Supporting Information

Catalytic Enantioselective Conjugate Addition of Cyanide to $\square,\square$ -Unsaturated *N*-Acylpyrroles

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General: Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^1H NMR, 126.65 MHz for ^{13}C NMR. Chemical shifts in CDCl_3 were reported in the scale relative to CHCl_3 (7.26 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to CDCl_3 (77.0 ppm) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. EI mass spectra were measured on JEOL JMS-BU20 GCmate. Column chromatographies were performed with silica gel Merck 60 (230-400 mesh ASTM). The enantiomeric excesses (ee's) were determined by HPLC. HPLC analysis was performed on JASCO HPLC systems containing of following: pump, PU-980; detector, UV-970, measured at 254 nm or 210 nm; column, Daicel Chiralpak AD-H, AS-H, or Daicel Chiralcel OD-H, OJ-H; mobile phase, 2-propanol/hexane; flow rate, 1.0 mL/min. In general, reactions were carried out in dry solvents under an argon atmosphere, unless noted otherwise. Dry solvents of tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were purchased from Kanto Chemical. Co., Inc. $\text{Gd}(\text{tPr})_3$ was purchased from Kojundo Chemical Laboratory Co., Ltd. (Fax: +81-492-84-1351, sales@kojundo.co.jp). Chiral ligand **1** and **2** were prepared by a reported method.¹ (These ligands are commercially available from Junsei Chemical. Co., Ltd.) Substrate $\square,\square$ -unsaturated *N*-acylpyrroles were prepared according to the reported procedure.² Propionitrile was distilled from calcium hydride. Other reagents were purified by usual methods.

(A) Data of Substrates

(*2E*)-3-Phenyl-1-pyrrol-1-yl-2-propen-1-one (**7a**), (*2E*)-3-(4-methoxyphenyl)-1-pyrrol-1-yl-2-propen-1-one (**7b**), and (*2E*)-5-phenyl-1-pyrrol-1-yl-2-penten-1-one (**7d**) were identified with the corresponding material reported previously².

(2E)-3-(4-*tert*-Butylphenyl)-1-pyrrol-1-yl-2-propen-1-one (7c): colorless solid; IR (KBr): 3141, 2961, 1680, 1622, 1467, 1350, 1255, 1123, 827, 777 cm^{-1} ; ^1H NMR (CDCl_3): $\square$ = 7.99 (d, J = 15.6 Hz, 1H), 7.58 (d, J = 8.1 Hz, 2H), 7.48 (t, J = 2.0 Hz, 2H), 7.46 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 15.6 Hz, 1H), 6.36

¹ Kato, N.; Tomita, D.; Maki, K.; Kanai, M.; Shibasaki, M. *J. Org. Chem.* **2004**, *69*, 6128.

² Matsunaga, S.; Kinoshita, T.; Okada, S.; Harada, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 7559. Improved synthetic method of *N*-acylpyrroles using Horner–Emmons reaction will be reported elsewhere: Qin, H.; Yamagiwa, N.; Sugita, M.; Matsunaga, S.; Shibasaki, M. *Manuscript in preparation*.

(t, $J = 2.0$ Hz, 2H), 1.35 (s, 9H); ^{13}C NMR(CDCl_3): $\delta = 163.1, 154.7, 147.5, 131.5, 128.3, 126.0, 119.2, 114.8, 113.2, 35.0, 31.1$; MS: m/z 253 [M^+]; Anal. calcd for $\text{C}_{17}\text{H}_{19}\text{NO}$: C, 80.60; H, 7.56; N, 5.53%. Found: C, 80.56; H, 7.62; N, 5.36%.

(2E)-1-Pyrrol-1-yl-2-hexen-1-one (7e): light yellow liquid; IR (neat): 3149, 2961, 1698, 1641, 1468, 1355, 1277, 1121, 1072, 940 cm^{-1} ; ^1H NMR (CDCl_3): $\delta = 7.38$ (t, $J = 2.3$ Hz, 2H), 7.27 (dt, $J = 7.2, 15.2$ Hz, 1H), 6.56 (d, $J = 15.2$ Hz, 1H), 6.32 (t, $J = 2.3$ Hz, 2H), 2.34-2.29 (m, 2H), 1.62-1.51 (m, 2H), 0.98 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR(CDCl_3): $\delta = 162.8, 152.7, 119.5, 119.2, 113.1, 34.8, 21.3, 13.7$; MS: m/z 163 [M^+]; HRMS (EI): m/z calcd for $\text{C}_{10}\text{H}_{13}\text{NO}$ [M^+]: 163.0997. Found: 163.0997.

(2E)-5-Methyl-1-pyrrol-1-yl-2-hexen-1-one (7f): colorless liquid; IR (neat): 3150, 2958, 1697, 1641, 1468, 1408, 1356, 1281, 1122, 742 cm^{-1} ; ^1H NMR (CDCl_3): $\delta = 7.41$ (t, $J = 2.1$ Hz, 2H), 7.29 (dt, $J = 7.6, 15.3$ Hz, 1H), 6.58 (d, $J = 15.3$ Hz, 1H), 6.35 (t, $J = 2.1$ Hz, 2H), 2.29-2.22 (m, 2H), 1.87 (sept, $J = 6.7$ Hz, 1H), 1.00 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR(CDCl_3): $\delta = 162.7, 151.8, 120.4, 119.2, 113.1, 42.0, 27.9, 22.4$; MS: m/z 177 [M^+]; HRMS (EI): m/z calcd for $\text{C}_{11}\text{H}_{15}\text{NO}$ [M^+]: 177.1154. Found: 177.1163.

(2E)-4,4-Dimethyl-1-pyrrol-1-yl-2-penten-1-one (7g): colorless liquid; IR (neat): 3150, 2962, 1696, 1635, 1469, 1343, 1308, 1274, 1123, 743 cm^{-1} ; ^1H NMR (CDCl_3): $\delta = 7.39$ (t, $J = 2.4$ Hz, 2H), 7.28 (d, $J = 15.4$ Hz, 1H), 6.45 (d, $J = 15.4$ Hz, 1H), 6.32 (t, $J = 2.4$ Hz, 2H), 1.16 (s, 9H); ^{13}C NMR(CDCl_3): $\delta = 163.4, 162.3, 119.2, 114.7, 113.1, 34.4, 28.6$; MS: m/z 177 [M^+]; Anal. calcd for $\text{C}_{11}\text{H}_{15}\text{NO}$: C, 74.54; H, 8.53; N, 7.90%. Found: C, 74.53; H, 8.56; N, 7.75%.

(2E)-3-Cyclohex-1-enyl-1-pyrrol-1-yl-2-propen-1-one (7h): colorless solid; IR (KBr): 3147, 2935, 1680, 1607, 1467, 1340, 1295, 1248, 1128, 822 cm^{-1} ; ^1H NMR (CDCl_3): $\delta = 7.59$ (d, $J = 15.2$ Hz, 1H), 7.40 (t, $J = 2.3$ Hz, 2H), 6.46 (d, $J = 15.2$ Hz, 1H), 6.37-6.27 (m, 3H), 2.32-2.18 (m, 4H), 1.79-1.70 (m, 2H), 1.70-1.63 (m, 2H); ^{13}C NMR(CDCl_3): $\delta = 163.6, 151.0, 141.5, 135.1, 119.2, 112.9, 112.0, 26.6, 24.3, 22.0, 21.9$; MS: m/z 201 [M^+]; Anal. calcd for $\text{C}_{13}\text{H}_{15}\text{NO}$: C, 77.58; H, 7.51; N, 6.96%. Found: C, 77.51; H, 7.56; N, 6.79%.

Synthesis of Cyclopent-1-enyl pyrrol-1-yl ketone (7i)

To a solution of pyrrole (2.0 mL, 28.8 mmol) in THF (17 mL), *n*-BuLi (1.60 M in hexane, 18.0 mL, 28.8 mmol) was added at -78°C . After 10 min, 1-cyclopentene-1-carbonyl chloride³ (3.2 g, 24.5 mmol) in THF (10 mL) was added at -78°C . After 1 h, water was added, followed by the addition of 1 M HCl and AcOEt. The organic layer was separated and washed with brine and dried over Na_2SO_4 . The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (hexane-AcOEt, 100:1) and bulb-to-bulb distillation to afford the titled compound (2.3 g) in 58% yield as colorless liquid.

IR (neat): 3149, 2956, 1692, 1615, 1466, 1401, 1354, 1320, 1072, 791 cm^{-1} ; ^1H NMR (CDCl_3): $\delta = 7.32$

³ Naito, T.; Tanada, H.; Suzuki, Y.; Saito, H.; Kiguchi, T.; Ninomiya, I. *Heterocycles* **1993**, *36*, 2345.

(t, $J = 2.1$ Hz, 2H), 6.53-6.46 (m, 1H), 6.30 (t, $J = 2.1$ Hz, 2H), 2.85-2.71 (m, 2H), 2.67-2.53 (m, 2H), 2.02 (quint, $J = 7.5$ Hz, 2H); ^{13}C NMR(CDCl_3): $\delta = 165.0, 143.2, 137.8, 120.3, 112.7, 34.1, 33.4, 22.7$; MS: m/z 161 [M^+]; Anal. calcd for $\text{C}_{10}\text{H}_{11}\text{NO}$: C, 74.51; H, 6.88; N, 8.69%. Found: C, 74.24; H, 6.82; N, 8.42%.

(B) General Procedure for Conjugate Addition of Cyanide to α,β -Unsaturated *N*-Acylpyrroles

To a solution of ligand **2** (27.6 mg, 0.060 mmol) in THF (0.3 mL), $\text{Gd}(\text{O}^i\text{Pr})_3$ (0.2 M in THF, 150 μL , 0.030 mmol) was added at 0 $^\circ\text{C}$. The mixture was stirred at 45 $^\circ\text{C}$ for 1 h, and then the solvent was evaporated at ambient temperature. After drying the resulting pre-catalyst under reduced pressure (< 5 mmHg) for 2 h, **7a** (59.2 mg, 0.30 mmol) was added as a solid in one portion. Propionitrile (500 μL) was added at r.t., then cooled to -20 $^\circ\text{C}$. After 20 min, TMSCN (40 μL , 0.30 mmol) was added, and after 10 min, HCN (4 M in propionitrile stock solution, 150 μL , 0.60 mmol) was added to start reaction. After 98 h, water was added followed by the addition of AcOEt . The organic layer was separated and the water layer was extracted with AcOEt two times and the combined organic layer was washed with brine and dried over Na_2SO_4 . The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (hexane- AcOEt , 6:1) to afford the **8a** (60.8 mg) in 90% yield as colorless solid. Enantiomerically pure **8a** ($>99\%$ ee) was obtained after recrystallization from 2-propanol (61% yield from **7a**).

(3S)-3-Cyano-3-phenyl-1-pyrrol-1-yl-propan-1-one (8a): colorless solid; IR (KBr): 3417, 3141, 3064, 2936, 2244, 1713, 1472, 1403, 1280, 1129 cm^{-1} ; ^1H NMR (CDCl_3): $\delta = 7.45\text{--}7.35$ (m, 5H), 7.26 (brs, 2H), 6.31 (t, $J = 2.3$ Hz, 2H), 4.54 (dd, $J = 6.3, 7.9$ Hz, 1H), 3.56 (dd, $J = 7.9, 17.3$ Hz, 1H), 3.35 (dd, $J = 6.3, 17.3$ Hz, 1H); ^{13}C NMR(CDCl_3): $\delta = 165.9, 134.3, 129.4, 128.7, 127.5, 119.9, 118.8, 114.0, 40.6, 32.4$; MS: m/z 224 [M^+]; Anal. calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}$: C, 74.98; H, 5.39; N, 12.49%. Found: C, 75.00; H, 5.57; N, 12.52%; $[\alpha]_D^{23} -19.9$ ($c = 0.985$, CHCl_3) (92% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane 1/9, flow 1.0 mL/min, detection at 254 nm.): t_R 24.2 min (major) and 30.8 min (minor).

3-Cyano-3-(4-methoxyphenyl)-1-pyrrol-1-yl-propan-1-one (8b): colorless solid; IR (KBr): 3421, 3142, 2934, 2836, 2245, 1718, 1510, 1287, 1033, 735 cm^{-1} ; ^1H NMR (CDCl_3): $\delta = 7.34$ (d, $J = 8.8$ Hz, 2H), 7.25 (brs, 2H), 6.91 (d, $J = 8.8$ Hz, 2H), 6.30 (t, $J = 2.3$ Hz, 2H), 4.47 (dd, $J = 6.4, 7.6$ Hz, 1H), 3.80 (s, 3H), 3.52 (dd, $J = 7.6, 17.4$ Hz, 1H), 3.32 (dd, $J = 6.4, 17.4$ Hz, 1H); ^{13}C NMR(CDCl_3): $\delta = 166.0, 159.7, 128.6, 126.2, 120.2, 118.8, 114.7, 113.9, 55.3, 40.6, 31.6$; MS: m/z 254 [M^+]; Anal. calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2$: C, 70.85; H, 5.55; N, 11.02%. Found: C, 70.76; H, 5.80; N, 10.85%; $[\alpha]_D^{25} -16.5$ ($c = 1.080$, CHCl_3) (90% ee); HPLC (Chiralpak AD-H, 2-propanol/hexane 1/50, flow 1.0 mL/min, detection at 254 nm.): t_R 66.5 min (minor) and 72.1 min (major).

3-Cyano-3-(4-*tert*-butylphenyl)-1-pyrrol-1-yl-propan-1-one (8c): colorless solid; IR (KBr): 3140, 3107,

2964, 2246, 1712, 1472, 1370, 1295, 1280, 1125 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.43 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.26 (brs, 2H), 6.31 (t, J = 2.3 Hz, 2H), 4.51 (dd, J = 6.2, 8.1 Hz, 1H), 3.55 (dd, J = 8.1, 17.5 Hz, 1H), 3.35 (dd, J = 6.2, 17.5 Hz, 1H), 1.32 (s, 9H); ^{13}C NMR(CDCl_3): δ = 166.1, 151.8, 131.2, 127.1, 126.3, 120.1, 118.8, 113.9, 40.5, 34.6, 31.9, 31.2; MS: m/z 280 [M^+]; Anal. calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}$: C, 77.11; H, 7.19; N, 9.99%. Found: C, 76.88; H, 7.30; N, 9.90%; $[\alpha]_D^{23}$ -21.9 (c = 1.422, CHCl_3) (89% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane 1/50, flow 1.0 mL/min, detection at 254 nm.): t_R 27.5 min (major) and 41.6 min (minor).

3-Cyano-5-phenyl-1-pyrrol-1-yl-pentan-1-one (8d): light yellow solid; IR (KBr): 3406, 3143, 3109, 3028, 2939, 2243, 1711, 1473, 1286, 919 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.42-7.17 (m, 7H), 6.35 (t, J = 2.3 Hz, 2H), 3.32-3.19 (m, 2H), 3.15-3.035 (m, 1H), 3.032-2.94 (m, 1H), 2.90-2.80 (m, 1H), 2.08-2.04 (m, 2H); ^{13}C NMR(CDCl_3): δ = 166.3, 139.5, 128.7, 128.3, 126.5, 120.7, 118.8, 113.9, 36.8, 33.3, 33.1, 26.3; MS: m/z 252 [M^+]; Anal. calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}$: C, 76.16; H, 6.39; N, 11.10%. Found: C, 76.11; H, 6.52; N, 11.04%; $[\alpha]_D^{24}$ +23.8 (c = 1.238, CHCl_3) (96% ee); HPLC (Chiralpak AS-H, 2-propanol/hexane 1/49, flow 1.0 mL/min, detection at 254 nm.): t_R 68.6 min (minor) and 72.8 min (major).

(3R)-3-Cyano-1-pyrrol-1-yl-hexan-1-one (8e): colorless solid; IR (KBr): 3412, 3165, 3143, 3125, 2959, 2871, 2244, 1721, 1473, 1291 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.28 (brs, 2H), 6.33 (t, J = 2.4 Hz, 2H), 3.30-3.20 (m, 2H), 3.07 (dd, J = 8.7, 19.3, 1H), 1.75-1.593 (m, 3H), 1.591-1.47 (m, 1H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C NMR(CDCl_3): δ = 166.5, 121.0, 118.8, 113.9, 36.9, 33.8, 26.6, 20.3, 13.4; MS: m/z 190 [M^+]; Anal. calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$: C, 69.45; H, 7.42; N, 14.73%. Found: C, 69.54; H, 7.48; N, 14.57%; $[\alpha]_D^{24}$ +19.1 (c = 0.858, CHCl_3) (98% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane 1/20, flow 1.0 mL/min, detection at 254 nm.): t_R 14.7 min (major) and 17.1 min (minor).

(3R)-3-Cyano-5-methyl-1-pyrrol-1-yl-hexan-1-one (8f): colorless solid; IR (KBr): 3402, 3145, 2960, 2931, 2242, 1708, 1474, 1374, 1292, 921 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.27 (brs, 2H), 6.32 (t, J = 2.3 Hz, 2H), 3.33-3.16 (m, 2H), 3.06 (dd, J = 6.1, 16.7, 1H), 1.98-1.82 (m, 1H), 1.75-1.57 (m, 1H), 1.49-1.34 (m, 1H), 1.00 (d, J = 6.4 Hz, 3H), 0.99 (d, J = 6.7 Hz, 3H); ^{13}C NMR(CDCl_3): δ = 166.5, 121.1, 118.8, 113.9, 40.8, 37.3, 26.2, 25.0, 22.9, 21.1; MS: m/z 204 [M^+]; Anal. calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}$: C, 70.56; H, 7.90; N, 13.71%. Found: C, 70.48; H, 8.03; N, 13.74%; $[\alpha]_D^{25}$ +26.2 (c = 0.940, CHCl_3) (97% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane 1/20, flow 1.0 mL/min, detection at 254 nm.): t_R 13.0 min (major) and 16.7 min (minor).

3-Cyano-4,4-dimethyl-1-pyrrol-1-yl-pentan-1-one (8g): colorless solid; IR (KBr): 3417, 3149, 2969, 2912, 2875, 2238, 1712, 1475, 1294, 1122 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.31 (brs, 2H), 6.34 (t, J = 2.3 Hz, 2H), 3.19-3.03 (m, 3H), 1.14 (s, 9H); ^{13}C NMR(CDCl_3): δ = 167.1, 120.4, 118.9, 113.9, 38.5, 33.2, 32.9, 27.2; MS: m/z 204 [M^+]; Anal. calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}$: C, 70.56; H, 7.90; N, 13.71%. Found: C, 70.44; H, 7.82; N, 13.64%; $[\alpha]_D^{25}$ -34.5 (c = 1.048, CHCl_3) (90% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane

1/9, flow 1.0 mL/min, detection at 254 nm.): t_R 7.8 min (minor) and 9.8 min (major).

3-Cyano-3-cyclohex-1-enyl-1-pyrrol-1-yl-propan-1-one (8h): colorless solid; IR (KBr): 3143, 2926, 2859, 2245, 1714, 1472, 1369, 1284, 1119, 922 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.29 (brs, 2H), 6.33 (t, J = 2.3 Hz, 2H), 5.88 (brs, 1H), 3.82 (dd, J = 5.8, 8.2 Hz, 1H), 3.28 (dd, J = 8.2, 17.0 Hz, 1H), 3.16 (dd, J = 5.8, 17.0 Hz, 1H), 2.21-1.97 (m, 4H), 1.76-1.65 (m, 2H), 1.64-1.51 (m, 2H); ^{13}C NMR(CDCl_3): δ = 166.4, 130.3, 127.6, 119.7, 118.9, 113.9, 36.7, 34.2, 26.2, 25.1, 22.4, 21.6; MS: m/z 228 [M^+]; Anal. calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}$: C, 73.66; H, 7.06; N, 12.27%. Found: C, 73.57; H, 7.17; N, 12.07%; $[\alpha]_D^{25}$ -3.9 (c = 1.235, CHCl_3) (95% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane 1/50, flow 1.0 mL/min, detection at 254 nm.): t_R 21.6 min (major) and 25.2 min (minor).

(1R,2R)-2-(Pyrrole-1-carbonyl)-cyclopentanecarbonitrile (trans-8i): light yellow oil; IR (neat): 3147, 2967, 2877, 2241, 1713, 1471, 1292, 1121, 1074, 746 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.31 (brs, 2H), 6.35 (t, J = 2.6 Hz, 2H), 3.75-3.65 (m, 1H), 3.54-3.49 (m, 1H), 2.39-2.21 (m, 2H), 2.12-2.00 (m, 1H), 1.99-1.78 (m, 3H); ^{13}C NMR(CDCl_3): δ = 170.2, 121.7, 119.2, 114.0, 48.3, 31.7, 31.5, 30.8, 25.5; MS: m/z 188 [M^+]; Anal. calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}$: C, 70.19; H, 6.43; N, 14.88%. Found: C, 70.08; H, 6.37; N, 14.78%; $[\alpha]_D^{25}$ -119.8 (c = 1.595, CHCl_3) (86% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane 1/50, flow 1.0 mL/min, detection at 254 nm.): t_R 16.9 min (major) and 20.1 min (minor).

(1R,2S)-2-(Pyrrole-1-carbonyl)-cyclopentanecarbonitrile (cis-8i): yellow solid; IR (KBr): 3141, 2957, 2876, 2240, 1713, 1470, 1279, 1125, 1076, 745 cm^{-1} ; ^1H NMR (CDCl_3): δ = 7.32 (brs, 2H), 6.33 (t, J = 2.3 Hz, 2H), 3.73-3.68 (m, 1H), 3.13-3.08 (m, 1H), 2.34-1.99 (m, 5H), 1.86-1.74 (m, 1H); ^{13}C NMR(CDCl_3): δ = 169.2, 119.6, 119.1, 113.8, 45.8, 32.5, 30.9, 29.5, 23.8; MS: m/z 188 [M^+]; Anal. calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}$: C, 70.19; H, 6.43; N, 14.88%. Found: C, 69.82; H, 6.49; N, 14.94%; $[\alpha]_D^{26}$ +21.1 (c = 1.265, CHCl_3) (83% ee); HPLC (Chiralcel OD-H, 2-propanol/hexane 1/50, flow 1.0 mL/min, detection at 254 nm.): t_R 40.1 min (minor) and 47.1 min (major).

(C) Transformation of the Products into Various Synthetically Useful Compounds

Synthesis of (4S)-4-Phenyl-2-pyrrolidinone

To a solution of **8a** (>99% ee; recrystallized from 2-propanol) (18.4 mg, 0.082 mmol) in MeOH (1 mL) and AcOEt (1 mL), AcOH (50 μL) and 10% Pd/C (11.1 mg, 0.010 mmol) was added, and the mixture was stirred under 20 atm pressure of hydrogen at room temperature. After 9 hr, catalyst was filtered off through celite, and the solvent was removed under reduced pressure. Sat. HCl / EtOH solution (1.5 mL) was added to the residue and the mixture was heated at 90 $^\circ\text{C}$. After 10 hr, solvent was removed, and toluene (2 mL) and Et_3N (500 μL) were added to the residue. The mixture was heated at 100 $^\circ\text{C}$ for 11 hr. Water and CH_2Cl_2 were added and the organic layer was separated. The water layer was extracted with CH_2Cl_2 and the combined organic layer was washed with 1 M HCl and brine,

and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (CH₂Cl₂-MeOH, 20:1) to afford (4*S*)-4-phenyl-2-pyrrolidinone (11.5 mg) in 87% yield as white solid.

IR (KBr): 3244, 2905, 2796, 1684, 1495, 1444, 1259, 1052, 746, 697 cm⁻¹; ¹H NMR (CDCl₃): δ = 7.38-7.31 (m, 2H), 7.29-7.21 (m, 3H), 6.65 (brs, 1H), 3.80-3.77 (m, 1H), 3.72-3.66 (m, 1H), 3.42 (dd, *J* = 7.4, 9.7 Hz, 1H), 2.73 (dd, *J* = 9.1, 17.0 Hz, 1H), 2.51 (dd, *J* = 8.5, 17.0, 1H); ¹³C NMR(CDCl₃): δ = 177.9, 142.1, 128.8, 127.0, 126.7, 49.5, 40.2, 38.0; MS: *m/z* 161 [M⁺]; HRMS (EI): *m/z* calcd for C₁₀H₁₁NO [M⁺]: 161.0841. Found: 161.0836; [α]_D²³ +37.7 (*c* = 0.160, MeOH). The absolute configuration was determined to be *S* based on the comparison of the optical rotation with the reported value.⁴ [lit. [α]_D²² +37.5 (*c* = 0.83, MeOH) for *S* enantiomer (optically pure).]

To determine the enantiomeric excess, the lactam was converted to its *N*-Boc derivative (90% yield).⁵ The ee of the carbamate was determined to be 98%. HPLC (Chiralpak AS-H, 2-propanol/hexane 1/20, flow 1.0 mL/min, detection at 210 nm.): *t*_R 24.7 min (major) and 28.2 min (minor).

Synthesis of (3*R*)-3-Cyano-5-methyl-hexanoic acid

To a solution of **8f** (90% ee) (44.8 mg, 0.219 mmol) in THF (440 μ L), 1 M NaOH (440 μ L, 0.440 mmol) was added at room temperature. After 1 hr, THF was removed by rotary evaporation and sat. NaHCO₃ was added to the residue. The aqueous phase was washed with CH₂Cl₂ three times, acidified to pH 1, and extracted with CH₂Cl₂ three times. The combined organic layer was dried over Na₂SO₄ and concentrated to afford (3*R*)-cyano-5-methyl-hexanoic acid (31.8 mg) in 94% yield as colorless oil.

IR (neat): 2961, 2244, 1714, 1469, 1414, 1371, 1175, 924, 619 cm⁻¹; ¹H NMR (CDCl₃): δ = 9.29 (brs, 1H), 3.12-2.96 (m, 1H), 2.76 (dd, *J* = 7.5, 17.0 Hz, 1H), 2.62 (dd, *J* = 6.1, 17.0 Hz, 1H), 1.95-1.78 (m, 1H), 1.74-1.57 (m, 1H), 1.43-1.30 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H); ¹³C NMR(CDCl₃): δ = 175.5, 120.8, 40.6, 36.8, 26.1, 25.5, 22.8, 21.2; MS: *m/z* 155 [M⁺]; HRMS (EI): *m/z* calcd for C₈H₁₄NO₂ [M+H⁺]: 156.1025. Found: 156.1026; [α]_D²¹ +15.0 (*c* = 0.590, CHCl₃). The absolute configuration of this product was determined to be *R* based on the comparison of the optical rotation with the reported value.⁶ [lit. [α]_D²⁵ -16.7 (*c* = 0.5, CHCl₃) for *S* enantiomer with 97% ee.]

Confirmation of Absolute Configuration of **8f**

To a solution of (3*R*)-cyano-5-methyl-hexanoic acid (**A**) derived from **8f** (76% ee) (21.2 mg, 0.137 mmol) in MeOH (280 μ L), *tert*-butylamine (30 μ L, 0.285 mmol) was added at 0 °C. After 30 min, the mixture was concentrated to afford *tert*-butylammonium (3*R*)-3-cyano-5-methyl-hexanoate (28.4 mg) in 91%

⁴ Zelle, R. E. *Synthesis* **1991**, 1023.

⁵ Meyers, A. I.; Snyder, L. J. *Org. Chem.* **1993**, 58, 36.

⁶ Sammis, G. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2003**, 125, 4442. The sign of the optical rotation of the α -cyanocarboxylic acid **A** was incorrect in this paper (personal communication from Prof. Jacobsen).

yield as colorless solid. The product was identical with the corresponding material reported previously.⁷ The absolute configuration of this *tert*-butylammonium salt was determined to be *R* based on the comparison of the optical rotation with the reported value.⁷ $[\alpha]^{25}_{\text{D}} +14.0$ ($c = 1.405$, MeOH) [lit. $[\alpha]^{25}_{\text{D}} -16.8$ ($c = 1.2$, MeOH) for *S* enantiomer with 97.7% ee.]

Synthesis of (1*R*,2*R*)-Cyclopentane-1,2-dicarboxylic acid

To a solution of **trans-8i** (79% ee) (21.4 mg, 0.114 mmol) in THF (230 μ L), 1 M NaOH (230 μ L, 0.230 mmol) was added at room temperature. After 1 hr, THF was removed by rotary evaporation, and sat. NaHCO₃ was added to the residue. The aqueous phase was washed with CH₂Cl₂ three times, acidified to pH 1, and extracted with CH₂Cl₂ three times. The combined organic layer was dried over Na₂SO₄, and the solvent was removed under reduced pressure. 12 M HCl was added to the residue, and the mixture was heated at 90 °C for 11 hr. Solvent was removed in *vacuo* to afford (1*R*,2*R*)-cyclopentane-1,2-dicarboxylic acid (12.8 mg) in 71% yield as white solid. The solid contained ammonium chloride as a byproduct of nitrile hydrolysis. The product was identical with the corresponding material reported previously.⁸ The absolute configuration was determined to be 1*R*,2*R* by comparison of the optical rotation with the reported value.⁸ $[\alpha]^{22}_{\text{D}} -39.6$ ($c = 0.640$, MeOH) [lit. $[\alpha]^{20}_{\text{D}} -55.25$ ($c = 0.80$, MeOH) for 1*R*,2*R* enantiomer.]

Determination of Absolute Configuration of 8e

To a solution of **8e** (98% ee) (42.9 mg, 0.226 mmol) in THF (450 μ L), 1.0 M NaOH (450 μ L, 0.450 mmol) was added at 0 °C. After 30 min, sat. NaHCO₃ was added to the mixture. The aqueous phase was washed with CH₂Cl₂ three times, acidified to pH 1, and extracted with CH₂Cl₂ three times. The combined organic layer was dried over Na₂SO₄ and concentrated to afford (3*R*)-3-cyano-hexanoic acid (22.9 mg) in 72% yield as colorless oil. The product was identical with the corresponding material reported previously.⁶ The absolute configuration of this product was determined to be *R* based on the comparison of the optical rotation with the reported value.⁶ $[\alpha]^{24}_{\text{D}} +1.2$ ($c = 1.065$, CHCl₃) [lit. $[\alpha]^{25}_{\text{D}} +1.3$ ($c = 1.1$, CHCl₃) for *R* enantiomer with 96% ee.]

Determination of Absolute Configuration of *Cis*-8i

To a solution of **cis-8i** (58% ee) (38.6 mg, 0.205 mmol) in THF (1.0 mL), LiBH₄ (16.3 mg, 0.748 mmol) was added at 0 °C and the mixture was warmed to room temperature. After 1 hr, NaBH₄ (25.0 mg, 0.661 mmol) was added at room temperature. After 15 hr, water and AcOEt were added and organic extract was

⁷ Burk, M. J.; De Koning, P. D.; Grote, T. M.; Hoekstra, M. S.; Hoge, G.; Jennings, R. A.; Kissel, W. S.; Le, T. V.; Lennon, I. C.; Mulhern, T. A.; Ramsden, J. A.; Wade, R. A. *J. Org. Chem.* **2003**, *68*, 5731.

⁸ Morimoto, Y.; Terao, Y.; Achiwa, K. *Chem. Pharm. Bull.* **1987**, *35*, 2266.

washed with 1 M HCl and brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure and the residue was treated with sat. HCl / EtOH solution (2 mL). The resulting mixture was heated at 80 °C for 18 hr. Solvent was removed under reduced pressure and the residue was purified by preparative TLC to afford (1*R*,5*S*)-3-oxabicyclo[3.3.0]octan-2-one (3.2 mg) in 12% yield as colorless oil. The product was identical with the corresponding material reported previously.⁹ The absolute configuration of this product was determined to be 1*R*,5*S* based on the comparison of the optical rotation with the reported value.¹⁰ [α]_D²⁴ -41.0 (*c* = 0.320, CHCl₃) [lit. [α]_D²⁵ +96.9 (*c* = 1.0, CHCl₃) for 1*S*,5*R* enantiomer with 100% ee.]

⁹ Sabbioni, G.; Jones, J. B. *J. Org. Chem.* **1987**, *52*, 4565.

¹⁰ Jakovac, I. J.; Goodbrand, H. B.; Lok, K. P.; Jones, J. B. *J. Am. Chem. Soc.* **1982**, *104*, 4659.