

Asymmetric Synthesis of Arylglycines and Their Use as Chiral Templates for the Stereocontrolled Synthesis of 7,8-Disubstituted 3-Aryl-1,2,3,4-tetrahydroisoquinolin-4-ols

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A synthetic technique for the asymmetric synthesis of arylglycines has been optimized, reaching the target amino acids in only four steps with good yields and with enantiomeric excesses higher than 99%. The key step consisted of a stereocontrolled electrophilic amination reaction of (*S,S*)-(+)-pseudoephedrine-based arylacetamide enolates with di-*tert*-butylazodicarboxylate. The arylglycines thus obtained

turned out to be excellent chiral templates for the production of chiral, nonracemic 7,8-disubstituted 3-aryl-1,2,3,4-tetrahydroisoquinolines, through use of a synthetic sequence involving: (1) reduction of the arylglycines to the parent arylglycins, (2) *N*-benzylation with appropriately substituted aromatic aldehydes and (3) Swern oxidation followed by acid-catalysed cyclization of the obtained α -amino aldehydes.

Introduction

The stereoselective synthesis of isoquinoline alkaloids is a field of growing interest in synthetic organic chemistry.^[1] As a consequence, many methods have already been published for the stereoselective syntheses of 1-substituted tetrahydroisoquinolines,^[1,2] which are very useful intermediates for the preparation of a wide range of enantiopure alkaloids.^[3] Although chiral, nonracemic tetrahydroisoquinolin-4-ol derivatives are of considerable interest, due to their biological activity and as naturally occurring alkaloids,^[4] research into their stereoselective synthesis is not as fully developed as that of the 1-substituted derivatives. Some reports have described the asymmetric synthesis of tetrahydroisoquinoline derivatives in which the substituent at C(4) bears a hydroxy function,^[5] but only a few reports can be found in which, in addition, the substituent at the 3-position is an aryl moiety,^[6,7,8] a pattern found quite often in nature, as in the protoberberine alkaloids ophiocarpine^[9] or papaverberine (Figure 1), among others.^[10]

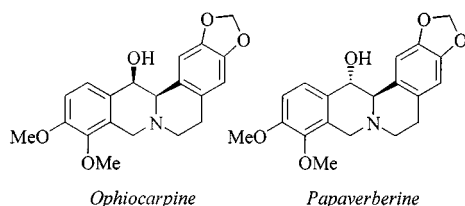
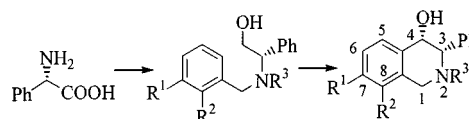


Figure 1. Natural 13-hydroxyprotoberberine alkaloids

One of the most widely employed method for the construction of the isoquinoline core involves a heterocycliz-

ation procedure using either Pictet–Spengler^[11] or Bischler–Napieralsky^[12] cyclizations. 3-Phenyl-1,2,3,4-tetrahydroisoquinolin-4-ols have therefore been obtained in enantiopure form by starting from chiral, nonracemic 1,2-diarylaminoethanols.^[7] The use of these cyclization procedures as key steps in the construction of the heterocyclic system has a severe limitation, however, which is that the substitution pattern in the aromatic ring of the isoquinoline skeleton is dictated by the electronic requirements of the cyclization step. Thus, these methodologies are more difficult to apply for the synthesis of 7,8-disubstituted derivatives,^[13] and this is the substitution pattern most commonly found in nature (see Figure 1). In this context, we recently developed a procedure for the asymmetric synthesis of 6,7-dimethoxy-4-phenyl-1,2,3,4-tetrahydroisoquinolin-4-ol using (*S*)-(+)-phenylglycine as the starting chiral source (Scheme 1).^[8] This would, in principle, allow access to enantiopure isoquinolin-4-ols with any kind of substitution pattern at the heterocyclic aromatic ring. However, this methodology is limited to the production of 3-phenyl isoquinolines because of the lack of commercially available chiral, nonracemic arylglycines. Development of a general procedure for the stereocontrolled synthesis of 3-aryl-1,2,3,4-tetrahydroisoquinolin-4-ols with any desired substitution pattern would therefore require a straightforward method for the synthesis of arylglycines in enantiopure form.

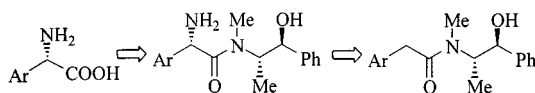
Although many of the reported methods for the stereocontrolled synthesis of arylglycines^[14] are quite effective,



Scheme 1

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some of them require multistep syntheses, the use of highly toxic reagents, laborious separation of diastereoisomers or harsh reaction conditions, while some lack the required high chemo- and diastereoselectivities for subsequent synthetic purposes. We have thus been engaged in the development of a suitable, high-yielding procedure for the stereocontrolled synthesis of this particular kind of racemization-prone amino acids.^[15] One possible route to these derivatives might be a stereocontrolled amination^[16,17] of arylacetamide enolates using (*S,S*)-(+)-pseudoephedrine as chiral auxiliary,^[18] as shown in Scheme 2. Subsequent hydrolysis of the obtained adducts would afford the wanted amino acids in enantiopure form, provided that no racemization at the newly created chiral centre occurred during these processes.



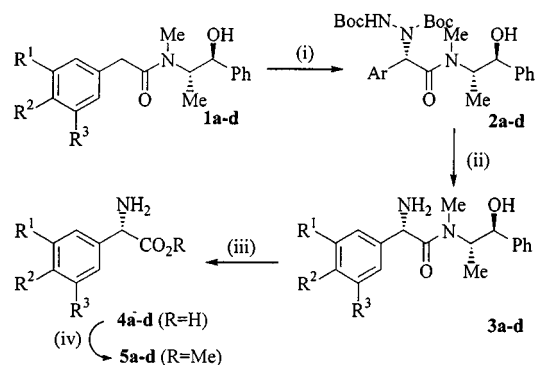
Scheme 2

In this paper we wish to report a detailed description of this procedure for the stereocontrolled synthesis of arylglycines and their use as precursors of chiral, nonracemic 7,8-disubstituted 3-aryl-1,2,3,4-tetrahydroisoquinolin-4-ols.

Results and Discussion

1. Asymmetric Synthesis of Arylglycines

As shown in Scheme 3, the arylacetic acid-derived (*S,S*)-(+)-pseudoephedrine amides **1a–d**, prepared as previously reported,^[19] were deprotonated under kinetic conditions, and subjected to amination reaction at -105°C , using di-*tert*-butyl azodicarboxylate (DTBAD) as a source of electrophilic nitrogen.^[16] The resulting adducts **2a–d** were obtained in $>95\%$ *de*, determined by ^1H NMR spectroscopy by comparison of the spectra of the obtained adducts with those of the corresponding mixtures of epimers at the newly created chiral centre. The amination reaction proved to be fast, and was complete within a few minutes, in contrast with other reports^[18,19] in which reactions of pseudoephed-



Reagents and conditions: (i) 1. LDA, THF, -78°C ; 2. DTBAD, THF, -105°C , (ii) 1. TFA, CH_2Cl_2 , rt.; 2. H_2 , Ni/Raney. (iii) 9M H_2SO_4 , dioxane, reflux. (iv) 2,2-dimethoxypropane, HCl, MeOH, rt.

Scheme 3

rine-derived enolates with other electrophiles required the aid of LiCl salts to accelerate the reaction.^[18,20]

The adducts **2a–d** were treated with trifluoroacetic acid, followed by hydrogenation of the resulting solution over Ni/Raney catalyst to yield the target arylglycine-based (*S,S*)-(+)-pseudoephedrine amides **3a–d**. These, upon acid hydrolysis (9 M H_2SO_4 /dioxane), afforded the corresponding amino acids **4a–d** in good yields after ion exchange chromatography. In addition, the chiral auxiliary (*S,S*)-(+)-pseudoephedrine could be recovered from the reaction mixture in ca. 88% yield and with no racemization, as indicated by the $[\alpha]_D^{20}$ value (Table 1). In order to calculate the *ee* with which the arylglycines **4a–d** had been obtained, they were converted into the corresponding methyl ester derivatives **5a–d** by treatment with 2,2-dimethoxypropane/HCl;^[21] chiral HPLC analysis then showed that they were of $>99\%$ *ee*. This confirmed that all of the transformations performed on the adducts **2a–d** had proceeded without racemization in any of the steps. It should also be pointed out that arylglycine **4d** has been employed as a key precursor in the total synthesis of vancomycin-like antibiotics.^[22]

The absolute configuration of the obtained arylglycines was assigned as *S* by comparison of the $[\alpha]_D^{20}$ value measured for arylglycine **4c** ($[\alpha]_D^{20} = +120.8$, $c = 0.4$, H_2O) with that reported in the literature ($[\alpha]_D^{20} = -119.7$ ($c = 0.8$, H_2O) for the *R* isomer).^[14k] The stereochemistry of the newly created chiral centre during the amination reaction of amides **1a–d** is hence in agreement with a previously

Table 1. Stereocontrolled synthesis of arylglycines

R ¹	R ²	R ³	Prod.	Yield (%)	<i>dr</i> (%) ^[a]	Prod.	Yield (%)	Prod.	Yield (%)	Prod.	Yield (%)	<i>ee</i> (%) ^[b]
OMe	OMe	H	2a	89	$>95:5$	3a	78	4a	86	5a	88	>99
OCH ₂ O		H	2b	91	$>95:5$	3b	79	4b	89	5b	79	>99
OMe	OMe	OMe	2c	90	$>95:5$	3c	78	4c	91	5c	90	>99
OBn	OMe	OBn	2d	86	$>95:5$	3d	75	4d	88	5d	87	>99

^[a] Determined by ^1H NMR. – ^[b] Determined by chiral HPLC analysis (Chiralcel OD, UV detector, Hexanes/2-propanol 50:50. Flow rate 0.60 mL/min).

proposed mechanism^[18] in which the high level of diastereocontrol observed in the reaction was attributed to exclusive formation of the *Z* enolate, followed by the attack of the nitrogen electrophile on a reactive open intermediate, held in a staggered, rigid conformation through the action of bridging solvent or *i*PrNH (from LDA) molecules (Figure 2).

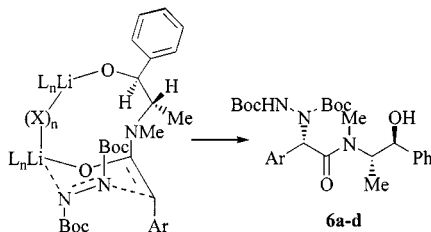
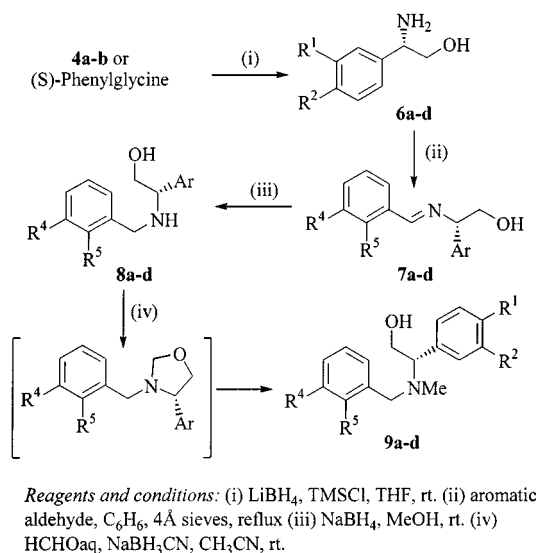


Figure 2. Proposed mechanism for the electrophilic amination of (*S,S*)-(+)-pseudoephedrine arylacetamide enolates

2. Asymmetric Synthesis of 7,8-Disubstituted 3-Aryl-1,2,3,4-tetrahydroisoquinolin-4-ols

With the focus now on the stereocontrolled synthesis of 3-aryl-1,2,3,4-tetrahydroisoquinolin-4-ols, arylglycines **4a–b** and the simple phenylglycine were reduced with $\text{LiBH}_4/\text{TMSCl}$,^[23] yielding the corresponding β -amino alcohols in good yields. Afterwards, these were easily transformed into the corresponding *N*-benzyl derivatives **8a–d** by initial formation of an imine intermediate **7a–d** with an aromatic aldehyde with the desired substitution pattern,



Scheme 4

Table 2. Synthesis of *N*-methylamino alcohols **9a–d**

R ¹	R ²	R ⁴	R ⁵	Prod.	Yield (%)	Prod.	Yield (%) ^[a]	Prod.	Yield (%)	Prod.	Yield (%)
OMe	OMe	OMe	OMe	6a	70	7a	81	8a	88	9a	78
OCH ₂ O		OMe	OMe	6b	72	7b	90	8b	91	9b	78
H	H	OMe	OMe	6c	86	7c	87	8c	98	9c	75
H	H	OMe	OBn	6c	86	7d	90	8d	98	9d	73

^[a] Yield of crude product.

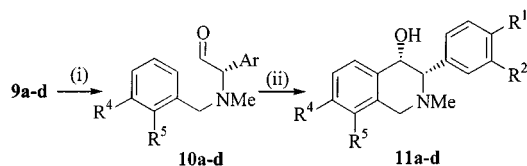
followed by reduction with NaBH_4 (Scheme 4, Table 2). The next step consisted of the methylation of the secondary amine functionality, which was performed by treatment of amino alcohols **8a–d** with aqueous formaldehyde in the presence of NaBH_3CN . The reaction proceeds through initial formation of oxazolidine intermediates (which could be isolated and identified) that, in the presence of excess of reducing agent, underwent ring-opening to yield the target *N*-methyl derivatives **9a–d** in good yields.

In order to complete the projected synthesis, amino alcohols **9a–d** were submitted to Swern oxidation reactions^[24] under modified conditions as previously reported by us.^[25] Thus, when amino alcohols **9a–d** were treated with oxalyl chloride, dimethyl sulfoxide and diisopropylethylamine, α -amino aldehydes **10a–d** could be detected in the ^1H NMR spectra of the crude mixtures and were isolated as colourless oils, prone to decomposition.^[26] Finally, with the freshly prepared aldehydes **10a–d** in hand, acid-catalysed aromatic electrophilic reactions^[8,27] were performed with a nondehydrating reagent, affording the desired 3-aryl-1,2,3,4-tetrahydroisoquinolin-4-ols **11a–d** as single diastereoisomers (*de* > 95%). The ^1H NMR spectra of the crude reaction mixtures each showed only one resonance for H(4), with a coupling constant ($J_{\text{H}3/\text{H}4}$ = 2.4–2.8 Hz) typical of a *cis* relationship between the substituents at the two adjacent stereogenic carbons. Moreover, the observation of strong nuclear Overhauser effects between protons H(3) and H(4) was consistent with the proposed *cis* relative relationships between these protons and so allowed (3*S*,4*S*) absolute configurations to be assigned to isoquinolines **11a–d**. In addition, the enantiomeric excesses in which these heterocycles **11a–d** had been obtained were determined by chiral HPLC, showing that little or no racemization had occurred during the process from arylglycines **4a–b** or phenylglycine to isoquinolines **11a–d** (*ee*: 81–90%, Scheme 5 and Table 3).

Table 3. Synthesis of the tetrahydroisoquinolin-4-ols **11a–d**

Prod.	R ¹	R ²	R ⁴	R ⁵	Yield (%)	<i>ee</i> (%) ^[a]
11a	OMe	OMe	OMe	OMe	80	81
11b	OCH ₂ O		OMe	OMe	85	90
11c	H	H	OMe	OMe	78	87
11d	H	H	OMe	OBn	83	90

^[a] Determined by chiral HPLC analysis (Chiralcel OD, UV detector, hexanes/2-propanol 75:25. Flow rate 0.50 mL/min)



Reagents and conditions: (i) (COCl)₂, DMSO, iPr₂EtN, CH₂Cl₂, -60 °C. (ii) HCl (conc), acetone, rt.

Scheme 5

Conclusion

In summary, a simple and highly efficient route for the stereoselective preparation of arylglycines has been developed, using a stereocontrolled amination procedure of (*S,S*)-(+)-pseudoephedrine arylacetamide enolates as a key step. This affords access to the arylglycine skeleton in only four steps, with easily performed and high-yielding reactions. These arylglycines proved to be excellent chiral templates for the stereocontrolled synthesis of 3-aryl-1,2,3,4-tetrahydroisoquinolin-4-ols with a 7,8-disubstitution pattern in the aromatic ring of the isoquinoline core, a pattern commonly found in nature and not accessible by conventional heterocyclization routes such as Pictet–Spengler or Bischler–Napieralsky cyclization. The most advantageous feature of the synthesis reported here is the fact that the target heterocycle can be obtained with any desired substitution pattern, provided that this substitution pattern can be introduced in the starting arylglycine and aromatic aldehyde.

Experimental Section

General Remarks: Melting points were determined in unsealed capillary tubes and are uncorrected. – IR spectra were obtained on KBr pellets (solids) or CHCl₃ solution (oils). NMR spectra were recorded at 20–25 °C, at 250 MHz for ¹H and 62.8 MHz for ¹³C, and resonances are reported in ppm relative to tetramethylsilane unless otherwise stated. Assignment of individual ¹³C resonances were supported by DEPT experiments. ¹H-¹H NOE experiments were carried out in the difference mode by irradiation of all the lines of a multiplet.^[28] – Mass spectra were recorded by electron impact at 70 eV. – TLC was carried out with 0.2 mm. thick silica gel plates (Merck Kieselgel GF₂₅₄). Viewing was by UV light or by spraying with Dragendorff's reagent.^[29] – Flash column chromatography^[30] on silica gel was performed with Merck Kieselgel 60 (230–400 mesh). Determination of enantiomeric excesses was performed by chiral HPLC analysis of noncrystallized samples using a Chiracel OD column with a UV detector, with eluents and flow rates as indicated in each case. – All solvents used in reactions were dried and purified according to standard procedures.^[31] *n*BuLi was titrated with diphenylacetic acid periodically prior to use. All air- or moisture-sensitive reactions were performed under argon. The glassware was oven-dried (140 °C) overnight and purged with argon.

(2*S*,1'*S*,2'*S*)-(+)-2-(3,4-Dimethoxyphenyl)-2-[*N,N'*-bis(1,1-dimethylethoxycarbonyl)hydrazino]-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methylacetamide (2a): *n*BuLi (3.87 mL of a 1.5 M solution in hexane, 5.8 mmol) was added to a cooled (–78 °C) solution of diisopropylamide (0.81 mL, 5.8 mmol) in dry THF (2 mL). The reaction mixture was stirred for 20 min at this temperature, and allowed to come to room temp. and stirred for additional 10 min. The mixture was cooled again to –78 °C and a THF (15 mL) solution of **1a** (1.00 g, 2.9 mmol) was added dropwise over 5 min. The reaction mixture was stirred for 1 h at this temperature, for 15 min. at 0 °C and for 5 min. at room temp., after which it was cooled again to –105 °C, at which temperature a solution of DTBAD (0.67 g, 2.9 mmol) in dry THF (10 mL) was added dropwise over 10 min. The resulting solution was stirred for 1 h at –105 °C, allowed to come to room temp. and quenched with a saturated NH₄Cl solution (30 mL). The mixture was extracted with CH₂Cl₂ (3 × 50 mL) and the combined organic fractions were collected, dried over Na₂SO₄ and filtered. The solvent was removed in vacuo to afford a yellowish oil, which was purified by flash column chromatography (hexanes/ethyl acetate, 2:8). Yield: 1.48 g, 89%. Mp: 89–92 °C (Et₂O). – [α]_D²⁰ = +110.7 (*c* = 0.9, CH₂Cl₂). – IR (KBr): $\tilde{\nu}$ = 3401, 1701 cm^{–1}. – ¹H NMR (CDCl₃) (5:1 rotamer ratio; *indicates minor rotamer resonances): δ = 0.55* (d, *J* = 6.7 Hz, 3 H), 0.99 (d, *J* = 6.7 Hz, 3 H), 1.18* (s, 18 H), 1.44 (s, 18 H), 2.28 (br. s, 1 H), 2.56* (s, 3 H), 2.67 (s, 3 H), 3.79 (s, 3 H), 3.81 (s, 3 H), 4.01 (m, 1 H), 4.45 (m, 2 H), 6.03 (s, 1 H), 6.45–6.95 (m, 3 H), 7.04–7.29 (m, 5 H). – ¹³C NMR (CDCl₃) (5:1 rotamer ratio; * indicates minor rotamer resonances): δ = 13.6, 13.9*, 26.4, 27.1*, 27.4, 27.5, 27.7*, 55.2, 55.3*, 61.8, 65.2, 75.0*, 76.5, 79.1, 80.7*, 80.9, 81.2*, 110.3, 110.5*, 112.3, 121.7*, 124.2, 124.8*, 126.3, 127.1*, 127.5*, 127.8, 127.9*, 130.2, 148.0, 148.2*, 148.3, 148.5*, 151.0*, 151.2, 152.0*, 152.3, 153.6, 154.2*, 155.0*, 155.6, 171.4, 172.0*. – MS (EI): *m/z* (rel. int.): 573 (1) [M⁺], 58 (100). – C₃₀H₄₃N₃O₈: calcd. C 62.81, H 7.56, N 7.32; found C 62.85, H 7.51, N 7.41.

[2*S*,1'*S*,2'*S*]-(+)-2-[*N,N'*-Bis(1,1-dimethylethoxycarbonyl)hydrazino]-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methyl-2-(3,4-methylenedioxyphenyl)acetamide (2b): Amide **2b** was prepared by the same procedure as employed for **2a**, using amide **1b** (1.00 g, 3.0 mmol) and DTBAD (0.70 g, 3.0 mmol). Yield: 1.54 g, 91%. Mp: 150–153 °C (Et₂O). [α]_D²⁰ = +74.5 (*c* = 1.2, CH₂Cl₂). – IR (KBr): $\tilde{\nu}$ = 3400, 1710 cm^{–1}. – ¹H NMR (CDCl₃) (7:1 rotamer ratio; *indicates minor rotamer resonances): δ = 0.59* (d, *J* = 6.6 Hz, 3 H), 1.02 (d, *J* = 6.6 Hz, 3 H), 1.23* (s, 18 H), 1.54 (s, 18 H), 2.59* (s, 3 H), 2.69 (s, 3 H), 4.12 (m, 1 H), 4.57 (m, 2 H), 6.09 (s, 1 H), 6.22 (s, 2 H), 6.31* (s, 2 H), 6.54–7.11 (m, 3 H), 7.22–7.35 (m, 5 H). – ¹³C NMR (CDCl₃) (7:1 rotamer ratio, *indicates minor rotamer resonances): δ = 13.9, 14.2*, 25.1, 27.6, 27.7*, 27.8*, 28.0, 61.6, 61.9, 75.6*, 76.5, 79.6*, 79.7, 80.7, 81.0*, 95.9, 110.2, 110.6*, 123.6, 126.0*, 126.3, 126.4*, 126.7, 127.5*, 127.9, 128.2*, 128.4*, 128.9, 141.0, 141.7*, 147.2, 147.4*, 151.2*, 151.4, 152.1*, 152.3, 153.7, 154.4*, 155.4*, 155.7, 171.8*, 172.2. – MS (EI): *m/z* (rel. int.): 557 (1) [M⁺], 237 (100). – C₂₉H₃₉N₃O₈: calcd. C 62.46, H 7.05, N 7.54; found C 62.39, H 7.11, N 7.50.

[2*S*,1'*S*,2'*S*]-(+)-2-[*N,N'*-Bis(1,1-dimethylethoxycarbonyl)hydrazino]-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methyl-2-(3,4,5-trimethoxyphenyl)acetamide (2c): Amide **2c** was prepared by the same procedure as employed for **2a**, using amide **1c** (1.00 g, 2.6 mmol) and DTBAD (0.61 g, 2.67 mmol). Yield: 1.45 g, 90%. M.p. 130–133 °C (Et₂O). [α]_D²⁰ = +118.2 (*c* = 0.9, CH₂Cl₂). – IR (KBr): $\tilde{\nu}$ = 3400, 1750 cm^{–1}. – ¹H NMR (CDCl₃) (5:2 rotamer ratio; *indicates minor rotamer resonances): δ = 0.56* (d, *J* =

6.7 Hz, 3 H), 0.85 (d, J = 6.7 Hz, 3 H), 1.12* (s, 18 H), 1.31 (s, 18 H), 2.28 (sa, 1 H), 2.49* (s, 3 H), 2.55 (s, 3 H), 3.63 (s, 3 H), 3.82 (s, 6 H), 3.98 (m, 1 H), 4.43 (m, 2 H), 6.00 (s, 1 H), 6.58 (s, 2 H), 6.62* (s, 2 H), 7.00–7.23 (m, 5 H). – ^{13}C NMR (CDCl_3) (5:2 rotamer ratio; *indicates minor rotamer resonances): δ = 13.5, 13.9*, 26.3, 27.2, 27.7, 27.9, 28.2*, 55.1, 55.4*, 61.7, 64.6, 75.1*, 76.3, 79.0*, 80.2, 80.7, 81.0*, 110.2, 110.4*, 124.2, 124.6*, 126.1, 127.1*, 127.4, 127.9*, 148.1, 148.3*, 148.5, 148.7*, 151.0*, 151.4, 152.2*, 152.4, 153.5, 154.3*, 155.0*, 155.5, 170.2*, 172.6. – MS (EI): m/z (rel. int.): 603 (1) [M^+], 58 (100). – $\text{C}_{31}\text{H}_{45}\text{N}_3\text{O}_9$: calcd. C 61.67, H 7.51, N 6.96; found C 61.70, H 7.53, N 7.00.

[2*S*,1'*S*,2'*S*]-(+)-2-[*N,N'*-Bis(1,1-dimethylethoxycarbonyl)-hydrazinol]-2-(3,5-dibenzyloxy-4-methoxyphenyl)-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methylacetamide (2d): Amide 2d was prepared by the same procedure as employed for 2a, using amide 1d (1.00 g, 1.9 mmol) and DTBAD (0.44 g, 1.9 mmol). Yield: 1.22 g, 85%. $[\alpha]_{\text{D}}^{20}$ = +121.4 (c = 0.9, CH_2Cl_2). – IR (CHCl_3): $\tilde{\nu}$ = 3388, 1698 cm^{-1} . – ^1H NMR (CDCl_3) (5:1 rotamer ratio; *indicates minor rotamer resonances): δ = 0.53* (d, J = 7.2 Hz, 3 H), 1.02 (d, J = 6.6 Hz, 3 H), 1.17* (s, 18 H), 1.46 (s, 18 H), 2.23 (sa, 1 H), 2.51* (s, 3 H), 2.57 (s, 3 H), 3.65 (m, 1 H), 3.74 (s, 3 H), 3.78* (s, 3 H), 4.45 (m, 2 H), 4.97* (s, 4 H), 5.01 (s, 4 H), 6.48 (s, 2 H), 7.23–7.47 (m, 15 H). – ^{13}C NMR (CDCl_3) (5:1 rotamer ratio; *indicates minor rotamer resonances): δ = 13.4, 14.1*, 26.1, 26.8, 27.2*, 27.4, 27.9*, 57.3, 57.8*, 60.1, 60.3*, 70.3*, 70.4, 74.4*, 75.3, 80.1*, 80.9, 81.3, 81.4*, 124.3, 124.6*, 125.2, 125.5*, 126.2, 126.4*, 126.7, 127.1*, 127.4, 127.8*, 127.9, 128.1*, 128.6, 130.1, 130.5*, 136.5, 136.8*, 137.2, 137., 151.2*, 151.4, 152.0*, 152.2, 153.4, 153.5*, 154.8, 171.6*, 172.3. – MS (EI): m/z (rel. int.): 412 (12), 91 (100). – $\text{C}_{43}\text{H}_{53}\text{N}_3\text{O}_9$: calcd. C 68.32, H 7.07, N 5.56; found C 68.39, H 7.01, N 5.47.

[2*S*,1'*S*,2'*S*]-(+)-2-Amino-2-(3,4-dimethoxyphenyl)-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methylacetamide (3a): Trifluoroacetic acid (15 mL) was added in one portion to a cooled (0 °C) solution of 2a (0.67 g, 1.2 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 30 min. at room temp. and transferred to a hydrogenation vessel. Ni/Raney was added and the mixture was shaken under H_2 pressure (150 psi) for 48 h. The catalyst was filtered and the resulting solution was basified with NaOH (aq) and extracted with CH_2Cl_2 (3 $\times$ 40 mL). The combined organic fractions were collected, dried over Na_2SO_4 and filtered, and the solvent was removed in vacuo to afford a yellowish oil, which was purified by normal pressure column chromatography (methanol/ethyl acetate 1:1). Yield: 0.32 g, 78%. M.p. 137–139 °C (Et_2O). $[\alpha]_{\text{D}}^{20}$ = +105.2 (c = 0.2, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3354, 1631 cm^{-1} . – ^1H NMR (CDCl_3) (3:2 rotamer ratio; *indicates minor rotamer resonances): δ = 0.38 (d, J = 6.7 Hz, 3 H), 0.92* (d, J = 6.7 Hz, 3 H), 2.54* (s, 3 H), 2.80 (s, 3 H), 3.0–3.5 (sa, 3 H), 2.51 (s, 3 H), 2.57* (s, 3 H), 2.60* (s, 3 H), 2.80 (s, 3 H), 4.02 (m, 1 H), 4.44 (m, 1 H), 4.88 (s, 1 H), 6.64–6.71 (m, 3 H), 7.14–7.21 (m, 5 H). – ^{13}C NMR (CDCl_3) (3:2 rotamer ratio; *indicates minor rotamer resonances): δ = 13.6, 14.2*, 27.0, 55.4, 55.5*, 55.9, 56.0*, 57.5, 59.2, 74.0*, 75.1, 109.7, 110.8*, 118.9, 119.3*, 126.2, 126.4*, 126.5, 127.1*, 127.5, 127.9*, 128.1*, 128.5, 141.8, 141.9*, 147.9, 148.1*, 153.6, 154.1*, 155.7*, 155.9, 173.6*, 173.8. – MS (EI): m/z (Int. rel.): 358 (1) [M^+], 165 (100). – $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_4$: calcd. C 67.02, H 7.31, N 7.82; found C 67.09, H 7.30, N 7.88.

(2*S*,1'*S*,2'*S*)-(+)-2-Amino-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methyl-2-(3,4-methylenedioxyphenyl)acetamide (3b): Amide 3b was prepared by the same procedure as employed for 3a, using 2b (0.58 g, 1.0 mmol) as starting material. Yield: 0.28 g, 79%. M.p. 161–163 °C (Et_2O). $[\alpha]_{\text{D}}^{20}$ = +67.2 (c = 1.8, CH_2Cl_2). – IR (KBr):

$\tilde{\nu}$ = 3330, 1622 cm^{-1} . – ^1H NMR (CDCl_3) (3:1 rotamer ratio; * indicates minor rotamer resonances): δ = 0.50 (d, J = 6.7 Hz, 3 H), 0.80* (d, J = 6.7 Hz, 3 H), 2.64* (s, 3 H), 2.87 (s, 3 H), 3.0–3.4 (sa, 3 H), 3.58 (m, 1 H), 4.49 (m, 1 H), 4.94 (s, 1 H), 5.86 (s, 2 H), 5.89* (s, 2 H), 6.63–6.73 (m, 3 H), 7.24–7.35 (m, 5 H). – ^{13}C NMR (CDCl_3) (3:1 rotamer ratio; *indicates minor rotamer resonances): δ = 13.8, 14.2*, 27.3, 55.9, 57.7, 74.4*, 75.0, 101.0, 107.2, 107.3*, 107.5, 108.4*, 120.4, 120.5*, 120.7, 120.9*, 126.4, 126.7*, 127.5*, 127.7, 134.1, 134.8*, 141.7, 141.8*, 146.9, 147.0*, 147.9*, 149.1, 173.6*, 173.8. – MS (EI): m/z (rel. int.): 342 (1) [M^+], 162 (100). – $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_4$: calcd. C 66.65, H 6.48, N 8.18; found C 66.60, H 8.12, N 8.22.

(2*S*,1'*S*,2'*S*)-(+)-2-Amino-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methyl-2-(3,4,5-trimethoxyphenyl)acetamide (3c): Amide 3c was prepared by the same procedure as employed for 3a, using 2c (0.73 g, 1.2 mmol) as starting material. Yield: 0.34 g, 78%. M.p. 172–175 °C (Et_2O). $[\alpha]_{\text{D}}^{20}$ = +112.6 (c = 0.2, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3350, 1660 cm^{-1} . – ^1H NMR (CDCl_3) (3:2 rotamer ratio; *indicates minor rotamer resonances): δ = 0.36 (d, J = 6.7 Hz, 3 H), 0.94* (d, J = 6.7 Hz, 3 H), 2.56* (s, 3 H), 2.81 (s, 3 H), 3.0–3.5 (sa, 3 H), 2.53 (s, 3 H), 2.56* (s, 3 H), 2.61* (s, 6 H), 2.83 (s, 6 H), 4.01 (m, 1 H), 4.42 (m, 1 H), 4.86 (s, 1 H), 6.58 (s, 2 H), 7.11–7.19 (m, 5 H). – ^{13}C NMR (CDCl_3) (3:2 rotamer ratio; *indicates minor rotamer resonances): δ = 13.5, 14.4*, 27.2, 55.3, 55.4*, 56.1, 56.6*, 57.2, 59.0, 74.5*, 75.4, 109.9, 110.2*, 126.2, 126.5*, 126.7, 127.0*, 127.5, 127.7*, 141.9, 142.2*, 147.8, 148.1*, 153.4, 154.1*, 155.3*, 155.6, 173.2*, 173.5. – MS (EI): m/z (rel. int.): 358 (1) [M^+], 164 (100). – $\text{C}_{21}\text{H}_{28}\text{N}_2\text{O}_5$: calcd. C 64.93, H 7.27, N 7.21; found C 64.90, H 7.30, N 7.18.

(2*S*,1'*S*,2'*S*)-(+)-2-Amino-2-(3,5-dibenzyloxy-4-methoxyphenyl)-*N*-(2'-hydroxy-1'-methyl-2'-phenylethyl)-*N*-methylacetamide (3d): Amide 3d was prepared by the same procedure as employed for 3a, using 2d (0.86 g, 1.16 mmol) as starting material. Yield: 0.51 g, 82%. $[\alpha]_{\text{D}}^{20}$ = +116.7 (c = 0.2, CH_2Cl_2). – IR (CHCl_3): $\tilde{\nu}$ = 3355, 1628 cm^{-1} . – ^1H -NMR (CDCl_3) (3:2 rotamer ratio; *indicates minor rotamer resonances): δ = 0.41 (d, J = 7.2 Hz, 3 H), 0.96* (d, J = 6.5 Hz, 3 H), 2.53* (s, 3 H), 2.78 (s, 3 H), 3.0–3.5 (sa, 3 H), 3.72 (m, 1 H), 3.77* (s, 3 H), 3.82 (s, 3 H), 4.44 (m, 1 H), 5.02* (s, 4 H), 5.06 (s, 4 H), 6.54 (s, 2 H), 7.28–7.52 (m, 15 H). – ^{13}C NMR (CDCl_3) (3:2 rotamer ratio; *indicates minor rotamer resonances): δ = 13.5, 14.4*, 27.2, 57.2, 57.9, 62.3*, 62.6, 70.1*, 70.4, 74.1*, 75.5, 124.2, 124.4*, 125.6, 125.8*, 126.1, 126.3*, 126.6, 127.2*, 127.5, 127.9*, 127.9, 128.4*, 128.5 (Ar{CH}), 130.3, 130.6*, 136.2, 136.9*, 137.1, 137.6*, 151.3, 151.5*, 151.9, 171.2*, 172.4. – MS (EI): m/z (rel. int.): 540 (1) [M^+], 91 (100). – $\text{C}_{33}\text{H}_{36}\text{N}_2\text{O}_5$: calcd. C 73.31, H 6.71, N 5.18; found C 73.28, H 6.65, N 5.12.

(2*S*)-(+)-3,4-Dimethoxyphenylglycine (4a): A solution of the α -aminoamide 3a (0.53 g, 1.5 mmol) in dioxane (10 mL) was added to a cooled (0 °C) 9 M H_2SO_4 solution and the mixture was refluxed for 6 h. Water (20 mL) was added, and the mixture was carefully basified to pH 12 and extracted with CH_2Cl_2 (3 $\times$ 20 mL) (from which (*S,S*)-(+)-pseudoephedrine could be recovered in ca. 88% yield). The aqueous layer was then basified with HCl to pH 3 and was washed with CH_2Cl_2 (3 $\times$ 30 mL). After reduction of the volume of the aqueous layer in vacuo to approx. 10 mL, it was loaded onto an ion-exchange column (DOWEX® 50WX4–50), washed with water until the collected fractions were at pH 7 and eluted with a 20% NH_4OH solution. These basic fractions were collected and the solvent was removed in vacuo, yielding arylglycine 4a as a white solid. Yield: 0.27 g, 86%. M.p. 178–181 °C. $[\alpha]_{\text{D}}^{20}$ = +98.6 (c = 0.02, H_2O). – IR (KBr): $\tilde{\nu}$ = 3450, 1660 cm^{-1} . – ^1H NMR

(D₂O+CD₃OD): δ = 3.72 (s, 3 H), 3.81 (s, 3 H), 4.05 (s, 1 H), 6.54–6.77 (m, 3 H). – ¹³C NMR (D₂O+CD₃OD): δ = 56.0, 57.2, 65.5, 109.1, 110.2, 111.1, 129.3, 132.0, 141.3, 177.0. – C₁₀H₁₃NO₄: calcd. C 56.86, H 6.20, N 6.63; found C 56.80, H 6.21, N 6.69.

(2S)-(+)-3,4-Methylenedioxyphenylglycine (4b): Arylglycine **4b** was prepared by the same procedure as employed for **4a**, using **3b** (0.61 g, 1.8 mmol) as starting material. Yield: 0.31 g, 89%. M.p. 195–198 °C. $[\alpha]_D^{20}$ = +95.5 (c = 0.05, H₂O). – IR (KBr): $\tilde{\nu}$ = 3455, 1662 cm⁻¹. – ¹H NMR (D₂O+CD₃OD): δ = 4.01 (s, 1 H), 5.84 (s, 2 H), 6.51–6.64 (m, 3 H). – ¹³C NMR (D₂O+CD₃OD): δ = 64.9, 100.9, 109.3, 110.6, 111.2, 129.6, 132.5, 141.7, 177.6. – C₉H₉NO₄: calcd. C 55.39, H 4.65, N 7.18; found C 55.31, H 4.61, N 7.12.

(2S)-(+)-3,4,5-Trimethoxyphenylglycine (4c): Arylglycine **4c** was prepared by the same procedure as employed for **4a**, using **3c** (0.58 g, 1.6 mmol) as starting material. Yield: 0.35 g, 91%. M.p. 201–203 °C. $[\alpha]_D^{20}$ = +120.8 (c = 0.04, H₂O). – IR (KBr): $\tilde{\nu}$ = 3500, 1600 cm⁻¹ (C=O). – ¹H NMR (D₂O+CD₃OD): δ = 3.74 (s, 3 H), 3.82 (s, 6 H), 4.07 (s, 1 H), 6.71 (s, 2 H). – ¹³C NMR (D₂O+CD₃OD): δ = 56.1, 57.1, 65.8, 109.3, 129.5, 132.2, 148.5, 177.1. – C₁₁H₁₅NO₅: calcd. C 54.77, H 6.27, N 5.81; found C 54.72, H 6.23, N 5.80.

(2S)-(+)-3,5-Dibenzoyloxy-4-methoxyphenylglycine (4d): Arylglycine **4d** was prepared by the same procedure as employed for **4a**, using **3d** (0.58 g, 1.1 mmol) as starting material. Yield: 0.35 g, 83%. M.p. 114–117 °C. $[\alpha]_D^{20}$ = +93.5 (c = 0.1, H₂O). – IR (KBr): $\tilde{\nu}$ = 3437, 1680 cm⁻¹. – ¹H NMR (D₂O+CD₃OD): δ = 3.87 (s, 3 H), 4.23 (s, 1 H), 5.31 (s, 4 H), 6.63 (s, 2 H), 7.25–7.41 (m, 10 H). – ¹³C NMR (D₂O+CD₃OD): δ = 60.6, 65.3, 71.2, 107.2, 127.1, 127.8, 128.5, 129.1, 136.3, 139.7, 152.6, 175.2. – C₂₃H₂₃NO₅: calcd. C 70.21, H 5.89, N 3.56; found C 70.16, H 5.94, N 3.49.

Methyl (2S)-(+)-2-Amino-2-(3,4-dimethoxyphenyl)acetate (5a): A suspension of arylglycine **4a** (0.33 g, 1.6 mmol) in MeOH (5 mL) and HCl_{conc} (5 mL) was refluxed until all the arylglycine was dissolved. It was then cooled to room temp., 2,2-dimethoxypropane (4 mL) was added, and the reaction mixture was stirred for 24 h. Water (20 mL) was added and the mixture was basified with NaOH and extracted with CH₂Cl₂ (3 × 20 mL). The combined organic extracts were dried over Na₂SO₄ and filtered, and the solvent was removed in vacuo to afford α -amino ester **5a** after flash column chromatography purification (hexanes/ethyl acetate 1:1). Yield: 0.31 g, 88%. M.p. (as HCl salt) 209–212 °C. $[\alpha]_D^{20}$ = +131.2 (c = 0.3, CH₂Cl₂). – IR (KBr): $\tilde{\nu}$ = 3350, 1750 cm⁻¹. – ¹H NMR (CDCl₃): δ = 2.11 (sa, 2 H), 3.70 (s, 3 H), 3.86 (s, 3 H), 3.88 (s, 3 H), 4.56 (s, 1 H), 6.82–6.91 (m, 3 H). – ¹³C NMR (CDCl₃): δ = 51.8, 55.4, 56.0, 60.1, 109.4, 110.6, 118.2, 132.2, 148.3, 148.9, 174.1. – MS (EI): m/z (rel. int.): 225 (1) [M⁺], 151 (100). – C₁₁H₁₆ClNO₄: calcd. C 50.48, H 6.16, N 5.35; found C 54.41, H 6.19, N 5.30.

Methyl (2S)-(+)-2-Amino-2-(3,4-methylenedioxyphenyl)acetate (5b): Amino ester **5b** was prepared by the same procedure as employed for **5a**, using **4b** (0.28 g, 1.4 mmol) as starting material. Yield: 0.24 g, 79%. M.p. (HCl salt) 221–223 °C. $[\alpha]_D^{20}$ = +128.4 (c = 0.3, CH₂Cl₂). – IR (KBr): $\tilde{\nu}$ = 3300, 1770 cm⁻¹. – ¹H NMR (CDCl₃): δ = 2.19 (sa, 2 H), 3.69 (s, 3 H), 4.54 (s, 1 H), 5.82 (s, 2 H), 6.81 (d, J = 8.6 Hz, 1 H), 6.88 (m, 2 H). – ¹³C NMR (CDCl₃): δ = 51.6, 60.6, 101.8, 109.5, 110.4, 118.7, 132.6, 148.9, 149.2, 174.6. – MS (EI): m/z (rel. int.): 209 (1) [M⁺], 135 (100). – C₁₀H₁₂ClNO₄: calcd. C 48.89, H 4.92, N 5.70; found C 48.92, H 4.97, N 5.69.

Methyl (2S)-(+)-2-Amino-2-(3,4,5-trimethoxyphenyl)acetate (5c): Amino ester **5c** was prepared by the same procedure as employed

for **5a**, using **4c** (0.19 g, 0.8 mmol) as starting material. Yield: 0.18 g, 90%. M.p. (as HCl salt) 231–233 °C. $[\alpha]_D^{20}$ = +113.5 (c = 0.3, CH₂Cl₂). – IR (KBr): $\tilde{\nu}$ = 3350, 1740 cm⁻¹. – ¹H NMR (CDCl₃): δ = 2.15 (sa, 2 H), 3.74 (s, 3 H), 3.84 (s, 3 H), 3.89 (s, 6 H), 4.54 (s, 1 H), 6.87 (s, 2 H). – ¹³C NMR (CDCl₃): δ = 51.6, 55.2, 56.2, 60.7, 110.1, 132.6, 148.1, 148.7, 174.6. – MS (EI): m/z (rel. int.): 255 (1) [M⁺], 151 (100). – C₁₂H₁₈ClNO₅: calcd. C 49.41, H 6.22, N 4.80; found C 49.46, H 6.20, N 4.82.

Methyl (2S)-(+)-2-Amino-2-(3,5-dibenzoyloxy-4-methoxyphenyl)-acetate (5d): Amino ester **5d** was prepared by the same procedure as employed for **5a**, using **4d** (0.23 g, 0.6 mmol) as starting material. Yield: 0.21 g, 87%. $[\alpha]_D^{20}$ = +118.4 (c = 0.3, CH₂Cl₂). – IR (CHCl₃): $\tilde{\nu}$ = 3344, 1736 cm⁻¹. – ¹H NMR (CDCl₃): δ = 2.10 (sa, 2 H), 3.71 (s, 3 H), 3.86 (s, 3 H), 4.51 (s, 1 H), 5.28 (s, 4 H), 6.57 (s, 2 H), 7.23–7.48 (m, 10 H). – ¹³C NMR (CDCl₃): δ = 51.4, 57.2, 60.9, 71.6, 107.5, 127.3, 128.0, 128.9, 129.1, 136.1, 139.8, 152.3, 173.6. – MS (EI): m/z (rel. int.): 407 (3) [M⁺], 91 (100). – C₂₄H₂₅NO₅: calcd. C 70.74, H 6.18, N 3.44; found C 70.81, H 6.15, N 3.41.

(2S)-(+)-2-Amino-2-(3,4-dimethoxyphenyl)ethanol (6a): TMSCl (14.37 g, 132.3 mmol) was added to a cooled (0 °C) suspension of LiBH₄ (1.44 g, 66.1 mmol) in dry THF (33 mL). Arylglycine **4a** (7.00 g, 33.1 mmol) was then added and the mixture was stirred at 0 °C for 1 h and at room temp. for 24 h. The mixture was then cooled to 0 °C, MeOH (50 mL) was added, and the resulting solution was stirred for an additional 10 min. The volatiles were removed in vacuo and a 20% KOH solution (20 mL) was added to the resulting oil, after which the mixture was stirred for 1 h. The mixture was extracted with CH₂Cl₂ (3 × 50 mL) and the combined organic extracts were dried over Na₂SO₄ and filtered, and the solvent was removed in vacuo to afford a yellowish oil, which was purified by crystallization (hexane/EtOAc 1:1). Yield: 5.21 g, 80%. $[\alpha]_D^{20}$ = +12.1 (c = 0.6, 1 M HCl). M.p. (hexane/EtOAc 1:1): 92–94 °C. – IR (KBr): $\tilde{\nu}$ = 3500–3000 cm⁻¹. – ¹H NMR (CDCl₃): δ = 2.67 (s, 3 H), 3.50 (dd, J = 10.7, 8.5 Hz, 1 H), 3.66 (dd, J = 10.7, 4.0 Hz, 1 H), 3.81 (s, 3 H), 3.84 (s, 3 H), 3.96 (dd, J = 8.5, 4.0 Hz, 1 H), 6.76–6.84 (m, 3 H). – ¹³C NMR (CDCl₃): δ = 55.7, 56.9, 67.8, 109.5, 110.9, 118.4, 134.8, 148.1, 148.8. – MS (EI): m/z (rel. int.): 166 (100) [M⁺ – 31]. – C₁₀H₁₅NO₃: calcd. C 60.9, H 7.67, N 7.10; found C 61.2, H 7.90, N 7.32.

(2S)-(–)-2-Amino-2-(3,4-methylenedioxyphenyl)ethanol (6b): Arylglycinol **6b** was prepared by the same procedure as employed for **6a**, using **4b** (6.45 g, 33.1 mmol) as starting material. Yield: 4.67 g, 78%. $[\alpha]_D^{20}$ = –45.0 (c = 0.1, HCl 1 M). M.p. (hexane/EtOAc 1:1): 76–78 °C. – IR (KBr): $\tilde{\nu}$ = 3500–3000 cm⁻¹. – ¹H NMR (CDCl₃): δ = 3.31 (s, 3 H), 3.48–3.69 (m, 2 H), 3.96 (s, 1 H), 5.92 (s, 2 H), 6.76–6.82 (m, 3 H). – ¹³C NMR (CDCl₃): δ = 57.0, 67.5, 101.0, 106.9, 108.2, 110.9, 119.8, 135.8, 146.9, 147.8. – MS (EI): m/z (Int. Rel.): 164 (100) [M⁺ – 17]. – C₉H₁₁NO₃: calcd. C 59.66, H 6.12, N 7.73; found C 60.12, H 6.15, N 7.41.

(2S)-(+)-2-Amino-2-phenylethanol (6c): Phenylglycinol **6c** was prepared by the same procedure as employed for **6a**, using (*S*)-(+)-phenylglycine (5.0 g, 33.1 mmol) as starting material. Yield: 3.9 g, 86%. $[\alpha]_D^{20}$ = +31.5 (c = 0.8, HCl 1 M). M.p. (hexane/EtOAc 1:1): 75–78 °C. – IR (KBr): $\tilde{\nu}$ = 3400–2860 cm⁻¹. – ¹H NMR (CDCl₃): δ = 2.94 (s, 3 H), 3.55 (dd, J = 10.8, 8.3 Hz, 1 H), 3.72 (dd, J = 10.8, 4.1 Hz, 1 H), 4.03 (dd, J = 8.3, 4.1 Hz, 1 H), 7.25–7.30 (m, 5 H). – ¹³C NMR (CDCl₃): δ = 57.3, 68.0, 126.4, 127.5, 128.6, 143.2. – C₈H₁₁NO: calcd. C 70.04, H 8.08, N 10.21; found C 70.65, H 8.15, N 10.45.

(2S)-(-)-2-[(E)-2,3-Dimethoxybenzylideneamino]-2-(3,4-dimethoxyphenyl)ethanol (7a): A suspension of arylglycinol **6a** (2.68 g, 13.6 mmol) and 2,3-dimethoxybenzaldehyde (2.50 g, 15.1 mmol) in benzene (100 mL) containing 4Å molecular sieves was refluxed for 4 h. The mixture was allowed to come to room temperature and filtered, and solvent was removed in vacuo, yielding imino alcohol **7a** as an oil. Yield: 4.23 g, 90%. $[\alpha]_D^{20} = -6.4$ ($c = 0.6$, EtOH). – IR (KBr): $\tilde{\nu} = 3600\text{--}3300$, 1630 cm^{-1} . – $^1\text{H NMR}$ (CD_3OD): $\delta = 3.75\text{--}3.90$ (m, 2 H), 3.82 (s, 12 H), 4.43 (t, $J = 6.3$ Hz, 1 H), 6.84–7.07 (m, 5 H), 7.56–7.58 (m, 1 H), 8.76 (s, 1 H). – $^{13}\text{C NMR}$ (CD_3OD): $\delta = 56.2$, 56.3, 62.0, 67.8, 78.3, 112.1, 115.9, 119.9, 120.8, 125.2, 130.7, 135.0, 149.6, 150.3, 150.7, 154.1, 159.6. – MS (EI): m/z (rel. int.): 315 (20) [$\text{M}^+ - 30$], 151 (100). – $\text{C}_{19}\text{H}_{23}\text{NO}_5$: calcd. C 66.07, H 6.71, N 4.05; found C 66.36, H 6.35, N 4.25.

(2S)-(+)-(E)-2-(2,3-Dimethoxybenzylideneamino)-2-(3,4-methylenedioxyphenyl)ethanol (7b): Imino alcohol **7b** was prepared by the same procedure as employed for **7a**, using arylglycinol **6b** (2.47 g, 13.6 mmol) and 2,3-dimethoxybenzaldehyde (2.50 g, 15.2 mmol) as starting materials. Yield: 3.81 g, 85%. $[\alpha]_D^{20} = +10.29$ ($c = 0.3$, EtOH). – IR (KBr): $\tilde{\nu} = 3600\text{--}3300$, 1631 cm^{-1} . – $^1\text{H NMR}$ (CD_3OD): $\delta = 3.71\text{--}3.79$ (m, 2 H), 3.78 (s, 3 H), 3.79 (s, 3 H), 4.34 (t, $J = 6.1$ Hz, 1 H), 5.84 (s, 2 H), 6.71–7.04 (m, 5 H), 7.53–7.56 (m, 1 H), 8.71 (s, 1 H). – $^{13}\text{C NMR}$ (CD_3OD): $\delta = 56.3$, 62.0, 67.8, 78.2, 102.2, 108.7, 109.1, 115.8, 119.9, 121.5, 125.2, 130.7, 136.2, 148.1, 149.0, 150.7, 154.1, 159.5. – MS (EI): m/z (rel. int.): 299 (20) [$\text{M}^+ - 30$], 135 (100). – $\text{C}_{18}\text{H}_{19}\text{NO}_5$: calcd. C 65.64, H 5.81, N 4.25; found C 65.32, H 6.01, N 4.41.

(2S)-(+)-(E)-2-(2,3-Dimethoxybenzylideneamino)-2-phenylethanol (7c): Imino alcohol **7c** was prepared by the same procedure as employed for **7a**, using (S)-(+)-phenylglycinol **6c** (4.00 g, 29.2 mmol) and 2,3-dimethoxybenzaldehyde (5.00 g, 30.1 mmol) as starting materials. Yield: 7.24 g, 87%. $[\alpha]_D^{20} = +10.5$ ($c = 1.5$, EtOH). M.p. (Et_2O /pentane 1:2.5): 68–71 °C. – IR (KBr): $\tilde{\nu} = 3500\text{--}3200$, 1631 cm^{-1} . – $^1\text{H NMR}$ (CD_3OD): $\delta = 3.89\text{--}3.99$ (m, 2 H), 3.94 (s, 6 H), 4.54 (t, $J = 6.4$ Hz, 1 H), 7.18 (d, $J = 4.9$ Hz, 2 H), 7.67 (m, 1 H), 7.30–7.56 (m, 5 H), 8.85 (s, 1 H). – $^{13}\text{C NMR}$ (CD_3OD): $\delta = 56.6$, 62.4, 68.1, 79.0, 116.3, 120.3, 125.5, 128.7, 129.8, 131.1, 142.6, 151.2, 154.6, 160.1. – MS (EI): m/z (Rel. Int): 284 (4) [$\text{M}^+ - 1$], 254 (100). – $\text{C}_{17}\text{H}_{19}\text{NO}_3$: calcd. C 71.59, H 6.71, N 4.91; found C 71.56, H 6.57, N 4.82.

(2S)-(+)-(E)-2-(2-Benzyloxy-3-methoxybenzylideneamino)-2-phenylethanol (7d): Imino alcohol **7d** was prepared by the same procedure as employed for **7a**, using (S)-(+)-phenylglycinol **6c** (0.26 g, 1.9 mmol) and 2-benzyloxy-3-methoxybenzaldehyde (0.48 g, 1.9 mmol) as starting materials. Yield: 0.63 g, 90%. $[\alpha]_D^{20} = +29.1$ ($c = 0.1$, EtOH). M.p.: 120–121 °C. – IR (KBr): $\tilde{\nu} = 3500\text{--}3100$, 1640 cm^{-1} . – $^1\text{H NMR}$ (CD_3OD): $\delta = 3.88$ (d, $J = 6.5$ Hz, 2 H), 3.99 (s, 3 H), 4.38 (t, $J = 6.4$ Hz, 1 H), 5.07 (d, $J = 11.0$ Hz, 1 H), 5.16 (d, $J = 11.0$ Hz, 1 H), 7.11–7.64 (m, 13 H), 8.69 (s, 1 H). – $^{13}\text{C NMR}$ (CD_3OD): $\delta = 56.4$, 67.3, 76.8, 115.9, 119.9, 125.3, 128.4, 128.5, 129.3, 129.4, 129.9, 131.2, 138.4, 142.2, 149.2, 154.3, 160.3. – MS (EI): m/z (%) = 300 [$\text{M}^+ - 61$] (7), 255 (6), 194 (39), 166 (16), 135 (66), 91 (100). – $\text{C}_{23}\text{H}_{23}\text{NO}_3$: calcd. C 76.43, H 6.41, N 3.87; found C 76.65, H 6.15, N 3.48.

(2S)-(+)-2-(2,3-Dimethoxybenzylamino)-2-(3,4-dimethoxyphenyl)ethanol (8a): NaBH_4 (0.07 g, 2.0 mmol) was added in three portions to a cooled (0 °C) solution of imino alcohol **2a** (0.28 g, 1.0 mmol) in MeOH (25 mL). The mixture was stirred at room temperature for 3 h and water (15 mL) was added. The mixture was extracted with CH_2Cl_2 (3 $\times$ 25 mL) and the combined organic extracts were collected, dried over Na_2SO_4 and filtered, and the solvent was re-

moved in vacuo to afford amino alcohol **3a** as a white solid. Yield: 0.31 g, 90%. $[\alpha]_D^{20} = +14.7$ ($c = 0.3$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3500\text{--}3200\text{ cm}^{-1}$. – $^1\text{H NMR}$ (CDCl_3): $\delta = 2.10$ (s, 2 H), 3.49–3.81 (m, 5 H), 3.78 (s, 3 H), 3.81 (s, 3 H), 3.85 (s, 3 H), 3.89 (s, 3 H), 6.80–7.04 (m, 6 H). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 46.4$, 55.6, 55.8, 60.7, 63.4, 66.8, 110.1, 110.9, 111.4, 119.5, 121.9, 123.9, 133.0, 133.6, 147.2, 148.2, 149.0; 152.6. – MS (EI): m/z (rel. int.): 316 (19) [$\text{M}^+ - 31$], 151 (100). – $\text{C}_{19}\text{H}_{25}\text{NO}_5$: calcd. C 65.69, H 7.25, N 4.03; found C 65.34, H 7.36, N 4.41.

(2S)-(+)-2-(2,3-Dimethoxybenzyl)amino-2-(3,4-methylenedioxyphenyl)ethanol (8b): Amino alcohol **8b** was prepared by the same procedure as employed for **7a**, using imino alcohol **7b** (0.33 g, 1.1 mmol) as starting material. Yield: 0.31 g, 90%. $[\alpha]_D^{20} = +5.43$ ($c = 0.3$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3500\text{--}3200\text{ cm}^{-1}$. – $^1\text{H NMR}$ (CDCl_3): $\delta = 3.41\text{--}3.82$ (m, 5 H), 3.81 (s, 3 H), 3.82 (s, 3 H), 5.94 (s, 2 H), 6.78–7.87 (m, 5 H), 6.96–6.99 (m, 1 H). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 46.3$, 55.6, 60.6, 63.5, 66.8, 100.9, 107.4, 108.1, 120.7, 121.8, 123.6, 133.6, 134.6, 146.7, 147.2, 147.7, 152.5. – MS (EI): m/z (rel. int.): 314 (3) [$\text{M}^+ - 17$], 151 (100). – $\text{C}_{18}\text{H}_{21}\text{NO}_5$: calcd. C 65.24, H 6.39, N 4.23; found C 65.54, H 6.15, N 4.20.

(2S)-(+)-2-(2,3-Dimethoxybenzyl)amino-2-phenylethanol (8c): Amino alcohol **8c** was prepared by the same procedure as employed for **7a**, using imino alcohol **7c** (0.28 g, 1.0 mmol) as starting material. Yield: 0.30 g, 98%. $[\alpha]_D^{20} = +46.0$ ($c = 1.8$, CH_2Cl_2). M.p.: 66–68 °C (Et_2O). – IR (KBr): $\tilde{\nu} = 3500\text{--}3200$, $3450\text{--}3300\text{ cm}^{-1}$. – $^1\text{H NMR}$ (CDCl_3): $\delta = 3.40\text{--}3.60$ (m, 3 H), 3.73 (s, 3 H), 3.78 (s, 3 H), 3.71–3.81 (m, 2 H), 6.77–6.81 (m, 2 H), 6.93–6.99 (m, 1 H), 7.29–7.33 (m, 5 H). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 45.9$, 55.2, 60.2, 63.6, 66.3, 111.1, 121.5, 123.5, 127.0, 127.2, 128.0, 133.1, 140.2, 146.9, 152.2. – MS (EI): m/z (rel. int.): 256 (21) [$\text{M}^+ - 31$], 151 (99), 136 (100). – $\text{C}_{17}\text{H}_{21}\text{NO}_3$: calcd. C 71.04, H 7.37, N 4.88; found C 71.45, H 7.15, N 4.50.

(2S)-(+)-2-(2-Benzyloxy-3-methoxybenzyl)amino-2-phenylethanol (8d): Amino alcohol **8d** was prepared by the same procedure as employed for **7a**, using imino alcohol **7d** (0.46 g, 1.3 mmol) as starting material. Yield: 0.45 g, 98%. $[\alpha]_D^{20} = +54.5$ ($c = 0.1$, CH_2Cl_2). M.p.: 65–67 °C (Et_2O). – IR (KBr): $\tilde{\nu} = 3600\text{--}3200\text{ cm}^{-1}$. – $^1\text{H NMR}$ (CDCl_3): $\delta = 3.1$ (s, 1 H), 3.47–3.81 (m, 5 H), 3.89 (s, 3 H), 4.99 (d, $J = 11.1$ Hz, 1 H), 5.09 (d, $J = 11.1$ Hz, 1 H), 7.04–7.07 (m, 2 H), 7.11–7.38 (m, 11 H). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 46.2$, 55.4, 63.7, 66.4, 74.5, 111.2, 121.7, 123.8, 127.1, 127.3, 127.6, 127.9, 128.1, 128.3, 133.7, 137.3, 140.2, 145.7, 152.3. – MS (EI): m/z (rel. int.): 280 (80) [$\text{M}^+ - 83$], 178 (100). – $\text{C}_{23}\text{H}_{25}\text{NO}_3$: calcd. C 76.01, H 6.93, N 3.85; found C 76.45, H 7.15, N 3.45.

(2S)-(+)-2-(2,3-Dimethoxybenzyl)-N-methylamino-2-(3,4-dimethoxyphenyl)ethanol (9a): A suspension of amino alcohol **8a** (1.70 g, 4.9 mmol) and 35% aq. HCHO (2.0 mL) in 40 mL of acetonitrile was stirred for 15 minutes. The solution was then cooled (0 °C) and NaBH_3CN (1.55 g, 24.7 mmol) was added in three portions. The mixture was stirred until TLC indicated full conversion (typically 24 h). Water (25 mL) was added, the mixture was extracted with CH_2Cl_2 (3 $\times$ 50 mL), and the combined organic fractions were collected, dried over Na_2SO_4 and filtered. The solvent was removed in vacuo to afford N-methylamino alcohol **4a** as a colourless oil after flash column chromatography (hexane/ethyl acetate 7:3). Yield: 1.43 g, 80%. $[\alpha]_D^{20} = +7.40$ ($c = 0.2$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3600\text{--}3300\text{ cm}^{-1}$. – $^1\text{H NMR}$ (CDCl_3): $\delta = 2.12$ (s, 3 H), 3.38 (d, $J = 12.7$ Hz, 1 H), 3.65–3.77 (m, 3 H), 3.84 (s, 3 H), 3.86 (s, 3 H), 3.89 (s, 3 H), 3.90 (s, 3 H), 4.05 (t, $J = 9.9$ Hz, 1 H), 6.80–6.89 (m, 5 H), 6.99–7.05 (m, 1 H). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 37.7$, 52.0, 55.7, 55.8, 55.9, 60.7, 61.0, 68.4, 110.6, 111.4, 112.2,

121.1, 122.6, 123.7, 128.2, 132.4, 147.6, 148.5, 152.7. – MS (EI): m/z (rel. int.): 330 (28) [$M^+ - 31$], 151 (100). – $C_{20}H_{27}NO_5$: calcd. C 66.46, H 7.53, N 3.87; found C 66.81, H 7.15, N 3.41.

(2S)-(–)-2-(2,3-Dimethoxybenzyl)-N-methylamino-2-(3,4-methylenedioxyphenyl)ethanol (9b): *N*-methylamino alcohol **9b** was prepared by the same procedure as employed for **9a**, using amino alcohol **8c** (1.62 g, 4.9 mmol) as starting material. Yield: 1.35 g, 80%. $[\alpha]_D^{20} = -19.67$ ($c = 0.3$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3600\text{--}3300\text{ cm}^{-1}$. – 1H NMR ($CDCl_3$): $\delta = 2.09$ (s, 3 H), 3.30 (d, $J = 12.7$ Hz, 1 H), 3.61–3.80 (m, 3 H), 3.85 (s, 3 H), 3.86 (s, 3 H), 4.00 (t, $J = 10.1$ Hz, 1 H), 5.96 (s, 2 H), 6.69–6.79 (m, 5 H), 6.97–7.04 (m, 1 H). – ^{13}C NMR ($CDCl_3$): $\delta = 37.6$, 51.9, 55.6, 60.6, 61.0, 68.5, 100.9, 107.9, 109.0, 111.4, 122.3, 122.6, 123.6, 129.4, 132.4, 146.9, 147.4, 147.5, 152.6. – MS (EI): m/z (rel. int.): 327 (1) [$M^+ - 18$], 151 (100). – $C_{19}H_{23}NO_5$: calcd. C 66.07, H 6.71, N 4.06; found C 66.20, H 6.55, N 4.41.

(2S)-(+)–2-(2,3-Dimethoxybenzyl)-N-methylamino-2-phenylethanol (9c): *N*-Methylamino alcohol **9c** was prepared by the same procedure as employed for **9a**, using amino alcohol **8c** (1.40 g, 4.9 mmol) as starting material. Yield: 1.14 g, 76%. $[\alpha]_D^{20} = +29.3$ ($c = 0.3$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3600\text{--}3300\text{ cm}^{-1}$. – 1H NMR ($CDCl_3$): $\delta = 2.11$ (s, 3 H), 3.51 (d, $J = 12.7$ Hz, 1 H), 3.70–3.77 (m, 3 H), 3.83 (s, 3 H), 3.85 (s, 3 H), 4.11 (t, $J = 10.1$ Hz, 1 H), 6.83–6.87 (m, 2 H), 7.00 (m, 1 H), 7.26–7.39 (m, 5 H). – ^{13}C NMR ($CDCl_3$): $\delta = 37.4$, 51.7, 55.2, 60.2, 60.6, 68.6, 111.1, 122.3, 123.3, 127.3, 127.8, 128.6, 132.1, 135.5, 147.3, 152.3. – MS (EI): m/z (%) = 270 (86) [$M^+ - 31$], 151 (100). – $C_{18}H_{23}NO_3$: calcd. C 71.72, H 7.70, N 4.65; found C 71.54, H 7.90, N 4.30.

(2S)-(+)–2-(2-Benzyloxy-3-methoxybenzyl)-N-methylamino-2-phenylethanol (9d): *N*-Methylamino alcohol **9d** was prepared by the same procedure as employed for **9a**, using amino alcohol **8d** (0.31 g, 0.80 mmol) as starting material. Yield: 0.23 g, 73%. $[\alpha]_D^{20} = +18.3$ ($c = 0.2$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3700\text{--}3100\text{ cm}^{-1}$. – 1H NMR ($CDCl_3$): $\delta = 2.09$ (s, 1 H), 3.29 (d, $J = 13.1$ Hz, 1 H), 3.52 (d, $J = 13.1$ Hz, 1 H), 3.65 (dd, $J = 10.1$, 4.8 Hz, 1 H), 3.82 (dd, $J = 10.1$, 4.8 Hz, 1 H), 3.94 (s, 3 H), 4.01 (t, $J = 10.1$ Hz, 1 H), 5.02 (d, $J = 11.1$ Hz, 1 H), 5.09 (d, $J = 11.1$ Hz, 1 H), 6.89–6.97 (m, 2 H), 7.09 (t, $J = 7.9$ Hz, 1 H), 7.35–7.41 (m, 8 H). – ^{13}C NMR ($CDCl_3$): $\delta = 37.1$, 51.8, 55.5, 60.4, 68.3, 74.7, 111.1, 122.0, 123.7, 127.5, 127.8, 127.9, 128.1, 128.5, 128.9, 132.8, 135.2, 137.2, 145.9, 152.5. – MS (EI): m/z (rel. int.): 273 (31) [$M^+ - 104$], 136 (100). – $C_{24}H_{27}NO_3$: calcd. C 76.39, H 7.21, N 3.71; found C 76.45, H 7.55, N 3.35.

(3S,4S)-(+)–7,8-Dimethoxy-3-(3,4-dimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-ol (11a): A solution of DMSO (0.25 mL, 3.5 mmol) in CH_2Cl_2 (3 mL) was added dropwise to a cooled ($-60^\circ C$) solution of oxalyl chloride (0.15 mL, 1.7 mmol) in CH_2Cl_2 (3 mL), and the mixture was stirred for 15 min. A solution of *N*-methylamino alcohol **9a** (0.57 g, 1.6 mmol) in 15 mL of CH_2Cl_2 was added dropwise and the reaction mixture was stirred for an additional 30 min. Diisopropylethylamine (1.40 mL, 8.0 mmol) was added dropwise and, after stirring for 15 min, the solution was allowed to reach room temp. The reaction was quenched with water (10 mL), the mixture was extracted with CH_2Cl_2 (3×25 mL), and the combined organic fractions were collected, dried over Na_2SO_4 and filtered. The solvent was removed in vacuo to afford the corresponding aldehyde **10**. The crude aldehyde was dissolved in acetone (8 mL), the solution was cooled to $0^\circ C$, and HCl_{conc} (2 mL) was added. The mixture was allowed to come to room temp., stirred for 2 h and quenched with a 1 M

NaOH solution (15 mL). The mixture was extracted with CH_2Cl_2 (3×25 mL) and the combined organic fractions were collected, dried over Na_2SO_4 and filtered, and the solvent was removed in vacuo, yielding isoquinoline **11a** after flash column chromatography (hexane/EtOAc = 2:8). Yield: 0.46 g, 80%. $[\alpha]_D^{20} = +130.1$ ($c = 0.5$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3550\text{--}3250\text{ cm}^{-1}$. – 1H NMR ($CDCl_3$): $\delta = 2.30$ (s, 3 H), 3.46 (d, $J = 16.6$ Hz, 1 H), 3.51 (d, $J = 2.8$ Hz, 1 H), 3.85 (s, 6 H), 3.87 (s, 3 H), 3.88 (s, 3 H), 4.17 (d, $J = 16.6$ Hz, 1 H), 4.57 (d, 1 H), 6.79–7.00 (m, 4 H), 7.12 (d, $J = 8.3$ Hz, 1 H). – ^{13}C NMR ($CDCl_3$): $\delta = 43.7$, 53.6, 55.7, 55.8, 60.1, 70.3, 70.4, 110.7, 111.1, 112.5, 121.8, 124.4, 128.5, 130.1, 130.2, 144.4, 148.5, 148.6, 151.7. – MS (EI): m/z (rel. int.): 357 (6) [$M^+ - 2$], 180 (100), 165 (12). – $C_{20}H_{25}NO_5$: calcd. C 66.83, H 7.01, N 3.90; found C 66.76, H 6.86, N 3.51.

(3S,4S)-(–)-7,8-Dimethoxy-2-methyl-3-(3,4-methylenedioxyphenyl)-1,2,3,4-tetrahydroisoquinolin-4-ol (11b): Isoquinoline **11b** was prepared by the same procedure as employed for **11a**, using *N*-methylamino alcohol **9b** (0.55 g, 1.6 mmol) as starting material. Yield: 0.44 g, 80%. $[\alpha]_D^{20} = -122.5$ ($c = 0.4$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3550\text{--}3250\text{ cm}^{-1}$. – 1H NMR ($CDCl_3$): $\delta = 2.29$ (s, 3 H), 3.45 (d, $J = 16.6$ Hz, 1 H), 3.50 (d, $J = 2.8$ Hz, 1 H), 3.85 (s, 3 H), 3.88 (s, 3 H), 4.13 (d, $J = 16.3$ Hz, 1 H), 4.53 (d, 1 H), 5.95 (s, 2 H), 6.78–6.93 (m, 4 H), 7.10 (d, $J = 8.3$ Hz, 1 H). – ^{13}C NMR ($CDCl_3$): $\delta = 43.5$, 53.5, 55.8, 60.1, 70.2, 70.4, 101.0, 107.9, 110.0, 111.1, 122.9, 124.3, 128.4, 130.2, 131.6, 144.4, 147.0, 147.5, 151.7. – MS (EI): m/z (rel. int.): 341 (3) [$M^+ - 2$], 164 (100). – $C_{19}H_{21}NO_5$: calcd. C 66.46, H 6.16, N 4.08; found C 66.81, H 6.15, N 4.41.

(3S,4S)-(+)–7,8-Dimethoxy-2-methyl-3-phenyl-1,2,3,4-tetrahydroisoquinolin-4-ol (11c): Isoquinoline **11b** was prepared by the same procedure as employed for **11a**, using *N*-methylamino alcohol **9b** (0.48 g, 1.6 mmol) as starting material. Yield: 0.37 g, 78%. $[\alpha]_D^{20} = +134.2$ ($c = 0.4$, CH_2Cl_2). M.p. $149\text{--}152^\circ C$ (Et_2O). – IR (KBr): $\tilde{\nu} = 3550\text{--}3250\text{ cm}^{-1}$. – 1H NMR ($CDCl_3$): $\delta = 2.20$ (s, 3 H), 3.29 (s, 1 H), 3.39 (d, $J = 16.6$ Hz, 1 H), 3.48 (d, $J = 2.4$ Hz, 1 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 4.11 (d, $J = 16.6$ Hz, 1 H), 4.48 (m, 1 H), 6.85 (d, $J = 8.3$ Hz, 1 H), 7.07 (d, $J = 8.3$ Hz, 1 H), 7.30 (m, 5 H). – ^{13}C NMR ($CDCl_3$): $\delta = 43.6$, 53.7, 56.7, 60.0, 70.1, 70.9, 111.0, 124.5, 127.5, 128.0, 129.6, 128.5, 130.2, 137.9, 144.3, 151.5. – MS (EI): m/z (rel. int.): 299 (1) [M^+], 120 (100). – $C_{18}H_{21}NO_3$: calcd. C 72.20, H 7.07, N 4.68; found C 72.40, H 7.15, N 4.41.

(3S,4S)-(+)–8-Benzyloxy-7-methoxy-2-methyl-3-phenyl-1,2,3,4-tetrahydroisoquinolin-4-ol (11d): Isoquinoline **11d** was prepared by the same procedure as employed for **11a**, using *N*-methylamino alcohol **9d** (0.11 g, 0.3 mmol) as starting material. Yield: 0.09 g, 83%. $[\alpha]_D^{20} = +73.9$ ($c = 0.2$, CH_2Cl_2). – IR (KBr): $\tilde{\nu} = 3600\text{--}3100\text{ cm}^{-1}$. – 1H NMR ($CDCl_3$): $\delta = 2.22$ (s, 3 H), 3.35 (d, $J = 16.6$ Hz, 1 H), 3.53 (d, $J = 2.7$ Hz, 1 H), 3.91 (s, 3 H), 4.09 (d, $J = 16.6$ Hz, 1 H), 4.55 (d, $J = 2.7$ Hz, 1 H), 5.02 (d, $J = 11.0$ Hz, 1 H), 5.09 (d, $J = 11.0$ Hz, 1 H), 6.91 (d, $J = 8.3$ Hz, 1 H), 7.14 (d, $J = 8.3$ Hz, 1 H), 7.34–7.49 (m, 10 H). – ^{13}C NMR ($CDCl_3$): $\delta = 43.5$, 53.8, 55.7, 70.0, 70.9, 74.0, 111.0, 124.6, 127.4, 127.8, 128.3, 129.7, 128.6, 130.2, 137.8, 143.2, 151.5. – MS (EI): m/z (rel. int.): 285 (4) [$M^+ - 90$], 91 (100). – $C_{24}H_{25}NO_3$: calcd. C 76.77, H 6.71, N 3.73; found C 76.55, H 6.55, N 3.35.

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