Supporting Information

© Wiley-VCH 2005

69451 Weinheim, Germany

Stereocontrolled Creation of Adjacent Quaternary and Tertiary Stereocenters via a Catalytic, Diastereoselective and Enantioselective Conjugate Addition

Hongming Li, Yi Wang, Liang Tang, Fanghui Wu, Xiaofeng Liu, Chengyun Guo, Bruce M. Foxman and Li Deng*

*Department of Chemistry
Brandeis University
Waltham, Massachusetts 02454-9110*

*To whom correspondence should be addressed

General Information. ^1H and ^{13}C NMR spectra were recorded on a Varian instrument (400 MHz and 100 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for ^1H NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ , ppm). Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer and are reported in frequency of absorption. Low resolution mass spectra for all the new compounds done by either 20 eV, CH_4/CI or NH_3/CI were recorded on a Hewlett-Packard 5989A GC/MS, and exact mass spectra on a VG 7070 high resolution mass spectrometer. Specific rotations were measured on a Jasco Digital Polarimeter. High pressure liquid chromatography (HPLC) analysis was performed on a Hewlett-Packard 1100 Series instrument equipped with a quaternary pump, using a Daicel Chiralcel OJ, OD Column (250 x 4.6 mm) or Chiralpak AD Column (250 x 4.6 mm). UV detection was monitored at 220 nm or at 215 nm.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication nos. CCDC-249709(**5Ba**), CCDC-249710(**5Dd**), CCDC-249711(**5De**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ. UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Materials: All the Michael donors **3** are commercially available and used without further purification. Nitroalkenes **4a-c** were purchased from Aldrich Inc. and used without further purifications. Nitroalkenes **4d-f** were prepared according to literature procedures.¹

Preparatio of catalysts:

1. Preparation of Q-**2b**:

To a solution of Quinine (4.0 g, 12.4 mmol) in DMF (40 mL, freshly distilled from the suspension of CaH_2 in DMF) under nitrogen atmosphere, NaH (1.36 g, 57 % suspension in mineral oil, 32.3 mmol) was added and the resulted mixture was stirred at room temperature for 2 h. Then BnCl (1.56 mL, 13.6 mmol) was added dropwise via a syringe over 10 minutes. The resulting mixture was stirred overnight. After the starting material was completely consumed, brine was added carefully (40 mL) and the resulting mixture was extracted with ethyl acetate (200 mL). The organic phase was washed with H_2O (5 x 100 mL), brine (100 mL) and dried over Na_2SO_4 . The solvent was removed in *vacuo* to afford a light yellow oil (5.1 g, 99%). This crude product (Q-Bn) was used for next reaction without further purification.

Under N_2 atmosphere, a suspension of Q-Bn (5.1 g, 12.3 mmol) and NaSEt (4.2g, 50.0 mmol) in dry DMF (75 mL, freshly distilled from the suspension of CaH_2 in DMF) was stirred at 110 °C for 9 hours until a TLC analysis showed that Q-Bn was completely consumed. The reaction mixture was cooled to room temperature, then mixed with sat. NH_4Cl (80 mL) and H_2O (60 mL). The resulting mixture was adjusted to pH = 2 by conc. HCl, washed by ethyl acetate (2x100 mL) and adjusted to pH = 8 by conc. ammonium hydroxide. The resulting mixture was extracted with ethyl acetate (2 x 150 mL). The combined organic phase was dried over Na_2SO_4 , and concentrated in *vacuo*. The residue was washed by CH_2Cl_2 (2x30 mL) and dissolved in HCl (2 N, 150 mL). The resulted

solution was washed by ethyl acetate (50 mL) and adjusted to pH = 7 by conc. ammonium hydroxide. The aqueous phase was extracted by ethyl acetate (300 mL). The combined organic phase was dried quickly over Na₂SO₄, and concentrated to afford **Q-2b** as a white powder (3.764g, 77%). $[\alpha]_D^{25} = -78.9$ (*c*, 0.98 EtOH); ¹H NMR (400 MHz, DMSO) 10.03 (br, 1H), 8.63 (d, *J* = 4.4 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 7.70-7.15 (m, 8H), 5.92-5.77 (m, 1H), 5.14-4.82 (m, 3H), 4.34 (d, *J* = 11.6 Hz, 1H), 4.27 (d, *J* = 11.6 Hz, 1H), 3.30-2.94 (m, 2H), 2.88-2.70 (m, 1H), 2.50-2.10 (m, 3H), 1.94-1.32 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 155.4, 146.6, 144.3, 143.4, 142.3, 138.1, 131.3, 128.2, 127.7, 127.55, 127.49, 121.4, 114.2, 104.7, 70.5, 59.9, 56.0, 54.9, 41.7, 39.4, 27.4, 27.3, 24.6; IR (KBr) ν 3395, 3063, 3033, 2953, 2908, 2863, 2753, 2686, 2613, 2539, 1906, 1638, 1613, 1591, 1509, 1499, 1463, 1401, 1355, 1331, 1280, 1241, 1215, 1132, 1100, 1030, 1014, 921, 853, 814, 751, 702 cm⁻¹; HRMS (ESI) *m/z* calcd for (C₂₆H₂₉N₂O₂+H⁺): 401.2229, found: 401.2228.

2. Preparation of **Q-2c**:²

To a three neck round bottom flask (250 mL) charged with quinine (5.0 g) in DMSO (60 ml, freshly distilled from the suspension of CaH₂ in DMSO) was added NaH (0.7g, 60% in mineral oil) in small portion to form an orange solution. Pyridine (2.6 mL), CuI (3.0 g) and 9-I-PHN (4.8 g) were added. The resulting mixture was heated in an oil bath (120 °C) for 70 h. The reaction mixture was cooled to room temperature, after which CH₂Cl₂ (40 ml) and H₂O (40 ml) and Et₂O (20 ml) were added. To the resulting reaction mixture, ethylenediaminetetraacetate disodium salt dihydrate (8.5g) and aqueous ammonia solution (6ml) were added. Air was bubbled through to agitate the resulting reaction mixture for 1 h. The brown organic phase was collected and the blue aqueous layer was extracted with CH₂Cl₂ (2 x 20 ml). The combined organic phase was washed with aqueous NH₄OH (5%, 3 x 20 ml,) and the brown solution was dried over Na₂SO₄ and concentrated. The residue was subjected to column

chromatography (SiO₂, CH₂Cl₂ : CH₃OH = 100:1) to furnish Q-PHN as a light yellow solid (3.3 g, 43% yield).

To a solution of Q-PHN (3.3g) in DMF (60 ml, freshly distilled from the suspension of CaH₂ in DMF)) was added NaSEt (3g). The resulting mixture was heated at 110°C for 6 hrs and cooled to room temperature. Saturated NH₄Cl solution (40 ml) and water (50 ml) was added sequentially. The resulting mixture was extracted with EtOAc (3 x 200 mL). The combined organic phase was washed with brine (3 x 100 mL), dried over Na₂SO₄, and concentrated. The residue was subjected to column chromatography (SiO₂, CH₂Cl₂ : CH₃OH = 50 :1) to afford Q-**2c** as a yellow solid (1.8 g, 56% yield). $[\alpha]_D^{25} = + 371.1$ (c, 0.64 CHCl₃); ¹H NMR (400 MHz, CDCl₃) 8.69-8.62 (m, 2H), 8.61 (br, 1H), 8.51 (d, *J* = 5.2 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 9.2 Hz, 1H), 7.77-7.71 (m, 2H), 7.41 (d, *J* = 4.4 Hz, 1H), 7.29-7.26 (m, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 6.88 (t, *J* = 8.0 Hz, 1H), 6.59 (s, 1H), 6.49 (d, 8.0 Hz, 1H), 6.29 (s, 1H), 5.79-5.70 (m, 1H), 5.30 (s, 1H), 5.00 (d, *J* = 17.2 Hz, 1H), 4.97 (d, *J* = 10.4 Hz, 1H), 3.70-3.62 (m, 1H), 3.49 (t, *J* = 9.2Hz, 1H), 3.33-3.27 (m, 1H), 2.90-2.85 (m, 1H), 2.58-2.53 (m, 1H), 2.47 (br, 1H), 2.60-2.20 (m, 1H), 2.10 (br, 1H), 1.82-1.76 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 156.9, 149.3, 146.8, 143.8, 142.2, 140.6, 131.9, 131.6, 127.4, 127.2, 127.0, 126.7, 126.5, 126.1, 124.6, 123.4, 122.9, 121.9, 121.8, 117.4, 115.2, 106.5, 105.1, 76.4, 59.3, 56.4, 43.3, 39.3, 27.8, 27.3, 20.4; IR (neat) ν 3500-2500, 3073, 2942, 1688, 1622, 1598, 1510, 1453, 1398, 1309, 1231, 1116 cm⁻¹; HRMS (ESI) *m/z* calcd. for (C₃₃H₃₀N₂O₂+H⁺): 487.2386, found: 487.2378.

General procedure for asymmetric Michael addition of 3A-H to nitroalkenes 4a-f:

Catalysts

For asymmetric conjugate additions generating **5Aa**, **5Ba**, **5Bb**, **5Bc**, **5Ea**, 0.4 mmol of **3A**, **3B** and **3E** (2.0 equiv.) and 0.2 mmol of **4a-c** were used; for reactions generating **5Ca**, 0.8 mmol of **3C** (4 equiv.) and 0.2 mmol of **4a** were used; for other reactions, 0.2 mmol of **3** and 0.4 mmol of **4** were used. Yields were calculated based on the limiting reagent. The choice of using either a donor or acceptor as the limiting reagent is based on how readily the product (**5**) can be separated from the excessive starting materials (**3** or **4**). Changing the ratio of **3** and **4** has no impact on both the diastereoselectivity and enantioselectivity of the asymmetric conjugate addition.

When catalyst **Q-2b** was used, it is first suspended in THF. The resulting suspension was subjected to ultrasound for 10-15 min. and became a milky mixture. To this solution, the starting materials were added according to the procedure described below.

Procedure: At the temperature specified in tables 1 and 2 to a solution of the limiting reagent (**3** or **4**, 0.2 mmol) and the chiral catalyst (**Q-2**, **QD-2** or **6**, 10-20 mol %) in THF (0.2 mL) was added the other reagent (**4** or **3**, 2 or 4 eq.). The resulting mixture was kept at the temperature until the limiting reagent is consumed. The reaction mixture was then passed through a plug of silica gel for the removal of the catalyst. The plug of silica gel was eluted with ether or ethyl acetate (2-3 mL). The combined filtrate was concentrated in *vacuo* and the residue was subjected to purification by flash chromatography on silica gel.

Data for the products 5

Q-2b (10 mol %) catalyzed reaction was run in THF at -60 °C for 48 h to furnish the crude product [dr = 95:5,

determined by integration of one set of ^1H NMR signal (δ_{major} 5.16–5.12 ppm, δ_{minor} 5.27–5.21 ppm). The crude product was purified by flash chromatography (hexane: ethyl acetate = 12:1) to give adduct **5Aa** as a colorless oil in 94% yield (dr = 95:5) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 80:20, 1.00 mL/min, λ = 220 nm, t (major) = 11.0 min, t (minor) = 17.0 min]. $[\alpha]_{\text{D}}^{25}$ = + 36.5 (c , 0.84 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.30–7.21 (m, 5H), 5.14 (dd, J = 4.0 Hz, 13.6 Hz, 1H), 4.99 (dd, J = 11.2 Hz, 2.4 Hz, 1H), 4.05 (dd, J = 3.6 Hz, 14.4 Hz, 1H), 3.73 (s, 3H), 2.38–2.28 (m, 2H), 2.04–1.85 (m, 3H), 1.82–1.77 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 212.2, 169.8, 135.2, 129.2, 128.8, 128.3, 76.4, 62.4, 53.0, 46.1, 37.9, 31.0, 19.3; IR (neat) ν 2957, 1718, 1543, 1496, 1229 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{15}\text{H}_{17}\text{NO}_5 + \text{H}^+$): 292.1185, found: 292.1193.

QD-**2c** (10 mol%) catalyzed reaction was run at $-60\text{ }^\circ\text{C}$ for 48 h to furnish the crude product (dr = 94:6) and was purified by flash chromatography to give adduct **5Aa** in 97% yield (dr = 94:6) and 99% ee (major diastereomer).

6 (10 mol%) catalyzed reaction was run at $-60\text{ }^\circ\text{C}$ for 36 h to furnish the crude product (dr = 97:3) and was purified by flash chromatography to give adduct **5Aa** in 97% yield (dr = 97:3) and 98% ee (major diastereomer).

Q-**2b** (10 mol %) catalyzed reaction was run in THF at $-60\text{ }^\circ\text{C}$ for 96 h to furnish the crude product [dr > 98:2, determined by integration of one set of ^1H NMR signal (δ_{major} 4.87–4.82 ppm, δ_{minor} 4.55–4.51 ppm, the minor peak can not be detected by ^1H NMR)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 15:1) to give adduct **5Ae** as a colorless oil in 87 % yield (dr > 98:2) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 95:5, 0.8 mL/min, λ = 215 nm, t (major) = 11.0 min, t (minor) = 16.6 min]. $[\alpha]_{\text{D}}^{25}$ = + 82.5 (c , 0.84 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 4.86 (dd, J = 6.0 Hz, 14.4 Hz, 1H), 4.29 (dd, J = 4.4 Hz, 14.4 Hz, 1H), 3.67 (s, 3H), 2.92–2.86 (m, 1H), 2.61–2.55 (m, 1H), 2.46–2.37 (m, 1H), 2.33–2.24 (m, 1H), 2.04–1.88 (m, 3H), 1.56–1.50 (m, 1H), 1.42 (ddd, J = 3.6 Hz, 10.4 Hz, 14.0 Hz, 1H), 0.97 (ddd, J = 2.4 Hz, 10.4 Hz, 12.8 Hz, 1H), 0.88 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3)

δ 213.2, 169.9, 76.6, 62.9, 52.7, 39.4, 38.4, 38.3, 31.0, 25.6, 23.7, 21.1, 19.4; IR (neat) ν 2959, 1750, 1722, 1557, 1435, 1380, 1230, 1164, 1230 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{13}\text{H}_{21}\text{NO}_5 + \text{H}^+$): 272.1498, found: 272.1497.

5Ba

Q-2a (10mol %) catalyzed reaction was run in THF at $-20\text{ }^\circ\text{C}$ for 72 h to furnish the crude product [dr > 98:2, determined by integration of one set of ^1H NMR signal (δ_{major} 5.06–5.02 ppm, δ_{minor} 5.17–5.11 ppm, the minor peak can not be detected by ^1H NMR)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 10:1) to give adduct **5Ba** as a white solid in 93 % yield (dr > 98:2) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 95:5, 0.9 mL/min, λ = 220 nm, t (major) = 12.3 min, t (minor) = 17.0 min]. $[\alpha]_{\text{D}}^{25}$ = -91.5 (c , 1.02 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.25–7.12 (m, 5H), 5.04 (dd, J = 3.2 Hz, 13.2 Hz, 1H), 4.77 (dd, J = 13.2 Hz, 1.6 Hz, 1H), 4.18 (qd, J = 1.6 Hz, 7.2 Hz, 2H), 3.97 (dd, J = 3.2 Hz, 10.8 Hz, 1H), 2.52–2.39 (m, 2H), 2.08–1.97 (m, 2H), 1.71–1.55 (m, 3H), 1.48–1.40 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 207.0, 169.6, 135.3, 129.4, 128.4, 128.1, 77.5, 62.9, 61.9, 47.7, 41.4, 37.0, 27.9, 22.3, 13.9; IR (neat) ν 3032, 2943, 2869, 1712, 1553, 1453, 1378, 1308, 1235 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{17}\text{H}_{21}\text{NO}_5 + \text{H}^+$): 320.1498, found: 320.1502.

The relative configuration of 5Ba was determined by X-ray crystallography of (-)-5Ba.

5Bb

Q-2a (10 mol %) catalyzed reaction was run in THF at $-20\text{ }^\circ\text{C}$ for 74 h to furnish the crude product [dr > 98:2, determined by integration of one set of ^1H NMR signal (δ_{major} 4.88–4.85 ppm, δ_{minor} 5.14–5.08 ppm, the minor peak can not be detected by ^1H NMR)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 10:1) to give adduct **5Bb** as a colorless oil in 91 % yield (dr > 98:2) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 95:5, 0.9 mL/min, λ = 220 nm, t (major) = 14.9 min, t (minor) = 24.6 min]. $[\alpha]_{\text{D}}^{25}$ = -69.0 (c , 1.06 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.20 (d, J = 4.8 Hz, 1H), 6.89–6.85 (m, 2H), 4.86 (dd, J = 3.2 Hz, 13.6 Hz, 1H), 4.77 (dd, J = 10.4 Hz, 1H), 4.31 (dd, J = 4.0 Hz, 10.4 Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 2.52 (m, 2H), 2.32–2.28 (m, 1H), 2.01–

1.97 (m, 1H), 1.79-1.77 (m, 1H), 1.69-1.56 (m, 3H), 1.22 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 206.9, 169.6, 137.7, 128.4, 126.5, 126.1, 78.7, 63.7, 62.1, 43.3, 41.0, 36.1, 27.5, 22.1, 13.9; IR (neat) ν 2942, 1718, 1702, 1559, 1543, 1524, 1437, 1376, 1232 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{15}\text{H}_{19}\text{NO}_5\text{S} + \text{H}^+$): 326.1055, found: 326.1058.

Q-2a (10 mol %) catalyzed reaction was run in THF at -20 °C for 74 h to furnish the crude product [dr > 98:2, determined by integration of one set of ^1H NMR signal (δ_{major} 5.01-4.97 ppm, δ_{minor} 5.16-5.10 ppm, the minor peak can not be detected by ^1H NMR)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 12:1) to give adduct **5Bc** as a colorless oil in 95 % yield (dr > 98:2) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 90:10, 0.8 mL/min, $\lambda = 220$ nm, t (major) = 11.4 min, t (minor) = 18.6 min]. $[\alpha]_{\text{D}}^{25} = -74.1$ (c, 0.56 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.38 (d, $J = 8.4$ Hz, 2H), 7.02 (d, $J = 8.4$ Hz, 2H), 4.98 (dd, $J = 3.2$ Hz, 14.0 Hz, 1H), 4.71 (dd, $J = 14.0$ Hz, 2.4 Hz, 1H), 4.21-4.13 (m, 2H), 3.92 (dd, $J = 3.2$ Hz, 11.6 Hz, 1H), 2.50-2.39 (m, 2H), 2.10-2.05 (m, 1H), 2.02-1.96 (m, 1H), 1.72-1.65 (m, 1H), 1.63-1.50 (m, 2H), 1.46-1.39 (m, 1H), 1.21 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 206.8, 169.5, 134.5, 131.5, 131.2, 122.3, 76.7, 62.7, 62.0, 47.2, 41.3, 37.0, 27.7, 22.3, 13.9; IR (neat) ν 2942, 1716, 1557, 1490, 1436, 1377, 1307, 1234, 1198, 1012 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{17}\text{H}_{20}\text{BrNO}_5 + \text{H}^+$): 398.0603, found: 398.0604.

QD-2a (10 mol%) catalyzed reaction was run at -20 °C for 72 h to furnish the crude product (dr > 98:2) and was purified by flash chromatography to give adduct **5Bc** in 96% yield (dr > 98:2) and 99% ee (major diastereomer).

6 (10 mol%) catalyzed reaction was run at -20 °C for 60 h to furnish the crude product (dr > 98:2) and was purified by flash chromatography to give adduct **5Bc** in 97% yield (dr > 98:2) and 98% ee (major diastereomer).

5Be

Q-2c (10 mol %) catalyzed reaction was run in THF at 23 °C for 96 h to furnish the crude product [dr > 98:2, determined by integration of one set of ^1H NMR signal (δ_{major} 4.55–4.50 ppm, δ_{minor} 4.62–4.57 ppm, the minor peak can not be detected by ^1H NMR)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 20:1) to give to give adduct **5Be** as a colorless oil in 83 % yield (dr >98:2) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 90:10, 0.8 mL/min, λ = 215 nm, t (major) = 11.0 min, t (minor) = 19.2 min]. $[\alpha]_{\text{D}}^{25}$ = - 33.7 (c , 0.92 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 4.53 (dd, J = 4.8 Hz, 14.0 Hz, 1H), 4.30 (dd, J = 4.8 Hz, 14.8 Hz, 1H), 4.22 (ddd, J = 2.4 Hz, 7.2 Hz, 14.0 Hz, 2H), 2.94 (m, 1H), 2.59 (m, 3H), 2.03 (m, 1H), 1.83 (m, 1H), 1.70–1.61 (m, 3H), 1.58–1.51 (m, 1H), 1.43 (ddd, J = 4.0 Hz, 10.4 Hz, 14.0 Hz, 1H), 1.30 (t, J = 1.30 Hz, 3H), 1.16 (ddd, J = 2.4 Hz, 9.6 Hz, 13.6 Hz, 1H), 0.91 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 207.3, 170.9, 77.9, 64.4, 61.8, 41.1, 39.9, 38.8, 33.9, 27.1, 25.9, 23.7, 22.2, 21.2, 14.0; IR (neat) ν 2957, 2896, 1713, 1554, 1465, 1439, 1379, 1235, 1208, 1137, 1020 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{15}\text{H}_{25}\text{NO}_5 + \text{H}^+$): 300.1811, found: 300.1811.

5Ca

Q-2c (15 mol %) catalyzed reaction was run in THF at -20 °C for 63 h to furnish the crude product [dr = 91:9, determined by integration of one set of ^1H NMR signal (δ_{major} 2.17 ppm, δ_{minor} 2.12 ppm)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 13:1) to give to give adduct **5Ca** as a colorless oil in 73 % yield (pure diastereomer) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 90:10, 0.9 mL/min, λ = 220 nm, t (major) = 10.3 min, t (minor) = 26.6 min]. $[\alpha]_{\text{D}}^{25}$ = - 69.9 (c , 0.93 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.33–7.27 (m, 3H), 7.14–7.12 (m, 2H), 4.97 (dd, J = 10.4 Hz, 13.2 Hz, 1H), 4.89 (dd, J = 3.6 Hz, 13.2 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 4.14 (dd, J = 4.0 Hz, 10.4 Hz, 1H), 2.17 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 204.2, 171.2, 135.3, 128.9, 128.7, 128.3, 77.5, 62.4, 62.1, 47.7, 26.4, 20.0, 13.9; IR (neat) ν 2986, 1717, 1557, 1457, 1378, 1236 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{15}\text{H}_{19}\text{NO}_5 + \text{H}^+$): 294.1341, found: 294.1343.

QD-2c (10 mol%) catalyzed reaction was run at -20 °C for 60 h to furnish the crude product (dr = 82:18) and was purified by flash chromatography to give adduct **5Ca** in 70 % yield (pure diastereomer) and 99 % ee (major diastereomer).

6 (10 mol%) catalyzed reaction was run at -20 °C for 64 h to furnish the crude product (dr = 89:11) and was purified by flash chromatography to give adduct **5Ca** in 75% yield (pure diastereomer) and 96% ee (major diastereomer).

Q-2b (10 mol %) catalyzed reaction was run in THF at -60 °C for 44 h to furnish the crude product [dr = 98:2, determined by integration of one set of ¹H NMR signal (δ_{major} 2.31 ppm, δ_{minor} 2.43 ppm)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 6:1) to give to give adduct **(-)-5Dd** as a white solid in 87 % yield (dr = 98:2) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 60:40, 1.0 mL/min, λ = 220 nm, t (major) = 10.3 min, t (minor) = 20.0 min]. $[\alpha]_D^{25}$ = - 23.5 (c, 1.18 CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.32 (dt, *J* = 8.4 Hz, 1.6 Hz, 2H), 7.20 (dt, *J* = 8.8 Hz, 1.6 Hz, 2H), 5.00 (dd, *J* = 11.6 Hz, 13.6 Hz, 1H), 4.70 (dd, *J* = 3.2 Hz, 13.6 Hz, 1H), 4.29 (dd, *J* = 3.2 Hz, 11.6 Hz, 1H), 4.10 (dt, *J* = 6.0 Hz, 9.2 Hz, 1H), 3.47 (dt, *J* = 6.0 Hz, 9.2 Hz, 1H), 2.55 (ddd, *J* = 6.0 Hz, 8.8 Hz, 14.0 Hz, 1H), 2.31 (s, 3H), 2.20 (ddd, *J* = 6.0 Hz, 8.8 Hz, 14.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 200.9, 175.0, 135.2, 132.7, 130.0, 129.6, 76.2, 66.2, 62.8, 45.6, 29.8, 26.5 ; IR (neat) ν 2994, 2923, 1755, 1716, 1555, 1494, 1434, 1417, 1378, 1175 cm⁻¹; HRMS (CI) *m/z* calcd for (C₁₄H₁₄ClNO₅ + H⁺): 312.0639, found: 312.0630.

The absolute configuration of (-)-5Dd was determined by X-ray crystallography of (-) -5Dd.

QD-2c (10 mol%) catalyzed reaction was run at -60 °C for 40 h to furnish the crude product (dr = 97:3) and was purified by flash chromatography to give adduct **(+)-5Dd** in 92% yield (dr = 97:3) and 98 % ee (major diastereomer).

6 (10 mol%) catalyzed reaction was run at -60 °C for 36 h to furnish the crude product (dr = 97:3) and was purified by flash chromatography to give adduct **(+)-5Dd** in 92% yield (dr = 97:3) and 98% ee (major diastereomer).

5De

Q-2c (10 mol %) catalyzed reaction was run in THF at $-60\text{ }^{\circ}\text{C}$ for 48 h to furnish the crude product [dr = 42 : 1, determined by integration of one set of ^1H NMR signal (δ_{major} 2.37 ppm, δ_{minor} 2.40 ppm)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 10:1) to give adduct **5De** as a white solid in 82 % yield (dr = 98:2) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 90:10, 0.8 mL/min, λ = 215 nm, t (major) = 20.4 min, t (minor) = 51.0 min]. $[\alpha]_{\text{D}}^{25}$ = + 80.9 (*c*, 0.92 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 4.44 (dd, J = 4.4 Hz, 13.6 Hz, 1H), 4.38 (dd, J = 6.4 Hz, 1H), 4.33 (dt, J = 2.0 Hz, 9.2 Hz, 1H), 4.12, (dt, J = 7.6 Hz, 9.6 Hz, 1H), 3.29–3.22 (m, 1H), 2.78 (ddd, J = 2.4 Hz, 7.2 Hz, 13.2 Hz, 1H), 2.35 (s, 3H), 1.99 (td, J = 9.6 Hz, 12.8 Hz, 1H), 1.56–1.50 (m, 1H), 1.26 (ddd, J = 4.4 Hz, 11.2 Hz, 14.8 Hz, 1H), 0.96 (ddd, J = 2.8 Hz, 10.8 Hz, 14.0 Hz, 1H), 0.89 (d, J = 6.0 Hz, 3H), 0.87 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.8, 173.8, 76.7, 66.4, 65.1, 39.0, 37.2, 26.2, 25.4, 25.1, 23.6, 21.1; IR (neat) ν 2958, 2930, 1758, 1715, 1560, 1448, 1380, 1223, 1159, 1022 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{12}\text{H}_{19}\text{NO}_5 + \text{H}^+$): 258.1341, found: 258.1341.

The relative configuration of 5De was determined by X-ray crystallography of (+)-5De.

5Ea

Q-2b (10 mol %) catalyzed reaction was run in THF at $-60\text{ }^{\circ}\text{C}$ for 48 h to furnish the crude product [dr = 86:14, determined by integration of one set of ^1H NMR signal (δ_{major} 4.39–4.35 ppm, δ_{minor} 4.28–4.24 ppm)]. Crude product was purified by flash chromatography (hexane: ethyl acetate = 12:1) to give adduct **5Ea** as a white solid (pure diastereomer) in 76 % yield (pure diastereomer) and 99% ee (major diastereomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 80:20, 1.0 mL/min, λ = 220 nm, t (major) = 12.6 min, t (minor) = 53.3 min]. $[\alpha]_{\text{D}}^{25}$ = - 43.3 (*c*, 1.11 CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.22 (m, 5H), 4.84 (dd, J = 11.6 Hz, 13.2 Hz, 1H), 4.48 (dd, J = 4.4 Hz, 14.0 Hz, 1H), 4.36 (dd, J = 3.6 Hz, 11.6 Hz, 1H), 2.57–2.51 (m, 1H), 2.30 (s, 3H), 2.21–2.12 (m, 1H), 1.99–1.91 (m, 1H), 1.76–1.64 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 213.1, 202.7, 134.2, 129.4, 128.8, 128.4, 75.5, 71.1, 46.3, 38.6, 27.2, 26.6, 19.4 ; IR (neat) ν 3033, 2971, 1740, 1702, 1554, 1378, 1140 cm^{-1} ; HRMS (CI) m/z calcd for ($\text{C}_{15}\text{H}_{17}\text{NO}_4 + \text{H}^+$): 276.12136, found: 276.1238.

QD-**2c** (10 mol%) catalyzed reaction was run at -60 °C for 48 h to furnish the crude product (dr = 88:12) and was purified by flash chromatography to give adduct **5Ea** in 70% yield (pure diastereomer) and 98 % ee (major diastereomer).

6 (10 mol%) catalyzed reaction was run at -60 °C for 48 h to furnish the crude product (dr = 90:10) and was purified by flash chromatography to give adduct **5Ea** in 79% yield (pure diastereomer) and 96% ee (major diastereomer).

Q-**2a** (10 mol%) catalyzed reaction was run in THF at -20 °C for 2.5 days to furnish the crude product [dr = 92:8, determined by ¹H NMR peaks at 5.04-5.17 ppm and 4.96-5.00 ppm]. Pure major diastereomer (-)-**5Fa** was obtained by flash chromatography (hexane : ethyl acetate = 15 :1-10:1) as white solid in 78% yield and 92% ee [determined by HPLC, Chiralcel OD, hexane: isopropanol = 80: 20, 1.00 mL/min, λ = 220 nm, t (major) = 7.9 min, t (minor) = 18.8 min]. [α]_D²⁵ = -50.2 (c 0.93, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.31 (t, J = 7.6 Hz, 3H), 1.65 (s, 3H), 4.33 (q, J = 6.8 Hz, 2H), 4.41 (dd, J = 3.6, 10.4 Hz, 1H), 5.07 (dd, J = 10.4, 14.0 Hz, 1H), 5.14 (dd, J = 3.6, 14.0 Hz, 1H), 7.12-7.15 (m, 2H), 7.35-7.37 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 13.74, 21.88, 48.65, 63.80, 77.00, 93.78, 128.88, 128.29, 129.34, 132.39, 166.57; IR (neat) ν 1753, 1561, 1549 cm⁻¹; HRMS (CI/MH⁺) Calcd for C₁₃H₁₇N₂O₆: 297.1084, found 297.1087.

QD-**2a** (10 mol%) catalyzed reaction was run in THF at -20 °C for 2.5 days to furnish the crude product (dr = 89:11). Major diastereomer (+)-**5Fa** was obtained by flash chromatography as a white solid in 74% yield and 89% ee.

6 (10 mol%) catalyzed reaction was run in THF at -20 °C for 2.5 days to furnish the crude product (dr = 95:5). Major diastereomer (+)-**5Fa** was obtained by flash chromatography as a white solid in 74% yield and 88% ee.

Q-**2a** (20 mol%) catalyzed reaction was run in THF at -50 °C for 6 days to furnish crude product [dr = 95:5, determined by ¹H NMR peaks at 4.58-4.62 ppm (minor) and 5.17-5.21 ppm (major)]. Pure product was obtained by flash chromatography (hexane : ethyl acetate = 20:1-15:1) as a white solid mixture of two

diastereomers (dr = 95:5) in 77% yield and 96% ee (major isomer) [determined by HPLC, Chiralcel OJ, hexane: isopropanol = 80: 20, 1.00 mL/min, λ = 220 nm, t (major) = 27.3 min, t (minor) = 31.5 min]. After recrystallization in Et₂O, pure diastereomer (-)-**5Ga** was obtained in 50 % yield and more than 99% ee. $[\alpha]_D^{25}$ = -68.1 (c 0.88, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.98 (t, J = 8.0 Hz, 3H), 1.34 (t, J = 7.2 Hz, 3H), 1.76-1.85 (m, 1H), 2.04-2.13 (m, 1H), 4.33-4.40 (m, 2H), 4.43 (dd, J = 3.2, 10.8 Hz, 1H), 4.97 (dd, J = 10.4, 13.2 Hz, 1H), 7.08-7.10 (m, 2H), 7.31-7.35 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 8.45, 13.89, 27.79, 46.74, 63.57, 77.72, 97.46, 128.52, 129.30, 129.33, 132.51, 165.65; IR (neat) ν 1753, 1560, 1552 cm⁻¹; HRMS (CI/MH⁺) Calcd for C₁₄H₁₉N₂O₆: 311.1246, found 311.1243.

Q-2b (20 mol%) catalyzed reaction was run in THF at -50 °C for 6 days to furnish the crude product [dr > 98:2, determined by ¹H NMR peaks at 4.82-4.86 ppm and 4.98-5.04 ppm]. Pure major diastereomer (-)-**5Ha** was obtained by flash chromatography (hexane: ethyl acetate = 10:1-8:1) as colorless oil in 78% yield and 99% ee [determined by HPLC, Chiralcel OD, hexane: isopropanol = 80: 20, 1.00 mL/min, λ = 220 nm, t (major) = 32.5 min, t (minor) = 21.5 min]. $[\alpha]_D^{25}$ = -38.0 (c 2.10, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.34 (t, J = 7.2 Hz, 3H), 1.38 (s, 3H), 4.02 (dd, J = 5.2, 10.4 Hz, 1H), 4.27-4.35 (m, 2H), 4.79 (dd, J = 4.8, 13.2 Hz, 1H), 4.98 (dd, J = 10.0, 13.6 Hz, 1H), 7.37 (brs, 5H); ¹³C NMR (101 MHz, CDCl₃) δ 13.86, 22.84, 46.58, 48.34, 63.84, 76.44, 117.81, 128.69, 129.21, 129.31, 133.04, 168.14; IR (neat) ν 1739, 1556 cm⁻¹; HRMS (CI/MH⁺) Calcd for C₁₄H₁₇N₂O₄: 277.1197, found 277.1188.

QD-2a (10 mol%) catalyzed reaction was run in THF at -20 °C for 2.5 days to furnish the crude product (dr = 86:14). Major diastereomer (+)-**5Ha** was obtained by flash chromatography as colorless oil in 76% yield and 95% ee.

6 (10 mol%) catalyzed reaction was run in THF at -20 °C for 2.5 days to furnish the crude product (dr = 86:14). Major diastereomer (+)-**5Ha** was obtained by flash chromatography as colorless oil in 74% yield and 88% ee.

Q-2a (10 mol%) catalyzed reaction was run in THF at -20 °C for 3.5 days to furnish crude product [dr = 93:7, determined by ¹H NMR peaks 3.40 ppm (minor), 3.20-3.25 ppm

(major)]. Pure major diastereomer (+)-**5Ff** was obtained by flash chromatography (hexane : ethyl acetate = 50 :1-20:1) as a colorless oil in 78% yield and 92% ee [determined by HPLC, Chiralcel OD, hexane: isopropanol = 99: 1, 1.00 mL/min, λ = 220 nm, t (major) = 31.6 min, t (minor) = 53.2 min]. $[\alpha]_D^{25}$ = +19.3 (c 2.15, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.24-1.42 (m, 10 H), 1.55-1.61 (m, 1H), 1.86 (s, 3H), 3.20-3.25 (m, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 4.46 (dd, *J* = 6.4, 14.8 Hz, 1H), 4.77 (dd, *J* = 3.6, 14.4 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 13.68, 13.82, 21.02, 22.23, 26.63, 29.34, 31.49, 42.47, 63.57, 77.00, 94.69, 166.47; IR (neat) ν 1751, 1560 cm⁻¹; HRMS (CI/MH⁺) Calcd for C₁₂H₂₃N₂O₆: 291.1561, found 291.1556.

Q-2a (10 mol%) catalyzed reaction was run in THF at -20 °C for 3.5 days to furnish crude product [dr = 93:7, determined by ¹H NMR peaks at 2.93-2.96 ppm (minor) and 2.82-2.88 ppm (major)]. Pure product **5Hf** was obtained by flash chromatography (hexane : ethyl acetate = 50:1-30:1) as a colorless oil mixture of two diastereomers (dr = 93:7) in 76% yield and 98% ee (major isomer) [determined by HPLC, Chiralcel OD, hexane: isopropanol = 99: 1, 0.50 mL/min, λ = 220 nm, t (major) = 45.8 min, t (minor) = 66.2 min]. $[\alpha]_D^{25}$ = +17.3 (c 1.81, CHCl₃); ¹H NMR of major diastereomer (400 MHz, CDCl₃) δ 0.90 (t, *J* = 6.0 Hz, 3H), 1.26-1.50 (m, 10H), 1.67 (s, 3H), 1.70-1.76 (m, 1H), 2.82-2.88 (m, 1H), 4.28 (q, *J* = 6.8 Hz, 2H), 4.43 (dd, *J* = 6.4, 14.0 Hz, 1H), 4.64 (dd, *J* = 4.8, 14.0 Hz, 1H); ¹³C NMR of major diastereomer (101 MHz, CDCl₃) δ 13.84, 21.64, 22.27, 26.49, 29.33, 31.48, 42.97, 46.87, 63.47, 76.04, 76.68, 118.34, 168.03; IR (neat) ν 1743, 1560 cm⁻¹; HRMS (CI/MH⁺) Calcd for C₁₃H₂₃N₂O₄: 271.1652, found 271.1658.

Kinetic Data:

The kinetic parameters of this reaction were determined by *in situ* monitoring of the consumption of nitroalkenes (at peak 1522 cm⁻¹) by the use of a ReactIR 1000 instrument. ReactIR 1000 fitted with a 5/8" Dicomp Probe, running software version 2.1a.

Order in nitroalkene (**4a**) was established by using a large excess of methyl 2-oxocyclopentane carboxylate (**3A**, 5 equiv) and 10 mol% **Q-2c**. Plotting in $\ln[4a]$ versus time gave a straight line ($R^2 = 0.9863$, Figure A), thus establishing a first-order dependence on Nitroalkene (**4a**).

Order in methyl 2-oxocyclopentane carboxylate (**3A**) was established by using a large excess of nitroalkene (**4a**, 5 equiv) and 10 mol% **Q-2c**. Plotting in $\ln[3A]$ versus time gave a straight line ($R^2 = 0.9952$, Figure C), thus establishing a first-order dependence on **3A**.

The reaction order in catalyst was established by determining the kinetic rate constants at various catalyst concentrations. A plot of the rate constants k_{obs} vs the catalyst concentration gave a straight line for **Q-2c** ($R^2 = 0.99$, Figure F) The reaction displays first-order dependence on catalysts **Q-2c**.

General procedure for kinetic study:

A mixture of nitroalkene (**4a**) (1.0 mmol) and **Q-2c** (2.5-12.5 mol%) in anhydrous THF (1.0 mL) was stirred at -30°C for 5 minutes, and then pre-cooled methyl 2-oxocyclopentane carboxylate (**3A**, 0.65ml, 5eq) was introduced in one portion via a syringe. The resulting reaction mixture was monitored every 2 seconds for 25 minutes.

Figure A. Determination of the order of nitroalkene (**4a**)

Figure A shows a linear relationship between $\ln[4a]$ and time indicating the reaction is first order on **4a**.

Figure B. Determination of the order of nitroalkene (**4a**)

Figure B shows clearly nonlinear relationship between $1/[4a]$ and time indicating the reaction is NOT second order in **4a**

Figure C. Determination of the order of methyl 2-oxocyclopentane carboxylate (**3A**).

Figure C shows a linear relationship between $\ln[3A]$ and time indicating the reaction is first order in **3A**.

Figure D. Determination of the order of methyl 2-oxocyclopentane carboxylate (**3A**)

Figure D shows clearly nonlinear relationship between $1/[\mathbf{3A}]$ and time indicating the reaction is NOT second order in **3A**.

Figure E. Kinetic profiles for the catalyst Q-2c

Catalyst 2.5 mol%	$k_{\text{obs}} = 0.0268$	$R^2 = 0.9974$
Catalyst 5.0 mol%	$k_{\text{obs}} = 0.0661$	$R^2 = 0.9976$
Catalyst 7.5 mol%	$k_{\text{obs}} = 0.1035$	$R^2 = 0.9978$
Catalyst 10.0 mol%	$k_{\text{obs}} = 0.1775$	$R^2 = 0.9965$
Catalyst 12.5 mol%	$k_{\text{obs}} = 0.2152$	$R^2 = 0.9936$

Figure F. Kinetic rate constant (k_{obs}) of different concentration of Q-2c

Figure F shows the linear relationship between the kinetic rate constant (k_{obs}) and the concentration of the catalyst, indicating the reaction is first order in catalyst Q-2c.

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 80/20,
1.0 mL/min, λ 220 nm

Racemic 5Aa

(+)-5Aa 99%ee
Product of **Q-2b**
catalyzed reaction

(-)-5Aa 99%ee
Product of QD-2c
catalyzed reaction

(-)-5Aa 98%ee
Product of 6
catalyzed reaction

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 95/5,
0.8 mL/min, λ 215 nm

Racemic 5Ae

(+)-5Ae 99%ee
Product of Q-2b
catalyzed reaction

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 95/5
0.9 mL/min, λ 220 nm

(-)-5Ba 99%ee
Product of **Q-2a**
catalyzed reaction

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 95/5
0.9 mL/min, λ 220 nm

Racemic 5Bb

(-)-5Bb 99%ee
Product of Q-2a
catalyzed reaction

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 90/10
0.8 mL/min, λ 220 nm

(-)-5Bc 99%ee
Product of **Q-2a**
catalyzed reaction

(+)-5Bc 99%ee
Product of QD-2a
catalyzed reaction

(+)-5Bc 98%ee
Product of 6
catalyzed reaction

HPLC conditions: Hypersil-Keystone plus Chiralcel OD,
Hexane/*iso*-propanol: 90/10 0.8 mL/min, λ 215 nm

Racemic 5Be

(-)-5Be 99%ee
Product of **Q-2c**
catalyzed reaction

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 90/10,
0.9mL/min, λ 220 nm

(-)-5Ca 99%ee
Product of **Q-2c**
catalyzed reaction

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
UN# 7801 JUN 16, 2004 16:55:21

PEAK FILE : M:SIGNAL.PRA
PEAK# RT AREA TYPE WIDTH SPB AREA
10.862 16793440 588 .420 12.05329
11.974 51353920 588 .479 36.85866
18.068 52247552 588 .694 37.50005
28.575 18931712 588 1.047 13.58800

TOTAL AREA=1.3933E+08
MUL FACTOR=1.0000E+00

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
UN# 7802 JUN 16, 2004 18:06:24

PEAK FILE : M:SIGNAL.PRA
PEAK# RT AREA TYPE WIDTH SPB AREA
10.328 171345920 588 .427 99.01894
11.443 669645 588 .298 38698
17.040 367974 588 1.380 21265
26.547 660053 588 .914 38144

TOTAL AREA=1.7304E+08
MUL FACTOR=1.0000E+00

(+)-5Ca 96%ee
Product of **6**
catalyzed reaction

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 7980 JUL 7, 2004 18:35:09
PEAK FILE : M:SIGNAL.PRA
AREA% RT AREA TYPE WIDTH AREA%
10.374 608563 BU .455 1.86460
25.819 32029248 PB .933 98.13539
TOTAL AREA=3.2638E+07
MUL FACTOR=1.0000E+00

(+)-5Ca 99%ee
Product of **QD-2c**
catalyzed reaction

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 8011 JUL 10, 2004 15:22:04
PEAK FILE : M:SIGNAL.PRA
AREA% RT AREA TYPE WIDTH AREA%
10.577 638139 BU .384 .73484
17.612 1471573 PB .751 1.69456
26.042 84731264 BB .965 97.57059
TOTAL AREA=8.6841E+07
MUL FACTOR=1.0000E+00

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 60/40,
1.0 mL/min, λ 220 nm

Racemic 5Dd

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 7599 MAY 28, 2004 09:49:02

AREA%	RT	AREA	TYPE	WIDTH	AREA%
10.542	56272152	SBB	.482	41.35301	
14.542	11919288	BU	.707	8.75841	
20.267	56916320	SPB	1.067	41.82267	
44.420	10976872	BB	2.144	8.06591	

TOTAL AREA=1.3609E+08
MUL FACTOR=1.0000E+00

(-)-5Dd 99%ee
Product of **Q-2b**
catalyzed reaction

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 7597 MAY 28, 2004 00:03:13
PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
10.335	223744640	SBB	.615	96.15098	
14.291	6394707	BB	.776	2.74803	
20.045	1492207	BB	1.045	.64125	
43.630	1069909	I PP	2.242	.45978	

TOTAL AREA=2.3270E+08
MUL FACTOR=1.0000E+00

Error storing signal to M:SIGNAL .BNA
 DIRECTORY FULL
 Storing processed peaks to M:SIGNAL .PRA

RUN# 7940 JUL 5, 2004 21:15:54

PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
9.985	3426749	BB	.439	1.08668	
13.620	949598	BB	.642	.30113	
17.723	307032800	SHB	.983	97.36493	
39.245	3933218	I PP	2.061	1.24728	

TOTAL AREA=3.1534E+08
 MUL FACTOR=1.0000E+00

Error storing signal to M:SIGNAL .BNA
 DIRECTORY FULL
 Storing processed peaks to M:SIGNAL .PRA

RUN# 8015 JUL 11, 2004 12:36:36

PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
10.172	232265	BB	.435	.88057	
13.817	130611	BB	.615	.40746	
18.826	30846608	BB	.927	96.23078	
40.076	795341	BB	2.007	2.48119	

TOTAL AREA=3.3055E+07
 MUL FACTOR=1.0000E+00

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 90/10,
0.8 mL/min, λ 215 nm

(+)-5De 99%ee
Product of **Q-2c**
catalyzed reaction

HPLC conditions: Chiralcel OD, Hexane/iso-propanol: 80/20,
1.0 mL/min, λ 220 nm

Racemic 5Ea

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA

RUN# 7752 JUN 12, 2004 10:07:57

PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
12.819	46416160	SPB	.705	38.29846	
15.809	13645768	BB	.843	11.25926	
23.971	13812768	PB	1.252	11.39706	
54.704	47321216	PB	2.838	39.04523	

TOTAL AREA=1.2120E+00
MUL FACTOR=1.0000E+00

(-)-5Ea 99%ee
Product of **Q-2b**
catalyzed reaction

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA

RUN# 7749 JUN 11, 2004 21:51:42

PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
12.680	30141216	BB	.679	98.27693	
15.660	302233	BP	.821	.98545	
53.321	226235	BU	2.431	.73765	

TOTAL AREA=3.0670E+07
MUL FACTOR=1.0000E+00

(+)-5Ea 96%ee
Product of **6**
catalyzed reaction

(+)-5Ea 98%ee
Product of **QD-2c**
catalyzed reaction

HPLC conditions: Chiralcel OD, hexane:isopropanol = 80:20,
1 mL/min, λ = 220 nm

(-)-**5Ha** 99% ee
Product of Q-2b
catalyzed reaction
at -50 °C

(+)-**5Ha** 95% ee
Product of QD-**2a**
catalyzed reaction
at -20 °C

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 7996 JUL 9, 2004 09:18:12
PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
19.454	21216544	P8	.811	97.34275	
29.145	579174	P8	1.129	2.65728	

TOTAL AREA=2.1796E+07
MUL FACTOR=1.0000E+00

(+)-**5Ha** 88% ee
Product of **6**
catalyzed reaction
at -20 °C

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA
RUN# 7997 JUL 9, 2004 09:59:42
PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
19.719	23802304	P8	.798	93.98653	
29.810	1510127	B8	1.190	6.01347	

TOTAL AREA=2.5112E+07
MUL FACTOR=1.0000E+00

HPLC conditions: Chiralcel OD, hexane:isopropanol = 80:20,
1 mL/min, λ = 220 nm

Racemic **5Fa**

Closing signal file M:SIGNAL.BMC
Storing processed peaks to M:Q84BC613.PRO
DIRECTORY FULL
RUN# 7282 APR 30, 2004 22:07:14
SIGNAL FILE: M:SIGNAL.BMC
PEAK FILE : M:Q84BC613.PRO

AREA%	RT	AREA	TYPE	WIDTH	SPB	BB	PB	AREA%
7.829	12210216	SPB	.291	36.45294				
9.060	4521082	BB	.353	13.49744				
10.673	4520458	PB	.412	13.49558				
19.106	12244072	PB	.748	36.55403				

TOTAL AREA=3.3496E+07
MUL FACTOR=1.0000E+00

(-)-**5Fa** 92% ee
Product of **Q-2a**
catalyzed reaction
at -20 °C

Error storing signal to M:SIGNAL.BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL.PRA
RUN# 7512 MAY 20, 2004 19:49:48
PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	SPB	BB	PB	AREA%
7.884	17088208	SPB	.272	96.08525				
18.786	696217	BB	.718	5.91476				

TOTAL AREA=1.7784E+07
MUL FACTOR=1.0000E+00

(+)-**5Fa** 89% ee
Product of QD-**2a**
catalyzed reaction
at -20 °C

(+)-**5Fa** 88% ee
Product of **6**
catalyzed reaction
at -20 °C

HPLC conditions: Chiralcel OJ, hexane:isopropanol = 80:20,
1 mL/min, λ = 220 nm

Racemic **5Ga**

(-)-**5Ga** 96% ee
Product of Q-**2a**
catalyzed reaction
at -50 °C

HPLC conditions: Chiralcel OD, hexane:isopropanol = 99:1,
0.5 mL/min, λ = 220 nm

(+)-**5Hf** 98%
 ee
 Product of Q-
2a
 catalyzed
 reaction
 at -20 °C

HPLC conditions: Chiralcel OD, hexane:isopropanol = 99:1,
0.5 mL/min, λ = 220 nm

(+)-**5Ff** 92% ee
Product of Q-**2a**
catalyzed
reaction
at -20 °C

X-Ray Structure Determination. Single crystals of **5Ba**, **5Dd** and **5De** (prepared using catalysts Q-2 as described in this supporting information) suitable for X-ray diffraction measurements were obtained by recrystallization from hexane/Ethyl Acetate, hexane/Ethyl Acetate, and hexane/Ethyl Acetate, respectively. Crystals were mounted in a glass capillary, in order to avoid previously-observed decomposition upon irradiation in air. Data collection was carried out at room temperature (low temperature apparatus was not available) on a CAD-4 Turbo diffractometer equipped with MoK α radiation (**5Ba**), or a CAD-4-U diffractometer equipped with CuK α radiation (**5Dd** and **5De**)³. The structures were solved by direct methods (SIR92).⁴ Full-matrix least squares refinement was carried out using the Oxford University *Crystals for Windows* system.^{5,6} All ordered nonhydrogen atoms were refined by using anisotropic displacement parameters. Disorder of the methyl moiety in the ethyl group of **5Ba** was resolved and refined, with a major component occupancy of 0.55(5). Hydrogen atoms were fixed at calculated geometric positions and updated after each round of least-squares cycles. For **5Dd** (Figure 1), the absolute configuration was established using anomalous scattering, with a Flack parameter value of 0.001(65). For **5De** (Figure 2) and **5Ba** (Figure 3), the relative configurations of the two chiral centers were unambiguously established. These results automatically establish that **5De** and **5Ba** prepared by using catalysts QD-2 have the same relative configuration as illustrated in Figure 2 and Figure 3. These results also establish that the absolute configuration of 1,4-adduct **5Dd** prepared by using catalysts QD-2 has the absolute configuration that is opposite to that illustrated in Figure 1.

Figure 1. Molecular Structure of **5Dd**

Figure 2. Molecular Structure of **5De**

References :

- ¹ (a) Denmark, S. E.; Marcin, L, R. *J. Org. Chem.* **1993**, 58, 3850-3856. (b) Bulbule, V. J.; Jnaneshwara, G. K.; Deshmukh, R. R.; Borate, H. B.; Deshpande, V. H. *Synthetic Comm.* **2001**, 31, 3623-3626.
- ² Amberg, W.; Bennani, Y.; Chadha, R. K.; Crispino, G. A.; Davis, W. D.; Hartung, J.; Jeong, K.; Ogino, Y.; Shibata, T.; Sharpless, K. B. *J. Org. Chem.* **1993**, 58, 844-849.
- ³ Straver, L.H. *CAD4-EXPRESS*, Enraf-Nonius: Delft, The Netherlands, 1992.
- ⁴Altomare, A.; Cascarano, G.; Giacovazzo G.; Guagliardi A.; Burla M.C.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994**, 27, 435.
- ⁵ Betteridge, P.W.; Carruthers, J.R; Cooper, R.I.; Prout, K.; Watkin, D.J. *J. Appl. Cryst.* **2003**, 36, 1487.
- ⁶Watkin, D. J.; Prout, C. K.; Pearce, L. J. *CAMERON*, Chemical Crystallography Laboratory, Oxford, UK, 1996.