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Enantiospecific synthesis of pyridinylmethyl pyrrolidinemethanols and catalytic asymmetric borane reduction of prochiral ketones

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Abstract—Three chiral pyridinylmethyl pyrrolidinemethanol derivatives have been synthesized from *N*-alkylation of (*S*)-α,α-diphenyl-2-pyrrolidinemethanol and *N*-carbonylation of L-proline methyl ester. The catalytic asymmetric borane reduction of prochiral ketones was examined in the presence of chiral oxazaborolidine catalysts prepared in situ from chiral pyridinylmethyl pyrrolidinemethanol derivatives. The corresponding chiral secondary alcohols were obtained with good to excellent enantiomeric excesses (up to 98% ee) using (*S*)-2-(diphenylmethanol)-l-(2-pyridylmethyl)pyrrolidine **1** in THF at reflux and moderate to good enantiomeric excesses using C_2-symmetric compound **2** (up to 86% ee) in THF.

1. Introduction

The enantioselective reduction of prochiral ketones with borane in the presence of a chiral ligand leading to enantiomerically pure secondary alcohols has received considerable attention in recent years.[1] Enantiomerically pure secondary alcohols are important intermediates for the synthesis of various other organic compounds such as halides, esters, ethers, ketones, and amines and many biologically active compounds.[2] The pioneering work of Itsuno et al.[3] and Corey et al.[4] inspired the research interests of chemists and the asymmetric reduction of prochiral ketones to optically active alcohols using chiral oxazaborolidine catalysts has become one of the most active research fields. A great number of studies have been reported and many new ligands have been prepared in order to find more effective catalysts.[5] The study of chiral amino alcohols based on prolinol is still an active research area and new derivatives such as sulfonyl prolinol,[6] polymer-supported sulfonamide,[7] chiral phosphinamides,[8] and chiral squaric prolinols[9] were reported recently and high yields and good enantioselectivities were obtained. The applications of pyridinylmethyl pyrrolidinemethanol *N*-oxides in asymmetric reduction of ketone[10a] and corresponding chiral *N*-oxide-titanium(IV) complexes in asymmetric cyanosilylation of ketones have been reported.[10b] To the best of our knowledge, the use of pyridinylmethyl pyrrolidinemethanol derivatives in the reduction of ketones has not been reported to date. It should be of interest to investigate the catalytic ability of pyridinylmethyl pyrrolidinemethanol derivatives. We have an ongoing project on the synthesis and application of chiral pyridine derivative in chiral molecular recognition[11] and asymmetric synthesis and we want to evaluate the effect resulting from the introduction of a pyridinyl moiety onto the catalysts. We expect that the cooperation of pyridine unit and chiral prolinol unit in the new ligands may result in unique properties for suitable catalytic reactions. Herein, the synthesis and structure of enantiomerically pure pyridinylmethyl pyrrolidinemethanol and their applications as ligands in the catalytic enantioselective reduction of ketones by borane.

2. Results and discussion

(*S*)-2-(Diphenylmethanol)-l-(2-pyridylmethyl)pyrrolidine **1** was first synthesized by Chelucci's group from *N*-alkylation of L-proline methyl ester with 2-chloromethylpyridine followed by a Grignard addition reaction.[12] We use an alternative convenient procedure, by treating (*S*)-α,α-diphenyl-2-pyrrolidinemethanol with 2-bromomethylpyridine in a mixture of K_2CO_3 and KI in ethanol at room temperature afforded the corresponding pyrrolidinemethanol **1** in 76% yield. The new

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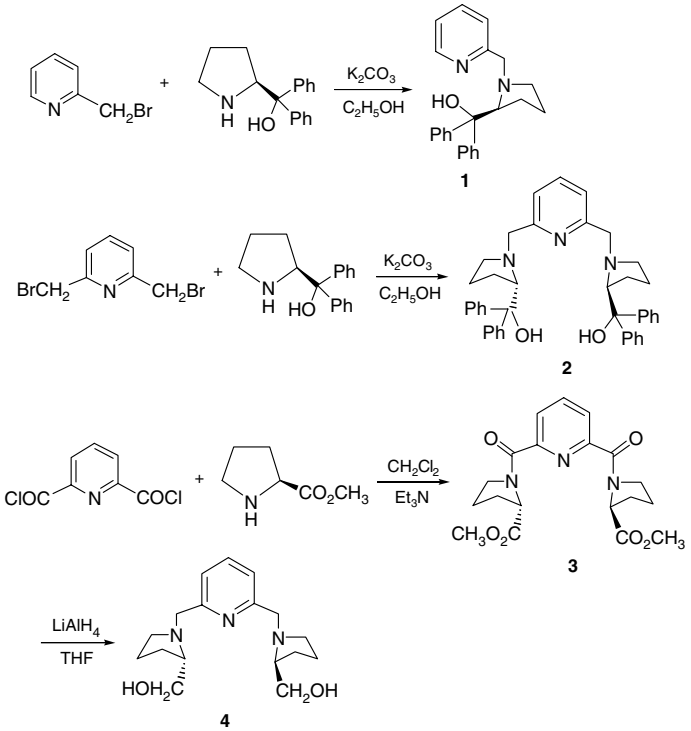
chiral C_2-symmetric pyridinylmethyl pyrrolidinemethanol derivatives **2** and **4** were synthesized from *N*-alkylation of (*S*)-α,α-diphenyl-2-pyrrolidinemethanol and *N*-carbonylation of L-proline methyl ester. Treatment of (*S*)-α,α-diphenyl-2-pyrrolidinemethanol with 2,6-dibromomethylpyridine using K_2CO_3 as base in ethanol afforded the corresponding chiral prolinol derivative **2** as a solid in 80% yield. The ligand **4** was easily synthesized (70% yield) through the lithium aluminum hydride reduction of compound **3**, which was obtained in 86% yield from with reaction of 2,6-pyridinedicarboxylic dichloride with L-proline methyl ester hydrochloride in the presence of triethylamine (Scheme 1).

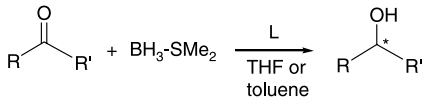
In order to evaluate the efficiency of these ligands in the catalytic asymmetric reduction, we carried out the enantioselective reduction of ketones with borane. We first examined the reduction of acetophenone in the presence of 10 mol% chiral catalyst **1** under various experimental conditions to find the optimum reaction conditions (Table 1). When the reaction was carried out at room temperature in THF, the reduction of acetophenone by the complex prepared in situ from compound **1** with $BH_3{\cdot}SMe_2$ afforded the corresponding (*R*)-1-phenylethanol in 62% ee (91% yield). When the reaction was carried out at reflux, the corresponding (*R*)-1-phenylethanol was obtained in 97% ee and 84% yield (entry 1). When the reaction was carried out in toluene, the ee value decreased from 97% to 48% (entries 2 and 3), though the yield increased. The results suggest that the temperature had a significant effect on the reaction. The best result (97% ee) was obtained at reflux catalyzed by **1**, lower temperatures reduced the catalytic activities, which may be ascribed to the difficulty in forming the catalytic complex in low temperature. On the other hand, solvent also has an effect on the enantioselectivity of the reaction, THF is better than toluene. These results demonstrated that mono-pyridyl prolinol ligand in refluxing THF was beneficial for the improvement of the enantioselectivity. This above result is the same as the previous reports that the higher enantioselectivity was obtained at a higher reaction temperature.[13] Then the reduction of 2-acetylnaphthalene with chiral catalyst **1** was carried out under similar experimental conditions, the corresponding (*R*)-α-2-naphthylethanol was obtained in 98% ee (93% yield) and 45% ee (94% yield) in THF and toluene solution at reflux, respectively. This result further confirmed that THF at reflux maintained good enantioselectivities and this condition was applied to the reduction of other prochiral ketones. We applied catalyst **1** to the reduction of various aromatic ketones, and the results are also shown in Table 1. For the examined ketones, the catalyst **1** gave moderate to high enantioselectivities and chemical yields. The results show that the reduction of bromoacetophenone could give a higher enantioselectivity (93% ee) than other ketones such as 1-methyl, 1-ethyl, 2′-methoxy, and 3′-methoxy substituted acetophenone (entries 6–10). The steric hindrance also had a significant effect on the reduction reaction, 1-acetylnaphthalene, and 1-naphthyl phenyl ketone give lower enantioselectivity and chemical yield (entries 11 and 12), this may be due to the steric repulsion of the substitution on C1 position of naphthalene.

Also as shown in Table 1, we found that the nature of catalyst has a dramatic influence on the catalytic activ-



Scheme 1. Synthesis of pyridine prolinol derivatives **1**–**4**.

Table 1. Asymmetric borane reduction of prochiral ketones catalyzed by pyridinyl prolinol ligand **1**, **2**, and **4**



Entry	Ligand	R	R′	Solvent	Temp.	Yield (%)[a]	Ee (%)[b]	Config.[c]
1	**1**	Ph	Me	THF	rt	91	62	*R*
2	**1**	Ph	Me	THF	Reflux	84	97	*R*
3	**1**	Ph	Me	Toluene	Reflux	95	48	*R*
4	**1**	2-Naphthyl	Me	THF	Reflux	93	98	*R*
5	**1**	2-Naphthyl	Me	Toluene	Reflux	94	45	*R*
6	**1**	Ph	Et	THF	Reflux	93	86	*R*
7	**1**	Ph	*n*-Pr	THF	Reflux	95	87	*R*
8	**1**	Ph	CH_2Br	THF	Reflux	95	93	*S*
9	**1**	2-MeOPh	Me	THF	Reflux	93	84	*R*
10	**1**	3-MeOPh	Me	THF	Reflux	93	84	*R*
11	**1**	1-Naphthyl	Ph	THF	Reflux	40	83	*R*
12	**1**	1-Naphthyl	Me	THF	Reflux	90	39	*R*
13	**1**	Et	Me	THF	Reflux	92	10	*R*
14	**2**	Ph	Me	THF	Reflux	71	81	*R*
15	**2**	Ph	*n*-Pr	THF	Reflux	93	54	*R*
16	**2**	Ph	CH_2Br	THF	Reflux	90	84	*S*
17	**2**	2-Naphthyl	Me	THF	Reflux	92	86	*R*
18	**2**	2-Naphthyl	Ph	THF	Reflux	90	53	*R*
19	**2**	Et	Me	THF	Reflux	90	0	—
20	**4**	Et	Me	THF	Reflux	90	0	—
21	**4**	Ph	Me	THF	Reflux	98	7	*R*
22	**4**	2-Naphthyl	Me	THF	Reflux	98	19	*R*

[a] Isolated yield by chromatographic purification.
[b] Ee values were determined by HPLC (Daicel Chiracel OB Column, elution with hexane/isopropanol 95:5, 0.5–1.0 mL/min) and Chiral GC (beta DEX Column).
[c] The absolute configuration of the product was determined by comparison of the sign of the specific rotation to the literature data.[4,14]

ity. For example, use of the above optimum reaction condition in the presence of 10 mol% C_2-symmetric catalysts **2** and **4** gave good chemical yields but with lower enantioselectivities (entries 14–22). From above results we can see that: (1) catalyst **1** containing a mono-prolinol gave the best enantioselectivities; (2) mono-prolinol catalyst **1** is more effective than C_2-symmetric ligands **2** and **4**; (3) the catalyst **2**, which has two phenyl groups on substituent, is move effective than catalyst **4**; (4) the results also indicated that the larger substitution and no C_2-symmetry of ligand is important for improving the enantioselectivity; (5) the enantioselectivities for the reduction of aromatic ketones are better than dialkyl ketone (entries 13, 19, and 20). (6) The stereochemical course of the reductions were the same, the (*R*)-isomer of corresponding secondary alcohol was formed preferentially for all ketones tested except α-bromoacetophenone (entries 8 and 16).

In order to obtain direct information of the pyridinyl-methyl pyrrolidinemethanol ligand, the stereostructure of ligands **1** was determined by X-ray crystallographic diffraction analysis.[15] Compound **1** was obtained as air-stable, colorless single crystals upon slow evaporation of a solution of **1** in ethyl acetate–petroleum ether (v/v 1:1). A perspective view of compound **1** is shown in Figure 1, there are two independent molecules in each unit cell of this molecule. The pyridine ring and pyrrolidine ring has

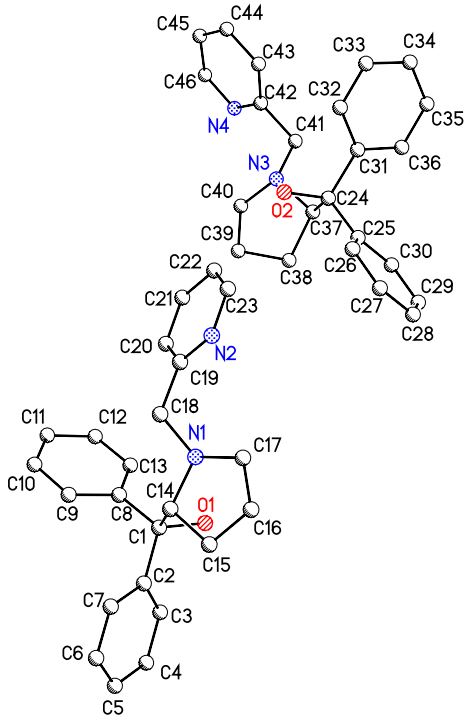
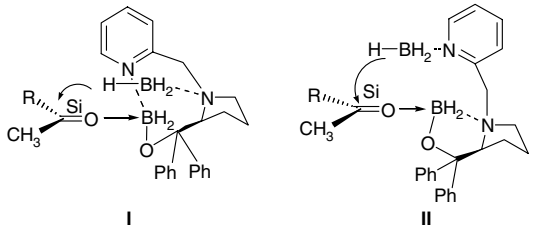


Figure 1. Perspective view of compound **1**, showing 30% probability ellipsoids for the nonhydrogen atoms and the numbering scheme of the atoms in the molecule.

dihedral angles 39.5° (mean planes C19–C20–C21–C22–C23–N2 and C14–C15–C16–C17–N1) and 57.9° (mean planes C42–C43–C44–C45–C46–N4 and C37–C38–C39–C40–N3), respectively. The two phenyl ring's dihedral angles are 112.1° (mean planes C2–C3–C4–C5–C6–C7 and C8–C9–C10–C11–C12–C13) and 67.7° (mean planes C25–C26–C27–C28–C29–C30 and C31–C32–C33–C34–C35–C36), respectively. The torsion angles between the pyridine and prollidine rings are −87.5° (N1–C18–C19–N2) and −89.9° (N3–C41–C42–N4), respectively. From the crystal structure we can see that the coordination of either of the two nitrogen atoms to the boron atom may provide a chiral environment for the asymmetric reduction.

Although the introduction of *N*-alkyl substituents prevents the formation of N–B covalent bond, an amine–borane complex could be formed instead of an oxazaborolidine. The strong coordination of the pyridinyl group to borane may provide an alternative catalytic pathway. The following catalytic model may be proposed based on the above explanation (Scheme 2). Model I is coordination of pyridinyl to borane form an eight-membered ring, the second borane coordination is to a pyrrolidine nitrogen atom. Model II is formation of oxazaborolidine-like five-membered ring, and pyridinyl nitrogen coordination to the second borane. Both pathways facilitate the formation of the *si*-face attack product. It may be difficult for the C_2-symmetric ligands **2** and **3** to form the above-mentioned complex, consistent with lower selectivities being obtained compared with **1**. As shown in Table 1 the reactivity and the enantioselectivity are decreased compared to the case of the corresponding oxazaborolidine catalyzed borane reduction of ketone, this may be ascribed to the lower stability of amine–borane complexes compared to oxazaborolidines.



Scheme 2.

In conclusion, we have synthesized a series of pyridinylmethyl pyrrolidinemethanol catalysts from (*S*)-α,α-diphenyl-2-pyrrolidinemethanol and L-proline methyl ester hydrochloride, respectively. The catalytic activity for the asymmetric borane reduction of prochiral ketones was investigated. Moderate to high enantiomeric excesses and excellent yields were obtained in the asymmetric borane reduction of prochiral aromatic ketones catalyzed by **1** or **2**, up to 98% ee was afforded by pyridinyl mono-prolinol catalyst **1**. In general, the pyridinyl mono-prolinol catalyst **1** demonstrated better enantioselectivity than the new C_2-symmetric pyridinyl prolinol catalysts **2** and **4**. These results should provide useful information for the design of new types of catalysts. The results presented also show that these pyridinyl prolinol compounds may have potential as new catalysts for other asymmetric reactions. Further modifications and studies are in progress in our laboratory in order to expand the applications of these chiral ligand to other asymmetric reactions.

3. Experimental section

Melting points were measured on an XT-4 melting point apparatus and were uncorrected. ^{1}H NMR spectra were recorded on a Mercury 200 MHz or Bruker ARX 400 MHz spectrometer with tetramethylsilane (TMS) serving as internal standard. Infrared spectra were obtained on a Bruker Vector 22 spectrometer. Mass spectra were obtained on a VG-ZAB-HS mass spectrometer. Optical rotations were measured on a Perkin–Elmer 241 MC spectrometer. Elemental analyses were carried out on an Elementar Vario EL instrument. The enantiomeric excesses were determined by HPLC analysis using a chiral column (Daicel Chiralcel OB; eluent, hexane–isopropyl alcohol 95:5; flow rate, 0.5 mL/min; UV detector, 254 nm). The absolute configuration of the major enantiomer was assigned according to the sign of the specific rotation. Solvents used were purified and dried by standard procedures. (*S*)-α,α-Diphenyl-2-pyrrolidinemethanol was synthesized according to the literature procedure.[16]

3.1. (*S*)-2-(Diphenylmethanol)-l-(2-pyridylmethyl)pyrrolidine 1

A solution of (*S*)-α,α-diphenyl-2-pyrrolidinemethanol (0.25 g, 1 mmol), 2-bromomethylpyridine hydrobromide (0.25 g, 1 mmol), potassium carbonate (0.27 g, 2 mmol), and KI (10 mg) in ethanol (15 mL) was stirred at room temperature for 10 h. The solution was filtered, the solvent was removed in vacuo and water (50 mL) was added to the residue. The aqueous solution was extracted with ethyl acetate (20 mL × 3). The organic phase was washed with brine and dried with anhydrous sodium sulfate. The solvent was concentrated and the crude product was purified by column chromatography (eluent: petroleum ether–ethyl acetate 1:1) to afford colorless solid 0.26 g (76% yield); mp 111–113 °C (lit.[12] mp 119 °C); $[\alpha]_D^{20} = 69.0$ ($c = 0.98$, $CHCl_3$); IR (KBr): ν 3415, 3068, 2951, 2864, 2829, 1639, 1591, 1482, 1442, 1375, 1309, 1188 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.43–8.40 (m, 1H, ArH), 7.71–7.54 (m, 5H, ArH), 7.33–7.04 (m, 8H, ArH), 4.98 (s, 1H, OH), 4.11–4.04 (q, $J = 4.6$ Hz, 1H, CH), 3.35 (s, 2H, CH_2), 3.00–2.95 (m, 1H, CH), 2.58–2.49 (m, 1H, CH_2), 1.96–1.61 (m, 4H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): 159.58, 148.52, 147.68, 146.34, 136.21, 128.02, 127.92, 126.30, 126.16, 125.55, 122.37, 121.71, 77.93, 70.85, 62.08, 55.63, 29.53, 24.28; MS (FAB): m/z 345 $(M+1)^+$; Anal. Calcd for $C_{23}H_{24}N_2O$: C,

80.20; H, 7.02; N, 8.13. Found: C, 80.34; H, 7.13; N, 8.19.

3.2. (*S*,*S*)-1,1′-(2,6-Pyridinyldimethyl)-bis[2-(diphenylmethanol)pyrrolidine] 2

A solution of (*S*)-α,α-diphenyl-2-pyrrolidinemethanol 0.54 g (2.05 mmol), 2,6-dibromomethylpyridine hydrobromide 0.265 g (1 mmol), potassium carbonate (0.4 g, 3 mmol), and KI (10 mg) in ethanol (15 mL) was stirred at room temperature for 8 h. The solution was filtered, the solvent was removed in vacuo, and dichloromethane (30 mL) was added to the residue. The solution was washed with water and brine (25 mL) for once. The aqueous solution was extracted with dichloromethane (30 mL). The combined organic phases was dried with anhydrous sodium sulfate. The solvent was concentrated and the crude product was purified by column chromatography (eluent: petroleum ether–ethyl acetate–dichloromethane 1:1:1) to afford colorless solid 0.49 g (80% yield); mp 210–212 °C (dec); $[\alpha]_D^{20} = +45.0$ ($c = 0.1$, CH_2Cl_2); IR (KBr): ν 3344, 3087, 3030, 2942, 2871, 2831, 2797, 1589, 1575, 1491, 1458, 1449, 1376, 1300, 1170, 1112 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.68–6.84 (m, 23H, ArH), 5.20 (s, 2H, OH), 4.12–4.05 (q, $J = 4.4$ Hz, 2H, CH), 3.30 (s, 4H, CH_2), 2.97–2.90 (q, $J = 4.6$ Hz, 2H, CH_2), 2.54–2.41 (q, 2H, $J = 8.2$ Hz, CH_2), 2.01–1.62 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$): 159.57, 156.21, 155.31, 147.58, 146.25, 138.02, 137.21, 128.01, 127.91, 126.75, 126.30, 126.17, 126.17, 125.74, 125.54, 122.00, 121.58, 120.75, 77.97, 70.80, 61.69, 55.64, 46.63, 46.31, 29.53, 24.33; MS (FAB): m/z 610 $(M+1)^+$; Anal. Calcd for $C_{41}H_{43}N_3O_2$: C, 80.75; H, 7.11; N, 6.89. Found: C, 80.91; H, 7.18; N, 6.79.

3.3. (*S*,*S*)-1,1′-(2,6-Pyridinyldimethyl)-bis[2-(methoxycarboxyl)pyrrolidine] 3

To an ice-cold solution of L-proline methyl ester hydrochloride (5.0 g, 30 mmol) in CH_2Cl_2 (60 mL), Et_3N (8.28 mL, 60 mmol) was added followed by dropwise addition of 2,6-pyridinedicarbonyl dichloride (2.95 g, 14.5 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred for 1 h at 0 °C, and then allowed to warm to room temperature and stirred for 8 h. The reaction mixture was washed with saturated citric acid solution to dissolve the precipitate. The organic layer was separated and was washed with water (40 mL), saturated $NaHCO_3$ solution (40 mL), and water (40 mL). The organic layer was then dried over anhydrous Na_2SO_4, and filtered. The filtrate was concentrated in vacuo to afford the crude yellow oil, which was recrystallized from petroleum ether (bp 60–90 °C) to give colorless solid 4.86 g (86% yield); mp 128–130 °C; IR (KBr): ν 3455, 3075, 2980, 2956, 2866, 1738, 1626, 1581, 1569, 1440, 1399, 1339, 1266, 1173 cm^{-1}; ^1HNMR ($CDCl_3$): δ 8.01–7.79 (m, 3H, ArH), 4.88–4.84 (m, 1H, CH), 4.73–4.61 (m, 1H, CH), 3.94–3.48 (m, 10H, CH_3+CH_2), 2.35–2.02 (m, 8H, CH_2); MS (FAB): m/z 390 $(M+1)^+$; Anal. Calcd for $C_{19}H_{23}N_3O_6$: C, 58.60; H, 5.95; N, 10.79. Found: C, 58.16; H, 5.76; N, 10.73.

3.4. (*S*,*S*)-1,1′-(2,6-Pyridinyldimethyl)-bis[2-(hydroxymethyl)pyrrolidine] 4

Compound **3** (0.55 g, 1.4 mmol) was dissolved in THF (30 mL), the mixture heated to reflux, and the suspension of $LiAlH_4$ (0.45 g, 12 mmol) in THF (25 mL) then added dropwise. The reaction mixture was further refluxed for 7 h. The reaction mixture was filtered through Celite, the filter cake was further refluxed with ethanol for 1 h, and filtered again. The filtrate were combined, the ethanol was evaporated, the residue was dissolved in dichloromethane (30 mL) and washed with 2 N HCl (30 mL). The aqueous phase was adjust to pH = 8 with saturated $NaHCO_3$ solution. The aqueous phase was then extracted with dichloromethane (30 mL × 3), dried over anhydrous Na_2SO_4. The solvent was concentrated and the crude product was purified by column chromatography (eluent: dichloromethane–methanol 9:1) to afford yellow liquid 0.30 g (70% yield); $[\alpha]_D^{20} = -29.2$ ($c = 1.0$, CH_2Cl_2): IR (KBr): ν 3380, 2960, 2875, 1655, 1594, 1577, 1459, 1086, 1044 cm^{-1}; ^1HNMR ($CDCl_3$): δ 7.62 (t, $J = 7.6$ Hz, 1H, ArH), 7.15 (d, 2H, $J = 11.4$ Hz, ArH), 4.18 (br s, 2H, OH), 4.11 (d, $J = 14$ Hz, 2H, CH_2), 3.68 (d, $J = 14$ Hz, 2H, CH_2), 3.64 (dd, $J = 2.5$, 11.5 Hz, 2H, CH), 3.47 (dd, $J = 4.8$, 11.5 Hz, 2H, CH), 3.10–3.03 (m, 2H, CH_2) 2.85–2.80 (m, 2H, CH_2), 2.50–2.43 (m, 2H, CH_2), 1.95–1.87 (m, 2H, CH_2), 1.75–1.72 (m, 6H, CH_2); ^{13}C NMR ($CDCl_3$): δ 158.84, 137.50, 121.38, 65.87, 63.37, 60.09, 55.31, 27.32, 23.44; MS (FAB): m/z 306 $(M+1)^+$.

3.5. Typical procedure for the reduction of prochiral ketones

$BH_3{\cdot}SMe_2$ (0.6 mL, 2 M) was added by syringe to a solution of chiral ligand (0.1 mmol) in dry THF (4 mL) under nitrogen at 0 °C. The mixture was stirred for 10 min at 0 °C and then was refluxed for 3 h. A solution of acetophenone (1 mmol) in dry THF (5 mL) was added dropwise over a period of 1 h at refluxing temperature. After refluxing for another 1 h, the cooled reaction mixture was then quenched by dropwise addition of 10% NH_4Cl (5 mL). The alcohol product was isolated by extraction with ethyl acetate (10 mL × 3). The organic phase was washed with brine, dried over anhydrous sodium sulfate. After concentration by rotatory evaporation, the product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 5:1) to afford the corresponding alcohol. The enantiomeric excess were determined by HPLC with a chiral column (Daicel Chiralcel OB; eluent, hexane–isopropyl alcohol 95:5; flow rate, 0.5 mL/min; UV detector, 254 nm).

3.6. X-ray crystallographic analysis

A colorless crystal was selected and mounted on a fine-focus sealed tube and used for data collection. Cell constants and an orientation matrix for data collection were obtained by least-squares refinement of the diffraction data from 25 reflections in the 2θ range from 2.31° to 27.48° in a Rigaku AFC6S diffractometer

equipped with a graphite crystal incident beam monochromator. Data were collected at 293(2) K using MoKα radiation ($\lambda = 0.71073$ Å) and the ω–2θ variable-scan mode. The intensity data obtained were corrected for Lorentz and polarization effects. An empirical absorption correction based on ψ-scan data was applied. The crystal structure was resolved by the direct method using SHELXS97,[17] and full-matrix least-squares refinement on F^2 was performed with SHELXL97 program.[18] All the nonhydrogen atoms were deduced from an E-map and refined anisotropically. The positions of hydrogen atoms were generated geometrically and included in structure factor calculations with assigned isotropic thermal parameters. All computations were performed on a FOUNDER FP$^+$ 5-166 586 personal computer.

1: $C_{23}H_{24}N_2O$, $F_W = 344.44$, monoclinic, space group $P(2)1$, $a = 10.855(2)$, $b = 7.9683(16)$, $c = 22.637(5)$ Å; $\alpha = 90°$, $\beta = 102.78(3)°$, $\gamma = 90°$, $V = 1909.5(7)$ Å^3, $Z = 4$, $F(000) = 736$, $Dc = 1.198$ g/cm^3, $\mu = 0.074$ mm^{-1}. Crystal size $0.30 \times 0.20 \times 0.15$ mm; index ranges $-14 \leqslant h \leqslant 14$, $-10 \leqslant k \leqslant 10$, $-29 \leqslant l \leqslant 28$; reflections collected/unique, 12,691/4640 ($R_{int} = 0.0531$); data/restraints/parameters, 4640/1/514; goodness-of-fit on F^2 0.879; absolute structure parameter: −3(2); extinction coefficient: 0.021(2); final R indices [$I > 2\sigma(I)$]: $R1 = 0.0493$, $wR2 = 0.1162$; R indices (all data): $R1 = 0.1075$, $wR2 = 0.1354$; largest diff. peak and hole, 0.147 and −0.143 e Å^{-3}.

Acknowledgements

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15. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-215883. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
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