Pergamon

Tetrahedron 55 (1999) 13947–13956

TETRAHEDRON

Diastereoselective Allylation and Alkylation of Optically Active Imines with Metallic Samarium and a Catalytic Amount of Iodine

Reiko Yanada,* Nobuyuki Negoro, Masanori Okaniwa, Toshiro Ibuka*

Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan

Received 24 August 1999; accepted 30 September 1999

Abstract: Barbier-type allylation and alkylation of optically active imines such as *N*-benzylidenevalinol methyl ether was performed with metallic samarium, a catalytic amount of iodine, and allyl or alkyl halides. This reaction proceeded in a highly diastereoselective manner in THF at room temperature.

Keyword: samarium, allylation, imine, chelation

Introduction

Samarium reagents have quite unique and useful properties such as long ion radius, high coordination number, strong Lewis acidity, and high oxophilicity. So the chemistry of samarium reagents to oxygen functional groups, especially carbonyl groups, has been extensively developed. Recently, several examples where high stereoselectivity was achieved by chelation between the Sm(III) cation and oxygen functional groups were reported.[1] The chemistry by the use of metallic samarium (Sm) is of current interest in organic synthesis. Though samarium iodide (SmI_2) is a good synthetic tool (a mild, neutral and ether-soluble one-electron reductant),[2] its sensitivity to air makes it rather difficult to handle. We have been studying the direct use of Sm to improve on this shortcoming of SmI_2.[3] The mildness and operational simplicity of this new protocol encouraged us to further investigate the scope and utility with a series of representative chiral imines. We report here the details of the diastereoselective Barbier-type allylation and alkylation of optically active imines with Sm and a catalytic amount of iodine.[3i]

Results and Discussion

Three types of imines, *N*-benzylidene amino acid alkyl ester (**1a**), *N*-benzylidene amino alcohol (**1b**), and *N*-benzylidene amino alcohol alkyl ethers (**1c-1l**), have been used for optically active substrates. The former two have been used for Barbier-type allylation and alkylation of imine to produce chiral amines.[4] No example has been reported on such reaction of *N*-benzylidene amino alcohol alkyl ethers (**1c-1l**), although some Grignard-type reactions have been reported.[5]

To determine the proper molecular ratio between Sm and iodine, allylation of imine (**1c**) (0.3 mmol) with allyl bromide (0.6 mmol), Sm (0.63 mmol) and various amounts of iodine (0.0-0.3 mmol) was examined in THF at room temperature (Table 1). No reaction occured without iodine (Entry 1). Addition of one mol eq. iodine to **1c** gave **2c** and **3c** accompanied with the starting material **1c** (30 %) (Entry 2). Addition of 0.1 mol eq. iodine was the best condition (Entry 4). The amounts of by-products increased when the THF volume was decreased (Entry 5). The major by-products are an amine produced by simple reduction of carbon-nitrogen double bond and C_2-2,2'-ethylenediimino-diethanol derivative produced by the intermolecular pinacol-like radical coupling of imine **1c**.[3j]

*E-mail: ryanada@pharm.kyoto-u.ac.jp
tibuka@pharm.kyoto-u.ac.jp

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00854-6

Table 2 summarizes the results of the allylation of imines. Ester-type imine **1a** gave a complex mixture (Entry 1). The ester moiety might be also changed because we were unable to detect the starting material after the reaction mixture was worked up. Alcohol-type imine **1b** gave allylation products in 47% yield in low diastereoselectivity (**2b**:**3b** = 62:38) and a simple reduction product, 2-hydroxy-1-isopropylbenzylamine in 30% yield (Entry 2). Among the imines (**1a-1d**), methyl ether-type imine **1c** was the best substrate to give allylation products in good yield (85%) and in high diastereoselectivity (**2c**:**3c** = 96:4) (Entry 3). The absolute configurations of **2c** (*S*, *S*) and **3c** (*R*, *S*) were determined by comparison with the authentic samples prepared by *O*-methylation of known products **2b** (*S*, *S*) and **3b** (*R*, *S*).[6] Unfortunately, the reaction of **1c** with allyl iodide, cinnamyl bromide, and prenyl bromide gave a complex mixture (Entries 4-6). Benzyl ether-type imine **1d** gave allylation products in 79% yield and in high diastereoselectivity (**2d**:**3d** = 97:3) (Entry 7). The absolute configuration of them was determined by comparison with the authentic samples prepared by *O*-benzylation of **2b** and **3b**. More bulkiness (phenyl, isopropyl, ethyl, and methyl) at the α position from the amino group in methyl ether-type imines increased the diastereoselectivity of allylation (Entries 11, 3, 8, and 9). Imine **1h** derived from (*R*)-phenylglycinol gave only one diastereomer **3h** in 77% yield and the other diastereomer could not be detected by ^{1}H-NMR (Entry 11). The substituent, such as phenyl, at the β-position of the amino group did not exert any influence upon the diastereoselectivity (Entries 9 and 10).

Table 3 shows that the allylation of imines, prepared from (*S*)-Valinol, with allyl bromide was considerably influenced by the substituents on the aryl group (Entries 1-3). Imine **1k**, bearing a 2-methoxyphenyl group, showed high diastereoselectivity (99:1) (Entry 3). This implies that the 2-methoxy group on phenyl also coordinates to the Sm(III) cation in the intermediate and constructs a stronger stereostructure. Imine **1l**, which has a 1-naphthyl group, gave the product in 62% yield with some by-products (Entry 4).

The chiral allylation product was readily converted into optically active homoallylic amine. For example, **2c** was converted into the optically pure (*S*)-**4** in 85% yield by demethylation with boron tribromide (BBr_3) in hexane-chloroform followed by oxidative cleavage of the C-N bond according to the Umani-Ronchi-Savoia's procedure[6b] (Scheme 1). Chiral homoallylamines are synthons for further transformation, for example, to 1,3-amino alcohols, 1-amino-3,4-epoxides, and β-amino acids. β-Amino acids are receiving attention for the synthesis of β-lactam antibiotics.[7]

Next we tried the alkylation of optically active imines. Table 4 represents the results. Alkylated amines **5** and **6** were obtained in good yield and in high diastereoselectivity (Entries 2, 3, 9, 10). The reaction with **1c** and *i*-PrI or *i*-PrBr gave poor yield and low diastereoselectivity (Entries 4 and 5). The reaction of BnBr with **1c** or **1j** gave the expected products in low yield and high diastereoselectivity (Entries 6 and 8). The major product was dibenzyl. It is well known that the exposure of benzyl bromide to SmI_2 leads cleanly to a dimerization product. The reaction with Sm probably proceeded in a similar manner as with SmI_2. This could be understandable by considering that the concentration of the benzyl radical is high

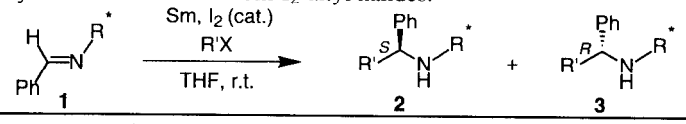
Table 1. Allylation of imine (**1c**) with Sm-I_2-allyl bromides

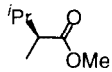
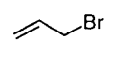
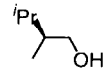
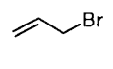
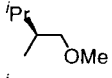
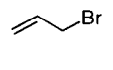
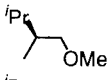
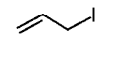
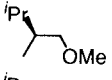
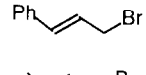
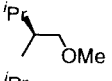
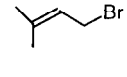
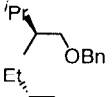
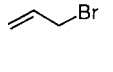
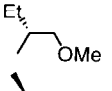
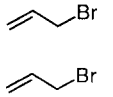
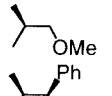
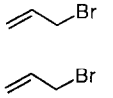
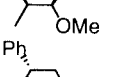
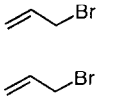
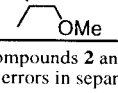
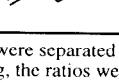
Entry	I_2 (eq.)	THF (ml)	Yield[a] (%)	Ratio[b] **2c** : **3c**
1	-	2	0	-
2	1.0	2	24	95 : 5
3	0.6	2	74	95 : 5
4	0.1	2	85	96 : 4
5	0.1	1	80	95 : 5

[a] Isolated yield.

[b] The ratios were determined on the basis of their ^{1}H NMR spectra.

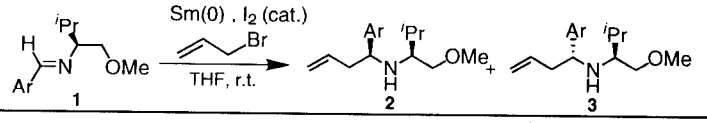
Table 2. Allylation of imines with Sm-I_2-allyl halides.



Entry	Imine	R*	R'X	Product	Yield (%)[a] 2 + 3	Ratio[b] 2 : 3
1	**1a**			complex mixture	-	-
2	**1b**			**2b , 3b**	47	62 : 38
3	**1c**			**2c , 3c**	85	96 : 4
4	**1c**			complex mixture	-	-
5	**1c**			complex mixture	-	-
6	**1c**			complex mixture	-	-
7	**1d**			**2d , 3d**	79	97 : 3
8	**1e**			**2e , 3e**	73	7 : 93
9	**1f**			**2f , 3f**	74	90 : 10
10	**1g**			**2g , 3g**	75	91 : 9
11	**1h**			**3h**	77	<1 : >99

[a] Isolated yield. [b] Compounds **2** and **3** were separated by flash column chromatography. In order to minimize the consequences of errors in separating, the ratios were determined on the basis of their ^{1}H NMR spectra.

Table 3. Allylation of imines with Sm-I_2-allyl bromide.

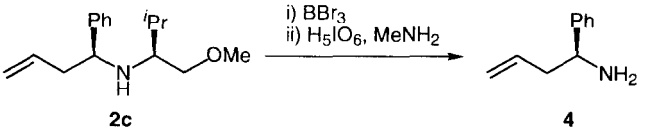


Entry	Imine	Ar	Product	Yield (%)[a] 2 + 3	Ratio[b] 2 : 3
1	**1i**	4-NC-C_6H_4	complex mixture	-	-
2	**1j**	4-MeO-C_6H_4	**2j , 3j**	93	97 : 3
3	**1k**	2-MeO-C_6H_4	**2k , 3k**	77	99 : 1
4	**1l**	1-naphthyl	**2l , 3l**	62	92 : 8

[a] Isolated yield.

[b] Compounds **2** and **3** were separated by flash column chromatography. In order to minimize the consequences of errors in separating, the ratios were determined on the basis of their ^{1}H NMR spectra.

Scheme 1. Preparation of chiral homoallylamine **4**.



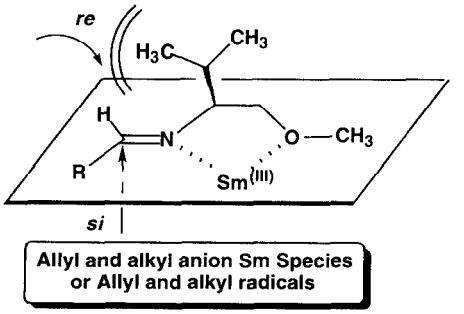
2c **4**

under our reaction conditions, thus the benzyl-benzyl coupling reaction becomes faster than the benzyl-imine coupling.[8] No reaction occurred when lower reactive benzyl chloride was used instead of benzyl bromide, although benzyl-benzyl coupling reaction by benzyl chloride with SmI_2 proceeds slowly (Entry 7).[9]

The configuration of the allyl or alkyl group in chiral amines could readily determined by ^{1}H-NMR spectroscopy. The characteristic ^{1}H-NMR peaks of the methoxy group of the chiral amines (**2**, **3**, **5**, and **6**) are summarized in Table 5. The peaks of the methoxy groups of major chiral amines were shifted to lower field in comparison with the minor ones except the benzylated products **5e** and **5f**. The chemical shifts of methoxy group of them are 3.11 and 3.12 ppm respectively. The absolute configuration of the demethylated product of **5e** by BBr_3 was determined by comparison with the known compound.[10]

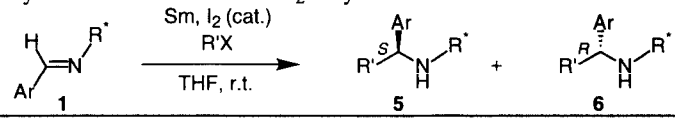
It is thought that there might be some competitive reaction mechanisms.[11] Fig 1 shows one of the plausible reaction mechanism. The formation of an allyl and alkyl anion Sm species or allyl and alkyl radicals is predominant because there is little C_2-2,2'-ethylenediimino-diethanol derivatives or amines under these experimental conditions.[3j] The Sm(III) species, which was probably deposited in the reaction mixture during the short induction period, is a strong Lewis acid. It would coordinate the nitrogen and oxygen atoms of the imine. In the case of imine **1c** derived from the (*S*)-valinol methyl ether, the bulky isopropyl group is oriented *re* face and obstructs the approach of the allyl samarium species from the *re* face. The nucleophilic species then approaches from the less hindered side *si* face to give the (*S*, *S*) isomer **2c** selectively.

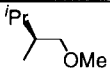
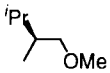
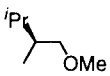
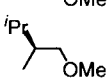
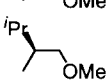
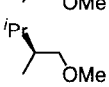
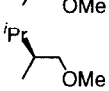
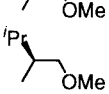
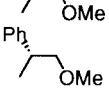
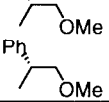
Figure 1. Plausible mechanism of Barbier-type allylation and alkylation with Sm and iodine (cat.).



In conclusion, the first diastereoselective Barbier-type allylation and alkylation of optically active imines was performed with Sm and a catalytic amount of iodine with high asymmetric induction. The optically pure homoallylic amines and alkylamines can be obtained easily.

Table 4. Alkylation of imines with Sm-I_2-alkyl halides.



Entry	Imine	Ar	R*	R'X	Product	Yield (%)[a] (5 + 6)	Ratio[b] (5 : 6)
1	**1c**	Ph		MeI	**5a , 6a**	85	(78 : 22)[c]
2	**1c**	Ph		EtI	**5b , 6b**[d]	90	96 : 4
3	**1c**	Ph		*n*-PrI	**5c , 6c**	90	94 : 6
4	**1c**	Ph		*i*-PrI	**5d , 6d**	29[e]	60 : 40
5	**1c**	Ph		*i*-PrBr	**5d , 6d**	41[e]	67 : 33
6	**1c**	Ph		BnBr	**5e , 6e**	33[e]	>99 : 1
7	**1c**	Ph		BnCl	-	0	-
8	**1j**	4-MeO-C_6H_4		BnBr	**5f , 6f**	34[e]	>99 : 1
9	**1h**	Ph		EtI	**5g , 6g**	86	1 : >99
10	**1h**	Ph		*n*-PrI	**5h , 6h**	73	6 : 94

[a] Isolated yield.
[b] Compounds **5** and **6** were separated by flash column chromatography. In order to minimize the consequences of errors in separating, the ratios were determined on the basis of their ^{1}H NMR spectra.
[c] Compound **5** and **6** could not be separated. The number in parenthesis was determined by ^{1}H-NMR integration.
[d] Reference 4(a).
[e] Amines and C_2-dimers were obtained as by-products. Reference 3(j).

Table 5. ^{1}H-NMR characteristics of diastereomeric amines **2**, **5** and **3**, **6**; chemical shifts (ppm from TMS) of the methoxy group in $CDCl_3$.

Compound	2	3	Compound	5	6
	δ (OCH_3)			δ (OCH_3)	
c	3.32	3.17	**a**	3.33	3.21
e	3.22	3.33	**b**	3.33	3.18
f	3.34	3.25	**c**	3.33	3.17
g	3.32	3.20	**d**	3.34	3.14
h	-	3.34	**e**	3.11	-
j	3.32	3.18	**f**	3.12	-
k	3.32	3.17	**g**	-	3.33
l	3.33	3.16	**h**	3.25	3.34

Experimental

General: All reactions were carried out under a positive pressure of argon or nitrogen. ^{1}H-NMR spectra were recorded on a JEOL JNM-EX-270 spectrometer using tetramethylsilane (TMS) as an internal standard. ^{13}C-NMR spectra were recorded on a JEOL JNM-EX-270 (67.8MHz) spectrometer. Optical rotations were measured with a JASCO DIP-360 digital polarimeter. Nominal (LRMS) and exact mass (HRMS) spectra were recorded on a JEOL JMS-HX/HX-110A instrument. Metallic samarium was purchased from Kojundo Chemical Laboratory Co., Ltd.

General procedure for the preparation of allylated and alkylated amines 2, 3, 5, and 6.

A mixture of imine (0.30 mmol), Sm (95 mg, 0.63 mmol), iodine (8 mg, 0.03 mmol), and allyl or alkyl halides (0.60 mmol) was stirred in THF (2 ml) at room temperature under argon or nitrogen for 30 min. The color changes of the mixture during the reaction served as indicator of the progress of the reaction. After a short induction period, the color of the solution turned to black-purple and then dark blue-green. After the reaction was quenched with 1*N*-hydrochloric acid and the resulting mixture was made basic with 10% NaOH aq., the product was extracted with diethyl ether, washed with brine, dried over anhydrous potassium carbonate, and concentrated under reduced pressure. Silica gel column chromatography or preparative thin-layer chromatography affroded pure **2**, **3**, **5**, and **6**.

(*S*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-phenyl-3-butenylamine (**2c**); a pale yellow oil: $[\alpha]_D^{20}$ -84.1 (c 2.07, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.79 (d, 3H, *J* = 6.9 Hz), 0.85 (d, 3H, *J* = 6.6 Hz), 1.57 (bs, 1H), 1.65 (m, 1H), 2.21 (ddd, 1H, *J* = 4.3, 4.5, 4.6 Hz), 2.33-2.39 (m, 2H), 3.31 (dd, 1H, *J* = 4.5, 9.7 Hz), 3.32 (s, 3H), 3.42 (dd, 1H, *J* = 4.6, 9.7 Hz), 3.78 (t, 1H, *J* = 6.8 Hz), 5.00-5.12 (m, 2H), 5.63-5.78 (m, 1H), 7.18-7.36 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 19.1, 19.4, 30.1, 43.8, 59.1, 59.7, 60.3, 72.1, 117.3, 127.0, 127.8, 128.3, 135.9, 145.0. LRMS (CI) *m/z*, 248 (MH^+), 206, 202, 170, 159, 131. HRMS Calcd for $C_{16}H_{26}NO$ (MH^+): 248.2016. Found: 248.2021.

(*R*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-phenyl-3-butenylamine (**3c**); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.86 (d, 3H, *J* = 6.8 Hz), 0.91 (d, 3H, *J* = 6.8 Hz), 1.76 (bs, 1H), 1.85-1.93 (m, 1H), 2.36-2.47 (m, 3H), 3.15-3.20 (m, 2H), 3.17 (s, 3H), 3.73 (dd, 1H, *J* = 6.5, 7.3 Hz), 4.98-5.10 (m, 2H), 5.66-5.80 (m, 1H), 7.19-7.35 (m, 5H). LRMS (CI) *m/z*, 248 (MH^+), 216, 206, 170, 131. HRMS Calcd for $C_{16}H_{26}NO$ (MH^+): 248.2016. Found: 248.2009.

(*S*)-*N*-((*S*)-1-(benzyloxymethyl)-2-methylpropyl)-1-phenyl-3-butenylamine (**2d**); a pale yellow oil: $[\alpha]_D^{20}$ -88.5 (c 1.02, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.78 (d, 3H, *J* = 6.6 Hz), 0.85 (d, 3H, *J* = 6.9 Hz), 1.62 (bs, 1H), 1.62-1.75 (m, 1H), 2.20-2.25 (m, 1H), 2.30-2.40 (m, 2H), 3.40 (dd, 1H, *J* = 4.3, 9.6 Hz), 3.52 (dd, 1H, *J* = 4.3, 9.6 Hz), 3.75 (dd, 1H, *J* = 6.3, 7.6 Hz), 4.50 (s, 2H), 4.98-5.10 (m, 2H), 5.60-5.75 (m, 1H), 7.17-7.40 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 19.2, 19.6, 30.3, 43.9, 59.7, 60.2, 69.3, 73.4, 117.4, 127.0, 127.7, 127.7, 127.8, 128.2, 128.5, 136.0, 138.9, 144.9. LRMS (FAB) *m/z*, 324 (MH^+), 282, 202, 131, 91. HRMS Calcd for $C_{22}H_{30}NO$ (MH^+): 324.2329. Found: 324.2332.

(*R*)-*N*-((*S*)-1-(benzyloxymethyl)-2-methylpropyl)-1-phenyl-3-butenylamine (**3d**); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.85 (d, 3H, *J* = 6.9 Hz), 0.91 (d, 3H, *J* = 6.9 Hz), 1.62 (bs, 1H), 1.88-1.96 (m, 1H), 2.35-2.42 (m, 2H), 2.50 (dd, 1H, *J* = 5.6, 10.2 Hz), 3.25-3.34 (m, 2H), 3.73 (t, 1H, *J* = 6.8 Hz), 4.33 (s, 2H), 4.98-5.09 (m, 2H), 5.66-5.79 (m, 1H), 7.19-7.42 (m, 10H). LRMS (FAB) *m/z*, 324 (MH^+), 282, 202, 131, 91. HRMS Calcd for $C_{22}H_{30}NO$ (MH^+): 324.2329. Found: 324.2322.

(*S*)-*N*-((*R*)-1-(methoxymethyl)propyl)-1-phenyl-3-butenylamine (**2e**); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.83(t, 3H), 1.44 (m, 2H,), 1.81 (bs, 1H), 2.37-2.44 (m, 2H), 2.46-2.53 (m, 1H), 3.21 (d, 2H, *J* = 6.3 Hz), 3.22 (s, 3H), 3.77 (t, 1H, *J* = 6.9 Hz), 4.99-5.10 (m, 2H), 5.63-5.79 (m, 1H), 7.20-7.36 (m, 5H). LRMS (FAB) *m/z*, 234 (MH^+), 192, 188, 131. HRMS Calcd for $C_{15}H_{24}NO$ (MH^+): 234.1859. Found: 234.1860.

(*R*)-*N*-((*R*)-1-(methoxymethyl)propyl)-1-phenyl-3-butenylamine (**3e**); a pale yellow oil: $[\alpha]_D^{19}$ 48.8 (c 1.26, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.79 (t, 3H, *J* = 7.6 Hz), 1.34 (dq, 2H, *J* = 4.6, 7.6 Hz), 1.82 (s, 1H), 2.35-2.46 (m, 3H), 3.23 (dd, 1H, *J* = 4.6, 9.4 Hz), 3.37 (dd, 1H, *J* = 4.6, 9.4 Hz), 3.33 (s, 3H), 3.80 (t, 1H, *J* = 6.8 Hz), 5.06-5.11 (m, 2H), 5.62-5.78 (m, 1H), 7.22-7.35 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 10.7, 26.0, 43.7,

56.2, 59.2, 60.3, 73.9, 117.4, 127.0, 127.5, 128.4, 135.8, 145.0. LRMS (FAB) *m/z*, 234 (MH^+), 232, 202, 192, 188, 131. HRMS Calcd for $C_{15}H_{24}NO$ (MH^+): 234.1859. Found: 234.1852.

(*S*)-*N*-((*S*)-2-methoxy-1-methylethyl)-1-phenyl-3-butenylamine (2f); a pale yellow oil: $[\alpha]_D^{20}$ -40.8 (c 3.55, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.89 (d, 3H, *J* = 6.8 Hz), 1.82 (bs, 1H), 2.17-2.41 (m, 2H), 2.76 (dd, 1H, *J* = 5.6, 6.8 Hz), 3.22 (dd, 1H, *J* = 5.6, 9.5 Hz), 3.31 (dd, 1H, *J* = 5.6, 9.5 Hz), 3.34 (s, 3H), 3.77 (t, 1H, *J* = 6.8 Hz), 5.01-5.12 (m, 2H), 5.62-5.77 (m, 1H), 7.18-7.36 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 19.2, 43.5, 50.8, 59.1, 60.7, 76.5, 117.5, 127.0, 127.4, 128.4, 136.5, 145.1. LRMS (FAB) *m/z*, 220 (MH^+), 178, 131. HRMS Calcd for $C_{14}H_{22}NO$ (MH^+): 220.1703. Found: 220.1708.

(*R*)-*N*-((*S*)-2-methoxy-1-methylethyl)-1-phenyl-3-butenylamine (3f); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.97 (d, 3H, *J* = 6.6 Hz), 1.83 (bs, 1H), 2.38-2.48 (m, 2H), 2.62-2.69 (m, 1H), 3.13-3.23 (m, 2H), 3.25 (s, 3H), 3.79 (t, 1H, *J* = 6.9 Hz), 4.98-5.09 (m, 2H), 5.60-5.76 (m, 1H), 7.19-7.40 (m, 5H). LRMS (FAB) *m/z*, 220 (MH^+), 178, 131. HRMS Calcd for $C_{14}H_{22}NO$ (MH^+): 220.1703. Found: 220.1700.

(*S*)-*N*-((1*S*,2*R*)-2-methoxy-1-methyl-2-phenylethyl)-1-phenyl-3-butenylamine (2g); a pale yellow oil: $[\alpha]_D^{20}$ -70.6 (c 1.26, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.83 (d, 3H, *J* = 6.9 Hz), 1.88 (bs, 1H), 2.27-2.39 (m, 2H), 2.61 (dq, 1H, *J* = 4.0, 6.9 Hz), 3.32 (s, 3H), 3.79 (dd, 1H, *J* = 5.6, 8.1 Hz), 4.30 (d, 1H, *J* = 4.0 Hz), 5.00-5.10 (m, 2H), 5.59-5.74 (m, 1H), 7.12-7.38 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 16.2, 43.7, 56.0, 57.7, 60.1, 84.4, 117.6, 127.0, 127.1, 127.3, 127.5, 128.3, 128.5, 135.7, 140.5, 144.8. LRMS (FAB) *m/z*, 296 (MH^+), 254, 174, 131. HRMS Calcd for $C_{20}H_{26}NO$ (MH^+): 296.2016. Found: 296.2021.

(*R*)-*N*-((1*S*,2*R*)-2-methoxy-1-methyl-2-phenylethyl)-1-phenyl-3-butenylamine (3g); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.97 (d, 3H, *J* = 6.3 Hz), 1.73 (bs, 1H), 2.30-2.36 (dd, 2H, *J* = 6.6, 6.9 Hz), 2.59 (dq, 1H, *J* = 5.3, 6.3 Hz), 3.20 (s, 3H), 3.76 (dd, 1H, *J* = 6.6, 6.9 Hz), 4.03 (d, 1H, *J* = 5.3 Hz), 4.96-5.06 (m, 2H), 5.56-5.72 (m, 1H), 7.09-7.34 (m, 10H). LRMS (FAB) *m/z*, 296 (MH^+), 254, 174, 131. HRMS Calcd for $C_{20}H_{26}NO$ (MH^+): 296.2016. Found: 296.2007.

(*R*)-*N*-((*R*)-2-methoxy-1-phenylethyl)-1-phenyl-3-butenylamine (3h); a pale yellow oil: $[\alpha]_D^{20}$ -12.1 (c 1.29, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 2.48 (m, 2H), 2.53 (bs, 1H), 3.34 (s, 3H), 3.44-3.52 (m, 2H), 3.71 (t, 1H, *J* = 6.6 Hz), 3.95 (dd, 1H, *J* = 5.3, 6.6 Hz), 4.98-5.09 (m, 2H), 5.57-5.72 (m, 1H), 7.13-7.26 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 41.5, 59.0, 60.3, 60.4, 77.2, 117.5, 126.8, 127.2, 127.5, 127.8, 128.2, 128.3, 135.3, 141.8, 144.4. LRMS (FAB) *m/z*, 282 (MH^+), 240, 131. HRMS Calcd for $C_{19}H_{24}NO$ (MH^+): 282.1859. Found: 282.1862.

(*S*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-(4-methoxyphenyl)-3-butenylamine (2j); a pale yellow oil: $[\alpha]_D^{20}$ -84.7 (c 1.05, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.78 (d, 3H, *J* = 6.9 Hz), 0.85 (d, 3H, *J* = 6.9 Hz), 1.56 (bs, 1H), 1.62 (m, 1H), 2.20 (ddd, 1H, *J* = 1.3, 4.2, 9.9 Hz), 2.31-2.36 (m, 2H), 3.31 (dd, 1H, *J* = 4.2, 9.7 Hz), 3.32 (s, 3H), 3.41 (dd, 1H, *J* = 4.2, 9.7 Hz), 3.74 (t, 1H, *J* = 6.7 Hz), 3.79 (s, 3H), 4.99-5.10 (m, 2H), 5.62-5.77 (m, 1H), 6.81-6.86 (m, 2H), 7.22-7.27 (m, 2H). ^{13}C-NMR ($CDCl_3$) δ: 19.1, 19.5, 30.1, 43.9, 55.4, 59.1, 59.6, 59.7, 72.2, 113.6, 117.2, 128.7, 136.0, 137.0, 158.7. LRMS (FAB) *m/z*, 278 (MH^+), 236, 161. HRMS Calcd for $C_{17}H_{28}NO$ (MH^+): 278.2121. Found: 278.2114.

(*R*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-(4-methoxyphenyl)-3-butenylamine (3j); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.85 (d, 3H, *J* = 6.9 Hz), 0.90 (d, 3H, *J* = 6.9 Hz), 1.61 (bs, 1H), 1.82-1.92 (m, 1H), 2.30-2.47 (m, 3H), 3.11-3.18 (m, 2H), 3.18 (s, 3H), 3.68 (t, 1H, *J* = 6.9 Hz), 3.80 (s, 3H), 4.99-5.08 (m, 2H), 5.65-5.81 (m, 1H), 6.85 (d, 2H, *J* = 8.6 Hz), 7.21 (d, 2H, *J* = 8.6 Hz). LRMS (FAB) *m/z*, 278 (MH^+), 236, 232, 161. HRMS Calcd for $C_{17}H_{28}NO$ (MH^+): 278.2121. Found: 278.2123.

(*S*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-(2-methoxyphenyl)-3-butenylamine (2k); a pale yellow oil: $[\alpha]_D^{20}$ -92.7 (c 1.03, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.80 (d, 3H, *J* = 6.9 Hz), 0.89 (d, 3H, *J* = 6.9 Hz), 1.69 (m, 1H), 1.73 (bs, 1H), 2.22 (dd, 1H, *J* = 4.8, 10.2 Hz), 2.30-2.52 (m, 2H), 3.32 (s, 3H), 3.32 (dd, 1H, *J* = 4.8, 9.6 Hz), 3.40 (dd, 1H, *J* = 4.9, 9.6 Hz), 3.81 (s, 3H), 4.15 (t, 1H, *J* = 6.9 Hz), 4.95-5.08 (m, 2H), 5.65-5.80 (m, 1H), 6.84 (dd, 1H, *J* = 1.0, 7.9 Hz), 6.92 (ddd, 1H, *J* = 1.0, 7.5, 7.8 Hz), 7.19 (ddd, 1H, *J* = 1.8, 7.8, 7.9 Hz), 7.39 (dd, 1H, *J* = 1.8, 7.5 Hz). ^{13}C-NMR ($CDCl_3$) δ: 18.9, 19.4, 29.9, 41.6, 54.1, 55.4, 59.0, 59.9, 72.4, 110.5, 116.6, 120.6, 127.6, 128.8, 132.5, 136.6, 157.5. LRMS (FAB) *m/z*, 278 (MH^+), 236,161. HRMS Calcd for $C_{17}H_{28}NO_2$ (MH^+): 278.2121. Found: 278.2124.

(*R*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-(2-methoxyphenyl)-3-butenylamine (3k); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.85 (d, 3H, *J* = 6.9 Hz), 0.90 (d, 3H, *J* = 6.9 Hz), 1.69 (bs, 1H), 1.85-1.93 (m, 1H), 2.39-2.47 (m, 3H), 3.17 (s, 3H), 3.20 (dd, 2H, *J* = 5.9 Hz), 3.82 (s, 3H), 4.08 (dd, 1H, *J* = 6.9, 7.3

Hz), 4.93-5.06 (m, 2H), 5.72-5.83 (m, 1H), 6.83-6.96 (m, 2H), 7.16-7.34 (m, 2H). LRMS (FAB) *m/z*, 278 (MH^+), 236, 232, 161. HRMS Calcd for $C_{17}H_{28}NO_2$ (MH^+): 278.2121. Found: 278.2127.

(*S*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-(1-naphthyl)-3-butenylamine (2l); a pale yellow oil: $[\alpha]_D^{19}$ -102.0 (c 0.94, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.80 (d, 3H, *J* = 6.9 Hz), 0.89 (d, 3H, *J* = 6.9 Hz), 1.69 (m, 1H), 1.70 (bs, 1H), 2.28 (ddd, 1H, *J* = 1.3, 4.9, 9.4 Hz), 2.41-2.63 (m, 2H), 3.32 (dd, 1H, *J* = 4.6, 9.6 Hz), 3.33 (s, 3H), 3.46 (dd, 1H, *J* = 4.3, 9.7 Hz), 4.70 (dd, 1H, *J* = 4.6, 8.2 Hz), 5.04-5.17 (m, 2H), 5.73-5.88 (m, 1H), 7.42-7.53 (m, 3H), 7.71-7.88 (m, 3H), 8.28 (d, 1H, *J* = 7.6 Hz). ^{13}C-NMR ($CDCl_3$) δ: 19.4, 19.5, 30.4, 43.1, 55.5, 59.1, 60.2, 72.2, 117.5, 123.4, 125.0, 125.3, 125.7, 127.2, 129.1, 131.8, 134.2, 136.0, 140.5. LRMS (FAB) *m/z*, 298 (MH^+), 256, 181. HRMS Calcd for $C_{20}H_{28}NO$ (MH^+): 298.2172. Found: 298.2169.

(*R*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-(1-naphthyl)-3-butenylamine (3l); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.85 (d, 3H, *J* = 6.9 Hz), 0.95 (d, 3H, *J* = 6.9 Hz), 1.73 (bs, 1H), 1.84-1.96 (m, 1H), 2.39-2.68 (m, 3H), 3.16 (s, 3H), 3.30-3.52 (m, 2H), 4.65 (dd, 1H, *J* = 4.6, 8.2 Hz), 4.99-5.18 (m, 2H), 5.74-5.95 (m, 1H), 7.36-7.60 (m, 3H), 7.62-7.93 (m, 3H), 8.19 (d, 1H, *J* = 6.5 Hz). LRMS (FAB) *m/z*, 298 (MH^+), 256, 252, 181. HRMS Calcd for $C_{20}H_{28}NO$ (MH^+): 298.2172. Found: 298.2175.

Preparation of (*S*)-1-phenyl-3-butenylamine (4) A solution of 99 mg (0.4 mmol) of methyl ether **2c** in 2 ml chloroform cooled to -78°C was treated with 2 ml (1M in hexane, 2 mmol) of boron tribromide. After 30 min the reaction mixture was warmed to -20 °C, where stirring was continued for 6 hr. The reaction mixture was warmed to room temperature and was stirred an additional 30 min followed by addition of water. Isolation of the product by ethyl acetate extraction gave a crude material. Purification of silica gel column chromatography using chloroform gave 83 mg (89%) of a pure demethylated product[6]: a pale yellow oil: $[\alpha]_D^{24}$ -32.4 (c 2.0, $CHCl_3$). *Anal* Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.27; H, 10.06; N, 5.88. To a solution of the demethyled product in 2 ml MeOH was added 40% aqueous $MeNH_2$ (310 μl, 4.0 mmol) and H_5IO_6 (330 mg, 1.45 mmol) dissolved in H_2O (1 ml). The mixture was stirred magnetically over 15 hr, 10% aqueous NaOH (1.3 ml) was added, MeOH was removed under reduced pressure, and the organic phase was extracted with ethyl acetate. Drying and concentration afforded crude (*S*)-**4**. Silicagel column chromatography using hexane/AcOEt=1/5 afforded pure (*S*)-**4** (50 mg, 95%): $[\alpha]_D^{26}$ -44.2 (c 2.0, $CHCl_3$).[6b,12]

(*S*)-1-(methoxymethyl)-2-methyl-*N*-((*S*)-1-phenylethyl)propylamine (5a); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.79 (d, 3H, *J* = 6.6 Hz), 0.86 (d, 3H, *J* = 6.9 Hz), 1.33 (d, 3H, *J* = 6.6 Hz), 1.54 (bs, 1H), 1.62-1.75 (m, 1H), 2.26 (ddd, 1H, *J* = 4.6, 4.8, 5.6 Hz), 3.31 (dd, 1H, *J* = 4.8, 9.6 Hz), 3.33 (s, 3H), 3.44 (dd, 1H, *J* = 4.6, 9.6 Hz), 3.90 (q, 1H, *J* = 6.6 Hz), 7.17-7.36 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 18.8, 19.0, 25.1, 29.7, 55.7, 59.0, 59.6, 72.2, 126.9, 128.2, 128.3, 146.4. LRMS (CI) *m/z*, 222 (MH^+), 206, 176, 105. HRMS Calcd for $C_{14}H_{24}NO$ (MH^+): 222,1859. Found: 222.1861.

(*S*)-1-(methoxymethyl)-2-methyl-*N*-((*R*)-1-phenylethyl)propylamine (6a); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.86 (d, 3H, *J* = 6.9 Hz), 0.92 (d, 3H, *J* = 6.9 Hz), 1.33 (d, 3H, *J* = 6.6 Hz), 1.54 (bs, 1H), 1.83-1.91 (m, 1H), 2.26 (ddd, 1H, *J* = 4.6, 4.9, 5.6 Hz), 3.21 (s, 3H), 3.21-3.26 (m, 2H), 3.85 (q, 1H, *J* = 6.6 Hz), 7.17-7.36 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 17.7, 18.9, 24.7, 28.3, 55.5, 58.6, 58.7, 72.9, 126.6, 126.9, 128.2, 146.3. LRMS (CI) *m/z*, 222 (MH^+), 206, 176, 105. HRMS Calcd for $C_{14}H_{24}NO$ (MH^+): 222,1859. Found: 222.1858.

(*S*)-1-(methoxymethyl)-2-methyl-*N*-((*S*)-1-phenylpropyl)propylamine (5b); a pale yellow oil: $[\alpha]_D^{26}$ -90.7 (c 2.00, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.77 (d, 3H, *J* = 6.9 Hz), 0.80 (t, 3H, *J* = 7.4 Hz), 0.85 (d, 3H, *J* = 6.9 Hz), 1.57 (bs, 1H), 1.54-1.74 (m, 3H), 2.21 (dt, 1H, *J* = 3.9, 5.6 Hz), 3.32 (dd, 1H, *J* = 4.3, 9.8 Hz), 3.33 (s, 3H), 3.44 (dd, 1H, *J* = 4.5, 9.8 Hz), 3.59 (dd, 1H, *J* = 6.1, 7.4 Hz), 7.18-7.30 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 10.9, 18.9, 19.1, 29.8, 31.7, 58.9, 59.6, 62.6, 71.8, 126.6, 127.6, 127.9, 144.9. LRMS (CI) *m/z*, 236 (MH^+). HRMS Calcd for $C_{15}H_{26}NO$ (MH^+): 236.2016. Found: 236.2016.

(*S*)-1-(methoxymethyl)-2-methyl-*N*-((*R*)-1-phenylpropyl)propylamine (6b); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.82 (t, 3H, *J* = 6.8 Hz), 0.85 (d, 3H, *J* = 6.9 Hz), 0.91 (d, 3H, *J* = 6.9 Hz), 1.56-1.78 (m, 3H), 2.41-2.46 (m, 1H), 2.42 (dt, 1H, *J* = 4.6, 5.8 Hz), 3.18 (s, 3H), 3.19 (d, 2H, *J* = 3.9, 5.8 Hz), 3.54 (t, 1H, *J* = 7.0 Hz), 7.21-7.34 (m, 5H). LRMS (CI) *m/z*, 236 (MH^+). HRMS Calcd for $C_{15}H_{26}NO$ (MH^+): 236.2016. Found: 236.2010.

(*S*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-phenylbutylamine (5c); a pale yellow oil: $[\alpha]_D^{30}$ -90.2 (c 1.96, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.77 (d, 3H, *J* = 6.9 Hz), 0.85 (d, 3H, *J* = 6.9 Hz), 0.88 (d, 3H, *J* = 7.3 Hz), 1.17-1.31 (m, 2H), 1.53-1.70 (m, 4H), 2.20 (ddd, 1H, *J* = 4.3, 4.6, 5.9 Hz), 3.31 (dd, 1H, *J* = 4.3, 9.8 Hz), 3.33 (s, 3H), 3.43 (dd, 1H, *J* = 4.6, 9.8 Hz), 3.69 (t, 1H, *J* = 6.9,Hz), 7.18-7.30 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 14.0, 18.9, 19.1, 19.6, 29.8, 41.2, 59.0, 59.6, 60.7, 71.9, 126.6, 127.5, 128.0, 145.3. LRMS (CI) *m/z*, 250 (MH^+), 218, 204, 133. HRMS Calcd for $C_{16}H_{28}NO$ (MH^+): 250.2172. Found: 250.2165.

(*R*)-*N*-((*S*)-1-(methoxymethyl)-2-methylpropyl)-1-phenylbutylamine (6c); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.85 (d, 3H, *J* = 6.9 Hz), 0.88 (d, 3H, *J* = 8.3 Hz), 0.91 (d, 3H, *J* = 6.9 Hz), 1.17-1.34 (m, 2H), 1.53-1.71 (m, 3H), 1.84-1.91 (m, 1H), 2.42 (dt, 1H, *J* = 4.6, 5.6 Hz), 3.17 (s, 3H), 3.18 (d, 2H, *J* = 4.6 Hz), 3.63 (t, 1H, *J* = 6.9,Hz), 7.20-7.34 (m, 5H). LRMS (CI) *m/z*, 250 (MH^+), 218, 204, 133. HRMS Calcd for $C_{16}H_{28}NO$ (MH^+): 250.2172. Found: 250.2175.

(*S*)-1-(methoxymethyl)-2-methyl-*N*-((*S*)-2-methyl-1-phenylpropyl)propylamine (5d); a pale yellow oil: $[\alpha]_D^{30}$ -96.0 (c 1.32, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.73 (d, 3H, *J* = 6.6 Hz), 0.76 (d, 3H, *J* = 6.9 Hz), 0.85 (d, 3H, *J* = 6.9 Hz), 0.96 (d, 3H, *J* = 6.6 Hz), 1.57-1.68 (m, 2H), 1.76-1.84 (m, 1H), 2.10-2.16 (m, 1H), 3.32 (dd, 1H, *J* = 4.3, 9.6 Hz), 3.34 (s, 3H), 3.41 (d, 1H, *J* = 6.9 Hz), 3.42 (dd, 1H, *J* = 4.6, 9.6 Hz), 7.18-7.29 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 19.0, 19.3, 19.6, 19.7, 30.0, 34.8, 59.0, 59.7, 67.1, 71.5, 126.5, 127.8, 128.4, 143.8. LRMS (CI) *m/z*, 250 (MH^+), 218, 206, 133. HRMS Calcd for $C_{16}H_{28}NO$ (MH^+): 250.2172. Found: 250.2174.

(*S*)-1-(methoxymethyl)-2-methyl-*N*-((*R*)-2-methyl-1-phenylpropyl)propylamine (6d); a pale yellow oil: $[\alpha]_D^{30}$ 39.7 (c 0.84, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.72 (d, 3H, *J* = 6.6 Hz), 0.84 (d, 3H, *J* = 6.9 Hz), 0.91 (d, 3H, *J* = 6.9 Hz), 1.01 (d, 3H, *J* = 6.6 Hz), 1.65 (bs, 1H), 1.77-1.91 (m, 2H), 2.38 (dt, 1H, *J* = 4.6, 5.3 Hz), 3.14 (s, 3H), 3.15 (d, 2H, *J* = 5.3 Hz), 3.31 (d, 1H, *J* = 7.3 Hz), 7.19-7.33 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 17.5, 18.9, 19.8, 19.9, 28.1, 34.8, 58.5, 58.6, 67.0, 72.8, 126.4, 127.7, 127.8, 143.9. LRMS (CI) *m/z*, 250 (MH^+), 218, 206, 133. HRMS Calcd for $C_{16}H_{28}NO$ (MH^+): 250.2172. Found: 250.2167.

(*S*)-*N*-((*S*)-1,2-diphenylethyl)-1-(methoxymethyl)-2-methylpropylamine (5e); a pale yellow oil: $[\alpha]_D^{20}$ -29.7 (c 1.58, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.75 (d, 3H, *J* = 6.9 Hz), 0.81 (d, 3H, *J* = 6.9 Hz), 1.56 (bs, 1H), 1.58 (dqq, 1H, *J* = 6.3, 6.6, 6.9 Hz), 2.13 (ddd, 1H, *J* = 4.4, 5.6, 6.3 Hz), 2.82 (dd, 1H, *J* = 8.3, 13.5 Hz), 2.91 (dd, 1H, *J* = 5.6, 13.5 Hz), 3.11 (s, 3H), 3.19 (dd, 1H, *J* = 5.6, 9.6 Hz), 3.23 (dd, 1H, *J* = 4.4, 9.6 Hz), 3.97 (dd, 1H, *J* = 5.6, 8.3 Hz), 7.11-7.36 (m, 10H). LRMS (FAB) *m/z*, 298 (MH^+), 252, 206, 181. HRMS Calcd for $C_{20}H_{28}NO$ (MH^+): 298.2172. Found: 298.2173.

(*S*)-1-(methoxymethyl)-*N*-((*S*)-1-(4-methoxyphenyl)-2-phenylethyl)-2-methylpropylamine (5f); a pale yellow oil: $[\alpha]_D^{26}$ -220.6 (c 1.40, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.75 (d, 3H, *J* = 6.9 Hz), 0.81 (d, 3H, *J* = 6.9 Hz), 1.57 (bs, 1H), 1.57-1.65 (m, 1H), 2.12 (td, 1H, *J* = 4.3, 4.6 Hz), 2.81 (dd, 1H, *J* = 8.3, 13.4 Hz), 2.88 (dd, 1H, *J* = 5.9, 13.4 Hz), 3.12 (s, 3H), 3.19 (dd, 1H, *J* = 4.3, 9.9 Hz), 3.24 (dd, 1H, *J* = 4.6, 9.9 Hz), 3.79 (s, 3H), 3.92 (dd, 1H, *J* = 5.9, 8.3 Hz), 6.82 (d, 2H, *J* = 8.6 Hz), 7.24 (d, 2H, *J* = 8.6 Hz), 7.10-7.29 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 19.0, 19.3, 29.9, 45.9, 55.2, 58.8, 59.5, 61.7, 71.5, 113.4, 126.1, 128.2, 128.6, 129.3, 136.6, 139.3, 158.5. LRMS (CI) *m/z*, 328 (MH^+), 296, 236, 211. HRMS Calcd for $C_{21}H_{30}NO_2$ (MH^+): 328.2278. Found: 328.2274.

(*R*)-*N*-((*R*)-2-methoxy-1-phenylethyl)-1-phenylpropylamine (6g); a pale yellow oil: $[\alpha]_D^{30}$ -4.7 (c 2.00, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.74 (t, 3H, *J* = 7.5 Hz), 1.65-1.71 (m, 1H), 1.81-1.84 (m, 1H), 2.16 (bs, 1H), 3.33 (s, 3H), 3.47-3.55 (m, 3H), 3.93 (dd, 1H, *J* = 5.3, 6.9 Hz), 7.14-7.32 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 10.3, 29.2, 58.9, 60.1, 62.0, 77.2, 126.5, 27.0, 127.6, 128.0, 128.1, 128.4, 141.6, 144.3. LRMS (CI) *m/z*, 270 (MH^+), 238, 192. HRMS Calcd for $C_{18}H_{24}NO$ (MH^+): 270.1859. Found: 270.1855.

(*S*)-*N*-((*R*)-2-methoxy-1-phenylethyl)-1-phenylbutylamine (5h); a pale yellow oil: ^{1}H-NMR ($CDCl_3$) δ: 0.80 (t, 3H, *J* = 7.3 Hz), 1.12-1.21 (m, 1H), 1.25-1.34 (m, 1H), 1.51-1.68 (m, 2H), 1.74 (bs, 1H), 3.25 (s, 3H), 3.26-3.44 (m, 3H), 3.62 (dd, 1H, *J* = 4.0, 9.2 Hz), 7.12 (d, 2H, *J* = 8.3 Hz), 7.20-7.35 (m, 8H). LRMS (CI) *m/z*, 284 (MH^+), 252, 238, 206, 133. HRMS Calcd for $C_{19}H_{26}NO$ (MH^+): 284.2016. Found: 284.2021.

(*R*)-*N*-((*R*)-2-methoxy-1-phenylethyl)-1-phenylbutylamine (6h); a pale yellow oil: $[\alpha]_D^{27}$ -18.1 (c 1.00, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.84 (t, 3H, *J* = 7.3 Hz), 1.08-1.24 (m, 2H), 1.55-1.90 (m, 3H), 3.34 (s, 3H), 3.48-3.52 (m, 2H), 3.61 (dd, 1H, *J* = 5.6, 8.3 Hz), 3.93 (dd, 1H, *J* = 5.2, 6.8 Hz), 7.12-7.31 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 14.0, 19.2, 39.0, 58.9, 60.2, 60.6, 77.0, 126.6, 127.1, 127.3, 127.7, 127.9, 128.1, 141.5,

144.5. LRMS (CI) *m/z*, 284 (MH^+), 252, 238, 206, 133. HRMS Calcd for $C_{19}H_{26}NO$ (MH^+): 284.2016. Found: 284.2011.

References

1 (a) Molander, G. A.; Kenny, C. *Tetrahedron Lett.* **1987**, *28*, 4367. (b) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236. (c) Kan, T.; Hosokawa, S.; Nara, S.; Oikawa, M.; Ito, S.; Matsuda, F.; Shirahama, H. *J. Org. Chem.* **1994**, *59*, 5532. (d) Kawatsura, M.; Matsuda, F.; Shirahama, H. *J. Org. Chem.* **1994**, *59*, 6900. (e) Kawatsura, M.; Hosaka, K.; Matsuda, F.; Shirahama, H. *Synlett* **1995**, 729. (f) Matsuda, F. *J. Synth. Org. Chem. Jpn.* **1995**, *53*, 987. (g) Kawatsura, M.; Dekura, F.; Shirahama, H.; Matsuda, F. *Synlett* **1996**, 373. (h) Kito, M.; Sakai, T.; Haruta, N.; Shirahama, H.; Matsuda, F. *Synlett* **1996**, 1057. (i) Kawatsura, M.; Kishi, E.; Kito, M.; Sakai, T.; Shirahama, H.; Matsuda, F. *Synlett* **1997**, 479.

2 (a) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573. (b) Kagan, H. B. *Nouv. J. Chim.* **1990**, *14*, 453. (c) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29. (d) Molander, G. A. *Organic Reactions* **1994**, *46*, 211. (e) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307. (f) Krief, A.; Laval, A.-M. *Chem. Rev.* **1999**, *99*, 745.

3 (a) Ogawa, A.; Takami, N.; Sekiguchi, M.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 8729. (b) Ogawa, A.; Nanke, T.; Takami, N.; Sumino, Y.; Ryu, I.; Sonoda, N. *Chem. Lett.* **1994**, 379. (c) Murakami, M.; Hayashi, M.; Ito, Y. *Synlett* **1994**, 179. (d) Yanada, R.; Bessho, K.; Yanada, K. *Chem. Lett.* **1994**, 1279. (e) Yanada, R.; Bessho, K.; Yanada, K. *Synlett* **1995**, 443. (f) Yanada, R.; Negoro, N.; Bessho, K.; Yanada, K. *Synlett* **1995**, 1261. (g) Yanada, R.; Negoro, N.; Yanada, K.; Fujita, T. *Tetrahedron Lett.* **1996**, *37*, 9313. (h) Yanada, R.; Negoro, N.; Yanada, K.; Fujita, T. *Tetrahedron Lett.* **1997**, *38*, 3271. (i) Negoro, N.; Yanada, R.; Okaniwa, M.; Yanada, K.; Fujita, T. *Synlett* **1998**, 835. (j) Yanada, R.; Negoro, N.; Okaniwa, M.; Miwa, Y.; Taga, T.; Yanada, K.; Fujita, T. *Synlett* **1999**, 537.

4 Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, *8*, 1895, and references cited therein.

5 Grignard-type allylation to optically active imines (*N*-benzylidene amino alcohol alkyl ether type): (a) Suzuki, Y.; Takahashi, H. *Chem. Pharm. Bull.* **1983**, *31*, 2895. (b) Ukaji, Y.; Watai, T.; Sumi, T.; Fujisawa, T. *Chem. Lett.* **1991**, 1555. (c) Hashimoto, Y.; Takaoki, K.; Sudo, A.; Ogasawara, T.; Saigo, K. *Chem. Lett.* **1995**, 235. (d) Alvaro, G.; Martelli, G.; Savoia, D. *J. Chem. Soc., Perkin Trans. 1.* **1998**, 775. (e) Higashiyama, K.; Fujikura, H.; Takahashi, H. *Chem. Pharm. Bull.* **1995**, *43*, 722. (f) Dembélé, Y. A.; Belaud, C.; Villiéras, J. *Tetrahedron: Asymmetry* **1992**, *3*, 511.

6 (a) Bocoum, A.; Savoia, D.; Umani- Ronchi, A. *J. Chem. Soc., Chem. Commun.* **1993**, 1542. (b) Basile, T.; Bocoum, A.; Savoia, D.; Umani-Ronchi, A. *J. Org. Chem.* **1994**, *59*, 7766. (c) Alvaro, G.; Pacioni, P.; Savoia, D. *Chem. Eur. J.* **1997**, *3*, 726.

7 Laschat, S.; Kunz, H. *J. Org. Chem.* **1991**, *56*, 5883, and references cited therein.

8 Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943.

9 (a) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem Soc.* **1980**, *102*, 2693. (b) Souppe, J.; Danon, L.; Namy, J. L.; Kagan, H. B. *J. Organomet. Chem.* **1983**, *250*, 227.

10 Takahashi, H.; Suzuki, Y.; Inagaki, H. *Chem. Pharm. Bull.* **1982**, *30*, 3160.

11 Curran, D. P.; Gu, X.; Zhang, W.; Dowd, P. *Tetrahedron* **1997**, *53*, 9023.

12 Tanaka, H.; Inoue, K.; Pokorski, U.; Taniguchi, M.; Torii, S. *Tetrahedron Lett.* **1990**, *31*, 3023.