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Enantioselective reduction of ketoxime ethers with borane–oxazaborolidines and synthesis of the key intermediate leading to (*S*)-rivastigmine

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ABSTRACT

The reduction of representative alkyl aryl (*E*)-ketoxime *O*-benzyl ethers with borane catalyzed by terpene oxazaborolidines, derived from (1*R*)-nopinone and (1*R*)-camphor, gave the corresponding amines with 82–99% ee. Oxazaborolidines derived from (1*S*)-2-carene and (1*S*)-3-carene were less selective. (*S*)-1-(3-Methoxyphenyl)ethanamine (94% ee) the key intermediate in the synthesis of (*S*)-rivastigmine, was obtained by the reduction of (*E*)-1-(3-methoxyphenyl)ethanone *O*-benzyl oxime with borane/oxazaborolidine generated from (*S*)-valinol.

1. Introduction

The enantioselective reduction of prochiral ketoxime *O*-ethers provides direct access to non-racemic primary amines which are important compounds widely used for the separation of enantiomers,[1,2] as auxiliaries and ligands for catalysts in asymmetric synthesis,[3,4] and as pharmaceuticals.[2,5] Boranes, in the presence of oxazaborolidines derived from enantiopure β-amino alcohols have emerged as convenient reagents for the reduction of ketoxime *O*-ethers.[6] Oxazaborolidines catalyze the reaction, however, a stoichiometric amount or an excess is usually required for the best enantioselectivity. In some cases, high selectivity at a lower catalyst load was also achieved,[7] for example, with a polymer-supported oxazaborolidine, generated from 2-piperazinomethanol.[7b] Spiroborates, obtained from β-amino alcohols or α-amino acids and diols, are also convenient catalysts for the reduction of ketoxime *O*-ethers with borane.[8] Recently, a highly selective reduction of alkyl aryl and heteroaryl ketoxime *O*-benzyl ethers with borane, catalyzed by 0.1 equiv of spiroborate generated from (*S*)-1,1-diphenylvalinol and ethylene glycol, was reported.[8e,f]

However, the reduction of certain ketoxime *O*-ethers with borane required an extensive search for a suitable oxazaborolidine. For example, in the reduction of 3-acetyl-7-benzyloxybenzofuran oxime ethers with borane/oxazaborolidines, generated from various β-amino alcohols, an acceptable selectivity was achieved only in the presence of oxazaborolidine generated from norephedrine.[9] In the synthesis of sphinganine, the reduction of certain oxoketoxime ethers with borane/oxazaborolidines generated from β-amino alcohols with the pinane skeleton, was more selective compared to oxazaborolidine generated from 1,1-diphenylprolinol.[10] Recently, we also observed high selectivity in the reduction of ketones and 2-acetylbenzothiphene oxime ethers with borane/oxazaborolidines derived from (1*R*)-nopinone and (1*R*)-camphor.[11] Consequently, we herein undertook the reduction of representative ketoxime *O*-benzyl ethers with borane, catalyzed by terpene oxazaborolidines derived from (1*R*)-nopinone, (1*R*)-camphor, (1*S*)-2-carene, and (1*S*)-3-carene.

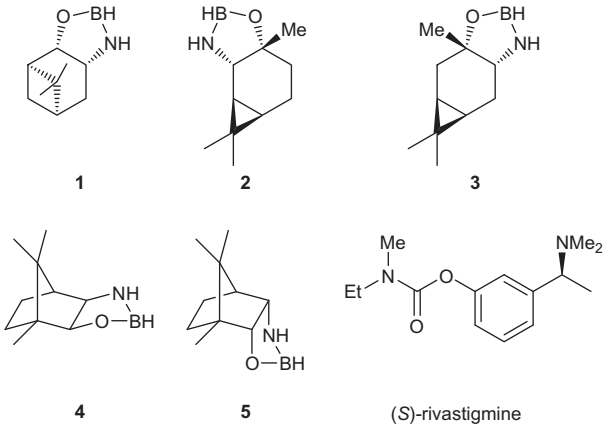

Figure 1.

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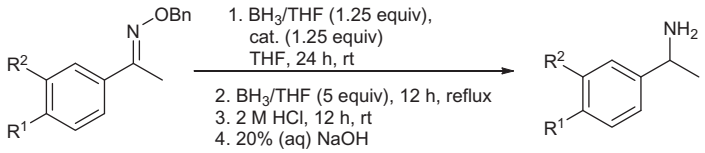
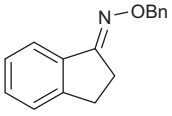
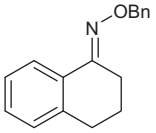
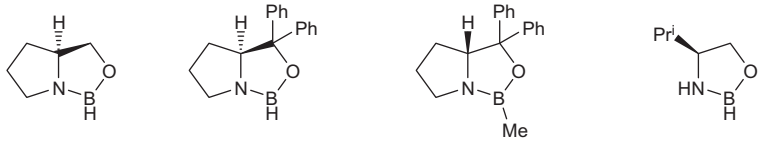
Table 1
Reduction of representative alkyl aryl (*E*)-ketoxime *O*-benzyl ethers with borane catalyzed by oxazaborolidines



6-13 **6a-13a**

Oxime ether			Catalyst	Product amine			
No.	R^1	R^2		No.	Yield[a] (%)	ee[b] (%)	Conf[c]
6	H	H	**1**	**6a**	85	85	(*R*)
			2		52	37	(*R*)
			3		73	26	(*S*)
			4		82	95	(*R*)
			5		82	84	(*S*)
7	OMe		**1**	**7a**	68	99	(*R*)
8	OBu		**1**	**8a**	90	82	(*R*)
9	Cl		**1**	**9a**	91	91	(*R*)
10	F		**1**	**10a**	83	84	(*R*)
11			**1**	**11a**	70	70	(*R*)
12			**1**	**12a**	70	40	(*R*)
13			**1**	**13a**	88	89	(*R*)
			4		71	93	(*R*)
			5		80	84	(*S*)
			14		74	79	(*S*)
			15		71	80	(*S*)
			16		76	57	(*R*)
			17		74	94	(*S*)



14 **15** **16** **17**

[a] Isolated yield.
[b] Determined by GC analysis of the TFA derivative on a Chiraldex-PN chiral capillary column 20 m × 0.25 mm.
[c] Determined by comparison of the sign of the specific rotation with an authentic sample or with the literature data, see the Section 4.

Our second aim was the synthesis of (*S*)-1-(3-methoxyphenyl)ethanamine by the reduction of (*E*)-1-(3-methoxyphenyl)ethanone *O*-benzyl oxime with borane/oxazaborolidines. The amine is the key intermediate in the synthesis of (*S*)-rivastigmine (Fig. 1), a cholinesterase inhibitor used for the treatment of mild to moderate dementia due to Alzheimer or Parkinson diseases.[12]

2. Results and discussion

Terpene oxazaborolidines **1**–**5** (Fig. 1), generated from the corresponding β-amino alcohols prepared as described in our earlier publications,[11,13] were used as catalysts for the reduction of representative alkyl aryl ketoxime *O*-benzyl ethers with borane.

The acetophenone oxime, its ring substituted derivatives, 1-indanone and 1-tetralone oximes were prepared by oximation of the ketones with hydroxylamine hydrochloride/sodium acetate in ethanol. (*E*)-Oximes were isolated by crystallization and immediately transformed into *O*-benzyl ethers **6**–**13** (Table 1) by benzylation of their sodium salts with benzyl chloride. The stereochemical purity of **6**–**13**, which was monitored by ^{1}H NMR, is important, since the selectivity of the reduction of oximes and oxime ethers with borane depends on their *E*/*Z* configuration.[6i] The selectivity is also influenced by the ether group; benzyl ethers were chosen since they can be readily isolated as pure (*E*)-isomers. Oxazaborolidines **1**–**5** were generated by the addition of borane–tetrahydrofuran (2.5 equiv) to a solution of the corresponding β-amino alcohol (1.25 equiv) at 0 °C, and the mixture was left until hydrogen evolution ceased. Next, the oxime ether (1.0 equiv) was added slowly at room temperature and the mixture was left for 24 h. The reduction to the amines proceeded by the borane addition to the C=N–OBn double bond and cleavage of the nitrogen–oxygen bond. The cleavage required an excess of borane and a higher temperature, otherwise a mixture of the product amine and N-substituted hydroxylamine *O*-ether was obtained, as was previously observed.[6j,14] Consequently, after 24 h an excess of borane was

added to complete the reaction at reflux. The results are presented in Table 1.

The selectivity obtained in the reduction of **6** in the presence of terpene oxazaborolidines **1**–**5** decreased in the order **4** > **1** > **5** > **2** > **3**, indicating that **1**, **4**, and **5** with more rigid skeletons than the carane derivatives **2** and **3**, were more selective catalysts. Product amines with opposite configurations were obtained in the reduction catalyzed by the isomeric carane derivatives **2** and **3**, and also by stereoisomeric bornane derivatives **4** and **5**. 4-Substituted acetophenone oxime *O*-benzyl ethers **7**–**10**, and also **11** and **12** were then reduced with borane/**1**. Ethers **7**–**10**, containing electron-donating substituents, were reduced with high selectivity reaching 99% ee for the 4-methoxy substituted **7a**. The selectivity in the reduction of **11** was lower, and decreased further for the more hindered **12**. In the presence of a lower load of **1** (0.5 equiv), **7a** was obtained with a lower enantiomeric excess (85% ee). When the reduction of **7** was carried out without an excess of borane in the second step of the procedure, a mixture of **7a** (99% ee, 58% yield) and the corresponding hydroxylamine *O*-benzyl ether (99% ee, 32% yield) were obtained.

Turning to the synthesis of (*S*)-**13a**, the key intermediate leading to (*S*)-rivastigmine, **13** was reduced with borane, catalyzed with oxazaborolidines **1**, **4**, and **5**. The reduction in the presence of **1** and **4** was selective; however, the product amine (*R*)-**13a** of opposite configuration was obtained. Although the desired (*S*)-**13a** (84% ee) was produced in the presence of **5**, the selectivity was unsatisfactory. Consequently, the reduction of **13** with borane, catalyzed by oxazaborolidines **14**–**17**, derived from the corresponding amino acids was examined, and the results are shown in Table 1. Fortunately, (*S*)-**13a** (94% ee) was obtained in the presence of oxazaborolidine generated from readily available (*S*)-valinol. The reduction catalyzed with oxazaborolidines **14**–**16** was less selective.

Several syntheses of (*S*)-rivastigmine have been reported.[15] Recently, the compound was synthesized from 1-(3-methoxphenyl)ethanone via its derivatives. Thus, the keto group was transformed into the corresponding (*S*)-*tert*-butylsulfinylimine, followed by asymmetric transfer hydrogenation or by reduction with sodium borohydride and hydrolysis to give (*S*)-**13a** (99% ee).[15l,m] Last year, this method, slightly modified, was used for the large scale synthesis of (*S*)-rivastigmine.[15n] Our synthesis provides a direct asymmetric reduction of **13** to (*S*)-**13a**, which can be transformed into (*S*)-rivastigmine following a straightforward three-step methylation–deprotection–carbamoylation route.[15a,m]

3. Conclusion

The results indicate that terpene oxazaborolidines **1**, **4**, and **5**, having rigid apopinane and bornane skeletons, are selective catalysts in the reduction of acetophenone *O*-benzyl oxime with borane, whereas **2** and **3** with a less rigid carane skeleton are less selective. The reduction of **6** and its ring substituted derivatives **7**–**10** and **13** with borane/**1** gave the corresponding amines with 82–99% ee. A simple synthesis of (*S*)-**13a** (94% ee) the key intermediate in the synthesis of (*S*)-rivastigmine, via reduction of **13** with borane/oxazaborolidine generated from readily available (*S*)-valinol, was developed. Its enantiomer (*R*)-**13a** (93% ee) was obtained by the reduction of **13** with borane/**5** derived from (*R*)-camphor.

4. Experimental

4.1. General

Experiments with air and moisture sensitive materials were carried out under a nitrogen atmosphere. Glassware was oven dried for several hours, assembled hot, and cooled in a stream of nitrogen. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 200, Bruker AMX 300 MHz, Avance III 400 MHz, and DRX 600 MHz instruments. EIMS spectra were recorded on Shimadzu QP5050A and ESIMS spectra on a Waters® Micromass® Q-TOF Micro™ spectrometer. HRMS were recorded on a JEOL (Japan) JMS-700 MStation spectrometer and Perspective Biosystems Mariner spectrometer. Optical rotations were measured on an automatic polarimeter Optical Activity polAAr 3000. GC analyses were performed on a Perkin–Elmer Auto System XL chromatograph, and HPLC analyses on a Shimadzu LC 10 chromatograph. Melting points were determined in open glass capillaries and are uncorrected. Elemental analyses were performed by microanalysis laboratories at the Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, and at the CSIR Indian Institute of Chemical Biology using Perkin–Elmer 2400, Series II elemental analyzer, Calcutta, India.

4.2. Materials

Acetophenone, substituted acetophenones, 1-indanone, 1-tetralone, amino acids, sodium hydride 60% suspension in mineral oil, hydroxylamine hydrochloride, and benzyl chloride were commercial products (Aldrich). Tetrahydrofuran was freshly distilled from sodium benzophenone ketyl, and DMF was dried over 3 Å molecular sieves. Dichloromethane and triethylamine were distilled from calcium hydride before use. Oxazaborolidines **1**–**5** were generated from the corresponding amino alcohols prepared as described earlier,[11,13] **14**, **15**, and **17** according to the literature,[16,17] and **16** was a commercial product (Aldrich).

4.3. (*E*)-1-(3-Methoxyphenyl)ethanone oxime 13. Typical procedure

To a solution of 1-(3-methoxyphenyl)ethanone (7.51 g, 50 mmol) in ethanol (50 mL), hydroxylamine hydrochloride (10.42 g, 150 mmol) and sodium acetate (12.30 g, 150 mmol) were added. The mixture was refluxed for 5 h, cooled, poured on crushed ice, and kept overnight in a refrigerator. The crystals formed were filtered off, washed with cold water (5 mL), and dried under vacuum over phosphorous pentoxide, 6.46 g, 79% yield, mp 45–46 °C (from *n*-hexane). Lit.[18] mp 44–45 °C. FT-IR (KBr): ν_{max} 3214, 1576, 1456, 1305, 1225 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.13 s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 6.93 (ddd, J = 7.8 Hz, 2.4 Hz, 1.2 Hz, 1H, CH), 7.17 (t, J = 1.5 Hz, 1H, CH), 7.20 (dt, J = 7.8 Hz, 2.2 Hz, 1H, CH), 7.29 (t, J = 7.8 Hz, 1H, CH), 11.20 (s, 1H, OH). ^{1}H NMR (C_6D_6, 600 MHz): δ 2.07 s, 3H, CH_3), 3.27 (s, 3H, CH_3), 6.77 (ddd, J = 8.4 Hz, 3.0 Hz, 1.2 Hz, 1H, CH), 7.04 (t, J = 8.4 Hz, 1H, CH), 7.18 (dd, J = 7.8 Hz, 1.2 Hz, 1H, CH), 7.35(br s, 1H, CH). ^{13}C NMR (DMSO-d_6, 150 MHz): δ 12.14 (CH_3), 55.33 (OCH_3), 111.39 (CH), 115.10 (CH), 118.65 (CH), 129.54 (CH) 137.92 (C), 155.99 (C), 159.66 (C). ESI-MS: m/z 188 $[M+Na]^+$. EI-HRMS: m/z M^+ 165.07736, requires 165.07898. Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: 65.40; H, 6.67; N, 8.43.

4.3.1. (*E*)-Acetophenone oxime

Yield 80%, mp 58–59 °C. Lit.[19] mp 58–59 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.14 (s, 3H, CH_3), 7.34–7.39 (m, 3H, CH), 7.62–7.63 (m, 2H, CH), 11.19 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 11.51 (CH_3), 125.51 (2CH), 128.32 (2CH), 128.55 (CH), 136.07 (C). 152.85 (C).

4.3.2. (*E*)-1-(4-Methoxyphenyl)ethanone oxime

Yield 76%, mp 86–87 °C. Lit.[20] mp 82–85 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.10 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 6.90–6.95 (m AA′, 2H, CH), 7.55–7.60 (m BB′, 2H, CH), 10.97 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 11.40 (CH_3), 55.10 (OCH_3), 113.68 (2CH), 126.79 (2CH), 129.43 (C), 152.34 (C), 159.60 (C).

4.3.3. (*E*)-1-(4-Benzyloxyphenyl)ethanone oxime

Yield 96%, mp 156–158 °C. ^{1}H NMR (DMSO-d_6, 200 MHz): δ 2.10 (s, 3H, CH_3), 5.11 (s, 2H, CH_2), 6.96–7.06 (m AA′, 2H, CH), 7.28–7.48 (m BB′, 5H, CH), 7.55–7.59 (m, 2H, CH), 10.98 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 11.43 (CH_3), 69.19 (CH_2), 114.58 (2CH), 126.81 (2CH), 127.62 (2CH), 127.81 (CH), 128.40 (2CH), 129.64 (C), 136.94 (C), 152.33 (C), 158.69 (C). HRMS: m/z M^+ 242.11761, requires 242.11758.

4.3.4. (*E*)-1-(4-Chlorophenyl)ethanone oxime

Yield 92%, mp 98–99 °C. Lit.[21] mp 96–97 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.13 (s, 3H, CH_3), 7.40–7.45 (m AA′, 2H, CH), 7.63–7.68 (m BB′, 2H, CH), 11.32 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 11.32 CH_3), 127.22 (2CH), 128.31 (2CH), 133.21 (C), 135.76 (C), 151.96 (C).

4.3.5. (*E*)-1-(4-Fluorophenyl)ethanone oxime

Yield 95%, mp 76–77 °C. Lit.[22] mp 75.6–76.2 °C. ^{1}H NMR (DMSO-d_6, 200 MHz): δ 2.13 (s, 3H CH_3), 7.13–7.26 (m AA′, 2H, CH), 7.62–7.73 (m BB′, 2H, CH), 11.20 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 11.52 (CH_3), 115.17 (d, J_{CF} = 20.3 Hz, 2CH), 127.60 (d, J_{CF} = 8.2 Hz, 2CH), 133.47 (d, J_{CF} = 3.4 Hz, C), 152.03 (C), 162.37 (d, J_{CF} = 244.2, C). HRMS: *m*/*z* M^+ 154.06620, requires 154.06627. Anal. Calcd for C_8H_8FNO: C, 62.74; H, 5.26; N, 9.15. Found: C, 62.55, H, 5.27; N, 9.34.

4.3.6. (*E*)-1-Indanone oxime

Yield 94%, mp 143–145 °C. Lit.[23] mp 148–150 °C. ^{1}H NMR (DMSO-d_6, 200 MHz): δ 2.71–2.83 (m AA′, 2H, CH_2), 2.93–3.05 (m BB′, 2H, CH_2), 7.20–7.40 (m, 3H, CH), 7.55 (d, J = 7.2 Hz, 1H, CH), 10.83 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 25.56 (CH_2), 27.92 (CH_2), 120.56 (CH), 125.72 (CH), 126.80 (CH), 129.68 (CH), 136.59 (C), 147.64 (C), 160.98 (C).

4.3.7. (*E*)-1-Tetralone oxime

Yield 71%, mp 101–102 °C. Lit.[24] mp 100–102 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.91 (quintet, J = 6.4 Hz, 2H, CH_2), 2.79 (t, J = 6.4 Hz, 2H, CH_2), 2.87 (t, J = 6.4 Hz, 2H, CH_2), 7.18 (ddd, J = 7.8 Hz, 1.6 Hz, 0.8 Hz, 1H, CH), 7.23 (tdd, J = 7.8 Hz, 1.6 Hz, 1.2 Hz, 1H, CH), 7.30 (td, J = 7.8 Hz, 1.2 Hz), 7.92 (dd, J = 8.0 Hz, 1.2 Hz, 1H, CH), 8.3 (br s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.29 (CH_2), 23.87 (CH_2), 29.81 (CH_2), 124.13 (CH), 126.50 (CH), 128.70 (CH), 129.31 (CH), 130.35 (C), 139.80 (C), 155.34 (C).

4.4. (*E*)-1-(3-Methoxyphenyl)ethanone *O*-benzyl oxime 13. Typical procedure

Sodium hydride 60% dispersion in mineral oil (5.80 g, 145 mmol) was washed with *n*-hexane (2 × 10 mL), after which dry DMF (150 mL) was added. Next **13** (16.52 g, 100 mmol) was added with cooling in ice-water, and the mixture was stirred for 24 h. Benzyl chloride (15.19 g, 120 mmol) was then added and the mixture was stirred overnight at room temperature. The solvent was removed under vacuum, after which cold water (100 mL) was added, and the mixture was extracted with diethyl ether (3 × 200 mL). The extract was washed with brine and dried over anhydrous magnesium sulfate, and the product was isolated by distillation, 24.25 g, 95%, bp 138–140 °C/0.1 mm Hg. FT-IR (KBr): ν_{max} 2932, 1577, 1457, 1321, 1228, 1042 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.26 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 5.25 (s, 2H, OCH_2), 6.91 (ddd, J = 7.6 Hz, 2.7 Hz, 1.8 Hz, 1H, CH), 7.20–7.50 (m, 8H, CH). ^{1}H NMR (C_6D_6, 600 MHz): δ 2.06 (s, 3H, CH_3), 3.03 (s, 3H, OCH_3), 5.26 (s, 2H, CH_2), 6.77 (ddd, J = 8.4 Hz, 2.4 Hz, 0.6 Hz, 1H, CH), 7.06 Hz (t, J = 7.8 Hz, 1H, CH), 7.09 (t, J = 7.2 Hz, 1H, CH phenyl), 7.14–7.18 (m, 2H, CH), 7.234 (ddd, J = 7.8 Hz, 2.4 Hz, 0.6 Hz, 1H, CH), 7.357 (d, J = 6.6 Hz, 2H, CH), 7.43 (dd, J = 2.4 Hz, 0.6 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 12.97 (CH_3), 55.25 (OCH_3), 76.19 (CH_2), 111.43 (CH), 114.76 (CH), 118.65 (CH), 127.73 (CH), 128.14 (2CH), 128.32 (2CH), 129.32 (CH), 138.00 (2C), 154.80 (C), 159.52 (C). ESI-MS *m*/*z*: 278 $[M+Na]^+$; EI-MS *m*/*z*: 255 (M^+, 5%), 237 (2), 148 (2), 105 (2), 91 (100), 76 (12), 65 (8), 51 (3), 39 (3). HRMS: *m*/*z* M^+ 255.1270, requires 255.1259. Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.23; H, 6.68; N, 5.45.

4.4.1. (*E*)-Acetophenone *O*-benzyl oxime 6

Yield 87%, bp 120–122 °C/0.2 mm Hg. Lit.[6b] bp 145 °C/15 mm Hg. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.33 (s, 3H, CH_3), 5.32 (s, 2H, CH_2), 7.33–7.52 (m, 8H, CH), 7.67–7.74 (m, 2H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 12.81 (CH_3), 76.14 (CH_2), 126.04 (2CH), 127.68 (CH), 128.09 (2CH), 128.30 (4CH), 128.98 (CH), 136.59 (C), 138.07 (C), 154.89 (C).

4.4.2. (*E*)-1-(4-Methoxphenyl)ethanone *O*-benzyl oxime 7

Yield 93%, bp 168–170 °C (0.7 mmHg), mp 42–44 °C. Lit.[8c] an oily liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.25 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 5.23 (s, 2H, CH_2), 6.86–6.91 (m AA′, 2H, CH), 7.30–7.44 (m, 5H, CH), 7.58–7.63 (m BB′, 2H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 12.75 (CH_3), 55.28 (OCH_3), 76.03 (OCH_2), 113.74 (2CH), 127.40 (2CH), 127.64 (CH), 128.09 (2CH), 128.30 (2CH), 129.23 (C), 138.25 (C), 154.50 (C), 160.38 (C).

4.4.3. (*E*)-1-(4-Benzyloxyphenyl)ethanone *O*-benzyl oxime 8

Yield 94%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.27 (s, 3H, CH_3), 5.10 (s, 2H, CH_2), 5.26 (s, 2H, CH_2), 6.95–7.01 (m AA′, 2H, CH), 7.30–7.48 (m, 10H, CH), 7.59–7.66 (m BB′, 2H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 12.74 (CH_3), 69.95 (CH_2), 76.01 (CH_2), 114.65 (2 CH), 127.39 (2CH), 127.40 (2CH), 127.64 (CH), 127.98 (CH), 128.07 (2CH), 128.29 (2CH), 128.57 (2CH), 129.40 (C), 136.74 (C), 138.19 (C), 154.45 (C), 159.51 (C). HRMS: *m*/*z* M^+ 332.16479, requires 332.16451. Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.47; H, 6.46; N, 4.16.

4.4.4. (*E*)-1-(4-Chlorophenyl)ethanone *O*-benzyl oxime 9

Yield 84%, bp 156–157 °C (0.7 mmHg), mp 58–60 °C. Lit.[8c] mp 57–58 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.25 (s, 3H, CH_3), 5.25 (s, 2H, CH_2), 7.30–7.36 (m AA′, 2H, CH), 7.28–7.45 (m, 5H, CH), 7.56–7.62 (m BB′, 2H, CH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 12.86 (CH_3), 75.94 (CH_2), 128.11 (2CH), 128.22 (CH), 128.48 (2CH), 128.81 (2CH), 128.97 (2CH), 134.42 (C), 135.15 (C), 138.35 (C), 154.06 (C).

4.4.5. (*E*)-1-(4-Fluorophenyl)ethanone *O*-benzyl oxime 10

Yield 93%, bp 152–153 °C (2.5 mmHg), mp 58–60 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.26 (s, 3H, CH_3), 5.24 (s, 2H, CH_2), 7.00–7.10 (m AA′, 2H, CH), 7.30–7.50 (m, 5H, CH), 7.60–7.70 (m BB′, 2H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 12.81 (CH_3), 76.21 (CH_2), 115.23 (d, J_{CF} = 21.85 Hz, 2CH), 127.77 (d, J_{CF} = 1.5 Hz, 2CH), 127.95 (CH), 128.12 (2CH), 128.35 (2CH), 132.48 (d, J_{CF} = 3.0 Hz, C), 138.02 (C), 153.90 (C), 162.85 (d, J_{CF} = 247.0 Hz, C). HRMS: *m*/*z* M^+ 244.11399, requires 244.11322. Anal. Calcd for $C_{15}H_{14}FNO$: C, 74.06; H, 5.80; N, 5.76. Found: C, 74.04; H, 5.90; N, 5.72.

4.4.6. (*E*)-1-Indanone *O*-benzyl oxime 11

Yield 70%, bp 130 °C (0.05 mmHg). ^{1}H NMR (C_6D_6, 400 MHz): δ: 2.90–2.99 (m AA′, 2H, CH_2), 2.40–2.46 (m BB′, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.90 (ddt, J = 7.2 Hz, 1.6 Hz, 0.8 Hz, 1H, CH), 6.96 (tdt, J = 7.2 Hz, 1.6 Hz, 0.8 Hz, 1H, CH), 7.02 (td, J = 7.2 Hz, 1.6 Hz, 1H, CH), 7.05–7.21 (m, 3H, CH), 7.38–7.42 (m, 2H, CH), 7.74 (ddd,

J = 7.2 Hz, 1.6 Hz, 0.8 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.65 (CH_2), 28.59 (CH_2), 76.19 (CH_2), 125.53 (CH), 126.91 (CH), 127.71 (CH), 128.08 (2CH), 128.34 (2CH), 130.25 (CH), 136.18 (C), 138.27 (C), 148.32 (C), 163.18 (C). HRMS: m/z M^+ 238.12166, requires 238.12264. Anal. Calcd for $C_{16}H_{15}NO$: C, 80.97; H, 6.37; N, 5.90. Found: C, 80.88; H, 6.47; N, 5.82.

4.4.7. (*E*)-1-Tetralone *O*-benzyl oxime 12

Yield 83%, bp 162–164 °C/3 mm Hg. Lit.[8c,25] bp 225–227 °C/15 mm Hg. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.87 (quintet, J = 6.0 Hz, 2H, CH_2), 2.77 (t, J = 6.0 Hz, 2H, CH_2), 2.82 (t, J = 6.0 Hz, 2H, CH_2), 5.27 (s, 2H, CH_2), 7.15 (ddd, J = 7.2 Hz, 1.2 Hz, 0.8 Hz, 1H, CH), 7.21 (tdd, J = 8.0 Hz, 1.6 Hz, 0.8 Hz, 1H, CH), 7.27 (td, J = 7.2 Hz, 1.2 Hz, 1H, CH), 7.31–7.47 (m, 5H, CH), 8.02 (dd, J = 8.0 Hz, 1.2 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.44 (CH_2), 24.58 (CH_2), 29.78 (CH_2), 76.24 (CH_2), 124.34 (CH), 126.31 (CH), 127.71 (CH), 128.14 (2CH), 128.34 (2CH), 128.54 (CH), 128.96 (CH), 130.75 (C), 138.24 (C), 139.57 (C), 154.39 (C).

4.5. (*S*)-1-(3-Methoxyphenyl)ethanamine 13a. Typical procedure

At first, borane/THF (25 mL, 25 mmol) was added to a solution of (*S*)-valinol (1.29 g, 12.5 mmol) in THF (10 mL) at 0 °C, and the mixture was stirred for 5 h in an ice-water bath. A solution of **13** (2.55 g, 10 mmol) in THF (10 mL) was then added dropwise and the mixture was stirred for 24 h at room temperature. Next, borane/THF (50 mL, 50 mmol) was added, the mixture was gently refluxed for 24 h, then cooled, acidified with 2 M hydrochloric acid, and stirred for 24 h at room temperature. It was then concentrated under vacuum, alkalized with 20% aqueous sodium hydroxide, and extracted with ethyl acetate (3 × 50 mL). The organic solution was washed with saturated brine (50 mL), and dried over anhydrous magnesium sulfate. The solvent was removed and the product was isolated by flash chromatography, silica gel, dichloromethane–methanol–triethylamine 9:1:0.1, 1.12 g, 74%, and distilled, bp 118–120 °C/2.5 mm Hg, $[\alpha]_D^{20} = -18.8$ (c 1.0, MeOH), 94% ee by GC analysis of trifluoroacetamide on a Chiraldex G-PN column, 20 m × 0.25 mm, t_R 29.74 (*R*), t_R 35.15 (*S*), T = 125 °C, f = 30 cm/s. Lit.[15m] $[\alpha]_D^{20} = -19.2$ (c 1, MeOH), 99.34% ee. IR (KBr): ν_{max} 3361, 2964, 1594, 1559, 1260, 1042 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.38 d, J = 6.6 Hz, 3H, CH_3), 1.86 (s, 2H, NH_2), 3.81 (s, 3H, OCH_3), 4.09 (q, J = 6.6 Hz, 1H, CH), 6.78 (ddd, J = 8.1 Hz, 2.7 Hz, 0.9 Hz, 1H, CH), 6.91 (s, 1H, CH), 6.92 (d, J = 7.2 Hz, 1H, CH), 7.24 (t, J = 8.1 Hz, 1H, CH). ^{1}H NMR (C_6D_6, 600 MHz): δ 1.21 d, J = 6.6 Hz, 3H, CH_3), 2.34 br s, 2H, NH_2), 3.40 (s, 3H, OCH_3), 4.83 q, J = 6.6 Hz, 1H, CH), 6.70 (d, J = 7.8 Hz, 1H, CH), 6.88 (d, J = 7.8 Hz, 1H, CH), 7.02 (s, 1H, CH), 7.12 (t, J = 7.8 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 25.42 (CH_3), 51.26 (OCH_3), 55.16 (CH), 111.35 (CH), 112.06 (CH), 118.00 (CH), 129.47 (CH), 149.28 (C), 159.72 (C). EIMS m/z: 151 (M^+, 23%), 136 (100), 121 (4), 109 (38), 94 (22), 77 (17), 6 (10), 44 (22). HR-MS m/z M^+ 151.0967, requires 151.0997. Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67 N; 9.26. Found: C, 71.55 H, 8.69 N, 9.29.

4.5.1. (*R*)-1-(Phenyl)ethanamine 6a

This Compound was obtained by the reduction of **6** with borane/**1**, 85% yield, $[\alpha]_D^{20} = +25.1$ (c 0.6 MeOH), 85% ee, determined by GC analysis of trifluoroacetamide on a Chiraldex G-PN column, 20 m × 0.25 mm, t_R 58.04 (*R*), t_R 59.36, (*S*), T = 130 °C, f = 30 cm/s. Lit.[6e] $[\alpha]_D^{20} = +28.7$ (c 4.1, MeOH), 99% ee. The racemate was also analyzed. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.44 (d, J = 6.6 Hz, 3H, CH_3), 3.31 (br s, 2H, NH_2), 4.15 (q, J = 6.6 Hz, 1H, CH), 7.20–7.40 (m, 5H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 24.64 (CH_3), 51.29 (CH), 125.83 (2CH), 127.10 (CH,) 128.52 (2CH), 145.91 (C).

4.5.2. (*R*)-1-(4-Methoxyphenyl)ethanamine 7a

This compound was obtained by the reduction of **7** with borane/**1**, 68% yield, $[\alpha]_D^{20} = +28.9$ (c 2.0, benzene), 99% ee, determined by GC analysis of trifluoroacetamide on a Chiraldex G-PN column, 20 m × 0.25 mm, t_R 41.18 (*R*), t_R 46.58, (*S*), T = 120 °C, f = 30 cm/s. Lit.[26] (*S*)-**7a**, $[\alpha]_D^{27} = -29.4$ (c 8, benzene), >99% ee. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.36 (d, J = 6.6 Hz, 3H, CH_3), 1.48 (s, 2H, NH_2), 3.80 (s, 3H, OCH_3), 4.08 (q, J = 6.6 Hz, 1H, CH), 6.84–6.89 (m AA′, 2H, CH), 7.24–7.29 (m BB′, 2H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.72 (CH_3), 50.64 (CH), 55.24 (OCH_3), 113.77 (2CH), 126.68 (2CH), 139.93 (C), 158.40 (C).

4.5.3. (*R*)-1(4-Benzyloxyphenyl)ethanamine 8a

This compound was obtained by the reduction of **8** with borane/**1**, 90% yield, $[\alpha]_D^{20} = +22.8$ (c 1.75, $CHCl_3$), 81.6% ee, determined by HPLC analysis of trifluoroacetamide on a Daicel Chiralcel OD-H column, 25 cm × 0.46 cm, 5 μm particles, *n*-hexane–isopropanol, 9:1, t_R 13.33 (*R*), t_R 15.91 (*S*), T = 25 °C, f = 0.7 mL/min. Lit.[9b] (*S*), $[\alpha]_D^{20} = -24.7$ (c 1.75 $CHCl_3$), 93% ee. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.37 (d, J = 6.6 Hz, 3H, CH_3), 1.51 (s, 2H, NH_2), 4.07 (q, J = 6.6 Hz, 1H, CH), 5.06 (s, 2H, CH_2), 6.92–7.00 (m AA′, 2H, CH), 7.24–7.32 (m BB′, 2H, CH), 7.33–7.50 (m, 5H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.70 (CH_3), 50.63 (CH), 70.01 (OCH_2), 114.74 (2CH), 126.69 (2CH), 127.39 (2CH), 127.84 (CH) 128.50 (2CH) 137.10 (C), 140.26 (C), 157.63 (C).

4.5.4. (*R*)-1-(4-Chlorophenyl)ethanamine 9a

This compound was obtained by the reduction of **9** with borane/**1**, 91% yield, $[\alpha]_D^{20} = +21.8$ (c 2.0, MeOH), 91% ee, determined by GC analysis of trifluoroacetamide on a Chiraldex G-PN column, 20 m × 0.25 mm, t_R 23.82 (*R*), t_R 27.21, (*S*), T = 130 °C, f = 30 cm/s. Lit.[26] $[\alpha]_D^{20} = -23.7$ (c 2, MeOH). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.35 (d, J = 6.6 Hz, 3H, CH_3), 1.49 (br s, 2H, NH_2), 4.10 (q, J = 6.6 Hz, 1H, CH), 7.28 (s, 4H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.75 (CH_3), 50.72 (CH), 127.14 (2CH), 127.85 (CH), 128.53 (2CH), 132.36 (C), 146.24 (C).

4.5.5. (*R*)-1-(-4-Fluorophenyl)ethanamine 10a

This compound was obtained by the reduction of **10** with borane/**1**, 83% yield, $[\alpha]_D^{20} = +21.4$ (c 1.0, MeOH), 84.2% ee, determined by GC analysis of trifluoroacetamide on a Chiraldex G-PN column, 20 m × 0.25 mm, t_R 22.61 (*R*), t_R 27.36 (*S*), T = 110 °C, f = 30 cm/s. Lit.[27] $[\alpha]_D^{20} = +25$ (c 1, MeOH). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.37 (d, J = 6.6 Hz, 3H, CH_3), 1.68 (s, 2H, NH_2), 4.12 (q, J = 6.6 Hz, H, CH) 6.96–7.04 (m AA′, 2H, CH), 7.27–7.35 (m BB′, 2H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.83 (CH_3) 50.67 (CH), 115.15 (d, J_{CF} = 20.9 Hz, 2CH), 127.21 (d, J_{CF} = 7.75 Hz, 2CH), 143.31 (d, J_{CF} = 2.9 Hz, C), 161.71 (d, J_{CF} = 242.7 Hz, C).

4.5.6. (*R*)-2,3-Dihydro-1*H*-inden-1-amine 11a

This compound was obtained by the reduction of **11** with borane/**1**, 70% yield, $[\alpha]_D^{20} = -12.2$ (c 1.0, MeOH), 69.5% ee, determined by GC analysis of trifluoroacetamide on a Supelco β-DEX 325 column, 30 m × 0.25 mm, t_R 103.18 (*R*), t_R 105.01 (*S*), T = 110 °C. Lit.[28] $[\alpha]_D^{20} = -17$ (c 1.3, MeOH). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.55 (s, 2H, NH_2), 1.69 (ddt, J = 12.6 Hz, 8.7 Hz, 7.8 Hz, 1H, CH_2), 2.52 (dddd, J = 12.6 Hz, 7.8 Hz, 7.2 Hz, 3.3 Hz, 1H, CH_2) 2.81 (dt, J = 15.9 Hz, 8.1 Hz, 1H, CH_2), 2.97 (ddd, J = 15.9 Hz, 8.7 Hz, 3.3 Hz, 1H, CH_2), 4.36 (t, J = 7.8 Hz, 1H, CH), 7.17–7.25 (m, 3H, CH) 7.31–7.36 (m, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 30.09 (CH_2) 37.39 (CH_2), 57.28 (CH), 123.29 (CH), 124.64 (CH), 126.46 (CH), 127.14 (CH), 143.06 (C), 147.50 (C).

4.5.7. (*R*)-1,2,3,4-Tetrahydronaphthalen-1-amine 12a

This compound was obtained by the reduction of **12** with borane/**1**, 70% yield, $[\alpha]_D^{20} = -12.1$ (c 1.3, MeOH), 40.0% ee, determined

by GC analysis of trifluoroacetamide on a Supelco β-DEX 325 column, 30 m × 0.25 mm, t_R 19.16 (*S*), t_R 19.73 (*R*), *T* = 160 °C, *f* = 30 cm/s. Lit.[28] $[\alpha]_D^{20} = -26$ (*c* 1.32, MeOH). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.61 (s, 2H, NH_2), 1.60–1.85 (m, 2H, CH_2), 1.90–2.15 (m, 2H, CH_2), 2.78 (q, *J* = 5.5 Hz 2H, CH_2), 3.98 (t, *J* = 5.5 Hz, 1H, CH), 7.05–7.25 (m, 3H, CH), 7.32–7.45 (m, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.51 (CH_2), 29.51 (CH_2), 33.53 (CH_2), 49.32 (CH), 125.94 (CH), 126.48 (CH), 127.97 (CH), 128.94 (CH), 136.64 (C), 141.14 (C).

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References

1. Kozma, D. *CRC Handbook of Optical Resolutions via Diastereomeric Salt Formation*; CRC Press: Boca Raton, Florida, 2001.
2. Lawrence, S. A. *Amines: Synthesis Properties and Applications*; Cambridge University Press: Cambridge, UK, 2004.
3. Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, *8*, 1895–1946.
4. Fache, F.; Schulz, E.; Tommasino, M. L.; Lamaire, M. *Chem. Rev.* **2000**, *100*, 2159–2232.
5. Corey, E. J.; Czako, B.; Kurti, L. *Molecules and Medicine*; J. Wiley: Hoboken, New Jersey, 2007.
6. (a) Deloux, L.; Srebnik, M. *Chem. Rev.* **1993**, *93*, 763–784; (b) Brunel, J-M. *Recent Res. Dev. Org. Chem.* **2003**, *7*, 155–190; (c) Glushkov, V. A.; Tolstikov, A. G. *Usp. Khim.* **2004**, *73*, 632–661; (d) Hirao, A.; Itsuno, S.; Nakahama, S.; Yamazaki, N. *J. Chem. Soc. Chem. Commun.* **1981**, 315–317; (e) Itsuno, S.; Nakano, M.; Miyazaki, K.; Masuda, H.; Ito, K. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2039–2044; (f) Itsuno, S.; Nakano, M.; Ito, K. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2615–2619; (g) Itsuno, S.; Sakurai, Y.; Shimizu, K.; Ito, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1859–1863; (h) Inoue, T.; Sato, D.; Komura, K.; Itsuno, S. *Tetrahedron Lett.* **1999**, *29*, 5379–5382; (i) Sakito, Y.; Yoneyoshi, Y.; Suzukamo, G. *Tetrahedron Lett.* **1988**, *29*, 223–224; (j) Fontaine, E.; Namane, C.; Meneyrol, J.; Geslin, M.; Serva, L.; Russey, E.; Tissandie, S.; Maftouh, M.; Roger, P. *Tetrahedron: Asymmetry* **2001**, *12*, 2185–2189; (k) Krzeminski, M. P.; Zaidlewicz, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1463–1466; (l) Dutheuil, G.; Bailly, L.; Couve-Bonnaire, S.; Pannecoucke, X. *J. Fluorine Chem.* **2007**, *128*, 34–39; (m) Demir, A. S.; Tanyeli, C.; Cagir, A.; Tahir, M. N.; Ulku, D. *Tetrahedron: Asymmetry* **1998**, *9*, 1035–1042; (n) Demir, A. S.; Sesenoglu, O.; Garcek-Arkin, Z. *Tetrahedron: Asymmetry* **2009**, *12*, 2309–2313; (o) Demir, A. S.; Sesenoglu, O.; Oksoy-Cam, H.; Kaya, H.; Aydogan, K. *Tetrahedron: Asymmetry* **2003**, *14*, 1335–1340; (p) Demir, A. S.; Sesenoglu, O.; Ulku, D.; Arci, C. *Helv. Chim. Acta* **2004**, *87*, 106–118; (q) Zheng, W.; Li, M.; Tian, A. *J. Mol. Struct. (Theochem)* **2004**, *668*, 13–23; (r) Salias, H. E.; Watts, J. P.; Whiting *J. Chem. Soc., Perkin Trans. 1* **2000**, 3362–3374; (s) Tillyer, R. D.; Boudreau, C.; Tschaen, D.; Dolling, U.-H.; Reider, P. J. *Tetrahedron Lett.* **1995**, *35*, 4337–4340; (t) Shimizu, M.; Kamei, M.; Fujisawa, T. *Tetrahedron Lett.* **1995**, *36*, 5239–5242; (u) Shimizu, M.; Tsukamoto, K.; Matsutani, T.; Fujisawa, T. *Tetrahedron* **1998**, *54*, 10265–10274.
7. (a) Matsui, M.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 5195–5198; (b) Itsuno, S.; Matsumoto, T.; Sato, D.; Inoue, T. *J. Org. Chem.* **2000**, *65*, 5879–5881.
8. (a) Chu, Y.; Shan, Z.; Liu, D.; Sun, N. *J. Org. Chem* **2006**, *71*, 3998–4001; (b) Stepanenko, V.; Huang, K.; Ortiz-Marciales, M. *Org. Synth.* **2010**, *87*, 26–33; (c) Huang, X.; Ortiz-Marciales, M.; Huang, K.; Stepanienko, V.; Merced, F. G.; Ayala, A. M.; Correa, W.; De Jesus, M. *Org. Lett.* **2007**, *9*, 1793–1795; (d) Huang, K.; Ortiz-Marciales, M.; Merced, F. G.; Melendez, H. J.; Correa, W.; De Jesus, M. *J. Org. Chem.* **2008**, *73*, 4017–4026; (e) Huang, K.; Ortiz-Marciales, M.; Stepanienko, V.; De Jesus, M.; Correa, W. *J. Org. Chem.* **2008**, *73*, 6928–6931; (f) Huang, X.; Ortiz-Marciales, M. *Org. Synth.* **2010**, *87*, 36–52.
9. (a) Lantos, I.; Flisak, J.; Liu, L.; Matsuoka, R.; Mendelson, W.; Stevenson, D.; Tubman, K.; Tucker, L.; Zhang, W.-Y.; Adams, J.; Sorensen, M.; Garigipati, R.; Erhard, K.; Ross, S. *J. Org. Chem.* **1997**, *62*, 5385–5391; (b) Łączkowski, K. Z.; Pakulski, M. M.; Krzeminski, M. P.; Jaisankar, P.; Zaidlewicz, M. *Tetrahedron: Asymmetry* **2008**, *19*, 788–792.
10. Matsui, M.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 5199–5200.
11. (a) Krzeminski, M. P.; Wojtczak, A. *Tetrahedron Lett.* **2005**, *46*, 8299–8303; (b) Bosiak, M. J.; Krzeminski, M. P.; Jaisankar, P.; Zaidlewicz, M. *Tetraherdon: Asymmetry* **2008**, *19*, 956–963.
12. (a) Spencer, M.; Noble, S. *Drugs Aging* **1998**, *13*, 391–411; (b) Teklin, S.; Lane, R. *Neurother. Neuropsychopharmacol.* **2006**, *1*, 13–25; (c) Weintraub, D.; Somogyi, M.; Meng, X. *Am. J. Alzheimers Dis. Demen.* **2011**, *26*, 443–449.
13. (a) Łączkowski, K. Z.; Kmieciak, A.; Kozakiewicz, A. *Tetrahedron: Asymmetry* **2009**, *20*, 1487–1492; (b) Bosiak, M. J.; Pakulski, M. M. *Synthesis* **2011**, 316–324.
14. Dougherty, J. T.; Flisak, J. R.; Hades, J.; Lantos, I.; Liu, L.; Tucker, L. *Tetrahedron: Asymmetry* **1997**, *8*, 497–499.
15. (a) Amstutz, R.; Enz, A.; Marzi, M.; Boelsterli, J.; Walkinsshaw, M. *Helv. Chim. Acta* **1990**, *73*, 739–753; (b) H. Stepankova, J. Hajicek, S. Simek, WO 2004037771; *Chem. Abstr.* **2004**, *142*, 6315.; (c) A. Gaitonde, M. Mangle, A. Pawar, WO 2005061446; *Chem. Abstr.* **2005**, *143*, 77963.; (d) Garrido, M. J. V., Monsterrat, A. M.; Juarez, M. J. WO 2007014973, *Chem. Abstr.* **2007**, *146*, 206113.; (e) Ma, D. W.; Pan, Q.; Pan, S. WO 2007025481; *Chem. Abstr.* **2007**, *146*, 295621.; (f) Mangas-Sanchez, J.; Rodriguez-Mata, M.; Busto, E.; Gotor-Fernandez, V.; Gotor, V. *J. Org. Chem.* **2009**, *74*, 5304–5310; (g) Kumar, K. A.; Reddy, M. A.; Kumar, T. S.; Kumar, B. V.; Chandrasekhar, K. B.; Kumar, P. P.; Pal, M. *Beilstein J. Org. Chem.* **2010**, *6*, 1174–1179; (h) Fuchs, M.; Koszlewski, D.; Tauber, K.; Kroutil, W.; Faber, K. *Chem. Commun.* **2010**, *46*, 5500–5502; (i) Han, K.; Kim, C.; Park, J.; Feng, M. J. *J. Org. Chem.* **2010**, *75*, 3105–3108; (j) Hu, M.; Zhang, F.-L.; Xie, M.-H. *Synth. Commun.* **2009**, *39*, 1527–1533; (k) Boezio, A. A.; Pytkowicz, J.; Cote, A.; Charette, A. B. *J. Am. Chem. Soc.* **2003**, *125*, 14260–14261; (l) Guijarro, D.; Pablo, O.; Yus, M. *J. Org. Chem.* **2010**, *75*, 5265–5270; (m) Arava, V. R.; Gorentla, L.; Dubey, P. K. *Pharma Chemica* **2011**, *3*, 426–433; (n) Arava, V. R.; Gorentla, L.; Dubey, P. K. *Int. J. Org. Chem.* **2011**, *1*, 26–32.
16. Itsuno, S.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2887–2893.
17. Mathre, D. J.; Jones, T. K.; Xawier, L. C.; Blacklock, T. J.; Reamer, R. A.; Mohan, J. J.; Jones, E. T. T.; Hoogsteen, K.; Baum, M. W.; Grabowski, E. J. J. *J. Org. Chem.* **1991**, *56*, 751–762.
18. Schlittler, E.; Mueller, J. *Helv. Chim. Acta* **1948**, *31*, 914–921.
19. (a) Mackor, A. *J. Org. Chem.* **1978**, *43*, 3241–3243; (b) Buchanan, G. W.; Dawson, B. A. *Can. J. Chem.* **1976**, *54*, 790–794.
20. Wang, H.-Y.; Mueller, D. S.; Sachwani, R.; Londino, H. N.; Andersson, L. L. *Org. Lett.* **2010**, *12*, 2290–2294.
21. (a) Celik, H. *J. Phys. Chem. B* **2006**, *110*, 6785–6796; (b) Pearson, D. E.; Baxter, J. F.; Martin, J. C. *J. Org. Chem.* **1952**, *17*, 1511–1518.
22. Beauchemin, A. M.; Moran, J.; Lebrun, M.-E.; Seguin, C.; Dimitrievic, E.; Zhang, L.; Gorelsky, S. *Angew Chem., Int. Ed.* **2008**, *47*, 1410–1413.
23. Clive, D. L. J.; Pham, M. P.; Subedi, R. *J. Am. Chem. Soc.* **2007**, *129*, 2713–2717.
24. Koenig, S. G.; Singh, S. P.; Bakale, R. P.; Zhao, H.; Vandenbossche, C. P. *Org. Synth.* **2010**, *87*, 275–287.
25. Lamart-Lucas, P.; Hoch, M. J.; Viale, M. *Bull. Soc. Chim. France* **1952**, 220–224.
26. Pallavicini, M.; Valoti, E.; Villa, L.; Piccolo, O. *Tetrahedron: Asymmetry* **1997**, *8*, 1069–1073.
27. Gao, Y.; Zou, X.-M.; Yu, L.-M.; Xu, H.; Liu, B.; Zhu, Y.-Q.; Hu, F-Z.; Yang, H.-Z. *Chin. J. Chem.* **2006**, *24*, 521–526.
28. Gutman, A. L.; Etinger, M.; Nisnevich, G.; Polyak, F. *Tetrahedron: Asymmetry* **1998**, *9*, 4369–4379.