Supporting Information

Highly Enantioselective Synthesis of (2*S*)- α -(Hydroxymethyl)-glutamic Acid by the Catalytic Michael Addition of 2-Naphthalen-1-yl-2-oxazoline-4-carboxylic acid *tert*-butyl ester

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General Methods.

The ^1H -NMR and ^{13}C -NMR were recorded at 300 MHz and 100 MHz, respectively. The chemical shifts were reported in ppm relative to CHCl_3 (δ 7.26) for ^1H -NMR and relative to the central CDCl_3 (δ 77.23) resonance for ^{13}C -NMR. Optical rotations were measured on a digital polarimeter. Melting points were not corrected. Flash column chromatography was carried out using silica gel (70~230 mesh). The enantiomeric excess (ee) of the products was determined by HPLC using 4.6 mm $\times$ 250 mm Daicel Chiralpak OD-H columns. All solvents and commercially available chemicals were used without additional purification.

Representative procedure for preparation of starting material. 2-Naphthalen-1-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester (3b).**Preparation of acyl serine intermediate. 3-Hydroxy-2-[(naphthalene-1-carbonyl)-amino]-propionic acid *tert*-butyl ester.**

To a solution of *L*-serine-*t*-butyl ester hydrochloride (3.10 g, 15.7 mmol) in methylene chloride (50 mL) at 0°C was added triethylamine (4.39 mL, 31.5 mmol) followed by 1-Naphthoyl chloride (2.37 mL, 15.7 mmol). The solution was warmed to ambient temperature and stirred for 12 hours. The reaction mixture was diluted with methylene chloride (200 mL), washed with water (50 mL $\times$ 2). The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo*. Purification by silica gel chromatography (hexane:EtOAc = 3:1) afforded the acyl serine intermediate (4.58 g, 98% yield) as pale yellow oil.

Procedure for cyclization of intermediate for 2-Naphthalen-1-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester (3b**).**

The 3-Hydroxy-2-[(naphthalene-1-carbonyl)-amino]-propionic acid *tert*-butyl ester (1.58 g, 5.00 mmol) described immediately above was dissolved in methylene chloride and cooled to -78°C . DAST (0.79 mL, 6.00 mmol) was added and the solution was stirred for 2 hours. After complete the reaction, the reaction mixture was diluted with 100 mL of methylene chloride, poured into 30 mL of saturated NaHCO_3 aqueous solution and the resulting mixture was stirred at room temperature for 30 minutes. The organic layer was separated and washed with water (20 mL), dried over MgSO_4 , filtered and concentrated *in vacuo*. Purification by silica gel chromatography (hexane:EtOAc = 15:1) afforded the desired product **3b** (1.37 g, 92% yield) as pale yellow oil.

^1H NMR (300 MHz, CDCl_3) δ 9.10 (d, $J = 8.6$ Hz, 1H), 8.08 (d, $J = 7.3$ Hz, 1H), 7.97 (d, $J = 8.3$ Hz, 1H), 7.87 (d, $J = 8.3$ Hz, 1H), 7.63-7.46 (m, 3H), 4.99 (dd, $J = 7.5, 10.4$ Hz, 1H), 4.67-4.56 (m, 2H), 1.54 (s, 9H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 170.5, 166.0, 133.6, 132.2, 131.2, 129.2, 128.3, 127.4, 126.4, 126.1, 124.5, 124.0, 82.1, 70.2, 69.0, 28.0 ppm; IR (KBr): 2978, 1734, 1640, 1588, 1512, 1365, 1293, 1220, 1156, 999, 845, 808, 778 cm^{-1} ; MS (FAB^+): m/z 320.0 $[\text{M}+\text{Na}]^+$

Representative Procedure for the Enantioselective Catalytic Michael reaction of *tert*-Butyl ester **3b under Phase-Transfer Catalytic Conditions.**

To a methylene chloride solution (0.15 mL) of 2-Naphthalen-1-yl-2-oxazoline-4-carboxylic acid *tert*-butyl ester **3b** (50.0 mg, 0.168 mmol), chiral catalyst **4** (3.65 mg, 0.004 mmol), BEMP (0.06mL, 0.210 mmol), and ethyl acrylate (23 μL , 0.210 mmol)

was added at -60 °C. The reaction solution was stirred for 20 hours. After complete the reaction, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes:EtOAc = 15:1) to afford **5b** (65 mg, 93% yield) as a pale yellow oil. The enantioselectivity was determined by chiral HPLC analysis (DAICEL Chiralcel OD-H, hexane:2-propanol = 99.0:1.0, flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention times; *S* (major) 14.6 min, *R* (minor) 18.3 min, 97% ee). Absolute configuration was determined by comparison of the optical rotation of α -(hydroxymethyl)glutamic acid from the acid hydrolysis of **5b** with the reported value.

^1H NMR (300 MHz, CDCl_3) δ 9.11 (d, J = 8.4 Hz, 1H), 8.06 (dd, J = 1.3, 7.5 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.63-7.46 (m, 3H), 4.71 (d, J = 9.0 Hz, 1H), 4.26 (d, J = 9.0 Hz, 1H), 4.14-4.07 (m, 2H), 2.67-2.55 (m, 1H), 2.50-2.40 (m, 2H), 2.29-2.17 (m, 1H), 1.53 (s, 9H), 1.22 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 172.9, 171.6, 164.6, 133.6, 132.2, 131.2, 129.1, 128.3, 127.3, 126.5, 126.1, 124.5, 124.0, 82.2, 78.6, 73.4, 60.4, 32.9, 29.3, 27.9, 14.1 ppm; IR (KBr): 2978, 1733, 1643, 1512, 1369, 1255, 1159, 1098, 1005, 846, 778 cm^{-1} ; MS (FAB^+): m/z 398.0 $[\text{M}+\text{H}]^+$

Representative Procedure for the Hydrolysis of **5b**.

4-(2-Ethoxycarbonyl-ethyl)-2-naphthalen-1-yl-4,5-dihydro-oxazole-4-carboxylic acid tert-butyl ester **5b** (200 mg, 0.50 mmol) was added to 6N HCl (2.0 mL) and the reaction mixture was refluxed for 24 hours. The reaction mixture was diluted with water (20 mL) and extracted with EtOAc (5 mL x 2). The extracted organic layer was concentrated to give pure 1-naphthoic acid (85 mg, 99% yield). The aqueous layer was concentrated and

purified by reverse-phased column chromatography to give α -(hydroxymethyl)glutamic acid hydrochloride (101 mg, 95% yield) as a white solid, $[\alpha]_D^{20} +2.3$ (c 0.5, H₂O) [lit. +1.8 (c 0.7, H₂O)].

Characterization of Substrate.

2-Naphthalen-2-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (3c)

¹H NMR (300 MHz, CDCl₃) δ 8.50 (s, 1H), 8.07 (dd, J = 1.7, 8.6 Hz, 1H), 7.93-7.85 (m, 3H), 7.58-7.49 (m, 2H), 4.89 (dd, J = 8.1, 10.2 Hz, 1H), 4.68-4.59 (m, 2H), 1.53 (s, 9H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 166.2, 134.9, 132.6, 129.3, 129.0, 128.1, 127.8, 127.7, 126.5, 125.0, 124.5, 82.2, 69.9, 69.6, 28.0 ppm; IR (KBr): 2978, 1733, 1645, 1474, 1366, 1299, 1224, 1156, 1076, 974, 910, 826, 756 cm⁻¹; MS (FAB⁺): m/z 320.0 [M+Na]⁺

2-Biphenyl-2-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (3d)

¹H NMR (300 MHz, CDCl₃) δ 7.82-7.79 (m, 1H), 7.54-7.48 (m, 1H), 7.41-7.30 (m, 7H), 4.70 (dd, J = 8.0, 10.4 Hz, 1H), 4.31-4.20 (m, 2H), 1.50 (s, 9H) ¹³C NMR (100 MHz, CDCl₃) δ 170.1, 167.9, 141.8, 140.9, 130.9, 130.4, 130.3, 128.3, 128.1, 127.2, 127.1, 126.8, 81.9, 70.1, 69.4, 28.0 ppm; IR (KBr): 2978, 1733, 1647, 1475, 1362, 1299, 1222, 1157, 1041, 962, 845, 746, 699 cm⁻¹; MS (FAB⁺): m/z 346.0 [M+Na]⁺

2-Anthracen-1-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (3e)

¹H NMR (300 MHz, CDCl₃) δ 9.64 (s, 1H), 8.44 (s, 1H), 8.22 (d, J = 7.0 Hz, 1H), 8.14 (d, J = 8.8 Hz, 1H), 8.08-8.05 (m, 1H), 8.00-7.97 (m, 1H), 7.51-7.43 (m, 3H), 5.08 (dd, J = 7.3, 10.3 Hz, 1H), 4.79-4.72 (m, 2H), 1.57(s, 9H) ppm; ¹³C NMR (100 MHz,

CDCl₃) δ 170.5, 165.8, 132.8, 132.4, 131.6, 131.4, 129.5, 129.1, 128.5, 127.7, 126.9, 125.9, 125.8, 125.6, 123.9, 123.7, 82.0, 70.3, 68.7, 28.0 ppm; IR (KBr): 2976, 1733, 1644, 1542, 1365, 1221, 1156, 1105, 992, 883, 734 cm⁻¹; MS (FAB⁺): m/z 370.1 [M+Na]⁺

2-Anthracen-9-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (3f)

¹H NMR (300 MHz, CDCl₃) δ 8.53 (s, 1H), 8.22 (d, *J* = 8.5 Hz, 2H), 8.00 (d, *J* = 7.8 Hz, 2H), 7.55-7.44 (m, 4H), 5.12 (dd, *J* = 7.1, 10.5 Hz, 1H), 4.87-4.64 (m, 2H), 1.59 (s, 9H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 166.0, 130.8, 130.1, 129.7, 128.4, 126.7, 125.3, 125.2, 121.7, 82.3, 70.3, 70.1, 28.0 ppm; IR (KBr) : 2978, 1731, 1652, 1453, 1367, 1198, 1155, 991, 894, 846, 740 cm⁻¹; MS (FAB⁺) : m/z 370.0 [M+Na]⁺

Characterization of Michael adduct.

4-(2-Ethoxycarbonyl-ethyl)-2-phenyl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (5a)

¹H NMR (300 MHz, CDCl₃) δ 7.96-7.93 (m, 2H), 7.49-7.43 (m, 1H), 7.40-7.34 (m, 2H), 4.63 (d, *J* = 9.0 Hz, 1H), 4.20 (d, *J* = 9.0 Hz, 1H), 4.13-4.03 (m, 2H), 2.53-2.41 (m, 1H), 2.38-2.27 (m, 2H), 2.17-2.02 (m, 1H), 1.46 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 172.8, 171.3, 164.6, 131.6, 128.5, 128.1, 127.0, 82.1, 74.0, 60.4, 32.9, 29.0, 27.8, 14.0 ppm; IR (KBr): 2979, 1733, 1646, 1452, 1368, 1263, 1159, 1101, 977, 846, 697 cm⁻¹; MS (FAB⁺): m/z 370.0 [M+Na]⁺

The enantioselectivity was determined by chiral HPLC analysis (DAICEL Chiralcel OD-H, hexane:2-propanol = 95.0:5.0, flow rate = 1.0 ml/min, 23 °C, λ = 254 nm,

retention times; *S* (major) 5.7 min, *R* (minor) 7.0 min)

4-(2-Ethoxycarbonyl-ethyl)-2-naphthalen-2-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (5c)

¹H NMR (300 MHz, CDCl₃) δ 8.47 (s, 1H), 8.04 (dd, *J* = 1.7, 8.6 Hz, 1H), 7.90-7.82 (m, 3H), 7.56-7.47 (m, 2H), 4.70 (d, *J* = 9.0 Hz, 1H), 4.28 (d, *J* = 9.0 Hz, 1H), 4.14-4.04 (m, 2H), 2.59-2.45 (m, 1H), 2.43-2.32 (m, 2H), 2.23-2.13 (m, 1H), 1.49 (s, 9H), 1.20 (t, *J* = 7.14 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 172.8, 171.4, 164.8, 134.8, 132.5, 129.2, 128.8, 127.9, 127.7, 127.6, 126.5, 124.9, 124.3, 82.2, 77.5, 74.1, 60.4, 33.0, 29.1, 27.9, 14.1 ppm; IR (KBr) : 2979, 1732, 1647, 1472, 1369, 1262, 1159, 1099, 981, 846, 758 cm⁻¹; MS (FAB⁺): *m/z* 420.1 [M+Na]⁺

The enantioselectivity was determined by chiral HPLC analysis (DAICEL Chiralcel OD-H, hexane:2-propanol = 97.0:3.0, flow rate = 1.0 ml/min, 23 °C, λ = 254 nm, retention times; *S* (major) 10.8 min, *R* (minor) 15.4 min)

2-Biphenyl-2-yl-4-(2-ethoxycarbonyl-ethyl)-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (5d)

¹H NMR (300 MHz, CDCl₃) δ 7.78-7.75 (m, 1H), 7.54-7.49 (m, 1H), 7.41-7.29 (m, 7H), 4.34 (d, *J* = 9.0 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.90 (d, *J* = 9.0 Hz, 1H), 2.43-2.22 (m, 3H), 2.13-1.99 (m, 1H), 1.49 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 172.9, 171.2, 166.9, 141.8, 140.8, 130.8, 130.4, 130.2, 128.3, 128.0, 127.3, 127.1, 126.9, 82.1, 74.8, 60.5, 32.4, 29.0, 27.9, 14.2 ppm; IR (KBr): 2979, 1732, 1649, 1476, 1367, 1259, 1160, 1097, 1038, 847, 746, 699 cm⁻¹; MS (FAB⁺): *m/z* 446.0 [M+Na]⁺

The enantioselectivity was determined by chiral HPLC analysis (DAICEL Chiralcel OD-H, hexane:2-propanol = 97.0:3.0, flow rate = 1.0 ml/min, 23 °C, λ = 254 nm, retention times; *S* (major) 8.6 min, *R* (minor) 13.5 min)

2-Anthracen-1-yl-4-(2-ethoxycarbonyl-ethyl)-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (5e)

^1H NMR (300 MHz, CDCl_3) δ 9.74 (s, 1H), 8.46 (s, 1H), 8.14-8.11 (m, 2H), 8.08-7.96 (m, 2H), 7.53-7.43 (m, 3H), 4.79 (d, J = 8.8 Hz, 1H), 4.33 (d, J = 8.8 Hz, 1H), 4.18-4.05 (m, 2H), 2.72-2.58 (m, 1H), 2.55-2.32 (m, 2H), 2.33-2.23 (m, 1H), 1.54 (s, 9H), 1.27-1.14 (m, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 173.0, 171.4, 165.2, 133.2, 132.5, 131.6, 131.4, 123.0, 129.2, 128.5, 127.8, 127.0, 126.0, 125.9, 125.8, 123.8, 82.5, 77.9, 73.7, 60.6, 32.8, 29.4, 28.0, 14.1 ppm; IR (KBr): 2978, 1732, 1644, 1608, 1453, 1369, 1264, 1159, 1099, 1002, 883, 845, 734 cm^{-1} ; MS (FAB^+) : m/z 470.0 $[\text{M}+\text{Na}]^+$

The enantioselectivity was determined by chiral HPLC analysis (DAICEL Chiralcel AD-H, hexane:2-propanol = 95.0:5.0, flow rate = 1.0 ml/min, 23 °C, λ = 254 nm, retention times; *R* (minor) 7.9 min, *S* (major) 8.9 min)

2-Anthracen-9-yl-4-(2-ethoxycarbonyl-ethyl)-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester. (5f)

^1H NMR (300 MHz, CDCl_3) δ 8.53 (s, 1H), 8.21 (d, J = 8.8 Hz, 2H), 8.01-7.98 (m, 2H), 7.58-7.44 (m, 4H), 4.91 (d, J = 9.1 Hz, 1H), 4.45 (d, J = 9.1 Hz, 1H), 4.20-4.06 (m, 2H), 2.76-2.67 (m, 1H), 2.61-2.50 (m, 2H), 2.44-2.36 (m, 1H), 1.61 (s, 9H), 1.23 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 173.0, 171.5, 165.0, 130.9, 130.2, 129.9, 128.5, 126.9, 125.4, 125.2, 121.6, 82.7, 78.3, 75.1, 60.6, 33.1, 29.6, 28.0, 14.2 ppm; IR

(KBr): 2979, 1731, 1653, 1449, 1370, 1261, 1156, 1099. 996, 894, 846, 738 cm^{-1} ; MS

(FAB⁺): m/z 470.1 [M+Na]⁺

The enantioselectivity was determined by chiral HPLC analysis (DAICEL Chiralcel OD-H, hexane:2-propanol = 95.0:5.0, flow rate = 1.0 ml/min, 23 °C, λ = 254 nm, retention times; *S* (major) 12.7 min, *R* (minor) 21.0 min)

2-Anthracen-1-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester

$C_{22}H_{21}NO_3$
Mol. Wt.: 347.41
300MHz, $CDCl_3$

2-Anthracen-1-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester

$C_{22}H_{21}NO_3$
Mol. Wt.: 347.41
400MHz, $CDCl_3$

2-Anthracen-9-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester

$C_{22}H_{21}NO_3$
Mol. Wt.: 347.41
300MHz, $CDCl_3$

2-Anthracen-9-yl-4,5-dihydro-oxazole-4-carboxylic acid *tert*-butyl ester

$C_{22}H_{21}NO_3$
Mol. Wt.: 347.41
400MHz, $CDCl_3$

2-Anthracen-1-yl-4-(2-ethoxycarbonyl-ethyl)-
4,5-dihydro-oxazole-4-carboxylic acid
tert-butyl ester

$C_{27}H_{29}NO_5$
Mol. Wt.: 447.52
300MHz, $CDCl_3$

2-Anthracen-1-yl-4-(2-ethoxycarbonyl-ethyl)-
4,5-dihydro-oxazole-4-carboxylic acid
tert-butyl ester

$C_{27}H_{29}NO_5$
Mol. Wt.: 447.52
500MHz, $CDCl_3$