Enantioselective Synthesis of Cyclohexenol Derivatives from γ-Aryl-substituted Enals via an Organocatalyzed Three-Component Reaction

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Supporting Information

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General Information

All reactions were carried out in closed vial and monitored by TLC and the products were visualized by UV detection. Flash column chromatography was performed with silica gel (32-63 μ). \( ^1H \) and \( ^{13}C \) NMR spectra were recorded on a 500 MHz (125 MHz for \( ^{13}C \) NMR) or a 300 MHz spectrometer (75 MHz for \( ^{13}C \) NMR). The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). FTIR spectra were measured on a Bruker Vector 22 instrument. Enantiomeric excesses (ee) were determined by HPLC analysis using a Shimadzu instrument with chiral HPLC columns. ChiralPak IB, IC, and ID columns (4.6 mm × 250 mm) were purchased from Daicel Chemical Industries. Melting points were recorded on MEL-TEMP melting point apparatus in open capillaries and uncorrected. HRMS analyses were conducted at the RCMI Proteomics and Protein Biomarkers Core Facility of the Department of Chemistry, UTSA.

Materials: All the α,β-unsaturated aldehydes were prepared by following the literature procedure.\(^{12}\) All the nitroalkenes were either purchased from commercial sources or synthesized by following known literature procedures.\(^{13}\) All catalysts, except for 5e, 5f, 5g, and 5y, are known compounds and were prepared by following the known procedures.\(^{14}\) Tetrahydrofuran was dried over sodium metal under argon atmosphere and distilled before prior to use.
Catalyst Preparation

Scheme S-1. Synthesis of the squaramide catalysts 5.

Preparation of intermediate c: Intermediate c was prepared according to the literature procedure. In a 250-mL round-bottom flask, the Boc-protected amino acid b (5.0 mmol), hydroxybenzotriazole (HOBT, 676 mg, 5.0 mmol, 1.0 equiv.), and EDC hydrochloride (959 mg, 5.0 mmol, 1.0 equiv.) were suspended in dry CH₂Cl₂ (35 mL) at room temperature. After 2 min., DIPEA (1.3 g, 10 mmol, 2.0 equiv.) was added, which was followed immediately by the benzylamine derivative a (5.0 mmol, 1.0 equiv.). The reaction mixture was allowed to stir further for 2 h at the same temperature. During the reaction progress, due to the consumption of HOBT, the mixture changed from turbid to a clear solution. The reaction was then quenched by adding 1N HCl (20 mL) and the mixture was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The resulting colorless liquid was further dissolved in CH₂Cl₂ (25 mL) and treated with trifluoroacetic acid (75 mmol, 15 equiv.) under stirring. After 1 h the reaction mixture was diluted with CH₂Cl₂ (30 mL) and quenched with chilled saturated solution of sodium carbonate (50 mL). After neutralization by adding more saturated sodium carbonate solution, the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL), and the combined organic layers were dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure to give a white solid that was used without further purification.
Synthesis of intermediate d: The crude intermediate c (5.0 mmol) was dissolved in CH₂Cl₂ (25 mL) and dimethylsquirate (710.6 mg, 5.0 mmol) was added portion wise over 10 min. at room temperature. The mixture was further stirred for 72 h to complete the reaction (monitored by TLC). The solvent was then removed under reduced pressure and the crude product was purified by in flash column chromatography using 98:2 CH₂Cl₂/MeOH as the eluent to give the intermediate d (63-72%).

Synthesis of 5: In an oven-dried round-bottom flask, the quinine- or quinidine-derived 9-amino(9-deoxy)cinchona alkaloid (255.5 mg, 0.79 mmol) was dissolved in dry methanol (10 mL) at room temperature. To that solution, d (0.79 mmol) was added in one portion and the mixture was further stirred for 48-90 h. During the progress, a white precipitate was observed. The precipitate was filtered and washed with cold MeOH/hexane (1:4), which gave the pure catalyst 5. The filtrate was further concentrated and purified by silica gel flash column chromatography using MeOH/CH₂Cl₂ (0:100 to 5:95) as a mobile phase to give an additional portion of the catalyst. Both the portions were combined for catalytic use (total yield 55-60%).

Detailed Experimental Procedures

**General procedure for the three-component reaction:** To a stirred solution of the appropriate nitroalkene (0.60 mmol, 3.0 equiv.) and the squaramide catalyst 5f (24.9 mg, 0.040 mmol, 20 mol %) in freshly distilled THF (0.7 mL) at room temperature, the γ-aryl-α,β-unsaturated aldehyde (0.20 mmol) was added. The mixture was further stirred at room temperature for 72 h (the progress of the reaction was monitored by TLC). After the completion of the reaction, the solvent was evaporated in a rotary evaporator under the reduced pressure and the crude product obtained was purified by flash column chromatography using 90:10 to 95:5 hexane/EtOAc as an eluent.

**1.0 mmol-scale reaction**
To a stirred solution of trans-β-nitrostyrene (2a, 447.5 mg, 3.0 mmol, 3.0 equiv.) and the squaramide catalyst 5f (124.4 mg, 0.20 mmol, 0.2 equiv) in freshly distilled THF (3.5 mL) at room temperature, 4-phenyl-2-butenal (1a, 146.2 mg, 1.0 mmol) was added. The mixture was further stirred at room temperature for 72 h (the progress of the reaction was monitored by TLC). After the completion of the reaction, the solvent was evaporated in a rotary evaporator under reduced pressure and the crude product obtained was purified by flash column chromatography using 95:5 hexanes/EtOAc as an eluent to give 4a as white color solid (310.5 mg, 70% yield, 87:1 dr, 99% ee).

**Acetylation of the adduct 4a**

To a solution of the adduct 4a (44.5 mg, 0.10 mmol) in CH₂Cl₂ (3.0 mL), acetic anhydride (0.10 mL, 1.0 mmol) and DMAP (2.5 mg, 0.020 mmol) were added at 0 °C and the reaction mixture was further stirred for 30 min at room temperature. After the completion the reaction, the solvent was evaporated under reduced pressure, and the crude product was purified by flash chromatography using 93:7 hexanes/EtOAc as an eluent to give 6 as white solid (38.7 mg, 80% yield).

**Oxidation of the adduct 4a**

To a solution of the adduct 4a (44.5 mg, 0.10 mmol) in CH₂Cl₂ (3.0 mL), 100 mg Celite was suspended and then PCC (64.7 mg, 0.30 mmol) were added at room temperature and the reaction mixture was further stirred for 12 h at the same temperature. After the completion the reaction, the mixture was filtered through a Celite pad and the crude product was purified by flash chromatography using 92:8 hexane/EtOAc as an eluent to give 7 as white solid. (37.6 mg, 85% yield).
Detailed Catalyst Screening and Condition Optimizations

Figure S-1. Structure of catalyst used in the screening
Table S-1: Screening of the catalysts

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<sup>a</sup>Unless otherwise noted, all reactions were carried out with 1a (0.20 mmol) and 2a (0.6 mmol) in dry THF (0.7 mL) at room temperature for 72 h, using 5 (20 mol %) as the catalyst. <sup>b</sup>Yield of the isolated product. <sup>c</sup>Diastereomeric ratio was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. <sup>d</sup>Determined by chiral HPLC analysis. <sup>e</sup>The opposite enantiomer was obtained as the major product. <sup>f</sup>The catalyst loading was 10 mol %.
Figure S-2. ORTEP drawing of compound 4a
Scheme S-2. Alternative reaction mechanism for the three-component reaction
3-{(S)-N’-[3,5-Bis(trifluoromethyl)benzyl]-3,3-dimethylbutanamid-2-ylamino}-4-{[(9R)-6’-methoxycinchonan-9-yl]amino}-3-cyclobutene-1,2-dione (5e)

The crude product was purified by silica gel flash column chromatography using MeOH/CH$_2$Cl$_2$ (0:100 to 5:95) to get 5e as a white solid, 2.01 g, 55% yield, m.p. 178-180 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ: 8.88 (s, 2H), 8.56 (s, 2H), 8.06 (d, $J = 9.2$ Hz, 1H), 7.95 (s, 1H), 7.70 (s, 1H), 7.44-7.40 (m, 2H), 7.27 (s, 1H), 7.12 (br, 1H), 6.51 (br, 1H), 5.97 (d, $J = 14.3$ Hz, 1H), 5.29 (d, $J = 16.9$ Hz, 1H), 5.13 (d, $J = 10.0$ Hz, 1H), 4.47 (s, 2H), 4.14 (br, 1H), 3.89 (s, 3H), 3.42 (br, 2H), 3.06 (s, 3H), 2.41 (s, 1H), 1.92 (s, 3H), 1.72 (s, 3H), 1.16-1.04 (m, 2H), 0.85 (s, 9H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 183.0, 181.7, 171.8, 169.2, 165.5, 159.0, 148.1, 145.2, 144.7, 141.0, 140.8, 132.2, 132.1 (q, $J_{C-F} = 33.7$ Hz), 125.8, 125.3 (q, $J_{C-F} = 273.0$ Hz), 122.7, 121.0, 119.8 (br.), 119.5, 115.1, 101.9, 64.8, 59.3, 56.0, 53.6, 49.5, 47.1, 42.1, 39.7, 35.6, 28.1, 27.4, 26.5, 26.1. $\nu_{\text{max}}$ (neat, cm$^{-1}$): 3234, 2936, 1660, 1622, 1582, 1509, 1434, 1379, 1349, 1275, 1243, 1170, 1128, 1021. HRMS (ESI) m/z calcd for C$_{39}$H$_{42}$F$_6$N$_5$O$_4$ $^+$ ([M+H]): 758.3136; found: 758.3146.

3-{(S)-N’-Benzyl-3,3-dimethylbutanamid-2-ylamino}-4-{[(9R)-6’-methoxycinchonan-9-yl]amino}-3-cyclobutene-1,2-dione (5f)

The crude product was purified by silica gel flash column chromatography using MeOH/CH$_2$Cl$_2$ (0:100 to 3:97) to get 5f as a white solid, 1.86 g, 60% yield, m.p. 190-192 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ: 8.70 (br, 1H), 8.54-8.62 (m, 1H), 8.42 (br, 1H), 8.05 (d, $J = 9.1$ Hz, 1H), 7.98 (s, 1H), 7.81 (s, 1H), 7.43 (d, $J = 9.3$ Hz, 1H), 7.26 (br, 1H), 7.08-7.06 (m, 3H), 6.84-6.83 (m, 2H), 6.51 (br, 1H), 5.90 (ddd, $J_1 = 17.0$ Hz, $J_2 = 10.5$, $J_3 = 6.2$ Hz, 1H), 5.20 (d, $J = 17.1$ Hz, 1H), 5.05 (d, $J = 10.3$ Hz, 1H), 4.54 (d, $J = 9.5$ Hz, 1H), 4.13 (s, 2H), 3.92 (s, 3H), 3.78-3.75 (m, 1H), 3.36 (s, 1H), 3.24 (s, 1H), 2.97-2.93 (m, 2H), 2.30-2.28 (m, 2H), 1.64-1.57 (m, 3H), 1.11 (s, 1H), 0.99 (s, 1H), 0.81 (s, 9H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 183.0,
182.1, 170.8, 168.9, 166.1, 158.8, 148.2, 145.1, 140.8, 137.7, 132.0, 128.8, 128.4, 127.6, 122.7, 119.9, 115.1, 101.9, 64.9, 59.3, 56.1, 53.3, 49.4, 47.2, 43.4, 39.8, 35.9, 28.2, 27.3, 26.7, 25.8, 23.0, 14.5, 12.4 ν\textsubscript{max} (neat, cm\textsuperscript{-1}): 3301, 2932, 1795, 1652, 1621, 1582, 1509, 1432, 1368, 1227, 1128.

HRMS (ESI) m/z calcd for C\textsubscript{37}H\textsubscript{44}N\textsubscript{5}O\textsubscript{4} ([M+H]+): 622.3388; found: 622.3390.

3-[(S)-N'-Benzyl-3,3-dimethylbutanamid-2-ylamino]-4-{{[8α,9S)-6'-methoxycinchonan-9-yl]amino}-3-cyclobutene-1,2-dione (5g)

The crude product was purified by silica gel flash column chromatography using MeOH/CH\textsubscript{2}Cl\textsubscript{2} (0:100 to 4:96) to get 5g as a white solid, 1.71 g, 55% yield, m.p. 182-184°C; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) δ: 8.45 (br, 1H), 8.01-7.98 (m, 3H), 7.57 (s, 2H), 7.38-7.36 (m, 1H), 7.02-6.94 (m, 4H), 6.28 (br, 1H), 5.89 (br, 1H), 5.03-4.93 (m, 2H), 4.58 (s, 1H), 3.94-3.88 (m, 5H), 3.40 (s, 1H), 3.24 (t, J = 10 Hz, 1H), 2.85-2.76 (m, 2H), 2.29 (d, J = 7.2 Hz, 1H), 1.64-1.44 (m, 4H), 0.88 (br, 9H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) δ: 183.3, 170.8, 168.8, 167.2, 159.0, 148.2, 145.1, 144.8, 142.1, 137.9, 132.2, 129.4, 128.7, 127.6, 122.6, 120.0, 114.9, 102.0, 64.9, 56.2, 53.9, 43.5, 41.2, 40.1, 35.4, 28.3, 26.5. ν\textsubscript{max} (neat, cm\textsuperscript{-1}): 33264, 2942, 1657, 1621, 1581, 1524, 1454, 1367, 1259, 1228, 1176, 1132, 1028. HRMS (ESI) m/z calcd for C\textsubscript{37}H\textsubscript{44}N\textsubscript{5}O\textsubscript{4} ([M+H]+): 622.3388; found: 622.3401.

3-[(S)-N'-Benzyl-3-methylbutanamid-2-ylamino]-4-{{[9R)-6'-methoxycinchonan-9-yl]amino}-3-cyclobutene-1,2-dione (5y)

The crude product was purified by silica gel flash column chromatography using MeOH/CH\textsubscript{2}Cl\textsubscript{2} (0:100 to 4:96) to get 5y as a white solid, 1.67 g, 58% yield, m.p. 170-172°C; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) δ: 8.75 (br, 2H), 8.50 (s, 1H), 8.09-8.04 (m, 2H), 7.81 (s, 1H), 7.46 (d, J = 9.3 Hz, 2H), 7.11 (s, 3H), 6.88 (s, 2H), 6.54 (s, 1H), 5.93 (td, J\textsubscript{1} = 11.0 Hz, J\textsubscript{2} = 10.3 Hz, J\textsubscript{3} = 5.7 Hz, 1H), 5.25 (d, J = 17.2 Hz, 1H), 5.09 (d, J = 10.4 Hz, 1H), 4.60 (s, 1H), 4.10-3.94 (m, 6H), 3.72 (s, 1H), 3.35 (s, 1H), 3.22 (s, 1H), 3.03-3.00 (m, 2H), 2.33 (d, J = 8.1 Hz, 1H), 1.94-1.86 (m, 2H), 1.67-1.62 (m, 3H), 1.14 (s, 1H), 1.07-0.89 (m, 2H), 0.81 (d, J = 6.4 Hz, 3H),
0.73 (d, J = 5 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 183.2, 181.55, 171.7, 169.2, 165.6, 158.7, 148.2, 145.3, 145.1, 140.9, 137.6, 132.0, 128.8, 128.3, 127.6, 127.4, 122.8, 119.9, 115.0, 101.9, 63.0, 59.2, 56.0, 53.4, 49.4, 47.1, 43.2, 39.8, 33.3, 28.2, 27.3, 25.8, 18.9, 18.7, 12.3. ν$_{\text{max}}$ (neat, cm$^{-1}$): 3232, 2933, 1655, 1621, 1509, 1452, 1367, 1260, 1241, 1228, 1159, 1080, 1027. HRMS (ESI) m/z calcd for C$_{36}$H$_{42}$N$_5$O$_4^+$ ([M+H]): 608.3231; found: 608.3249.

(1'R,2'S,3'S,4'S)-3'-Nitro-5'-[(R)-2-nitro-1-phenylethyl]-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4a)

The crude material was purified by flash column chromatography using hexanes/EtOAc (95:5) as an eluent to get 4a as a white solid, 71 mg, 80% yield, m.p. 140-142 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ: 7.46-7.31 (m, 5H), 7.21-7.19 (m, 1H), 7.17-7.09 (m, 3H), 7.05 (t, J = 7.4 Hz, 2H), 6.61-6.55 (m, 4H), 6.02 (d, J = 4.2 Hz, 1H), 5.24 (dd, J$_1$ = 12.3 Hz, J$_2$ = 9.7 Hz, 1H), 5.11 (dd, J$_1$ = 12.0 Hz, J$_2$ = 8.5 Hz, 1H), 4.95 (dd, J$_1$ = 12.2 Hz, J$_2$ = 6.9 Hz, 1H), 4.80 (t, J = 8.0 Hz, 1H), 4.63 (dd, J$_1$ = 9.6 Hz, J$_2$ = 7.0 Hz, 1H), 3.79-3.76 (m, 2H), 2.63 (d, J = 7.5 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 137.23, 137.0, 136.5, 136.2, 130.8, 130.2, 129.6, 128.5, 128.1, 128.0, 79.0, 73.4, 49.0, 48.7, 47.8. ν$_{\text{max}}$ (neat, cm$^{-1}$): 3586, 3029, 1550, 1453, 1433, 1378, 1246, 1060, 1033, 970. HRMS (ESI) m/z calcd for C$_{26}$H$_{24}$N$_2$NaO$_5$ ([M+Na]$: 467.1577; found: 467.1573. Enantiomeric excess of 4a was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t$_R$ = 18.0 min, major enantiomer: t$_R$ = 50.0 min.

(1'R,2'S,3'S,4'S)-4''-Methyl-3'-nitro-5'-[(R)-2-nitro-1-(p-tolyl)ethyl]-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4b)

The crude material was purified by flash column chromatography using hexanes/EtOAc (93:7) as an eluent to get 4b as a white solid, 68.9 mg, 73% yield, m.p. 130-132 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ: 7.29-7.24 (m, 3H), 7.23-7.19 (m, 4H), 7.17-7.14 (m, 2H), 6.85 (d, J = 7.7 Hz, 3H), 6.63 (d, J = 7.4 Hz, 2H), 6.44 (br, 2H), 6.00 (d, J = 3.4 Hz, 1H), 5.21 (dd, J$_1$ = 12.2 Hz, J$_2$ = 9.7 Hz, 1H), 5.08 (dd, J$_1$ = 12.6 Hz, J$_2$ = 8.5 Hz, 1H), 4.91 (dd, J$_1$ = 12.3 Hz, J$_2$ = 7.0 Hz, 1H), 4.79 (t, J = 8.1 Hz, 1H), 4.59 (d, J = 7.3 Hz, 1H), 3.80-3.65 (m, 2H), 2.55 (d, J = 7.6 Hz, 1H), 2.36 (s, 3H),
(1'R,2'S,3'S,4'S)-4''-Fluoro-5'-(R)-1-(4-fluorophenyl)-2-nitroethyl]-3'-nitro-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4c)

The crude material was purified by flash column chromatography using hexanes/EtOAc (91:9) as an eluent to get 4c as a white solid, 67.2 mg, 70% yield, m.p. 134-136 °C; ^1H NMR (500 MHz, CDCl_3) δ: 7.36-7.33 (m, 2H), 7.24-7.21 (m, 1H), 7.18-7.15 (m, 2H), 7.08-7.05 (m, 2H), 6.76 (t, J = 8.5 Hz, 2H), 6.64-6.57 (m, 3H), 6.52 (br, 2H), 5.98 (d, J = 3.3 Hz, 1H), 5.18 (dd, J_1 = 12.4 Hz, J_2 = 9.5 Hz, 1H), 5.09-5.02 (m, 1H), 4.91 (dd, J_1 = 12.3 Hz, J_2 = 7.1 Hz, 1H), 4.78 (t, J = 7.4 Hz, 1H), 4.62 (dd, J_1 = 9.3, J_2 = 7.2 Hz, 1H), 3.77-3.73 (m, 2H), 2.81 (d, J = 7.3 Hz, 1H). ^13C NMR (126 MHz, CDCl_3) δ: 162.7 (d, J_{C-F} = 239.4 Hz), 162.5 (d, J_{C-F} = 239.4 Hz), 137.0, 136.3, 133.0, 131.9, 130.7, 130.2, 130.1 (d, J_{C-F} = 7.5 Hz), 129.8 (d, J_{C-F} = 7.5 Hz), 128.7, 128.2, 116.5 (d, J_{C-F} = 21.3 Hz), 115.4 (d, J_{C-F} = 21.3 Hz), 90.7, 79.0, 73.1, 48.6, 48.0, 47.1. v_max (neat, cm^{-1}): 3526, 2922, 1603, 1548, 1507, 1452, 1347, 1224, 1160, 1050. HRMS (ESI) m/z calcd for C_{26}H_{21}F_{2}N_{2}O_{5} ([M-H]): 479.1424; found: 479.1430. Enantiomeric excess of 4c was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t_R = 10.3 min, major enantiomer: t_R = 31.8 min.

(1'R,2'S,3'S,4'S)-4''-Chloro-5'-(R)-1-(4-chlorophenyl)-2-nitroethyl]-3'-nitro-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4d)
The crude material was purified by flash column chromatography using hexanes/EtOAc (92:8) as an eluent to get 4d as a white solid, 71.8 mg, 70% yield, m.p. 140-142 °C; 1H NMR (500 MHz, CDCl3) δ: 7.37-7.34 (m, 3H), 7.31-7.29 (m, 2H), 7.23-7.20 (m, 2H), 7.19-7.16 (m, 2H), 7.05 (d, J = 8.2 Hz, 2H), 6.60 (d, J = 7.5 Hz, 2H), 6.49 (br, 2H), 5.97 (d, J = 3.2 Hz, 1H), 5.15 (dd, J1 = 12.5 Hz, J2 = 9.2 Hz, 1H), 5.06 (dd, J1 = 12.1 Hz, J2 = 8.3 Hz, 1H), 4.92-4.88 (m, 2H), 4.76 (t, J = 7.6 Hz, 1H), 4.61 (dd, J1 = 9.1 Hz, J2 = 7.3 Hz, 1H), 3.79-3.69 (m, 2H), 2.92 (d, J = 7.1 Hz, 1H). 13C NMR (125 MHz, CDCl3) δ: 136.8, 136.1, 135.8, 134.6, 134.0, 130.7, 130.2, 129.8, 129.7, 129.5, 128.2, 90.5, 78.7, 73.0, 48.4, 47.9, 47.2. v_max (neat, cm⁻¹): 3501, 2918, 1548, 1490, 1452, 1373, 1091, 1051, 1013, 972. HRMS (ESI) m/z calcd for C26H21Cl2N2O5 ([M-H]⁻): 511.0833; found: 511.0830. Enantiomeric excess of 4d was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t_R = 11.0 min, major enantiomer: t_R = 32.5 min.

(1'R,2'S,3'S,4'S)-4''-Bromo-5'-(R)-1-(4-bromophenyl)-2-nitroethyl]-3'-nitro-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4e)

The crude material was purified by flash column chromatography using hexanes/EtOAc (91:9) as an eluent to get 4e as a light green solid, 90.3 mg, 75% yield, m.p. 150-152 °C; 1H NMR (500 MHz, CDCl3) δ: 7.51 (d, J = 8.4 Hz, 2H), 7.26-7.16 (m, 9H), 6.63 (br, 2H), 6.43 (d, J = 3.5 Hz, 1H), 5.16 (dd, J1 = 12.5 Hz, J2 = 9.3 Hz, 1H), 5.05 (dd, J1 = 12.6 Hz, J2 = 8.4 Hz, 1H), 4.90 (dd, J1 = 12.5 Hz, J2 = 7.2 Hz, 1H), 4.76 (t, J = 7.6 Hz, 1H), 4.63-4.56 (m, 1H), 3.80-3.67 (m, 2H), 2.75 (d, J = 7.2 Hz, 1H). 13C NMR (125 MHz, CDCl3) δ: 136.7, 136.3, 136.0, 135.1, 132.7, 131.7, 130.8, 130.2, 129.8, 128.8, 128.3, 122.5, 122.2, 90.4, 78.6, 73.1, 48.3, 48.1, 47.3. v_max (neat, cm⁻¹): 3500, 2918, 1547, 1487, 1452, 1432, 1373, 1099, 1073, 1009, 904. HRMS (ESI) m/z calcd for C26H21Br2N2O5 ([M-H]⁻): 598.9823; found: 598.9813. Enantiomeric excess of 4e was determined by chiral stationary phase HPLC analysis using a
ChiralPak IC column (92.5:7.5 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t_R = 15.1 min, major enantiomer: t_R = 53.3 min.

(1'R,2'S,3'S,4'S)-2''-Bromo-5''-[(S)-1-(2-bromophenyl)-2-nitroethyl]-3'-nitro-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4f)

The crude material was purified by flash column chromatography using hexanes/EtOAc (93:7) as an eluent to get 4f as a brown solid, 78.3 mg, 65% yield, m.p. 125-127 °C; ¹H NMR (500 MHz, CDCl₃) δ: 7.66 (d, J = 6.7 Hz, 1H), 7.56 (dd, J₁ = 7.9 Hz, J₂ = 1.3 Hz, 1H), 7.43-7.41 (m, 1H), 7.25-7.23 (m, 1H), 7.16 (t, J = 7.6 Hz, 2H), 7.11 (t, J = 7.1 Hz, 2H), 6.98 (td, J₁ = 7.7 Hz, J₂ = 1.6 Hz, 1H), 6.79 (td, J₁ = 7.6 Hz, J₂ = 1.3 Hz, 1H), 6.61-6.68 (m, 2H), 6.04 (dd, J₁ = 7.9 Hz, J₂ = 1.6 Hz, 1H), 5.93 (d, J = 3.7 Hz, 1H), 5.20-5.13 (m, 3H), 4.76 (dd, J₁ = 8.5 Hz, 6.9 J₂ = Hz, 1H), 4.36 (dd, J₁ = 12.9 Hz, J₂ = 6.1 Hz, 1H), 4.03 (t, J = 4.9 Hz, 1H), 2.90 (d, J = 7.1 Hz, 1H).¹³C NMR (125 MHz, CDCl₃) δ: 136.7, 135.9, 135.3, 134.7, 134.5, 133.4, 132.1, 129.9, 129.9, 129.3, 128.5, 128.4, 128.3, 128.3, 128.0, 127.2, 125.8, 125.0, 90.2, 77.8, 73.1, 47.4, 45.9, 45.1. v_max (neat, cm⁻¹): 3503, 2919, 2850, 1548, 1489, 1471, 1452, 1373, 1263, 1062, 1021, 973. HRMS (ESI) m/z calcd for C₂₆H₂₁Br₂N₂O₅ ([M-H]⁻): 598.9823; found: 598.9822. Enantiomeric excess of 4f was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t_R = 19.6 min, major enantiomer: t_R = 40.4 min.

(1'R,2'S,3'S,4'S)-3''-Bromo-5''-[(R)-1-(3-bromophenyl)-2-nitroethyl]-3'-nitro-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4g)

The crude material was purified by flash column chromatography using hexanes/EtOAc (95:5) as an eluent to get 4g as a light green solid, 86.7 mg, 68% yield, m.p. 125-127 °C; ¹H NMR (500 MHz, CDCl₃) δ: 7.52 (s, 1H), 7.48-7.45 (m, 2H), 7.33-7.18 (m, 8H), 6.91 (t, J = 7.9 Hz, 1H), 6.80 (br, 1H), 6.61 (d, J = 6.8 Hz, 2H), 6.41 (br, 1H), 6.00 (d, J = 4.1 Hz, 1H), 5.15 (dd, J₁ = 12.6 Hz,
$J_2 = 9.4$ Hz, 1H), 5.06 (dd, $J_1 = 12.3$ Hz, $J_2 = 8.4$ Hz, 1H), 4.93-4.87 (m, 1H), 4.77 (t, $J = 10.0$ Hz, 1H), 4.60 (dd, $J_1 = 9.5$ Hz, $J_2 = 6.9$ Hz, 1H), 3.80-3.73 (m, 2H), 2.81 (d, $J = 7.1$ Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 139.6, 138.4, 136.6, 136.0, 132.0, 131.6, 131.3, 131.2, 130.4, 129.9, 128.7, 128.3, 126.7, 123.6, 122.5, 90.2, 78.6, 73.1, 48.4, 48.1, 47.3. v$_{\text{max}}$ (neat, cm$^{-1}$): 3501, 2921, 2851, 1594, 1547, 1489, 1474, 1452, 1373, 1260, 1199, 996. HRMS (ESI) m/z calcd for C$_{26}$H$_{21}$Br$_2$N$_2$O$_5$ ([M-H$^{-}$]: 598.9823; found: 598.9833. Enantiomeric excess of 4g was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (95:5 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t$_R$ = 32.3 min, major enantiomer: t$_R$ = 85.3 min.

(1R,2R,3S,4S)-3-Nitro-5-[(R)-2-nitro-1-(thiophen-2-yl)ethyl]-2-(thiophen-2-yl)-1,2,3,4-tetrahydro-[1,1'-biphenyl]-4-ol (4h)

The crude material was purified by flash column chromatography using hexanes/EtOAc (90:10) as an eluent to get 4h as a white solid, 62.1 mg, 68% yield, m.p. 140-142 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ: 7.30-7.28 (m, 1H), 7.25-7.17 (m, 3H), 7.08-6.98 (m, 3H), 6.75 (d, $J = 6.7$ Hz, 2H), 6.69-6.68 (m, 1H), 6.10 (d, $J = 3.5$ Hz, 1H), 6.05 (d, $J = 4.6$ Hz, 1H), 5.19 (dd, $J_1 = 12.2$ Hz, $J_2 = 9.1$ Hz, 1H), 5.05 (dd, $J_1 = 12.6$ Hz, $J_2 = 8.5$ Hz, 1H), 4.96 (dd, $J_1 = 12.2$ Hz, $J_2 = 6.9$ Hz, 1H), 4.92-4.89 (m, 2H), 4.08 (dd, $J_1 = 12.7$ Hz, $J_2 = 6.1$ Hz, 1H), 3.86 (t, $J = 5.4$ Hz, 1H), 2.74 (d, $J = 7.3$ Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 139.9, 138.1, 136.6, 136.0, 130.9, 130.1, 129.9, 128.7, 128.6, 128.2, 127.8, 127.0, 127.0, 126.3, 126.1, 125.9, 124.9, 91.5, 79.5, 72.8, 48.9, 44.3, 42.9. v$_{\text{max}}$ (neat, cm$^{-1}$): 3581, 2918, 2849, 1550, 1490, 1430, 1379, 1330, 1246, 1201, 1049, 967. HRMS (ESI) m/z calcd for C$_{22}$H$_{19}$N$_2$O$_5$S$_2$ ([M-H$^{-}$]): 455.0741; found: 455.0750. Enantiomeric excess of 4h was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t$_R$ = 19.4 min, major enantiomer: t$_R$ = 46.2 min.
The crude material was purified by flash column chromatography using hexanes/EtOAc (90:10) as an eluent to get 4i as a white solid, 64.5 mg, 68% yield, m.p. 120-122 °C; 1H NMR (500 MHz, CDCl3) δ: 7.48-7.33 (m, 5H), 7.15-7.06 (m, 3H), 6.68 (d, J = 8.8 Hz, 2H), 6.59 (br, 2H), 6.50 (d, J = 8.2 Hz, 2H), 6.01 (d, J = 3.2 Hz, 1H), 5.25 (dd, J1 = 12.2 Hz, J2 = 9.8 Hz, 1H), 5.08 (dd, J1 = 12.0 Hz, J2 = 8.5 Hz, 1H), 4.94 (dd, J1 = 12.2 Hz, J2 = 6.8 Hz, 1H), 4.79-4.76 (m, 1H), 4.61 (dd, J1 = 9.7 Hz, J2 = 6.9 Hz, 1H), 3.76 (s, 3H), 3.73-3.70 (m, 2H), 2.62 (d, J = 7.5 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ: 159.4, 137.3, 136.6, 136.4, 131.3, 132.3, 129.6, 128.5, 128.5, 128.4, 128.0, 127.9, 113.8, 90.7, 79.1, 77.6, 73.4, 55.6, 49.1, 47.9. νmax (neat, cm⁻¹): 3501, 2920, 2850, 1606, 1547, 1508, 1495, 1454, 1374, 1333, 1247, 1176, 1112, 1030. HRMS (ESI) m/z calcld for C27H25N2O6 ([M-H]⁻): 473.1718; found: 473.1720. Enantiomeric excess of 4i was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: tR = 23.4 min, major enantiomer: tR = 71.7 min.

The crude material was purified by flash column chromatography using hexanes/EtOAc (95:5) as an eluent to get 4j as a white solid, 58.3 mg, 63% yield, m.p. 130-132 °C; 1H NMR (500 MHz, CDCl3) δ: 7.37-7.32 (m, 6H), 7.14 (d, J = 7.1 Hz, 1H), 7.09 (t, J = 7.3 Hz, 2H), 6.83 (t, J = 8.5 Hz, 2H), 6.67-6.57 (m, 2H), 6.55 (dd, J1 = 8.3 Hz, J2 = 5.3 Hz, 2H), 5.99 (q, J = 2.0 Hz, 1H), 5.26 (dd, J1 = 12.2 Hz, J2 = 9.8 Hz, 1H), 5.06 (dd, J1 = 12.1 Hz, J2 = 8.5 Hz, 1H), 4.93 (dd, J1 = 12.2 Hz, J2 = 6.7 Hz, 1H), 4.77 (t, J = 7.8 Hz, 1H), 4.62 (dd, J1 = 9.7 Hz, J2 = 6.7 Hz, 1H), 3.78-3.74 (m, 2H), 2.79 (d, J = 7.4 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ: 162.5 (d, JCF = 248.2 Hz), 137.3, 137.2, 136.1, 132.3 (d, JCF = 2.5 Hz), 131.6 (d, JCF = 7.5 Hz), 130.7, 129.6, 128.6, 128.5, 128.3, 128.3, 128.1, 128.0, 115.3 (d, JCF = 7.5 Hz).
\[ \nu_{\text{max}} \text{ (neat, cm}^{-1}) = 3523, 3029, 1547, 1489, 1454, 1374, 1274, 1091, 1013. \]

HRMS (ESI) \( m/z \) calcd for \( \text{C}_{26}\text{H}_{23}\text{ClN}_{2}\text{O}_{5} \) ([M-H]): 461.1518; found: 461.1519. Enantiomeric excess of \( 4j \) was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, \( \lambda = 220 \text{ nm} \)), minor enantiomer: \( t_R = 15.0 \text{ min} \), major enantiomer: \( t_R = 44.0 \text{ min} \).

\( (1'R,2'S,3'S,4'S)-4-\text{Chloro}-3'-\text{nitro}-5'-[(R)-2-\text{nitro}-1\text{-phenylethyl}]-1',2',3',4'-\text{tetrahydro}-[1,1':2',1''-\text{terphenyl}]-4'-\text{ol (4k)} \)

The crude material was purified by flash column chromatography using hexanes/EtOAc (95:5) as an eluent to get \( 4k \) as a pale yellow solid, 58.3 mg, 61% yield, m.p. 135-137 \textdegree C; \( ^1\text{H} \text{NMR (500 MHz, CDCl}_3 \) \( \delta: 7.38-7.32 \text{ (m, 6H)}, 7.15-7.10 \text{ (m, 6H)}, 6.60 \text{ (br, 2H)}, 6.51 \text{ (d, } J = 8.1 \text{ Hz, 2H)}, 5.96 \text{ (d, } J = 2.9 \text{ Hz, 1H}), 5.26 \text{ (dd, } J_1 = 12.2 \text{ Hz, } J_2 = 9.8 \text{ Hz, 1H}), 5.05 \text{ (dd, } J_1 = 12.3 \text{ Hz, } J_2 = 8.4 \text{ Hz, 1H}), 4.92 \text{ (dd, } J_1 = 12.2 \text{ Hz, } J_2 = 6.7 \text{ Hz, 1H}), 4.77 \text{ (t, } J = 7.6 \text{ Hz, 1H}), 4.61 \text{ (dd, } J_1 = 9.9 \text{ Hz, } J_2 = 6.7 \text{ Hz, 1H}), 3.80-3.74 \text{ (m, 2H)}, 2.80 \text{ (d, } J = 7.4 \text{ Hz, 1H}). \)

\( ^{13}\text{C} \text{NMR (125 MHz, CDCl}_3 \) \( \delta: 137.6, 137.1, 136.0, 135.1, 134.0, 131.4, 130.4, 129.6, 128.7, 128.6, 128.5, 128.3, 128.1, 128.0, 90.4, 79.0, 73.2, 48.9, 48.0, 47.5. \nu_{\text{max}} \text{ (neat, cm}^{-1}) = 3523, 3029, 1547, 1489, 1454, 1374, 1274, 1091, 1013. \) HRMS (ESI) \( m/z \) calcd for \( \text{C}_{26}\text{H}_{23}\text{ClN}_{2}\text{O}_{5} \) ([M+Na]?): 501.1188; found: 501.1172. Enantiomeric excess of \( 4k \) was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, \( \lambda = 220 \text{ nm} \)), minor enantiomer: \( t_R = 15.7 \text{ min} \), major enantiomer: \( t_R = 49.3 \text{ min} \).

\( (1'R,2'S,3'S,4'S)-4-\text{Bromo}-3'-\text{nitro}-5'-[(R)-2-\text{nitro}-1\text{-phenylethyl}]-1',2',3',4'-\text{tetrahydro}-[1,1':2',1''-\text{terphenyl}]-4'-\text{ol (4l)} \)
The crude material was purified by flash column chromatography using hexanes/EtOAc (95:5) as an eluent to get 4l as a pale yellow solid, 64.9 mg, 62% yield, m.p. 140-142 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 7.41-7.30 (m, 7H), 7.27-7.25 (m, 4H), 7.18-7.08 (m, 4H), 6.60 (br, 2H), 6.45 (d, \(J = 8.0\) Hz, 2H), 5.96 (d, \(J = 3.1\) Hz, 1H), 5.26 (dd, \(J_1 = 12.2\) Hz, \(J_2 = 9.9\) Hz, 1H), 5.05 (dd, \(J_1 = 12.1\) Hz, \(J_2 = 8.4\) Hz, 1H), 4.92 (dd, \(J_1 = 12.2\) Hz, \(J_2 = 6.7\) Hz, 1H), 4.77 (t, \(J = 7.9\) Hz, 1H), 4.61 (dd, \(J_1 = 9.9\) Hz, \(J_2 = 6.7\) Hz, 1H), 3.79-3.73 (m, 2H), 2.75 (d, \(J = 7.4\) Hz, 1H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 137.62, 137.10, 135.96, 135.65, 131.78, 131.54, 130.35, 129.60, 128.67, 128.49, 128.32, 128.39, 128.15, 127.98, 122.14, 90.34, 78.96, 73.21, 48.91, 48.07, 47.44. \(\nu_{\text{max}}\) (neat, cm\(^{-1}\)): 2522, 2360, 2340, 2159, 2016, 1868, 1699, 1683, 1652, 1558, 1540, 1456, 1418, 1072. HRMS (ESI) \(m/z\) calcd for C\(_{26}\)H\(_{23}\)BrN\(_2\)O\(_5\)Na ([M+Na\(^+\)]: 545.0683; found: 545.0663. Enantiomeric excess of 4l was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, \(\lambda = 220\) nm), minor enantiomer: \(t_R = 16.7\) min, major enantiomer: \(t_R = 50.9\) min.

\((1'R,2'S,3'S,4'S)-4''-Bromo-5'-(\(R\)-1-(4-bromophenyl)-2-nitroethyl]-4-methoxy-3'-nitro-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-ol (4m)\)

The crude material was purified by flash column chromatography using hexanes/EtOAc (95:5) as an eluent to get 4m as a white solid, 82.2 mg, 65% yield, m.p. 135-137 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 7.51 (d, \(J = 8.4\) Hz, 2H), 7.25-7.21 (m, 6H), 6.71 (d, \(J = 8.8\) Hz, 2H), 6.50 (d, \(J = 8.2\) Hz, 2H), 6.45 (br, 2H), 5.97 (d, \(J = 3.9\) Hz, 1H), 5.18 (dd, \(J_1 = 12.4\) Hz, \(J_2 = 9.5\) Hz, 1H), 5.02 (dd, \(J_1 = 12.5\) Hz, \(J_2 = 8.4\) Hz, 1H), 4.90 (dd, \(J_1 = 12.4\) Hz, \(J_2 = 7.1\) Hz, 1H), 4.74 (t, \(J = 6.9\) Hz, 1H), 4.57 (dd, \(J_1 = 9.4\) Hz, \(J_2 = 7.1\) Hz, 1H), 3.78 (s, 3H), 3.72-3.65 (m, 2H), 2.75 (d, \(J = 7.2\) Hz, 1H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 159.6, 136.3, 136.3, 135.3, 132.7, 131.7, 131.3, 131.2, 130.2, 129.8, 127.8, 122.1, 114.1, 90.5, 78.7, 73.1, 55.6, 48.3, 47.6, 47.4. \(\nu_{\text{max}}\) (neat, cm\(^{-1}\)): 3420, 2918, 2849, 1703, 1608, 1548, 1508, 1488, 1462, 1373, 1248, 1176, 1112, 1073. HRMS (ESI) \(m/z\) calcd for C\(_{27}\)H\(_{23}\)Br\(_2\)N\(_2\)O\(_6\) ([M-H]): 628.9928; found: 628.9925.
Enantiomeric excess of 4m was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t_R = 16.0 min, major enantiomer: t_R = 55.5 min.

(1'R,2'S,3'S,4'S)-3'-Nitro-5'-'[(R)-2-nitro-1-phenylethyl]-1',2',3',4'-tetrahydro-[1,1':2',1''-terphenyl]-4'-yl acetate (6)

The crude material was purified by flash column chromatography using hexanes/EtOAc (93:7) as an eluent to get 6 as a white solid, 38.7 mg, 80% yield, m.p. 181-183 °C; 1H NMR (500 MHz, CDCl_3) δ 7.40 (t, J = 7.4 Hz, 2H), 7.36 – 7.31 (m, 1H), 7.29 (d, J = 7.1 Hz, 2H), 7.23 (d, J = 7.3 Hz, 1H), 7.18 (t, J = 10.0 Hz, 2H), 7.13 (t, J = 7.4 Hz, 1H), 7.06 (t, J = 7.5 Hz, 2H), 6.68 (d, J = 7.1 Hz, 2H), 6.59 (br, 2H), 6.34 (d, J = 8.4 Hz, 1H), 6.08 (d, J = 5.7 Hz, 1H), 5.23 (dd, J_1 = 13.0 Hz, J_2 = 8.4 Hz, 1H), 4.87 (dd, J_1 = 13.4 Hz, J_2 = 8.8 Hz, 1H), 4.68 (dd, J_1 = 13.4 Hz, J_2 = 7.6 Hz, 1H), 4.43 (t, J = 8.2 Hz, 1H), 3.94 (dd, J_1 = 13.0 Hz, J_2 = 5.8 Hz, 1H), 3.85 (t, J = 5.7 Hz, 1H), 1.84 (s, 3H). 13C NMR (125 MHz, CDCl_3) δ 170.4, 137.4, 136.5, 135.8, 134.3, 131.0, 130.3, 129.6, 128.6, 128.5, 128.4, 128.1, 128.0, 87.3, 78.5, 73.8, 48.4, 47.8, 46.0, 20.7. ν_max (neat, cm⁻¹): 3028, 1739, 1547, 1491, 1453, 1427, 1368, 1271, 1209, 1087, 1015. HRMS (ESI) m/z calcd for C_{28}H_{30}N_{3}O_{6}([M+NH_4]^+): 504.2129; found: 504.2132.

Enantiomeric excess of 6 was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: t_R = 22.2 min, major enantiomer: t_R = 55.3 min.

(1'R,2'S,3'S)-3'-Nitro-5'-'((R)-2-nitro-1-phenylethyl)-2',3'-dihydro-[1,1':2',1''-terphenyl]-4'(1'H)-one (7)
The crude material was purified by flash column chromatography using hexanes/EtOAc (92:8) as an eluent to get 7 as a white solid, 37.6 mg, 85% yield, m.p. 125-127 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.40-7.33 (m, 5H), 7.25 – 7.05 (m, 7H), 6.65 (d, $J = 7.5$ Hz, 2H), 6.56 (d, $J = 7.6$ Hz, 2H), 5.78 (d, $J = 14.1$ Hz, 1H), 5.17 (dd, $J_1 = 12.7$ Hz, $J_2 = 8.9$ Hz, 1H), 4.92 (t, $J = 8.0$ Hz, 1H), 4.84 (dd, $J_1 = 12.7$ Hz, $J_2 = 7.1$ Hz, 1H), 4.41 (dd, $J_1 = 14.1$ Hz, $J_2 = 5.6$ Hz, 1H), 4.11 (t, $J = 5.8$ Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 187.4, 148.9, 137.0, 136.9, 135.6, 133.2, 130.0, 129.7, 129.0, 128.9, 128.8, 128.7, 128.5, 128.3, 127.9, 90.4, 76.9, 48.8, 48.5, 44.5. $\nu$ max (neat, cm$^{-1}$): 1689, 1551, 1493, 1453, 1374, 1205, 1085, 1032, 918, 789, 766, 747. HRMS (ESI) m/z calcd for C$_{26}$H$_{26}$N$_3$O$_5$ ([M+NH$_4$]$^+$): 460.1867; found: 460.1871. Enantiomeric excess of 7 was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (70:30 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), minor enantiomer: $t_R = 25.6$ min, major enantiomer: $t_R = 37.3$ min.
Additional References


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### Shimadzu LCsolution Analysis Report

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