Full paper/Mémoire

Synthesis of allenylzinc reagents by 1,2-rearrangement of alkynyl(disilyl)zincates derived from acetylenic epoxides and acetylenic aziridines

Valentin N. Bochatay, Laurent Debien, Fabrice Chemla[**], Franck Ferreira[***], Olivier Jackowski, Alejandro Perez-Luna[*]

Sorbonne Universités, UPMC Université Paris-6, CNRS UMR 8232, Institut parisien de chimie moléculaire, 75005, Paris, France

A B S T R A C T

Lithium alkynyl(disilyl)zincates obtained from metalated ethynyloxiranes, as well as from *N-tert*-butanesulfinyl(ethynyl)aziridines or *N-tert*-butanesulfonyl(ethynyl)aziridines, undergo 1,2-migration of the organosilyl group with ring opening of the oxirane or aziridine ring by S_Ni displacement. A developed protocol that involves *n*BuLi for the metalation step offers a straightforward approach to the corresponding δ-oxy- and δ-amino α-silyl allenylzinc intermediates. The reagents derived from the epoxides are amenable to subsequent in situ condensation with aldehydes or ketones to provide 1,3-diols but not those derived from aziridines that only react sluggishly in similar condensations.

© 2017 Académie des sciences. Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Allenylmetal reagents [1], including allenylzincs [2], are versatile organometallic species that have been used intensively in organic synthesis. For more than a decade, work from our laboratories [3] and others [1,2] have demonstrated that α-silyl−substituted allenylzincs are a particularly useful substrate class of this family. Typically, allenylzinc reagents exist in a solution as mixture of two rapidly interconverting metallotropic forms: the propargylic and the allenic one. When opposed to carbonyl derivatives (i.e., aldehydes, ketones, or imines), each form has the potential to undergo electrophilic substitution through an S_E2' mechanism providing either allenes (from

the propargylic form) or alkynes (from the allenic form). Lack of regioselectivity is thus a common drawback for such condensations [2].

A key feature of α-silyl−substituted allenylzinc reagents is that the organosilyl group geminal to the carbon−zinc bond stabilizes the allenic form (α-silicon effect) and thereby shifts the propargyl/allenyl metallotropic equilibrium toward the latter form (Scheme 1) [4]. Hence, condensation with carbonyl derivatives occurs with exquisite regioselectivity and affords exclusively the propargylic adducts [3,5]. Furthermore, in cases where two stereogenic centers are created during the condensation event, excellent levels of diastereocontrol are usually observed. In addition, their high functional-group tolerance and the fact that they lead to silylated alkynes that can be easily protodesilylated to unmask a terminal alkyne that then serves as handle for further synthetic elaboration are also important qualities of these propargylating reagents [6].
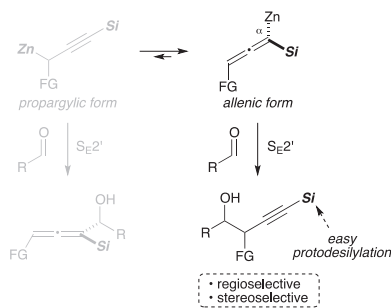
α-Substituted allenylmetals can be conveniently accessed by the 1,2-metalate rearrangement of alkynylogous carbenoids. Commonly, migration of alkyl groups is

---

* Corresponding author.
** Corresponding author.
*** Corresponding author.

E-mail addresses: fabrice.chemla@upmc.fr (F. Chemla), franck. ferreira@upmc.fr (F. Ferreira), alejandro.perez_luna@upmc.fr (A. Perez-Luna).

Scheme 1. Condensation of aldehydes with α-silyl–substituted propargyl/allenylzinc reagents.

involved and α-alkyl–substituted allenylmetals are obtained [7–10]. However, the approach is also suitable to access α-silyl allenylmetals, but this prospect has remained so far virtually unexplored [10b,11]. In seminal studies, Harada et al. demonstrated that zincate complexes **II**, obtained from bromopropargyl mesylates **I** by halogen–metal exchange with (Me₂PhSi)₃ZnLi, provided α-silyl allenylzinc intermediates **III** after 1,2-migration of the organosilyl group with displacement of the propargylic leaving group through an $S_{N}i$ mechanism (Scheme 2, top) [10b,12]. Inspired by these results and as part of our longstanding interest in ring-opening reactions of acetylenic epoxides [13] and aziridines [14], we reasoned that implementation of a similar approach with lithium alkynyl(disilyl)zincates **V** derived from those substrates and disilylzinc reagents would lead to δ-heteroatom substituted α-silyl allenylzinc intermediates **VI** that could offer an expeditious stereoselective access to valuable 1,3-diols (**VII**, X = O) or 1,3-aminoalcohols (**VII**, X = NR) on condensation with aldehydes (Scheme 2, bottom). In this article, we describe our research endeavors in this area combining an overview of
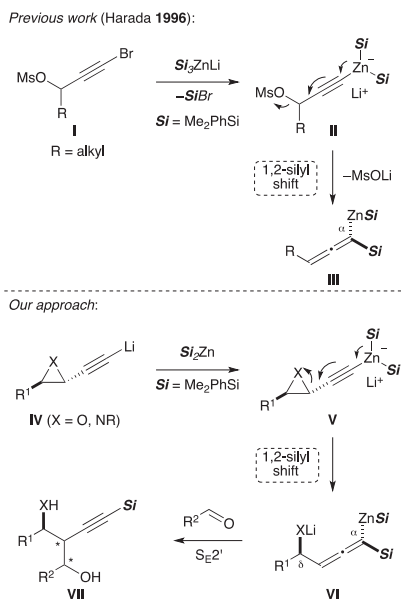
previous work on acetylenic epoxides [10e] and recent results on the ring-opening of *N-tert*-butanesulfinylaziridines and *N-tert*-butanesulfonylaziridines.
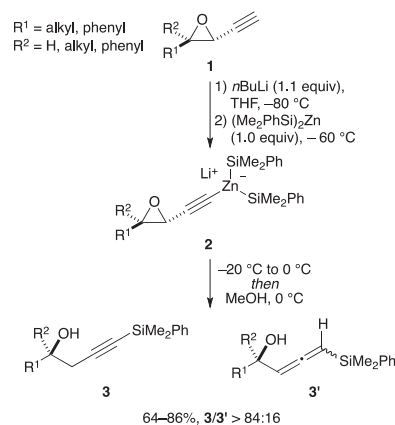
2. 1,2-Rearrangement of alkynyl(disilyl)zincates derived from acetylenic epoxides

Our first foray in this field was the result of our studies on the rearrangement of lithiated ethynylepoxides by reaction with dialkylzinc reagents [10e]. As part of this work, it was found that lithiated acetylenic epoxides also underwent transmetalation with (Me₂PhSi)₂Zn at −60 °C to afford lithium alkynyl(disilyl)zincates **2** (Scheme 3). 1,2-Silyl migration inducing opening of the oxirane ring occurred on warming the reaction mixture to −20 °C and afforded the corresponding α-silyl allenylzinc intermediates. After acidic aqueous workup, a mixture of homopropargylic (**3**) and allenic (**3′**) alcohols was obtained. The **3/3′** ratio was found to be highly dependent on the quench conditions and difficult to control. Ultimately, it was possible to find conditions to prepare regioselectively homopropargylic alcohols **3** using MeOH (0 °C) to quench the reaction mixture after rearrangement. This optimized protocol was suitable for di- and tri-substituted acetylenic epoxides having either alkyl or aryl substituents and the corresponding alcohols **3** were obtained in 64–86% yield with good to excellent regioselectivity (**3/3′** > 84:16).
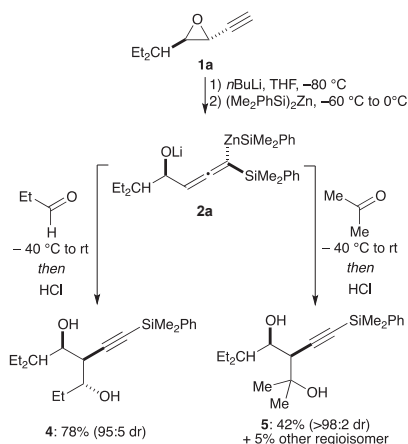
The possibility to use this chemistry to access 1,3-diols was also demonstrated. Condensation of propionaldehyde with the α-silyl allenylzinc intermediate **2a′** (obtained from epoxide **1a**) was achieved at −40 °C and led to diol **4** [15] in a remarkable 78% yield with excellent regio- and stereoselectivity (Scheme 4). Trapping with acetone was less efficient and tertiary alcohol **5** was obtained in a lower 42% yield, still with excellent stereoselectivity. Interestingly, in the latter case, the presence of allenic regioisomers was also detected to some extent.

## 3. 1,2-Rearrangement of alkynyl(disilyl)zincates derived from acetylenic aziridines

Following on these results, we considered the rearrangement of acetylenic aziridines and focused on *N-tert-*

Scheme 2. Formation of α-silyl–substituted propargyl/allenylzinc reagents by 1,2-metalate rearrangement of alkynylogous carbenoids.

Scheme 3. Rearrangement of lithium alkynyl(disilyl)zincates.

**Scheme 4.** Preparation of 1,3-diols **4** and **5**.

butanesulfinylethynylaziridines (**6**) and *N-tert*-butane-sulfonylethynylaziridines (**7**) (Scheme 5). Model substrates **6a**–**c** were prepared as pure stereoisomers in two steps from *N-tert*-butanesulfinylimines, according to a procedure previously reported by our group [14,16]. Oxidation of **6a**–**c**
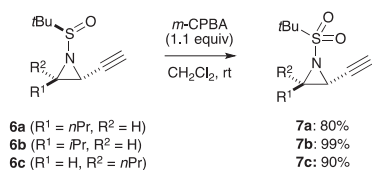
Scheme 5. Preparation of *N-tert*-butanesulfonyl(ethynyl)aziridines **7a**–**c**.

with *meta*-Chloroperoxybenzoic acid (*m*-CPBA) afforded the corresponding *N-tert*-butanesulfonylethynylaziridines **7a**–**c** in excellent yields.

First, the lithiation step was examined (Table 1). To this end, substrate **6a** (representative of *N-tert*-butanesulfiny-lethynylaziridines) was treated with *n*BuLi in THF at −80 °C for 15 min and the reaction mixture was then quenched with MeOD. After workup, [²H]-**6a** was obtained in low 25% yield along with 71% of unreacted **6a** (entry 1). To drive the metalation to completion, the reaction time was then increased to 1 h: [²H]-**6a** was obtained in 57% yield along with 7% of **6a** (entry 2). Hence, although the deuteration grade was significantly improved (89%), the overall lith-iation yield remained modest because around 30% of the starting material had been consumed unproductively to yield unidentified material. Sulfoxide **8** was also isolated from this reaction in 5% yield, suggesting that substitution at the sulfur atom of the *tert*-butanesulfinyl moiety was at the origin of the starting material degradation. To minimize this possible side reaction, changing *n*BuLi for other alkyl-lithium reagents was considered. When *t*BuLi was used (entry 3), sulfoxide **9** was isolated in a higher 16% yield and some starting material was lost. In contrast, degradation did not occur using MeLi or PhLi (entries 4 and 5). Yet, complete metalation was not achieved (65–68% deutera-tion grades) even after prolonged reaction times (3 h).

Following these failures, we contemplated deprotona-tion of **6a** with LDA. On reaction at −80 °C for 1 h, only partial metalation was obtained, but without any signifi-cant starting material degradation (entry 6). Finally, add-ing HMPA (2.0 equiv) as additive and performing the reaction at −30 °C allowed for convenient lithiation of **6a** as [²H]-**6a** was obtained in 81% yield (entry 7). An addi-tional solution for the metalation of **6a** came out of

Table 1
Deprotonation studies of **6a**.
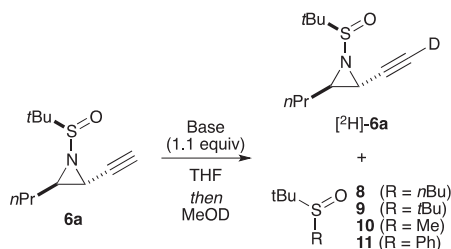
Entry	Base	Conditions	[²H]-**6a** (%)[a]	**6a**[a] (%)	*t*BuS(O)R[a] (%)
1	*n*BuLi	−80 °C, 15 min	25	71	**8**: —[b]
2	*n*BuLi	−80 °C, 1 h	57	7	**8**: 5
3	*t*BuLi	−80 °C, 1 h	52	11	**9**: 16
4	MeLi	−80 °C, 3 h	62	34	**10**: —[b]
5	PhLi	−80 °C, 3 h	63	30	**11**: 7
6	LDA	−80 °C, 1 h	47	39	—
7	LDA	HMPA[c], −30 °C, 2 h	81	9	—
8	*n*Bu₃ZnLi[d]	0 °C, 2 h	89	11	**8**: —[b]

LDA, Lithium diisopropylamide; HMPA, Hexamethylphosphoramide.
[a] Yield determined by ¹H NMR spectroscopy using biphenyl as an internal standard.
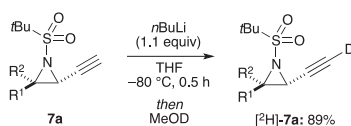[b] Product not detected.
[c] 2.0 equiv.
[d] 2.2 equiv.

serendipity. Although studying the ring-opening of ethynylaziridines with triorganozincates [17], we found that [²H]-**6a** could be obtained in 89% yield by treatment with 2.2 equiv nBu$_3$ZnLi at 0 °C for 2 h followed by quenching with MeOD (entry 8) [18].

Unlike for *N-tert*-butanesulfinylethynylaziridine **6a**, lithiation of **7a** (representative of *N-tert*-butanesulfonylaziridines) was not problematic and occurred readily at −80 °C on treatment with nBuLi (1.1 equiv). This was confirmed by the isolation of [²H]-**7a** in 89% yield after addition of MeOD to the reaction mixture and aqueous workup (Scheme 6).
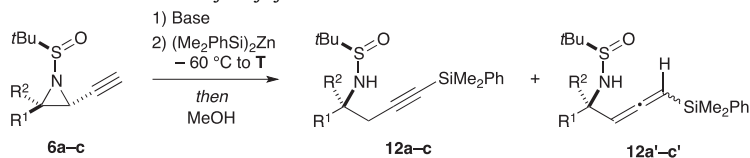
With suitable metalation procedures in hand for **6** and **7**, the 1,2-metalate rearrangement of the corresponding alkynyl(disilyl)zincates (**V**) arising from reaction with (Me$_2$PhSi)$_2$Zn was investigated. *N-tert*-butanesulfinylethynylaziridines **6** were considered first (Table 2).

Trace amounts of rearrangement products were obtained with the initial set of conditions involving LDA as base, addition of 1.1 equiv (Me$_2$PhSi)$_2$Zn at −60 °C, and warming the reaction mixture to −30 °C (Table 2, entry 1). After addition of MeOH (at −30 °C) and work up, around 80% of the starting aziridine **6a** was recovered. To our delight, when a larger amount of (Me$_2$PhSi)$_2$Zn was introduced (2.2 equiv), complete ring opening of **6a** was observed and δ-amino allenylsilane **12a′** was isolated in 57% yield as a 68:32 mixture of diastereomers (entry 2). 1,2-Rearrangement also occurred at 0 °C with the zincate

obtained using nBu$_3$ZnLi for the metalation step (entry 3). In this case, a mixture of **12a** and **12a′** in a **12a**/**12a′** = 66:34 ratio was isolated in 63% yield. Quite unexpectedly, given the apparent moderate efficiency of the lithiation step (see above), similar yields (60–65%) in rearranged products were obtained when nBuLi was used as base (entries 4–6). Here, mixtures of **12a**/**12a′** were isolated in regio- and stereoselectivities that were difficult to control and varied with the workup conditions [19]. Importantly, these substantial disparities provided good evidence for the intermediate formation of a δ-amino α-silyl allenylzinc intermediate **VI** and, in-line with the behavior of the related δ-oxy α-silyl allenylzinc reagents obtained from ethynylepoxides, are likely the result of the difficulty to control the selectivity of the protodemetalation reaction.

The 1,2-metalate rearrangement also occurred efficiently in the case of ethynylaziridine **6b** having a secondary alkyl substituent (entry 7). Interestingly, with the protocol relying on nBuLi for the metalation step, the exclusive formation of δ-amino allenylsilane **12b′** (97:3 dr) was obtained in 75% yield. On the contrary, ring-opening by 1,2-metalate rearrangement did not occur for the alkynyl(disilyl)zincate derived from *cis*-configured ethynylaziridine **6c** and the starting material was recovered (entry 8) [20].

N-tert-Butanesulfonylethynylaziridines **7** were considered next (Table 3). The rearrangement of the alkynyl(disilyl)zincate derived from lithiated **7a** and (Me$_2$PhSi)$_2$Zn (1.5 equiv) occurred fully at −30 °C and a mixture of products **13a** and **13a′** (**13a**/**13a′** = 78:22) was isolated after methanolysis and workup in 54% yield (entry 1). Performing the rearrangement at 0 °C led to a better 70% yield (entry 2).

In the case of substrate **7b** having a secondary alkyl substituent, the yield in rearranged products **13b** and **13b′** was already good when the rearrangement was

Scheme 6. Deprotonation of **7a**.

Table 2
Rearrangement of *N-tert*-butanesulfinylethynylaziridines **6**.

Entry	**6**	Base	(Me$_2$PhSi)$_2$Zn [equiv], T	Product	**12**/**12′**[a]	**12′**(dr)[a]	Yield[b] (%)
1	**6a**	LDA/HMPA	1.1, −30 °C	**12a**/**12a′**	nc[c]	nc[c]	<5
2	**6a**	LDA/HMPA	2.2, −30 °C	**12a**/**12a′**	<2:98	68:32	57
3	**6a**	(nBu)$_3$ZnLi[d]	2.2, 0 °C	**12a**/**12a′**	66:34	91:9	63
4	**6a**	nBuLi	1.5, 0 °C	**12a**/**12a′**	84:16	33:67	60
5[e]	**6a**	nBuLi	1.5, 0 °C	**12a**/**12a′**	<2:98	77:23	64
6[f]	**6a**	nBuLi	1.5, 0 °C	**12a**/**12a′**	90:10	54:46	65
7	**6b**	nBuLi	1.5, 0 °C	**12b**/**12b′**	<2:98	97:3	75
8	**6c**	nBuLi	1.5, 0 °C	**12c**/**12c′**	–	–	–[g]

[a] Measured by ^{1}H NMR spectroscopy before purification.
[b] Combined isolated yield of **12** and **12′**.
[c] Not calculated.
[d] 2.2 equiv.
[e] Quenched at −20 °C.
[f] Quenched with 1 M HCl at −30 °C.
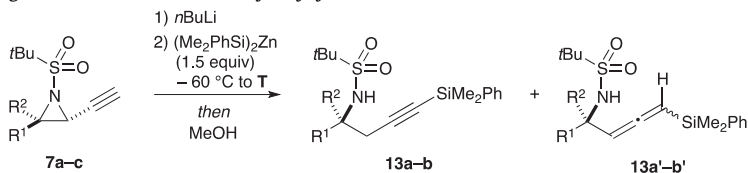[g] The starting material was recovered.

Table 3
Rearrangement of *N-tert*-butanesulfonylethynylaziridines **7**.

| Entry	7	T	Product	13/13'[a]	13'(dr)[a]	Yield[b] (%)
1	**7a**	−30 °C	**13a/13a'**	78:22	90:10	54
2	**7a**	0 °C	**13a/13a'**	93:7	nc	70
3[c]	**7b**	−30 °C	**13b/13b'**	98:2	nc	70
4	**7c**	−30 °C	**13a/13a'**	87:13	74:16	80

[a] Measured by ^{1}H NMR spectroscopy before purification.
[b] Combined isolated yield of **13** and **13'**.
[c] Quench was performed at −80 °C.

carried out at −30 °C (entry 3). Here, in sharp contrast with *N-tert*-butanesulfinyl substrates, no significant reactivity difference was noted between *trans* and *cis* configured ethynylaziridines. Thus, starting from *cis*-configured **7c**, the ring-opening products **13a** and **13a'** were isolated in 80% combined yield after rearrangement at −30 °C and treatment with MeOH (entry 4). Again, evidencing the formation of δ-amino α-silyl allenylzinc intermediates (**VI**), the regio- and stereoselectivity of the process was, for all the substrates, somewhat erratic and dependent on the workup conditions. Nevertheless, quenching the reactions with MeOH before aqueous workup favored in general the formation of homo-propargylamines **13**, as indicated in Table 3.

Finally, the reactivity against aldehydes of the δ-amino α-silyl allenylzinc intermediates (**VI**) obtained from ethynylaziridines was investigated. Despite extensive experimentation, condensation was not observed to significant extents (<10–15%) between the allenylzinc species obtained from *N*-sulfinylated ethynylaziridines **6a** or **6b** and neither propionaldehyde nor acetone. The allenylzinc intermediates arising from *N*-sulfonylated ethynylaziridines **7a** or **7b** were slightly more prone to react but still satisfactory results were not achieved. The most promising reaction was that of **7b** that afforded 1,3-aminodiol **14** as a single stereoisomer in 30% yield [21], by sequential ring opening by 1,2-metalate rearrangement and condensation with benzaldehyde (Scheme 7).
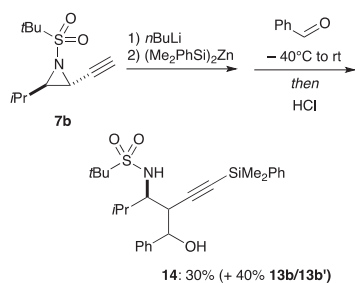
Scheme 7. Preparation of 1,3-aminoalcohol **14**.

4. Conclusion

To sum up, lithium alkynyl(disilyl)zincates derived from ethynylepoxides and ethynylaziridines undergo 1,2-migration of the organosilyl group with ring opening of the oxirane or aziridine ring by S$_N$i displacement. This protocol, initially developed for the rearrangement of ethynylepoxides, was successfully extended to aziridines and thus offers a straightforward approach to both δ-oxy- and δ-amino α-silyl allenylzinc intermediates. δ-Oxy α-silyl allenylzinc intermediates could undergo condensation with aldehydes or ketones to provide 1,3-diols in good yields and stereoselectivities. In contrast, the δ-amino α-silyl allenylzinc intermediates only reacted sluggishly. Understanding the reasons for this lack of reactivity and finding suitable conditions allowing for the preparation of 1,3-aminoalcohols with satisfactory yields using this chemistry are currently our research objectives in this promising field.

5. Experimental section

5.1. General methods

Experiments involving organometallic compounds were carried out in dried glassware under a positive pressure of dry argon or nitrogen using Schlenk techniques. THF was dried over Na/benzophenone and distilled before use. Commercial *n*BuLi (Sigma–Aldrich or Acros) was titrated with Sufferts's reagent [22]. Commercial ZnBr$_2$ was melted under nitrogen and immediately after cooling to room temperature dissolved in dry THF. Chloro(dimethyl)phenylsilane (Sigma–Aldrich) and all other reagents were of commercial quality and were used without purification. Flash column chromatography was performed using the indicated solvents on silica gel 60 (15–40 or 40–63 μm particle size) by Merck. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker AV 400. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual solvent resonance as the internal standard (CHCl$_3$: δ = 7.26 ppm for ^{1}H NMR and CDCl$_3$: δ = 77.16 ppm for ^{13}C NMR). Data are reported as

follows: chemical shift, multiplicity (br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant, and integration. Infrared (IR) spectra were recorded on a Bruker Tensor 27 ATR diamond spectrophotometer equipped with an ATR unit. High-resolution mass spectra (HRMS) were obtained using a Bruker micrOTOF instrument equipped with ESI source. Product characterization data for compounds **5** [10e] and **12′ a**−**c** [14,19b] have been previously reported.

5.1.1. Preparation of PhMe₂SiLi (~0.40 M in THF)

Under argon, Li (557 mg, 80.0 mmol) was washed with dry THF (3 × 5 mL). TMSCl (5.1 mL, 40.0 mmol) and THF (20 mL) were added. After 15 min of sonication, Li was washed with dry THF (4 × 5 mL) and then taken up in dry THF (40 mL). After an additional 5 min of sonication, PhMe₂SiCl (3.3 mL, 20.0 mmol) was added and the resulting mixture was sonicated for 2 h at 0 °C to give a dark red THF solution of PhMe₂SiLi (~0.40 M). The halogen−lithium exchange was assumed to be effective at 80% [23]. The solution was stored at −18 °C and used within 2 weeks.

5.1.2. Preparation of (PhMe₂Si)₂Zn (~0.16 M in THF)

To a stirred THF solution of PhMe₂SiLi (~0.40 M, 3.75 mL, 1.50 mmol) was added dropwise a THF solution of ZnBr₂ (1.0 M, 0.75 mL, 0.75 mmol) at −20 °C giving a dark green solution within 10 min.

5.2. Preparation of N-tert-butanesulfonylaziridines 7a−c

5.2.1. Typical procedure for the oxidation of N-tert-butanesulfinylaziridines (preparation of 7a)

To a stirred CH₂Cl₂ (40 mL) solution of *N*-*tert*-butanesulfinylaziridine **6a** (1.54 g, 7.22 mmol) at room temperature was added *m*-CPBA (≤77% assay, 1.96 g, 7.94 mmol). The mixture was stirred for 10 min and an aqueous saturated solution of Na₂S₂O₃ (40 mL) was added. After 30 min of stirring, the layers were separated and the aqueous layer was extracted with AcOEt (×2). The combined organics were washed with an aqueous saturated solution of NaHCO₃ (×3), water (×2), and brine, dried over anhydrous MgSO₄, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (cyclohexane/AcOEt = 90:10) afforded analytically pure **7a** (1.32 g, 80%) as a pale yellow solid. ¹H NMR (400 MHz, CDCl₃): δ = 3.00 (dd, J = 4.3, 2.0 Hz, 1H), 2.87 (dt, J = 8.2, 4.3 Hz, 1H), 2.33 (d, J = 2.0 Hz, 1H), 2.07−1.97 (m, 1H), 1.70 −1.59 (m, 3H), 1.48 (s, 9H), 0.99 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ = 78.3, 72.8, 60.6, 49.1, 34.8, 31.4, 24.1 (3C), 20.4, 13.8. IR (neat): 3244, 2967, 2935, 2875, 2361, 1301, 1123, 1018, 881, 729, 669 cm⁻¹. HRMS (ESI): *m/z* [M + Na]⁺ calcd for C₁₁H₁₉NNaO₂S, 252.1029; found, 252.1020.

5.2.2. Preparation of product 7b

The typical procedure was followed with **6b** (320 mg, 1.50 mmol). Purification by flash column chromatography on silica gel (cyclohexane/AcOEt = 70:30) afforded analytical pure **7b** (340 mg, 99%) as a pale yellow amorphous solid. ¹H NMR (400 MHz, CDCl₃): δ = 2.99 (dd, J = 4.3, 2.0 Hz, 1H), 2.79 (dd, J = 7.1, 4.3 Hz, 1H), 2.36 (d, J = 2.0 Hz,

1H), 1.94−1.85 (m, 1H), 1.47 (s, 9H), 1.11 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ = 77.9, 73.6, 60.5, 53.8, 32.8, 28.7, 24.2 (3C), 20.2, 19.0. IR (neat): 3245, 2977, 2929, 2361, 1303, 1131, 886, 703, 670 cm⁻¹. HRMS (ESI): *m/z* [M + Na]⁺ calcd for C₁₁H₁₉NNaO₂S, 252.1029; found, 252.1035.

5.2.3. Preparation of product 7c

The typical procedure was followed with **6c** (516 mg, 2.42 mmol). Purification by flash column chromatography on silica gel (cyclohexane/AcOEt) afforded analytical pure **7c** (500 mg, 90%) as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃): δ = 3.19 (dd, J = 6.8, 1.9 Hz, 1H), 2.86−2.76 (m, 1H), 2.24 (d, J = 1.9 Hz, 1H), 1.69−1.59 (m, 2H), 1.57−1.48 (m, 2H), 1.48 (s, 9H), 0.98 (t, J = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ = 72.7, 72.6, 59.6, 41.6, 35.0, 30.5, 24.1 (3C), 19.9, 13.8.

5.3. Typical procedure for the rearrangement of ethynylepoxides and ethynylaziridines (preparation of 13a (Table 3, entry 2))

*n*BuLi (2.40 M in hexanes, 0.23 mL, 0.55 mmol) was added dropwise at −80 °C to a THF (5 mL) solution of ethynylaziridine **7a** (115 mg, 0.50 mmol). The mixture was stirred for 1 h at this temperature, then warmed to −60 °C, and added via cannula to a THF solution of (PhMe₂Si)₂Zn (0.16 M, 4.7 mL, 0.75 mmol) at −60 °C. The reaction mixture was then warmed to 0 °C and stirred for 2 h. MeOH (1 mL) was added and the mixture was left to warm to room temperature. Et₂O (10 mL) was then added and the layers were separated. The aqueous layer was extracted with Et₂O (×2), and the combined organics were washed with water and brine, dried over MgSO₄, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (cyclohexane/AcOEt = 90:10) afforded analytical pure **13a** (127 mg, 70%) as a yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 7.62−7.60 (m, 2H), 7.44 −7.38 (m, 3H), 4.01 (d, J = 9.9 Hz, 1H, NH), 3.55−3.43 (m, 1H), 2.68 (AB system, J = 17.1, 5.7 Hz, 1H), 2.56 (AB system, J = 17.1, 4.4 Hz, 1H), 1.76−1.65 (m, 2H), 1.46−1.34 (m, 2H), 1.40 (s, 9H), 0.99 (t, J = 7.5 Hz, 3H), 0.41 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ = 137.2, 133.7 (2C), 129.5, 128.0 (2C), 104.2, 86.3, 60.0, 54.7, 28.4, 26.9, 24.4 (3C), 10.6, −0.67, −0.69 (one C missing). HRMS (ESI): *m/z* [M + Na]⁺ calcd for C₁₉H₃₁NNaO₂SSi, 388.1737; found, 388.1728.

5.3.1. Preparation of product 12a (Table 2, entry 6)

The typical procedure was followed with **6a** (107 mg, 0.50 mmol) but using an aqueous solution of HCl (1.0 M) for hydrolysis instead of MeOH. Purification by flash column chromatography on silica gel (cyclohexane/AcOEt = 90:10) afforded **12a** contaminated with **12a′** (114 mg, **12a**/**12a′** = 90:10, 65%). Data for **12a**: ¹H NMR (400 MHz, CDCl₃): δ = 7.64−7.58 (m, 2H), 7.40−7.30 (m, 3H), 3.57 (d, J = 8.1 Hz, 1H, NH), 3.39 (m, 1H), 2.72 (ABX system, J = 16.9, 5.8, 0.7 Hz, 1H), 2.56 (ABX system, J = 16.9, 4.7, 0.7 Hz, 1H), 1.65 −1.51 (m, 2H), 1.48−1.30 (m, 2H), 1.19 (s, 9H), 0.92 (t, J = 7.4 Hz, 3H), 0.40 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ = 137.3, 133.7 (2C), 129.5, 128.0 (2C), 104.8, 86.3, 56.0,

54.5, 37.2, 28.2, 22.8 (3C), 19.1, 14.0, −0.61, −0.65. IR (neat): 3209, 3069, 2957, 2870, 2173, 1939, 1457, 1248, 114, 1051, 835, 814, 779, 730, 698 cm^{-1}.

5.3.2. Preparation of product 13b (Table 3, entry 3)

The typical procedure was followed with **7b** (115 mg, 0.50 mmol) but methanolysis was carried out at −80 °C. Purification by flash column chromatography on silica gel (cyclohexane/AcOEt = 90:10) afforded analytical pure **13b** (127 mg, 70%) as a pale yellow oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.62–7.60 (m, 2H), 7.39–7.35 (m, 3H), 3.92 (d, J = 10.0 Hz, 1H, NH), 3.36 (dddd, J = 10.1, 6.5, 5.7, 4.6 Hz, 1H), 2.68 (AB system, J = 17.3, 5.7 Hz, 1H), 2.60 (AB system, J = 17.3, 4.7 Hz, 1H), 2.05 (dq, J = 13.5, 6.8 Hz, 1H), 1.40 (s, 9H), 1.02 (d, J = 6.8 Hz, 3H), 1.00 (d, J = 6.8 Hz, 3H), 0.40 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 137.2, 133.7 (2C), 129.5, 128.0 (2C), 104.6, 86.3, 60.2, 58.4, 32.2, 24.9, 24.5 (3C), 19.1 (2C), −0.7 (2C). IR (neat): 3275, 2959, 2360, 2341, 1939, 1305, 1122, 814 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for C$_{19}$H$_{31}$NNaO$_2$SSi, 388.1737; found, 388.1722.

5.4. Typical procedure for sequential rearrangement–condensation with aldehydes (preparation of 4)

nBuLi (2.40 M in hexanes, 0.23 mL, 0.55 mmol) was added dropwise at −80 °C to a THF (5 mL) solution of ethynylepoxide **1a** (69 mg, 0.50 mmol). The mixture was stirred for 1 h at this temperature, then warmed to −60 °C and added via cannula to a THF solution of (PhMe$_2$Si)$_2$Zn (0.16 M, 4.7 mL, 0.75 mmol) at −60 °C. The reaction mixture was warmed to −20 °C for 1.5 h and then to 0 °C for 45 min before being cooled to −80 °C. Propionaldehyde (180 μL, 2.5 mmol) was added at this temperature and the mixture was warmed to −40 °C and stirred for 2.5 h. After warming to room temperature, aqueous HCl (1.0 M, 10 mL) and Et$_2$O (10 mL) were added and the layers were separated. The aqueous layer was extracted with Et$_2$O (×2) and the combined organics were washed with water and brine, dried over MgSO$_4$, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (n-pentane/Et$_2$O = 85:15) afforded analytical pure **4** (129 mg, 78%, 95:5 dr) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.66–7.61 (m, 2H), 7.43–7.35 (m, 3H), 3.97 (dd, J = 8.7, 3.1 Hz, 1H), 3.84 (m, 1H), 2.74 (dd, J = 8.7, 2.1 Hz, 1H), 1.75–1.25 (m, 7H), 1.00 (t, J = 7.4 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H), 0.40 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 137.3, 133.7 (2C), 129.6, 128.0 (2C), 105.7, 88.4, 72.6, 71.8, 44.2, 43.1, 29.0, 22.9, 20.6, 12.4, 11.9, 10.7, −0.6 (2C). IR (neat): 3393, 3070, 2961, 2929, 2876, 2169, 1719, 1462, 1428, 1250, 115, 837, 817, 780, 731, 700 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for C$_{20}$H$_{32}$NaO$_2$Si, 355.2064; found, 355.2066.

5.4.1. Preparation of 1,3-aminoalcohol 14

The typical procedure was followed with **7b** (115 mg, 0.50 mmol) and benzaldehyde (254 μL, 2.5 mmol). Purification by flash column chromatography on silica gel (n-pentane/Et$_2$O = 90:10–70:30) afforded analytical pure **14** (71 mg, 30%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.53–7.51 (m, 2H), 7.42–7.28 (m, 8H), 4.98 (m, 1H), 4.0 (d, J = 10.2 Hz, 1H, NH), 3.43 (ddd, J = 10.2, 7.4, 2.9 Hz, 1H),

3.14 (d, J = 5.5 Hz, 1H, OH), 2.94 (dd, J = 7.4, 4.2 Hz, 1H), 2.28 (septd, J = 6.9, 2.9 Hz, 1H), 1.33 (s, 9H), 0.97 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 0.28 (s, 3H), 0.27 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 141.5, 136.9, 133.7 (2C), 129.5, 128.3 (2C), 128.0 (2C), 127.8, 126.5 (2C), 105.1, 90.0, 71.8, 60.7, 59.5, 48.1, 31.0, 24.6 (3C), 21.6, 17.2, −0.8, −0.9. IR (neat): 3490, 3278, 3060, 2964, 2170, 1427, 1297, 1115, 1018, 907, 819, 727 cm^{-1}. HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{26}$H$_{37}$NNaO$_3$SSi, 494.2156; found, 494.2166.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.crci.2017.02.001.

References

[1] For selected recent reviews on the use of allenylmetals in synthesis:
(a) J.A. Marshall, J. Org. Chem. 72 (2007) 8153;
(b) S. Yu, S. Ma, Angew. Chem., Int. Ed. 51 (2012) 3074;
(c) C.-H. Ding, X.-L Hou, Chem. Rev. 111 (2011) 1914.
[2] J.A. Marshall, Synthesis and reactions of allenylzinc reagents, in: Z. Rappoport (Ed.), Patai's Chemistry of Functional Groups; Organozinc Compounds (2007), John Wiley & Sons, Ltd, Chichester, 2009.
[3] (a) C. Botuha, F. Chemla, F. Ferreira, A. Pérez-Luna, B. Roy, New J. Chem. 31 (2007) 1552;
(b) C. Botuha, F. Chemla, F. Ferreira, J. Louvel, A. Pérez-Luna, Tetrahedron: Asymmetry 21 (2010) 1147.
[4] For theoretical support, see: P. Quinio, C. François, A. Escribano Cuesta, A.K. Steib, F. Achrainer, H. Zipse, K. Karaghiosoff, P. Knochel Org. Lett. 17 (2015) 1010.
[5] J. Bejjani, C. Botuha, F. Chemla, F. Ferreira, S. Magnus, A. Pérez-Luna, Organometallics 31 (2012) 4876.
[6] Recent applications in synthesis from our group: (a) A. Voituriez, F. Ferreira, F. Chemla, J. Org. Chem. 72 (2007) 5358;
(b) A. Voituriez, F. Ferreira, A. Pérez-Luna, F. Chemla, Org. Lett. 9 (2007) 4705;
(c) F. Ferreira, C. Botuha, F. Chemla, A. Pérez-Luna, J. Org. Chem. 74 (2009) 2238;
(d) C. Séguin, F. Ferreira, C. Botuha, F. Chemla, A. Pérez-Luna, J. Org. Chem. 74 (2009) 6986;
(e) B. Hélal, F. Ferreira, C. Botuha, F. Chemla, A. Pérez-Luna, Synlett (2009) 3115;
(f) J. Louvel, C. Botuha, F. Chemla, E. Demont, F. Ferreira, A. Pérez-Luna, Eur. J. Org. Chem. (2010) 2921;
(g) J. Louvel, F. Chemla, E. Demont, F. Ferreira, A. Pérez-Luna, A. Voituriez, Adv. Synth. Catal. 353 (2011) 2137;
(h) J. Louvel, F. Chemla, E. Demont, F. Ferreira, A. Pérez-Luna, Org. Lett. 13 (2011) 6452.
[7] Allenylboron reagents: (a) T. Leung, G. Zweifel, J. Am. Chem. Soc. 96 (1974) 5620;
(b) G. Zweifel, S.J. Blacklund, T. Leung, J. Am. Chem. Soc. 100 (1978) 5561;
(c) M.M. Midland, J. Org. Chem. 42 (1977) 2650;
(d) D. Carrié, B. Carboni, M. Vaultier, Tetrahedron Lett. 36 (1995) 8209.
[8] Allenylaluminium reagents: N.R. Pearson, G. Hanh, G. Zweifel J. Org. Chem. 47 (1982) 3364.
[9] Allenylzirconium reagents: (a) E. Negishi, K. Akiyoshi, B. O'Connor, K. Takagi, G. Wu, J. Am. Chem. Soc. 111 (1989) 3089;
(b) T. Luker, R.J. Whitby, Tetrahedron Lett. 35 (1994) 785;
(c) G.J. Gordon, R.J. Whitby, Chem. Commun. (1997) 1321;
(d) J. Steck, A.R. Henderson, R.J. Whitby, Tetrahedron Lett. 53 (2012) 112.
[10] Allenylzinc reagents: (a) T. Katsuhira, T. Harada, K. Maejima, A. Osada, A. Oku, J. Org. Chem. 58 (1993) 6166;

(b) T. Harada, T. Katsuhira, A. Osada, K. Iwazaki, K. Maejima, A. Oku, J. Am. Chem. Soc. 118 (1996) 11377;
(c) T. Harada, E. Kutsuwa, J. Org. Chem. 68 (2003) 6716;
(d) J.A. Marshall, G.S. Barley, J. Org. Chem. 59 (1994) 7169;
(e) A. Denichoux, L. Debien, M. Cyklinsky, M. Kaci, F. Chemla, F. Ferreira, A. Pérez-Luna, J. Org. Chem. 78 (2013) 134.

[11] M. Shimizu, T. Kurahashi, H. Kitagawa, T. Hiyama, Org. Lett. 5 (2003) 225.

[12] The reaction between $(Me_2PhSi)_3ZnLi$ and propargylic mesylates having terminal alkynes was also contemplated. In that case, direct S_N2' displacement seemed to be the major operating pathway, see Ref. [10b].

[13] (a) A. Denichoux, F. Ferreira, F. Chemla, Org. Lett. 6 (2004) 3509;
(b) A. Denichoux, M. Cyklinsky, F. Chemla, F. Ferreira, A. Pérez-Luna, Synlett (2013) 1001.

[14] V.N. Bochatay, Y. Sanogo, F. Chemla, F. Ferreira, O. Jackowski, A. Perez-Luna, Adv. Synth. Catal. 357 (2015) 2809.

[15] The configuration of diol **4** was determined by ^1H NMR analysis of the cyclic 6-membered acetal obtained from **4** and dimethoxymethane.

[16] Our studies were carried out with racemic *N-tert*-butanesulfinyle-thynylaziridines, but these substrates can also be prepared in enantiomerically pure form starting from enantiopure *N-tert*-buta-nesulfinylimines. For relevant references, see: (a) F. Chemla,

F. Ferreira, J. Org. Chem. 69 (2004) 8244;
(b) F. Ferreira, M. Audouin, F. Chemla, Chem.—Eur. J. 11 (2005) 5269.

[17] The ring opening of ethynyloxiranes on reaction with nBu$_3$ZnLi (2.4 equiv) has been previously reported and it involves direct S_N2' displacement to some extent, see Ref. [10d].

[18] It is documented that nBu$_3$ZnLi can abstract acetylenic protons from propargylic mesylates and propargylic ethers under similar conditions; 2 equiv of zincate were used, but this issue was not discussed in any detail, see Ref. [10a].

[19] Optimization of the regio- and stereoselectivity was not pushed further because we have previously disclosed more efficient synthetic strategies to access the same products: (a) (**12**) M. Cyklinsky, C. Botuha, F. Chemla, F. Ferreira, A. Pérez-Luna, Synlett (2011) 2681;
(b) (**12′**) V.N. Bochatay, Z. Neouchy, F. Chemla, F. Ferreira, O. Jackowski, A. Perez Luna, Synthesis 48 (2016) 3287 and Ref. [14].

[20] This surprising difference of reactivity between *trans* and *cis* isomers was further confirmed by an experiment wherein a 1:1 mixture of **6a** (0.5 equiv) and **6c** (0.5 equiv) was treated under the rearrangement conditions (0 °C): ring opening of **6a** was complete, whereas **6c** was recovered intact.

[21] The relative configurations of product **14** were not determined.

[22] J. Suffert, J. Org. Chem. 54 (1989) 509.

[23] M. Oestrich, B. Weiner, Synlett (2004) 2139.