DOI: 10.1002/ejoc.200600214

Diastereoselective Ethynylation of Chiral α-(Dibenzylamino) Aldehydes: Synthesis of *meso*- and Homochiral C_2-Symmetrical 1,6-Diamino-2,5-diols

José M. Andrés,[a] Rafael Pedrosa,*[a] and Alfonso Pérez-Encabo[a]

Keywords: Amino acids / Amino aldehydes / Asymmetric synthesis / Ethynylation

Homochiral α-(dibenzylamino) aldehydes, prepared from the corresponding α-amino acids, react with ethynylmagnesium bromide in THF/Et_2O at 0 °C to afford, in good yields and *dr*, propargylic 1,2-amino alcohols; *anti* diastereomers were always formed as the major products in this reaction. These compounds are versatile intermediates in the synthesis of *meso*- and enantiopure 1,6-diamino-2,5-diols with C_2 symmetry.

Introduction

Propargyl 1,2-amino alcohols (**I**) are very important starting compounds in organic synthesis (Figure 1). They can be transformed into 4-amino-3-hydroxy acids (**II**) by hydroboration/oxidation or into protected 3-amino-2-hydroxy acids (**III**) by ruthenium-catalyzed oxidation of the acetylenic bond.[1] Chiral 3-substituted 2-ethynylaziridines (**IV**) have also been prepared by Mitsunobu[2] reaction or intramolecular amination[3] of bromoallenes obtained from **I**. Methods for the asymmetric synthesis of these intermediates, such as diastereoselective reduction of acetylenic ketones,[1,4] diastereoselective condensation of propargyl aldehydes with tin enolates,[5] addition of alkoxyallenylzinc compounds to imines[6] and some others,[7] have been described, but the most direct synthesis involves the addition of metal acetylides to protected chiral α-amino aldehydes.

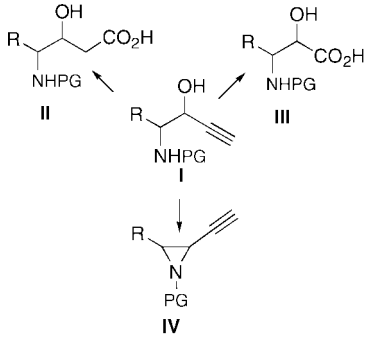


Figure 1. Different transformations for amino propargyl alcohols.

Nevertheless, the control of facial selectivity in these addition reactions is not easy and mixtures of *syn* and *anti* adducts can be obtained depending on the nature of the protecting groups at the nitrogen atom.[8] *N*-Boc-protected amino aldehydes give the *syn* diastereoisomer on reaction with lithium acetylides[2] and also the *syn* diastereoisomer was obtained from the reaction of ethynylmagnesium bromide with 9-fluorenylamino aldehydes.[9] In contrast, benzyl(tosyl)amino aldehydes yielded the *anti* diastereoisomer with high diastereoselectivity[10] and the alkynylation of dibenzylamino aldehydes with lithium acetylides also gave the *anti* adducts exclusively.[11,12]

Recently, we reported on the diastereoselective alkylation of α-(dibenzylamino) aldehydes with diethylzinc leading to *syn*-1,2-amino alcohols[13] as a complementary route to the preparation of *anti* adducts obtained by reaction with lithium, magnesium or copper derivatives.[14] In addition, dibenzylamino aldehydes react with diethylaluminium cyanide,[15] Reformatsky reagents,[16] or CF_3TMS[17] to yield the *anti* diastereoisomer as the major product.

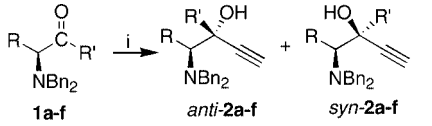
In this paper we summarize our results on the reaction of α-(dibenzylamino) aldehydes **1a**–**e** and ketone **1f** with ethynylmagnesium bromide leading to propargyl 1,2-amino alcohols and their transformations into *meso*- and enantiopure amino alcohol derivatives with C_2 symmetry. The asymmetric synthesis of these compounds has attracted much interest because they have been used as chiral ligands[18] and are an important part of pseudopeptides which act as HIV protease inhibitors.[19] In addition, although the synthesis of 1,4-diamino-2,3-diols with C_2 symmetry has been thoroughly developed[20] the asymmetric preparation of 1,5-diamino-2,4-diols[21] and 1,6-diamino-2,5-diols[22] has attracted less attention.

Results and Discussion

The reaction of α-(dibenzylamino) aldehydes **1a**–**e** with ethynylmagnesium bromide in a mixture of THF/Et_2O at

[a] Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid,
Doctor Mergelina s/n, 47011 Valladolid, Spain
Fax: +34-983-423013
E-mail: pedrosa@qo.uva.es

0 °C yielded the propargyl 1,2-amino alcohols **2a**–**e** in good chemical yields. The *anti* adducts were formed as the major diastereoisomer in high diastereomeric excess (*de*) and the diastereoselectivity was not affected by the size of the substituent when R was an alkyl group (Scheme 1 and Table 1, Entries 1–3). In contrast, the facial discrimination was lower in the reaction of D-phenylglycinal (*ent*-**1e**, R = Ph) or in the presence of additional heteroatoms in the chain of the amino aldehyde, **1d** (L-serinal) (Table 1, Entries 4 and 5). α-(Dibenzylamino) ketone **1f** also reacted with ethynylmagnesium bromide to give the tertiary propargyl carbinol *anti*-**2f** in excellent *de* (Table 1, Entry 6). This behavior is similar to that described for reactions with other magnesium or lithium derivatives.[23]



a: R = Me; R' = H **d**: R = $CH_2OTBDMS$; R' = H
b: R = *i*Pr; R' = H **e**: R = Ph; R' = H
c: R = CH_2Ph; R' = H **f**: R = CH_2Ph; R' = Me

Scheme 1. Reagents and conditions: (i) 1. HC≡CMgBr, THF/Et_2O, 0 °C; 2. NH_4Cl.

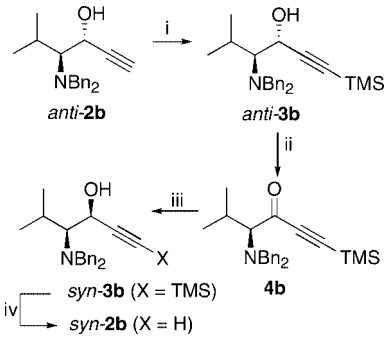
Table 1. Stereoselective ethynylation of α-(dibenzylamino) aldehydes **1a**–**e** and α-(dibenzylamino) ketone **1f**.

Entry	**1**[a]	R	R′	**2**	Yield [%][b]	*anti*/*syn*[c]
1	**1a**	Me	H	**2a**	78	91:9
2	**1b**	*i*Pr	H	**2b**	73	90:10
3	**1c**	$PhCH_2$	H	**2c**	71	92:8
4	**1d**	$CH_2OTBDMS$	H	**2d**	47	82:18
5	*ent*-**1e**	Ph	H	*ent*-**2e**	70	82:18
6	**1f**	$PhCH_2$	Me	**2f**	66	95:5

[a] Reactions were carried out with 1.2 equiv. of ethynylmagnesium bromide. [b] Numbers correspond to the combined yield of pure, isolated diastereoisomers. [c] The diastereomeric ratio was determined by integration of the signals of the ^1H NMR spectrum of the reaction mixture.

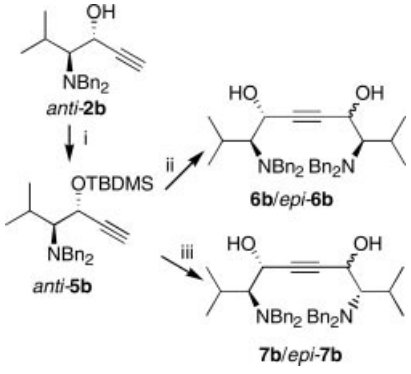
Pure diastereoisomers were obtained from the reaction mixtures by flash chromatography except for the L-serinal derivatives *syn*- and *anti*-**2d**. In this case, the mixture of diastereoisomers was desilylated by reaction with TBAF in THF at room temperature, but the resulting 2-amino-1,3-diols were also inseparable by flash chromatography.

Amino alcohol *syn*-**2b** was synthesized from *anti*-**2b** as summarized in Scheme 2. Amino alcohol *anti*-**2b** was converted into *anti*-**3b** by deprotonation with *n*BuLi (2 equiv.) in THF at –78 °C and treatment with TMSCl (1 equiv.). Swern oxidation of *anti*-**3b** led to propargyl ketone **4b**, which was reduced with lithium aluminium hydride to *syn*-**3b** as a single diastereoisomer. Deprotection of this compound by reaction with TBAF in THF at room temperature yielded *syn*-**2b** in good yield.



Scheme 2. Reagents and conditions: (i) 1. *n*BuLi (2.1 equiv.), THF, –78 °C, 1 h; 2. TMSCl, THF, –78 °C; 3. NH_4Cl; (ii) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –78 °C; (iii) $LiAlH_4$, Et_2O, –78 °C; (iv) TBAF, THF, room temp.

The transformation of these propargyl 1,2-amino alcohols into 1,6-diamino-2,5-diols was envisaged by their reaction with α-(dibenzylamino) aldehydes, taking as a model *anti*-**2b** and its TBDMS derivative *anti*-**5b** and L- or D-valinal as the aldehyde. If the stereochemical behavior of these reactions is in agreement with the Felkin–Anh model, a *meso*-diamino diol would be obtained as the major diastereoisomer in the reaction with D-dibenzylvalinal (*ent*-**1b**) and the C_2-symmetrical homochiral 1,6-diamino-2,5-diol derivative from L-dibenzylvalinal (**1b**). In fact, the dianion prepared by treatment of *anti*-**2b** with *n*BuLi (2 equiv.) reacted with *ent*-**1b** in THF at –78 °C to yield a mixture of **6b** and its C-7 epimer (*epi*-**6b**) but in low yield and with moderate diastereoselectivity (Scheme 3 and Table 2, Entry 1). The same behavior was observed in the reaction of *anti*-**2b** with L-dibenzylvalinal (**1b**), leading to a mixture of **7b** and *epi*-**7b** in low yield and with moderate diastereoselectivity (Table 2, Entry 4).



Scheme 3. Reagents and conditions: (i) TBDMSCl, imidazole, DMAP, CH_2Cl_2, room temp.; (ii) 1. *n*BuLi, THF, –78 °C, 1 h; 2. *ent*-**1b**, THF, –78 °C; 3. TBAF, room temp.; 4. NH_4Cl; (iii) 1. *n*BuLi, THF, –78 °C, 1 h; 2. **1b**, THF, –78 °C; 3. TBAF, room temp.; 4. NH_4Cl.

Much better results were obtained when the lithium derivative of the silylated compound *anti*-**5b** was used as the nucleophile. Deprotonation of *anti*-**5b** with *n*BuLi followed by reaction with *ent*-**1b** yielded a mixture of **6b** and *epi*-**6b** in 70% yield and with a good diastereomeric ratio after desilylation of the condensation product with TBAF in

Table 2. Reaction of propargyl derivatives *anti*-**2b** and *anti*-**5b** with amino aldehydes *ent*-**1b** and **1b**.

Entry	Acetylenic derivative	*n*BuLi [equiv.]	Amino aldehyde	Product	Yield [%][a]	*dr*[b]
1	*anti*-**2b**	2.1	*ent*-**1b**	**6b**	40	65:35
2	*anti*-**5b**	1.1	*ent*-**1b**	**6b**	70	84:16
3[c]	*anti*-**5b**	1.1	*ent*-**1b**	**6b**	63	88:12
4	*anti*-**2b**	2.1	**1b**	**7b**	38	72:28
5	*anti*-**5b**	1.1	**1b**	**7b**	67	86:14

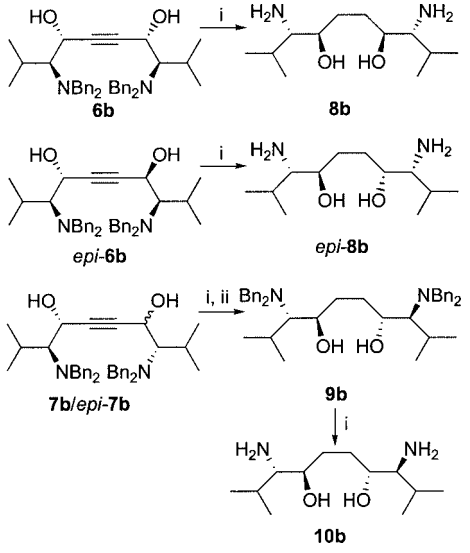
[a] Numbers correspond to the combined yield of pure and isolated diastereoisomers. [b] The diastereomeric ratio was determined by integration of the signals of the ^{1}H NMR spectrum of the reaction mixture. [c] The reaction was carried out at –95 °C and with HMPA (2 equiv.) as additive.

THF (Table 2, Entry 2). The diastereomeric ratio was improved to 88:12 when the reaction was carried out at –95 °C in the presence of HMPA, but the yield was slightly lower (63%) (Table 2, Entry 3).

After isolation of the diastereoisomers by flash chromatography, the structure of the major isomer (**6b**) was determined to be a *meso* form (3*S*,4*R*,7*S*,8*R*) on the basis of its ^{1}H NMR spectral[24] and optical rotation data ($[\alpha]_D^{23}$ = 0). This fact led us to assign the stereochemistry for *epi*-**6b** as (3*S*,4*R*,7*R*,8*R*).

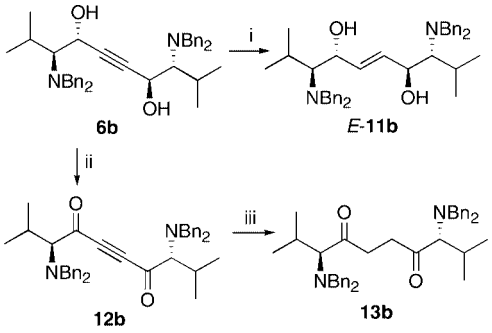
The lithium salt of *anti*-**5b** also reacted with **1b** to yield, after desilylation, a mixture of **7b** and *epi*-**7b** in 67% yield and good diastereoselectivity (Table 2, Entry 5). This mixture was inseparable by flash chromatography.

All these compounds were transformed into the corresponding saturated diamino diols **8b** and **10b**, as summarized in Scheme 4. Reduction and debenzylation of **6b** by stirring with Pearlman's catalyst under hydrogen led to the *meso* form of **8b**, as determined by ^{1}H NMR and optical rotation measurements, and the same treatment of *epi*-**6b** yielded *epi*-**8b** also in excellent yield. The mixture of diastereoisomers **7b** and *epi*-**7b** was subjected to hydrogenation as described above and benzylated with excess benzyl bromide and potassium carbonate in refluxing acetonitrile to give a mixture of saturated bis(dibenzylamino) diols **9b** and *epi*-**9b**. Now the epimers were easily separated by flash chromatography and the stereochemistry of **9b** was assigned as the C_2-symmetrical homochiral (3*S*,4*R*,7*R*,8*S*)-3,8-bis(dibenzylamino)-2,9-dimethyldecane-4,7-diol on the basis of its ^{1}H NMR spectral characteristics. Compound **9b** was debenzylated to **10b** by hydrogenolysis as described above.



Scheme 4. Reagents and conditions: (i) H_2, $Pd(OH)_2$/C, THF/MeOH; (ii) BnBr, K_2CO_3, CH_3CN, reflux.

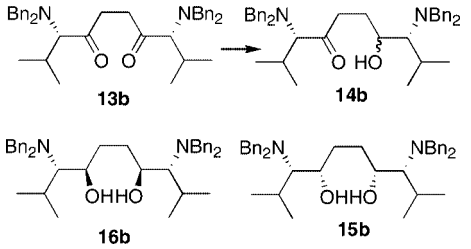
Two different transformations of **6b** were studied (Scheme 5). Treatment of this compound with lithium aluminium hydride[25] in refluxing THF led to the *meso* form of (*E*)-1,6-diaminohex-3-ene-2,5-diol derivative (*E*)-**11b** in good yield as a single diastereoisomer. On the other hand, Swern oxidation of **6b** gave, in moderate yield, the propargyl diketone **12b**, which was transformed into the *meso* form of the saturated 1,6-diamino-2,5-dione derivative **13b** by reduction with sodium borohydride in THF/methanol at –20 °C. The same diketone **13b** was also obtained from **8b** after complete benzylation with benzyl bromide and potassium carbonate in acetonitrile and Swern oxidation of the tetrabenzylated amino alcohol.



Scheme 5. Reagents and conditions: (i) $LiAlH_4$, THF, reflux; (ii) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –78 °C; (iii) $NaBH_4$, THF/MeOH, –20 to 0 °C.

Taking into account the stereochemistry of the reduction of chiral α-(dibenzylamino) ketones, compound **13b** could be used as the starting material for the synthesis of a different *meso* form of **8b** that differs in the relative stereochemistry of the vicinal dibenzylamino and hydroxy groups. In this case the relative stereochemistry of the vicinal substituents would be *syn* whereas in compound **8b** the relative stereochemistry was *anti*.

Compound **13b** was allowed to react with different metal hydrides and the results are summarized in Scheme 6 and Table 3.



Scheme 6. Reduction of **13b** by metal hydrides (see Table 3).

Table 3. Reaction of diketone **13b** with differents hydrides.

Entry	Hydride	Solvent	Temp. [°C]	**14b** [%][a]	**15b** [%][a]	**16b** [%][a]
1	$NaBH_4$	MeOH/THF	20	40	–	–
2	$LiAlH_4$	THF	0 → 65	21	45	11
3	$LiBH_4$	THF/EtOH	0 → 20	–	46	19

[a] Isolated yield.

Treatment of **13b** with excess of sodium borohydride in THF/methanol at room temperature for 72 h led to an epimeric mixture of diamino hydroxy ketone **14b** and unreacted diketone. Lithium aluminium hydride reduced compound **13b** to yield the semireduced product **14b** and a mixture of diastereoisomeric diamino diols **15b** and **16b** in a ratio of 4:1; further addition of lithium aluminium hydride did not modify the reaction mixture (Table 3, Entry 2). Finally, **13b** was totally reduced to a mixture of **15b** and **16b** (*dr* ≈ 7:3) when treated with lithium borohydride in THF/ethanol at 20 °C. The stereochemistry of **16b** was established by comparison with the tetrabenzylated diamino diol prepared by the reaction of **8b** with excess benzyl bromide and potassium carbonate in acetonitrile, while the stereochemistry of **15b** was assigned on the basis of ^{1}H NMR spectroscopic data[24] and the value of the optical rotation ($[\alpha]_D^{23} = 0$).

Conclusion

In summary, the reaction of chiral α-(dibenzylamino) aldehydes with ethynylmagnesium bromide yielded *anti*-amino alcohols as the major diastereoisomer; *syn*-amino alcohols can also be prepared from the *anti* isomers. Lithium derivatives of these propargyl amino alcohols reacted with chiral α-(dibenzylamino) aldehydes to give *meso*- or C_2-homochiral propargyl diamino diols which were further elaborated to the corresponding saturated diamino diols. The addition reactions of both the magnesium derivative and the acetylide derived from the propargyl amino alcohol occurred in good yields and diastereomeric excesses, and enantio-enriched compounds were easily obtained by flash chromatography.

Experimental Section

General: The reactions were carried out in oven-dried glassware under argon and with anhydrous solvents. Starting α-(dibenzylamino) aldehydes **1a**–**e** and α-amino ketone **1f** were prepared as described previously.[13,26] Ethynylmagnesium bromide, as 0.5 M solution in THF, is commercially available. The ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded using TMS as the internal standard. IR spectra were recorded as a film or KBr dispersion. Optical rotations were measured with a digital polarimeter in a 1-dm cell. Microanalyses were performed by the Departamento de Química Inorgánica.

General Procedure for the Ethynylation of α-Amino Aldehydes: A 0.5 M solution of HC≡CMgBr (7.2 mL) in THF (3.6 mmol, 1.2 equiv.) was added dropwise to a solution of amino aldehyde (3 mmol, 1.0 equiv.) in anhydrous diethyl ether (15 mL) at 0 °C (ice bath) under argon. The mixture was stirred at 0 °C until the reaction was finished (TLC) and then quenched with an aqueous saturated solution of ammonium chloride (30 mL). The THF was then removed and the aqueous phase was extracted with diethyl ether (3 × 15 mL). The combined organic layers were washed with brine and dried with anhydrous $MgSO_4$. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel; hexane/ethyl acetate, 15:1–50:1).

(3*R*,4*S*)-4-(Dibenzylamino)pent-1-yn-3-ol (*anti*-2a): This compound was obtained as the major diastereomer from the reaction of amino aldehyde **1a** (760 mg, 3 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 15:1) and recrystallization from *n*-hexanes; 594 mg (2.13 mmol, 71%); colorless solid, m.p. 53–54 °C. $[\alpha]_D^{23} = +31.7$ (*c* = 0.6, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3410, 3295, 2110, 1030, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.27 (d, *J* = 6.9 Hz, 3 H, CH_3), 2.48 (d, *J* = 1.3 Hz, 1 H, HC≡), 3.08 (m, 1 H, CHN), 3.42 (d, *J* = 13.3 Hz, 2 H, C*H*HPh), 4.19 (m, 1 H, C*H*OH), 4.21 (d, *J* = 13.3 Hz, 2 H, CH*H*Ph), 7.25–7.50 (m, 10 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.2 (CH_3), 54.5 (CH_2Ph), 55.4 (CHN), 62.6 (CHOH), 74.2 (C≡*C*H), 83.8 (*C*≡CH), 127.2, 128.4, 129.0 (CHar), 139.0 (Car) ppm. $C_{19}H_{21}NO$ (279.4): calcd. C 81.68, H 7.58, N 5.01; found C 81.45, H 7.43, N 4.89.

(3*S*,4*S*)-4-(Dibenzylamino)-5-methylhex-1-yn-3-ol (*syn*-2b): This compound was obtained as the minor diastereomer from the reaction of amino aldehyde **1b** (844 mg, 3 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 30:1); 65 mg (0.21 mmol, 7%); colorless oil. $[\alpha]_D^{23}$ = +31.2 (*c* = 0.95, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3405, 3303, 1050, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.12 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.15 (d, *J* = 7.1 Hz, 3 H, CH_3), 2.28 [m, 1 H, C*H*(CH_3)$_2$], 2.43 (d, *J* = 2.1 Hz, 1 H, HC≡), 2.64 (dd, *J* = 8.5, 4.0 Hz, 1 H, CHN), 3.57 (d, *J* = 13.2 Hz, 2 H, C*H*HPh), 3.81 (d, *J* = 13.2 Hz, 2 H, CH*H*Ph), 4.00 (br. s, 1 H, OH), 4.46 (dd, *J* = 8.5, 2.1 Hz, 1 H, C*H*OH), 7.20–7.40 (m, 10 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.4, 23.4 (CH_3), 25.8 [*C*H(CH_3)$_2$], 53.8 (CH_2Ph), 58.9 (CHN), 66.6 (CHOH), 74.3 (C≡*C*H), 83.9 (*C*≡CH), 127.3, 128.5, 129.2 (CHar), 138.7 (Car) ppm. $C_{21}H_{25}NO$ (307.4): calcd. C 82.04, H 8.20, N 4.56; found C 81.92, H 8.32, N 4.61.

(3*R*,4*S*)-4-(Dibenzylamino)-5-methylhex-1-yn-3-ol (*anti*-2b): This compound was obtained as the major diastereomer from the reaction of amino aldehyde **1b** (844 mg, 3 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 30:1); 606 mg (1.97 mmol, 66%); colorless oil. $[\alpha]_D^{23}$ = –56.8 (*c* = 1.1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3400, 3300, 2590, 755, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.95 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.30 (d, *J* = 6.4 Hz, 3 H, CH_3), 2.37 (d, *J* = 2.1 Hz, 1 H, HC≡), 2.44 [m, 1 H, C*H*(CH_3)$_2$], 2.54 (dd, *J* = 10.6, 5.0 Hz, 1 H, CHN), 3.70 (d, *J* = 13.0 Hz, 2 H, C*H*HPh), 4.25 (m, 1 H, C*H*OH), 4.29 (d, *J* = 13.0 Hz, 2 H, CH*H*Ph), 7.15–7.40 (m, 10 H, Har) ppm.

^{13}C NMR ($CDCl_3$): δ = 20.4, 22.4 (CH_3), 28.9 [*C*H(CH_3)$_2$], 55.6 (*C*H_2Ph), 59.8 (CHN), 65.9 (CHOH), 73.4 (C≡*C*H), 83.8 (*C*≡CH), 127.2, 128.4, 129.4 (CHar), 139.2 (Car) ppm. $C_{21}H_{25}NO$ (307.4): calcd. C 82.04, H 8.20, N 4.56; found C 82.18, H 8.02, N 4.70.

(3*S*,4*S*)-4-(Dibenzylamino)-5-phenylpent-1-yn-3-ol (*syn*-2c): This compound was obtained as the minor diastereomer from the reaction of amino aldehyde **1c** (988 mg, 3 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 20:1); 60 mg (0.17 mmol, 6%); colorless solid, mp. 134–135 °C (from hexane/EtOAC). $[a]_D^{23}$ = +88.7 (*c* = 0.3, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3436, 3273, 2118, 1019, 755, 736, 692 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.39 (d, *J* = 2.1 Hz, 1 H, HC≡), 3.01 (dd, *J* = 14.3, 9.2 Hz, 1 H, C*H*HPh), 3.11 (dd, *J* = 14.3, 3.8 Hz, 1 H, CH*H*Ph), 3.19 (m, 1 H, CHN), 3.39 (d, *J* = 13.2 Hz, 2 H, C*H*HN), 3.77 (d, *J* = 13.2 Hz, 2 H, CH*H*N), 4.05 (br. s, 1 H, OH), 4.29 (dd, *J* = 9.2, 2.1 Hz, 1 H, C*H*OH), 7.05–7.40 (m, 15 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 33.0 (*C*H_2Ph), 53.7 (CH_2N), 61.9 (CHN), 64.7 (CHOH), 74.1 (C≡*C*H), 83.2 (*C*≡CH), 126.4, 127.4, 128.5, 128.6, 129.0, 129.5 (CHar), 138.4, 139.9 (Car) ppm. $C_{25}H_{25}NO$ (355.5): calcd. C 84.47, H 7.09, N 3.94; found C 84.32, H 6.94, N 3.74.

(3*R*,4*S*)-4-(Dibenzylamino)-5-phenylpent-1-yn-3-ol (*anti*-2c): This compound was obtained as the major diastereomer from the reaction of amino aldehyde **1c** (988 mg, 3 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 20:1); 696 mg (1.96 mmol, 65%); colorless solid, m.p. 131–132 °C (from hexane/EtOAc). $[a]_D^{23}$ = +63.4 (*c* = 1.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3272, 2107, 1494, 1024, 747, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.60 (d, *J* = 2.0 Hz, 1 H, HC≡), 3.03 (dd, *J* = 12.2, 9.7 Hz, 1 H, C*H*HPh), 3.16 (m, 1 H, CHN), 3.24 (dd, *J* = 12.2, 4.1 Hz, 1 H, CH*H*Ph), 3.53 (d, *J* = 13.2 Hz, 2 H, C*H*HN), 4.07 (m, 1 H, C*H*OH), 4.19 (br. s, 1 H, OH), 4.36 (d, *J* = 13.2 Hz, 2 H, CH*H*N), 7.20–7.50 (m, 15 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 31.4 (*C*H_2Ph), 54.9 (CH_2N), 60.0 (CHN), 62.1 (CHOH), 75.1 (C≡*C*H), 83.8 (*C*≡CH), 126.4, 127.4, 128.5, 128.6, 129.1, 129.2 (CHar), 138.3, 138.8 (Car) ppm. $C_{25}H_{25}NO$ (355.5): calcd. C 84.47, H 7.09, N 3.94; found C 84.22, H 6.80, N 4.09.

(2*S*,3*R*)- and (2*S*,3*S*)-1-(*tert*-Butyldimethylsilyloxy)-2-(dibenzylamino)pent-4-yn-3-ol (*anti*/*syn*-2d): This compound was obtained as an inseparable mixture of diastereomers from the reaction of amino aldehyde **1d** (844 mg, 2.2 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 30:1); 420 mg (1.03 mmol, 47%); colorless oil. IR (film): $\tilde{\nu}$ = 3421, 3305, 2110, 1100, 838, 749, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.16, 0.17 (s, 3 H, CH_3Si), 0.98 [s, 9 H, (CH_3)$_3$CSi], 2.40 (d, *J* = 2.1 Hz, 1 H, C≡CH_{syn}), 2.46 (d, *J* = 2.4 Hz, 1 H, C≡CH_{anti}), 2.97 (m, 1 H, CHN$_{syn}$), 3.16 (m, 1 H, CHN$_{anti}$), 3.71 (d, *J* = 13.1 Hz, 2 H, CH*H*Ph), 3.89 (dd, *J* = 10.4, 6.4 Hz, 1 H, CH*H*OTBDMS), 4.04 (br. s, 1 H, OH), 4.17 (dd, *J* = 10.4, 6.8 Hz, 1 H, C*H*HOTBDMS), 4.21 (d, *J* = 13.1 Hz, 2 H, C*H*HPh), 4.41 (m, 1 H, C*H*OH), 7.25–7.40 (m, 10 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.5 (CH_3Si), 18.1 [(CH_3)$_3$*C*Si], 25.9 [(CH_3)$_3$Si], 54.5 (*C*H_2Ph$_{syn}$), 55.2 (*C*H_2Ph$_{anti}$), 59.8 (CHN), 60.9 (CHOH and *C*H_2OTBDMS), 74.1 (C≡*C*H), 83.8 (*C*≡CH), 127.2, 128.4, 129.0 (CHar), 138.9 (Car$_{syn}$), 139.3 (Car$_{anti}$) ppm.

(1*R*,2*R*)-1-(Dibenzylamino)-1-phenylbut-3-yn-2-ol (*ent*-*syn*-2e): This compound was obtained as the minor diastereomer from the reaction of amino aldehyde *ent*-**1e** (1.58 g, 5 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 12:1); 215 mg (0.63 mmol, 13%); colorless solid, m.p. 117–118 °C (from hexane). $[a]_D^{23}$ = –162.7 (*c* = 1.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3392, 3286, 2119, 1454, 1055, 747, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.13 (d, *J* = 2.1 Hz, 1 H, HC≡), 3.08 (d, *J* = 13.3 Hz, 2 H, C*H*HPh), 3.86 (d, *J* = 10.6 Hz, 1 H, CHN), 3.89 (d, *J* = 13.3 Hz, 2 H, CH*H*Ph), 4.36 (br. s, 1 H, OH), 4.93 (dd, *J* = 10.6, 2.1 Hz, 1 H, C*H*OH), 7.25–7.50 (m, 15 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 53.5 (*C*H_2Ph), 59.7 (CHN), 67.2 (CHOH), 73.6 (C≡*C*H), 82.2 (*C*≡CH), 127.5, 128.3, 128.7, 129.0, 129.6 (CHar), 133.0, 138.0 (Car) ppm. $C_{24}H_{23}NO$ (341.5): calcd. C 84.42, H 6.79, N 4.10; found C 84.22, H 6.62, N 4.14.

(1*R*,2*S*)-1-(Dibenzylamino)-1-phenylbut-3-yn-2-ol (*ent*-*anti*-2e): This compound was obtained as the minor diastereomer from the reaction of amino aldehyde *ent*-**1e** (1.58 g, 5 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 12:1); 980 mg (2.87 mmol, 57%); colorless oil. $[a]_D^{23}$ = –94.5 (*c* = 1.0, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3425, 3292, 1494, 1454, 1028, 748, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.66 (d, *J* = 2.2 Hz, 1 H, HC≡), 2.70 (br. s, 1 H, OH), 3.22 (d, *J* = 13.6 Hz, 2 H, C*H*HPh), 3.98 (d, *J* = 7.4 Hz, 1 H, CHN), 4.11 (d, *J* = 13.6 Hz, 2 H, CH*H*Ph), 4.84 (dd, *J* = 7.4, 2.2 Hz, 1 H, C*H*OH), 7.25–7.55 (m, 15 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.9 (*C*H_2Ph), 62.4 (CHN), 66.0 (CHOH), 74.9 (C≡*C*H), 84.0 (*C*≡CH), 127.1, 128.0, 128.2, 128.3, 129.0, 129.7 (CHar), 134.3, 139.2 (Car) ppm. $C_{24}H_{23}NO$ (341.5): calcd. C 84.42, H 6.79, N 4.10; found C 84.18, H 6.65, N 4.26.

(3*S*,4*S*)-4-(Dibenzylamino)-3-methyl-5-phenylpent-1-yn-3-ol (*syn*-2f): This compound was obtained as the minor diastereomer from the reaction of amino ketone **1f** (1.38 g, 4 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 20:1); 49 mg (0.13 mmol, 3%); colorless oil. $[a]_D^{23}$ = +54.1 (*c* = 1.0, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3298, 1495, 1454, 1074, 745, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$, 333 K): δ = 1.54 (s, 3 H, CH_3), 2.54 (s, 1 H, HC≡), 2.63 (br. s, 1 H, OH), 3.25 (m, 3 H, C*HH*Ph and CHN), 3.49 (d, *J* = 13.4 Hz, 2 H, C*H*HN), 4.12 (d, *J* = 13.4 Hz, 2 H, CH*H*N), 7.15–7.45 (m, 15 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.8 (CH_3), 32.3 (*C*H_2Ph), 55.6 (CH_2N), 67.1 (CHN), 70.6 (COH), 73.1 (C≡*C*H), 87.6 (*C*≡CH), 126.3, 127.1, 128.3, 128.7, 129.0, 129.5 (CHar), 139.3, 140.9 (Car) ppm. $C_{26}H_{27}NO$ (369.5): calcd. C 84.51, H 7.37, N 3.79; found C 84.31, H 7.20, N 3.68.

(3*R*,4*S*)-4-(Dibenzylamino)-3-methyl-5-phenylpent-1-yn-3-ol (*anti*-2f): This compound was obtained as the major diastereomer from the reaction of amino ketone **1f** (1.38 g, 4 mmol) with ethynylmagnesium bromide and was purified by flash chromatography (silica gel; hexane/EtOAc, 20:1); 931 mg (2.52 mmol, 63%); colorless solid, m.p. 104–105 °C (from hexane). $[a]_D^{23}$ = +26.2 (*c* = 1.0, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3295, 2104, 1495, 1115, 740, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$, 333 K): δ = 1.21 (s, 3 H, CH_3), 2.54 (s, 1 H, HC≡), 3.05 (m, 2 H, C*H*$_2$Ph), 3.35 (dd, *J* = 14.3, 7.0 Hz, 1 H, CHN), 3.40 (d, *J* = 12.6 Hz, 2 H, C*H*HN), 4.32 (br. s, 2 H, CH*H*N), 5.44 (br. s, 1 H, OH), 7.20–7.50 (m, 15 H, Har) ppm. ^{13}C NMR ($CDCl_3$, 333 K): δ = 29.5 (CH_3), 32.6 (*C*H_2Ph), 55.1 (CH_2N), 67.3 (COH), 67.7 (CHN), 73.0 (C≡*C*H), 87.7 (*C*≡CH), 126.5, 127.4, 128.5, 128.7, 129.3, 129.5 (CHar), 138.8, 140.3 (Car) ppm. $C_{26}H_{27}NO$ (369.5): calcd. C 84.51, H 7.37, N 3.79; found C 84.25, H 7.23, N 3.60.

(3*R*,4*S*)-4-(Dibenzylamino)-5-methyl-1-(trimethylsilyl)hex-1-yn-3-ol (*anti*-3b): *n*BuLi in hexanes (1.6 M, 2 mL, 3.2 mmol, 2.1 equiv.) was added to a solution of *anti*-**2b** (460 mg, 1.5 mmol) in anhydrous THF (6 mL) at –78 °C under argon. After stirring the mixture at –78 °C for 45 min, TMSCl (0.22 mL, 1.65 mmol, 1.1 equiv.) was added. The mixture was warmed to 0 °C and maintained at this temperature for 2 h and then quenched with saturated aqueous NH_4Cl solution (20 mL). The 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 concen-

trated under reduced pressure. The crude product was purified by flash chromatography (silica gel; hexane/ethyl acetate, 30:1); 250 mg (0.66 mmol, 44%); colorless solid, m.p. 72–73 °C. $[\alpha]_D^{23}$ = –118.0 (*c* = 0.5, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3330, 2165, 1030, 760, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.01 [s, 9 H, $Si(CH_3)_3$], 0.90 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.23 (d, *J* = 6.4 Hz, 3 H, CH_3), 2.36 [m, 1 H, C*H*$(CH_3)_2$], 2.45 (dd, *J* = 10.6, 4.9 Hz, 1 H, CHN), 3.63 (d, *J* = 13.0 Hz, 2 H, C*H*HPh), 4.03 (d, *J* = 8.6 Hz, 1 H, OH), 4.12 (m, 1 H, C*H*OH), 4.25 (d, *J* = 13.0 Hz, 2 H, CH*H*Ph), 7.15–7.30 (m, 10 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = –0.3 [$Si(CH_3)_3$], 20.6, 22.6 (CH_3), 29.1 [*C*H$(CH_3)_2$], 55.8 (*C*H_2Ph), 60.6 (CHN), 66.6 (CHOH), 90.0 (C≡*C*Si), 106.0 (*C*≡CSi), 127.3, 128.4, 129.5 (CHar), 139.5 (Car) ppm. $C_{24}H_{33}NOSi$ (379.6): calcd. C 75.93, H 8.76, N 3.69; found C 75.79, H 8.89, N 3.83.

(*S*)-4-(Dibenzylamino)-5-methyl-1-(trimethylsilyl)hex-1-yn-3-one (4b): DMSO (0.1 mL, 1.4 mmol) was added dropwise to a stirred solution of oxalyl chloride (60 μL, 0.7 mmol) in dichloromethane (2 mL) cooled to –78 °C under argon. After 15 min, a solution of *anti*-**3b** (190 mg, 0.5 mmol) in dichloromethane (2 mL) was added and the mixture was stirred at –78 °C for 30 min and triethylamine (0.2 mL, 1.43 mmol) was added. Then the reaction mixture was allowed to warm to room temperature whilst being stirred for 45 min and the mixture quenched with water (2 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ and water. The organic phase was dried ($MgSO_4$) and concentrated to yield an oil that was purified by flash chromatography (silica gel; hexane/EtOAc, 30:1); 122 mg (0.32 mmol, 64%); colorless oil. $[\alpha]_D^{23}$ = –196.3 (*c* = 1.2, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2145, 1660, 1250, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.30 [s, 9 H, $Si(CH_3)_3$], 0.84 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.05 (d, *J* = 6.6 Hz, 3 H, CH_3), 2.28 [m, 1 H, C*H*$(CH_3)_2$], 3.06 (d, *J* = 10.7 Hz, 1 H, CHN), 3.58 (d, *J* = 14.0 Hz, 2 H, C*H*HPh), 4.03 (d, *J* = 14.0 Hz, 2 H, CH*H*Ph), 7.20–7.50 (m, 10 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = –0.9 [$Si(CH_3)_3$], 19.6, 19.8 [$CH(CH_3)_2$], 26.4 [*C*H$(CH_3)_2$], 54.0 (*C*H_2Ph), 72.9 (CHN), 100.1 (C≡*C*Si), 104.2 (*C*≡CSi), 126.9, 128.1, 128.8 (CHar), 139.1 (Car), 189.7 (C=O) ppm. $C_{24}H_{31}NOSi$ (377.6): calcd. C 76.34, H 8.28, N 3.71; found C 76.55, H 8.45, N 3.80.

(3*S*,4*S*)-4-(Dibenzylamino)-5-methyl-1-(trimethylsilyl)hex-1-yn-3-ol (*syn*-3b): A solution of compound **4b** (100 mg, 0.26 mmol) in anhydrous Et_2O (1 mL) was added to a suspension of $LiAlH_4$ (15 mg, 0.40 mmol, 1.5 equiv.) in anhydrous THF (2 mL) at –78 °C and the suspension was stirred at this temperature for 15 min. Then the mixture was treated at –78 °C with H_2O (15 μL), a 15% NaOH solution (15 μL) and H_2O (45 μL), and then warmed to room temperature. The solids were removed by filtration, the solvent was evaporated and the residue purified by flash chromatography (silica gel; hexane/EtOAc, 30:1); 79 mg (0.21 mmol, 65%), colorless oil. $[\alpha]_D^{23}$ = +36.1 (*c* = 1.0, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3413, 2170, 1250, 1059, 844, 749, 699 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.16 [s, 9 H, $Si(CH_3)_3$], 1.13 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.15 (d, *J* = 6.8 Hz, 3 H, CH_3), 2.28 [m, 1 H, C*H*$(CH_3)_2$], 2.62 (dd, *J* = 8.4, 3.9 Hz, 1 H, CHN), 3.58 (d, *J* = 13.3 Hz, 2 H, C*H*HPh), 3.78 (br. s, 1 H, OH), 3.83 (d, *J* = 13.3 Hz, 2 H, CH*H*Ph), 4.49 (d, *J* = 8.4 Hz, 1 H, C*H*OH), 7.20–7.40 (m, 10 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = –0.3 [$Si(CH_3)_3$], 19.2, 23.5 (CH_3), 25.6 [$CH(CH_3)_2$], 53.8 (*C*H_2Ph), 59.4 (CHN), 66.9 (CHOH), 91.0 (C≡*C*Si), 105.7 (*C*≡CSi), 127.2, 128.4, 129.1 (CHar), 138.8 (Car) ppm. $C_{24}H_{33}NOSi$ (379.6): calcd. C 75.93, H 8.76, N 3.69; found C 75.73, H 8.92, N 3.85.

(3*R*,4*S*)-3-(*tert*-Butyldimethylsilyloxy)-4-(dibenzylamino)-5-methyl-1-hexyne (*anti*-5b): TBDMSCl (340 mg, 2.25 mmol, 1.5 equiv.), imidazole (225 mg, 3.75 mmol, 2.5 equiv.) and DMAP (20 mg, 0.15 mmol, 0.1 equiv.) were added to a solution of *anti*-**2b** (461 mg, 1.5 mmol) in CH_2Cl_2 (10 mL) at 0 °C and the mixture was stirred at room temperature for 48 h. The reaction was quenched with aqueous saturated NH_4Cl solution (10 mL) and decanted. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL), the combined organic phases were washed with water, dried ($MgSO_4$) and the solvent was evaporated. The product was purified by flash chromatography (silica gel; hexane/EtOAc, 30:1) to yield *anti*-**5b** as a colorless oil; 538 mg (1.28 mmol, 85%). $[\alpha]_D^{23}$ = –76.7 (*c* = 1.1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3305, 1255, 1083, 745, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.25 and 0.27 [2s, 6 H, $Si(CH_3)_2$], 0.97 [s, 9 H, $C(CH_3)_3$], 1.00 (d, *J* = 6.7 Hz, 6 H, C*H*$_3$CH), 2.19 [m, 1 H, C*H*$(CH_3)_2$], 2.49 (d, *J* = 2.3 Hz, 1 H, ≡CH), 2.55 (dd, *J* = 10.1, 2.5 Hz, 1 H, CHN), 3.56 (d, *J* = 13.9 Hz, 2 H, C*H*HPh), 4.02 (d, *J* = 13.9 Hz, 2 H, CH*H*Ph), 4.90 (m, 1 H, CHO), 7.20–7.40 (m, 10 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = –4.9, –4.0 (CH_3Si), 18.1 [*C*$(CH_3)_3$], 20.8, 21.4 (*C*H_3CH), 25.9 [C(*C*$H_3)_3$], 27.2 [*C*H$(CH_3)_2$], 55.0 (*C*H_2Ph), 60.7 (CHN), 68.2 (CHO), 74.7 (C≡*C*H), 85.9 (*C*≡CH), 126.7, 128.0, 129.1 (CHar), 140.3 (Car) ppm. $C_{27}H_{39}NOSi$ (421.7): calcd. C 76.90, H 9.32, N 3.32; found C 76.79, H 9.44, N 3.38.

(3*S*,4*R*,7*S*,8*R*)-3,8-Bis(dibenzylamino)-2,9-dimethyldec-5-yne-4,7-diol (6b): *n*BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol, 1.1 equiv.) was added to a solution of *anti*-**5b** (422 mg, 1 mmol) in anhydrous THF (5 mL) at –78 °C under argon. After stirring the mixture at –78 °C for 1 h, a solution of amino aldehyde *ent*-**1b** (282 mg, 1 mmol, 1 equiv.) was added. The mixture was kept at –78 °C for 2 h and then warmed to room temperature overnight. Then TBAF (315 mg, 1.0 mmol, 1 equiv.) was added at 0 °C and the mixture was stirred at room temperature for 4 h. Saturated aqueous NH_4Cl (10 mL) was added to quench the reaction, the THF was removed and the aqueous phase 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; $CHCl_3/Et_2O$, 80:1) to yield *anti*-**6b** (347 mg, 0.59 mmol, 59%) as the major product; colorless solid, m.p. 207–208 °C. $[\alpha]_D^{23}$ = 0 (*c* = 0.8, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3360, 1070, 755, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.77 (d, *J* = 6.5 Hz, 6 H, CH_3), 1.14 (d, *J* = 6.5 Hz, 6 H, CH_3), 2.29 [m, 2 H, C*H*$(CH_3)_2$], 2.46 (dd, *J* = 10.7, 4.5 Hz, 2 H, CHN), 3.65 (d, *J* = 13.1 Hz, 4 H, C*H*HPh), 4.25 (m, 6 H, C*H*OH and CH*H*Ph), 7.15–7.40 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.4, 22.3 (CH_3), 29.2 [*C*H$(CH_3)_2$], 55.7 (*C*H_2Ph), 60.1 (CHN), 66.2 (CHOH), 85.1 (C≡), 127.2, 128.4, 129.4 (CHar), 139.3 (Car) ppm. $C_{40}H_{48}N_2O_2$ (588.8): calcd. C 81.59, H 8.22, N 4.76; found C 81.36, H 8.16, N 4.95.

(3*S*,4*R*,7*R*,8*R*)-3,8-Bis(dibenzylamino)-2,9-dimethyldec-5-yne-4,7-diol (*epi*-6b): This compound was obtained as the minor product in the reaction of the lithiated compound derived from *anti*-**5b** (422 mg, 1 mmol) with the amino aldehyde *ent*-**1b** and purified by flash chromatography (silica gel; $CHCl_3/Et_2O$, 80:1); 64 mg (0.11 mmol, 11%); colorless oil. $[\alpha]_D^{23}$ = –64.6 (*c* = 0.9, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3380, 1093, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.94 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.03 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.08 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.28 (d, *J* = 6.4 Hz, 3 H, CH_3), 2.19 [m, 1 H, C*H*$(CH_3)_2$], 2.38 [m, 1 H, C*H*$(CH_3)_2$], 2.54 (m, 2 H, CHN), 3.61 (d, *J* = 13.2 Hz, 2 H, C*H*HPh), 3.67 (m, 4 H, C*HH*Ph), 4.22 (d, *J* = 13.2 Hz, 2 H, C*H*HPh), 4.28 (m, 1 H, C*H*OH), 4.55 (d, *J* = 6.8 Hz, 1 H, C*H*OH), 7.10–7.40 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.9, 20.6, 22.5 (CH_3), 26.9, 29.2 [*C*H$(CH_3)_2$], 54.0, 55.5 (*C*H_2Ph), 59.7, 60.1 (CHN), 66.3, 66.9 (CHOH), 85.2, 86.2 (C≡), 127.1, 127.3, 128.3, 128.4, 129.0, 129.5 (CHar), 138.8, 139.3 (Car) ppm. $C_{40}H_{48}N_2O_2$ (588.8): calcd. C 81.59, H 8.22, N 4.76; found C 81.44, H 8.08, N 4.90.

(3*R*,4*R*,7*R*,8*S*)-3,8-Bis(dibenzylamino)-2,9-dimethyldec-5-yne-4,7-diol (7b): This compound was obtained as the major product in the reaction of the lithiated compound derived from *anti*-**5b** (717 mg, 1.7 mmol) with the amino aldehyde **1b** by the procedure described for the preparation of **6b** and was purified by flash chromatography (silica gel; hexane/EtOAc, 8:1); 670 mg (1.14 mmol, 67%); colorless oil. $[\alpha]_D^{23}$ = –103.0 (*c* = 0.9, $CHCl_3$) (for an 86:14 mixture of diastereomers). IR (KBr): $\tilde{\nu}$ = 3402, 1453, 1044, 749, 698 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.76 (d, *J* = 6.5 Hz, 6 H, CH_3), 1.15 (d, *J* = 6.5 Hz, 6 H, CH_3), 2.22 [m, 2 H, C*H*(CH_3)$_2$], 2.48 (dd, *J* = 10.7, 4.3 Hz, 2 H, CHN), 3.63 (d, *J* = 13.0 Hz, 4 H, C*H*HPh), 4.18 (d, *J* = 13.0 Hz, 4 H, CH*H*Ph), 4.29 (m, 4 H, C*H*OH and OH), 7.15–7.40 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.5, 22.4 (CH_3), 29.3 [*C*H(CH_3)$_2$], 55.4 (*C*H_2Ph), 60.1 (CHN), 66.1 (CHOH), 85.2 (*C*≡C), 127.2, 128.4, 129.3 (CHar), 139.1 (Car) ppm.

(3*S*,4*R*,7*S*,8*R*)-3,8-Diamino-2,9-dimethyldecane-4,7-diol (8b): $Pd(OH)_2$/C (22 mg) was added in one portion to a solution of **6b** (88 mg, 0.15 mmol) in MeOH (3 mL). 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 and the residue was purified by flash chromatography (silica gel; CH_2Cl_2/MeOH/NH_4OH, 6:4:0.2) to give **8b** as a colorless solid; 33 mg (0.14 mmol, 95%); m.p. 151–152 °C. $[\alpha]_D^{23}$ = 0 (*c* = 1, MeOH). IR (KBr): $\tilde{\nu}$ = 3350, 1590, 1045 cm^{-1}. ^1H NMR (CD_3OD): δ = 0.97 (d, *J* = 6.8 Hz, 6 H, CH_3), 0.99 (d, *J* = 6.7 Hz, 6 H, CH_3), 1.32 (m, 2 H, C*H*HCHOH), 1.85 [m, 4 H, CH*H*CHOH and C*H*(CH_3)$_2$], 2.60 (dd, *J* = 7.0, 5.2 Hz, 2 H, CHN), 3.67 (m, 2 H, C*H*OH) ppm. ^{13}C NMR (CD_3OD): δ = 18.9, 20.5 [CH(*C*H_3)$_2$], 28.9 (CH_2), 30.1 [*C*H(CH_3)$_2$], 63.2 (CHN), 72.8 (CHOH) ppm. $C_{12}H_{28}N_2O_2$ (232.4): calcd. C 62.03, H 12.15, N 12.06; found C 61.78, H 11.97, N 11.95.

(3*S*,4*R*,7*R*,8*R*)-3,8-Diamino-2,9-dimethyldecane-4,7-diol (*epi*-8b): This compound was obtained by hydrogenation of *epi*-**6b** (59 mg, 0.1 mmol) with $Pd(OH)_2$/C in MeOH by the procedure described for the preparation of **8b** and was purified by flash chromatography (silica gel; CH_2Cl_2/MeOH/NH_4OH, 6:4:0.2); 18 mg (0.08 mmol, 80%); colorless oil. $[\alpha]_D^{23}$ = +35.0 (*c* = 0.5, MeOH). ^1H NMR ($CDCl_3$): δ = 0.94 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.95 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.96 (d, *J* = 7.1 Hz, 3 H, CH_3), 1.00 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.65 (m, 4 H, CH_2), 1.85 [m, 2 H, C*H*(CH_3)$_2$], 2.42 (m, 1 H, CHN), 2.50 (m, 1 H, CHN), 3.60 (m, 2 H, C*H*OH), 4.90 (br. s, 6 H, OH and NH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.6, 18.3, 20.6, 20.8 (CH_3), 28.5 (CH_2), 30.3, 30.9 [*C*H(CH_3)$_2$], 31.7 (CH_2), 62.2, 62.8 (CHN), 72.6, 72.8 (CHOH) ppm. $C_{12}H_{28}N_2O_2$ (232.4): calcd. C 62.03, H 12.15, N 12.06; found C 62.25, H 12.34, N 12.01.

(3*S*,4*R*,7*R*,8*S*)-3,8-Bis(dibenzylamino)-2,9-dimethyldecane-4,7-diol (9b): This compound was obtained from an 86:14 mixture of **7b**/*epi*-**7b** (588 mg, 1 mmol) by catalytic hydrogenation with $Pd(OH)_2$/C (150 mg) in MeOH (10 mL) followed by treatment with BnBr (0.25 mL, 2.1 mmol, 2.1 equiv.) and K_2CO_3 (276 mg, 2 mmol, 2 equiv.) in acetonitrile (6 mL) at reflux. After flash chromatography (silica gel; hexane/EtOAc, 8:1), compound **9b** was obtained as a colorless oil; 450 mg (0.76 mmol, 76%). $[\alpha]_D^{23}$ = –21.9 (*c* = 1.2, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3400, 1453, 1071, 749, 699 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.90 (d, *J* = 6.5 Hz, 6 H, CH_3), 1.19 (d, *J* = 6.5 Hz, 6 H, CH_3), 1.54 (m, 2 H, C*H*HCHOH), 1.72 (m, 2 H, CH*H*CHOH), 2.17 [m, 2 H, C*H*(CH_3)$_2$], 2.46 (dd, *J* = 9.4, 4.4 Hz, 2 H, CHN), 3.48 (br. s, 2 H, OH), 3.60 (m, 2 H, C*H*OH), 3.74 (d, *J* = 13.5 Hz, 4 H, C*H*HPh), 3.82 (d, *J* = 13.5 Hz, 4 H, CH*H*Ph), 7.15–7.35 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.9, 23.1 (CH_3), 27.9 [*C*H(CH_3)$_2$], 31.5 (CH_2), 56.1 (*C*H_2Ph), 67.2 (CHN), 70.2 (CHOH), 127.1, 128.4, 129.1 (CHar), 139.9 (Car) ppm. $C_{40}H_{52}N_2O_2$ (592.8): calcd. C 81.04, H 8.84, N 4.73; found C 81.12, H 8.73, N 4.86.

(3*S*,4*R*,7*R*,8*S*)-3,8-Diamino-2,9-dimethyldecane-4,7-diol (10b): This compound was obtained by hydrogenation of **9b** (318 mg, 0.54 mmol) as described for the preparation of **8b** and was purified by flash chromatography (silica gel; CH_2Cl_2/MeOH/NH_4OH, 6:4:0.2); 113 mg (0.49 mmol, 90%); colorless solid, m.p. 111–112 °C. $[\alpha]_D^{23}$ = +46.0 (*c* = 0.4, MeOH). IR (KBr): $\tilde{\nu}$ = 3348, 1597, 1474, 1060, 942 cm^{-1}. ^1H NMR (CD_3OD): δ = 0.98 (d, *J* = 6.7 Hz, 12 H, CH_3), 1.60 (m, 4 H, CH_2), 1.88 [m, 2 H, C*H*(CH_3)$_2$], 2.59 (dd, *J* = 6.8, 5.4 Hz, 2 H, CHN), 3.69 (m, 2 H, C*H*OH) ppm. ^{13}C NMR (CD_3OD): δ = 18.8, 20.5 (CH_3), 28.1 (CH_2), 30.1 [*C*H(CH_3)$_2$], 63.0 (CHN), 71.8 (CHOH) ppm. $C_{12}H_{28}N_2O_2$ (232.4): calcd. C 62.03, H 12.15, N 12.06; found C 61.78, H 11.96, N 12.23.

(3*S*,4*R*,7*S*,8*R*)-3,8-Bis(dibenzylamino)-2,9-dimethyldec-5-ene-4,7-diol [(*E*)-11b]: Compound **6b** (118 mg, 0.2 mmol, 1.0 equiv.) was added to a suspension of $LiAlH_4$ (30 mg, 0.8 mmol, 4 equiv.) in anhydrous THF (4 mL) at 0 °C. The ice bath was removed and the suspension was stirred at reflux for 1 h. Then the mixture was treated at 0 °C with H_2O (30 μL), a 15% NaOH solution (30 μL) and H_2O (90 μL) and stirred for 2 h. The white solids were removed by filtration, the filtrate was concentrated and the residue purified by flash chromatography (silica gel; $CHCl_3$/Et_2O, 60:1); 77 mg (0.13 mmol, 65%); colorless solid, m.p. 195–196 °C. $[\alpha]_D^{23}$ = 0 (*c* = 1, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3350, 1453, 1090, 1070, 753, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.88 (d, *J* = 6.4 Hz, 6 H, CH_3), 1.20 (d, *J* = 6.5 Hz, 6 H, CH_3), 2.17 [m, 2 H, C*H*(CH_3)$_2$], 2.52 (dd, *J* = 10.7, 4.9 Hz, 2 H, CHN), 3.55 (d, *J* = 8.4 Hz, 2 H, OH), 3.63 (d, *J* = 13.3 Hz, 4 H, C*H*HPh), 3.87 (d, *J* = 13.3 Hz, 4 H, CH*H*Ph), 3.94 (m, 2 H, C*H*OH), 6.10 (s, 2 H, C*H*=CH), 7.10–7.40 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.8, 23.1 (CH_3), 28.7 [*C*H(CH_3)$_2$], 56.0 (*C*H_2Ph), 67.3 (CHN), 68.5 (CHOH), 127.2, 128.3, 129.1 (CHar), 129.5 (CH=), 139.8 (Car) ppm. $C_{40}H_{50}N_2O_2$ (590.8): calcd. C 81.31, H 8.53, N 4.74; found C 81.07, H 8.37, N 4.56.

(3*S*,8*R*)-3,8-Bis(dibenzylamino)-2,9-dimethyldec-5-yne-4,7-dione (12b): DMSO (0.12 mL, 1.7 mmol) was added dropwise to a stirred solution of oxalyl chloride (71 μL, 0.8 mmol) in CH_2Cl_2 (2 mL) cooled to –78 °C under argon. After 15 min, a solution of **6b** (177 mg, 0.3 mmol) in CH_2Cl_2 (2 mL) was added, the mixture was stirred at –78 °C for 45 min and then triethylamine (0.24 mL, 1.7 mmol) was added. Then the mixture was allowed to reach room temperature whilst being stirred for 45 min and quenched with water (2 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ and water. The organic phase was dried ($MgSO_4$) and concentrated to yield an oil that was purified by flash chromatography (silica gel; hexane/EtOAc, 8:1); 131 mg (0.22 mmol, 75%); colorless oil. $[\alpha]_D^{23}$ = 0 (*c* = 1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1665, 1100, 735, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.83 (d, *J* = 6.5 Hz, 6 H, CH_3), 1.08 (d, *J* = 6.5 Hz, 6 H, CH_3), 2.29 [m, 2 H, C*H*(CH_3)$_2$], 3.13 (d, *J* = 10.8 Hz, 2 H, CHN), 3.55 (d, *J* = 14.0 Hz, 4 H, C*H*HPh), 4.02 (d, *J* = 14.0 Hz, 4 H, CH*H*Ph), 7.15–7.45 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.8, 20.0 (CH_3), 26.6 [*C*H(CH_3)$_2$], 54.2 (*C*H_2Ph), 73.1 (CHN), 88.0 (C≡), 127.2, 128.4, 128.8 (CHar), 138.6 (Car), 189.0 (C=O) ppm. $C_{40}H_{44}N_2O_2$ (584.8): calcd. C 82.15, H 7.58, N 4.79; found C 82.01, H 7.54, N 4.84.

(3*S*,8*R*)-3,8-Bis(dibenzylamino)-2,9-dimethyldecane-4,7-dione (13b): This compound was obtained by reduction of **12b** (88 mg, 0.15 mmol) with $NaBH_4$ (51 mg, 1.35 mmol, 9 equiv.) in MeOH/THF (2 mL, 9:2) at –20 °C and purified by flash chromatography (silica gel; hexane/EtOAc, 20:1); 35 mg (0.06 mmol, 40%); colorless solid, m.p. 136–137 °C. $[\alpha]_D^{23}$ = 0 (*c* = 1, $CHCl_3$). IR (KBr): $\tilde{\nu}$ =

3435, 1700, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.86 (d, J = 6.5 Hz, 6 H, CH_3), 1.17 (d, J = 6.6 Hz, 6 H, CH_3), 2.26 [m, 2 H, C*H*(CH_3)$_2$], 2.56 (m, 2 H, C*H*HCO), 2.72 (m, 2 H, CH*H*CO), 3.16 (d, J = 10.6 Hz, 2 H, CHN), 3.57 (d, J = 14.2 Hz, 4 H, C*H*HPh), 4.06 (d, J = 14.2 Hz, 4 H, CH*H*Ph), 7.20–7.50 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.1, 20.3 (CH_3), 27.2 [*C*H(CH_3)$_2$], 39.7 (*C*H_2CO), 54.4 (*C*H_2Ph), 70.7 (CHN), 126.9, 128.3, 128.7 (CHar), 139.7 (Car), 210.7 (C=O) ppm. $C_{40}H_{48}N_2O_2$ (588.8): calcd. C 81.59, H 8.22, N 4.76; found C 81.29, H 7.96, N 4.51.

(3*S*,8*R*)-3,8-Bis(dibenzylamino)-7-hydroxy-2,9-dimethyldecan-4-one (14b): This compound was obtained as the sole isolated product in the reduction of **13b** (30 mg, 0.05 mmol) with $NaBH_4$ (15 mg, 0.4 mmol, 8 equiv.) in THF/MeOH (1:1, 1.5 mL) at room temperature and was purified by flash chromatography (silica gel; hexane/EtOAc, 10:1); 12 mg (0.02 mmol, 40%); colorless oil. $[a]_D^{23}$ = 0 (c = 1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3435, 1700, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.70 (d, J = 6.5 Hz, 3 H, CH_3), 1.07 (d, J = 6.7 Hz, 3 H, CH_3), 1.10 (d, J = 7.3 Hz, 3 H, CH_3), 1.18 (d, J = 7.0 Hz, 3 H, CH_3), 1.61 (m, 1 H, C*H*HCHOH), 1.95 (m, 1 H, CH*H*CHOH), 2.17 [m, 1 H, C*H*(CH_3)$_2$], 2.32 [m, 3 H, CHN, C*H*HCO and C*H*(CH_3)$_2$], 2.63 (dt, J = 18.5, 7.5 Hz, 1 H, CH*H*CO), 2.99 (d, J = 10.6 Hz, 1 H, CHNCO), 3.46 (d, J = 14.2 Hz, 2 H, C*H*HPh), 3.47 (d, J = 13.0 Hz, 2 H, C*H*HPh), 3.76 (m, 1 H, CHOH), 3.95 (d, J = 13.0 Hz, 2 H, CH*H*Ph), 3.99 (d, J = 14.2 Hz, 2 H, CH*H*Ph), 4.58 (br. s, 1 H, OH), 7.20–7.40 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.2, 20.1, 20.2, 24.1 (CH_3), 24.8, 27.1 [*C*H(CH_3)$_2$], 28.4 (*C*H_2CHOH), 42.8 (*C*H_2CO), 53.9, 54.5 (*C*H_2Ph), 66.1 (CHN and CHOH), 71.0 (*C*HNCO), 126.9, 127.3, 128.3, 128.5, 128.7, 129.2 (CHar), 138.9, 139.8 (Car), 213.1 (C=O) ppm. $C_{40}H_{50}N_2O_2$ (590.8): calcd. C 81.31, H 8.53, N 4.74; found C 81.51, H 8.69, N 4.60.

(3*S*,4*S*,7*R*,8*R*)-3,8-Bis(dibenzylamino)-2,9-dimethyldecane-4,7-diol (15b): This compound was obtained as the major product in the reduction of **13b** (30 mg, 0.05 mmol) with $LiBH_4$ (9 mg, 0.4 mmol, 8 equiv.) in THF/EtOH (1:1, 1.5 mL) at room temperature and was purified by flash chromatography (silica gel; hexane/EtOAc, 8:1); 14 mg (0.023 mmol, 46%); colorless solid, m.p. 170–171 °C (from hexane/EtOAc). $[a]_D^{23}$ = 0 (c = 1, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3370, 1450, 1065, 755, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.01 (d, J = 7.3 Hz, 6 H, CH_3), 1.02 (d, J = 7.1 Hz, 6 H, CH_3), 1.13 (m, 2 H, C*H*HCHOH), 1.78 (m, 2 H, CH*H*CHOH), 2.21 [m, 2 H, C*H*(CH_3)$_2$], 2.32 (dd, J = 9.3, 1.9 Hz, 2 H, CHN), 3.43 (d, J = 13.0 Hz, 4 H, C*H*HPh), 3.70 (m, 2 H, CHOH), 3.90 (d, J = 13.0 Hz, 4 H, CH*H*Ph), 4.55 (br. s, 2 H, OH), 7.15–7.40 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.2, 24.0 (CH_3), 24.6 [*C*H(CH_3)$_2$], 31.5 (CH_2), 53.9 (*C*H_2Ph), 65.7 (CHN), 67.3 (CHOH), 127.1, 128.4, 129.2 (CHar), 139.0 (Car) ppm. $C_{40}H_{52}N_2O_2$ (592.8): calcd. C 81.04, H 8.84, N 4.73; found C 80.86, H 8.61, N 4.54.

(3*S*,4*R*,7*S*,8*R*)-3,8-Bis(dibenzylamino)-2,9-dimethyldecane-4,7-diol (16b): A mixture of **8b** (41 mg, 0.18 mmol), benzyl bromide (95 μL, 0.8 mmol, 4.4 equiv.) and K_2CO_3 (100 mg, 0.72 mmol, 4 equiv.) in CH_3CN (2 mL) was stirred at reflux until the reaction was finished (TLC). The solid was separated by filtration, the filtrate was concentrated under reduced pressure and the residue purified by flash chromatography (silica gel; CH_2Cl_2); 75 mg (0.13 mmol, 70%); colorless solid, m.p. 168–169 °C. $[a]_D^{23}$ = 0 (c = 1, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3385, 1070, 753, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.91 (d, J = 6.5 Hz, 6 H, CH_3), 1.22 (d, J = 6.5 Hz, 6 H, CH_3), 1.30 (m, 2 H, C*H*HCHOH), 1.82 (m, 2 H, CH*H*CHOH), 2.21 [m, 2 H, C*H*(CH_3)$_2$], 2.49 (dd, J = 9.4, 5.1 Hz, 2 H, CHN), 3.31 (br. s, 2 H, OH), 3.49 (m, 2 H, C*H*OH), 3.70 (d, J = 13.4 Hz, 4 H, C*H*HPh), 3.83 (d, J = 13.4 Hz, 4 H, CH*H*Ph), 7.20–7.40 (m, 20 H, Har) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.8, 23.3 (CH_3), 28.1 [*C*H(CH_3)$_2$], 30.6 (CH_2), 56.2 (*C*H_2Ph), 66.9 (CHN), 70.4 (CHOH), 127.1, 128.3, 129.1 (CHar), 139.8 (Car) ppm. $C_{40}H_{52}N_2O_2$ (592.8): calcd. C 81.04, H 8.84, N 4.73; found C 81.08, H 8.68, N 4.85.

Acknowledgments

The authors thank the Spanish Ministerio de Educación y Ciencia (DGI, Project CTQ2005-01191/BQU) for financial support.

[1] C. Alemany, J. Bach, J. Farràs, J. García, *Org. Lett.* **1999**, *1*, 1831–1834.
[2] H. Ohno, A. Toda, Y. Takemoto, N. Fuji, T. Ibuka, *J. Chem. Soc., Perkin Trans. 1* **1999**, 2949–2962.
[3] H. Ohno, H. Hamaguchi, T. Tanaka, *Org. Lett.* **2001**, *3*, 2269–2271.
[4] A. Dondoni, D. Perrone, E. Turturici, *J. Org. Chem.* **1999**, *64*, 5557–5564.
[5] J. J. Gridley, M. P. Coogan, D. W. Knight, K. M. Abdul Malik, C. M. Sharland, J. Singkhonrat, S. Williams, *Chem. Commun.* **2003**, 2550–2551.
[6] J.-F. Poisson, J. F. Normant, *Org. Lett.* **2001**, *3*, 1889–1891.
[7] L. He, H. S. Byun, R. Bittman, *J. Org. Chem.* **2000**, *65*, 7627–7633.
[8] a) P. G. Cozzi, R. Hilgraf, N. Zimmermann, *Eur. J. Org. Chem.* **2004**, 4095–4105; b) F. D'Aniello, A. Schoenfelder, A. Mann, M. Taddei, *J. Org. Chem.* **1996**, *61*, 9631–9634.
[9] B. W. Lee, J. H. Lee, K. C. Jang, J. E. Kang, J. H. Kim, K.-M. Park, K. H. Park, *Tetrahedron Lett.* **2003**, *44*, 5905–5907.
[10] M. Heneghan, G. Procter, *Synlett* **1992**, 489–490.
[11] For a review, see: M. T. Reetz, *Chem. Rev.* **1999**, *99*, 1121–1162.
[12] J. Clayden, C. McCarthy, J. G. Cumming, *Tetrahedron: Asymmetry* **1998**, *9*, 1427–1440.
[13] J. M. Andrés, R. Barrio, M. A. Martínez, R. Pedrosa, A. Pérez-Encabo, *J. Org. Chem.* **1996**, *61*, 4210–4213.
[14] M. T. Reetz, M. W. Drewes, A. Schmitz, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1141–1143.
[15] J. M. Andrés, M. A. Martínez, R. Pedrosa, A. Pérez-Encabo, *Tetrahedron: Asymmetry* **2001**, *12*, 347–353.
[16] J. M. Andrés, R. Pedrosa, A. Pérez, A. Pérez-Encabo, *Tetrahedron* **2001**, *57*, 8521–8530.
[17] J. M. Andrés, R. Pedrosa, A. Pérez-Encabo, *Eur. J. Org. Chem.* **2004**, 1558–1566.
[18] a) B. Jiang, Y. Feng, J.-F. Hang, *Tetrahedron: Asymmetry* **2001**, *12*, 2323–2329; b) B. Jiang, Y. Feng, *Tetrahedron Lett.* **2002**, *43*, 2975–2977.
[19] P. Ciapetti, M. Falorni, M. Taddei, *Tetrahedron* **1996**, *52*, 7379–7390.
[20] a) A. Aravind, S. K. Mohanty, T. V. Pratap, S. Baskaran, *Tetrahedron Lett.* **2005**, *46*, 2965–2968; b) D. Spielvogel, J. Kammerer, M. Keller, H. Prinzbach, *Tetrahedron Lett.* **2000**, *41*, 7863–7867; c) A. Dondoni, D. Perrone, M. Rinaldi, *Tetrahedron Lett.* **1998**, *39*, 2651–2654; d) F. Benedetti, F. Berti, S. Norbedo, *Tetrahedron Lett.* **1998**, *39*, 7971–7974; e) S. H. Kang, D. H. Ryu, *Tetrahedron Lett.* **1997**, *38*, 607–610; f) M. E. Pierce, G. D. Harris, Q. Islam, L. A. Radesca, L. Storace, R. E. Waltermire, E. Wat, P. K. Jadhav, G. C. Emmett, *J. Org. Chem.* **1996**, *61*, 444–450; g) L. T. Rossano, Y. S. Lo, L. Anzalone, Y.-C. Lee, D. J. Meloni, J. R. Moore, T. M. Gale, J. F. Arnett, *Tetrahedron Lett.* **1995**, *36*, 4967–4970.
[21] a) S. Dagorne, S. Bellemin-Laponnanz, R. Welter, *Organometallics* **2004**, *23*, 3053–3061; b) P. Y. S. Lam, Y. Ru, P. K. Jadhav, P. E. Aldrich, G. V. DeLucca, C. J. Eyermann, C.-H. Chang, G. Emmett, E. R. Holler, W. F. Daneker, L. Li, P. N. Confalone, R. J. McHugh, Q. Han, R. Li, J. A. Markwalder, S. P. Seitz, T. R. Sharpe, L. T. Bacheler, M. M. Rayner, R. M. Klabe, L. Shum, D. L. Winslow, D. M. Kornhauser, D. A. Jackson, S. Erickson-Viitanen, C. N. Hodge, *J. Med. Chem.* **1996**, *39*, 3514–3525.

[22] a) N. Aguilar, A. Moyano, M. A. Pericás, A. Riera, *Tetrahedron Lett.* **1999**, *40*, 3917–3920; b) T. K. Chakraborty, S. Dutta, *Synth. Commun.* **1997**, *27*, 4163–4172.
[23] M. T. Reetz, A. Schmitz, *Tetrahedron Lett.* **1999**, *40*, 2737–2740.
[24] a) A. A. A. van der Zeijden, *Tetrahedron: Asymmetry* **1995**, *6*, 913–918; b) K. Ishimaru, K. Tsuru, K. Yabuta, M. Wada, Y. Yamamoto, K.-y. Akiba, *Tetrahedron* **1996**, *52*, 13137–13144.
[25] E. J. Corey, J. A. Katzenellenbongen, G. H. Posner, *J. Am. Chem. Soc.* **1967**, *89*, 4245–4247.
[26] J. M. Andrés, N. de Elena, R. Pedrosa, A. Pérez-Encabo, *Tetrahedron: Asymmetry* **2001**, *12*, 1503–1509.

Received: March 9, 2006
Published Online: May 30, 2006

