

Silylzincation of carbon–carbon multiple bonds revisited

Gertrud Auer and Martin Oestreich*

Received (in Cambridge, UK) 23rd September 2005, Accepted 28th October 2005

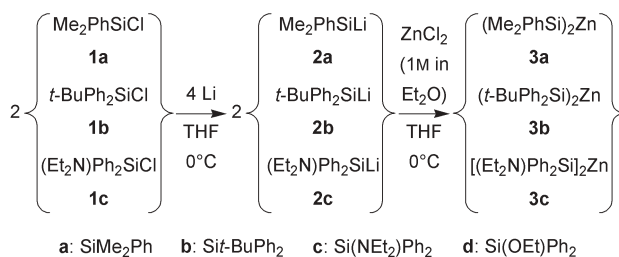
First published as an Advance Article on the web 22nd November 2005

DOI: 10.1039/b513528a

The first investigation of the copper-catalyzed silylzincation of alkynes as well as a diene and styrene using bis(triorganosilyl) zinc reagents led to the development of an efficient procedure and the disclosure of an unexpected bissilylation and unforeseen regioselectivity.

Regiocontrolled addition of a silicon–metal bond across a carbon–carbon triple bond is a prevalent method for the preparation of stereodefined vinylic silanes.¹ In this regard, stoichiometric silylcupration [(R₃Si)₂CuLi·LiCN] of terminal as well as symmetric internal alkynes has already been investigated by Fleming *et al.* to considerable extent.^{2–4} Interestingly, a competitive silylmagnesiation catalytic in copper [R₃SiMgMe with CuI (5.0 mol%)] was subsequently elaborated by Oshima *et al.*, yet attracted somewhat less attention.^{5,6} Almost simultaneously, a copper-catalyzed silylzincation of alkynes using (mixed) zincates [R₃SiZnR₂Li or (R₃Si)₃ZnLi with CuCN (1.0 mol%)] originated from the same laboratories.⁷ In all these transformations, regioselective silylmetalation of terminal and internal non-symmetric triple bonds was mostly realized for specific substrates often employing sterically hindered reagents. This issue has recently been successfully addressed by Uchiyama *et al.* in the silylzincation of terminal alkynes using dianion-type zincates [R₃SiZnR(OR)₂Mg₂Cl] in the absence of any transition metal catalyst.⁸

Based on a report by Oshima *et al.*,⁹ we have established the copper-catalyzed chemistry of bis(triorganosilyl) zincs as moderately nucleophilic silicon sources [(R₃Si)₂Zn with CuI (5.0 mol%)].¹⁰ These reagents are conveniently accessed by reductive lithiation of silyl chlorides (1 → 2)¹¹ followed by transmetalation (2 → 3)^{9,10} (Scheme 1). † In this communication, we report the extension of this reagent–copper catalyst combination to the silylzincation of carbon–carbon multiple bonds with particular focus on alkynes. Within our study, we have disclosed an unexpected bissilylation



Scheme 1 Preparation of bis(triorganosilyl) zinc reagents.

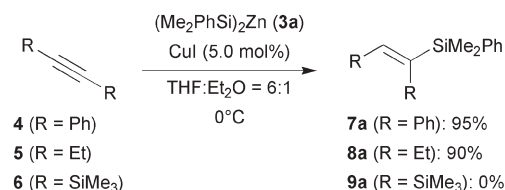
Institut für Organische Chemie und Biochemie,
Albert-Ludwigs-Universität, Albertstrasse 21, D-79104 Freiburg im
Breisgau, Germany.
E-mail: martin.oestreich@orgmail.chemie.uni-freiburg.de;
Fax: +49 (0)761 203-6100; Tel: +49 (0)761 203-6020

of terminal triple bonds and, importantly, a regioselective silylzincation of non-symmetric triple bonds. Moreover, installation of a heteroatom-substituted silyl group serves as a linchpin for subsequent cross-coupling reactions, thereby enabling the synthesis of trisubstituted alkenes with defined double bond geometry.

Our investigation commenced with the silylzincation of symmetric internal alkynes using (Me₂PhSi)₂Zn (3a)^{9,10} in the presence of catalytic amounts of CuI (Scheme 2). Both bisarylated 4 and bisalkylated 5 performed equally well affording 7a and 8a, respectively in high yield whereas the bissilylated alkyne 6 emerged as inert not forming 9a under these standard reaction conditions. A control experiment proved that 3a alone does not effect silylzincation of internal alkynes. We routinely used 5.0 mol% of the copper catalyst but 1.0 mol% was also sufficient. It must be noted that, unless otherwise indicated, all reactions were conducted with equimolar amounts of alkyne and zinc reagent.

We then examined the silylcupration of terminal alkynes 10–13 (Table 1). Using (Me₂PhSi)₂Zn (3a), phenylacetylene (10) gave the expected linear regioisomer 14a (Table 1, Entry 1) while, under identical reaction conditions, 1-hexyne (11) produced a mixture of linear and branched 15a with opposite regioselectivity (Table 1, Entry 2). Remarkably, this result provides a rough picture of the catalytically active copper intermediate: In a related situation using pre-formed cuprates, Fleming *et al.* showed that (Me₂PhSi)₂CuLi·LiCN selectively favours the linear isomer (*rs* = 100 : 0) while Me₂PhSiCu·LiCN favours the branched isomer with moderate selectivity (*rs* = 25 : 75).^{2a,b} We believe that these observations imply the intermediacy of a monosilylcopper compound such as Me₂PhSiCu·ZnX₂ (X = Me₂PhSi, Cl, and/or I). The strong influence of reaction temperature on yield and regioselectivity, partially due to competing deprotonation, still remains unclear (Table 1, Entries 3–5).²

The regioselectivity of the silylcupration of terminal alkynes might be steered towards the linear isomer by employing silylmethyls bearing the sterically demanding *t*-BuPh₂Si group.^{3b} Accordingly, (*t*-BuPh₂Si)₂Zn (3b) and catalytic amounts of CuI facilitated the silylzincation of 10–13 with good to excellent regioselectivities (Table 1, Entries 6–9). Conversely, functionalized [(Et₂N)Ph₂Si]₂Zn (3c) failed to undergo the silylzincation with reasonable regiocontrol and useful yields (35–50%).¹²



Scheme 2 Copper-catalyzed silylzincation of symmetric internal alkynes.

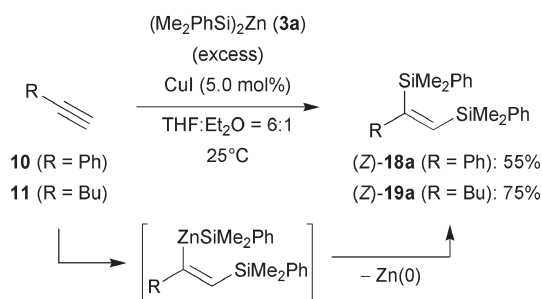
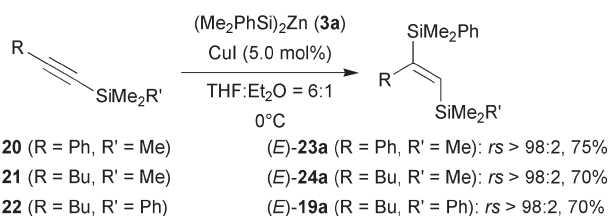
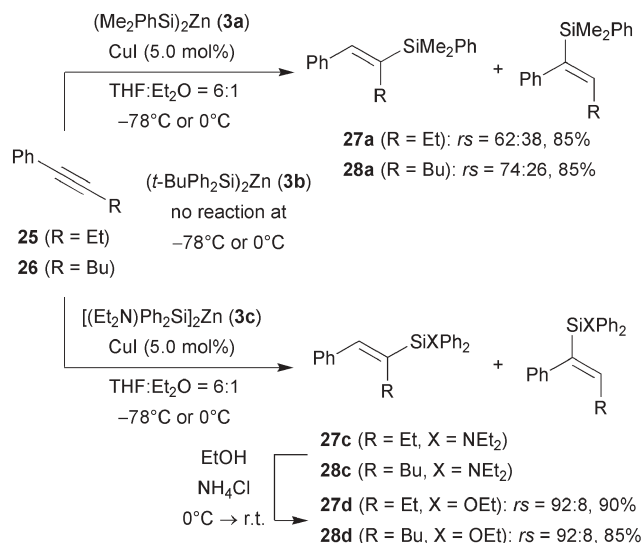
Table 1 Copper-catalyzed silylzincation of terminal alkynes

Entry	Alkyne 10–13	R	Zinc reagent	T/ ^o C	Product 14–17	rs ^a	Yield (%) ^b
1	10	Ph	3a	0	14a	>98 : 2	95
2	11	Bu	3a	0	15a	25 : 75	50
3	11	Bu	3a	–50	15a	78 : 22	85
4	11	Bu	3a	–78	15a	22 : 78	65
5	11	Bu	3a	–100	15a	10 : 90	70
6	10	Ph	3b	0	14b	>98 : 2	90
7	11	Bu	3b	0	15b	95 : 5	85
8	12	CH ₂ OH	3b	0	16b	86 : 14	95
9	13	CH ₂ OBn	3b	0	17b	94 : 6	95

^a Ratio of regioisomers was determined from the ¹H NMR spectra by integration of baseline-separated resonance signals prior to purification. ^b Averaged yield (two or more runs) of product after purification by flash chromatography and/or Kugelrohr distillation in order to remove traces of R₃Si–H and R₃Si–SiR.

To our surprise, when performing the silylcupration of **10** and **11** at ambient temperature, we isolated the bisilylated alkenes (*Z*)-**18a** and (*Z*)-**19a** in minor quantities (Scheme 3). Increasing the amount of (Me₂PhSi)₂Zn (**3a**) to 2.5–3.0 equiv. led to smooth bisilylation accompanied by formation of elementary zinc. Initial silylmatalation followed by reductive elimination with carbon–silicon coupling is well-precedented for manganese-based silicon reagents [(R₃Si)₃MnMgMe].^{13,14}

We were pleased to find that copper-catalyzed silylzincation of silicon-substituted non-symmetric alkynes **20–22** proceeded highly regioselectively with the less hindered (Me₂PhSi)₂Zn (**3a**) (Scheme 4). As demonstrated for one pair of alkene diastereomers, bisilylation of a terminal alkyne (**11** → (*Z*)-**19a**, Scheme 3) and

**Scheme 3** Copper-catalyzed bisilylation of terminal alkynes.**Scheme 4** Copper-catalyzed silylzincation of silicon-substituted non-symmetric internal alkynes.**Scheme 5** Unforeseen regiocontrol for non-symmetric internal alkynes.

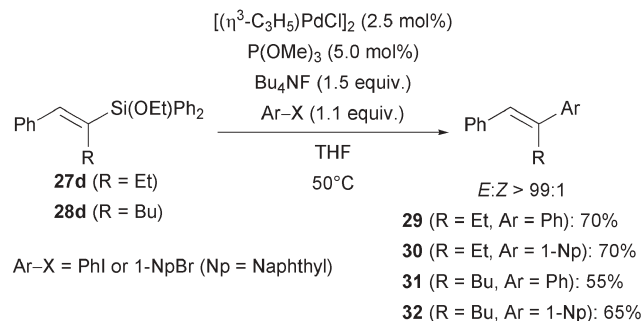
silylzincation of silicon-substituted internal alkynes (**22** → (*E*)-**19a**, Scheme 4) complement each other nicely.

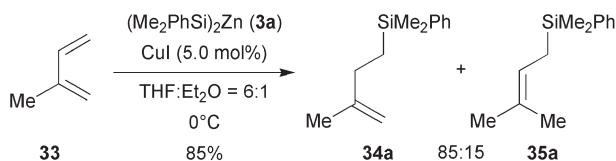
Finally, we targeted the demanding silylzincation of non-symmetric internal alkynes. These silylmatalations normally proceed without any regiocontrol^{15,16} and, therefore, these substrates have been almost invariably omitted in previous studies.^{2–4} Not unexpectedly, **25** and **26** reacted unselectively with (Me₂PhSi)₂Zn (**3a**) at –78 °C and 0 °C and (*t*-BuPh₂Si)₂Zn (**3b**) was too unreactive (Scheme 5).

To our great delight, zinc reagent **3c** incorporating an amino-substituted silyl group cleanly added across the internal triple bond (**25** → **27c** and **26** → **28c**). After treatment with dry ethanol and solid NH₄Cl,¹² the alkoxy-substituted vinylic silanes **27d** and **28d**, respectively were obtained with substantial regioselectivity (*rs* = 92 : 8) and in excellent yield.†

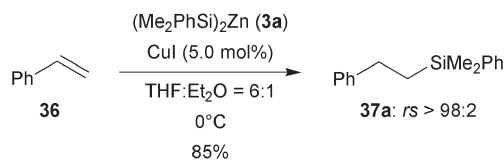
Heteroatom-functionalized silicon moieties are predestined for palladium-catalyzed cross-coupling reactions.¹⁷ Thus, **27d** and **28d** were subjected to a standard Hiyama coupling protocol reported by Tamao *et al.* (Scheme 6).¹⁸ Under these reaction conditions, iodobenzene as well as 1-bromonaphthalene afforded the trisubstituted alkenes **29–32** as single diastereomers (*E* : *Z* > 99 : 1).

Based on recent reports by Liepins and Bäckvall on the stoichiometric silylcupration with Me₂PhSiCu–LiCN of 1,3-dienes¹⁹ and even styrenes,²⁰ we tested our method for these acceptors. Treatment of isoprene (**33**) with **3a** under copper

**Scheme 6** Hiyama cross-coupling reaction of alkenyl alkoxy silanes.



Scheme 7 Copper-catalyzed silylzincation of 1,3-dienes.



Scheme 8 Copper-catalyzed silylzincation of styrene.

catalysis formed the isomers **34a** and **35a** in a ratio of 85 : 15 and in high yield (Scheme 7) which compares well with reported data.¹⁹ Similarly, copper-catalyzed silylzincation of styrene (**36**) gave desired silane **37a** with perfect regioselectivity (Scheme 8).

This experiment once more supports our previous hypothesis (*vide supra*) that $\text{Me}_2\text{PhSiCu}\cdot\text{ZnX}_2$ is the actual silyl transfer reagent since, according to Liepins and Bäckvall,²⁰ $(\text{Me}_2\text{PhSi})_2\text{CuLi}\cdot\text{LiCN}$ polymerizes the starting material **36**.

In summary, we have presented a novel transition metal-catalyzed silylmetalation of carbon–carbon multiple bonds. The catalyst system $(\text{R}_3\text{Si})_2\text{Zn}$ (**3**) and catalytic amounts of CuI enables smooth silylzincation not only of alkynes but also of 1,3-dienes and styrenes; experimental evidence suggests the *in-situ* formation of a R_3SiCu species. Increasing the amount of zinc reagent **3** from 1.0 to 3.0 equiv. allows for the stereoselective bisilylation of terminal alkynes. For the first time, we have successfully utilized functionalized $[(\text{Et}_2\text{N})\text{Ph}_2\text{Si}]_2\text{Zn}$ (**3c**) in silylmetalation chemistry which added regioselectively across non-symmetric internal triple bonds. Extension of this noteworthy feature to the stereoselective synthesis of tetrasubstituted alkenes is under investigation.

M. O. is indebted to the Deutsche Forschungsgemeinschaft for an Emmy Noether fellowship (2001–2006) and to Professor Reinhard Brückner for his continuous encouragement. The authors thank the Dr Otto Röhm Gedächtnisstiftung for additional financial support.

Notes and references

† *Representative experimental procedures.* Bis[(diethylamino)diphenylsilyl] zinc (**3c**): (diethylamino)diphenylsilyl chloride (**1e**) (725 mg, 2.50 mmol, 2.50 equiv.) was maintained with freshly cut lithium wire (large excess and pre-treated with Me_3SiCl) in dry THF (4.00 mL) at 0 °C for 12 h under argon atmosphere. The resulting dark green solution of (diethylamino)diphenylsilyl lithium (**2c**) (2.00 mmol, 80% average conversion) and THF was separated from unreacted lithium metal by transfer *via* a double-ended cannula into a separate flask. Addition of ZnCl_2 (1.00 mL, 1.00 equiv., 1 M in Et_2O) at 0 °C was accompanied by a color change from dark green to greenish yellow and afforded ready-to-use zinc reagent **3c**.

(*E*)-2-[(Ethoxy)diphenylsilyl]-1-phenyl-1-butene (**27d**): a suspension of CuI (9.6 mg, 0.050 mmol, 5.0 mol%) and THF (1.00 mL) was pre-cooled to –78 °C and **3c** (1.00 mmol, 1.00 equiv.) was added *via* syringe. The dark brown reaction mixture was allowed to warm to 0 °C and maintained at this temperature for 0.5 h. Addition of 1-phenyl-1-butyne (**25**) (130 mg, 1.00 mmol, 1.00 equiv.) in THF (1.00 mL) was followed by stirring at 0 °C for 1.0 h. The reaction mixture was then treated with dry ethanol (2.50 mL) and solid NH_4Cl (100 mg) at 0 °C and was maintained at room temperature for several hours. Upon completion of the reaction, the mixture was poured into water (10 mL) and the flask was rinsed with

t-butyl methyl ether (10 mL). The aqueous phase was separated and extracted with *t*-butyl methyl ether (3 × 10 mL). The combined organic phases were extracted with brine (10 mL) and dried over Na_2SO_4 . The solvents were evaporated under reduced pressure and the crude product was purified by flash chromatography on silica gel initially using cyclohexane and then cyclohexane : *t*-butyl methyl ether = 9 : 1 as eluent. The title compound **27d** along with its regioisomer (321 mg, *rs* = 92 : 8, 90%) was isolated as a pale yellow oil. Depending on conversion in the reductive metalation step, trace amounts of $[(\text{EtO})\text{Ph}_2\text{Si}]_2$ needed to be removed by Kugelrohr distillation to obtain an analytically pure sample.

- (a) A. Barbero and F. J. Pulido, *Acc. Chem. Res.*, 2004, **37**, 817–825; (b) R. K. Dieter, in *Modern Organocopper Chemistry*, ed. N. Krause, Wiley-VCH, Weinheim, 2002, pp. 79–144.
- (a) I. Fleming and F. Roessler, *J. Chem. Soc., Chem. Commun.*, 1980, 276–277; (b) I. Fleming, T. W. Newton and F. Roessler, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2527–2532; (c) I. Fleming and E. Martínez de Marigorta, *J. Chem. Soc., Perkin Trans. 1*, 1999, 889–900.
- For studies probing the steric demand at silicon, see: (a) H.-M. Chen and J. P. Oliver, *J. Organomet. Chem.*, 1986, **316**, 255–260; (b) A. Barbero, P. Cuadrado, I. Fleming, A. M. González, F. J. Pulido and A. Sánchez, *J. Chem. Soc., Perkin Trans. 1*, 1995, 1525–1532.
- For the silylcupration of functionalized alkynes, see: (a) L. Capella, A. Degl'Innocenti, G. Reginato, A. Ricci and M. Taddei, *J. Org. Chem.*, 1989, **54**, 1473–1476; (b) A. Casarini, B. Jousseume, D. Lazzari, E. Porciatti, G. Reginato, A. Ricci and G. Seconi, *Synlett*, 1992, 981–983; (c) L. Capella, A. Capperucci, G. Curotto, D. Lazzari, P. Dembech, G. Reginato and A. Ricci, *Tetrahedron Lett.*, 1993, **34**, 3311–3314; (d) G. Reginato, A. Mordini, M. Valacchi and E. Grandini, *J. Org. Chem.*, 1999, **64**, 9211–9216.
- (a) H. Hayami, M. Sato, S. Kanemoto, Y. Morizawa, K. Oshima and H. Nozaki, *J. Am. Chem. Soc.*, 1983, **105**, 4491–4492; (b) Y. Okuda, Y. Morizawa, K. Oshima and H. Nozaki, *Tetrahedron Lett.*, 1984, **25**, 2483–2486.
- V. Liepins, A. S. E. Karlström and J.-E. Bäckvall, *J. Org. Chem.*, 2002, **67**, 2136–2143.
- (a) Y. Okuda, K. Wakamatsu, W. Tückmantel, K. Oshima and H. Nozaki, *Tetrahedron Lett.*, 1985, **26**, 4629–4632; (b) K. Wakamatsu, T. Nonaka, Y. Okuda, W. Tückmantel, K. Oshima, K. Utimoto and H. Nozaki, *Tetrahedron*, 1986, **42**, 4427–4436.
- S. Nakamura, M. Uchiyama and T. Ohwada, *J. Am. Chem. Soc.*, 2004, **126**, 11146–11147.
- Y. Morizawa, H. Oda, K. Oshima and H. Nozaki, *Tetrahedron Lett.*, 1984, **25**, 1163–1166.
- (a) M. Oestreich and B. Weiner, *Synlett*, 2004, 2139–2142; (b) M. Oestreich and G. Auer, *Adv. Synth. Catal.*, 2005, **347**, 637–640.
- A. Kawachi and K. Tamao, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 945–955.
- In a single example, 1-octyne was subjected to silylcupration using $(\text{Et}_2\text{N})\text{Ph}_2\text{SiMgMe}$ and CuI (50 mol%). Treatment with ethanol and NH_4Cl provided the linear product in 56% yield which matches the regioselectivity seen for $(\text{Me}_2\text{PhSi})_2\text{CuLi}\cdot\text{LiCN}^{2a,b}$: K. Tamao, A. Kawachi, Y. Tanaka, H. Ohtani and Y. Ito, *Tetrahedron*, 1996, **52**, 5765–5772.
- (a) J.-i. Hibino, S. Nakatsukasa, K. Fugami, S. Matsubara, K. Oshima and H. Nozaki, *J. Am. Chem. Soc.*, 1985, **107**, 6416–6417; (b) K. Fugami, J.-i. Hibino, S. Nakatsukasa, S. Matsubara, K. Oshima, K. Utimoto and H. Nozaki, *Tetrahedron*, 1988, **44**, 4277–4292.
- For a palladium-catalyzed bisilylation of alkynes, see: Y. Ito, M. Sugimoto and M. Murakami, *J. Org. Chem.*, 1991, **56**, 1948–1951.
- J.-F. Betzer and A. Pancrazi, *Synlett*, 1998, 1129–1131.
- (a) A. Zakarian, A. Batch and R. A. Holton, *J. Am. Chem. Soc.*, 2003, **125**, 7822–7824; (b) B. Shi, N. A. Hawrylyuk and B. B. Snider, *J. Org. Chem.*, 2003, **68**, 1030–1042; (c) S. C. Archibald, D. J. Barden, J. F. Y. Bazin, I. Fleming, C. F. Foster, A. K. Mandal, A. K. Mandal, D. Parker, K. Takaki, A. C. Ware, A. R. B. Williams and A. B. Zwicky, *Org. Biomol. Chem.*, 2004, **2**, 1051–1064.
- (a) S. E. Denmark and R. F. Sweis, in *Metal-catalyzed Cross-coupling Reactions*, ed. A. de Meijere and F. Diederich, Wiley-VCH, Weinheim, 2004, vol. **1**, pp. 163–216; (b) S. Rendler and M. Oestreich, *Synthesis*, 2005, 1727–1747.
- K. Tamao, K. Kobayashi and Y. Ito, *Tetrahedron Lett.*, 1989, **30**, 6051–6054.
- (a) V. Liepins and J.-E. Bäckvall, *Org. Lett.*, 2001, **3**, 1861–1864; (b) V. Liepins and J.-E. Bäckvall, *Eur. J. Org. Chem.*, 2002, 3527–3535.
- V. Liepins and J.-E. Bäckvall, *Chem. Commun.*, 2001, 265–266.