Supporting Information for: An Asymmetric, Bifunctional Catalytic Approach to Non-Natural α -Amino Acid Derivatives

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General. Unless otherwise stated, all reactions were carried out under anhydrous, air-free conditions. All solvents were dried and distilled by standard procedures. The ^1H (400 MHz) and ^{13}C (101 MHz) chemical shifts are given in parts per million (δ) with respect to internal TMS standards and residual chloroform or DMSO. Optical rotations were recorded at room temperature. Enantiomeric ratios were obtained by HPLC using the Chiracel OD and Regis Technologies (*R,R*)-Whelk-01 chiral phase columns. Racemic reactions employ the combination of catalysts BQd and BQ (**3a** and **3b**, 5 mol% each), which have been shown to give complimentary enantiomers.¹ Masses were determined by positive ion electrospray using NaCl solution. Benzoylquinidine **3a** was formed from quinidine and benzoyl chloride according to the method of Pracejus.² All quinone imide used was prepared by following analogous procedures by Wolfer et al.¹

General procedure for the synthesis of reported products (aliphatic) (4a-d):

Benzoylquinidine (**3a**) (0.012 mmol) and scandium (III) triflate (0.012 mmol) were placed into a 10 mL round bottom flask equipped with a magnetic stir bar and 2 mL of THF was added. The reaction mixture was cooled to -78°C and Hünig's base (0.12 mmol) was added followed by the quinone imide (0.12 mmol) as a solution in 1 mL of THF. The acid chloride (0.12 mmol) as a solution in 1 mL of THF was added dropwise over 0.25 h. The reaction was kept at -78°C during the addition. The reaction was monitored by TLC and, when finished, quenched with 3 mL of methanol and allowed to warm to room temperature overnight. The reaction mixture was concentrated, dried *in vacuo*, adsorbed onto silica gel, and purified by flash chromatography using EtOAc/hexanes.

General procedure for the synthesis of reported products (aryl) (4e-h).

Benzoylquinidine (**3a**) (0.012 mmol) and scandium (III) triflate (0.012 mmol) were placed into a 10 mL round bottom flask equipped with a magnetic stir bar and 2 mL of THF was added. The reaction was cooled to -78°C and Hünig's base (0.12 mmol) was added followed by the quinone imide (0.12 mmol) as a solution in 1 mL of THF. The acid chloride (0.12 mmol) as a solution in 2 mL of THF was added to the reaction via syringe pump (6h, this slow-addition method was necessary to avoid dimerization of the intermediate aryl ketenes). The reaction was kept at -78°C during the addition. The reaction was monitored by TLC and, when finished, quenched with 3 mL of methanol and allowed to warm to room temperature overnight. The reaction mixture was concentrated, dried *in vacuo*, adsorbed onto silica gel, and purified by flash chromatography using EtOAc/hexanes.

(R)-methyl 2-(N-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)propanoate (4a). Pale yellow crystalline solid: % yield = 91; % ee = >99; mp = 55-57 °C; Lit. value mp = 56 °C.¹

(S)-methyl 2-(N-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)propanoate (4b). Pale yellow crystalline solid: % yield = 92; % ee = >99; mp = 56-57 °C; Lit. value = 56 °C.²

(R)-methyl 2-(N-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)butanoate (4c). Pale yellow crystalline solid: % yield = 86; % ee = >99; mp = 74-75 °C; Lit. value mp = 74 °C.²

(R)-methyl 2-(N-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)-3-methylbutanoate (4d). White crystalline solid: % yield = 84; % ee = >99; mp = 68-69 °C; $[\alpha]_D = -46.9^\circ$ (c = 0.84, CHCl₃); ¹H NMR (CDCl₃) (@ 95 °C) δ 10.45 (s, 1H), 8.06 (m, 2H), 7.50 (m, 3H), 6.87 (s, 1H), 4.79 (m, 1H), 3.66 (s, 3H), 2.15 (m, 1H), 1.10 (s, 3H), 0.85 (s, 3H) ppm; ¹H NMR (CDCl₃) (@ 25 °C) δ 10.26 (s, 0.7H) 9.82 (s, 0.3H), 8.01 (m, 2H), 7.35 (m, 2H), 7.20 (s, 0.4H), 7.09 (s, 0.3H), 6.94 (m, 1.6H), 4.80 (m, 0.7H), 3.91 (s, 0.5H), 3.88 (s, 2.5H), 3.48 (m, 0.3H), 2.93 (m, 0.2H), 1.86 (m, 0.8H), 1.14 (m, 1.9H), 1.05 (m, 2.6H), 0.67 (m, 2.5H) ppm; ¹³C NMR (CDCl₃) δ 177.2, 170.6, 154.7, 152.9, 141.1, 134.9, 132.9, 130.2, 128.2, 127.6, 125.9, 124.2, 122.5, 120.4, 119.8, 118.2, 66.0, 54.1, 53.6, 28.1, 27.6, 22.4, 21.0, 18.6 ppm; IR (CH₂Cl₂) 3150, 1710, 1664 cm⁻¹; HRMS (ESI+) Calcd for C₁₉H₁₈Cl₂N₂O₆Na⁺: 463.0434, found: 463.0432; HPLC (Whelk-01, 10% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 14.222, (S) = 14.222.

(R)-methyl 2-(N-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)-2-phenylacetate (4e). Pale yellow crystalline solid: % yield = 92; % ee = >99; mp = 91 °C; Lit. value = 91 °C.²

(*R*)-methyl 2-(*N*-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)-3-phenylpropanoate (4f). Yellow crystalline solid: % yield = 81; % ee = >99; mp = 82 °C; Lit. value = 82 °C.²

(*R*)-methyl 2-(*N*-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)-2-(4-methoxyphenyl)acetate (4g). White crystalline solid: % yield = 87; % ee = >99; mp = 90 °C; $[\alpha]_D = -10.9^\circ$ ($c = 1.14$, CHCl_3); ^1H NMR (CDCl_3) δ 9.72 (s, 1H), 8.07 (m, 2H), 7.47 (m, 2H), 6.98 (m, 2H), 6.84 (s, 1H), 6.78 (m, 2H), 6.35 (s, 1H), 6.23 (s, 1H), 3.91 (s, 3H), 3.76 (s, 3H) ppm; ^{13}C NMR (CDCl_3) δ 175.7, 169.9, 160.7, 154.1, 148.5, 140.6, 134.2, 132.6, 130.9, 128.2, 125.1, 123.3, 122.7, 122.4, 119.6, 114.7, 64.3, 55.4, 54.2 ppm; IR (CH_2Cl_2) 3207, 1715, 1662 cm^{-1} ; HRMS (ESI+) Calcd for $\text{C}_{23}\text{H}_{18}\text{Cl}_2\text{N}_2\text{O}_7\text{Na}^+$: 527.0383, found: 527.0379; HPLC (Whelk-01, 10% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 42.77, (S) = 27.01.

(R)-methyl 2-(N-(4,5-dichloro-2-hydroxyphenyl)-4-nitrobenzamido)-3-(1,3-dioxoisindolin-2-yl)propanoate (4h). White crystalline solid: % yield = 90; % ee = >99; mp = 88°C; $[\alpha]_D^{25} = +102.3^\circ$ (c = 0.9467, CHCl₃); ¹H NMR (CDCl₃) δ 9.37 (s, 0.85H), 9.10 (s, 0.15H), 8.01 (m, 2H), 7.85 (m, 2H), 7.42 (m, 2H), 7.38 (m, 2H), 6.85 (s, 1H), 6.29 (s, 1H), 4.93 (m, 1H), 4.24 (m, 2H), 3.93, (m, 2.6H), 3.73 (s, 0.4H) ppm; ¹³C NMR (CDCl₃) δ 172.5, 169.4, 168.2, 152.5, 148.5, 139.8, 134.8, 134.4, 131.4, 129.2, 128.7, 128.0, 123.9, 123.4, 122.9, 120.2, 64.4, 63.5, 54.5 ppm; IR (CH₂Cl₂) 3193, 1774, 1719, 1672 cm⁻¹; HRMS (ESI+) Calcd for C₂₅H₁₇Cl₂N₃O₈Na⁺: 580.0285, found: 580.0282; HPLC (Chiracel OD, 20% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 17.00, (S) = 47.04.

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11/5/07

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