Silylzincation of carbon–carbon multiple bonds revisited

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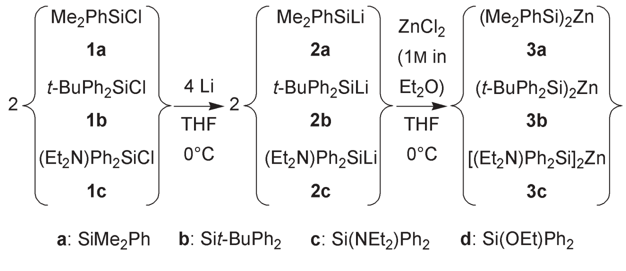
The first investigation of the copper-catalyzed silylzincation of alkynes as well as a diene and styrene using bis(triorganosilyl) zinc reagents led to the development of an efficient procedure and the disclosure of an unexpected bissilylation and unforeseen regioselectivity.

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 [$(R_3Si)_2CuLi\cdot LiCN$] of terminal as well as symmetric internal alkynes has already been investigated by Fleming *et al.* to considerable extent.[2–4] Interestingly, a competitive silylmagnesation catalytic in copper [$R_3SiMgMe$ 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 [R_3SiZnR_2Li or $(R_3Si)_3ZnLi$ 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 [$R_3SiZnR(OR)_2Mg_2Cl$] 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 [$(R_3Si)_2Zn$ 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 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.

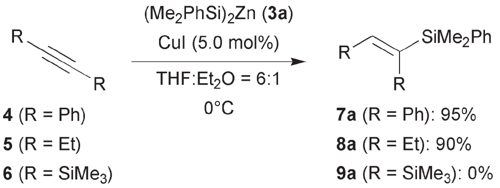


Scheme 1 Preparation of bis(triorganosilyl) zinc reagents.

Our investigation commenced with the silylzincation of symmetric internal alkynes using $(Me_2PhSi)_2Zn$ (**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 $(Me_2PhSi)_2Zn$ (**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 $(Me_2PhSi)_2CuLi\cdot LiCN$ selectively favours the linear isomer (*rs* = 100 : 0) while $Me_2PhSiCu\cdot LiCN$ 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 $Me_2PhSiCu\cdot ZnX_2$ (X = Me_2PhSi ,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 silylmetals bearing the sterically demanding t-$BuPh_2Si$ group.[3b] Accordingly, $(t\text{-}BuPh_2Si)_2Zn$ (**3b**) and catalytic amounts of CuI facilitated the silylzincation of **10–13** with good to excellent regioselectivities (Table 1, Entries 6–9). Conversely, functionalized $[(Et_2N)Ph_2Si]_2Zn$ (**3c**) failed to undergo the silylzincation with reasonable regiocontrol and useful yields (35–50%).[12]



Scheme 2 Copper-catalyzed silylzincation of symmetric internal alkynes.

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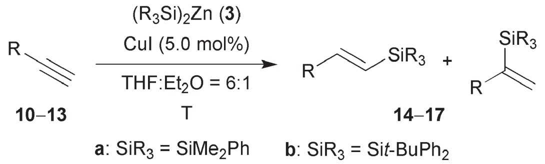
Table 1 Copper-catalyzed silylzincation of terminal alkynes

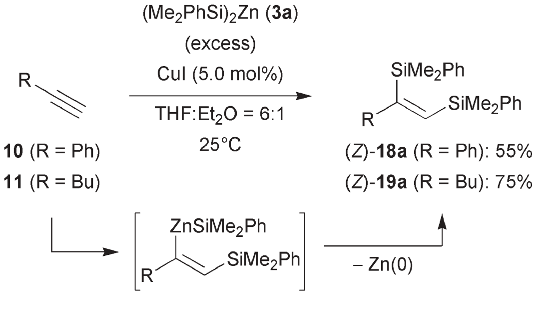


Entry	Alkyne **10–13**	R	Zinc reagent	*T*/°C	Product **14–17**	*rs*[a]	Yield (%)[b]
1	**10**	Ph	**3a**	0	**14a**	>98 : 2	95
2	**11**	Bu	**3a**	0	**15a**	25 : 75	50
3	**11**	Bu	**3a**	−50	**15a**	78 : 22	85
4	**11**	Bu	**3a**	−78	**15a**	22 : 78	65
5	**11**	Bu	**3a**	−100	**15a**	10 : 90	70
6	**10**	Ph	**3b**	0	**14b**	>98 : 2	90
7	**11**	Bu	**3b**	0	**15b**	95 : 5	85
8	**12**	CH_2OH	**3b**	0	**16b**	86 : 14	95
9	**13**	CH_2OBn	**3b**	0	**17b**	94 : 6	95

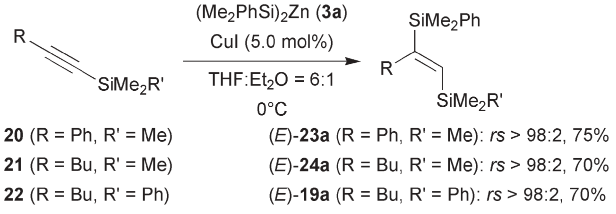
[a] Ratio of regioisomers was determined from the ^1H NMR spectra by integration of baseline-separated resonance signals prior to purification. [b] Averaged yield (two or more runs) of product after purification by flash chromatography and/or Kugelrohr distillation in order to remove traces of $R_3Si–H$ and $R_3Si–SiR$.

To our surprise, when performing the silylcupration of **10** and **11** at ambient temperature, we isolated the bissilylated alkenes (*Z*)-**18a** and (*Z*)-**19a** in minor quantities (Scheme 3). Increasing the amount of $(Me_2PhSi)_2Zn$ (**3a**) to 2.5–3.0 equiv. led to smooth bissilylation accompanied by formation of elementary zinc. Initial silylmetalation followed by reductive elimination with carbon–silicon coupling is well-precedented for manganese-based silicon reagents $[(R_3Si)_3MnMgMe]$.[13,14]

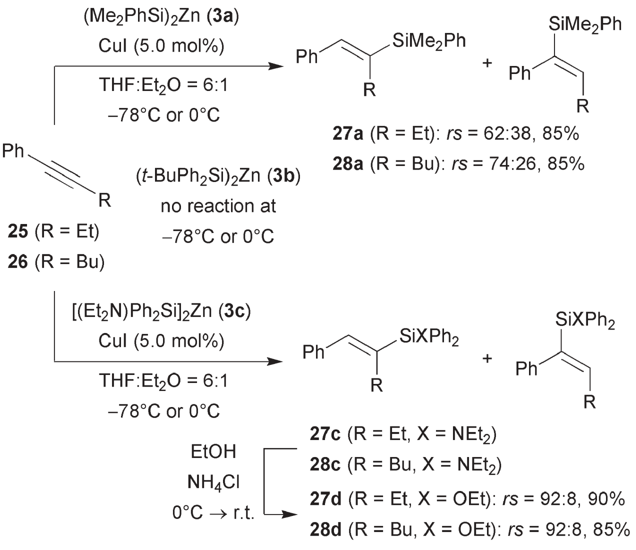
We were pleased to find that copper-catalyzed silylzincation of silicon-substituted non-symmetric alkynes **20–22** proceeded highly regioselectively with the less hindered $(Me_2PhSi)_2Zn$ (**3a**) (Scheme 4). As demonstrated for one pair of alkene diastereomers, bissilylation of a terminal alkyne (**11** → (*Z*)-**19a**, Scheme 3) and silylzincation of silicon-substituted internal alkynes (**22** → (*E*)-**19a**, Scheme 4) complement each other nicely.



Scheme 3 Copper-catalyzed bissilylation of terminal alkynes.



Scheme 4 Copper-catalyzed silylzincation of silicon-substituted non-symmetric internal alkynes.



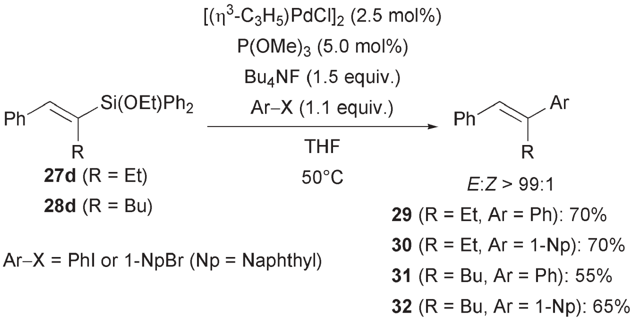
Scheme 5 Unforeseen regiocontrol for non-symmetric internal alkynes.

Finally, we targeted the demanding silylzincation of non-symmetric internal alkynes. These silylmetalations 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 $(Me_2PhSi)_2Zn$ (**3a**) at −78 °C and 0 °C and $(t\text{-}BuPh_2Si)_2Zn$ (**3b**) was too unreactive (Scheme 5).

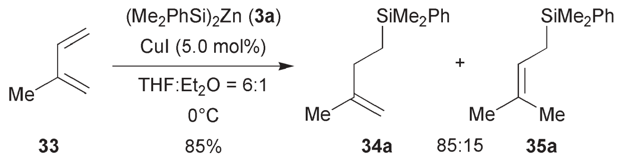
To our great delight, zinc reagent **3c** incorporating an amino-substituted silyl group cleanly added across the internal triple bond (**25** → **27c** and **26** → **28c**). After treatment with dry ethanol and solid NH_4Cl,[12] the alkoxy-substituted vinylic silanes **27d** and **28d**, respectively 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).

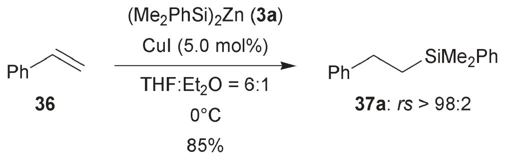
Based on recent reports by Liepins and Bäckvall on the stoichiometric silylcupration with $Me_2PhSiCu·LiCN$ of 1,3-dienes[19] and even styrenes,[20] we tested our method for these acceptors. Treatment of isoprene (**33**) with **3a** under copper



Scheme 6 Hiyama cross-coupling reaction of alkenyl alkoxysilanes.



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 $Me_2PhSiCu{\cdot}ZnX_2$ is the actual silyl transfer reagent since, according to Liepins and Bäckvall,[20] $(Me_2PhSi)_2CuLi{\cdot}LiCN$ polymerizes the starting material **36**.

In summary, we have presented a novel transition metal-catalyzed silylmetalation of carbon–carbon multiple bonds. The catalyst system $(R_3Si)_2Zn$ (**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 bissilylation of terminal alkynes. For the first time, we have successfully utilized functionalized $[(Et_2N)Ph_2Si]_2Zn$ (**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.

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Notes and references

† *Representative experimental procedures*. Bis[(diethylamino)diphenylsilyl] zinc (**3c**): (diethylamino)diphenylsilyl chloride (**1c**) (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 $[(EtO)Ph_2Si]_2$ needed to be removed by Kugelrohr distillation to obtain an analytically pure sample.

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