Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 1735–1741

Synthesis and characterization of chiral 1,2-diamines from 5-oxo-pyrrolidine-(*S*)-2-carboxylic acid

Uwe Köhn,[a] Andrea Schramm,[a] Florian Kloß,[a] Helmar Görls,[b] Evelyn Arnold[a] and Ernst Anders[a,*]

[a]*Institut für Organische und Makromolekulare Chemie der Friedrich-Schiller-Universität, Humboldtstr. 10, D-07745 Jena, Germany*
[b]*Institut für Anorganische und Analytische Chemie der Friedrich-Schiller-Universität, Lessingstr. 8, D-07743 Jena, Germany*

Received 2 July 2007; accepted 16 July 2007

Abstract—Unsymmetrical chiral secondary vicinal diamines were synthesized by applying a modified three-step reaction. The key step in this sequence is a primary amine mediated ring opening reaction of a diastereomeric oxazolidinone derivative. A possible mechanism for this step is described.

1. Introduction

Various compounds with a biologically active vicinal diamine function play an important role in medicinal chemistry as anti-depressant agents, anti psychotics, cytostatics or antihypertensives.[1] Moreover, vicinal 1,2-diamine derivatives are important compounds or key structural units in organic and supramolecular chemistry as valuable intermediates,[2] additives for metal organic compounds, and as synthetic components for the building of nitrogenous macrocycles (cryptates).[3] Enantiopure 1,2-diamines are used as chiral auxiliaries or ligands and have achieved considerable importance in stereoselective syntheses.[4] Lucet, Le Gall and Mioskowski reviewed the chemistry of vicinal diamines in 1998.[1] Since that report, the development of new or improved synthetic methods of diamines and their applications has continued. Alexakis et al. reported the synthesis of a new tertiary pseudo C_2-symmetric 1,2-diamine derived from (1*S*,2*S*)-(+)-pseudoephedrine, which was subsequently applied as a chiral auxiliary in the enantioselective addition of MeLi to aromatic imines.[5] Recently, Alexakis et al. described the further synthesis of a chiral 1,2-diamine with C_2 symmetry and its successful application as an auxiliary.[6] Enders et al. have developed an efficient and flexible method for the preparation of different protected C_2 symmetric 1, *n*-diamines in high diastereo- and enantiomeric purity.[7] An efficient aldimine cross-coupling route to unsymmetrical vicinal diamine compounds capitalizes upon the reaction of N-monosubstituted α-amino nitriles and imines as exploited by Opatz et al. in 2005.[8] Recent work by Wang et al. using chiral β-amino imines selectively afforded after reduction with different reducing agents *syn*- or *anti*-1,3-diamines in high diastereoselectivities.[9] Denmark et al. reported the synthesis of several enantiopure 1,2-diphenyl-1,2-ethanediamine compounds by the reductive coupling of the corresponding *N*-silylimine derivates with $NbCl_4(THF)_2$.[10] A general route to chiral vicinal diamines via the formation of a 2-trichloromethyloxazolidin-4-one precursor, a ring opening reaction with secondary amines and subsequent reduction has been described by Amedjouk et al.[11] The strategy of oxazolidinone formation during the first step is derived from the self-reproduction of chirality methodology of Seebach et al.,[12] which was modified by Wang and Germanas.[13]

In continuation of our interest in chiral guanidine chemistry[14] we have focused our attention onto the synthesis of chiral 1,2-diamine compounds with two NH functions. With Amedjouk's three-step procedure in hand, we developed an alternative and efficient approach, which involves the ring opening reaction between diastereomeric oxazolidinone intermediates and different primary aliphatic and aromatic amines as the key step. Herein, we report the

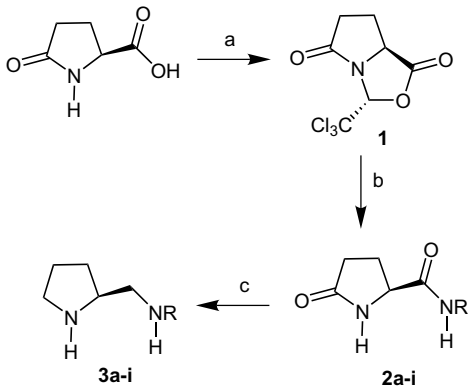
* Corresponding author. Tel.: +49 0 3641 948210; fax: +49 0 3641 948212; e-mail: Ernst.Anders@uni-jena.de

0957-4166/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2007.07.012

synthesis of unsymmetrical chiral vicinal diamines via a three-step reaction starting with commercially available 5-oxo-pyrrolidine-2-carboxylic acid as the chiral source.

2. Results and discussion

The starting point of the three-step reaction is the synthesis of the known diastereomeric oxazolidinone derivative **1**, which was performed by the reaction of equivalent amounts of 5-oxo-pyrrolidine-(*S*)-2-carboxylic acid and anhydrous chloral in the presence of catalytic amounts of *p*-toluenesulfonic acid in toluene (Scheme 1, a).[11]



Scheme 1. The synthesis of chiral vicinal diamines **3a–i**. Reagents and conditions: (a) 5-oxo-L-proline, anhydrous chloral, toluene, reflux, 40 h; (b) **1**, primary amines (cf. Table 1) , toluene, reflux, 2 h; (c) **2a–i**, $LiAlH_4$, THF, reflux, 2 h.

Upon refluxing for 40 h and filtration of the hot reaction mixture, the air-stable diasteromeric compound **1** was obtained in yields over 90%. Our NMR investigations confirmed the formation of only one diastereomeric form of **1** according to the literature.[11] The ^{1}H NMR spectrum of compound **1** exhibited a sharp singlet at $\delta = 6.05$ ppm for the formation of the characteristic hemiaminal function. The corresponding ^{13}C NMR signal was detected at $\delta = 92.2$ ppm. In addition, the structure of the oxazolidinone derivate **1** and, accordingly the, configurations of the two stereogenic centres [C(2), C(6)] were firmly established by using X-ray crystallographic analysis. Suitable single-crystals were obtained by crystallisation from ethyl acetate. As shown in Figure 1, the predetermined (*S*)-configuration at the C(2) carbon could be confirmed, since the

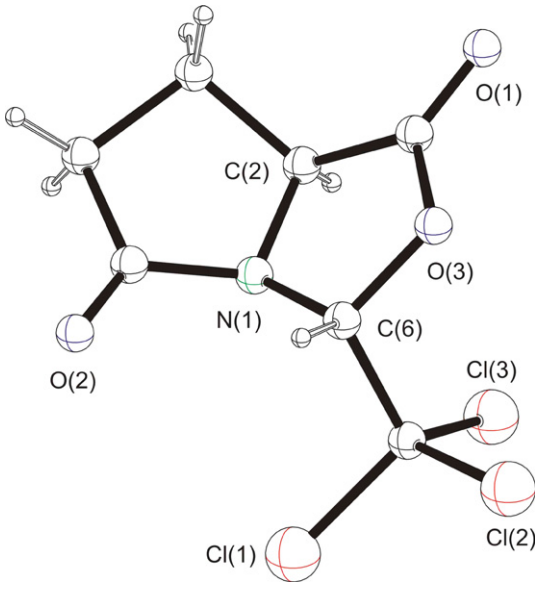


Figure 1. Molecular structure of **1**.

asymmetric carbon atom does not change its configuration during the reaction sequence. The absolute configuration of the newly formed asymmetric centre C(6) was determined to be (*R*)-configuration.

Treatment of **1** (1 equiv) with primary aromatic amines (3 equiv) in refluxing toluene (30 mL) for 2 h afforded, via a nucleophilic oxazolidinone ring opening reaction, *N*-aryl-5-oxopyrrolidine-(*S*)-2-carboxamides **2a–i** in high yields (Scheme 1, b, Table 1). Under these optimized conditions, amide compounds **2a–i** partly separated as solid during the reflux procedure and could be obtained upon filtration in high purity. Filtration of the slightly warm reaction mixture was found to be an appropriate procedure for obtaining **2a–i** in high enantiomeric excess.

However, this filtration procedure is accompanied by a minor decrease of the yields. For compound **2c**, the increase in the steric hindrance of the nucleophilic nitrogen atom caused by the methyl groups at the *o*/*o*′-positions led to an extension of the reaction time (6 h). All products **2a–i** were fully characterized by NMR spectroscopy, mass spectrometry and elemental analysis. The ^{1}H NMR spectra of **2a–i** in deuterated DMSO revealed the presence of two amide NH signals in the characteristic range of

Table 1. Preparation of *N*-aryl-5-oxopyrrolidine-(*S*)-2-carboxamides **2a–i** and the corresponding vicinial diamines **3a–i**

Primary amine	Chiral diamides	Yields[a] (%)	Chiral 1,2-diamines	Yields[a] (%)	$[\alpha]_D^{rt}$
Aniline	**2a**	95.4	**3a**	44.7	31.0
p-Toluidine	**2b**	98.0	**3b**	80.2	29.5
2,4,6-Trimethylaniline	**2c**	77.4	**3c**	38.1	23.25
4-Chloroaniline	**2d**	84.0	**3d**	70.7	27.1
α-Naphthylamine	**2e**	73.6	**3e**	64.1	52.0
Benzylamine	**2f**	97.0	**3f**	47.0	15.15
p-Methylbenzylamine	**2g**	99.1	**3g**	34.1	14.95
(*R*)-Phenylethylamine	**2i**	81.7	**3i**	53.6	27.1
(*S*)-Phenylethylamine	**2h**	98.4	**3h**	49.2	−15.3

[a] Isolated yields.

7–11 ppm, which indicate that the nucleophilic ring opening reaction, by means of primary aromatic amines, has occurred. The final evidence for the existence of the two NH protons was found by HMQC and HMBC NMR correlation experiments. Using the reaction conditions described in the literature,[11] we observed in all our attempts no or only minor ring opening reaction products. In addition, we performed NMR investigations of the resulting filtration solution of **2b** to obtain insight into the oxazolidinone ring opening reaction. The residue obtained upon the removal of the solvent and stirring in petrol ether was determined to be the *N*-tolylaminal of chloral **4**[15] by NMR analysis, including ^{1}H, ^{13}C, HMQC and HMBC experiments and elemental analysis. Aminal **4** was characterized by two peaks at $\delta = 75.7$ (CH) and $\delta = 104.6$ (Cl_3C) ppm in the ^{13}C NMR spectrum. In the ^{1}H NMR spectrum, the observed peaks at $\delta = 5.83$ ppm and $\delta = 5.57$ ppm were assigned to both the NH and CH protons, respectively. Their characteristic CH_3 group resonances were observed as a singlet at $\delta = 2.13$ ppm.

In order to explain the formation of **4**, we performed the reaction of **1** with 2 equiv of *p*-toluidine and investigated the resulting filtration solution by NMR analysis. The ^{1}H and ^{13}C NMR studies showed that the tolylimine of chloral **5**,[16] 2,2,2-trichloroethylidene-*p*-toluidine, was formed during this step.

A plausible mechanism for the ring opening is shown in Scheme 2. According to NMR data obtained, we can assume that the lactone functionality of **1** was converted under ring opening to the corresponding amide group and a hemiaminal unit by the nucleophilic attack of the first equivalent *p*-toluidine. Under our chosen reflux conditions an excess of *p*-toluidine led directly to the formation of vicinal diamide **2b** and a carbinolamine based on chloral. This carbinolamine likely undergoes a dehydration to form imine **5** followed by the addition of *p*-toluidine to the imine function generating aminal **4**.[17]

Finally, the resulting diamides **2a**–**i** were converted without further purification into the corresponding chiral 1,2-diamines **3a**–**i** by reduction with lithium aluminium hydride. Diamides **2a**–**i** were added to a THF suspension of $LiAlH_4$ and heated at refluxing for 2 h at this juncture. Upon aqueous basic workup, the purification of **3a**–**i** was carried out by bulb to bulb distillation, in which moderate to good yields (34–80%) and very high enantioselectivities (ee >96%) were obtained. It should be noted that the washing step of the residue with hot THF during the aqueous workup is very important for obtaining yields of the crude products over 90%. The enantiomeric excesses of diamines **3a**–**i** were determined by using a chiral stationary phase (Daicel Chiracel OD–H column).[18] The ability to separate the enantiomers with the HPLC method used was shown by comparison with the racemic compounds of diamines **3a**–**i**. The preservation of the given (*S*)-configuration of the starting material is shown by the polarimetric data of **3a**–**i** and their comparison with known diamines. Additionally, the structural analysis of **3d** to confirm the absolute configuration of vicinal diamines **3a**–**i** has been performed using X-ray crystallography. It should be noted that the vicinal diamines **3b** and **3d** crystallize at room temperature after standing for several days.

The X-ray structural data of the isolated crystals of **3d** confirmed the preservation of the (*S*)-configuration at the C2 carbon in 5-oxo-pyrrolidine-(*S*)-2-carboxylic acid during the three-step reaction (Fig. 2). All chiral 1,2-diamines **3a**–**i** were fully characterized by 1D and 2D NMR (HMCQ, HMBC, and COSY) measurements and high resolution mass-spectrometry investigations. Their ^{13}C NMR spectra generally exhibit the expected number of signals and show the loss of the two amide C=O signals indicating the successful reduction of **2a**–**i**.

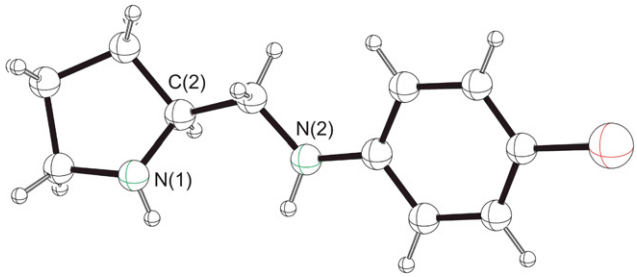
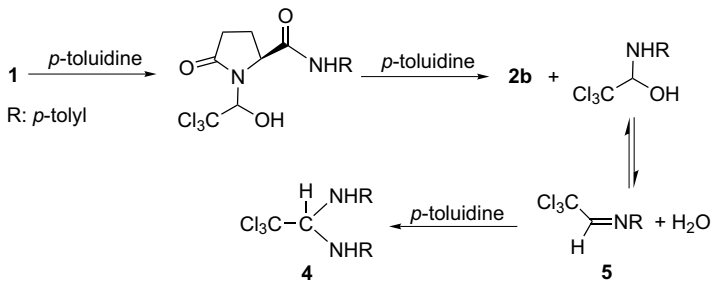


Figure 2. Molecular structure of **3d**.

3. Conclusion

In conclusion, an improved and efficient three-step methodology has been successfully applied to synthesize unsymmetrical enantiopure 1,2-diamines with two secondary amine functions. This vicinal diamine method demon-



Scheme 2. Proposed mechanism for step 2.

strates good generality, since the synthesized chiral 1,2-diamines can be derived from commercially available 5-oxo-L-proline and a variety of primary aromatic amines. The easy accessibility and the stability over a long period of time of these chiral 1,2-diamines make them useful as possible chiral ligands for catalysts in asymmetric syntheses.

4. Experimental

4.1. General

NMR spectra were recorded on a Bruker AC 250 MHz and AC 400 MHz using the residual solvent resonance as an internal standard. $CDCl_3$ (H $\delta = 7.24$, C $\delta = 77.0$ ppm) and DMSO-d_6 (H $\delta = 2.49$, C $\delta = 35.5$ ppm) were used as solvent. The geminal protons of the CH_2 groups were listed as $\delta = X/X$ ppm. The multiplicities of the ^{13}C NMR signals were determined with the DEPT 135 technique. Optical rotations were recorded on a Polartronic E and are reported as $[\alpha]_D^{rt}$ (c in g per 100 mL, solvent). Elemental analyses were conducted by the microanalytical service of our department. IR spectra were recorded on an ATR–BIO-RAD FTS-25. MS spectra were recorded on a Finnigan MAT SAQ 710 (EI). All compounds were fully characterized and given microanalytical data (±0.4%) or HRMS (Micro-ESI). Enantiomeric purity was determined on a Jasco liquid chromatograph with a Knauer UV detector, using a Daicel Chiralcel ODH column. 5-Oxo-pyrrolidine-(*S*)-2-carboxylic acid, anhydrous chloral and the corresponding amine were commercially available and used without further purification.

4.2. General procedure for the preparation of chiral carboxamides 2a–i

4.2.1. (2*R*,5*S*)-2-Trichloromethyl-1-aza-3-oxabicyclo-[3,3,0]-octan-4,8-dione 1. Compound **1** was synthesized according to the published procedure of Amedjkouh and Ahlberg,[11] in which we have increased the reaction time from 16 to 40 h.

Diastereomer **1** (2 g, 7.75 mmol) and the corresponding primary aliphatic or aromatic amine (23.3 mmol) were dissolved in toluene (30 mL) followed by reflux for 2 h. For **2c**, the amount of toluene (60 mL) and the reaction time (6 h) were increased. It should be noted that in the majority of cases the products were separated from the solution during the refluxing. After refluxing, the reaction mixture was allowed to cool gradually to 50 °C and was then filtered. The solid obtained was washed with diethyl ether and was dried in vacuum. The purity could be further increased by re-crystallization from ethyl acetate/ethanol or ethyl acetate.

4.2.2. *N*-Phenyl-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2a.[19] Yield 95.4%, mp 185 °C (white solid). $[\alpha]_D^{20} = +14.1$ (c 2.27, DMSO). Found: C, 64.69; H, 5.92; N, 13.67. $C_{11}H_{12}N_2O_2$ requires C, 64.69; H, 5.92; N, 13.72. IR (ATR): 3322, 3255, 3198, 3140, 3092, 1685, 1661, 1619, 1601, 1552, 1483, 1445 cm^{-1}. ^1H NMR (250 MHz, DMSO-d_6, rt): $\delta = 10.00$ (s, NH), 7.89 (s, NH), 7.61 (d, $^3J = 8.8$ Hz, 2 × CH), 7.30 (t, $^3J = 7.7$ Hz, 2 × CH), 7.05 (t, $^3J = 7.3$ Hz, CH), 4.19 (m, CH), 2.31/1.99 (m, $COCH_2$), 2.17 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 177.4$ (CO), 171.2 (CO), 138.7 (C), 128.7 (2 × CH), 123.4 (CH), 119.3 (2 × CH), 56.3 (CH), 29.2 ($COCH_2$), 25.3 (CH_2) ppm. MS (EI, 70 eV): m/z (%) = 204 (60) $[M^+]$, 84 (100) $[M-C_7H_6NO]^+$.

4.2.3. *N*-Tolyl-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2b.[20] Yield 98.0%, mp 206–208 °C (fawn solid). $[\alpha]_D^{20} = +16.11$ (c 2.11, DMSO). Found: C, 65.79; H, 6.41; N 12.72. $C_{12}H_{14}N_2O_2$ requires C, 66.04; H, 6.47; N, 12.86. IR (ATR): 3319, 3247, 3124, 3083, 3053, 1687, 1660, 1612, 1509 cm^{-1}. ^1H NMR (250 MHz, DMSO-d_6, rt): $\delta = 9.32$ (s, NH), 7.68 (s, NH), 7.49 (d, $^3J = 8.4$ Hz, 2 × CH), 7.01 (d, $^3J = 8.4$ Hz, 2 × CH), 4.16 (m, CH), 2.28/2.15 (m, $COCH_2$), 2.23 (s, CH_3), 2.18 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 177.4$ (CO), 171.0 (CO), 136.2 (C), 132.4 (C), 129.3 (2 × CH), 119.3 (2 × CH), 56.3 (CH), 29.2 ($COCH_2$), 25.2 (CH_2), 20.4 (CH_3) ppm. MS (EI, 70 eV): m/z (%) = 218 (50) $[M^+]$, 84 (100) $[M-C_4H_6NO]^+$.

4.2.4. *N*-Mesityl-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2c. Yield 77.4%, mp 255 °C (white solid). $[\alpha]_D^{20} = +23.4$ (c 2.22, DMSO). Found: C, 68.12; H, 7.45; N, 11.35. $C_{14}H_{18}N_2O_2$ requires C, 68.27; H, 7.37; N 11.37. IR (ATR): 3233, 3081, 2914, 2856, 1709, 1659, 1610, 1525, 1484 cm^{-1}. ^1H NMR (250 MHz, DMSO-d_6, rt): $\delta = 9.25$ (s, NH), 7.94 (s, NH), 6.86 (s, 2 × CH), 4.21 (m, CH), 2.49 (m, $COCH_2$), 2.21 (s, CH_3), 2.18/2.05 (m, CH_2), 2.08 (s, 2 × CH_3) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 177.3$ (CO), 171.0 (CO), 135.4 (C), 134.8 (2 × C), 131.9 (C), 128.6 (2 × CH), 55.8 (CH), 29.3 ($COCH_2$), 25.6 (CH_2), 20.4 (CH_3), 17.8 (2 × CH_3) ppm. MS (EI, 70 eV): m/z (%) = 246 (60) $[M^+]$, 135 (100) $[M-C_5H_5NO_2]^+$.

4.2.5. *N*-(4-Chlorophenyl)-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2d.[21] Yield 84.0%, mp 202–204 °C (fawn solid). $[\alpha]_D^{20} = +13.8$ (c 2.18, DMSO). Found: C, 55.29; H, 4.61; N, 11.64. $C_{11}H_{11}N_2O_2Cl$ requires C, 55.36; H, 4.65; N, 11.74. IR (ATR): 3328, 3242, 3228, 3119, 3078, 1690, 1663, 1613, 1595, 1550, 1489 cm^{-1}. ^1H NMR (250 MHz, DMSO-d_6, rt): $\delta = 10.20$ (s, NH), 7.87 (s, NH), 7.64 (d, $^3J = 8.8$ Hz, 2 × CH), 7.36 (d, $^3J = 8.4$ Hz, 2 × CH), 4.17 (m, CH), 2.31/2.03 (m, $COCH_2$), 2.16 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 177.4$ (CO), 171.4 (CO), 137.7 (C), 128.6 (2 × CH), 127.0 (C), 120.9 (2 × CH), 56.4 (CH), 29.1 ($COCH_2$), 25.2 (CH_2) ppm. MS (EI, 70 eV): m/z (%) = 238 (30) $[M^+]$, 84 (100) $[M-C_7H_5ClNO]^+$.

4.2.6. *N*-(1-Naphthyl)-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2e.[22] Yield 73.6%, mp 210 °C (paly violet solid). $[\alpha]_D^{20} = +34.65$ (c 2.02, DMSO). Found: C, 70.50; H, 5.53; N, 10.99. $C_{15}H_{14}N_2O_2$ requires C, 70.85; H, 5.55; N, 11.02. IR (ATR): 3246, 3053, 1717, 1667, 1541, 1504 cm^{-1}. ^1H NMR (250 MHz, DMSO-d_6, rt): $\delta = 10.03$ (s, NH), 8.10–7.45 (m, 7 × CH), 8.00 (s, NH), 4.42 (m, CH), 2.41/2.12 (m, $COCH_2$), 2.21 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 177.4$ (CO), 172.0

(CO), 136.6 (C), 136.0 (C), 127.9 (C), 128.1, 126.4, 125.8, 2 × 125.5, 122.7, 121.9 (7 × CH), 56.1 (CH), 29.3 ($COCH_2$), 25.5 (CH_2) ppm. MS (EI, 70 eV): m/z (%) = 254 (60) [M^+], 143 (100) [$M-C_5H_5NO_2$]$^+$.

4.2.7. *N*-Benzyl-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2f.[11] Yield 97.0%, mp 130 °C (white solid). $[\alpha]_D^{20} = +13.7$ (c 2.04, DMSO). Found: C, 66.00; H, 6.53; N, 12.73. $C_{12}H_{14}N_2O_2$ requires C, 66.04; H, 6.46; N, 12.83. IR (ATR): 3273, 3226, 1682, 1639, 1572 cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6, rt): $\delta = 8.48$ (s, NH), 7.84 (s, NH), 7.37–7.18 (m, 5 × CH), 4.28 (d, $^3J = 5.74$ Hz, Ph–CH_2), 4.03 (m, CH), 2.27/1.89 (m, $COCH_2$), 2.12 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 177.3$ (CO), 172.3 (CO), 139.1 (C), 128.2, 127.1, 126.7 (5 × CH), 55.8 (CH), 42.0 (CH_2), 29.1 ($COCH_2$), 25.3 (CH_2) ppm. MS (EI, 70 eV): m/z (%) = 218 (10) [M^+], 84 (100) [$M-C_8H_8NO$]$^+$.

4.2.8. *N*-(4-Methylbenzyl)-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2g.[23] Yield 99.1%, mp 128 °C (white solid). $[\alpha]_D^{20} = +7.8$ (c 2.04, DMSO). Found: C, 67.22; H, 6.94; N 12.06. $C_{13}H_{16}N_2O_2$ requires C, 67.22; H, 6.94; N, 12.06. IR (ATR): 3288, 3082, 2918, 1697, 1655, 1647, 1533, 1516 cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6, rt): $\delta = 8.45$ (s, NH), 7.84 (s, NH), 7.12 (m, 4 × CH), 4.21 (d, $^3J = 5.7$ Hz, Ph–CH_2), 4.02 (m, CH), 2.26 (s, CH_3), 2.22/1.87 (m, 2H, $COCH_2$), 2.12 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 177.3$ (CO), 172.2 (CO), 136.1 (C), 135.8 (C), 128.7 (2 × CH), 127.2 (2 × CH), 55.8 (CH), 41.8 (CH_2), 29.2 ($COCH_2$), 25.3 (CH_2), 20.6 (CH_3) ppm. MS (EI, 70 eV): m/z (%) = 232 (10) [M^+], 84 (100) [$M-C_9H_{10}NO$]$^+$.

4.2.9. *N*-(*R*)-1-Phenylethyl-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2h.[11] Yield 98.4%, mp 151 °C (white solid). $[\alpha]_D^{20} = +84.85$ (c 1.98, DMSO). Found: C, 67.06; H, 6.81; N, 12.08. $C_{13}H_{16}N_2O_2$ requires C, 67.22; H, 6.94; N, 12.06. IR (ATR): 3292, 3242, 1679, 1646, 1561 cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6, rt): $\delta = 7.27$ (m, 5 × CH), 7.22 (s, NH), 6.94 (d, $^3J = 7.6$ Hz, NH), 5.03 (m, CH), 4.13 (m, CH), 2.42/2.08 (m, CH_2), 2.23 (m, $COCH_2$), 1.47 (t, $^3J = 6.9$ Hz, CH_3) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 179.5$ (CO), 171.0 (CO), 142.9 (C), 2 × 128.7, 127.4, 2 × 126.1 (5 × CH), 57.1 (CH), 48.8 (CH), 29.3 ($COCH_2$), 25.7 (CH_2), 21.6 (CH_3) ppm. MS (EI, 70 eV): m/z (%) = 232 (10) [M^+], 84 (100) [$M-C_9H_{10}NO$]$^+$.

4.2.10. *N*-(*S*)-1-Phenylethyl-5-oxo-pyrrolidine-(*S*)-2-carboxamide 2i. Yield 81.7%, mp 134 °C (white solid). $[\alpha]_D^{20} = -89.6$ (c 2.21, DMSO). Found: C, 67.26; H, 6.92; N, 12.04. $C_{13}H_{16}N_2O_2$ requires C, 67.22; H, 6.94; N, 12.06. IR (ATR): 3296, 1707, 1648, 1528 cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6, rt): $\delta = 7.27$ (m, 5 × CH), 7.26 (s, NH), 7.21 (d, $^3J = 7.6$ Hz, NH), 5.05 (m, CH), 4.02 (m, CH), 2.38/2.11 (m, CH_2), 2.22 (m, $COCH_2$), 1.45 (t, $^3J = 7.3$ Hz, CH_3) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 179.4$ (CO), 171.2 (CO), 143.0 (C), 2 × 128.6, 127.4, 2 × 126.1 (5 × CH), 57.1 (CH), 48.9 (CH), 29.3 ($COCH_2$), 25.6 (CH_2), 21.7 (CH_3) ppm. MS (EI, 70 eV): m/z (%) = 232 (5) [M^+], 84 (100) [$M-C_9H_{10}NO$]$^+$.

4.3. General procedure for the preparation of chiral 1,2-diamines

Anhydrous THF (50 mL) was added to $LiAlH_4$ (23.3 mmol) under an argon atmosphere and the mixture was cooled to 0 °C. Upon slow addition of the solid carboxamides **2a**–**i** (2 g, 7.75 mmol), the resulting mixture was refluxed for 2 h until the reduction was completed as monitoring by IR and ^{13}C NMR spectroscopies. The reaction mixture was then treated with aqueous 2 M NaOH solution under ice bath cooling until the reaction was completed by forming a solid residue. After stirring for 2 h at room temperature, the mixture was filtered and the solid residue washed with hot THF (50 mL). The combined organic phases were dried over $MgSO_4$ and concentrated in vacuum to afford a crude yellow oil. Purification of the residue by bulb-to-bulb distillation gave **3a**–**i** as colourless to light yellow oils.

4.3.1. *N*-(Pyrrolidin-2-ylmethyl)-aniline 3a.[10] Yield 44.7%, bp 147 °C/5.0 × 10^{-2} Torr (colourless oil). $[\alpha]_D^{20} = +31.0$ (c 4.77, $CHCl_3$). HRMS m/z 177.1369 [M+H]$^+$. $C_{11}H_{17}N_2$ requires 177.1392. IR (ATR): 3326, 2956, 2868, 1601, 1502, 746 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$, rt): $\delta = 7.04$ (m, CH), 6.55 (m, 2 × CH), 6.50 (m, 2 × CH), 5.38 (s, NH), 3.19 (m, CH), 2.91 (m, CH_2), 2.77 (m, CH_2), 2.62 (s, NH), 1.77/1.35 (m, CH_2), 1.64 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 149.1$ (C), 128.7 (2 × CH), 115.4 (CH), 111.9 (2 × CH), 56.9 (CH), 48.1 (CH_2), 45.7 (CH_2), 29.2 (CH_2), 25.1 (CH_2) ppm.

4.3.2. 4-Methyl-*N*-(pyrrolidin-2-ylmethyl)-aniline 3b.[24] Yield 80.2%, bp 125 °C/1.0 × 10^{-2} Torr (colourless oil), **3b** crystallize after standing for several days at room temperature, mp 112 °C. HRMS m/z 191.1542 [M+H]$^+$ $C_{12}H_{19}N_2$ requires 191.1543. $[\alpha]_D^{20} = +29.5$ (c 2.85, $CHCl_3$). IR (ATR): 3337, 2948, 2864, 1616, 1519, 805 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$, rt): $\delta = 6.99$ (d, $^3J = 8.5$ Hz, 2 × CH), 6.58 (d, $^3J = 8.5$ Hz, 2 × CH), 3.95 (s, NH), 3.36 (m, CH), 3.15/2.94 (m, CH_2), 2.94 (m, CH_2), 2.25 (s, CH_3), 1.90/1.46 (m, CH_2), 1.80 (s, NH), 1.76 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 146.3$ (C), 129.7 (2 × CH), 126.5 (C), 113.2 (2 × CH), 57.7 (CH), 49.1 (CH_2), 46.5 (CH_2), 29.6 (CH_2), 25.8 (CH_2) 20.3 (CH_3) ppm.

4.3.3. 2,4,6-Trimethyl-*N*-(pyrrolidin-2-ylmethyl)-aniline 3c.[10] Yield 38.1%, bp 164 °C/7.8 × 10^{-2} Torr (colourless oil). $[\alpha]_D^{20} = +23.25$ (c 5.85, $CHCl_3$). HRMS m/z 219.1844 [M+H]$^+$. $C_{14}H_{23}N_2$ requires 219.1861. IR (ATR): 3336, 2945, 2914, 2864, 1484, 852 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt): $\delta = 6.83$ (s, 2 × CH), 3.33 (m, CH), 2.96 (m, CH_2), 2.96/2.79 (m, CH_2), 2.30 (s, 2 × CH_3), 2.25 (s, CH_3), 1.91/1.43 (m, CH_2), 1.81/1.72 (m, CH_2) ppm, NH protons were not detected. ^{13}C NMR (100 MHz, $CDCl_3$, rt): $\delta = 143.7$ (C), 131.0 (C), 129.6 (2 × C), 129.4 (2 × CH), 58.9 (CH), 53.5 (CH_2), 46.6 (CH_2), 29.5 (CH_2), 25.9 (CH_2), 20.5 (CH_3), 18.4 (2 × CH_3) ppm.

4.3.4. 4-Chloro-*N*-(pyrrolidin-2-ylmethyl)-aniline 3d. Yield 70.7%, bp 160 °C/6.5 × 10^{-2} Torr (yellow oil). **3d** crystallize

after standing for several days at room temperature, mp 143 °C. $[\alpha]_D^{20} = +27.1$ (*c* 2.58, $CHCl_3$). HRMS *m/z* 211.1002 $[M+H]^+$. $C_{11}H_{16}N_2Cl$ requires 211.1017. IR (ATR): 3375, 3304, 2955, 2853, 1599, 814 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, rt): $\delta = 7.10$ (d, $^3J = 8.8$ Hz, $2 \times CH$), 6.54 (d, $^3J = 8.8$ Hz, $2 \times CH$), 4.17 (s, NH), 3.36 (m, CH), 3.12/2.89 (m, CH_2), 2.92 (m, 2H, CH_2), 1.90 (m, 2H, CH_2), 1.84 (s, 1H, NH), 1.72 (m, 2H, CH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 147.1$ (C), 128.9 ($2 \times CH$), 121.7 (C), 114.0 ($2 \times CH$), 57.5 (CH), 48.6 (CH_2), 46.5 (CH_2), 29.5 (CH_2), 25.8 (CH_2) ppm.

4.3.5. *N*-(Pyrrolidin-2-ylmethyl)-naphthalene-1-amine 3e.[25] Yield 64.1%, bp 220 °C/7.2×10^{-2} Torr (brown yellow oil). $[\alpha]_D^{20} = +52.0$ (*c* 3.27, $CHCl_3$). HRMS *m/z* 227.1536 $[M+H]^+$. $C_{15}H_{19}N_2$ requires 227.1548. IR (ATR): 3380, 3051, 2951, 2863, 1580, 766 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, rt): $\delta = 7.97$–6.57 (m, $7 \times CH$), 5.00 (s, NH), 3.55 (m, CH), 3.32/3.09 (m, CH_2), 2.97 (m, CH_2), 2.06 (s, NH), 1.99/1.57 (m, CH_2), 1.85/1.76 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 143.9$ (C), 134.3 (CH), 128.5, 126.6, 125.7, 124.6, 120.2, 117.2, 104.4 ($7 \times CH$), 123.7 (C), 57.5 (CH), 48.6 (CH_2), 46.6 (CH_2), 29.8 (CH_2), 25.9 (CH_2) ppm.

4.3.6. Benzyl-(pyrrolidin-2-ylmethyl)-amine 3f.[10] Yield 47.0%, bp 198 °C/4.0×10^{-2} Torr (colourless oil). $[\alpha]_D^{20} = +15.15$ (c 5.81, $CHCl_3$). HRMS *m/z* 191.1548 $[M+H]^+$. $C_{12}H_{19}N_2$ requires 191.1536. IR (ATR): *v* 3314, 2954, 2869, 2813, 1452, 773 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, rt): $\delta = 7.25$–7.06 (m, $5 \times CH$), 3.68 (s, Ph–CH_2), 3.10 (m, CH), 2.76 (m, CH_2), 2.50/2.42 (m, CH_2), 1.70/1.23 (m, CH_2), 1.81–1.46 (s, $2 \times NH$), 1.58 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 140.1$ (C), 127.8 ($2 \times CH$), 127.5 ($2 \times CH$), 126.2 (CH), 57.8 (CH), 54.0 (CH_2), 53.6 (CH_2), 45.9 (CH_2), 29.1 (CH_2), 25.2 (CH_2) ppm.

4.3.7. 4-Methylbenzyl-(pyrrolidin-(*S*)-2-ylmethyl)-amine 3g. Yield 34.1%, bp 140 °C/6.5×10^{-2} Torr (colourless oil). $[\alpha]_D^{20} = +14.95$ (*c* 3.88, $CHCl_3$). HRMS *m/z* 205.1712 $[M+H]^+$. $C_{13}H_{21}N_2$ requires 205.1705. IR (ATR): 3309, 2951–2817, 1514, 1452 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, rt): $\delta = 7.18$ (d, $^3J = 8.0$ Hz, $2 \times CH$), 7.09 (d, $^3J = 8.0$ Hz, $2 \times CH$), 3.73 (s, N–CH_2), 3.20 (m, CH), 2.86 (m, CH_2), 2.59/2.49 (m, CH_2), 2.30 (s, CH_3), 2.07 (s, $2 \times NH$), 1.81/1.30 (m, CH_2), 1.69 (m, CH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 137.3$ (C), 136.2 (C), 128.8 ($2 \times CH$), 127.9 ($2 \times CH$), 58.2 (CH), 54.3 (CH_2), 53.7 (CH_2), 46.3 (CH_2), 29.5 (CH_2), 25.5, 20.9 (CH_3) ppm.

4.3.8. (*R*)-1-Phenylethyl-(pyrrolidin-(*S*)-2-ylmethyl)-amine 3i.[11] Yield 53.6%, bp 111 °C/5.4×10^{-2} Torr (colourless oil). $[\alpha]_D^{20} = +27.13$ (*c* 2.58, $CHCl_3$). HRMS 205.1708 *m/z* $[M+H]^+$. $C_{13}H_{21}N_2$ requires 205.1705. IR (ATR): 3304, 2959, 2868, 1450, 760, 669 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, rt): $\delta = 7.25$ (m, $3 \times CH$), 7.16 (m, CH), 3.70 (q, $^3J = 6.9$ Hz, CH), 3.13 (m, CH), 2.77 (m, CH_2), 2.46/2.24 (m, CH_2), 2.23 (s, $2 \times NH$), 1.75/1.20 (m, CH_2), 1.59 (m, CH_2), 1.29 (d, $^3J = 6.9$ Hz, CH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 145.6$ (C), 128.2 ($2 \times CH$), 126.5 (CH), 126.3 ($2 \times CH$), 58.2 (CH), 58.1 (CH), 52.3 (CH_2), 46.1 (CH_2), 29.4 (CH_2), 25.4 (CH_2), 24.2 (CH_3) ppm.

4.3.9. (*S*)-1-Phenylethyl-(pyrrolidin-(*S*)-2-ylmethyl)-amine 3h.[25] Yield 49.2%, bp 117 °C/1.0×10^{-1} Torr (colourless oil). $[\alpha]_D^{20} = -15.3$ (*c* 3.40, $CHCl_3$). HRMS *m/z* 205.1703 $[M+H]^+$. $C_{13}H_{21}N_2$ requires 205.1705. IR (ATR): 3343, 2958, 2867, 1450, 760, 700 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, rt): $\delta = 7.25$ (m, $2 \times CH$), 7.23 (m, $2 \times CH$), 7.13 (m, CH), 3.65 (q, $^3J = 6.4$ Hz, CH), 3.05 (m, CH), 2.78 (m, CH_2), 2.32 (m, CH_2), 2.27 (s, $2 \times NH$), 1.72/1.19 (m, CH_2), 1.60 (m, CH_2), 1.28 (d, $^3J = 6.4$ Hz, CH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, rt): $\delta = 145.6$ (C), 128.2 ($2 \times CH$), 126.5 (CH), 126.3 ($2 \times CH$), 58.2 (CH), 58.1 (CH), 52.3 (CH_2), 46.1 (CH_2), 29.4 (CH_2), 25.4 (CH_2), 24.2 (CH_3) ppm.

4.4. X-ray crystallography

The intensity data for the compound were collected on a Nonius KappaCCD diffractometer using graphite-monochromated Mo-K_α radiation. Data were corrected for Lorentz, polarization effects and not for absorption effects.[26,27] The structure was solved by direct methods (SHELXS[28]) and refined by full-matrix least squares techniques against F_o^2 (SHELXL-97[29]). All the hydrogen atoms of **1** and the hydrogen atoms of the amine group and of the water molecules of **3d** were located by difference Fourier synthesis and refined isotropically. All non-hydrogen atoms were refined anisotropically.[26] XP (SIEMENS Analytical X-ray Instruments, Inc.) was used for structure representations.

Crystal data for **1**:[30] $C_7H_6Cl_3NO_3$, $M_r = 258.48$ g mol^{-1}, colourless prism, size $0.10 \times 0.10 \times 0.10$ mm^3, orthorhombic, space group $P2_12_12_1$, $a = 6.0396(2)$, $b = 10.1568(4)$, $c = 15.5495(6)$ Å, $V = 953.85(6)$ $Å^3$, $T = -90$ °C, $Z = 4$, $\rho_{calcd.} = 1.800$ g cm^{-3}, μ (Mo-K_α) = 9.37 cm^{-1}, $F(000) = 520$, 6815 reflections in $h(-7/7)$, $k(-13/13)$, $l(-17/20)$, measured in the range $2.40° \leqslant \Theta \leqslant 27.46°$, completeness $\Theta_{max} = 99.9\%$, 2154 independent reflections, $R_{int} = 0.0333$, 1911 reflections with $F_o > 4\sigma(F_o)$, 151 parameters, 0 restraints, $R1_{obs} = 0.0287$, $wR^2_{obs} = 0.0660$, $R1_{all} = 0.0368$, $wR^2_{all} = 0.0696$, GOOF = 1.027, Flack-parameter 0.06(7), largest difference peak and hole: 0.253/−0.308 e $Å^{-3}$.

Crystal data for **3d**:[30] $C_{11}H_{15}ClN_2 \cdot 0.5H_2O$, $M_r = 219.71$ g mol^{-1}, colourless prism, size $0.05 \times 0.05 \times 0.05$ mm^3, orthorhombic, space group $P2_12_12_1$, $a = 7.9859(2)$, $b = 13.5576(6)$, $c = 20.9296(8)$ Å, $V = 2266.04(14)$ $Å^3$, $T = -90$ °C, $Z = 8$, $\rho_{calcd.} = 1.288$ g cm^{-3}, μ (Mo-K_α) = 3.07 cm^{-1}, $F(000) = 936$, 19015 reflections in $h(-9/10)$, $k(-17/16)$, $l(-27/22)$, measured in the range $1.79° \leqslant \Theta \leqslant 27.48°$, completeness $\Theta_{max} = 99.7\%$, 5175 independent reflections, $R_{int} = 0.0401$, 4203 reflections with $F_o > 4\sigma(F_o)$, 286 parameters, 0 restraints, $R1_{obs} = 0.0449$, $wR^2_{obs} = 0.1105$, $R1_{all} = 0.0614$, $wR^2_{all} = 0.1205$, GOOF = 1.023, Flack-parameter −0.04(7), largest difference peak and hole: 0.194/−0.407 e $Å^{-3}$.

Acknowledgements

Financial support by the Deutsche Forschungsgemeinschaft (Sonderforschungsbereich 436), the Fond der Chemischen Industrie (Germany) and by the Thüringer Ministerium für Wissenschaft, Forschung und Kultur (Erfurt, Germany) is gratefully acknowledged.

References

1. Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580, and references cited therein.
2. (a) Ryan, K.; Gershell, L. J.; Still, W. C. *Tetrahedron* **2000**, *56*, 3309; (b) Torneiro, M.; Still, W. C. *Tetrahedron* **1997**, *53*, 8739; (c) Yoon, S. S.; Still, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 823; (d) Popter, A. E. A. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 3, p 179.
3. (a) Cronin, L. Annu *Rep. Prog. Chem., Sect. A: Inorg. Chem.* **2005**, *101*, 319; (b) Lehn, J. M. *Acc. Chem. Res.* **1978**, *11*, 49.
4. (a) Jiang, M.; Zhu, S.-F.; Yang, Y.; Gong, L.-Z.; Zhou, X.-G.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2006**, *17*, 384; (b) Mikami, K.; Wakabayashi, K.; Yusa, Y.; Aikawa, K. *Chem. Commun.* **2006**, 2365; (c) Bette, V.; Mortreux, A.; Ferioli, F.; Martelli, G.; Savoia, D.; Carpentier, J.-F. *Eur. J. Org. Chem.* **2004**, *10*, 3040; (d) Berkessel, A.; Schroeder, M.; Sklorz, C. A.; Tabanella, S.; Vogl, N.; Lex, J.; Neudoerfl, J. M. *J. Org. Chem.* **2004**, *69*, 3050; (e) Kizirian, J.-C.; Caille, J.-C.; Alexakis, A. *Tetrahedron Lett.* **2003**, *44*, 8893; (f) Andrey, O.; Alexakis, A.; Bernardinelli, G. *Org. Lett.* **2003**, *5*, 2559; (g) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581.
5. Gille, S.; Cabello, N.; Kizirian, J.-C.; Alexakis, A. *Tetrahedron: Asymmetry* **2006**, *17*, 10451.
6. (a) Alexakis, A.; Tomassini, A.; Andrey, O.; Bernardinelli, G. *Eur. J. Org. Chem.* **2005**, *11*, 1332; (b) Alexakis, A.; Tomassini, A.; Chouillet, C.; Roland, S.; Mangeney, P.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 4093.
7. (a) Enders, D.; Meiers, M. *Synthesis* **2002**, *17*, 2542; (b) Enders, D.; Meiers, M. *Angew. Chem., Int. Ed.* **1996**, *35*, 2261.
8. Kison, C.; Meyer, N.; Opatz, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5662.
9. Zhao, C.-H.; Liu, L.; Wang, D.; Chen, Y.-J. *Eur. J. Org. Chem.* **2006**, 2977.
10. Denmark, S. E.; Su, X.; Nishigaichi, Y.; Coe, D. M.; Wong, K.-T.; Winter, S. B. D.; Choi, J. Y. *J. Org. Chem.* **1999**, *64*, 1958.
11. Amedjkouh, M.; Ahlberg, P. *Tetrahedron: Asymmetry* **2002**, *13*, 2229.
12. Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. *J. Am. Chem. Soc.* **1983**, *105*, 5390.
13. Wang, H.; Germanas, J. P. *Synlett* **1999**, 33.
14. Köhn, U.; Klopfleisch, M.; Goerls, H.; Anders, E. *Tetrahedron: Asymmetry* **2006**, *17*, 811.
15. Analytical data for **5**: Mp 97 °C; ^{1}H NMR (250 MHz, DMSO-d_6, rt): $\delta = 6.89$ (d, $^{3}J = 8.4$ Hz, 2H, 2 × CH), 6.75 (d, $^{3}J = 8.8$ Hz, 2H, 2 × CH), 5.83 (m, 2 × NH), 5.57 (m, 2H, CH), 2.13 (s, 3H, CH_3) ppm. ^{13}C NMR (62.9 MHz, DMSO-d_6, rt): $\delta = 144.0$ (C), 129.3 (2 × CH), 126.2 (C), 113.6 (2 × CH), 104.6 (Cl_3C), 75.7 (CH), 20.0 (CH_3) ppm. Anal. Calcd for $C_{16}H_{17}Cl_3N_2$: C, 55.92; H, 4.99; N, 8.15. Found: C, 55.81; H, 4.99; N, 7.92.
16. Davies, A. G.; Kennedy, J. D. *J. Chem. Soc.* **1971**, 68.
17. Crampton, M. R.; Lord, S. D.; Millar, R. *J. Chem. Soc., Perkin Trans. 2* **1997**, 909.
18. HPLC conditions: column Chiralcel-OD–H, Compound **3a**: *n*-hexane/*i*-propanol (80:20), butylamine (0.1%), detection wavelength 250, 0.6 ml/min, temperature 30 °C. Compound **3b**: *n*-hexane/*i*-propanol (95:5), butylamine (0.1%), detection wavelength 250, 0.6 ml/min, temperature 30 °C. Compound **3c**: *n*-hexane/*i*-propanol (99.3:0.7), butylamine (0.1%), detection wavelength 250, 0.6 ml/min, temperature 40 °C. Compound **3d**: *n*-hexane/*i*-propanol (98:2), butylamine (0.2%), detection wavelength 250, 1.0 ml/min, temperature 40 °C. Compound **3e**: *n*-hexane/*i*-propanol (60:40), butylamine (0.1%), detection wavelength 250, 0.6 ml/min, temperature 30 °C. Compound **3f**: *n*-hexane/*i*-propanol (98:2), butylamine (0.5%), detection wavelength 267, 0.8 ml/min, temperature 40 °C. Compound **3g**: *n*-hexane/*i*-propanol (98:2), butylamine (0.5%), detection wavelength 253, 0.6 ml/min, temperature 30 °C. Compound **3h**: *n*-hexane/*i*-propanol (99.7:0.3), butylamine (0.5%), detection wavelength 245, 0.3 ml/min, temperature 45 °C. Compound **3i**: *n*-hexane/*i*-propanol (99.3:0.7), butylamine (0.5%), detection wavelength 245, 0.6 ml/min, temperature 40 °C.
19. Edwards, C. W.; Shipton, M. R.; Alcock, N. W.; Clase, H.; Wills, M. *Tetrahedron* **2003**, *59*, 6473.
20. Rigo, B.; Erb, B.; El Ghammarti, S.; Gautret, P. *J. Heterocycl. Chem.* **1995**, *32*, 1599.
21. Basavaiah, D.; Rao, K. V.; Reddy, B. S. *Tetrahedron: Asymmetry* **2007**, *18*, 968–974.
22. Szewczuk, A.; Mulczyk, M. *Eur. J. Biochem.* **1969**, *8*, 63.
23. Angier, R. B.; Smith, V. K. *J. Org. Chem.* **1956**, *21*, 1540.
24. Brunel, J.-M.; Chiodi, O.; Faure, B.; Fotiadu, F.; Buono, G. *J. Organomet. Chem.* **1997**, *529*, 285.
25. Asami, M.; Ohno, H.; Kobayashi, S.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1869.
26. COLLECT, Data Collection Software; Nonius B.V., Netherlands, **1998**.
27. Z. Otwinowski, W. Minor, 'Processing of X-Ray Diffraction Data Collected in Oscillation Mode', in Methods in Enzymology, Vol. 276, Macromolecular Crystallography, Part A, edited by C.W. Carter, R. M. Sweet, pp 307, Academic Press **1997**.
28. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467.
29. Sheldrick, G. M. SHELXL-*97 (Release 97-2)*; University of Göttingen: Germany, 1997.
30. CCDC 628359 (**1**) and CCDC 635916 (**3d**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).