Comparative Study of the Diastereoselective Addition of Allenyl Zinc Reagents to α-Alkoxy (or Silyloxy) Aldehydes and Imines. A Straightforward Synthesis of Amino Alcohols from Imines

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The addition of allenylzinc bromides to α-chiral imines proceeds with very high diastereoselectivity. This result is in contrast with the addition to the corresponding aldehydes, leading to poor diastereoselectivity. The anti/anti adducts are explained by Felkin−Ahn and Gaudemar−Yamamoto models of the transition state.

Introduction

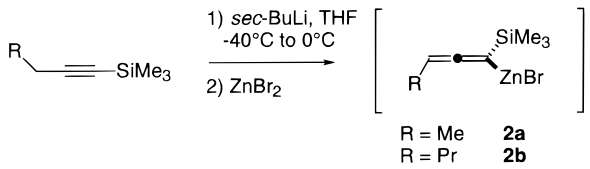
Little is known about double diastereoselection during the addition of chiral allenylzinc reagents to chiral electrophiles (aldehydes, imines...). The reaction of allenylzinc reagents with simple aldehydes has been studied extensively. As shown by Zweifel et al., an excellent anti/syn ratio (>96:4) is achieved for the homopropargylic alcohol thus formed.[1] However, this selectivity depends on the nature of the allenyl moiety substituent groups and may drop (in the 70:30 range) so that the titanium or boron reagents are considered more useful.[2,3] For a double diastereoselection, excellent results were obtained by Marshall et al.[4,5] when stannyl or indium[6] reagents were reacted with α-alkoxy or α-alkyl aldehydes.[7] Recently, the same group showed that nonracemic allenylzinc mesylates, derived from "umpolung" of propargylic mesylates via a palladium intermediate, displayed little mismatching during their addition to enantioenriched α-chiral aldehydes: one enantiomer of the latter leads to an anti/syn sequence while the other leads to the anti/anti isomer.[4,5]

In a study of carbozincation,[8] using allenylzinc bromides derived from the corresponding lithium derivatives, we were interested in knowing whether these reagents would follow the same reactivity.

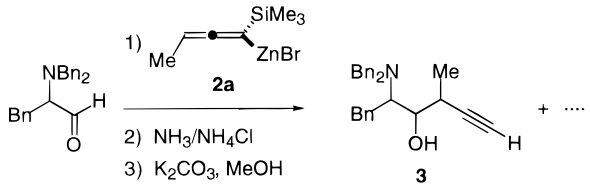
Results and Discussion

We easily obtained the allenic zinc species **2** by means of propargylic deprotonation using *sec*-BuLi in THF at −40 °C, followed by standard transmetalation of the lithium species using zinc (II) bromide (Scheme 1).

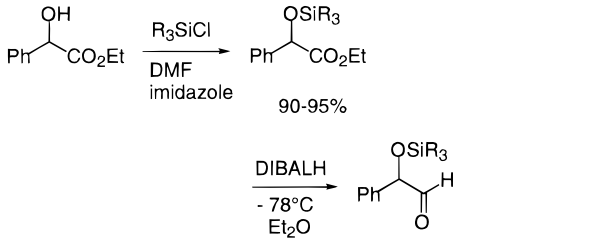
Scheme 1



Scheme 2



Scheme 3



Reaction of **2a** with 2-(*N*,*N*-dibenzylamino)-3-phenylpropionaldehyde,[9] at 25 °C, gave an impure product with many side products (Scheme 2). At −50 °C, **3** was obtained as a mixture of two diastereomers with an approximate d.r. of 85:15. However the aldehyde reacted incompletely and unidentified side products were still present.

We then turned to α-oxygenated aldehydes, and studied silyl protected mandelaldehydes **4**. They are prepared

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(1) Zweifel, G.; Hahn, G. *J. Org. Chem.* **1984**, *49*, 4565−4567.
(2) Furuta, K.; Ishiguro, M.; Haruta, R.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2768−2776.
(3) Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Org. Chem.* **1982**, *47*, 2225−2227.
(4) (a) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1998**, *63*, 3812−3813. (b) Marshall, J. A.; Johns, B. A. *J. Org. Chem.* **1998**, *63*, 7885−7892.
(5) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1999**, *64*, 5201−5204.
(6) (a) Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 696−697. (b) Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 8214−8219.
(7) (a) Marshall, J. A.; Palovitch, M. R. *J. Org. Chem.* **1998**, *64*, 3701−3705. (b) Marshall, J. A.; Fitzgerald, R. N. *J. Org. Chem.* **1999**, *64*, 4477−4478.
(8) Meyer, C.; Marek, I.; Courtemanche, G.; Normant, J. F. *J. Org. Chem.* **1995**, *60*, 863−871.
(9) Reetz, M. T.; Drewes, M. W.; Schmidtz, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1141−1143.

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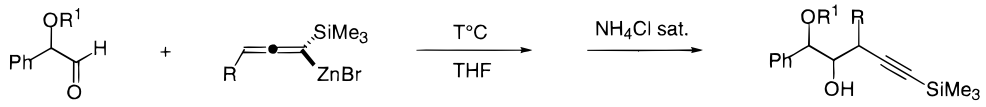
Scheme 4



4a R^1 = TIPS
4b R^1 = TBDMS
4c R^1 = TBDPS

2a R = Me
2b R = *n*-Pr

5a	R = Me	R^1 = TIPS
5b	"	R^1 = TBDMS
5c	"	R^1 = TBDPS
5d	R = *n*-Pr	R^1 = TBDMS
5e	"	R^1 = TBDPS

Table 1. Addition of Allenylzinc Reagents 2a,b to Silyl Derivatives of Mandelic Aldehyde 4a−c

2	4	*T* (°C)	product	conversion (%)	d.r.
2a	**4a**	−50	**5a**	85	53:47
2a	**4b**	−70	**5b**	90	55:45
2a	**4c**	−50	**5c**	97	58:42
2b	**4b**	−70	**5b**	90	58:42
2b	**4c**	−70	**5e**	90	67:33

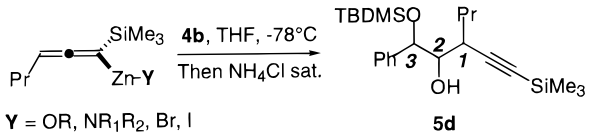
according to Leahy by a controlled DIBALH reduction of the corresponding ethyl mandelate derivatives (Scheme 3).[10c]

Reaction of **2a** with **4a**, **4b,** and **4c** at −50 °C led this time to a clean conversion to **5** (conversion of 85, 90, 97%, respectively) consisting of two diastereomers, but still with low diastereoselection (7, 9, and 17% respectively). The same outcome was observed with zinc reagent **2b** with slightly better diastereoselection (Scheme 4 and Table 1).

We then decided to use a lactaldehyde derivative. This substrate was obtained by TIPS protection of the free hydroxyl of cheap, commercially available, (*S*)-ethyl lactate, racemization using LDA and DIBALH reduction of the ester function. Upon reaction with **2a**, a low diastereoselection (57:43) was again observed.

We have no interpretation for the slight drop of selectivity when the silicon protecting group is varied from TBDPS to TBDMS or TIPS (Table 1, entries 1−3). Our results are close to those obtained by Marshall et al., who used α-methylated aldehydes, but our α-silyloxy aldehydes displayed a higher diastereoselection. In another connection, Tamaru,[11] in early reports concerning zinc reagents prepared by "umpolung" via a palladium intermediate, found a notable difference of reactivity between the in situ generated zinc species via a palladium intermediate and the "standard" alkylzinc bromide species. Indeed, the diastereoselectivity of the reaction of a 1,3-dimethylallylzinc reagent toward benzaldehyde varied from >95% de, in the "umpolung" case, to a 62:38 ratio in the "zinc bromide" case. The influence of Y in RZnY derivatives has never been studied thoroughly. Preliminarily, we found that replacement of

Scheme 5



Y = OR, NR_1R_2, Br, I

5d

Table 2. Influence of Y in RZn-Y on the Diastereoselectivity

entry	Y	conversion (%)	d.r.
1	Br	77	58:42
2	I	81	55:45
3	MeO	88	67:33
4	*t*-BuO	75	70:30
5	$MeSO_3$	91	55:45
6	$N(i\text{-}Pr)_2$	78	50:50
7	$NMe(CH_2)_2NMe_2$	76	71:29

bromide, in reagent **2b**, by different groups had a notable influence on the diastereoselectivity of the addition to **4b** (Scheme 5 and Table 2).[12]

The diasteroselection varied with Y according to $Me_2N(CH_2)_2NMe$ > *t*-BuO > MeO > Br > I ≈ MesO > $i\text{-}Pr_2N$ and no difference in reactivity was observed. This sequence is difficult to interpret, both in terms of bulkiness of Y and polarization of the Zn−Y bond.

Conversion of both diastereomers of **5d** to the corresponding cyclic carbonates **6** allowed us to assess the relative configuration of the products by NOE. The major diastereomer is of 2,3-anti relationship while the minor diastereomer is of 2,3-syn relationship (Scheme 6). For both isomers, we consider a common 1,2-anti relationship as obvious, considering the previous studies realized by Marshall et al.[4,5]

At this point, we suspected that the nucleophilicity of allenylzinc bromides toward aldehydes was too great and responsible for the low diastereoselection. Consequently, we decided to use an aldehyde derivative of lower electrophilicity: an imine.

Imines derived from aldehydes are easily available,[13] and their electrophilicity can be finely tuned by a simple variation of the nitrogen substituent. The addition of allenylmetals (Ti, B, Al, Li) derived from 1-(trimethylsilyl)but-1-yne to simple imines has been described by Yamamoto et al.[14] With imines derived from aliphatic

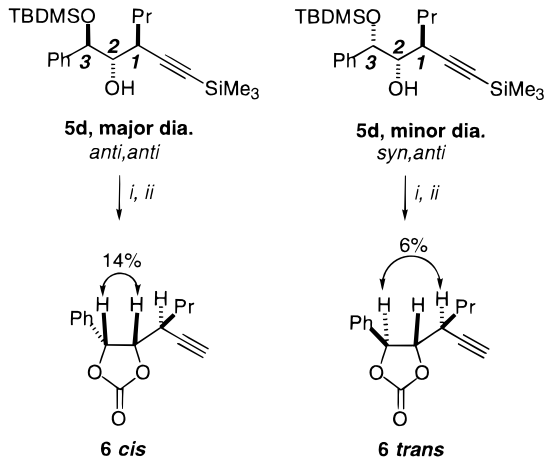
(10) Lactic series. For OTBDMS, see: (a) Massad, S. K.; Hawkins, L. D.; Baker, D. C. *J. Org. Chem.* **1983**, *62*, 5180−5182. For OBn, see: (b) Hoppe, D.; Tarara, G.; Wilckens, M. *Synthesis* **1995**, 723−725. Mandelic series. For OTIPS, see: (c) Gardinier, K. M.; Leahy, J. W. *J. Org. Chem.* **1997**, *48*, 7098−7099. For OTBDPS, see: (d) Raczko, J. *Tetrahedron*: *Asymmetry* **1997**, *8*, 3821−3828. For OTBDMS, see: (e) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Ponzini, F. *J. Org. Chem.* **1993**, *58*, 4746−4748. For OMOM, see: (f) Corey, E. J.; Hannon, F. J.; Boaz, N. W. *Tetrahedron* **1989**, *45*, 545−555.

(11) (a) Tamaru, Y.; Tanaka, A.; Yasui, K.; Goto, S.; Tanaka, S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 787−789. For an allenyl report from the same author, see: (b) Tamaru, Y.; Goto, S.; Tanaka, A.; Shimizu, M.; Kimura, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 878−880. (c) Shimizu, M.; Kimura, M.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1998**, *39*, 609−612.

(12) The aminozinc derivatives were prepared by displacement of the bromide with the corresponding lithium amides. The alkoxyzinc derivatives were prepared by hydrolysis of the diallenylzinc species by 0.5 equiv of the corresponding alcohol. The iodide derivative was prepared by transmetalation using zinc(II) iodide.

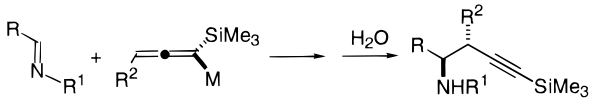
(13) (a) Midland, M. M.; Koops, R. W. *J. Org. Chem.* **1992**, *57*, 1158−1161. (b) Kobayashi, Y.; Takemoto, Y.; Kamijo, T.; Harada, H.; Ito, Y.; Terashima, S. *Tetrahedron* **1992**, *48*, 1853−1868. (c) Franz, T.; Hein, M.; Veith, U.; Jäger, V.; Peters, E.-M.; Peter, K.; Von Schnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1298−1300.

Scheme 6[a]



[a] Key: (i) TBAF, THF; (ii) $Cl_3COCOCl$, CH_2Cl_2, NEt(*i*-Pr)$_2$.

Scheme 7[a]



[a] Key: M = Ti, B, Al, Li; R^2 = alkyl, R^1 = benzyl or alkyl.

aldehydes the exclusive formation of an anti product was observed (Scheme 7).

The addition of allenylzinc derivatives to simple imines derived from benzaldehyde[15] has also been reported and led to the major formation of the anti product, but to our knowledge,[16] the use of imines derived from *aliphatic* aldehydes either simple or α-substituted has never been reported. On the other hand, the reaction of allylic zinc reagents with imines derived from aliphatic α-substituted aldehydes is well documented[17] and gives rather low diastereomeric excesses as compared to the allylic titanium and boron reagents.[17d,k,l]

For our first attempts, we selected benzyl imines of mandelaldehyde blocked as silyl or MOM ethers. They are formed quantitatively by simply adding the desired primary amine to a suspension of the aldehyde and magnesium sulfate in toluene at 0 °C, as already reported.[18] They are unstable on silica gel, and the slight excess of amine must be removed either by a rapid filtration on a short pad of neutral alumina, or better by washing the organic phase with a cold dilute solution of NH_4Cl, followed by drying on $MgSO_4$. Even under argon at 0 °C, they cannot be stored for days and are preferably used immediately after preparation. Those imines were reacted with zinc reagent **2b** derived from 1-(trimethylsilyl)hex-1-yne and **2a** derived from 1-(trimethylsilyl)but-1-yne (Scheme 8). The results are quoted in Table 3.

Table 3. Addition of Allenyl Reagents 2b and 2a to the Benzyl Imine of Mandelic Aldehyde Protected as Silyl Derivatives or MOM Ether

entry	zinc reagent	imine	*T* (°C)	product	yield[b] (%)	de[a] (%)
1	**2b**	**7a**	−70	**8a**	90	93:7
2	**2b**	**7b**	−70	**8b**	70	>35:1
3	**2b**	**7c**	−70	**8c**	85	>35:1
4	**2b**	**7c**	−35	**8c**	75 (68)	96:4
5	**2b**	**7c**	0	**8c**	78 (70)	68:32
6	**2b**	**7d**	−60	**8d**	80	>35:1
7	**2b**	**7e**	−70	**8e**	80 (74)	>35:1
8	**2b**	**7f**	−60	**8f**	68 (52)	>35:1
9	**2b**	**7f**	−35	**8f**	62 (55)	93:7
10	**2b**	**7f**	0	*c*	*c*	*c*
11	**2a**	**7f**	−70	**8g**	73 (61)	>35:1
12	**2a**	**7f**	−35	**8g**	70	93:7
13	**2a**	**7c**	−70	**8h**	68	>35:1

[a] Determined by ^{1}H NMR using the crude adduct. [b] In parentheses, calculated from the aldehyde (two steps). [c] See text.

To our delight, at −70 °C, only one diastereomer is formed (except for entry 1), as is the case at −35 °C with the TBDMS protection (entry 4). Even at 0 °C, a significant diastereoselection occurs (entry 5). It must be noted that the strongly chelating OMOM substituent also allows for excellent diastereoselection (entry 6). With reagent **2b**, benzyl imines **7e** and **7f**, derived from lactaldehyde led to a similar diastereoselection (Scheme 8 and Table 3). At −70 °C, **7e** gives one diastereomer (entry 7). At −60 °C or −35 °C, **7f** gives a slightly lower yield of a single diastereomer **8f** (entries 8 and 9), whereas at 0 °C, **7f** delivers four diastereomers (1.1/0.5/5.5/0.4). An attempt at reversing the diastereoselectivity of the reaction, by precomplexing imine **7f** with $MgBr_2 \cdot OEt_2$, led to a slight drop of selectivity, furnishing an adduct with 97:3 dr of the same major isomer (see structure determination). Unfortunately, an analogous attempt with **7d** led to the decomposition of the imine.

In the case of **2a**, similar high selectivity (a single isomer formed at −70 °C) and similar isolated yield are obtained with both mandelic and lactic derivatives, thus showing that a methyl or a primary alkyl group on the allenic species are equally diastereodiscriminating in this reaction (entries 11−13 in Table 3).

Structure Determination

For the determination of the structure of the major isomer of **8**, we attempted to synthesize a crystalline amide via reaction of **8c** with *p*-nitrobenzenesulfonyl chloride or *p*-nitrobenzoyl chloride. This very sterically demanding amine did not react under these reaction conditions (Scheme 7). However, double deprotection of the silyl groups in **8c** by TBAF, followed by reaction with

(14) Yamamoto, Y.; Ito, W.; Maruyama, K. *J. Chem. Soc., Chem. Comun.* **1984**, 1004−1005.

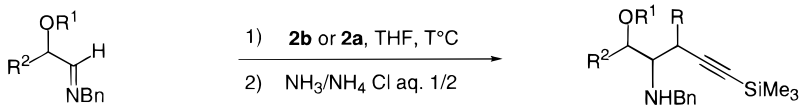
(15) (a) Moreau, J. L.; Gaudemar, M. *Bull. Soc. Chem. Fr.* **1975**, 1211−1215; (b) *Bull. Soc. Chem. Fr.* **1973**, 2549−2554.

(16) For an example where the diastereoselection was not studied, see: Leboutet, L.; Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1991**, *420*, 155−161.

(17) For generality, see: (a) Kleinman, E. F.; Volkmann, R. A. In *Comprehensive Organic Synthesis*; Trost, B., Fleming, I., Eds.; Pergamon Press, New York, 1991; Vol. 2, p 984. (b) Bloch, R. *Chem. Rev.* **1998**, 1407−1438. (c) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, 2207−2293. With allyltitanium, see: (d) Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, *8*, 1895−1946. For allylzinc, see: (e) Baside, T.; Bocum, A.; Savoia, D.; Umani-ronchi, A. *J. Org. Chem.* **1994**, *59*, 7766−7773. (f) Dembele, Y. A.; Beland, C.; Hitchcock, P.; Villieras, J. *Tetrahedron: Asymmetry* **1992**, *8*, 351−354. (g) Nyzam, V.; Beland, C.; Zammatio, F.; Villieras, J. *Tetrahedron: Asymmetry* **1996**, *8*, 1835−1843. (h) Chtara, R. A.; Moreau, J. L.; Gaudemar, M. *C. R. Acad. Sci. Ser. C* **1975**, *280*, 1157−1159. (i) Yamamoto, Y.; Nishii, S.; Maruyama, K.; Komatsu, T.; Ito, W. *J. Am. Chem. Soc.* **1986**, *108*, 7778−7786. (j) Yamamoto, Y.; Komatsu, T.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1985**, 814−816. For allyl Boron see: (k) Yamamoto, Y.; Komatsu, T.; Muruyama, K. *J. Am. Chem. Soc.* **1984**, *106*, 5031−5033. (l) Yamamoto, Y.; Komatsu, T.; Muruyama, K. *J. Org. Chem.* **1985**, *50*, 3115−3121.

(18) (a) Kobayashi, Y.; Takemoto, Y.; Kajimo, T.; Harada, H.; Ito, Y.; Terashima, S. *Tetrahedron* **1992**, *48*, 1853−1868. (b) Midland, M. M.; Koops, R. *J. Org. Chem.* **1992**, *57*, 1158−1161. (c) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Ponzini, F. *J. Org. Chem.* **1993**, *58*, 4746−4748.

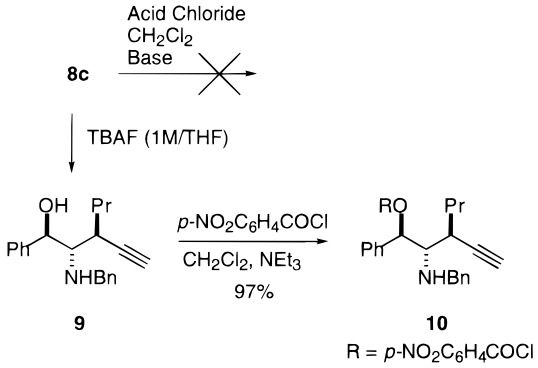
Scheme 8



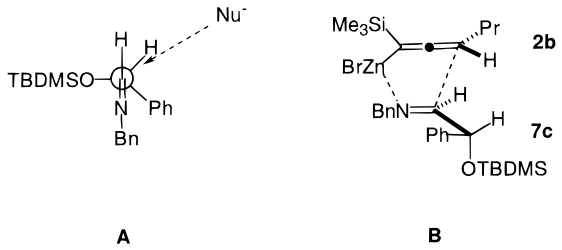
7a	R^2 = Ph	R^1 = TBDPS	
7b	"	R^1 = TIPS	
7c	"	R^1 = TBDMS	
7d	"	R^1 = MOM	
7e	R^2 = Me	R^1 = Bn	
7f	"	R^1 = TBDMS	

8a	R = *n*-Pr	R^2 = Ph	R^1 = TBDPS
8b	"	"	R^1 = TIPS
8c	"	"	R^1 = TBDMS
8d	"	"	R^1 = MOM
8e	"	R^2 = Me	R^1 = Bn
8f	"	"	R^1 = TBDMS
8g	R = Me	R^2 = Me	R^1 = TBDMS
8h	"	R^2 =Ph	R^1 = TBDMS

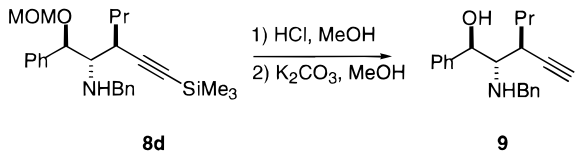
Scheme 9



Scheme 10



Scheme 11



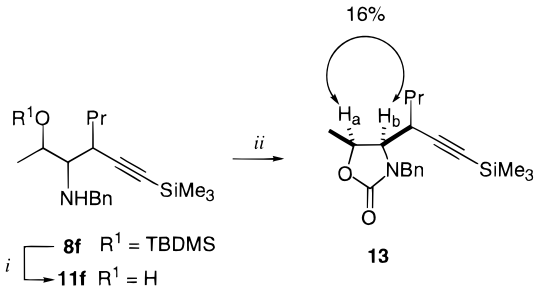
p-nitrobenzoyl chloride on **9**, furnished the crystalline ester **10** whose single-crystal X-ray pattern showed an anti-anti relationship of the substituents (Scheme 9).

Such stereochemistry corresponds to a Felkin−Anh attack on the imine center, (see **A** in Scheme 10) by an allenyl reagent such that interactions between Pr (in **2b**) and PhCHOTBDMS (in **7c**) are minimized. Such modes of attack have been proposed by Zweifel[1] for aldehydes and by Gaudemar[15] and Yamamoto[14] for imines (see **B** in Scheme 10).

The same diastereoisomer is formed for **8d** (MOM protection), as shown by removal of the MOM moiety and the TMS group leading to **9** (Scheme 11).

In the lactic series, the alcohol **11f** derived from **8f** gave no satisfactory crystalline ester when submitted to the same derivatization. We decided to ensure both relative

Scheme 12[a]



[a] Key: (i) $HF(NEt_3)_3$, CH_3CN; (ii) disphosgene, NEt_3, CH_2Cl_2, 30%.

relationships stepwise. We first checked that the Felkin attack (A, Scheme 10) is still valid by conversion of **11f** to the oxazolidinone **13**. H_a and H_b in **13** display a strong NOE (16%), confirming the cis stereochemistry of the oxazolidinone **13** (Scheme 12) and therefore the anti relationship between the oxygen and the nitrogen in **8f**. In a second step, **8f** was twice desilylated to **12f**, semi-hydrogenated to **14**, and submitted to iodoetherification, giving a major diastereomer **15**. The known relative configurations of H_a, H_b allowed the confirmation of the cis relationship of H_b and H_c (NOE of 6% and 11%) in **15**, thus securing the anti/anti configuration of **8f** (Scheme 13).

To broaden the scope of this easy access to α-substituted vicinal amino alcohols, we tried the use of silylated imines, to obtain free primary amines.

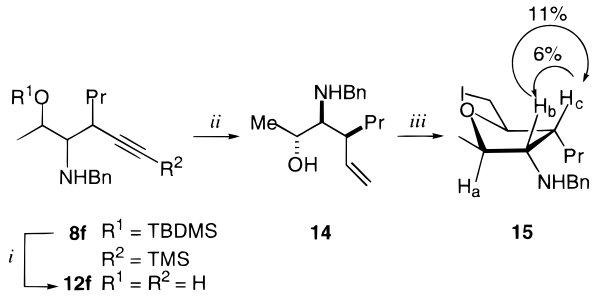
These silylamines are easily prepared[19] but are not very stable.[16] They have been previously reacted, with low yield, with the Grignard reagent analogous to **2a**.[16] Under our reaction conditions, **2b** reacted with imine **16** giving a single diastereomer **17** in good yield, which was subsequently benzylated to give a product analogous to **8f** (Scheme 14).

Conclusion

In summary, the addition of allenylzinc bromides to α-silyloxyaldehydes proceeds with low to moderate diastereoselectivity. Changing the bromide ligand of zinc for

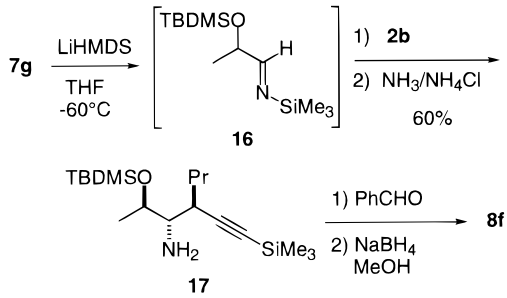
(19) (a) Hart, D. J.; Kanai, K.; Thomas, D. G.; Yang, T. K. *J. Org. Chem.* **1983**, *48*, 283−294. (b) Ha, D. C.; Hart, D. J.; Yang, T. K. *J. Am. Chem. Soc.* **1984**, *106*, 4819−4848. (c) Colvin, E. W.; MacGarry, D. G. *Chem. Commun.* **1985**, 539−540. (d) Cainelli, G.; Giacomini, D.; Panunzio, M.; Martelli, G.; Spunta, G. *Tetrahedron Lett.* **1987**, *28*, 5369−5372.

Scheme 13[a]



[a] Key: (i) TBAF (1 M/THF); (ii) H_2, Pd Lindlar, quinoline, AcOEt; (iii) I_2, CH_3CN, $NaHCO_3$.

Scheme 14



other halides, alkoxides, amides, showed that these substituents have an influence on the diastereoselectivity which, however, never exceeded 40% de. On the contrary, α-benzyloxy or α-silyloxy imines, either benzylated or silylated at nitrogen, undergo a highly diastereoselective addition of substituted allenylzinc reagents to give α-ethynyl vicinal amino alcohols of anti/anti type. Further insight to this reaction is undertaken as well as the study of the configurational stability of zinc derivatives **2a** and **2b** by means of the "Hoffmann test" which will be reported in due course.

Experimental Section

The 1:2 solution of NH_4OH/NH_4Cl is prepared by mixing two volumes of a saturated aqueous solution of NH_4Cl and one volume of a 30% aqueous solution of ammonia.

General Procedure for the Formation of the Intermediate Allenylzinc: Allenylzinc Reagent 2a. *s*-BuLi (1.3 M/hexane, 1.7 mL, 2.2 mmol) was added dropwise to a solution of 1-(trimethylsilyl)but-1-yne (252 mg, 2.0 mmol) in dry THF (10 mL) at −40 °C under a nitrogen atmosphere. The reaction mixture was stirred for 1 h at 0 °C and cooled to −20 °C. $ZnBr_2$ (1M/THF, 2.2 mL, 2.2 mmol) was then added dropwise leading to a colorless solution of **2a**.

Allenylzinc Reagent 2b. Prepared according to the general procedure, using 1-(trimethylsilyl)hex-1-yne (308 mg, 2 mmol).

Aldehydes 4a−f. Aldehydes, derived from either ethyl lactate or ethyl mandelate, were prepared by protection of the free alcohol by standard methods, followed by a controlled (−78 °C) DIBALH reduction of the ester function. All data were in accord with literature reports.[12a−f]

General Procedure A: Addition of Allenylzinc Reagents 2 to α-Chiral Aldehydes 4. A solution of aldehyde **4** (2 mmol) in THF (5 mL) was added dropwise to the allenylzinc reagent **2** (2 mmol) at −50 °C (unless otherwise specified) under a nitrogen atmosphere. The reaction mixture was stirred for 1 h at −50 °C and allowed to warm to 0 °C. It was subsequently quenched by addition of a 1:2 solution of NH_4OH/NH_4Cl (10 mL) and stirred for 30 min at room temperature. Water (10 mL) and ether (10 mL) were added, followed by a vigorous stirring. The layers were separated and the aqueous phase extracted twice with ether. The combined organic layers were washed with brine and dried over $MgSO_4$. The volatiles were removed under reduced pressure and the residue purified (unless otherwise specified) by flash chromatography on silica gel (eluent pentane/ether, 95/5) to yield **5**.

4-Hydroxy-3-methyl-5-phenyl-5-triisopropylsilyloxy-1-(trimethylsilyl)pent-1-yne (5a). General procedure A was applied to **4a** (585 mg, 2 mmol) and **2a** (2 mmol). **5a** (753 mg, 90%) was obtained as a colorless oil, consisting of a mixture of two diastereomers (de = 7%). **Minor diastereomer**: IR (neat) ν cm^{-1} 3500, 2170; ^1H NMR (400 MHz, $CDCl_3$) δ 0.21 (9H, s), 0.98−1.22 (21H, m), 1.23 (3H, d, J = 7.2 Hz), 2.24 (1H, ddd, J = 0.9, 2.2, 7.1 Hz), 3.03 (1H, dd, J = 1.0, 1.8 Hz), 3.46 (1H, app dt, J = 2.2, 8.6 Hz), 4.94 (1H, d, J = 8.5 Hz), 7.28−7.43 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 13.9, 17.6 17.8, 18.0, 28.2, 77.9, 79.7, 86.8, 107.0, 127.0, 127.9, 128.0, 141.0. **Major diastereomer**: IR (neat) ν cm^{-1} 3580, 2170; ^1H NMR (400 MHz, $CDCl_3$) δ 0.20 (9H, s), 0.95−1.03 (21H, m), 1.28 (1H, d, J = 7.2 Hz), 1.76 (1H, br d, J = 6.8 Hz), 3.12 (1H, dq, J = 3.1, 7.1 Hz), 3.48 (1H, m), 4.74 (1H, d, J = 7.4 Hz), 7.28−7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 12.3, 17.8, 17.9, 18.1, 29.7, 76.9, 78.4, 87.7, 107.0, 127.6, 127.8, 127.9, 141.8; MS (CI) 436 ($M + NH_4^+$), 419 (MH^+), 262 (MH^+ − TIPS), 245 (MH^+ − TIPSOH). Anal. Calcd for $C_{24}H_{42}O_2Si_2$: C, 68.84; H, 10.11. Found: C, 68.74; H, 10.26.

5-*tert*-Butyldimethylsilyloxy-4-hydroxy-3-methyl-5-phenyl-1-(trimethylsilyl)pent-1-yne (5b). General procedure A was applied to **4b** (500 mg, 2 mmol) and allenylzinc **2a** (2 mmol). **5b** was obtained as a crude mixture of diastereomers (5:3:1). Due to the poor diastereoselectivity, no further purification of this product was realized.

5-*tert*-Butyldiphenylsilyloxy-4-hydroxy-3-methyl-5-phenyl-1-(trimethylsilyl)pent-1-yne (5c). General procedure A was applied to **4c** (750 mg, 2 mmol) and allenylzinc **2a** (2 mmol). The title compound (511 mg, 51%) was obtained as a colorless oil consisting in a mixture of diastereomers (de = 17%). **Major diatereomer**: IR (neat) ν cm^{-1} 3580, 2250, 2170; ^1H NMR (400 MHz, $CDCl_3$) δ 0.15 (9H, s), 1.13 (9H, s), 1.20 (1H, d, J = 7.0 Hz), 2.25 (1H, dq, J = 2.4, 7.0 Hz), 2.68 (1H, d, J = 4.2), 3.62 (1H, ddd, J = 2.6, 4.2, 8.2 Hz), 4.89 (1H, d, J = 8.2 Hz), 7.24−7.73 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 18.1, 19.3, 26.9, 28.6, 78.5, 79.0, 87.0, 106.6, 127.1, 127.2, 127.5, 127.8, 129.4, 129.5, 131.0, 131.2, 135.6, 135.7; 140.3. **Minor diastereomer**: IR (neat) ν cm^{-1} 3560, 2060, 2165; ^1H NMR (400 MHz, $CDCl_3$) δ 0.22 (9H, s), 1.13 (9H, s), 1.27 (3H, d, J = 7.1 Hz), 1.93 (1H, d, J = 7.4 Hz), 3.08 (1H, dq, J = 3.6, 7.1 Hz), 3.68 (1H, app. dt, J = 3.6, 7.0 Hz), 4.77 1H, d, J = 6.8 Hz), 7.20−7.71 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 18.2, 19.4, 26.9, 28.5, 77.6, 77.7, 87.6, 106.8, 127.0, 127.3, 127.4, 127.7, 129.2; 129.3, 131.4, 131.5, 135.5, 137.7, 140.4; MS (CI) 518 ($M + NH_4^+$), 501 (MH^+), 423, 392, 262 (MH^+ − TBDPS), 245 (MH^+ − TBDPSOH). Anal. Calcd for $C_{31}H_{40}O_2Si_2$: C, 74.34; H, 8.05. Found: C, 74.28; H, 8.14.

4-Hydroxy-5-phenyl-3-*n*-propyl-5-triisopropylsilyloxy-1-(trimethylsilyl)pent-1-yne (5d). General procedure A was applied to **4b** (500 mg, 2 mmol) and allenylzinc **2b** (2 mmol) with an addition temperature of the aldehyde of −70 °C. **5d major** (320 mg, 40%) and **5d minor** (200 mg, 25%) were obtained as a colorless oils (de = 20%). **Major diastere-**

omer: IR (neat) ν cm^{-1} 3500, 2180; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.15 (3H, s), 0.13 (3H, s), 0.27 (9H, s), 1.00 (3H, t, J = 6.8 Hz), 1.40−1.80 (5H, m), 3.13 (1H, ddd, J = 2.0, 5.6, 9.2 Hz), 3.50 (1H, app dt, J = 2.0, 8.0 Hz), 4.64 (1H, d, J = 8.0 Hz), 7.32−7.47 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.3−4.8, 0.0, 13.4, 17.8, 20.4, 25.5, 33.9, 34.9, 76.6, 76.7, 88.4, 105.9, 127.1, 127.5, 127.9, 142.1. **Minor diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (3H, s), 0.20 (3H, s), 0.21 (9h, s), 0.80−1.00 (12H, m), 1.30−1.70 (4H, m), 2.31 (1H, m), 3.51 (1H, dd, J = 2.4 and 7.2 Hz), 4.74 (1H, d, J = 7.6 Hz), 7.32−7.53 (5H, m); MS (CI) 422 ($M + NH_4^+$), 405 (MH^+), 290 (MH^+ − TBDMS), 273 (MH^+ − TBDMSOH). Anal. Calcd for $C_{23}H_{40}O_2Si_2$: C, 68.25; H, 9.96. Found: C, 68.14, H, 10.14.

5-*tert*-Butyldiphenylsilyloxy-4-hydroxy-5-phenyl-3-*n*-propyl-1-(trimethylsilyl)pent-1-yne (5e). General procedure A was applied to **4c** (750 mg, 2 mmol) and **2b** (2 mmol), with an addition temperature of the aldehyde of −70 °C. **5e** was obtained as a crude mixture of diastereomer (3:1).

(4,5-*cis*)-5-Phenyl-4-(3-(1-(trimethylsilyl)hex-1-ynoyl))-1,2-dioxolan-2-one (6-*cis*). TBAF (1 M in THF) was added dropwise to a THF solution of **5d major** (100 mg, 0.2 mmol). After completion, the reaction was diluted with water and the aqueous phase extracted twice with ether. The combined organic phases were dried over $MgSO_4$ and the volatiles removed under reduced pressure. CH_2Cl_2 (5 mL) and NEt_2-Pr (1.2 equiv) were added to the residue. This solution was subsequently treated with diphosgene (1.1 equiv) at 0 °C. The reaction was monitored by TLC. After completion, the reaction was diluted with water (5 mL) and the aqueous phase extracted twice with ether. The combined organic phases were dried over $MgSO_4$ and the volatiles removed under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent pentane/ether, 70/30) to yield **6-*cis*** (31 mg, 51%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (1H, t, J = 7.2 Hz), 1.23−1.61 (4H, m), 2.17 (2H, m), 4.80 (1H, d, J = 3.3, 7.8 Hz), 5.83 (1H, d, J = 7.8 Hz), 7.40−7.47 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 19.9, 32.7, 34.2, 73.7, 80.4, 80.8, 81.5, 126.6, 128.8, 129.4, 132.2, 154.5.

(4,5-*trans*)-5-Phenyl-4-(3-(1-(trimethylsilyl)hex-1-ynoyl))-1,2-dioxolan-2-one (6-*trans*). The same procedure was applied to **5d minor** (50 mg, 0.12 mmol) to yield **6-*trans*** (15 mg, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, J = 7.2 Hz), 1.46−1.76 (4H, m), 2.30 (1H, d, J = 2.5 Hz), 2.75−2.79 (1H, m), 4.52 (1H, dd, J = 2.9, 6.3 Hz), 5.58 (1H, d, J = 6.3 Hz), 7.37−7.46 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 20.5, 29.8, 32.6, 35.3, 73.8, 80.0, 81.0, 84.3, 125.9, 129.4, 129.8, 136.4, 154.3.

Imines (7a−f). Imines were prepared, according to known procedures,[13] by slow addition of the amine to a cold solution (0 °C) of the aldehyde in toluene in the presence of anhydrous $MgSO_4$. The reaction mixture was then diluted with ether and washed with a cold dilute aqueous solution of NH_4Cl. The organic phase was dried over $MgSO_4$ and the volatiles removed under reduced pressure. They were used without further purification.

General Procedure B: Addition of Allenylzincs 2 to α-Chiral Imines 7. A solution of imine **7** (2 mmol) in THF (5 mL) was added dropwise, over 10 min, to the allenylzinc **2** (2 mmol) at −70 °C (unless otherwise specified), under a nitrogen atmosphere. The reaction mixture was further stirred for 1 h at −70 °C, slowly allowed to warm to 0 °C, and subsequently quenched by addition of 10 mL of a 1:2 solution of NH_4OH/NH_4Cl. After vigorous stirring, water (10 mL) and ether (10 mL) were added. The layers were separated, and the aqueous phase was extracted twice with Et_2O. The combined organic layers were washed with brine and dried over $MgSO_4$. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent pentane/ether 98:2) to yield **8**.

4-*N*-Benzylamino-5-*tert*-butyldiphenylsilyloxy-*5*-phenyl-*3*-*n*-propyl-1-(trimethylsilyl)pent-1-yne (8a). General procedure B was applied to **7a** (695 mg, 2 mmol) and **2b** (2 mmol). **8a** (820 mg, 90%) was obtained as a colorless oil consisting of a mixture of two diastereomers (de = 86%). **Minor diastereomer**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 0.00 (9H, s), 0.91 (3H, t, = 7.2 Hz), 1.08 (9H, s), 1.20−1.70 (4H, m), 5.57 (1H, m), 2.63 (1H, m), 3.68 (1H, d, J = 13.6 Hz), 3.84 (1H, d, J = 13.6 Hz), 5.01 (1H, d, J = 5.6 Hz), 7.09−7.68 (20H, m). **Major diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.13 (9H, s), 0.86 (3H, t, J = 7.2 Hz), 1.08 (9H, s), 1.20−1.70 (4H, m), 2.75 (1H, dd, J = 3.62, 6.4 Hz), 3.00 (1H, ddd, J = 3.2, 5.2, 8.8 Hz), 3.39 (1H, d, J = 13.2 Hz), 3.50 (1H, d, J = 13.2 Hz), 4.83 (1H, d, 6.4 Hz), 7.09−7.68 (20H, m); ^{13}C NMR ($CDCl_3$) δ 0.3, 13.8, 19.5, 20.7, 26.9, 27.1, 35.1, 35.7, 53.1, 65.5, 78.4, 87.4, 108.2, 127.1, 127.3, 127.5, 127.9, 128.0, 133.7, 133.9, 135.9, 141.2, 142.2; MS (CI) 618 (MH^+). Anal. Calcd for $C_{40}H_{51}NOSi_2$: C, 77.74; H, 8.32; N, 2.27. Found: C, 77.80; H, 8.48; N, 2.20.

4-*N*-Benzylamino-*5*-phenyl-*3*-*n*-propyl-5-triisopropylsilyloxy-1-(trimethylsilyl)pent-1-yne (8b). General procedure B was applied to **7b** (149 mg, 0.39 mmol) and **2b** (0.39 mmol). **8b** (145 mg, 70%) was obtained as a colorless oil as a single diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.16 (9H, s), 0.96 (3H, t, J = 7.1 Hz), 1.00 (21H, m), 1.10−1.70 (4H, m), 2.65 (1H, dd, J = 2.9, 7.7 Hz), 3.12 (1H, ddd, J = 2.9, 5.5, 8.7 Hz), 3.22 (1H, d, J = 12.9 Hz), 3.38 (1H, d, J = 12.9 Hz), 4.78 (1H, d, J = 7.7 Hz), 7.03−7.47 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2, 12.6, 13.8, 18.0, 18.1, 20.9, 35.2, 53.4, 66.3, 77.8, 87.5, 108.3, 126.5, 127.3, 127.7, 127.9, 128.0, 128.2, 141.2, 143.9.

4-*N*-Benzylamino-5-*tert*-butyldimethylsilyloxy-*5*-phenyl-*3*-*n*-propyl-1-(trimethylsilyl)pent-1-yne (8c). General procedure B was applied to **7c** (509 mg, 1.5 mmol) and **2b** (1.5 mmol). **8c** (564 mg, 76%) was obtained as a colorless oil consisting of a single diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.21 (3H, s), 0.09 (3H, s), 0.89 (9H, s), 0.91 (3H, t, J = 4.8 Hz), 1.37−1.43 (3H, m), 1.60−1.80 (1H, m), 2.59 (1H, dd, J = 2.8, 8.4 Hz), 3.10−3.17 (3H, m), 3.29 (1H, d, J = 12.8 Hz), 4.61 (1H, d, J = 8.4 Hz), 7.16−7.41 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.4, 0.3, 13.7, 16.1, 20.8, 25.8, 35.0, 53.1, 65.7, 77.0, 87.5, 108.3, 126.5, 127.2, 127.7, 127.8, 127.9, 128.2, 141.1, 144.0; MS (CI) 494 (MH^+), 354. Anal. Calcd for $C_{30}H_{47}NOSi_2$: C, 72.96; H, 9.59; N, 2.84. Found: C, 72.65; H, 9.79; N, 2.80.

4-*N*-Benzylamino-5-methoxymethyloxy-*5*-phenyl-*3*-*n*-propyl-1-(trimethylsilyl)pent-1-yne (8d). General procedure B was applied to **7d** (808 mg, 3 mmol) and **2b** (3 mmol) with an addition temperature of the imine of −60 °C. **8d** (1.0 g, 80%) was obtained as a colorless oil consisting in a single diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.21 (9H, s), 0.95 (3H, t, J = 7.1 Hz), 1.30−1.60 (3H, m), 1.70−1.85 (1H, m), 2.78 (1H, dd, J = 2.9, 8.7 Hz), 3.17 (1H, app sext, J = 2.6 Hz), 3.27 (1H, d, J = 12.8 Hz), 3.42−3.39 (4H, m), 4.58 (2H, ab syst, J = 1.5, 6.6 Hz), 4.70 (1H, d, J = 8.7 Hz), 7.01−7.46 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 13.7, 20.7, 34.8, 35.1, 52.8, 55.6, 63.7, 79.5, 83.3, 93.8, 107.7, 126.3, 127.7, 127.89, 127.94, 128.1, 140.3, 140.6; MS (CI) 424 (MH^+). Anal. Calcd for $C_{26}H_{37}NO_2Si$: C, 73.71; H, 8.80; N, 3.31. Found: C, 73.63; H, 8.97; N, 3.15.

4-*N*-Benzylamino-5-benzyloxy-*3*-*n*-propyl-1-(trimethylsilyl)hex-1-yne (8e). General procedure B was applied to **7e** (615 mg, 2.43 mmol) and **2b** (2.43 mmol). **8e** (724 mg, 74%) was obtained as a colorless oil consisting of a single diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (9H, s), 0.78 53H, t, J = 7.2 Hz), 1.17 (3H, d, J = 6.4 Hz), 1.20−1.55 (4H, m), 2.43 (1H, dd, J = 3.6, 7.2 Hz), 2.85 (1H, m), 3.46 (1H, dq, J = 6.4, 7.2 Hz), 4.33 (1H, d, J = 11.4 Hz), 4.45 (1H, d, J = 11.4 Hz), 7.00−7.25 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.6, 14.3, 17.0, 21.4, 35.7, 36.0, 54.2, 63.9, 71.8, 78.1, 87.8, 108.7, 127.1, 127.8, 128.1, 128.6, 128.7, 139.2, 141.5; MS (CI) 408 (MH^+). Anal. Calcd for $C_{26}H_{37}NOSi$: C, 76.60; H, 9.15; N, 3.44. Found: C, 76.42; H, 9.32; N, 3.34.

4-*N*-Benzylamino-5-*tert*-butyldimethylsilyloxy-3-*n*-propyl-1-(trimethylsilyl)hex-1-yne (8f). General procedure B was applied to **7f** (438 mg, 1.58 mmol) and **2b** (1.58 mmol). **8f** (335 mg, 52%) was obtained as a colorless oil consisting of a single diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.12 (3H, s), 0.13 (3H, s), 0.16 (9H, s), 0.91 (9H, s), 0.95 (3H, t, J = 7.2 Hz), 1.29 (3H, d, J = 6.0 Hz), 1.40−1.60 (4H, m), 2.38 (1H, dd, J = 3.2, 7.2 Hz), 2.98 (1H, ddd, J = 3.6, 5.2, 8.8 Hz), 3.83 (1H,

dt, J = 6.0, 7.2 Hz), 3.92 (1H, d, J = 12.8 Hz), 4.01 (1H, d, J = 13.0 Hz), 7.27−7.41 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.9, −4.2, 0.1, 13.8, 17.9, 20.8, 20.9, 25.9, 35.2, 35.3, 54.3, 65;8, 70.9, 87.3, 108.0, 126.7, 128.2, 141.2.

4-*N*-Benzylamino-5-*tert*-butyldimethylsilyloxy-3-methyl-1-(trimethylsilyl)hex-1-yne (8g). General procedure B was applied to **7f** (555 mg, 2.1 mmol) and **2a** (2.1 mmol). **8f** (309 mg, 61%) was obtained as a colorless oil consisting of a single diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.10 (3H, s), 0.11 (3H, s), 0.15 (9H, s), 0.91 (9H, s), 1.25 (3H, d, J = 6.0 Hz), 1.26 (3H, d, J = 7.2 Hz), 2.36 (1H, dd, J = 4.0, 6.8 Hz), 3.02 (1H, dq, J = 4.0, 7.2 Hz), 3.82 51H, app. qt, J = 6.0 Hz), 3.93 (1H, d, J = 13.0 Hz), 4.00 (1H, d, J = 13.0 Hz), 7.25−7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.4, 0.0, 17.9, 19.1, 20.3, 25.7, 29.4, 54.3, 67.1, 70.7, 86.2, 109.1, 126.6, 128.1, 132.5, 141.1; MS (CI) 404 (MH^+). Anal. Calcd for $C_{23}H_{41}NOSi_2$: C, 68.42; H, 10.24; N, 3.47. Found: C, 68.52, H, 10.33; N, 3.30.

4-*N*-Benzylamino-5-*tert*-butyldimethylsilyloxy-3-methyl-5-phenyl-1-(trimethylsilyl)pent-1-yne (8h). General procedure B was applied to **7c** (679 mg, 2.0 mmol) and **2a** (2.0 mmol). **8h** (630 mg, 68%) was obtained as a colorless oil consisting of a single diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.20 (3H, s), 0.10 (3H, s), 0.20 (9H, s), 0.89 (9H, s), 1.26 (3H, t, J = 7.2 Hz), 2.55 (1H, dd, J = 3.2, 8.4 Hz), 3.18 (1H, d, J = 13.2 Hz), 3.22 (1H, dq, J = 3.2, 7.2 Hz), 3.31 (1H, d, J = 13.2 Hz), 4.61 (1H, d, J = 8.4 Hz), 7.03−7.42 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.5, 0.3, 18.1, 25.8, 29.4, 53.4, 67.3, 77.7, 86.3, 109.2, 126.6, 127.8, 127.9, 128.0, 128.3, 141.0, 143.8; MS (CI) 466 ((MH^+). Anal. Calcd for $C_{28}H_{43}NOSi_2$: C, 72.20; H, 9.30; N, 3.01. Found: C, 72.34; H, 9.14; N, 3.01.

Structure Determination. 4-*N*-Benzylamino-5-*p*-nitrobenzoyloxy-*5*-phenyl-3-*n*-propyl-pent-1-yne (10). TBAF (3 mL, 3 mmol, 1 M/THF) was added at room temperature to a THF (2 mL) solution of **8c** (645 mg, 1.3 mmol). The reaction was followed by TLC. When no starting material was left (5 h), the volatiles were removed under reduced pressure to yield **9** as a crude material that was used as such. *p*-Nitrobenzoyl chloride (291 mg, 1.6 mmol) was added to a solution of **9** and DMAP (160 mg, 1.3 mmol) in dry CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 3 h. Water (3 mL) and ether (10 mL) were then added. The layers were separated, and the aqueous one was extracted twice with ether. The combined organic phase was washed with brine and dried over $MgSO_4$. The volatiles were removed under reduced pressure and the residue purified by flash chromatography on silica gel (eluent cyclohexane/EtOAc, 9/1) to yield **10** (500 mg, 97%) as orange crystals. It was recrystallized from pentane/ether (4/1) to obtain satisfactory monocrystals: mp = 84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86−0.96 (6H, m), 1.30−1.36 (3H, m), 1.45 (1H, m), 2.23 (1H, d, J = 2.4 Hz), 2.84 (1H, m), 3.10 (1H, dd, J = 2.2, 6.3 Hz), 3.77 (2H, s), 6.33 (1H, d, J = 6.3 Hz), 7.27−7.50 (10H, m), 8.33 (2H, d, J = 8.9 Hz), 8.39 (2H, d, J = 8.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 19.9, 33.1, 35.6, 52.4, 62.6, 68.8, 77.8, 35.2, 123.8, 127.0, 127.1, 128.4, 128.5, 128.6, 128.8, 131.3, 135.8, 138.7, 140.3, 150.8, 164.0.

3-Benzyl-4-(3-(1-(trimethylsilyl)hex-1-ynoyl))-5-methyl-2-oxazolidinone (13). $HF(NEt_3)_3$ (0.5 mL, 3 mmol) was added dropwise to a solution of **8f** (405 mg, 0.95 mmol) in CH_3CN (5 mL). The reaction mixture was stirred for 1 h, and a saturated solution of $NaHCO_3$ (2 mL) was added. The organic phase was extracted twice with ether and dried over $MgSO_4$. The volatiles were removed under reduced pressure to yield **11f**, which was used without purification, and some fully desilylated product. **11f** was added to a solution of NEt_3 (870 μL, 5.0 mmol) in CH_2Cl_2 (5 mL) at room temperature under nitrogen. Diphosgene (181 μL, 1.5 mmol) was added dropwise to this solution maintained at room temperature by means of a water bath. After 30 min of stirring, the reaction was quenched with water and diluted with ether (10 mL). The layers were separated, and the aqueous phase was extracted twice with ether. The combined organic phase was dried over $MgSO_4$. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent cyclohexane/EtOAc, 98/2) to yield **13** (100 mg, 30%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.18 (9H, s), 0.9 (3H, t, J = 7.4 Hz), 1.15−1.35 (3H, m), 1.56 (1H, d, J = 6.8 Hz), 1.55−1.70 (1H, m), 2.64 (1H, ddd, J = 2.9, 4.1, 7.3 Hz), 3.58 (1H, dd, J = 2.8, 7.6 Hz), 4.16 (1H, d, J = 15.6 Hz), 4.66 (1H, app quint, J = 6.7 Hz), 5.02 (1H, d, J = 15.6 Hz), 7.26−7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2, 14.0, 15.7, 21.6, 33.5, 34.4, 47.3, 59.9, 78.0, 90.2, 105.3, 128.2, 128.2, 129.2, 136.6, 158.9; MS (CI) 361 ($M + NH_4^+$), 344 (MH^+). Anal. Calcd for $C_{20}H_{29}NO_2Si$: C, 69.92; H, 8.51; N, 4.08. Found: C, 70.11; H, 9.03; N, 3.88.

4-*N*-Benzylamino-5-hydroxy-3-*n*-propyl-hex-1-ene (14). TBAF (2 mL, 2 mmol, 1 M/THF) was added at room temperature to a solution of **8f** (209 mg, 0.48 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 5 h, and the volatiles were removed under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent cyclohexane/EtOAc, 4/1) to yield **12f** (103 mg, 94%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, J = 7.2 Hz), 1.21 (3H, d, J = 6.5 Hz), 1.30−1.75 (4H, m), 2.17 (1H, d, J = 2.5 Hz), 2.55 (1H, dd, J = 3.7, 5.0 Hz), 2.68 (1H, m), 3.86 (2H, m), 4.02 (1H, d, J = 12.9 Hz), 7.26−7.39 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 19.0, 20.6, 33.3, 35.9, 53.3, 63.5, 68.1, 71.9, 85.0, 127.1, 128.2, 128.4, 140.5. Amino alcohol **12f** (103 mg, 0.42 mmol) in EtOAc (5 mL) was hydrogenated under 1 atm of H_2 in the presence of quinoline (12 μL, 0.1 mmol) and Lindlar catalyst (5 mg, 0.05 mmol). The reaction was followed on TLC. After complete consumption of the starting material, the reaction mixture was filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent cyclohexane/EtOAc, 4/1) to yield **14** in quantitative yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, m), 1.15 (3H, d, J = 6.4 Hz), 1.16−1.44 (4H, m), 2.19 (1H, m), 2.54 (1H, dd, J = 4.3, 6.6 Hz), 3.03 (1H, br. d, J = 6.6 Hz), 3.75 (1H, d, J = 12.6 Hz), 3.88 (2H, m), 5.08 (1H, dd, J = 1.9, 16.7 Hz), 5.14 (1H, dd, J = 1.9, 10.2 Hz), 5.82 (1H, ddd, J = 9.4, 10.2, 17.0 Hz), 7.35 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 18.5, 22.5, 34.1, 46.5, 54.3, 64.8, 66.9, 116.6, 127.4, 218.6, 128.7, 140.7, 140.9.

4-*N*-Benzylamino-2-iodomethyl-5-methyl-3-*n*-propyltetrahydrofuran (15). 14 (0.48 mmol) in solution in CH_3CN (3 mL) was added dropwise to a CH_3CN (5 mL) solution of iodine (190 mg, 0.73 mmol) at −40 °C. The reaction mixture was slowly allowed to warm to 0 °C. A saturated solution of Na_2SO_3 (5 mL) was then added. The reaction mixture was diluted with ether, the layers were separated, and the aqueous phase was extracted twice with ether. The combined organic phase was dried over $MgSO_4$, and the volatiles were removed under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent cyclohexane/EtOAc, 9/1) to afford **15** (55 mg, 30%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (3H, t, J = 7.1 Hz), 1.15−1.45 (7H, m), 2.05 (1H, app quint, J = 7.4 Hz), 2.93 (1H, dd, J = 5.4, 6.5 Hz), 3.24 (1H, dd, J = 5.0, 10.5 Hz), 3.37 (1H, dd, J = 4.7, 10.5 Hz), 3.67 (1H, app q, J = 6.0 Hz), 3.71 (1H, d, J = 13.1 Hz), 3.84 (1H, d, J = 13.1 Hz), 3.96 (1H, app quint, J = 6.0 Hz), 7.25−7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9, 14.3, 20.7, 45.9, 52.3, 65.3, 79.2, 81.8, 127.1, 128.1, 128.4, 140.2.

4-Amino-3-*n*-propyl-5-*tert*-butyldimethylsilyloxy-1-(trimethylsilyl)hex-1-yne (17). LiHMDS (2.1 mL, 2.1 mmol, 1 M/THF) was added dropwise to a solution of 2-*tert*-butyldimethylsilyloxypropanal (377 mg, 2 mmol) in THF (10 mL) at −60 °C under a nitrogen atmosphere. The reaction mixture was allowed to warm to −40 °C and stirred for 40 min at this temperature. It was subsequently cooled to −70 °C, and **2b** (2.2 mmol) was added dropwise. The reaction mixture was stirred overnight as the temperature of the reaction raised to −30 °C. The reaction was quenched by addition of 10 mL of a 1:2 solution of NH_4OH/NH_4Cl. After vigorous stirring, water (10 mL) and ether (10 mL) were added. The layers were separated, and the aqueous phase was extracted twice with Et_2O. The combined organic layers were washed with brine and dried over $MgSO_4$. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent pentane/ether 9:1) to yield

17 (102 mg, 60%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (3H, s), 0.10 (3H, s), 0.16 (9H, s), 0.90 (9H, s), 0.93 (3H, t, J = 4.0 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.30−1.65 (4H, m), 2.40 (1H, dd, J = 3.2, 8.0 Hz), 2.88 (1H, ddd, J = 3.2, 5.2, 8.8 Hz), 3.66 (1H, dq, J = 6.0, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.3, 0.12, 13.7, 17.9, 20.3, 20.6, 25.8, 34.6, 35.0, 60.0, 70.8, 87.6, 107.3; MS (CI) 342 (MH^+). Anal. Calcd for $C_{18}H_{39}NOSi_2$: C, 63.27; H, 11.50; N, 4.10. Found: C, 63.09; H, 11.61; N, 3.98.

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Supporting Information Available: ORTEP diagram and crystallographic table of **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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