

## Chiral Pyrrolidine Derivatives as Catalysts for the Enantioselective Addition of Diethylzinc to Aldehydes

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**A chiral hydroxylated pyrrolidine derivative (4) and an *N*-(2-mercaptoethyl)pyrrolidine derivative (1c) were synthesized from D-ribonolactone and were used as chiral catalyst ligands in the reaction of diethylzinc and aldehydes. High asymmetric induction of up to 95% ee was observed in the addition to aromatic aldehydes using the chiral hydroxylated pyrrolidine derivative 4.**

**Key words** asymmetric addition; chiral hydroxylated pyrrolidine; D-ribonolactone; chiral catalyst ligand; diethylzinc; optically active secondary alcohol

Asymmetric additions of dialkylzinc to aldehydes<sup>1)</sup> and enones<sup>2)</sup> in the presence of a catalytic amount of various chiral  $\beta$ -amino alcohols, including camphor-derived amino alcohols,  $\alpha$ -amino acid-derived  $\beta$ -amino alcohols, ephedrine derivatives, chiral pyrrolidinylmethanol derivatives, and C<sub>2</sub>-symmetric pyrrolidine derivatives, have been extensively studied in recent years. In connection with our studies on the synthesis of chiral polyhydroxylated amines,<sup>3)</sup> we describe here the synthesis of a chiral hydroxylated pyrrolidine derivative (4) and an *N*-(2-mercaptoethyl)pyrrolidine derivative (1c), and their use as chiral catalysts in the asymmetric addition of diethylzinc to aldehydes.

(2*S*,3*R*,4*S*)-*N*-Methyl-4-hydroxy-3-methoxymethoxy-2-trityloxymethylpyrrolidine (4) was prepared from (2*S*,3*R*,4*S*)-3,4-isopropylidenedioxy-2-trityloxymethylpyrrolidine (1a), which in turn was synthesized starting from D-ribonolactone.<sup>4a)</sup> Thus, 1a was converted into the corresponding *N*-benzyloxycarbonylpyrrolidine (1b), which was treated under acidic condition (concentrated HCl: MeOH = 1 : 20) to afford a trihydroxypyrrolidine (2) in 76% yield. Tritylation of the primary hydroxy group in 2 (trityl chloride (1.15 eq), triethylamine, 4-dimethylaminopyridine, dichloromethane) followed by silylation with *tert*-butyldimethylsilyl chloride in the presence of imidazole in *N,N*-dimethylformamide at 0 °C afforded 3a and 3b (3a:3b = 12.3:1) in 75% yield. Protection of the secondary hydroxy group in the major isomer (3a) as the methoxymethyl ether (chloromethyl methyl ether, *N,N*-diisopropylethylamine, tetrahydrofuran (THF)), followed by desilylation of 3c with tetrabutylammonium fluoride in THF, gave 3d in 73% yield from 3a. The structure of 3d was confirmed by transformation of 3d into (2*S*,3*S*)-*N*-benzyloxycarbonyl-3-methoxymethoxy-2-trityloxymethylpyrrolidine (5b) (1,1'-thiocarbonyldimidazole, pyridine, THF; then tributyltin hydride, benzene), which was identical with an authentic sample prepared from (2*S*,3*S*)-3-methoxymethoxy-2-trityloxymethylpyrrolidine (5a)<sup>4b)</sup> by *N*-benzyloxycarbonylation in terms of the <sup>1</sup>H- and <sup>13</sup>C-NMR spectra and the optical rotation. Reduction of 3d with LiAlH<sub>4</sub> in THF gave the corresponding *N*-methylpyrrolidine derivative (4) in 68% yield.

Recently, Kang *et al.*,<sup>5a)</sup> Kellogg *et al.*,<sup>5b)</sup> and Masaki *et al.*<sup>5c)</sup> have reported the use of sulfur derivatives of

ephedra alkaloids and C<sub>2</sub>-symmetrical chiral pyrrolidine derivatives for the addition of diethylzinc to aldehydes. (2*S*,3*R*,4*S*)-*N*-(2-Mercaptoethyl)-3,4-isopropylidenedioxy-2-trityloxymethylpyrrolidine (1c) was prepared from 1a by treatment with ethylene sulfide in acetonitrile at room temperature in 80% yield.

The asymmetric addition of diethylzinc to aldehydes was performed in cyclohexane–hexane (1 : 1) at 0 °C using 2.0 eq of diethylzinc in the presence of 0.08 eq of the chiral pyrrolidine (1c or 4) for 10–30 h. The enantiomeric excess of the secondary alcohols was determined by optical rotation measurement and <sup>1</sup>H-NMR analysis of the corresponding Mosher's ester.<sup>6)</sup> The results are summarized in Table 1. The *N*-methyl-4-hydroxypyrrolidine derivative (4) exhibited a high efficiency in chiral induction for aromatic aldehydes (up to 95% ee). However, hexanal could only be ethylated with moderate enantioselectivity (55% ee). On the other hand, enantiomeric excess for the addition of diethylzinc to benzaldehyde using 1c was low (41% ee). Interestingly, a dramatic change of enantioselectivity was observed between 1c, which gave (*S*)-1-phenylpropanol, and 4, which afforded the (*R*)-alcohol.

Further studies on asymmetric reactions employing chiral polyhydroxylated amines are in progress.

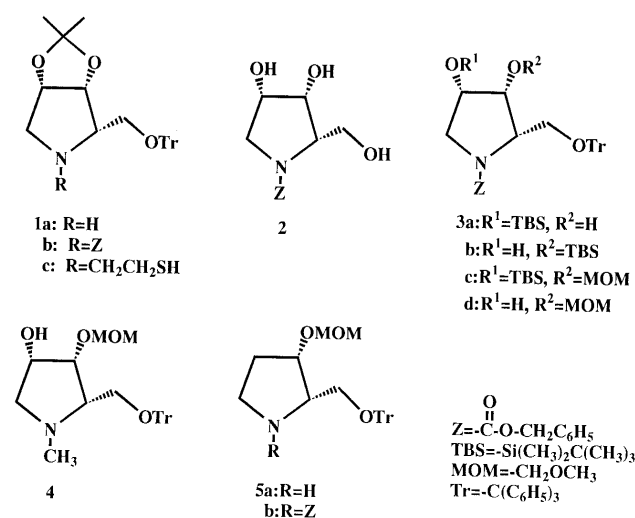


Chart 1

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Table 1. Asymmetric Addition of Diethylzinc to Aldehydes in the Presence of a Chiral Pyrrolidine Derivative as a Catalyst Ligand

| $\text{R-CHO} + \text{Et}_2\text{Zn} \xrightarrow{\text{chiral ligand (0.08 eq)}} \text{R-CH(OH)Et}$ |          |                                                     |          |           |                                                            |                       |         |
|------------------------------------------------------------------------------------------------------|----------|-----------------------------------------------------|----------|-----------|------------------------------------------------------------|-----------------------|---------|
| Entry                                                                                                | Catalyst | Aldehyde                                            | Time (h) | Yield (%) | $[\alpha]_D^{20}$ (c, solvent)                             | % ee <sup>a)</sup>    | Config. |
| 1                                                                                                    | 4        | PhCHO                                               | 20       | 90        | +46.1° (5.8, CHCl <sub>3</sub> ) <sup>b)</sup>             | 95 (94)               | R       |
| 2                                                                                                    | 4        | 4-ClPhCHO                                           | 20       | 64        | +22.7° (1.9, C <sub>6</sub> H <sub>6</sub> ) <sup>c)</sup> | 90 (88)               | R       |
| 3                                                                                                    | 4        | (E)-PhCH=CHCHO                                      | 20       | 65        | +4.7° (4.1, CHCl <sub>3</sub> ) <sup>d)</sup>              | 79 (75)               | R       |
| 4                                                                                                    | 4        | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> CHO | 30       | 41        | -5.3° (4.3, CHCl <sub>3</sub> ) <sup>e)</sup>              | 55 (62) <sup>f)</sup> | R       |
| 5                                                                                                    | 1c       | PhCHO                                               | 10       | 82        | -20.1° (5.2, CHCl <sub>3</sub> ) <sup>b)</sup>             | 41 (38)               | S       |

a) Based on the reported value of  $[\alpha]_D$ . Numbers in parentheses are based on the NMR analysis of the corresponding Moscher's esters. b) Reported value for (S)-1-phenylpropanol in 98% ee is  $[\alpha]_D^{22} -47.6^\circ$  (c=6.11, CHCl<sub>3</sub>); ref. 1c. c) Reported value for (S)-1-(4-chlorophenyl)propanol in 93% ee is  $[\alpha]_D^{22} -23.5^\circ$  (c=0.82, C<sub>6</sub>H<sub>6</sub>); ref. 1c. d) Reported value for (S)-1-phenylpent-1-en-3-ol in 96% ee is  $[\alpha]_D^{22} -5.7^\circ$  (CHCl<sub>3</sub>); ref. 1c. e) Reported value for (S)-3-nonanol is  $[\alpha]_D^{24} +9.6^\circ$  (c=8.3, CHCl<sub>3</sub>); Mukaiyama T., Hojo K., *Chem. Lett.*, **1976**, 893–896. f) <sup>1</sup>H-NMR spectrum of Moscher's ester was recorded in the presence of a shift reagent [Eu(fod)<sub>3</sub>].

## Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectral measurements were performed on a JEOL JIR-110 FT-IR spectrophotometer. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded on a JEOL JNM-FX100 (100 MHz) spectrometer. Data are recorded in parts per million (ppm) downfield from internal tetramethylsilane (TMS). The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). MS were taken on JEOL JMS-D302 and JEOL JMS-FX-102A spectrometers. Optical rotations were measured in CHCl<sub>3</sub> solution at 20°C on a JASCO DIP-360 polarimeter unless otherwise mentioned. The organic solvents were dried over anhydrous MgSO<sub>4</sub> before vacuum evaporation, and column chromatography was carried out with silica gel (Wakogel C-200).

**(2S,3R,4S)-N-Benzoyloxycarbonyl-3,4-isopropylidenedioxy-2-trityloxymethylpyrrolidine (1b)** Benzyl chloroformate (1.1 ml, 7.2 mmol) was added to a mixture of **1a** (2.5 g, 6 mmol) in ether (15 ml) and saturated aqueous NaHCO<sub>3</sub> (25 ml). The whole was stirred at room temperature for 3 h, then diluted with AcOEt (200 ml), and the organic layer was separated and washed with half-saturated aqueous NaCl. Drying, followed by evaporation and purification of the residue by column chromatography (AcOEt:hexane=1:3), gave **1b** (3.01 g, 91% yield) as crystals, mp 105°C (AcOEt-hexane),  $[\alpha]_D +30.9^\circ$  (c=1.2). IR  $\nu_{\text{max}}^{\text{Nujol}}$  cm<sup>-1</sup>: 1705. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.21 and 1.25 (2×3H, each s, 2×CH<sub>3</sub>), 3.13–3.48 (3H, m, CH, CH<sub>2</sub>OTr), 3.81–4.01 (1H, m, CH), 4.08–4.31 (1H, m, CH), 4.56–4.78 (2H, m, CH), 5.01 and 5.13 (2H, AB, J=12 Hz, OCH<sub>2</sub>Ph), 7.07–7.59 (20H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 23.61 (q), 24.77 (q), 49.75 (t), 58.34 (d), 60.78 (t), 66.82 (t), 77.63 (d), 79.26 (d), 86.62 (s), 113.76 (s), 127.76 (d), 128.46 (d), 128.87 (d), 129.33 (d), 129.62 (d), 137.46 (s), 145.59 (s), 156.16 (s). *Anal.* Calcd for C<sub>35</sub>H<sub>35</sub>NO<sub>5</sub>: C, 76.48; H, 6.42; N, 2.55. Found: C, 76.22; H, 6.65; N, 2.41.

**(2S,3R,4S)-N-Benzoyloxycarbonyl-3,4-dihydroxy-2-hydroxymethylpyrrolidine (2)** A solution of **1b** (2.5 g, 4.55 mmol) in concentrated HCl-MeOH (1:20, 25 ml) was stirred at room temperature for 1.5 h. After dilution with AcOEt (200 ml), the mixture was washed with saturated aqueous NaHCO<sub>3</sub> and half-saturated aqueous NaCl. Drying, followed by evaporation and purification of the residue by column chromatography (AcOEt:MeOH=20:1), gave **2** (1.02 g, 84% yield) as an oil,  $[\alpha]_D +33.8^\circ$  (c=0.8). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 3400, 1668, 1417, 1103, 1018. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.31–3.64 (2H, m), 3.64–4.30 (6H, m), 4.30–5.40 (4H, m), 7.30 (5H, s, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 52.04 and 52.16 (each t), 58.28 and 58.87 (each t), 59.31 and 60.23 (each d), 67.16 (t), 69.05 and 69.93 (each d), 71.58 and 71.97 (each d), 127.72 (d), 128.01 (d), 128.40 (d), 136.00 (s), 155.55 (s). MS *m/z*: 267 (M<sup>+</sup>).

**(2S,3R,4S)-N-Benzoyloxycarbonyl-4-tert-butylidimethylsiloxy-3-hydroxy-2-trityloxymethylpyrrolidine (3a) and (2S,3R,4S)-N-Benzoyloxycarbonyl-3-tert-butylidimethylsiloxy-4-hydroxy-2-trityloxymethylpyrrolidine (3b)** A mixture of **2** (1.0 g, 3.75 mmol), trityl chloride (1.2 g, 4.32 mmol), triethylamine (0.68 ml, 4.58 mmol), and 4-dimethylaminopyridine (50 mg) in dichloromethane (15 ml) was stirred at room temperature for 8 h. After dilution with AcOEt (100 ml), the mixture was washed with half-saturated aqueous NaCl. Drying, followed by evaporation, gave a residue, which was treated with *tert*-butyldimethylsilyl chloride (650 mg, 4.3 mmol) and imidazole (640 mg, 9.4 mmol) in

*N,N*-dimethylformamide (12 ml) at 0°C for 2 h. After dilution with AcOEt (200 ml), the mixture was washed with half-saturated aqueous NaCl. Drying, followed by evaporation and purification of the residue by column chromatography (AcOEt:hexane=1:5), gave **3a** (1.60 g, 69% yield) and **3b** (130 mg, 5.6%) as an oil. **3a**:  $[\alpha]_D +27.8^\circ$  (c=2). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 3465, 1703, 1099. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 0.12 and 0.14 (2×3H, each s, 2×CH<sub>3</sub>), 0.91 (9H, s, *tert*-Bu), 3.02–3.08 (1H, m, OH), 3.20–3.40 (1H, m, CH<sub>2</sub>OTr), 3.40–3.97 (3H, m, CH<sub>2</sub>OTr, CH<sub>2</sub>), 4.12–4.45 (3H, m, 3×CH), 4.96–5.34 (2H, m, OCH<sub>2</sub>Ph), 7.0–7.60 (20H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): -4.97 and -5.07 (each q), 17.88 (s), 25.58 (q), 51.51 (t), 58.33 (d), 62.13 (t), 66.76 (t), 70.85 (d), 72.41 (d), 87.03 (s), 126.80 (d), 127.62 (d), 128.45 (d), 136.39 (s), 143.80 (s), 154.86 (s). MS *m/z*: 622 (M<sup>+</sup>-1). **3b**:  $[\alpha]_D +5.3^\circ$  (c=1.5). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 3460, 1700, 1100. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 0.01 and 0.09 (2×3H, each s, 2×CH<sub>3</sub>), 0.81 (9H, s, *tert*-Bu), 3.22–3.36 (1H, m, CH<sub>2</sub>OTr), 3.42–3.78 (3H, m), 3.80–4.41 (3H, m), 4.70–4.96 (1H, m), 5.15 (2H, brs, OCH<sub>2</sub>Ph), 7.03–7.56 (20H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): -5.36 and -5.02 (each q), 17.98 (s), 25.58 (q), 53.46 (t), 58.67 (d), 60.42 (t), 66.57 and 66.90 (each t), 69.54 and 70.51 (each d), 72.27 and 72.46 (each d), 88.20 (s), 126.89 (d), 127.58 (d), 128.65 (d), 136.15 (s), 142.97 (s), 154.67 (s). MS *m/z*: 622 (M<sup>+</sup>-1).

**(2S,3R,4S)-N-Benzoyloxycarbonyl-4-tert-butylidimethylsiloxy-3-methoxymethoxy-2-trityloxymethylpyrrolidine (3c)** A mixture of **3a** (1.54 g, 2.47 mmol), *N,N*-diisopropylethylamine (2.38 g, 18.5 mmol), and chloromethyl methyl ether (1.49 g, 18.5 mmol) in THF (15 ml) was heated under reflux for 20 h. After dilution with AcOEt (100 ml), the mixture was washed with half-saturated aqueous NaCl. Drying, followed by evaporation and purification of the residue by column chromatography (AcOEt:hexane=1:5), gave **3c** (1.46 g, 89% yield) as an oil,  $[\alpha]_D +10.8^\circ$  (c=1). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 1703, 1411, 1151. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): -0.03 and 0.00 (2×3H, each s, 2×CH<sub>3</sub>), 0.77 (9H, s, *tert*-Bu), 3.20 (3H, s, OCH<sub>3</sub>), 3.20–3.35 (1H, m, CH), 3.35–3.40 (1H, m, CH), 3.40–3.70 (2H, m, 2×CH), 3.90–4.30 (2H, m, 2×CH), 4.30–4.70 (2H, m, OCH<sub>2</sub>O), 4.90–5.30 (3H, m, OCH<sub>2</sub>Ph, CH), 7.06–7.60 (20H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): -5.31 and -5.17 (each q), 17.74 (s), 25.44 (q), 52.19 (t), 55.50 (q), 58.14 (d), 62.47 (t), 66.57 (t), 70.37 (d), 75.92 (d), 86.49 (s), 95.76 (t), 126.45 (d), 127.28 (d), 127.55 (d), 127.72 (d), 128.11 (d), 128.50 (d), 136.45 (s), 143.95 (s), 155.20 (s). MS *m/z*: 666 (M<sup>+</sup>-1).

**(2S,3R,4S)-N-Benzoyloxycarbonyl-4-hydroxy-3-methoxymethoxy-2-trityloxymethylpyrrolidine (3d)** A mixture of **3c** (1.5 g, 2.25 mmol) and tetrabutylammonium fluoride (3.5 ml of 1 M solution in THF) in THF (8 ml) was stirred at room temperature for 30 min. After dilution with AcOEt (100 ml), the mixture was washed with half-saturated aqueous NaCl. Drying, followed by evaporation and purification of the residue by column chromatography (AcOEt:hexane=1:1), gave **3d** (1.01 g, 82% yield) as an oil,  $[\alpha]_D +6.0^\circ$  (c=1.5). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 3407, 1700, 1413, 1101. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.25 (3H, s, OCH<sub>3</sub>), 3.20–3.35 (1H, m, CH), 3.45–3.85 (3H, m, CH<sub>2</sub>, CH), 3.90–4.40 (3H, m, 2×CH, OH), 4.50 and 4.60 (2H, AB, J=7 Hz, OCH<sub>2</sub>O), 4.70–5.26 (3H, m, OCH<sub>2</sub>Ph, CH), 7.02–7.60 (20H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 53.36 (t), 55.75 (q), 57.60 and 57.89 (each d), 59.45 and 60.23 (each t), 66.52 and 66.86 (each t), 68.32 and 69.05 (each d), 76.36 (d), 88.10 (s), 96.05 (t), 126.99 (d), 127.58 (d), 128.55 (d), 136.11 (s), 142.82 (s), 154.72 (s). MS *m/z*: 552 (M<sup>+</sup>-1).

**(2S,3R,4S)-N-Methyl-4-hydroxy-3-methoxymethoxy-2-trityloxy-methylpyrrolidine (4)** LiAlH<sub>4</sub> (200 mg, 5.3 mmol) was added at room temperature to a solution of **3d** (1 g, 1.8 mmol) in THF (15 ml) and the reaction mixture was stirred at room temperature for 1 h. After addition of H<sub>2</sub>O (0.2 ml), 15% aqueous NaOH (0.2 ml), and H<sub>2</sub>O (0.6 ml), the mixture was filtered and the filtrate was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Evaporation, followed by purification of the residue by column chromatography (AcOEt:MeOH=10:1), gave **4** (530 mg, 68% yield) as an oil,  $[\alpha]_D^{25} +22.9^\circ$  ( $c=1$ ). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 3432, 1448, 1151, 1070. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 2.26 (3H, s, NCH<sub>3</sub>), 2.18–2.68 (2H, m, CH<sub>2</sub>), 2.92–3.77 (4H, m, CH<sub>2</sub>, CH, OH), 3.24 (3H, s, OCH<sub>3</sub>), 4.08–4.31 (2H, m, 2 × CH), 4.48 and 4.58 (2H, AB,  $J=4$  Hz, OCH<sub>2</sub>O), 7.02–7.60 (15H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 41.47 (q), 55.89 (q), 61.69 (d), 62.42 (t), 67.35 (d), 69.63 (d), 78.31 (d), 87.03 (s), 97.07 (t), 126.80 (d), 127.58 (d), 128.45 (d), 143.75 (s). HRMS  $m/z$ : Calcd for C<sub>27</sub>H<sub>31</sub>NO<sub>4</sub> (M<sup>+</sup>): 433.2253. Found: 433.2256.

**(2S,3S)-N-Benzyloxycarbonyl-3-methoxymethoxy-2-trityloxymethylpyrrolidine (5b)** A mixture of **3d** (150 mg, 0.27 mmol), 1,1'-thiocarbonyldiimidazole (120 mg, 0.68 mmol), and pyridine (80 mg, 1.0 mmol) in THF (2 ml) was heated under reflux for 12 h. After dilution with AcOEt (50 ml), the mixture was washed with half-saturated aqueous NaCl. Drying, followed by evaporation, gave a residue, which was dissolved in benzene (1 ml). This benzene solution was added to a solution of tributyltin hydride (190 mg, 0.65 mmol) in benzene (1 ml) at 80 °C, and the mixture was heated under reflux for 1 h. After evaporation of benzene *in vacuo*, the residue was purified by column chromatography (AcOEt:hexane=4:1) to give **5b** (45 mg, 31% yield) as an oil ( $[\alpha]_D^{25} +10.5^\circ$  ( $c=0.7$ )). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 3458, 1700, 1417, 1091. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 2.00–2.36 (2H, m, CH<sub>2</sub>), 3.22 (3H, s, OCH<sub>3</sub>), 3.20–3.60 (4H, m, 2 × CH<sub>2</sub>), 3.85–4.36 (2H, m, 2 × CH), 4.36–4.70 (2H, m, OCH<sub>2</sub>O), 4.82–5.19 (2H, m, OCH<sub>2</sub>Ph), 7.04–7.60 (20H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 29.72 (t), 55.26 (q), 58.33 (d), 60.13 and 60.67 (each t), 66.57 (t), 76.21 (d), 86.79 (s), 96.14 (s), 126.55 (s), 127.04 (s), 127.38 (s), 127.58 (d), 136.25 (s), 143.80 (s), 154.67 (s). MS  $m/z$ : 538 (M<sup>+</sup> + 1), 536 (M<sup>+</sup> – 1), which was identical with an authentic sample prepared from (2S,3S)-3-methoxymethoxy-2-trityloxymethylpyrrolidine (**5a**)<sup>4b</sup> by *N*-benzyloxycarbonylation as described above for the preparation of **1b**.

**(2S,3R,4S)-N-(2-Mercaptoethyl)-3,4-isopropylidenedioxy-2-trityloxy-methylpyrrolidine (1c)** A mixture of **1a** (230 mg, 0.55 mmol) and ethylene sulfide (0.4 ml) in acetonitrile (1.5 ml) was stirred at room temperature for 6 h. After evaporation of the ethylene sulfide and the acetonitrile *in vacuo*, the residue was purified by column chromatography (AcOEt:hexane=1:5) to afford **1c** (206 mg, 80% yield) as an oil,  $[\alpha]_D^{25} +69.3^\circ$  ( $c=1$ ). IR  $\nu_{\text{max}}^{\text{neat}}$  cm<sup>-1</sup>: 1448, 1216, 1070, 757. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.26 and 1.32 (2 × 3H, each s, 2 × CH<sub>3</sub>), 1.42–1.78 (1H, m, CH), 1.91–2.10 (1H, m, CH), 2.15–2.60 (4H, m, 2 × CH<sub>2</sub>), 2.82–3.30 (3H, m, CH<sub>2</sub>OTr, CH), 3.55–3.71 (1H, m, CH), 4.47–4.66 (2H, m, OCH<sub>2</sub>O), 7.10–7.60 (15H, m, aromatic protons). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 22.95 (q), 25.44 (q), 26.07 (q), 56.33 (t), 59.16 (t), 62.38 (t), 67.49 (d), 77.87 (d), 80.70 (d), 86.88 (s), 110.91 (s), 126.75 (d), 127.53 (d), 128.65 (d), 143.95 (s). HRMS  $m/z$ : Calcd for C<sub>29</sub>H<sub>33</sub>NO<sub>3</sub>S (M<sup>+</sup>): 475.2181. Found: 475.2177.

**General Procedure for the Chiral Pyrrolidine Derivative (1c or 4)-Catalyzed Addition of Diethylzinc to Aldehydes** A mixture of the chiral

pyrrolidine derivative (0.1 mmol, 8 mol%) and an aldehyde (1.3 mmol) in cyclohexane (1.5 ml) and hexane (1.5 ml) was warmed at 60 °C for 5 min, then cooled to 0 °C, and diethylzinc (2.6 ml of a 1 M hexane solution) was added. The mixture was stirred for 10–30 h at 0 °C, quenched by the addition of 10% aqueous HCl and extracted with dichloromethane. Drying, followed by evaporation and purification of the residue by column chromatography (AcOEt:hexane=1:3–1:5), afforded the optically active secondary alcohols, which were identical with authentic racemic samples in terms of <sup>1</sup>H-NMR spectra. Moscher's esters were prepared by the reaction of the secondary alcohols with (*R*)-(–)-methoxy- $\alpha$ -(trifluoromethyl)phenylacetyl chloride and 4-dimethylaminopyridine in CCl<sub>4</sub> at room temperature.

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## References and Notes

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