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Cu-Catalyzed Silylation of Alkynes: A Traceless 2-Pyridylsulfonyl Controller Allows Access to either Regioisomer on Demand

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KEYWORDS: silylcupration · Cu-catalysis · hydrosilylation · vinyl silane · 2-pyridyl sulfone

ABSTRACT: The Cu-catalyzed silylation of terminal and internal alkynes bearing a 2-pyridyl sulfonyl group (SO_2Py) at the propargylic position affords a breadth of vinyl silanes in good yields and excellent regio- and stereocontrol under mild conditions. The directing SO_2Py group is essential in terms of reaction efficiency and chemoselectivity. Importantly, this group also provides the ability to reverse the regiochemical outcome of the reaction, opening the access to either regioisomer without modification of the starting substrate by virtue of an in situ base-promoted alkyne to allene equilibration which takes place prior to the silylcupration process. Furthermore, removal of the directing SO_2Py allows for further elaboration of the silylation products. In particular, a one-pot tandem alkyne silylation/allylic substitution sequence, in which both steps are catalyzed by the same Cu species, opens up a new approach for the access to either formal hydrosilylation regioisomer of unsymmetrical aliphatic-substituted internal alkynes from propargyl sulfones.

INTRODUCTION

Vinyl silanes have found widespread applications in modern synthetic organic chemistry as versatile building blocks, and methods for their production continue to be an area of unquestionable interest.[1] The catalytic hydrosilylation of alkynes is arguably the most powerful and direct reaction for the synthesis of these reagents since it offers potential for complete control of the regio- and stereoselectivity.[2] While most of the examples reported in the literature have focused on the hydrosilylation of terminal alkynes, internal alkynes have received considerably less attention due to their lower reactivity and the inherent difficulty to achieve useful regiocontrol. Indeed, the problem of regioselectivity truly comes to the fore when unbiased unsymmetrical (internal) alkynes with close similarity in terms of electronic and steric properties of the acetylenic substituents are employed. It is thus of great importance to broaden the applicability of alkyne metallation reactions to this type of substrates, as it would open up new ground for design approaches.

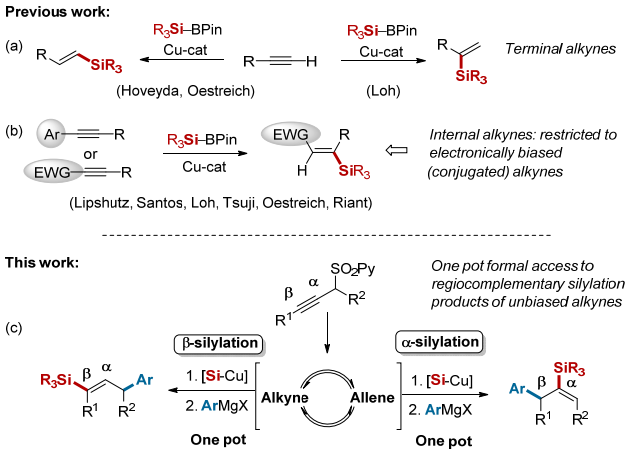
The development of methods that result in a formal umpolung of the standard electrophilic reactivity of boron reagents to nucleophilic[3] (boryl-Cu complexes obtained by transmetalation of B_2Pin_2 with LCuOR species), independently reported in 2000 by the Miyaura and Hosomi groups,[4] has fueled the invention of new technologies directed at solving the issue of regioselectivity in the hydrometallation of alkynes. Work pioneered by the Hoveyda laboratories using this nucleophilic boryl-Cu species has inspired solutions for the regioselective hydroborylation of alkynes, both terminal[5] and internal,[6] in which the introduction of directing atoms at the propargylic position is crucial to effect regiocontrol.

The development of a family of boron-silicon reagents by Suginome and co-workers (most notably $PhMe_2Si$–BPin)[7] has facilitated the extension of some of the prototypical B_2Pin_2 reactivity to the hydrosilylation of alkynes via silyl-Cu complexes (it is only the R_3Si group in the transmetalation with LCuOR that is transferred to an acceptor molecule).[8-14] However, the regioselectivity trends observed for the borylation of alkylalkynes do not appear to be extensive to silylation. For instance, in a recent elegant example of sequential silylation/borylation of terminal alkynes catalyzed by Cu-NHC complexes,[9] Hoveyda observed exclusive generation of the β-hydrosilylation isomer (linear), regardless of the electronic attributes of the alkyne substituent (Scheme 1a), which is in sharp contrast with the analogous borylation process.[5,6] In 2011, Loh described the complementary highly α-regioselective synthesis of vinylsilanes (branched) through $PhMe_2Si$-BPin addition to alkyl-substituted terminal alkynes catalyzed by a Cu-bulky phosphine complex (Scheme 1a).[10] More recently, Oestreich has reported a linear-selective Cu-catalyzed $PhMe_2Si$-BPin-silylation of terminal alkynes without added ligand, in which the solvent was found to greatly influence the regioselectivity.[11]

However, even after these important advances, the regiocontrolled silylation of internal alkynes still represents a major challenge. Only recently have appeared the first successful reports on the Cu-catalyzed silylation of internal alkynes, albeit high regiocontrol has only been achieved in substrates with a marked electronic bias such as conjugated electron-deficient internal alkynes (e.g., propyolates),[12] 1-aryl-1-alkynes or 1,3-enynes,[11,13] (Scheme 1b). To the best of our knowledge, a general method to achieve the direct catalytic hydrosilylation of unbiased unsymmetrical aliphatic-substituted internal alkynes with high regiocontrol is yet to be reported. Moreover, the ability to reverse the regiochemical outcome of the reaction without modification of the starting substrate or the catalyst, thereby providing access to both regiocomplementary alkyne

silylation products, would notably expand further the structural scope of vinyl silane synthesis. Literature precedents for tuning of regioselectivity in metalation of alkynes are rare and typically rely on structural modification of the starting substrate or ligand control;[15] however, an emerging alternative for controlling regioselectivity based on the use of alkynes as allene surrogates is receiving increasing attention from the synthetic community.[16]

Scheme 1. Control of regioselectivity in the Cu-catalyzed hydrosilylation of alkynes.

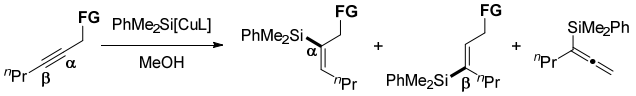


We recently described the development of a two-step protocol to access formal hydroboration products of unbiased internal alkynes.[6a,17] This strategy relies on the use of a propargylic SO_2Py group[18] as a traceless element of site-selectivity control to produce one specific regioisomer. We envisioned that our findings could be brought further to bear on the formulation of unique methods that would facilitate switching of the regiochemistry of a given reaction on demand, starting from the same substrate, by simply changing the reaction conditions (e.g., by virtue of an in situ base-promoted alkyne to allene isomerization). Herein, we demonstrate the successful implementation of this concept applied to the α- and β-regioselective silylation of alkynes using the SO_2Py as powerful element of regiochemistry and reactivity control, as well as a flexible handle for further elaboration of the resulting products, which enables ready regiodivergent access to structurally diverse vinyl silanes (Scheme 1c).

RESULTS AND DISCUSSION

Optimization studies: search for a convenient directing group. At the outset of our studies, we prepared several internal alkynes bearing polar functions at the propargylic position that could act as directing groups, and explored their reactivity under standard conditions extrapolated from borylation precedents[5,6] and using Suginome's reagent $PhMe_2SiBPin$ as the silicon source (substrates **1-9**, Table 1). In contrast to the high regioselectivity observed in hydroborylations,[5,6] the hydrosilylation of substrates bearing typical O- and N-based functional groups at the propargylic position, such as OH (entry 1), the bulkier OTIPS (entry 2), or tosylamino (entry 3), afforded silylation products in high conversion but poor regioselectivities. In agreement with observations reported by Sawamura and Szabó for Cu-catalyzed borylations of propargylic carbonates,[19] and by Oestreich in the Cu-catalyzed silylation of propagylic chlorides and phosphates,[20] the use of functional groups with high leaving group abilities such as phosphate or carbonate (entries 4 and 5, respectively) resulted in formation of the corresponding silyl-allene. Finally, we observed that the installation of sulfur-based moieties at the propargylic position had a marked effect in regioselectivity, although only sulfones afforded hydrosilylated compounds in high yields (entries 7-9). Among them, the use of 2-$PySO_2$ (entry 8) resulted in almost exclusive β-silylation and 78% of pure isolated product **10**. Although the precise role of the 2-$PySO_2$ group in this transformatiojn is unclear at this stage, this result suggests that the 2-pyridyl unit has an additional effect on regiocontrol that enhances the primary effect of the sulfonyl group (entry 7). This secondary effect could be due to the potentially coordinating ability of the 2-pyridiyl unit since the use of the electronically related 4-$PySO_2$ group led to a lower regioselectivity level (entry 9).

Table 1. β-Silylation of propargylic substituted 2-hexynes.



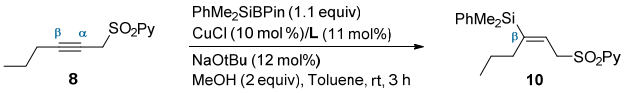
Entry	FG (alkyne)	Conv. (%)[b]	α/β/allene [b]	Yield (%)[c]
1	OH (**1**)	95	43:57:<2	33
2	OTIPS (**2**)	>98	38:62:<2	62[d]
3	NHTs (**3**)	80	19:81:<2	60
4	$OPO(OEt)_2$ (**4**)	35	<2:<2:>98	–
5	OCO_2Me (**5**)	87	<2:<2:>98	64
6	S(2-Py) (**6**)	9	<2:>98:<2	–
7	SO_2Ph (**7**)	74	15:85:<2	60
8	SO_2(2-Py) (**8**)	>98	4:96:<2	78
9	SO_2(4-Py) (**9**)	85	22:78:<2	68

[a]Reaction conditions: Alkyne (1.0 equiv), $PhMe_2SiBPin$ (1.1 equiv), CuCl (10 mol %), PCy_3 (11 mol %), NaO*t*Bu (12 mol %), MeOH (2 equiv), toluene, rt, 2 h. [b]Determined by ^1H NMR in the crude mixture. [c]Isolated yield in major product after chromatography. [d]Obtained as an inseparable mixture of regioisomers.

Influence of the ligand. During the development of the hydrosilylation reaction, we noticed that the use of a proper phosphine ligand was crucial in terms of both reactivity and selectivity. This observation was in accordance with literature precedents. For example, in the context of Cu-catalyzed silylation of terminal alkynes, the utilization of an electron-rich and bulky monophosphine ligand such as $PtBu_3$ and Johnphos[21] was found to be crucial by the group of Loh to achieve high levels of reactivity and branched(α)-selectivity,[10a] whereas exclusive linear(β)-selectivity was achieved by Hoveyda's group using copper complexes of NHC ligands (SIMes).[5a,5b] To evaluate the effect of the ligand in the silylation of the model internal propargyl sulfone **8**, a ligand screen was performed which corroborated that PCy_3 was optimal in fulfilling the subtle balance of steric and electronic requirements for achieving high reactivity and regiocontrol in this reaction (Table 2). The IMes NHC

ligand was poorly effective, providing the hydrosilylation product **10** in 40% conversion and modest levels of β-regioselectivity (β/α = 75:25, entry 1). Unexpectedly, the saturated analogue SIMes ligand was totally ineffective (no reaction observed, entry 2). The use of Ph_3P improved both yield (71%) and regioselectivity (β/α = 86:14) of the vinyl silane **10**, albeit to unpractical levels (entry 3). Phosphines with more electron-donating ability such as P(2-furyl)$_3$ or P*n*Bu$_3$ slightly improved further the β-selectivity to 90%, but at the cost of a decline in reactivity (<50% conversion, entries 4 and 5). Finally, whereas PCy_3 provided full conversion and excellent β-regioselectivity (β/α = 96:4, entry 6), the bulkier P*t*Bu$_3$ was found to be much less effective in terms of both reactivity (26% conversion) and regioselectivity (β/α= 16:84; entry 7), thus suggesting that the steric hindrance of the ligand is also an important factor for catalytic activity and selectivity.

Table 2. β-Silylation of propargylic substituted 2-hexynes.

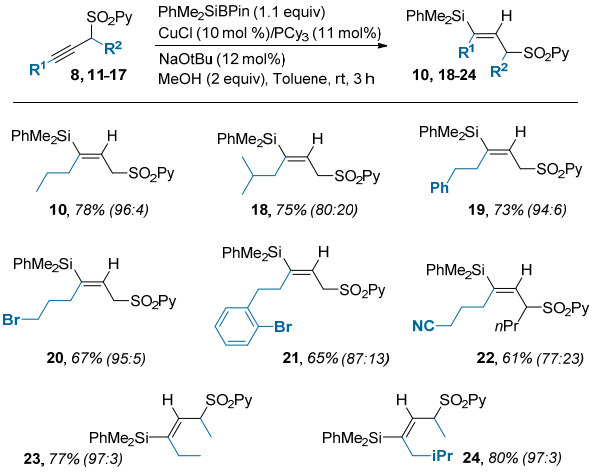


Entry[a]	Ligand (**L**)	α/β Ratio[b]	Conversion (%)[b]
1	IMes[c]	25:75	40
2	SIMes[d]	–	<5
3	PPh_3	14:86	71
4	P(2-furyl)$_3$	9:91	28
5	P(^{n}Bu)$_3$	10:90	47
6	PCy_3	4:96	>98
7	P(^{t}Bu)$_3$	16:84	26

[a]Reaction conditions: Alkyne (1.0 equiv), $PhMe_2SiBPin$ (1.1 equiv), CuCl (10 mol %), PCy_3 (11 mol %), NaOtBu (12 mol %), MeOH (2 equiv), toluene, rt, 3 h. [b]Determined by ^1H NMR in the crude mixture. [c] IMes:1,3-bis-(2,6-diisopropylphenyl) imidazolinium chloride. [d] SIMes: 1,3-bis(2,6-diisopropylphenyl)-1,3-dihydro-2*H*-imidazol-2-ylidene. SO_2Py = 2-$PySO_2$

Cu-catalyzed β-silylation of propargylic 2-pyridyl sulfones. With the optimal catalysis conditions in hand, we next sought to examine the scope of the alkyne substitution of this new β-silylation protocol. As shown in Table 3, the reaction of a range of structurally diverse internal propargylic (2-Py)-sulfones resulted in formation of the corresponding trisubstituted β-silylated allylic sulfones in good yields (products **18-24**, 61-80%) and good to excellent selectivities (β/α ratio 77:23–97:3). The mild reaction conditions allow for good compatibility with a variety of functional groups: substrates bearing primary alkyl bromides, aryl bromides or potentially coordinating nitriles (products **20**, **21**, and **22**, respectively) were shown to be amenable to the transformation, which demonstrates the ability of this silylation protocol to generate vinyl silane products containing synthetically useful functional handles that might be readily exploited in subsequent transformations. The reaction was found to be equally effective for the more sterically congested internal alkynes with branched propargylic substitution (R^2 = Me or *n*Pr, **22-24**).

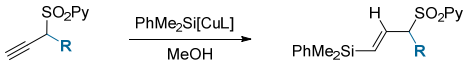
Table 3. β-Silylation of internal propargylic 2-pyridyl sulfones.[a]



[a]Same reaction conditions as in Table 1; reaction time 2-3 h. In parenthesis, regioselectivity (β/α ratio) determined by ^1H NMR in the crude mixtures. Isolated yield for the mixture of regioisomers. SO_2Py = 2-$PySO_2$

We also examined the feasibility of extending this reactivity profile to propargyl 2Py-sulfones derived from terminal alkynes. This was indeed the case and several terminal propargylic sulfones reacted cleanly under the optimized conditions to afford the corresponding β-silylated allylic sulfones (**29-32**) in good yields and satisfactory regioselectivities (ranging from 90:10 to >97:<3, Scheme 2).

Scheme 2. Extension of the β-silylation to terminal alkynes

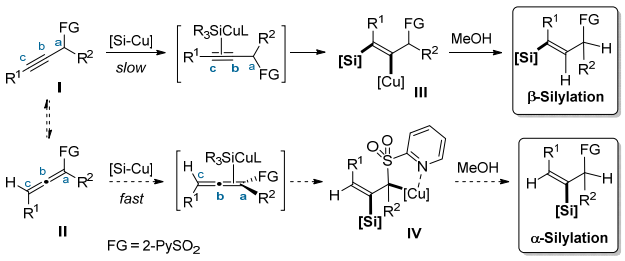


Substrate	R	Product	yield (%)	β/α ratio
25	^{n}Pr	**29**	70	*>97:<3*
26	Cy	**30**	82	*>97:<3*
27	Me	**31**	75	*>97:<3*
28	Phenethyl	**32**	77	*90:10*

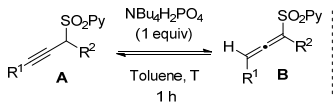
Studies towards regioselectivity switch: from β- to α-selective silylation. Once established an efficient silylation protocol that provides high control of both β-regioselectivity and stereoselectivity across a broad range of substrates, our attention was shifted to developing a method with the ability to reverse the regiochemical outcome of the reaction, since it would provide access to the opposite α-regioisomer without modification of the starting substrate. The accumulated knowledge on the chemistry of sulfones led us to envision an opportunity to invert the regioselectivity of the silylation process: taking advantage of a well-known isomerization process that transforms propargylic sulfones (**I**) into allenyl sulfones (**II**, Scheme 3)[22]. Allenes have been shown to undergo hydrosilylation and hydroborylation processes, with the regiochemistry of these processes being significantly affected by substitution.[12c,23] In particular, previous work in Cu-catalyzed hydroboration[23c] and hydrosilylation[12c] of electron-deficient allenes has shown that the electron density bias imposed by the electron withdrawing group directs the exclusive installation of the boryl or silyl moiety on the central allene carbon, leading to a stabilized allyl Cu-enolate intermediate which then undergo protonolysis by

ROH. On the basis of these precedents, we reasoned that the putative intermediate allenyl sulfone **II** would undergo addition of the Si-Cu complex across the C^a–C^b double bond (instead of the C^b–C^c centers of the starting propargyl sulfone **I**), resulting in the allylic copper intermediate **IV**, which could find additional stabilization by coordination of the metal to the pyridyl nitrogen of the SO_2Py group[18] (Scheme 3). If a base-promoted equilibration between **I** and **II** occurs prior to the hydrosilylation reaction, and assuming that the allene species (**II**) is more reactive than the parent alkyne, this regime for reversible alkyne-allene interconversion would provide a Curtin-Hammett scenario, thus enabling a complementary approach for α-selective silylation. Under such conditions, product selectivity should be largely dependent upon the relative silylation rate constant of both equilibrating species (**I** and **II**) rather than their relative stability. If successful, this method would provide access to both regioisomers of the same starting material by simply switching the reactive species.

Scheme 3. Propargyl and allenyl (2-Py)sulfones: potential divergent reactivity.



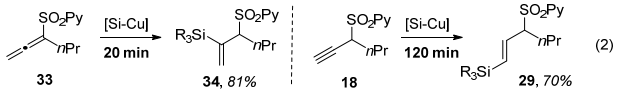
To secure the success of our work plan, two conditions needed to be fulfilled: firstly, the base required to effect the rearrangement should not inhibit the silylation reaction. Along these lines, several bases have been shown to be compatible with Me_2PhSi–BPin in related transformations.[11] Secondly, the allene should be more reactive than the corresponding alkyne in order to shift a hypothetical equilibrium. To examine these hypotheses, we treated substrates **16** and **18** with several bases in toluene, and observed that a number of them promoted this rearrangement; the propargyl/allenyl ratio was shown to depend on the substitution pattern of the starting material: in particular, we observed that for terminal alkyne **18** the equilibrium was completely shifted towards the allene, whereas a 1:1 mixture of species in equilibrium was detected in the case of internal alkyne **16** (eq 1).[24] Among the bases tested, $NBu_4H_2PO_4$ was chosen in light of its very low coordinating ability, which should not inhibit the formation of the required copper catalyst. Additionally, its poor nucleophilicity constitutes an additional advantage in terms of functional group tolerance.



Subst	R^1	R^2	T (°C)	A:B
16	Et	Me	45	50:50
18	H	^{n}Pr	rt	<2:>98

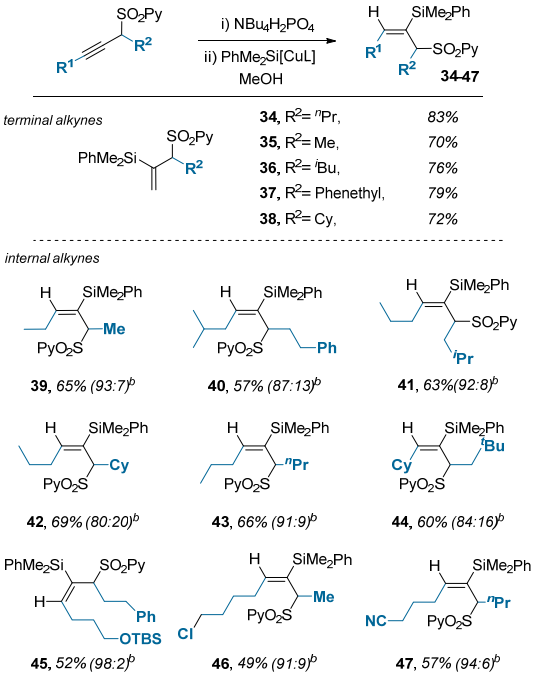
(1)

Strong support for the second premise was found in silylation experiments carried out using preformed allenyl sulfone **33**. When this compound was submitted to the optimized silylation reaction conditions (eq. 2), the corresponding α-silylated allyl sulfone **34** was exclusively formed after only 20 minutes, as opposed to 120 minutes required for the β-silylation of the corresponding propargylic sulfone **18**. This result indicates that the allenyl sulfones are more reactive than the propargylic sulfones under our Cu-catalyzed silylation conditions.[25,26]



Cu-catalyzed α-silylation of propargylic 2-pyridyl sulfones. With this information in hand, we reasoned that prestirring our substrates in the presence of an equivalent of base would result in a relatively fast equilibration of the initial propargylic sulfone to the allenyl sulfone.[27] Assuming that the allene species are more reactive than the alkyne, this scenario could enable a new approach for a selective α-silylation process. Gratifyingly, under these reaction conditions, we found that both terminal and internal alkynes underwent a smooth α-silylation process (Table 4), in which the only products detected in the reaction mixtures were the desired regio- and diastereomerically pure α-silylated isomers. When internal alkynes were used as substrates, the silylation products were obtained as mixtures of rotamers about the C–S/C–Si sigma bond (ranging from 80:20 to 98:2). The high chemoselectivity was also demonstrated in the α-silylation reaction of alkynes bearing functional groups such as silyl ethers, alkyl chlorides or nitriles (**45**, **46**, and **47**, respectively).

Table 4. α-Silylation of propargylic 2-pyridyl sulfones.[a]



[a]Reaction conditions: Alkyne (1.0 equiv), $NBu_4H_2PO_4$ (1.0 equiv), toluene, rt for internal alkynes or 50 °C for terminal alkynes, 1 h; then, $PhMe_2SiBPin$ (1.0-1.5 equiv), CuCl (10 mol %), PCy_3 (11 mol %), NaOtBu (12 mol %), MeOH (2 equiv), rt or 50 °C. [b]In parenthesis, ratio of rotamers determined by ^1H NMR in the crude mixtures. SO_2Py = 2-$PySO_2$

The presence of rotamers in equilibrium was unambiguously determined by NMR studies on compound **42** (Figure 1). In particular, ^{1}H NMR studies at variable temperatures resulted in coalescence of those peaks attributed to equivalent protons at temperatures above 85 °C. Additionally, cooling back to 25 °C resulted in recovery of exactly the same ratio of rotamers, while no signs of decomposition were observable in the spectrum. Furthermore, the existence of an equilibrium between the two rotamers in **42** was supported by the observation of strong exchange cross-peaks (EXSY) between equivalent protons of each rotameric pair in a 2D NOESY experiment (signals derived from NOE or from chemical exchange will appear in different phases).[28]

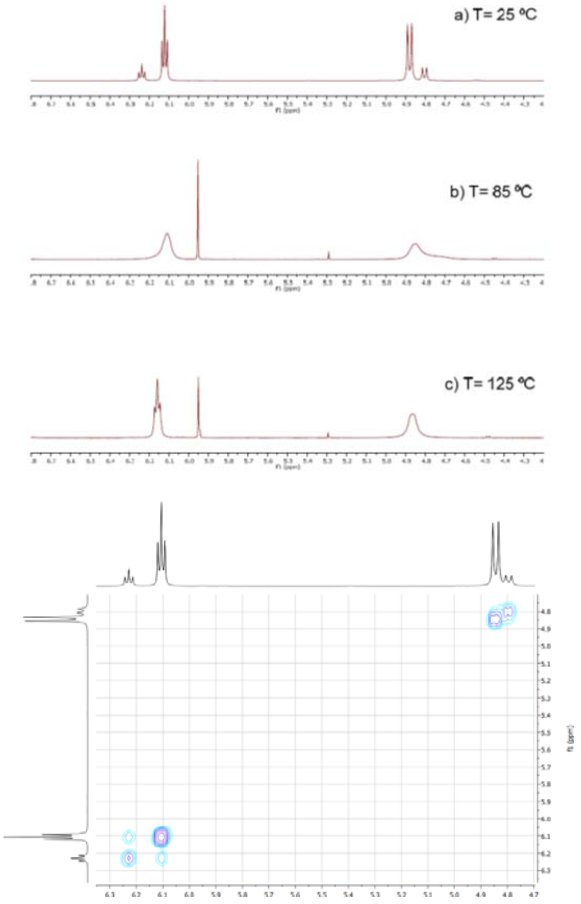
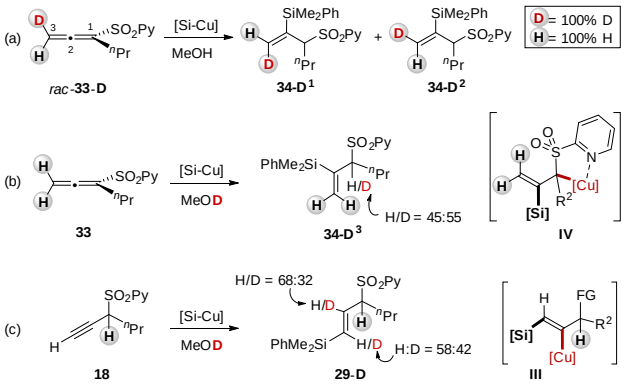


Figure 1. Olefinic and allylic peaks attributed to rotamers in compound **42**. (i) Coalescence of at higher temperature. (ii) Exchange cross-peaks observed in a 2D NOESY experiment.

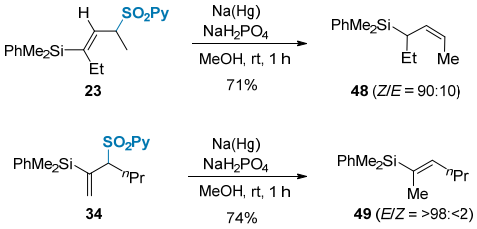
Mechanistic insights: isotope tracer experiments. Support for the participation of the catalytic intermediate species **IV** and **III** in the α-silylation *via allene* and β-silylation *via alkyne*, respectively (see Scheme 2), was obtained from deuterium labeling experiments shown in Scheme 4. Firstly, a 1:1 mixture of deuterated diastereoisomers across the terminal double bond (**34-D**^{1} + **34-D**^{2}) was obtained after 20 minutes when the deuterated allene *rac*-**33-D** was submitted to the standard reaction conditions (Scheme 4a), adding additional weight to our previous observations depicted in equation 2. The formation of both diastereomers in equal amounts is consistent with a silylcupration process at C_1 and C_2 of the proposed allene intermediate. Assuming the accepted mechanism of coordination/*syn*-addition of the Si-Cu complex to the unsaturated substrate, the formation of the diastereomer **34-D**^{2} would be largely unexpected if an equilibration of *rac*-**33-D** to the corresponding alkyne followed by silylcupration on the latter intermediate had taken place. In addition, hydrosilylation of substrate **33** in the presence of MeOD resulted in significant levels of deuterium incorporation at the allylic position, whereas no deuterium scrambling was detected at the vinylic positions (product **34-D**^{3}): this observation is consistent with the participation of the proposed pyridinium-stabilized Cu intermediate **IV** (Scheme 4b).[22] Conversely, the hydrosilylation of alkyne **18** in the presence of MeOD allowed the deuterium interception of the presumed intermediate **III**, furnishing the β-silylated product **29-D** with significant incorporation of deuterium at the α-vinylic position. Notably, hydrogen was completely retained at the methine adjacent to the sulfonyl group, which strongly supports the participation of the proposed intermediate **III**. The partial H/D exchange observed at the terminal vinylic position is ascribable to partial deprotonation of the acidic acetylenic position under the basic reaction conditions prior to silyl-cupration of the alkyne, which also might justify the incomplete deuteration at C2. In agreement with this proposal, when propargyl sulfone **18** was subjected to the standard reaction conditions (*t*BuOCu-PCy_3) in the absence of the Si-B reagent and in the presence of MeOD, 17% deuterium incorporation at the acetylenic position was observed. Importantly, except for the latter case, no deuterium scrambling was observed in those positions not directly involved in the metalation step for each proposed mechanism (vinylic positions in the reaction from allene **33** and allylic position in the reaction from alkyne **18**, Scheme 4), which strongly supports the notion that both regiochemistry patterns originate from different reaction intermediates.

Scheme 4. D-labeling studies on the reaction mechanism.



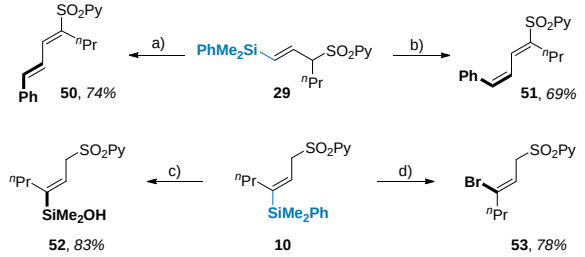
Further elaboration of vinyl silanes: selective transformations on vinyl silanes/allylic sulfones. In hopes of illustrating further the utility of the method described above, we looked into representative transformations of vinyl silanes and allylic sulfones which would selectively remove either one of these functional groups. Firstly, the sulfonyl group in the silylation products could be smoothly removed without interference by the silicon moiety by standard treatment with Na(Hg) with concomitant migration of the olefin to give rise to synthetically useful stereochemically enriched (or pure) allyl and vinyl silanes (Scheme 5, products **48** and **49**, respectively).

Scheme 5. Selective removal of the SO_2Py group.



In our exploratory studies of the selective reactivity of the silicon group, we observed that treatment of vinyl silane **29** with a strong base (KHMDS), followed by addition of benzaldehyde, resulted in formation of sulfonyl diene **50** in 74% yield by formal Peterson olefination (Scheme 6). Interestingly, the stereochemistry of the process was easily inverted by switch to LiHMDS in the presence of the crown ether 12-crown-4 (product **51**, 69%). Other studies performed along these lines involved the transformation of the vinyl silanes obtained above in other practical functionalities. For example, vinyl silane **10** was smoothly converted in silanol **52** by treatment with TfOH in cold DCM.[29] The utility of silanols as partners in Hiyama couplings has been extensively studied by Denmark.[30] Also, treatment of **10** with bromine in DCM resulted in formation of vinyl bromide **53** in good yield and with complete stereocontrol (inversion of the *E*/*Z* stereochemistry).[31]

Scheme 6. Transformations that involve removal of the $Si(Me)_2Ph$ group.

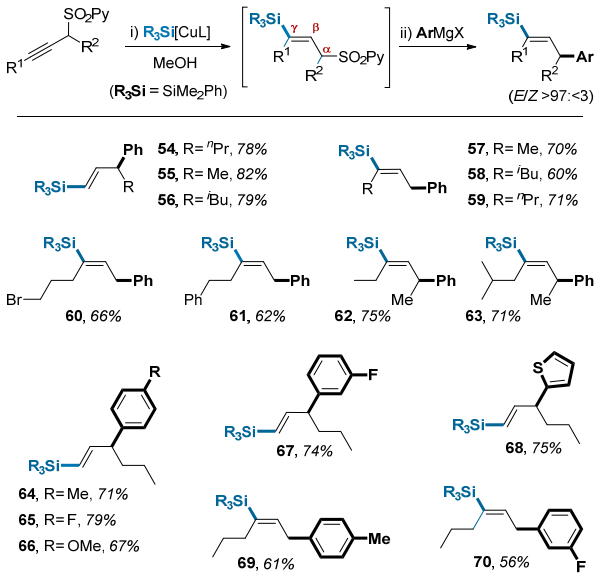


Conditions: a) KHMDS, DME, −78 °C, 30 min; then, PhCHO. b) LHMDS, 12-crown-4, DME, −78 °C, 30 min; then, PhCHO. c) TfOH, CH_2Cl_2, 0 °C, 1 h. d) Br_2, CH_2Cl_2, rt. SO_2Py = 2-$PySO_2$

One-pot formal access to hydrosilylation products of unbiased alkynes. In accordance with our desired goal of accessing formal hydrosilylation products of unsymmetrical aliphatic-substituted internal alkynes, we next focussed on a potential Cu-catalyzed allylic substitution reaction with Grignard reagents, similar to the one reported by us for vinyl boronates.[17] In this case, however, we pondered the feasibility of a condensed tandem one-pot silylation/allylic alkylation sequence starting directly from the alkyne instead of using the preformed vinyl-metal species, as it would significantly improve the synthetic value of this process while simplifying the reaction setup. The main challenge to be solved is that both steps need to be compatible under the same Cu-catalyst system. If such requirement is met, simple addition of a Grignard reagent to the reaction vessel on completion of the silylation step would in principle enable tandem silylation-arylation.

Ensuring high conversion in the overall process required, however, careful adjustments of the excess of MeOH used in the silylation step and the amount of Grignard reagent needed for the allylic substitution. We were glad to find that using 2.0 equiv of MeOH and 2.0 equiv of RMgX, the tandem β-silylation/allylic substitution was productive for the model reaction of alkyne **18** using PhMgBr as Grignard reagent to give cleanly the SN2-type product **54**, resulting from α-addition to the unsymmetrical allyl sulfone intermediate, with complete levels of regiocontrol (>98% α-selectivity, Table 5). The observed regioselectivity can be attributed to the high steric demand at the γ-allylic position imposed by the R_3Si group (attack favored at the less sterically congested allylic terminus).

Table 5. One-pot regio- and stereoselective synthesis of di- and trisubstituted vinyl silanes.[a,b]



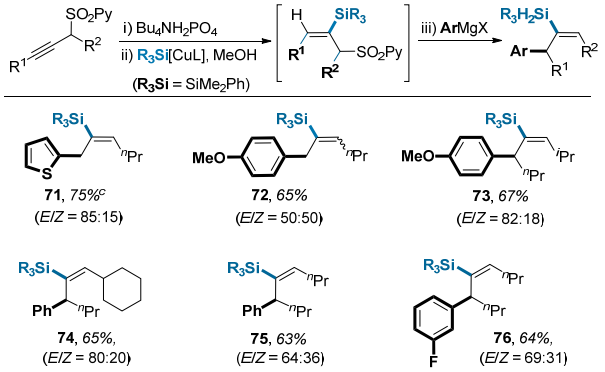
[a] Reaction conditions: Alkyne (1.0 equiv), $PhMe_2SiBPin$ (1.1 equiv), CuCl (10 mol %), PCy_3 (11 mol %), NaO*t*Bu (12 mol %), MeOH (2 equiv), toluene, rt, 2 h; then, ArMgX (2 equiv), rt, 2-16h. [b]Isolated yields after flash chromatography. SO_2Py = 2-$PySO_2$

By following the one-pot protocol, the scope of this reaction was next explored (Table 5). Other terminal alkynes with linear or branched substituents at the propargylic position (R^2) proved to be equally effective (**55** and **56**, 82% and 79%, respectively). To our delight, this tandem reaction is not limited to terminal alkynes. Internal alkynes, with or without branched propargylic substitution, were also found to be fully compatible, affording the corresponding products in good yields while preserving the complete α-regiocontrol in the allylic substitution step (**57**-**63**, 60-75%). A sensitive alkyl bromide substitution was tolerated under the present conditions (**60**, 66%). A variety of aryl Grignard reagents of different steric and electronic properties (**64**-**70**, 56-79%), including heteroaromatics (**68**, 75%) are applicable. The current tandem one-pot reaction produced structurally elaborated vinyl silanes in good yields. In all examples described in Table 5 (17 cases studied), a single regioisomer (>98% β-site selectivity in the silylation reaction and >98% α-site selectivity in the allylic substitution) and diastereoisomer (>98% *E*-

stereoselectivity) of the product is formed (products **54**-**70**, 56-82% yield).

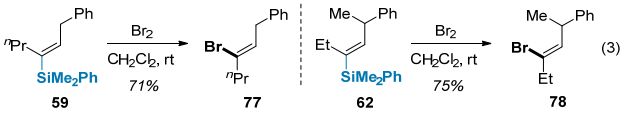
This one-pot silylation/allylic substitution sequence is also compatible with the base-promoted α-silylation via allene, even though the presence of stoichiometric amounts of $NBu_4H_2PO_4$ makes this process more challenging. Interestingly, in this case the regiochemical outcome of the allylic substitution step was reversed, providing exclusively the S_N2'-type product, as a result of the attack of the Grignard reagent to the γ-terminus of the allyl sulfone intermediate (>98% γ-selectivity Table 6). The lack of a sterically hindered silyl group at the γ-allylic position could be the reason behind this S_N2'-type selectivity, which on the other hand is typically observed in Cu-catalyzed allylic substitutions.[32] A variety of trisubstituted vinyl silanes with different substitution pattern were obtained regioisomerically pure with acceptable yields in this protocol (products **71**-**76**, 63-75% yields). The compatibility with heteroarenes at the substrate was remarkable (product **71**, 75%). Unfortunately, however, the hydrosilylation products were obtained with consistently lower stereoselectivity, the *E*/*Z* ratio ranging from 1:1 to 5.7:1. Except for one case (product **71**), no significant improvement of stereocontrol could be obtained by lowering the temperature (down to −78 °C). The different levels of stereoselectivity observed for both processes can be attributed to the divergence in the reaction mechanism (formal S_N2 versus S_N2').

Table 6. Extension to the one-pot regio- and stereoselective α–silylation/allylic substitution[a,b]



[a]Reaction conditions: Alkyne (1.0 equiv), $NBu_4H_2PO_4$ (1.0 equiv), toluene, rt for internal alkynes or 50 °C for terminal alkynes, 1 h; then, $PhMe_2SiBPin$ (1.0-1.5 equiv), CuCl (10 mol %), PCy_3 (11 mol %), NaOtBu (12 mol %), MeOH (2 equiv), rt or 50 °C; then, ArMgX (2 equiv), rt, 2-16h. [b]Yields after flash chromatography. [c] Reaction performed at −78 °C. SO_2Py = 2-$PySO_2$

Finally, the facile silicon-bromine exchange process described for compound **52**[30] was successfully applied to the synthesis of non-functionalized, trisubstituted, vinyl bromides **77** and **78** in good yields and complete stereocontrol (eq 3). At this point it is important to note that, in spite of the significance of alkenyl halides as versatile coupling partners in transition metal catalyzed cross-coupling reactions and as precursors to a wide range of organometallic reagents, the synthesis of alkenyl halides, especially those involving trisubstituted alkenes in a stereodefined manner is challenging.



CONCLUSIONS

In summary, we report on a general and practical method for the regio- and stereocontrolled synthesis of di- and trisubstituted vinyl silanes by Cu-catalyzed hydrosilylation of both internal and terminal alkynes. The use of a SO_2Py group at the propargylic position is essential in three ways: firstly, it controls the reactivity of the system, preventing alternative reaction pathways such as nucleophilic displacement of the directing group; secondly, it enables an alkyne/allene rearrangement that results in efficient control of the regioselectivity of the hydrosilylation process; thirdly, its formal elimination promotes a series of useful transformations, even in a one-pot fashion. In particular, we have shown, for the first time, a tandem silylation/allylic arylation of propargyl sulfones, using the same Cu-catalyst to access in a single operation novel vinyl sylanes that cannot be accessed directly from dialkyl alkynes. The overall transformation can be accomplished in the presence of a wide range of functional groups. The wide scope highlights the validity of the method to construct, in a one-pot operation, a variety of trisubstituted vinyl silanes having various substitution patterns from simple propargyl sulfones. This work thus contributes to the emerging use of alkynes as allene surrogates in transition metal-catalyzed reactions as a strategy for selectivity control.

EXPERIMENTAL SECTION

General methods. Dichloromethane, toluene, acetonitrile, and tetrahydrofuran were taken from a PureSolv MD purification system. Sodium amalgam [Na(Hg)] 6% was prepared following a reported procedure.[33] Metal precatalysts, Grignard reagents and *m*CPBA (≤77% purity) were purchased from commercial sources and used without further purification. All reactions were carried out under inert atmosphere, unless otherwise noted.

Typical procedure for the β-silylation of propargylic sulfones. CuCl (2.0 mg, 0.020 mmol, 10 mol %) was placed in a Schlenck tube. The tube was purged and backfilled with argon. Then was added dry toluene (0.7 mL), tri-cyclohexyl-phosphine (20 % in toluene, min 88 %) (50 µl, 0.022 mmol, 11 mol %) and NaOtBu (2M in THF) (12 µL, 0.024 mmol, 12 mol %) and the solution was allowed to stir at 22 °C for five minutes. Silylborane reagent (60 µL, 0.22 mmol, 1.1 equiv) was added to the solution, causing it to turn dark brown immediately. The mixture was allowed to stir at 22 °C for 5 min under an argon atmosphere. The corresponding propargylic sulfone (0.2 mmol, 1.0 equiv) dissolved in toluene (0.5 mL), and MeOH (17 µL, 0.4 mmol, 2 equiv) were sequentially added through syringes. The resulting mixture was allowed to stir at 22 °C until no starting material was detected (TLC monitoring, 2-16 h). Then, the reaction was quenched by passing the mixture through a short plug of celite and silica gel, and then eluted with DCM (3 × 4 mL). The filtrate was concentrated *in vacuo* and purified by silica gel chromatography.

Typical procedure for the α-silylation of propargylic sulfones. The corresponding propargylic sulfone (0.2 mmol, 1.0 equiv) and $(NBu_4)H_2PO_4$ (67.8 mg, 0.2 mmol, 1.0 equiv) were placed

in a Schlenck tube. The Schlenck tube was purged and backfilled with argon, and dry toluene (1.0 mL) was added. The mixture was stirred at 50 °C for 1 h. In a separate Schlenck tube, CuCl (2.0 mg, 0.020 mmol, 10 mol %) was placed. The Schlenck tube was purged and backfilled with argon. Then, dry toluene (0.7 mL), tri-cyclohexyl-phosphine (20% in toluene, min 88%) (50 µl, 0.022 mmol, 11 mol %) and NaO*t*Bu (2M in THF) (12 µL, 0.024 mmol, 12 mol %) were sequentially added and the solution was allowed to stir at 22 °C for five minutes. Silylborane reagent (90 µL, 0.3 mmol, 1.5 equiv) was added to the solution, causing it to turn dark brown immediately. The mixture was allowed to stir at 22 °C for 5 min under an atmosphere of argon. This solution and MeOH (17 µL, 0.4 mmol, 2 equiv) were sequentially added through syringes to the first Schlenck tube. The resulting mixture was allowed to stir at 50 °C (for internal alkynes) or 22 °C (for terminal alkynes) until no starting material was detected (TLC monitoring, 30 min-16 h). Then, the reaction was quenched by passing the mixture through a short plug of celite and silica gel, and then eluted with DCM (3 × 4 mL). The filtrate was concentrated *in vacuo* and purified by silica gel chromatography.

ASSOCIATED CONTENT

Experimental details as well as spectroscopic and analytical data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) (a) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435; (b) Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221. (c) Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, 853. (d) Lim, D. S. W; Anderson, E. A. *Synthesis* **2012**, *44*, 983.

(2) (a) Iannazzo, L.; Molander, G. A. *Eur. J. Org. Chem.* **2012**, 4923. (b) *Hydrosilylation: A Comprehensive Review on Recent Advances*; Marciniec, B., Ed.; Springer: Berlin, 2009. (c) Roy, A. K. *Adv. Organomet. Chem.* **2008**, 55, 1.

(3) General reviews: (a) Dang, Li.; Lin, Z.; Marder, T. B. *Chem. Commun.* **2009**, 3987; (b) Schiffner, J. A.; Müther, K.; Oestreich, Martin *Angew. Chem. Int. Ed.* **2010**, *49*, 1194 ; (c) Yamashita, M. *Bull. Chem. Soc. Jpn.* **2011**, *84*, 983; (d) Hartmann, E.; Vyasab D. J.; Oestreich M. *Chem. Commun.* **2011**, *47*, 7917; (e) Cid, J.; Gulyás, H.; Carbó J. J.; Fernández, E. *Chem. Soc. Rev.* **2012**, *41*, 3558; (f) Calow, A. D. J.; Whiting, A. *Org. Biomol. Chem.* **2012**, *10*, 5485. For reviews on Cu-catalyzed borylation of alkynes with diboron reagents: (g) Yun, J. *Asian J. Org. Chem.*, 2013, 2, 1016; (h) Alfaro, R.; Parra, A.; Alemán J.; Tortosa, M. *Synlett* **2013**, 804; (i) Fujihara, T.; Semba, K.; Terao J.; Tsuji, Y. *Catal. Sci. Technol.* **2014**, *4*, 1699.

(4) (a) Ito, H.; Yamanaka, H.; Tateiwa, J.-i.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821; (b) Takahashi, K.; Ishiyama, T.; Miyaura, N. *Chem. Lett.* **2000**, 982.

(5) (a) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859. See also: (b) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234. For a very recent Co-catalyzed hydrosilylation, see: (c) Mo, Z.; Xiao, J.; Gao, Y.; Deng L. *J. Am. Chem. Soc.* **2014**, *136*, 17414.

(6) (a) Moure, A. L.; Gómez Arrayás, R.; Cárdenas, D. J.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2012**, *134*, 7219; (b) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2012**, *18*, 4179; (c) Park, J. K.; Ondrusek, B. A.; McQuade, D. T. *Org. Lett.* **2012**, *14*, 4790; (d) Yuana W.; Ma, S. *Org. Biomol. Chem.* **2012**, *10*, 7266; (e) Liu, P.; Fukui, Y.; Tian, P.; He, Z.-T.; Sun, C.-Y.; Wu, N.-Y.; Lin, G.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 11700. For Cu-catalyzed borylation of propargylic silylalkynes, see: (f) Kim, Y. E.; Li, D.-X.; Yun J. *Dalton Trans.* **2015**, DOI: 10.1039/c5dt00144g.

(7) (a) Ohmura, T.; Suginome, M. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29; (b) Suginome, M.; Ito, Y. *J. Organomet. Chem.* **2003**, *680*, 43.

(8) For a comprehensive review on the rich chemistry that has been developed based on Si–B bond activation, see: (a) Oestreich, M.; Hartmann, E.; Mewald M. *Chem. Rev.* **2013**, *113*, 402. For seminal references on Cu-catalyzed silylation using Si–B reagent, see: conjugate addition: (b) Lee, K.-s.; Hoveyda, A H. *J. Am. Chem. Soc.* **2010**, *132*, 2898; allylic substitution: (c) Vyas, D. J.; Oestreich, M. *Angew. Chem. Int. Ed.* **2010**, *49*, 8513; isonitrile insertion: Tobisu, M.; Fujihara, H.; Koh, K.; Chatani, N. *J. Org. Chem.* **2010**, *75*, 4841.

(9) (a) Meng, F.; Jang H.; Hoveyda, A. H. *Chem. Eur. J.* **2013**, *19*, 3204. For a recent report on Co-catalyzed β-selective hydrosilylation of terminal alkynes, see: (b) Mo, Z.; Xiao, J.; Gao, Y.; Deng, L. *J. Am. Chem. Soc.* **2014**, *136*, 17414.

(10) (a) P. Wang, X.-L. Yeo and T.-P. Loh, *J. Am. Chem. Soc.* **2011**, *133*, 1254; (b) Zhou, H.; Wang, Y.-B. *ChemCatChem* **2014**, 6, 2512.

(11) Hazra, C. K.; Fopp, C.; Oestreich, M. *Chem. Asian J.* **2014**, 9, 3005.

(12) (a) Linstadt, R. T. H.; Peterson, C. A.; Lippincott, D. J.; Jette, C. I.; Lipshutz, B. H. *Angew. Chem. Int. Ed.* **2014**, *53*, 4159; (b) Calderone, J. A.; Santos, W. L. *Angew. Chem. Int. Ed.* **2014**, *53*, 4154; (c) Xu, Y.-H.; Wu, L.-H.; Wang, J.; Loh, T.-P. *Chem. Commun.* **2014**, 50, 7195. For tandem Cu-catalyzed $PhMe_2Si$-BPin-silylation of propiolate esters and Pd-catalyzed allylation: (d) Vercruysse, S.; Cornelissen, L.; Nahra, F.; Collard, L.; Riant, O. *Chem. Eur. J.* **2014**, *20*, 1834. For Pt-catalyzed hydrosilylation: (e) Rooke, D. A.; Ferreira, E. M. *Angew. Chem. Int. Ed.* **2012**, *51*, 3225. For phosphine-catalyzed silaboration: (f) Nagao, K.; Ohmiya, H.; Sawamura, M. *Org. Lett.* **2015**, *17*, 1304.

(13) For Cu-catalyzed silacarboxylation (a) Fujihara, T.; Tani, Y.; Semba, K.; Terao, J.; Tsuji Y. *Angew. Chem. Int. Ed.* **2012**, *51*, 11487. For Pd-catalyzed hydrosilylation: Zhou H.; Moberg, C. *Org. Lett.* **2013**, *15*, 1444.

(14) For a review on silaboration of alkynes with Si–B reagents catalyzed by Pd via an oxidative addition/reductive elimination mechanism, see: (a) Ohmura, T.; Suginome, M. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29. See also: (b) Ohmura, T.; Oshima, K.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 12194; (c) Ohmura, T.; Oshima, K.; Suginome, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 12501; (d) Miura, T.; Nishida, Y.; Murakami M. *J. Am. Chem. Soc.* **2014**, *136*, 6223.

(15) For examples of ligand-controlled regioselectivity switch in catalytic metalation of alkynes, see: (a) Miller, K. M.; Jamison, T. F. *J. Am. Chem. Soc.* **2004**, *126*,15342; (b) Ohmura, T.; Oshima, K.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 12194; (c) Malik, H. A.; Sormunen, G. J.; Montgomery, J. *J. Am. Chem. Soc.* **2010**, *132*, 6304; (d) González-Rodríguez, C.; Pawley, R. J.; Chaplin, A. B.; Thompson, A. L.; Weller, A. S.; Willis M. C. *Angew. Chem. Int. Ed.* **2011**, *50*, 5134; (e) Park, J. K.; Ondrusek, B. A.; McQuade, D. T. *Org. Lett.* **2012**, *14*, 4790; (f) Di Giuseppe, A.; Castarlenas, R.; Pérez-Torrente, J. J.; Crucianelli, M.; Polo, V.; Sancho, R.; Lahoz, F. J.; Oro L. A. *J. Am. Chem. Soc.*

2012, *134*, 8171; (g) Park, J. K.; Ondrusek, B. A.; McQuade, D. T. *Org. Lett.* **2012**, *14*, 4790; (h) Ding, S. T.; Song, L. J.; Chung, L. W.; Zhang, X. H.; Sun, J. W.; Wu, Y. D. *J. Am. Chem. Soc.* **2013**, *135*, 13835. See also ref. 5a. For controlling regioselectivity by choice of catalytic species, see ref. 6b. For an elegant example of switching regioselectivity via alteration in reversibility of a key mechanistic step, see: (i) Jackson, E. P.; Montgomery, J. *J. Am. Chem. Soc.* **2015**, *137*, 958.

(16) For very recent elegant examples of regioselectivity switch in Ru-catalyzed functionalization of unsymmetrical aliphatic-substituted internal alkynes that rely on an in situ catalyst-promoted alkyne-allene isomerization, see: (a) Chen, Q.-A.; Cruz, F. A.; Dong V. M. *J. Am. Chem. Soc.* **2015**, *137*, 3157. (b) Liang, T.; Nguyen, K. D.; Zhang, W.; Krische, M. J. *J. Am. Chem. Soc.* **2015**, *137*, 3161. See references therein for further examples of metal-catalyst-promoted in situ alkyne-allene isomerization.

(17) Moure, A. L.; Mauleón, P.; Gómez-Arrayás, R.; Carretero, J. C., *Org. Lett.* **2013**, *15*, 2054.

(18) For early reports on the metal-coordinating ability of 2-pyridylsulfones, see: (a) Mauleón, P.; Carretero, J. C. *Org. Lett.* **2004**, *6*, 3195; (b) Llamas, T.; Gómez Arrayás, R.; Carretero J. C. *Angew. Chem. Int. Ed.* **2007**, *46*, 3329; (c) Mauleón, P.; Carretero, J. C. *Chem. Commun.* **2005**, 4961. For the Cu-coordinating ability of SO_2Py, see: (d) Esquivias, J.; Gómez Arrayás, R.; Carretero, J. C. *Angew. Chem. Int. Ed.* **2007**, *46*, 9257. For the use of SO_2Py as leaving group in Cu-catalyzed allylic substitution of allylic sulfones with Grignard reagents: (e) Llamas, T.; Gómez Arrayás, R.; Carretero, J. C. *Adv. Synth. Catal.* **2004**, *346*, 1651 and ref 17. Other selected examples of the use of SO_2Py group as regio-/stereocontrolling unit: (f) Desrosiers, J.-N.; Bechara, W. S.; Charette, A. B. *Org. Lett.* **2008**, *10*, 2315; (g) Bos, P. H.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2008**, *10*, 4219; (h) Nakamura, S.; Nakashima, H.; Sugimoto, H.; Sano, H.; Hattori, M.; Shibata, N.; Toru T. *Chem. Eur. J.* **2008**, *14*, 2145; (i) García-Rubia, A.; Urones, B.; Gómez Arrayás, R.; Carretero, J. C. *Angew. Chem. Int. Ed.* **2011**, *50*, 10927. (j) Hussain, N.; Hussain, M. M.; Ziauddin, M.; Triyawatanyu, P.; Walsh P. J. *Org. Lett.* **2011**, *13*, 6464; (k) Urones, B.; Martínez, A. M.; Rodríguez, N.; Gómez Arrayás, R.; Carretero, J. C. *Chem. Commun.* **2013**, *49*, 11044; (l) Urones, B.; Gómez Arrayás, R.; Carretero, J. C. *Org. Lett.* **2013**, *15*, 1120. (l) Nakamura, S.; Ohara, M.; Koyari, M.; Hayashi, M.; Hyodo, K.; Nabisaheb, N. R.; Funahashi, Y. *Org. Lett.* **2014**, *16*, 4452.

(19) (a) Ito, H.; Sasaki, Y.; Sawamura, M. *J. Am. Chem. Soc.* **2008**, *130*, 15774. (b) Zhao, T. S. N.; Yang, Y.; Lessing, T.; Szabó, K. J. *J. Am. Chem. Soc.* **2014**, *136*, 7563.

(20) Vyas, D. J.; Hazra, C. K.; Oestreich, M. *Org. Lett.* **2011**, *13*, 4462.

(21) For the development of Johnphos ligand, see: Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369.

(22) (a) Kitagaki, S.; Teramoto, S.; Mukai C. *Org. Lett.* **2007**, *9*, 2549; (b) Back, T. G. *Tetrahedron Lett.* **2001**, *57*, 5263.

(23) For the regioselective silyl-cupration of allenes, see: (a) Rae, J.; Hu, Y. C.; Procter, D. J. *Chem. Eur. J.* **2014**, *20*, 13143. For regioselective boryl-cupration of allenes: (b) Yuana, W.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1867; (c) Yuan, W.; Zhang, X.; Yu, Y.; Ma, S. *Chem. Eur. J.* **2013**, *19*, 7193; (d) Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2013**, *19*, 7125; (e) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 12400. For site-selectivity control in hydroboration of allenes, see: (f) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414. For Cu-catalyzed silacarboxylation: (g) Tani, Y.; Fujihara, T.; Terao, J.; Tsuji Y. *J. Am. Chem. Soc.* **2014**, *136*, 17706. See also: (h) Miller, Z. D.; Li W.; Belderrain, T. R.; Montgomery, J. *J. Am. Chem. Soc.* **2013**, *135*, 15282.

(24) See SI for a more complete study on the effect of several bases such as KOAc, NaOtBu, KOtBu, and the effect of temperature.

(25) See SI for experimental details.

(26) After completion of our study, Loh and Xu reported that pre-formed allenes with electron-withdrawing groups directly attached to the allene moiety undergo silylation at the internal position (ref. 12c).

(27) A pre-stirring time of 1 h in the presence of 1 equiv of base ($NBu_4H_2PO_4$) before addition of the silylating reagent was found to be necessary for achieving complete α-regiocontrol. Nevertheless, even in the absence of pre-treatment with base a good, albeit not complete, α-silylation regioselectivity was observed in agreement with the higher reactivity of the allenyl sulfone over the propargyl sulfone. For example, the α-silylation reaction of the internal propargyl sulfone **16** in the presence of base but with no pre-stirring time (i.e., adding the silylborane reagent at time zero) produced product **39** with a regioselectivity ratio of α/β = 90:10.

(28) For other examples of use of this technique for the identification of rotamers, see: Rayyan, S.; Fossen, T.; Solheim Nateland, H.; Andersen Ø. M., *Phytochem. Anal.* **2005**, *16*, 334, and references cited therein.

(29) Ghosh, S. K.; Singh, R.; Singh, G. C., *Eur. J. Org. Chem.* **2004**, 4141. For the use of related silanols in Hiyama-Denmark coupling reactions, see: Anderson, J. C.; Munday, R. H. *J. Org. Chem.* **2004**, *69*, 8971.

(30) (a) Denmark, S. E.; Regens, C. S. *Acc. Chem. Res.* **2008**, *41*, 1486. (b) Denmark, S. E.; Ramzi F. Sweis, R. F. *J. Am. Chem. Soc.* **2001**, *123*, 6439.

(31) Chan, T. H.; Lau, P. W. K.; Mychajlowskij, W., *Tetrahedron Lett.* **1977**, *18*, 3317.

(32) Karlström, A. S. E.;Bäckvall, J.-E. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinhem, Germany, 2001; p 259.

(33) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1345.

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