Supporting Information for

Highly Enantioselective Reformatsky Reaction of Ketones: Chelation Assisted Enantioface Discrimination

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General:

Infrared spectra were obtained on a Perkin Elmer FT-IR Spectrometer PARAGON 1000. ¹H-NMR spectra were recorded on JEOL JMT-C400 /5(400 MHz). Chemical shifts were given in ppm with tetramethylsilane as an internal standard, and coupling constants (*J*) were given in hertz (Hz). The following abbreviations were used; s=singlet, d=doublet, t=triplet, m=multiplet, dd=double doublet, br=broad, DEA=diethyl amine. The chiral stationary phase columns, CHIRALCEL[®] OD, CHIRALCEL[®] OJ, CHIRALCEL[®] OJ-H and CHIRALPAK[®] AD were purchased from Daicel Chemical Industries, Ltd. Mega Bond Elut[®] was purchased from Varian Incorporated.

General Procedure

(*S*)-*tert*-Butyl 3-hydroxy-3-(2-naphthyl)-3-(1-trityl-1*H*-imidazol-4-yl)propanoate (2).

The Reformatsky reagent (0.45 M in THF, 4.4 ml, 2.0 mmol) was added dropwise to a cooled (0 °C) suspension of cinchonine (220 mg, 0.75 mmol) in THF (1 ml), and the mixture was stirred for 10 min at 0 °C under an argon atmosphere. Pyridine (0.15 ml, 2.0 mmol) was added, and the mixture was stirred for 20 min at 0 °C. After being cooled to -42 °C, a solution of 2-naphthyl(1-trityl-1*H*-imidazol-4-yl)methanone (232 mg, 0.5 mmol) in THF (2 ml) was added dropwise over a period of 10 min, and the mixture was stirred for 4 h at -40 °C. The mixture was diluted with 1 mol/L HCl, and then extracted with AcOEt. The organic layer was successively washed with water, saturated NaHCO₃, and brine followed by drying over MgSO₄. After removal of

the solvent *in vacuo*, the enantiomer excess (97% ee) and yield (97%) were determined by HPLC analysis. The resulting crude product was purified by column chromatography on silica gel (*n*-hexane: AcOEt = 3:1) to give a colorless amorphous powder.

$^1\text{H-NMR}$ (CDCl_3) δ : 1.32(9H, s), 3.12(1H, d, $J = 16.0$ Hz), 3.40(1H, d, $J = 16.0$ Hz), 5.25(1H, s), 6.85(1H, s), 7.0 – 7.8(22H, m), 8.01(1H, s).

IR (KBr) $\nu \text{ cm}^{-1}$: 3455, 2977, 1706, 1493, 1446, 1368, 1155, 742, 701.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/2-propanol (90/10), flow rate: 1.0 ml/min, detection: UV (254 nm), column temp.: room temperature, retention time: 24.5 min (minor: 17.8 min, substrate: 19.8 min).

$[\alpha]_{\text{D}}^{25} = +13.5^\circ$ ($c = 0.5$, EtOH).

***tert*-Butyl 3-hydroxy-3-phenyl-3-(1-trityl-1*H*-imidazol-4-yl)propanoate (16).**

colorless amorphous powder (97% ee, >99%): $^1\text{H-NMR}$ (CDCl_3) δ : 1.32(9H, s), 3.02(1H, d, $J = 15.9$ Hz), 3.30(1H, d, $J = 15.9$ Hz), 5.09(1H, s), 6.80(1H, s), 7.0 – 7.4(19H, m), 7.5 – 7.6(2H, s).

IR (KBr) $\nu \text{ cm}^{-1}$: 3468, 2978, 1704, 1493, 1447, 1368, 1346, 1153, 748, 701.

HPLC conditions: column, CHIRALCEL OD connected with CHIRALPAK[®] AD, mobile phase: *n*-hexane/ethanol (95/5), flow rate: 1.0 ml/min, detection: UV (254 nm), column temp.: room temperature, retention time: 21.9 min (minor: 19.5 min, substrate: 29.1 min).

$[\alpha]_{\text{D}}^{25} = -8.02^\circ$ ($c = 0.46$, EtOH).

***tert*-Butyl 3-hydroxy-4-methyl-3-(1-trityl-1*H*-imidazol-4-yl)pentanoate (17).**

colorless oil (94% ee, 73%): $^1\text{H-NMR}$ (CDCl_3) δ : 0.84(3H, d, $J = 6.9$ Hz), 0.88(3H, d, $J = 6.9$ Hz), 1.37 (9H, s), 1.94 – 2.05(1H, m), 2.66(1H, d, $J = 15.6$ Hz), 3.01(1H, d, $J = 15.6$ Hz), 4.57(1H, s), 6.79(1H, s), 7.0 – 7.2 (6H, m), 7.2 – 7.4(10H, m).

IR (KBr) $\nu \text{ cm}^{-1}$: 3453, 2978, 1693, 1446, 1365, 1335, 1150, 951, 819, 749, 700.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/ethanol (95/5), flow rate:

0.5 ml/min, detection: UV (254 nm), column temp.: room temperature, retention time: 35.4 min (minor: 15.6 min, substrate: 18.0 min).

(S)-tert-Butyl 3-hydroxy-3-phenyl-3-(2-pyridyl)propanoate (18).

colorless solid (90% ee, 98%): $^1\text{H-NMR}$ (CDCl_3) δ : 1.32(9H, s), 3.12(1H, d, $J = 15.8$ Hz), 3.52(1H, d, $J = 15.8$ Hz), 5.51(1H, s), 7.1 – 7.3 (4H, m), 7.5 – 7.7(4H, m), 8.5(1H, m).

IR (neat) $\nu \text{ cm}^{-1}$: 3461, 2978, 1702, 1368, 1154, 700.

HPLC conditions: column, CHIRALCEL[®] OJ-H, mobile phase: *n*-hexane/ethanol (975/25), flow rate: 1.0 ml/min, detection: UV (220 nm), column temp.: 30 °C, retention time: 12.0 min (minor: 14.4 min, substrate: 27.0 min).

$[\alpha]_{\text{D}}^{25} = -49.8^\circ$ ($c = 0.5$, EtOH)

tert-Butyl 3-hydroxy-3-(2-pyridyl)butanoate (19).

colorless oil (86% ee, 94%): $^1\text{H-NMR}$ (CDCl_3) δ : 1.30(9H, s), 1.53(3H, s), 2.73(1H, d, $J = 15.5$ Hz), 3.10(1H, d, $J = 15.5$ Hz), 4.95(1H, s), 7.1(1H, m), 7.6 – 7.7(2H, m), 8.5(1H, m).

IR (neat) $\nu \text{ cm}^{-1}$: 3477, 2979, 1704, 1591, 1472, 1434, 1392, 1368, 1228, 1159, 1107, 793, 751.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/ethanol (975/25), flow rate: 0.5 ml/min, detection: UV (220 nm), column temp.: room temperature, retention time: 17.4 min (minor: 15.8 min, substrate: 12.5 min).

tert-Butyl 3-hydroxy-3-phenyl-3-(3-pyridyl)propanoate (20).

colorless solid (28% ee, 27%): $^1\text{H-NMR}$ (CDCl_3) δ : 1.32 (9H, s), 3.16(1H, d, $J = 16.0$ Hz), 3.21(1H, d, $J = 16.0$ Hz), 5.27(1H, s), 7.2 – 7.5 (6H, m), 7.7 – 7.8 (1H, m), 8.4 – 8.5(1H, m), 8.6 – 8.7 (1H,

m).

IR (KBr) ν cm^{-1} : 3150, 2982, 1718, 1427, 1367, 1318, 1217, 1174, 1145, 1062, 1027, 1015, 817, 714, 699.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/ethanol (90/10), flow rate: 1.0 ml/min, detection: UV (220 nm), column temp.: room temperature, retention time: 12.3 min (minor: 11.6 min, substrate: 22.1 min).

***tert*-Butyl 3-hydroxy-3-phenyl-3-(4-pyridyl)propanoate (21).**

colorless solid (13% ee, 41%): ¹H-NMR (CDCl₃) δ : 1.32(9H, s), 3.12(1H, d, J = 16.1 Hz), 3.18(1H, d, J = 16.1 Hz), 5.25(1H, s), 7.2 – 7.4(7H, m), 8.5(2H, m).

IR (KBr) ν cm^{-1} : 3092, 2975, 2859, 1717, 1606, 1367, 1331, 1228, 1151, 1062, 697, 626, 585.

HPLC conditions: column, CHIRALCEL[®] OJ-H, mobile phase: *n*-hexane/ethanol (975/25), flow rate: 1.0 ml/min, detection: UV (220 nm), column temp.: 35 °C, retention time: 31.1 min (minor: 27.4 min, substrate: 22.7 min).

***tert*-Butyl 3-hydroxy-3-(2-naphthyl)butanoate (22).**

colorless solid (15% ee, 42%): ¹H-NMR (CDCl₃) δ : 1.26(9H, s), 1.46(3H, s), 2.80(1H, d, J = 15.9 Hz), 3.00(1H, d, J = 15.9 Hz), 4.61(1H, s), 7.43 – 7.94(7H, m).

IR (neat) ν cm^{-1} : 3484, 2978, 1708, 1369, 1225, 1153, 751.

HPLC conditions: column, CHIRALCEL[®] OJ-H, mobile phase: *n*-hexane/2-propanol (90/10), flow rate: 1.0 ml/min, detection: UV (280 nm), column temp.: room temperature, retention time: 7.5 min (minor: 11.3 min, substrate: 16.3 min).

***tert*-Butyl 4-(*N,N*-dibenzylamino)-3-hydroxy-3-(2-naphthyl)butanoate (23).**

colorless solid (racemic, >99%): $^1\text{H-NMR}$ (CDCl_3) δ : 1.30(9H, s), 2.68(1H, d, $J = 15.4$ Hz), 2.87(2H, s), 2.98(1H, d, $J = 15.4$ Hz), 3.44(2H, d, $J = 13.5$ Hz), 3.75(1H, s), 3.81(2H, d, $J = 13.5$ Hz), 7.2 – 7.5(14H, m), 7.7 – 7.9(3H, m).

IR (KBr) $\nu \text{ cm}^{-1}$: 3464, 2978, 1702, 1369, 1156, 747, 699.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/ethanol (99/1), flow rate: 1.0 ml/min, detection: UV (254 nm), column temp.: room temperature, retention time: 7.1 and 8.5 min (substrate: 17.1 min).

***tert*-Butyl 3-hydroxy-3-(1-trityl-1*H*-imidazol-4-yl)propanoate (24).**

colorless amorphous powder (66% ee, 84%): $^1\text{H-NMR}$ (CDCl_3) δ : 1.42(9H, s), 2.74(1H, dd, $J = 16.4$ and 7.8 Hz), 2.81(1H, dd, $J = 16.4$ and 4.6 Hz), 3.42(1H, d, $J = 4.9$ Hz), 5.06(1H, m), 6.79(1H, s), 7.1 – 7.2(7H, m), 7.29 – 7.36(8H, m), 7.37(1H, d, $J = 1.4$ Hz). IR (KBr) $\nu \text{ cm}^{-1}$: 3197, 2974, 1726, 1493, 1444, 1148, 701.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/2-propanol (90/10), flow rate: 1.0 ml/min, detection: UV (220 nm), column temp.: 30 °C, retention time: 22.5 min (minor: 16.8 min, substrate: 14.9 min).

***tert*-Butyl 3-hydroxy-3-(2-pyridyl)propanoate (25).**

colorless amorphous powder (70% ee, 94%): $^1\text{H-NMR}$ (CDCl_3) δ : 1.44(9H, s), 2.65 – 2.72(1H, m), 2.81 – 2.87(1H, m), 4.27(1H, d, $J = 4.9$ Hz), 5.13(1H, m), 7.1 – 7.3(1H, m), 7.4(1H, d, $J = 7.8$ Hz), 7.6 – 7.8(1H, m), 8.54(1H, d, $J = 3.0$ Hz). IR (KBr) $\nu \text{ cm}^{-1}$: 2979, 1727, 1594, 1368, 1152.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/ethanol (95/5), flow rate: 1.0 ml/min, detection: UV (220 nm), column temp.: 30 °C, retention time: 20.1 min (minor: 18.0 min, substrate was not detected)

Determination of Absolute Configuration.

(S)-1-(2-Naphthyl)-1-(1-trityl-1*H*-imidazol-4-yl)propane-1,3-diol.

A solution of *tert*-butyl 3-hydroxy-3-(2-naphthyl)-3-(1-trityl-1*H*-imidazol-4-yl)propanoate (**2**) (175 mg, 0.3 mmol) in THF (1 ml) was added to a suspension of LiAlH₄ (23 mg, 0.6 mmol) in THF (2 ml) at –10 °C over a period of 20 min. The reaction mixture was stirred at –10 °C for an hour and at 0 °C for another an hour. After being cooled to –20 °C, a solution of 10% aqueous NaHCO₃ (0.5 ml) was added, and the mixture was stirred for 30 min. The precipitates were removed off by decantation, and washed with AcOEt (20 ml). The combined organic layer was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by Mega Bond Elut[®] (BE-NH₂ 5 g) (AcOEt) to give an amorphous powder (80 mg, 52%).

¹H-NMR (CDCl₃) δ: 1.68 – 1.71(1H, m), 1.82 – 1.86(1H, m), 2.36 – 2.42(1H, m), 2.48 – 2.57(1H, m), 3.7(1H, br s), 6.77(1H, s), 7.1 – 7.2(6H, m), 7.3 – 7.4(9H, m), 7.4 – 7.5(4H, m), 7.7 – 7.8(4H, m), 7.95(1H, s).

IR (KBr) ν cm^{–1} : 3400, 2924, 1490, 1444, 701.

(S)-1-(1*H*-Imidazol-4-yl)-1-(2-naphthyl)propane-1,3-diol (**3**).

A mixture of 1-(2-naphthyl)-1-(1-trityl-1*H*-imidazol-4-yl)propane-1,3-diol (70 mg, 0.13 mmol), formic acid (1 ml), THF (1 ml) and water (0.5 ml) was stirred at 60 °C for an hour. After being concentrated *in vacuo*, the residue was dissolved in AcOEt (10 ml), washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by Mega Bond Elut[®] (BE-NH₂ 5 g) (acetone) to give a colorless oil (16 mg, 46%). The retention time of the product was identical with that of (S)-1-(1*H*-Imidazol-4-yl)-1-(2-naphthyl)-propane-1,3-diol (**3**) described below.

¹H-NMR (CDCl₃) δ: 2.68 – 2.71(1H, m), 2.75 – 2.82(1H, m), 3.74(1H, br s), 4.20 – 4.28(1H, m), 4.34 – 4.42(1H, m), 6.97(1H, s), 7.4 – 7.6(5H, m), 7.7 – 7.9(3H, m), 7.95(1H, s), 8.04(1H, s).

IR (KBr) ν cm^{–1} : 3058(br), 1717, 1625, 1357, 1171, 778, 758.

HPLC conditions: column, CHIRALCEL[®] OJ, mobile phase: *n*-hexane/2-propanol/DEA

(85/15/0.1), flow rate: 1.0 ml/min, detection: UV (235 nm), column temp.: 30 °C, retention time: 19.7 min (minor: 31.4 min).

(4*S*,3'*S*)-3-[3-Hydroxy-3-(2-naphthyl)-3-(1-trityl-1*H*-imidazol-4-yl)propanoyl]-4-phenyl-1,3-oxazolidin-2-one.

A solution of (*S*)-3-acetyl-4-phenyl-1,3-oxazolidin-2-one (920 mg, 4.5 mmol) dissolved in THF (8.0 ml) was added to a solution of lithium bis(trimethylsilyl)amide (1 M in THF, 4.0 ml) in THF (8.0 ml) at -78 °C, and the mixture was stirred for 30 min. A solution of 2-naphthyl(1*H*-imidazol-4-yl)methanone (**1**) (929 mg, 1.99 mmol) in THF (8.0 ml) was added to the mixture at -78 °C. After being stirred for 4 h, lithium bis(trimethylsilyl)amide (1 M in THF, 3.0 ml) was added, and the reaction mixture was stirred at the same temperature for 3.5 h. Water was added to the reaction mixture, which was extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (*n*-hexane/AcOEt = 1/1 to 1/2) to give a colorless solid (199 mg, 15%).

¹H-NMR (CDCl₃) δ: 4.03(1H, d, *J* = 16.8 Hz), 4.13(1H, m), 4.14(1H, d, *J* = 16.8 Hz), 4.61(1H, t, *J* = 8.8 Hz), 5.03(1H, s), 5.34(1H, dd, *J* = 3.6 and 8.8 Hz), 6.68(1H, d, *J* = 1.4 Hz), 6.90(2H, d, *J* = 7.6 Hz), 6.98(2H, t, *J* = 8.0 Hz), 7.06 – 7.13(7H, m), 7.25 – 7.30(9H, m), 7.37(1H, d, *J* = 1.4 Hz), 7.45(2H, m), 7.63(1H, dd, *J* = 1.7 and 8.6 Hz), 7.72-7.80(3H, m), 7.93(1H, br s).

IR (KBr) ν cm⁻¹: 3469, 1785, 1683, 1381, 1197, 755, 701.

(4*S*,3'*S*)-3-[3-Hydroxy-3-(1*H*-imidazol-4-yl)-3-(2-naphthyl)propanoyl]-4-phenyl-1,3-oxazolidin-2-one (5**).**

A mixture of (4*S*, 3'*S*)-3-[3-hydroxy-3-(2-naphthyl)-3-(1-trityl-1*H*-imidazol-4-yl)-propanoyl]-4-phenyl-1,3-oxazolidin-2-one (131 mg, 0.196 mmol), THF (2 ml), water (0.2 ml), and formic acid (2 ml) was stirred at 60 °C for an hour. The reaction mixture was concentrated *in vacuo*.

The residue was dissolved in AcOEt, washed with saturated aqueous NaHCO₃ solution and brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by Mega Bond Elut[®] (BE 10 g, acetone) to give a colorless solid (31 mg, 37%). This solid was crystallized from acetone for single crystal X-ray analysis. Crystallographic data have been deposited with the Cambridge Crystallographic Data Center (CCDC 187194). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

¹H-NMR (CDCl₃) δ : 4.13(3H, m), 4.64(1H, t, J = 8.8 Hz), 5.16(1H, br s), 5.34(1H, dd, J = 3.6 and 8.8 Hz), 6.86(3H, d-like, J = 7.6 Hz), 6.95(2H, t, J = 7.2 Hz), 7.11 (1H, t, J = 7.2 Hz), 7.47(2H, m), 7.58(1H, s), 7.64(1H, d-like, J = 8.0 Hz), 7.77-7.83(3H, m), 7.97(1H, br s).

IR (KBr) ν cm⁻¹: 3400 (br), 1781, 1699, 1684, 1380, 1197, 757, 698.

Stereoscopic Molecular View.

Thermal ellipsoids represent 50% probability level.

Summary of the Crystal Data

Empirical Formula	C ₂₅ H ₂₁ N ₃ O ₄
Formula Weight	427.46
Crystal Color, Habit	colorless, prismatic
Crystal Dimensions	0.60 X 0.30 X 0.20 mm
Crystal System	monoclinic
Space Group	P2 ₁ (#4)
Lattice Parameters	a = 8.910(2) Å
	b = 11.253(2) Å
	c = 10.988(1) Å
	β = 108.91(1)°
	V = 1042.3(3) Å ³

Z	2
Dcalc	1.362 g/cm ³
Residuals: R1, wR2	0.042, 0.113

(S)-1-(1*H*-Imidazol-4-yl)-1-(2-naphthyl)propane-1,3-diol (3).

A solution of (4*R*,3'*S*)-3-[3-hydroxy-3-(1*H*-imidazol-4-yl)propanoyl-3-(2-naphthyl)]-4-phenyl-1,3-oxazolidin-2-one (15 mg, 0.035 mmol) in THF (0.5 ml) was added to a suspension of LiAlH₄ (7 mg, 0.18 mmol) in THF (1 ml) at –10 °C over a period of 10 min. The reaction mixture was stirred at –10 °C for an hour and at 0 °C for another an hour. After being cooled to –20 °C, a solution of 10% aqueous NaHCO₃ (0.5 ml) was added, and the mixture was stirred for 30 min. The precipitates were removed off by decantation, and washed with diethyl ether (10 ml). The combined organic layer was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was subjected to HPLC analysis.

HPLC conditions: column, CHIRALCEL[®] OJ, mobile phase: *n*-hexane/2-propanol/DEA (85/15/0.1), flow rate: 1.0 ml/min, detection: UV (235 nm), column temp.: 30 °C, retention time: 19.7 min.

(S)-1-Phenyl-1-pyridin-2-ylpropane-1,3-diol.

A solution of (*S*)-*tert*-butyl 3-hydroxy-3-phenyl-3-(2-pyridyl)propanoate (600 mg, 2 mmol, 51% ee) in THF (5 ml) was added to a suspension of LiAlH₄ (100 mg, 2.6 mmol) in THF (10 ml) at –10 °C over a period of 10 min. The reaction mixture was stirred at –10 °C for an hour and at 0 °C for another an hour. After being cooled to –20 °C, a solution of 10% aqueous NaHCO₃ (1.5 ml) was added, and the mixture was stirred for 30 min. The precipitates were removed off by decantation, and washed with diethyl ether (50 ml). The combined organic layer was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by Mega Bond Elut[®] (BE-NH₂ 10 g) (AcOEt) to give colorless oil (87 mg, 19%). The enantiomer excess (51% ee) was determined by HPLC analysis. The HPLC analysis also showed that the major product was *S* isomer. The retention time of the minor product was identical with that of

(*R*)-1-phenyl-1-pyridin-2-ylpropane-1,3-diol described below.

¹H-NMR (CDCl₃) δ: 2.53(1H, ddd, *J* = 3.8, 7.0 and 14.5 Hz), 2.67(1H, ddd, *J* = 3.8, 7.0 and 14.5 Hz), 3.12(1H, br s), 3.5 – 3.81 (2H, m), 6.32(1H, s), 7.1 – 7.6(7H, m), 7.66-7.69(1H, m), 8.51-8.53(1H, m).

IR (neat) ν cm⁻¹: 3437, 3282, 1585, 1446, 1406, 1020, 698.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/2-propanol (90/10), flow rate: 1.0 ml/min, detection: UV (230 nm), column temp.: 30 °C, retention time: 15.5 min (minor: 13.8 min).

(4*S*,3'*R*)-3-(3-Hydroxy-3-phenyl-3-pyridin-2-ylpropanoyl)-4-phenyl-1,3-oxazolidin-2-one.

A solution of (*S*)-3-acetyl-4-phenyl-1,3-oxazolidin-2-one (1840 mg, 9.0 mmol) in THF (16 ml) was added to a stirred, cooled (–78 °C) solution of lithium bis(trimethylsilyl)amide (1 M in THF, 8 ml) in THF (16 ml), and the mixture was stirred for 30 min. A solution of 2-benzoylpyridine (733 mg, 4.0 mmol) in THF (8.0 ml) was added at –78 °C. After being stirred for 3 h, water was added, and the mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (*n*-hexane / AcOEt = 2/1) to give two diastereomers as colorless solids (less polar isomer: *R*_f = 0.3, yield: 470 mg, 30%, more polar isomer: *R*_f = 0.2, yield: 570 mg, 37%). The less polar diastereomer was crystallized from acetone/diisopropyl ether, then diisopropyl ether for single-crystal X-ray analysis. The configuration of the diastereomer was determined to be (4*S*,3'*R*). Crystallographic data have been deposited with the Cambridge Crystallographic Data Center (CCDC 187195). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

¹H-NMR (400 MHz, CDCl₃) δ: 3.47(1H, d, *J* = 17.3 Hz), 4.23(1H, dd, *J* = 4.0 and 8.8 Hz), 4.65(1H, d, *J* = 17.4 Hz), 4.65(1H, t, *J* = 8.8 Hz), 5.25(1H, s), 5.38(1H, dd, *J* = 4.0 and 8.8 Hz), 7.01(1H, m), 7.19 – 7.34(8H, m), 7.44 – 7.51(4H, m), 8.31(1H, m).

IR (KBr) ν cm⁻¹: 3496, 1787, 1766, 1687, 1389, 1362, 1212, 749, 696.

Stereoscopic Molecular View.

Thermal ellipsoids represent 50% probability level.

Summary of the Crystal Data

Empirical Formula	C ₂₃ H ₂₀ N ₂ O ₄
Formula Weight	388.42
Crystal Color, Habit	colorless, prismatic
Crystal Dimensions	0.70 X 0.10 X 0.10 mm
Crystal System	orthorhombic
Space Group	P2 ₁ 2 ₁ 2 ₁ (#19)
Lattice Parameters	a = 9.826(4) Å b = 22.629(6) Å c = 8.752(4) Å V = 1946(1) Å ³
Z	4
D _{calc}	1.326 g/cm ³
Residuals: R1, wR2	0.042, 0.116

(R)-1-Phenyl-1-pyridin-2-ylpropane-1,3-diol.

A solution of (4*S*,3'*R*)-3-(3-hydroxy-3-phenyl-3-pyridin-2-ylpropanoyl)-4-phenyl-1,3-oxazolidin-2-one (199 mg, 0.5 mmol) in THF (2.5 ml) was added to a stirred, and cooled (−20 ~ −10 °C) suspension of LiAlH₄ (75 mg, 1.9 mmol) in THF (5 ml) at −10 °C over a period of 10 min. The reaction mixture was stirred at −10 °C for an hour and at 0 °C for another an hour. After being cooled to −20 °C, a solution of 10% aqueous NaHCO₃ (0.5 ml) was added, and the mixture was

stirred for 30 min. The precipitates were removed off by decantation, and washed with diethyl ether (20 ml). The combined organic layer was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by Mega Bond Elut[®] (BE-NH₂ 5 g) (acetone) to give a colorless solid (87 mg, 76%). The product was subjected to HPLC analysis. The retention time of this enantiomer was identical with that of the antipode of **18**, so that the absolute configuration of **18** was determined to be *S*.

HPLC conditions: column, CHIRALPAK[®] AD, mobile phase: *n*-hexane/2-propanol (90/10), flow rate: 1.0 ml/min, detection: UV (230 nm), column temp.: 30 °C, retention time: 13.8 min .