Supporting Information

Experimental details for the synthesis and product characterizations and X-ray structures of **5a** and **5d**.

Experimental

General procedure for preparing lactone 1: To a solution of aldehyde (10 mmol), (*R*) -α-phenylglycinol (11 mmol), ammonium chloride (13 mmol) in 10 mL of MeOH and 10 mL of H_2O was added sodium cyanide (10 mmol) under ice-water bath. The resultant solution was stirred at room temperature for 12 h. After MeOH was evaporated in vacuo, the aqueous phase was extracted with ethyl acetate for three times. The combined organic phase was washed with brine and dried over anhydrous sodium sulfate. The solvent was evaporated in vacuo and the residue was dissolved in a saturated methanolic HCl. After the resultant solution was stirred overnight, the solvent was evaporated in vacuo and the residue was dissolved in 20 mL of water. The solution was neutralized with aqueous sodium bicarbonate until pH = 8 before it was extracted with ethyl acetate for three times, the combined organic phase was washed with brine and dried over anhydrous sodium sulfate. After the solvent had been evaporated in vacuo, the residue was purified by chromatography to give the corresponding amino ester in about 80% yield.

The above amino ester (1.0 mmol) in 20 mL of toluene was added PTSA (34.4 mg, 0.2 mmol). The solution was heated to reflux for 2 days under argon. After the reaction was completed as monitored by TLC, the solvent was evaporated in vacuo and the residue was purified by chromatography to give lactone **1** as a mixture of two diastereomers.

General procedure for preparing compounds 4a and 4b: To a solution of **1** in dry DMF (0.5 M) was added benzyl bromide and anhydrous potassium carbonate with stirring. After the mixture was warmed to 60 ~ 65 ^{o}C slowly, the stirring was continued

for 8 h at the same temperature. The cooled solution was evaporated in vacuo and the residue was purified by chromatography to give **4** as a mixture of two diastereomers.

4a: 83% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.17 (m, 10H), 4.31-4.14 (m, 2H), 3.97 (dd, *J* = 11.1, 3.6 Hz, 1H), 3.80 (d, *J* = 13.7 Hz, 1H), 3.65 (dd, *J* = 6.8, 5.9 Hz, 1H), 3.52 (d, *J* = 13.7 Hz, 1H), 1.72-1.60 (m, 2H), 1.51-1.27 (m, 2H), 0.89-0.77 (m, 3H). EIMS *m/z* 308 (M^+ - H^+), 266, 91.

5b: 85% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.20 (m, 10H), 4.33-4.14 (m, 2H), 3.95 (dd, *J* = 10.3, 3.8 Hz, 1H), 3.82 (d, *J* = 13.9 Hz, 1H), 3.67 (m, 1H), 3.52 (d, *J* = 13.9 Hz, 1H), 1.37 (d. *J* = 7.1 Hz, 3H). EIMS *m/z* 282 (M^+ - H^+), 132, 91.

Typical procedure for functionalization of 4: A solution of **4** (5 mmol) in DME-THF (1:1, 1 mL) was cooled to -78 ^{o}C under argon before NaHMDS in THF (6 mmol) was added over 15 min. The stirring was continued for 1 h and then benzyl bromide (6 mmol) was added. After the reaction was completed as monitored by TLC, a solution of saturated aqueous ammonium chloride was added to quench the reaction. The mixture was partitioned between ethyl acetate and brine and the organic phase was separated, dried over anhydrous sodium sulfate. After the solvent was evaporated in vacuo, the residue was purified by chromatography to give product.

5a: $[\alpha]_D^{20}$ -20.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.22 (m, 10H), 4.61 (dd, *J* = 10.3, 3.0 Hz, 1H), 4.47 (t, *J* = 10.8 Hz, 1H), 4.28 (dd, *J* = 11.0, 3.2 Hz, 1H), 3.79 (s, 3H), 3.75 (d, *J* = 15.2 Hz, 1H), 3.40 (d, *J* = 15.2 Hz, 1H), 3.24 (d, *J* = 17.6 Hz, 1H), 3.03 (d, *J* = 17.6 Hz, 1H), 2.06 (m, 1H), 1.51-1.10 (m, 3H), 0.79 (t, *J* = 7.1 Hz, 3H); EIMS *m/z* 381 (M^+); HRMS found *m/z* 381.1917 (M^+), $C_{23}H_{29}NO_4$ requires 381.1894.

5b: $[\alpha]_D^{14}$-53.3 (*c* 2.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.07 (m, 15H), 4.40 (dd, *J* = 10.7, 3.6 Hz, 1H). 4.11-4.04 (m, 2H), 3.85-3.80 (m, 2H), 3.30 (d, *J* = 13.9 Hz, 1H), 3.14 (d, *J* = 13.9 Hz), 1.32 (s, 3H); EIMS *m/z* 280 (M^+ - Bn), 91; HRMS found *m/z* 280.1355 (M^+ - Bn), $C_{25}H_{25}NO_2$ requires 280.1373.

5c: $[\alpha]_D^{14}$ -65.3 (*c* 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.09 (m, 10H) , 4.78 (dd , *J* = 10.8, 3.7 Hz, 1H) , 4.66 (dd , *J* = 10.8, 3.7 Hz, 1H) , 4.00 (m, 1H) , 3.90 (d, *J* = 14.8 Hz, 1H) , 3.69 (d, *J* = 14.8 Hz, 1H), 2.00-1.85 (m, 2H), 1.21-1.10 (m, 6H); EIMS *m/z* 309 (M^+); HRMS found *m/z* 309.1734 (M^+), $C_{20}H_{23}NO_2$ requires 309.1739.

5d: $[\alpha]_D^{14}$ +17.5 (*c* 2.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-6.92 (m, 10H), 4.59 (t, *J* = 10.7 Hz, 1H), 4.22-4.09 (m, 2H), 3.84 (d, *J* = 15.0 Hz, 1H), 3.77 (br s, 1H), 3.60 (d, *J* = 15.0, 1H), 3.38-0.93 (m, 7H), 0.85 (dd, *J* = 13.1, 6.3 Hz, 3H); EIMS *m/z* 354(M^+), 280, 132; Anal. Cacld. for $C_{22}H_{27}NO_3$: C: 74.75, H: 7.69, N: 3.96; found: C: 74.77, H: 7.39, N: 3.98.

5e: $[\alpha]_D^{14}$ +47.1 (*c* 4.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.26 (m, 10H), 4.87 (dd, *J* = 10.6, 3.5 Hz, 1H), 4.66 (dd, *J* = 10.6, 3.5 Hz, 1H), 3.97 (m, 1H), 3.82 (s, 3H), 3.75 (d, *J* = 8.8 Hz, 1H), 3.65 (d, *J* = 8.8 Hz, 1H), 3.18 (d, *J* = 16.4 Hz, 1H), 2.96 (d, *J* = 16.4 Hz, 1H), 1.21 (s, 3H); EIMS *m/z* 353 (M^+); HRMS found *m/z* 353.1636 (M^+); $C_{21}H_{23}NO_4$ requires 353.1645.

5f: $[\alpha]_D^{25}$ -53.6 (*c* 3.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-6.79 (m, 15H), 4.40 (t, *J* = 10.3 Hz, 1H), 4.19 (d, *J* = 15.5 Hz, 1H), 3.94 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.77 (d, *J* = 15.5 Hz, 1H), 3.60 (dd, *J* = 10.0, 3.9 Hz, 1H), 3.50 (d, *J* = 14.2 Hz, 1H), 3.34 (d, *J* = 14.1 Hz, 1H), 1.98-1.84 (m, 2H), 1.53-1.36 (m, 2H), 0.81 (t, *J* = 7.1 Hz, 3H); EIMS *m/z*

308 (M^+ -Bn), 91; Anal. Cacld. for $C_{27}H_{29}NO_2$: C: 81.11, H: 7.31, N: 3.51; found C: 80.81, H: 7.08, N: 3.45.

5g: $[\alpha]_D^{14}$ +20.5 (*c* 2.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.41-7.16 (m, 10H), 4.53 (t, *J* = 9.7 Hz, 1H), 4.36-4.32 (m, 2H), 4.26-4.21 (m, 1H), 3.88 (d, *J* = 11.2 Hz, 1H), 3.80 (m, 2H), 2.17-2.07 (m, 1H), 1.89-1.80 (m, 1H), 1.28-1.22 (m, 2H), 0.82 (t, *J* = 7.0 Hz, 3H); EIMS *m/z* 354 ($M^+ + H^+$), 308, 266, 91; Anal. Cacld. for $C_{22}H_{27}NO_3$: C: 74.75, H: 7.69, N: 3.96; found C: 74.87, H: 7.75, N, 4.06.

Following a similar procedure, **2** and **3** were obtained from **1a**. **2:** $[\alpha]_D^{18}$ +17.5 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.46-7.27 (m, 5H), 4.59 (m, 1H), 4.48-4.43 (m, 2H), 3.70 (s, 3H), 3.15 (d, *J* = 15.6 Hz, 1H), 2.68 (d, *J* = 15.6 Hz, 1H), 1.95-1.76 (m, 2H), 1.70-1.61 (m, 1H), 1.44-1.38 (m, 1H), 0.95 (t, *J* = 7.7 Hz, 3H). EIMS *m/z* 292 ($M^+ + H^+$), 248, 156; Anal. Calcd. for $C_{16}H_{21}NO_4$: C: 65.96, H: 7.26, N: 4.81; found C: 66.00, H: 7.30; N: 4.80. **3:** $[\alpha]_D^{18}$ -6.4 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38-7.26 (m, 5H), 4.43-4.36 (m, 3H), 3.74 (s, 3H), 3.14 (d, *J* = 16.4 Hz, 1H), 2.59 (d, *J* = 16.4 Hz, 1H), 2.15 (br s, 1H), 2.07-1.96 (m, 1H), 1.82-1.72 (m, 1H), 1.50-1.37 (m, 2H), 0.96 (t, *J* = 7.2 Hz, 3H); EIMS *m/z* 292 ($M^+ + H^+$), 248, 156; Anal. Calcd. for $C_{16}H_{21}NO_4$: C: 65.96, H: 7.26, N: 4.81; found C: 66.01; H: 7.30; N: 4.78.

General procedure for synthesis of amino acid:

Method A: The substrate was suspended in aqueous hydrochloride (6 M) and the mixture was heated to reflux. After the reaction completed, the solvent was evaporated in vacuo, and the residue was dissolved in mixture of MeOH-H_2O (v/v, 1/1). After Pd-C (10%, w/w) was added, the mixture was stirred under H_2 (40 atm, 40 ^oC) for 36 h. The

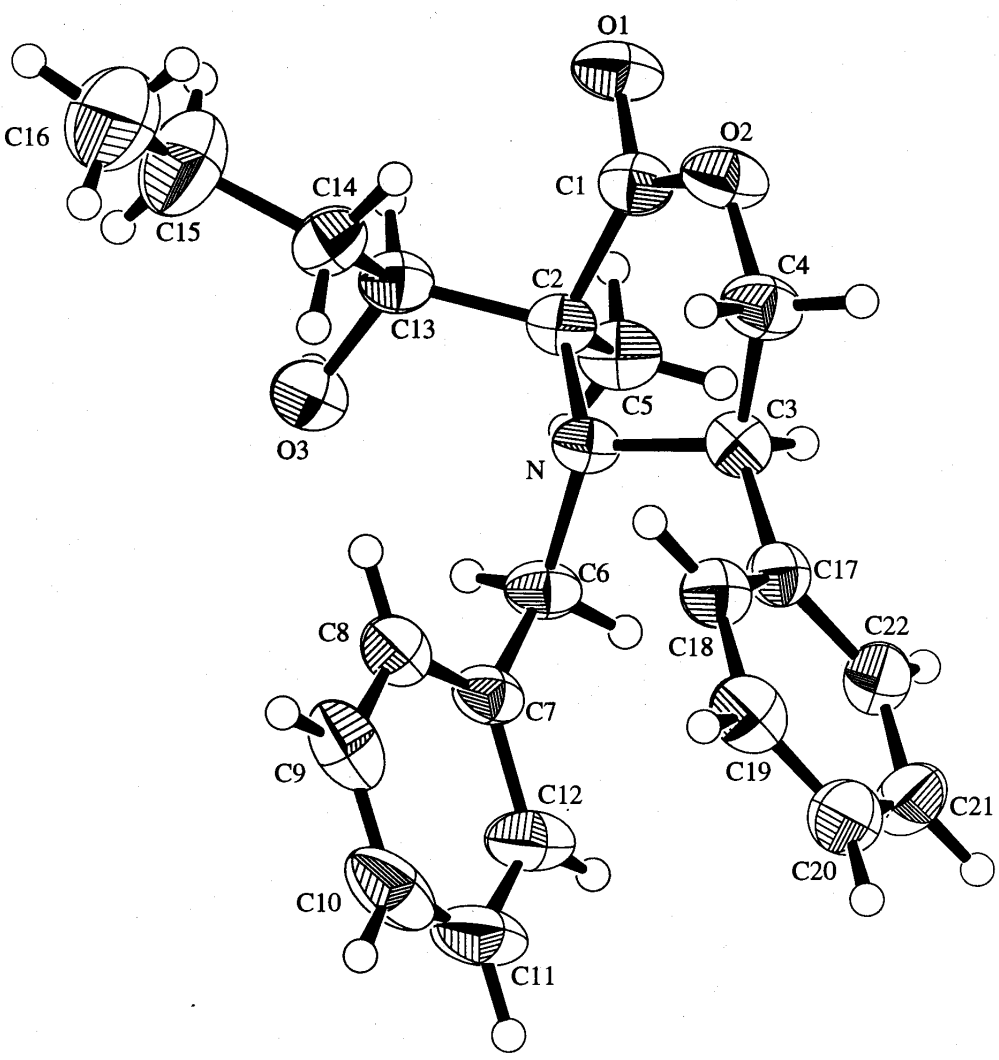
catalyst was filtered off and the filtrate was concentrated, the residue was purified by ion exchanged column (Dowex-50W) to give the product.

Method B: The substrate was dissolved in MeOH and then 10% NaOH was added. The mixture was stirred at room temperature until no more starting material was detected by TLC. To this solution was added 2 M of hydrochloride until pH = 4. The solvent was evaporated in vacuo and the residue was dissolved in ethanol. After Pd-C (10%, w/w) was added, the mixture was stirred under H_2 (40 atm, 40 ^oC) for 36 h. The catalyst was filtered off and the filtrate was concentrated, the residue was purified by ion exchanged column (Dowex-50W) to give the product.

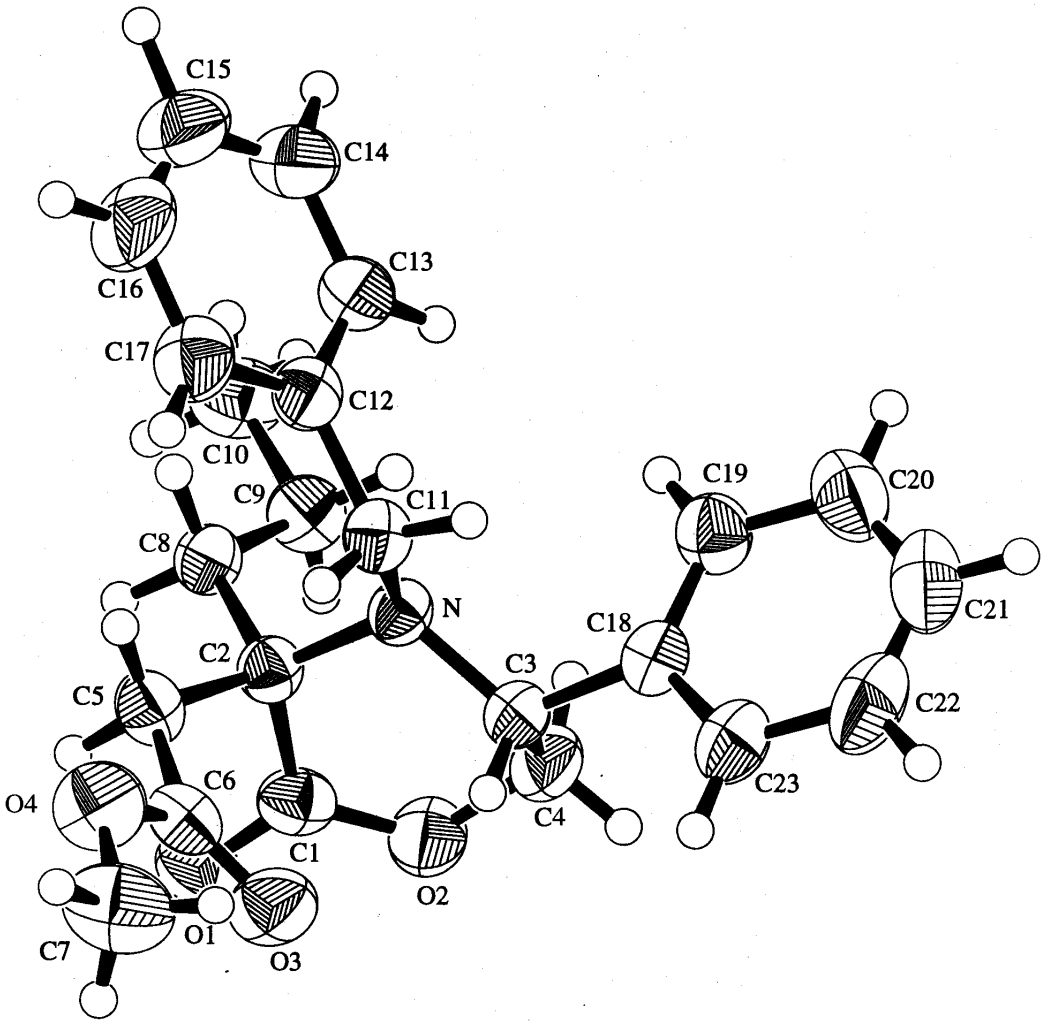
6: $[\alpha]_D^{16}$ -22.2 (*c* 2.8, H_2O) (lit. $[\alpha]_D^{25}$ -22 (*c* 1, H_2O)); ^{1}H NMR (300 MHz, D_2O) δ 7.36-7.24 (m, 5H), 3.32 (d, *J* = 14.5 Hz, 1H), 3.03 (d, *J* = 14.5 Hz, 1H), 1.58 (s, 3H); ESIMS *m/z* 179 (M^+).

7: $[\alpha]_D^{17}$ -57.8 (*c* 0.41, H_2O, as hydrochloride salt) (lit. $[\alpha]_D^{20}$ -52.9 (*c* 1.0, H_2O, as hydrochloride salt)); ^{1}H NMR (300 MHz, D_2O) δ 3.17 (d, *J* = 18.2 Hz, 1H), 2.90 (d, *J* = 18.2 Hz, 1H), 1.56 (s, 3H).

8: $[\alpha]_D^{25}$ -7.0 (*c* 1, MeOH); ^{1}H NMR (300 MHz, D_2O) δ 3.78 (m, 1H), 1.53-1.31 (m, 7H), 0.81 (t, *J* = 6.9 Hz, 3H); ESIMS *m/z* 162 ($M^+ - H^+$).



X-ray structure of 5a



X-ray Structure of 5d