield (Scheme 3).[7] It is well-known that the silyl enolate reacts with various electrophiles, so the procedure make the four components coupling possible.



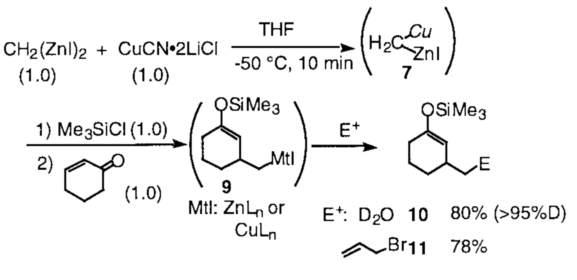
Scheme 2



Scheme 3

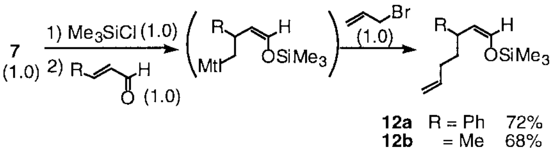
A treatment of 2-cyclohexen-1-one with bis(iodozincio)methane and chlorotrimethylsilane resulted into the recovery of enone. In this case, we tried to prepare organocopper species from *gem*-dizinc compound and copper salt.[7] A reaction of bis(iodozincio)methane (**1**) in THF with a THF solution of CuCN·2 LiCl at -30 °C was monitored by ^1H NMR. A treatment of **1** with an equimolar amount of CuCN·2 LiCl showed a new signal at -0.7 ppm, while the signal of bis(iodozincio)methane (**1**, -1.35 ppm) disappeared completely. This fact imply the new copper species **7** was formed by the above procedure.[8]

To the species **7**, chlorotrimethylsilane[4] and 2-cyclohexen-1-one were added sequentially. After the reaction was completed, D_2O was added to quench C-Zn bond. The silyl enolate **10** was obtained in 80% yield via **9** (Scheme 4). The intermediary organozinc **9** reacted also with organic halides. The copper salt which already existed in the reaction mixture mediated reaction of **9** with allyl halide to give **11** as a product in 78% yield.

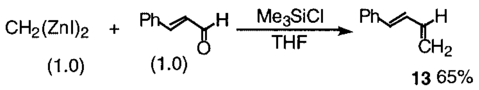


Scheme 4

The copper-mediated reaction of **1** with α,β-unsaturated aldehyde was also examined. As shown in Scheme 5, the species **7** was treated with chlorotrimethylsilane and aldehyde, and followed by an addition of allyl bromide afforded the silyl enolate **12** having *Z*-configuration.[9] The reaction without copper salt proceeded to give diene **13** via methylenation as shown in Scheme 6.[3]



Scheme 5



Scheme 6

The chlorotrimethylsilane-mediated addition of bis(iodozincio)-methane to acyclic α,β-unsaturated carbonyl compounds proceeded in 1,4-manner and gave the β-zinciomethylketone in a silyl enolate form. The reaction with *s-trans* cyclic ketone required a mediation with copper salt. The reaction of these highly reactive species, the reactivity of β-zinciomethylketone in the silyl enolate form is now under investigation.

Acknowlegement

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas (No. 10208208), from The Ministry of Education, Science, Sports, and Culture.

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(5) **3a**: ^{1}H NMR ($CDCl_3$) δ 7.1-7.6 (m, 10 H), 5.90 (d, *J* = 10.2 Hz, 1H), 4.24 (dt, *J* = 10.2, 7.6 Hz, 1H), 0.78 (d, *J* = 7.6 Hz, 1H), 0.10 (s, 9H).

(6) An existence of chlorotrimethylsilane is required for completion of the reaction. A reaction of **2a** with **1** in THF at 20 ° C for 12 h was quenched with H_2O. 2-Phenylpropyl phenyl ketone was obtained in 43% yield; a recovery of **2a** was 51%. **4a**: ^{1}H NMR ($CDCl_3$) δ 7.1-7.6 (m, 10 H), 5.39 (d, *J* = 7.2 Hz, 1H), 4.0 (dt, *J* = 7.2, 7.2 Hz, 1H), 1.40 (dt, *J* = 7.2, 0.8 Hz, 2 H).

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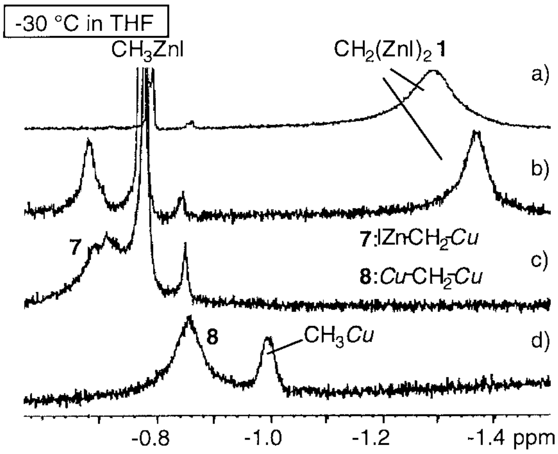
(8) The signal of methylene in **1** appeared at -1.3 ppm as a broad peak (Figure 1). By an addition of a THF solution of CuCN•2LiCl, the mixture showed newly formed signal at -0.7 ppm. This signal was supposed to be a mono copper species IZn-CH_2-*Cu* **7**. The substituent and ligand on copper could not be identified. An addition of excess amount of copper salt would form a dicopper species *Cu*-CH_2-*Cu* **8**, which was detected in ^{1}H NMR spectra as the signal at -0.85 ppm. A broad peak at -1.0 ppm in d) came from CH_3ZnI and copper salt. From these results, the tendency of transmetalation from zinc to copper was appeared in the following order: $CH_2(ZnI)_2$ > *Cu*-CH_2-ZnI > CH_3ZnI. The reaction of 2-cyclohexen-1-one with **8** in the presence of chlorotrimethlsilane did not give any adduct, and resulted in quantitative recovery of the starting material.



a) **1** in THF, b) **1** (1.0) + CuCN•2LiCl (0.25) in THF, c) **1** (1.0) + CuCN•2LiCl (1.0) in THF, d) **1** (1.0) + CuCN•2LiCl (4.0) in THF

Figure 1 ^{1}H NMR Spectra of Copper Reagent Prepared from $CH_2(ZnI)_2$ and CuCN•2LiCl in THF at -30 ° C.

(9) To a solution of bis(iodozincio)methane in THF[3b] (0.4 M, 2.0 mmol) was added dropwise a solution of CuCN (2.0 mmol) and LiCl (4.0 mmmol) in THF (5.0 mL) at -50 ° C over 15 min. The mixture was stirred for 5 min at the same temperature. To the mixture, cinnamyl aldehyde (2.0 mmol) and chlorotrimethylsilane (2.0 mmol) were added at -50 ° C. The resulting mixture was allowed to warm up to 0 ° C and allyl bromide (2.0 mmol) in THF (3.0 mL) was added at 0 ° C. The mixture was stirred for 1 h at 20 ° C. The resulting mixture was poured into ice cooled sat. NH_4Cl aq, and extracted with ether. The organic layers were washed with sat. $Na_2S_2O_3$ and brine. The ethereal solution was dried over $MgSO_4$. A short silica-gel column chromatography gave **12a** in 72 % yield. **12a**: ^{1}H NMR ($CDCl_3$) δ 7.1-7.3 (m, 5 H), 6.26 (d, *J* = 11.2 Hz, 1H), 5.82 (ddt, *J* = 15.5, 11.0, 7.2 Hz, 1H), 5.18 (dd, *J* = 11.2, 7.5 Hz, 1H), 5.01 (d, *J* = 15.5 Hz, 1H), 4.96 (d, *J* = 11.0 Hz, 1H), 3.18 (dt, *J* = 7.5, 7.5 Hz, 1H), 1.9-2.1 (m, 2H), 1.6-1.85 (m, 2H), 0.20 (s, 9H).

Article Identifier:
1437-2096,E;1999,0,08,1253,1254,ftx,en;Y11799ST.pdf