Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 62 (2006) 9166–9173
Tetrahedron

Synthesis of enantiopure *cis*-decahydroquinolines from homotyramines by Birch reduction and aminocyclization

Marisa Mena, Nativitat Valls, Mar Borregán and Josep Bonjoch*

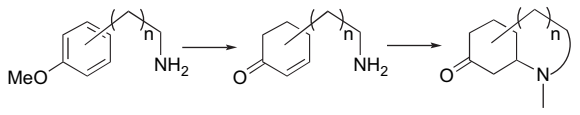
Laboratori de Química Orgànica, Facultat de Farmàcia, Universitat de Barcelona, Av. Joan XXIII s/n, 08028-Barcelona, Spain

Received 20 June 2006; accepted 11 July 2006
Available online 4 August 2006

Abstract—Birch reduction of homotyramines with a *syn*-β-amino alcohol unit followed by acid treatment of formed dihydroanisole derivatives gives polysubstituted enantiopure *cis*-decahydroquinolines. The stereoselectivity of the process differs if the hydroxyl group is free or protected. The procedure allows the synthesis of 7-oxodecahydroquinolines embodying four stereogenic centres with the same relative configuration as that of lepadins F and G.

1. Introduction

The use of (ω-aminoalkyl)methoxybenzene derivatives (e.g., tyrosine and tyramine compounds) as starting materials to elaborate azabicyclic compounds through a Birch reduction followed by an intramolecular cyclization of the resulting amino-tethered cyclohexenone (Scheme 1) is well-precedented in the literature. Following this methodology, octahydroindoles,[1,2] azaspiroundecanes,[3] 6-azabicyclo-[3.2.1]octanes,[4] 2-azabicyclo[3.3.1]nonanes,[5] and decahydroquinolines[6] have been prepared, but, apart from of our work on the synthesis of enantiopure octahydroindoles,[2] all described processes lead to racemic compounds.



Scheme 1. The Birch reduction/aminocyclization process leading to azabicyclic compounds.

In this paper, we describe the synthesis of enantiopure polysubstituted decahydroquinolines from homotyramine precursors following the aforementioned Birch reduction/aminocyclization sequence.[7] The interest of this work, aside from studying the stereocontrol of the process, lies in the possible usefulness of the resulting compounds in the synthesis of lepadin alkaloids. These natural products are structurally characterized by the presence of a 2,3,5-trisubstituted cis-fused decahydroquinoline ring. The substitution pattern, which has a methyl group at C(2), a hydroxyl group, free or protected, at C(3) and a functionalized side chain at C(5), shows a variety of stereochemical arrangements.[8] Total enantioselective syntheses of lepadins A,[9] B,[9–11] C,[9] D–E[11] and H,[11] as well as a formal route to *rac*-lepadin B[12] have been reported.

We focused our attention on the synthesis of *cis*-decahydroquinolines incorporating a methyl at C(2) and a hydroxyl at C(3), with an *S* configuration at both stereogenic centres, as occurs in lepadins A, B and C. In lepadins F and G both substituents also have a cis relationship, although their absolute configuration is unknown (see Scheme 2). The strategies described for the construction of 3-hydroxy-2-methyldecahydroquinolines involve the elaboration of a polyfunctionalized piperidine followed by carbocyclic ring closure through aldol processes[9,10] or the construction of the piperidine ring from cyclohexanone derivatives either by an intramolecular enamine alkylation[11] or by using a xanthate-mediated radical cyclization.[12] In our approach, we envisaged enantiopure anisole derivatives of type **I** (R=H or Me) as potential intermediates for the aforementioned *cis*-decahydroquinolines, as they would bring about ring closure by forming the N–C(8a) bond.[13]

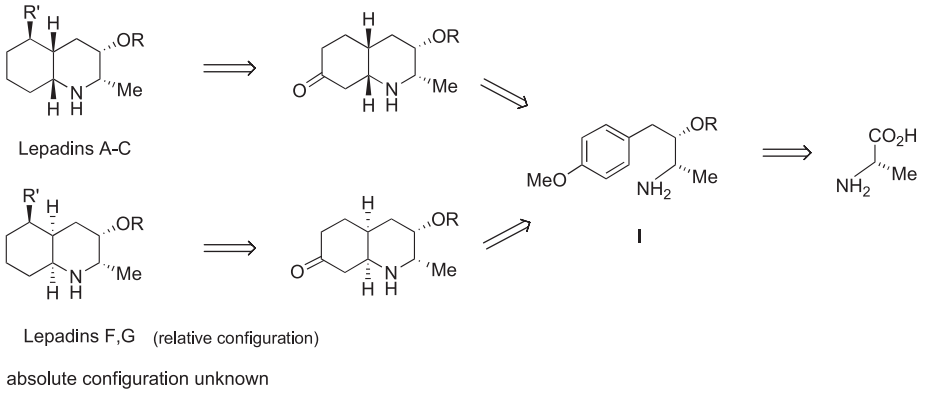
2. Results and discussion

2.1. Synthetic aspects

For the proposed studies of Birch reduction of homotyramines followed by an aminocyclization process to achieve *cis*-decahydroquinolines of interest in the lepadin field, α-methyl-β-aminoalcohol **I** was required. The synthesis of *syn*-α-methyl-β-amino alcohols (**II**, Scheme 3) is

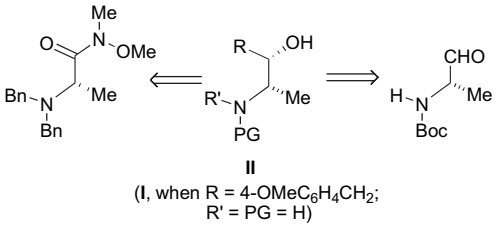
Keywords: Lepadin alkaloids; Decahydroquinolines; Epoxides; Conformational analysis; Nitrogen heterocycles.
* Corresponding author. Tel.: +34 934024540; fax: +34 934024539; e-mail: josep.bonjoch@ub.edu

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.07.035

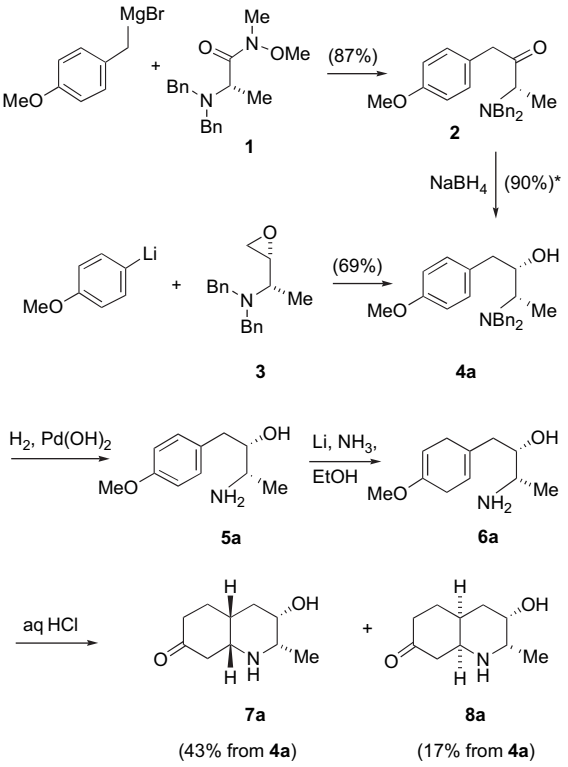


Scheme 2. Retrosynthetic approach to lepadin alkaloids.

well-precedented not only by the methodological studies of the reactivity of alanine derivatives but also by the presence of this structural motif in several natural products other than the aforementioned lepadins, such as various piperidine alkaloids[14] (i.e., carpamic acid, azimic acid, julifloridine and cassine inter alia). The most suitable procedures for *syn* amino alcohols of type **II** are the organometallic addition upon the Weinreb amide of *N*,*N*-dibenzylalanine[15] followed by hydride reduction of the resulting α-amino ketone[16] or the organometallic addition upon the *N*-Boc-alaninal.[17,18] To our knowledge, none of these versatile approaches have been used in reactions involving *p*-methoxybenzylmagnesium bromide, as was required in the present work. We decided to use the protocol involving the Weinreb amide of *N*,*N*-dibenzylalanine and, in addition, introduced a new approach based on the ring-opening of a suitable epoxide with a lithium reagent is introduced to achieve aminoalcohol **I**.



Scheme 3. Synthesis of enantiopure *syn*-α-methyl-β-amino alcohols.

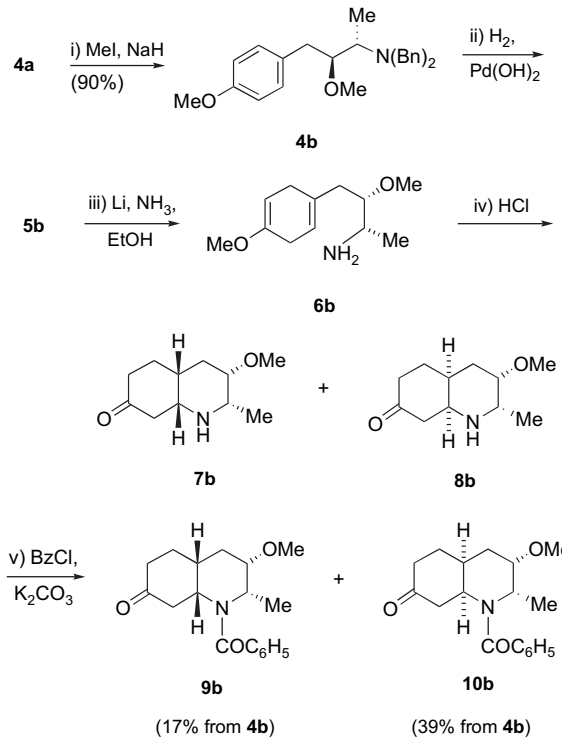


Scheme 4. Synthesis of *cis*-decahydroquinolines.

Coupling of either the *p*-methoxybenzylmagnesium bromide with Weinreb amide **1**[19,20] or the *p*-methoxyphenyllithium with the (*R*) isomer of [(*S*)-1′-(dibenzylamino)ethyl]oxirane (**3**)[21] in the presence of $BF_3 \cdot Et_2O$ (Ganem's conditions)[22,23] gave synthetic access to the required aminoalcohol **4a**, a diastereoselective reduction of the initially formed β-amino ketone **2** being necessary in the former sequence (Scheme 4, * denotes that 10% of the epimer of **4a**[24] was additionally isolated in this route, see Section 3). A loss of enantiopurity observed in this sequence (**1**→**4a**) when the coupling of the Weinreb amide **1** was carried out at 0 °C[25] and was avoided at −40 °C.

Debenzylation of **4a** gave the primary amine **5a**, which was submitted to the Birch reduction conditions (Li/NH_3) to allow the formation of dihydroanisole **6a**. This was treated with a 2 N HCl solution at 75 °C, and the decahydroquinoline ring was formed after enol ether hydrolysis, double bond isomerization and an intramolecular 1,4-addition of the amino group across the cyclohexenone intermediate. The process is stereoselective, with the exclusive formation of *cis*-isomers of the decahydroquinoline ring. Polysubstituted decahydroquinolines **7a** (43%) and **8a** (17%) were isolated in a 2.5:1 ratio and a overall yield of 60% from the sequence **4a**→**7a**+**8a**.

We then carried out the same sequence of reactions but starting from *syn*-amino ether **4b**, which was obtained by *O*-methylation of aminoalcohol **4a** (Scheme 5). In this series, the aminocyclization step starting from dihydroanisole **6b** gave a 1:2.3 mixture of decahydroquinolines **7b** and **8b**, which were only partially separated. However, when the reaction mixture was basified and treated with benzoyl chloride after aminocyclization, the corresponding amides **9b** and **10b** were isolated in 17 and 39% overall yields (four steps from **4b**).



Scheme 5.

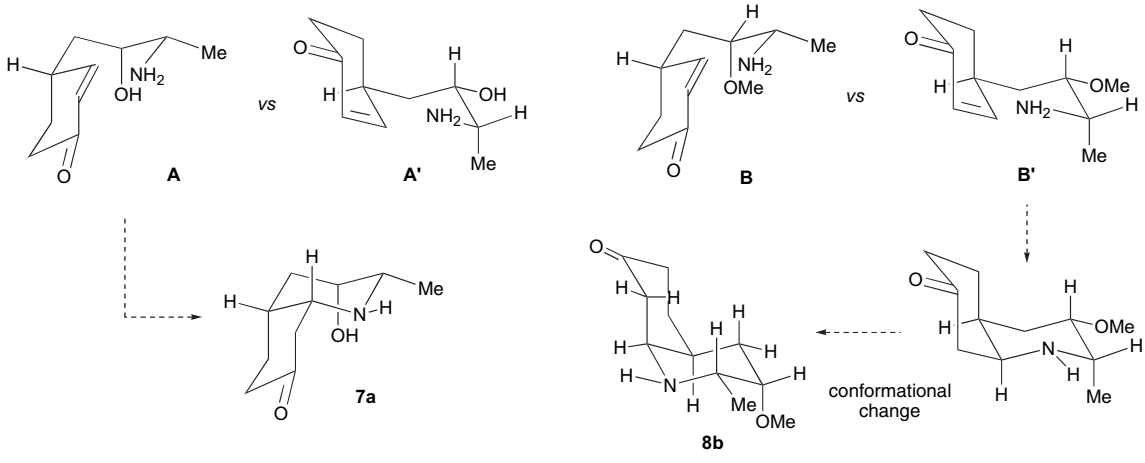
In the cyclization processes (**6**→**7**+**8**), both in series **a** (3-OH) and series **b** (3-OMe), the isolated decahydroquinolines showed a cis-fused relationship. The major compound of series **a** (i.e., **7a**) showed the same pattern of absolute configuration in its four stereocentres as lepadins A–C, while that of series **b** (i.e., **8b**) matched the relative configuration of lepadins F and G, allowing them to be considered as advanced building blocks for elaborating the aforementioned alkaloids.

The stereoselective *cis*-perhydroquinoline formation through a 6-*exo* process agreed with the stereochemical outcome observed in related cyclizations,[6] and with both the steric and electronic preferences for a pseudo axial addition of the nucleophilic species to the cyclohexenone moiety. Interestingly, the configuration of the new methine carbons (i.e., C-4a and C-8a) is controlled to some extent by the oxygenated function. Why does the decalin ring formation change diastereoselectivity if there is a free or protected hydroxyl group? Considering that the axial attack proceeds through a chair-like transition state in the hydroxyl series perhaps a hydrogen bonding favours the formation of enone **A** with respect to the epimeric enone **A′**, which could be in equilibrium by means of a tautomeric process through their corresponding dienol ether. On the contrary in series **b**, in which the hydroxyl group is protected as methyl ether, the steric factors (a 1,3-diaxial relationship between the C3–OMe and C4a–C5 bonds) prevent to some extent the formation of epimer **B**, and the formation of **B′** being favoured (Scheme 6). Thus, the ratio of *cis*-decahydroquinoline with an *S* configuration at the two new stereogenic centres formed in the aminocyclization to the diastereoisomers with a *R* configuration was higher in compounds with a methoxy rather than hydroxyl substituent.

2.2. NMR studies of decahydroquinolines 7–10 (series a and b)

The stereochemistry of the synthesized azabicyclic compounds was elucidated by 2D NMR spectra (COSY, HSQC). The N-inside (**7a** and **7b**) and N-outside (**8a** and **8b**) *cis*-decahydroquinoline isomers[26] in the amino series are clearly differentiated by two NMR features: (i) the ^{1}H NMR chemical shift of H-2, which appears more deshielded (δ 3.1) in the N-outside than in the N-inside derivatives (δ 2.8), due to the compression upon H-2 of the C8–C8a bond, which has a 1,3-cis relationship, on the N-outside derivatives; (ii) the ^{13}C NMR chemical shift of C(2) is more upfielded (∼10 ppm) in compounds with the N-outside conformation than those with the N-inside conformation; moreover the signals given by the carbon atoms at C-4, C-6 and C-8 also appear in a higher field in the N-outside derivatives.

The key evidence for the conformational elucidation of **7a** was found in the ^{1}H NMR coupling pattern for the methylene protons at C-8, which appear as dd (J=14.6, 5.4 Hz). The relative configuration for methoxy derivative **7b** is the same as that observed in **7a** and their NMR data follows the same pattern of chemical shifts (Scheme 2). The absolute configuration of **7a** was deduced by considering that: (a) the



Scheme 6.

coupling constants for H-2 (qd, J=6.6, 2 Hz) and H-3 (q, J=2.4 Hz) determined their location and hence fixed the methyl at C(2) and the hydroxyl at C(3) to an equatorial and axial disposition, respectively; (b) the multiplicity of H-8a (br s) implied an equatorial relationship with respect to the cyclohexane ring, which discarded not only a trans junction of the decaline ring but also, taking into account the preferred conformation, implied a *R* configuration for C(8a). For the major component in the methoxy series **8b**, the axial proton H-8a is strongly coupled to one adjacent axial. Hence, its resonance signal appears as a deceptively simple doublet (J=10.4 Hz) of triplets (J=4.8 Hz) centred at δ 3.43.

In summary, the twin chair conformation with the nitrogen axially substituting the carbocyclic ring is the lowest energy conformation for **7a**, whereas the twin chair conformation with the nitrogen equatorially substituting the carbocyclic ring is the lowest energy conformation for **8b** (Fig. 1).

Interestingly, the *N*-benzoyl derivatives **9a**, prepared from amine **7a** in quantitative yield, and **10b** (Fig. 2) showed a different preferred conformations to that of their precursors **7a** and **8b**, respectively, as has been observed in synthetic intermediates in lepadin synthesis[9–11] when the amino group is converted to a carbamate or amide group.

In summary, a new synthetic entry to enantiopure polysubstituted *cis*-decahydroquinolines has been reported. Since the observed stereoselectivity allows lepadin-type stereochemistries to be achieved, further studies using decahydroquinolines **9a** and **10b** as advanced synthetic intermediates are in progress with the aim of achieving lepadins A–C and F and G, respectively.

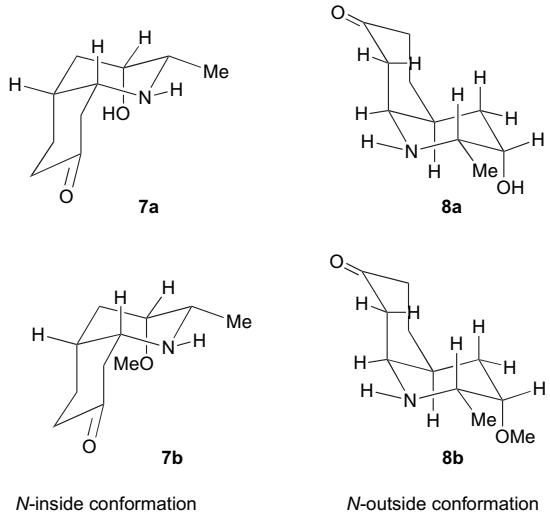


Figure 1. Preferred conformation of decahydroquinolines **7** and **8**.

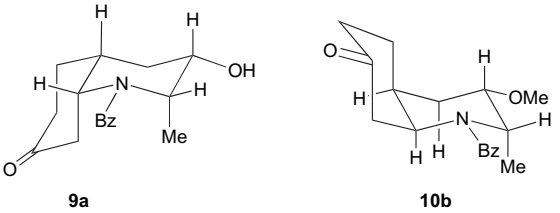


Figure 2. Preferred conformation of decahydroquinolines **9** and **10**.

3. Experimental

3.1. General

All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions. Analytical TLC was performed on SiO_2 (silica gel 60 F_{254}, Merck) or Al_2O_3 (ALOX N/UV_{254}, Polygram), and the spots were located with iodoplatinate reagent (compounds **1**–**8**) or 1% aqueous $KMnO_4$ (compounds **9** and **10**). Chromatography refers to flash chromatography and was carried out on SiO_2 (silica gel 60, SDS, 230–240 mesh ASTM) or Al_2O_3 (aluminium oxide 90, Merck). Drying of organic extracts during workup of reactions was performed over anhydrous Na_2SO_4. Optical rotations were recorded with a Perkin–Elmer 241 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Gemini 200 or 300, or a Varian Mercury 400 instrument. Chemical shifts are reported in parts per million downfield (δ) from Me_4Si. All new compounds were determined to be >95% pure by ^{1}H NMR spectroscopy.

3.1.1. (*S*)-(*N*,*N*-Dibenzyl)amino-*N*-methoxy-*N*-methylpropionamide (1). To a solution of benzyl (*S*)-2-(*N*,*N*-dibenzylamino)propionate[27] (2.15 g, 6 mmol) and HCl·HN(OMe)Me (3.0 g, 30 mmol) in THF (90 mL) at −20 °C, ^{i}PrMgCl (30 mL of a 2 M in THF, 60 mmol) was added dropwise over a period of 30 min. The reaction mixture was stirred for 2 h at this temperature and then warmed to rt for 2.5 h. NH_4Cl (20 mL) was added and the product was extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was dried and concentrated to an oil, which contained **1** and BnOH. The latter was removed under vacuum to afford compound **1** (1.94 g), which was used without further purification. The ^{1}H NMR data were identical to those previously reported.[20] R_f=0.1 (SiO_2, 9:1 hexane/EtOAc); ^{13}C NMR (50 MHz, $CDCl_3$) 14.9 (CH_3), 54.4 (CH_2), 56.1 (CH), 60.1 (CH_2), 126.8 (CH), 127.4 (CH), 127.6 (CH), 128.1 (CH), 128.3 (CH), 128.5 (CH), 139.8 (C), 173.9 (C).

3.1.2. (3*S*)-3-(*N*,*N*-Dibenzyl)amino-1-(4-methoxyphenyl)butan-2-one (2). To a solution of **1** (1.81 g, 5.8 mmol) in THF (50 mL) at −40 °C, 2-methoxybenzylmagnesium chloride 0.25 M in THF (46 mL, 11.6 mmol) was added dropwise. The reaction mixture was stirred for 2 h 30 min at −40 °C and then quenched with NH_4Cl. The organic layer was dried and concentrated to an oil, which was purified by chromatography (SiO_2, 9:1 hexane/EtOAc) to give **2** as a colourless oil (2.17 g, 87%). R_f=0.5 (SiO_2, 9:1 hexane/EtOAc); $[\alpha]_D^{25}$ −8.8 (*c* 1.0, $CHCl_3$); IR (KBr) 1715, 1611 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 1.15 (d, J=6.6 Hz, 3H), 3.47 (d, J=13.2 Hz, 2H), 3.52 (q, J=6.6 Hz, 1H), 3.72 (d, J=15.0 Hz, 1H), 3.74 (d, J=13.2 Hz, 2H), 3.76 (s, 3H), 3.88 (d, J=15.3 Hz, 1H), 6.74 (d, J=8.6 Hz, 2H), 6.84 (d, J=8.6 Hz, 2H), 7.20–7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) 7.1 (CH_3), 45.3 (CH_2), 54.6 (CH_2), 55.2 (CH_3), 60.6 (CH), 113.8 (CH), 126.5 (C), 127.2 (CH), 128.4 (CH), 128.9 (CH), 130.3 (CH), 139.2 (C), 158.3 (C). Anal. Calcd for $C_{25}H_{27}NO_2$: C, 80.40; H, 7.29; N, 3.75. Found: 80.00; H, 7.29; N, 3.67.

3.1.3. (2*S*,3*S*)-3-(*N*,*N*-Dibenzyl)amino-1-(4-methoxyphenyl)butan-2-ol (4a). *Method A* (from ketone **2**): to a solution of **2** (2.15 g, 5.75 mmol) in MeOH (68 mL) at −20 °C, $NaBH_4$ (453 mg, 11.5 mmol) was added. The reaction mixture was stirred for 1 h at this temperature, and then quenched with brine (30 mL). The product was extracted with CH_2Cl_2 (3×30 mL), dried and concentrated to give a mixture of alcohols **4a** and *epi*-**4a**[24] in a 9:1 ratio according to the NMR spectrum. Purification by chromatography (SiO_2, 9:1 hexane/EtOAc) gave **4a** (1.94 g, 90%) and *epi*-**4a** (216 mg, 10%).

Compound **4a**: colourless oil. R_f=0.24 (SiO_2, 9:1 hexane/EtOAc); $[\alpha]_D^{25}$ −5.6 (*c* 1.4, $CHCl_3$); IR (KBr) 3600–3100, 1611 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.07 (d, *J*=6.6 Hz, 3H), 2.38 (dd, *J*=14.0, 7.8 Hz, 1H), 2.60 (dq, *J*=9.3, 6.6 Hz, 1H), 2.78 (dd, J_1=14.3, 3.0 Hz, 1H), 3.30 (d, *J*=13.5 Hz, 2H), 3.68 (m, 1H), 3.77 (s, 3H), 3.82 (d, *J*=13.5 Hz, 2H), 6.77 (d, *J*=9 Hz, 2H), 7.11 (d, *J*=9 Hz, 2H), 7.20–7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) 8.3 (CH_3), 39.1 (CH_2), 53.2 (CH_2), 55.2 (CH_3), 57.7 (CH), 71.9 (CH), 113.5 (CH), 127.1 (CH), 128.4 (CH), 128.9 (CH), 130.1 (CH), 131.0 (C), 138.7 (C), 157.8 (C). Anal. Calcd for $C_{25}H_{29}NO_2 \cdot 1/2H_2O$: C, 78.12; H, 7.81; N, 3.64. Found: C, 77.84; H, 8.16; N, 3.34.

Compound *epi*-**4a**: colourless oil. R_f=0.14 (SiO_2, 9:1 hexane/EtOAc); IR (KBr) 3600–3100, 1611 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.17 (d, *J*=6.6 Hz, 3H), 2.30 (dd, *J*=13.8, 9.6 Hz, 1H), 2.75 (quint, *J*=6.9 Hz, 1H), 3.21 (dd, *J*=13.8, 3.0 Hz, 1H), 3.50 (*J*=13.8 Hz, 2H), 3.73–3.81 (m, 1H), 3.80 (d, *J*=14.1 Hz, 2H), 6.80 (d, *J*=9.0 Hz, 2H), 7.02 (d, *J*=9.0 Hz, 2H), 7.20–7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) 8.6 (CH_3), 40.6 (CH_2), 54.7 (CH_2), 55.3 (CH_3), 57.2 (CH), 74.7 (CH), 113.9 (CH), 126.8 (CH), 128.2 (CH), 128.8 (CH), 130.2 (CH), 131.0 (C), 140.0 (C), 158.1 (C).

Method B (from epoxide **3**): to a solution of *n*-BuLi (1.6 M in hexanes, 1.05 mL, 1.68 mmol) in THF (3.5 mL) at −78 °C was added 4-bromoanisole (0.2 mL, 1.56 mmol). The reaction mixture was stirred for 90 min, treated with a solution of (2*R*)-[1′(*S*)-(dibenzylamino)ethyl]oxirane[21] (162 mg, 0.6 mmol) in THF (2 mL) and $BF_3 \cdot Et_2O$ (0.21 mL, 1.68 mmol) and continuously stirred at −78 °C for 2 h prior to being quenched with saturated NH_4Cl (4 mL) and warmed to rt. The product was extracted with CH_2Cl_2 (3×10 mL), and the organic layer was dried and concentrated to give an oil, which was purified by chromatography (SiO_2, 9:1 hexane/EtOAc) to give **4a** as a colourless oil (153 mg, 69%). The spectroscopic data and specific rotation were identical with the product obtained by *method A*.

3.1.4. (2*S*,3*S*)-*N*,*N*-Dibenzyl-3-methoxy-4-(4-methoxyphenyl)-2-butanamine (4b). To a suspension of NaH (195 mg, 4.89 mmol) in THF (2 mL) at 0 °C a solution of **4a** (1.22 g, 3.26 mmol) in THF was transferred (1 mL+1 mL). The reaction mixture was warmed over 20 min to rt and then MeI (2 mL, 32.6 mmol) was added. The reaction was sealed and stirred for 48 h. NH_4Cl was added (10 mL) and the product was extracted with CH_2Cl_2 (3×20 mL). The resulting organic layer was washed with H_2O (15 mL) and brine (15 mL), dried and concentrated to give an oil, which was purified by chromatography (SiO_2, 9:1 hexane/EtOAc) to give **4b** as a colourless oil (1.14 g, 90%). R_f=0.42 (SiO_2, 9:1 hexane/EtOAc); $[\alpha]_D^{25}$ −4.6 (*c* 1.0, $CHCl_3$); IR (KBr) 1611 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.13 (d, *J*=6.9 Hz, 3H), 2.74–2.88 (m, 3H), 3.13 (s, 3H), 3.22 (dt, *J*=7.2, 4.8 Hz, 1H), 3.43 (d, *J*=13.5 Hz, 2H), 3.77 (s, 3H), 4.01 (d, *J*=13.5 Hz, 2H), 6.73 (d, *J*=8.7 Hz, 2H), 6.94 (d, *J*=8.7 Hz, 2H), 7.20–7.32 (m, 6H), 7.39–7.41 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) 10.1 (CH_3), 37.4 (CH_2), 55.1 (CH), 55.2 (CH_2), 55.2 (CH_3), 59.2 (CH_3), 88.1 (CH), 113.5 (CH), 126.6 (CH), 128.1 (CH), 128.9 (CH), 130.2 (CH), 132.3 (C), 140.9 (C), 157.7 (C). Anal. Calcd for $C_{26}H_{31}NO_2$: C, 80.17; H, 8.02; N, 3.60. Found: C, 80.07; H, 8.31; N, 3.40.

3.1.5. (2*S*,3*S*)-3-Amino-1-(4-methoxyphenyl)butan-2-ol (5a). A suspension of **4a** (2.16 g, 5.75 mmol) and $Pd(OH)_2/C$ (210 mg, 20%) in EtOH (110 mL) was stirred at rt under hydrogen atmosphere overnight. The catalyst was removed by filtration through Celite and the filtrate was concentrated to give **5a** as an oil (1.12 g), which was used directly in the next step. An analytical sample was obtained by chromatography (Al_2O_3, CH_2Cl_2 saturated with NH_3). $[\alpha]_D^{25}$ −15.5 (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) 1.12 (d, *J*=6.6 Hz, 3H), 2.56 (dd, *J*=14.0, 8.6 Hz, 1H), 2.74–2.86 (m, 2H), 3.40–3.46 (m, 1H), 3.78 (s, 3H), 6.84 (d, *J*=8.7 Hz, 2H), 7.14 (d, *J*=8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 20.5 (CH_3), 39.6 (CH_2), 50.3 (CH), 54.7 (CH_2), 55.2 (CH_3), 76.4 (CH), 113.7 (CH), 130.1 (C), 130.2 (CH), 158.0 (C).

3.1.6. (2*S*,3*S*)-3-Methoxy-4-(4-methoxyphenyl)-2-butanamine (5b). Operating as above, starting from **4b** (1.14 g, 2.92 mmol), **5b** was obtained (615 mg) as an oil, which was used directly in the next step. An analytical sample was obtained by chromatography (Al_2O_3, 98:2 CH_2Cl_2 saturated with NH_3/MeOH). $[\alpha]_D^{25}$ +8.4 (*c* 1.0, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) 1.11 (d, *J*=6.3 Hz, 3H), 2.56 (dd, *J*=14.3, 6.5 Hz, 1H), 2.90–2.81 (m, 2H), 3.07 (dt, *J*=6.6, 5.4 Hz, 1H), 3.30 (s, 3H), 3.79 (s, 3H), 6.84 (d, *J*=8.4 Hz, 2H), 7.15 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) 20.1 (CH_3), 35.8 (CH_2), 49.2 (CH), 55.2 (CH_3), 58.8 (CH_3), 87.6 (CH), 113.7 (CH), 130.4 (CH), 130.8 (C), 158.0 (C).

3.1.7. (2*S*,3*S*)-3-Amino-1-(4-methoxy-2,5-dihydrophenyl)butan-2-ol (6a). To a solution of **5a** (1.12 g, 5.75 mmol) in EtOH (6 mL) at −78 °C, ammonia (46 mL) was added. Small chips of lithium (280 mg, 40 mmol) were added until the solution become a persistent deep blue for 1.5 h. The cooling bath was removed, the ammonia was allowed to evaporate overnight and the reaction mixture was evaporated. The dried extract was dissolved in brine (15 mL) and the product was extracted with CH_2Cl_2 (3×15 mL), dried with Na_2SO_4 and concentrated to give **6a** (1.112 g) as an oil, which was used directly in the next step. ^1H NMR (200 MHz, $CDCl_3$) 1.11 (d, *J*=6.3 Hz, 3H), 2.08 (dd, *J*=14.1, 9.0 Hz, 1H), 2.21 (dd, *J*=13.5, 3.3 Hz, 1H), 2.69–2.84 (m, 6H), 3.33–3.40 (m, 1H), 3.55 (s, 3H), 4.63 (m, 1H), 5.51 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 20.2 (CH_3), 29.1 (CH_2), 29.4 (CH_2), 41.6 (CH_2), 50.8 (CH), 53.7 (CH_3), 73.1 (CH), 90.2 (CH), 120.2 (CH), 132.4 (C), 152.6 (C).

3.1.8. (2*S*,3*S*)-3-Methoxy-4-(4-methoxy-2,5-dihydrophenyl)-2-butanamine (6b). Operating as above, starting from **5b** (611 mg, 2.92 mmol), **6b** was obtained (620 mg) as an oil, which was used directly in the next step. ^{1}H NMR (200 MHz, $CDCl_3$) 1.09 (d, J=6.6 Hz, 3H), 2.14–2.29 (m, 2H), 2.74–2.84 (m, 3H), 2.87–2.96 (m, 1H), 3.02–3.07 (m, 1H), 3.40 (s, 3H), 3.55 (s, 3H), 4.62 (m, 1H), 5.49 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) 20.1 (CH_3), 29.2 (CH_2), 30.0 (CH_2), 37.9 (CH_2), 49.3 (CH), 53.9 (CH_3), 58.4 (CH_3), 84.7 (CH), 90.4 (CH), 120.1 (CH), 132.6 (C), 152.9 (C).

3.1.9. Aminocyclization of 6a. A solution of **6a** (95 mg, 0.48 mmol) in 2 N HCl (1.6 mL) was stirred for 3.5 h at 70 °C. The mixture was basified with NaOH (1 N, 10 mL) and the solution was extracted with CH_2Cl_2 (4×10 mL) and $CHCl_3$/MeOH (4×10 mL), dried and concentrated to give a brown oil. Purification by chromatography (Al_2O_3, CH_2Cl_2 saturated with NH_3) gave a partially separated 2.5:1 mixture of **7a** (37 mg, 43%) and **8a** (15 mg, 17%).

3.1.9.1. (2*S*,3*S*,4a*R*,8a*R*)-3-Hydroxy-2-methyloctahydroquinolin-7-one (7a). White solid; mp 112–114 °C; R_f=0.17 (Al_2O_3, 99:1 CH_2Cl_2 saturated with NH_3/MeOH); ^{1}H NMR (400 MHz, $CDCl_3$, gCOSY) 1.11 (d, J=6.8 Hz, 3H, Me), 1.81 (ddd, J=14.8, 5.6, 3.6 Hz, H-4eq), 1.87 (dm, J=14 Hz, H-5eq), 1.95 (dt, J=14.4, 2 Hz, H-4ax), 2.05 (m, H-4a), 2.24 (dt, J=14.4, 2 Hz, H-6eq), 2.29 (dd, J=14.4, 5.6 Hz, H-8ax), 2.32 (m, H-6ax), 2.50 (qd, J=13.6, 4.8 Hz, H-5ax), 2.65 (ddd, J=14.8, 4.8, 0.8 Hz, H-8eq), 2.80 (qd, J=6.6, 2 Hz, H-2ax), 3.35 (br s, H-8a), 3.58 (q, J=2.4 Hz, H-3eq); ^{13}C NMR (100 MHz, $CDCl_3$, gHSQC) 18.1 (Me), 28.8 (C-5), 33.5 (C-4a), 36.4 (C-4), 41.6 (C-6), 47.5 (C-8), 56.8 (C-8a), 59.3 (C-2), 68.2 (C-3), 210.8 (C-7). HRMS (ESI-TOF) calcd for $C_{10}H_{18}NO_2$ (M^++1) 184.1332, found 184.1337.

3.1.9.2. (2*S*,3*S*,4a*S*,8a*S*)-3-Hydroxy-2-methyloctahydroquinolin-7-one (8a). Colourless oil; R_f=0.14 (Al_2O_3, 99:1 CH_2Cl_2 saturated with NH_3/MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) 1.10 (d, J=6.6 Hz, 3H, Me), 1.72–1.98 (m, 4H), 2.15–2.44 (m, 4H), 2.93 (t, J=12.6 Hz, H-8ax), 3.06 (qd, J=6.5, 1.8 Hz, H-2ax), 3.39 (dt, J=11.7, 4.8 Hz, H-8a), 3.76 (br s, H-3eq); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) 17.7 (Me), 28.0 (C-5), 28.1 (C-4a), 31.9 (C-4), 36.6 (C-6), 42.6 (C-8), 47.5 (C-2), 55.9 (C-8a), 68.2 (C-3), 210.9 (C-7). HRMS (ESI-TOF) calcd for $C_{10}H_{18}NO_2$ (M^++1) 184.1332, found 184.1331.

3.1.10. Aminocyclization of 6b. Following the above procedure for the aminocyclization of **6a** using methoxy derivative **6b** (225 mg, 1.07 mmol), heating at 70 °C for 3 h and purifying by chromatography (Al_2O_3, 99:1 CH_2Cl_2 saturated with NH_3/MeOH), a partially separated mixture of **7b** (36 mg, 17%) and **8b** (50 mg, 22%) was obtained.

3.1.10.1. (2*S*,3*S*,4a*R*,8a*R*)-3-Methoxy-2-methyldecahydroquinolin-7-one (7b). White solid; mp 45–47 °C; R_f=0.25 (Al_2O_3, 99:1 CH_2Cl_2 saturated with NH_3/MeOH); $[\alpha]_D^{25}$ +14.6 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, gCOSY) 1.12 (d, J=6.8 Hz, 3H, Me), 1.62 (ddd, J=14.8, 5.6, 3.2 Hz, H-4eq), 1.74 (m, H-5eq), 2.00 (dm, J=12 Hz, H-4a), 2.13 (dt, J=14.8, 2.2 Hz, H-4ax), 2.23 (td, J=14, 6 Hz, H-6ax), 2.26 (dm, J=14.8 Hz, H-8), 2.32 (dddd, J=14, 4.8, 2.4, 2.4 Hz, H-6eq), 2.61 (dd, J=14.8, 5.6 Hz, H-8), 2.63 (qd, J=14, 4.2 Hz, H-5ax), 2.78 (qd, J=6.5, 2.4 Hz, H-2ax), 3.05 (q, J=2.7 Hz, H-3eq), 3.30 (masked, H-8a), 3.31 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$, gHSQC) 18.1 (Me), 26.9 (C-5), 30.9 (C-4), 33.4 (C-4a), 41.4 (C-6), 47.6 (C-8), 56.3 (C-2), 56.9 (OMe), 58.7 (C-8a), 76.9 (C-3), 210.6 (C-7). HRMS (ESI-TOF) calcd for $C_{11}H_{20}NO_2$ (M^++1) 198.1489, found 198.1487.

3.1.10.2. (2*S*,3*S*,4a*S*,8a*S*)-3-Methoxy-2-methyldecahydroquinolin-7-one (8b). Colourless oil; R_f=0.19 (Al_2O_3, 99:1 CH_2Cl_2 saturated with NH_3/MeOH); ^{1}H NMR (400 MHz, $CDCl_3$, gCOSY) 1.11 (d, J=6.8 Hz, 3H, Me), 1.75–2.00 (m, 4H, H-4, H-5), 2.20–2.30 (m, 3H, H-4a, H-6), 2.39 (ddd, J=14.4, 4.4, 1.5 Hz, H-8eq), 2.62 (dd, J=14.4, 10 Hz, H-8ax), 3.13 (qd, J=6.5, 3.2 Hz, H-2ax), 3.34 (masked, H-3eq), 3.36 (s, 3H, OMe), 3.43 (ddd, J=10, 4.8, 4.8 Hz, H-8a); ^{13}C NMR (100 MHz, $CDCl_3$, gHSQC) 16.0 (Me), 27.6 (C-5), 27.8 (C-4), 29.6 (C-4a), 37.7 (C-6), 43.7 (C-8), 48.1 (C-2), 53.3 (C-8a), 56.7 (OMe), 76.4 (C-3), 210.9 (C-7). HRMS (ESI-TOF) calcd for $C_{11}H_{20}NO_2$ (M^++1) 198.1489, found 198.1487.

3.1.11. (2*S*,3*S*,4a*R*,8a*R*)-1-Benzoyl-3-hydroxy-2-methyloctahydroquinolin-7-one (9a). A solution of **7a** (12 mg, 0.07 mmol) was dissolved in THF (0.2 mL) and H_2O (0.2 mL) was added. Then, K_2CO_3 (39 mg, 0.28 mmol) and BzCl (8.4 μL, 0.074 mmol) were added. The reaction mixture was stirred for 2 h at rt, extracted with CH_2Cl_2 (4×15 mL), dried and concentrated to give a brown oil. Purification by column chromatography (Al_2O_3, from CH_2Cl_2 saturated with NH_3 to 98:2 CH_2Cl_2 saturated with NH_3/MeOH) gave **9a** (19 mg, 99%). R_f=0.44 (Al_2O_3, 98:2 CH_2Cl_2 saturated with NH_3); ^{1}H NMR (300 MHz, $CDCl_3$, mixture of rotamers) 1.20 and 1.30 (2br d, CH_3), 1.70–2.20 (m, 6H), 2.34 (br, 1H), 2.75 (m, 1H), 3.85–4.15 (br, 2H), 5.07 (br, 1H), 7.25–7.45 (m, 5H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) 14.1 and 15.7 (CH_3), 27.5 and 28.6 (C-4), 29.7 (C-5), 31.9 (C-4a), 36.2 (C-6), 49.1 (C-8), 53.4 (C-2), 55.3 (C-8a), 74.6 (C-3), 125.9, 128.8, 129.5, 136.5 (Ar), 171.6 and 172.2 (NCO), 208.0 (C-7). HRMS (ESI-TOF) calcd for $C_{17}H_{22}NO_3$ (M^++1) 288.1594, found 288.1585.

3.1.12. (2*S*,3*S*,4a*R*,8a*R*)-1-Benzoyl-3-methoxy-2-methyloctahydroquinolin-7-one (9b). Operating as above, starting from **7b** (16 mg, 0.08 mmol) and after purification by chromatography (Al_2O_3, CH_2Cl_2 saturated with NH_3), amide **9b** (24 mg, 99%) was obtained as a white solid. Mp 100–102 °C; R_f=0.52 (Al_2O_3, CH_2Cl_2 saturated with NH_3); ^{1}H NMR (300 MHz, $CDCl_3$, mixture of rotamers) 1.05 and 1.25 (2br d, CH_3), 1.70–2.20 (m, 6H), 2.35 (br, 1H), 2.75 (m, 1H), 3.20 and 3.40 (2s, 3H, OCH_3), 3.25–3.45 (masked, 2H), 3.95 (br, 0.5H), 4.15 (br, 0.5H), 5.0 (br, 0.5H), 5.20 (br, 0.5H), 7.20–7.65 (m, 4H, ArH), 8.20 (d, J=7.5 Hz, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) 15.0 and 16.0 (CH_3), 25.3 and 25.7 (C-4), 27.6 (C-5), 32.6 and 33.5 (C-4a), 36.0 and 36.4 (C-6), 43.6 and 45.2 (C-8), 45.4, 49.4, 51.2 and 56.2 (C-2 and C-8a), 55.6 and 56.6 (OCH_3), 77.9 and 78.4 (C-3), 125.7, 128.7, 129.4, 136.6 (Ar), 171.6 (NCO), 207.4 and 207.9 (C-7). HRMS (ESI-TOF) calcd for $C_{18}H_{24}NO_3$ (M^++1) 302.1751, found 302.1752.

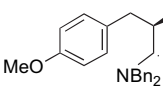
3.1.13. (2*S*,3*S*,4a*R*,8a*R*)- and (2*S*,3*S*,4a*S*,8a*S*)-1-Benzoyl-3-methoxy-2-methyloctahydroquinolin-7-one (9b and 10b). A solution of **6b** (90 mg, 0.42 mmol) in 2 N HCl (2 mL) was stirred for 3 h at 75 °C. The mixture was basified with K_2CO_3 (464 mg, 3.36 mmol) and BzCl (0.06 mL, 0.5 mmol) in THF (2 mL) was added. The reaction mixture was stirred for 2 h at rt, concentrated and extracted with CH_2Cl_2 (4×20 mL). The dried organic layers were concentrated to give a brown oil, which was purified by chromatography (SiO_2, from hexane/EtOAc 7:3 to EtOAc) to give a 1:2.3 mixture of **9b** (22 mg, 17% from **4b**) and **10b** (50 mg, 39% from **4b**). For data of **9b**, see above.

Compound **10b**: colourless oil; R_f=0.14 (SiO_2, 1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +16 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, gCOSY) 1.25 (d, *J*=6.8 Hz, 3H, Me), 1.80 (m, H-5), 1.87 (m, H-4), 1.99 (dt, *J*=14, 5.2 Hz, H-4eq), 2.11 (dddd, *J*=12, 11, 9.4, 4.4 Hz, H-5ax), 2.25 (ddd, *J*=15.4, 10, 5.4 Hz, H-6ax), 2.36 (m, H-4a), 2.64 (masked, 1H, H-6), 2.59 and 2.67 (2dd, *J*=16.8, 5.6 Hz, 1H each, H-8), 3.20 (s, 3H, OMe), 3.51 (ddd, *J*=10.8, 5.4, 5.4 Hz, H-3ax), 4.12 (ddd, *J*=5.6, 5.6, 2.8 Hz, H-8a), 4.24 (quint, *J*=6.4 Hz, H-2eq), 7.40 (s, 5H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, gHSQC) 12.5 (Me), 26.5 (C-5), 28.5 (C-4), 33.3 (C-4a), 38.5 (C-6), 43.0 (C-8), 51.9 (C-8a), 52.8 (C-2), 56.2 (OMe), 75.0 (C-3), 126.8, 128.6, 130.0, 136.6 (Ar), 173.2 (NCO), 205.4 (C-7). HRMS (ESI-TOF) calcd for $C_{18}H_{24}NO_3$ (M^++1) 302.1751, found 302.1750.

Acknowledgements

This research was supported by the MEC (Spain)-FEDER through project CTQ2004-04701/BQU. Thanks are also due to the DURSI (Catalonia) for Grant 2005SGR-00442 and the Ministry of Education and Science (Spain) for fellowships to M.M. and M.B.

References and notes

1. (a) Ueda, N.; Tokuyama, T.; Sakan, T. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 2012–2014; (b) Bonjoch, J.; Catena, J.; Valls, N. *J. Org. Chem.* **1996**, *61*, 7106–7115.
2. (a) Bonjoch, J.; Catena, J.; Isábal, E.; López-Canet, M.; Valls, N. *Tetrahedron: Asymmetry* **1996**, *7*, 1899–1902; (b) Bonjoch, J.; Catena, J.; Terricabras, D.; Fernández, J.-C.; López-Canet, M.; Valls, N. *Tetrahedron: Asymmetry* **1997**, *8*, 3143–3151; (c) Valls, N.; López-Canet, M.; Vallribera, M.; Bonjoch, J. *Chem.—Eur. J.* **2001**, *7*, 3446–3460.
3. Venit, J. J.; DiPierro, M.; Magnus, P. *J. Org. Chem.* **1989**, *54*, 4298–4301.
4. (a) Gensler, W. J.; Gatsonis, C. D.; Ahmed, Q. A. *J. Org. Chem.* **1968**, *33*, 2968–2971; (b) Furstoss, R.; Esposito, G.; Teissier, P.; Waegell, B. *Bull. Soc. Chim. Fr.* **1974**, 2485–2494.
5. Adachi, J.; Nomura, K.; Mitsuhashi, K. *Chem. Pharm. Bull.* **1976**, *24*, 85–91.
6. (a) Momose, T.; Uchida, S.; Kinoshita, M.; Imanishi, T. *Chem. Pharm. Bull.* **1977**, *25*, 1797–1802; (b) Momose, T.; Uchida, S.; Kinoshita, M.; Imanishi, T. *Chem. Pharm. Bull.* **1978**, *26*, 620–626; (c) Liu, D.; Wikström, H. V.; Dijkstra, D.; deVries, J. B.; Venhuis, B. J. *J. Med. Chem.* **2006**, *49*, 1494–1498.
7. For studies of decahydroquinol-7-ones by this strategy in the racemic series, see Ref. 6. For other synthesis of decahydroquinoline derivatives by intramolecular aza-Michael ring closure upon cyclohexenones, see: Taber, D. F.; Joshi, P. V.; Kanai, K. *J. Org. Chem.* **2004**, *69*, 2268–2271.
8. (a) For Lepadin A, see: Steffan, B. *Tetrahedron* **1991**, *47*, 8729–8732; (b) For Lepadins B and C, see: Kubanek, J.; Williams, D. E.; de Silva, E. D.; Allen, T.; Anderson, R. J. *Tetrahedron Lett.* **1995**, *36*, 6189–6192; (c) For Lepadins D–F, see: Wright, A. D.; Goclik, E.; König, G. M.; Kaminsky, R. *J. Med. Chem.* **2002**, *45*, 3067–3072; (d) For Lepadins F–H, see: Davis, R. A.; Carroll, A. R.; Quinn, R. J. *J. Nat. Prod.* **2002**, *65*, 454–457.
9. (a) Toyooka, N.; Okumura, M.; Takahatam, H. *J. Org. Chem.* **1999**, *64*, 2182–2183; (b) Toyooka, N.; Okumura, M.; Takahatam, H.; Nemoto, H. *Tetrahedron* **1999**, *55*, 10673–10684.
10. (a) Osawa, T.; Aoyagi, S.; Kobayashi, C. *Org. Lett.* **2000**, *2*, 2955–2958; (b) Osawa, T.; Aoyagi, S.; Kobayashi, C. *J. Org. Chem.* **2001**, *66*, 3338–3347.
11. Pu, X.; Ma, D. *Angew. Chem., Int. Ed.* **2004**, *43*, 4222–4225.
12. Kalai, C.; Tate, E.; Zard, S. Z. *Chem. Commun.* **2002**, 1430–1431.
13. For a previous work in this field, see: Mena, M.; Bonjoch, J. *Tetrahedron* **2005**, *61*, 8264–8270.
14. (a) Sato, S.; Aoyagi, S.; Kibayashi, C. *Org. Lett.* **2003**, *5*, 3839–3842; (b) Cassidy, M. P.; Padwa, A. *Org. Lett.* **2004**, *6*, 4029–4031; (c) Tsai, M.-R.; Chen, B.-F.; Cheng, C.-C.; Chang, N.-C. *J. Org. Chem.* **2005**, *70*, 1780–1785; (d) Lemire, A.; Charette, A. B. *Org. Lett.* **2005**, *7*, 4029–4031.
15. For a review in the chemistry of *N*,*N*-dibenzylamino aldehydes, see: Reetz, M. T. *Chem. Rev.* **1999**, *99*, 1121–1162.
16. For the formation of *syn*-amino alcohols in the reduction of *N*,*N*-dibenzyl α-alkyl-α-amino ketones, see: Hart, S. A.; Sabat, M.; Etzkorn, F. A. *J. Org. Chem.* **1998**, *63*, 7580–7581.
17. For a review in the chemistry of *N*-protected-α-amino aldehydes, see: Gryko, D.; Chalko, J.; Jurczak, J. *Chirality* **2003**, *15*, 514–541.
18. (a) Ibuka, T.; Habashita, H.; Otaka, A.; Fujii, N.; Oguchi, Y.; Uyehara, T.; Yamamoto, Y. *J. Org. Chem.* **1991**, *56*, 4370–4382; (b) Angle, S. R.; Breitenbucher, J. G.; Arnaiz, D. O. *J. Org. Chem.* **1992**, *57*, 5947–5955; (c) Kumar, K. K.; Datta, A. *Tetrahedron* **1999**, *55*, 13899–13906; (d) Randl, S.; Blechert, S. *Tetrahedron Lett.* **2004**, *45*, 1167–1169.
19. Weinreb amide **1**, although previously reported,[20] was here reported by reaction of tribenzyl alanine with *N*,*O*-dimethylhydroxylamine using isopropylmagnesium chloride according to a protocol introduced by Williams, J. M.; Jobson, R. B.; Yasuda, N.; Marchesini, G.; Dolling, U.-H.; Grabowski, E. J. J. *Tetrahedron Lett.* **1995**, *36*, 5461–5464.
20. Beaulieu, P. L.; Wernic, D. *J. Org. Chem.* **1996**, *61*, 3635–3645.
21. Barluenga, J.; Baragaña, B.; Concellón, J.-M. *J. Org. Chem.* **1995**, *60*, 6696–6699.
22. Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, *106*, 3693–3694.
23. For a precedent, in the ring-opening of epoxide **3** by an organolithium reagent in the presence of $BF_3{\cdot}Et_2O$, see Ref. 13. For the reductive alkylation of epoxide **3** with organolithium reagents, see: Concellón, J. M.; Suárez, J. R.; Del Solar, V. *Org. Lett.* **2006**, *8*, 349–351.
24.  *epi*-**4a**

25. Reetz, M. T.; Drewes, M. W.; Lennick, K.; Schmitz, A.; Holdgrün, X. *Tetrahedron: Asymmetry* **1990**, *1*, 375–378.
26. For NMR studies of decahydroquinolines, see: (a) Eliel, E. L.; Vierhapper, F. W. *J. Org. Chem.* **1976**, *41*, 199–208; (b) Vierhapper, F. W.; Eliel, E. L. *J. Org. Chem.* **1977**, *42*, 51–62; (c) Spande, T. F.; Jain, P.; Garraffo, H. M.; Pannell, L. K.; Yeh, H. J. C.; Daly, J. W.; Fukumoto, S.; Imamura, K.; Torres, J. A.; Snelling, R. R.; Jones, T. H. *J. Nat. Prod.* **1999**, *62*, 5–21; (d) Phuan, P.-W.; Kozlowski, M. C. *J. Org. Chem.* **2002**, *67*, 6339–6346.
27. (a) Reetz, M. T.; Drewes, M. W.; Schmitz, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1141–1143; (b) Reetz, M. T.; Drewes, M. W.; Schwickardi, R. *Org. Synth.* **1999**, *76*, 110–122.