Supporting Information-I

Rawal's Catalyst as an Effective Stimulant for the Highly Asymmetric Michael Addition of β-Keto Esters to Functionally Rich Nitro-olefins

A. Suresh Kumar, T. Prabhakar Reddy, R. Madhavachary, and Dhevalapally B. Ramachary*

Catalysis Laboratory, School of Chemistry, University of Hyderabad, Central University (P.O.), Hyderabad 500 046, India

E-mail: ramsc@uohyd.ernet.in or ramchary.db@gmail.com

General Methods: The ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS (δ = 0) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0) for ^{13}C NMR. *In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment, and is given in parentheses.* The coupling constants *J* are given in Hz. Column chromatography was performed using Acme's silica gel (particle size 0.063-0.200 mm). High-resolution mass spectra (HRMS) were recorded on ESI-TOF maXis. IR spectra were recorded on JASCO FT/IR-5300. Elemental analyses were recorded on a Thermo Finnigan Flash EA 1112 analyzer. Mass spectra were recorded on either VG7070H mass spectrometer using EI technique or Shimadzu-LCMS-2010 a mass spectrometer. The X-ray diffraction measurements were carried out at 298 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite monochromated, Mo-Kα (λ = 0.71073 Å) radiation with CAD4 software or the X-ray intensity data were measured at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å). For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

Materials: All solvents and commercially available chemicals were used as received. Functionalized 2-amino-β-nitrostyrenes **1a-j** was prepared according to the literature procedure.[1]

General Experimental Procedures

Procedure A: General procedure for quinidine-squaramide catalyzed asymmetric Michael reaction of (*E*)-2-(2-nitrovinyl)anilines 1 with β-keto esters 2: In an ordinary glass vial equipped with a magnetic stirring bar, to the **3d** or **3e** (5 mol%) in DCM (1.0 mL), were added (*E*)-2-(2-nitrovinyl)anilines **1a-i** (0.3 mmol) and β-keto esters **2a-l** (0.4 mmol, 1.33 equiv.). After stirring the reaction mixture at 25 °C as shown in Tables 1-3, the crude reaction mixture was concentrated and pure chiral products **4** were obtained by quick filtration (silica gel, mixture of hexane/ethyl acetate).

Procedure B: General procedure for quinidine-squaramide catalyzed one-pot synthesis of 1,4-dihydroquinolines from (*E*)-2-(2-nitrovinyl)anilines 1 and β-keto esters 2: In an ordinary glass vial equipped with a magnetic stirring bar, to the **3e** (5 mol%) in DCM (1.0 mL), were added (*E*)-2-(2-nitrovinyl)anilines **1a-i** (0.3 mmol) and β-keto esters **2a-l** (0.4 mmol, 1.33 equiv.). The resulting mixture was stirred at 25 °C until complete consumption of (*E*)-2-(2-nitrovinyl)anilines **1a-i** and added trifluoroacetic acid (3.0 equiv.) at room temperature. After stirring at 25 °C as shown in Table 3, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layer was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified using silica gel column chromatography using ethyl acetate and hexane as eluents to afford the desired 1,4-dihydroquinoline compounds **5**.

Procedure C: General procedure for amine-catalyzed racemic Michael reaction of (*E*)-2-(2-nitrovinyl)anilines with 1 with keto-esters 2: In an ordinary glass vial equipped with a magnetic stirring bar, to the 1:1 mixture of quinine and quinidine (each 5 mol%) in DCM (1.0 mL), were added (*E*)-2-(2-nitrovinyl)anilines **1a-i** (0.3 mmol) and β-keto esters **2a-l** (0.4 mmol, 1.33 equiv.). After stirring the reaction mixture at 25 °C as shown in Table S1, the crude reaction mixture was concentrated and pure racemic products **4** were obtained by quick filtration (silica gel, mixture of hexane/ethyl acetate).

Procedure D: General procedure for amine-catalyzed one-pot synthesis of racemic 1,4-dihydroquinolines from (E)-2-(2-nitrovinyl)anilines 1 and keto-esters 2: In an ordinary glass vial equipped with a magnetic stirring bar, to the 1:1 mixture of quinine and quinidine (each 5 mol%) in DCM (1.0 mL), were added (*E*)-2-(2-nitrovinyl)anilines **1a-i** (0.3 mmol) and β-keto esters **2a-l** (0.4 mmol, 1.33 equiv.). The resulting mixture was stirred at 25 °C until complete consumption of (*E*)-2-(2-nitrovinyl)anilines **1a-i** was observed as determined by TLC and added trifluoroacetic acid (3.0 equiv) at room temperature. After stirring at 25 °C as shown in Table S2, the reaction mixture was quenched with

saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layer was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified using silica gel column chromatography using ethyl acetate and hexane as eluents to afford the desired 1,4-dihydroquinoline compounds **5**.

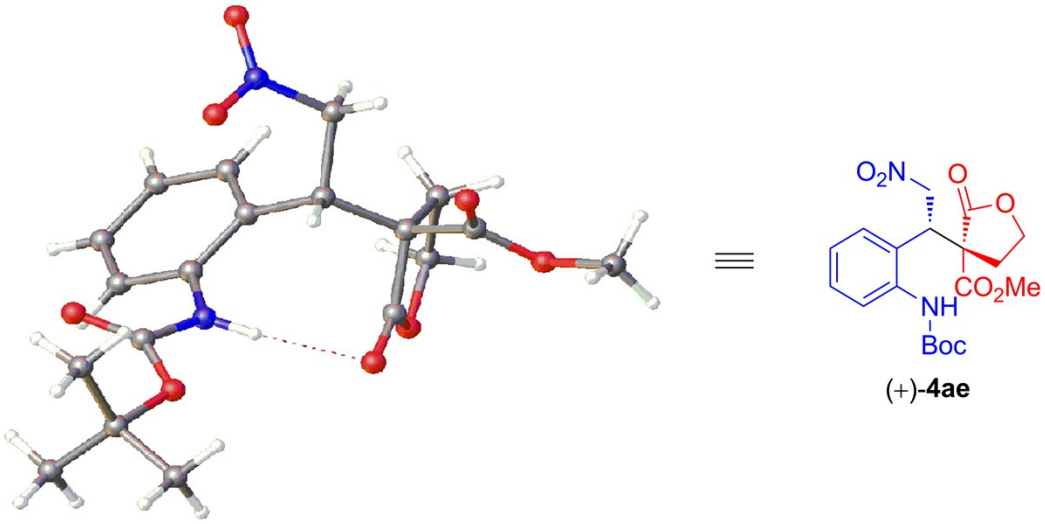
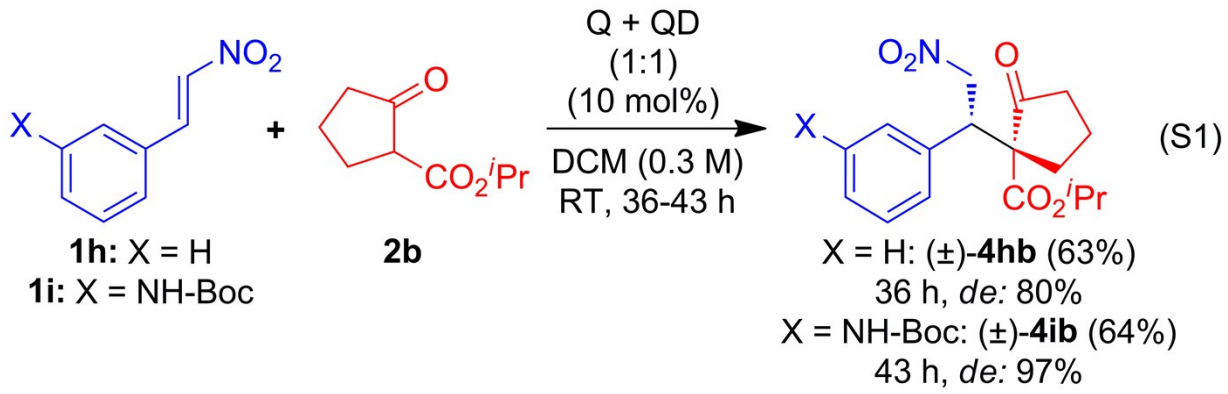
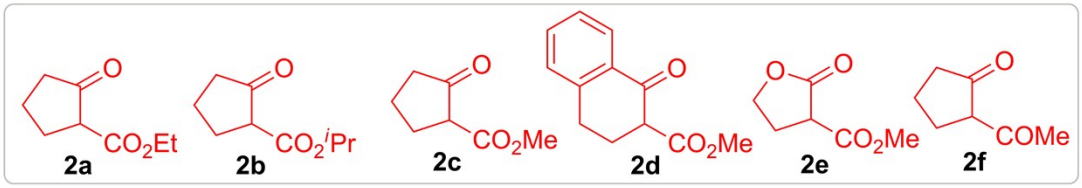


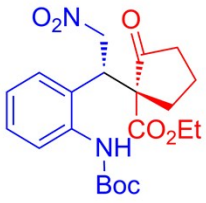
Figure S1: X-ray crystal structure of chiral (*S*)-methyl 3-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxotetrahydrofuran-3-carboxylate (**4ae**).



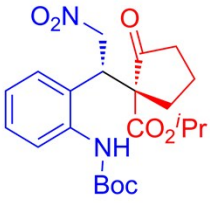
[Q = Quinine and QD = Quinidine]

Table S1: Synthesis of racemic Michael products

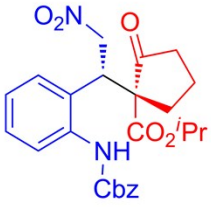




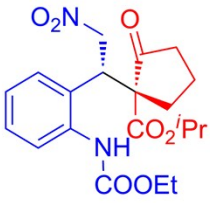
(±)-**4aa** (70%)
12 h, *de*: 59%



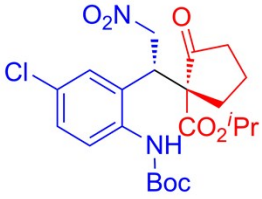
(±)-**4ab** (73%)
12 h, *de*: 35%



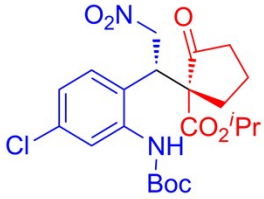
(±)-**4bb** (74%)
12 h, *de*: 59%



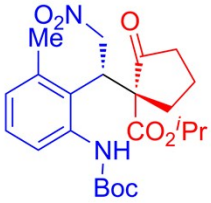
(±)-**4cb** (40%)
12 h, *de*: 77%



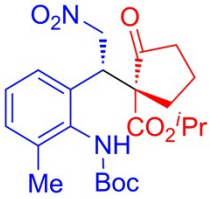
(±)-**4db** (64%)
12 h, *de*: 48%



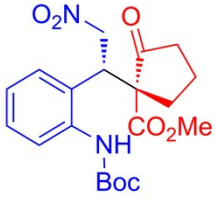
(±)-**4eb** (64%)
12 h, *de*: 56%



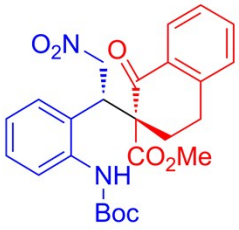
(±)-**4fb** (47%)
36 h, *de*: 58%



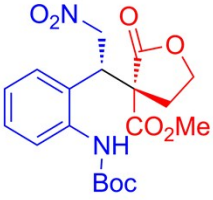
(±)-**4gb** (64%)
24 h, *de*: 75%



(±)-**4ac** (83%)
15 h, *de*: 58%



(±)-**4ad** (20%)
48 h, *de*: 3%

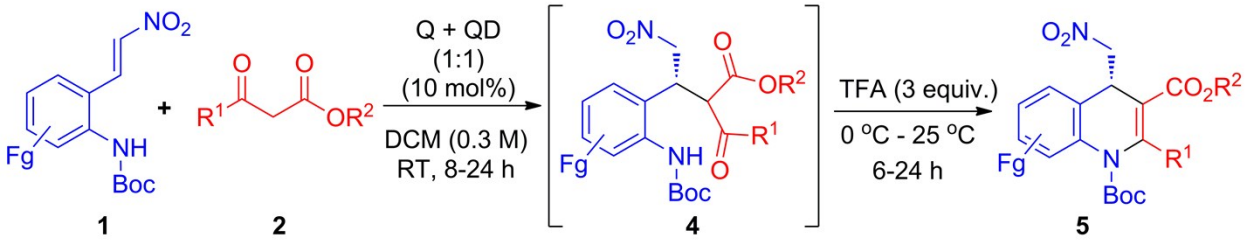


(±)-**4ae** (43%)
24 h, *de*: 44%

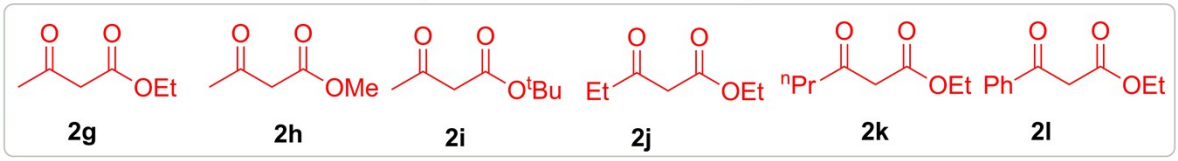
(±)-**4af** (36%)
20 h, *de*: 17%

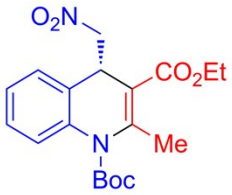
[a] Yield refers to the column purified product. [b] de was determined by CSP HPLC analysis.

Table S2: Synthesis of racemic 1,4-dihydroquinolines[a,b]

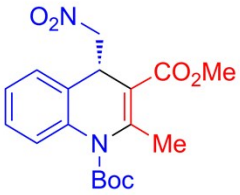


[Q = Quinine; QD = Quinidine]

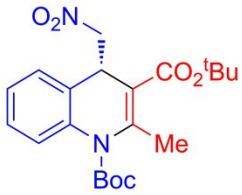




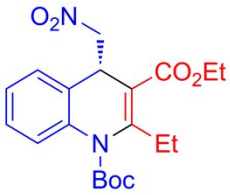
(±)-**5ag** (59%), 30 h



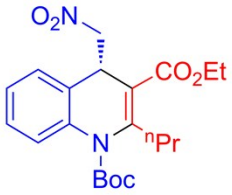
(±)-**5ah** (69%), 14 h



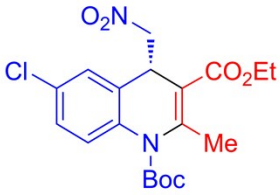
(±)-**5ai** (54%), 30 h



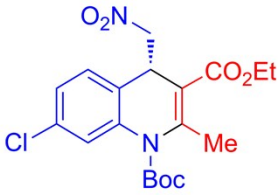
(±)-**5aj** (37%), 48 h



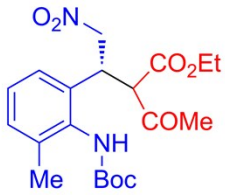
(±)-**5ak** (21%), 48 h



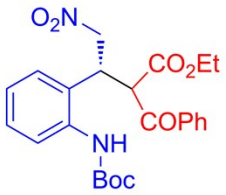
(±)-**5dg** (44%), 20 h



(±)-**5eg** (51%), 30 h



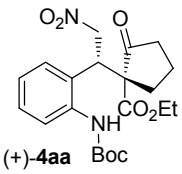
(±)-**4gg** (31%)[c], 24 h
de: 1%



(±)-**4al** (70%)[c], 12 h
de: 10%

[a] Yield refers to the column purified product. [b] de were determined by CSP HPLC analysis. [c] Only Micheal product obtained.

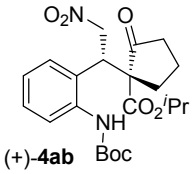
(*R*)-Ethyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxocyclopentane carboxylate (4aa): Prepared by following the procedure **A** and purified by column chromatography using



(+)-**4aa**

EtOAc/hexane and isolated as white solid. Mp 107-109 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u Cellulose-2 column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 9.55 min (minor), t_R = 14.92 min (major); **$[\alpha]_D^{25}$ = +3.4° (*c* = 0.17 g/100 mL, $CHCl_3$, 98% *ee* and >99% *de*)**; IR (KBr): ν_{max} 3408 (N-*H*), 2980, 1720 (C=O), 1555 (NO_2), 1450, 1367 (NO_2), 1229, 1154, 1023 and 855 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.54 (1H, d, *J* = 8.0 Hz), 7.38 (1H, dd, *J* = 7.6, 1.2 Hz), 7.30-7.26 (1H, m), 7.18-7.12 (1H, m), 6.93 (1H, br s, N*H*), 5.18 (1H, dd, *J* = 14.4, 4.4 Hz), 4.97 (1H, dd, *J* = 14.4, 10.0 Hz), 4.45 (1H, dd, *J* = 10.4, 4.4 Hz), 4.23 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.44-2.36 (2H, m), 2.19-2.10 (1H, m), 2.07-1.99 (1H, m), 1.98-1.88 (2H, m), 1.55 (9H, s, $OC(CH_3)_3$), 1.29 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 213.0 (C, *C*=O), 169.4 (C, O-*C*=O), 154.0 (C, O-*C*=O), 137.0 (C), 130.2 (C), 128.6 (CH), 127.5 (CH), 127.2 (CH), 125.8 (CH), 80.4 (C), 77.0 (CH_2), 63.0 (C), 62.3 (CH_2, OCH_2CH_3), 38.5 (CH), 37.7 (CH_2), 31.4 (CH_2), 28.3 (3 x CH_3, $OC(CH_3)_3$), 19.4 (CH_2), 13.8 (CH_3, OCH_2CH_3); HRMS m/z 443.1795 (M + Na), calcd for $C_{21}H_{28}N_2O_7Na$ 443.1795.

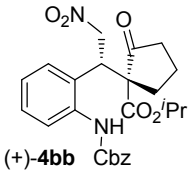
(*R*)-Isopropyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxocyclopentane carboxylate (4ab): Prepared by following the procedure **A** and purified by column chromatography using



(+)-**4ab**

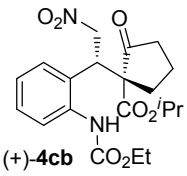
EtOAc/hexane and isolated as white solid. Mp 108-110 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak ID-H column (hexane/2-propanol = 90:10, flow rate 0.8 mL/min, λ = 254 nm), t_R = 14.72 min (major), t_R = 23.55 min (minor); **$[\alpha]_D^{25}$ = +12.1° (*c* = 0.07 g/100 mL, $CHCl_3$, >99% *ee* and >99% *de*)**; IR (KBr): ν_{max} 3383 (N-*H*), 2980, 1717 (C=O), 1556 (NO_2), 1451, 1368 (NO_2), 1230, 1155, 1047 and 906 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.54 (1H, d, *J* = 8.0 Hz), 7.41 (1H, d, *J* = 7.6 Hz), 7.28 (1H, dt, *J* = 7.6, 1.2 Hz), 7.16 (1H, t, *J* = 7.6 Hz), 6.96 (1H, br s, N*H*), 5.15 (1H, dd, *J* = 14.0, 4.4 Hz), 5.08 (1H, septet, *J* = 6.4 Hz), 4.96 (1H, dd, *J* = 14.0, 10.0 Hz), 4.46 (1H, dd, *J* = 10.0, 4.0 Hz), 2.45-2.35 (2H, m), 2.19-2.07 (1H, m), 2.05-1.98 (1H, m), 1.96-1.90 (2H, m), 1.55 (9H, s, $OC(CH_3)_3$), 1.28 (6H, d, *J* = 6.0 Hz, $OCH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 213.1 (C, *C*=O), 168.9 (C, O-*C*=O), 154.0 (C, O-*C*=O), 137.0 (C), 130.2 (C), 128.6 (CH), 127.5 (CH), 127.2 (CH), 125.7 (CH), 80.3 (C), 77.0 (CH_2), 70.3 (CH, $OCH(CH_3)_2$), 63.1 (C), 38.5 (CH), 37.7 (CH_2), 31.4 (CH_2), 28.3 (3 x CH_3, $OC(CH_3)_3$), 21.5 (CH_3, $OCH(CH_3)_2$), 21.3 (CH_3, $OCH(CH_3)_2$), 19.4 (CH_2); HRMS m/z 457.1951 (M + Na), calcd for $C_{22}H_{30}N_2O_7Na$ 457.1951.

(*R*)-Isopropyl 1-((*S*)-1-(2-(((benzyloxy)carbonyl)amino)phenyl)-2-nitroethyl)-2-oxocyclopentane carboxylate (4bb): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 77-79 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak ID-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 17.13 min (major), t_R = 33.06 min (minor); **$[\alpha]_D^{25}$ = +18.7° (*c* = 0.14 g/100 mL, $CHCl_3$, >99% *ee* and >99% *de*)**; IR (KBr): ν_{max} 3402 (N-*H*), 2987, 1719 (C=O), 1555 (NO_2), 1471, 1376 (NO_2), 1215, 1183, 1043, 906 and 733 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.59 (1H, d, *J* = 7.6 Hz), 7.46-7.44 (2H, m), 7.42-7.37 (3H, m), 7.35-7.28 (3H, m), 7.18 (1H, t, *J* = 7.6 Hz), 5.26 (2H, s, OCH_2Ph), 5.12 (1H, dd, *J* = 14.0, 4.0 Hz), 5.06 (1H, septet, *J* = 6.4 Hz), 4.93 (1H, dd, *J* = 14.0, 10.4 Hz), 4.46 (1H, dd, *J* = 10.0, 4.0 Hz), 2.44-2.30 (2H, m), 2.06-1.94 (2H, m), 1.92-1.80 (2H, m), 1.25 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$), 1.23 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 213.2 (C, *C*=O), 168.8 (C, O-*C*=O), 154.6 (C, O-*C*=O), 136.7 (C), 136.5 (C), 130.0 (C), 128.8 (CH), 128.5 (2 x CH), 128.1 (2 x CH), 128.1 (CH), 127.6 (CH), 126.9 (CH), 126.0 (CH), 76.9 (CH_2), 70.4 (CH, O*C*H(CH$_3$)$_2$), 67.0 (CH_2, O*C*H_2Ph), 63.2 (C), 38.5 (CH), 37.6 (CH_2), 31.3 (CH_2), 21.4 (CH_3, OCH(*C*H$_3$)$_2$), 21.3 (CH_3, OCH(*C*H$_3$)$_2$), 19.3 (CH_2); HRMS m/z 491.1795 (M + Na), calcd for $C_{25}H_{28}N_2O_7Na$ 491.1795.



(+)-**4bb**

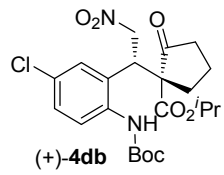
(*R*)-Isopropyl 1-((*S*)-1-(2-((ethoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxocyclopentane carboxylate (4cb): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 110-112 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.7 min (major), t_R = 55.8 min (minor) [for minor isomer], t_R = 20.7 min (major), t_R = 27.6 min (minor) [for major isomer]; **$[\alpha]_D^{25}$ = +20.9° (*c* = 0.07 g/100 mL, $CHCl_3$, 96% *ee* and >99% *de*)**; IR (KBr): ν_{max} 3386 (N-*H*), 2986, 1719 (C=O), 1555 (NO_2), 1470, 1376 (NO_2), 1219, 1147, 1098 and 906 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.58 (1H, d, *J* = 8.0 Hz), 7.39 (1H, dd, *J* = 7.6, 1.2 Hz), 7.28 (1H, dt, *J* = 7.6, 1.2 Hz), 7.20 (1H, br s, N*H*), 7.16 (1H, dt, *J* = 7.6, 1.2 Hz), 5.10 (1H, dd, *J* = 14.0, 4.0 Hz), 5.06 (1H, septet, *J* = 6.4 Hz), 4.91 (1H, dd, *J* = 14.0, 10.0 Hz), 4.49 (1H, dd, *J* = 10.0, 4.4 Hz), 4.25 (2H, dq, *J* = 7.2, 1.6 Hz, OCH_2CH$_3$), 2.45-2.32 (2H, m), 2.10-1.99 (2H, m), 1.97-1.88 (2H, m), 1.34 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 1.27 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$), 1.25 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 213.2 (C, *C*=O), 168.9 (C, O-*C*=O), 154.8 (C, O-*C*=O), 136.9 (C), 129.7 (C), 128.7 (CH), 127.6 (CH), 126.7 (CH), 125.7 (CH), 76.9 (CH_2), 70.4 (CH, O*C*H(CH$_3$)$_2$), 63.2 (C), 61.3 (CH_2, O*C*H_2CH$_3$), 38.4 (CH), 37.6 (CH_2), 31.1 (CH_2), 21.4 (CH_3,



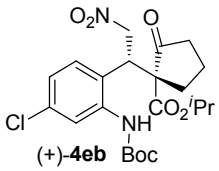
(+)-**4cb**

OCH(CH_3)$_2$), 21.3 (CH_3, OCH(CH_3)$_2$), 19.4 (CH_2), 14.5 (CH_3, OCH_2CH_3); HRMS m/z 429.1633 (M + Na), calcd for $C_{20}H_{26}N_2O_7Na$ 429.1638.

(*R*)-Isopropyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)-5-chlorophenyl)-2-nitroethyl)-2 oxo cyclopentanecarboxylate (4db): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 78-80 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 16.3 min (minor), t_R = 21.4 min (major) [for minor isomer], t_R = 18.9 min (major), t_R = 38.3 min (minor) [for major isomer]; **$[\alpha]_D^{25}$ = +2.6° (*c* = 0.27 g/100 mL, $CHCl_3$, >99% *ee* and 97% *de*)**; IR (KBr): ν_{max} 3381 (N-*H*), 2980, 1716 (C=O), 1556 (NO_2), 1456, 1368 (NO_2), 1231, 1155, 1098 and 906 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.50 (1H, d, *J* = 8.4 Hz), 7.44 (1H, d, *J* = 2.0 Hz), 7.25 (1H, dd, *J* = 8.4, 2.4 Hz), 6.89 (1H, br s, N*H*), 5.17 (1H, dd, *J* = 14.4, 4.0 Hz), 5.09 (1H, septet, *J* = 6.4 Hz), 4.93 (1H, dd, *J* = 14.4, 10.4 Hz), 4.36 (1H, dd, *J* = 10.4, 4.0 Hz), 2.45-2.38 (2H, m), 2.23-2.14 (1H, m), 1.98-1.92 (3H, m), 1.54 (9H, s, OC(CH_3)$_3$), 1.29 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$), 1.27 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 212.8 (C, *C*=O), 168.7 (C, O-*C*=O), 153.7 (C, O-*C*=O), 135.8 (C), 132.2 (C), 131.2 (C), 128.8 (CH), 128.3 (CH), 127.7 (CH), 80.7 (C), 76.8 (CH_2), 70.6 (CH, O*C*H(CH_3)$_2$), 62.9 (C), 38.5 (CH), 37.6 (CH_2), 31.7 (CH_2), 28.3 (3 x CH_3, OC(CH_3)$_3$), 21.5 (CH_3, OCH(CH_3)$_2$), 21.3 (CH_3, OCH(CH_3)$_2$), 19.3 (CH_2); HRMS m/z 491.1560 (M + Na), calcd for $C_{22}H_{29}N_2O_7ClNa$ 491.1561.

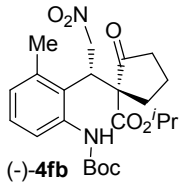


(*R*)-Isopropyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)-4-chlorophenyl)-2-nitroethyl)-2-oxo cyclopentanecarboxylate (4eb): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 102-104 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OJ-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.1 min (minor), t_R = 54.0 min (major) [for minor isomer], t_R = 19.4 min (minor), t_R = 26.8 min (major) [for major isomer]; **$[\alpha]_D^{25}$ = +6.9° (*c* = 0.18 g/100mL, $CHCl_3$, 99% *ee* for major isomer, 85% *ee* for minor isomer and 70% *de*)**; IR (KBr): ν_{max} 3376 (N-*H*), 2981, 1717 (C=O), 1556 (NO_2), 1456, 1368 (NO_2), 1230, 1154, 1098 and 938 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.65 (1H, br d, *J* = 2.0 Hz), 7.36 (1H, d, *J* = 8.4 Hz), 7.12 (1H, dd, *J* = 8.4, 2.0 Hz), 7.06 (1H, br s, N*H*), 5.11-5.05 (2H, m), 4.90 (1H, dd, *J* = 14.4, 10.4 Hz), 4.38 (1H, dd, *J* = 10.4, 4.0 Hz), 2.44-2.37 (2H, m), 2.17-2.07 (1H, m), 2.03-1.90 (3H, m), 1.55 (9H, s, OC(CH_3)$_3$), 1.27 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$), 1.26 (3H, d, *J* = 6.4 Hz, OCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 213.0 (C, *C*=O), 168.8 (C, O-*C*=O), 153.4 (C, O-*C*=O), 138.5 (C), 134.4 (C), 128.8 (CH), 127.8 (C), 126.4 (CH),



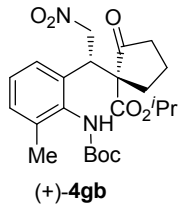
125.5 (CH), 80.8 (C), 76.7 (CH_2), 70.5 (CH, O*C*H(CH_3)$_2$), 63.1 (C), 38.1 (CH), 37.6 (CH_2), 31.4 (CH_2), 28.3 (3 x CH_3, OC(*C*H$_3$)$_3$), 21.4 (CH_3, OCH(*C*H$_3$)$_2$), 21.3 (CH_3, OCH(*C*H$_3$)$_2$), 19.4 (CH_2); HRMS m/z 491.1558 (M + Na), calcd for $C_{22}H_{29}N_2O_7ClNa$ 491.1561.

(*R*)-Isopropyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)-6-methylphenyl)-2-nitroethyl)-2-oxocyclopentanecarboxylate (4fb): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.8 mL/min, λ = 254 nm), t_R = 7.8 min (minor), t_R = 12.2 min (major) [for major isomer]; t_R = 11.2 min (minor), t_R = 13.5 min (major) [for minor isomer]; **$[\alpha]_D^{25}$ = –15.0° (*c* = 0.12 g/100 mL, $CHCl_3$, >99% *ee* for major, >99% *ee* for minor and dr = 3:1);** IR (Neat): ν_{max} 3285 (N-*H*), 2978, 1720 (C=O), 1556 (NO_2), 1454, 1367 (NO_2), 1232, 1157, 1099 and 905 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, at 50 °C, major isomer) δ 8.35 (1H, br s, N*H*), 7.54 (1H, d, *J* = 8.0 Hz), 7.19-7.14 (1H, m), 6.92 (1H, d, *J* = 7.6 Hz), 5.04-4.94 (2H, m), 4.85-4.75 (1H, m), 4.56-4.53 (1H, m), 2.66-2.62 (1H, m), 2.56-2.48 (1H, m), 2.38 (3H, s, C*H*$_3$), 2.03-1.96 (1H, m), 1.88-1.78 (3H, m), 1.57 (9H, s, OC(C*H*$_3$)$_3$), 1.11 (3H, d, *J* = 6.4 Hz, OCH(C*H*$_3$)$_2$), 1.04 (3H, d, *J* = 6.4 Hz, OCH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C, major isomer) δ 213.8 (C, *C*=O), 174.2 (C, O-*C*=O), 169.2 (C, O-*C*=O), 154.0 (C), 139.0 (C), 137.5 (C), 128.4 (CH), 127.1 (CH), 124.2 (CH), 80.1 (C), 75.2 (CH_2), 71.1 (CH, O*C*H(CH_3)$_2$), 64.3 (C), 40.3 (CH), 37.0 (CH_2), 35.7 (CH_2), 28.4 (3 x CH_3, OC(*C*H$_3$)$_3$), 21.5 (CH_3, OCH(*C*H$_3$)$_2$), 21.2 (CH_3, OCH(*C*H$_3$)$_2$), 20.9 (CH_3), 19.1 (CH_2); HRMS m/z 471.2100 (M + Na), calcd for $C_{23}H_{32}N_2O_7Na$ 471.2108.



(-)-**4fb**

(*R*)-Isopropyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)-3-methylphenyl)-2-nitroethyl)-2-oxocyclopentanecarboxylate (4gb): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak ID-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 7.5 min (major), t_R = 8.7 min (minor) [for minor isomer]; t_R = 10.1 min (major), t_R = 14.5 min (minor) [for major isomer]; **$[\alpha]_D^{25}$ = +2.6° (*c* = 0.52 g/100 mL, $CHCl_3$, >99% *ee*, >99% *ee* and dr = 15:1)**; IR (Neat): ν_{max} 3380 (N-*H*), 2979, 1716 (C=O), 1555 (NO_2), 1488, 1375 (NO_2), 1231, 1185, 1100, 907 and 777 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.32 (1H, m), 7.18-7.15 (2H, m), 6.57 (1H, br s, N*H*), 5.23 (1H, d, *J* = 11.6 Hz), 5.13-4.98 (2H, m), 4.47 (1H, br s), 2.47-2.32 (2H, m), 2.29 (3H, s, C*H*$_3$), 2.24-2.10 (1H, m), 2.06-1.98 (1H, m), 1.95-1.84 (2H, m), 1.54 (9H, s, OC(C*H*$_3$)$_3$), 1.28 (3H, d, *J* = 6.4 Hz, OCH(C*H*$_3$)$_2$), 1.27 (3H, d, *J* = 6.4 Hz, OCH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 213.7 (C, *C*=O), 169.1 (C, O-*C*=O), 153.8 (C, O-*C*=O), 138.1 (C), 135.1 (C), 134.6 (C), 130.7 (CH),



(+)-**4gb**

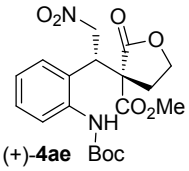
127.6 (CH), 125.1 (CH), 80.1 (C), 77.6 (CH_2), 70.1 (CH, O*C*H(CH_3)$_2$), 62.7 (C), 39.1 (CH), 37.9 (CH_2), 32.0 (CH_2), 28.3 (3 x CH_3, OC(*C*H$_3$)$_3$), 21.6 (CH_3, OCH(*C*H$_3$)$_2$), 21.5 (CH_3, OCH(*C*H$_3$)$_2$), 19.5 (CH_2), 18.7 (CH_3); HRMS m/z 471.2103 (M + Na), calcd for $C_{23}H_{32}N_2O_7Na$ 471.2108.

(*R*)-Methyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxocyclopentane carboxylate (4ac): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as semisolid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u Cellulose-2 column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 8.19 min (minor), t_R = 10.12 min (major) [for minor isomer]; t_R = 14.60 min (minor), t_R = 16.13 min (major) [for major isomer]; **[α]$_D^{25}$ = –7.6° (*c* = 0.60 g/100 mL, $CHCl_3$, 94% *ee* for major, 46% *ee* for minor** and **dr = 39:1)**; IR (Neat): ν_{max} 3393 (N-*H*), 2981, 1720 (C=O), 1556 (NO_2), 1450, 1367 (NO_2), 1230, 1154, 1048, 985 and 751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.53 (1H, d, *J* = 8.0 Hz), 7.36 (1H, br d, *J* = 7.6 Hz), 7.28 (1H, dt, *J* = 7.6, 1.6 Hz), 7.16 (1H, br t, *J* = 7.6 Hz), 6.89 (1H, br s, N*H*), 5.20 (1H, dd, *J* = 14.0, 4.0 Hz), 4.98 (1H, dd, *J* = 14.0, 10.0 Hz), 4.42 (1H, dd, *J* = 10.0, 4.0 Hz), 3.78 (3H, s, CO_2CH_3), 2.45-2.36 (2H, m), 2.21-2.12 (1H, m), 2.07-1.98 (1H, m), 1.96-1.90 (2H, m), 1.55 (9H, s, OC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 212.9 (C, *C*=O), 170.0 (C, O-*C*=O), 154.0 (C, O-*C*=O), 137.1 (C), 130.2 (C), 128.6 (CH), 127.4 (CH), 127.3 (CH), 125.9 (CH), 80.4 (C), 76.9 (CH_2), 62.9 (C), 53.0 (CH_3, CO_2CH_3), 38.4 (CH), 37.7 (CH_2), 31.5 (CH_2), 28.3 (3 x CH_3, OC(*C*H$_3$)$_3$), 19.3 (CH_2); HRMS m/z 429.1632 (M + Na), calcd for $C_{20}H_{26}N_2O_7Na$ 429.1638.

(*R*)-Methyl 2-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-1-oxo-1,2,3,4-tetrahydro naphthalene-2-carboxylate (4ad): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 21.20 min (major), t_R = 24.11 min (minor) [for major isomer]; t_R = 33.09 min (major), t_R = 38.81 min (minor) [for minor isomer]; **[α]$_D^{25}$ = +100.7° (*c* = 0.33 g/100 mL, $CHCl_3$, 94% *ee* for major, 36% *ee* for minor** and **dr = 12:1)**; IR (Neat): ν_{max} 3370 (N-*H*), 2979, 1724 (C=O), 1555 (NO_2), 1451, 1367 (NO_2), 1233, 1155, 1052, 906 and 736 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 8.04 (1H, d, *J* = 7.6 Hz), 7.57 (1H, d, *J* = 8.0 Hz), 7.49-7.43 (2H, m), 7.34-7.29 (1H, m), 7.28-7.24 (1H, m), 7.20-7.14 (3H, m), 5.23 (1H, dd, *J* = 14.4, 4.0 Hz), 4.95 (1H, dd, *J* = 14.4, 10.0 Hz), 4.66 (1H, dd, *J* = 10.0, 4.0 Hz), 3.65 (3H, s, O*CH*$_3$), 3.08-3.00 (1H, m), 2.94-2.87 (1H, m), 2.50-2.45 (1H, m), 2.19-2.10 (1H, m), 1.51 (9H, s, OC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 194.4 (C, *C*=O), 170.2 (C, O-*C*=O), 154.0 (C, O-*C*=O), 142.7 (C), 137.3 (C), 134.1 (CH), 131.6 (C), 129.8 (C), 128.6 (CH),

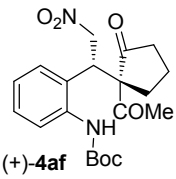
128.5 (CH), 128.4 (2 x CH), 126.9 (CH), 126.8 (CH), 125.4 (CH), 80.3 (C), 77.8 (CH_2), 60.1 (C), 52.8 (CH_3, CO_2CH_3), 39.3 (CH), 30.3 (CH_2), 28.3 (3 x CH_3, $OC(CH_3)_3$), 25.7 (CH_2); HRMS m/z 491.1794 (M + Na), calcd for $C_{25}H_{28}N_2O_7Na$ 491.1795.

(*S*)-Methyl 3-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxotetrahydrofuran-3-carboxylate (4ae): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 153-155 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak ID-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 220 nm), t_R = 18.6 min (minor), t_R = 20.4 min (major) [for minor isomer], t_R = 25.6 min (major), t_R = 35.9 min (minor) [for major isomer]; **$[\alpha]_D^{25}$ = +23.3° (*c* = 0.17 g/100 mL, $CHCl_3$, >99% *ee* and >99% *de*)**; IR (KBr): ν_{max} 3378 (N-*H*), 2983, 1763 (C=O), 1556 (NO_2), 1450, 1368 (NO_2), 1236, 1157, 1025 and 909 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, at 50 °C) δ 7.53 (1H, d, *J* = 8.0 Hz), 7.37-7.31 (2H, m), 7.21 (1H, t, *J* = 7.6 Hz), 6.85 (1H, br s, N*H*), 5.41 (1H, dd, *J* = 14.4, 4.0 Hz), 5.09 (1H, dd, *J* = 14.4, 10.4 Hz), 4.54 (1H, dd, *J* = 10.4, 4.0 Hz), 4.32-4.29 (2H, m), 3.87 (3H, s, OCH_3), 2.64-2.58 (1H, m), 2.40-2.33 (1H, m), 1.55 (9H, s, $OC(CH_3)_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 173.3 (C, O-*C*=O), 168.4 (C, O-*C*=O), 154.2 (C, O-*C*=O), 137.1 (C), 130.3 (C), 129.1 (CH), 128.0 (CH), 127.0 (CH), 126.6 (CH), 80.7 (C), 76.7 (CH_2), 66.5 (CH_2), 56.9 (C), 53.6 (CH_3, CO_2CH_3), 39.1 (CH), 30.9 (CH_2), 28.3 (3 x CH_3, $OC(CH_3)_3$); HRMS m/z 426.1877 (M + NH_4), calcd for $C_{19}H_{28}N_3O_8$ 426.1877.



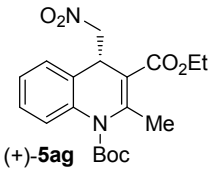
(+)-**4ae**

***tert*-Butyl (2-((*S*)-1-((*S*)-1-acetyl-2-oxocyclopentyl)-2-nitroethyl)phenyl)carbamate (4af):** Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak ID-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 16.85 min (major), t_R = 39.48 min (minor) [for major isomer]; t_R = 18.25 min (major), t_R = 19.0 min (minor) [for minor isomer]; **$[\alpha]_D^{25}$ = +20.0° (*c* = 0.10 g/100 mL, $CHCl_3$, >99% *ee*, 94% *ee* and dr = 8:1)**; IR (Neat): ν_{max} 3376 (N-*H*), 2920, 1704 (C=O), 1556 (NO_2), 1453, 1367 (NO_2), 1234, 1156, 1024 and 756 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, at 50 °C, major isomer) δ 7.54 (1H, d, *J* = 7.6 Hz), 7.29 (2H, m), 7.18-7.09 (2H, m), 4.83-4.77 (1H, m), 4.66-4.63 (2H, m), 2.62-2.60 (1H, m), 2.31 (3H, s, $COCH_3$), 2.26-2.23 (1H, m), 2.18-2.11 (1H, m), 2.01-1.94 (2H, m), 1.84-1.78 (1H, m), 1.55 (9H, s, $OC(CH_3)_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C, major isomer) δ 215.0 (C, *C*=O), 202.4 (C, *C*=O), 154.0 (C, O-*C*=O), 137.2 (C), 129.3 (C), 128.8 (CH), 127.6 (CH), 127.58 (CH), 125.7 (CH), 80.4 (C), 76.5 (CH_2), 71.7 (C), 38.5 (CH), 38.4 (CH_2), 28.4 (CH_2), 28.3 (3 x CH_3, $OC(CH_3)_3$), 26.6 (CH_3, $COCH_3$), 19.5 (CH_2); HRMS m/z 413.1684 (M + Na), calcd for $C_{20}H_{26}N_2O_6Na$ 413.1689.



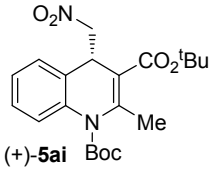
(+)-**4af**

(*S*)-1-*tert*-Butyl 3-ethyl 2-methyl-4-(nitromethyl)quinoline-1,3(4*H*)-dicarboxylate (5ag): Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak ID-H column (hexane/2-propanol = 90:10, flow rate 0.8 mL/min, λ = 254 nm), t_R = 6.80 min (minor), t_R = 7.41 min (major); **$[\alpha]_D^{25}$ = +212.1° (*c* = 0.17 g/100 mL, $CHCl_3$, 98% *ee*)**; IR (Neat): ν_{max} 2979, 1716 (C=O), 1587 (NO_2), 1487, 1370 (NO_2), 1232, 1151, 1076 and 917 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.70 (1H, d, *J* = 8.0 Hz), 7.34-7.30 (1H, m), 7.24-7.16 (2H, m), 4.72 (1H, dd, *J* = 9.2, 6.0 Hz), 4.46 (1H, dd, *J* = 11.6, 6.0 Hz), 4.35-4.23 (2H, m, OCH_2CH_3), 4.20 (1H, dd, *J* = 11.6, 9.2 Hz), 2.54 (3H, s, CH_3), 1.56 (9H, s, $OC(CH_3)_3$), 1.37 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.5 (C, O-*C*=O), 152.7 (C), 151.5 (C, O-*C*=O), 138.3 (C), 129.9 (C), 127.6 (CH), 127.5 (CH), 126.0 (CH), 124.1 (CH), 117.3 (C), 83.5 (C), 77.6 (CH_2), 61.1 (CH_2, OCH_2CH_3), 38.9 (CH), 28.1 (3 x CH_3, $OC(CH_3)_3$), 21.6 (CH_3), 14.2 (CH_3, OCH_2CH_3); HRMS m/z 399.1529 (M + Na), calcd for $C_{19}H_{24}N_2O_6Na$ 399.1532.



(+)-**5ag**

(*S*)-1-*tert*-Butyl 3-methyl-2-methyl-4-(nitromethyl)quinoline-1,3(4*H*)-dicarboxylate (5ah): Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.60 min (minor), t_R = 12.06 min (major); **$[\alpha]_D^{25}$ = +208.9° (*c* = 0.21 g/100 mL, $CHCl_3$, 98% *ee*)**; IR (Neat): ν_{max} 2930, 1720 (C=O), 1552 (NO_2), 1484, 1369 (NO_2), 1222, 1153, 1078 and 998 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.71 (1H, d, *J* = 8.0 Hz), 7.35-7.33 (1H, m), 7.22-7.19 (2H, m), 4.73 (1H, dd, *J* = 9.2, 6.0 Hz), 4.48 (1H, dd, *J* = 12.0, 6.0 Hz), 4.20 (1H, dd, *J* = 12.0, 9.2 Hz), 3.84 (3H, s, OCH_3), 2.55 (3H, s, CH_3), 1.57 (9H, s, $OC(CH_3)_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.9 (C, O-*C*=O), 153.2 (C), 151.5 (C, O-*C*=O), 138.2 (C), 129.8 (C), 127.6 (CH), 127.5 (CH), 126.0 (CH), 124.1 (CH), 116.9 (C), 83.6 (C), 77.5 (CH_2), 52.0 (OCH_3, $COOCH_3$), 38.9 (CH), 28.1 (3 x CH_3, $OC(CH_3)_3$), 21.7 (CH_3); HRMS m/z 385.1314 (M + Na), calcd for $C_{18}H_{22}N_2O_6Na$ 385.1376.



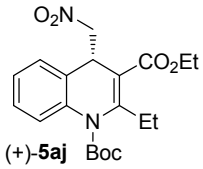
(+)-**5ah**

(*S*)-di-*tert*-Butyl 2-methyl-4-(nitromethyl)quinoline-1,3(4*H*)-dicarboxylate (5ai): Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 8.28 min (minor), t_R = 10.70 min (major); **$[\alpha]_D^{25}$ = +226.9° (*c* = 0.32 g/100 mL, $CHCl_3$, >99% *ee*)**; IR (Neat): ν_{max} 2979, 1716 (C=O), 1552 (NO_2), 1487, 1370 (NO_2), 1217, 1151, 1076 and 917 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ

(+)-**5ai**

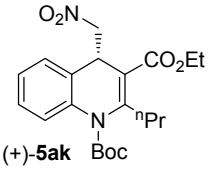
7.68 (1H, d, J = 8.0 Hz), 7.34-7.29 (1H, m), 7.23-7.16 (2H, m), 4.65 (1H, dd, J = 9.2, 6.4 Hz), 4.45 (1H, dd, J = 11.6, 6.4 Hz), 4.18 (1H, dd, J = 11.6, 9.2 Hz), 2.50 (3H, s, CH_3), 1.56 (9H, s, OC(CH_3)$_3$), 1.55 (9H, s, OC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 164.8 (C, O-*C*=O), 151.6 (C), 151.3 (C, O-*C*=O), 138.4 (C), 130.1 (C), 127.6 (CH), 127.4 (CH), 125.9 (CH), 124.2 (CH), 118.9 (C), 83.4 (C), 81.9 (C), 77.8 (CH_2), 39.3 (CH), 28.2 (3 x CH_3, OC(*C*H_3)$_3$), 28.1 (3 x CH_3, OC(*C*H_3)$_3$), 21.5 (CH_3); HRMS m/z 427.1844 (M + Na), calcd for $C_{21}H_{28}N_2O_6Na$ 427.1845.

(*S*)-1-*tert*-Butyl 3-ethyl-2-ethyl-4-(nitromethyl)quinoline-1,3(4*H*)-dicarboxylate (5aj): Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.32 min (minor), t_R = 11.71 min (major); **$[\alpha]_D^{25}$ = +225.7° (*c* = 0.13 g/100 mL, $CHCl_3$, >99% *ee*)**; IR (Neat): ν_{max} 2978, 1717 (C=O), 1553 (NO_2), 1487, 1369 (NO_2), 1224, 1151, 1080 and 894 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (1H, d, J = 8.0 Hz), 7.34-7.29 (1H, m), 7.22-7.16 (2H, m), 4.65 (1H, dd, J = 9.6, 6.4 Hz), 4.52 (1H, dd, J = 12.0, 6.0 Hz), 4.36-4.24 (2H, m, OCH_2CH$_3$), 4.18 (1H, dd, J = 12.0, 9.6 Hz), 3.34 (1H, sextet, J = 7.2 Hz), 2.90 (1H, sextet, J = 7.6 Hz), 1.56 (9H, s, OC(CH_3)$_3$), 1.37 (3H, t, J = 7.2 Hz, OCH$_2$CH_3), 1.09 (3H, t, J = 7.6 Hz, CH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.5 (C, O-*C*=O), 158.2 (C), 151.7 (C, O-*C*=O), 139.0 (C), 130.7 (C), 127.6 (CH), 127.5 (CH), 126.0 (CH), 124.3 (CH), 118.1 (C), 83.4 (C), 77.5 (CH_2), 61.1 (CH_2, O*C*H$_2$CH$_3$), 39.4 (CH), 28.1 (3 x CH_3, OC(*C*H_3)$_3$), 25.7 (CH_2, *C*H$_2$CH$_3$), 14.1 (CH_3, OCH$_2$*C*H$_3$), 12.7 (CH_3, CH$_2$*C*H$_3$); HRMS m/z 413.1681 (M + Na), calcd for $C_{20}H_{26}N_2O_6Na$ 413.1689.



(+)-**5aj**

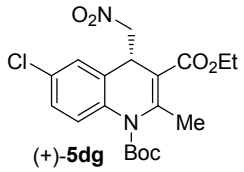
(*S*)-1-*tert*-Butyl 3-ethyl-4-(nitromethyl)-2-propylquinoline-1,3(4*H*)-dicarboxylate (5ak): Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 97:3, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.79 min (minor), t_R = 13.62 min (major); **$[\alpha]_D^{25}$ = +159.5° (*c* = 0.14 g/100 mL, $CHCl_3$, 97% *ee*)**; IR (Neat): ν_{max} 2964, 1714 (C=O), 1553 (NO_2), 1487, 1369 (NO_2), 1219, 1151, 1078 and 919 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63 (1H, d, J = 8.0 Hz), 7.33-7.28 (1H, m), 7.22-7.16 (2H, m), 4.66 (1H, dd, J = 9.6, 6.0 Hz), 4.52 (1H, dd, J = 12.0, 6.0 Hz), 4.35-4.24 (2H, m, OCH_2CH$_3$), 4.18 (1H, dd, J = 12.0, 9.6 Hz), 3.38-3.30 (1H, m), 2.89-2.82 (1H, m), 1.55 (9H, s, OC(CH_3)$_3$), 1.37 (3H, t, J = 6.8 Hz, OCH$_2$CH_3), 0.89-0.85 (5H, m, CH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.5 (C, O-*C*=O), 157.1 (C), 151.7 (C, O-*C*=O), 138.8 (C), 130.7 (C), 127.6 (CH), 127.5 (CH), 126.0 (CH), 124.4 (CH), 118.7 (C), 83.4 (C), 77.5 (CH_2), 61.1 (CH_2,



(+)-**5ak**

OCH_2CH_3), 39.4 (CH), 34.0 (CH_2), 28.1 (3 x CH_3, OC(CH_3)$_3$), 21.9 (CH_2), 14.2 (CH_3, OCH_2CH_3), 13.9 (CH_3, $CH_2CH_2CH_3$); HRMS m/z 427.1842 (M + Na), calcd for $C_{21}H_{28}N_2O_6Na$ 427.1845.

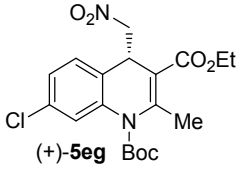
(*S*)-1-*tert*-Butyl 3-ethyl-6-chloro-2-methyl-4-(nitromethyl)quinoline-1,3(4*H*)-dicarboxylate (5dg):



(+)-**5dg**

Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.66 min (minor), t_R = 11.31 min (major); **$[\alpha]_D^{25}$ = +199.2° (*c* = 0.18 g/100 mL, $CHCl_3$, 99% *ee*)**; IR (Neat): ν_{max} 2980, 1717 (C=O), 1552 (NO_2), 1483, 1370 (NO_2), 1232, 1152, 1093 and 987 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (1H, d, *J* = 8.8 Hz), 7.28 (1H, dd, *J* = 8.8, 2.4 Hz), 7.22 (1H, d, *J* = 2.0 Hz), 4.67 (1H, dd, *J* = 9.2, 5.6 Hz), 4.45 (1H, dd, *J* = 12.0, 5.6 Hz), 4.35-4.23 (2H, m, OCH_2CH$_3$), 4.19 (1H, dd, *J* = 12.0, 9.2 Hz), 2.53 (3H, s, CH_3), 1.56 (9H, s, OC(CH_3)$_3$), 1.36 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.2 (C, O-*C*=O), 152.7 (C), 151.2 (C, O-*C*=O), 136.9 (C), 131.6 (C), 131.4 (C), 127.6 (CH), 127.4 (CH), 125.4 (CH), 116.8 (C), 83.9 (C), 77.2 (CH_2), 61.2 (CH_2, OCH_2CH_3), 38.6 (CH), 28.1 (3 x CH_3, OC(CH_3)$_3$), 21.5 (CH_3), 14.2 (CH_3, OCH$_2$CH_3); HRMS m/z 433.1141 (M + Na), calcd for $C_{19}H_{23}N_2O_6ClNa$ 433.1143.

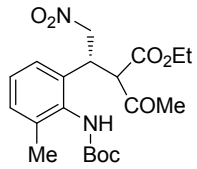
(*S*)-1-*tert*-Butyl 3-ethyl-7-chloro-2-methyl-4-(nitromethyl)quinoline-1,3(4*H*)-dicarboxylate (5eg):



(+)-**5eg**

Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.06 min (minor), t_R = 10.27 min (major); **$[\alpha]_D^{25}$ = +229.8° (*c* = 0.18 g/100 mL, $CHCl_3$, 98% *ee*)**; IR (Neat): ν_{max} 2980, 1717 (C=O), 1553 (NO_2), 1484, 1370 (NO_2), 1238, 1151, 1094 and 921 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 (1H, d, *J* = 2.0 Hz), 7.19-7.13 (2H, m), 4.69 (1H, dd, *J* = 9.5, 6.0 Hz), 4.47 (1H, dd, *J* = 12.0, 5.5 Hz), 4.35-4.25 (2H, m, OCH_2CH$_3$), 4.16 (1H, dd, *J* = 12.0, 9.5 Hz), 2.53 (3H, s, CH_3), 1.58 (9H, s, OC(CH_3)$_3$), 1.37 (3H, t, *J* = 7.0 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.3 (C, O-*C*=O), 152.4 (C), 151.1 (C, O-*C*=O), 139.1 (C), 133.4 (C), 128.5 (CH), 128.1 (C), 126.1 (CH), 124.4 (CH), 117.0 (C), 84.1 (C), 77.4 (CH_2), 61.2 (CH_2, OCH_2CH_3), 38.4 (CH), 28.1 (3 x CH_3, OC(CH_3)$_3$), 21.6 (CH_3), 14.2 (CH_3, OCH$_2$CH_3); HRMS m/z 433.1136 (M + Na), calcd for $C_{19}H_{23}N_2O_6ClNa$ 433.1143.

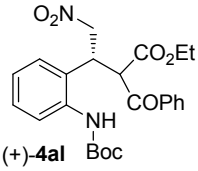
(3*R*)-Ethyl 2-acetyl-3-(2-((*tert*-butoxycarbonyl)amino)-3-methylphenyl)-4-nitrobutanoate (4gg):



(+)-**4gg**

Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 220 nm), t_R = 20.55 min (major), t_R = 27.96 min (minor); t_R = 34.92 min (minor), t_R = 40.41 min (major); **$[\alpha]_D^{25}$ = +4.3° (*c* = 0.19 g/100 mL, $CHCl_3$, 99% *ee*, 94% *ee* and dr = 1:1)**; IR (Neat): ν_{max} 3392 (N-*H*), 2981, 1710 (C=O), 1555 (NO_2), 1489, 1367 (NO_2), 1244, 1159, 1052, 955 and 836 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, at 50 °C, *dr* = 1.5:1.0) δ 7.18-7.12 (3H, m), 7.06-7.00 (3H, m), 6.22 (2H, br s, N*H*), 4.91-4.87 (3H, m), 4.67-4.60 (2H, m), 4.25 (4H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.17 (1H, br d, *J* = 7.6 Hz), 4.05 (2H, br q, *J* = 7.2 Hz), 2.29 (6H, br s, 2 x CH_3), 2.13 (6H, br s, 2 x CH_3), 1.52 (18H, s, 2 x $OC(CH_3)_3$), 1.30 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.10 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C, *dr* = 1.5:1.0) δ 200.74 (C, *C*=O), 200.67 (C, *C*=O), 167.8 (C, O-*C*=O), 167.5 (C, O-*C*=O), 154.4 (2 x C, O-*C*=O), 137.96 (C), 137.90 (C), 134.2 (2 x C), 131.9 (C), 131.78 (C), 130.41 (CH), 130.37 (CH), 127.65 (CH), 127.62 (CH), 124.3 (2 x CH), 80.4 (2 x C), 77.1 (CH_2), 76.95 (CH_2), 61.9 (2 x CH), 61.86 (2 x CH_2, OCH_2CH_3), 36.3 (2 x CH), 29.6 (2 x CH_3), 28.2 (6 x CH_3, 2 x $OC(CH_3)_3$), 18.46 (CH_3), 18.42 (CH_3), 13.89 (CH_3, OCH_2CH_3), 13.68 (CH_3, OCH_2CH_3); HRMS m/z 431.1797 (M + Na), calcd for $C_{20}H_{28}N_2O_7Na$ 431.1795.

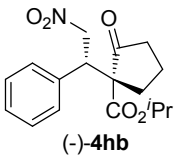
(3*R*)-Ethyl 2-benzoyl-3-(2-((*tert*-butoxycarbonyl)amino)phenyl)-4-nitrobutanoate (4al):



(+)-**4al**

Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 31.90 min (major), t_R = 41.18 min (minor) [for major isomer]; t_R = 45.22 min (major), t_R = 51.52 min (minor) [for minor isomer]; **$[\alpha]_D^{25}$ = +69.2° [*c* = 0.37 g/100 mL, $CHCl_3$, 90% *ee*, 91% *ee* and dr = 3.7:1]**; IR (Neat): ν_{max} 3412 (N-*H*), 2980, 1726(C=O), 1554 (NO_2), 1473, 1367 (NO_2), 1230, 1154, 1023, 976 and 729 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, major isomer) δ 8.05 (2H, dd, *J* = 8.0, 0.8 Hz), 7.65-7.54 (2H, m), 7.52-7.48 (2H, m), 7.29-7.25 (1H, m), 7.20-7.17 (1H, m), 7.15-7.09 (1H, m), 6.99 (1H, br s, N*H*), 5.05-4.7 (4H, m), 3.97-3.84 (2H, m, OCH_2CH_3), 1.57 (9H, s, $OC(CH_3)_3$), 0.92 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135, major isomer) δ 193.5 (C, *C*=O), 167.4 (C, O-*C*=O), 154.2 (C, O-*C*=O), 136.3 (C), 135.8 (C), 134.3 (CH), 130.0 (C), 129.0 (2 x CH), 128.9 (2 x CH), 128.7 (CH), 126.9 (CH), 126.5 (CH), 125.7 (CH), 80.6 (C), 77.3 (CH_2), 62.2 (CH_2, OCH_2CH_3), 56.7 (CH), 35.9 (CH), 28.3 (3 x CH_3, $OC(CH_3)_3$), 13.5 (CH_3, OCH_2CH_3); HRMS m/z 479.1796 (M + Na), calcd for $C_{24}H_{28}N_2O_7Na$ 479.1795.

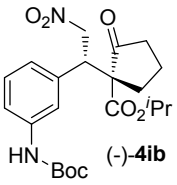
(*R*)-Isopropyl 1-((*S*)-2-nitro-1-phenylethyl)-2-oxocyclopentanecarboxylate (4hb):



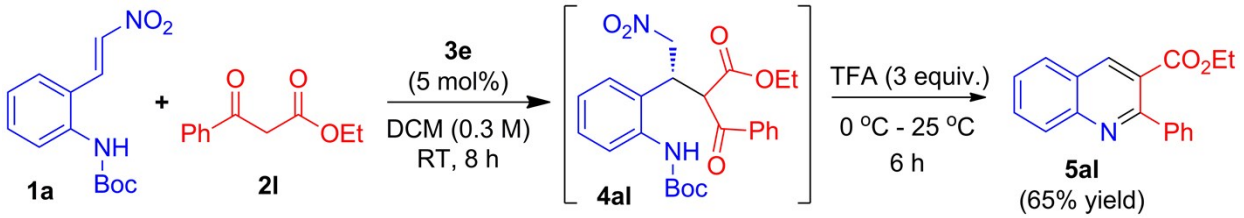
(-)-**4hb**

Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u Cellulose-2 column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 220 nm), t_R = 29.91 min (minor), t_R = 39.68 min (major); **$[\alpha]_D^{25}$ = –25.4° (*c* = 0.33 g/100 mL, $CHCl_3$, 98% *ee*)**; IR (Neat): ν_{max} 2975, 1715 (C=O), 1551 (NO_2), 1457, 1375 (NO_2), 1227, 1101, 1036 and 904 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.33-7.26 (5H, m), 5.19 (1H, dd, *J* = 13.5, 4.0 Hz), 5.09-5.00 (2H, m), 4.07 (1H, dd, *J* = 11.0, 4.0 Hz), 2.39-2.33 (2H, m), 2.05-1.87 (4H, m), 1.26 (3H, d, *J* = 6.0 Hz, $OCH(CH_3)_2$), 1.25 (3H, d, *J* = 6.0 Hz, $OCH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 212.3 (C, *C*=O), 168.8 (C, O-*C*=O), 135.5 (C), 129.4 (2 x CH), 128.8 (2 x CH), 128.2 (CH), 76.5 (CH_2), 70.1 (CH, O*C*H(CH_3)$_2$), 62.5 (C), 46.3 (CH), 37.8 (CH_2), 31.4 (CH_2), 21.6 (CH_3, $OCH(CH_3)_2$), 21.4 (CH_3, $OCH(CH_3)_2$), 19.3 (CH_2); HRMS m/z 342.1319 (M + Na), calcd for $C_{17}H_{21}NO_5Na$ 342.1318.

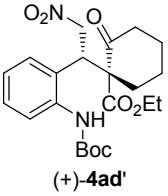
(*R*)-Isopropyl 1-((*S*)-1-(3-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxocyclopentane carboxylate (4ib): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 103-105 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.8 mL/min, λ = 254 nm), t_R = 10.76 min (minor), t_R = 12.40 min (major); **$[\alpha]_D^{25}$ = –18.5°(*c* = 0.28 g/100 mL, $CHCl_3$, 99% *ee*)**; IR (KBr): ν_{max} 3397 (N-*H*), 2981, 1731 (C=O), 1540 (NO_2), 1441, 1381 (NO_2), 1238, 1156, 1041 and 860 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37 (1H, br d, *J* = 7.5 Hz), 7.25 (1H, s), 7.23 (1H, t, *J* = 8.0 Hz), 6.95 (1H, d, *J* = 7.5 Hz), 6.50 (1H, br s, N*H*), 5.18 (1H, dd, *J* = 13.5, 3.5 Hz), 5.08 (1H, septet, *J* = 6.5 Hz), 5.01 (1H, dd, *J* = 13.5, 11.0 Hz), 4.02 (1H, dd, *J* = 11.0, 3.5 Hz), 2.41-2.36 (2H, m), 2.09 (1H, dd, *J* = 18.5, 9.5 Hz), 2.05-1.97 (1H, m), 1.96-1.92 (1H, m), 1.91-1.82 (1H, m), 1.53 (9H, s, $OC(CH_3)_3$), 1.27 (3H, d, *J* = 6.5 Hz, $OCH(CH_3)_2$), 1.26 (3H, d, *J* = 6.5 Hz, $OCH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 212.4 (C, *C*=O), 168.8 (C, O-*C*=O), 152.5 (C, O-*C*=O), 138.8 (C), 136.6 (C), 129.4 (CH), 123.7 (CH), 119.4 (CH), 118.2 (CH), 80.7 (C), 76.5 (CH_2), 70.1 (CH, O*C*H(CH_3)$_2$), 62.4 (C), 46.2 (CH), 37.8 (CH_2), 31.5 (CH_2), 28.3 (3 x CH_3, $OC(CH_3)_3$), 21.6 (CH_3, $OCH(CH_3)_2$), 21.4 (CH_3, $OCH(CH_3)_2$), 19.4 (CH_2); HRMS m/z 457.1952 (M + Na), calcd for $C_{22}H_{30}N_2O_7Na$ 457.1951.



(-)-**4ib**



Ethyl 2-phenylquinoline-3-carboxylate (5al): Prepared by following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as oil. IR (Neat): ν_{max} 2926, 1715 (C=O), 1594, 1485, 1370, 1101, 1036, 767 and 696 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.68 (1H, s), 8.21 (1H, d, *J* = 8.5 Hz), 7.95 (1H, d, *J* = 8.0 Hz), 7.86-7.82 (1H, m), 7.66-7.61 (3H, m), 7.51-7.46 (3H, m), 4.21 (2H, q, *J* = 7.0 Hz, OCH_2CH_3), 1.10 (3H, t, *J* = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.0 (C, O-*C*=O), 158.2 (C), 148.4 (C), 140.8 (C), 139.1 (CH), 131.6 (CH), 129.5 (CH), 128.6 (3 x CH), 128.25 (CH), 128.22 (2 x CH), 127.3 (CH), 125.9 (C), 125.5 (C), 61.6 (CH_2, OCH_2CH_3), 13.7 (CH_3, OCH_2CH_3); LRMS m/z 278.15 (M + H+), calcd for $C_{18}H_{15}NO_2$ 277.1103.



(*R*)-Ethyl 1-((*S*)-1-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-nitroethyl)-2-oxocyclohexane carboxylate (4ad'): Prepared by following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as oil. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak ID-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 29.9 min (major), t_R = 36.8 min (minor); **$[\alpha]_D^{25}$ = +42.8° (*c* = 0.30 g/100 mL, $CHCl_3$, >99% *ee* and >99% *de*)**; IR (Neat): ν_{max} 3364 (N-*H*), 2970, 1709 (C=O), 1556 (NO_2), 1463, 1375 (NO_2), 1227, 1156, 1019 and 762 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.52 (1H, br s), 7.27 (1H, t, *J* = 8.0 Hz), 7.13 (1H, t, *J* = 8.0 Hz), 7.07 (1H, br d, *J* = 7.5 Hz), 6.73 (1H, br s, N*H*), 5.14 (1H, dd, *J* = 14.5, 3.0 Hz), 4.70 (1H, dd, *J* = 14.5, 11.0 Hz), 4.46 (1H, dd, *J* = 11.0, 3.0 Hz), 4.26 (2H, q, *J* = 7.0 Hz, OCH_2CH_3), 2.53-2.50 (1H, m), 2.44-2.38 (1H, m), 2.14 (1H, dd, *J* = 14.0, 2.0 Hz), 2.03-2.01 (1H, m), 1.70-1.68 (1H, m), 1.64-1.57 (2H, m), 1.52 (9H, s, $OC(CH_3)_3$), 1.42-1.37 (1H, m), 1.28 (3H, t, *J* = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 207.2 (C, *C*=O), 169.7 (C, O-*C*=O), 154.0 (C, O-*C*=O), 137.0 (C), 129.5 (C), 128.5 (CH), 127.4 (CH), 126.9 (CH), 125.6 (CH), 80.4 (C), 77.5 (CH_2), 63.0 (C), 62.2 (CH_2, OCH_2CH_3), 41.4 (CH_2), 39.3 (CH), 35.9 (CH_2), 28.3 (3 x CH_3, $OC(CH_3)_3$), 27.9 (CH_2), 22.3 (CH_2), 14.0 (CH_3, OCH_2CH_3); HRMS m/z 452.2397 (M + NH_4^+), calcd for $C_{22}H_{34}N_3O_7$ 452.2397.

References:

[1] For the synthesis of substituted 2-(2-nitrovinyl)anilines **1a-j**, see: Y. Lee, S. –G. Kim, *J. Org. Chem.* **2014**, *79*, 8234−8243.