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Diastereoselective synthesis of enantioenriched homopropargyl amino alcohols from α-dibenzylamino aldehydes and their use as chiral synthons

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Abstract—Homochiral α-dibenzylamino aldehydes, prepared from the corresponding α-amino acids, react with propargyl bromide and zinc in DMF/THF (1:1) or DMF/Et_2O (1:1) at 20 °C to afford, in good yields and *dr*, homopropargylic 1,2-amino alcohols. *anti* Diastereomers were always formed as major products in this reaction. These compounds are versatile intermediates for a variety of synthetic targets: γ-amino-β-hydroxy-ketones, 4-amino-1,3-diols, 1,7-diamino-2,6-diols, and ω-amino-δ-hydroxy esters.
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1. Introduction

Homopropargyl alcohols are interesting intermediates in organic synthesis that are prepared by reaction of carbonyl compounds with propargyl or allenyl organometallics.[1] In some cases, mixtures of allenyl and homopropargyl alcohols are obtained depending on the nature of the carbonyl compound, propargyl halide, and the metal and solvent used in the reaction.[2]

The diastereoselective propargylation of carbonyl compounds was first described for α-alkoxy aldehydes with zinc and propargyl bromide in DMF/THF leading to the *anti* adducts as major diastereoisomers in good yield and diastereomeric excess (de).[3,4] Propargylation of some protected α-amino aldehydes has also been studied. For instance, *N*-Boc-leucinal reacts with propargyl bromide and zinc in DMF/Et_2O leading to the corresponding *anti* homopropargyl amino alcohol with very good de,[5] and diastereoselective propargylation of α-acetamido aldehyde constitutes a key step in the synthesis of Neu5Ac.[6] There are no antecedents on propargylation of α-dibenzylamino aldehydes although allenylation of 2-dibenzylamino-3-phenylpropionaldehyde leads to the *anti* homopropargyl amino alcohol in moderate de,[7] and some enantioselective propargylation of aldehydes leading to homochiral propargyl alcohols are also known.[8]

As a part of a project on the reactivity of α-dibenzylamino aldehydes with different nucleophiles,[9] we present now the results obtained on the diastereoselective propargylation of those compounds and the transformation of the resulting homopropargyl amino alcohols into useful synthetic intermediates.

2. Results and discussion

The reaction of α-dibenzylamino aldehydes with propargyl bromide and zinc dust was initially tested by taking L-alaninal derivative **1a** as a model. The reaction did not take place when diethyl ether was used as a solvent (entry 1 in Table 1), but led to a mixture of diastereomeric dibenzylamino homopropargyl alcohols *anti*-**2a** and *syn*-**2a** in good yield and de when the reaction was carried out in mixtures of Et_2O or THF and DMF as solvents (entries 2–6 in Table 1). The ratio of diastereoisomers did not appreciably change with the

Table 1. Stereoselective propargylation of α-dibenzylamino aldehydes **1a–f**

Entry	**1**[a]	Solvent	T[a] (°C)	Yield (%)[b]	*anti*/*syn*[c]
1	**1a**	Et_2O	20	—	—
2	**1a**	DMF/Et_2O (1:1)	20	**2a** (63)	80:20
3	**1a**	DMF/Et_2O (1:1)	0→20	**2a** (71)	81:19
4	**1a**	DMF/THF (1:1)	0→20	**2a** (81)	82:18
5	**1a**	DMF/Et_2O (1:5)	0	**2a** (60)	82:18
6	**1a**	DMF/Et_2O (5:1)	0	**2a** (54)	85:15
7	**1b**	DMF/Et_2O (1:1)	20	**2b** (80)	90:10
8	**1c**	DMF/Et_2O (1:1)	0→20	**2c** (70)	85:15
9	**1d**	DMF/THF (1:1)	0→20	**2d** (57)	89:11
10	**1e**	DMF/THF (1:1)	0→20	**2e** (61)	70:30
11	**1f**	DMF/Et_2O (1:1)	0→20	**2f** (61)	18:82

[a] Reactions were run with 2 equiv of propargyl bromide and 3 equiv of zinc.
[b] Numbers correspond to combined yield of pure and isolated diastereoisomers.
[c] The diastereomeric ratio was determined by integration of the signals of ^{1}H NMR spectra of the reaction mixture.

Keywords: Propargylation; Amino acids; Amino aldehydes; Asymmetric synthesis; Zinc.
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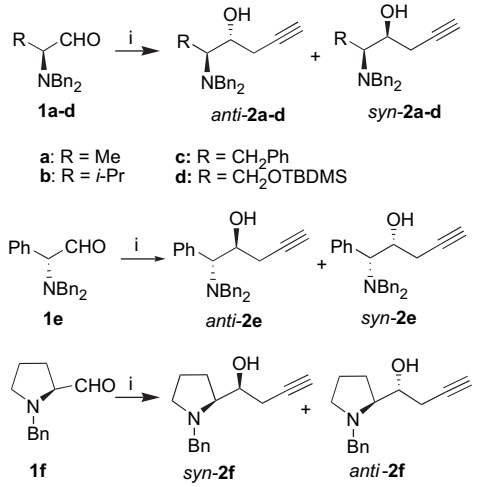
temperature of the reaction or by the ethereal solvent or by the ratio of Et_2O and DMF, but the best yield was obtained for the reaction in THF/DMF at 0–20 °C (entry 4 in Table 1). The best diastereoselection for the reaction was observed when a mixture of DMF/Et_2O 5:1 was used as solvent (entry 6 in Table 1). The reaction was extended to dibenzylamino aldehydes **1b–f** and the results are summarized in Scheme 1 and Table 1.



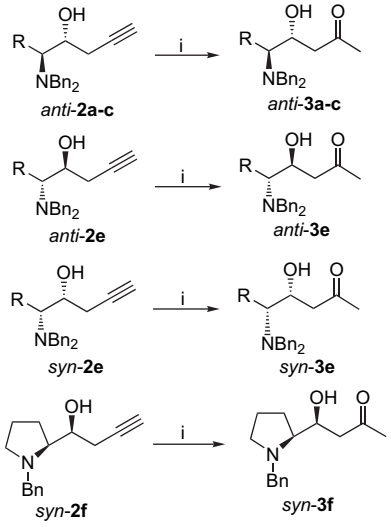
Scheme 1. Reagents and conditions: (i) 1. Zn dust, HC≡CCH$_2$Br, DMF/THF (1:1) or DMF/Et_2O (1:1), rt. 2. NH_4Cl.

The stereoselection was improved when increasing the size of the chain in the starting amino aldehyde, raising to ca. 9:1 for L-dibenzylamino valinal **1b** and L-dibenzylamino serinal derivative **1d**. On the contrary, the presence of a phenyl group in **1e** decreased the ratio of diastereoisomers to 7:3 (entry 10 in Table 1). This fact has been previously observed for nucleophilic additions to phenylglycinal derivatives.[9b–d]

Interestingly, the reaction of L-*N*-benzyl prolinal **1f** with propargyl bromide and zinc dust in DMF/Et_2O at room temperature leads to a mixture of *anti*- and *syn*-**2f** in moderate yield and good de, but in this case the *syn* adduct was formed as major diastereoisomer. This behavior, which can be explained through a Cram-chelated model, had been previously observed for additions to prolinal derivatives.[9c,10]

All the diastereoisomers, except *anti*- and *syn*-**2d**, were purified by flash chromatography and their stereochemistry was determined on the basis of ^{1}H NMR spectral data[9c,10,11] and confirmed for *anti*-**2b** by transformation into (3*S*,4*R*)-3-dibenzylamino-2-methyl-4-heptanol by reduction on Pearlman's catalyst and dibenzylation with benzyl bromide and K_2CO_3 in acetonitrile. This amino alcohol was also obtained by reaction of **1b** with propylmagnesium bromide as previously described.[12]

γ-Amino-β-hydroxy carbonyl compounds are important parts of biologically interesting molecules,[13] and their synthesis has attracted much attention.[14] In this way, we consider the transformation of dibenzylamino homopropargyl alcohols **2** into γ-amino-β-hydroxy ketones **3** as an alternative to the aldol type reaction of α-amino aldehydes with acetone.[15] The versatility of our method allowed the synthesis of either *anti*- or *syn* diastereoisomers depending on the stereochemistry of the starting compound, avoiding the stereochemical problem associated with the aldol reaction. To this end, *anti*-**2a–e** and *syn*-**2e**,**f** were subjected to hydration by reaction with 10% solution of H_2SO_4 and a catalytic amount of $HgSO_4$ at room temperature.[16] Ketones *anti*-**3a–e** and *syn*-**3e**,**f** were isolated in moderate to good yield as single diastereoisomers (Scheme 2 and Table 2), as shown by the identity of their physical and spectral data with those previously described for *anti*-**3a** and **3b**.[15]



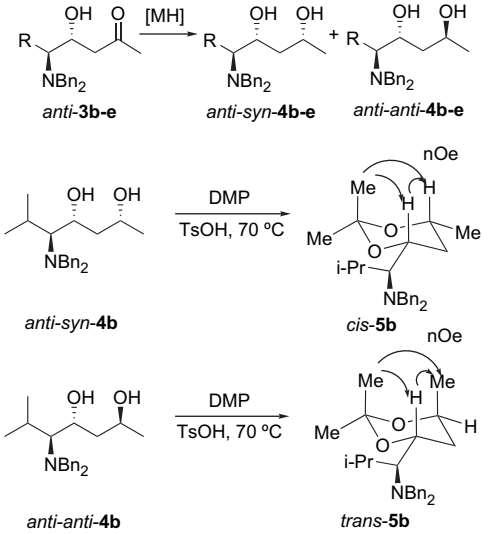
Scheme 2. Reagents and conditions: (i) H_2SO_4, $HgSO_4$, MeOH, rt.

Table 2. Hydration of the triple bond of compounds *syn*- and *anti*-**2**

Entry	**2**	R	*t* (h)	Aldol	Yield (%)[a]
1	*anti*-**2a**	Me	7	*anti*-**3a**	75
2	*anti*-**2b**	^{i}Pr	5	*anti*-**3b**	65
3	*anti*-**2c**	$PhCH_2$	6	*anti*-**3c**	75
4	*syn*-**2e**	Ph	3	*syn*-**3e**	51
5	*anti*-**2e**	Ph	5	*anti*-**3e**	56
6	*syn*-**2f**	—	5	*syn*-**3f**	51

[a] Numbers correspond to yield of pure and isolated products.

Compounds **3b–e** were transformed into 4-amino-1,3-diols **4b–e** in moderate to good yields and excellent de by reduction with different complex metal hydrides (Scheme 3 and



Scheme 3.

Table 3. Stereoselective reduction of β-hydroxy ketones *anti*-**3**

Entry	**3**	Hydride	Solvent	T[a] (°C)	Yield[a] (%)	*syn*/*anti*[b]
1	*anti*-**3b**	$NaBH_4$	MeOH	−20	62	80:20
2	*anti*-**3b**	$Et_3B/NaBH_4$	THF/MeOH (4:1)	−78	52	>95:5
3	*anti*-**3b**	$NaBH(OAc)_3$	CH_3CN/HOAc	−40	66	23:77
4	*anti*-**3c**	$Et_3B/NaBH_4$	THF/MeOH (4:1)	−78	50	>95:5
5	*anti*-**3c**	$NaBH(OAc)_3$	CH_3CN/HOAc	−40	40	34:66
6	*anti*-**3e**	$Et_3B/NaBH_4$	THF/MeOH (4:1)	−78	68	>95:5
7	*anti*-**3e**	$NaBH(OAc)_3$	CH_3CN/HOAc	−40	88	37:63

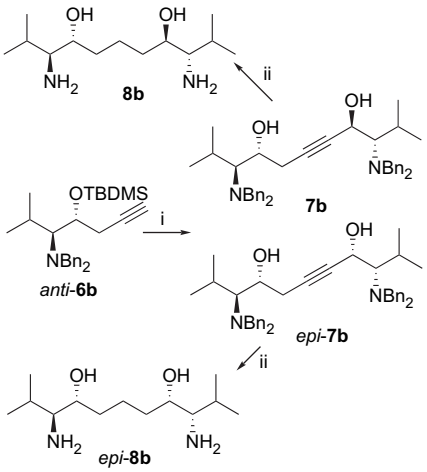
[a] Numbers correspond to combined yield of pure and isolated diastereoisomers.
[b] The diastereomeric ratio was determined by integration of the signals of ^1H NMR spectra of the reaction mixture.

Table 3). The selection of the reducing agent allowed the preparation of either diastereoisomers of **4b–e**.

The reduction of *anti*-**3b** with $NaBH_4$ in methanol yielded a mixture of *anti-syn*-**4b** and *anti-anti*-**4b** in a ratio 4:1 but the reduction in the presence of Et_2BOMe, generated in situ from Et_3B and MeOH,[17] leads to *anti-syn*-**4b** as a single diastereoisomer. Alternatively, the reaction of *anti*-**3b** with Evans's reagent ($NaBH(OAc)_3$)[18] in a mixture of acetonitrile/acetic acid as solvent at −40 °C gave *anti-anti*-**4b** as major diastereoisomer although in moderate de (entry 3 in Table 3). The reduction of *anti*-**3c–e** follows the same pattern as described for *anti*-**3b**. The reduction with $NaBH_4$/Et_2BOMe yielded *anti-syn*-**4c–e** as a single diastereoisomer, whereas the reaction with $NaBH(OAc)_3$ leads to *anti-anti*-**4c–e** as major isomers in moderate de.

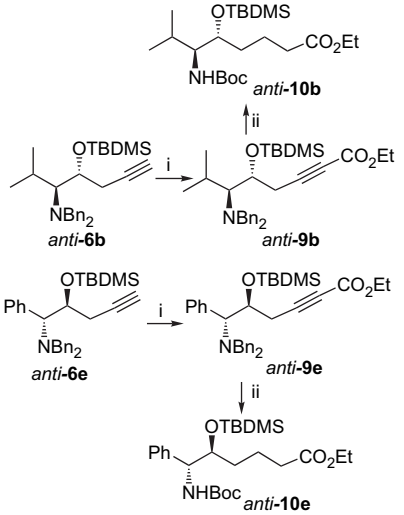
The stereochemistry of the amino diols *anti-syn*-**4b** and *anti-anti*-**4b** was established by transformation into 1,3-dioxane derivatives *cis*-**5b** and *trans*-**5b**, respectively, by reaction with 2,2-dimethoxypropane and *p*-toluenesulfonic acid as catalyst (Scheme 3). The NOESY experiment of *cis*-**5b** shows cross peak for the signal of the axial methyl group at C-2 and the hydrogen atoms at C-4 and C-6, demonstrating the *cis*-relationship of the substituents at C-4 and C-6. For *trans*-**5b** the cross peaks appeared for the signals of the methyl groups at C-2 and C-4 and the hydrogen atom at C-6 in the dioxane ring, pointing a *trans*-disposition of the methyl at C-4 and the substituent at C-6. The stereochemistry was generalized for amino diols **4c–e**.

The interest in homopropargyl amino alcohols **2** as synthetic intermediates was extended to the preparation of ω-amino-δ-hydroxy acids and C_2-symmetrical 1,7-diamino-2,6-diols previously used as chiral ligands[19] and in the synthesis of pharmacological active compounds.[20] Homopropargyl amino alcohol *anti*-**2b** was transformed into *anti*-**6b** by treatment with TBDMSCl and imidazole in DMF. Lithium acetylide, prepared by deprotonation of *anti*-**6b** with *n*-BuLi in THF at −78 °C, was reacted with L-dibenzylamino valinal **1b** and after desilylation with TBAF yielded a mixture (4:1) of diastereomeric bis-amino alcohols **7b** and *epi*-**7b** in 66% yield (Scheme 4). After separation, the major diastereoisomer **7b** was transformed into the homochiral C_2-symmetrical 1,7-diamino-2,6-diol derivative **8b** by hydrogenation/hydrogenolysis on Pearlman's catalyst. The same treatment on *epi*-**7b** leads to *epi*-**8b** also in excellent yield.



Scheme 4. Reagents and conditions: (i) 1. *n*-BuLi (1.1 equiv), THF, −78 °C, 1 h. 2. **1b** (1.1 equiv), THF, −78 °C, 1 h. 3. TBAF (1.2 equiv), THF, 0 °C, 5 h. 4. NH_4Cl. (ii) H_2, $Pd(OH)_2/C$, MeOH.

Finally, both *anti*-**6b** and *anti*-**6e** were transformed into the ω-amino-δ-hydroxy ethyl esters *anti*-**10b** and *anti*-**10e**, respectively, in two steps as summarized in Scheme 5. Deprotonation with *n*-BuLi in THF at −78 °C of *anti*-**6b** and **6e**, followed by reaction with ethyl chloroformate in THF at −40 °C lead to esters *anti*-**9b** and *anti*-**9e** in good yields. These esters cannot be purified because extensive decomposition was observed when subjected to flash chromatography, but they were transformed in moderate yields into the saturated amino hydroxyl ester derivatives *anti*-**10b** and *anti*-**10e** by hydrogenation on Pearlman's catalyst in the presence of Boc_2O using EtOAc as solvent.



Scheme 5. Reagents and conditions: (i) 1. *n*-BuLi (1.5 equiv), THF, −78 °C, 1 h. 2. $ClCO_2Et$ (2 equiv), THF, −78 °C to −40 °C, 0.5 h. 3. NH_4Cl. (ii) H_2, $Pd(OH)_2/C$, Boc_2O, EtOAc.

In summary, reaction of chiral α-dibenzylamino aldehydes with propargyl bromide and zinc yielded *anti* amino alcohols as major diastereoisomer. As an alternative to the aldol reaction, these compounds were transformed in good yields to γ-amino-β-hydroxy ketones, by hydration of the triple bond. In a different way, lithium derivatives of these homopropargyl amino alcohols reacted with ethyl chloroformate to

yield enantioenriched ω-amino-δ-hydroxy esters or with chiral α-dibenzylamino aldehydes leading to propargyl diamino diols, which were further elaborated to the corresponding saturated homochiral C_2 diamino diols.

3. Experimental

3.1. General

The reactions were carried out in oven-dried glassware under argon atmosphere and using anhydrous solvents. Starting *N*,*N*-dibenzyl α-amino aldehydes **1a–e** were prepared as previously described.[9a] Propargyl bromide, as 80 wt % solution in toluene, is commercially available. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were registered using TMS as an internal standard. IR spectra were recorded as film or KBr dispersion. Optical rotations were measured in a 1 dm cell. Microanalyses were performed by the Departamento de Química Inorgánica.

3.2. General procedure for propargylation of α-amino aldehydes

The amino aldehyde (2 mmol) and propargyl bromide (80 wt % in toluene, 0.44 mL, 4 mmol) were dissolved in a mixed solvent (DMF/ether or DMF/THF, 1:1, 8 mL). To this well-stirred solution was added activated zinc dust (washed with 2% HCl, water, methanol, and dried in vacuum; 392 mg, 6 mmol) slowly at 0 °C. After 5 min, the exothermic reaction brought itself to reflux. The whole reaction mixture was stirred at room temperature until the reaction was finished (TLC) and then quenched with aqueous saturated solution of ammonium chloride (20 mL). The organic layer was separated and the aqueous phase was extracted with diethyl ether (3×20 mL). The combined organic layers were washed with brine, and dried over anhydrous $MgSO_4$. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel, hexane/ethyl acetate 15:1 to 50:1).

3.2.1. (2*S*,3*R*)-2-Dibenzylaminohex-5-yn-3-ol (*anti*-2a). This compound was obtained as the major diastereomer in the propargylation of amino aldehyde **1a** (760 mg, 3 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 15:1): 586 mg (2.0 mmol, 67%). Colorless oil. $[\alpha]_D^{23}$ +37.8 (*c* 1.0, $CHCl_3$). IR (film): 3435, 3300, 2117, 1028, 748, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.20 (d, 3H, *J*=6.6 Hz, C*H*$_3$); 1.96 (t, 1H, *J*=2.6 Hz, ≡C–*H*); 2.12 (br s, 1H, O*H*); 2.27 (ddd, *J*=16.7, 8.0, 2.6 Hz, C*H*HCHOH); 2.72 (dq, 1H, *J*=8.2, 6.6 Hz, C*H*N); 2.82 (ddd, *J*=16.7, 3.6, 2.7 Hz, CH*H*CHOH); 3.44 (d, 2H, *J*=13.7 Hz, C*H*HPh); 3.76 (d, 2H, *J*=13.7 Hz, CH*H*Ph); 7.20–7.45 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 8.3 (*C*H$_3$); 25.1 (*C*H$_2$C≡C); 54.3 (*C*H$_2$Ph); 56.7 (*C*HN); 70.7 (C≡*C*H); 71.8 (*C*HOH); 81.5 (CH≡*C*); 126.9, 128.2, 128.7 (*C*Har); 139.6 (*C*ar). $C_{20}H_{23}NO$ (293.4): calcd C 81.87, H 7.90, N 4.77; found C 81.64, H 7.75, N 4.65.

3.2.2. (4*R*,5*S*)-5-Dibenzylamino-6-methylhept-1-yn-4-ol (*anti*-2b). This compound was obtained as the major diastereoisomer in the propargylation of amino aldehyde **1b** (844 mg, 3 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 30:1): 694 mg (2.16 mmol, 72%). Colorless oil. $[\alpha]_D^{23}$ −5.5 (*c* 1.0, $CHCl_3$). IR (film): 3568, 3457, 3303, 2116, 1064, 748, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.03 (d, 1H, *J*=6.7 Hz, C*H*$_3$); 1.13 (d, 1H, *J*=6.9 Hz, C*H*$_3$); 1.98 (m, 1H, ≡C*H*); 2.24 (m, 1H, C*H*(CH$_3$)$_2$); 2.30 (m, 1H, C*H*HCHOH); 2.43 (m, 2H, C*H*N and O*H*); 2.62 (ddd, 1H, *J*=16.6, 3.5, 2.5 Hz, CH*H*CHOH); 3.64 (d, 2H, *J*=13.5 Hz, C*H*HPh); 3.96 (d, 2H, *J*=13.5 Hz, CH*H*Ph); 7.15–7.40 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 20.0 (*C*H$_3$); 23.4 (*C*H$_3$); 25.5 (*C*H$_2$–C≡C); 26.3 (*C*H(CH$_3$)$_2$); 55.2 (*C*H$_2$Ph); 65.4 (*C*HN); 68.7 (*C*HOH); 70.4 (≡*C*H); 81.9 (*C*≡CH); 127.0, 128.3, 129.0 (*C*Har); 139.5 (*C*ar). $C_{22}H_{27}NO$ (321.5): calcd C 82.20, H 8.47, N 4.36; found C 82.34, H 8.30, N 4.49.

3.2.3. (2*S*,3*R*)-2-Dibenzylamino-1-phenylhex-5-yn-3-ol (*anti*-2c). This compound was obtained as the major diastereomer in the propargylation of amino aldehyde **1c** (659 mg, 2 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 15:1): 440 mg (1.19 mmol, 60%). Colorless oil. $[\alpha]_D^{23}$ +14.3 (*c* 1.1, $CHCl_3$). IR (film): 3450, 3297, 3300, 2117, 1072, 744, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.95 (t, 1H, *J*=2.6 Hz, ≡C*H*); 2.05 (br s, 1H, O*H*); 2.24 (ddd, 1H, *J*=16.7, 8.4, 2.6 Hz, C*H*HC≡CH); 2.60 (ddd, 1H, *J*=16.7, 4.2, 2.7 Hz, CH*H*C≡CH); 3.61 (d, 2H, *J*=13.8 Hz, NC*H*HPh); 3.02 (m, 3H, C*H*$_2$C*H*N); 3.73 (d, 2H, *J*=13.8 Hz, NCH*H*Ph); 3.99 (m, 1H, C*H*OH); 7.15–7.35 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 25.7 (*C*H$_2$C≡C); 32.0 (*C*H$_2$Ph); 54.6 (N*C*H$_2$Ph); 62.7 (*C*HN); 70.5 (*C*HOH); 70.8 (C≡*C*H); 81.2 (*C*≡CH); 125.8, 126.9, 128.2, 128.3, 128.7, 129.4 (*C*Har); 139.5, 140.8 (*C*ar). $C_{26}H_{27}NO$ (369.5): calcd C 84.51, H 7.37, N 3.79; found C 84.28, H 7.07, N 3.94.

3.2.4. (2*S*,3*S*)-2-Dibenzylamino-1-phenylhex-5-yn-3-ol (*syn*-2c). This compound was obtained as the minor diastereomer in the propargylation of amino aldehyde **1c** (659 mg, 2 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 15:1): 74 mg (0.2 mmol, 10%). Colorless oil. $[\alpha]_D^{23}$ +23.0 (*c* 0.54, $CHCl_3$). IR (film): 3300, 2118, 1072, 744, 701 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.81 (t, 1H, *J*=2.6 Hz, ≡C*H*); 2.15 (ddd, 1H, *J*=17.0, 6.3, 2.6 Hz, C*H*HC≡CH); 2.25 (ddd, 1H, *J*=17.0, 3.6, 2.6 Hz, CH*H*C≡CH); 2.76 (dd, 1H, *J*=13.0, 6.0 Hz, PhC*H*H); 3.09 (m, 2H, C*H*N and CH*H*Ph); 3.39 (d, 2H, *J*=13.2 Hz, NC*H*HPh); 3.94 (d, 2H, *J*=13.2 Hz, NCH*H*Ph); 3.69 (m, 1H, C*H*OH); 4.31 (br s, 1H, O*H*); 7.10–7.40 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 24.6 (*C*H$_2$C≡C); 32.0 (*C*H$_2$Ph); 54.1 (N*C*H$_2$Ph); 62.5 (*C*HN); 68.9 (*C*HOH); 70.1 (C≡*C*H); 80.9 (*C*≡CH); 126.4, 127.2, 128.4, 128.6, 129.1, 129.2 (*C*Har); 138.7, 139.8 (*C*ar). $C_{26}H_{27}NO$ (369.5): calcd C 84.51, H 7.37, N 3.79; found C 84.36, H 7.22, N 3.59.

3.2.5. (2*S*,3*R*)-2-Dibenzylamino-1-(*tert*-butyldimethylsilyloxy)hex-5-yn-3-ol (*anti*-2d). This compound was obtained as the major product together with the diastereomer *syn*-**2b** in the propargylation of amino aldehyde **1d** (1.53 g, 4 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 50:1): 970 mg (2.3 mmol, 57% combined yield, de=78%). Colorless oil. $[\alpha]_D^{23}$ +39.5 (*c* 1.1, $CHCl_3$). IR (film): 3307, 1602, 1493, 1089, 777, 746, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.94 (t, 1H, *J*=2.6 Hz,

*H*C≡); 2.29 (ddd, 1H, *J*=16.7, 7.7, 2.6 Hz, C*H*HCHOH); 2.77 (m, 2H, C*H*N, CH*H*CHOH); 3.63 (d, 1H, *J*=13.7 Hz, CH*H*Ph); 3.90 (d, 1H, *J*=13.7 Hz, C*H*HPh); 4.07 (m, 3H, C*H*OH, CH_2OTBDMS); 7.20–7.40 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 18.0 ($C(CH_3)_3$); 25.2 ($CH_2C{\equiv}C$); 25.8 ($C(CH_3)_3$); 55.1 (CH_2Ph); 60.5 (CH_2O); 60.8 (*C*HN); 70.1 (*C*HOH); 126.9 (*C*≡C); 128.2, 128.4, 128.8 (*C*Har); 139.6 (*C*ar).

3.2.6. (1*R*,2*S*)-1-Dibenzylamino-1-phenylpent-4-yn-2-ol (*anti*-2e). This compound was obtained as the major diastereomer in the propargylation of amino aldehyde **1e** (1.58 g, 5 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 15:1): 759 mg (2.14 mmol, 43%). Colorless oil. $[\alpha]_D^{23}$ −110.0 (*c* 0.9, $CHCl_3$). IR (film): 3550, 3447, 3300, 2118, 1028, 748, 703 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.99 (t, 1H, *J*=2.6 Hz, ≡C*H*); 2.43 (ddd, 1H, *J*=16.9, 7.9, 2.6 Hz, C*H*HCHOH); 3.02 (m, 1H, CH*H*CHOH); 3.07 (d, 2H, *J*=13.7 Hz, C*H*HPh); 3.67 (d, 1H, *J*=9.2 Hz, C*H*N); 3.83 (d, 2H, *J*=13.7 Hz, CH*H*Ph); 4.45 (m, 1H, C*H*OH); 7.20–7.55 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 24.8 (CH_2); 54.6 (CH_2Ph); 66.7 (*C*HN); 69.1 (*C*HOH); 70.8 (C≡*C*H); 81.4 (*C*≡CH); 127.1, 127.8, 128.3, 128.4, 128.8, 129.9 (*C*Har); 134.4, 139.1 (*C*ar). $C_{25}H_{25}NO$ (355.5): calcd C 84.47, H 7.09, N 3.94; found C 84.23, H 6.95, N 4.10.

3.2.7. (1*R*,2*R*)-1-Dibenzylamino-1-phenylpent-4-yn-2-ol (*syn*-2e). This compound was obtained as the minor diastereomer in the propargylation of amino aldehyde **1e** (1.58 g, 5 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 15:1): 325 mg (0.91 mmol, 18%). Colorless oil. $[\alpha]_D^{23}$ −74.9 (*c* 1.1, $CHCl_3$). IR (film): 3405, 3305, 1074, 753, 702 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.81 (t, 1H, *J*=2.6 Hz, ≡C*H*); 1.92 (ddd, 1H, *J*=17.0, 6.5, 2.6 Hz, C*H*HCHOH); 2.28 (ddd, 1H, *J*=17.0, 3.2, 2.6 Hz, CH*H*CHOH); 3.05 (d, 2H, *J*=13.2 Hz, CH*H*Ph); 3.72 (d, 1H, *J*=10.3 Hz, C*H*N); 3.95 (d, 2H, *J*=13.2 Hz, C*H*HPh); 4.36 (ddd, 1H, *J*=10.3, 6.5, 3.2 Hz, C*H*OH); 4.62 (br s, 1H, O*H*); 7.20–7.50 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 23.8 (CH_2); 53.6 (CH_2Ph); 66.1 (*C*HN); 66.5 (*C*HOH); 69.9 (≡*C*H); 80.4 (C≡*C*H); 127.3, 128.2, 128.5, 128.6, 129.0, 129.8 (*C*Har); 133.1, 138.3 (*C*ar). $C_{25}H_{25}NO$ (355.5): calcd C 84.47, H 7.09, N 3.94; found C 84.27, H 6.92, N 3.99.

3.2.8. (*R*)-1-[(*S*)-1-Benzyl-2-pyrrolidinyl]but-3-yn-1-ol (*anti*-2f). This compound was obtained as the minor diastereomer in the propargylation of amino aldehyde **1f** (568 mg, 3 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 2:1): 62 mg (0.27 mmol, 9%). Colorless oil. $[\alpha]_D^{23}$ +20.5 (*c* 0.3, MeOH). IR (film): 3198, 1617, 1388, 1053, 733, 706 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.73 (m, 4H, CH_2); 2.03 (t, 1H, *J*=5.4 Hz, C≡C*H*); 2.15 (s, 1H, C*H*HCN); 2.28 (m, 1H, C*H*HC≡C); 2.57 (ddd, 1H, *J*=9.6, 7.0, 2.7 Hz, CH*H*C≡C); 2.80 (td, 1H, *J*=7.7, 2.7 Hz, C*H*N); 2.97 (m, 1H, CH*H*CN); 3.32 (d, 1H, *J*=13.0 Hz, C*H*HPh); 3.98 (dt, 1H, *J*=7.2, 2.7 Hz, C*H*OH); 4.06 (d, 1H, *J*=13.0 Hz, CH*H*Ph); 7.20–7.45 (m, 5H, *H*ar). ^{13}C NMR ($CDCl_3$): 22.9, 23.0 (CH_2); 23.1 ($CH_2C{\equiv}CH$); 54.4 (CH_2Ph); 58.1 (CH_2N); 66.2 (*C*HN); 67.2 (*C*HOH); 69.8 (C≡*C*H); 80.8 (*C*≡CH); 127.0, 128.3, 128.7 (*C*Har); 139.0 (*C*ar). $C_{15}H_{19}NO$ (229.3): calcd C 78.56, H 8.35, N 6.11; found C 78.71, H 8.42, N 6.04.

3.2.9. (*S*)-1-[(*S*)-1-Benzyl-2-pyrrolidinyl]but-3-yn-1-ol (*syn*-2f). This compound was obtained as the major diastereomer in the propargylation of amino aldehyde **1f** (568 mg, 3 mmol) and purified by flash chromatography (silica gel, hexane/EtOAc 2:1): 282 mg (1.23 mmol, 41%). Colorless oil. $[\alpha]_D^{23}$ −24.7 (*c* 1.0, MeOH). IR (film): 3410, 3293, 2117, 1072, 744, 701 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.70 (m, 3H, CH_2 and C*H*HCN); 1.97 (m, 1H, CH*H*CHN); 2.03 (t, 1H, *J*=2.6 Hz, C≡C*H*); 2.38 (m, 1H, C*H*HN); 2.43 (m, 2H, C*H*HC≡CH); 2.91 (m, 1H, CH*H*N); 3.05 (ddd, 1H, *J*=8.9, 5.2, 3.3 Hz, C*H*N); 3.48 (q, 1H, *J*=6.3, 5.2 Hz, C*H*OH); 3.58 (d, 1H, *J*=13.3 Hz, C*H*HPh); 4.02 (d, 1H, *J*=13.3 Hz, CH*H*Ph); 7.20–7.30 (m, 5H, *H*ar). ^{13}C NMR ($CDCl_3$): 24.5, 24.7 (CH_2); 29.1 ($CH_2C{\equiv}C$); 54.3 (CH_2Ph); 61.6 (CH_2N); 66.3 (*C*HN); 70.1 (C≡*C*H); 72.0 (*C*HOH); 81.2 (*C*≡CH); 127.0, 128.1, 128.3, 128.4 (*C*Har); 139.4 (*C*ar). $C_{15}H_{19}NO$ (229.3): calcd C 78.56, H 8.35, N 6.11; found C 78.75, H 8.29, N 6.04.

3.2.10. (4*R*,5*S*)-5-Dibenzylamino-4-hydroxyhexan-2-one (*anti*-3a). To a solution of amino alcohol *anti*-**2a** (293 mg, 1.0 mmol) and $HgSO_4$ (75 mg, 0.25 mmol) in MeOH (4 mL) at 0 °C was added 10% H_2SO_4 (1.0 mL), and the resultant reaction mixture was stirred at room temperature for 2–5 h (TLC). The pH of the reaction was adjusted to 7 with saturated $NaHCO_3$ and the mixture extracted with Et_2O (3×10 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, concentrated, and chromatographed (silica gel, hexane/EtOAc 6:1): 232 mg of *anti*-**3a** (0.75 mmol, 75%). Colorless oil. $[\alpha]_D^{23}$ +43.5 (*c* 1, $CHCl_3$). Lit.[15] $[\alpha]_D^{23}$ +45.2 (*c* 1.1, $CHCl_3$). IR (film): 3452, 1704, 1061, 748, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.16 (d, 3H, *J*=6.6 Hz, CH_3CH); 2.08 (s, 3H, CH_3CO); 2.37 (dd, 1H, *J*=18.1, 8.9 Hz, C*H*HCO); 2.64 (dq, 1H, *J*=8.6, 6.6 Hz, C*H*N); 3.03 (dd, 1H, *J*=18.1, 2.3 Hz, CH*H*CO); 3.06 (br s, 1H, O*H*); 3.39 (d, 2H, *J*=13.6 Hz, CH*H*Ph); 3.72 (d, 2H, *J*=13.6 Hz, C*H*HPh); 3.98 (m, 1H, C*H*OH); 7.20–7.40 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 8.2 (CH_3CH); 30.6 (CH_3CO); 47.5 (CH_2CO); 54.2 (CH_2Ph); 56.4 (*C*HN); 69.6 (*C*HOH); 126.8, 128.2, 128.7 (*C*Har); 139.7 (*C*ar); 210.7 (*C*O).

3.2.11. (4*R*,5*S*)-5-Dibenzylamino-4-hydroxy-6-methylheptan-2-one (*anti*-3b). This compound was obtained from *anti*-**2b** (450 mg, 1.4 mmol), by the method described for *anti*-**3a** and purified by flash chromatography (silica gel, hexane/EtOAc 8:1): 309 mg (0.91 mmol, 65%). Colorless oil. $[\alpha]_D^{23}$ +10.6 (*c* 1.1, $CHCl_3$). Lit.[15] $[\alpha]_D^{23}$ +10.3 (*c* 1.0, $CHCl_3$). IR (film): 3470, 1705, 1069, 749, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.08 (d, 3H, *J*=6.7 Hz, CH_3); 1.18 (d, 3H, *J*=6.8 Hz, CH_3); 2.17 (s, 3H, CH_3CO); 2.22 (m, 1H, $CH(CH_3)_2$); 2.45 (t, 1H, *J*=6.3 Hz, C*H*N); 2.56 (dd, 1H, *J*=17.0, 10.0 Hz, C*H*HCO); 2.76 (dd, 1H, *J*=17.0, 2.0 Hz, CH*H*CO); 3.20 (br s, 1H, O*H*); 3.70 (d, 2H, *J*=13.6 Hz, CH*H*Ph); 3.76 (d, 2H, *J*=13.6 Hz, C*H*HPh); 4.34 (m, 1H, C*H*OH); 7.20–7.40 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 20.0 (CH_3); 23.3 (CH_3); 26.4 ($CH(CH_3)_2$); 30.8 (CH_3CO); 48.2 (CH_2CO); 55.1 (CH_2Ph); 65.3 (*C*HN); 66.3 (*C*HOH); 127.0, 128.3, 129.3 (*C*Har); 139.6 (*C*ar); 209.9 (*C*O).

3.2.12. (4*R*,5*S*)-5-Dibenzylamino-4-hydroxy-6-phenylhexan-2-one (*anti*-3c). This compound was obtained from *anti*-**2c** (259 mg, 0.7 mmol) by the method described for

anti-**3a** and purified by flash chromatography (silica gel, hexane/EtOAc 8:1): 203 mg (0.52 mmol, 75%). Colorless oil. $[\alpha]_D^{23}$ +17.2 (*c* 1.1, $CHCl_3$). IR (film): 3482, 1706, 1365, 1073, 736, 702 cm^{-1}. ^1H NMR ($CDCl_3$): 2.06 (s, 3H, C*H*$_3$); 2.41 (dd, 1H, *J*=17.8, 9.5 Hz, C*H*HCO); 2.77 (dd, 1H, *J*=17.8, 2.3 Hz, CH*H*CO); 2.92 (m, 1H, C*H*N); 3.00 (m, 1H, C*H*HPh); 3.08 (dd, 1H, *J*=14.0, 7.6 Hz, CH*H*Ph); 3.61 (d, 2H, *J*=13.8 Hz, CH*H*Ph); 3.72 (d, 2H, *J*=13.8 Hz, C*H*HPh); 4.27 (m, 1H, C*H*OH); 7.15–7.35 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 30.6 (*C*H$_3$); 32.1 (*C*H$_2$Ph); 48.0 (*C*H$_2$CO); 54.5 (N*C*H$_2$Ph); 62.7 (*C*HN); 68.1 (*C*HOH); 125.8, 126.8, 128.1, 128.2, 128.7, 129.4 (*C*Har); 139.6, 141.1 (*C*ar); 210.2 (*C*O). $C_{26}H_{29}NO_2$ (387.5): calcd C 80.59, H 7.54, N 3.61; found C 80.74, H 7.74, N 3.42.

3.2.13. (4*S*,5*R*)-5-Dibenzylamino-4-hydroxy-5-phenylpentan-2-one (*anti*-3e). This compound was obtained from *anti*-**2e** (427 mg, 1.2 mmol) by the method described for *anti*-**3a** and purified by flash chromatography (silica gel, hexane/EtOAc 8:1): 250 mg (0.67 mmol, 56%). Colorless solid, mp 112–113 °C. $[\alpha]_D^{23}$ −119.8 (*c* 1, $CHCl_3$). IR (KBr): 3581, 1716, 748, 701 cm^{-1}. ^1H NMR ($CDCl_3$): 2.20 (s, 3H, C*H*$_3$); 2.45 (br s, 1H, O*H*); 2.54 (dd, 1H, *J*=17.7, 9.2 Hz, C*H*HCO); 3.07 (d, 2H, *J*=13.7 Hz, CH*H*Ph); 3.29 (dd, 1H, *J*=17.7, 2.3 Hz, CH*H*CO); 3.62 (d, 1H, *J*=9.5 Hz, C*H*N); 3.83 (d, 2H, *J*=13.7 Hz, C*H*HPh); 4.78 (m, 1H, C*H*OH); 7.20–7.50 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 30.9 (*C*H$_3$); 47.8 (*C*H$_2$CO); 54.4 (*C*H$_2$Ph); 66.3 (*C*HN); 66.9 (*C*HOH); 127.0, 127.6, 128.2, 128.3, 128.8, 129.9 (*C*Har); 134.5, 139.3 (*C*ar); 209.7 (*C*O). $C_{25}H_{27}NO_2$ (373.5): calcd C 80.40, H 7.29, N 3.75; found C 80.50, H 7.45, N 3.60.

3.2.14. (4*R*,5*R*)-5-Dibenzylamino-4-hydroxy-5-phenylpentan-2-one (*syn*-3e). This compound was obtained from *syn*-**2e** (355 mg, 1.0 mmol) by the method described for *anti*-**3a** and purified by flash chromatography (silica gel, hexane/EtOAc 6:1): 190 mg (0.51 mmol, 51%). Colorless solid, mp 100–101 °C (from hexane). $[\alpha]_D^{23}$ −132.4 (*c* 1, $CHCl_3$). IR (KBr): 3388, 1710, 1076, 757, 701 cm^{-1}. ^1H NMR ($CDCl_3$): 2.04 (s, 3H, C*H*$_3$); 2.10 (dd, 1H, *J*=16.0, 2.2 Hz, C*H*HCO); 2.30 (dd, 1H, *J*=16.0, 9.1 Hz, CH*H*CO); 3.02 (d, 2H, *J*=13.3 Hz, CH*H*Ph); 3.50 (d, 1H, *J*=10.4 Hz, C*H*N); 3.98 (d, 2H, *J*=13.3 Hz, C*H*HPh); 4.40 (br s, 1H, O*H*); 4.74 (m, 1H, C*H*OH); 7.15–7.50 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 30.8 (*C*H$_3$); 47.9 (*C*H$_2$CO); 53.4 (*C*H$_2$Ph); 64.5 (*C*HN); 66.9 (*C*HOH); 127.2, 128.1, 128.5, 128.9, 129.7 (*C*Har); 133.1, 138.3 (*C*ar); 207.2 (*C*O). $C_{25}H_{27}NO_2$ (373.5): calcd C 80.40, H 7.29, N 3.75; found C 80.03, H 7.13, N 3.75.

3.2.15. (*S*)-4-[(*S*)-1-Benzyl-2-pyrrolidinyl]-4-hydroxybutan-2-one (*syn*-3f). This compound was obtained from *syn*-**2f** (92 mg, 0.4 mmol) by the method described for *anti*-**3a** and purified by flash chromatography (silica gel, hexane/EtOAc 3:2): 52 mg (0.21 mmol, 52%). Colorless oil. $[\alpha]_D^{23}$ −53.1 (*c* 0.52, $CHCl_3$). IR (film): 3438, 1711, 1357, 1073, 746, 701 cm^{-1}. ^1H NMR ($CDCl_3$): 1.69 (m, 3H, C*H*$_2$ and C*H*HCHN); 1.93 (m, 1H, CH*H*CHN); 2.21 (s, 3H, C*H*$_3$CO); 2.39 (m, 1H, C*H*HN); 2.53 (dd, 1H, *J*=16.2, 9.1 Hz, CH*H*CO); 2.64 (dd, 1H, *J*=16.2, 3.4 Hz, C*H*HCO); 2.82 (m, 1H, C*H*N); 2.93 (m, 1H, CH*H*N); 3.54 (d, 1H, *J*=13.2 Hz, C*H*HPh); 3.88 (m, 1H, C*H*OH); 3.96 (d, 1H, *J*=13.2 Hz, CH*H*Ph); 7.30–7.40 (m, 5H, *H*ar). ^{13}C NMR ($CDCl_3$): 24.2 (*C*H$_2$); 27.5 (*C*H$_2$); 30.9 (*C*H$_3$); 47.3 (*C*H$_2$CO); 54.2 (*C*H$_2$Ph); 61.1 (*C*H$_2$N); 67.4 (*C*HN); 69.7 (*C*HOH); 126.9, 128.3, 128.5 (*C*Har); 139.5 (*C*ar); 209.0 (*C*O). $C_{15}H_{21}NO_2$ (247.3): calcd C 72.84, H 8.56, N 5.66; found C 72.72, H 8.40, N 5.80.

3.2.16. (2*R*,4*R*,5*S*)-5-Dibenzylamino-6-methylheptane-2,4-diol (*anti-syn*-4b). A solution of triethylborane (1.0 M in hexane, 0.23 mL, 0.23 mmol, 1.1 equiv) was added to a mixture of anhydrous THF (2 mL) and MeOH (0.5 mL) at 0 °C under nitrogen. After stirring for 1 h at room temperature, the mixture was cooled to −78 °C followed by the addition of β-hydroxy ketone *anti*-**3b** (71 mg, 0.21 mmol, 1 equiv) in THF (0.5 mL) and stirring was continued for 30 min. Then sodium borohydride (10 mg, 0.25 mmol, 1.2 equiv) was added, and the mixture was stirred for 3–4 h, depending on the substrate used. The reaction mixture was quenched with aqueous NH_4Cl (3 mL) and extracted with Et_2O (3×5 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and the volatiles were evaporated. The crude product was dissolved in THF (1 mL) and aqueous 10% NaOH solution (1 mL) and the mixture was stirred vigorously for 1 h. Then THF was removed and the aqueous phase was extracted with $CHCl_3$ (3×5 mL). The combined organic extracts were washed with H_2O and dried with anhydrous $MgSO_4$. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel, hexane/EtOAc 6:1): 37 mg (0.11 mmol, 52%). Colorless oil. $[\alpha]_D^{23}$ −12.1 (*c* 0.5, $CHCl_3$). IR (film): 3380, 1452, 1070, 749, 699 cm^{-1}. ^1H NMR ($CDCl_3$): 0.91 (d, 3H, *J*=6.6 Hz, (C*H*$_3$)$_2$CH); 1.16 (d, 3H, *J*=6.2 Hz, (C*H*$_3$CH)); 1.28 (d, 3H, *J*=6.5 Hz, (C*H*$_3$)$_2$CH); 1.50 (m, 1H, C*H*HCHOH); 1.61 (m, 1H, CH*H*CHOH); 2.16 (m, 1H, C*H*(CH$_3$)$_2$); 2.54 (dd, 1H, *J*=10.3, 4.9 Hz, C*H*N); 3.69 (m, 1H, C*H*OH); 3.74 (d, 2H, *J*=13.3 Hz, CH*H*Ph); 3.93 (d, 2H, *J*=13.3 Hz, C*H*HPh); 3.95 (m, 1H, CH$_3$C*H*OH); 4.17 (br s, 1H, O*H*); 7.20–7.40 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 20.8 (*C*H$_3$); 23.2 (*C*H$_3$); 23.7 (*C*H$_3$); 28.4 (*C*H(CH$_3$)$_2$); 39.8 (*C*H$_2$); 56.4 (*C*H$_2$Ph); 66.8 (*C*HOH); 69.5 (*C*HOH); 71.7 (*C*HN); 127.5, 128.6, 129.2 (*C*Har); 139.4 (*C*ar). $C_{22}H_{31}NO_2$ (341.5): calcd C 77.38, H 9.15, N 4.10; found C 77.21, H 9.29, N 3.98.

3.2.17. (2*S*,4*R*,5*S*)-5-Dibenzylamino-6-methylheptane-2,4-diol (*anti-anti*-4b). To a solution of $NaBH(OAc)_3$ (407 mg, 1.92 mmol, 8 equiv) in anhydrous acetonitrile (1 mL) was added anhydrous acetic acid (1 mL) and the mixture was stirred at ambient temperature for 30 min. The mixture was cooled to −40 °C and a solution of hydroxy ketone *anti*-**3b** (81 mg, 0.24 mmol, 1 equiv) in anhydrous acetonitrile (0.5 mL) was added via syringe. After stirring at −40 °C for 2 h (TLC), the reaction mixture was quenched by addition of 0.5 M aqueous sodium potassium tartrate (3 mL). The mixture was allowed to warm to 23 °C and stirred for 30 min. The mixture was then diluted with CH_2Cl_2 (5 mL) and washed with aqueous saturated $NaHCO_3$ (5 mL). The aqueous layer was back extracted with CH_2Cl_2 (3×10 mL), and the combined organic layers were washed with aqueous saturated $NaHCO_3$, dried with anhydrous $MgSO_4$, and concentrated in vacuo. The crude product was dissolved in THF (1 mL) and aqueous 10% NaOH solution (1 mL) and then the mixture was stirred vigorously for 1 h. Then THF was removed and the aqueous phase was

extracted with $CHCl_3$ (3×5 mL). The combined organic extracts were washed with H_2O and dried with anhydrous $MgSO_4$. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel, hexane/EtOAc 6:1) to give 42 mg of *anti-anti*-**4b** (0.12 mmol, 51%) and 12 mg of *anti-syn*-**4b** (0.036 mmol, 15%). Colorless oil. $[\alpha]_D^{23}$ +20.3 (*c* 0.66, $CHCl_3$). IR (film): 3398, 1452, 1070, 759, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 0.95 (d, 3H, *J*=6.6 Hz, $(CH_3)_2CH$); 1.19 (d, 3H, *J*=6.3 Hz, (CH_3CH)); 1.25 (d, 3H, *J*=6.6 Hz, $(CH_3)_2CH$); 1.54 (ddd, 1H, *J*=13.9, 7.4, 2.0 Hz, C*H*HCHOH); 1.67 (ddd, 1H, *J*=13.9, 10.7, 3.1 Hz, CH*H*CHOH); 2.16 (m, 1H, $CH(CH_3)_2$); 2.58 (dd, 1H, *J*=9.5, 5.3 Hz, C*H*N); 3.25 (br s, 1H, O*H*); 3.73 (d, 2H, *J*=13.4 Hz, CH*H*Ph); 3.89 (d, 2H, *J*=13.4 Hz, C*H*HPh); 3.93 (m, 1H, C*H*OH); 4.03 (m, 1H, CH_3CHOH); 7.15–7.40 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 20.6 (CH_3); 23.4 (CH_3); 28.1 ($CH(CH_3)_2$); 39.8 (CH_2); 56.3 (CH_2Ph); 65.8 (*C*HOH); 66.7 (*C*HOH); 66.9 (*C*HN); 127.4, 128.5, 129.2 (*C*Har); 139.7 (*C*ar). $C_{22}H_{31}NO_2$ (341.5): calcd C 77.38, H 9.15, N 4.10; found C 77.24, H 9.28, N 4.24.

3.2.18. (2*R*,4*R*,5*S*)-5-Dibenzylamino-6-phenylhexane-2,4-diol (*anti-syn*-4c). This compound was obtained from *anti*-**3c** (77 mg, 0.2 mmol), by the method described for *anti-syn*-**4b** and purified by flash chromatography (silica gel, hexane/EtOAc 4:1): 39 mg (0.1 mmol, 50%). Colorless oil. $[\alpha]_D^{23}$ +16.7 (*c* 0.7, $CHCl_3$). IR (film): 3378, 1602, 1452, 1121, 1072, 744, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 1.20 (d, 3H, *J*=6.2 Hz, C*H*$_3$); 1.48 (m, 1H, C*H*HCHOH); 1.76 (m, 1H, CH*H*CHOH); 2.78 (dd, 1H, *J*=12.9, 6.5 Hz, PhC*H*HCHN); 3.04 (m, 1H, C*H*N); 3.11 (m, 1H, PhCH*H*CHN); 3.45 (s broad, 2H, O*H*); 3.57 (d, 1H, *J*=13.6 Hz, NC*H*HPh); 3.81 (d, 1H, *J*=13.6 Hz, NCH*H*Ph); 3.83 (m, 1H, C*H*OH); 3.91 (m, 1H, CH_3CHOH); 7.15–7.35 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 24.0 (CH_3); 31.9 (CH_2CHN); 41.4 (CH_2CHOH); 55.2 (NCH_2Ph); 63.3 (CH_3CHOH); 69.3 (*C*HN); 72.6 (*C*HOH); 126.1, 127.2, 128.4, 128.5, 128.8, 129.2 (*C*Har); 139.4, 140.0 (*C*ar). $C_{26}H_{31}NO_2$ (389.5): calcd C 80.17, H 8.02, N 3.60; found C 80.01, H 7.90, N 3.55.

3.2.19. (2*S*,4*R*,5*S*)-5-Dibenzylamino-6-phenylhexane-2,4-diol (*anti-anti*-4c). This compound was obtained as the major diastereomer in the reaction of *anti*-**3c** (85 mg, 0.22 mmol) with $NaBH(OAc)_3$ by the method described for *anti-anti*-**4b** and purified by flash chromatography (silica gel, hexane/EtOAc 4:1): 23 mg (0.06 mmol, 27%). Colorless oil. $[\alpha]_D^{23}$ +27.8 (*c* 0.36, $CHCl_3$). IR (film): 3368, 1453, 1122, 1074, 740, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 1.16 (d, 3H, *J*=6.3 Hz, C*H*$_3$); 1.63 (m, 2H, C*H*$_2$CHOH); 2.86 (dd, 1H, *J*=12.7, 5.8 Hz, C*H*HCHN); 3.07 (m, 1H, C*H*N); 3.12 (m, 1H, CH*H*CHN); 3.59 (d, 1H, *J*=13.7 Hz, NCH*H*Ph); 3.79 (d, 1H, *J*=13.7 Hz, NC*H*HPh); 3.93 (m, 1H, CH_3CHOH); 4.05 (m, 1H, C*H*OH); 7.15–7.35 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 23.3 (CH_3); 32.1 (CH_2CHN); 40.9 (CH_2CHOH); 55.0 (CH_2Ph); 63.2 (CH_3CHOH); 65.7 (*C*HN); 68.9 (*C*HOH); 126.0, 127.1, 128.3, 128.4, 128.8, 129.3 (*C*Har); 139.5, 140.6 (*C*ar). $C_{26}H_{31}NO_2$ (389.5): calcd C 80.17, H 8.02, N 3.60; found C 80.34, H 7.91, N 3.71.

3.2.20. (1*R*,2*S*,4*S*)-1-Dibenzylamino-1-phenylpentane-2,4-diol (*anti-syn*-4e). This compound was obtained from *anti*-**3e** (45 mg, 0.12 mmol), by the method described for *anti-syn*-**4b** and purified by flash chromatography (silica gel, hexane/EtOAc 4:1): 30 mg (0.08 mmol, 68%). Colorless oil. $[\alpha]_D^{23}$ −48.1 (*c* 0.5, $CHCl_3$). IR (film): 3385, 1452, 1070, 744, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 1.26 (d, 3H, *J*=6.1 Hz, CH_3); 1.38 (ddd, 1H, *J*=14.7, 10.1, 5.4 Hz, CH*H*CHOH); 2.37 (ddd, 1H, *J*=14.7, 2.3, 1.9 Hz, C*H*HCHOH); 3.10 (d, 1H, *J*=13.8 Hz, C*H*HPh); 3.58 (d, *J*=8.8 Hz, C*H*N); 3.84 (d, 1H, *J*=13.8 Hz, CH*H*Ph); 4.10 (m, 1H, CH_3CHOH); 4.50 (m, 1H, C*H*OH); 7.20–7.50 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 24.1 (CH_3); 42.0 (CH_2); 54.7 (CH_2Ph); 68.3 (CH_3CHOH); 68.9 (*C*HN); 72.0 (*C*HOH); 127.1, 127.9, 128.4, 128.7, 128.9, 130.0 (*C*Har); 134.5, 139.4 (*C*ar). $C_{25}H_{29}NO_2$ (375.5): calcd C 79.96, H 7.78, N 3.73; found C 80.17, H 7.95, N 3.82.

3.2.21. (1*R*,2*S*,4*R*)-1-Dibenzylamino-1-phenylpentane-2,4-diol (*anti-anti*-4e). This compound was obtained as the major diastereomer in the reaction of *anti*-**3e** (49 mg, 0.13 mmol) with $NaBH(OAc)_3$ by the method described for *anti-anti*-**4b** and purified by flash chromatography (silica gel, hexane/Et_2O 1:1): 27 mg (0.07 mmol, 55%). Colorless oil. $[\alpha]_D^{23}$ −102.3 (*c* 0.44, $CHCl_3$). IR (film): 3402, 1452, 1071, 741, 701 cm^{-1}. ^1H NMR ($CDCl_3$): 1.26 (d, 3H, *J*=6.2 Hz, C*H*$_3$); 1.81 (ddd, 1H, *J*=14.6, 7.7, 2.5 Hz, C*H*HCHOH); 2.16 (ddd, 1H, *J*=14.6, 8.5, 3.1 Hz, CH*H*CHOH); 3.10 (d, 1H, *J*=13.7 Hz, C*H*HPh); 3.70 (d, 1H, *J*=9.3 Hz, C*H*N); 3.9 (d, 1H, *J*=13.7 Hz, CH*H*Ph); 3.80 (m, 1H, CH_3CHOH), 4.70 (dt, 1H, *J*=9.1, 3.0 Hz, C*H*OH); 7.20–7.50 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): 23.6 (CH_3); 40.7 (CH_2); 54.5 (CH_2Ph); 65.1 (CH_3CHOH); 67.1 (*C*HN); 68.1 (*C*HOH); 127.8, 128.3, 128.8, 130.0 (*C*Har); 134.7, 139.4 (*C*ar). $C_{25}H_{29}NO_2$ (375.5): calcd C 79.96, H 7.78, N 3.73; found C 79.85, H 7.90, N 3.80.

3.2.22. (2*R*,4*R*,5*S*)-5-Dibenzylamino-2,4-isopropylidendioxy-6-methylheptano (*cis*-5b). To a solution of amino diol *anti-syn*-**4b** (34 mg, 0.1 mmol) in 2,2-dimethoxypropane (2 mL), at room temperature, was added *p*-$TsOH\cdot H_2O$ (8 mg). The mixture was stirred at 70 °C for 2 h, and then quenched with aqueous saturated solution of $NaHCO_3$ (3 mL). The aqueous phase was extracted with EtOAc (3×10 mL) and dried over anhydrous $MgSO_4$. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel, hexane/EtOAc 30:1) to yield 33 mg of *cis*-**5b** (0.087 mmol, 87%) as a colorless oil. $[\alpha]_D^{23}$ −21.1 (*c* 0.5, $CHCl_3$). IR (film): 1454, 1378, 1258, 1179, 746, 698 cm^{-1}. ^1H NMR ($CDCl_3$): 0.99 (d, 3H, *J*=6.6 Hz, $(CH_3)_2CH$); 1.02 (d, 3H, *J*=6.1 Hz, $(CH_3)_2CH$); 1.17 (d, 3H, *J*=6.1 Hz, CH_3CH); 1.35 (s, 3H, C*H*$_3$); 1.48 (s, 3H, C*H*$_3$); 1.67 (m, 1H, C*HH*CHO); 2.20 (m, 1H, $CH(CH_3)_2$); 2.30 (dd, 1H, *J*=6.5, 4.4 Hz, C*H*N); 3.61 (d, 2H, *J*=13.7 Hz, CH*H*Ph); 3.67 (d, 2H, *J*=13.7 Hz, C*H*HPh); 3.99 (m, 1H, CH_3CHO); 4.25 (ddd, 1H, *J*=11.7, 6.2, 2.4 Hz, C*H*O); 7.20–7.40 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): 19.4, 20.0 ($(CH_3)_2CH$); 22.4 (CH_3CHO); 23.1 (CH_3); 25.5 ($CH(CH_3)_2$); 30.2 (CH_3); 38.1 (CH_2); 54.8 (CH_2Ph); 65.2 (*C*HO); 65.6 (CH_3CHO); 67.3 (*C*HN); 98.2 ($O_2C(CH_3)_2$), 126.8, 128.1, 128.9 (*C*Har); 140.1 (*C*ar). $C_{25}H_{35}NO_2$ (381.5): calcd C 78.70, H 9.25, N 3.67; found C 78.49, H 9.30, N 3.51.

3.2.23. (2*S*,4*R*,5*S*)-5-Dibenzylamino-2,4-isopropylidendioxy-6-methylheptane (*trans*-5b). This compound was

obtained from *anti-anti*-**4b** (34 mg, 0.1 mmol), by the method described for *cis*-**5b** and purified by flash chromatography (silica gel, hexane/EtOAc 15:1): 18 mg (0.048 mmol, 48%). Colorless oil. $[\alpha]_D^{23}$ −11.7 (*c* 0.5, $CHCl_3$). IR (film): 1454, 1378, 1224, 1120, 748, 701 cm^{-1}. ^1H NMR ($CDCl_3$): 1.03 (d, 3H, *J*=6.6 Hz, $(CH_3)_2CH$); 1.04 (d, 3H, *J*=6.5 Hz, $(CH_3)_2CH$); 1.21 (d, 3H, *J*=6.2 Hz, CH_3CH); 1.33 (s, 3H, CH_3); 1.45 (s, 3H, CH_3); 1.60 (ddd, 1H, *J*=12.7, 9.8, 7.0 Hz, CHHCHO); 1.74 (ddd, 1H, *J*=12.7, 9.3, 5.6 Hz, CHHCHO); 2.25 (m, 1H, $CH(CH_3)_2$); 2.28 (m, 1H, CHN); 3.57 (d, 2H, *J*=13.7 Hz, CHHPh); 3.73 (d, 2H, *J*=13.7 Hz, CHHPh); 3.88 (m, 1H, CH_3CHO); 4.27 (ddd, 1H, *J*=12.2, 9.2, 7.0 Hz, CHO); 7.20–7.40 (m, 10H, Har). ^{13}C NMR ($CDCl_3$): 20.2, 21.6 ($(CH_3)_2CH$); 22.8 (CH_3CHO); 24.5 (CH_3); 25.0 (CH_3); 25.9 ($CH(CH_3)_2$); 40.1 (CH_2); 54.7 (CH_2Ph); 62.8 (CHO); 64.3 (CH_3CHO); 65.3 (CHN); 100.3 ($O_2C(CH_3)_2$); 126.7, 128.1, 129.0 (CHar); 140.2 (Car). $C_{25}H_{35}NO_2$ (381.5): calcd C 78.70, H 9.25, N 3.67; found C 78.55, H 9.20, N 3.60.

3.2.24. (4*R*,5*S*)-5-Dibenzylamino-4-(*tert*-butyldimethylsilyloxy)-6-methyl-1-heptyne (*anti*-6b). To a solution of *anti*-**2b** (482 mg, 1.55 mmol) and imidazole (270 mg, 4.5 mmol, 3 equiv) in DMF (3 mL) was added TBDMSCl (340 mg, 2.25 mmol, 1.5 equiv) at 0 °C and the mixture was stirred at room temperature overnight. The reaction mixture was quenched with aqueous saturated NH_4Cl solution (10 mL) and decanted. The aqueous phase was extracted with ether (3×10 mL), and the combined organic phases were washed with brine, dried ($MgSO_4$), and the solvent was evaporated. The product was purified by flash chromatography (silica gel, hexane/EtOAc 50:1) yielding *anti*-**6b** as a colorless solid: 425 mg (0.98 mmol, 65%). Mp 57–58 °C. $[\alpha]_D^{23}$ −19.8 (*c* 1.2, $CHCl_3$). IR (film): 3310, 1952, 1090, 745, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 0.20, 0.21 (s, 3H, CH_3Si); 0.92 (s, 9H, $(CH_3)_3C$); 0.97 (d, 3H, *J*=6.6 Hz, CH_3); 1.09 (d, 3H, *J*=6.8 Hz, CH_3); 1.94 (t, 1H, *J*=2.8 Hz, ≡CH); 2.22 (m, 1H, $CH(CH_3)_2$); 2.52 (m, 2H, $CH_2C{\equiv}CH$); 3.50 (d, 2H, *J*=14.1 Hz, CHHPh); 3.91 (d, 2H, *J*=14.1 Hz, CHHPh); 4.37 (m, 1H, CHO); 7.15–7.45 (m, 10H, Har). ^{13}C NMR ($CDCl_3$): −4.4, −3.3 (CH_3Si); 18.1 ($(CH_3)_3CSi$); 21.2, 21.8 (CH_3); 25.9 ($(CH_3)_3C$); 27.0 ($(CH_3)_2CH$); 28.1 ($CH_2C{\equiv}CH$); 54.7 (CH_2Ph); 66.1 (CHN); 69.5 (CHOTBDMS); 71.0 (C≡CH); 81.8 (C≡CH); 126.6, 127.9, 129.0 (CHar); 140.4 (Car). $C_{28}H_{41}NOSi$ (435.7): calcd C 77.18, H 9.48, N 3.21; found C 76.76, H 9.08, N 2.99.

3.2.25. (4*S*,5*R*)-5-Dibenzylamino-4-(*tert*-butyldimethylsilyloxy)-5-phenyl-1-pentyne (*anti*-6e). This compound was obtained from *anti*-**2e** (249 mg, 0.7 mmol) by the method described for *anti*-**6b** and purified by flash chromatography (silica gel, hexane/EtOAc 50:1): 221 mg (0.47 mmol, 67%). Colorless oil. $[\alpha]_D^{23}$ −45.0 (*c* 0.77, $CHCl_3$). IR (film): 3309, 2122, 1454, 1252, 1109, 745, 699 cm^{-1}. ^1H NMR ($CDCl_3$): −0.31 (s, 3H, CH_3Si); 0.08 (s, 3H, CH_3Si); 0.62 (s, 9H, $(CH_3)_3C$); 1.91 (t, 1H, *J*=2.6 Hz, ≡CH); 2.69 (ddd, 1H, *J*=16.9, 4.9, 2.6 Hz, CHHCHO); 3.01 (m, 1H, CHHCHO); 3.16 (d, 2H, *J*=13.7 Hz, CHHPh); 3.79 (d, 1H, *J*=9.1 Hz, CHN); 3.90 (d, 2H, *J*=13.7 Hz, CHHPh); 4.53 (m, 1H, CHOTBDMS); 7.20–7.50 (m, 15H, Har). ^{13}C NMR ($CDCl_3$): −5.4, −4.0 (CH_3Si); 17.8 ($(CH_3)_3CSi$); 25.1 (CH_2); 25.5 ($(CH_3)_3CSi$); 54.5 (CH_2Ph); 66.4 (CHN); 70.5 (C≡CH); 71.7 (CHO); 82.1 (C≡CH); 126.9, 127.1, 127.7, 128.3, 128.9, 130.3 (CHar); 135.7, 139.4 (Car). $C_{31}H_{39}NOSi$ (469.7): calcd C 79.26, H 8.37, N 2.98; found C 79.02, H 8.18, N 2.86.

3.2.26. (3*S*,4*R*,8*R*,9*S*)-3,9-Bis-dibenzylamino-2,10-dimethyl-5-undecyne-4,8-diol (7b). To a solution of *anti*-**6b** (323 mg, 0.74 mmol) in anhydrous THF (4 mL) at −78 °C was added 1.6 M *n*-BuLi in hexane (0.51 mL, 0.81 mmol, 1.1 equiv) under argon. After the mixture was stirred for 1 h at −78 °C, a solution of amino aldehyde **1b** (229 mg, 0.81 mmol, 1.1 equiv) in THF was added. The mixture was kept at −78 °C for 2 h and then allowed to warm to room temperature overnight. Then, TBAF (281 mg, 0.89 mmol, 1.2 equiv) was added at 0 °C and the mixture was stirred at room temperature for 6 h. Saturated aqueous NH_4Cl (5 mL) was added to quench the reaction, then THF was removed, and the aqueous phase was extracted with $CHCl_3$ (3×10 mL). The organic extracts were combined, washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by flash chromatography (silica gel, hexane/ethyl acetate 15:1 to 8:1): 235 mg (0.39 mmol, 53%). Colorless oil. $[\alpha]_D^{23}$ −68.0 (*c* 0.6, $CHCl_3$). IR (film): 3415, 2227, 1736, 1604, 750, 695 cm^{-1}. ^1H NMR ($CDCl_3$): 0.96 (d, 3H, *J*=6.4 Hz, CH_3); 0.98 (d, 3H, *J*=6.5 Hz, CH_3); 1.08 (d, 3H, *J*=6.8 Hz, CH_3); 1.30 (d, 3H, *J*=7.1 Hz, CH_3); 2.20 (m, 2H, $CH(CH_3)_2$ and CHHC≡C); 2.32 (m, 1H, CHHC≡C); 2.41 (m, 1H, $CH(CH_3)_2$); 2.53 (dd, 1H, *J*=10.6, 4.6 Hz, CHN); 2.64 (dd, 1H, *J*=16.7, 3.0 Hz, CHN) 3.60 (s, 4H, CH_2Ph); 3.73 (d, 2H, *J*=13.1 Hz, CHHPh); 3.93 (m, 1H, CH_2CHOH); 4.25 (m, 1H, CHOH); 4.31 (d, 2H, *J*=13.1 Hz, CHHPh); 7.15–7.35 (m, 20H, Har). ^{13}C NMR ($CDCl_3$): 20.0 (CH_3); 20.6 (CH_3); 22.5 (CH_3); 23.3 (CH_3); 26.1 ($CH(CH_3)_2$); 26.4 (CH_2CHOH); 29.2 ($CH(CH_3)_2$); 55.0, 55.9 (CH_2Ph); 60.3 (CHOH); 65.6 (CHN); 66.5 (CHN); 68.9 (CH_2CHOH); 82.1 (C≡C); 83.2 (C≡C); 126.9, 127.2, 128.2, 128.4, 128.9, 129.3 (CHar); 139.6 (Car). $C_{41}H_{50}N_2O_2$ (602.8): calcd C 81.69, H 8.36, N 4.65; found C 81.25, H 7.96, N 4.34.

3.2.27. (3*S*,4*S*,8*R*,9*S*)-3,9-Bis-dibenzylamino-2,10-dimethyl-5-undecyne-4,8-diol (*epi*-7b). This compound was obtained as the minor product in the reaction of the lithiated compound derived from *anti*-**6b** (323 mg, 0.74 mmol) with the amino aldehyde **1b** and purified by flash chromatography (silica gel, hexane/EtOAc 15:1 to 8:1): 60 mg (0.1 mmol, 13%). Colorless oil. $[\alpha]_D^{23}$ −52.0 (*c* 1.1, MeOH). $[\alpha]_D^{23}$ −2.0 (*c* 1.1, $CHCl_3$). IR (film): 3405, 2232, 1450, 745, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 1.05 (d, 3H, *J*=6.7 Hz, CH_3); 1.10 (d, 3H, *J*=7.0 Hz, CH_3); 1.13 (d, 3H, *J*=6.8 Hz, CH_3); 1.15 (d, 3H, *J*=6.9 Hz, CH_3); 2.28 (m, 2H, $CH(CH_3)_2$); 2.40 (m, 2H, $CH_2C{\equiv}C$); 2.61 (dd, 1H, *J*=8.5, 3.8 Hz, CHN); 2.71 (d, 1H, *J*=16.6 Hz, CHN); 3.58 (d, 2H, *J*=13.2 Hz, CHHPh); 3.66 (d, 2H, *J*=13.6 Hz, CHHPh); 3.73 (d, 2H, *J*=13.6 Hz, CHHPh); 3.84 (d, 2H, *J*=13.2 Hz, CHHPh); 4.04 (m, 1H, CH_2CHOH); 4.46 (d, 1H, *J*=8.5 Hz, CHOH); 7.20–7.45 (m, 20H, Har). ^{13}C NMR ($CDCl_3$): 19.5 (CH_3); 20.1 (CH_3); 23.4 (CH_3); 25.8 ($CH(CH_3)_2$); 26.2 ($CH(CH_3)_2$); 26.4 (CH_2CHOH); 53.8, 55.1 (CH_2Ph); 59.2 (CHOH); 65.4 (CHN); 66.8 (CHN); 68.7 (CH_2CHOH); 82.1 (C≡C); 83.9 (C≡C); 127.0,

127.3, 128.3, 128.4, 129.0, 129.2 (*C*Har); 138.8, 139.7 (*C*ar). $C_{41}H_{50}N_2O_2$ (602.8): calcd C 81.69, H 8.36, N 4.65; found C 81.32, H 8.05, N 4.40.

3.2.28. (3*S*,4*R*,8*R*,9*S*)-3,9-Diamino-2,10-dimethylundecane-4,8-diol (8b). To a solution of diol **7b** (316 mg, 0.52 mmol) in MeOH (5 mL) was added $Pd(OH)_2$/C (95 mg) in one portion. The mixture was stirred under hydrogen for 1 h and the catalyst was removed by filtration and washed with methanol. The solvent was evaporated under reduced pressure to give **8b** as a colorless solid: 128 mg (0.52 mmol, 100%). Mp 152–153 °C. $[\alpha]_D^{23}$ +38.8 (*c* 1.0, MeOH). IR (KBr): 3348, 1598, 1473, 1062, 980 cm^{-1}. ^1H NMR (CD_3OD): 0.96 (d, 6H, *J*=6.8 Hz, CH_3); 0.97 (d, 6H, *J*=6.7 Hz, CH_3); 1.35–1.65 (m, 6H, CH_2CH_2CH_2); 1.86 (m, 2H, CH(CH_3)$_2$); 2.56 (dd, 2H, *J*=6.6, 5.4 Hz, CHN); 3.65 (m, 2H, CHOH). ^{13}C NMR (CD_3OD): 18.7 (*C*H_3); 20.6 (*C*H_3); 23.7 (*C*H_2); 30.1 (*C*H(CH_3)$_2$); 32.0 (*C*H_2CHOH); 63.1 (*C*HN); 72.4 (*C*HOH). $C_{13}H_{30}N_2O_2$ (246.4): calcd C 63.37, H 12.27, N 11.37; found C 63.30, H 12.11, N 11.49.

3.2.29. (3*S*,4*S*,8*R*,9*S*)-3,9-Diamino-2,10-dimethylundecane-4,8-diol (*epi*-8b). This compound was obtained by debenzylation of *epi*-**7b** (54 mg, 0.09 mmol) as described for **8b**: 15 mg (0.063 mmol, 70%). Colorless solid. $[\alpha]_D^{23}$ +15.9 (*c* 0.3, MeOH). ^1H NMR (CD_3OD): 1.00 (d, 6H, *J*=6.9 Hz, CH_3); 1.03 (d, 3H, *J*=6.9 Hz, CH_3); 1.06 (d, 3H, *J*=7.0 Hz, CH_3); 1.30–1.85 (m, 6H, CH_2CH_2CH_2); 1.94 (m, 1H, CH(CH_3)$_2$); 1.99 (m, 1H, CH(CH_3)$_2$); 2.76 (m, 2H, CHN); 3.73 (dd, 1H, *J*=8.4, 4.4 Hz, CHOH); 3.80 (dd, 1H, *J*=10.0, 4.6 Hz, CHOH). ^{13}C NMR (CD_3OD): 17.9 (*C*H_3); 19.2 (*C*H_3); 20.2 (*C*H_3); 20.3 (*C*H_3); 23.2 (*C*H_2); 29.3 (*C*H(CH_3)$_2$); 29.8 (*C*H(CH_3)$_2$); 31.4 (*C*H_2CHOH); 35.3 (*C*H_2CHOH); 62.4 (*C*HN); 63.6 (*C*HN); 70.1 (*C*HOH); 70.6 (*C*HOH). $C_{13}H_{30}N_2O_2$ (246.4): calcd C 63.37, H 12.27, N 11.37; found C 63.56, H 12.37, N 11.22.

3.2.30. (5*R*,6*S*)-Ethyl 6-dibenzylamino-5-*tert*-butyldimethylsilyloxy-7-methyloct-2-ynoate (*anti*-9b). To a solution of *anti*-**6b** (958 mg, 2.2 mmol) in anhydrous THF (20 mL) at −78 °C was added 1.6 M *n*-BuLi in hexane (2.1 mL, 3.3 mmol, 1.5 equiv) under argon. After the mixture was stirred for 1 h at −78 °C, ethyl chloroformate (0.42 mL, 4.4 mmol, 2 equiv) was added. The mixture was kept at −40 °C for 1 h and then allowed to warm to 0 °C and quenched with saturated aqueous NH_4Cl solution (20 mL). Then THF was removed and the aqueous phase was extracted with Et_2O (3×20 mL). The organic extracts were combined, washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to yield an oil that was used without further purification in the next step: 970 mg (1.91 mmol, 87%). Colorless oil. IR (film): 2234, 1712, 1252, 1072, 748, 699 cm^{-1}. ^1H NMR ($CDCl_3$): 0.19 (s, 6H, CH_3Si); 0.90 (s, 9H, (CH_3)$_3$C); 0.96 (d, 3H, *J*=6.5 Hz, CH_3CH); 1.05 (d, 3H, *J*=6.8 Hz, CH_3CH); 1.31 (t, 3H, *J*=7.1 Hz, CH_3CH$_2$); 2.19 (m, 1H, CH(CH_3)$_2$); 2.42 (dd, 1H, *J*=7.6, 2.9 Hz, CHN); 2.65 (d, 2H, *J*=6.6 Hz, CH_2CHO); 3.50 (d, 2H, *J*=13.9 Hz, CHHPh); 3.86 (d, 2H, *J*=13.9 Hz, CHHPh); 4.23 (q, 2H, *J*=7.1 Hz, CH_2CH$_3$); 4.37 (m, 1H, CHO); 7.15–7.45 (m, 10H, *H*ar). ^{13}C NMR ($CDCl_3$): −4.4, −3.5 (*C*H_3Si); 14.0 (*C*H_3CH$_2$); 18.1 (*C*(CH_3)$_3$); 21.1, 21.8 (*C*H_3CH); 25.9 ((*C*H_3)$_3$C); 26.9 ((CH$_3$)$_2$*C*H); 28.1 (CH_2CHO); 54.8 (*C*H_2Ph); 61.7 (*C*H_2CH$_3$); 66.5 (*C*HN); 69.1 (*C*HO); 75.1 (C≡*C*CO$_2$Et); 86.5 (*C*≡CCO$_2$Et); 126.7, 128.0, 128.9 (*C*Har); 140.0 (*C*ar); 153.5 (*C*O$_2$Et).

3.2.31. (5*S*,6*R*)-Ethyl 6-dibenzylamino-5-(*tert*-butyldimethylsilyloxy)-6-phenyl hex-2-ynoate (*anti*-9e). This compound was obtained as a product in the reaction of the lithiated compound derived from *anti*-**6e** (188 mg, 0.4 mmol) with ethyl chloroformate by the procedure described for *anti*-**9b**. Yield: 145 mg (0.27 mmol, 67%). Colorless oil. IR (film): 2238, 1710, 1254, 1100, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): −0.42 (s, 3H, CH_3Si); 0.02 (s, 3H, CH_3Si); 0.55 (s, 9H, (CH_3)$_3$C); 1.28 (t, 3H, *J*=7.1 Hz, CH_3CH$_2$); 2.75 (dd, 1H, *J*=17.4, 5.5 Hz, CHHC≡C); 3.08 (d, 2H, *J*=13.7 Hz, CHHPh); 3.19 (dd, 1H, *J*=17.4, 3.7 Hz, CHHC≡C); 3.63 (d, 1H, *J*=9.4 Hz, CHN); 3.81 (d, 2H, *J*=13.7 Hz, CHHPh); 4.18 (q, 2H, *J*=7.1 Hz, CH_2CH$_3$); 4.51 (m, 1H, CHO); 7.15–7.45 (m, 15H, *H*ar). ^{13}C NMR ($CDCl_3$): −5.5, −4.2 (*C*H_3Si); 14.0 (*C*H_3CH$_2$); 17.8 ((CH$_3$)$_3$*C*Si); 25.4 ((*C*H_3)$_3$C); 25.6 (*C*H_2C≡C); 54.5 (*C*H_2Ph); 61.6 (*C*H_2CH$_3$); 66.8 (*C*HN); 70.9 (*C*HOTBDMS); 75.0 (C≡*C*CO$_2$Et); 87.5 (*C*≡CCO$_2$Et); 127.0, 127.3, 127.9, 128.4, 128.7, 130.3 (*C*Har); 135.2, 139.1 (*C*ar); 153.6 (*C*O$_2$Et).

3.2.32. (5*R*,6*S*)-Ethyl 5-(*tert*-butyldimethylsilyloxy)-6-*tert*-butoxycarbonylamino-7-methyl octanoate (*anti*-10b). To a solution of *anti*-**9b** (1.02 g, 2 mmol) in EtOAc (20 mL) were added di-*tert*-butyl dicarbonate (655 mg, 3 mmol, 1.5 equiv) and $Pd(OH)_2$/C (250 mg) in one portion. The mixture was stirred under 1 hydrogen atmosphere and the reaction was monitored by TLC. When the reaction was completed, the catalyst was removed by filtration and washed with EtOAc. The solvent was concentrated under reduced pressure and the residue was purified by flash chromatography (silica gel, hexane/EtOAc 30:1): 276 mg (0.64 mmol, 32%). Colorless oil. $[\alpha]_D^{23}$ −10.0 (*c* 1.0, $CHCl_3$). IR (film): 3462, 3369, 1734, 1720, 1705, 1171, 837 cm^{-1}. ^1H NMR ($CDCl_3$): 0.05 (s, 3H, CH_3Si); 0.07 (s, 3H, CH_3Si); 0.87 (d, 3H, *J*=6.8 Hz, CH_3CH); 0.89 (s, 9H, (CH_3)$_3$CSi); 0.92 (d, 3H, *J*=6.8 Hz, CH_3CH); 1.25 (t, 3H, *J*=7.1 Hz, CH_3CH$_2$); 1.43 (s, 9H, (CH_3)$_3$CO); 1.63 (m, 4H, CH_2CH_2CH$_2$CO$_2$Et); 1.92 (m, 1H, CH(CH_3)$_2$); 2.29 (m, 2H, CH_2CO$_2$Et); 3.49 (m, 1H, CHN); 3.72 (m, 1H, CHO); 4.12 (q, 2H, *J*=7.1 Hz, CH_2CH$_3$); 4.53 (d, 1H, *J*=10.3 Hz, NH). ^{13}C NMR ($CDCl_3$): −4.8, −4.5 (*C*H_3Si); 14.1 (*C*H_3CH$_2$); 17.4 (*C*H_3CH); 17.9 ((CH$_3$)$_3$*C*Si); 20.8 (*C*H_3CH and *C*H_2); 25.8 ((*C*H_3)$_3$CSi); 27.5 ((CH$_3$)$_2$*C*H); 28.3 ((*C*H_3)$_3$CO); 32.9 (*C*H_2); 34.4 (CH$_2$); 57.5 (*C*HN); 60.1 (*C*H_2CH$_3$); 73.1 (*C*HO); 78.7 ((CH$_3$)$_3$*C*O); 155.8 (*C*O$_2^t$Bu); 173.2 (*C*O$_2$Et). $C_{22}H_{45}NO_5Si$ (431.7): calcd C 61.21, H 10.51, N 3.24; found C 61.39, H 10.59, N 3.30.

3.2.33. (5*S*,6*R*)-Ethyl 5-(*tert*-butyldimethylsilyloxy)-6-*tert*-butoxycarbonylamino-6-phenyl hexanoate (*anti*-10e). This compound was obtained from *anti*-**9e** (135 mg, 0.25 mmol) by the method described for *anti*-**10b** and purified by flash chromatography (silica gel, hexane/EtOAc 15:1): 55 mg (0.12 mmol, 47%). Colorless oil. $[\alpha]_D^{23}$ −14.9 (*c* 1.0, $CHCl_3$). IR (film): 3366, 1713, 1170, 776, 701 cm^{-1}. ^1H NMR ($CDCl_3$): 0.08 (s, 3H, CH_3Si); 0.09 (s,

3H, CH_3Si); 0.92 (s, 9H, (CH_3)$_3$CSi); 1.20 (t, 3H, J=7.2 Hz, CH_3CH$_2$); 1.40 (s, 9H, (CH_3)$_3$CO$_2$); 1.65 (m, 4H, CH_2CH_2CHO); 2.19 (m, 2H, CH_2CO$_2$Et); 3.98 (m, 1H, C*H*O); 4.06 (q, 2H, J=7.2 Hz, CH_2CH$_3$); 4.65 (m, 1H, CHN); 5.28 (m, 1H, N*H*); 7.15–7.35 (m, 5H, *H*ar). ^{13}C NMR ($CDCl_3$): −4.7, −4.5 (*C*H$_3$Si); 14.1 (*C*H$_3$); 18.1 ((CH$_3$)$_3$*C*Si); 21.1 (*C*H$_2$); 25.9 ((*C*H$_3$)$_3$CSi); 28.3 ((*C*H$_3$)$_3$CO$_2$C); 32.8 (*C*H$_2$CHO); 34.2 (*C*H$_2$CO$_2$); 60.2 (*C*H$_2$CH$_3$); 74.4 (*C*HOTBDMS); 79.3 ((CH$_3$)$_3$*C*O$_2$); 127.3, 128.0, 128.1 (*C*Har); 155.2 (NH*C*O$_2$^{t}Bu); 173.2 (*C*O$_2$Et). $C_{25}H_{43}NO_5Si$ (465.7): calcd C 64.48, H 9.31, N 3.01; found C 64.57, H 9.14, N 3.05.

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References and notes

1. (a) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163–3186; (b) Knochel, P. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, p 212; (c) Panek, J. S. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, p 595; (d) Yamamoto, H. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 1.3.
2. (a) Cabezas, J. A.; Álvarez, L. X. *Tetrahedron Lett.* **1998**, *39*, 3935–3938; (b) Kurono, N.; Sugita, K.; Tokuda, M. *Tetrahedron* **2000**, *56*, 847–854; (c) Jogi, A.; Mäeorg, U. *Molecules* **2001**, *6*, 964–968; (d) Yanagisawa, A.; Okitsu, S.; Arai, T. *Synlett* **2005**, 1679–1682; (e) Lee, P.-H.; Kim, H.; Lee, K. *Adv. Synth. Catal.* **2005**, *347*, 1219–1222.
3. Wu, W.-L.; Yao, Z.-J.; Li, Y.-L.; Li, J.-C.; Xia, Y.; Wu, Y.-L. *J. Org. Chem.* **1995**, *60*, 3257–3259.
4. (a) Wu, Y.-L.; Wu, W.-L.; Li, Y.-L.; Sun, X.-L.; Peng, Z.-H. *Pure Appl. Chem.* **1996**, *68*, 727–734; (b) Li, L.-S.; Wu, Y.-L. *Tetrahedron* **2002**, *58*, 9049–9054; (c) Hu, S.-G.; Hu, T.-S.; Wu, Y.-L. *Org. Biomol. Chem.* **2004**, *2*, 2305–2310.
5. (a) Ghosh, A. K.; Cappiello, J. *Tetrahedron Lett.* **1998**, *39*, 8803–8806; (b) Gosh, A. K.; Bischoff, A.; Cappiello, J. *Eur. J. Org. Chem.* **2003**, 821–832.
6. Liu, K.-G.; Yan, S.; Wu, Y.-L.; Yao, Z.-J. *J. Org. Chem.* **2002**, *67*, 6758–6763.
7. Poisson, J.-F.; Normant, J. F. *J. Org. Chem.* **2000**, *65*, 6553–6560.
8. For recent examples of enantioselective propargylation: (a) Lai, C.; Soderquist, J. A. *Org. Lett.* **2005**, *7*, 799–802; (b) Inoue, M.; Nakada, M. *Org. Lett.* **2004**, *6*, 2977–2980; (c) Lee, K.-C.; Lin, M.-J.; Loh, T.-P. *Chem. Commun.* **2004**, 2456–2457; (d) Loh, T.-P.; Lin, M.-J.; Tan, K.-L. *Tetrahedron Lett.* **2003**, *44*, 507–509; (e) Konishi, S.; Hanawa, H.; Maruoka, K. *Tetrahedron: Asymmetry* **2003**, *14*, 1603–1605.
9. (a) Andrés, J. M.; Barrio, R.; Martínez, M. A.; Pedrosa, R.; Pérez-Encabo, A. *J. Org. Chem.* **1996**, *61*, 4210–4213; (b) Andrés, J. M.; Martínez, M. A.; Pedrosa, R.; Pérez-Encabo, A. *Tetrahedron: Asymmetry* **2001**, *12*, 347–353; (c) Andrés, J. M.; Pedrosa, R.; Pérez, A.; Pérez-Encabo, A. *Tetrahedron* **2001**, *57*, 8521–8530; (d) Andrés, J. M.; Pedrosa, R.; Pérez-Encabo, A. *Eur. J. Org. Chem.* **2004**, 1558–1666.
10. Andrés, J. M.; de Elena, N.; Pedrosa, R.; Pérez-Encabo, A. *Tetrahedron* **1999**, *55*, 14137–14144.
11. (a) van der Zeijden, A. A. H. *Tetrahedron: Asymmetry* **1995**, *6*, 913–918; (b) Ishimaru, K.; Tsuru, K.; Yabuta, K.; Wada, M.; Yamamoto, Y.; Akiba, K. *Tetrahedron* **1996**, *52*, 13137–13144.
12. Reetz, M. T.; Drewes, M. W.; Schmitz, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1141–1143.
13. See for instance: (a) Jurczak, J.; Golebiowski, A. *Chem. Rev.* **1989**, *89*, 149–164; (b) Reetz, M. T. *Chem. Rev.* **1999**, *99*, 1121–1162; (c) Gryko, D.; Chalko, J.; Jurczak, J. *Chirality* **2003**, *15*, 514–541.
14. (a) Reetz, M. T.; Rivanedeira, E.; Niemeyer, C. *Tetrahedron Lett.* **1990**, *31*, 3863–3866; (b) Hamada, Y.; Hayashi, K.; Shioiri, T. *Tetrahedron Lett.* **1991**, *32*, 931–934; (c) Gennari, C.; Moresca, D.; Vulpetti, A.; Pain, G. *Tetrahedron* **1997**, *53*, 5593–5608; (d) McWilliams, J. C.; Armstrong, J. D.; Zheng, N.; Bhupathy, M.; Volante, R. P.; Reider, P. *J. Am. Chem. Soc.* **1996**, *118*, 11970–11971; (e) Kiyooka, S.; Goh, K.; Nakamura, Y.; Takeose, H.; Hena, M. *Tetrahedron Lett.* **2000**, *41*, 6599–6603.
15. Pan, Q.; Zou, B.; Wang, Y.; Ma, D. *Org. Lett.* **2004**, *6*, 1009–1012.
16. Poss, A. J.; Belter, R. K. *J. Org. Chem.* **1987**, *52*, 4812–4814.
17. Chen, K.; Gunderson, K. G.; Hardtman, G. E.; Prasad, K.; Repic, O.; Shapiro, M. J. *Chem. Lett.* **1987**, 1923–1926.
18. (a) Evans, D. A.; Chapman, K. T. *Tetrahedron Lett.* **1986**, *27*, 5939–5942; (b) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578.
19. Jiang, B.; Feng, Y. *Tetrahedron Lett.* **2002**, *43*, 2975–2977.
20. Ciapetti, P.; Falorni, M.; Taddei, M. *Tetrahedron* **1996**, *52*, 7379–7390.