Asymmetric Syntheses of New Functionalized β-Amino Alcohols via Diastereoselective Addition of Organometallic Reagents onto Oxazolidines

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Diastereoselective reactions between (*S*)-phenylglycinol-derived oxazolidines and two unsaturated organolithium reagents afforded chiral β-amino alcohols having vinyl and alkynylsilane moieties. When the same reactions were performed in the presence of titanium isopropoxide, a dramatic change of regioselectivity was observed, from the α- to the γ-position, thus producing β-amino alcohols with allyl or allenylsilane functions. A rationalization of the observed diastereoselectivity was suggested for each case.

Diastereoselective additions of Grignard reagents to imines or oxazolidines derived from β-amino alcohols are well documented,[1] but works related to similar reactions with organolithium derivatives are scarcer. Pioneering works in this field[2] have been concerned with the diastereoselective addition of alkyl or aryllithium reagents onto oxazolidines derived from amino alcohol and especially from phenylglycinol. As part of a program aimed at emphasizing the efficiency of asymmetric syntheses of pipecolic acid derivatives from functionalized β-amino alcohols,[3] we have recently explored[4] the reactions between unsaturated organolithium reagents and oxazolidines **1**.

Results

Condensation of (*S*)-phenylglycinol and various aldehydes quantitatively afforded oxazolidines **1a**−**f**. We observed that reaction of the allyltrimethylsilane-derived lithium reagent[5] **2** with these oxazolidines gave β-amino alcohols **3 a**−**f**, whose vinylsilane moiety showed an *E*-geometry. In the same way, the lithiated anion[2g] derived from propynyltrimethylsilane **4** reacts with compound **1** to afford β-amino alcohols **5 a**−**e** with an alkynyl appendage (Scheme 1).

Oxazolidines with various R substituents were reacted with the lithium derivatives **2** and **4**, and the results are listed in Table 1. Yields are substantially lowered in the case of R = Me, and the corresponding diastereoisomeric ratios have not been determined. In all cases, the major isomer shows the absolute configuration for the carbon bearing the R-group indicated in Scheme 1.

As shown in Table 2, which shows data for experiments performed on oxazolidines **1a** (R = Ph), anion **2** was best generated with 5 equiv of *sec*-BuLi containing an equimolar amount of tetramethylethylenediamine at −78 °C in THF (entry 2). As regards medium effects, the beneficial influence of TMEDA can be ascribed to the fact that it favors the existence of unaggregated lithium species.[6]

A change of regioselectivity was found when the above reactions were performed in the presence of titanium isopropoxide.[7] In this case, addition of Ti(O-*i*-Pr)$_4$ onto the organolithium reagents **2** and **4** transforms these species into covalent allyl or propargyl titanium derivatives **6** and **7**, respectively (Scheme 2).

The action of these organometallic compounds onto oxazolidines **1** thus produces compounds **8** and **9**, as described in Scheme 3.

The use of the titanium derivative **6** gives rise to the formation of β-amino alcohols possessing an allylsilane function. Thus, substrates **1c** and **1e** (R = Et and *i*-Pr) reacted with this reagent and afforded allylsilanes **8c** (50% yield, dr = 95/5) and **8e** (48% yield, dr = 77/23),

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Scheme 1

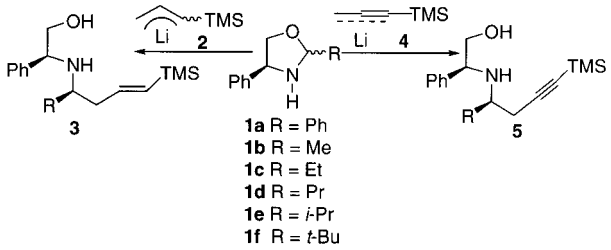


Table 1. Reaction between Oxazolidines 1 with Organolithium Reagents 2[a] and 4[b]

entry	product	R	yield (%)	dr[(c)]
1	**3a**	Ph	81	92/8
2	**3b**	Me	26	
3	**3c**	Et	45	80/20
4	**3d**	Pr	46	80/20
5	**3e**	*i*-Pr	75	90/10
6	**3f**	*t*-Bu	80	95/5
7	**5a**	Ph	70	80/20
8	**5b**	Me	17	
9	**5c**	Et	55	90/10
10	**5d**	Pr	55	90/10
11	**5e**	*i*-Pr	68	95/5

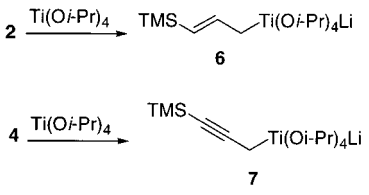
[a] $(CH_3)_3SiCH_2CH{=}CH_2$ (5 equiv), *sec*-BuLi (5 equiv), TMEDA (5 equiv). [b] $(CH_3)_3SiC{\equiv}CCH_3$ (5 equiv), *sec*-BuLi (5 equiv), TMEDA (5 equiv). [c] Diastereoisomeric ratios were determined by ^{1}H NMR analysis of the crude mixture.

Table 2. Diastereoselective Addition of the Lithium Derivative 2 on Compound 1a (R = Ph)

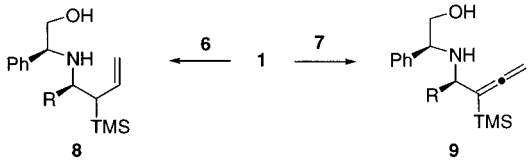
entry	solvent	additive	yield of **3a** (%)	dr of **3a**[f]
1	THF	TMEDA[a]	60	90/10
2	THF	TMEDA[b]	81	92/8
3	THF	HMPA[c]	62	56/44
4	THF	none[d]	72	84/16
5	THF	PMDTA[e]	73	84/16
6	Et_2O	TMEDA[b]	59	72/28

[a] *sec*-BuLi (2.5 equiv), TMEDA (2.5 equiv). [b] *sec*-BuLi (5 equiv), TMEDA (5 equiv). [c] *sec*-BuLi (2.5 equiv), HMPA/THF (10% v/v). [d] *sec*-BuLi (5 equiv). [e] *sec*-BuLi (5 equiv), PMDTA (1,1,4,7,7-pentamethylenetriamine, 5 equiv). [f] Diastereoisomeric ratios were determined by ^{1}H NMR analysis of the crude mixture.

Scheme 2



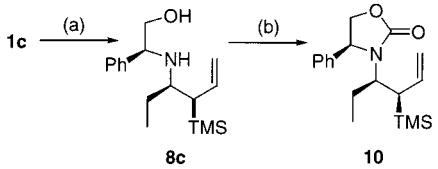
Scheme 3



respectively, in which two stereogenic centers were created. The action of triphosgene on compound **8c** afforded oxazolidinone **10** whose absolute configuration was determined previously by X-ray analysis.[4]

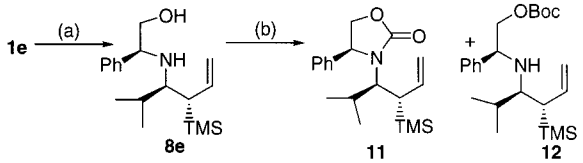
Major isomer **8e** was isolated from the mixture of four isomers obtained in the case of the isopropyl substituent. The action of triphosgene being unsuccessful, amino alcohol **8e** was treated with Boc_2O in the presence of DMAP to obtain oxazolidinone **11**, together with the O−Boc derivative **12**. The absolute configuration of compound **8e** was deduced from X-ray analysis[8] of compound **11** (Scheme 5).

Scheme 4



Reaction conditions: (a) **6**, 50%; (b) $(CCl_3O)_2CO$, 6 N NaOH, CH_2Cl_2, 53%.

Scheme 5

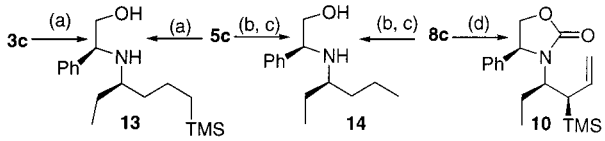


Reaction conditions: (a) **6**, 48%; (b) Boc_2O, DMAP, AcOEt, 42% (for **11**) and 46% (for **12**).

Table 3. Diastereoselective Addition of Organotitanium Derivative 7 onto Oxazolidine 1

product	R	yield (%)	diastereoisomeric ratio
9a	Ph	78	>95/5
9c	Et	70	90/10
9e	*i*-Pr	55	90/10

Scheme 6



Reaction conditions: (a) H_2, Pd/C, abs EtOH, 2 h, 57% from **3c** and 67% from **5c**; (b) *n*-Bu_4NF, THF, 1 h; (c) H_2, Pd/C, abs EtOH, 40 min, 89% from **5c** and 56% from **8c**; (d) $(CCl_3O)_2CO$, 6 N NaOH, CH_2Cl_2, 53%.

Reaction of the organotitanium reagent **7** with oxazolidines **1a**, **1c**, and **1e** (Scheme 3) led to the formation of the β-amino alcohols **9a**, **9c**, and **9e**, respectively, possessing an allenylsilane function (Table 3). The absolute configuration of compound **9a** was determined from X-ray analysis.[4]

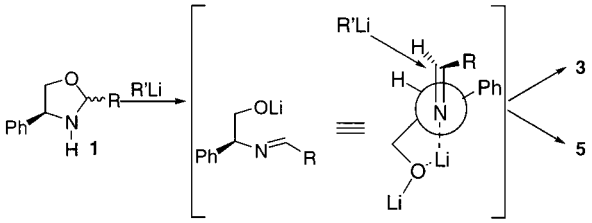
The absolute configuration of the β-amino alcohols having either a vinylsilane function **3** or an alkynylsilane moiety **5** was determined by a chemical correlation (Scheme 6) from the known compound **10**. Hydrogenation of compounds **3c** and **5c** furnished the same product **13**; desilylation followed by hydrogenation of products **8c** and **5c** gave the same amino alcohol **14**, thus disclosing an *R* absolute configuration for the stereocenter in **5c**. Compound **13**, which was obtained from **3c** or **5c**, also exhibits an *R* configuration for the created stereocenter in **3c**.

Discussion

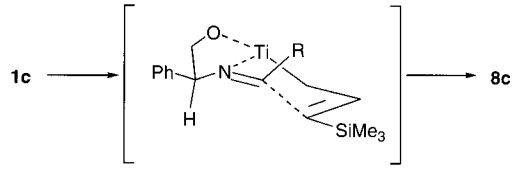
The preceding results show that this methodology can be applied for the synthesis of various amino alcohols

(8) The X-ray analysis was performed by Dr. J.-C. Daran in the Laboratoire de Chimie de Coordination at Toulouse, France.

Scheme 7



Scheme 8



possessing an unsaturated silane moiety. However, a limitation was found when a 2-methyl-substituted oxazolidine was used as a substrate (see entries 2 and 8 in Table 1). This unsatisfactory result can be ascribed to the instability of such oxazolidine[2b] whose methyl moiety is very sensitive to a base-mediated deprotonation.

Rationalization of the results (cf Scheme 1) obtained with the organolithium derivatives **2** or **4** can be made on the basis of the model described by Block.[1a] A first equivalent of organolithium compound reacts with the oxazolidine to give an imine with an *E*-geometry, and a second equivalent attacks this intermediate in an anti position relative to the phenyl group, as depicted in Scheme 7.

The change of regioselectivity observed with titanium isopropoxide can be ascribed to the nature of the organometallic species. As described above, the titanium species **6** afforded amino alcohols **8c** and **8e** from oxazolidines **1c** and **1e** (Schemes 4 and 5). The complete stereoselectivity observed during the formation of compound **8c** can be rationalized by a chair cyclic transition state, analogous to the transition state involved in the case of addition of allyltitanium derivatives onto imines[9] (Scheme 8). In such a fixed conformation, the pseudoaxial geometry of the ethyl group of the imine and the chelation between titanium, nitrogen, and oxygen atoms explain the favored attack on the *Si* face of the imine. In this transition state, the bulky phenyl group occupies a pseudoequatorial position.

The selectivity observed during the reaction with the titanium derivative **7** could hardly be explained by a chairlike transition state, which is incompatible with the geometry of the triple bond. An open transition state analogous to those involved in the attack of organolithium derivative (Scheme 7) can be also operative during the formation of β-amino alcohols **9**. The excellent stereoselectivity that results from such open transition states was already pointed out.[1a]

In conclusion, we have synthesized a large range of β-amino alcohols variously functionalized. These compounds present considerable interest as starting materials in asymmetric syntheses. Further studies on the synthetic applications of these compounds are actively underway.

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Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra ($CDCl_3$ solution) were recorded on a Bruker ARX 250 spectrometer at 250 and 62.9 MHz, respectively; chemical shifts are reported in ppm from TMS. Optical rotations were determined with a Perkin-Elmer 141 instrument. All reactions were carried out under argon. Column chromatography was performed on silica gel, 230−400 mesh, by using various mixtures of ethyl acetate (AcOEt) and petroleum ether (PE). Melting points are uncorrected. THF was distilled from sodium/benzophenone ketyl. THF was degassed for 30 min with argon before use. Compositions of stereoisomeric mixtures were determined by NMR analysis on crude products before any purification.

General Procedure for the Preparation of Oxazolidines. The required aldehyde (5.85 mmol) was added dropwise to a solution of (2*S*)-phenylglycinol (800 mg, 5.85 mmol) in THF (12 mL) in the presence of $MgSO_4$. The mixture was stirred at room temperature for 1 h (for **1e**) or 2 h (for **1f**) and filtered over Celite 545. The solution was concentrated under reduced pressure to afford a mixture of cis and trans oxazolidines in a quantitative yield. This mixture was engaged in the next step without further purification.

(4*S*)-2-Isopropyl-4-phenyloxazolidine (1e). Oil. ^{1}H NMR: 7.23−7.11 (m, 5H), 4.33 (t, J = 7.0 Hz, 0.35H), 4.26−4.19 (m, 1.65H), 4.12 (dd, J = 7.2 and 8.0 Hz, 0.35H), 3.99 (t, J = 7.5 Hz, 0.65H), 3.54−3.46 (m, 1H), 2.03 (m, 1H), 1.83−1.66 (m, 1H), 1.00−0.83 (m, 6H).^{13}C NMR: 142.4, 140.4, 128.9, 128.7, 127.9, 127.2, 126.9, 126.5, 97.7, 97.3, 72.7, 71.8, 62.5, 60.8, 32.7, 32.3, 18.5, 18.3, 18.2.

(4*S*)-2-*tert*-Butyl-4-phenyloxazolidine (1f). Oil. ^{1}H NMR: 7.28−7.16 (m, 5H), 4.38 (t, J = 6.6 Hz, 0.4H), 4.29 (t, J = 7.7 Hz, 0.6H), 4.27 (s, 0.4H), 4.26 (s, 0.6H), 4.19−4.13 (m, 0.4H), 4.07 (t, J = 7.5 Hz, 0.6H), 3.60 (dd, J = 6.5 and 8.1 Hz, 0.4H), 3.52 (t, J = 7.7 Hz, 0.6H), 1.94 (s, 1H), 0.95−0.92 (m, 9H). ^{13}C NMR: 142.3, 140.2, 128.9, 128.7, 128.5, 127.9, 127.3, 127.0, 126.6, 99.7, 99.3, 73.1, 72.2, 62.4, 61.0, 34.4, 33.8, 25.4, 25.3.

General Procedure for the Syntheses of β-Amino Alcohols 3a−f and 5a−e. *sec*-Butyllithium (1.3 M in cyclohexane, 3.4 mL, 4.40 mmol) was added at −78 °C to a solution of allyltrimethylsilane (0.70 mL, 4.40 mmol) (for **3**) or propyntrimethylsilane (0.65 mL, 4.40 mmol) (for **5**) and tetramethylethylenediamine (0.65 mL, 4.40 mmol) in THF (8 mL). After stirring for 15 min at −78 °C and 15 min at room temperature, the mixture was cooled at −78 °C and a solution of oxazolidine (0.88 mmol) in THF (4 mL) was added dropwise. After an additional stirring of 20 min at this temperature, the mixture was allowed to reach 0 °C in 1 h, and the reaction was then quenched by addition of an aqueous solution saturated with NH_4Cl (15 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL), and the organic layers were combined, dried over K_2CO_3, and evaporated. The residue was then chromatographed on silica gel.

[2*S*,2(1*S*)]-2-Phenyl-2-(1-phenyl-4-trimethylsilanylbut-3-enylamino)ethanol (3a). Oil (AcOEt/PE, 10:90). Yield: 81%. ^{1}H NMR: 7.27−7.16 (m, 10H), 5.86 (dt, J = 6.5 and 18.5 Hz, 1H), 5.65 (d, J = 18.5 Hz, 1H), 3.84 (dd, J = 4.5 and 7.0 Hz, 1H), 3.76−3.69 (m, 2H), 3.50 (dd, J = 7.0 and 10.5 Hz, 1H), 2.59−2.41 (m, 4H), 0.00 (s, 9H). ^{13}C NMR: 143.8, 143.1, 141.3, 133.8, 128.6, 128.3, 127.4, 126.2, 126.1, 65.6, 61.4, 59.8, 44.5, −1.2.

[2(1*R*),2*S*]-2-(1-Methyl-4-trimethylsilanylbut-3-enylamino)-2-phenylethanol (3b). Oil (AcOEt/PE, 15:85). Yield: 26%. ^{1}H NMR: 7.30−7.21 (m, 5H), 5.93 (dt, J = 6.6 and 18.5 Hz, 1H), 5.65 (d, J = 18 Hz, 1H), 3.83 (dd, J = 4.4 and 8.6 Hz, 1H), 3.61 (dd, J = 4.4 and 10.6 Hz, 1H), 3.40 (dd, J = 8.6 and 10.6 Hz, 1H), 2.70−2.63 (m, 1H), 2.50−2.20 (m, 2H), 2.31−2.22 (m, 1H), 2.14−2.03 (m, 1H), 0.93 (d, J = 7. 5 Hz, 3H), 0.01−0.04 (m, 9H). ^{13}C NMR: 143.6, 141.6, 133.5, 128.7, 127.6, 127.2, 66.8, 61.9, 50.1, 43.7, 21.7, −1.1.

[2(1*R*),2*S*]-2-(1-Ethyl-4-trimethylsilanylbut-3-enylamino)-2-phenylethanol (3c). Oil (AcOEt/PE, 15:85). Yield: 45%. $[\alpha]^{20}_D$: +87 (*c* 0.9, $CHCl_3$). ^{1}H NMR: 7.31−7.17 (m, 5H), 5.94 (dt, J = 6.5 and 18.5 Hz, 1H), 5.67 (dd, J = 0.9 and 18.5 Hz, 1H), 3.85 (dd, J = 4.6 and 8.6 Hz, 1H), 3.60 (dd, J = 4.6

and 10.5 Hz, 1H), 3.43 (dd, J = 8.6 and 10.5 Hz, 1H), 2.75 (bs, 2H), 2.48−2.39 (m, 1H), 2.25−2.18 (m, 2H), 1.40−1.20 (m, 2H), 0.76 (t, J = 7.4 Hz, 3H), 0.00 (s, 9H).^{13}C NMR: 143.4, 141.2, 133.5, 128.6, 127.6, 127.3, 66.8, 61.8, 55.5, 40.5, 27.6, 10.4, −1.1. Anal. Calcd for $C_{17}H_{29}NOSi$: C, 70.04; H, 10.33; N, 4.80. Found: C, 69.92; H, 10.15; N, 4.61.

[2*S*,2(1*R*)]-2-Phenyl-2-(1-propyl-4-trimethylsilanylbut-3-enylamino)ethanol (3d). Oil (AcOEt/PE, 20:80). Yield: 46%. $[\alpha]^{20}_D$: +84 (*c* 1.4, $CHCl_3$). ^{1}H NMR: 7.32−7.18 (m, 5H), 5.94 (dt, J = 6.6 and 18.5 Hz, 1H), 5.67 (dt, J = 1.0 and 18.5 Hz, 1H), 3.83 (dd, J = 4.5 and 8.6 Hz, 1H), 3.60 (dd, J = 4.5 and 10.6 Hz, 1H), 3.42 (dd, J = 8.6 and 10.6 Hz, 1H), 2.52−2.48 (m, 1H), 2.35 (bs, 2H), 2.22−2.17 (m, 2H), 1.30−1.11 (m, 4H), 0.73 (t, J = 7.0 Hz, 3H), 0.00 (s, 9H).^{13}C NMR: 143.6, 141.4, 133.5, 128.6, 127.6, 127.3, 66.9, 61.7, 53.7, 41.1, 37.3, 19.1, 14.2, −1.1. IR: 3326, 2956, 1615, 1454 cm^{-1}.

[2*S*,2(1*R*)]-2-Phenyl-2-(1-isopropyl-4-trimethylsilanylbut-3-enylamino)ethanol (3e). Oil (AcOEt/PE, 15:85). Yield: 75%. $[\alpha]^{20}_D$: +96 (*c* 1.5, $CHCl_3$). ^{1}H NMR: 7.30−7.17 (m, 5H), 5.96 (dt, J = 6.5 and 18.5 Hz, 1H), 5.67 (dt, J = 1.2 and 18.5 Hz, 1H), 3.80 (dd, J = 4.5 and 8.5 Hz, 1H), 3.59 (dd, J = 4.5 and 10.5 Hz, 1H), 3.40 (dd, J = 8.5 and 10.5 Hz, 1H), 2.70 (bs, 1H), 2.32−2.28 (m, 1H), 2.22−2.17 (m, 2H), 1.65−1.52 (m, 2H), 0.79 (d, J = 6.7 Hz, 3H), 0.73 (d, J = 6.7 Hz, 3H), 0.00 (m, 9H). ^{13}C NMR: 144.7, 141.7, 133.0, 128.7, 127.6, 127.5, 67.1, 62.1, 59.7, 38.5, 31.0, 18.8, 18.5, −1.0. Anal. Calcd for $C_{18}H_{31}NOSi$: C, 70.76; H, 10.23; N, 4.58. Found: C, 70.61; H, 10.23; N, 4.41.

[2(1*R*),2*S*]-2-(1-*tert*-Butyl-4-trimethylsilanylbut-3-enylamino)-2-phenylethanol (3f). Oil (AcOEt/PE, 15:85). Yield: 80%. $[\alpha]^{20}_D$: +119 (*c* 0.9, $CHCl_3$). ^{1}H NMR: 7.29−7.16 (m, 5H), 6.09−5.97 (m, 1H), 5.68−5.60 (m, 1H), 3.88 (dd, J = 4.6 and 8.5 Hz, 1H), 3.58 (dd, J = 4.6 and 10.6 Hz, 1H), 3.44 (dd, J = 8.5 and 10.6 Hz, 1H), 2.80−2.30 (m, 2H), 2.49−2.40 (m, 1H), 2.19−2.07 (m, 2H), 0.79 (s, 9H), 0.02−0.00 (m, 9H). ^{13}C NMR: 147.0, 141.3, 131.4, 128.5, 127.9, 127.5, 67.2, 62.7, 62.4, 39.3, 35.2, 27.2, −1.5.

[2*S*,2(1*S*)]-2-Phenyl-2-(1-phenyl-4-trimethylsilanylbut-3-ynylamino)ethanol (5a). Oil (AcOEt/PE, 20:80). Yield: 70%. ^{1}H NMR: 7.23−7.05 (m, 10H), 3.79−3.71 (m, 2H), 3.63 (dd, J = 4.5 and 10.7 Hz, 1H), 3.42 (dd, J = 7.2 and 10.7 Hz, 1H), 2.70−2.55 (m, 2H), 2.50 (t, J = 6.1 Hz, 2H), 0.0 (s, 9H). ^{13}C NMR: 142.9, 140.9, 128.6, 128.3, 127.5, 127.2, 127.0, 104.1, 87.6, 66.0, 61.6, 58.4, 28.3, 0.0. Anal. Calcd for $C_{21}H_{27}NOSi$: C, 74.73; H, 8.06; N, 4.15. Found: C, 74.30; H, 8.25; N, 3.98.

[2(1*R*),2*S*]-2-(1-Methyl-4-trimethylsilanylbut-3-ynylamino)-2-phenylethanol (5b). Solid (AcOEt/PE, 40:60). Yield: 17%. Mp: 94 °C. $[\alpha]^{20}_D$: +94 (*c* 0.6, $CHCl_3$). ^{1}H NMR: 7.31−7.16 (m, 5H), 3.80 (dd, J = 4.5 and 8.7 Hz, 1H), 3.60 (dd, J = 4.5 and 10.5 Hz, 1H), 3.40 (dd, J = 8.7 and 10.5 Hz, 1H), 2.80−2.68 (m, 1H), 2.37−2.17 (ABX system, J^{AB} = 17 Hz, J^{AX} = 4.7 Hz, J^{BX} = 5.8 Hz, 2H), 2.40−1.90 (m, 2H), 1.02 (d, J = 7.5 Hz, 3H), 0.04 (s, 9H). ^{13}C NMR: 141.3, 128.7, 127.7, 127.2, 104.3, 87.0, 67.1, 61.9, 49.2, 27.0, 21.6, 0.2. Anal. Calcd for $C_{16}H_{25}NOSi$: C, 69.76; H, 9.15; N, 5.08. Found: C, 69.92; H, 9.11; N, 4.86.

[2(1*R*),2*S*]-2-(1-Ethyl-4-trimethylsilanylbut-3-ynylamino)-2-phenylethanol (5c). Solid (AcOEt/PE, 20:80). Yield: 55%. Mp: 78 °C. $[\alpha]^{20}_D$: +108 (*c* 1.1, $CHCl_3$). ^{1}H NMR: 7.22−7.08 (m, 5H), 3.74 (dd, J = 4.4 and 8.6 Hz, 1H), 3.52 (dd, J = 4.4 and 10.6 Hz, 1H), 3.32 (dd, J = 8.6 and 10.6 Hz, 1H), 2.40−2.32 (m, 1H), 2.36−2.07 (ABX system, J^{AB} = 16.6 Hz, J^{AX} = 4.2 Hz, J^{BX} = 5.5 Hz, 2H), 1.99 (bs, 2H), 1.38−1.26 (m, 2H), 0.69 (t, J = 7.5 Hz, 3H), 0.0 (s, 9H). ^{13}C NMR: 141.1, 128.5, 127.5, 127.2, 104.2, 88.0, 67.2, 61.6, 54.4, 27.7, 24.3, 10.5, 0.3. Anal. Calcd for $C_{17}H_{27}NOSi$: C, 70.53; H, 9.40; N, 4.83. Found: C, 70.44; H, 9.57; N, 4.82.

[2*S*,2(1*R*)]-2-Phenyl-2-(1-propyl-4-trimethylsilanylbut-3-ynylamino)ethanol (5d). Solid (AcOEt/PE, 20:80). Yield: 55%. Mp: 66 °C. $[\alpha]^{20}_D$: +99 (*c* 1.1, $CHCl_3$). ^{1}H NMR: 7.20−7.06 (m, 5H), 3.94 (dd, J = 4.5 and 8.6 Hz, 1H), 3.73 (dd, J = 4.5 and 10.5 Hz, 1H), 3.32 (dd, J = 10.5 and 8.5 Hz, 1H), 2.49−2.40 (m, 1H), 2.30 (ABX, J^{AB} = 16.8 Hz, and J^{AX} = 5.6 Hz, 1H), 2.20 (bs, 2H), 2.10 (ABX, J^{AB} = 16.8 and J^{BX} = 4.2 Hz, 1H), 1.33−1.04 (m, 4H), 0.66 (t, J = 7.4 Hz, 3H), 0.00 (s, 9H). ^{13}C NMR: 141.1, 128.6, 127.6, 127.3, 104.4, 87.0, 67.3, 61.6, 52.6, 37.3, 24.8, 19.2, 14.1, 0.2. Anal. Calcd for $C_{18}H_{29}NOSi$: C, 71.23; H, 9.63, N, 4.61. Found: C, 71.24; H, 9.54; N, 4.68.

[2*S*,2(1*S*)]-2-Phenyl-2-(1-isopropyl-4-trimethylsilanylbut-3-ynylamino)ethanol (5e). Solid (AcOEt/PE, 10:90). Yield: 68%. Mp: 43 °C. $[\alpha]^{20}_D$: +114 (*c* 1.0, $CHCl_3$). ^{1}H NMR: 7.20−7.06 (m, 5H), 3.75 (dd, J = 4.5 and 8.5 Hz, 1H), 3.53 (dd, J = 4.5 and 10.5 Hz, 1H), 3.34 (dd, J = 8.5 and 10.5 Hz, 1H), 2.38−2.11 (m, 3H), 2.15−1.85 (m, 2H), 1.70−1.55 (m, 1H), 0.75 (d, J = 7.5 Hz, 3H), 0.68 (d, J = 7.5 Hz, 3H), 0.0 (s, 9H).^{13}C NMR: 141.2, 128.6, 127.6, 127.5, 105.1, 86.8, 67.5, 62.1, 58.6, 31.6, 22.2, 19.1, 18.8, 0.2. Anal. Calcd for $C_{18}H_{29}NOSi$: C, 71.23; H, 9.63; N, 4.61. Found: C, 71.01, H, 9.72; N, 4.68.

General Procedure for the Syntheses of β-Amino Alcohols 8c, 8e, and 9. *sec*-Butyllithium (1.3 M in cyclohexane, 3.4 mL, 4.40 mmol) was added at −78 °C to a solution of allyltrimethylsilane (for **8c** and **8e**) or propyntrimethylsilane (for **9**) (4.40 mmol) and tetramethylethylenediamine (0.65 mL, 4.40 mmol) in THF (8 mL). After stirring for 15 min at −78 °C and 15 min at room temperature, the mixture was cooled at −78 °C and titanium isopropoxide (1.35 mL, 4.40 mmol) was added slowly. The mixture was stirred at −78 °C for 1 h, and a solution of oxazolidine (0.88 mmol) in THF (4 mL) was added dropwise. After an additionnal stirring of 20 min at this temperature, the mixture was allowed to reach 0 °C in 1 h, and the reaction was then quenched by addition of an aqueous solution saturated with NH_4Cl (15 mL) and water (15 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL), and the organic layers were combined, dried over K_2CO_3, and evaporated. The residue was then chromatographed on silica gel.

[2(1*R*,2*S*),2*S*]-2-(1-Ethyl-2-trimethylsilanylbut-3-enylamino)-2-phenylethanol (8c). Solid (AcOEt/PE, 10:90). Yield: 50%. Mp: 43 °C. $[\alpha]^{20}_D$: +154 (*c* 1.2, $CHCl_3$). ^{1}H NMR: 7.39−7.29 (m, 5H), 5.81 (dt, J = 17.0 and 10.5 Hz, 1H), 5.11 (dd, J = 10.0 and 2.0 Hz, 1H), 5.04 (dd, J = 17.0 and 2.2 Hz, 1H), 3.89 (dd, J = 8.5 and 4.5 Hz, 1H), 3.72 (dd, J = 10.5 and 4.5 Hz, 1H), 3.60 (dd, J = 10.5 and 8.5 Hz, 1H), 2.54−2.50 (m, 1H), 2.39 (bs, 2H), 2.10 (dd, J = 11.0 and 3.7 Hz, 1H), 1.52−1.33 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H), 0.00 (s, 9H).^{13}C NMR: 141.1, 135.9, 128.5, 127.6, 127.5, 115.7, 67.2, 61.0, 55.9, 38.8, 25.9, 11.4, −2.0. Anal. Calcd for $C_{17}H_{29}NOSi$: C, 70.04; H, 10.03; N, 4.80. Found: C, 70.02; H, 10.02; N, 4.76.

[2(1*R*,2*S*),2*S*]-2-(1-Isopropyl-2-trimethylsilanylbut-3-enylamino)-2-phenylethanol (8e). Oil (AcOEt/PE, 7:93). Yield: 48%. Mp: 64 °C. $[\alpha]^{20}_D$: +37 (*c* 0.6, $CHCl_3$). ^{1}H NMR: 7.25−7.14 (m, 5H), 5.85 (dt, J = 16.7 and 10.5 Hz, 1H), 4.86 (dd, J = 10.0 and 2.0 Hz, 1H), 4.81 (dd, J = 16.7 and 2.2 Hz, 1H), 3.72 (dd, J = 7.2 and 5.2 Hz, 1H), 3.58 (dd, J = 10.7 and 7.2 Hz, 1H), 3.56 (dd, J = 10.7 and 5.2 Hz, 1H), 2.62 (t, J = 4.0 Hz, 1H), 2.30−1.50 (m, 2H), 1.81 (dd, J = 11.0 and 4.5 Hz, 1H), 1.72−1.60 (m, 1H), 0.71 (d, J = 5.0 Hz, 3H), 0.57 (d, J = 7.5 Hz, 3H), 0.00 (s, 9H).^{13}C NMR: 142.4, 138.1, 128.3, 127.4, 127.3, 113.7, 66.4, 63.2, 60.3, 38.6, 32.6, 18.4, 18.3, 0.0. Anal. Calcd for $C_{18}H_{31}NOSi$: C, 70.76; H, 10.23; N, 4.58. Found: C, 70.64; H, 10.28; N, 4.42.

[2*S*,2(1*R*)]-2-Phenyl-2-(1-phenyl-4-trimethylsilanylbuta-2,3-dienylamino)ethanol (9a). Solid (AcOEt/PE, 12:88). Yield: 78%. Mp: 49 °C. $[\alpha]^{20}_D$: −97 (*c* 0.9, $CHCl_3$). ^{1}H NMR: 7.47−7.31 (m, 5H), 4.87 (dd, J = 2.5 and 11.0 Hz, 1H), 4.81 (dd, J = 2.5 and 11 Hz, 1H), 4.21 (t, J = 2.5 Hz, 1H), 4.08 (dd, J = 4.5 and 8.5 Hz, 1H), 3.82 (dd, J = 4.5 and 10.5 Hz, 1H), 3.65 (dd, J = 8.5 and 10.5 Hz, 1H), 2.49 (bs, 2H), 0.0 (t, J = 2.5 Hz, 9H). ^{13}C NMR: 208.7, 143.4, 140.9, 128.7, 128.4, 127.9, 127.7, 127.4, 98.6, 72.2, 67.1, 62.4, 58.8, −1.3. Anal. Calcd for $C_{21}H_{27}NOSi$: C, 74.73; H, 8.06; N, 4.15. Found: C, 74.71; H, 8.09; N, 3.99.

[2(1*R*),2*S*]-2-(1-Ethyl-2-trimethylsilanylbuta-2,3-dienylamino)-2-phenylethanol (9c). Oil (AcOEt/PE, 8:92). Yield: 70%. ^{1}H NMR: 7.31−7.18 (m, 5H), 4.49 (dd, J = 1.5 and 10.8 Hz, 1H), 4.41 (dd, J = 1.3 and 10.8 Hz, 1H), 3.82 (dd, J = 4.8 and 8.8 Hz, 1H), 3.60 (dd, J = 4.8 and 10.8 Hz, 1H), 3.47 (dd, J = 8.8 and 10.8 Hz, 1H), 2.84−2.78 (m, 1H), 2.39 (bs, 2H),

1.51−1.34 (m, 2H), 0.91−0.88 (t, J = 7.5 Hz, 3H), 0.0 (s, 9H). ^{13}C NMR: 208.3, 140.9, 128.5, 128.4, 127.4, 98.4, 71.0, 67.6, 61.8, 56.3, 30.3, 10.6, −1.0.

[2(1*R*),2*S*]-2-(1-Isopropyl-2-trimethylsilanylbuta-2,3-dienylamino)-2-phenylethanol (9e). Oil (AcOEt/PE, 10:90). Yield: 55%. $[\alpha]^{20}_D$: +159 (*c* 1.0, $CHCl_3$). ^{1}H NMR: 7.35−7.20 (m, 5H), 4.56 (dd, J = 1.5 and 10.8 Hz, 1H), 4.45 (dd, J = 1.3 and 10.8 Hz, 1H), 3.82 (dd, J = 4.5 and 8.8 Hz, 1H), 3.64 (dd, J = 4.5 and 10.8 Hz, 1H), 3.53 (dd, J = 8.8 and 10.8 Hz, 1H), 2.73−2.70 (m, 1H), 2.53 (bs, 2H), 1.70−1.62 (m, 1H), 0.91−0.88 (m, 6H), 0.0 (t, J = 2.5 Hz, 9H). ^{13}C NMR: 208.5, 140.7, 128.3, 127.8, 127.4, 97.6, 70.9, 67.7, 62.0, 59.7, 33.4, 20.5, 16.7, −1.0.

[3(1*R*,2*S*),4*S*]-3-(1-Ethyl-2-trimethylsilanylbut-3-enyl)-4-phenyloxazolidin-2-one (10). An aqueous solution of 6 N NaOH (1.6 mL) was added to a vigorously stirred solution of amino alcohol **8c** (2.0 mmol) in CH_2Cl_2 (4.5 mL). The mixture was cooled to −5 °C, and triphosgene (237 mg, 0.8 mmol) in CH_2Cl_2 (1.6 mL) was added dropwise over a period of 30 min. After the mixture was stirred for 4 h at room temperature, water (15 mL) was added and the resulting mixture was extracted with CH_2Cl_2 (3 × 15 mL). After evaporation, the resulting mixture was chromatographed to give starting material **8c** (yield 29%) and compound **10** as a solid (AcOEt/PE, 5:95). Yield: 53%. Mp: 141 °C. $[\alpha]^{20}_D$: +104 (*c* 1.0, $CHCl_3$). ^{1}H NMR: 7.48−7.37 (m, 5H), 5.80 (dt, J = 10.8 and 16.8 Hz, 1H), 4.89 (dd, J = 2.0 and 10.0 Hz, 1H), 4.83−4.68 (m, 2H), 4.62 (t, J = 8.8 Hz, 1H), 4.20 (dd, J = 7.5 and 8.8 Hz, 1H), 3.23−3.15 (m, 1H), 2.56−2.37 (m, 1H), 2.07 (dd, J = 5.3 and 10.8 Hz, 1H), 1.53−1.37 (m, 1H), 0.88 (t, J = 7.5 Hz, 3H), 0.0 (s, 9H). ^{13}C NMR: 158.1, 138.8, 135.3, 129.3, 128.1, 115.0, 69.9, 60.1, 57.3, 39.8, 23.1, 12.1, −2.1. Anal. Calcd for $C_{18}H_{27}NO_2Si$: C, 68.09; H, 8.57; N, 4.41. Found: C, 68.03; H, 8.62; N, 4.35.

[3(1*R*,2*R*),4*S*]-3-(1-Isopropyl-2-trimethylsilanylbut-3-enyl)-4-phenyloxazolidin-2-one (11) and [2(1*R*,2*R*),2*S*]-Carbonic Acid-*tert*-butylester-2-(1-iso-propyl-2-trimethylsilanyl but-3-enylamino)-2-phenylester (12). Di-*tert*-butyl dicarbonate (200 mg, 0.89 mmol) in AcOEt (10 mL) was added to a solution of amino alcohol **8e** (248 mg, 0.81 mmol) and DMAP (100 mg, 0.81 mmol) in AcOEt (20 mL). The mixture was stirred at room temperature for 1 h, evaporated, and chromatographed to afford compound **12** (152 mg) and oxazolidinone **11** (109 mg).

Compound (11). Solid. Yield: 42%. Mp: 108 °C. $[\alpha]^{20}_D$: +27 (*c* 1.0, $CHCl_3$). ^{1}H NMR: 7.39−7.28 (m, 5H), 5.53 (dt, J = 10.4 and 17.0 Hz, 1H), 4.94 (dd, J = 1.8 and 10.4 Hz, 1H), 4.85 (dd, J = 1.5 and 17.0 Hz, 1H), 4.66 (dd, J = 5.7 and 9.0 Hz, 1H), 4.53 (t, J = 8.7 Hz, 1H), 4.23 (dd, J = 5.7 and 8.5 Hz, 1H), 3.27−3.21 (m, 1H), 2.42 (t, J = 10.1 Hz, 1H), 2.05−1.92 (m, 1H), 0.85 (d, J = 7.0 Hz, 3H), 0.55 (d, J = 6.7 Hz, 3H), 0.04−0.00 (m, 9H). ^{13}C NMR: 158.7, 149.2, 137.0, 129.1, 128.8, 127.7, 115.6, 69.6, 63.2, 62.4, 37.1, 31.2, 21.6, 19.4, −1.5. Anal. Calcd for $C_{19}H_{29}NO_2Si$: C, 68.83; H, 8.82; N, 4.22. Found: C, 68.89; H, 9.10; N, 3.84.

X-ray Crystallographic Study. Data were collected on a Brucker Smart 1000 diffractometer. The final unit cell parameters were obtained by the least-squares refinement of 10 000 reflections. Only statistical fluctuations were observed in the intensity monitors over the course of the data collections. The structure was solved by direct methods (SIR97[10]) and refined by least-squares procedures on F^2. All H atoms attached to carbon were introduced in calculation in idealized positions [d(CH) = 0.96 Å] and treated as riding models. Due to the value of the Flack's parameter of 0.1 and to the standard uncertainty of 0.2, the absolute configuration could not be unambiguously determined. However, inverting the configuration led to a Flack's parameter of 0.9(2), and it may be assumed that the value of 0.1 is indicative of the true configuration. There is some residual electron density that develops around the 2-fold screw axis. This electron density might be related to a mix up of solvent molecules (hexane, pentane, Et_2O, etc.), but no correct models could be defined. Least-squares refinements were carried out by minimizing the function $\Sigma w(F_o^2 - F_c^2)^2$, where F_o and F_c are the observed and calculated structure factors. The weighting scheme used in the last refinement cycles was $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$, where $P = (F_o^2 + 2F_c^2)/3$. Models reached convergence with $R = \Sigma(||F_o| - |F_c||)/\Sigma(|F_o|)$ and $wR_2 = \{\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2\}^{1/2}$, having values listed in Table 1. The calculations were carried out with the SHELXL-97 program[11] using the integrated system WINGX(1.63).[12] A molecular view was realized with the help of ORTEP.[13] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-178136. Copies of the data can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 IEZ, U.K. [Fax: int. code +44-(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

Compound (12): Oil. Yield: 46%. ^{1}H NMR: 7.39−7.20 (m, 5H), 5.87 (dt, J = 10.5 and 16.7 Hz, 1H), 4.93−4.82 (m, 2H), 4.19−4.00 (m, 3H), 2.67 (t, J = 3.9 Hz, 1H), 1.86 (dd, J = 4.3 and 11.0 Hz, 1H), 1.78−1.68 (m, 1H), 1.43 (s, 9H), 0.83 (d, J = 6.7 Hz, 3H), 0.69 (d, J = 7.0 Hz, 3H), 0.02 (s, 9H). ^{13}C NMR: 153.5, 141.6, 137.8, 128.4, 128.0, 127.6, 113.9, 81.8, 71.0, 60.2, 59.7, 39.0, 32.9, 27.8, 18.9, 18.3, −1.9.

[1(1*R*),2*S*]-1-(1-Ethyl-4-trimethylsilanylbutylamino)-2-phenylethanol (13). A mixture of amino alcohol **3c** or **5c** (0.32 mmol) and palladium on carbon (8 mg) in absolute ethanol (5 mL) was hydrogenated under stirring for 2 h. After filtration over Celite 545 and evaporation, the crude product was chromatographed to afford compound **13** as an oil. Yield 57% from **3c** and 67% from **5c**. ^{1}H NMR: 7.39−7.25 (m, 5H), 3.85 (dd, J = 4.5 and 8.5 Hz, 1H), 3.69 (dd, J = 4.5 and 10.5 Hz, 1H), 3.49 (dd, J = 8.5 and 10.5 Hz, 1H), 2.46−2.35 (m, 1H), 2.40−2.10 (m, 2H), 1.50−1.28 (m, 6H), 0.81 (t, J = 7.5 Hz, 3H), 0.48 (dd, J = 7.5 and 8.0 Hz, 2H), 0.00 (s, 9H). ^{13}C NMR: 141.8, 128.6, 127.5, 127.2, 66.7, 61.7, 55.8, 37.5, 27.4, 19.7, 17.1, 10.2, −1.5.

[1(1*R*),2*S*]-1-(1-Ethylbutylamino)-2-phenylethanol (14). A solution of *n*-Bu_4NF (1 M in THF, 640 μL, 0.64 mmol) was added to a solution of β-amino alcohol **5c** or **8c** (0.32 mmol) in THF (3 mL). The mixture was stirred for 1 h, and water was added. Extraction with Et_2O and evaporation of the organic layers gave a mixture that was treated with palladium on carbon (8 mg) in absolute ethanol (5 mL) under an atmosphere of hydrogen. After stirring for 40 min, filtration over Celite 545, and evaporation, the crude product was chromatographed to afford amino alcohol **14** as an oil. Yield: 89% (from **5c**) and 56% (from **8c**). $[\alpha]^{20}_D$: +105 (*c* 1.1, $CHCl_3$) (from **5c**) and $[\alpha]^{20}_D$: +102 (*c* 1.1, $CHCl_3$) (from **8c**). ^{1}H NMR: 7.29−7.15 (m, 5H), 3.76 (dd, J = 4.5 and 8.5 Hz, 1H), 3.59 (dd, J = 4.5 and 10.5 Hz, 1H), 3.40 (dd, J = 8.5 and 10.5 Hz, 1H), 2.40−2.27 (m, 3H), 1.38−1.14 (m, 6H), 0.82 (t, J = 7.0 Hz, 3H), 0.72 (t, J = 7.5 Hz, 3H). ^{13}C NMR: 141.7, 128.6, 127.5, 127.3, 66.7, 61.7, 55.6, 35.6, 27.4, 18.4, 14.6, 10.2. IR: 3391, 2957, 1493, 1455 cm^{-1}.

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Supporting Information Available: X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

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