Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 1209–1217

TETRAHEDRON: *ASYMMETRY*

Application of optically active 1,2-diol monotosylates for synthesis of β-azido and β-amino alcohols with very high enantiomeric purity. Synthesis of enantiopure (*R*)-octopamine, (*R*)-tembamide and (*R*)-aegeline

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Received 16 May 2002; accepted 13 June 2002

Abstract—A very convenient and highly efficient synthesis of near enantiopure β-azido and β-amino alcohols including biologically active substances such as (*R*)-octopamine, (*R*)-tembamide and (*R*)-aegeline from optically active 1,2-diol monotosylates is reported. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Optically active β-azido alcohols are of great significance as potential precursors for non-racemic aziridines[1] and β-amino alcohols.[2] The latter compounds are not only a common structural component in a vast group of naturally occurring and synthetic molecules, but also can be widely used as versatile chiral building blocks and chiral catalysts[3] in organic synthesis. In particular, chiral 2-amino-1-arylethanols are important structural elements in pharmaceuticals such as α- or β-adrenergic blockers and agonists in the treatment of cardiovascular disease, cardiac failure, asthma and glaucoma.[4] Accordingly, the development of practical methods for regio- and enantioselective synthesis of enantiopure 2-azido-1-arylethanols is of great interest. For the synthesis of these compounds, many methods, including the enzymatic resolution of a racemic mixture,[5] enantio- or regioselective azidolysis of aryloxiranes using biological[6a] and chemical methods,[6b–f] and reductions of 2-azido-1-arylethanones by catalytic asymmetric hydrogenation,[7a] CBS-oxazaborolidine-catalyzed borane,[7b] sodium borohydride in the presence of β-cyclodextrin[8] and baker's yeast[9] have been reported. However, the resolution methods suffer from the fact that the theoretical yields are limited to 50%.[5b] The azidolysis of aryloxiranes is commonly accompanied by the formation of undesired regioisomers having the azido group at the benzylic position.[6b–f] For other methods for synthesis of chiral 2-amino-1-arylethanols, reduction of non-racemic arylcyanohydrins,[10] baker's yeast-mediated reduction of α-(acyl or alkoxycarbonylamino)-acetophenones and lipase-catalyzed resolution of 2-(acyl or alkoxycarbonylamino)-1-arylethanols have been published.[11] On the other hand, (*R*)-octopamine **1** is a potent chiral drug possessing β-adrenergic activity[12] and (*R*)-tembamide **2** and (*R*)-aegeline **3** are naturally occurring biologically active substances which are used in traditional Indian medicine and have been shown to have hypoglycemic activity.[13] To date only a few methods for the preparation of these compounds have been presented, involving the resolution of a racemic mixture[12] and a multi-step synthesis using optically active cyanohydrins as starting materials.[13] Very recently, the asymmetric synthesis of (*R*)-**2** and (*R*)-**3** via enzymatic reduction of α-azido arylketones has been reported.[14] Recently, we reported a convenient method for the preparation of 1,2-diol monotosylates with high optical purity via CBS-oxazaborolidine-catalyzed borane reduction of 1-substituted-2-(*p*-tosyloxy)ethanones.[15] The results encouraged us to develop a convenient route to the synthesis of optically active β-azido alcohols that avoid the formation of undesired regioisomers. We report herein a highly effective new method for synthesis of these compounds from 1,2-diol monotosylates and the corresponding β-amino alcohols with very high enantiomeric purity including (*R*)-**1**, (*R*)-**2** and (*R*)-**3** (Fig. 1).

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PII: S0957-4166(02)00322-1

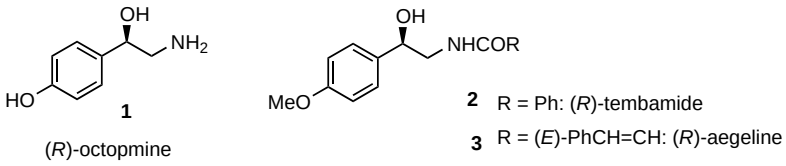


Figure 1.

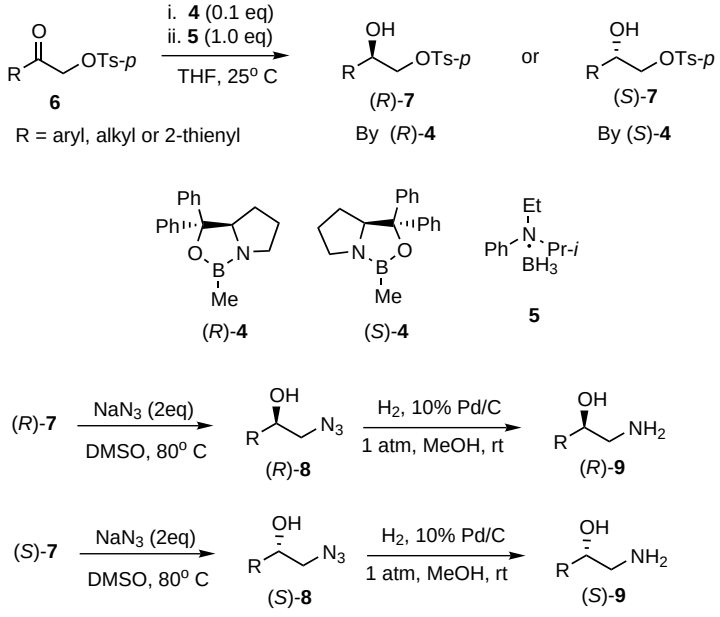
2. Results and discussion

According to our previous procedure,[15] we carried out (*R*)- or (*S*)-CBS-oxazaborolidine **4**-catalyzed asymmetric borane reduction of 1-substituted-2-(*p*-tosyloxy)ethanones **6** using an environmentally benign borane carrier, *N*-ethyl-*N*-isopropylaniline-borane complex **5**, as the hydride source. The reduction provided optically active 1,2-diol monotosylates **7** with very high enantiomeric purity (approaching 100% e.e.) by performing recrystallization when necessary. To prepare non-racemic 2-azido alcohols **8**, (*R*)- or (*S*)-**7** obtained was treated with 2 equiv of sodium azide in DMSO at 80°C for 2–3 h (Scheme 1). As shown in Table 1, all the reaction proceeded smoothly to give the desired products **8** in high yields. The enantiomeric purities of **8**, determined by HPLC analysis using Whelk-O1, Chiralcel OD, Chiralcel OD-H chiral columns or GC analysis using α- or β-Dex 120 chiral columns, were very high, with near 100% e.e. for all the products bearing aryl, alkyl and 2-thienyl groups. The results indicate that no racemization occurred during the azidation reaction. The β-azido alcohols **8** obtained were hydrogenated under atmospheric pressure over 10% Pd/C to give the optically active 2-amino alcohols **9** in high yields. The results are summarized in Table 2.

We applied this methodology to the synthesis of (*R*)-**1**, (*R*)-**2** and (*R*)-**3**. Thus asymmetric borane reduction of 1-(*p*-benzyloxyphenyl)-2-tosyloxyethanone **6d** catalyzed by (*R*)-CBS-oxazaborolidine afforded (*R*)-1-(*p*-benzyloxyphenyl)-2-tosyloxyethanol (*R*)-**7d** in almost quantitative yield. Azidation of (*R*)-**7d** with sodium azide in DMSO provided (*R*)-**8d** with 99% e.e. in 96% yield (entry 4 in Table 1). Subsequent reduction and debenzylation of (*R*)-**8d** by catalytic hydrogenation on 20% $Pd(OH)_2/C$ at 55 psi for 15 h furnished enantiopure (*R*)-**1** in 94% yield. On the other hand, acylation of β-amino alcohol (*R*)-**9c** (entry 3 in Table 2) with benzoyl chloride in the presence of pyridine at 0°C gave (*R*)-**2** in 89% yield. Similarly (*R*)-**9c** was treated with (*E*)-cinnamoyl chloride to afford (*R*)-**3** in 88% yield (Scheme 2).

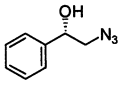
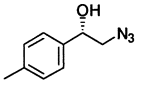
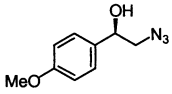
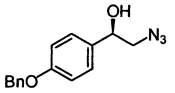
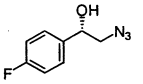
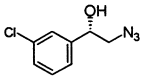
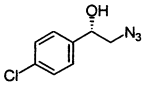
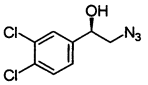
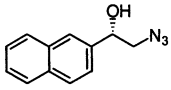
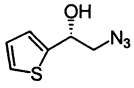
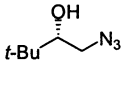
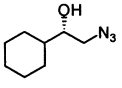
3. Conclusion

We have developed a simple and highly efficient method for obtaining optically active 2-azido and 2-amino-1-substituted alcohols including biologically active substances such as (*R*)-octopamine, (*R*)-tembamide and (*R*)-aegeline with near 100% enantiomeric purity from the corresponding chiral 1,2-diol monotosylates. It is noteworthy that this method provides a convenient route to optically active β-azido and β-amino alcohols with near 100% e.e. that avoids the formation of undesired regioisomers.



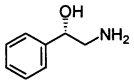
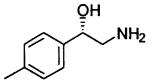
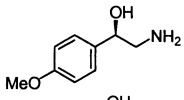
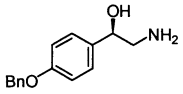
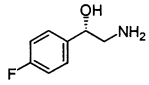
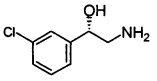
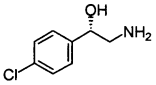
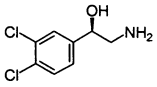
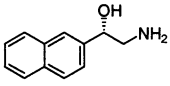
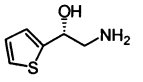
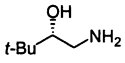
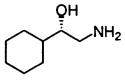
Scheme 1.

Table 1. Preparation of optically active 2-azido-1-substituted ethanols **8**[a]

Entry	Product **8**		Yield (%)[b]	$[\alpha]_D$ in $CHCl_3$		E.e. (%)	Config[m]
				This study[c]	Literature data[d]		
1		**8a**	99	+104.5 (*c* 1.30)	-80.1 (*c* 0.78) 100% ee, *R*	99[h]	*S*
2		**8b**	96	+103.2 (*c* 1.46)	-28.2 (*c* 1.2) 96% ee, *R*	99[h]	*S*
3		**8c**	99	-117.4 (*c* 1.30)	-39.0 (*c* 1.0) 97% ee, *R*	99[h]	*R*
4		**8d**	96	-72.2 (*c* 1.10)	f	99[h]	*R*[n]
5		**8e**	97	+92.8 (*c* 2.07)	-14.7 (*c* 2.0) 98% ee, *R*	99[h]	*S*
6		**8f**	96	+84.5 (*c* 1.42)	f	99[h]	*S*[n]
7		**8g**	98	+96.4 (*c* 1.25)	-79.1 (*c* 1.25) 100% ee, *R*	99[h]	*S*
8		**8h**	98	-103.9 (*c* 0.92)	f	100[h]	*R*[n]
9		**8i**	99	+125.2 (*c* 0.55)	-80.1 (*c* 0.55) 96% ee, *R*	99[h]	*S*
10		**8j**	98	+75.2 (*c* 1.00)	-34.2 (*c* 1.2) 92% ee, *S*	98[j]	*R*[o]
11		**8k**	85	+1.4 (*c* 1.05) -6.57 (*c* 1.05)[e]	-6.8 (*c* 2)[c,e,g]	98[k]	*S*[n]
12		**8l**	94	+14.2 (*c* 1.04)	f	99[l]	*S*[n]

[a]Reaction was carried out with (*R*)- or (S)-**7** with NaN_3 (2 eq) in DMSO at 80°C. [b]Isolated and purified yields. [c]Measured at 20°C. [d]Measured at 25°C: ref. 9. [e]Measured in CH_2Cl_2. [f]Not reported [g]Ref. 5b. [h]Determined by HPLC analysis using Whelk-O1 column; eluent: hexane-*i*PrOH 9:1. [i]Determined by HPLC analysis using Chiralcel OD-H column; eluent: hexane-*i*PrOH 95:5. [j]Determined by HPLC analysis of Chiralcel OD column; eluent: hexane-*i*PrOH 40:1. [k]Determined by GC analysis using β-Dex 120 column. [l]Determined by GC analysis using α-Dex 120 column. [m]By comparison with reported data, unless otherwise indicated: ref. 9. [n]The absolute configuration is unknown, but is probably *S* based on comparison of the order of elution in HPLC analysis using a chiral column and comparison of the sign of the optical rotation with their analogues. [o]By sequence rule.

Table 2. Preparation of optically active 2-amino-1-substituted ethanols **9**[a]

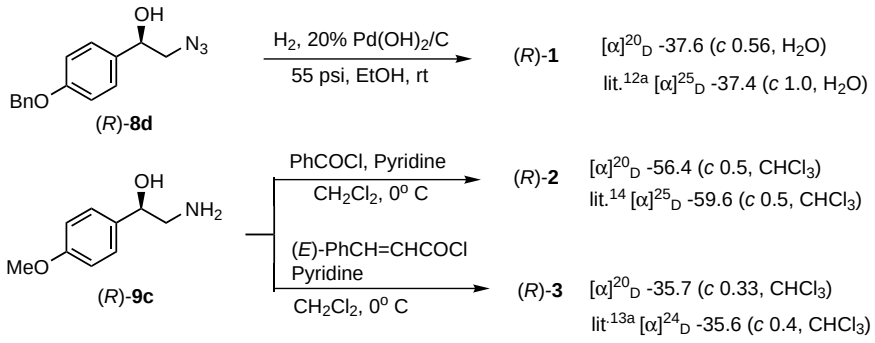
Entry	Product **9**		Yield (%)[b]	$[\alpha]_D^{20}$ in EtOH		E.e. (%)[j]	Config
				This study	Literature data		
1		**9a**	99	+48.6 (*c* 2.01)	+47.9 (*c* 2.4)[d] 100% ee, *S*	99	*S*[k]
2		**9b**	95	+51.8 (*c* 0.24)[e] +42.3 (*c* 0.54)	-49.0 (*c* 0.6)[e] 98% ee, *R*	99	*S*[k]
3		**9c**	98	-39.9 (*c* 1.03)	-38.6 (*c* 1)[f] 96% ee, *R*	99	*R*[k]
4		**9d**	98	-75.7 (*c* 0.53)	g	99	*R*[l]
5		**9e**	97	+40.9 (*c* 0.48)	-40.8 (*c* 1.68)[m] 96% ee	99	*S*[l]
6		**9f**	97	+78.9 (*c* 0.21)	g	99	*S*[l]
7		**9g**	98	+67.4 (*c* 0.35)[c] +40.5 (*c* 0.53)	+65.1 (*c* 0.48)[c,h] 99% ee, *S*	99	*S*[k]
8		**9h**	99	-34.7 (*c* 0.42)	g	100	*R*[l]
9		**9i**	99	+40.0 (*c* 0.31)	-23.8 (*c* 0.32)[i] 70% ee, *R*	99	*S*[k]
10		**9j**	98	+18.1 (*c* 0.72) +31.0 (*c* 0.53)[n]	+30.9 (*c* 1.03)[n,o] *R*	98	*R*[k,p]
11		**9k**	90	+25.9 (*c* 0.47)	g	98	*S*[l]
12		**9l**	97	+12.1 (*c* 0.37)	g	99	*S*[l]

[a](*R*)- or (*S*)-**8** was hydrogenated on 10% Pd/C at room temperature under atmospheric pressure. [b]Isolated and purified yields. [c]Measured in $CHCl_3$. [d]Measured at 23°C: ref. 16. [e]Measured in ether: ref. 10a. [f]Measured at 20°C: ref. 17. [g]Not reported. [h]Measured in $CHCl_3$ at 20°C: ref. 11a. [i]Measured at 20°C: ref. 10c. [j]By comparison with optical rotation value reported and those of **8** shown in Table 1. [k]By comparison with literature values. [l]By comparison with those of **8** and the sign of the optical rotation of the known compounds. [m]Ref. 7a. [n]Measured in CH_2Cl_2. [o]Ref. 18. [p]*R* configuration by sequence rule.

4. Experimental

4.1. General

All operations with air-sensitive materials were carried out under a nitrogen atmosphere with oven-dried glassware. Liquid materials were transferred with a double-ended needle. The reactions were monitored by TLC using silica gel plates and the products were purified by flash column chromatography on silica gel (Merck; 230–400 mesh). NMR spectra were recorded at 200 or 400 MHz for ^1H and 50 or 100 MHz for ^{13}C using Me_4Si as the internal standard in $CDCl_3$, DMSO-d_6, or DCl/D_2O. Optical rotations were measured with a high



Scheme 2.

resolution digital polarimeter. Melting points were uncorrected. Enantiomeric excesses (e.e.s) of the product 2-azido alcohols were determined with a HPLC apparatus fitted with a 25 cm Whelk-O1 (Regis), Chiralcel OD or Chiralcel OD-H (Daicel) chiral column and/or a capillary GC using a 25 m α- or β-Dex 120 chiral column (Supelco).

4.2. Materials

Most of the organic compounds utilized in this study were commercial products of the highest purity. They were further purified by distillation where necessary. THF was distilled over sodium benzophenone ketyl and stored in ampules under nitrogen atmosphere. (*R*)- and (*S*)-CBS-oxazaborolidine reagent and *N*-ethyl-*N*-isopropylaniline-borane complex were purchased from the Aldrich Chemical Company. Optically active 1.2-diol monotosylates, (*R*)- or (*S*)-**7** with 99% e.e., used as starting materials were prepared from CBS-oxazaborolidine-catalyzed borane reduction of 1-substituted-2-(*p*-tosyloxy)ethanones **6** according to the reported procedure.[15]

4.3. General procedure for preparation of optically active β-azido alcohols 8 from 7

A mixture of (*R*)- or (*S*)-**7** (2 mmol) and sodium azide (4 mmol) in DMSO (5 mL) was heated at 80°C for 2–3 h and then cooled to room temperature. To this was added water (5 mL) and the mixture was extracted with CH_2Cl_2 (3×5 mL). The combined extract was dried over anhydrous $MgSO_4$, filtered and concentrated. The crude 2-azido-1-arylethanols (*R*)- or (*S*)-**8** obtained were further purified by a flash column chromatography on silica gel (230–400 mesh) using ethyl acetate/hexane (1/2) unless otherwise indicated. The enantiomeric excesses of **8** were determined by HPLC analysis using a Whelk-O1 column [*iso*-PrOH/hexane: 1/9; flow rate: 1.0 mL/min; detector: 254 nm] unless otherwise indicated. Absolute configurations were assigned by comparison with those of **8** reported.[9]

4.3.1. (*S*)-(+)-2-Azido-1-phenylethanol 8a. R_f 0.61; 99% yield; oil; IR (neat, cm^{-1}) 3414, 3065, 2922, 2093, 1493, 1452; ^1H NMR (200 MHz, $CDCl_3$) δ 2.38 (br s, 1H), 3.40–3.55 (m, 2H), 4.89 (m, 1H), 7.26–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.7, 74.1, 126.6, 129.4, 141.2; Calcd. for $C_8H_9N_3O$: C, 58.88; H, 5.56; N, 25.75. Found: C, 58.92; H, 5.58; N, 25.80; $[\alpha]_D^{20}$ +104.5 (*c* 1.3, $CHCl_3$) {lit.[9] $[\alpha]_D^{25}$ −80.1 (*c* 0.78, $CHCl_3$), *R*, 100% e.e.}; HPLC analysis showed it to be 99% e.e., *S* [*iso*-PrOH/hexane: 1/99; $t_R(S)$ 13.58 min and $t_R(R)$ 16.07 min].

4.3.2. (*S*)-(+)-2-Azido-1-(*p*-tolyl)ethanol 8b. R_f 0.51; 96% yield; oil; IR (neat, cm^{-1}) 3425, 2924, 2099, 1513, 1439; ^1H NMR (200 MHz, $CDCl_3$) δ 2.30 (d, 1H, $J=2.44$ Hz); 2.35 (s, 3H), 3.38–3.54 (m, 2H), 4.85 (m, 1H), 7.17–7.29 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.8, 58.7, 74.0, 126.5, 130.1, 138.3, 138.9; $[\alpha]_D^{20}$ +103.2 (*c* 1.46, $CHCl_3$) {lit.[9] $[\alpha]_D^{25}$ −28.2 (*c* 1.2, $CHCl_3$), *R*, 96% e.e.}; HPLC analysis showed it to be 99% e.e., *S* [flow rate = 0.5 ml/min; $t_R(S)$ 9.36 min and $t_R(R)$ 10.27 min].

4.3.3. (*R*)-(−)-2-Azido-1-(*p*-methoxyphenyl)ethanol 8c. R_f 0.48; 99% yield; oil; IR (neat, cm^{-1}) 3451, 2930, 2100, 1611, 1512; ^1H NMR (200 MHz, $CDCl_3$) δ 2.36 (br s, 1H); 3.34–3.53 (m, 2H), 3.81 (s, 3H), 4.82 (m, 1H), 6.90 (d, 2H, $J=8.55$ Hz), 7.29 (d, 2H, $J=8.85$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 55.9, 58.7, 73.7, 114.7, 127.9, 133.4, 160.3; $[\alpha]_D^{20}$ −117.2 (*c* 1.3, $CHCl_3$) {lit.[9] $[\alpha]_D^{25}$ −39.0 (*c* 1.0, $CHCl_3$), *R*, 97% e.e.}; HPLC analysis showed it to be 99% e.e., *R* [*iso*-PrOH/hexane = 1: 40; flow rate = 0.8 ml/min; $t_R(S)$ 15.56 min and $t_R(R)$ 20.07 min].

4.3.4. (*R*)-(−)-2-Azido-1-(*p*-benzyloxyphenyl)ethanol 8d. R_f 0.70 (EtOAc/hexane 1: 1); 96% yield; mp 69–70°C; IR (KBr, cm^{-1}) 3434, 3129, 3004, 2877, 2096, 1611, 1512, 1454; ^1H NMR (200 MHz, $CDCl_3$) δ 2.33 (d, 1H, $J=3.05$ Hz); 3.40–3.46 (m, 2H), 4.81 (m, 1H), 5.06 (s, 2H), 6.97 (d, 2H, $J=8.85$ Hz), 7.25–7.41 (m, 7H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.7, 70.7, 73.7, 115.8, 118.7, 127.9, 128.1, 128.7, 129.3, 133.7, 137.5, 159.6; Calcd. for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.93; H, 5.29; N, 15.57; EIMS: $m/z=267$ (M^+); $[\alpha]_D^{20}$ −72.2 (*c* 1.1, $CHCl_3$); HPLC analysis showed it to be 99% e.e., *R* [flow rate = 0.5 ml/min; $t_R(S)$ 15.77 min and $t_R(R)$ 18.69 min].

4.3.5. (*S*)-(+)-2-Azido-1-(*p*-fluorophenyl)ethanol 8e. R_f 0.45; 97% yield; mp 37–39°C; IR (KBr, cm^{-1}) 3417, 2925, 2105, 1605, 1512, 1228; ^1H NMR (200 MHz, $CDCl_3$) δ 2.40 (d, 1H, $J=3.36$ Hz), 3.43–3.47 (m, 2H), 4.87 (m, 1H), 7.02–7.11 (m, 2H), 7.32–7.39 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.7, 73.4, 116.1, 116.5,

128.3, 128.4, 136.9, 160.8; $[\alpha]_D^{20}$ +92.8 (*c* 2.07, $CHCl_3$); {lit.[9] $[\alpha]_D^{25}$ −14.7 (*c* 2.0, $CHCl_3$), *R*, 98% e.e.}; HPLC analysis showed it to be 99% e.e., *S* [*iso*-PrOH/hexane: 1/99; $t_R(S)$ 11.07 min and $t_R(R)$ 13.04 min].

4.3.6. (*S*)-(+)-2-Azido-1-(*m*-chlorophenyl)ethanol 8f. R_f 0.53; 96% yield; oil; IR (neat, cm^{-1}) 3392, 2898, 2083, 1616, 1577; ^1H NMR (200 MHz, $CDCl_3$) δ 2.48 (d, 1H, $J=3.36$ Hz); 3.45 (d, 2H, $J=5.80$ Hz), 4.86 (m, 1H), 7.24–7.39 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.6, 73.4, 124.7, 126.8, 129.2, 130.7, 135.4, 143.2; Calcd. for $C_8H_8ClN_3O$: C, 48.62; H, 4.08; N, 21.26. Found: C, 48.73; H, 4.23; N, 21.25; EIMS: $m/z=198$ $(M+H)^+$; $[\alpha]_D^{20}$ +84.5 (*c* 1.42, $CHCl_3$); HPLC analysis using Daicel OD-H chiral column showed it to be 99% e.e., *S* [$t_R(R)$ 7.64 min and $t_R(R)$ 8.64 min].

4.3.7. (*S*)-(+)-2-Azido-1-(*p*-chlorophenyl)ethanol 8g. R_f 0.48; 98% yield; mp 47–49°C [lit.[9] 47–48.5°C]; IR (KBr, cm^{-1}) 3417, 2974, 2099, 1598, 1493; ^1H NMR (200 MHz, $CDCl_3$) δ 2.55 (br s, 1H); 3.43 (d, 2H, $J=5.80$ Hz), 4.86 (t, 1H, $J=5.95$ Hz), 7.26–7.38 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.6, 73.4, 128.0, 129.5, 134.8, 139.6; Calcd. for $C_8H_8ClN_3O$: C, 48.62; H, 4.08; N, 21.26. Found: C, 48.78; H, 4.15; N, 21.29 $[\alpha]_D^{20}$ +96.4 (*c* 1.25, $CHCl_3$); {lit.[9] $[\alpha]_D^{25}$ −79.1 (*c* 1.25, $CHCl_3$), *R*, 100% e.e.}; HPLC analysis showed it to be 99% e.e., *S* [*iso*-PrOH/hexane = 1: 99; $t_R(S)$ 11.72 min and $t_R(R)$ 13.42 min].

4.3.8. (*R*)-(−)-2-Azido-1-(3',4'-dichlorophenyl)ethanol 8h. R_f 0.60 (EtOA*c*/hexane 1: 1); 98% yield; oil; IR (neat, cm^{-1}) 3421, 2924, 2092, 1390, 1469; ^1H NMR (200 MHz, $CDCl_3$) δ 2.49 (d, 1H, $J=3.66$ Hz); 3.45 (d, 2H, $J=5.80$ Hz), 4.85 (m, 1H), 7.22 (m, 1H), 7.43–7.50 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.5, 72.8, 125.9, 128.7, 131.4, 133.0, 133.6, 141.4; Calcd. for $C_8H_7Cl_2N_3O$: C, 41.40; H, 3.04; N, 18.11. Found: C, 41.51; H, 3.24; N, 18.14; EIMS: $m/z=231$ (M^+); $[\alpha]_D^{20}$ −103.9 (*c* 0.92, $CHCl_3$); HPLC analysis showed it to be >99% e.e., *R* [*iso*-PrOH/hexane = 1: 99; flow rate = 0.8 ml/min; $t_R(S)$ 18.15 min and $t_R(R)$ 19.07 min].

4.3.9. (*S*)-(+)-2-Azido-1-(2'-naphthyl)ethanol 8i. R_f 0.57; 99% yield; mp 81–82°C (lit.[9] mp 80–81.5°C); IR (KBr, cm^{-1}) 3423, 2926, 2102, 1609, 1277; ^1H NMR (200 MHz, $CDCl_3$) δ 2.48 (d, 1H, $J=3.05$ Hz); 3.44—3.63 (m, 2H), 5.04 (m, 1H), 7.43–7.52 (m, 3H), 7.82–7.88 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.6, 74.2, 124.3, 125.7, 127.0, 127.1, 128.4, 128.7,129.2, 133.9, 138.6; Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.59; H, 4.97; N, 19.67; $[\alpha]_D^{20}$ +125.2 (*c* 0.55, $CHCl_3$); {lit.[9] $[\alpha]_D^{25}$ −80.1 (*c* 0.55, $CHCl_3$), *R*, 96% e.e.}; HPLC analysis showed it to be 99% e.e., *S* [$t_R(S)$ 6.99 min and $t_R(R)$ 8.30 min].

4.3.10. (*R*)-(+)-2-Azido-1-(2'-thienyl)ethanol 8j. R_f 0.58; 98% yield; oil; IR (neat, cm^{-1}) 3418, 3100, 2924, 2104, 1438; ^1H NMR (200 MHz, $CDCl_3$) δ 2.68 (d, 1H, $J=3.66$ Hz); 3.42–3.64 (m, 2H), 5.12 (m, 1H), 6.98–7.04 (m, 2H), 7.29 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.4, 70.2, 125.3, 126.2, 127.6, 144.6; Calcd. for $C_6H_7N_3OS$: C, 42.59; H, 4.17; N, 24.83; S, 18.95. Found: C, 42.71; H, 4.21; N, 24.91; S, 18.98; $[\alpha]_D^{20}$ +75.2 (*c* 1.0, $CHCl_3$); {lit.[9] $[\alpha]_D^{25}$ −34.2 (*c* 1.2, $CHCl_3$), *S*, 92% e.e.}; HPLC analysis using Daicel OD chiral column showed it to be 98% e.e., *S* [*iso*-PrOH/hexane = 1: 40; flow rate = 0.8 ml/min; $t_R(S)$ 45.09 min and $t_R(R)$ 49.40 min].

4.3.11. (*S*)-(+)-1-Azido-3,3-dimethyl-2-butanol 8k. R_f 0.66; 85% yield; oil; IR (neat, cm^{-1}) 3452, 2963, 2095, 1500, 1390; ^1H NMR (200 MHz, $CDCl_3$) δ 0.94 (s, 9H), 2.05 (d, 1H, $J=3.66$ Hz), 3.28 (m, 1H), 3.40–3.46 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.4, 34.7, 54.4, 79.0; EIMS: $m/z=144$ $(M+H)^+$; $[\alpha]_D^{20}$ +1.4 (*c* 1.05, $CHCl_3$); $[\alpha]_D^{20}$ −6.58 (*c* 1.05, CH_2Cl_2); {lit.[5b] $[\alpha]_D^{20}$ −6.8 (*c* 2, CH_2Cl_2), *R*, >98% e.e.}; GC analysis using β-Dex 120 (Supelco) chiral capillary column showed it to be 98% e.e., *S* [isothemal; 100°C; $t_R(S)$ 34.42 min and $t_R(R)$ 36.17 min].

4.3.12. (*S*)-(+)-2-Azido-1-(cyclohexyl)ethanol 8l. R_f 0.61; 94% yield; oil; IR (neat, cm^{-1}) 3415, 2928, 2101, 1449; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00–1.82 (m, 11H), 1.89 (d, 1H, $J=4.58$ Hz), 3.33–3.41 (m, 2H), 3.49 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.5, 26.7, 26.9, 28.9, 29.6, 42.0, 55.8, 75.7; Calcd. for $C_8H_{15}N_3O$: C, 56.78; H, 8.93; N, 24.83. Found: C, 56.93; H, 8.74; N, 24.64; FAB MS: $m/z=169$ (M^+); $[\alpha]_D^{20}$ +14.2 (*c* 1.04, $CHCl_3$); GC analysis using α-Dex 120 (Supelco) chiral capillary column showed it to be 99% e.e., *S* [isothemal; 140°C; $t_R(S)$ 25.92 min and $t_R(R)$ 26.72 min].

4.4. General procedure for preparation of optically active 2-amino-1-substituted ethanols 9 from 8

A mixture of **8** (2 mmol) and 10% Pd/C (140 mg) in MeOH (1m mL) was hydrogenated using hydrogen balloon at room temperature for 15 h, filtered on a celite pad and the filtrate was concentrated. Solid products obtained were washed with ether to give **9**. If necessary, **9** was further purified by a flash column chromatography on silica gel (230–400 mesh) using *n*-BuOH/AcOH/H_2O(3/1/1). The enantiomeric excesses and absolute configurations of **9** were determined by comparison of those reported in literatures or on the base of the values for the corresponding 2-azido alcohols **8** determined as above.

4.4.1. (*S*)-(+)-2-Amino-1-phenylethanol 9a. R_f 0.72; 99% yield; mp 55–57°C (lit.[16] 55–57°C; IR (KBr, cm^{-1}) 3357, 3248, 3123, 2922, 1640, 1611, 1492, 1466; ^1H NMR (200 MHz, DMSO-d_6) δ 2.52–2.78 (m, 3H), 2.89–3.43 (m, 2H), 4.45 (t, 1H, $J=5.80$ Hz), 7.20–7.33 (m, 5H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.43–2.61 (m, 2H), 4.29 (m, 1H), 6.70 (s, 5H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 50.3, 74.4, 126.4, 127.2, 128.4, 144.8; Calcd. for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.02; H, 8.11; N, 10.32; $[\alpha]_D^{20}$ +48.6 (*c* 2.01, EtOH) from (*S*)-**8a** with 99% e.e. {lit.[16] $[\alpha]_D^{23}$ +47.9 (*c* 2.4, EtOH), *S*, 100% e.e.}.

4.4.2. (*S*)-(+)-2-Amino-1-(*p*-tolyl)ethanol 9b. R_f 0.71; 95% yield; mp 68–70°C [lit.[10a] 76–78°C]; IR (KBr, cm^{-1}) 3433, 3216, 3101, 2973, 1513; ^1H NMR (200 MHz, DMSO-d_6) δ 2.35 (s, 3H), 2.49–2.84 (m, 2H), 3.52–4.04 (br s, 3H), 4.51(m, 1H), 7.18–7.30 (m, 4H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 1.81 (s, 3H), 2.71–2.77 (m, 2H), 4.47 (m, 1H), 6.75–6.85 (m, 4H); ^{13}C NMR (50

MHz, DMSO-d_6) δ 20.8, 50.0, 73.9, 125.9, 128.5, 135.7, 141.3; Calcd. for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.52; H, 8.66; N, 9.28; $[\alpha]_D^{20}$ +42.3 (*c* 0.54, EtOH); $[\alpha]_D^{20}$ +51.8 (*c* 0.24, Et_2O) from (*S*)-**8b** with 99% e.e. {lit.[10a] $[\alpha]_D^{20}$ −49 (*c* 0.6, Et_2O), >98% e.e., *R*}.

4.4.3. (*R*)-(−)-2-Amino-1-(*p*-methoxyphenyl)ethanol 9c. R_f 0.69; 98% yield; 100–102°C (lit.[17] 102–103°C); IR (KBr, cm^{-1}) 3350, 3199, 3083, 2977, 1627, 1513; ^1H NMR (200 MHz, $CDCl_3$) δ 1.68–2.12 (br s, 3H), 2.67–3.02 (m, 2H), 3.80 (s, 3H), 4.58 (br s, 1H), 6.89 (d, 2H, $J=8.24$ Hz), 7.27 (d, 2H, $J=8.24$ Hz); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.46–2.50 (m, 2H), 3.07 (s, 3H), 4.22 (m, 1H), 6.27 (d, 2H, $J=8.85$ Hz), 6.64 (d, 2H, $J=8.55$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.3, 55.9, 74.8, 114.5, 127.8, 135.3, 159.8; Calcd. for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.63; H, 7.59; N, 8.32; $[\alpha]_D^{20}$ −39.9 (*c* 1.03, abs. EtOH) from (*R*)-**8c** with 99% e.e. {lit.[17] $[\alpha]_D^{20}$ −38.6 (*c* 1.0, abs. EtOH), *R*, 96% e.e.}.

4.4.4. (*R*)-(−)-2-Amino-1-(*p*-benzyloxyphenyl)ethanol 9d. R_f 0.81; 98% yield; mp 130–132 °C; IR (KBr, cm^{-1}) 3345, 3063, 2908, 1611, 1586, 1502, 1468; ^1H NMR (400 MHz, DMSO-d_6) δ 2.50–2.71 (m, 3H), 2.94–3.15 (m, 2H), 4.46 (m, 1H), 5.08 (s, 2H), 6.95 (d, 2H, $J=8.59$ Hz), 7.23 (d, 2H, $J=8.55$ Hz), 7.30–7.45 (m, 5H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.70–3.09 (m, 2H), 4.72 (m, 1H), 6.82–7.07 (m, 2H), 7.13–7.50 (m, 7H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 55.8, 70.0, 80.0, 115.1, 127.9, 128.0, 128.6, 129.3, 138.1, 158.1; Calcd. for $C_{15}H_{16}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.11; H, 7.17; N, 5.78; EIMS: $m/z=243$ (M^+); $[\alpha]_D^{20}$ −75.7 (*c* 0.53, EtOH) from (*R*)-**8d** with 99% e.e..

4.4.5. (*S*)-(+)-2-Amino-1-(*p*-fluorophenyl)ethanol 9e. R_f 0.65; 97% yield; mp 63–65 °C; IR (KBr, cm^{-1}) 3357, 2998, 2878, 1603, 1501; ^1H NMR (200 MHz, DMSO-d_6) δ 2.37–2.79 (m, 2H), 2.95–3.62 (m, 2H), 4.46 (m, 1H), 7.08–7.16 (m, 2H), 7.31–7.38 (m, 2H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.43–2.50 (m, 2H), 4.23 (m, 1H), 6.33–6.41 (m, 2H), 6.61–6.68 (m, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 50.0, 73.5, 114.4, 114.9, 127.7, 127.9, 140.6, 163.6; EIMS: $m/z=155$ (M^+); $[\alpha]_D^{20}$ +40.9 (*c* 0.48, EtOH) from (*S*)-**8e** with 99% e.e. {lit.[7a] $[\alpha]_D^{20}$ −40.8 (*c* 1.68, EtOH), *R*, 96% e.e.}.

4.4.6. (*S*)-(+)-2-Amino-1-(*m*-chlorophenyl)ethanol 9f. R_f 0.69; 97% yield; mp 120–122°C; IR (KBr, cm^{-1}) 3348, 2989, 2884, 1596, 1480, 1070; ^1H NMR (200 MHz, DMSO-d_6) δ 2.95–3.19 (m, 2H), 3.21–3.81 (m, 3H), 4.88 (m, 1H), 7.23–7.65 (m, 4H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.50–2.61 (m, 2H), 4.35 (m, 1H), 6.77 (s, 4H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 46.3, 69.6, 126.0, 127.6, 128.4, 142.3; Calcd. for $C_8H_{10}ClNO$: C, 55.99; H, 5.87; N, 8.16. Found: C, 56.01; H, 5.88; N, 8.19; EIMS: $m/z=171$ (M^+); $[\alpha]_D^{20}$ +78.9 (*c* 0.21, EtOH) from (*S*)-**8f** with 99% e.e..

4.4.7. (*S*)-(+)-2-Amino-1-(*p*-chlorophenyl)ethanol 9g. R_f 0.70; 98% yield; mp 95–97°C [lit.[11a] 96–98°C]; IR (KBr, cm^{-1}) 3357, 3214, 3104, 2964, 2853, 1595, 1491; ^1H NMR (200 MHz, DMSO-d_6) δ 2.39–2.77 (m, 3H), 2.87–3.32 (m, 2H), 4.46 (m, 1H), 7.14–7.52 (m, 4H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.27–2.41 (m, 2H), 4.09 (m, 1H), 6.43–6.53 (s, 4H);^{13}C NMR (50 MHz, DMSO-d_6) δ 50.0, 73.7, 127.8, 127.9, 131.2, 143.5; Calcd. for $C_8H_{10}ClNO$: C, 55.99; H, 5.87; N, 8.16. Found: C, 56.12; H, 5.91; N, 8.22; $[\alpha]_D^{20}$ +40.5 (*c* 0.53, EtOH); $[\alpha]_D^{20}$ +67.4 (*c* 0.35, $CHCl_3$) from (*S*)-**8g** with 99% e.e.; {lit.[11a] $[\alpha]_D^{20}$ +65.1 (*c* 0.48, $CHCl_3$), 99% e.e., *S*}.

4.4.8. (*R*)-(−)-2-Amino-1-(3′,4′-dichlorophenyl)ethanol 9h. R_f 0.74; 99% yield; oil; IR (neat, cm^{-1}) 3362, 3179, 2922, 2740, 1589, 1566, 1467; ^1H NMR (200 MHz, DMSO-d_6) δ 2.67 (m, 1H), 2.97–3.92 (m, 4H), 4.50 (m, 1H), 7.31 (m, 1H), 7.55–7.96 (m, 2H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.12–2.24 (m, 2H), 3.96 (m, 1H), 6.25 (m, 1H), 6.46–6.52 (m, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 49.4, 72.8, 126.4, 127.0, 129.1, 130.1, 130.6, 145.6; Calcd. for $C_8H_9Cl_2NO$: C, 46.63; H, 4.40; N, 6.80. Found: C, 46.66; H, 4.47; N, 6.76; EIMS: $m/z=206$ $(M+H)^+$; $[\alpha]_D^{20}$ −34.7 (*c* 0.42, EtOH) from (*S*)-**8h** with 100% e.e..

4.4.9. (*S*)-(+)-2-Amino-1-(2'-naphthyl)ethanol 9i. R_f 0.81; 99% yield; mp 101–103°C [lit.[10c] 115–118°C]; IR (KBr, cm^{-1}) 3354, 3247, 3057, 2910, 1601; ^1H NMR (200 MHz, DMSO-d_6) δ 2.53–2.93 (m, 3H), 2.98–3.41 (m, 2H), 4.62 (m, 1H), 7.47–7.50 (m, 3H), 7.83–7.90 (m, 4H); ^1H NMR (200 MHz, DCl/D_2O/DMSO-d_6) δ 2.24–2.48 (m, 2H), 4.54 (m, 1H), 6.73–6.76 (m, 3H), 7.11 (br s, 4H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 49.9, 74.4, 124.2, 124.6, 125,4, 125.9, 127.3, 127.4, 127.6, 132.2, 132.8, 141.9; Calcd. for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.97; H, 7.02; N, 7.50; $[\alpha]_D^{20}$ +40.0 (*c* 0.31, EtOH) from (*S*)-**8i** with 99% e.e. {lit.[10c] $[\alpha]_D^{20}$ −23.8 (*c* 0.322, EtOH), 70% e.e., *R*}.

4.4.10. (*R*)-(+)-2-Amino-1-(2'-thienyl)ethanol 9j. R_f 0.63; 98% yield; mp 59–61°C [lit.[18] 58–61°C]; IR (KBr, cm^{-1}) 3418, 3282, 2955, 1591, 1491, 1438; ^1H NMR (200 MHz, $CDCl_3$) δ 1.93 –2.47 (br s, 3H), 2.77–3.19 (m, 2H), 4.88 (br s, 1H), 6.97–6.99 (m, 2H), 7.25 (m, 1H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.43–2.65 (m, 2H), 4.50 (m, 1H), 6.32 (m, 1H), 6.40 (m, 1H), 6.71 (m,1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 49.8, 71.2, 124.3, 125.2, 127.5, 147.2; Calcd. for C_6H_9NOS: C, 50.32; H, 6.33; N, 9.78; S, 22.39. Found: C, 50.35; H, 6.20; N, 9.41; $[\alpha]_D^{20}$ +18.1 (*c* 0.72, EtOH); $[\alpha]_D^{20}$ +31.0 (*c* 0.53, CH_2Cl_2) from (*R*)-**8j** with 98% e.e. {lit.[18] $[\alpha]_D^{20}$ +30.9 (*c* 1.03, CH_2Cl_2), *R*}.

4.4.11. (*S*)-(+)-1-Amino-3,3-dimethyl-2-butanol 9k. R_f 0.63; 90% yield; mp 76–78°C; IR (KBr, cm^{-1}) 3427, 3287, 2878, 1597, 1501; ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (s, 9H), 2.17–2.64 (m, 3H), 2.90 (br s, 1H), 3.16 (br s, 1H), 3.47 (s, 1H); ^1H NMR (200 MHz, 2.2 N DCl/D_2O) δ 0.14 (d, 9H, $J=2.14$ Hz), 2.16 (m, 1H), 2.49 (m, 1H), 2.77 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.5, 34.5, 43.1, 80.0; EIMS: $m/z=117$ (M^+); $[\alpha]_D^{20}$ +25.9 (*c* 0.47, EtOH) from (*S*)-**8k** with 98% e.e..

4.4.12. (*S*)-(+)-2-Amino-1-(cyclohexyl)ethanol 9l. R_f 0.78; 97% yield; mp 70–72°C (lit.[10d] 70–80°C); IR (KBr, cm^{-1}) 3365, 2927, 2666, 1609, 1588; ^1H NMR (200 MHz,

DMSO-d_6) δ 0.90–1.52 (m, 6H), 1.53–1.96 (m, 5H), 2.36–2.71 (m, 3H), 2.73–3.28 (m, 3H); ^{1}H NMR (200 MHz, 2.2 N DCl/D_2O) δ 0.24–0.84 (m, 11H), 2.05 (m, 1H), 2.31 (m, 1H), 2.68 (m, 1H); ^{13}C NMR (50 MHz, DMSO–d_6) δ 25.5, 25.8, 26.0, 26.3, 27.9, 29.0, 45.0, 75.9; EIMS: $m/z=143$ (M^+); $[\alpha]_D^{20}$ +12.1 (c 0.37, EtOH) from (S)-**8l** with 99% e.e..

4.5. Preparation of (*R*)-octopamine 1, (*R*)-tembamide 2 and (*R*)-aegeline 3

4.5.1. (*R*)-(−)-Octopamine 1. The azido alcohol (*R*)-**8d** (539 mg, 2 mmol) was dissolved in EtOH (10 mL) and stirred under a hydrogen atmosphere (55 psi) in the presence of 20% $Pd(OH)_2$ on charcoal (150 mg) at room temperature for 12 h. The catalyst was filtered on a pad of celite and the filtrate was concentrated and purified by a flash column chromatography to give (*R*)-**1**; R_f 0.57 (n-BuOH/AcOH/H_2O 3:1:1); 94% yield; mp 245–246°C (lit.[12a] <254°C); IR (KBr, cm^{-1}) 3344, 3152, 2925, 1605; ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.55 (br s, 3H), 2.93-3.38 (m, 3H), 4.29 (t, 1H, $J=5.95$ Hz), 6.83 (d, 2H, $J=8.55$ Hz), 7.08 (d, 2H, $J=8.24$ Hz); ^{1}H NMR (200 MHz, 2.2 N DCl/D_2O) δ 2.21–2.26 (m, 2H), 3.94 (m, 1H), 5.92 (d, 2H, $J=8.55$ Hz), 6.31 (d, 2H, $J=8.55$ Hz); ^{13}C NMR (50 MHz, DMSO-d_6) δ 50.3, 74.3, 114.7, 127.0, 134.7, 156.2; Calcd. for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.67; H, 7.24; N, 9.23; $[\alpha]_D^{20}$ –37.6 (c 0.56, H_2O), 100% e.e., R {lit.[12a] $[\alpha]_D^{20}$ −37.4 (c 1.0, H_2O), R}.

4.5.2. (*R*)-(−)-Tembamide 2. To a solution of the amino alcohol (*R*)-**9c** (167 mg, 1 mmol) in CH_2Cl_2 (10 mL) in the presence of pyridine (3 mL) was added benzoyl chloride (1.1 mmol) dropwise through a syringe at 0°C and the mixture was stirred at the same temperature for 2 h. The reaction mixture was added water (8 ml), stirred and extracted with CH_2Cl_2 (3×5 mL). The organic layer separated was washed with 10% HCl (5 mL) and brine (5 mL) and dried over anhydrous $MgSO_4$. After $MgSO_4$ was removed by filtration, the filtrate was concentrated and purified by a flash column chromatography to give (*R*)-**5**; R_f 0.54 (EtOAc/hexane 2:1); 89% yield; mp 145–146°C (lit.[14] 154–155°C); IR (KBr, cm^{-1}) 3372, 1630, 1543, 1510, 1243; ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.23–3.51 (m, 2H), 3.73 (s, 3H), 4.72 (m, 1H), 5.43 (d, 1H, $J=4.27$ Hz), 6.90 (d, 2H, $J=8.55$ Hz), 7.28 (d, 2H, $J=4.27$ Hz), 7.42–7.52 (m, 3H), 7.81–7.85 (m, 2H), 8.49 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 47.7, 55.0, 70.8, 113.5, 127.2, 128.2, 131.1, 134.6, 135.8, 158.4, 166.4; Calcd. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.81; H, 6.47; N, 5.02; $[\alpha]_D^{20}$ −57.6 (c 0.3, $CHCl_3$), 99% e.e., R {lit.[14] $[\alpha]_D^{25}$ −59.6 (c 0.52, $CHCl_3$), R; lit.[12b] $[\alpha]_D^{21}$ −55.3 (c 0.5, $CHCl_3$), R}.

4.5.3. (*R*)-Aegeline 3. Acylation of (*R*)-**9c** with (*E*)-cinnamoyl chloride under similar condition as described above gave (*R*)-5; R_f 0.35 (EtOAc/hexane 2:1); 88% yield; mp 194–196°C (lit.[14] 196–197°C); IR (KBr, cm^{-1}) 3356, 2964, 1657, 1606, 1242; ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.15–3.47 (m, 2H), 3.73 (s, 3H), 4.60 (m, 1H), 5.45 (d, 1H, $J=4.27$ Hz), 6.72 (d, 1H, $J=15.87$ Hz), 6.90 (d, 2H, $J=8.55$ Hz), 7.28 (d, 2H, $J=8.55$ Hz), 7.39–7.45 (m, 3H), 7.53–7.57 (m, 2H), 8.16 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 47.1, 55.0, 71.0, 113.5, 122.4, 127.2, 127.5, 129.0, 129.4, 135.0, 135.8, 138.6, 158.4, 165.1; Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.72; H, 6.47; N, 4.75; $[\alpha]_D^{20}$ −35.7 (c 0.5, $CHCl_3$), >99% e.e., R {lit.[14] $[\alpha]_D^{25}$ −36.1 (c 0.45, $CHCl_3$), R; lit.[13a] $[\alpha]_D^{24}$ −35.6 (c 0.4, $CHCl_3$), R; lit.[12b] $[\alpha]_D^{25}$ −35.1 (c 0.4, $CHCl_3$), R}.

Acknowledgements

This work was supported by the grant No. R05-2002-000-00003-0 from the Basic Research Program of the Korea Science and Engineering Foundation.

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