Palladium-catalysed *cis*- and *trans*-silaboration of terminal alkynes: complementary access to stereo-defined trisubstituted alkenes†

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Palladium-catalysed *cis*- and *trans*-silaboration of terminal alkynes has been developed *via* the addition of (chlorodimethylsilyl)pinacolborane, followed by a one-pot conversion of the chloro group on the silicon atom to an isopropoxy group.

There is increasing demand for the development of an efficient way to synthesise stereodefined organometallic compounds for stereoselective access to complex organic molecules. Vicinally dimetallated alkenes are attractive intermediates for the synthesis of highly substituted alkenes, *via* C–C bond forming reactions using appropriate carbon electrophiles (Fig. 1).[1] Regio- and stereoselective synthesis of dimetallic alkenes has been achieved *via* the transition metal-catalysed addition of dimetallic compounds, consisting of silicon, boron, or tin, to alkynes.[2] These reactions generally proceed in a *cis* fashion to give *cis*-1,2-bismetallated alkenes. In contrast, selective synthesis of the corresponding *trans* isomers has been only partly achieved by hydrometallation of monometallated internal alkynes, which often suffers from low regio- and stereoselectivity.[3–5] Complementary synthesis of *cis*- and *trans*-bismetallated alkenes from common starting materials is highly attractive for the preparation of desirable stereoisomers of highly substituted alkenes.[6]

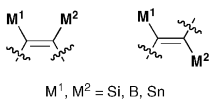
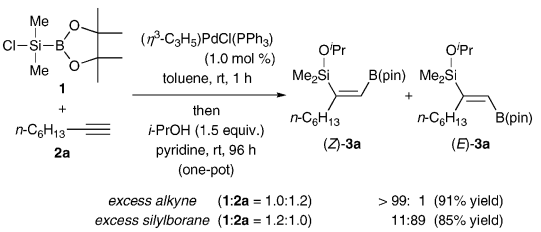


Fig. 1 Vicinally dimetallated alkenes.

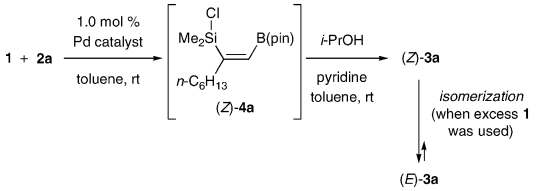
As a part of our silaboration study,[7] we have recently reported on the palladium-catalysed reaction of alkynes with silylboranes bearing a heteroatom functional group on the silicon atom.[8] We found that addition of (chlorodimethylsilyl)pinacolborane (**1**)[9] to 1-octyne was much faster than that of conventional triorganosilylboranes, such as (dimethylphenylsilyl)pinacolborane.[10,11] The efficiency of the reaction and the potential synthetic utility of the product, which has an easily convertible silyl group,[12] led us to an investigation aimed at the application of these products in stereoselective alkene synthesis. Herein, we describe the palladium-catalysed silaboration of terminal alkynes with **1**. Depending on the reaction conditions of the silaboration, either the *cis*- or *trans*-silaboration products were obtained selectively through a one-pot conversion into the alkoxysilane derivative.

(Chlorodimethylsilyl)pinacolborane (**1**) was reacted with 1-octyne (**2a**) in toluene at room temperature in the presence of (η^3-C_3H_5)PdCl(PPh_3)[13] (1.0 mol%) (Scheme 1). After a period of 1 h, isopropyl alcohol (1.5 equiv.) and pyridine were added to the reaction mixture to convert the chloro group on the silicon atom to an isopropoxy group, giving the chromatographically stable 1-boryl-2-silyloct-1-ene **3a**. When the reaction was carried out with a small excess of alkyne (**1** : **2a** = 1.0 : 1.2), the *cis*-addition product, (*Z*)-**3a**, was isolated in a 91% yield as a single stereoisomer (*Z* : *E* = >99 : 1). In sharp contrast, when a small excess of silylborane (**1** : **2a** = 1.2 : 1.0) was used under the same reaction conditions, the *trans*-addition product, (*E*)-**3a**, was isolated in an 85% yield (*Z* : *E* = 11 : 89) after treatment of the reaction mixture with *i*-PrOH–pyridine.



Scheme 1 Palladium-catalysed silaboration of **2a** with **1**.

The reaction process, which was highly influenced by the stoichiometry of the reagents used, was traced in order to elucidate the mechanism of the *cis*- and *trans*-silaboration (Scheme 2). In the first step, the palladium-catalysed addition of **1** to **2a** proceeded in a *cis* fashion to give (*Z*)-**4a** selectively,[14] regardless of the stoichiometry of the substrate used. The subsequent reaction of (*Z*)-**4a** with isopropyl alcohol also proceeded stereospecifically to give (*Z*)-**3a**, which was also



Scheme 2 Tracing of the reaction.

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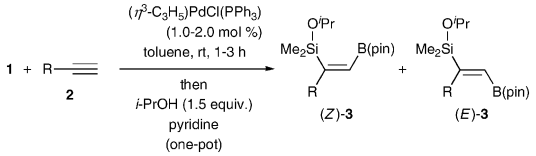
Table 1 Palladium-catalysed *cis*- and *trans*-silaboration of terminal alkynes



Entry	R (Alkyne)	Product	Excess alkyne % yield (Z : E)	Excess Si–B % yield (Z : E)
1	*n*-C_6H_{13} (**2a**)	**3a**	93 (>99 : 1)	92 (11 : 89)[e]
2	*n*-C_4H_9 (**2b**)	**3b**	93 (>99 : 1)	87 (8 : 92)
3	*n*-C_8H_{17} (**2c**)	**3c**	91 (>99 : 1)	91 (8 : 92)
4	TBSO$(CH_2)_2$ (**2d**)	**3d**	90 (>99 : 1)	82 (9 : 91)
5	TBSO$(CH_2)_3$ (**2e**)	**3e**	81 (>99 : 1)	82 (7 : 93)
6	Cl$(CH_2)_3$ (**2f**)	**3f**	94 (>99 : 1)	84 (11 : 89)
7	NC$(CH_2)_3$ (**2g**)	**3g**	87 (>99 : 1)	81 (7 : 93)
8	Ph (**2h**)	**3h**	87 (>99 : 1)	80 (62 : 38)
9	*cyclo*-C_6H_{11} (**2i**)	**3i**	90 (>99 : 1)	91 (67 : 33)
10	*t*-Bu (**2j**)	**3j**	87 (>99 : 1)	76 (90 : 10)[f]

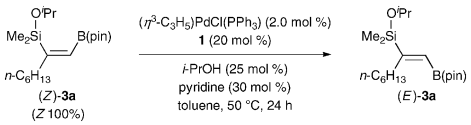
[a] (η^3-C_3H_5)PdCl(PPh_3) (1.0 mol%), **1** (0.40 mmol), and **2** (0.48 mmol) in toluene (0.2 mL) were stirred at room temperature for 1–3 h. Pyridine (0.72 mmol) and *i*-PrOH (0.60 mmol) were added and the mixture was stirred at room temperature for 1 h. [b] (η^3-C_3H_5)-PdCl(PPh_3) (2.0 mol%), **1** (0.48 mmol), and **2** (0.40 mmol) in toluene (0.2 mL) were stirred at room temperature for 1–3 h. Pyridine (0.72 mmol) and *i*-PrOH (0.60 mmol) were added and the mixture was stirred at 50 °C for 24 h. [c] Isolated yield. [d] Determined by GC analysis of the crude mixture. [e] Carried out with **1** (2.4 mmol) and **2** (2.0 mmol). [f] Determined by ^{1}H NMR analysis.

not dependent on the reaction conditions. However, it was found that (*Z*)-**3a** underwent slow isomerization to (*E*)-**3a** only when an excess of **1** was used in the first step. The ratio of (*Z*)-**3a** : (*E*)-**3a** became constant (*ca.* 1 : 9) after a period of 96 h at room temperature.[15]

Various terminal alkynes were subjected to the *cis*- and *trans*-silaboration protocols (Table 1). To obtain *cis*-addition products, the silaboration was performed with excess alkyne (**1** : **2** = 1.0 : 1.2) in the presence of (η^3-C_3H_5)PdCl(PPh_3) (1.0 mol%), followed by treatment with *i*-PrOH at room temperature for a period of 1 h. The reaction of various aliphatic alkynes **2a–g** proceeded efficiently at room temperature to give the corresponding (*Z*)-**3a–g** in yields of 81–94% with perfect *Z* selectivities (entries 1–7). Functional groups such as silyloxy, chloro, and cyano groups were tolerated under these reaction conditions (entries 4–7). Phenylacetylene (**2h**), cyclohexylacetylene (**2i**), and 3,3-dimethylbut-1-yne (**2j**) also successfully underwent the *cis*-silaboration to produce (*Z*)-**3h–j** in yields of 87–90% with the Z/E ratios of >99 : 1 (entries 8–10).

On the other hand, to obtain the *trans*-silaboration products, the silaboration step was carried out with excess silylborane (**1** : **2** = 1.2 : 1.0) in the presence of 2.0 mol% of (η^3-C_3H_5)PdCl(PPh_3), followed by treatment with *i*-PrOH at 50 °C for a period of 24 h. The reaction of the primary alkyl-substituted alkynes **2a–g** successfully gave (*E*)-**3a–g** in 81–92% yields with high *E*-selectivities (Z : E = 11 : 89–7 : 93, entries 1–7). Functional groups such as silyloxy, chloro, and cyano groups were tolerated (entries 4–7). However, the *trans*-silaboration protocol was not applicable to the sterically demanding alkynes, such as **2h**, **2i**, and **2j** (entries 8–10). These results clearly indicate that the sterically less-hindered alkynes are suitable for the *trans*-silaboration.

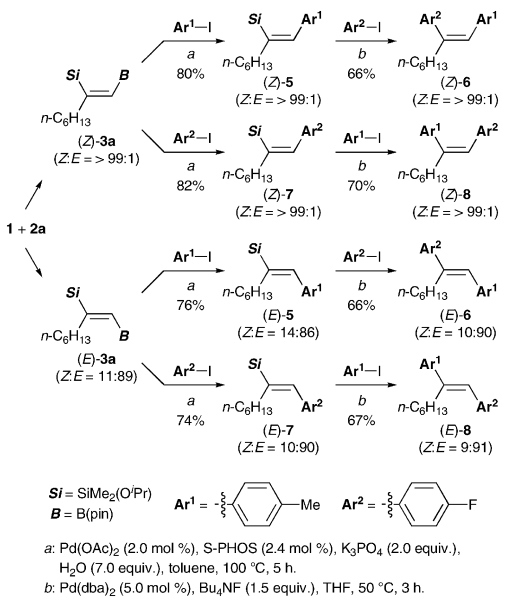
Table 2 Isomerization of (*Z*)-**3a** to (*E*)-**3a**



Entry	Pd	**1**	*i*-PrOH	Pyridine	(*Z*)-**3a** : (*E*)-**3a**[a,b]
1	+	+	+	+	13 : 87
2	–	+	+	+	>99 : 1
3	+	–	+	+	>99 : 1
4	+	+	–	+	>99 : 1
5	+	+	+	–	8 : 92
6	+	–[c]	+	+	>99 : 1
7	+	–[c]	+	–	>99 : 1

[a] Determined by GC analysis. [b] Small amounts of structure-undefined products were formed for all reactions investigated. [c] Me_3SiCl was used instead of **1**.

The isomerization step was examined separately from the silaboration step using isolated (*Z*)-**3a** (Table 2). In the presence of (η^3-C_3H_5)PdCl(PPh_3) (2.0 mol%), **1** (20 mol%), *i*-PrOH (25 mol%), and pyridine (30 mol%), geometrically pure (*Z*)-**3a** was isomerized to (*E*)-**3a** to the same extent as in the one-pot reaction (Z : E = 13 : 87) after heating to 50 °C for a period of 24 h (entry 1). On the other hand, no isomerization took place in the absence of either the palladium complex, **1**, or *i*-PrOH (entries 2–4), whereas pyridine was not essential for driving the isomerization (entry 5). Two additional experiments were carried out to elucidate the role of the chloro-substituted silylborane (entries 6 and 7). In the presence of



Scheme 3 A synthetic application to stereoselective preparation of all isomers of 1,2-diaryloct-1-ene.

trimethylsilyl chloride instead of the silylborane, no isomerization proceeded in either the presence or absence of pyridine. These results clearly suggest that the isomerization is promoted by a catalytically active palladium species that is formed with **1** and *i*-PrOH.[16]

Synthetic application of the silaboration products was demonstrated by the stereoselective synthesis of 1,2-diaryloct-1-ene *via* a Suzuki–Miyaura coupling followed by a Hiyama coupling (Scheme 3). The Suzuki–Miyaura coupling of (*Z*)-**3a** with 4-iodotoluene (Ar^1–I) in the presence of a Pd–S-PHOS catalyst[17] gave alkenylsilane (*Z*)-**5** in an 80% yield. The subsequent Hiyama coupling of (*Z*)-**5** with 4-fluoroiodobenzene (Ar^2–I) under phosphine-free conditions[18] afforded (*Z*)-2-(4-fluorophenyl)-1-(4-methylphenyl)oct-1-ene [(*Z*)-**6**] in a 66% yield. On the other hand, the Suzuki–Miyaura coupling of (*Z*)-**3a** with Ar^2–I followed by Hiyama coupling with Ar^1–I gave (*Z*)-**8**, the regioisomer of (*Z*)-**6**, in a comparable yield. A complementary two-step transformation was applied to (*E*)-**3a**, producing (*E*)-**6** and (*E*)-**8** in reasonable yields. These reactions demonstrate that all four isomers of 1,2-diarylalk-1-enes are accessible from a single set of reactants, *i.e.*, 1-octyne, *p*-tolyl iodide, and *p*-fluorophenyl iodide, with the use of common reagents for each step. The methods of synthesis are only differentiated by the reagent ratio in the silaboration step and the order of the aryl iodides.

In conclusion, we have established palladium-catalysed *cis*- and *trans*-silaboration of terminal alkynes, which can be controlled by the stoichiometry of the silylborane and alkyne. The products, (*Z*)- and (*E*)-1-boryl-2-silylalk-1-enes, serve as useful synthetic buiilding blocks for the stereoselective synthesis of stilbene derivatives.

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Notes and references

1 (*a*) E. Piers and R. T. Skerlj, *J. Org. Chem.*, 1987, **52**, 4421; (*b*) G. Zweifel and W. Leong, *J. Am. Chem. Soc.*, 1987, **109**, 6409; (*c*) T. Ishiyama, N. Matsuda, N. Miyaura and A. Suzuki, *J. Am. Chem. Soc.*, 1993, **115**, 11018; (*d*) T. Ishiyama, M. Yamamoto and N. Miyaura, *Chem. Lett.*, 1996, 1117; (*e*) S. D. Brown and R. W. Armstrong, *J. Am. Chem. Soc.*, 1996, **118**, 6331; (*f*) S. D. Brown and R. W. Armstrong, *J. Org. Chem.*, 1997, **62**, 7076; (*g*) R. Mabon, A. M. E. Richecœur and J. B. Sweeney, *J. Org. Chem.*, 1999, **64**, 328; (*h*) L.-E. Perret-Aebi and A. von Zelewsky, *Synlett*, 2002, 773; (*i*) M. Wenckens, P. Jakobsen, P. Vedsø, P. O. Huusfeldt, B. Gissel, M. Barfoed, B. L. Brockdorff, A. E. Lykkesfeldt and M. Begtrup, *Bioorg. Med. Chem.*, 2003, **11**, 1883; (*j*) T. Yamamoto, K. Kobayashi, T. Yasuda, Z.-H. Zhou, I. Yamaguchi, T. Ishikawa and S. Koshihara, *Polym. Bull.*, 2004, **52**, 315; (*k*) C. Baldoli, A. Bossi, C. Giannini, E. Licandro, S. Maiorana, D. Perdicchia and M. Schiavo, *Synlett*, 2005, 1137; (*l*) F. R. Wüst, A. Höhne and P. Metz, *Org. Biomol. Chem.*, 2005, **3**, 503; (*m*) E. Licandro, C. Rigamonti, M. T. Ticozzelli, M. Monteforte, C. Baldoli, C. Giannini and S. Maiorana, *Synthesis*, 2006, 3670; (*n*) N. B. Carter, R. Mabon, R. Walmsley, A. M. E. Richecœur and J. B. Sweeney, *Synlett*, 2006, 1747.

2 (*a*) I. Beletskaya and C. Moberg, *Chem. Rev.*, 2006, **106**, 2320; (*b*) M. Suginome, T. Matsuda, T. Ohmura, A. Seki and M. Murakami, in *Comprehensive Organometallic Chemistry III*, ed. R. H. Crabtree, D. M. P. Mingos and I. Ojima, Elsevier, Oxford, 2007, vol. 10, p. 725.

3 Hydrometallation of R′–C≡C–M (M = SiR_3, BR_2, and SnR_3) tends to give *gem*-dimetallated alkenes. For examples, see: (*a*) J. J. Eisch and M. W. Foxton, *J. Org. Chem.*, 1971, **36**, 3520; (*b*) K. Uchida, K. Utimoto and H. Nozaki, *J. Org. Chem.*, 1976, **41**, 2941; (*c*) G. Zweifel and S. J. Backlund, *J. Am. Chem. Soc.*, 1977, **99**, 3184; (*d*) A. Hassner and J. A. Soderquist, *J. Organomet. Chem.*, 1977, **131**, C1; (*e*) T. N. Mitchell and A. Amamria, *J. Organomet. Chem.*, 1983, **252**, 47; (*f*) B. H. Lipshutz, R. Kell and J. C. Barton, *Tetrahedron Lett.*, 1992, **33**, 5861; (*g*) L. Deloux, E. Skrzypczak-Jankun, B. V. Cheesman and M. Srebnik, *J. Am. Chem. Soc.*, 1994, **116**, 10302.

4 For hydrometallation of 1-silyl-1-alkynes yielding *trans*-1,2-bismetallated 1-alkenes, see: (*a*) P. F. Hudrlik, R. H. Schwartz and J. C. Hogan, *J. Org. Chem.*, 1979, **44**, 155; (*b*) J. A. Soderquist, J. C. Colberg and L. D. Valle, *J. Am. Chem. Soc.*, 1989, **111**, 4873; (*c*) H. X. Zhang, F. Guibé and G. Balavoine, *J. Org. Chem.*, 1990, **55**, 1857; (*d*) H. Urabe, T. Hamada and F. Sato, *J. Am. Chem. Soc.*, 1999, **121**, 2931.

5 Stereoselective catalytic *trans*-bismetallation has been achieved only for ethyne (C_2H_2): (*a*) B. L. Chenard and C. M. Van Zyl, *J. Org. Chem.*, 1986, **51**, 3561; (*b*) T. Hayashi, H. Yamashita, T. Sakakura, Y. Uchimaru and M. Tanaka, *Chem. Lett.*, 1991, 245. For *trans*-bisstannylation of 1,3-diynes with a stannylcopper reagent, see ref. 1*b*.

6 (*a*) T. N. Mitchell, A. Amamria, H. Killing and D. Rutschow, *J. Organomet. Chem.*, 1986, **304**, 257; (*b*) E. Piers and R. T. Skerlj, *J. Chem. Soc., Chem. Commun.*, 1986, 626.

7 For recent examples, see: (*a*) T. Ohmura and M. Suginome, *Org. Lett.*, 2006, **8**, 2503; (*b*) T. Ohmura, H. Furukawa and M. Suginome, *J. Am. Chem. Soc.*, 2006, **128**, 13366; (*c*) T. Ohmura, H. Taniguchi and M. Suginome, *J. Am. Chem. Soc.*, 2006, **128**, 13682; (*d*) T. Ohmura, H. Taniguchi, Y. Kondo and M. Suginome, *J. Am. Chem. Soc.*, 2007, **129**, 3518.

8 T. Ohmura, K. Masuda and M. Suginome, *J. Am. Chem. Soc.*, 2008, **130**, 1526.

9 T. Ohmura, K. Masuda, H. Furukawa and M. Suginome, *Organometallics*, 2007, **26**, 1291.

10 (*a*) M. Suginome, H. Nakamura and Y. Ito, *Chem. Commun.*, 1996, 2777; (*b*) S.-y. Onozawa, Y. Hatanaka and M. Tanaka, *Chem. Commun.*, 1997, 1229; (*c*) M. Suginome, T. Matsuda, H. Nakamura and Y. Ito, *Tetrahedron*, 1999, **55**, 8787; (*d*) J. C. A. Da Silva, M. Birot, J.-P. Pillot and M. Pétraud, *J. Organomet. Chem.*, 2002, **646**, 179; (*e*) M. Suginome, H. Noguchi, T. Hasui and M. Murakami, *Bull. Chem. Soc. Jpn.*, 2005, **78**, 323.

11 For a related study on the catalytic silaboration of alkynes, see: (*a*) M. Suginome, T. Matsuda and Y. Ito, *Organometallics*, 1998, **17**, 5233; (*b*) T. Segawa, Y. Asano and F. Ozawa, *Organometallics*, 2002, **21**, 5879.

12 (*a*) T. Hiyama, in *Metal-Catalyzed Cross-Coupling Reactions*, ed. F. Diedrich and P. J. Stang, Wiley-VCH, Weinheim, 1998, ch.10; (*b*) T. Hiyama and E. Shirakawa, *Top. Curr. Chem.*, 2002, **219**, 61.

13 P. Kisanga and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2000, **122**, 10017.

14 A possible mechanism of *cis*-silaboration involves oxidative addition of the Si–B bond to Pd(0), followed by regioselective *cis*-insertion of the C–C triple bond into the Pd–B bond and subsequent reductive elimination of the (*Z*)-adduct with regeneration of Pd(0). See ref. 10*c*.

15 For a related study on the *Z*/*E* isomerization under the catalytic bismetallation conditions, see: (*a*) H. Watanabe, M. Kobayashi, K. Higuchi and Y. Nagai, *J. Organomet. Chem.*, 1980, **186**, 51; (*b*) H. Matsumoto, I. Matsubara, T. Kato, K. Shono, H. Watanabe and Y. Nagai, *J. Organomet. Chem.*, 1980, **199**, 43; see also refs. 5*b* and 10*c*.

16 For a general description of alkene isomerization, see (*a*) F. J. McQuillin, D. G. Parker and G. R. Stephenson, in *Transition Metal Organometallics for Organic Synthesis*, Cambridge University Press, Cambridge, 1991, ch. 2, p. 27; (*b*) G. W. Parshall and S. D. Ittel, in *Homogeneous Catalysis*, Wiley Interscience, New York, 1992, ch. 2, p. 9; (*c*) R. H. Crabtree, in *The Organometallic Chemistry of the Transition Metals*, Wiley Interscience, New York, 3rd edn, 2001, p. 226.

17 T. E. Barder, S. D. Walker, J. R. Martinelli and S. L. Buchwald, *J. Am. Chem. Soc.*, 2005, **127**, 4685.

18 (*a*) K. Tamao, K. Kobayashi and Y. Ito, *Tetrahedron Lett.*, 1988, **30**, 6051; (*b*) L. Li and N. Navasero, *Org. Lett.*, 2004, **6**, 3091; (*c*) S. E. Denmark, L. Neuville, M. E. L. Christy and S. A. Tymonko, *J. Org. Chem.*, 2006, **71**, 8500.

