

## Organocatalytic Asymmetric 5-Hydroxyisoxazolidinone Synthesis: A Highly Enantioselective Route to $\beta$ -Amino acids

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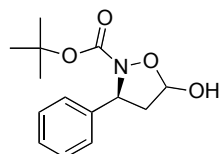
### Supporting Information

**General.** Chemicals and solvents were either purchased *puriss p.A.* from commercial suppliers or purified by standard techniques. Catalyst **9** was synthesized according to literature procedures.<sup>1</sup> For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid (25 g), Ce(SO<sub>4</sub>)<sub>2</sub>·H<sub>2</sub>O (10 g), conc. H<sub>2</sub>SO<sub>4</sub> (60 mL), and H<sub>2</sub>O (940 mL) followed by heating or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H<sub>2</sub>SO<sub>4</sub> (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating. Flash chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm), <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on Varian AS 400. Chemical shifts are given in  $\delta$  relative to tetramethylsilane (TMS), the coupling constants *J* are given in Hz. The spectra were recorded in CDCl<sub>3</sub> as solvent at room temperature, TMS served as internal standard ( $\delta = 0$  ppm) for <sup>1</sup>H NMR, and CDCl<sub>3</sub> was used as internal standard ( $\delta = 77.0$  ppm) for <sup>13</sup>C NMR. HPLC was carried out using a Waters 2690 Millennium with photodiode array detector. Optical rotations were recorded on a Perkin Elmer 241 Polarimeter ( $\lambda = 589$  nm, 1 dm cell). High-resolution mass spectra were recorded on a Bruker MicrOTOF spectrometer.

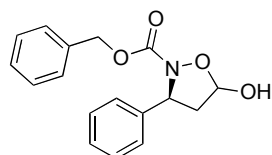
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1. a) M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2005**, *44*, 794. b) M. Marigo, D. Fielenbach, A. Braunton, A. Kjaersgaard, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2005**, *44*, 3703. c) J. Franzén, M. Marigo, D. Fielenbach, T. C. Wabnitz, A. Kjaersgaard, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 18296. d) Y. Hayashi, H. Gotoh, T. Hayashi, M. Shoji, *Angew. Chem. Int. Ed.* **2005**, *44*, 4212. e) M. Marigo, J. Franzén, T. B. Poulsen, W. Zhuang, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 6964. g) H. Sundén, I. Ibrahim, A. Córdova, *Tetrahedron Lett.* **2006**, *47*, 99. h) I. Ibrahim, A. Córdova, *Chem. Commun.* **2006**, 1760.

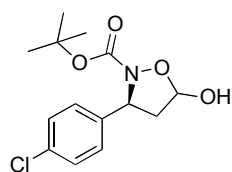
**Typical experimental procedure:** To a stirred solution of catalyst **9** (20 mol %) in chloroform (0.5 mL) at 4 °C was added  $\alpha,\beta$ -unsaturated aldehyde **2** (1.0 equiv. 0.25 mmol) and hydroxycarbamate **1** (1.2 equiv. 0.3 mmol). The reaction was vigorously stirred for 3 hours or 16 hours. Next, the reaction mixture was directly loaded upon a silica-gel column and immediate chromatography (pentane:EtOAc-mixtures or toluene:EtOAc-mixtures) furnished the pure 5-hydroxyisoxazolidines **3**.



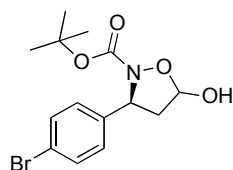
**3a:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.35-7.28 (m, 5H), 5.89 (d,  $J$  = 4.9Hz, 1H), 5.29 (t,  $J$  = 8.4Hz, 1H), 2.76 (dd,  $J$  = 8.3Hz,  $J'$  = 12.5Hz, 1H), 2.31-2.25 (m, 1H), 1.43 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 160.0, 142.3, 128.8, 127.5, 126.4, 98.8, 82.8, 61.7, 45.5, 28.3;  $[\alpha]_{\text{D}}^{25}$  = - 8.0 ( $c$  = 1.0,  $\text{CHCl}_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with *iso*-hexane/*i*-PrOH (97:3) as the eluent. Flow: 0.5 mL/min; minor isomer:  $t_{\text{R}}$  = 14.9 min; major isomer:  $t_{\text{R}}$  = 13.4 min.; HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{14}\text{H}_{19}\text{NO}_4)$  requires  $m/z$  288.1206, found 288.1197.



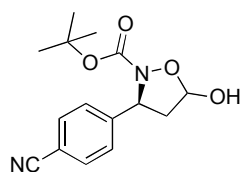
**3b:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.40-7.20 (m, 10H), 5.84 (d,  $J$ =4.4Hz, 1H), 5.39 (t,  $J$ =8.4Hz, 1H), 5.18 (s, 2H), 2.78 (dd,  $J$ =8.4Hz,  $J'$ =12.8Hz, 1H), 2.32-2.28 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 159.3, 141.4, 135.6, 128.6, 128.4, 128.1, 127.7, 127.4, 126.0, 98.7, 68.1, 61.3, 45.2.  $[\alpha]_{\text{D}}^{25}$  = - 22.2 ( $c$  = 1.0,  $\text{CHCl}_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with *iso*-hexane/*i*-PrOH (98:2) as the eluent; Flow: 1.0 mL/min; minor isomer:  $t_{\text{R}}$  = 35.89 min; major isomer:  $t_{\text{R}}$  = 30.78 min. HRMS (ESI): calcd. for  $[\text{M}+\text{H}]^+(\text{C}_{17}\text{H}_{17}\text{NO}_4)$  requires  $m/z$  300.1230, found 300.1233.



**3c:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.30$  (d,  $J=8.8\text{Hz}$ , 2H), 7.27 (d,  $J=8.8\text{Hz}$ , 2H), 5.85 (d,  $J=4.5\text{Hz}$ , 1H), 5.26 (t,  $J=8.4\text{Hz}$ , 1H), 2.76 (dd,  $J=8.3\text{Hz}$ ,  $J'=12.6\text{Hz}$ , 1H), 2.25-2.19 (m, 1H), 1.41 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 159.0$ , 141.0, 133.3, 129.0, 127.7, 98.8, 83.0, 61.2, 45.5, 28.3.  $[\alpha]_{\text{D}}^{25} = -10.7$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with *iso*-hexane/*i*-PrOH (98:2) as the eluent; Flow: 0.5 mL/min; minor isomer:  $t_{\text{R}} = 16.5$  min; major isomer:  $t_{\text{R}} = 18.3$  min. HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{14}\text{H}_{18}\text{ClNO}_4)$  requires  $m/z$  322.0817, found 322.0820.

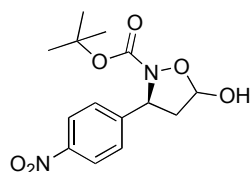


**3d:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.45$  (d,  $J=8.3\text{Hz}$ , 2H), 7.20 (d,  $J=8.3\text{Hz}$ , 2H), 5.83 (d,  $J=4.5\text{Hz}$ , 1H), 5.20 (t,  $J=8.2\text{Hz}$ , 1H), 2.74 (dd,  $J=8.3\text{Hz}$ ,  $J'=12.6\text{Hz}$ , 1H), 2.25-2.19 (m, 1H), 1.41 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 159.0$ , 141.4, 132.0, 128.1, 121.4, 99.0, 83.1, 61.2, 45.5, 28.3.  $[\alpha]_{\text{D}}^{25} = -11.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with *iso*-hexane/*i*-PrOH (98:2) as the eluent; Flow: 0.5 mL/min; minor isomer:  $t_{\text{R}} = 18.8$  min; major isomer:  $t_{\text{R}} = 20.9$  min. HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{14}\text{H}_{18}\text{Br}^{79}\text{NO}_4)$  requires  $m/z$  366.0311, found 366.0326.

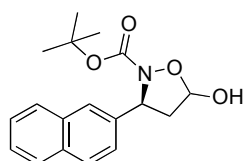


**3e:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.63$  (d,  $J=8.2\text{Hz}$ , 2H), 7.44 (d,  $J=8.2\text{Hz}$ , 2H), 5.85 (d,  $J=4.5\text{Hz}$ , 1H), 5.31 (t,  $J=8.3\text{Hz}$ , 1H), 2.79 (dd,  $J=8.3\text{Hz}$ ,  $J'=12.6\text{Hz}$ , 1H), 2.22-2.18 (m, 1H), 1.41 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 159.0$ , 147.7, 132.8, 127.1, 119.0, 111.5, 98.7, 83.4, 61.4, 45.4, 28.3.  $[\alpha]_{\text{D}}^{25} = -12.1$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD with *iso*-hexane/*i*-PrOH (96:4) as the eluent; Flow: 0.5 mL/min; minor isomer:  $t_{\text{R}} =$

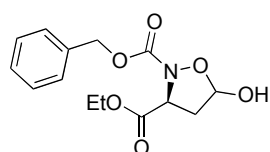
52.9 min; major isomer:  $t_R = 58.8$  min. HRMS (ESI): calcd. for  $[M+Na]^+(C_{15}H_{18}N_2O_4)$  requires  $m/z$  313.1159, found 313.1147.



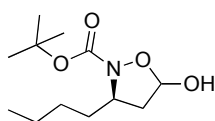
**3f:**  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta = 8.20$  (d,  $J=11.7$ Hz, 2H), 7.51 (d,  $J=11.7$ Hz, 2H), 5.87 (d,  $J=4.2$ Hz, 1H), 5.38 (t,  $J=8.1$ Hz, 1H), 2.83 (dd,  $J=8.1$ Hz,  $J'=12.3$ Hz, 1H), 2.23-2.19 (m, 1H), 1.43 (s, 9H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta = 158.5$ , 149.3, 147.3, 126.9, 124.0, 98.5, 83.2, 60.9, 45.2, 28.1.  $[\alpha]_D^{25} = -15.5$  ( $c = 1.0$ ,  $CHCl_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with *iso*-hexane/*i*-PrOH (90:10) as the eluent; Flow: 1.0 mL/min; minor isomer:  $t_R = 13.16$  min; major isomer:  $t_R = 10.75$  min. HRMS (ESI): calcd. for  $[M+Na]^+(C_{14}H_{18}N_2O_6)$  requires  $m/z$  333.1057, found 333.1041.



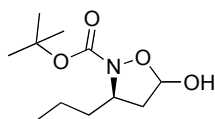
**3g:**  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta = 7.84$ -7.78 (m, 4H), 7.48-7.42 (m, 3H), 5.90 (d,  $J=4.2$ Hz, 1H), 5.46 (t,  $J=8.4$ Hz, 1H), 2.84 (dd,  $J=8.4$ Hz,  $J'=12.6$ Hz, 1H), 2.38-2.34 (m, 1H), 1.43 (s, 9H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta = 158.8$ , 139.3, 133.3, 132.8, 128.6, 127.8, 127.6, 126.2, 125.8, 124.8, 124.1, 98.6, 82.5, 61.5, 45.4, 28.1.  $[\alpha]_D^{25} = -6.6$  ( $c = 1.0$ ,  $CHCl_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with *iso*-hexane/*i*-PrOH (95:5) as the eluent; Flow: 1.0 mL/min; minor isomer:  $t_R = 6.77$  min; major isomer:  $t_R = 8.24$  min. HRMS (ESI): calcd. for  $[M+H]^+(C_{18}H_{22}NO_4)$  requires  $m/z$  316.1543, found 316.1531.



**3h:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.39\text{-}7.31$  (m, 5H), 5.73 (d,  $J=4.4\text{Hz}$ , 1H), 5.23 (d,  $J=12.4\text{Hz}$ , 1H), 5.17 (d,  $J=12.4\text{Hz}$ , 1H), 4.90 (t,  $J=8.4\text{Hz}$ , 1H), 4.20 (q,  $J=7.2\text{Hz}$ , 2H), 2.59 (dd,  $J=8.4\text{Hz}$ ,  $J'=12.8\text{Hz}$ , 1H), 2.49-2.45 (m, 1H) 1.25 (t,  $J=7.2\text{Hz}$ , 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 170.5$ , 159.1, 135.5, 128.7, 128.7, 128.5, 128.4, 128.1, 98.4, 68.7, 62.0, 58.9, 39.7, 14.3.  $[\alpha]_{\text{D}}^{25} = -34.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with *iso*-hexane/*i*-PrOH (95:5) as the eluent; Flow: 1.0 mL/min; minor isomer:  $t_{\text{R}} = 27.2$  min; major isomer:  $t_{\text{R}} = 23.8$  min. HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_6)$  requires  $m/z$  296.1129, found 296.1138.

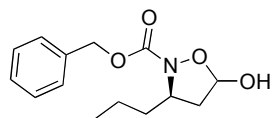


**3i:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.69 (d,  $J = 4.4$  Hz, 1H), 4.21 (t,  $J = 7.2$  Hz, 1H), 2.36 (dd,  $J = 12.4$ , 8.0 Hz, 1H), 1.83-1.88 (m, 1H), 1.61-1.62 (m, 1H), 1.49-1.51 (m, 2H), 1.47 (s, 9H), 1.30-1.37 (m, 3H), 0.89 (t,  $J = 6.0$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  159.4, 98.8, 82.2, 58.2, 41.8, 36.1, 28.6, 28.3, 22.5, 14.1;  $[\alpha]_{\text{D}}^{25} = -3.4$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ); The enantiomeric excess was determined on a Chromasil CP-Chirasil-DexCB column, temperature program: 70-170  $^{\circ}\text{C}$ , rate: 10  $^{\circ}\text{C}/\text{min}$ , hold 10 min, 170-200  $^{\circ}\text{C}$ , rate: 80  $^{\circ}\text{C}/\text{min}$ , hold 5 min. Major isomer:  $t_{\text{R}} = 13.958$  min; minor isomer:  $t_{\text{R}} = 14.211$  min; HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{12}\text{H}_{23}\text{NO}_4)$  requires  $m/z$  268.1519, found 268.1524.



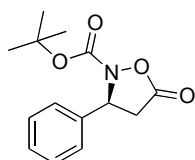
**3j:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) major rotamer  $\delta$  5.70 (d,  $J = 3.9$  Hz, 1H), 5.45 (br s, 1H), 4.23 (t,  $J = 6.6$  Hz, 1H), 2.37 (dd,  $J = 12.4$ , 8.4 Hz, 1H), 1.85-1.94 (m, 1H), 1.55-1.66 (m, 1H), 1.48-1.49 (m, 2H), 1.46 (s, 9H), 1.32-1.39 (m, 1H), 0.90-0.96 (m, 3H); minor rotamer  $\delta$  5.73 (d,  $J = 3.6$  Hz, 1H), 4.38 (t,  $J = 5.7$  Hz, 1H), 3.82 (br s, 1H), 2.63 (dd,  $J = 12.9$ , 6.6 Hz, 1H), 2.03-2.05 (m, 1H), 1.55-1.66 (m, 1H), 1.48-1.49 (m, 2H), 1.46 (s, 9H), 1.32-1.39 (m, 1H), 0.90-0.96 (m, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) mixture of two rotamer:  $\delta$  159.4, 155.4, 98.7, 82.4, 82.1, 57.9, 42.7, 41.8,

38.6, 28.4, 28.3, 19.3, 19.8, 14.0, 13.9;  $[\alpha]_D^{25} = -1.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ); The enantiomeric excess was determined on a Chromasil CP-Chirasil-DexCB column, temperature program: 70-160 °C, rate: 10 °C/min, hold 1 min, 160-200 °C, rate: 80 °C/min, hold 5 min. Major isomer:  $t_R = 11.164$  min; minor isomer:  $t_R = 11.248$  min; HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{11}\text{H}_{21}\text{NO}_4)$  requires  $m/z$  254.1363, found 254.1373.

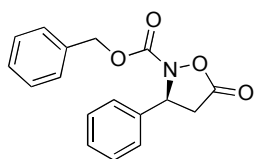


**3k:** Mixture of rotamers:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.43$ - $7.31$  (m, 5H), 5.80 (dd,  $J=3.6\text{Hz}$ ,  $J'=6.4\text{Hz}$ , 1H minor rotamer), 5.69 (dd,  $J=4.8\text{Hz}$ ,  $J'=32.4\text{Hz}$ , 1H major rotamer), 5.25-5.20 (m, 2H), 4.45-4.30 (m, 1H, major rotamer), 4.05-4.00 (m, 1H, minor rotamer), 2.7-2.6 (m, 1H, minor rotamer), 2.43-2.28 (m, 1H, major rotamer), 2.10-1.35 (m, 5H), 0.96-0.93 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 155.6$ , 135.9, 135.6, 128.6, 128.5, 128.4, 128.2, 128.1, 128.1, 98.7, 79.6, 67.9, 67.8, 58.0, 42.3, 41.5, 41.4, 38.2, 34.9, 34.6, 19.4, 19.0, 19.0, 13.9, 13.7.  $[\alpha]_D^{25} = -5.4$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD with *iso*-hexane/*i*-PrOH (98.5:1.5) as the eluent; Flow: 1.0 mL/min; minor isomer:  $t_R = 44.1$  min; major isomer:  $t_R = 37.4$  min. HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{14}\text{H}_{19}\text{NO}_4)$  requires  $m/z$  288.1206, found 288.1198.

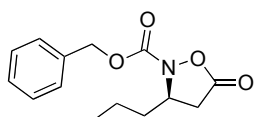
**Typical experimental procedure for the direct enantioselective catalytic Synthesis of 5-isoxazolidinones 10:** To a stirred solution of catalyst **9** (20 mol %) in chloroform (0.5 mL) at 4 °C was added  $\alpha,\beta$ -unsaturated aldehyde **2** (1.0 equiv. 0.25 mmol) and hydroxycarbamate **1** (1.2 equiv. 0.3 mmol). (In the case of the synthesis of **10a**, the reaction temperature was 25 °C). The reaction was vigorously stirred for 3 hours. Upon completion (a small aliquot was removed for ee determination) The reaction temperature was increased to room temperature, isobutene (0.1 mL), *tert*-butanol (0.4 mL),  $\text{H}_2\text{O}$  (0.2mL)  $\text{KH}_2\text{PO}_4$  (54.4 mg, 4 mmol), and  $\text{NaClO}_2$  (36 mg, 4mmol) were added sequentially. After 16h, the crude product **10** was purified by column chromatography (pentane/EtOAc mixtures) to afford the desired 5-isoxazolidinones **10**.



**10a:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.42-7.29 (m, 5H), 5.50 (d,  $J=8.1\text{Hz}$ , 1H), 3.25 (dd,  $J=8.4\text{Hz}$ ,  $J'=15.0\text{Hz}$ , 1H), 2.85 (dd,  $J=4.8\text{Hz}$ ,  $J'=15.4\text{Hz}$ , 1H), 1.43 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 175.7, 157.4, 138.9, 128.8, 128.2, 127.3, 83.2, 59.6, 37.4, 28.5.  $[\alpha]_{\text{D}}^{25}$  = - 13.0 ( $c$  = 1.0,  $\text{CHCl}_3$ ). HRMS (ESI): calcd. for  $[\text{M}+\text{Na}]^+(\text{C}_{14}\text{H}_{17}\text{NO}_4)$  requires  $m/z$  286.1050, found 286.1047.



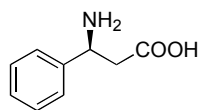
**10b:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.42-7.20 (m, 10H), 5.60 (dd,  $J=5.1\text{Hz}$ ,  $J'=10.5\text{Hz}$ , 1H), 5.20-5.10 (m, 2H), 3.26 (dd,  $J=10.5\text{Hz}$ ,  $J'=15.9\text{Hz}$ , 1H), 2.85 (dd,  $J=5.1\text{Hz}$ ,  $J'=15.9\text{Hz}$ , 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 175.3, 157.4, 138.1, 135.5, 128.6, 128.5, 128.2, 128.1, 127.9, 127.2, 68.3, 59.1, 36.6.  $[\alpha]_{\text{D}}^{25}$  = - 33.2 ( $c$  = 1.0,  $\text{CHCl}_3$ ). HRMS (ESI): calcd. for  $[\text{M}+\text{H}_2\text{O}+\text{Na}]^+(\text{C}_{17}\text{H}_{15}\text{NO}_4)$  requires  $m/z$  338.0999, found 338.1002.



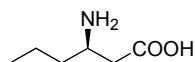
**10c:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.38-7.32 (m, 5H), 5.19 (s, 2H), 4.20-4.10 (m, 1H), 2.61 (t,  $J=5.2\text{Hz}$ , 2H), 1.72-1.35 (m, 4H), 0.91 (t,  $J=6.4\text{Hz}$ , 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 175.6, 158.9, 135.1, 128.6, 128.5, 128.4, 82.6, 68.2, 38.5, 34.5, 18.7, 13.8.  $[\alpha]_{\text{D}}^{25}$  = - 24.2 ( $c$  = 0.7,  $\text{CHCl}_3$ ). HRMS (ESI): calcd. for  $[\text{M}+\text{H}_2\text{O}+\text{Na}]^+(\text{C}_{14}\text{H}_{17}\text{NO}_4)$  requires  $m/z$  304.1155, found 304.1159.

**$\beta$ -amino acid synthesis:** To a stirred solution of Cbz-protected isoxazolidinones **10** in MeOH (0.1 M), was added 10% (in weight) of Pd/C (10%). The reaction was stirred under 90 atm of Hydrogen overnight. Then the crude reaction was filtered

through a plug of Celite®. The solvent was removed under reduced pressure to afford the pure  $\beta$ -aminoacid **11**.

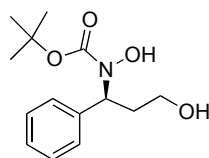


**11b**:<sup>2</sup> <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O/K<sub>2</sub>CO<sub>3</sub>):  $\delta$  = 7.40-7.30 (m, 5H), 4.27 (t,  $J$ =7.2Hz, 1H), 2.60-2.45 (m, 2H); <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O/K<sub>2</sub>CO<sub>3</sub>):  $\delta$  = 179.4, 128.9, 128.8, 128.7, 127.6, 53.1, 46.7.;  $[\alpha]_D^{25}$  = - 6.9 (c = 1, H<sub>2</sub>O).



**11c**:<sup>3</sup> <sup>1</sup>H NMR (300 MHz, MeOD)  $\delta$  3.96-3.90 (m, 1H), 2.40-2.25 (m, 2H), 1.50-1.35 (m, 4H), 0.93 (t,  $J$ =7.2Hz, 3H);  $[\alpha]_D^{25}$  = + 30.8 (c = 1, H<sub>2</sub>O).

**Experimental procedure for the one-pot synthesis of amino alcohols 12:** To a stirred solution of the catalyst **9** (16 mg, 20 mol %) in CHCl<sub>3</sub> (1 mL) was added *trans*-cinnamaldehyde **2a** (33 mg, 0.25 mmol) and **1a** (40 mg, 0.3 mmol). The reaction was vigorously stirred at room temperature for 4 hours. Then the reaction mixture was diluted with MeOH (1 mL) and cooled to 0°C followed by addition of NaBH<sub>4</sub> (19 mg, 0.5 mmol). The mixture was then stirred for 10 min., quenched with HCl (1 N), and extracted with EtOAc. The organic layer was separated, dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed. The residue was purified by silica gel (pentane: ethyl acetate = 4:1) to give the product 58 mg (yield 87%).



**12a**: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.27-7.42 (m, 5H), 6.91 (br s, 1H), 5.21 (dd,  $J$  = 10.8, 2.1 Hz, 1H), 3.76-3.81 (m, 2H), 2.36-2.47 (m, 1H), 2.02-2.11 (m, 1H), 1.43 (s, 9H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  157.2, 140.3, 128.5, 127.6, 127.4, 82.0, 60.3, 60.1, 34.2, 28.4;  $[\alpha]_D^{25}$  = - 52.0 (c = 0.5, CHCl<sub>3</sub>). HRMS (ESI): calcd. for  $[M+Na]^+$ (C<sub>14</sub>H<sub>21</sub>NO<sub>4</sub>) requires  $m/z$  290.1363, found 290.1355.



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