Diastereoselective Addition of Grignard Reagents to Chiral 1,3-Oxazolidines Having a *N*-Diphenylmethyl Substituent

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Chiral 1,3-oxazolidines having a diphenylmethyl group at the 3-position of the oxazolidine ring as a bulky substituent were synthesized. The reaction of Grignard reagents with the chiral 1,3-oxazolidines afforded the corresponding amines with very high diastereoselectivity. Furthermore, the method for the synthesis of optically active amines was applied to the asymmetric synthesis of (−)-dihydropinidine, a piperidine alkaloid.

Key words diastereoselective reaction; chiral 1,3-oxazolidine; diphenylmethyl group; Grignard reagent; (−)-dihydropinidine

The asymmetric reaction of organometallic reagents with the chiral imine function or its derivative is one of the most powerful construction methods for the preparation of optically active amines.[1] We have developed a synthetic method for the stereoselective preparation of both amine enantiomers starting from a single enantiomeric source, (*R*)-phenylglycinol, using the diastereoselective addition of Grignard reagents to chiral imines and 1,3-oxazolidines (Chart 1).[2] The former addition proceeded with high diastereoselectivity (99—88% de), but the latter showed much lower selectivity (82—32% de). However, we have found that the diastereoselectivity of the addition is improved when the 1,3-oxazolidine ring is *N*-substituted, in the order of methyl, benzyl and isopropyl groups.[3] This suggests that the *N*-substituent of the chiral 1,3-oxazolidine plays an important role in the appearance of the diastereoselectivity. Selectivity is high using isopropyl as the *N*-substituent, but unfortunately its subsequent removal is difficult.

On the basis of the above information, we describe here the stereoselective addition of Grignard reagents to chiral 1,3-oxazolidine having the bulkier diphenylmethyl group *versus* the isopropyl group. The diphenylmethyl group can be easily eliminated by using various methods. Furthermore, we synthesized the natural product, (−)-dihydropinidine (**12**), in order to confirm the utility of this method.

Synthesis of *N*-Diphenylmethyl-1,3-oxazolidine (3a—d) from (*R*)-Phenylglycinol First, the synthesis of (*R*)-*N*-diphenylmethylphenylglycinol (**2**), as the chiral source, was performed as follows.

The crystalloid **1** was obtained *via* the dehydrative condensation of (*R*)-phenylglycinol and benzophenone, with *p*-toluenesulfonic acid as a catalyst in toluene. This compound exists as an equilibrium mixture of the imine form and 1,3-oxazolidine form in the ratio of 1:2, as determined from the ^{1}H-NMR spectrum in $CDCl_3$ solution. Also, IR spectral measurement with the solution method ($CHCl_3$) showed a wide absorption mainly at 3460 cm^{-1} and a characteristic C=N absorption at 1660 cm^{-1}. Furthermore, in the Nujol mull method, the wide absorption at 3460 cm^{-1} which was found with the solution method shifted to 3270 cm^{-1} and no C=N absorption was observed.

The reduction of **1** with $LiAlH_4$ in tetrahydrofuran (THF) progressed easily to afford *N*-diphenylmethylphenylglycinol (**2**) in high yield. Chiral 1,3-oxazolidines were synthesized by the dehydrative condensation of **2** and various kinds of aldehydes. First, chiral 1,3-oxazolidine (**3a**) was obtained in the reaction of **2** and acetaldehyde with anhydrous $MgSO_4$ as the dehydrating agent in CH_2Cl_2 as a solvent, by stirring for 5 d. The diastereomers (**3a**) were obtained as an inseparable equilibrium mixture. The existence ratio was calculated from the peak

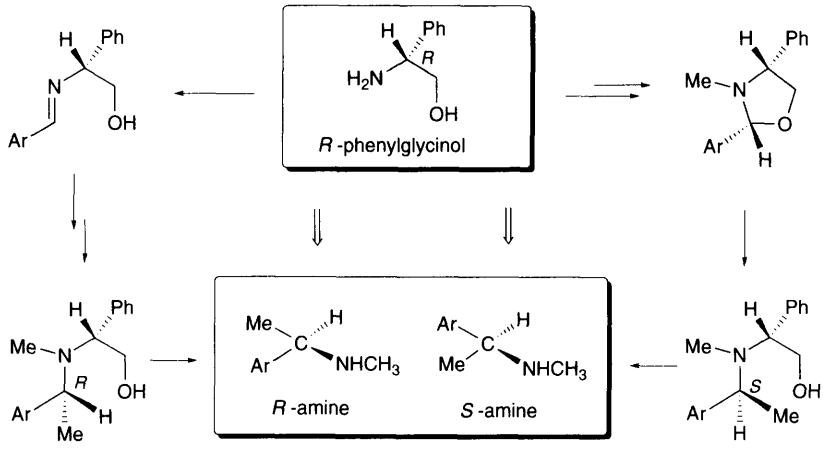

Chart 1

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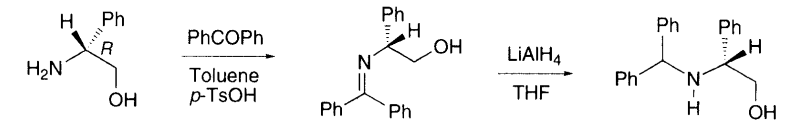


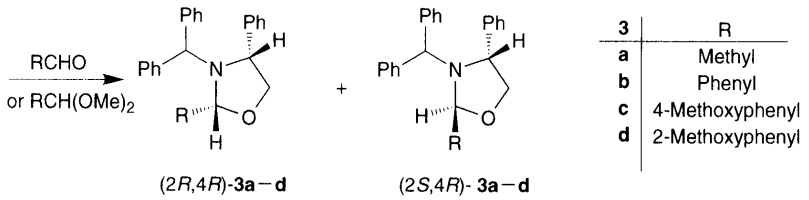


Chart 2

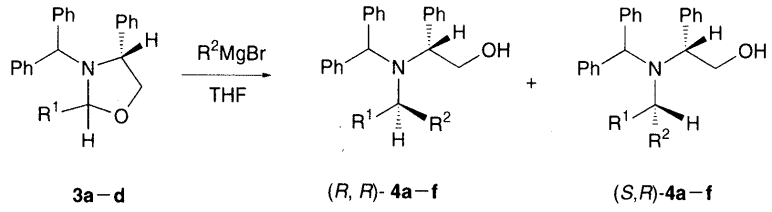


Chart 3

Table 1. Synthesis of Chiral 1,3-oxazolidines (**3a—d**)

3	R	Yield[a] (%)	Ratio[b] (2R:2S)
a	Methyl	81	98: 2
b	Phenyl	72	89: 1
c	4-Methoxyphenyl	66	89:11
d	2-Methoxyphenyl	69	90:10

a) Isolated yield. *b*) Estimated from the ^{1}H-NMR (270 MHz)spectrum.

Table 2. Diastereoselective Reaction of **3a—d** with Grignard Reagents

4	R^1	R^2	Reaction time (d)	Yield[a] (%)	Ratio[b] (R, R):(S, R)
a	Methyl	Phenyl	7	82	89:11
b	Phenyl	Methyl	6	85	6:94
c	4-Methoxyphenyl	Methyl	6	87	1: >99
d	2-Methoxyphenyl	Methyl	10	98	4:6
e	Methyl	iso-Propyl	19	79	>99: 1
f	Methyl	Ethyl	19	96	84:16

a) Isolated yield. *b*) Estimated from the ^{1}H-NMR (270 MHz) spectrum.

height of 2-Me in the ^{1}H-NMR spectrum.

In the reaction of **2** and aromatic aldehydes, the reactivity was increased by conversion into dimethylacetals by treatment with methyl orthoformate. Compounds **3b—d** were obtained by refluxing **2** and various acetals with *p*-toluenesulfonic acid as the catalyst in anhydrous toluene for 1—4 h. Generally, the chiral 1,3-oxazolidine was easily hydrolyzed by silica gel, but **3b—d** were comparatively stable, so they could be purified by means of column chromatography with silica gel. They were mixtures of diastereomers, like **3a**, and the existence ratio was calculated from the peak height of the **2** position proton of the 1,3-oxazolidine ring in the ^{1}H-NMR spectrum (Chart 2, Table 1). The single crystal X-ray analysis of *cis*-(2*R*,4*R*)-2-(*p*-bromophenyl)-*N*-methyl-4-phenyl-1,3-oxazolidine has already been reported.[3] In the same way, the absolute configurations of the major products of the chiral 1,3-oxazolidines (**3a—d**) were estimated to be (2*R*,4*R*), which means that functionalities of the 2 and 4 positions of the 1,3-oxazolidine ring are in the *cis* configuration.

Diastereoselective Addition of *N*-Diphenylmethyl-1,3-oxazolidines with Grignard Reagents Chiral 1,3-oxazolidines (**3a—d**) in anhydrous THF were reacted with various Grignard reagents at 50 °C under argon. The reaction progressed in a highly stereoselective manner, and **4a—f** were obtained as diastereomeric mixtures (Chart 3).

The existence ratio of the diastereomers was decided from the peak height of the methyl group in the ^{1}H-NMR spectrum, but only single products were found for **4c** and **4e** (Table 2). In these stereoselective reactions, high selectivity was observed in each case. Based on the ^{1}H-NMR spectra of **4a** and **4b**, it was found that the major product of **4a** and the minor one of **4b** have similar structure, like the minor product of **4a** and the major one of **4b**. This reaction may be very useful, as the desired stereogenic center can be obtained by changing the combinations of Grignard reagent and aldehyde, in spite of using the same chiral starting material, (*R*)-*N*-diphenylmethylphenylglycinol.

Removal of the Diphenylmethyl Group and Determination of Absolute Configuration The diphenylmethyl group of each compound was removed, and the absolute configuration was determined.

The elimination of the diphenylmethyl group of **4a** was carried out with concentrated hydrochloric acid in ethanol solution, and **5a** was obtained in quantitative yield. This

is a known compound, and it was found that the major product of **4a** was (*R*, *R*) by comparing the ^{1}H-NMR spectrum with the literature data.[3] Therefore, the major product of **4b** was determined to be (*S*, *R*), as it is in a diastereomer relation with the major product of **4a**.

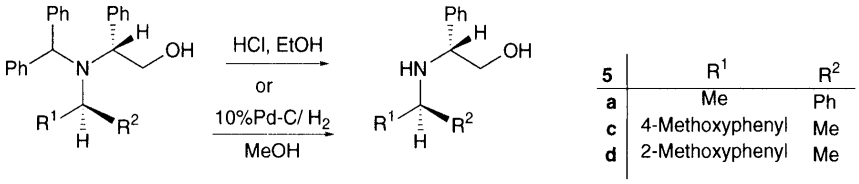
Catalytic hydrogenation of **4c** and **4d** treated with 10% palladium–carbon in methanol gave **5c** and **5d** in high yield. The stereochemistry of **5c** was identified as (*S*, *R*) from a comparison with the authentic compound.[2] Oxidation of **5d** with lead tetraacetate led to **6**, followed by acetylation to afford a known compound (**7**)[4] (Chart 4).

The treatment of **4e** and **4f** with NaH and MeI gave *O*-methyl products. The removal of the diphenylmethyl group using ethanol and concentrated hydrochloric acid afforded **8e** and **8f** in high yield (Chart 5). They are known compounds,[5] and their configurations were (*R*, *R*) as judged from a comparison of the ^{1}H-NMR spectra.

All the absolute configurations of newly formed chiral centers of **4a**—**f** were determined. It is considered that the reaction proceeds *via* an iminium intermediate by cleavage of the 1,3-oxazolidine ring, as proposed by Takahashi *et al.*[2,6]

Synthesis of (−)-Dihydropinidine Dihydropinidine is a piperidine alkaloid distributed in many *Pinaceae* plants, and a variety of asymmetric syntheses have been reported.[7] An asymmetric synthesis of (−)-dihydropinidine with our method was investigated. The condensation of (*R*)-*N*-diphenylmethylphenylglycinol (**2**), *n*-butyraldehyde and molecular sieves (MS 3 Å) in CH_2Cl_2 afforded **9** in 89% yield. The chiral 1,3-oxazolidine (**9**) in anhydrous THF was alkylated with the Grignard reagent which was prepared from 5-bromo-1-pentene to give **10** in quantitative yield and high stereoselectivity (96% yield, >99% de).

Wacker oxidation of **10** with $PdCl_2$ $(CH_3CN)_2$ as a catalyst produced the methyl ketone (**11**) in 63% yield. The next task was the cleavage of the diphenylmethyl group and the ring closure. The reaction of **11** with 10% palladium–carbon as a catalyst in hydrochloric acid



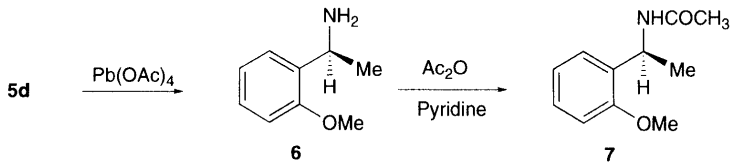


Chart 4

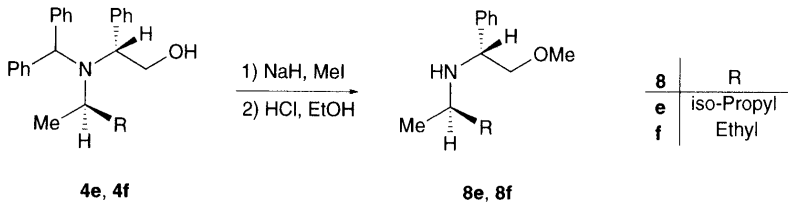


Chart 5

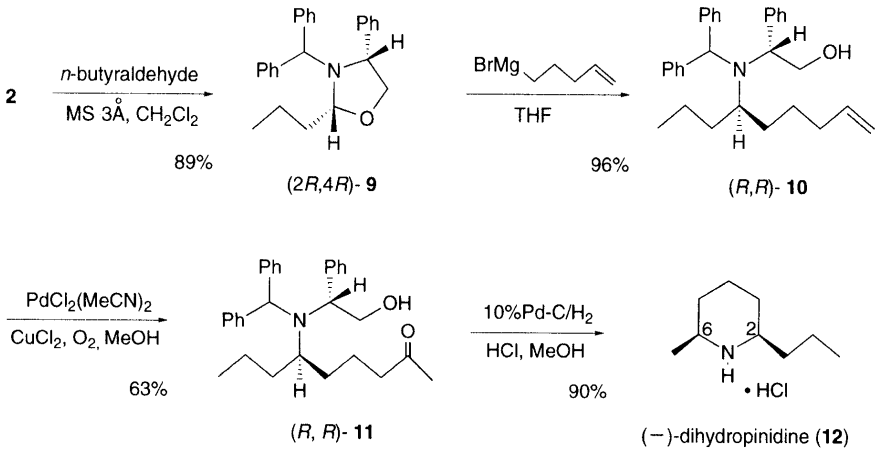


Chart 6

afforded the dihydropinidine hydrochloric acid salt (**12**) without difficulty in 90% yield (Chart 6). As the ^{1}H-NMR spectrum and specific rotation of synthesized **12** were identical with those in the literature,[8] the structure of **12** was confirmed.

In conclusion, chiral 1,3-oxazolidines having an *N*-diphenylmethyl group, prepared from (*R*)-phenylglycine, were allowed to react with Grignard reagents to afford chiral amines with high diastereoselectivity. These reactions allowed us to obtain chiral amine compounds which have the desired absolute configuration of the newly formed chiral carbon, according to the combination of aldehydes and Grignard reagents used. The stereoselectivity was much better than could be obtained with a methyl, benzyl or isopropyl group. Further, the diphenylmethyl was easily introduced and cleaved. To confirm the usefulness of these reactions, we applied them to the asymmetric synthesis of (−)-dihydropinidine in 48% total yield from **2**.

Experimental

General Procedures Melting points were measured with a Yanagimoto micro melting point apparatus without correction. IR spectra were recorded on a 215 Hitachi grating IR spectrophotometer. ^{1}H-NMR spectra were obtained on a JEOL GSX 270 instrument, and chemical shifts are reported in ppm on the δ-scale from internal Me_4Si. Mass spectra were measured with a JEOL JMS D-300 spectrometer by using the chemical ionization (CI) with isobutane and the electron impact (EI) methods. Elemental analyses were performed on a Perkin-Elmer 240-B instrument. Optical rotations were taken with a JASCO DIP-370 polarimeter at room temperature. A Shibata glass tube oven GTO-350RD was used as a distillation apparatus. Column chromatography was performed on silica gel (45—75 mm, Wakogel C-300). The reaction solvents were prepared as follows. THF was distilled over potassium metal. Ether and toluene were distilled over sodium metal.

(*R*)-2-Diphenylmethylideneamino-2-phenylethanol (1) A mixture of (*R*)-phenylglycinol (20.9 g, 152.4 mmol), benzophenone (27.77 g, 152.4 mmol), and *p*-toluenesulfonic acid (1.45 g, 7.6 mmol) in toluene (300 ml) was refluxed for 40 h using a Dean–Stark trap. After cooling, the mixture was poured into saturated aqueous $NaHCO_3$ (200 ml), the organic layer was separated and the aqueous layer was extracted with C_6H_6 (2 × 50 ml). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was crystallized to afford the imine **1** as colorless needles. Yield: 60%; mp 125—126 °C (from CH_2Cl_2–hexane). $[\alpha]_D$ −27.61° (c=1.03, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: Imine component; 2.00 (1H, br s, OH), 3.81 (1H, dd, J=4.3, 10.4 Hz, C$\underline{H}_2$OH), 3.98 (1H, dd, J=7.6, 10.4 Hz, C$\underline{H}_2$OH), 4.56 (1H, dd, J=4.3, 7.6 Hz, PhC$\underline{H}$N), 7.02—7.75 (15H, m, aromatic H). Oxazolidine component; 2.00 (1H, br s, NH), 3.87 (1H, t, J=7.3 Hz, PhC$\underline{H}$N), 4.24 (1H, t, J=7.3 Hz, C$\underline{H}_2$OH), 4.38 (1H, t, J=7.3 Hz, C$\underline{H}_2$OH), 7.02—7.75 (15H, m, aromatic H). IR ($CHCl_3$): 3460, 1660, 1600, 1450, 1320, 1280 cm^{-1}. MS *m/z*: CI, 302(M^++1); EI, 301 (M^+), 270 (M^+−CH_2OH). *Anal.* Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.65; H, 6.30; N, 4.57.

(*R*)-2-Diphenylmethylamino-2-phenylethanol (2) A solution of the imine (27.81 g, 92.26 mmol) in THF (100 ml) was added dropwise to a suspension of lithium aluminum hydride (5.25 g, 138.4 mmol) in dry THF (200 ml) at room temperature over a 20 min period. The reaction mixture was refluxed for 2.5 h, after which the excess hydride was decomposed by the slow addition of water (10 ml) and the mixture was filtered through a little Celite. Evaporation of the filtrate gave a colorless oil, which was distilled to give the *N*-diphenylmethylphenylglycinol (**2**) as a colorless viscous oil. Yield: 99%; bp 274 °C (1.1 mmHg). $[\alpha]_D$ −74.58° (c=3.90, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 2.38 (2H, br s, OH, NH), 3.58 (1H, dd, J=8.5, 10.4 Hz, C$\underline{H}_2$OH), 3.66 (1H, dd, J=4.3, 10.4 Hz, C$\underline{H}_2$OH), 3.72 (1H, dd, J=4.3, 8.5 Hz, PhC$\underline{H}$N), 4.71 (1H, s, $Ph_2C\underline{H}$), 7.15—7.39 (15H, m, aromatic H). IR ($CHCl_3$): 3500, 2850, 1600, 1450, 1100, 1020 cm^{-1}. MS *m/z*: CI, 304 (M^++1). *Anal.* Calcd for $C_{21}H_{21}NO$: C, 83.15; H, 6.98; N, 4.62. Found: C, 83.27; H, 6.92; N, 4.59.

(2*R*,4*R*)-3-Diphenylmethyl-2-methyl-4-phenyl-1,3-oxazolidine (3a) Acetaldehyde (14.22 g, 322.8 mmol) was added to a solution of **2** (6.53 g, 21.52 mmol) in dry CH_2Cl_2 (100 ml) in the presence of anhydrous $MgSO_4$ (10 g) at room temperature. After the reaction mixture had been stirred for 5 d it was filtered through a little Celite. Evaporation of the filtrate gave a oil, which was purified by bulb-to-bulb distillation to give the oxazolidine (**3a**) as a colorless oil. Yield: 81% (98 : 2 mixture); oven temperature 217 °C (4.7 mmHg). $[\alpha]_D$ −57.14° (c=1.14, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: Major component: 1.16 (3H, d, J=5.5 Hz, CH_3), 3.81 (1H, dd, J=5.5, 7.9 Hz, CH_2O), 4.10 (1H, dd, J=5.5, 7.3 Hz, CH_2O), 4.21 (1H, dd, J=7.3, 7.9 Hz, PhC$\underline{H}$N), 4.79 (1H, q, J=5.5 Hz, $CHCH_3$), 4.97 (1H, s, Ph_2CH), 7.01—7.50 (15H, m, aromatic H); minor component: 0.96 (3H, d, J=6.1 Hz, CH_3), 4.73 (1H, s, $Ph_2C\underline{H}$). IR($CHCl_3$): 2840, 1590, 1480, 1440, 1380, 1100, 1010, 980, 850 cm^{-1}. MS *m/z*: CI, 330 (M^++1); EI, 329 (M^+), 314 (M^+−CH_3). *Anal.* Calcd for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.91; H, 7.08; N, 4.26.

General Procedure for the Condensation of 2 with Aromatic Carbaldehyde Dimethylacetals A mixture of an aromatic carbaldehyde dimethylacetal [benzaldehyde dimethylacetal, 4-methoxybenzaldehyde dimethylacetal, or 2-methoxy-benzaldehyde dimethylacetal (30 mmol)], **2** (3.03 g, 10 mmol) and *p*-toluenesulfonic acid (19.0 mg, 0.1 mmol) in toluene (50 ml) was refluxed for 4—48 h. After cooling, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (20 ml), the organic layer was separated, and the aqueous layer was extracted with C_6H_6 (2 × 10 ml). The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to give the crude product, which was subjected to column chromatography on silica gel with CH_2Cl_2–hexane (98 : 2 v/v) to give the corresponding oxazolidine (**3b—d**) as colorless crystals.

(2*R*,4*R*)-3-Diphenylmethyl-2,4-diphenyl-1,3-oxazolidine (**3b**): Colorless needles. Yield: 72% (89 : 11 mixture); mp 129—130 °C (from CH_2Cl_2–hexane). $[\alpha]_D$ −13.48° (c=1.00, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: Major component: 3.90 (1H, dd, J=6.1, 8.5 Hz, CH_2O), 4.22 (1H, dd, J=6.1, 7.3 Hz, CH_2O), 4.32 (1H, dd, J=7.3, 8.5 Hz, PhC$\underline{H}$N), 5.11 (1H, s, $Ph_2C\underline{H}$), 5.61 (1H, s, NCHO), 7.01—7.47 (20H, m, aromatic H); minor component: 4.52 (1H, s, Ph_2CH), 5.49 (1H, s, NCHO). IR ($CHCl_3$): 2830, 1590, 1480, 1440, 1060, 1010 cm^{-1}. MS *m/z*: CI, 392 (M^++1); EI, 391 (M^+), 167 (base peak). *Anal.* Calcd for $C_{28}H_{25}NO$: C, 85.90; H, 6.44; N, 3.58. Found: C, 85.99; H, 6.42; N, 3.55.

(2*R*,4*R*)-3-Diphenylmethyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine (**3c**): Colorless plates. Yield: 66% (89 : 11 mixture); mp 106 °C (from CH_2Cl_2–hexane). $[\alpha]_D$ +10.56° (c=1.05, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: Major component: 3.78 (3H, s, OCH_3), 3.88 (1H, dd, J=6.1, 7.9 Hz, CH_2O), 4.20 (1H, dd, J=6.1, 7.3 Hz, CH_2O), 4.28 (1H, dd, J=7.3, 7.9 Hz, PhC$\underline{H}$N), 5.08 (1H, s, $Ph_2C\underline{H}$), 5.54 (1H, s, NCHO), 6.77 (2H, d, J=8.6 Hz, aromatic H), 7.01—7.39 (17H, m, aromatic H); minor component: 3.74 (3H, s, OCH_3), 4.53 (1H, s, $Ph_2C\underline{H}$), 5.49 (1H, s, NCHO), 6.64 (2H, d, J=8.6 Hz, aromatic H). IR ($CHCl_3$): 2840, 1610, 1500, 1460, 1300, 1170, 1020 cm^{-1}. MS *m/z*: CI, 422 (M^++1); EI, 421 (M^+), 167 (base peak). *Anal.* Calcd for $C_{29}H_{27}NO_2$: C, 82.63; H, 6.46; N, 3.32. Found: C, 82.53; H, 6.42; N, 3.28.

(2*R*,4*R*)-3-Diphenylmethyl-2-(2-methoxyphenyl)-4-phenyl-1,3-oxazolidine (**3d**): Colorless plates. Yield: 69% (90 : 10 mixture); mp 121 °C (from CH_2Cl_2–hexane). $[\alpha]_D$ +3.85° (c=1.07, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: Major component: 3.61 (3H, s, OCH_3), 3.98 (1H, dd, J=4.3, 6.7 Hz, CH_2O), 4.18 (1H, dd, J=4.3, 7.3 Hz, CH_2O), 4.23 (1H, dd, J=6.7, 7.3 Hz, PhC$\underline{H}$N), 5.07 (1H, s, $Ph_2C\underline{H}$), 5.98 (1H, s, NCHO), 6.61 (1H, d, J=7.3 Hz, aromatic H), 6.89—7.26 (17H, m, aromatic H), 7.92 (1H, dd, J=1.8, 7.3 Hz, aromatic H); minor component: 3.53 (3H, s, OCH_3), 4.60 (1H, s, $Ph_2C\underline{H}$), 6.02 (1H, s, NCHO), 6.46 (1H, d, J=7.3 Hz, aromatic H), 7.76 (1H, dd, J=1.8, 7.3 Hz, aromatic H). IR ($CHCl_3$): 2830, 1600, 1490, 1460, 1450, 1270, 1120, 1070, 1020 cm^{-1}. MS *m/z*: CI, 422 (M^++1); EI, 421 (M^+), 167 (base peak). *Anal.* Calcd for $C_{29}H_{27}NO_2$: C, 82.63; H, 6.46; N, 3.32. Found: C, 82.59; H, 6.44; N, 3.27.

General Procedure for the Reaction of 3a—d with Grignard Reagents Grignard reagent [C_6H_5MgBr, CH_3MgBr, iso-C_3H_7MgBr or C_2H_5MgBr (18 mmol)] was added dropwise to a stirred solution of **3a—d** (1.8 mmol) in THF (10 ml) at room temperature under an argon atmosphere over a 15 min period. After the reaction mixture had been stirred at 50 °C for 5—19 d, it was quenched with a small amount of water and diluted with ether (20 ml). The resulting white precipitate was filtered off, and the filtrate was washed with saturated ammonium chloride (20 ml). The organic layer was separated and the aqueous layer was extracted with ether (2 × 10 ml). The combined extracts were washed

with brine, dried over Na_2SO_4 and evaporated to give a residue, which was subjected to column chromatography on silica gel with hexane–ethyl acetate (3 : 1 v/v) to give a diastereomeric mixture of **4a—f**.

(*R*)-2-{(Diphenylmethyl)[(*R*)-1-phenylethyl]amino}-2-phenylethanol (**4a**): The Grignard reagent C_6H_5MgBr was added to the oxazolidine (**3a**) according to the general procedure to give a diastereomeric mixture of **4a** (82%) (89 : 11 mixture), which was recrystallized to afford the major product as colorless needles. Yield: 65%; mp 132 °C (from ether–hexane). $[\alpha]_D$ −63.44° (c = 1.03, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: Major component: 1.01 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 2.12 (1H, br s, OH), 3.71 (1H, dd, J = 6.7, 11.0 Hz, $C\underline{H}_2OH$), 3.96 (1H, dd, J = 8.6, 11.0 Hz, $C\underline{H}_2OH$), 4.39 (1H, dd, J = 6.7, 8.6 Hz, $PhC\underline{H}N$), 4.42 (1H, q, J = 6.7 Hz, $C\underline{H}CH_3$), 5.17 (1H, s, $Ph_2C\underline{H}$), 6.92—7.34 (20H, m, aromatic H). IR ($CHCl_3$): 2930, 1590, 1490, 1450, 1370, 1120, 1070, 1010 cm^{-1}. MS m/z: CI, 408 ($M^+ + 1$); EI, 376 ($M^+ - CH_2OH$), 167 (base peak). *Anal.* Calcd for $C_{29}H_{29}NO$: C, 85.46; H, 7.17; N, 3.44. Found: C, 85.28; H, 7.12; N, 3.37.

(*R*)-2-{(Diphenylmethyl)[(*S*)-1-phenylethyl]amino}-2-phenylethanol (**4b**): The Grignard reagent CH_3MgBr was added to the oxazolidine (**3b**) according to the general procedure to give a diastereomeric mixture of **4b** (6 : 94 mixture) as a colorless viscous oil. Yield: 85%. ^{1}H-NMR ($CDCl_3$) δ: Major component: 1.45 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 1.72 (1H, br s, OH), 3.93 (2H, d, J = 7.9 Hz, $C\underline{H}_2OH$), 4.41 (1H, t, J = 7.9 Hz, $PhC\underline{H}N$), 4.49 (1H, q, J = 6.7 Hz, $C\underline{H}CH_3$), 5.20 (1H, s, $Ph_2C\underline{H}$), 6.82—7.38 (20H, m, aromatic H). IR ($CHCl_3$): 2950, 1600, 1490, 1450, 1380, 1130, 1010 cm^{-1}. MS m/z: CI, 408 ($M^+ + 1$); EI, 407 (M^+), 376 ($M^+ - CH_2OH$), 167 (base peak). HR-MS m/z: Calcd for $C_{29}H_{29}NO$ (M^+): 407.2247. Found: 407.2241.

(*R*)-2-{(Diphenylmethyl)[(*S*)-1-(4-methoxyphenyl)ethyl]amino}-2-phenylethanol (**4c**): The Grignard reagent CH_3MgBr was added to the oxazolidine (**3c**) according to the general procedure to give a diastereomeric mixture of **4c** (1 : >99 mixture) as a colorless viscous oil. Yield: 87%. $[\alpha]_D$ −51.15° (c = 0.76, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.41 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 1.94 (1H, br s, OH), 3.75 (3H, s, OCH_3), 3.91 (2H, d, J = 7.9 Hz, $C\underline{H}_2OH$), 4.39 (1H, t, J = 7.9 Hz, $PhC\underline{H}N$), 4.43 (1H, q, J = 6.7 Hz, $C\underline{H}CH_3$), 5.16 (1H, s, $Ph_2C\underline{H}$), 6.65—7.37 (19H, m, aromatic H). IR ($CHCl_3$): 2940, 1610, 1500, 1460, 1180, 1020 cm^{-1}. MS m/z: CI, 438 ($M^+ + 1$); EI, 437 (M^+), 406 ($M^+ - CH_2OH$), 272 (base peak). HR-MS m/z: Calcd for $C_{30}H_{31}NO_2$ (M^+): 437.2353. Found: 437.2348.

(*R*)-2-{(Diphenylmethyl)[(*S*)-1-(2-methoxyphenyl)ethyl]amino}-2-phenylethanol (**4d**): The Grignard reagent CH_3MgBr was added to the oxazolidine (**3d**) according to the general procedure to give a diastereomeric mixture of **4d** (4 : 96 mixture) as a colorless viscous oil. Yield: 98%. ^{1}H-NMR ($CDCl_3$) δ: Major component: 1.18 (3H, d, J = 7.3 Hz, $CHC\underline{H}_3$), 2.56 (1H, br s, OH), 3.51—3.59 (2H, m, $C\underline{H}_2OH$), 3.77 (3H, s, OCH_3), 4.42 (1H, t, J = 7.3 Hz, $PhC\underline{H}N$), 4.71 (1H, q, J = 7.3 Hz, $C\underline{H}CH_3$), 5.47 (1H, s, $Ph_2C\underline{H}$), 6.82—7.53 (19H, m, aromatic H); minor component: 1.07 (3H, d, J = 7.3 Hz, $CHC\underline{H}_3$), 2.74 (1H, br s, OH), 3.92 (3H, s, OCH_3), 4.85 (1H, q, J = 7.3 Hz, $C\underline{H}CH_3$), 5.22 (1H, s, $Ph_2C\underline{H}$). IR ($CHCl_3$): 3500, 2940, 1600, 1590, 1490, 1020 cm^{-1}. MS m/z: CI, 438 ($M^+ + 1$); EI, 437 (M^+), 406 ($M^+ - CH_2OH$), 167 (base peak). HR-MS m/z: Calcd for $C_{30}H_{31}NO_2$ (M^+): 437.2353. Found: 437.2364.

(*R*)-2-{(Diphenylmethyl)[(*R*)-1,2-dimethylpropyl]amino}-2-phenylethanol (**4e**): The Grignard reagent iso-C_3H_7MgBr was added to the oxazolidine (**3a**) according to the general procedure to give a diastereomeric mixture of **4e** (>99 : 1 mixture) as a colorless viscous oil. Yield: 79%. $[\alpha]_D$ −8.12° (c = 1.01, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.55 [3H, d, J = 6.7 Hz, $CH(C\underline{H}_3)_2$], 0.65 [3H, d, J = 6.7 Hz, $CH(C\underline{H}_3)_2$], 1.01 [1H, m, $C\underline{H}(CH_3)_2$], 1.05 (3H, d, J = 6.7 Hz, $NCHC\underline{H}_3$), 2.32 (1H, br s, OH), 2.73 (1H, dd, J = 6.7, 8.5 Hz, $NC\underline{H}CH_3$), 3.74 (1H, dd, J = 6.7, 11.0 Hz, $C\underline{H}_2OH$), 4.10 (1H, dd, J = 8.6, 11.0 Hz, $C\underline{H}_2OH$), 4.35 (1H, dd, J = 6.7, 8.6 Hz, $PhC\underline{H}N$), 5.09 (1H, s, $Ph_2C\underline{H}$), 7.01—7.47 (15H, m, aromatic H). IR ($CHCl_3$): 3600, 2900, 1600, 1590, 1490, 1010 cm^{-1}. MS m/z: CI, 374 ($M^+ + 1$); EI, 342 ($M^+ - CH_2OH$), 167 (base peak). *Anal.* Calcd for $C_{26}H_{31}NO$: C, 83.60; H, 8.37; N, 3.75. Found: C, 83.54; H, 8.39; N, 3.75.

(*R*)-2-{(Diphenylmethyl)[(*R*)-1-methylpropyl]amino}-2-phenylethanol (**4f**): The Grignard reagent C_2H_5MgBr was added to the oxazolidine (**3a**) according to the general procedure to give a diastereomeric mixture of **4f** (84 : 16 mixture) as colorless needles. Yield: 96%; mp 41 °C (from ether–hexane). ^{1}H-NMR ($CDCl_3$) δ: Major component: 0.63 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 0.81 (3H, t, J = 7.3 Hz, $CH_2C\underline{H}_3$), 1.08—1.43 (2H, m, $C\underline{H}_2CH_3$), 2.56 (1H, br s, OH), 3.03—3.11 (1H, m, $NC\underline{H}CH_3$), 3.71 (1H, dd, J = 6.7, 11.0 Hz, $C\underline{H}_2OH$), 4.01 (1H, dd, J = 8.6, 11.0 Hz, $C\underline{H}_2OH$), 4.34 (1H, dd, J = 6.7, 8.6 Hz, $PhC\underline{H}N$), 5.22 (1H, s, $Ph_2C\underline{H}$), 7.10—7.45 (15H, m, aromatic H); minor component: 0.48 (3H, t, J = 7.3 Hz, $CH_2C\underline{H}_3$), 1.09 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 5.31 (1H, s, $Ph_2C\underline{H}$). IR ($CHCl_3$): 3470, 2940, 1600, 1450, 1370, 1010 cm^{-1}. MS m/z: CI, 360 ($M^+ + 1$); EI, 328 ($M^+ - CH_2OH$), 167 (base peak). *Anal.* Calcd for $C_{25}H_{29}NO$: C, 83.52; H, 8.13; N, 3.90. Found: C, 83.22; H, 8.36; N, 3.79.

(*R*)-2-[(*R*)-1-Phenylethylamino]-2-phenylethanol (5a) A solution of the diastereomeric mixture of **4a** (89 : 11) (0.5 g, 1.23 mmol) in concentrated hydrochloric acid–ethanol (1 : 2 v/v; 10 ml) was heated under reflux for 2.5 h. After having been cooled to room temperature, the reaction mixture was diluted with water–ether (1 : 1 v/v; 20 ml) and the organic layer was separated. The resulting aqueous layer was basified with 10% NaOH solution and extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to give a viscous oil, which was subjected to column chromatography on silica gel with CH_2Cl_2–MeOH (96 : 4 v/v) to give a diastereomeric mixture of **5a** (90 : 10 mixture) as a pale yellow oil. Yield 90%. ^{1}H-NMR ($CDCl_3$) δ: Major component: 1.36 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 2.48 (2H, br s, NH, OH), 3.51 (1H, dd, J = 7.9, 11.0 Hz, $C\underline{H}_2OH$), 3.72(1H, dd, J = 4.3, 11.0 Hz, $C\underline{H}_2OH$), 3.76 (1H, q, J = 6.7 Hz, $C\underline{H}CH_3$), 3.88 (1H, dd, J = 4.3, 7.9 Hz, $PhC\underline{H}N$), 7.19—7.35 (10H, m, aromatic H); minor component: 1.33 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$); whose spectral data were identical with those of an authentic specimen.[3]

(*R*)-2-[(*S*)-1-(4-Methoxyphenyl)ethylamino]-2-phenylethanol (5c) A solution of **4c** (0.5 g, 1.14 mmol) in methanol (10 ml) was hydrogenated over 10% palladium on carbon (15 mg) at atmospheric pressure for 2 d. The catalyst was filtered off and washed with methanol and the combined filtrate and washings were evaporated under reduced pressure. The residual oil was subjected to column chromatography on silica gel with CH_2Cl_2–MeOH (96 : 4 v/v) to give the amine **5c** as a colorless oil. Yield: 89%. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 2.24 (2H, br s, NH, OH), 3.46—3.64 (4H, m, $C\underline{H}_2OH$, $C\underline{H}CH_3$, $PhC\underline{H}N$), 3.80 (3H, s, OCH_3), 6.85—7.39 (9H, m, aromatic H).

(*S*)-1-(2-Methoxyphenyl)ethylamine (6) The hydrogenation of **4d** (0.5 g, 1.14 mmol) (96 : 4 mixture) was carried out as described above to give **5d** (>99 : 1 mixture) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 2.04 (2H, br s, NH, OH), 3.52—3.62 (3H, m, $C\underline{H}_2OH$, $PhC\underline{H}N$), 3.75 (3H, s, OCH_3), 3.96 (1H, q, J = 6.7 Hz, $C\underline{H}CH_3$), 6.85—7.36 (9H, m, aromatic H); which, without further purification, was used for the next reaction.

A solution of the crude **5d** (0.07 g, 0.24 mmol) in CH_2Cl_2–methanol (2 : 1 v/v, 6 ml) was stirred, and lead tetraacetate (0.12 g, 0.29 mmol) was added at 0 °C in a single portion. The reaction mixture was stirred for 5 min, basified with 10% NaOH solution and extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to give the residue, which was dissolved in ether–10% HCl solution (1 : 2 v/v, 6 ml). This solution was stirred for 15 h at room temperature. The two layers were separated, then the aqueous layer was basified with 10% NaOH solution and extracted with ether (3 × 10 ml). The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to give a viscous oil, which was subjected to column chromatography on silica gel with methanol–ethyl acetate (1 : 1 v/v) to give the amine (**6**) as a pale yellow oil. Yield: 67% from **4d**. ^{1}H-NMR ($CDCl_3$) δ: 1.40 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 2.13 (2H, br s, NH_2), 3.85 (3H, s, OCH_3), 4.35 (1H, q, J = 6.7 Hz, $C\underline{H}CH_3$), 6.87 (1H, dd, J = 1.6, 7.6 Hz aromatic H), 6.94 (1H, dt, J = 1.6, 7.6 Hz aromatic H), 7.22 (1H, dt, J = 1.6, 7.6 Hz aromatic H), 7.32 (1H, dd, J = 1.6, 7.6 Hz aromatic H).

(*S*)-*N*-[1-(2-Methoxyphenyl)ethyl]acetamide (7) Acetic anhydride (4 ml) was added dropwise to a stirred solution of **6** (0.2 g, 1.32 mmol) in pyridine (4 ml) at 0 °C. After having been stirred for 18 h, the reaction mixture was quenched with ether (10 ml) and washed with saturated $KHSO_4$ solution, 10% $NaHCO_3$ solution and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give an oily residue, which was subjected to column chromatography on silica gel with ethyl acetate–hexane (1 : 2 v/v) to give the acetate (**7**) as colorless plates. Yield: 89%; mp 165 °C (from benzene). $[\alpha]_D$ −134.8° (c = 0.12, $CHCl_3$). {lit.,[5] (*R*)-**7**; $[\alpha]_D$ +133° (c = 2.0, $CHCl_3$)}. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (3H, d, J = 6.7 Hz, $CHC\underline{H}_3$), 1.97 (3H, s, $COCH_3$), 3.89 (3H, s, OCH_3), 5.26 (1H, dq, J = 6.7, 9.2 Hz, $C\underline{H}CH_3$), 6.37 (1H, d, J = 9.2 Hz, NH), 6.94 (2H, t, J = 7.3 Hz aromatic H), 7.20 (1H, dd, J = 1.8, 7.3 Hz

aromatic H), 7.24 (1H, dd, $J=1.8$, 7.3 Hz aromatic H).

(*R*)-*N*-[(*R*)-1,2-Dimethylpropyl]-2-methoxy-1-phenylethylamine (8e) NaH (60%, 30.4 mg, 0.76 mmol) was added in one portion to a stirred solution of **4e** (0.14 g, 0.38 mmol) in dry THF (5 ml) under argon at room temperature. After the reaction mixture had been stirred for 2 h, methyl iodide (0.13 g, 0.92 mmol) was added over a 20 min period, and the whole was stirred for an additional 15 h at ambient temperature. It was then diluted with ether (20 ml), washed with brine (2 × 10 ml), and concentrated under reduced pressure to give a residue. This was dissolved in concentrated hydrochloric acid–ethanol (1 : 2 v/v 10 ml) and heated under reflux for 2.5 h. After having been cooled to room temperature, the solution was diluted with water–ether (1 : 1 v/v; 20 ml) and the organic layer was separated. The resulting aqueous layer was basified with 10% NaOH solution and extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to give a viscous oil, which was subjected to column chromatography on silica gel with ethyl acetate–hexane (1 : 2 v/v) to give the amine (**8e**) as a colorless oil. Yield: 81%. ^{1}H-NMR ($CDCl_3$) δ: 0.83 [3H, d, $J=6.7$ Hz, $CH(CH_3)_2$], 0.85 [3H, d, $J=6.7$ Hz, $CH(CH_3)_2$], 0.96 (3H, d, $J=6.7$ Hz, $CHCH_3$), 1.48—1.58 [1H, m, $CH(CH_3)_2$], 1.60 (1H, br s, NH), 2.22 (1H, dq, $J=4.9$, 6.7 Hz, $CHCH_3$), 3.35 (3H, s, OCH_3), 3.38 (1H, dd, $J=7.9$, 9.2 Hz, CH_2OCH_3), 3.41 (1H, dd, $J=4.9$, 9.2 Hz, CH_2OCH_3), 4.03 (1H, dd, $J=4.9$, 7.9 Hz, PhCHN), 7.21—7.39 (5H, m, aromatic H). The spectral data were identical with those of an authentic specimen.[6]

(*R*)-*N*-[(*R*)-1-Methylpropyl]-2-methoxy-1-phenylethylamine (**8f**): *O*-Alkylation and debenzylation of **4f** (0.22 g ,0.50 mmol) (84 : 16 mixture) were carried out as above to give a diastereomeric mixture of the amine (**8f**) as a colorless viscous oil. Yield: 83%. ^{1}H-NMR ($CDCl_3$) δ: Major component: 0.85 (3H, t, $J=7.3$ Hz, CH_2CH_3), 1.01 (3H, d, $J=6.1$ Hz, $NCHCH_3$), 1.20—1.45 (2H, m, CH_2CH_3), 1.83 (1H, br s, NH), 2.36 (1H, sixtet, $J=6.1$ Hz, $NCHCH_3$), 3.35 (3H, s, OCH_3), 3.39 (1H, dd, $J=8.5$, 9.2 Hz, CH_2OCH_3), 3.44 (1H, dd, $J=4.3$, 9.2 Hz, CH_2OCH_3), 4.04 (1H, dd, $J=4.3$, 8.5 Hz, PhCHN), 7.22—7.39 (5H, m, aromatic H); minor component: 2.52 (1H, m, $NCHCH_3$), 3.39 (3H, s, OCH_3), 4.03 (1H, dd, $J=4.3$, 8.5 Hz, PhCHN). The spectral data were identical with those of an authentic specimen.[6]

(2*R*,4*R*)-3-Diphenylmethyl-4-phenyl-2-propyl-1,3-oxazolidine (9) The reaction was performed as previously described for the oxazolidine (**3a**), using **2** (6.77 g, 22.33 mmol) in dry CH_2Cl_2 (120 ml), *n*-butyraldehyde (16.1 g, 223.30 mmol) and MS 3 Å (10 g) in dry CH_2Cl_2 (10 ml) to yield the oxazolidine (**9**) as a pale yellow oil. Yield: 89% (91 : 9 mixture); oven temperature 233 °C (5.2 mmHg). $[\alpha]_D$ −54.69° ($c=1.02$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: Major component: 0.70 (3H, t, $J=7.3$ Hz, CH_3), 1.15—1.59 (4H, m, $CH_2CH_2CH_3$), 3.74 (1H, dd, $J=6.1$, 7.9 Hz, CH_2O), 4.14 (1H, dd, $J=6.1$, 7.3 Hz, CH_2O), 4.25 (1H, dd, $J=7.3$, 7.9 Hz, PhCHN), 4.67 (1H, dd, $J=3.7$, 9.2 Hz, NCHO), 4.99 (1H, s, Ph_2CH), 6.99—7.50 (15H, m, aromatic H); minor component: 3.85 (1H, dd, $J=1.8$, 7.3 Hz, PhCHN), 4.63 (1H, s, Ph_2CH), 4.73 (1H, dd, $J=2.4$, 7.3 Hz, NCHO). IR ($CHCl_3$): 2964, 2870, 1730, 1660, 1600, 1450, 1100, 1070, 1020, 910 cm^{-1}. MS *m/z*: CI, 358 ($M^+ + 1$); EI, 314 ($M^+ - C_3H_7$), 167 (base peak). *Anal.* Calcd for $C_{25}H_{27}NO$: C, 83.99; H, 7.61; N, 3.92. Found: C, 84.25; H, 7.58; N, 3.95.

(*R*)-2-{(Diphenylmethyl)[(*R*)-1-propyl-5-hexenyl]amino}-2-phenylethanol (10) A solution of the oxazolidine (**9**) (3.96 g, 11.08 mmol) in dry THF (20 ml) was added dropwise to a stirred solution of pent-4-enylmagnesium bromide, [prepared from pent-4-enyl bromide (11.60 g, 77.83 mmol) and Mg (2.0 g, 82.27 mmol)] in dry THF (150 ml) at room temperature under argon. After the reaction mixture had been stirred for 5 d at 50 °C, it was quenched with water (10 ml) and filtered through a little Celite. The filtrate was dried over Na_2SO_4 and concentrated under reduced pressure to give a pale yellow oil, which was subjected to column chromatography on silica gel with CH_2Cl_2–hexane (1 : 2 v/v) to give the amine (**10**) as a colorless oil. Yield: 96%. $[\alpha]_D$ −21.78° ($c=1.02$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.50 (3H, t, $J=6.7$ Hz, CH_3), 0.75—1.96 (10H, m, 5 × CH_2), 2.16 (1H, br s, OH), 2.84 (1H, m, NCH), 3.74 (1H, dd, $J=7.3$, 11.0 Hz, CH_2OH), 3.99 (1H, dd, $J=7.9$, 11.0 Hz, CH_2OH), 4.34 (1H, dd, $J=7.3$, 7.9 Hz, PhCHN), 4.80—5.01 (2H, m, $CH=CH_2$), 5.19 (1H, s, Ph_2CH), 5.75 (1H, ddt, $J=6.7$, 10.4, 17.1 Hz, $CH=CH_2$), 7.06—7.48 (15H, m, aromatic H). IR ($CHCl_3$): 3630, 3480, 3070, 2860, 1640, 1600, 1450, 1350, 1010, 910 cm^{-1}. MS *m/z*: CI, 428 ($M^+ + 1$), 410 ($M^+ - OH$), 396 ($M^+ - CH_2OH$); EI, 396 ($M^+ - CH_2OH$), 167 (base peak). The product was too unstable to give a satisfactory microanalysis.

(*R*)-6-{(Diphenylmethyl)[(*R*)-2-hydroxy-1-phenylethyl]amino}-2-nonanone (11) Oxygen was bubbled into a stirred mixture of **10** (3.0 g, 7.03 mmol), $(MeCN)_2PdCl_2$ (175.5 mg, 0.7 mmol) and $CuCl_2$ (1.23 g, 9.14 mmol) in methanol (70 ml) at room temperature for 4 h. The catalyst was filtered off, the catalyst was washed with methanol, and the combined filtrates were evaporated under reduced pressure. The resulting residue was dissolved in 10% ammonia water (30 ml) and benzene (30 ml) and extracted with benzene (3 × 20 ml). The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated to give a brown oil. This was subjected to column chromatography on silica gel with ethyl acetate–hexane (1 : 3 v/v) to give the ketone (**11**) as colorless needles. Yield: 63%; mp 118.5 °C (from hexane). $[\alpha]_D$ −29.48° ($c=1.04$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.52 (3H, t, $J=6.7$ Hz, CH_3), 0.77—1.85 (8H, m, 4 × CH_2), 2.06 (3H, s, $COCH_3$), 2.12 (1H, br s, OH), 2.23 (2H, t, $J=7.3$ Hz, CH_2COCH_3), 2.81 (1H, m, NCH), 3.78 (1H, dd, $J=7.9$, 11.0 Hz, CH_2OH), 3.99 (1H, dd, $J=7.9$, 11.0 Hz, CH_2OH), 4.34 (1H, t, $J=7.9$ Hz, PhCHN), 5.18 (1H, s, Ph_2CH), 7.06—7.48 (15H, m, aromatic H). IR ($CHCl_3$): 3490, 2940, 1710, 1600, 1450, 1160, 1010 cm^{-1}. MS *m/z*: CI, 444 ($M^+ + 1$), 412 ($M^+ - CH_2OH$); EI, 412 ($M^+ - CH_2OH$), 167 (base peak). *Anal.* Calcd for $C_{30}H_{37}NO_2$: C, 81.22; H, 8.41; N, 3.16. Found: C, 81.31; H, 8.46; N, 3.11.

(2*R*,6*S*)-Dihydropinidine Hydrochloride (12) A solution of **11** (643.22 mg, 1.45 mmol) in methanol (20 ml) and 3% aqueous HCl (4 ml) was hydrogenated over 10% palladium on carbon (70 mg) at atmospheric pressure for 3 d. The reaction mixture was then filtered through a little Celite and the filtrate was diluted with water–ether (1 : 2 v/v; 10 ml). The aqueous layer was separated and concentrated under reduced pressure to give a crystalline residue, which was recrystallized from ether to afford the (2*R*,6*S*)-dihydropinidine hydrochloride (**12**) as colorless needles. Yield: 90%; mp 234 °C (from ether). $[\alpha]_D$ −12.74° ($c=0.47$, EtOH). {lit.,[8] (2*R*,6*S*)-**12**; $[\alpha]_D$ −12.7° ($c=2.00$, EtOH)}. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, t, $J=7.3$ Hz, CH_2CH_3), 1.31—2.11 (10H, m, 5 × CH_2), 1.58 (3H, d, $J=6.1$ Hz, $CHCH_3$), 2.71—3.09 (2H, m, CHNCH), 9.07, 9.43 (2H, br s, N^+H2).

References and Notes

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