Preparation of Silyl-substituted Dizinciomethanes and Their Reactions with Electrophiles

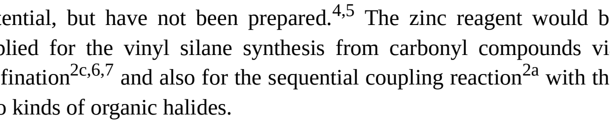
Seijiro Matsubara,* Yasuyuki Otake, Takuya Morikawa, and Kiitiro Utimoto
Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Yoshida, Sakyo, Kyoto 606-8501, Japan
Fax: 75-753-4863; E-mail: matsubara@orgrx2.kuic.kyoto-u.ac.jp

Received 25 August 1998

Abstract: Silyl-substituted bis(bromozincio)methanes ($RMe_2Si-CH(ZnBr)_2$; R = Me, Ph, and *p*-MeO-C_6H_4), prepared from the corresponding dibromides by Pb catalyzed reaction with zinc, reacted stepwise with two different electrophiles, R^1X and E^+, yielding R^1–CH($SiMe_2R$)–E.

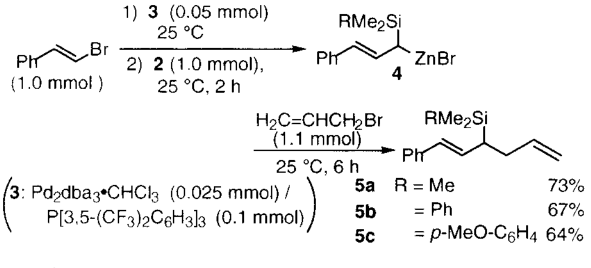
gem-Dimetallic reagents have attracted considerable attention as versatile reagents in organic synthesis.[1] Among various combinations of metals involved in the reagents, *gem*-dizincio reagents showed high reactivity.[2,3] The silyl substituted ones were expected to possess high potential, but have not been prepared.[4,5] The zinc reagent would be applied for the vinyl silane synthesis from carbonyl compounds via olefination[2c,6,7] and also for the sequential coupling reaction[2a] with the two kinds of organic halides.

We had reported the preparation of bis(iodozincio)methane from diiodomethane and zinc dust in the presence of catalytic amount of lead.[8] Analogously $RMe_2SiCHBr_2$ (**1a**: R = Me; **1b**: R = Ph; **1c**: R = *p*-MeO-C_6H_4) was treated with zinc dust in the presence of a catalytic amount of lead in THF. The reaction temperature was crucial; at 60 °C, the corresponding dizincio compounds (**2a-c**) were obtained in 72–80% yields (Scheme 1).[9]



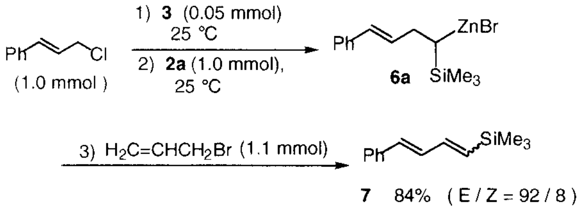
Scheme 1

A coupling reaction with an organic halide under influence of transition metal compounds were examined.[2a,b] As shown in Scheme 2, a reaction of **2** with (*E*)-bromostyrene using Pd catalyst **3** at 25 °C gave organozinc **4**;[10] this compound reacted with allyl bromide, which was added sequentially into the reaction mixture, to give **5a-c** in 64–73% overall yields. Thus two kinds of organic halides were connected with silyl-substituted methylene group (Scheme 2).



Scheme 2

Reaction of **2a** with allyl halides gave mono-adduct **6a** in good yields, but the sequential addition of allyl bromide afforded trimethylsilylbutadienes **7** by β-elimination (Scheme 3). The reaction may proceed via transmetalation of **6a** to palladium(II) species; the reductive elimination would form **7** with forming Pd(0) species which are oxidized into Pd(II) species again by allyl bromide. An improvement was required for the second step reaction. The use of organocopper species gave the way.



Scheme 3

The sequential use of palladium catalyst and copper salt also made the following transformations possible as shown in Table 1. A solution of organozinc species **6** in THF, prepared from an organic halide and **2** in the presence of Pd(0) catalyst **3**, was treated with CuCN•2LiCl followed by the reaction with various organic halides.[11] The homolallyl zinc species **6a** prepared from cinnamyl chloride was reacted with allyl bromide after a treatment with CuCN•2LiCl to give the coupling product **8a** in 88% yield (entry 1). It is the sharp contrast with the result of Scheme 3. The use of propargyl bromide instead of allyl bromide afforded the corresponding allene derivative (entries 4 and 5). The zinc species prepared from iodobenzene and propargyl bromide by the Pd catalyzed reaction with **2** as described above reacted with allyl bromide via organocopper species (entries 6-9).

As organosilyl group can be oxidized into hydroxyl group,[4] silyl-substituted dizinciomethanes described above can be used as hydroxymethyl dianion equivalent. The oxidation detailed methods are under investigation.

Experimental Procedure:

Preparation of bis(bromozincio)trimethylsilylmethane (**2a**):

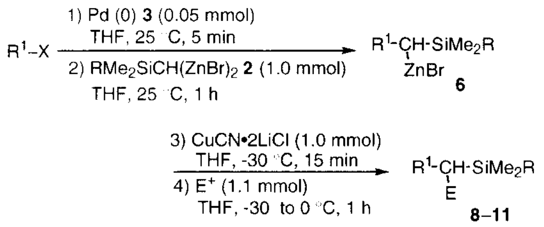
A mixture of Zn (4.9 g, 75 mmol) with catalytic amount of $PbCl_2$ (0.02 g) and **1a** (0.74 g, 3 mmol) in 3.0 ml of THF was sonicated for 2 h at 25°C. To the mixture THF (30 ml) and **1a** (6.7 g, 27 mmol) were added, then the mixture was stirred at 60 °C for 4 h affording **2a** in 72% yield.

Reaction of **2a** with bromostyrene:

Bromostyrene (0.18 g, 1.0 mmol) was added to a THF solution (10 ml) containing Pd_2dba_3•$CHCl_3$ (26 mg, 0.025 mmol) and tris[3,5(trifluoromethyl)phenyl]phosphine (67 mg, 0.15 mmol), then the mixture was stirred for 5 min. To the reaction mixture, **2a** (0.7 M in THF, 1.4 ml, 1.0 mmol) was added. The mixture was stirred for 2 h. Yield of **4a** was measured by ^1H NMR spectroscopy using 2,2,3,3-tetramethylbutane as an internal standard.[10] To the obtained THF solution of **4a**, allyl bromide (0.13 g, 1.1 mmol) was added and the resultant solution was stirred for 6 h. Aqueous workup, extraction with hexane-ethyl acetate, wash with brine, concentration, and purification by column chromatography of the reaction mixture afforded **5a** (0.17 g) in 73% yield.

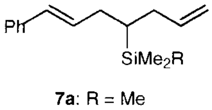
5a: ^1H NMR ($CDCl_3$, 20 °C); δ 0.04 (s, 9H), 1.79 (dt, *J* = 4.2, 9.6 Hz, 1H), 2.1-2.4 (m, 2H), 4.93 (dt, *J* = 0.9, 9.0 Hz, 1H), 5.00 (dt, *J* = 1.5,

Table 1. Copper Salt Mediated Coupling Reactions of **6** [a]

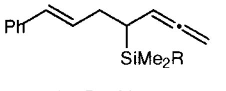


entry	R^1-X	R	E^+	Product	Y[b]
1	(*E*)-PhCH=CHCH$_2$Br	Me	CH$_2$=CHCH$_2$Br	**8a**	88 %
2		Ph		**8b**	76
3		*p*-MeOC$_6$H$_4$		**8c**	83
4		Me	HC≡CCH$_2$Br	**9a**	83[c]
5		*p*-MeOC$_6$H$_4$		**9c**	79[c]
6	PhI	Me	CH$_2$=CHCH$_2$Br	**10a**	92
7		*p*-MeOC$_6$H$_4$		**10c**	96
8	*n*-C$_8$H$_{11}$-C≡C-CH$_2$Br	Me	CH$_2$=CHCH$_2$Br	**11a**	65[d]
9		*p*-MeOC$_6$H$_4$		**11c**	77[d]

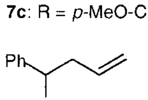
a) All reactions were carried out as a one pot reaction. b) Isolated yields. c) The allene isomer was not observed in the reaction mixture. d) The alkyne isomer was not observed in the reaction mixture



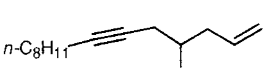
7a: R = Me
7b: R = Ph
7c: R = *p*-MeO-C$_6$H$_4$



8a: R = Me
8c: R = *p*-MeO-C$_6$H$_4$



9a: R = Me
9c: R = *p*-MeO-C$_6$H$_4$



10a: R = Me
10c: R = *p*-MeO-C$_6$H$_4$

17.1 Hz, 1H), 5.83 (ddt, J = 17.4, 9.0, 6.9 Hz, 1H), 6.10 (dd, J = 15.9, 9.6 Hz, 1H), 6.23 (d, J = 15.9 Hz, 1H), 7.1- 7.4 (m, 5H); ^{13}C NMR (CDCl$_3$, 20 °C); δ -3.1, 33.4, 34.1, 114.7, 125.7, 126.4, 127.6, 128.5, 132.5, 138.4, 139.1.

Reaction of **2a** with cinnamyl chloride:

Cinnamyl chloride (0.15 g, 1.0 mmol) was added to a THF solution (10 ml) containing Pd$_2$dba$_3$•CHCl$_3$ (26 mg, 0.025 mmol) and tris[3,5(trifluoromethyl)phenyl]phosphine (67 mg, 0.15 mmol), then the mixture was stirred for 5 min. To the reaction mixture, **2a** (0.7 M in THF, 1.4 ml, 1.0 mmol) was added and the solution was stirred for 1 h. Yield of homoallylzinc species **6a** was measured by ^{1}H NMR spectroscopy. To a THF solution of **6a**, a mixture of CuCN (90 mg, 1.0 mmol) and LiCl (85 mg, 2. 0 mmol) in THF (3 ml) was added at -30 °C. The mixture was stirred for 15 min at the same temperature. Allyl bromide (0.13 g, 1.1 mmol) was added and the resulting solution was stirred for 1 h. During the stirring, the reaction temperature was raised to 0 °C. Aqueous workup, extraction with hexane-ethyl acetate, wash with brine, concentration, and purification by column chromatography of the reaction mixture afforded **8a** (0.24 g) in 88% yield.

6a: ^{1}H NMR (THF-d_8, 20 °C); δ -0.11 (s, 9H), 2.37-2.51 (m, 2H), 6.16 (d, J = 15.9 Hz, 1H), 6.28 (d, J = 15.9, 6.9 Hz, 1H), 6.93-7.19 (m, 5H).

8a: ^{1}H-NMR (CDCl$_3$, 20 °C); δ 0.03 (s, 9H), 0.87 (tt, J = 5.7, 7.8 Hz, 1H), 2.1-2.38 (m, 4H), 4.97-5.09 (m, 2H), 5.80 (ddt, J = 17.4, 10.2, 6.9 Hz, 1H), 6.18 (dt, J = 15.9, 6.9 Hz, 1H), 6.36 (d, J = 15.9 Hz, 1H), 7.1-7.4 (m, 5H); ^{13}C NMR (CDCl$_3$, 20 °C); δ -2.1, 26.1, 32.9, 33.8, 115.2, 126.0, 126.8, 128.6, 130.5, 131.1, 137.9, 139.1.

Acknowledgement. Financial support from the Ministry of Education, Science, Sports and Culture, Japan (No. 10125217, 10132227) are acknowledged.

References and Notes

(1) Marek, I.; Normant, J.-F. *Chem. Rev.* **1996**, *96*, 3241.

(2) (a) Utimoto, K.; Toda, N.; Mizuno, T.; Kobata, M.; Matsubara, S. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2804. (b) Matsubara, S.; Kawamoto, K.; Utimoto, K. *Synlett* **1998**, 267. (c) Matsubara, S.; Sugihara, M.; Utimoto, K. *Synlett* **1998**, 313.

(3) Knochel, P.; Normant, J.-F. *Tetrahedron Lett.* **1986**, *27*, 4427, 4431; Nakamura, E.; Kubota, K.; Sakata, G. *J. Am. Chem. Soc.*, **1997**, *119*, 5457.

(4) Oxidation of C-Si bond into C-O bond: Colvin, E. W. In *Comprehensive Organic Synthesis*, Vol. 7; Ley, S.V.; Trost, B. M.; Fleming, I. Eds.; Pergamon Press: Oxford, **1991**, p641.

(5) *gem*-Dimagnesium derivatives: Bertini, F.; Grasselli, P.; Zubiani, G.; Cainelli, G. *Tetrahedron* **1970**, *26*, 1281; van de Heisteeg, B. J. J.; Schat, G.; Tinga, M. A. G. M.; Akkerman, O. S.; Bickelhaupt, F. *Tetrahedron Lett.* **1986**, *27*, 6123.

(6) Okazoe, T.; Takai, K.; Oshima, K.; Utimoto, K. *J. Org. Soc.* **1987**, *52*, 4410; Takai, K.; Kataoka, Y.; Miyai, J.; Okazoe, T.; Oshima, K.; Utimoto, K. *Org. Synth.* **1996**, *73*, 73; Lombardo, L. *Org. Synth.* **1987**, *65*, 81.

(7) Takai, K.; Kataoka, Y.; Okazoe, T.; Utimoto, K. *Tetrahedron Lett.* **1987**, *28*, 1443.

(8) Bis(iodozincio)methane was prepared by the reaction of diiodomethane with Zn under Pb catalysis; Takai, K.; Kakiuchi, T.; Kataoka, Y.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 2668.

(9) Yield was determined by ^{1}H NMR measurement using 2,2,3,3-tetramethylbutane as an internal standard. Reaction temperature is crucial to obtain **2** in good yield; for example **2a**, 72 % at 60 °C, whereas 30% at 25 °C with contamination of bromo(bromozincio)trimethyl-silylmethane (40%). ^{1}H NMR of **2a** (THF-d_8 at –63 °C): δ –1.62 (s, 1H), –0.09 (s, 9H).

(10) **4a**: ^{1}H NMR (THF-d_8, 20 °C); δ 0.05 (s, 9H), 1.52 (d, J = 12.9 Hz, 1H), 5.94 (d, J = 15.0 Hz, 1H), 6.66 (dd, J = 15.0, 12.9 Hz, 1H), 6.87-7.37 (m, 5H).

(11) Knochel, P.; Singer, R. D. *Chem. Rev.*, **1993**, *93*, 2117; Knochel, P. *Synlett* **1995**, 393.