An Efficient Preparation of Optically Active Allylic Alcohols, 2-Furyl Alcohols and 2-Thienyl Alcohols by Catalytic Asymmetric Alkylation

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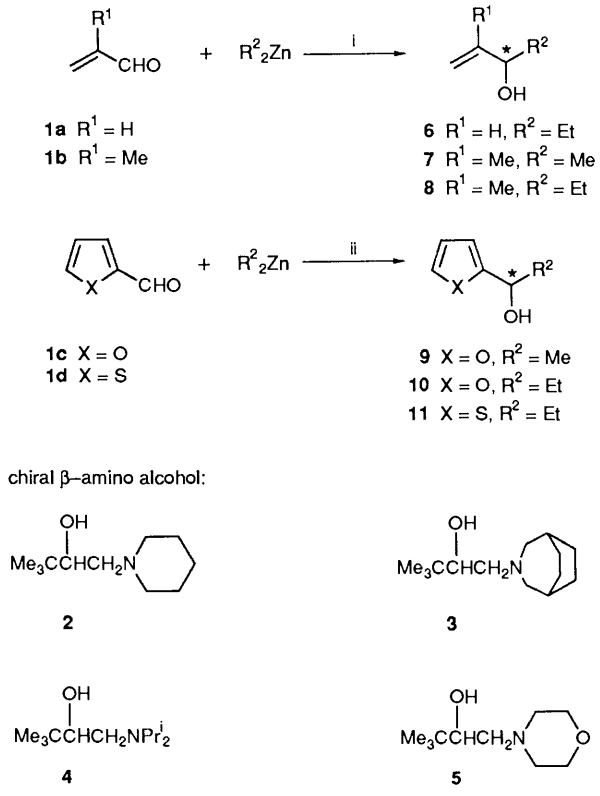
Highly enantioselective alkylation of some kinds of α,β-unsaturated aldehydes with dialkylzinc proceeds in the presence of a small amount of a chiral β-amino alcohol, thus providing an efficient method of obtaining optically active secondary allylic alcohols. Optically active 2-furyl and 2-thienyl alcohols are also available by this catalytic asymmetric alkylation method.

Optically active allylic secondary alcohols play very important roles in organic synthesis, and many efforts have been made to obtain these compounds.[1] Among those methods, kinetic resolution of racemic secondary allylic alcohols by enantioselective epoxidation using t-butyl hydroperoxide (TBHP) in the presence of chiral titanium/tartrate system (Sharpless oxidation) is widely recognized as a useful method of obtaining optically active allylic alcohols. Recently, Sato and co-workers reported the preparation of optically active 2-furyl and 2-thienyl alcohols by kinetic resolution using the Sharpless reagent.[2] They also demonstrated the synthetic utility of these compounds for the synthesis of useful homochiral compounds, such as α-alkoky carboxylic acids and γ-lactones. By this kinetic resolution method, however, the yield of the desired alcohol cannot exceeed 50% in principle, since the substrates are a racemic mixture.

On the other hand, enantioselective addition of dialkylzincs to aldehydes proceeds in the presence of a small amount of a chiral β-amino alcohol to give optically active secondary alcohols.[3] So, if this catalytic enantioselective alkylation of some α,β-unsaturated aldehydes using dialkylzincs affords corresponding allylic alcohols in high chemical yield and in high optical purity, this alkylation method will be superior to that by kinetic resolution in view of the chemical yield and operational simplicity.† In this paper we describe the efficient preparation of optically active allylic alcohols, 2-furyl alcohols and 2-thienyl alcohols by catalytic asymmetric alkylation.



Scheme 1 *Reagents and conditions:* i, 5 mol% chiral β-amino alcohol, −10 to +15 °C, 24–100 h; ii, 2 mol% chiral β-amino alcohol, −10 to +15 °C, 24–88 h

Results and Discussion

Enantioselective Alkylation of Acrylaldehyde **1a** *and Methylacrylaldehyde* **1b**.—We first examined the asymmetric reactions of acrylaldehyde **1a** and methylacrylaldehyde **1b** with dialkylzincs $R^2{}_2Zn$ (R^2 = Me, Et) in the presence of 5 mol% of a chiral amino alcohol. The chiral β-amino alcohols used in this alkylation possessed a t-butyl substituent on the carbon atom bonded to the hydroxy group.‡ Three kinds of *N*-substituent, *viz.* piperidino **2**, 3-azabicyclo[3,2,2]nonan-3-yl **3**, and diisopropylamino **4** derivatives, were employed. These β-amino alcohols could be prepared by epoxy opening of (*R*)-t-butylethylene oxide with a bromomagnesium dialkylamide,[3e] or by kinetic resolution of racemic amino alcohols *via* enantioselective *N*-oxide formation.[6] Asymmetric alkylation reactions were carried out in non-polar solvents such as toluene or hexane, with dimethylzinc or diethylzinc (2 mol equiv.) under argon. Some of our results are summarized in Table 1. Yield of the product in Table 1 was determined by GLC analysis using naphthalene as internal standard, and enantiomeric excess (ee) was determined by HPLC analysis after conversion into the corresponding 3,5-dinitrophenyl carbamate by means of a chiral stationary phase (column, Sumitomo Chemical Co. Sumipax OA 4000). In all cases, the corresponding allylic alcohols were obtained in good yield and in high optical purity. Highest enantioselection (98% ee) was attained in reaction of methylacrylaldehyde with diethylzinc catalysed by compound **3**. In enantioselective ethylation of acrylaldehyde, the optical yield of the product was not so influenced by the type of *N*-substituent in the chiral β-amino alcohols (88–90% ee). Although dimethylzinc was less reactive than diethylzinc, enantioselectivity was high (94% ee) using this reagent. It should be noted that when we used β-amino alcohols possessing the *R* configuration, *R*-alcohols were always obtained.

† Another method used to obtain optically active allylic alcohols by treatment with diorganozincs is the reaction of divinylzinc and aldehydes. See ref. 4.

‡ We have already presented the effectiveness of chiral β-amino alcohols possessing a t-butyl substituent: in highly enantioselective alkylation, see ref. 3*e*; in asymmetric amplification, see ref. 5*a*; in kinetic resolution of racemic aldehydes, see ref. 5*b*.

Table 1 Enantioselective alkylation of acrylaldehyde **1a** and methylacrylaldehyde **1b**[a]

			Conditions				Product		
Entry	Aldehyde	R^2	Catalyst	Solvent	Temp./°C	Time/h	Yield[b] (%)	$[\alpha]_D^{25}$ (*c*, $CHCl_3$)	ee[c] (Config.) (%)
1	**1a**	Et	(*R*)-(−)-**2**	toluene	−10	24	72	−23.9° (2.3)[d]	88 (*R*)[e]
2	**1a**	Et	(*R*)-(−)-**3**	toluene	−10	24	75	−24.0° (1.5)[d]	89 (*R*)[e]
3	**1a**	Et	(*R*)-(−)-**4**	toluene	−10	24	78	−24.3° (1.6)[d]	90 (*R*)[e]
4	**1b**	Me	(*R*)-(−)-**2**	hexane	15	100	64	+6.0° (1.8)	89 (*R*)[f]
5	**1b**	Me	(*R*)-(−)-**3**	hexane	15	100	69	+6.2° (2.1)	94 (*R*)[f]
6	**1b**	Et	(*R*)-(−)-**2**	hexane	−10	24	67	+3.6° (2.0)	95 (*R*)[g]
7	**1b**	Et	(*R*)-(−)-**3**	toluene	−10	24	78	+3.8° (2.1)	98 (*R*)[g]
8	**1b**	Et	(*R*)-(−)-**3**	toluene	0	24	100	+3.5° (2.0)	95 (*R*)[g]
9	**1b**	Et	(*R*)-(−)-**4**	toluene	0	24	69	+3.0° (2.0)	89 (*R*)[g]

[a] All reactions were carried out using 2.0 mol equiv. of dialkylzinc and 5 mol% of (*R*)-(−)-β-amino alcohol (>99% ee) per mol of aldehyde under argon. [b] GLC analysis using naphthalene as internal standard. [c] HPLC analysis (Sumipax OA 4000) of 3,5-dinitrophenyl carbamate. [d] Measured in ethanol. [e] Ref. 7. [f] Ref. 8. [g] Ref. 9.

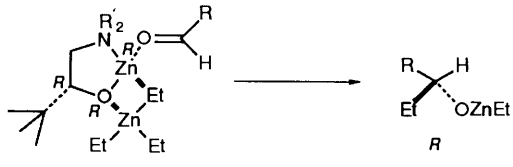
Table 2 Preparation of optically active 2-furyl alcohols and the 2-thienyl alcohol[a]

			Conditions				Product		
Entry	Aldehyde	R^2	Catalyst	Solvent	Temp./°C	Time/h	Yield[b] (%)	$[\alpha]_D^{25}$ (*c*, $CHCl_3$)	ee[c] (Config.) (%)
1	**1c**	Me	(*R*)-(−)-**2**	hexane	15	88	88	+9.0° (0.3)	42 (*R*)[d]
2	**1c**	Me	(*R*)-(−)-**2**	Et_2O	15	88	76	+15.5° (2.0)	75 (*R*)[d]
3	**1c**	Et	(*R*)-(−)-**2**	hexane	−10	24	96	+17.4° (1.8)	92 (*R*)[e]
4	**1c**	Et	(*R*)-(−)-**3**	hexane	−10	24	85	+12.8° (3.2)	66 (*R*)[e]
5	**1c**	Et	(*R*)-(−)-**4**	hexane	−10	24	81	+9.2° (0.2)	73 (*R*)[e]
6	**1c**	Et	(*R*)-(−)-**5**	hexane	−10	24	79	+25.9° (1.6)	55 (*R*)[e]
7	**1d**	Et	(*R*)-(−)-**2**	hexane	−10	24	90	+25.9° (2.1)	95 (*R*)[f]
8	**1d**	Et	(*R*)-(−)-**3**	hexane	−10	24	94	+26.4° (3.4)	93 (*R*)[f]
9	**1d**	Et	(*R*)-(−)-**4**	hexane	−10	24	94	+25.0° (3.9)	89 (*R*)[f]
10	**1d**	Et	(*R*)-(−)-**5**	hexane	−10	24	92	+24.7° (3.4)	88 (*R*)[f]

[a] All reactions were carried out using 1.1 mol equiv. of dialkylzinc and 2 mol% of (*R*)-(−)-β-amino alcohol (>99% ee) per mol of aldehydes under argon. [b] Isolated yield after silica gel column chromatography. [c] HPLC analysis (Sumipax OA 4000) of 3,5-dinitrophenyl carbamate. [d] Ref. 2*b*. [e] Ref. 10. [f] Determined by conversion into the corresponding (*R*)-2-hydroxybutyric acid according to Sato's procedure, ref. 2*b*.

Preparation of Optically Active 2-Furyl and 2-Thienyl Alcohols.—Enantioselective addition of dimethylzinc or diethylzinc to 2-furaldehyde **1c** in the presence of a chiral β-amino alcohol proceeded to afford the corresponding optically active 1-(2-furyl)ethanol **9** and 1-(2-furyl)propan-1-ol **10**, respectively. All reactions were carried out using 1.1 mol equiv. of diethylzinc and 2 mol% of chiral β-amino alcohol per mol of aldehyde. Some of our results are shown in Table 2. Yields in Table 2 show that of the isolated product after silica gel column chromatography, and the ee (%) of the products was determined by HPLC analysis. In enantioselective ethylation of 2-furaldehyde **1c** the effects of the *N*-substituent on enantioselection was remarkable. The reaction catalysed by 1-t-butyl-2-piperidinoethanol (3,3-dimethyl-1-piperidinobutan-2-ol) **2** afforded 92% ee of product, whereas the reactions using the chiral β-amino alcohol substituted by other amino groups (compounds 3–5), resulted in only a moderate level of enantioselectivity (55–73% ee). In the asymmetric methylation of 2-furaldehyde, a solvent effect on enantioselectivity was observed. Diethyl ether was found to be a more suitable solvent than hexane which is commonly used in this aklylation. The alkylation method that we have developed here was also available for the preparation of optically active 2-thienyl alcohols. In this case the effect of the *N*-substituent in the chiral β-amino alcohol on enantioselectivity was not so marked as in case of the reaction of 2-furaldehyde **2**. The reaction of thiophene-2-carboxaldehyde **1d** with diethylzinc aided by 2 mol% of catalyst **2** proceeded to give 1-(2-thienyl)propan-1-ol **11**, 95% ee, in 96% chemical yield. In this case *R*-alkylation products were also obtained using *R*-β-amino alcohols.

The stereochemical outcome observed in this asymmetric alkylation can reasonably be explained by consideration of the mechanism of asymmetric induction proposed by Noyori.[3d,e] The enantioselective alkylation proceeds *via* dinuclear zinc complexes, and the chirality of the 5/4-fused bicyclic intermediates determines the chirality of the alcoholic product. That is, a dinuclear intermediate possessing *R*-configurational Zn and O atoms leads to the *R*-products (Scheme 2).



Scheme 2

In conclusion, catalytic alkylation of some kinds of α,β-unsaturated aldehydes using dialkylzinc provides a new, efficient synthetic tool for the synthesis of optically active allylic alcohols, 2-furyl alcohols and 2-thienyl alcohols.

Experimental

General.—^1H NMR spectra were measured on a Hitachi R-250 Fourier Transfer NMR spectrometer (250 MHz) with [^2H]chloroform as solvent and are recorded in ppm relative to internal tetramethylsilane standard. IR spectra were obtained with a JASCO A-202 spectrometer. Elemental analyses were performed at the Faculty of General Education, Osaka University. Optical rotations were measured on a JASCO DIP-4 digital polarimeter for solutions in a 5 dm cell. Preparative column chromatography was performed on Wacogel-200. HPLC analyses were carried out on a JASCO TWINCLE

or JASCO 880-PU liquid chromatograph with a JASCO UVIDEC 100 UV detector. GLC analyses were performed on a Hitachi 263-30 instrument.

Materials.—Toluene, hexane and diethyl ether for asymmetric alkylation were distilled from sodium benzophenone ketyl under argon and degassed before use. Dimethylzinc and diethylzinc were kindly donated by Tosoh Akzo Co. Acrylaldehyde, methylacrylaldehyde, 2-furaldehyde and thiophene-2-carboxaldehyde were purchased from Tokyo Kasei Co. and distilled before use.

Preparation of (R)-1-*Dialkylamino*-3,3-*dimethylbutan*-2-*ols. General Procedure for the Reaction of* (R)-*t-Butylethylene Oxide with a Bromomagnesium Dialkylamide.*—To a solution of ethylmagnesium bromide prepared from magnesium (120 mg, 5.0 mmol) and ethyl bromide (540 mg, 5.0 mmol) in tetrahydrofuran (THF) (10 cm^3) was added a solution of a secondary amine (5.0 mmol) in THF (5 cm^3). After the mixture had been stirred at 35 °C for 1 h, (*R*)-t-butylethylene oxide (400 mg, 4 mmol) was added to the solution, which was then stirred for 12 h at room temperature before being poured into saturated aq NH_4Cl. The aq solution was acidified with 1 mol dm^{-3} HCl (20 cm^3) and extracted with ethyl acetate (30 cm^3 × 2), then was made alkaline by 10% aq. sodium hydroxide and extracted with ethyl acetate (20 cm^3 × 2). The combined organic layer was washed with brine (20 cm^3 × 2), dried over Na_2SO_4, and distilled or recrystallized to give the corresponding (*R*)-1-dialkylamino-3,3-dimethylbutan-2-ol. The enantiomeric excess of the β-amino alcohol thus obtained was determined as 99% ee by HPLC analysis of the corresponding 3,5-dinitrophenyl carbamate, using a chiral stationary phase (column, Sumitomo Chemical Co. SUMIPAX OA 4000). The procedure for the preparation of the carbamate was as follows: 3,5-dinitrophenyl isocyanate (10 mg) and pyridine (0.5 mm^3) were added to a toluene solution (0.5 cm^3) of amino alcohol (10 mg). After being vigorously stirred for 30 min at 20 °C, an aliquot (2 mm^3) of the reaction mixture containing the 3,5-dinitrophenyl carbamate was analysed by HPLC. The following compounds were thus prepared.

(R)-3,3-*Dimethyl*-1-*piperidinobutan*-2-*ol* **2**. Yield 594 mg (80%). Purification by distillation (b.p. 59–61 °C/1 mmHg). HPLC t_R of (*R*)-carbamate 9 min; t_R of (*S*)-carbamate 11 min [column, Sumitomo Chemical Co. SUMIPAX OA 4000; eluent hexane-ethanol (97:3)]; $[\alpha]_D^{25}$ −72.4° (*c* 1.8, $CHCl_3$); $[\alpha]_D^{25}$ −62.1° (*c* 1.9, EtOH); ν_{max}(neat)/cm^{-1} 3400; δ_H($CDCl_3$) 0.9 (9 H, s), 1.4–1.6 (6 H, m), 2.2–2.4 (4 H, m), 2.6–2.7 (2 H, m), 3.3 (1 H, dd, *J* 4.9 and 14.3 Hz) and 4.3 (1 H, br s) (Found: C, 71.2; H, 12.3; N, 7.7. Calc. for $C_{11}H_{23}NO$: C, 71.30; H, 12.51; N, 7.56%).

(R)-1-(3-*Azabicyclo*[3.2.2]*nonan*-3-*yl*)-3,3-*dimethylbutan*-2-*ol* **3**. Yield 893 mg (88%). Purification by recrystallization (m.p. 105–108 °C). HPLC t_R of (*R*)-carbamate 11.5 min; t_R of (*S*)-carbamate 13.2 min [column, Sumitomo Chemical Co. SUMIPAX OA 4000; eluent hexane–ethanol (97:3), 1.0 cm^3 min^{-1}]; $[\alpha]_D^{22}$ −64.2° (*c* 1.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3450; δ_H($CDCl_3$) 0.91 (9 H, s), 1.6–1.8 (8 H, m), 1.9 (2 H, br s), 2.3–2.4 (2 H, m), 2.47 (2 H, dd, *J* 11.4 and 4.1 Hz), 2.83 (2 H, dd, *J* 11.4 and 4.1 Hz), 3.35 (1 H, dd, *J* 9.9 and 4.4 Hz) and 4.25 (1 H, s) (Found: C, 74.3; H, 12.1; N, 6.3. Calc. for $C_{14}H_{27}NO$: C, 74.61; H, 12.08; N, 6.22%).

(R)-1-(*Diisopropylamino*)-3,3-*dimethylbutan*-2-*ol* **4**. Yield 665 mg (82%). Purification by distillation (b.p. 98–100 °C/14 mmHg). HPLC t_R of (*R*)-carbamate 8.8 min; t_R of (*S*)-carbamate 9.5 min [column, Sumitomo Chemical Co. SUMIPAX OA 4000; eluent hexane–ethanol (97 : 3), 1.0 cm^3 min^{-1}]; $[\alpha]_D^{25}$ −80.1° (*c* 1.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3450; δ_H($CDCl_3$) 0.9 (9 H, s), 1.0–1.1 (12 H, m), 2.2–2.6 (2 H, m), 3.0–3.1 (2 H, m), 3.1–3.2 (1 H, m) and 4.3 (1 H, br s) (Found: C, 71.4; H, 13.5; N, 7.0. Calc. for $C_{12}H_{27}NO$: C, 71.58; H, 13.52; N, 6.96%).

(R)-3,3-*Dimethyl*-1-*morpholinobutan*-2-*ol* **5**. Yield 680 mg (90%). Purification by distillation (b.p. 67 °C/1 mmHg). HPLC t_R of (*R*)-carbamate 7.7 min; t_R of (*S*)-carbamate 8.5 min [column, Sumitomo Chemical Co. SUMIPAX OA 4000; eluent hexane–ethanol (97:3), 1.0 cm^3 min^{-1}]; $[\alpha]_D^{24}$ −69.2° (*c* 1.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3400; δ_H ($CDCl_3$) 0.9 (9 H, s), 2.3–2.5 (4 H, m), 2.6–2.8 (2 H, m), 3.3–3.4 (1 H, m), 3.6 (1 H, br s), 3.7–3.8 (4 H, m) (Found: C, 64.0; H, 11.0; N, 7.5. Calc. for $C_{10}H_{21}NO_2$: C, 64.17; H, 11.30; N, 7.48%).

(R)-*Pent*-1-*en*-3-*ol* **6**.—In a flame-dried Schlenk tube were placed (*R*)-1-(diisopropylamino)-3,3-dimethylbutan-2-ol **4** (36.5 mg, 0.18 mmol), naphthalene (210 mg) and dry toluene (12 cm^3). To this solution at −10 °C was added diethylzinc (0.74 cm^3, 7.2 mmol) and the mixture was stirred for 20 min at 15 °C, then cooled to −10 °C, when freshly distilled acrylaldehyde **1a** (202 mg, 3.6 mmol) was added. After being stirred for 24 h at this temperature, the solution was quenched by 1 mol dm^{-3} HCl (20 cm^3). The yield of pent-1-en-3-ol **6** was determined as 78% by GLC analysis after extraction with diethyl ether (20 cm^3 × 3). GLC: t_R of compound **6** 4 min. t_R of naphthalene 12 min. The enantiomeric excess of compound **6** was determined as 90% ee by HPLC analysis of the corresponding 3,5-dinitrophenyl carbamate, using a chiral stationary phase (column, Sumitomo Chemical Co. SUMIPAX OA 4000). t_R of (*R*)-carbamate 41 min. t_R of (*S*)-carbamate 44 min [hexane–ethanol (100:1.5), 1.0 cm^3 min^{-1}]. Isolation was by molecular distillation. $[\alpha]_D^{25}$ −24.3° (*c* 1.6, EtOH); δ_H($CDCl_3$) 1.29 (3 H, d, *J* 6.7 Hz), 1.60 (1 H, s), 1.75 (3 H, s) and 4.25 (1 H, q, *J* 6.7 Hz).

(R)-3-*Methylbut*-3-*en*-2-*ol* **7**.—To a solution of (*R*)-1-(3-azabicyclo[3.2.2]nonan-3-yl)-3,3-dimethylbutan-2-ol **3** (45.7 mg, 0.18 mmol) and naphthalene (100 mg) in hexane (10 cm^3) at −10 °C was added dimethylzinc (0.69 cm^3, 7.2 mmol). This solution was allowed to warm up 15 °C and was stirred for 20 min at this temperature. To this mixture was added methylacrylaldehyde **1b** (252 mg, 3.6 mmol). After being stirred for 100 h at 15 °C, the solution was quenched by 1 mol dm^{-3} HCl (20 cm^3). Yield of the product was determined as 69%, after extraction with diethyl ether (20 cm^3 × 3), by GLC analysis. GLC t_R of compound **7** 3.4 min. t_R of naphthalene 12.3 min. The ee of compound **7** was determined as 94% by HPLC analysis as described above. HPLC t_R of (*R*)-carbamate 31 min. t_R of (*S*)-carbamate 36 min [hexane–ethanol (100:1.5), 1.0 cm^3 min^{-1}]. Isolation was by molecular distillation. $[\alpha]_D^{25}$ +6.2° (*c* 2.1, $CHCl_3$) [lit.,[8] $[\alpha]_D^{21}$ −5.6 ± 1° (*c* 8, $CHCl_3$) for the *S*-enantiomer in >95% ee]; δ_H($CDCl_3$) 1.29 (3 H, d, *J* 6.7 Hz), 1.60 (1 H, s), 1.75 (3 H, s), 4.25 (1 H, q, *J* 6.7 Hz), 4.80 (1 H, s) and 4.96 (1 H, s).

(R)-2-*Methylpent*-1-*en*-3-*ol* **8**.—In a Schlenk tube were placed (*R*)-1-(3-azabicyclo[3.2.2]nonan-3-yl)-3,3-dimethylbutan-2-ol **3** (0.157 g, 0.62 mmol), naphthalene (115 mg) and dry hexane (20 cm^3). To this solution was added diethylzinc (2.6 mL, 25.4 mmol) and the mixture was stirred at 0 °C for 30 min and was then cooled to −10 °C and freshly distilled methylacrylaldehyde **1b** (880 mg, 12.5 mmol) was added. The mixture was stirred for 24 h at this temperature and the solution was then quenched with 1 mol dm^{-3} HCl (20 cm^3). Extraction by diethyl ether (50 cm^3 × 2) followed by silica gel column chromatography [hexane–diethyl ether (3:1)] of the residue gave 2-methylpent-1-en-3-ol **8** (925 mg, 74%); $[\alpha]_D^{22}$ +3.5° (*c* 2.1, $CHCl_3$) {lit.,[9] $[\alpha]_D^{25}$ −4.9° (*c* 0.63, $CHCl_3$) for the *S*-enantiomer in >98% ee}; δ_H($CDCl_3$) 0.90 (3 H, t, *J* 7.5 Hz), 1.5–1.6 (2 H, m), 1.61 (1 H, s), 1.72 (3 H, s), 4.00 (1 H, t, *J* 6.6 Hz), 4.85

(1 H, m) and 4.94 (1 H, m). Yield was determined as 78% by GLC analysis. GLC t_R of compound **8** 4 min.; t_R of naphthalene 12.5 min. The ee of this alcohol was determined as 98% by HPLC analysis as described above. HPLC t_R of (*R*)-carbamate 27 min; t_R of (*S*)-carbamate 30 min [hexane–ethanol (100:1.5), 1.0 cm^3 min^{-1}].

(R)-1-(2-*Furyl*)*ethanol* **9**.—To a solution of (*R*)-3,3-dimethyl-1-piperidinobutan-2-ol **2** (14.9 mg, 0.08 mmol) in hexane (7.5 cm^3) at −10 °C was added dimethylzinc (0.39 cm^3, 4.1 mmol). The solution was warmed up to 15 °C, stirred for 20 min, and cooled to −10 °C again, and freshly distilled 2-furaldehyde **1c** (360 mg, 3.75 mmol) was added. After being stirred for 88 h at 15 °C, the solution was quenched by 1 mol dm^{-3} HCl (20 cm^3). Extraction by diethyl ether (20 cm^3 × 2) followed by silica gel column chromatography [hexane–methylene dichloride (1:2.5)] of the residue gave 1-(2-furyl)ethanol **9** (320 mg, 76%). The ee was determined as 75% by HPLC analysis of the corresponding carbamate. HPLC t_R of (*R*)-carbamate 21 min. t_R of (*S*)-carbamate 32 min; $[\alpha]_D^{24}$ 15.5° (*c* 2.02, $CHCl_3$) {lit.,[2b] $[\alpha]_D^{24}$ +20.8° (*c* 1.27, $CHCl_3$)}; $\delta_H(CDCl_3)$ 1.55 (3 H, d, *J* 6.7 Hz), 1.9 (1 H, br s), 4.89 (1 H, q, *J* 6.7 Hz), 6.33 (1 H, dd, *J* 1.8 and 3.3 Hz) and 7.38 (1 H, dd, *J* 0.9 and 1.8 Hz).

(R)-1-(2-*Furyl*)*propan*-1-*ol* **10**.—To a solution of (*R*)-3,3-dimethyl-1-piperidinobutan-2-ol **2** (14.9 mg, 0.08 mmol) in hexane (7.5 cm^3) at −10 °C was added diethylzinc (0.42 cm^3, 4.1 mmol). The solution was warmed up to 15 °C, stirred for 20 min and then cooled to −10 °C again, when freshly distilled 2-furaldehyde **1c** (360 mg, 3.75 mmol) was added. The mixture was stirred for 24 h at this temperature and was then quenched by 1 mol dm^{-3} HCl (20 cm^3). Extraction with diethyl ether (20 cm^3 × 2) followed by silica gel column chromatography [hexane–methylene dichloride (1:2.5)] of the residue gave 1-(2-furyl(propan-1-ol **10** (454 mg, 96%). The ee was determined as 92% by HPLC analysis of the corresponding carbamate. HPLC t_R of (*R*)-carbamate 19 min. t_R of (*S*)-carbamate 28 min [hexane–ethanol (96:4), 1.0 cm^3 min^{-1}]; $[\alpha]_D^{25}$ +17.4° (*c* 2.5, $CHCl_3$) {lit.,[10] $[\alpha]_D^{25}$ +12.6° (*c* 2.09, $CHCl_3$) for 95% ee}; $\delta_H(CDCl_3)$ 0.96 (3 H, t, *J* 7.5 Hz), 1.8–2.0 (3 H, m), 4.61 (1 H, t, *J* 6.7 Hz), 6.2–6.4 (2 H, m) and 7.3–7.4 (1 H, m).

(R)-1-(2-*Thienyl*)*propan*-1-*ol* **11**.—To a solution of (*R*)-3,3-dimethyl-1-piperidinobutan-2-ol **2** (14.9 mg, 0.08 mmol) in hexane (7.5 cm^3) at −10 °C was added diethylzinc (0.42 cm^3, 4.1 mmol). The solution was warmed up to 15 °C, stirred for 20 min and then cooled to −10 °C, when freshly distilled thiophene-2-carboxaldehyde **1d** (420 mg, 3.75 mmol) was added. The mixture was stirred for 24 h at −10 °C and was then quenched by 1 mol dm^{-3} HCl (20 cm^3). Extraction by diethyl ether (20 cm^3 × 2) followed by silica gel column chromatography [hexane–methylenedichloride (1:3)] of the residue gave 1-(2-thienyl)propan-1-ol **11** (480 mg, 90%). The ee was determined as 95% by HPLC analysis of the corresponding carbamate. HPLC t_R of (*R*)-carbamate 19 min. t_R of (*S*)-carbamate 29 min [hexane–ethanol (96:4), 1.0 cm^3 min^{-1}]; $[\alpha]_D^{24}$ +25.9° (*c* 2.02, $CHCl_3$); $\delta_H(CDCl_3)$ 0.97 (3 H, t, *J* 7.5 Hz), 1.9–2.0 (3 H, m), 4.85 (1 H, t, *J* 6.7 Hz), 7.0–7.1 (2 H, m) and 7.2–7.3 (1 H, m). Absolute configuration was confirmed by conversion into the corresponding (*R*)-2-hydroxybutyric acid according to Sato's procedure.[2b]

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