Supporting Information
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Supporting Information

Asymmetric Synthesis and Structural Elucidation of $C_2$-Symmetrical Optically Active Macrocycles Consisting of Two Biaryl and Two $\alpha$-Amino Acid Moieties

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Experimental Procedures

Unless noted otherwise, all reagents were commercially available and used without further purification. All solvents were distilled from the appropriate drying agents immediately before use. All air and moisture sensitive reactions were carried out under an inert atmosphere of dry nitrogen. Purification of the crude products was performed using flash column chromatography on silica gel (0.035-0.070 mm). Reaction were monitored by TLC carried out on 0.25 mm SDS silica gel coated glass plates (60F254) and compounds were detected with UV light and/or with iodide. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. NMR spectra were recorded on Bruker DRX 400 instrument and calibrated using tetramethylsilane as internal reference. CD spectra were recorded on a J-815 spectrometer (JASCO Deutschland, gross-Umstadt, Germany) at room temperature using a 0.1 cm standard cell and spectrophotometric-grade MeOH. High resolution mass spectra (HRMS) were recorded under electrospray ionization (ESI) conditions. Melting points were taken on an XT-4 melting point apparatus and are uncorrected. The X-ray structures were determined with a Rigaku RAXIS RAPID IP diffractometer and a Rigaku Saturn CCD area detector diffractometer respectively.

**Tributyl(2-nitrophenyl)stannane (2)**

\[
\begin{align*}
\text{SnBu}_3 \quad \text{NO}_2
\end{align*}
\]

Under nitrogen to a well stirred solution of 1-bromo-2-nitrobenzene (600.0 mg, 3.0 mmol) and Pd(PPh₃)₄ (346.8 mg, 0.3 mmol) in anhydrous toluene (20.0 mL) was added Hexa-n-butylditin (2.3 mL, 4.5 mmol) dropwise via a syringe. The reaction solution was stirred at 110°C for 15 h, and the excess solvent was removed under reduced pressure. The residue was dissolved in CH₂Cl₂ (20.0 mL), and the resulting solution was treated with aqueous KF solution (c = 1.40 M, 2.0 mL) for 30 min. The aqueous mixture was passed through a celite bed, and the corresponding filtrate was dried over anhydrous Na₂SO₄, filtered and evaporated under vacuum. The residue was purified by flash column chromatography on silica gel (eluent: EtOAc / petroleum ether = 1:40) to furnish 2 (991.2 mg, 80.0% yield) as yellow oil.³¹H NMR (CDCl₃): δ 8.24-8.39 (m, 1H), 7.43-7.77 (m, 3H), 1.11-1.62 (m, 18H), 0.87 (t, J = 7.2Hz, 9H).

**2'-nitro[1,1'-biphenyl]-2-carbaldehyde (4)**

\[
\begin{align*}
\text{CHO} \quad \text{NO}_2
\end{align*}
\]

Under nitrogen to a mixture of compound 2 (1.0 g, 2.4 mmol, 1.0 equiv) and 2-bromobenzaldehyde (420 μl, 3.6 mmol, 1.5 equiv) in anhydrous THF (20.0 mL) was added Pd(PPh₃)₄ (277.4 mg, 0.2 mmol, 0.1 equiv) and CuBr (27.5 mg, 0.2 mmol, 0.08 equiv). The resulting reaction solution was allowed to stir at 65°C for 5h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (eluent: EtOAc / petroleum ether = 1:5) to afford compound 4 (490.3 mg, 90.0% yield) as yellow semi-solid.²³H NMR (CDCl₃): δ 9.85 (s, 1H), 8.10 (dd, J = 7.8Hz, 1H), 7.99 (dd, J = 7.8Hz, 1.2Hz, 1H), 7.55-7.69 (m, 4H), 7.34 (dd, J = 7.4Hz, 1.2Hz, 1H), 7.25 (dd, J = 7.4Hz, 1.2Hz, 1H). HRMS (ESI) calculated for C₁₃H₉O₃Na(M⁺Na⁺): 250.0474, found 250.0474 (-0.2 ppm, -0.06 mmu).
2-[2-(1,3-dioxolan-2-yl)phenyl]nitrobenzene (5)

![Structure of 5]

Under nitrogen p-toluenesulfonic acid monohydrate (41.9 mg, 0.22 mmol, 0.1 equiv) was added to a well stirred suspension of compound 4 (500.0 mg, 2.2 mmol, 1.0 equiv), glycol (0.5 mL, 8.8 mmol, 4.0 equiv) and catalytic amount of molecular sieves (40.0 mg) in dried benzene (20.0 mL) at room temperature. The mixture was stirred at reflux for 2.5 h. The reaction mixture was diluted with EtOAc (50.0 mL) and washed with sat. NaHCO₃ (aq) (10 mL x 3). The organic layers was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified with flash column chromatography on silica gel (eluent: EtOAc / petroleum ether = 1:4) to afford 5 (470.0 mg, 80.0% yield) as yellow semi-solid. ¹H NMR (CDCl₃): δ 8.03 (dd, J = 8.4Hz, 1.2Hz, 1H), 7.39-7.65 (m, 6H), 7.16-7.21 (m, 1H), 5.52 (s, 1H), 3.91-4.77 (m, 4H); ¹³C NMR (CDCl₃): δ 148.6, 137.3, 134.8, 134.4, 132.4, 131.9, 128.9, 128.6, 128.2, 127.7, 126.8, 123.5, 102.0, 64.8, 64.6; HRMS (ESI) calculated for C₁₅H₁₃NO₄Na (M⁺Na⁺): 294.0744, found 294.0736 (+2.4 ppm, +0.7 mmu).

2-[2-(1,3-dioxolan-2-yl)phenyl]aniline (6)

A mixture of compound 5 (542.0 mg, 2.0 mmol) and PtO₂·3H₂O (56.2 mg, 0.2 mmol) in absolutely anhydrous EtOH (20.0 mL) was hydrogenated under 1 atm for 4.0 h. The catalyst was removed through a celite bed, and the resulted filtrate was concentrated under reduced pressure. The residue was purified with flash column chromatography on silica gel (eluent: petroleum ether / EtOAc = 1:4) to provide compound 6 (453.1 mg, 94% yield) as yellow semi-solid. ¹H NMR (CDCl₃): δ 7.67-7.71 (m, 1H), 7.40-7.44 (m, 2H), 7.20-7.28 (m, 1H), 7.16 (td, J = 7.6 Hz, 1.6Hz, 1H), 7.06 (dd, J = 7.4Hz,1.2Hz, 1H), 6.79 (td, J = 7.6 Hz, 1.2Hz, 1H), 6.73 (dd, J = 7.8Hz,1.2Hz, 1H), 5.60 (s,1H), 3.87-4.07 (m, 4H), 3.35 (br, NH₂); ¹³C NMR (CDCl₃): δ 144.3, 139.5, 138.9, 136.3, 131.0, 130.8, 130.5, 129.7, 128.8, 128.5, 128.1, 127.9, 127.2, 126.5, 125.4, 118.0, 115.3, 101.6, 101.5, 65.5, 65.3; HRMS (ESI) calculated for C₁₅H₁₆NO₂ (M⁺H⁺): 242.1183, found 242.1175 (+3.0 ppm, +0.7 mmu).

N-[2'-(1,3-dioxolan-2-yl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(R)-alanine amide ((R)-8a)

![Structure of 8a]

Under nitrogen to a well stirred solution of compound 6 (48.0 mg, 0.2 mmol, 1.0 equiv) and (R)-7a (45.4 mg, 0.24 mmol, 1.2 equiv) in dried CH₂Cl₂ (5.0 mL) was added EDCI (57.5 mg, 0.3 mmol, 1.5 equiv) in one portion. The resulting solution was stirred at room temperature for 4.0 h. The reaction mixture was diluted with CH₂Cl₂ (5.0 mL), and then washed with water (5 mL x 3). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified

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with flash column chromatography on silica gel (eluent: EtOAc / petroleum ether = 1:4) to afford (R)-8a (77.7 mg, 92% yield) as colorless semi-solid. \( \alpha_d^{23} = +21.2 \) (c = 1.7, CHCl₃); \(^1\)H NMR (CDCl₃) indicated a 64:36 ratio of two inseparable rotamers: \( \delta 8.16 \) (d, \( J = 8.0 \) Hz, 0.7H), 8.05 (brs, 0.3H), 7.82 (brs, 0.7H), 7.63-7.75 (m, 1.3H), 7.32-7.55 (m, 3H), 7.10-7.24 (m, 3H), 5.50 (s, 0.3H), 5.43 (s, 0.7H), 5.20, 4.85, 4.25 (brs, 3H, NHBOC), 3.75-4.15 (m, 5H), 1.39 (s, 3H), 1.34 (s, 6H), 1.23 (d, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (CDCl₃): \( \delta 170.9, 170.6, 154.9, 137.4, 137.3, 135.8, 135.6, 135.4, 135.1, 131.0, 130.4, 130.3, 130.2, 130.1, 129.9, 129.4, 128.6, 128.5, 128.3, 128.2, 127.4, 127.0, 124.3, 121.6, 101.6, 101.3, 79.4, 65.4, 65.1, 50.6, 28.2, 28.1, 18.2, 18.0; HRMS (ESI) calculated for C₂₃H₂₈N₂O₅Na (M+Na\(^+\)) : 435.1895, found 435.1890 (+1.0 ppm, +0.5 mmu).

\( N-[2'-(1,3-dioxolan-2-yl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(S)-alanine amide ((S)-8a) \)

\( \alpha_d^{23} = +21.2 \) (c = 1.7, CHCl₃); \(^1\)H NMR (CDCl₃) indicated a 64:36 ratio of two inseparable rotamers: \( \delta 8.16 \) (d, \( J = 8.0 \) Hz, 0.7H), 8.05 (brs, 0.3H), 7.82 (brs, 0.7H), 7.63-7.75 (m, 1.3H), 7.32-7.55 (m, 3H), 7.10-7.24 (m, 3H), 5.50 (s, 0.3H), 5.43 (s, 0.7H), 5.20, 4.85, 4.25 (brs, 3H, NHBOC), 3.75-4.15 (m, 5H), 1.39 (s, 3H), 1.34 (s, 6H), 1.23 (d, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (CDCl₃): \( \delta 170.9, 170.6, 154.9, 137.4, 137.3, 135.8, 135.6, 135.4, 135.1, 131.0, 130.4, 130.3, 130.2, 130.1, 129.9, 129.4, 128.6, 128.5, 128.3, 128.2, 127.4, 127.0, 124.3, 121.6, 101.6, 101.3, 79.4, 65.4, 65.1, 50.6, 28.2, 28.1, 18.2, 18.0; HRMS (ESI) calculated for C₂₃H₂₈N₂O₅Na (M+Na\(^+\)) : 435.1895, found 435.1890 (+1.0 ppm, +0.5 mmu).

\( \alpha_d^{23} = +21.2 \) (c = 1.7, CHCl₃); \(^1\)H NMR (CDCl₃) indicated a 64:36 ratio of two inseparable rotamers: \( \delta 8.16 \) (d, \( J = 8.0 \) Hz, 0.7H), 8.05 (brs, 0.3H), 7.82 (brs, 0.7H), 7.63-7.75 (m, 1.3H), 7.32-7.55 (m, 3H), 7.10-7.24 (m, 3H), 5.50 (s, 0.3H), 5.43 (s, 0.7H), 5.20, 4.85, 4.25 (brs, 3H, NHBOC), 3.75-4.15 (m, 5H), 1.39 (s, 3H), 1.34 (s, 6H), 1.23 (d, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (CDCl₃): \( \delta 170.9, 170.6, 154.9, 137.4, 137.3, 135.8, 135.6, 135.4, 135.1, 131.0, 130.4, 130.3, 130.2, 130.1, 129.9, 129.4, 128.6, 128.5, 128.3, 128.2, 127.4, 127.0, 124.3, 121.6, 101.6, 101.3, 79.4, 65.4, 65.1, 50.6, 28.2, 28.1, 18.2, 18.0; HRMS (ESI) calculated for C₂₃H₂₈N₂O₅Na (M+Na\(^+\)) : 435.1895, found 435.1890 (+1.0 ppm, +0.5 mmu).

\( N-[2'-(1,3-dioxolan-2-yl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(R)-leucine amide ((R)-8b) \)

\( \alpha_d^{23} = +30.7 \) (c = 0.9, CHCl₃); \(^1\)H NMR (CDCl₃) indicated a 67:33 ratio of two inseparable rotamers: \( \delta 8.16 \) (d, \( J = 8.0 \) Hz, 0.7H), 8.03 (brs, 0.3H), 7.79 (brs, 0.7H), 7.63-7.75 (m, 1.3H), 7.42-7.53 (m, 2H), 7.33-7.41 (m, 1H), 7.13-7.24 (m, 3H), 5.48 (s, 0.3H), 5.42 (s, 0.7H), 5.16, 4.90, 4.23 (brs, 3H, NHBOC), 3.80-4.14 (m, 5H), 1.39 (s, 3H), 1.34 (s, 6H), 1.22 (d, \( J = 6.8 \) Hz, 3H); \(^{13}\)C NMR (CDCl₃): \( \delta 171.0, 170.7, 155.0, 137.5, 137.3, 135.8, 135.5, 135.3, 135.1, 131.0, 130.5, 130.4, 130.3, 130.1, 130.0, 129.6, 129.8, 128.8, 128.7, 128.5, 128.45, 127.4, 127.0, 124.4, 121.6, 101.8, 101.5, 79.7, 65.5, 65.2, 65.15, 50.6, 28.3, 28.2, 18.4, 18.36; HRMS (ESI) calculated for C₂₆H₃₄N₂O₅Na (M+Na\(^+\)) : 477.2378, found 477.2359 (+1.2 ppm, +0.6 mmu).
(S)-8b was prepared from (S)-7b by following the same procedure as described for (R)-8a: compound 6 (48.0 mg, 0.2 mmol, 1.0 equiv), (S)-7b (59.8 mg, 0.24 mmol, 1.2 equiv) and EDCI (57.5 mg, 0.3 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature overnight. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 4:1) provided (S)-8b (84.7 mg, 93% yield) as colorless semi-solid. [α]D^23 = -30.6 (c = 1.5, CHCl3); 1H NMR (CDCl3) indicated a 70:30 ratio of two inseparable rotamers: δ 8.159 (d, J = 8.0Hz, 0.7H), 8.08 (brs, 0.3H), 7.95 (brs, 0.7H), 7.65-7.81 (m, 1.3H), 7.35-7.55 (m, 3H), 7.10-7.27 (m, 3H), 5.53 (s, 0.3H), 5.46 (s, 0.7H), 5.04, 4.72, 4.15 (3brs, NHBoc), 3.80-4.15 (m, 5H), 1.50-1.65 (m, 1H), 1.40 (s, 3H), 1.37 (s, 6H), 1.20-1.34 (m, 1H), 0.72-0.92 (m, 7H); 13C NMR (CDCl3): δ 170.7, 155.2, 137.5, 135.5, 135.4, 135.1, 131.4, 130.7, 130.6, 130.4, 130.2, 130.1, 129.9, 129.6, 128.7, 128.6, 128.5, 128.4, 128.3, 127.7, 127.3, 126.4, 124.5, 121.9, 101.8, 101.6, 79.5, 65.6, 65.5, 65.4, 65.2, 65.15, 53.5, 41.9, 41.6, 28.3, 28.2, 24.7, 23.0, 22.9, 21.7; HRMS (ESI) calculated for C_{26}H_{34}N_{2}O_{5}Na (M+Na^+): 477.2365, found 477.2357 (+1.0 ppm, +0.5 mmu).

(R)-8c was prepared from (R)-7c by following the same procedure as described for (R)-8a: compound 6 (48.0 mg, 0.2 mmol, 1.0 equiv), (R)-7c (63.7 mg, 0.24 mmol, 1.2 equiv) and EDCI (57.5 mg, 0.3 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature overnight. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 7:2) provided (R)-8c (93.8 mg, 97% yield) as colorless semi-solid. [α]D^23 = +11.7 (c = 1.1, CHCl3); 1H NMR (CDCl3) indicated a 70:30 ratio of two inseparable rotamers: δ 8.25 (d, J = 8.4Hz, 0.7H), 8.03 (brs, 0.3H), 7.87 (brs, 0.7H), 7.87 (brs, 0.7H), 7.62-7.74 (m, 1H), 7.30-7.52 (m, 3H), 7.13-7.29 (m, 3H), 7.00-7.13 (m, 3H), 5.46 (s, 0.3H), 5.39 (s, 0.7H), 5.14, 4.63, 4.42, 4.32 (4brs, NHBoc), 3.50-4.15 (m, 5H), 2.70-3.30 (m, 2H), 1.32 (s, 3H), 1.26 (s, 6H); 13C NMR (CDCl3): δ 169.3, 155.1, 137.2, 137.1, 136.7, 135.8, 135.5, 135.2, 135.1, 130.6, 130.4, 130.3, 130.2, 130.1, 129.6, 129.5, 129.4, 128.8, 128.7, 128.6, 128.4, 127.5, 127.1, 127.0, 126.8, 126.6, 124.4, 121.0, 101.8, 101.4, 79.6, 65.6, 65.5, 65.4, 65.2, 65.17, 56.1, 55.8, 38.0, 28.2, 28.15; HRMS (ESI) calculated for C_{29}H_{32}N_{2}O_{5}Na (M+Na^+): 511.2194, found 511.2203 (-1.8 ppm, -0.9 mmu).
(S)-8c was prepared from (S)-7c by following the same procedure as described for (R)-8a: compound 6 (48.0 mg, 0.2 mmol, 1.0 equiv), (S)-7c (63.7 mg, 0.24 mmol, 1.2 equiv) and EDCI (57.5 mg, 0.3 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 3.0 h. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 7:2) provided (S)-8c (87.0 mg, 90.0% yield) as colorless semi-solid. [α]D23 = -11.8 (c = 1.5, CHCl3); 1H NMR (CDCl3) indicated a 70:30 ratio of two inseparable rotamers: δ 8.28 (d, J = 8.4Hz, 0.7H), 8.05 (brs, 0.3H), 7.90 (brs, 0.7H), 7.85 (brs, 0.3H), 7.65-7.74 (m, 1H), 7.30-7.52 (m, 3H), 7.13-7.29 (m, 5H), 7.00-7.16 (m, 3H), 5.48 (s, 0.3H), 5.41 (s, 0.7H), 5.17, 4.66, 4.46, 4.35 (4brs, NHBoc), 3.52-4.15 (m, 5H), 2.70-3.30 (m, 2H), 1.35 (s, 3H), 1.29 (s, 6H); 13C NMR (CDCl3): δ 169.3, 155.1, 137.2, 137.1, 136.8, 135.9, 135.6, 135.3, 135.2, 130.6, 130.4, 130.3, 130.2, 130.0, 129.6, 129.5, 128.8, 128.5, 128.4, 127.5, 127.1, 126.8, 126.6, 124.4, 122.4, 121.0, 101.7, 101.4, 79.6, 79.5, 65.5, 65.4, 65.2, 65.15, 56.1, 55.9, 38.0, 28.2, 28.15; HRMS (ESI) calculated for C29H32N2O5Na (M+Na+): 511.2184, found 511.2203 (-3.8 ppm, -1.9 mmu).

N-methyl-N-[2'-(1,3-dioxolan-2-yl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(R)-alanine amide ((R)-9a)

To a stirred solution of (R)-8a (500.0 mg, 1.21 mmol, 1.0 equiv) in CH3CN (10.0 mL), Cs2CO3 (1182.7 mg, 3.63 mmol, 3.0 equiv) and CH3I (113 μL, 1.82 mmol, 1.5 equiv) were added. The resulting solution was stirred overnight at room temperature under nitrogen atmosphere. Complete conversion of starting material was ascertained by TLC. The reaction mixture was concentrated under reduced pressure. The crude product was purified with flash column chromatography on silica gel (eluent: petroleum ether / EtOAc = 2:1) to afford (R)-9a (422.7 mg, 82% yield) as colorless semi-solid. [α]D23 = +80.9 (c = 1.8, CHCl3); 1H NMR (CDCl3): δ 7.14-7.80 (m, 8H), 5.42 (s, 1H), 5.36-5.41 (m, 1H), 4.35-4.45 (m, 1H), 3.80-4.18 (m, 4H) 2.81 (s, 3H), 1.36-1.55 (m, 9H), 1.33 (d, J = 6.4 Hz, 3H); 13C NMR (CDCl3): δ 173.2, 154.6, 141.7, 140.6, 137.8, 137.4, 135.1, 132.9, 132.6, 132.1, 131.8, 131.0, 129.4, 129.1, 129.0, 128.3, 128.2, 128.0, 127.6, 127.3, 126.9, 101.3, 79.3, 65.5, 65.4, 47.1, 46.5, 37.7, 36.2, 28.4; HRMS (ESI) calculated for C24H31N2O5(M+H+): 427.2227, found 427.2225 (+0.5 ppm, +0.2 mmu).

N-methyl-N-[2'-(1,3-dioxolan-2-yl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(S)-alanine amide ((S)-9a)

(S)-9a was prepared from (S)-8a by following the same procedure as described for (R)-9a: (S)-8a (500.0 mg, 1.21 mmol, 1.0 equiv), anhydrous CH3CN (10.0 mL), Cs2CO3 (1182.7 mg, 3.63 mmol, 3.0 equiv) and CH3I (113 μL, 1.82 mmol, 1.5 equiv). The reaction mixture was stirred overnight at room temperature under nitrogen atmosphere. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 2:1) provided (S)-9a (463.9 mg, 90% yield) as colorless semi-solid. [α]D23 = -80.9 (c = 2.2, CHCl3); 1H NMR (CDCl3): δ 7.15-7.80 (m, 8H), 5.42 (s, 1H), 5.36-5.41 (m, 1H), 4.34-4.45 (m, 1H), 3.80-4.19 (m, 4H) 2.80 (s, 3H), 1.36-1.55 (m, 9H), 1.33 (d, J = 6.4 Hz, 3H); 13C NMR (CDCl3): δ 173.2, 154.5, 141.7, 140.6, 137.8, 137.4, 135.1, 132.9, 132.6, 132.1, 131.8, 129.4, 129.1, 129.0, 128.3, 128.2, 128.0, 127.6, 127.3, 126.9, 101.3, 79.3, 65.5, 65.4, 47.1, 46.5, 37.7, 36.2, 28.4; HRMS (ESI) calculated for C24H31N2O5Na (M+Na+): 427.2227, found 427.2225 (+0.5 ppm, +0.2 mmu).
N-methyl-N-[2'-(1,3-dioxolan-2-yl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(R)-leucine amide ((R)-9b)

(9b) was prepared from (R)-8b by following the same procedure as described for (R)-9a: (R)-8b (500.0 mg, 1.10 mmol, 1.0 equiv), anhydrous CH$_3$CN (10.0 mL), Cs$_2$CO$_3$ (1075.0 mg, 3.30 mmol, 3.0 equiv) and CH$_3$I (103 μL, 1.65 mmol, 1.5 equiv). The reaction mixture was stirred overnight at room temperature under nitrogen atmosphere. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 5:2) provided (R)-9b (422.1 mg, 82% yield) as colorless semi-solid. $[\alpha]_D^{23} = +102.4$ (c = 1.7, CHCl$_3$); $^1$H NMR (CDCl$_3$): $\delta$ 7.12-7.72 (m, 8H), 5.42 (s, 1H), 5.20-5.30 (m, 1H), 4.32-4.46 (m, 1H), 3.77-4.18 (m, 4H), 2.78 (s, 3H), 1.21-1.70 (m, 12H), 0.63-0.95 (m, 6H); $^{13}$C NMR (CDCl$_3$): $\delta$ 173.2, 155.0, 141.9, 140.4, 137.8, 137.5, 135.1, 132.9, 132.5, 132.1, 131.8, 129.6, 129.1, 128.9, 128.7, 128.5, 128.4, 128.3, 128.1, 128.0, 127.2, 126.8, 101.4, 79.2, 65.5, 65.4, 65.3, 65.2, 49.5, 49.0, 48.8, 44.3, 37.8, 36.1, 28.3, 28.0, 24.5, 23.8, 23.4, 21.1; HRMS (ESI) calculated for C$_{27}$H$_{37}$N$_2$O$_5$(M+H$^+$): 469.2697, found 469.2704 (-1.8 ppm, -0.9 mmu).

N-methyl-N-[2'-(1,3-dioxolan-2-yl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(S)-leucine amide ((S)-9b)

(S)-9b was prepared from (S)-8b by following the same procedure as described for (R)-9a: (S)-8b (500.0 mg, 1.10 mmol, 1.0 equiv), anhydrous CH$_3$CN (10.0 mL), Cs$_2$CO$_3$ (1076.5 mg, 3.30 mmol, 3.0 equiv) and CH$_3$I (103 μL, 1.65 mmol, 1.5 equiv). The reaction mixture was stirred overnight at room temperature under nitrogen atmosphere. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 5:2) provided (S)-9b (432.4 mg, 84% yield) as colorless semi-solid. $[\alpha]_D^{23} = -102.9$ (c = 1.1, CHCl$_3$); $^1$H NMR (CDCl$_3$): $\delta$ 7.13-7.72 (m, 8H), 5.42 (s, 1H), 5.20-5.30 (m, 1H), 4.32-4.46 (m, 1H), 3.77-4.18 (m, 4H), 2.78 (s, 3H), 1.21-1.70 (m, 12H), 0.60-1.00 (m, 6H); $^{13}$C NMR (CDCl$_3$): $\delta$ 173.2, 155.0, 141.9, 140.5, 137.9, 137.5, 135.1, 132.9, 132.6, 132.1, 131.8, 129.6, 129.2, 129.1, 128.7, 128.5, 128.3, 128.2, 128.1, 127.5, 127.2, 126.8, 101.4, 79.2, 65.5, 65.3, 49.6, 44.3, 36.1, 28.3, 28.0, 24.5, 23.8, 23.4, 21.2; HRMS (ESI) calculated for C$_{27}$H$_{37}$N$_2$O$_5$(M+H$^+$): 469.2697, found 469.2706 (-1.8 ppm, -0.9 mmu).
\( \text{N-methyl-N-[2'-\{1,3-dioxolan-2-yl\}[1,1'-biphenyl]-2-yl]-N-\text{tert-butoxycarbonyl-(R)-phenylalanine amide (}(R)\text{-9c}) } \)

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\text{(R-9c) was prepared from (R)-8c by following the same procedure as described for (R)-9a: (R)-8c (500.0 mg, 1.02 mmol, 1.0 equiv), anhydrous CH}_3\text{CN (10.0 mL), Cs}_2\text{CO}_3 (1000.3 mg, 3.07 mmol, 3.0 equiv) and CH}_3\text{I (95 µL, 1.53 mmol, 1.5 equiv). The reaction mixture was stirred overnight at room temperature under nitrogen atmosphere. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 5:2) provided (R)-9c (399.4 mg, 78% yield) as colorless semi-solid. } \]

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\left[\alpha\right]_\text{D}^{23} = +101.4 \text{ (c = 0.7, CHCl}_3); \text{ 1H NMR (CDCl}_3): 7.65-7.80 \text{ (m, 1H), 7.04-7.52 \text{ (m, 11H), 6.24 (d, } J = 8.0 \text{ Hz, 1H), 5.39 (s, 1H), 5.28 (d, } J = 8.0 \text{ Hz, 1H), 4.40-4.60 \text{ (m, 4H), 3.80-4.20 \text{ (m, 4H), 3.0-3.20 \text{ (m, 1H), 2.82-2.90 \text{ (m, 1H), 2.80 (s, 3H), 1.20-1.50 \text{ (m, 9H); 13C NMR (CDCl}_3): } \delta 171.7, 154.4, 140.3, 137.8, 137.5, 136.9, 135.1, 132.6, 129.8, 129.7, 129.6, 129.2, 128.9, 128.8, 128.5, 128.4, 128.3, 128.2, 128.1, 127.3, 127.1, 126.8,126.6, 101.3, 101.2, 79.7, 79.4, 65.5, 65.4, 65.3, 54.0, 52.6, 41.1, 38.0, 36.4, 35.7, 28.3, 27.6; \text{ HRMS} (\text{ESI}) \text{ calculated for C}_{30}\text{H}_{35}\text{N}_2\text{O}_5(\text{M}+\text{H}^+): 503.2540, found 503.2544 (-0.4 ppm, -0.2 mmu).} \]

\( \text{N-methyl-N-[2'-\{1,3-dioxolan-2-yl\}[1,1'-biphenyl]-2-yl]-N-\text{tert-butoxycarbonyl-(S)-Phenylalanine amide (}(S)\text{-9c}) } \)

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\text{(S-9c) was prepared from (S)-8c by following the same procedure described for above for (R)-9a: (S)-8c (500.0 mg, 1.02 mmol, 1.0 equiv), anhydrous CH}_3\text{CN (10.0 mL), Cs}_2\text{CO}_3 (1000.0 mg, 3.07 mmol, 3.0 equiv) and CH}_3\text{I (95 µL, 1.53 mmol, 1.5 equiv). The reaction mixture was stirred overnight at room temperature under nitrogen atmosphere. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 5:2) provided (S)-9c (409.6 mg, 80% yield) as colorless semi-solid. } \]

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\left[\alpha\right]_\text{D}^{23} = -101.4 \text{ (c = 0.9, CHCl}_3); \text{ 1H NMR (CDCl}_3): 7.65-7.80 \text{ (m, 1H), 7.04-7.52 \text{ (m, 11H), 6.23 (d, } J = 8.0 \text{ Hz, 1H), 5.39 (s, 1H), 5.28 (d, } J = 8.0 \text{ Hz, 1H), 4.40-4.60 \text{ (m, 4H), 3.80-4.20 \text{ (m, 4H), 3.0-3.20 \text{ (m, 1H), 2.82-2.90 \text{ (m, 1H), 2.80 (s, 3H), 1.20-1.50 \text{ (m, 9H); 13C NMR (CDCl}_3): } \delta 171.7, 154.4, 140.3, 137.8, 137.5, 136.9, 135.1, 132.6, 129.8, 129.7, 129.6, 129.2, 128.9, 128.8, 128.5, 128.4, 128.3, 128.2, 128.1, 127.3, 127.1, 126.8,126.6, 101.3, 101.2, 79.7, 79.4, 65.5, 65.4, 65.3, 54.0, 52.6, 41.1, 38.0, 36.4, 35.7, 28.3, 27.6; \text{ HRMS} (\text{ESI}) \text{ calculated for C}_{30}\text{H}_{35}\text{N}_2\text{O}_5(\text{M}+\text{H}^+): 503.2540, found 503.2542 (-0.3 ppm, -0.2 mmu).} \]

\( \text{N-methyl-N-[2'-\{formyl\}[1,1'-biphenyl]-2-yl]-N-\text{tert-butoxycarbonyl-(R)-alanine amide (}(R)\text{-10a}) } \)

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\text{To a stirred solution of (R)-9a (422.7 mg, 0.99 mmol, 1.0 equiv) in acetone (12.0 mL), TsOH·H}_2\text{O (18.9 mg, 0.10 mmol, 0.1 equiv) was added. The resulting solution was stirred at room temperature for 1.2 h. The resulting mixture was concentrated under reduced pressure at room temperature. The crude product} \]
was purified with flash column chromatography on silica gel (Eluent: petroleum ether / EtOAc = 2:1) to afford (R)-10a (351.7 mg, 93% yield) as colorless semi-solid. $[\alpha]_D^{23} = +91.0$ (c = 1.0, CHCl$_3$); $^1$H NMR (CDCl$_3$): $\delta$ 9.81 (s, 1H), 7.93-8.10 (m, 1H), 7.18-7.68 (m, 7H), 5.25-5.40 (m, 1H), 4.30-4.40 (m, 1H), 2.84 (s, 3H), 1.30-1.52 (m, 9H), 1.25 (d, J = 6.8 Hz, 3H); $^{13}$C NMR (CDCl$_3$): $\delta$ 192.2, 191.4, 173.2, 154.5, 141.2, 140.8, 136.7, 133.9, 132.5, 131.5, 130.8, 129.9, 129.8, 129.6, 128.8, 128.7, 128.6, 79.4, 47.2, 46.3, 38.8, 36.9, 29.7, 28.4, 20.4; HRMS (ESI) calculated for C$_{22}$H$_{27}$N$_2$O$_4$(M+H$^+$): 383.1965, found 383.1967 (-0.5 ppm, -0.2 mmu).

N-methyl-N-[2'-(formyl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(S)-alanine amide ((S)-10a)

(S)-10a was prepared from (S)-9a by following the same procedure as described for (R)-10a: (S)-9a (463.9 mg, 1.09 mmol, 1.0 equiv) and TsOH·H$_2$O (20.9 mg, 0.11 mmol, 0.1 equiv) was added. The resulting solution was stirred at room temperature for 1 h. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 2:1) provided (S)-10a (374.7 mg, 90% yield) as colorless semi-solid. $[\alpha]_D^{23} = -91.0$ (c = 0.5, CHCl$_3$); $^1$H NMR (CDCl$_3$): $\delta$ 9.81 (s, 1H), 7.93-8.10 (m, 1H), 7.18-7.68 (m, 7H), 5.25-5.40 (m, 1H), 4.30-4.40 (m, 1H), 2.84 (s, 3H), 1.30-1.52 (m, 9H), 1.25 (d, J = 6.8 Hz, 3H); $^{13}$C NMR (CDCl$_3$): $\delta$ 192.2, 191.3, 173.1, 155.1, 154.5, 142.2, 141.1, 140.8, 136.7, 134.0, 133.9, 133.7, 132.8, 132.5, 131.5, 131.4, 130.8, 130.1, 129.9, 129.8, 129.7, 128.7, 128.6, 128.3, 128.2, 127.6, 127.4, 126.9, 79.4, 47.2, 46.5, 38.8, 36.8, 29.7, 28.4, 20.4, 20.0; HRMS (ESI) calculated for C$_{22}$H$_{27}$N$_2$O$_4$(M+H$^+$): 383.1965, found 383.1977 (-2.8 ppm, -1.2 mmu).

N-methyl-N-[2'-(formyl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(R)-leucine amide ((R)-10b)

(R)-10b was prepared from (R)-9b by following the same procedure as described for (R)-10a: (R)-9b (422.1 mg, 0.91 mmol, 1.0 equiv) and TsOH·H$_2$O (17.2 mg, 0.09 mmol, 0.1 equiv) was added. The resulting solution was stirred at room temperature for 1.0 h. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 5:2) provided (R)-10b (378.1 mg, 98% yield) as colorless semi-solid. $[\alpha]_D^{23} = +97.5$ (c = 0.8, CHCl$_3$); $^1$H NMR (CDCl$_3$): $\delta$ 9.78 (s, 1H), 7.90-8.10 (m, 1H), 7.17-7.66 (m, 7H), 5.20-5.31 (m, 1H), 4.30-4.40 (m, 1H), 2.83 (s, 3H), 1.20-1.70 (m, 12H), 0.52-1.10 (m, 6H); $^{13}$C NMR (CDCl$_3$): $\delta$ 192.3, 191.4, 173.2, 155.0, 142.5, 141.2, 140.7, 136.8, 133.9, 133.7, 132.5, 131.3, 131.0, 129.8, 129.6, 128.8, 128.7, 128.6, 128.5, 128.2, 128.1, 127.6, 127.4, 127.3, 127.0, 79.4, 49.6, 48.7, 44.3, 36.8, 28.3, 28.1, 24.5, 24.0, 23.7, 23.4, 21.4, 21.0; HRMS (ESI) calculated for C$_{25}$H$_{33}$N$_2$O$_4$(M+H$^+$): 425.2435, found 425.2452 (-3.9 ppm, -1.7 mmu).
**N-methyl-N-[2’-(formyl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(S)-leucine amide ((S)-10b)**

(S)-10b was prepared from (S)-9b by following the same procedure as described for (R)-10a: (S)-9b (432.4 mg, 1.02 mmol, 1.0 equiv) and TsOH·H2O (19.4 mg, 0.10 mmol, 0.1 equiv) was added. The resulting solution was stirred at room temperature for 0.7 h. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 5:2) provided (S)-10b (410.9 mg, 95% yield) as colorless semi-solid. [α]D23 = -97.8 (c = 1.2, CHCl3); 1H NMR (CDCl3): δ 9.79 (s, 1H), 7.91-8.13 (m, 1H), 7.15-7.66 (m, 7H), 5.19-5.31 (m, 1H), 4.30-4.40 (m, 1H), 2.83 (s, 3H), 1.20-1.72 (m, 12H), 0.52-1.10 (m, 6H); 13C NMR (CDCl3): δ 192.3, 191.4, 173.2, 155.0, 142.5, 141.2, 140.7, 136.8, 133.9, 133.7, 132.5, 131.3, 131.0, 129.8, 129.6, 128.7, 128.6, 128.5, 128.2, 127.6, 127.3, 127.0, 79.4, 79.2, 49.6, 48.7, 44.3, 36.8, 28.3, 28.1, 24.5, 24.2, 23.7, 23.4, 21.4, 21.1; HRMS (ESI) calculated for C25H33N2O4(M+H+): 425.2435, found 425.2442 (-1.6 ppm, -0.7 mmu).

**N-methyl-N-[2’-(formyl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(R)-Phenylalanine amide ((R)-10c)**

(R)-10c was prepared from (R)-9c by following the same procedure described for above for (R)-10a: (R)-9c (473.8 mg, 0.94 mmol, 1.0 equiv) and TsOH·H2O (18.0 mg, 0.09 mmol, 0.1 equiv) was added. The resulting solution was stirred at room temperature for 1 h. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 3:1) provided (R)-10c (413.3 mg, 96% yield) as colorless semi-solid. [α]D23 = +46.2 (c = 1.0, CHCl3); 1H NMR (CDCl3): δ 9.80 (s, 1H), 7.95-8.00 (m, 1H), 6.90-7.70 (m, 12H), 6.25 (d, J = 7.6 Hz, 1H), 5.18 (d, J = 9.2 Hz, 1H), 4.41 (q, J = 8.8 Hz, 1H), 2.95-3.10 (m, 1H), 2.52-2.90 (m, 3H), 1.00-1.50 (m, 9H); 13C NMR (CDCl3): δ 191.4, 171.6, 154.4, 141.2, 140.6, 136.6, 133.8, 133.6, 132.0, 131.1, 129.7, 128.6, 128.5, 127.5, 126.9, 126.8, 79.4, 52.8, 41.1, 37.0, 28.3; HRMS (ESI) calculated for C28H31N2O4(M+H+): 459.2278, found 459.2292 (-2.8 ppm, -1.4mmu).

**N-methyl-N-[2’-(formyl)[1,1'-biphenyl]-2-yl]-N-tert-butoxycarbonyl-(S)-phenylalanine amide ((S)-10c)**

(S)-10c was prepared from (S)-9c by following the same procedure as described for (S)-10a: (S)-9c (409.6 mg, 0.82 mmol, 1.0 equiv) and TsOH·H2O (16.0 mg, 0.08 mmol, 0.1 equiv) was added. The resulting solution was stirred at room temperature for 1 h. Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 3:1) provided (S)-10c (371.8 mg, 99% yield) as colorless semi-solid. [α]D23 = -46.4 (c = 0.9, CHCl3); 1H NMR (CDCl3): δ 9.81 (s, 1H), 7.90-8.10 (m, 1H), 7.10-7.60 (m, 7H), 5.18-5.30 (m, 1H), 4.30-4.40 (m, 1H), 2.83 (s, 3H), 1.20-1.72 (m, 12H), 0.52-1.10 (m, 6H); 13C NMR (CDCl3): δ 192.3, 191.4, 173.2, 155.0, 142.5, 141.2, 140.7, 136.8, 133.9, 133.7, 132.5, 131.3, 131.0, 129.8, 129.6, 128.7, 128.6, 128.5, 128.2, 127.6, 127.3, 127.0, 79.4, 79.2, 49.6, 48.7, 44.3, 36.8, 28.3, 28.1, 24.5, 24.2, 23.7, 23.4, 21.4, 21.1; HRMS (ESI) calculated for C28H31N2O4(M+H+): 459.2278, found 459.2292 (-2.8 ppm, -1.4mmu).
6.90-7.70 (m, 12H), 6.25 (d, J = 8.0 Hz, 1H), 5.21 (d, J = 9.2 Hz, 1H), 4.43 (q, J = 9.2 Hz, 1H), 2.95-3.10 (m, 1H), 2.52-2.90 (m, 3H), 1.10-1.50 (m, 9H); 13C NMR (CDCl3): δ 191.4, 171.6, 154.4, 141.2, 140.6, 136.6, 133.8, 133.6, 132.0, 131.1, 129.7, 128.6, 128.5, 127.5, 126.9, 126.8, 79.4, 52.8, 41.1, 37.0, 28.3, 27.8; HRMS (ESI) calculated for C28H31N2O4(M+H+): 459.2278, found 459.2285 (-1.4 ppm, -0.7 mmu).

Chiral macrocycle (R,R,M,M)-11a

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\text{To a well stirred solution of (R)-10a (351.7 mg, 0.92 mmol) in anhydrous CH}_2\text{Cl}_2 (10 mL) was added trifluoroacetic acid (0.92 mL). The resulting solution was stirred at room temperature for 2 hour. The excess trifluoroacetic acid was removed under reduced pressure. The resulted residue was dissolved in CH}_2\text{Cl}_2 (10 mL) and washed with saturated aqueous NaHCO}_3 (3 x 10 mL). The organic layers were dried over anhydrous Na}_2\text{SO}_4, filtered, and concentrated under reduced pressure. The crude product was treated with 5\% AcOH (0.46 mL) in CH}_2\text{Cl}_2 (10 mL) at 40\textdegree C overnight. The reaction mixture was diluted with CH}_2\text{Cl}_2 (10 mL) and washed with water (3 x 10 mL). The organic layers were dried over anhydrous Na}_2\text{SO}_4, filtered, and concentrated under reduced pressure. The crude product was purified with flash column chromatography on silica gel (eluent: EtOAc) to afford (R,R,M,M)-11a (87.5 mg, 36% yield) as white solid, m.p. 209-212 \textdegree C. [\textalpha]D\textsubscript{23} = -296.0 (c = 1.0, CHCl3); 1H NMR (CDCl3): δ 7.63 (dd, J = 8.0Hz, 1.2Hz, 2H), 7.53 (s, 2H), 7.23-7.49 (m, 10H), 7.12 (d, J = 7.6Hz, 2H), 7.07 (dd, J = 7.6Hz, 1.2Hz, 2H), 3.64 (q, J = 6.8 Hz, 2H), 3.38 (s, 6H), 1.15 (d, J = 6.8Hz, 6H); 13C NMR (CDCl3): δ 172.6, 160.3, 142.2, 138.1, 133.5, 132.9, 132.9, 129.7, 128.9, 128.7, 128.3, 128.1, 127.6, 63.1, 39.8, 21.8; HRMS (ESI) calculated for C34H33N4O2(M+H+): 529.2598, found 529.2601 (-0.5 ppm, -0.3 mmu); HPLC: t\textsubscript{r} 37.0 min [Chiracel OD-H (25 cm x 0.46 cm) (from Daicel Chemical Ind., Ltd.)], Hexane/i-PrOH, 90/10, 1.0 mL/min, >99% ee.

Chiral macrocycle (S,S,P,P)-11a

(S,S,P,P)-11a was prepared from (S)-10a by following the same procedure as described for (R,R,M,M)-11a: (S)-10a (374.7 mg, 0.98 mmol), trifluoroacetic acid (0.98 mL) and 5\% AcOH (0.49 mL). Purification with flash column chromatography on silica gel (eluent: EtOAc) provided (S,S,P,P)-11a (111.2 mg, 43% yield) as white solid, m.p. 209-212\textdegree C. [\textalpha]D\textsubscript{23} = +295.0 (c = 0.8, CHCl3); 1H NMR (CDCl3): δ 7.64 (dd, J = 8.0Hz, 1.2Hz, 2H), 7.54 (s, 2H), 7.24-7.54 (m, 10H), 7.13 (dd, J = 7.6Hz, J = 0.8Hz, 2H), 7.08 (dd, J = 7.6Hz, 1.2Hz, 2H), 3.64 (q, J = 6.8 Hz, 2H), 3.40 (s, 6H), 1.17 (d, J = 6.8Hz, 6H); 13C NMR (CDCl3): δ 172.7, 160.4, 142.2, 138.1, 138.0, 133.6, 132.8, 130.2, 129.7, 128.9, 128.7, 128.3, 128.1, 127.5, 63.2, 39.8, 21.8; HRMS (ESI) calculated for C34H33N4O2(M+H+): 529.2598, found 529.2601 (-0.5 ppm, -0.3 mmu); HPLC: t\textsubscript{r} 44.5 min [Chiracel OD-H (25 cm x 0.46 cm) (from Daicel Chemical Ind., Ltd.)], Hexane/i-PrOH, 90/10, 1.0 mL/min, >99% ee.
Chiral macrocycle (R,R,M,M)-11b

(R,R,M,M)-11b was prepared from (R)-10b by following the same procedure as described for (R,R,M,M)-11a: (R)-10b (378.1 mg, 0.89 mmol), trifluoroacetic acid (0.89 mL) and 5% AcOH (0.45 mL). Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 1:6) provided (R,R,M,M)-11b (144.3 mg, 53% yield) as white solid, m.p. 261-263°C. [α]D23 = -208.4 (c = 1.1, CHCl3); 1H NMR (CDCl3): δ 7.63 (dd, J = 8.2Hz, 0.8Hz, 2H), 7.47 (s, 2H), 7.18-7.42 (m, 10H), 7.11 (d, J = 7.6Hz, 2H), 7.04 (dd, J = 7.4Hz, 1.2Hz, 2H), 3.59 (dd, J = 8.8Hz, 4.0Hz, 2H), 3.32 (s, 6H), 1.56-1.72 (m, 2H), 1.41-1.52 (m, 2H), 1.28 (brs, 2H), 0.75 (d, J = 6.4Hz, 6H), 0.34 (d, J = 6.4Hz, 6H); 13C NMR (CDCl3): δ 172.3, 160.2, 141.6, 138.2, 138.1, 133.5, 133.4, 130.1, 129.4, 129.1, 129.0, 128.3, 128.2, 127.5, 67.0, 44.1, 39.8, 23.3, 23.2, 21.1; HRMS (ESI) calculated for C40H45N4O2(M+H+): 613.3537, found 613.3540 (-0.5 ppm, -0.3 mmu).

Chiral macrocycle (S,S,P,P)-11b

(S,S,P,P)-11b was prepared from (S)-10b by following the same procedure as described for (R,R,M,M)-11a: (S)-10b (410.9 mg, 0.97 mmol), trifluoroacetic acid (0.97 mL) and 5% AcOH (0.48 mL). Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 1:6) provided (S,S,P,P)-11b (142.5 mg, 48% yield) as white solid, m.p. 261-263°C. [α]D23 = +208.9 (c = 0.9, CHCl3); 1H NMR (CDCl3): δ 7.66 (dd, J = 8.2Hz, 0.8Hz, 2H), 7.51 (s, 2H), 7.22-7.47 (m, 10H), 7.14 (dd, J = 7.6Hz, 0.8Hz, 2H), 7.10 (dd, J = 7.4Hz, 1.2Hz, 2H), 3.64 (dd, J = 8.8Hz, 4.0Hz, 2H), 3.32 (s, 6H), 1.61-1.72 (m, 2H), 1.47-1.57 (m, 2H), 1.32 (brs, 2H), 0.79 (d, J = 6.4Hz, 6H), 0.39 (d, J = 6.4Hz, 6H); 13C NMR (CDCl3): δ 172.3, 160.3, 141.7, 138.4, 138.0, 133.6, 133.4, 130.1, 129.3, 129.1 (2C), 128.4, 128.3, 127.5, 67.0, 44.2, 39.9, 23.4, 23.2, 21.2; HRMS (ESI) calculated for C40H45N4O2(M+H+): 613.3537, found 613.3542 (-0.7 ppm, -0.5 mmu).

Chiral macrocycle (R,R,M,M)-11c

(R,R,M,M)-11c was prepared from (R)-10c by following the same procedure as described for (R,R,M,M)-11a: (R)-10c (413.3 mg, 0.90 mmol), trifluoroacetic acid (0.9 mL) and 5% AcOH (0.5 mL). Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 1:2) provided (R,R,M,M)-11c
(134.6 mg, 44% yield) as yellow solid, m.p. 236-238°C. \([\alpha]_D^{23} = -179.1\) (c = 0.9, CHCl₃); \(^1\)H NMR (CDCl₃): \(\delta\) 7.60 (dd, \(J = 7.8\) Hz, 1.2Hz, 2H), 7.47 (s, 2H), 6.99-7.42 (m, 20H), 6.77-6.87 (m, 2H), 5.92-6.15 (m, 2H), 3.74 (dd, \(J = 9.6\) Hz, 5.6Hz, 2H), 3.28 (dd, \(J = 12.6\)Hz, 9.6Hz, 2H), 3.23 (s, 6H), 2.42 (dd, \(J = 12.6\) Hz, 5.6Hz, 2H); \(^{13}\)C NMR (CDCl₃): \(\delta\) 170.9, 160.5, 141.5, 137.9, 137.6, 136.9, 133.0, 132.7, 130.2, 129.9 (2C), 129.2, 129.1, 129.0, 128.7, 128.5 (2C), 127.9, 127.2, 127.0, 71.1, 43.2, 39.6; HRMS (ESI) calculated for C₄₆H₄₁N₄O₂(M+H\(^+\)): 681.3224, found 681.3243 (-2.6 ppm, -1.9mmu).

**Chiral Macrocycle (S,S,P,P)-11c**

(S,S,P,P)-11c was prepared from (S)-10c by following the same procedure as described for (R,R,M,M)-11a: (S)-10c (371.8 mg, 0.81 mmol), trifluoroacetic acid (0.8 mL) and 5% AcOH (0.4 mL). Purification with flash column chromatography on silica gel (petroleum ether / EtOAc = 1:2) provided (S,S,P,P)-11c (137.7 mg, 50% yield) as yellow solid, m.p. 236-238°C. \([\alpha]_D^{23} = +179.1\) (c = 1.0, CHCl₃); \(^1\)H NMR (CDCl₃): \(\delta\) 7.61(dd, \(J = 7.8\)Hz, 1.2Hz, 2H), 7.47(s, 2H), 6.97-7.42(m, 20H), 6.74-6.86(m, 2H), 5.91-6.27(m, 2H), 3.73(dd, \(J = 9.6\) Hz, 5.6Hz, 2H), 3.28(dd, \(J = 12.6\)Hz, 9.6Hz, 2H), 3.23(s, 6H), 2.42(dd, \(J = 12.6\)Hz, 5.6Hz, 2H); \(^{13}\)C NMR (CDCl₃): \(\delta\) 170.9, 160.5, 141.5, 137.9, 137.4, 136.8 , 133.0, 132.7, 130.2, 129.9 (2C), 129.2, 129.1, 129.0, 128.6, 128.5 (2C), 127.9, 127.2, 127.0, 71.2, 43.2, 39.7; HRMS (ESI) calculated for C₄₆H₄₁N₄O₂(M+H\(^+\)): 681.3224, found 681.3236 (-1.8 ppm, -1.2mmu).

**X-ray Crystallography**

Crystal data for (S,S,P,P)-11b: C₄₀H₄₄N₄O₂, \(M = 612.79\), monoclinic, \(a = 11.592\) (2), \(b = 13.305\) (3), \(c = 11.772\) (2) Å, \(U = 1805.7\) (6) Å\(^3\), \(T = 298\) K, space group \(P2_1\), \(Z = 2\), 8055 reflections measured, 3132 unique (\(R_{int} = 0.061\)) which were used in all calculations. The final \(R_1 = 0.067\) with \(wR_2 = 0.163\). (CCDC # 773495)
Crystal data for \((S,S,P,P)-11c\): \(C_{64}H_{58}N_4O_2\), \(M = 915.14\), orthorhombic, \(a = 9.5708\) (19), \(b = 17.399\) (4), \(c = 30.787\) (6) Å, \(U = 5126.6\) (18) \(\text{Å}^3\), \(T = 113\) K, space group \(P2_12_12_1\), \(Z = 4\), 4926 reflections measured, 4841 unique \((R_{int} = 0.054)\) which were used in all calculations. The final \(R_1 = 0.074\) with \(wR_2 = 0.173\). (CCDC # 773496)

References

$^1$H and $^{13}$C NMR Spectra for Compounds 11a-11c.
Compound (R,R,M,M)-11a

Current Data Parameters
NAME  zhachongmu
EXPMOD  31B
PROCND  1

F2 - Acquisition Parameters
Date  2009.10.29
Time  16.13
INSTRUM  spec1
PRMOD  5 nm PAERG 88-
PULPROG  Aqpp30
TD  85.536
SOLVENT  CDCl3
NS  50
DS  4
":.  24.58384.61 Hz
PIDRES  0.366790 Hz
AQ  1.3663188 sec
DS  2050
DM  20.800 usec
DE  1.00 usec
TE  296.7 K
DI  2.00000 sec
dd1  0.300000 sec
DELTA  1.6999999 sec
DS/3  1
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MZC1  13C
F1  11.10 usec
PL1  -2.00 dB
SFU1  100.6280888 MHz
--- CHANNEL F2 ---
CSMPAD1  wait.16
NCC2  18
PCP02  80.00 usec
PL2  -3.00 dB
PL12  10.71 dB
PL13  14.00 dB
SPC02  406.176 MHz
F2 - Processing parameters
HI  32768
LY  100.6280 MHz
PSW  4
LH  1.00 Hz
GD  1.40
2009.10.26 C-J-P4 cdcl3

(compound (R,R,M,M)-11c)