Highly Diastereoselective Addition of Grignard Reagents to Aliphatic, Enolizable *N*-Alkylketimines and 2,2-Disubstituted 1,3-Oxazolidines. Asymmetric Synthesis of the Antidepressant Cericlamine

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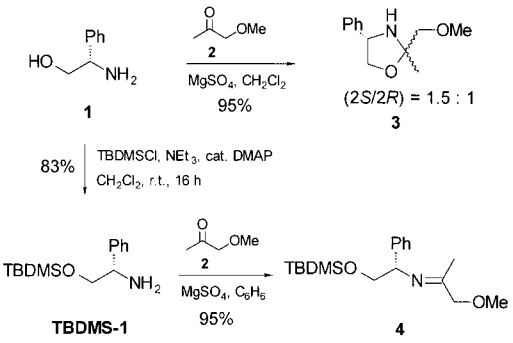
Grignard reagents were added to 2,2-disubstituted 1,3-oxazolidines and enolizable ketimines prepared from hydroxyacetone and phenylglycinol derivatives, with high to excellent diastereoselectivity, to yield 2,2-disubstituted 1,2-amino alcohol derivatives. Lewis acids had considerable influence on the yield and diastereoselectivity of the addition. This method was applied to the first asymmetric synthesis of the 5-HT reuptake inhibitor Cericlamine.

Although the asymmetric synthesis of amines by addition of organometallic reagents to aldimines and 2-monosubstituted 1,3-oxazolidines has gained much interest in recent years,[1] the corresponding reactions with ketimines and 2,2-disubstituted 1,3-oxazolidines remain largely unexplored. This is due to their poorer reactivity toward nucleophilic addition and their propensity to enolize on addition of Grignard reagents.[2] Hua et al. observed that addition of allylmagnesium bromide to *N*-sulfinylketimines, which have one potential site for enolization, occurred in 47−98% yields, but more basic Grignard reagents gave only enolization.[3] We recently showed[4] that a broad variety of Grignard reagents could be added in a highly diastereoselective manner to (2-heteroaryl)alkylimines with phenylglycinol derivatives as chiral auxiliaries,[5] the key feature being chelate formation of $MgBr_2$ with the imine nitrogen and the heteroatom of the arene. The chelate activated the imine toward nucleophilic attack and "locked" it into the (*E*) configuration. After demonstrating the first example of an asymmetric addition of a Grignard reagent to a phenylglycinol-derived ketimine, we set out to broaden the scope of the methodology. We report here the unprecedented addition of Grignard reagents to imines and oxazolidines prepared from hydroxyacetone and phenylglycinol derivatives. In this work, we demonstrate that the chelating substituent on the imine can be extended to include not only aromatic heterocycles but also an aliphatic CH_2OR group. These substrates have two potential sites for enolization; therefore, the addition of Grignard reagents to them represents a significant synthetic challenge.

Scheme 1. Preparation of the Starting Materials



In this study, we have focused on two types of substrates, the oxazolidine **3** and the *O*-TBDMS-protected imine **4**. The oxazolidine **3** was prepared from (*S*)-phenylglycinol (**1**) and methoxyacetone (**2**) by stirring with $MgSO_4$ in CH_2Cl_2.[6] The imine **4** was prepared from (*S*)-*O*-TBDMS-phenylglycinol (**TBDMS-1**) and **2** with $MgSO_4$ in benzene (Scheme 1). The configuration of the double bond in **4** and the configuration at C-2 of **3** were determined by NOESY experiments in CD_2Cl_2.

With the starting materials in hand, we investigated the feasibility of the addition of Grignard reagents. The reactions were carried out in CH_2Cl_2 instead of the more commonly used THF to increase the coordination of Lewis acids to the substrates.[4] We were gratified to find that Grignard reagents could indeed be added with high selectivity. We optimized the addition of Grignard reagents to **3** and **4** using benzylmagnesium halides by

(1) Reviews: (a) Enders, D.; Reinhold, U. *Tetrahedron*: *Asymmetry* **1997**, *8*, 1895−1946. (b) Pridgen, L. N. *Adv. Asymm. Synth.* **1997**, *2*, 55−117. (c) Risch, N.; Arend, M. In *Methods of Organic Chemistry* (*Houben-Weyl*): *Stereoselective Synthesis*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Georg Thieme Verlag: Stuttgart, 1995; Vol. E 21b, 1833−1893. (d) Volkmann, R. A. In *Comprehensive Organic Synthesis, Additions to C−X π Bonds, Part 1*; Schreiber, S. L., Ed.; Pergamon Press: Oxford, 1991; Vol. 1, Chapter 1.12. (e) Kleinmann, E. F.; Volkmann, R. A. In *Comprehensive Organic Synthesis, Additions to C−X π Bonds, Part 2*; Heathcock, C. H., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, Chapter 4.3.

(2) Stork, G.; Dowd, S. R. *J. Am. Chem. Soc.* **1963**, *85*, 2178−2180.

(3) (a) Hua, D. H.; Miao, S. W.; Chen, J. S.; Iguchi, S. *J. Org. Chem.* **1991**, *56*, 4−6. (b) Hua, D. H.; Lagneau, N.; Wang, H.; Chen, J. *Tetrahedron*: *Asymmetry* **1995**, *6*, 349−352.

(4) Spero, D. M.; Kapadia, S. R. *J. Org. Chem.* **1997**, *62*, 5537−5541.

(5) The pioneering work by Takahashi et al. on the use of phenylglycinol as chiral auxiliary for additions to imines and 1,3-oxazolidines was later explored widely by Pridgen et al.; see ref 1 and (a) Takahashi, H.; Chida, Y.; Higashiyama, K.; Onishi, H. *Chem. Pharm. Bull.* **1985**, *33*, 4662−4670. (b) Poerwono, H.; Higashiyama, K.; Takahashi, H. *J. Org. Chem.* **1998**, *63*, 2711−2714 and references therein. (c) Wu, M.-J.; Pridgen, L. N. *J. Org. Chem.* **1991**, *56*, 1340−1344. (d) Mokhallalati, M. K.; Wu, M.-J.; Pridgen, L. N. *Tetrahedron Lett.* **1993**, *34*, 47−50. (e) Pridgen, L. N.; Mokhallalati, M. K.; McGuire, M. A. *Tetrahedron Lett.* **1997**, *38*, 1275−1278 and references therein.

(6) It is interesting to note that oxazolidine **3** does not exist as a mixture of the open-chain hydroxyimine and the cyclized oxazolidines, as was observed in our earlier work with the corresponding pyridyl-substituted compounds.

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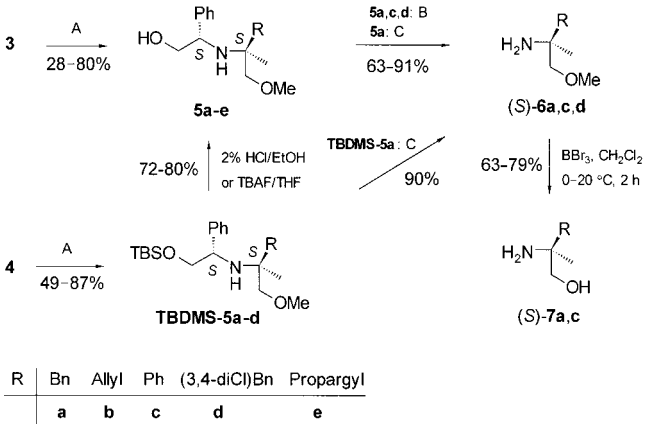
Table 1. Addition of RMgX to Oxazolidines 3 and Imine 4

entry	substrate	RMgX	Lewis acid	product	yield (%)	de (ee[a]) (%)
1	(*S*)-**3**	BnMgCl	-	**5a**	29	92
2	(*S*)-**3**[b]	BnMgCl	$MgBr_2$	**5a**	28	94
3	(*S*)-**3**	BnMgCl	$EtAlCl_2$	**5a**	34	24
4	(*S*)-**3**	**BnMgBr**	**$MgBr_2$**	**5a**	**38**	**99.5**
5	(*S*)-**4**	BnMgCl	-	**TBDMS-5a**	56	93
6	(*S*)-**4**	BnMgCl	$MgBr_2$	**TBDMS-5a**	71	98.4
7	(*S*)-**4**	BnMgCl	$EtAlCl_2$	**TBDMS-5a**	49	92
8	(*S*)-**4**	**BnMgBr**	**$MgBr_2$**	**TBDMS-5a**	**87**	**98.8**
9	(*S*)-**3**	AllylMgBr	$MgBr_2$	**5b**	80	96
10	(*S*)-**4**	AllylMgBr	$MgBr_2$	**TBDMS-5b**	73	96
11	(*S*)-**4**	PhMgBr	$MgBr_2$	**TBDMS-5c**	50	95
12	(*S*)-**3**	AllenylMgBr	$MgBr_2$	**5e**[b]	54	98
13	(*S*)-**4**	$ArCH_2MgCl$[c]	$MgBr_2$	**TBDMS-5d**	59	89
14	(*S*)-**4**	**$ArCH_2MgBr$**[c]	**$MgBr_2$**	**TBDMS-5d**	**67**	**95**

[a] ee of **6a** and **6d**, determined by HPLC.[10] [b] Homopropargylamine **5e**:allenylamine **8** ≥ 99:1. [c] Ar = (3,4-diCl)Ph.

Scheme 2. Addition of RMgX to 3 and 4 and Removal of the Auxiliary[a]

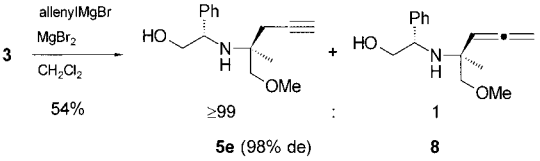


[a] Conditions: (A) RMgX, Lewis acid, CH_2Cl_2; (B) $Pb(OAc)_4$, $MeOH/CH_2Cl_2$; (C) NH_4HCO_2, 10% Pd/C, MeOH, reflux, overnight.

varying the Lewis acids and the halide (Table 1, entries 1−8[7,8]). Selectivity was highest with $MgBr_2$ and BnMgBr (entries 4 and 8). Addition of BnMgBr to the oxazolidine **3** afforded the amine **5a** in 38% yield with a 99.5% de. The yield could be improved by the addition of BnMgBr to the *O*-TBDMS-protected imine **4**. In this case, an 87% yield of amine product was realized with a 98.8% de.

This method can be extended to a variety of Grignard reagents. For example, under the optimized conditions, allylmagnesium bromide was added to **3** and **4** in 80% and 73% yield, respectively (entries 9 and 10). Even phenylmagnesium bromide could be added to **4** (entry 11, 50% yield), despite the considerably higher basicity of this Grignard reagent and the fact that the substrate has two sites for enolization.[9] In all of the above cases, the de was ≥95%. The addition of allenylmagnesium bromide (entry 12) to **3** deserves special comment. It proceeded with 98% de and a ratio of homopropargylamine **5e**:allenylamine **8** of ≥99:1 (Scheme 3). To the best of our knowledge, this

Scheme 3



is the first highly diastereo- and chemoselective addition of this Grignard reagent to a 1,3-oxazolidine.

The auxiliary was efficiently removed from **5** by $Pb(OAc)_4$ oxidation[10] to give the 2,2-disubstituted 1,2-amino alcohol derivatives **6**.[11] This reaction requires an unprotected 1,2-amino alcohol moiety, so the compounds **TBDMS-5** had to be desilylated. Both acidic and TBAF/THF deprotection worked in good yield. We found that the desilylation of **TBDMS-5** and also the hydrolysis of the intermediate benzaldimine generated from **5** by $Pb(OAc)_4$ could be performed very conveniently by using disposable syringe barrel columns containing a bonded silica support functionalized with ethylbenzenesulfonic acid (SCX), designed for solid-phase extraction.[12] To our knowledge, these are the first examples of performing synthetic reactions on these columns. Additionally, from both **TBDMS-5a** and **5a**, the auxiliary could be removed by transfer hydrogenation (NH_4HCO_2, 10% Pd/C, MeOH, reflux).[13] The methyl ether of **6a** and **6c** was cleaved with BBr_3 in good yield to give the 1,2-amino alcohols **7a** and **7c** (Scheme 2).

Both the oxazolidine **3** and the imine **4** gave predominantly the same diastereomer of the addition product. On the basis of the sign of optical rotation of the known amino alcohols **7a**,[14] **7c**,[15] and **10**,[14] the (*S*) configuration of the auxiliary leads to the (*S*) configuration at the newly formed stereocenter. A possible transition structure is

(7) Other Lewis acids such as $BF_3{\cdot}OEt_2$, $CuI/BF_3{\cdot}OEt_2$, $CeCl_3$, $Yb(OTf)_3$, ZnI_2, and TMSOTf gave inferior results.

(8) We observed that the yields for the addition of BnMgCl in the presence of $MgBr_2$ to imine **4** increased from 53% and 66% to 71% with 3, 4, and 5 equiv of this Grignard reagent, respectively. The selectivity dropped slightly (98.7%, 98.5%, 98.4% ee, respectively). With oxazolidine **3** and BnMgCl, the yields did not change; however, the selectivity increased (83% and 92% ee with 3 and 5 equiv, respectively).

(9) We also tried to add ethylmagnesium bromide (as an example for very basic alkyl Grignard reagents) but obtained only poor yields of the desired addition product.

(10) Mokhallalati, M. K.; Pridgen, L. N. *Synth. Commun.* **1993**, *23*, 2055−2064.

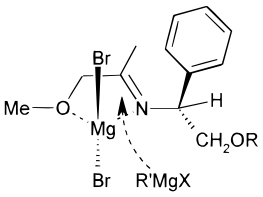
(11) **6a**: Chiralcel OD column eluting with hexanes/*i*PrOH/NEt_3 3873:90:1 at 0.5 mL/min, UV detection at 254 nm; t_R (*S*,*R*) 18.3 min, (*S*,*S*) 20.3 min. **6d**: Chiralcel OD column eluting with hexanes/EtOH/$HNEt_2$ 960:30:1 at 0.5 mL/min, UV detection at 254 nm; t_R (*S*,*R*) 15.5 min, (*S*,*S*) 18.4 min. The ee of **6a** and **6d** determined under these conditions were in accord with the de of the addition products **5a**,**d** and **TBDMS-5a,d** determined by ^1H NMR.

(12) See, for example: Lawrence, R. M.; Biller, S. A.; Fryszman, O. M.; Poss, M. A. *Synthesis* **1997**, 553−558.

(13) With **5d** and **TBDMS-5d**, the 3,4-dichlorophenyl ring was dechlorinated prior to cleavage of the auxiliary, giving **6a** instead of **6d**.

(14) Kaptein, B.; Moody, H. M.; Broxterman, Q. B.; Kamphuis, J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1495−1498.

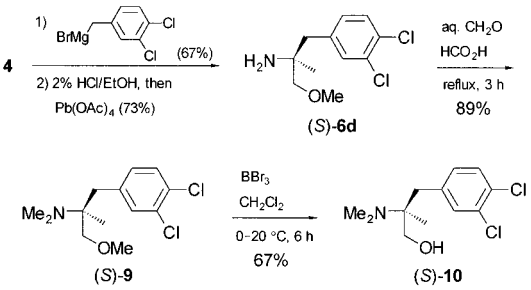
(15) Terashima, S.; Yamada, S.-I. *Chem. Pharm. Bull.* **1968**, *16*, 1953−1971.



R = MgX, TBDMS

Figure 1. Possible transition structure.

Scheme 4. Synthesis of (*S*)-Cericlamine [(*S*)-10]



shown in Figure 1. We postulate that the stereochemistry can be explained by A[1,3] strain, which favors the conformation shown. The phenyl group blocks the *re* face, and the delivery of the nucleophile occurs from the less hindered *si* face.[16] The $MgBr_2$ seems to activate the imine through complexation.[17] In addition, the methoxyl oxygen could also participate in coordination with magnesium.[18] This transition structure is analogous to the one we previously reported.[4]

To demonstrate the utility of this methodology, we have synthesized the serotonin reuptake inhibitor Cericlamine (**10**)[19] which is in clinical trials as an antidepressant.[20] The patented synthesis of enantiopure **10** starts from the corresponding amino acid that has been resolved by crystallization with tyrosine hydrazide.[21] An enzymatic resolution of the amino acid amide has also been published.[14]

The key step is the addition of 3,4-dichlorobenzylmagnesium halides to imine **4** (see Table 1, entries 13 and 14). Both 3,4-dichlorobenzylmagnesium halides gave high selectivities (89% and 95% de). The bromide was more selective than the chloride and also gave a higher yield (67% vs 59%), as was observed with the simple BnMgCl and BnMgBr.[22]

Scheme 4 shows our final synthesis. After addition of 3,4-dichlorobenzylmagnesium bromide to ketimine **4**, the phenylglycinol auxiliary was desilylated and removed by oxidative cleavage with $Pb(OAc)_4$ (73% for desilylation and removal of auxiliary). Dimethylation of **6d** with formic acid/formaldehyde gave the amine **9** in high yield (89%). Cleavage of the methyl ether with BBr_3 (67%) yielded (*S*)-Cericlamine (**10**).

In summary, we have developed an unprecedented, asymmetric synthesis of 2,2-disubstituted 1,2-amino alcohols[23] via a highly diastereoselective addition of Grignard reagents to ketimines and 2,2-disubstituted 1,2-oxazolidines. We applied this to the first asymmetric synthesis of the 5-HT reuptake inhibitor Cericlamine. In the course of that work, we used solid-phase extraction SCX columns for cleaving TBDMS ethers and hydrolysis of benzaldimines.

Experimental Section

General Procedures. Proton NMR spectra were recorded at 270 or 400 MHz in $CDCl_3$ using TMS (δ 0.00) or $CHCl_3$ (δ 7.26) as the internal standard. ^{13}C NMR spectra were recorded at 100.6 MHz in $CDCl_3$ using $CDCl_3$ (δ 77.00) as the internal standard. Multiplicities were determined by the DEPT sequence and are given as follows: (+) CH or CH_3, (−) CH_2, (C_{quat}) C. Commercially available chemicals were used as received. Column chromatography was carried out on silica gel 60 (E. Merck, 230−400 or 60−230 mesh). Solid-phase extraction SCX columns were obtained from Varian Sample Preparation Products.

(*S*)-*O*-TBDMS-phenylglycinol (TBDMS-1).[4] To a solution of (*S*)-**1** (5.00 g, 36.4 mmol) and TBDMSCl (6.03 g, 40.0 mmol) in dry CH_2Cl_2 (50 mL) were added NEt_3 (10.15 mL, 7.367 g, 72.8 mmol) and DMAP (178 mg, 1.5 mmol). After the mixture was stirred at room temperature for 21 h, saturated NH_4Cl solution (25 mL) was added; the crude product was extracted with CH_2Cl_2, dried over solid Na_2SO_4, and distilled (bp 120 °C/0.5 Torr) to give **TBDMS-1** (7.62 g, 83%) as a colorless oil, $[\alpha]^{25.2}_D = +15.6°$ (*c* 1.94, EtOH). MS (ES+) *m/z* 252 (83) [MH^+], 235 (84) [$MH^+ - NH_3$], 220 (35), 156 (100); ^1H NMR (270 MHz, $CDCl_3$) δ 0.03 (s, 6 H), 0.90 (s, 9 H), 1.8 (br s, 2 H), 3.51 (dd, ^2J = 9.8, ^3J = 8.4 Hz, 1 H), 3.72 (dd, ^2J = 9.8, ^3J = 4.0 Hz, 1 H), 4.07 (dd, ^3J = 8.4, ^3J = 4.0 Hz, 1 H), 7.25−7.40 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.47 (+, 2 C), 18.25 (C_{quat}), 25.85 (+, 3 C), 57.57 (+), 69.52 (−), 126.86 (+, 2 C), 127.21 (+), 128.22 (+, 2 C), 142.63 (C_{quat}).

2-Methoxymethyl-2-methyl-4*S*-phenyloxazolidine (3). A mixture of phenylglycinol [(*S*)-**1**] (1.37 g, 10.0 mmol), methoxyacetone (**2**) (969 mg, 11.0 mmol), and $MgSO_4$ (2.5 g) in CH_2Cl_2 (20 mL) was stirred at room temperature for 3 h. Filtration and evaporation of the solvent gave **3** (1.97 g, 95%) as a yellow oil, (2*S*/2*R*) = 1.5:1. The compound was used without further purification. IR (neat) ν 3329, 1445, 1102, 1040, 753, 679 cm^{-1}; MS (ES+) *m/z* 208 (100) [MH^+], 162 (45) [MH^+ − MeOMe]. **Major isomer (2*S*):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 3 H), 2.6 (br s, 1 H), 3.44 (s, 3 H), 3.48 and 3.50 (AB, ^2J = 10.4 Hz, 2 H), 3.61 (dd, ^3J = 8.9, ^2J = 7.7 Hz, 1 H), 4.25 (dd, ^2J = 7.7, ^3J = 6.8 Hz, 1 H), 4.49 (dd, ^3J = 8.9, ^3J = 6.8 Hz, 1 H), 7.25−7.39 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.42 (+), 59.32 (+), 61.18 (+), 72.37 (−), 76.00 (−), 96.49 (C_{quat}), 126.57 (+, 2 C), 127.54 (+), 128.52 (+, 2 C), 139.30

(16) When R = MgX, as would occur upon treatment of **3** with a Grignard reagent, the oxygen of the auxiliary might also participate in chelation with the Mg.

(17) In a related case, Corey et al. recently observed the superiority of MgI_2 over $MgBr_2$ in the addition of a silyl enol ether to an α-aminoaldehyde in terms of yield and reactivity. This was explained by the more facile dissociation of the iodide: Corey, E. J.; Weidong, L.; Reichard, G. A. *J. Am. Chem. Soc.* **1998**, *120*, 2330−2336.

(18) For examples of additions of Grignard reagents to aliphatic aldimines with an oxygen atom as coordination site α to C=N, see: (a) Kobayashi, Y.; Matsumoto, T.; Takemoto, Y.; Nakatani, K.; Ito, Y.; Kamijo, T.; Harada, H.; Terashima, S. *Chem. Pharm. Bull.* **1991**, *39*, 2550−2555. (b) Beresford, K. J. M.; Howe, G. P.; Procter, G. *Tetrahedron Lett.* **1992**, *33*, 3355−3358. (c) Franz, T.; Hein, M.; Veith, U.; Jäger, V.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Angew. Chem.* **1994**, *106*, 1308; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1298−1301.

(19) Aubard, G.; Bure, J.; Calvet, A. P.; Gouret, C.; Grouhel, A. G.; Junien, J.-L. Eur. Pat. 0237366, 1987.

(20) (a) Wettstein, J. G.; Gouret, C. J.; Junien, J.-L. *Eur. J. Pharmacol.* **1990**, *183*, 1477. (b) Gouret, C. J.; Wettstein, J. G.; Porsolt, R. D.; Puech, A.; Junien, J.-L. *Eur. J. Pharmacol.* **1990**, *183*, 1478. (c) Gouret, C. J.; Porsolt, R.; Wettstein, J. G.; Puech, A.; Pascaud, X.; Junien, J.-L. *Arzneim.-Forsch.* **1990**, *40*, 633−640. (d) *Drugs Future* **1991**, *16*, 301−304. (e) *Drugs Future* **1992**, *17*, 319−320. (f) *Drugs Future* **1993**, *18*, 365−366. (g) *Drugs Future* **1995**, *20*, 410.

(21) Dimsdale, M. J. *Fr. Demande* 2378746, 1977.

(22) The addition of 3,4-dichlorobenzylmagnesium bromide to *N*-**Me-3** gave an excellent yield (82%) but poor selectivity (38% de).

(23) We also prepared the compounds corresponding to **3** and **4** with a methylthio or dimethylamino substituent in place of the methoxy group, aiming at 1,2-aminothiols and 1,2-diamines, respectively. However, only poor yields were obtained. This may be explained in the methylthio case by the enhanced acidity of the adjacent methylene protons, leading to deprotonation instead of addition.

(C_{quat}). **Minor isomer (2*R*):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 3 H), 2.6 (br s, 1 H), 3.37 and 3.42 (AB, ^2J = 9.8 Hz, 2 H), 3.44 (s, 3 H), 3.70 (dd, $^3J = {}^2J$ = 8.0 Hz, 1 H), 4.28 (dd, ^2J = 8.0, ^3J = 6.9 Hz, 1 H), 4.51 (dd, ^3J = 8.0, ^3J = 6.9 Hz, 1 H), 7.25−7.39 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.69 (+), 59.36 (+), 61.60 (+), 71.95 (−), 76.69 (−), 96.02 (C_{quat}), 126.49 (+, 2 C), 127.44 (+), 128.49 (+, 2 C), 140.19 (C_{quat}).

(*S*)-[2-(*tert*-Butyldimethylsilyloxy)-1-phenylethyl]-(2-methoxy-1-methylethylidene)-amine (4). A mixture of (*S*)-**TBDMS-1** (1.26 g, 5.01 mmol), **2** (493 mg, 5.60 mmol), and $MgSO_4$ (2 g) in C_6H_6 (10 mL) was stirred at room temperature for 3 h. Filtration and evaporation of the solvent gave **4** (1.53 g, 95%) as a yellow oil. The compound was used without further purification. IR (neat) ν 1688, 1252, 1103, 832, 775, 699 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.05 (s, 6 H), 0.83 (s, 9 H), 1.89 (s, 3 H), 3.34 (s, 3 H), 3.83−3.86 (m, 2 H), 4.00 (s, 2 H), 4.65 (dd, $^3J = {}^3J$ = 6.7 Hz, 1 H), 7.18−7.42 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.51(+), −5.46 (+), 15.21 (+), 18.22 (C_{quat}), 25.81 (+, 3 C), 58.23 (+), 66.31 (+), 69.08 (−), 78.75 (−), 127.00 (+), 127.60 (+, 2 C), 128.17 (+, 2 C), 141.37 (C_{quat}), 168.17 (C_{quat}).

(*S,S*)-(1-Benzyl-2-methoxy-1-methylethyl)-[2-(*tert*-butyldimethylsilyloxy)-1-phenylethyl]-amine (TBDMS-5a). A suspension of $MgBr_2$ (183 mg, 0.994 mmol) and the imine **4** (160 mg, 0.498 mmol) in CH_2Cl_2 (6 mL) was stirred for 20 min at room temperature. BnMgBr (0.9 M in Et_2O, 2.8 mL, 2.5 mmol) was added, and stirring was continued overnight. The reaction was quenched with a saturated solution of NH_4Cl (10 mL), the mixture was extracted with CH_2Cl_2, and the CH_2Cl_2 extract was dried over solid Na_2SO_4 and concentrated. The crude product was chromatographed on silica gel eluting with hexanes/EtOAc (100:0 → 2:1) to give **TBDMS-5a** (179 mg, 87%) as a colorless oil, de 98.8%. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.01 (s, 3 H), 0.02 (s, 3 H), 0.76 (s, 3 H), 0.88 (s, 9 H), 2.2 (br s, 1 H), 2.79 (B of AB, ^2J = 13.0 Hz, 1 H), 2.84−2.94 (m, 3 H), 3.17 (s, 3 H), 3.46 (dd, ^3J = 9.0, ^2J = 9.9 Hz, 1 H), 3.57 (dd, ^3J = 4.7, ^2J = 9.9 Hz, 1 H), 4.05 (dd, ^3J = 4.7, ^3J = 9.0 Hz, 1 H), 7.16−7.33 (m, 8 H), 7.43−7.47 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.53 (+), −5.44 (+), 18.17 (C_{quat}), 21.72 (+), 25.81 (+, 3 C), 43.61 (−), 56.73 (C_{quat}), 58.30 (+), 58.84 (+), 68.72 (−), 77.70 (−), 125.82 (+), 126.82 (+), 127.65 (+, 2 C), 127.79 (+, 2 C), 127.92 (+, 2 C), 130.63 (+, 2 C), 138.79 (C_{quat}), 144.32 (C_{quat}); MS (ES+) *m*/*z* 414 (100) [MH$^+$].

(*S,S*)-2-(1-Benzyl-2-methoxy-1-methylethylamino)-2-phenylethanol (5a). Method A (addition of Grignard reagent). A suspension of $MgBr_2$ (188 mg, 1.02 mmol) and the oxazolidine **3** (106 mg, 0.511 mmol) in CH_2Cl_2 (6.5 mL) was stirred for 20 min at room temperature. BnMgBr (0.9 M in Et_2O, 2.8 mL, 2.5 mmol) was added, and stirring was continued overnight. The reaction was quenched with 2 N HCl (10 mL), and the mixture was extracted with Et_2O. Disodium EDTA (2 g) and 25% NH_3 (to adjust pH to 9−10) were added, and the crude product was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated. Chromatography on silica gel eluting with hexanes/EtOAc (5:1 → 2:1) gave **5a** (58 mg, 38%) as a colorless oil, de 99.5%. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.94 (s, 3 H), 2.4 (br s, 2 H), 2.71 and 2.73 (AB, ^2J = 13.0 Hz, 2 H), 2.65 and 2.89 (AB, ^2J = 9.0 Hz, 2 H), 2.95 (s, 3 H), 3.30 (dd, ^3J = 9.7, ^2J = 10.4 Hz, 1 H), 3.52 (dd, ^3J = 4.8, ^2J = 10.4 Hz, 1 H), 3.87 (dd, ^3J = 4.8, ^3J = 9.7 Hz, 1 H), 7.15−7.38 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.12 (+), 45.55 (−), 56.66 (C_{quat}), 58.00 (+), 58.29 (+), 67.09 (−), 76.38 (−), 126.21 (+), 126.77 (+, 2 C), 127.21 (+), 127.89 (+, 2 C), 128.40 (+, 2 C), 130.67 (+, 2 C), 137.83 (C_{quat}), 143.21 (C_{quat}); MS (PB-NH_3-CI) *m*/*z* 300 (100) [MH$^+$]. **Method B (desilylation of TBDMS-5a on SCX column).** A solution of **TBDMS-5a** (32 mg, 0.077 mmol) in CH_2Cl_2 (1 mL) was loaded on a SCX column (500 mg of sorbent). The column was washed with MeOH (2 × 2.5 mL) and eluted with 1:1 CH_2Cl_2/2 N NH_3 in MeOH to give **5a** (19 mg, 82%).

(*S,S*)-[2-(*tert*-Butyldimethylsilyloxy)-1-phenylethyl]-(1-methoxymethyl-1-methyl-3-butenyl)-amine (TBDMS-5b). As described for **TBDMS-5a**, allylMgBr in Et_2O (1.0 M, 2.6 mL, 2.6 mmol) was reacted with **4** (164 mg, 0.510 mmol) and $MgBr_2$ (190 mg, 1.03 mmol) in CH_2Cl_2 (6 mL) for 26 h. Chromatography on silica gel eluting with hexanes/EtOAc (40:1 → 2:1) gave **TBDMS-5b** (136 mg, 73%) as a colorless oil, de 96%. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.00 (s, 3 H), 0.01 (s, 3 H), 0.82 (s, 3 H), 0.88 (s, 9 H), 2.10−2.30 (m, 3 H), 2.93 and 3.01 (AB, ^2J = 9.0 Hz, 2 H), 3.15 (s, 3 H), 3.42 (dd, ^3J = 9.0, ^2J = 9.8 Hz, 1 H), 3.52 (dd, ^3J = 4.7, ^2J = 9.8 Hz, 1 H), 3.94 (dd, ^3J = 4.7, ^3J = 9.0 Hz, 1 H), 5.01−5.07 (m, 2 H), 5.75−5.90 (m, 1 H), 7.17−7.31 (m, 3 H), 7.37−7.42 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.51 (+), −5.44 (+), 18.19 (C_{quat}), 22.45 (+), 25.83 (+, 3 C), 42.03 (−), 55.93 (C_{quat}), 58.72 (+), 58.85 (+), 68.72 (−), 78.90 (−), 117.45 (−), 126.85 (+), 127.65 (+, 2 C), 127.94 (+, 2 C), 134.95 (+), 144.21 (C_{quat}); MS (ES+), *m*/*z*: 364 (100) [MH$^+$].

(*S,S*)-2-(1-Methoxymethyl-1-methyl-3-butenylamino)-2-phenylethanol (5b). Method A. As described for **5a**, allylMgBr in Et_2O (1.0 M, 2.5 mL, 2.5 mmol) was reacted with **3** (108 mg, 0.521 mmol) and $MgBr_2$ (193 mg, 1.05 mmol) in CH_2Cl_2 (6.5 mL) for 21 h. Chromatography on silica gel eluting with hexanes/EtOAc (5:1 → 2:1) gave **5b** (104 mg, 80%) as a colorless oil, de 96%. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.98 (s, 3 H), 1.8−2.1 (br s, 2 H), 2.11 and 2.16 (AB of ABX, ^3J = 7.1, ^3J = 7.7, ^2J = 13.8 Hz, 2 H), 2.82 and 3.06 (AB, ^2J = 9.0 Hz, 2 H), 3.21 (s, 3 H), 3.28 (dd, ^3J = 9.7, ^2J = 10.4 Hz, 1 H), 3.52 (dd, ^3J = 4.7, ^2J = 10.4 Hz, 1 H), 3.85 (dd, ^3J = 4.7, ^3J = 9.7 Hz, 1 H), 4.98−5.08 (m, 2 H), 5.75 (ddt, ^3J = 7.4, ^3J = 10.2, ^3J = 16.9 Hz, 1 H), 7.21−7.34 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.12 (+), 43.41 (−), 55.85 (C_{quat}), 58.15 (+), 58.42 (+), 67.25 (−), 77.71 (−), 117.88 (−), 126.73 (+, 2 C), 127.10 (+), 128.35 (+, 2 C), 134.17 (+), 143.39 (C_{quat}); MS (ES+), *m*/*z*: 250 (100) [MH$^+$]. **Method B.** Desilylation of **TBDMS-5b** was carried out as described for **TBDMS-5a** (80% yield).

(*S,S*)-[2-(*tert*-Butyldimethylsilyloxy)-1-phenylethyl]-(2-methoxy-1-methyl-1-phenylethyl)-amine (TBDMS-5c). As described for **TBDMS-5a**, PhMgBr (3.0 M in Et_2O, 1.0 mL, 3.0 mmol) was reacted with **4** (161 mg, 0.501 mmol) and $MgBr_2$ (184 mg, 1.00 mmol) in CH_2Cl_2 (6 mL) for 27 h. Chromatography on silica gel eluting with hexanes/EtOAc (100:0 → 2:1) gave **TBDMS-5c** (100 mg, 50%) as a pale yellow oil, de 95%. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.00 (s, 3 H), 0.02 (s, 3 H), 0.92 (s, 9 H), 1.09 (s, 3 H), 3.23 (s, 3 H), 3.30 and 3.36 (AB, ^2J = 8.8 Hz, 2 H), 3.47 (d, J = 6.5 Hz, 2 H), 3.64 (dd, $^3J = {}^3J$ = 6.9 Hz, 1 H), 7.18−7.36 (m, 8 H), 7.49−7.53 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.60 (+), −5.47 (+), 18.25 (C_{quat}), 23.84 (+), 25.85 (+, 3 C), 59.23 (+), 59.40 (+), 59.62 (C_{quat}), 68.66 (−), 82.87 (−), 126.36 (+), 126.81 (+), 127.33 (+, 2 C), 127.72 (+, 2 C), 127.75 (+, 2 C), 127.90 (+, 2 C), 144.30 (C_{quat}), 144.80 (C_{quat}); MS (PB-NH_3-CI) *m*/*z* 400 (100) [MH$^+$].

(*S,S*)-2-(2-Methoxy-1-methyl-1-phenylethylamino)-2-phenylethanol (5c). TBDMS-5c (69 mg, 0.17 mmol) was stirred at room temperature in 2% HCl/EtOH (4 mL) for 4 h. After evaporation of solvent and addition of 2 N HCl, the mixture was extracted with Et_2O. The aqueous layer was basified (2 N NaOH) and extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over Na_2SO_4 and concentrated to give **5c** (35 mg, 72%) as a colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.26 (s, 3 H), 2.77 (br s, 2 H), 3.21 (d, ^2J = 8.9 Hz, 1 H), 3.24 (s, 3 H), 3.37 (dd, ^3J = 9.0, ^2J = 10.7 Hz, 1 H), 3.43 (dd, ^3J = 5.0, ^2J = 10.7 Hz, 1 H), 3.55 (d, ^2J = 8.9 Hz, 1 H), 3.59 (dd, ^3J = 9.0, ^3J = 5.0 Hz, 1 H), 7.16−7.34 (m, 8 H), 7.46−7.48 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.18 (+), 58.84 (+), 59.00 (+), 59.58 (C_{quat}), 67.40 (−), 81.12 (−), 126.73 (+, 2 C), 126.87 (+, 2 C), 126.98 (+), 127.05 (+), 128.15 (+, 2 C), 128.35 (+, 2 C), 143.48 (C_{quat}), 144.26 (C_{quat}); MS (ES+), *m*/*z*: 286 (38) [MH$^+$], 149 (62) [MH$^+$ − **1**·H$^+$], 138 (100) [**1**·H$^+$].

(*S,S*)-[2-(*tert*-Butyldimethylsilyloxy)-1-phenylethyl]-[1-(3,4-dichlorobenzyl)-2-methoxy-1-methylethyl)-amine (TBDMS-5d). As described for **TBDMS-5a**, 3,4-dichlorobenzylmagnesium bromide (0.9 M in Et_2O, 2.9 mL, 2.6 mmol) was reacted with **4** (162 mg, 0.504 mmol) and $MgBr_2$ (190 mg, 1.03 mmol) in CH_2Cl_2 (7 mL) for 22 h. Chromatography on silica gel eluting with hexanes/EtOAc (100:0 → 20:1 → 2:1) gave **TBDMS-5d** (163 mg, 67%) as a colorless oil, de 95%. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.01 (s, 3 H), 0.02 (s, 3 H), 0.76 (s, 3 H), 0.88 (s, 9 H), 2.74 and 2.80 (AB, ^2J = 12.9 Hz, 2 H), 2.83 (s, 2 H), 3.16 (s, 3 H), 3.43 (dd, ^3J = 9.1, ^2J = 9.9 Hz, 1 H), 3.56

(dd, ^3J = 4.5, ^2J = 9.9 Hz, 1 H), 4.00 (dd, ^3J = 4.5, ^3J = 9.1 Hz, 1 H), 7.04 (dd, ^3J = 8.2, ^4J = 2.0 Hz, 1 H), 7.20−7.33 (m, 5 H), 7.40−7.44 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.55 (+), −5.44 (+), 18.14 (C_{quat}), 21.71 (+), 25.77 (+, 3 C), 42.81 (−), 56.72 (C_{quat}), 58.32 (+), 58.86 (+), 68.58 (−), 77.64 (−), 126.98 (+), 127.58 (+, 2 C), 128.01 (+, 2 C), 129.64 (+), 129.88 (C_{quat}), 130.01 (+), 131.66 (C_{quat}), 132.39 (+), 139.18 (C_{quat}), 143.99 (C_{quat}); MS (ES+) *m*/*z* 486/484/482 (14/75/100) [MH^+].

(*S*,*S*)-2-[1-(3,4-Dichlorobenzyl)-2-methoxy-1-methylethylamino]-2-phenylethanol (5d). TBDMS-5d (143 mg, 0.296 mmol) was stirred at room temperature in 2% HCl/EtOH (4 mL) for 3 h. After evaporation of solvent and addition of 2 N NaOH, the product was extracted with CH_2Cl_2, dried over Na_2SO_4 and concentrated. The crude **5d** (106 mg, 97%) was used without further purification. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.91 (s, 3 H), 2.60−2.71 (m, 5 H), 2.81 (A of AB, ^2J = 9.2 Hz, 1 H), 2.94 (s, 3 H), 3.33 (dd, ^3J = 9.6, ^2J = 10.5 Hz, 1 H), 3.53 (dd, ^3J = 4.7, ^2J = 10.5 Hz, 1 H), 3.86 (dd, ^3J = 4.7, ^3J = 9.6 Hz, 1 H), 6.99 (dd, ^3J = 8.2, ^4J = 1.8 Hz, 1 H), 7.23−7.38 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.94 (+), 44.46 (−), 56.71 (C_{quat}), 57.96 (+), 58.44 (+), 67.10 (−), 76.02 (−), 126.76 (+, 2 C), 127.35 (+), 128.46 (+, 2 C), 129.72 (+), 130.01 (+), 130.26 (C_{quat}), 131.79 (C_{quat}), 132.40 (+), 138.19 (C_{quat}), 142.91 (C_{quat}); MS (ES+) *m*/*z* 372/370/368 (11/68/100) [MH^+].

(*S*,*S*)-2-(1-Methoxymethyl-1-methyl-3-butynylamino)-2-phenylethanol (5e). As described for **5a**, allenylMgBr (1.1 M in Et_2O, 2.5 mL, 2.8 mmol) was reacted with **3** (110 mg, 0.531 mmol) and $MgBr_2$ (195 mg, 1.06 mmol) in CH_2Cl_2 (6.5 mL) for 20 h. Chromatography on silica gel eluting with hexanes/EtOAc (5:1 → 2:1) gave **5e** (70 mg, 54%) as a colorless oil, de 98%. IR (neat) ν 3294, 2115, 634 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.08 (s, 3 H), 1.8−2.3 (br s, 2 H), 2.01 (t, ^4J = 2.6 Hz, 1 H), 2.93 (d, ^4J = 2.6 Hz, 2 H), 2.93 and 3.19 (AB, ^2J = 8.9 Hz, 2 H), 3.10 (s, 3 H), 3.29 (dd, ^3J = 9.7, ^2J = 10.5 Hz, 1 H), 3.54 (dd, ^3J = 4.6, ^2J = 10.5 Hz, 1 H), 3.86 (dd, ^3J = 4.6, ^3J = 9.7 Hz, 1 H), 7.20−7.35 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.07 (+), 29.03 (−), 55.79 (C_{quat}), 58.44 (+), 58.66 (+), 67.28 (−), 70.64 (+), 77.19 (−), 81.30 (C_{quat}), 126.65 (+, 2 C), 127.25 (+), 128.44 (+, 2 C), 142.94 (C_{quat}); MS (ES+), *m*/*z*: 248 (100) [MH^+].

(*S*)-3-Phenyl-2-methyl-2-amino-1-methoxypropane [(*S*)-6a]. A mixture of **TBDMS-5a** (130 mg, 0.314 mmol), NH_4HCO_2 (208 mg, 3.3 mmol) and 10% Pd/C (51 mg) in MeOH (4 mL) was refluxed overnight. Then Pd/C was filtered off, the solvent was evaporated, the residue was dissolved in 2 N HCl (2.5 mL) and extracted with Et_2O (3 × 6 mL), and the aqueous layer was basified (6 N NaOH) and extracted with CH_2Cl_2 (5 × 5 mL). The CH_2Cl_2 extract was dried over Na_2SO_4 and concentrated to give amine (*S*)-**6a** (53 mg, 90%), bp 20 °C/0.5 Torr (Kugelrohr distillation), colorless oil, $[\alpha]^{25.2}_D$ = +2.50° (*c* 2.04, EtOH). Starting from **5a**, the yield was 83%. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.04 (s, 3 H), 1.5 (br s, 2 H), 2.71 (s, 2 H), 3.08 and 3.09 (AB, ^2J = 8.7 Hz, 2 H), 3.39 (s, 3 H), 7.16−7.33 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.12 (+), 45.98 (−), 52.64 (C_{quat}), 58.99 (+), 80.52 (−), 126.23 (+), 128.02 (+, 2 C), 130.50 (+, 2 C), 137.95 (C_{quat}); MS (PB-NH_3-CI), *m*/*z* 180 (100) [MH^+].

(*S*)-2-Amino-2-phenyl-1-methoxypropane [(*S*)-6c]. Removal of the auxiliary of **5c** (35 mg, 0.12 mmol) by $Pb(OAc)_4$ (69 mg, 0.16 mmol) was done following the procedure by Pridgen et al.[10] Instead of hydrolyzing the intermediate benzaldimine by aqueous HCl in EtOH as described in ref 10 the hydrolysis was performed on a SCX column. A solution of the benzaldimine (29 mg, 95%) in CH_2Cl_2 (1 mL) was loaded on a SCX column (500 mg of sorbent, prewet with CH_2Cl_2). The column was then washed with MeOH (2 × 2.5 mL), and 1:1 CH_2Cl_2/2 N NH_3 in MeOH (2.5 mL) eluted the amine (*S*)-**6c** (18 mg, 91% from **5c**) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 3 H), 1.74 (br s, 2 H), 3.35 (s, 3 H), 3.43 and 3.47 (AB, ^2J = 8.9 Hz, 2 H), 7.21−7.25 (m, 1 H), 7.32−7.36 (m, 2 H), 7.49−7.52 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.88 (+), 55.40 (C_{quat}), 59.33 (+), 82.52 (−), 125.40 (+, 2 C), 126.54 (+), 128.15 (+, 2 C), 146.67 (C_{quat}); MS (ES+) *m*/*z* 166 (5) [MH^+], 149 (100) [$MH^+ - NH_3$].

(*S*)-1-(3,4-Dichlorobenzyl)-2-methoxy-1-methylethylamine [(*S*)-6d]. Oxidative cleavage of **5d** (106 mg, 0.288 mmol) with $Pb(OAc)_4$ (166 mg, 0.374 mmol) as described above for the preparation of **6c** gave (*S*)-**6d** (53.5 mg, 75%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (s, 3 H), 1.4 (br s, 2 H), 2.66 (s, 2 H,), 3.02 and 3.06 (AB, ^2J = 8.8 Hz, 2 H), 3.38 (s, 3 H), 7.03 (dd, ^3J = 8.2, ^4J = 1.9 Hz, 1 H), 7.29 (d, ^4J = 1.9 Hz, 1 H), 7.35 (d, ^3J = 8.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.98 (+), 45.00 (−), 52.64 (C_{quat}), 58.94 (+), 80.20 (−), 129.83 (+), 129.87 (C_{quat}), 130.31 (+), 131.91 (C_{quat}), 132.21 (+), 138.40 (C_{quat}); MS (CI, NH_3) *m*/*z* 252/250/248 (13/70/100) [MH^+].

(*S*)-2-Amino-2-methyl-3-phenylpropan-1-ol [(*S*)-7a].[14] To a solution of the methyl ether (*S*)-**6a** (27 mg, 0.15 mmol) in dry CH_2Cl_2 (1.5 mL) was added at 0 °C BBr_3 (57 μL, 150 mg, 0.60 mmol). After 30 min, the cooling bath was removed, and stirring at room temperature was continued for 2 h. The mixture was poured into 2 N HCl (4 mL) and extracted with Et_2O, and the aqueous layer was refluxed for 1.5 h. After basification (6 N NaOH), the product was extracted with $CHCl_3$, dried over Na_2SO_4, and concentrated. (*S*)-**7a** was obtained in 79% yield. The characterization data were in accord with the literature values.[14]

(*S*)-α-Methylphenylglycinol [(*S*)-7c].[15] As described above for **7a**, (*S*)-**6c** (18 mg, 0.11 mmol) was reacted with BBr_3 (47 μL, 125 mg, 0.50 mmol) to give (*S*)-**7c** (10.4 mg, 63% yield) as a colorless oil, $[\alpha]^{25}_D$ = +16° (*c* 0.535, EtOH) [ref 15 $[\alpha]^{23}_D$ = +14.3° (*c* 0.978, EtOH)]. NMR data are not reported in ref 15. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 3 H), 1.9 (br s, 3 H), 3.58 and 3.63 (AB, ^2J = 10.7 Hz, 2 H), 7.23−7.28 (m, 1 H), 7.34−7.38 (m, 2 H), 7.44−7.46 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.11 (+), 56.27 (C_{quat}), 71.74 (−), 125.24 (+, 2 C), 126.78 (+), 128.43 (+, 2 C), 146.40 (C_{quat}); MS (ES+) *m*/*z* 152 (6) [MH^+], 135 (100) [$MH^+ - NH_3$].

(*S*)-[1-(3,4-Dichlorobenzyl)-2-methoxy-1-methylethyl]-dimethylamine [(*S*)-9]. A mixture of (*S*)-**6d** (53.5 mg, 0.215 mmol), formic acid (372 mg, 8.08 mmol) and aqueous formaldehyde (37%, 200 mg, 2.46 mmol) was heated at 105 °C for 3 h and stirred at room temperature overnight. After the addition of 2 N NaOH (5 mL) and extraction with CH_2Cl_2 (5 × 2 mL), the combined extracts were loaded on a SCX column (500 mg of sorbent). The column was washed with MeOH (2 × 2.5 mL) and eluted with 1:1 CH_2Cl_2/2 N NH_3 in MeOH to give (*S*)-**9** (53 mg, 89%) as a clear oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (s, 3 H), 2.34 (s, 6 H), 2.69 and 2.89 (AB, ^2J = 13.0 Hz, 2 H), 2.90 and 3.12 (AB, ^2J = 9.9 Hz, 2 H), 3.31 (s, 3 H), 7.04 (dd, ^3J = 8.2, ^4J = 2.1 Hz, 1 H), 7.31 (d, ^4J = 2.1 Hz, 1 H), 7.33 (d, ^3J = 8.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.48 (+), 38.59 (+, 2 C), 39.34 (−), 58.52 (+), 59.54 (C_{quat}), 74.91 (−), 129.63 (+), 129.93 (C_{quat}), 130.05 (+), 131.65 (C_{quat}), 132.41 (+), 139.32 (C_{quat}).

(*S*)-3-(3,4-Dichlorophenyl)-2-(dimethylamino)-2-methylpropan-1-ol (Cericlamine) [(*S*)-10].[14] (*S*)-**9** (52 mg, 0.19 mmol) was reacted for 6 h with BBr_3 (72 μL, 190 mg, 0.76 mmol) as described above for **7a** to give (*S*)-**10** (33 mg, 67%). The characterization data are in accord with the literature values.[14]

Supporting Information Available: Spectroscopic data for the (*S*,*R*) isomers of **5** and for **8** and proton and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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