Ni(II)–bis[(*R,R*)-*N,N'*-Dibenzylcyclohexane-1,2-diamine]Br₂ Catalyzed Enantioselective Michael Additions of 1,3-Dicarbonyl Compounds to Nitroalkenes

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Supporting Information

General Information. Michael additions were carried out in screw cap vials with magnetic stirring; no special precautions were taken to exclude water or air from the reaction vessel. NiBr₂ and nitrostyrenes were obtained from commercial sources and were used as received. Malonates and β -ketoesters were obtained from commercial sources and distilled prior to use except of benzyl malonate and diethyl acetamidomalonate which were used as received. Aliphatic nitroalkenes were prepared according to literature procedures.¹ Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and either ceric ammonium nitrate or permanganate stain, followed by heating. Optical rotations were measured on a Jasco DIP-0181 digital polarimeter with a sodium lamp and are reported as follows: $[\alpha]_D^{25}$ (c = g/100 mL, solvent). Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. ¹H-NMR spectra were recorded on a Varian Inova-500 (500 MHz) or on a Varian Mercury 400 (400 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data are reported as app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; integration; coupling constant(s) in Hz. Proton-decoupled ¹³C-NMR spectra were recorded on a Varian Inova-500 (125 MHz) or on a Varian Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Low- and high-resolution mass spectra were obtained on Jeol AX-505 or SX-102 spectrometers in the Harvard University Mass Spectrometry Laboratory.

Stereochemical Assignments: The absolute configurations of compounds **4a-g**, **4n-q** and **6e** were assigned by comparison of their optical rotations with literature values.^{2,3} The absolute configuration of compound **6f** was assigned by transforming it into **7f** (X-ray). These assignments showed the reaction to be stereochemically homogeneous, giving products with the same sense of induction (in compliance with the convention this may correspond to either (*R*) or (*S*) configuration). The absolute configurations of the remaining examples **4h-m** and **6a-d** were assigned by analogy.

Ni(II)–bis[(*R,R*)-*N,N'*-Dibenzylcyclohexane-1,2-diamine]Br₂ (1**).** A mixture of 437 mg (2 mmol) of NiBr₂ and 1266 mg (4.3 mmol) of (*R,R*)-*N,N'*-Dibenzylcyclohexane-1,2-diamine⁴ in 50 mL of acetonitrile were heated under reflux for five hours. Subsequent to solvent removal, the residue was dissolved in dichloromethane

and filtered through a fritted glass funnel. The solvent was evaporated off and the crude product was recrystallized from dichloromethane/acetonitrile to yield the title compound as a microcrystalline pale

blue powder in 82% yield. IR (cell, CH₂Cl₂) 3272, 3043, 2942, 2862, 1454, 1089, 1030, 977, 938, 901, 876, 785 cm⁻¹; [α]_D²² -73.3 (*c* 1.14, CHCl₃).

The complex was further characterized by X-ray crystallography:

The requisite CIF file has been submitted to the journal.

General Procedure for the NiBr₂ – chiral diamine catalyzed Michael reaction of 1,3-dicarbonyl compounds with conjugated nitroalkenes. The preformed complex **1** (16.2 mg, 0.02 mmol), the 1,3-dicarbonyl compound (1.2 mmol) and the nitroalkene (1 mmol) were added to a screw cap vial containing a stir bar. Solvent (1 mL) was added and the mixture was stirred for the amount of time indicated. The volatile components were removed under reduced pressure and the crude product purified by column chromatography.

(S)-Methyl-2-carbomethoxy-4-nitro-3-phenylbutyrate (4a). The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a white solid (99% yield) which was judged to be >95% pure by ¹H NMR spectroscopy. mp: 64 °C; IR (cell, CH₂Cl₂) 3064, 2957, 1739, 1558, 1498, 1456, 1437, 1380, 1327, 1294, 1240, 1197, 1159, 1020, 982, 906, 576 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 7.34-7.26 (m, 3H), 7.24-7.21 (m, 2H), 4.92 (dd, 1H, *J*_{AB} = 13.2, *J*_{AX} = 4.8 Hz), 4.88 (dd, 1H, *J*_{AB} = 13.2, *J*_{BX} = 9.2 Hz), 4.24 (ddd, 1H, *J* = 9.0, 9.0, 4.9 Hz), 3.86 (d, 1H, *J* = 8.8 Hz), 3.75 (s, 3H), 3.55 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 167.8, 167.2, 136.1, 129.0, 128.4, 127.8, 77.3, 54.7, 53.0, 52.8, 42.9; HRMS (ES⁺): Exact mass calcd for C₁₃H₁₆NO₆ [M + H]⁺, 282.0977. Found 282.0982; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer *t*_r = 21.7 min, major enantiomer *t*_r = 29.3 min; 94% ee; [α]_D²⁵ +6.2 (*c* 1.38, CHCl₃).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: [α]_D²⁵ +4.4 (*c* 1.02, CHCl₃), (93% ee, (*S*)-isomer).

(S)-Ethyl-2-carboethoxy-4-nitro-3-phenylbutyrate (4b). The title compound was prepared according to the General Procedure and purified by column chromatography (15% EtOAc/hexanes) to give a white solid (99% yield) which was judged to be >95%

pure by ^1H NMR spectroscopy. mp: 41-42 °C (hexanes/EtOAc); IR (cell, CH_2Cl_2) 3065, 2984, 1748, 1733, 1558, 1371, 1301, 1232, 1180, 1157, 1096, 1029, 861, 574 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.32-7.23 (m, 5H), 4.92 (dd, 1H, $J_{AB} = 13.2$, $J_{AX} = 4.7$ Hz), 4.86 (dd, 1H, $J_{AB} = 13.2$, $J_{BX} = 9.5$ Hz), 4.26-4.17 (m, 3H), 4.00 (q, 2H, $J = 7.1$ Hz), 3.82 (d, 1H, $J = 9.3$ Hz), 1.25 (t, 3H, $J = 7.3$ Hz), 1.03 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.4, 166.7, 136.2, 128.8, 128.3, 127.9, 77.6, 62.1, 61.8, 54.9, 42.9, 13.9, 13.6; HRMS (ES^+): Exact mass calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_6$ $[\text{M} + \text{H}]^+$, 310.1290. Found 310.1280; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer $t_r = 18.5$ min, major enantiomer $t_r = 43.1$ min; 95% ee; $[\alpha]_D^{23} +7.3$ (c 1.07, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_D^{25} +7.09$ (c 1.00, CHCl_3), (95% ee, (*S*)-isomer).

(*S*)-1-Methylethyl-2-(1-methylethoxycarbo)-4-nitro-3-phenylbutyrate (4c).

The title compound was prepared according to the General Procedure and purified by column chromatography (15% EtOAc/hexanes) to give a white solid (99% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 51 °C; IR (cell, CH_2Cl_2) 2985, 2937, 1728, 1558, 1467, 1444, 1377, 1290, 1243, 1182, 1147, 1101, 970, 904, 827, 580 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.32-7.22 (m, 5H), 5.08 (septet, 1H, $J = 6.3$ Hz) 4.92 (dd, 1H, $J_{AB} = 12.9$, $J_{AX} = 4.5$ Hz), 4.84 (dd, 1H, $J_{AB} = 12.9$, $J_{BX} = 9.7$ Hz), 4.83 (septet, 1H, $J = 6.3$ Hz) 4.20 (ddd, 1H, $J = 9.5$, 9.5, 4.4 Hz), 3.67 (d, 1H, $J = 9.3$ Hz), 1.24 (d, 3H, $J = 6.3$ Hz), 1.23 (d, 3H, $J = 6.3$ Hz), 1.06 (d, 3H, $J = 6.3$ Hz), 1.01 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.01, 166.28, 136.25, 128.81, 128.23, 128.10, 128.08, 77.88, 69.88, 69.49, 55.11, 42.88, 21.53, 21.41, 21.24, 21.21; HRMS (ES^+): Exact mass calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_6$ $[\text{M} + \text{H}]^+$, 338.1603. Found 338.1600; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer $t_r = 13.6$ min, major enantiomer $t_r = 30.1$ min; 95% ee; $[\alpha]_D^{25} +10.1$ (c 1.11, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_D^{25} +8.17$ (c 1.01, CHCl_3), (94% ee, (*S*)-isomer).

(*S*)-1,1-Dimethylethyl-2-(1,1-dimethylethoxycarbo)-4-nitro-3-phenylbutyrate (4d).

The title compound was prepared according to the General Procedure and purified by column chromatography (10% EtOAc/hexanes) to give a white solid (98% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 126-127 °C; IR (cell, CH_2Cl_2) 2982, 2934, 1728, 1557, 1456, 1370, 1300, 1163, 1142, 964, 845 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.31-7.23 (m, 5H), 4.92 (dd, 1H, $J_{AB} = 12.9$, $J_{AX} = 4.1$ Hz), 4.79 (dd, 1H, $J_{AB} = 12.9$, $J_{BX} = 10.1$ Hz), 4.12 (ddd, 1H, $J = 9.8$, 9.8, 4.4 Hz), 3.62 (d, 1H, $J = 9.8$ Hz), 1.46 (s, 9H), 1.22 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) 166.9, 166.0, 136.5, 128.7, 128.3, 128.1, 82.8, 82.2, 78.2, 56.4, 43.0, 27.8, 27.4; HRMS (ES^+): Exact mass calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_6$ $[\text{M} + \text{H}]^+$, 366.1916. Found 366.1928; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer $t_r = 11.2$ min, major enantiomer $t_r = 28.1$ min; 94% ee; $[\alpha]_D^{22} +13.6$ (c 1.06, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_D^{25} +3.86$ (c 1.03, CHCl_3), (33% ee, (*S*)-isomer).

(S)-Benzyl-2-carbobenzyloxy-4-nitro-3-phenylbutyrate (4e). The title compound was prepared according to the General Procedure and purified by column chromatography (15% EtOAc/hexanes) to give a white solid (99% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 72-73 °C; IR (cell, CH_2Cl_2) 3068, 3036, 2963, 1736, 1558, 1498, 1456, 1378, 1326, 1286, 1217, 1156, 1003, 975, 908, 562; ^1H NMR (500 MHz, CDCl_3) 7.37-7.26 (m, 11H), 7.22-7.20 (m, 2H), 7.12-7.11 (m, 2H), 5.21 (d, 1H, J_{AB} = 12.2 Hz), 5.18 (d, 1H, J_{AB} = 12.2 Hz), 4.98 (d, 1H, J_{AB} = 12.2 Hz), 4.96 (d, 1H, J_{AB} = 12.2 Hz), 4.91-4.83 (m, 2H), 4.30 (ddd, 1H, J = 8.9, 8.9, 5.1 Hz), 3.98 (d, 1H, 9.3 Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.06, 166.45, 135.88, 134.66, 134.57, 128.90, 128.55, 128.53, 128.45, 128.37, 128.27, 128.24, 128.16, 127.85, 77.32, 67.68, 67.50, 54.83, 42.85; HRMS (ES^+): Exact mass calcd for $\text{C}_{25}\text{H}_{27}\text{N}_2\text{O}_6$ [$\text{M} + \text{NH}_4$] $^+$, 451.1869. Found 451.1870; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer t_r = 99.6 min, major enantiomer t_r = 110.1 min; 95% ee; $[\alpha]_{\text{D}}^{23}$ -2.9 (c 1.11, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_{\text{D}}^{25}$ -4.82 (c 1.03, CHCl_3), (89% ee, (*S*)-isomer).

(R)-Methyl-2-carbomethoxy-2-methyl-4-nitro-3-phenylbutyrate (4f). The title compound was prepared according to the General Procedure and purified by column chromatography (CH_2Cl_2) to give a white solid (96% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 131-132 °C; IR (cell, CH_2Cl_2) 3065, 3007, 2956, 1735, 1557, 1456, 1436, 1379, 1308, 1284, 1252, 1152, 1109, 982, 886, 835, 618 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.32-7.26 (m, 3H), 7.16-7.14 (m, 2H), 5.05 (dd, 1H, J_{AB} = 13.7, J_{AX} = 11.1 Hz), 5.03 (dd, 1H, J_{AB} = 13.7, J_{BX} = 3.1 Hz), 4.18 (dd, 1H, J = 10.0, 4.6 Hz), 3.77 (s, 3H), 3.72 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) 171.3, 170.7, 134.9, 128.9, 128.7, 128.4, 77.4, 56.7, 53.0, 52.8, 48.3, 20.2; HRMS (ES^+): Exact mass calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_6$ [$\text{M} + \text{H}$] $^+$, 296.1134. Found 296.1134; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); major enantiomer t_r = 9.6 min, minor enantiomer t_r = 10.4 min; 94% ee; $[\alpha]_{\text{D}}^{25}$ -34.9 (c 1.16, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*R*) by comparison of the optical rotation with the following literature value: Lit³: $[\alpha]_{\text{D}}^{32}$ +32.3 (c 1.06, CHCl_3), (93% ee, (*S*)-isomer).

(S)-Ethyl-2-acetamido-2-carboethoxy-4-nitro-3-phenylbutyrate (4g). The title compound was prepared according to the General Procedure and purified by column chromatography (5% ether in CH_2Cl_2) to give a white solid (92% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 135-136 °C; IR (cell, CH_2Cl_2) 3390, 2985, 1743, 1687, 1556, 1492, 1375, 1301, 1276, 1257, 1211, 1100, 1064, 1011, 858, 614; ^1H NMR (500 MHz, CDCl_3) 7.29-7.26 (m, 3H), 7.20-7.17 (m, 2H), 6.72 (s, 1H), 5.50 (dd, 1H, J = 21.7, 12.2 Hz), 4.72-4.65 (m, 2H), 4.29 (dq, 1H, J = 10.7, 7.2 Hz), 4.24 (dq, 1H, J = 10.7, 7.2 Hz), 4.15 (dq, 1H, J = 10.7, 7.2 Hz), 4.03 (dq, 1H, J = 10.7, 7.2 Hz), 1.25 (t, 3H, J = 7.1 Hz), 1.23 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, CDCl_3) 170.09, 166.41, 165.71, 133.81, 128.78, 128.74, 128.66, 76.81, 67.17, 63.58, 62.77, 48.31, 22.98, 13.86, 13.75; HRMS (ES^+): Exact mass calcd for $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_7$ [$\text{M} + \text{H}$] $^+$, 367.1505. Found 367.1510; Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H

column (85:15 hexanes:isopropanol, 0.8 mL/min, 215 nm); major enantiomer t_r = 18.1 min, minor enantiomer t_r = 29.8 min; 94% ee; $[\alpha]_D^{25}$ -42.5 (*c* 1.04, CHCl₃).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_D^{25}$ -26.33 (*c* 1.01, CHCl₃), (41% ee, (*S*-isomer).

(*S*)-Ethyl-2-carboethoxy-4-nitro-3-(4-methylphenyl)butyrate (4h). The title compound was prepared according to the General Procedure and purified by column chromatography (15% EtOAc/hexanes) to give a colorless oil (99% yield) which was judged to be >95% pure by ¹H NMR spectroscopy. IR (film) 2984, 2939, 1732, 1557, 1516, 1446, 1371, 1301, 1256, 1179, 1096, 1029, 861, 819, 720, 680, 601, 562; ¹H NMR (500 MHz, CDCl₃) 7.13-7.09 (m, 4H), 4.89 (dd, 1H, J_{AB} = 13.2, J_{AX} = 4.7 Hz), 4.83 (dd, 1H, J_{AB} = 13.2, J_{BX} = 9.5 Hz), 4.27-4.17 (m, 3H), 4.01 (q, 2H, J = 7.2 Hz), 3.80 (d, 1H, J = 9.8 Hz), 2.29 (s, 3H), 1.26 (t, 3H, J = 7.1 Hz), 1.06 (t, 3H, J = 7.3 Hz); ¹³C NMR (125 MHz, CDCl₃) 167.4, 166.8, 138.0, 133.0, 129.5, 127.8, 77.7, 62.0, 61.7, 54.9, 42.5, 21.0, 13.9, 13.7; HRMS (ES⁺): Exact mass calcd for C₁₆H₂₂NO₆ [M + H]⁺, 324.1447. Found 324.1439; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer t_r = 17.5 min, major enantiomer t_r = 40.9 min; 95% ee; $[\alpha]_D^{22}$ +6.25 (*c* 1.36, CHCl₃).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by analogy.

(*S*)-Ethyl-2-carboethoxy-4-nitro-3-(4-methoxyphenyl)butyrate (4i). The title compound was prepared according to the General Procedure and purified by column chromatography (15% EtOAc/hexanes) to give a colorless oil (99% yield) which was judged to be >95% pure by ¹H NMR spectroscopy. IR (film) 2984, 2939, 2908, 1732, 1613, 1556, 1556, 1515, 1465, 1444, 1371, 1302, 1256, 1182, 1117, 1032, 860, 836, 744, 602, 564; ¹H NMR (500 MHz, CDCl₃) 7.16-7.13 (m, 2H), 6.84-6.81 (m, 2H), 4.88 (dd, 1H, J_{AB} = 13.0, J_{AX} = 4.5 Hz), 4.80 (dd, 1H, J_{AB} = 13.0, J_{BX} = 9.7 Hz), 4.25-4.15 (m, 3H), 4.01 (q, 2H, J = 7.0 Hz), 3.78 (d, 1H, J = 9.3 Hz), 3.76 (s, 3H), 1.26 (t, 3H, J = 7.1 Hz), 1.06 (t, 3H, J = 7.1 Hz); ¹³C NMR (125 MHz, CDCl₃) 167.5, 166.8, 159.4, 129.1, 127.9, 114.2, 77.9, 62.1, 61.8, 55.2, 55.0, 42.3, 13.9, 13.7; HRMS (ES⁺): Exact mass calcd for C₁₆H₂₂NO₇ [M + H]⁺, 340.1396. Found 340.1394; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (90:10 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer t_r = 22.9 min, major enantiomer t_r = 67.6 min; 95% ee; $[\alpha]_D^{25}$ +7.7 (*c* 1.01, CHCl₃).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by analogy.

(*S*)-Ethyl-2-carboethoxy-4-nitro-3-(4-bromophenyl)butyrate (4j). The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a white solid (99% yield) which was judged to be >95% pure by ¹H NMR spectroscopy. mp: 59-60 °C (EtOH); IR (film) 2983, 2950, 1732, 1556, 1490, 1445, 1371, 1301, 1256, 1180, 1112, 1075, 1028, 998, 860, 825, 716, 633, 595, 553; ¹H NMR (500 MHz, CDCl₃) 7.46-7.43 (m, 2H), 7.14-7.11 (m, 2H), 4.90 (dd, 1H, J_{AB} = 13.2, J_{AX} = 4.7 Hz), 4.82 (dd, 1H, J_{AB} = 13.2, J_{BX} = 9.4 Hz), 4.27-4.16 (m, 3H), 4.02 (q, 2H, J = 7.2 Hz), 3.77 (d, 1H, J = 9.3 Hz), 1.25 (t, 3H, J = 7.1 Hz), 1.08 (t, 3H, J = 7.1 Hz); ¹³C NMR (125 MHz, CDCl₃) 167.1, 166.5, 135.2, 132.0, 129.7, 122.4, 77.3, 62.2, 62.0, 54.6, 42.3, 13.9, 13.7; HRMS (ES⁺): Exact mass calcd for C₁₅H₁₉BrNO₆ [M + H]⁺, 388.0395. Found 388.0403; Enantiomeric

excess was determined by HPLC with a Chiralcel AD column (90:10 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer t_r = 23.5 min, major enantiomer t_r = 56.3 min; 95% ee; $[\alpha]_D^{25}$ +8.4 (c 1.04, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by analogy.

(*S*)-Ethyl-2-carboethoxy-4-nitro-3-(2-chlorophenyl)butyrate (4k).

The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a colorless oil (98% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. IR (film) 2984, 1733, 1557, 1478, 1445, 1371, 1301, 1253, 1231, 1181, 1097, 1038, 860, 758, 703; ^1H NMR (500 MHz, CDCl_3) 7.41-7.38 (m, 1H), 7.27-7.20 (m, 3H), 5.10 (dd, 1H, J_{AB} = 13.7, J_{AX} = 8.6 Hz), 4.95 (dd, 1H, J_{AB} = 13.7, J_{BX} = 4.4 Hz), 4.73 (ddd, 1H, J = 8.6, 8.6, 4.4 Hz), 4.25-4.14 (m, 2H), 4.09-4.04 (m, 3H), 1.23 (t, 3H, J = 7.3 Hz), 1.09 (t, 3H, J = 7.3 Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.3, 166.7, 134.0, 133.6, 130.4, 129.4, 128.8, 127.2, 75.6, 62.1, 62.0, 53.0, 39.3, 13.9, 13.7; HRMS (ES^+): Exact mass calcd for $\text{C}_{15}\text{H}_{19}\text{ClNO}_6$ $[\text{M} + \text{H}]^+$, 344.0901. Found 344.0916; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); minor enantiomer t_r = 11.0 min, major enantiomer t_r = 56.5 min; 92% ee; $[\alpha]_D^{22}$ +11.1 (c 1.13, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by analogy.

(*S*)-Ethyl-2-carboethoxy-4-nitro-3-(2,3-dimethoxyphenyl)butyrate (4l).

The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a colorless oil (99% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. IR (film) 2983, 2941, 1733, 1587, 1556, 1482, 1440, 1370, 1272, 1224, 1178, 1096, 1012, 860, 790, 749, 678, 624; ^1H NMR (500 MHz, CDCl_3) 6.94 (app t, 1H, J = 8.1 Hz), 6.84 (app d, 1H, J = 8.3 Hz), 6.72 (app d, 1H, J = 7.8 Hz), 4.98 (dd, 1H, J_{AB} = 13.2, J_{AX} = 8.9 Hz), 4.89 (dd, 1H, J_{AB} = 13.2, J_{BX} = 4.3 Hz), 4.46 (ddd, 1H, J = 9.3, 9.3, 4.4 Hz), 4.24-4.13 (m, 2H), 4.05-3.97 (m, 3H), 3.94 (s, 3H), 3.83 (s, 3H), 1.23 (t, 3H, J = 7.2 Hz), 1.06 (t, 3H, J = 7.8 Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.7, 167.1, 152.6, 147.1, 129.1, 123.8, 120.8, 112.5, 76.5, 61.9, 61.7, 60.6, 55.6, 53.4, 38.6, 13.9, 13.7; HRMS (ES^+): Exact mass calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_8$ $[\text{M} + \text{H}]^+$, 370.1502. Found 370.1494; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (90:10 hexanes:isopropanol, 0.8 mL/min, 215 nm); minor enantiomer t_r = 11.4 min, major enantiomer t_r = 19.1 min; 93% ee; $[\alpha]_D^{24}$ +12.0 (c 1.15, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by analogy.

(*S*)-Ethyl-2-carboethoxy-4-nitro-3-(2,4-dimethoxyphenyl)butyrate (4m).

The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a white solid (98% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 67°C; IR (film) 2982, 2941, 2840, 1732, 1614, 1598, 1587, 1556, 1509, 1466, 1440, 1376, 1288, 1221, 1159, 1135, 1031, 936, 860, 836, 804, 640; ^1H NMR (500 MHz, CDCl_3) 7.03 (app d, 1H, J = 8.8 Hz), 6.41 (app d, 1H, J = 2.4 Hz), 6.37 (app dd, 1H, J = 8.3, 2.4 Hz), 4.97 (dd, 1H, J_{AB} = 12.7, J_{AX} = 9.3 Hz), 4.82 (dd, 1H, J_{AB} = 12.7, J_{BX} = 4.4 Hz), 4.28 (ddd, 1H, J = 9.8, 9.8, 4.4 Hz), 4.26-4.16 (m, 2H), 4.11 (d, 1H, 10.3 Hz), 3.95 (q, 2H, J = 7.2 Hz), 3.83 (s, 3H), 3.75 (s, 3H), 1.26 (t, 3H, J = 7.2 Hz), 1.02 (t, 3H, J = 7.2 Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.9, 167.2, 160.8, 158.4, 131.5, 115.8, 104.2, 99.0, 76.3, 61.9, 61.5, 55.4, 55.3, 52.7, 40.1, 13.9, 13.7; HRMS (ES^+): Exact mass calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_8$ $[\text{M} + \text{H}]^+$,

370.1502. Found 370.1505; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (90:10 hexanes:isopropanol, 0.8 mL/min, 215 nm); minor enantiomer t_r = 15.4 min, major enantiomer t_r = 22.9 min; 94% ee; $[\alpha]_D^{22}$ +22.2 (c 1.17, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by analogy.

(S)-Ethyl-2-carboethoxy-4-nitro-3-(3,4-methylenedioxyphenyl)butyrate (4n). The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a white solid (97% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 69°C (ether/hexanes); IR (film) 2984, 2906, 2781, 1729, 1611, 1556, 1490, 1445, 1371, 1248, 1181, 1106, 1039, 935, 907, 860, 815, 642; ^1H NMR (500 MHz, CDCl_3) 6.73-6.67 (m, 3H), 5.93 (s, 2H), 4.87 (dd, 1H, J_{AB} = 13.2, J_{AX} = 4.5 Hz), 4.78 (dd, 1H, J_{AB} = 13.2, J_{BX} = 9.4 Hz), 4.27-4.17 (m, 2H), 4.14 (ddd, 1H, J = 9.4, 9.4, 4.6 Hz), 4.04 (q, 2H, J = 7.2 Hz), 3.74 (d, 1H, J = 9.8 Hz), 1.26 (t, 3H, J = 7.1 Hz), 1.10 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.4, 166.7, 147.9, 147.5, 129.7, 121.5, 108.5, 108.2, 101.2, 77.8, 62.1, 61.8, 55.0, 42.7, 13.9, 13.8; HRMS (ES^+): Exact mass calcd for $\text{C}_{16}\text{H}_{20}\text{NO}_8$ $[\text{M} + \text{H}]^+$, 354.1189. Found 354.1193; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (90:10 hexanes:isopropanol, 0.8 mL/min, 215 nm); minor enantiomer t_r = 27.2 min, major enantiomer t_r = 41.2 min; 95% ee; $[\alpha]_D^{22}$ +6.3 (c 1.03, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_D^{25}$ +4.85 (c 1.01, CHCl_3), (93% ee, (*S*)-isomer).

(R)-Ethyl-2-carboethoxy-4-nitro-3-(2-furyl)butyrate (4o). The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a colorless oil (98% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. IR (film) 2985, 2940, 1734, 1559, 1506, 1466, 1448, 1376, 1301, 1261, 1243, 1179, 1150, 1097, 1017, 918, 861, 817, 744, 599; ^1H NMR (500 MHz, CDCl_3) 7.31 (app d, 1H, J = 2.0 Hz), 6.26 (app dd, 1H, J = 2.9, 2.0 Hz), 6.19 (app d, 1H, J = 2.9 Hz), 4.91-4.84 (m, 2H), 4.34 (ddd, 1H, J = 7.8, 7.8, 5.4 Hz), 4.19 (dq, 2H, J = 7.2, 2.0 Hz), 4.11 (q, 2H, J = 7.2 Hz), 3.87 (d, 1H, J = 7.8 Hz), 1.23 (t, 3H, J = 7.1 Hz), 1.16 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.0, 166.7, 149.5, 142.6, 110.4, 108.3, 75.3, 62.0, 52.9, 36.7, 13.8, 13.7; HRMS (ES^+): Exact mass calcd for $\text{C}_{13}\text{H}_{18}\text{NO}_7$ $[\text{M} + \text{H}]^+$, 300.1083. Found 300.1088; Enantiomeric excess was determined by HPLC with a Chiralcel AD column (90:10 hexanes:isopropanol, 0.8 mL/min, 215 nm); minor enantiomer t_r = 11.7 min, major enantiomer t_r = 13.6 min; 95% ee; $[\alpha]_D^{22}$ -2.8 (c 1.22, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*R*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_D^{25}$ -4.04 (c 1.03, CHCl_3), (89% ee, (*R*)-isomer).

(R)-Ethyl-2-carboethoxy-3-(nitromethyl)octanoate (4p). The title compound was prepared according to the General Procedure but using two equivalents of ethylmalonate and no solvent. Purification by column chromatography (CH_2Cl_2) gave a colorless oil (84% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. IR (film) 2949, 2934, 2863, 1734, 1556, 1466, 1447, 1381, 1370, 1301, 1207, 1178, 1159, 1097, 1032, 862, 726; ^1H NMR (500 MHz, CDCl_3) 4.68 (dd, 1H, J_{AB} = 13.4, J_{AX} = 4.9 Hz), 4.51 (dd, 1H, J_{AB} = 13.4, J_{BX} = 7.1 Hz), 4.22-4.16 (m, 4H), 3.60 (d, 1H, J = 5.9 Hz), 2.90-2.83 (m, 1H), 1.46-1.41 (m,

2H), 1.36-1.31 (m, 2H), 1.30-1.23 (m, 10H), 0.85 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.92, 167.72, 76.61, 61.81, 61.66, 52.54, 36.83, 31.33, 29.88, 26.14, 22.26, 13.93, 13.91, 13.81; HRMS (ES^+): Exact mass calcd for $\text{C}_{14}\text{H}_{26}\text{NO}_6$ $[\text{M} + \text{H}]^+$, 304.1760. Found 304.1754; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (99:1 hexanes:isopropanol, 0.6 mL/min, 215 nm); major enantiomer $t_r = 20.3$ min, minor enantiomer $t_r = 25.1$ min; 89% ee; $[\alpha]_{\text{D}}^{24} +5.5$ (c 1.13, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*R*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_{\text{D}}^{25} +4.82$ (c 1.00, CHCl_3), (89% ee, (*R*)-isomer).

(*R*)-Ethyl-2-carboethoxy-3-(nitromethyl)-5-methylhexanoate (4q). The title compound was prepared according to the General Procedure but using two equivalents of ethylmalonate and no solvent. Purification by column chromatography (CH_2Cl_2) gave a colorless oil (94% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. IR (film) 2961, 2887, 1733, 1556, 1468, 1447, 1384, 1370, 1302, 1269, 1245, 1216, 1177, 1097, 1032, 863; ^1H NMR (500 MHz, CDCl_3) 4.67 (dd, 1H, $J_{AB} = 13.4$, $J_{AX} = 5.4$ Hz), 4.50 (dd, 1H, $J_{AB} = 13.4$, $J_{BX} = 6.6$ Hz), 4.19 (q, 2H, $J = 7.2$ Hz), 4.18 (q, 2H, $J = 7.2$ Hz), 3.58 (d, 1H, $J = 5.9$ Hz), 2.96-2.89 (m, 1H), 1.68-1.57 (m, 1H), 1.31-1.28 (m, 2H), 1.25 (t, 6H, $J = 7.1$ Hz), 0.89 (d, 3H, $J = 6.3$ Hz), 0.88 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 167.90, 167.70, 76.75, 61.80, 61.63, 52.52, 38.84, 34.73, 24.98, 22.24, 22.10, 13.94, 13.90; HRMS (ES^+): Exact mass calcd for $\text{C}_{13}\text{H}_{24}\text{NO}_6$ $[\text{M} + \text{H}]^+$, 290.1603. Found 290.1607; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (99:1 hexanes:isopropanol, 0.6 mL/min, 215 nm); major enantiomer $t_r = 16.5$ min, minor enantiomer $t_r = 19.8$ min; 88% ee; $[\alpha]_{\text{D}}^{24} +7.1$ (c 1.31, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*R*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_{\text{D}}^{25} +6.58$ (c 0.99, CHCl_3), (90% ee, (*R*)-isomer).

(*R*)-Ethyl-2-carboethoxy-3-(nitromethyl)-4-methylpentanoate (4r). The title compound was prepared according to the General Procedure but using two equivalents of ethylmalonate and no solvent. Purification by column chromatography (CH_2Cl_2) gave a colorless oil (82% yield) which was judged to be >95% pure by ^1H NMR spectroscopy. IR (film) 2971, 2940, 2879, 1732, 1557, 1466, 1383, 1325, 1262, 1228, 1177, 1160, 1097, 1027, 861; ^1H NMR (500 MHz, CDCl_3) 4.70 (dd, 1H, $J_{AB} = 14.5$, $J_{AX} = 4.2$ Hz), 4.56 (dd, 1H, $J_{AB} = 14.5$, $J_{BX} = 5.6$ Hz), 4.22-4.12 (m, 4H), 3.64 (d, 1H, $J = 5.5$ Hz), 2.89-2.85 (m, 1H), 1.86-1.76 (m, 1H), 1.25 (t, 3H, $J = 7.1$ Hz), 1.24 (t, 3H, $J = 7.1$ Hz), 0.95 (d, 3H, $J = 7.0$ Hz), 0.92 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 168.3, 168.1, 75.3, 62.0, 61.7, 51.6, 42.2, 29.6, 19.7, 19.1, 13.8; HRMS (ES^+): Exact mass calcd for $\text{C}_{12}\text{H}_{22}\text{NO}_6$ $[\text{M} + \text{H}]^+$, 276.1447. Found 276.1452; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (98:2 hexanes:isopropanol, 0.7 mL/min, 215 nm); major enantiomer $t_r = 11.5$ min, minor enantiomer $t_r = 26.2$ min; 90% ee; $[\alpha]_{\text{D}}^{23} +12.85$ (c 1.31, CHCl_3).

Configuration assignment: The absolute stereochemistry was assigned as (*R*) by analogy.

(3*S*)-Methyl-2-acetyl-4-nitro-3-phenylbutyrate (6a). The title compound was prepared according to the General Procedure and purified by column chromatography (20% EtOAc/hexanes) to give a white solid (94% yield, ~ 1:1 mixture of diastereomers) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 92-106 °C; IR (cell,

CH₂Cl₂) 3064, 3034, 2956, 1747, 1721, 1557, 1496, 1456, 1436, 1379, 1360, 1274, 1219, 1175, 1147, 982, 625 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 7.32-7.24 (m, 3H), 7.20-7.17 (m, 2H), 4.84 (dd, 0.5H, *J*_{AB} = 12.7, *J*_{AX} = 4.5 Hz), 4.80 (dd, 0.5H, *J*_{AB} = 12.7, *J*_{BX} = 9.2 Hz), 4.76 (d, 1H, *J* = 6.3 Hz) 4.25-4.18 (m, 1H), 4.13 (d, 0.5H, *J* = 9.8 Hz), 4.04 (d, 0.5H, *J* = 9.8 Hz), 3.75 (s, 1.5H), 3.50 (s, 1.5H), 2.27 (s, 1.5H), 2.03 (s, 1.5H); ¹³C NMR (125 MHz, CDCl₃) 201.07, 200.23, 167.93, 167.30, 136.34, 136.20, 129.09, 128.92, 128.31, 128.21, 128.19, 127.80, 127.76, 77.69, 77.57, 61.72, 61.30, 52.90, 52.69, 52.67, 42.52, 42.49, 42.22, 30.32, 30.18; HRMS (ES⁺): Exact mass calcd for C₁₃H₁₆NO₅ [M + H]⁺, 266.1028. Found 266.1024; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); First diastereomer: major enantiomer *t*_r = 14.2 min, minor enantiomer *t*_r = 20.4 min; 94% ee; Second diastereomer: minor enantiomer *t*_r = 19.4 min, major enantiomer *t*_r = 23.7 min, 94% ee; [α]_D²⁴ +69.1 (*c* 1.08, CHCl₃).

Configuration assignment: The absolute stereochemistry at carbon 3 was assigned as (*S*) by analogy.

(3*S*)-Ethyl-2-acetyl-4-nitro-3-phenylbutyrate (6b). The title compound was prepared according to the General Procedure and purified by column chromatography (CH₂Cl₂) to give a white solid (96% yield, ~ 1:1 mixture of diastereomers) which was judged to be >95% pure by ¹H NMR spectroscopy. mp: 71-74 °C (MeOH); IR (cell, CH₂Cl₂) 3065, 2984, 2940, 1743, 1719, 1557, 1496, 1456, 1433, 1379, 1275, 1379, 1275, 1248, 1218, 1180, 1146, 1019, 858, 626 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 7.32-7.24 (m, 3H), 7.21-7.18 (m, 2H), 4.87-4.71 (m, 2H), 4.25-4.18 (m, 2H), 4.11 (d, 0.5H, *J* = 10.0 Hz), 4.02 (d, 0.5H, *J* = 10.0 Hz), 3.95 (q, 1H, *J* = 7.2 Hz), 2.29 (s, 1.5H), 2.05 (s, 1.5H), 1.27 (t, 1.5H, *J* = 7.1 Hz), 0.99 (t, 1.5H, *J* = 7.1 Hz); ¹³C NMR (125 MHz, CDCl₃) 201.12, 200.33, 167.45, 166.78, 136.33, 136.27, 129.08, 128.87, 128.29, 128.21, 127.91, 127.83, 77.82, 77.71, 62.15, 61.89, 61.88, 61.55, 42.46, 42.21, 30.28, 30.04, 13.91, 13.60; HRMS (ES⁺): Exact mass calcd for C₁₄H₁₈NO₅ [M + H]⁺, 280.1185. Found 280.1187; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); First diastereomer: major enantiomer *t*_r = 12.1 min, minor enantiomer *t*_r = 17.8 min; 93% ee; Second diastereomer: minor enantiomer *t*_r = 19.0 min, major enantiomer *t*_r = 32.6 min, 93% ee; [α]_D²⁴ +50.5 (*c* 1.00, CHCl₃).

Configuration assignment: The absolute stereochemistry at carbon 3 was assigned as (*S*) by analogy.

(3*S*)-1',1'-Dimethylethyl-2-acetyl-4-nitro-3-phenylbutyrate (6c). The title compound was prepared according to the General Procedure and purified by column chromatography (15% EtOAc/hexanes) to give a white solid (97% yield, 1.5:1 mixture of diastereomers + a small amount of the enol tautomer) which was judged to be >95% pure by ¹H NMR spectroscopy. mp: 128-136 °C; IR (cell, CH₂Cl₂) 2983, 2934, 1737, 1718, 1557, 1456, 1433, 1371, 1289, 1258, 1144, 840, 549 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 7.31-7.23 (m, 3H), 7.21-7.19 (m, 2H), 4.85 (dd, 0.4H, *J*_{AB} = 12.7, *J*_{AX} = 4.3 Hz), 4.81 (dd, 0.4H, *J*_{AB} = 12.7, *J*_{BX} = 9.7 Hz), 4.72 (dd, 0.6H, *J*_{AB} = 12.3, *J*_{AX} = 4.4 Hz), 4.67 (dd, 0.6H, *J*_{AB} = 12.3, *J*_{BX} = 8.4 Hz), 4.20-4.11 (m, 1H), 4.00 (d, 0.6H, *J* = 10.0 Hz), 3.92 (d, 0.4H, *J* = 9.0 Hz), 2.29, (s, 1.8H), 2.04 (s, 1.2H), 1.46 (s, 3.6H), 1.15 (s, 5.4H); ¹³C NMR (125 MHz, CDCl₃) 201.27, 200.59, 166.57, 165.78, 136.55, 128.94, 128.74, 128.19, 128.16, 128.11, 127.89, 83.37, 82.82, 78.28, 77.79, 62.96, 62.60, 42.45, 42.26, 30.04, 29.59, 27.73, 27.25; HRMS (ES⁺): Exact mass calcd for C₁₆H₂₅N₂O₅ [M + NH₄]⁺, 325.1763. Found 325.1771; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); First (major) diastereomer: major enantiomer *t*_r = 8.6 min,

minor enantiomer $t_r = 12.4$ min; 93% ee; Second (minor) diastereomer: minor enantiomer $t_r = 15.2$ min, major enantiomer $t_r = 19.9$ min, 93% ee; $[\alpha]_D^{24} +93.9$ (c 1.1, CHCl_3).

Configuration assignment: The absolute stereochemistry at carbon 3 was assigned as (*S*) by analogy.

Ethyl-4-methyl-2-(2-nitro-1(*S*)-phenylethyl)-3-oxopentanoate (6d). The title compound was prepared according to the General Procedure and purified by column chromatography (CH_2Cl_2) to give a white solid (96% yield, ~ 1:1 mixture of diastereomers) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 55-58 °C; IR (cell, CH_2Cl_2) 2979, 2937, 2876, 1742, 1716, 1557, 1497, 1460, 1380, 1290, 1236, 1213, 1179, 1114, 1026, 860, 572 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.30-7.19 (m, 5H), 4.90-4.73 (m, 2H), 4.26-4.12 (m, 3H), 3.95 (q, 1H, $J = 7.2$ Hz), 2.73 (septet, 0.5H, $J = 6.9$ Hz), 2.43 (septet, 0.5H, $J = 6.8$ Hz), 1.24 (t, 1.5H, $J = 7.1$ Hz), 1.07 (d, 1.5H, $J = 6.8$ Hz), 1.04 (d, 1.5H, $J = 7.0$ Hz), 1.00 (t, 1.5H, $J = 7.1$ Hz), 0.67 (d, 1.5H, $J = 6.8$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 207.43, 206.36, 167.34, 166.88, 136.49, 136.37, 128.93, 128.82, 128.18, 128.16, 128.07, 127.95, 77.48, 77.43, 61.99, 61.82, 59.68, 59.63, 42.87, 42.50, 41.92, 41.23, 18.15, 17.67, 17.62, 17.26, 13.90, 13.63; HRMS (ES^+): Exact mass calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_5$ [$\text{M} + \text{H}$] $^+$, 308.1498. Found 308.1497; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); First diastereomer: major enantiomer $t_r = 10.1$ min, minor enantiomer $t_r = 17.7$ min; 93% ee; Second diastereomer: major enantiomer $t_r = 13.2$ min, minor enantiomer $t_r = 16.2$ min, 93% ee; $[\alpha]_D^{24} +51.7$ (c 1.0, CHCl_3).

Configuration assignment: The absolute stereochemistry at carbon 3 was assigned as (*S*) by analogy.

(3*S*)-Ethyl-2-phenylcarbonyl-4-nitro-3-phenylbutyrate (6e). The title compound was prepared according to the General Procedure and purified by column chromatography (15% EtOAc/hexanes) to give a white solid (99% yield, 2.5:1 mixture of diastereomers) which was judged to be >95% pure by ^1H NMR spectroscopy. mp: 100-111 °C; IR (cell, CH_2Cl_2) 3066, 2982, 1737, 1687, 1598, 1558, 1449, 1379, 1286, 1226, 1186, 1156, 1095, 1027, 979, 880, 849, 562 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 8.06-8.05 (m, 1.4H), 7.86-7.85 (m, 0.6 H), 7.63-7.60 (m, 0.7H), 7.57-7.54 (m, 0.3H), 7.50-7.47 (m, 1.4H), 7.43-7.40 (m, 0.6H), 7.34-7.26 (m, 3.6H), 7.22-7.15 (m, 1.4H), 4.99-4.91 (m, 1.6H), 4.80 (dd, 0.7H, $J_{AB} = 13.2$, $J_{AX} = 4.3$ Hz), 4.77 (dd, 0.7H, $J_{AB} = 13.2$, $J_{BX} = 9.2$ Hz), 4.50 (ddd, 0.7H, $J = 10.0$, 8.5, 4.9 Hz), 4.44 (ddd, 0.3H, $J = 9.0$, 9.0, 4.9 Hz), 4.18 (q, 0.6H, 7.2 Hz), 3.88 (dq, 0.7H, $J = 7.1$, 5.4 Hz), 3.85 (dq, 0.7H, $J = 7.1$, 5.4 Hz), 1.17 (t, 0.9H, $J = 7.1$ Hz), 0.89 (t, 2.1H, $J = 7.1$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 192.65, 167.64, 166.89, 136.64, 136.12, 135.89, 135.69, 133.79, 128.88, 128.83, 128.68, 128.50, 128.29, 128.22, 128.05, 127.90, 77.91, 62.18, 61.89, 56.93, 56.23, 43.02, 43.00, 13.82, 13.52; HRMS (ES^+): Exact mass calcd for $\text{C}_{19}\text{H}_{20}\text{NO}_5$ [$\text{M} + \text{H}$] $^+$, 342.1341. Found 342.1345; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 245 nm); First (major) diastereomer: major enantiomer $t_r = 16.2$ min, minor enantiomer $t_r = 36.4$ min; 90% ee; Second (minor) diastereomer: major enantiomer $t_r = 28.3$ min, minor enantiomer $t_r = 55.8$ min, 85% ee; $[\alpha]_D^{24} -1.5$ (c 1.36, CHCl_3).

Configuration assignment: The absolute stereochemistry at carbon 3 was assigned as (*S*) by comparison of the optical rotation with the following literature value: Lit²: $[\alpha]_D^{25} -2.31$ (c 1.03, CHCl_3), (87% ee, (3*S*)-isomer, 1:1 mixture of diastereomers).

(3*S*)-1',1'-Dimethylethyl-2-acetyl-4-nitro-3-(4-bromophenyl)butyrate (6f). The title compound was prepared according to the General Procedure and purified by column

chromatography (CH₂Cl₂) to give a white solid (97% yield, 1.75:1 mixture of diastereomers + a small amount of the enol tautomer) which was judged to be >95% pure by ¹H NMR spectroscopy. mp: 101-112 °C; IR (cell, CH₂Cl₂) 2983, 2933, 1737, 1716, 1557, 1496, 1456, 1433, 1371, 1289, 1144, 840 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 7.45-7.42 (m, 2H), 7.11-7.08 (m, 2H), 4.83 (dd, 0.35H, *J*_{AB} = 12.8, *J*_{AX} = 4.1 Hz), 4.78 (dd, 0.35H, *J*_{AB} = 12.8, *J*_{BX} = 10.2 Hz), 4.71 (dd, 0.65H, *J*_{AB} = 12.5, *J*_{AX} = 4.3 Hz), 4.65 (dd, 0.65H, *J*_{AB} = 12.5, *J*_{BX} = 8.7 Hz), 4.16 (ddd, 0.35H, *J* = 9.3, 9.3, 4.4 Hz), 4.10 (ddd, 0.65H, *J* = 10.3, 8.3, 4.4 Hz), 3.96 (d, 0.65H, *J* = 10.0 Hz), 3.88 (d, 0.35H, *J* = 9.5 Hz), 2.29 (s, 1.95H), 2.08 (s, 1.05H), 1.46 (s, 3.15H), 1.20 (s, 5.85H); ¹³C NMR (125 MHz, CDCl₃) 200.96, 200.19, 166.31, 165.58, 135.75, 135.68, 132.17, 131.93, 129.92, 129.65, 122.25, 122.17, 83.69, 83.21, 77.93, 77.49, 62.67, 62.47, 41.83, 41.71, 30.08, 29.67, 27.76, 27.37; HRMS (CI⁺): Exact mass calcd for C₁₆H₂₄BrN₂O₅ [M + NH₄]⁺, 403.0869. Found 403.0869; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (95:5 hexanes:isopropanol, 1 mL/min, 215 nm); First (major) diastereomer: major enantiomer *t*_r = 11.8 min, minor enantiomer *t*_r = 22.7 min; 94% ee; Second (minor) diastereomer: minor enantiomer *t*_r = 25.6 min, major enantiomer *t*_r = 39.0 min, 91% ee; [α]_D²² +59.0 (*c* 1.0, CHCl₃).

Configuration assignment: The absolute stereochemistry at carbon 3 was assigned as (*S*) by converting **6f** into **7f** (X-ray, see below).

(*S*)-4-(4-bromophenyl)-5-nitropentan-2-one (7f). A mixture of 72 mg (0.186 mmol) of **6f** and 6.4 mg (0.037 mmol) of *p*-toluenesulfonic acid in 5 mL of benzene was heated under reflux for four hours. After solvent removal the crude product was purified by column chromatography (2% ether in CH₂Cl₂) to give the title compound as a white solid (51.5 mg, 97% yield) which was judged to be >95% pure by ¹H NMR spectroscopy. mp: 112 °C; IR (cell, CH₂Cl₂) 2921, 1720, 1557, 1492, 1433, 1412, 1378, 1163, 1076, 818, 650, 538 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 7.46-7.44 (m, 2H), 7.11-7.09 (m, 2H), 4.69-4.65 (m, 1H), 4.59-4.54 (m, 1H), 4.00-3.94 (m, 1H), 2.89 (app d, 2H, *J* = 7.0 Hz), 2.12 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 204.9, 137.8, 132.1, 129.1, 121.8, 79.0, 45.9, 38.4, 30.3; HRMS (CI⁺): Exact mass calcd for C₁₁H₁₆BrN₂O₃ [M + NH₄]⁺, 303.0344. Found 303.0340; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 215 nm); major enantiomer *t*_r = 16.3 min, minor enantiomer *t*_r = 18.7 min; 93% ee; [α]_D²³ +4.28 (*c* 1.19, CHCl₃).

Configuration assignment: The absolute stereochemistry was assigned as (*S*) by X-ray analysis of crystals that were grown by layering a dichloromethane solution of **7f** with hexanes.

The requisite CIF file has been submitted to the journal.

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All ^1H -NMR spectra were recorded as described in the General Information section. The corresponding FIDs were processed using MestReC v4.4.6 which is available free of charge at <http://www.mestrec.com>.

^1H -NMR of (*S*)-Methyl-2-carbomethoxy-4-nitro-3-phenylbutyrate (**4a**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-phenylbutyrate (**4b**)

^1H -NMR of (*S*)-1-Methylethyl-2-(1-methylethoxycarbo)-4-nitro-3-phenylbutyrate (**4c**)

^1H -NMR of (*S*)-1,1-Dimethylethyl-2-(1,1-dimethylethoxycarbo)-4-nitro-3-phenylbutyrate (**4d**)

¹H-NMR of (*S*)-Benzyl-2-carbobenzyloxy-4-nitro-3-phenylbutyrate (**4e**)

^1H -NMR of (*R*)-Methyl-2-carbomethoxy-2-methyl-4-nitro-3-phenylbutyrate (**4f**)

^1H -NMR of (*S*)-Ethyl-2-acetamido-2-carboethoxy-4-nitro-3-phenylbutyrate (**4g**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-(4-methylphenyl)butyrate (**4h**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-(4-methoxyphenyl)butyrate (**4i**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-(4-bromophenyl)butyrate (**4j**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-(2-chlorophenyl)butyrate (**4k**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-(2,3-dimethoxyphenyl)butyrate (**4l**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-(2,4-dimethoxyphenyl)butyrate (**4m**)

¹H-NMR of (*S*)-Ethyl-2-carboethoxy-4-nitro-3-(3,4-methylenedioxyphenyl)butyrate (**4n**)

¹H-NMR of (*R*)-Ethyl-2-carboethoxy-4-nitro-3-(2-furyl)butyrate (**4o**)

^1H -NMR of (*R*)-Ethyl-2-carboethoxy-3-(nitromethyl)-octanoate (**4p**)

¹H-NMR of (*R*)-Ethyl-2-carboethoxy-3-(nitromethyl)-5-methylhexanoate (**4q**)

^1H -NMR of (*R*)-Ethyl-2-carboethoxy-3-(nitromethyl)-4-methylpentanoate (**4r**)

¹H-NMR of (3*S*)-Methyl-2-acetyl-4-nitro-3-phenylbutyrate (**6a**)

¹H-NMR of (3*S*)-Ethyl-2-acetyl-4-nitro-3-phenylbutyrate (**6b**)

^1H -NMR of (3*S*)-1',1'-Dimethylethyl-2-acetyl-4-nitro-3-phenylbutyrate (**6c**)

¹H-NMR of Ethyl-4-methyl-2-(2-nitro-1(S)-phenylethyl)-3-oxopentanoate (**6d**)

¹H-NMR of (3*S*)-Ethyl-2-phenylcarbonyl-4-nitro-3-phenylbutyrate (**6e**)

^1H -NMR of (3*S*)-1',1'-Dimethylethyl-2-acetyl-4-nitro-3-(4-bromophenyl)butyrate (**6f**)

^1H -NMR of (*S*)-4-(4-bromophenyl)-5-nitropentan-2-one (**7f**)