Highly Enantioselective Conjugate Addition of Malonate and β -Ketoester to Nitroalkenes: Asymmetric C-C Bond Formation with New Bifunctional Organic Catalysts Based on Cinchona Alkaloids

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Supporting Information

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), integration, coupling constant (Hz). 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 were 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.

Nitroalkenes **5a**, **5d**, **5k**, **5m** were purchased from Aldrich Inc. and **5o** was purchased from TCI America. They were used without other purifications. Other nitroalkenes were prepared according to literature procedures.¹

Structure of the catalysts

Figure 1. The Structure of Cinchona Alkaloids

Preparation of Quinidine 9-*O*-(9'-Phenanthryl) Ether, QD-PHN:²

A three-necked round-bottomed flask (500 mL) equipped with a mechanical stirrer, reflux condenser, and inert gas in- and outlet was charged with quinidine (QD-1, 12.8g, 39.5 mmol, 1.2 eq). The flask was flushed for 30 min with a gentle stream of argon. Anhydrous dimethyl sulfoxide (130 mL, freshly distilled in the presence of CaH₂) was added, and the reaction mixture was stirred at room temperature until all the quinidine was dissolved. Sodium hydride (60% oil dispersion, 2.0g, 1.5 eq.) was added in small portions yielding an orange, slightly cloudy solution of the corresponding sodium alkoxide. Upon addition of pyridine (6.4 mL, 2.4 eq.) and copper(I) iodide (7.8 g, 1.2 eq.) to the reaction mixture at room temperature, the color of the reaction mixture was changed from orange to dark green. After 30 min all of the precipitate dissolved, and a clear solution was formed. 9-iodophenanthrene (10.0 g, 32.9 mmol), was added, and the reaction mixture was kept at 113°C for 70h (oil bath, temperature: 120°C). The reaction

mixture was allowed to cool to room temperature. Water (100 mL), methylene chloride (100 mL), and diethyl ether (100 mL) were successively added to the brown solution followed by ethylenediaminetetraacetate disodium salt dihydrate (20 g) and concentrated aqueous ammonia solution (20 mL, 29%, w/w). The argon inlet was removed, and a gentle stream of air was flushed through the well-agitated reaction mixture for about 1 h. The reaction mixture was transferred to a separatory funnel and the turquoise blue aqueous phase separated from the dark brown organic phase. The aqueous layer was washed twice with methylene chloride (100 mL), and the combined organic phases were extracted three times with aqueous ammonia solution (200 mL, 5%, w/w) until the aqueous phase remained colorless. Then the organic layer was washed with aqueous HCl (1.0N, 2 x 50 mL) twice, with H₂O three times (3 x 50 mL) to remove the excess QD. The organic layer was washed with NH₄OH and dried over Na₂SO₄ and the solvent was removed in *vacuo*. The residue was dissolved in Et₂O (300 mL) and treated with HCl (1N in Et₂O) until no further precipitates were generated. The precipitates were collected and dissolved in CH₂Cl₂ and basified with saturated aqueous NH₄OH. The organic phase was washed with brine, dried over Na₂SO₄. The solvent was removed in *vacuo* to furnish QD-PHN as a yellowish foam (5.6g, 66% yield). $[\alpha]_D^{25} = +310.7$ (c 0.89 EtOH); ¹H NMR (CDCl₃, 400 MHz) δ 8.65-8.71 (m, 2H), 8.61 (d, *J* = 4.8 Hz, 1H), 8.52 (d, *J* = 8 Hz, 1H), 8.07 (d, *J* = 9.2 Hz, 1H), 7.70-7.75 (m, 2H), 7.55 (d, *J* = 2.4 Hz, 1H), 7.38-7.46 (m, 5H), 6.66 (s, 1H), 6.35 (br, 1H), 6.12-6.21 (m, 1H), 5.18 (d, *J* = 10.4 Hz, 1H), 5.12 (m, 1H), 4.03 (s, 3H), 3.32-3.42 (m, 2H), 2.97-3.06 (m, 2H), 2.79-2.87 (m, 1H), 2.44-2.50 (t, *J* = 10.0 Hz, 1H), 2.34-3.25 (m, 1H), 1.97 (br, 1H), 1.55-1.62 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 158.1, 150.4, 147.71, 144.7, 143.7, 140.3, 132.3, 132.2, 131.5, 127.5, 127.3, 126.8, 126.7, 126.6, 126.4, 124.5, 122.8, 122.7, 122.3, 121.8, 118.2, 114.7, 104.8, 100.8, 78.8, 60.5, 55.8, 50.2, 49.9, 39.6, 27.8, 26.5, 22.1; IR (CHCl₃) ν 3062, 2935, 2863, 1622, 1594, 1507, 1454, 1226, 1117, 750; HRMS (EI) *m/z* calcd for (C₃₄H₃₂N₂O₂)⁺: 500.2464, found: 500.2481.

Preparation of Quinidine 9-*O*-Benzyl Ether, QD-OBn:

To the solution of QD (2.0 g, 6.2 mmol) in DMF (20 mL, freshly distilled from a suspension of CaH₂ in DMF) was added NaH (0.68 g, 57 % suspension in mineral oil, 2.5 eq.). The resulting mixture was stirred at room temperature for 2h. Then BnCl (0.78 mL, 1.1 eq.) was added dropwisely via a syringe in 10 minutes. The resulting mixture was stirred overnight. When the reaction was completed, brine (20 mL) was added carefully and the resulting mixture was extracted with EtOAc (100 mL). The organic phase was washed with brine (3 x 50 mL), dried over Na₂SO₄, and concentrated in *vacuo*. The residue was purified by flash chromatography (MeOH/EtOAc: 1/40) to give a yellowish oil (2.3 g, 90% yield). $[\alpha]_D^{25} = +137.4$ (c 0.86 CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ

8.77 (d, $J = 5.2$ Hz, 1H), 8.05 (d, $J = 9.2$ Hz, 1H), 7.49 (d, $J = 4.0$ Hz, 1H), 7.40-7.31 (m, 7H), 6.00-5.92 (m, 1H), 5.23 (br, 1H), 5.02-5.00 (m, 1H), 4.97 (s, 1H), 4.49-4.37 (AB, 2H), 3.90 (s, 3H), 3.26 (m, 1H), 3.09-3.08 (m, 1H), 2.93-2.71 (m, 3H), 2.26-2.22 (m, 1H), 2.11-2.05 (m, 1H), 1.75 (br, 1H), 1.51-1.43 (m, 2H), 1.29-1.24 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.7, 147.6, 144.8, 144.7, 140.7, 137.8, 131.9, 128.3, 127.9, 127.7, 127.5, 121.7, 119.1, 114.3, 101.2, 80.9, 71.2, 60.1, 55.5, 50.1, 49.5, 40.1, 28.1, 26.6, 22.4; IR (CHCl_3) ν 2935, 2869, 1620, 1589, 1507, 1240, 1029.

General Procedure for the Preparation of QD-4a, QD-4b, QD-4c and Q-4a:³

Under N_2 atmosphere, a suspension of the starting cinchona alkaloid derivative (8.0 mmol) and NaSEt (4 equiv.) in dry DMF (50 ml, freshly distilled from the suspension of CaH_2 in DMF) was stirred at 110 °C until a TLC analysis showed that the starting material was completely consumed (4-6 hours). The reaction mixture was cooled down to room temperature, mixed with sat. NH_4Cl (40 ml) and H_2O (50 ml). The pH value of the solution was determined to be around 7. The resulting mixture was extracted with EtOAc (2 x 200 mL). The organic phase was washed with brine (4 x 50 ml), dried over Na_2SO_4 , and concentrated in *vacuo*. The residue was subjected to flash chromatography to afford the desired product.

QD-4a was obtained as a yellowish solid in 92% yield from quinidine after flash chromatography (elution gradient: Ethyl Acetate/MeOH / Et_3N = 100/2/3). $[\alpha]_{\text{D}}^{25} = +240.3$ (c 1.13, EtOH); ^1H NMR (400 MHz, CD_3OD) δ 8.58 (d, $J = 4.4$ Hz, 1H), 7.88 (d, $J = 9.2$ Hz, 1H), 7.62 (d, $J = 5.2$ Hz, 1H), 7.31 (dd, $J = 2.4$ Hz, 9.2 Hz, 1H), 7.25 (d, $J = 2.4$ Hz, 1H), 6.10-6.19 (m, 1H), 5.58 (d, $J = 2.8$ Hz, 1H), 5.10 (d, $J = 18.8$ Hz, 1H), 5.06 (d, $J = 10.4$ Hz, 1H), 3.60 (ddd, $J = 2.0$ Hz, 8.0 Hz, 13.6 Hz, 1H), 3.03 (dt, $J = 2.4$ Hz, 9.2 Hz, 1H), 2.87-2.94 (m, 2H), 2.74-2.82 (m, 1H), 2.30 (dt, $J = 8.8$ Hz, 8.4 Hz, 1H), 2.18-2.23 (m, 1H), 1.71 (br, 1H), 1.50-1.58 (m, 2H), 1.00-1.07 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.0, 149.8, 147.4, 143.9, 141.6, 131.4, 128.4, 123.3, 119.7, 115.2, 105.1, 72.2, 60.6, 50.8, 50.4, 41.3, 29.7, 27.0, 21.2; IR (CHCl_3) ν 3062, 2929, 2300-3500 (br), 1616, 1505, 1229, 739 cm^{-1} ; HRMS (FAB) m/z calcd for ($\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_2 + \text{H}^+$): 311.1760, found: 311.1755.

QD-4b was obtained as a yellowish powder in 87% yield from **QD-Bn** after flash chromatography (elution gradient: Ethyl Acetate/MeOH = 50/1 to 10/1). $[\alpha]_{\text{D}}^{25} = 154.7$ (c 1.05, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 10.92 (br, 1H), 8.67 (d, $J = 4.4$ Hz, 1H), 8.01 (d, $J = 9.2$ Hz, 1H), 7.86 (s, 1H), 7.44 (br, 1H), 7.35 (dd, $J = 2.4$ Hz, 8.8 Hz, 1H), 7.24-7.28 (m, 5H), 5.97-5.89 (m, 1H), 5.53 (br, 1H), 4.97 (d, $J = 10.0$ Hz, 1H), 4.94 (s,

1H), 4.34-4.25 (AB, 2H), 3.56 (br, 1H), 3.05-3.03 (m, 2H), 2.87-2.78 (m, 2H), 2.26-2.24 (m, 2H), 1.74 (br, 1H), 1.52-1.39 (m, 2H), 1.13 (br, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 157.0, 146.5, 143.6, 139.9, 137.7, 131.3, 128.3, 127.9, 127.8, 127.7, 127.6, 123.4, 114.9, 106.7, 79.0, 71.2, 59.0, 49.7, 49.2, 39.6, 28.0, 25.9. IR (CHCl₃) ν 2400-3500 (br.), 2939, 2873, 1617, 1590, 1511, 1468, 1240, 1068, 750 cm⁻¹; HRMS (ESI) m/z calcd for (C₂₆H₂₈N₂O₂ + H⁺): 401.2229, found: 401.2229.

QD-4c was obtained as a yellowish solid in 91% yield from **QD-PHN** after flash chromatography (elution gradient: Ethyl Acetate/MeOH = 20/1). [α]_D²⁵ = -304.6 (c 0.98, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 8.69-8.67 (m, 1H), 8.63-8.61 (m, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 8.20 (d, 1H, *J* = 2.0 Hz, 1H), 7.78 (d, *J* = 9.2 Hz, 1H), 7.74-7.70 (m, 2H), 7.35 (d, *J* = 5.2 Hz, 1H), 7.25-7.26 (m, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.80 (t, *J* = 7.2 Hz, 1H), 6.64 (s, 1H), 6.50 (d, *J* = 7.2 Hz, 1H), 6.33 (s, 1H), 6.23-6.15 (m, 1H), 5.27 (d, *J* = 14.4 Hz, 1H), 5.12 (d, *J* = 17.2 Hz, 1H), 3.58-3.53 (m, 1H), 3.36 (t, *J* = 9.2 Hz, 1H), 3.09-2.99 (m, 2H), 2.79-2.68 (m, 2H), 2.30-2.28 (m, 1H), 2.00 (br, 1H), 1.54-1.52 (m, 2H), 1.43-1.34 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 157.0, 149.6, 146.9, 143.7, 142.4, 139.4, 131.9, 131.8, 131.5, 127.3, 127.2, 127.1, 126.6, 126.4, 126.3, 126.1, 124.5, 123.4, 122.8, 122.6, 121.9, 117.5, 115.3, 106.1, 105.0, 76.8, 59.2, 49.7, 49.5, 38.8, 27.4, 25.7, 20.3; IR (CHCl₃) ν 3300-2800 (br), 3070, 2939, 2870, 1622, 1506, 1455, 1225, 1115, 753 cm⁻¹; HRMS (ESI) m/z calcd for (C₃₃H₃₀N₂O₂ + H⁺): 487.2386, found: 487.2370.

Q-4a was obtained as a white solid in 80% yield from quinine after flash chromatography (elution gradient: Ethyl Acetate/MeOH/Et₃N = 100/2/3). [α]_D²⁵ = -162.8 (c 0.93, EtOH); ¹H NMR (400 MHz, CD₃OD) δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 7.61 (d, *J* = 4.8 Hz, 1H), 7.32 (dd, *J* = 2.4 Hz, 9.2 Hz, 1H), 7.28 (d, *J* = 2.4 Hz, 1H), 5.69-5.78 (m, 1H), 5.51 (d, *J* = 3.2 Hz, 1H), 4.95 (d, *J* = 17.2 Hz, 1H), 4.88 (d, *J* = 9.2 Hz, 1H), 3.66-3.73 (m, 1H), 3.05-3.13 (m, 2H), 2.63-2.74 (m, 2H), 2.34 (br, 1H), 1.80-1.89 (m, 2H), 1.77-1.78 (m, 1H), 1.54-1.61 (m, 1H), 1.39-1.46 (m, 1H); ¹³C NMR (100 MHz, CD₃OD) δ 157.9, 149.8, 147.4, 144.0, 142.6, 131.4, 128.4, 123.3, 119.8, 115.0, 105.1, 72.2, 60.9, 57.6, 48.4, 44.2, 40.9, 29.2, 28.1, 21.8; IR (CHCl₃) ν 3055, 2937, 2870, 2300-3500 (br), 1616, 1457, 1236, 1067 cm⁻¹; HRMS (FAB) m/z calcd. for (C₁₉H₂₂N₂O₂ + H⁺): 311.1760, found: 311.1761.

Preparation of Racemic adducts (6a-r): At room temperature to a solution of a nitroalkene (0.1 mmol) in THF (1.0 M) was added dimethyl malonate (34 μL, 3 eq.) and base [for aryl substituted **5a-5o**, DABCO (20 mol%) was used; for alkyl substituted **5p-r**, KOBu^t (5 mol%) was used]. After the reaction went to completion, the reaction mixture was diluted with ethyl acetate, washed with HCl (1.0 N, aq.) and brine. The organic layer was dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography.

General procedure for enantioselective Michael addition of dimethyl malonate to nitroalkenes:

At -20°C, to a solution of a nitroalkene (0.2 mmol) in THF (0.2 mL) was added dimethyl malonate (68 μ L, 3 eq.) and the chiral catalyst (6.2 mg, 10 mol%). The resulting mixture was kept at -20 °C until **5** is consumed. The reaction mixture was then passed through a plug of silica gel for the removal of the catalyst (eluent: ether or ethyl acetate). The filtrate was concentrated in *vacuo* and the residue was purified by flash chromatography.

(S)-(+)-6a

(S)-(+)-Methyl 2-carbomethoxy-4-nitro-3-phenyl-butyrate (S)-(+)-6a. This product was obtained as a colorless oil in 97 % yield after flash chromatography (elution gradient: Ethyl Acetate / Hexane = 1/15 to 1/10) and 96 % ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 70:30, 0.9 ml/min, λ 220 nm, *t* (major) = 11.6 min, *t* (minor) = 13.7 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = +5.9$ (c 1.02, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.22 (m, 5H), 4.95-4.85 (m, 2H), 4.25 (dt, *J* = 5.2 Hz, 8.8 Hz, 1H), 3.86 (d, *J* = 9.2 Hz, 1H), 3.77 (s, 3H), 3.57 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.8, 167.2, 136.1, 128.9, 128.3, 127.8, 77.3, 54.7, 52.9, 52.7, 42.9; IR (CHCl₃) ν 3034, 2957, 1732, 1557, 1435, 1259 cm⁻¹; HRMS (CI) *m/z* calcd. for (C₁₃H₁₅NO₆ + H⁺) 282.0964, found 282.0969.

The absolute configuration of (+)-6a was determined to be S isomer by comparing the specific optical rotation with literature value⁴. $[\alpha]_D^{25} = +5.9$ (c 1.02, CHCl₃) for 96% ee [lit. $[\alpha]_D^{25} = +4.40$ (c 1.02, CHCl₃) 93% ee].

(-)-Methyl 2-carbomethoxy-4-nitro-3-phenyl-butyrate R-(-)-6a. This product was obtained as a colorless oil in 99 % yield and 93 % ee from a reaction catalyzed by **QD-4a** (10 mol %) at -20 °C for 36 hours.

6b

(+)-Methyl 2-carbomethoxy-4-nitro-3-(4-fluoro-phenyl)-butyrate (+)-6b. This product was obtained as a colorless oil in 97 % yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/12 to 1/6) and 97% ee as determined by HPLC analysis [Chiralpak AD, Hexanes:IPA, 70:30, 1.0 ml/min, λ 220 nm, *t* (minor)= 7.6 min, *t*(major)= 12.4 min] from a reaction catalyzed by **Q-4a** (10 mol%) at - 20 ° C for 36 hours. $[\alpha]_D^{25} = +6.2$ (c 1.04, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.22 (dd, *J* = 4.8 Hz, 8.4 Hz, 2H), 7.02 (t, *J* = 8.4 Hz, 2H), 4.91 (dd, *J* = 4.8 Hz, 12.8 Hz, 1H), 4.84 (dd, *J* = 9.2 Hz, 12.8 Hz, 1H), 4.24 (dt, *J* = 5.6 Hz, 9.2 Hz, 1H), 3.82 (d, *J* = 9.2 Hz, 1H), 3.77 (s, 3H), 3.58 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 167.1, 163.7, 161.2, 131.84, 131.80, 129.68, 129.60, 116.1, 115.9, 77.4, 54.6, 53.0, 52.9, 42.2; IR (CHCl₃) ν 3011, 2958, 2915, 1733, 1606, 1557,

1436, 1231 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{13}\text{H}_{14}\text{FNO}_6 + \text{H}^+$): 300.0883, found 300.0886.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(4-fluoro-phenyl)-butyrate (-)-6b. This product was obtained as a colorless oil in 97 % yield and 94 % ee from a reaction catalyzed by **QD-4a** (10 mol %) at -20 °C for 36 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(4-chloro-phenyl)-butyrate. (+)-6c This product was obtained as a white solid in 97% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/10 to 1/8) and 97% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 70:30, 1.0 ml/min, λ 220 nm, t (major) = 10.5 min, t (minor) = 15.6 min]

from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_{\text{D}}^{25} = +7.5$ (c 1.08, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.31 (d, $J = 8.4$ Hz, 2H), 7.18 (d, $J = 8.4$ Hz, 2H), 4.91 (dd, $J = 4.8$ Hz, 12.8 Hz, 1H), 4.85 (dd, $J = 8.4$ Hz, 13.6 Hz, 1H), 4.23 (dt, $J = 4.8$ Hz, 9.2 Hz, 1H), 8.83 (d, $J = 9.2$ Hz, 1H), 3.77 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 167.0, 134.6, 134.4, 129.3, 129.2, 77.1, 54.4, 53.0, 52.9, 42.3; IR (CHCl_3) ν 3011, 2956, 1736, 1653, 1557, 1494, 1436, 1259, 1015 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{13}\text{H}_{14}\text{ClNO}_6 + \text{H}^+$): 316.0583, found 316.0582.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(4-chloro-phenyl)butyrate (-)-6c This product was obtained as a white solid in 97 % yield and 94 % ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 36 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(4-bromo-phenyl)-butyrate (+)-6d This product was obtained as a white solid in 99% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/10 to 1/6) and 96% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 60:40, 1.0 ml/min, λ 220 nm, t (major) = 9.6 min, t (minor) = 12.9 min]

from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_{\text{D}}^{25} = +6.9$ (c 1.12, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, $J = 8.4$ Hz, 1H), 7.12 (d, $J = 8.8$ Hz, 1H), 4.91 (dd, $J = 5.6$ Hz, 13.6 Hz, 1H), 4.85 (dd, $J = 9.2$ Hz, 13.6 Hz, 1H), 4.22 (dt, $J = 4.8$ Hz, 9.2 Hz, 1H), 3.82 (d, $J = 9.2$ Hz, 1H), 3.77 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 167.0, 135.1, 132.2, 129.6, 122.5, 77.1, 54.4, 53.1, 52.9, 42.3; IR (CHCl_3) ν 2952, 1734, 1653, 1558, 1507, 1436 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{13}\text{H}_{14}\text{BrNO}_6 + \text{H}^+$): 360.0083, found 360.0082.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(4-bromo-phenyl)-butyrate (-)-6d This product was obtained as a white solid in 98% yield and 94% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 36 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(4-methylphenyl) butyrate (+)-6e This product was obtained as a colorless oil in 97 % yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/15 to 1/10) and 98% ee as determined by HPLC analysis

[Daicel chiralcel OD, Hexanes:IPA, 70:30, 1.0 ml/min, λ 220 nm, $t(\text{major}) = 9.8$ min, $t(\text{minor}) = 11.0$ min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20°C for 36 hours. $[\alpha]_{\text{D}}^{25} = +3.0$ (c 1.40, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.14-7.09 (m, 4H), 4.93-4.82 (m, 2H), 4.20 (dt, $J = 9.2$ Hz, 5.6 Hz, 1H), 3.85 (d, $J = 9.2$ Hz, 1H), 3.76 (s, 3H), 3.58 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.9, 167.2, 138.1, 132.9, 129.7, 127.6, 77.5, 54.7, 52.9, 52.8, 42.5, 21.1; IR (CHCl_3) ν 3018, 2956, 1736, 1557, 1436, 1259 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{14}\text{H}_{17}\text{NO}_6 + \text{H}^+$): 296.1134, found 296.1141.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(4-methylphenyl)-butyrate (-)-6e This product was obtained as a colorless oil in 97% yield and 94% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20°C for 44 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(4-isopropenylphenyl)-butyrate (+)-6f This product was obtained as a white solid in 95% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/20 to 1/10) and 97% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 70:30, 1.0 ml/min, λ 220 nm, $t(\text{major}) = 10.1$ min, $t(\text{minor}) = 13.4$ min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20°C for 36 hours. $[\alpha]_{\text{D}}^{25} = +4.7$ (c 1.08, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.15 (dd, $J = 8.0$ Hz, 14.0 Hz, 4H), 4.94-4.84 (m, 2H), 4.22 (dt, $J = 5.6$ Hz, 8.8 Hz, 1H), 3.85 (d, $J = 9.2$ Hz, 1H), 3.76 (s, 3H), 3.57 (s, 3H), 2.90-2.82 (m, 1H), 1.21 (d, $J = 7.6$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.9, 167.3, 148.9, 133.3, 127.7, 127.0, 77.4, 54.8, 52.9, 52.7, 42.5, 33.6, 23.8; IR (CHCl_3) ν 2960, 1735, 1558, 1436, 1259 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{16}\text{H}_{21}\text{NO}_6 + \text{H}^+$): 324.1447, found 324.1444.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(4-isopropenylphenyl)-butyrate (-)-6f This product was obtained as a white solid in 96% yield and 93% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20°C for 39 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(4-methoxyphenyl)-butyrate (+)-6g This product was obtained as a colorless oil in 90 % yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/15 to 1/10) and 97% ee as determined by HPLC analysis [Chiralpak AD, Hexanes:IPA, 60:40, 1.0 ml/min, λ 220 nm, $t(\text{minor}) = 7.6$ min, $t(\text{major}) = 11.9$ min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20°C for 44 hours. $[\alpha]_{\text{D}}^{25} = +5.0$ (c 1.18, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.14 (d, $J = 9.2$ Hz, 2H), 6.84 (d, $J = 8.8$ Hz, 2H), 4.89 (dd, $J = 4.8$ Hz, 12.8 Hz, 1H), 4.83 (dd, $J = 8.8$ Hz, 13.6 Hz, 1H), 4.19 (dt, $J = 4.8$ Hz, 13.2 Hz, 1H), 3.82 (d, $J = 9.2$ Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.9, 167.3, 159.4, 129.0, 127.8, 114.3, 77.6, 55.2, 54.8, 52.9, 52.8, 42.2; IR (CHCl_3) ν 3011, 2957, 2841, 1733, 1557, 1516, 1436, 1258, 1032 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{14}\text{H}_{17}\text{NO}_7 + \text{H}^+$): 312.1070, found 312.1076.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(4-methoxy-phenyl)butyrate (-)-6g This product was obtained as a colorless oil in 94% yield and 95% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 47 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(3-methylphenyl)-butyrate (+)-6h This product was obtained as a colorless oil in 97% yield after flash chromatography (elution gradient: Ethyl Acetate / Hexane = 1/15 to 1/10) and 97% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes : IPA, 92:8, 0.9 ml/min, λ 220 nm, t(major) = 19.8 min, t(minor) = 22.2 min]

from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = +1.0$ (c 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.21 (t, J = 7.2 Hz, 1H), 7.09 (d, J = 7.2 Hz, 1H), 7.02 (s, 1H), 7.01 (d, J = 7.2 Hz, 1H), 4.94-4.84 (m, 2H), 4.24-4.18 (dt, J = 5.6 Hz, 8.4 Hz, 1H), 3.86-3.84 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H), 3.58 (s, 3H), 2.32 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.9, 167.2, 138.6, 136.0, 129.1, 128.8, 128.6, 124.6, 77.3, 54.7, 52.9, 52.8, 42.8, 21.3; IR (CHCl₃) ν 3029, 2957, 1736, 1557, 1436, 1259 cm⁻¹; HRMS (CI) m/z calcd. for (C₁₄H₁₇NO₆ + H⁺): 296.1134, found 296.1141.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(3-methylphenyl)butyrate (-)-6h This product was obtained as a colorless oil in 99% yield and 93% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 36 hours.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(2-methylphenyl)-butyrate (-)-6i This product was obtained as a colorless oil in 95 % yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/15) and 98% ee as determined by HPLC analysis [Chiralpak AD, Hexanes:IPA, 80:20, 1.0 ml/min, λ 220 nm, t(minor) = 6.5 min, t(major) = 12.2 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = -1.6$ (c 1.25, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.17-7.11 (m, 4H), 4.94-4.83 (m, 2H), 4.57 (dt, J = 5.6 Hz, 9.2 Hz, 1H), 3.83 (d, J = 9.2 Hz, 1H), 3.77 (s, 3H), 3.54 (s, 3H), 2.44 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.9, 167.3, 136.9, 134.4, 131.2, 128.0, 126.5, 125.7, 77.3, 54.4, 52.9, 52.7, 37.7, 19.4; IR (CHCl₃) ν 3011, 2956, 1734, 1558, 1436, 1260 cm⁻¹; HRMS (CI) m/z calcd for (C₁₄H₁₇NO₆ + H⁺): 296.1134, found 296.1128.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(2-methylphenyl)butyrate (+)-6i This product was obtained as a colorless oil in 97% yield and 96% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 36 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(2-fluorophenyl)-butyrate (+)-6j This product was obtained as a colorless oil in 97% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/15 to 1/10) and 97% ee as determined by HPLC analysis [Chiralpak AD, Hexanes:IPA, 80:20, 1.0 ml/min, λ

220 nm, t (minor) = 8.2 min, t (major) = 10.1 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = +14.6$ (c 1.08, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.22 (m, 2H), 7.12-7.05 (m, 2H), 4.95-4.93 (d, *J* = 7.2 Hz, 2H), 4.46-4.4 (m, 1H), 4.00 (d, *J* = 9.6 Hz, 1H), 3.78 (s, 3H), 3.56 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.7, 167.1, 162.1, 159.7, 130.47, 130.44, 130.36, 130.3, 124.61, 24.58, 123.0, 122.9, 116.2, 116.0, 76.00, 75.98, 53.05, 52.99, 52.97, 52.81, 38.5; IR (CHCl₃) ν 3011, 2958, 2848, 1733, 1557, 1495, 1436, 1259 cm⁻¹; HRMS (CI) *m/z* calcd. for (C₁₃H₁₄FNO₆ + H⁺): 300.0883, found 300.0879.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(2-fluorophenyl)butyrate (-)-6j This product was obtained as a colorless oil in 94% yield and 95% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 36 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(2-nitrophenyl)butyrate (+)-6k This product was obtained as a yellowish oil in 90% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/9 to 1/6) and 97% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 50:50, 0.9 ml/min, λ 220 nm, t(major) = 8.5 min, t(minor) = 15.7 min] from a reaction catalyzed by **Q-4a**

(10 mol%) at -55 °C for 69 hours. $[\alpha]_D^{25} = +18.9$ (c 1.04, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.95 (dd, *J* = 1.2 Hz, 8.8 Hz, 1H), 7.60 (dt, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.49 (dt, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.41 (dd, *J* = 1.2 Hz, 8.0 Hz, 1H), 5.17 (dd, *J* = 8.0 Hz, 14.0 Hz, 1H), 5.06 (dd, *J* = 4.0 Hz, 14.0 Hz, 1H), 4.77 (td, *J* = 4.0 Hz, 8.0 Hz, 1H), 4.25 (d, *J* = 8.0 Hz, 1H), 3.77 (s, 3H), 3.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 167.0, 149.8, 133.3, 131.1, 129.3, 128.7, 125.4, 75.9, 53.4, 53.11, 53.08, 37.4; IR (CHCl₃) ν 3018, 2958, 1733, 1558, 1436, 1361 cm⁻¹; HRMS (CI) *m/z* calcd. for (C₁₃H₁₄N₂O₈ + H⁺): 327.0828, found 327.0822.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(2-nitrophenyl)butyrate (-)-6k This product was obtained as a yellowish oil in 88% yield and 92% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -55 °C for 72 hours.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(1-naphthyl)butyrate (-)-6l

This product was obtained as a colorless oil in 99% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/10) and 98% ee as determined by HPLC analysis [Chiralpak AD, Hexanes:IPA, 80:20, 1.0 ml/min, λ 280 nm, t(minor) = 9.5 min, t(major) = 13.7 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = -3.8$ (c 1.32, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 8.18 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.45-7.28 (m, 2H), 5.24-5.05 (m, 3H), 4.13-4.10 (d, *J* = 7.2 Hz, 1H), 3.72 (s, 3H), 3.55 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.9, 167.4, 134.1, 132.2, 130.9, 129.2, 128.9, 127.0, 126.1, 125.1, 123.9, 122.1, 76.6, 54.3, 52.9, 36.7; IR (CHCl₃) ν 3040, 3011, 2955, 1734, 1557, 1436, 1252, 1028 cm⁻¹; HRMS (CI) *m/z* calcd. for (C₁₇H₁₇NO₆ + H⁺): 311.1056, found 311.1055.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(1-naphthyl)butyrate (+)-6l This product was obtained as a colorless oil in 99% yield and 92% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 36 hours.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(2-thienyl)butyrate (-)-6m

This product was obtained as a colorless oil in 99% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/15 to 1/10) and 98% ee as determined by HPLC analysis [Chiralpak AD, Hexanes:IPA, 80:20, 1.0 mL/min, λ 220 nm, t (minor) = 8.8 min, t (major) = 10.6 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = -7.8$ (c 2.70, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.24 (d, $J = 5.2\text{ Hz}$, 1H), 6.96-6.93 (m, 2H), 4.98-4.89 (m, 2H), 4.60-4.54 (dt, $J = 5.2\text{ Hz}$, 8.0 Hz, 1H), 3.92 (d, $J = 7.2\text{ Hz}$, 1H), 3.77 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 167.1, 138.3, 127.1, 126.7, 125.6, 77.8, 55.2, 53.1, 53.0, 38.3; IR (CHCl_3) ν 3099, 3003, 2957, 1733, 1557, 1436, 1264 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{11}\text{H}_{13}\text{NO}_6\text{S} + \text{H}^+$): 288.0528, found 288.0530.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(2-thienyl)butyrate (+)-6m This product was obtained as a colorless oil in 96% yield and 95% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 44 hours.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(2-furyl)butyrate (-)-6n

This product was obtained as a yellowish oil in 97% yield after flash chromatography (elution gradient: Ethyl Acetate / Hexane = 1/15) and 98% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 60:40, 1.0 ml/min, λ 220 nm, t (major) = 6.2 min, t (minor) = 14.9 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = -4.9$ (c 1.10, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.35 (d, $J = 1.6\text{ Hz}$, 1H), 6.30 (dd, $J = 1.6\text{ Hz}$, 3.2 Hz, 1H), 6.23 (d, $J = 3.2\text{ Hz}$, 1H), 4.96-4.86 (m, 2H), 4.39 (dt, $J = 4.8\text{ Hz}$, 8.0 Hz, 1H), 3.95 (d, $J = 8.0\text{ Hz}$, 1H), 3.77 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.5, 167.2, 149.3, 142.8, 110.5, 108.4, 75.2, 53.03, 52.99, 52.5, 36.7; IR (CHCl_3) ν 3018, 2958, 1733, 1558, 1436, 1263, 1014 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{11}\text{H}_{13}\text{NO}_7 + \text{H}^+$): 272.0770, found 272.0768.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(2-furyl)butyrate (+)-6n This product was obtained as a yellowish oil in 99% yield and 96% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20 °C for 36 hours.

(+)-Methyl 2-carbomethoxy-4-nitro-3-(3-pyridinyl)butyrate (+)-6o

This product was obtained as a white solid in 98% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/2 to 1/1) and 96% ee as determined by HPLC analysis [Chiralpak AD, Hexanes:IPA, 60:40, 1.0 ml/min, λ 220 nm, t (minor) = 6.6 min, t (major) = 9.2 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20 °C for 36 hours. $[\alpha]_D^{25} = +3.3$ (c 1.30, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ : 8.56 (dd, $J = 1.6\text{ Hz}$, 4.8

Hz, 1H), 8.54 (d, $J = 2.8$ Hz, 1H), 7.61 (dt, $J = 8.0$ Hz, 2.0 Hz, 1H), 7.28 (dd, $J = 4.8$ Hz, 8.0 Hz, 1H), 4.99-4.88 (m, 2H), 4.28 (dt, $J = 5.2$ Hz, 9.2 Hz, 1H), 3.88 (d, $J = 9.2$ Hz, 1H), 3.78 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.4, 166.9, 149.8, 149.6, 135.3, 131.9, 123.6, 76.7, 54.1, 53.2, 53.0, 40.5; IR (CHCl_3) ν 3025, 2957, 1733, 1558, 1435, 1265, 1025 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_6 + \text{H}^+$): 283.0930, found 283.0923.

(-)-Methyl 2-carbomethoxy-4-nitro-3-(3-pyridinyl)butyrate (-)-6o This product was obtained as a white solid in 99% yield and 92% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20°C for 36 hours.

(+)-Methyl 2-carbomethoxy-3-nitromethyloctanoate (+)-6p

This product was obtained as a colorless oil in 81% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/20) and 94% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 90:10, 1.0 ml/min, λ 215 nm, t (major) = 6.1 min, t (minor) = 12.3 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20°C for 72 hours. $[\alpha]_{\text{D}}^{25} = +7.6$ (c 1.75, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 4.71 (dd, $J = 5.6$ Hz, 13.2 Hz, 1H), 4.53 (dd, $J = 6.8$ Hz, 13.6 Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.68 (d, $J = 5.6$ Hz, 1H), 2.92-2.87 (m, 1H), 1.48-1.42 (m, 2H), 1.39-1.26 (m, 6H), 0.88 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.4, 168.2, 76.5, 52.8, 52.7, 52.3, 36.9, 31.3, 29.9, 26.2, 22.3, 13.9; IR (CHCl_3) ν 2957, 2929, 1735, 1558, 1436, 1160 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{12}\text{H}_{21}\text{NO}_6 + \text{H}^+$): 276.1447, found 276.1446.

(-)-Methyl 2-carbomethoxy-3-nitromethyloctanoate (-)-6p This product was obtained as a colorless oil in 82% yield and 91% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20°C for 72 hours.

(+)-Methyl 2-carbomethoxy-5-methyl-3-nitromethylhexanoate (+)-6q

This product was obtained as a colorless oil in 86 % yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/20) and 94 % ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 90:10, 1.0 ml/min, λ 215 nm, t (major) = 5.6 min, t (minor) = 11.2 min] from a reaction catalyzed by **Q-4a** (10 mol%) at -20°C for 72 hours. $[\alpha]_{\text{D}}^{25} = +9.0$ (c 2.05, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 4.68 (dd, $J = 4.8$ Hz, 13.6 Hz, 1H), 4.49 (dd, $J = 6.4$ Hz, 13.6 Hz, 1H), 3.740 (s, 3H), 3.736 (s, 3H), 3.63 (d, $J = 5.6$ Hz, 1H), 2.96-2.91 (m, 1H), 1.65-1.58 (m, 1H), 1.32-1.22 (m, 2H), 0.90-0.88 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.4, 168.2, 76.7, 52.8, 52.7, 52.3, 38.9, 34.9, 25.1, 22.3, 22.1; IR (CHCl_3) ν 2959, 2878, 1732, 1557, 1436, 1161, 1027 cm^{-1} ; HRMS (CI) m/z calcd. for ($\text{C}_{11}\text{H}_{19}\text{NO}_6 + \text{H}^+$): 262.1291, found 262.1297.

(-)-Methyl 2-carbomethoxy-5-methyl-3-nitromethylhexanoate (-)-6q This product was obtained as a colorless oil in 84% yield and 92% ee from a reaction catalyzed by **QD-4a** (10 mol%) at -20°C for 72 hours.

This product was obtained as a colorless oil in 71 % yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/20) and 94% ee as determined by HPLC analysis [Daicel chiralcel OD, Hexanes:IPA, 90:10, 1.0 ml/min, λ 215 nm, t (major) = 6.0 min, t (minor) = 14.8 min] from a reaction catalyzed by **Q-4a** (20 mol%) at -20 °C for 108 hours. $[\alpha]_D^{25} = +12.0$ (c 0.95, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 4.73 (dd, $J = 4.4$ Hz, 14.8 Hz, 1H), 4.62 (dd, $J = 6.8$ Hz, 14.8 Hz, 1H), 3.77-3.75 (m, 7H), 2.92-2.88 (m, 1H), 1.78-1.59 (m, 5H), 1.49-1.42 (m, 1H), 1.26-1.10 (m, 3H), 1.07-0.95 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 168.9, 168.6, 75.4, 52.9, 52.7, 50.9, 42.1, 39.6, 30.1, 29.8, 26.22, 26.17, 25.9; IR (CHCl₃) ν 2931, 2855, 1735, 1557, 1436, 1160, 1024 cm⁻¹; HRMS (CI) m/z calcd. for (C₁₃H₂₁NO₆ + H⁺): 288.1447, found 288.1443.

(-)-Methyl 2-carbomethoxy-4-nitro-3-cyclohexylbutyrate (-)-6r This product was obtained as a colorless oil in 80% yield and 91% ee from a reaction catalyzed by **QD-4a** (20 mol%) at -20 °C for 108 hours.

Ethyl 2-acetyl-4-3-phenylbutyrate 8 This product was obtained as a white solid in 93% yield after flash chromatography (elution gradient: Ethyl Acetate/Hexane = 1/10 to 1/5) as a ~ 1/1 mixture of two compounds which are diastereomeric at the ester-bearing stereocenter (which agrees with the literature report⁴) and 91% ee as determined by HPLC analysis [Daicel chiralpak AD, Hexanes:ethanol, 90:10, 0.8 ml/min, λ 210 nm, t(major) = 12.8 min, 19.8 min, t(minor) = 17.3 min, 22.3min] from a reaction catalyzed by **Q-4a** (10 mol%) at 23 °C for 6 hours.

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 (**5a**) was established by using a large excess of Dimethyl malonate (5 equiv) and 10 mol% **QD-4a**. Plotting in ln[**5a**] versus time gives a straight line ($R^2 = 0.9999$, Figure A), thus establishing first-order dependence in nitroalkene **5a**.

Order in dimethyl malonate was established by using a large excess of nitroalkene (**5a**, 5 equiv) and 10 mol% **QD-4a**. In this case, the reaction was monitored by following the formation of the product (at peak 1557 cm⁻¹). Plotting in ln[Dimethyl malonate] versus time gives a straight line ($R^2 = 0.9975$, Figure C), thus establishing the first-order dependence in malonate.

The reaction order in catalyst was established by determining the rate constants (k_{obs}) at various catalyst concentrations. A plot of the rate constants k_{obs} versus the catalyst

loading gives a straight line for **QD-4a** ($R^2 = 0.99$, Figure F), indicating the first-order dependence on catalyst.

General procedure for kinetic study:

A mixture of Nitroalkene (**5a**) (1.0 mmol) and **QD-4a** (5-15 mol%) in anhydrous THF (1.0 mL) was stirred at room temperature for 5 minutes, and then dimethyl malonate (0.57ml, 5eq) was introduced in one portion via a syringe. The resulting reaction mixture was monitored every 2 minutes for 6 hours.

Figure A. Determination of the order of Nitroalkene (**5a**)

Figure A shows a linear relationship between $\ln[5a]$ and time, indicating the reaction is first order in **5a**.

Figure B. Determination of the order of Nitroalkene (**5a**)

Figure B shows clearly a nonlinear relationship between $1/[5a]$ and time, indicating the reaction is NOT second order in **5a**

Figure C. Determination of the order of Dimethyl malonate.

Figure C shows a linear relationship between $\ln[\text{dimethyl malonate}]$ and time, indicating the reaction is first order in dimethyl malonate.

Figure D. Determination of the order of dimethyl malonate.

Figure D shows clearly nonlinear relationship between $1/[\text{dimethyl malonate}]$ and time, indicating the reaction is NOT second order in dimethyl malonate

Figure E. Kinetic profiles for the catalyst QD-4a

5.0 mol% catalyst	$k_{\text{obs}} = 0.01635$	$R^2 = 0.9999$
7.5 mol% catalyst	$k_{\text{obs}} = 0.0189$	$R^2 = 0.9999$
10.0 mol% catalyst	$k_{\text{obs}} = 0.02414$	$R^2 = 0.9999$
12.5 mol% catalyst	$k_{\text{obs}} = 0.0259$	$R^2 = 0.9997$
15.0 mol% catalyst	$k_{\text{obs}} = 0.03115$	$R^2 = 0.9999$

Figure F. Kinetic rate constant (k_{obs}) of different concentration of QD-4a

Figure F shows the linear relationship between the kinetic rate constant (k_{obs}) and the loading of the catalyst, indicating the reaction is first order in catalyst **QD-4a**.

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 Smith, A. B.; Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4015-4018.

⁴ Ji, J.; Barnes, D. M.; Zhang, J.; King, S. A.; Wittenberger, S. J.; Morton, H. *J. Am. Chem. Soc.* **1999**, *121*, 10215-10216.

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 70:30, 0.9 mL/min, λ 220 nm

Racemic **6a**

(+)-**6a** 96% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6a** 93% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Chiralpak AD, Hexane:IPA, 70:30, 1.0 mL/min, λ 220 nm

(+)-**6b** 97% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6b** 94% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 70:30, 1.0 mL/min, λ 220 nm

(+)-**6c** 97% ee
Product of **Q 4a**
catalyzed reaction

(-)-**6c** 94% ee
Product of **Q D 4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 60:40, 1.0 mL/min, λ 220 nm

(+)-**6d** 96% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6d** 94% ee
Product of **Q D-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 70:30, 1.0 mL/min, λ 220 nm

(+)-**6e** 98% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6e** 94% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 70:30, 0.9 mL/min, λ 220 nm

Racemic 6f

(+)-6f 97% ee
Product of Q 4a
catalyzed reaction

(-)-6f 93% ee
Product of Q D 4a
catalyzed reaction

HPLC Conditions: Chiralpak AD, Hexane:IPA, 60:40, 1.0 mL/min, λ 220 nm

Racemic **6g**

(+)-**6g** 97% ee
Product of **Q-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 92:8, 0.9 mL/min, λ 220 nm

Racemic **6h**

(+)-**6h** 97% ee
Product of **QD-4a**
catalyzed reaction

(-)-**6h** 93% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Chiralpak AD, Hexane:IPA, 80:20, 1.0 mL/min, λ 220 nm

Racemic **6i**

(-)-**6i** 98% ee
Product of **Q-4a**
catalyzed reaction

(+)-**6i** 96% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Chiralpak AD, Hexane:IPA, 80:20, 1.0 mL/min, λ 220 nm

(+)-**6j** 97% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6j** 95% ee
Product of **QD-4a**
catalyzed reaction

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

RT	AREA	TYPE	WIDTH	AREA
8.235	10655088	BB	.416	50.14016
10.107	10595520	BB	.487	49.85988

TOTAL AREA=2.1261E+07
MUL FACTOR=1.0000E+00

RUN# 6501 FEB 7, 2004 13:15:10
PEAK FILE : M:SIGNAL.PRA

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

RT	AREA	TYPE	WIDTH	AREA
8.225	1034248	BB	.408	1.36616
10.102	13242668	BB	.502	98.63386

TOTAL AREA=1.3426E+08
MUL FACTOR=1.0000E+00

RUN# 6500 FEB 7, 2004 13:33:24
PEAK FILE : M:SIGNAL.PRA

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

RT	AREA	TYPE	WIDTH	AREA
8.249	23110000	BB	.391	97.45546
10.115	603409	BB	.465	2.54457

TOTAL AREA=2.3714E+07
MUL FACTOR=1.0000E+00

RUN# 6503 FEB 7, 2004 15:13:45
PEAK FILE : M:SIGNAL.PRA

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 50:50, 0.9 mL/min, λ 220 nm

(+)-**6k** 97% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6k** 92% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Chiralpak AD, Hexane:IPA, 80:20, 1.0 mL/min, λ 280 nm

(-)-**61** 98% ee
Product of **Q-4a**
catalyzed reaction

(+)-**61** 92% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Chiralpak AD, Hexane:IPA, 80:20, 1.0 mL/min, λ 220 nm

Racemic **6m**

(-)-6m 98% ee
Product of **Q-4a**
catalyzed reaction

(+)-6m 95% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 60:40, 1.0 mL/min, λ 220 nm

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

RUN# 6337 JAN 25, 2004 17:16:47

PEAK FILE : M:\SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
6.324	19009320	SPB	278	50	30157
15.120	18781408	PB	594	49	63945

TOTAL AREA=3.7791E+07
 MUL FACTOR=1.0000E+00

(-)-6n 98% ee
 Product of **Q-4a**
 catalyzed reaction

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

RUN# 6335 JAN 25, 2004 16:05:42

PEAK FILE : M:\SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
6.250	119394600	SPB	262	98	97024
14.961	1242283	PB	593	1	02977

TOTAL AREA=1.2064E+08
 MUL FACTOR=1.0000E+00

(+)-6n 96% ee
 Product of **QD-4a**
 catalyzed reaction

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

RUN# 6336 JAN 25, 2004 16:24:58

PEAK FILE : M:\SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
6.299	3546448	PB	273	1	03329
14.917	183770000	SPB	605	98	10672

TOTAL AREA=1.8732E+08
 MUL FACTOR=1.0000E+00

HPLC Conditions: Chiralpak AD, Hexane:IPA, 60:40, 1.0 mL/min, λ 220 nm

(+)-**6o** 96% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6o** 92% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 90:10, 1.0 mL/min, λ 215 nm

Racemic **6p**

(+)-**6p** 94% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6p** 91% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 90:10, 1.0 mL/min, λ 215 nm

Racemic **6q**

(+)-**6q** 94% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6q** 92% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 90:10, 1.0 mL/min, λ 215 nm

(+)-**6r** 94% ee
Product of **Q-4a**
catalyzed reaction

(-)-**6r** 91% ee
Product of **QD-4a**
catalyzed reaction

HPLC Conditions: Daicel chiralpak AD, Hexane:Ethanol, 90:10, 0.8 mL/min, λ 210 nm

Racemic 8

8 91% ee as an around 1:1 mixture of diastereomer product of **Q-4a** catalyzed reaction