Supporting Information

Enantioselective Total Synthesis of (+)-Arborescidine C and Related Tetracyclic Indole Alkaloids Using Organocatalysis.

Vishal M. Sheth,† Bor-Cherng Hong,*† and Gene-Hsiang Lee‡

†Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi, 621, Taiwan, R.O.C.
‡Instrumentation Center, National Taiwan University, Taipei, 106, Taiwan, R.O.C.

chebch@ccu.edu.tw

SUPPORTING INFORMATION:
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General Procedure. All solvents were reagent grade. Reactions were normally carried out under nitrogen atmosphere in glassware. Merck silica gel 60 (particle size 0.04-0.063 mm) was employed for flash chromatography. Melting points are uncorrected. 1H NMR spectra were obtained in CDCl₃ unless otherwise noted at 400 MHz (Bruker DPX-400) or 500 MHz (Varian-Unity INOVA-500). 13C NMR spectra were obtained at 100 MHz or 125 MHz. E.e. values were measured by HPLC on a chiral column (chiralpak IA, or OD-H, 0.46 cm ID x 25 cm, particle size 5 µ). The flow rate of the indicated elution solvent is maintained at 1 mL/min, and the retention time of a compound is recorded accordingly. HPLC was equipped with the ultraviolet and refractive index detectors. The melting point was recorded on a melting point apparatus (MPA100 – Automated melting point system, Stanford Research Systems, Inc.) and is uncorrected. The optical rotation values were recorded with a Jasco-P-2000 digital polarimeter.
Representative Procedure for the preparation of catalyst IX.¹

To a solution of (1R,2R)-cyclohexane-1,2-diamine (160 mg, 1.40 mmol) in methanol (7 mL) was sequentially added acetic acid (80 µL, 1.40 mmol) and 1-phenylpentane-1,4-dione (234 µL, 1.40 mmol). The solution was heated to reflux for 50 °C and stirred for 12 h, followed by cooled to room temperature and concentrated in vacuo. The residue was diluted with CH₂Cl₂ (20 mL), and the solution was washed with an aqueous MeOH solution (4 M, 20 mL). The aqueous solution was extracted twice with CH₂Cl₂ (50 mL). The combined organic extracts were dried over MgSO₄ and concentrated in vacuo to give the crude product, which was directly used for the next-step reaction without further purification.

**Step 1:** To a suspension of (L)-(S)-Boc-tert-leucine (200 mg, 0.865 mmol) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC, 148 mg, 0.95 mmol, 1.1 equiv) and 1-hydroxybenzotriazole (HOBt, 128 mg, 0.95 mmol, 1.1 equiv) in CH₂Cl₂ (9 mL) was sequentially added diisopropylethylamine (0.33 mL, 1.89 mmol, 2.2 equiv) and diallylamine (0.12 mL, 0.95 mmol, 1.1 equiv) at room temperature. The reaction solution was stirred at

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room temperature for 36 h, then diluted with CH$_2$Cl$_2$ (20 mL). The solution was washed twice with 1N aqueous HCl solution (10 mL), twice with saturated aqueous NaHCO$_3$ solution (20 mL), brine, and dried over MgSO$_4$. The solution was concentrated in vacuo to give the crude product which was used in the following step without further purification.

**Step 2**: To a solution of the above crude product in CH$_2$Cl$_2$ (2 mL) was added trifluoroacetic acid (330 µL, 4.32 mmol, excess), and the resulting solution was stirred at room temperature for 2h. The solution was concentrated *in vacuo* to yield the crude product, which was used in step 3 without further purification.

**Step 3**: To a solution of the above crude product in CH$_2$Cl$_2$ (6 mL) was added a saturated aqueous NaHCO$_3$ solution (6 mL) at 0 °C. The mixture was stirred for 5 mins, then stirring was stopped, and thiophosgene (73 µL, 0.95 mmol, 1.1 equiv) was added to the organic (lower) phase by syringe. The resulting orange mixture was restored to stir at 0 °C for 20 mins. To this mixture was added CH$_2$Cl$_2$ (10 mL), and the organic layer was separated. The aqueous layer was extracted twice with CH$_2$Cl$_2$ (15 mL). The combined organic extracts were dried over MgSO$_4$ and concentrated in vacuo to give the crude product as a yellow oil, which was used in step 4 immediately, without further purification.

**Step 4**: To a solution of the above crude product in CH$_2$Cl$_2$ (1 mL) was added by syringe of a solution of (1$R$,2$R$)-2-(2-methyl-5-phenyl-1$H$-pyrrol-1-yl)cyclohexanamine (283 mg, 1.11 mmol 1.3 equiv) in CH$_2$Cl$_2$ solution (2 mL, including the rinsing of the round bottom flask) at room temperature. The resulting solution was stirred at room temperature for 15 h, and then concentrated *in vacuo* to give the residue. The crude product was purified by flash column chromatography with 10% to 15% EtOAc-hexane ($R_f$ = 0.38 for IX in 20 % EtOAc-hexane) to afford the product IX as a yellow foam (375 mg, 85% yield from Boc-tert-leucine).

Selected spectroscopic data for IX: IR (neat): 3297, 3075, 2936, 2861, 1629, 1521, 1446, 1416, 1364, 1321, 1231, 925, 755, 701 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.42 – 7.39 (m, 2 H), 7.32 – 7.28 (m, 3 H), 5.99 (brs, 2 H), 5.84 – 5.67 (m, 3 H), 5.22 – 5.02 (m, 5 H), 4.48 (brs, 1 H), 4.22 – 3.96 (m, 4 H), 3.72 – 3.65 (m, 1 H), 2.46 (s, 3 H), 2.28 – 2.16 (m, 3 H), 1.90 – 1.64 (m, 4 H), 1.42 – 1.20 (m, 2 H), 0.94 (s, 9 H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 181.9 (C), 171.5 (C), 135.8 (C), 134.3 (C), 133.4 (two CH), 132.7 (two CH), 130.0 (C), 129.5 (CH), 128.8 (CH), 127.0 (CH), 118.4 (CH$_2$), 117.6 (CH$_2$), 110.0 (CH), 108.7 (CH), 60.0 (CH), 59.6 (CH), 56.0 (CH), 50.3 (CH$_2$), 47.3 (CH$_2$), 36.1 (C), 33.7 (CH$_3$), 32.3 (CH$_2$), 26.7 (three CH$_3$), 25.7 (CH$_2$), 24.6 (CH$_2$), 15.4 (CH$_3$); MS (m/z, relative intensity): 508 (M$^+$+2, 4), 507 (M$^+$+1, 14), 506 (M$^+$, 40), 411 (22), 410 (78), 409 (17), 348 (9), 297 (48), 253 (15), 237 (100), 157 (34), 86 (67); exact mass calculated for C$_{30}$H$_{42}$N$_4$OS (M$^+$): 506.3079; found: 506.3076.
Preparation of adduct 6.

\[ \text{tryptamine} + \text{aldehyde} \rightarrow \text{imine} \]

To a solution of tryptamine (40 mg, 0.25 mmol) in CH\(_2\)Cl\(_2\) (6 mL) was added a solution of aldehyde 2a\(^1\) (36 mg, 0.25 mmol) in CH\(_2\)Cl\(_2\) (3 mL), followed by the addition of Et\(_2\)O (3 mL). The solution was stirred at room temperature for 2 h, followed by the addition of Na\(_2\)SO\(_4\) (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was filtered by cannula transfer, and the remaining was rinsed twice with dichloromethane (2 x 5 mL). The combined solution was concentrated in vacuo to give the crude imine as a pale yellow oil, which was immediately dissolved in CH\(_2\)Cl\(_2\) (15 mL) for the next step reaction. To this solution was added catalyst IX (6.5 mg, 0.013 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at –78 °C, and the solution was stirred for 5 min. To the reaction mixture was added acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at –78 °C for 10 min, followed by warming to –60 °C and stirred at the same temperature for 37 h. The resulting heterogeneous mixture was allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 50 to 60% EtOAc-hexane (\(R_f = 0.40\) in 80% EtOAc-hexane) to afford product 6 (61 mg, 74% yield) as a white solid. M.p. 169–170 °C; \([\alpha]_D^{25} = 100.6\) (c 1, CHCl\(_3\)). The enantiomeric excess was determined to be 95 % by HPLC with chiral column CHIRALPAK\(^\circledR\) IA, 12% i-PrOH/n-hexane, flow rate 1.0 mL, \(\lambda = 254\) nm (t\(_{\text{major}} = 22.2\) min, t\(_{\text{minor}} = 25.0\) min). IR (neat): 3276, 3008, 2951, 2888, 1619, 1447, 1361, 1301, 1140, 1031, 945, 746 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)): the compound exists as a 4:1 mixture of amide rotamers, signals corresponding to the major rotamer: \(\delta\) 8.46 (brs, 1 H), 7.43 (d, \(J = 8.0\) Hz, 1 H), 7.29 (d, \(J = 8.0\) Hz, 1 H), 7.16 – 7.04 (m, 2 H), 5.78 (t, \(J = 8.0\) Hz, 1 H), 4.86 (t, \(J = 4.5\) Hz, 1 H), 4.00 – 3.80 (m, 5 H), 3.56 – 3.45 (m, 1 H), 2.86 – 2.74 (m, 2 H), 2.21 (s, 3 H), 2.00 – 1.55 (m, 6 H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) signals corresponding to the major rotamer: \(\delta\) 169.6 (C), 136.0 (C), 134.5 (C), 126.6 (C), 121.7 (CH), 119.4 (CH), 117.9 (CH), 110.9 (CH), 107.4 (C), 104.4 (CH), 64.84 (CH\(_2\)), 64.78 (CH\(_2\)), 48.6 (CH), 41.1 (CH\(_2\)), 34.0 (CH\(_2\)), 33.2 (CH\(_2\)), 22.0 (CH\(_2\)), 21.9 (CH\(_3\)), 20.5 (CH\(_2\)); MS (m/z, relative intensity): 329 (M\(^+\), 4), 328 (15), 285 (3), 213 (74), 171 (70), 101 (36), 73 (36), 58 (100); exact mass calculated for C\(_{19}\)H\(_{24}\)O\(_3\)N\(_2\) (M\(^+\)): 328.1789; found: 328.1787.

\(^1\) For best results, the aldehyde was used immediately after purification.
One-pot operation of the preparation of adduct 6.

To a solution of tryptamine (40 mg, 0.25 mmol) in CH$_2$Cl$_2$ (6 mL) was added dropwise a solution of aldehyde 2a (36 mg, 0.25 mmol) in CH$_2$Cl$_2$ (3 mL), followed by the addition of Et$_2$O (3 mL). The solution was stirred at room temperature for 2 h, followed by the addition of Na$_2$SO$_4$ (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was carefully concentrated in vacuo and applied in high vacuum for complete removal of solvent. The crude imine, as a pale yellow oil, was diluted with Et$_2$O (15 mL). To this solution was added catalyst IX (6.5 mg, 0.013 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at –78 °C, and the solution was stirred for 5 min. To the reaction mixture was added acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at –78 °C for 10 min, followed by warming to –60 °C and stirred at the same temperature for 35 h. The resulting heterogeneous mixture was allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 50 to 60% EtOAc-hexane ($R_f = 0.40$ in 80% EtOAc-hexane) to afford product 6 (52 mg, 63% yield) as a white solid. The enantiomeric excess was determined to be 93 % by chiral HPLC with chiral column CHIRALPAK® IA.
Preparation of amine 10.

To a solution of diisopropylamine (0.61 mL, 4.35 mmol, 7.1 equiv) in THF (4.4 mL) was added a solution of n-butyllithium (2.04 mL, 2.15 M in hexane, 4.39 mmol, 7.2 equiv) at −78 °C and stirred at the same temperature for 10 min, followed by warm up to 0 °C and stirred for 15 min. To this solution was added borane-ammonia complex (118 mg, 90% purity, 3.44 mmol, 5.6 equiv), and the suspension solution was stirred at 0 °C for 15 min, followed by warm up to room temperature and stirred for additional 10 min. To the solution was added 6 (200 mg, 0.609 mmol) at 0 °C and stirred for 2 min, followed by heating up to 60 °C and stirred for 4 h. The resulting suspension was cooled to 0°C and the reaction was quenched by dropwise addition of 2N aqueous HCl solution (10 mL), followed by stirring for 30 min. The pH value of the solution was adjusted to 8 by the addition of saturated aqueous NaHCO₃. The reaction mixture was extracted five times with ethyl acetate (5 x 20 mL), and the combined organic extracts were dried over MgSO₄ and concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 5 to 10% MeOH-CH₂Cl₂ ($R_f=0.38$ in 20% MeOH-CH₂Cl₂) to afford product 10 (120 mg, 69% yield) as a colorless oil. Selected spectroscopic data for 10: [α]D₂⁵ −51.2 (c 0.65, MeOH); IR (neat): 3169, 2922, 2767, 1583, 1456, 1307, 1140, 943, 741 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.93 (brs, 1 H), 7.46 (d, J = 8.0 Hz, 1 H), 7.29 (d, J = 7.5 Hz, 1 H), 7.14 – 7.05 (m, 2 H), 4.87 (t, J = 4.5 Hz, 1 H), 4.08 – 4.04 (m, 1 H), 3.98 – 3.95 (m, 1 H), 3.87 – 3.83 (m, 2 H), 3.35 – 3.30 (m, 1 H), 3.05 – 2.98 (m, 1 H), 2.75 – 2.69 (m, 2 H), 1.94 – 1.86 (m, 1 H), 1.78 – 1.60 (m, 6 H); ¹³C NMR (125 MHz, CDCl₃): δ 136.1 (C), 135.6 (C), 127.5 (C), 121.5 (CH), 119.3 (CH), 118.0 (CH), 110.7 (CH), 109.1 (C), 104.4 (CH), 64.88 (CH₂), 64.86 (two CH₂), 52.4 (CH) 42.5 (CH₂), 34.6 (CH₂), 33.4 (CH₂), 22.7 (CH₂), 20.2 (CH₂); MS (m/z, relative intensity): 286 (M⁺, 10), 285 (M⁺-1, 4), 241 (2), 184 (6), 172 (23), 171 (100), 144 (11), 115 (4), 99 (3), 73 (8); exact mass calculated for C₁₇H₂₂O₂N₂ (M⁺): 286.1681; found: 286.1681.
Preparation of 5.

To a solution of 10 (90 mg, 0.314 mmol) in methanol (3.2 mL) was added NaCNBH₃ (50 mg, 0.80 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 5 min followed by the addition of 37% aqueous HCHO solution (3 mL). The solution was stirred at room temperature for 12 h until the completion of the reaction, as monitored by TLC. The solution was concentrated in vacuo to give the residue. The residue was dissolved in THF (3.2 mL), followed by the addition of an aqueous solution of 2N HCl (3 mL), and the reaction mixture was stirred for 3 h at room temperature. The reaction was quenched with the addition of solid NaHCO₃ and the pH value of the solution was adjusted to 8. The reaction mixture was extracted with EtOAc (3 x 15 mL), and the combined organic extracts were dried over MgSO₄ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 10% MeOH–CH₂Cl₂ (Rf = 0.45 in 15% MeOH–CH₂Cl₂) to afford product 5 (58 mg, 72% yield) as a white solid. M.p. 143–144 °C, lit.² 140–142 °C. The enantiomeric excess was determined to be 97 % by HPLC analysis with chiral column CHIRALCEL® OD-H, 10% (10% MeOH–EtOAc) / 90% Hexane, flow rate 1.0 mL, λ = 280 nm (tₘajor = 12.3 min, tₘininor = 19.2 min). Selected spectroscopic data for 10: [α]D²⁵ = +3.0 (c 1, CHCl₃), lit.² [α]D²⁵ = +3.2; IR (neat): 3337, 3053, 2928, 2854, 1464, 1262, 1103, 1020, 802, 739 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.43 (d, J = 7.5 Hz, 1 H), 7.25 (d, J = 8.5 Hz, 1 H), 7.14 (dd, J = 7.5, 8.5 Hz, 1 H), 7.07 (dd, J = 7.5, 8.5 Hz, 1 H), 6.18 (d, J = 3.0 Hz, 1 H), 3.63 (d, J = 11.5 Hz, 1 H), 3.03 – 2.96 (m, 1 H), 2.80 – 2.62 (m, 3 H), 2.47 (s, 3 H), 2.35 – 2.07 (m, 3 H), 1.82 – 1.75 (m, 1 H), 1.67 – 1.59 (m, 1 H), 1.47 – 1.37 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 137.4 (C), 136.0 (C), 126.7 (C), 121.2 (CH), 119.3 (CH), 118.2 (CH), 108.8 (C), 108.4 (CH), 76.4 (CH), 61.6 (CH), 50.9 (CH₂) 42.7 (CH₃), 34.3 (CH₂), 32.7 (CH₂), 20.4 (CH₂), 20.2 (CH₂); MS (m/z, relative intensity): 257 (M⁺, 20), 256 (100), 255 (68), 227 (11), 213 (98), 185 (63), 184 (80), 183 (60), 156 (40), 143 (30); exact mass calculated for C₁₆H₂₀O N₂ (M⁺): 256.1576; found: 256.1575.

Figure S1. ORTEP and Stereo plots for X-ray crystal structures of (+)-5.

CCDC 1523958 contains the supplementary crystallographic data for (+)-5. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Table S1. Crystal data and structure refinement for (+)-5, ic18036.

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General procedure for Preparation of racemic compound (representative procedure for the preparation of (±)-6 and (±)-5:

![Chemical structure diagram](Image)

1. **Step 1:**
   A solution of tryptamine (30 mg, 0.187 mmol) and aldehyde 2a\(^3\) (27 mg, 0.187 mmol) in CH\(_2\)Cl\(_2\) (2 mL) was stirred at 0 °C, followed by the addition of a solution of trifluoroacetic acid (32 mg, 0.28 mmol, 1.5 equiv) in CH\(_2\)Cl\(_2\) (0.5 mL) and sodium sulfate (100 mg). The mixture was vigorously stirred at 0 °C and gradually warm up to room temperature for 8 h until the completion of the reaction, monitored by TLC. The reaction was quenched by the addition of saturated aqueous NaHCO\(_3\) solution (10 mL). The reaction mixture was extracted with CH\(_2\)Cl\(_2\) (5 mL x 3), and the combined organic extracts were dried over MgSO\(_4\) and concentrated *in vacuo* to give a residue. The crude product was purified by flash column chromatography with 5 to 10% EtOAc-hexane (*R*\(_f\) = 0.38 in 20% MeOH-CH\(_2\)Cl\(_2\)) to afford product 10 (40 mg, 75% yield).

2. **Step 2:**
   To a solution of 10 (25 mg, 0.087 mmol) and triethylamine (36 µL, 0.26 mmol, 3 equiv) in CH\(_2\)Cl\(_2\) (0.4 mL) was added acetyl chloride (12 µL, 0.17 mmol, 1.9 equiv) at room temperature, and the solution was stirred for 2 h until the completion of the reaction, monitored by TLC. The reaction mixture was diluted with water and extracted with CH\(_2\)Cl\(_2\). The organic layer was washed with brine and dried over MgSO\(_4\) to give the residue. The crude product was purified by flash column chromatography with 50–60% ethyl acetate in hexane, (*R*\(_f\) = 0.40 in 80% EtOAc-hexane) to afford 6 (18 mg, 63% yield).

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\(^3\) For best results, the aldehyde was used immediately after purification.
Step 1:
Followed the same procedure as mentioned in the previous reaction to give 10.

Step 2:
To a solution of 10 (60 mg, 0.21 mmol) in MeOH (2.1 mL) was added NaCNBH₃ (39 mg, 0.62 mmol, 3.0 equiv) at 0 °C, followed by the addition of 37% HCHO (2.1 mL). The solution was gradually warm up to room temperature and stirred for 12 h. The solution was concentrated in vacuo to give a residue.

Step 3:
To this residue was diluted with THF (2.1 mL) and added an aqueous 2N HCl solution (2.1 mL). The resulting mixture was stirred at room temperature for 3 h. The reaction was quenched by the addition of NaHCO₃ (solid), and the pH of the solution was adjusted to 8. The mixture was extracted with EtOAc, and the combined organic extracts were dried over MgSO₄ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 7% MeOH–CH₂Cl₂ (Rf = 0.45 in 15% MeOH–CH₂Cl₂) to afford product 5 (37 mg, 69% yield).
Preparation of 11.

To a solution of 5 (30 mg, 0.117 mmol) and Et₃N (46 µL, 0.33 mmol) in CH₂Cl₂ (3.2 mL) was added methanesulfonyl chloride (14 µL, 0.18 mmol) at 0 °C. The resulting solution was stirred at 0 °C to room temperature for 2h. The reaction was quenched by the addition of water (2 mL), and the mixture was extracted with CH₂Cl₂ (3 x 5 mL). The organic solution was washed with saturated aqueous NaHCO₃ solution, brine, dried over Na₂SO₄, and the solution was concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 7% MeOH–CH₂Cl₂ (Rf = 0.7 in 15% MeOH–CH₂Cl₂) to afford product 11 (20 mg, 72% yield) as a white solid. M.p. 99–100 °C; lit. 98–100 °C.

Selected spectroscopic data for 11: [α]D₂⁶ +60.6 (c 1, CHCl₃), lit. [4] +61 (c 1, CHCl₃), lit. [5] [α]D₂⁵ +62.1 (c 0.36, CHCl₃); IR (neat): 2956, 2920, 1459, 1378, 1260, 1092, 1022, 802 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.46 (d, J = 8.0 Hz, 1 H), 7.32 (d, J = 8.5 Hz, 1 H), 7.19 (dd, J = 7.5, 7.5 Hz, 1 H), 7.12 (dd, J = 7.5, 7.5 Hz, 1 H), 6.91 (d, J = 10.0 Hz, 1 H), 5.07 – 5.02 (m, 1 H), 3.40 (d, J = 10.0 Hz, 1 H), 3.16 – 3.10 (m, 1 H), 2.96 – 2.88 (m, 1 H), 2.75 – 2.66 (m, 2 H), 2.57 – 2.49 (m, 1 H), 2.53 (s, 3 H), 2.45 – 2.30 (m, 2 H), 1.92 – 1.83 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 137.3 (C), 136.1 (C), 126.9 (C), 122.0 (CH), 121.8 (CH), 120.1 (CH), 118.2 (CH), 110.0 (CH), 109.2 (C), 109.1 (CH), 62.5 (CH), 52.9 (CH₂), 42.5 (CH₃), 30.0 (CH₂), 28.0 (CH₂), 20.7 (CH₂); MS (m/z, relative intensity): 238 (M⁺, 100), 237 (87), 209 (30), 195 (89), 194 (62), 180 (26), 167 (33), 71 (27); exact mass calculated for C₁₆H₁₈N (M⁺): 238.1470; found: 238.1472.

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Another one-pot Preparation of 3.

To a solution of tryptamine (40 mg, 0.25 mmol) in CH$_2$Cl$_2$ (6 mL) was added a solution of aldehyde 2a$^6$ (36 mg, 0.25 mmol) in CH$_2$Cl$_2$ (3 mL), followed by the addition of Et$_2$O (3 mL). The solution was stirred at room temperature for 2 h, prior to the addition of Na$_2$SO$_4$ (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was filtered by cannula transfer, and the remaining was rinsed twice with dichloromethane (2 x 5 mL). The combined solution was concentrated in vacuo to give the crude imine as a pale yellow oil, which was immediately dissolved in Et$_2$O (10 mL) for the next step reaction. To this solution was added catalyst IX (6.5 mg, 0.013 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at –78 °C, and the solution was stirred for 5 min. To the reaction mixture was added methyl chloroformate (19.3µL, 0.25 mmol), and the resulting solution was stirred at –78 °C for 10 min, followed by warming to –60 °C and stirred at the same temperature for 30 h. The resulting heterogeneous mixture was allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 25 to 30% EtOAc-hexane ($R_f = 0.35$ in 50% EtOAc-hexane) to afford product 3 (55 mg, 64% yield) as a colorless oil; $[\alpha]_D^{27} = +47.5$ (c = 1 in CHCl$_3$). The enantiomeric excess was determined to be 74 % by HPLC with chiral column CHIRALPAK$^o$ IA, 15% i-PrOH/n-hexane, flow rate 1.0 mL, $\lambda = 254$ nm ($t_{major} = 22.6$ min, $t_{minor} = 12.7$ min). IR (neat): 3321, 2958, 2924, 2856, 1680, 1450, 1410, 1261, 1229, 1110, 1029, 800, 745 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): the compound exists as a nearly 1.2:1 mixture of amide rotamers, signals corresponding to the major rotamer: $\delta$ 8.23 (br s, 1 H), 7.45 (brs, 1 H), 7.28 (d, $J = 8.5$ Hz, 1 H), 7.16 – 7.04 (m, 2 H), 5.33 (brs, 1 H), 4.87 (t, $J = 4.5$ Hz, 1 H), 4.49 (d, $J = 10.5$ Hz, 1 H), 4.03 – 3.92 (m, 2 H), 3.91 – 3.80 (m, 2 H), 3.73 (brs, 3 H), 3.64 – 3.10 (m, 1 H), 2.88 – 2.64 (m, 2 H), 1.94 – 1.55 (m, 6 H); $^{13}$C NMR (125 MHz, CDCl$_3$) signals corresponding to the major rotamer: $\delta$ 156.5 (C), 135.9 (C), 134.3 (C), 126.7 (C), 121.7 (CH), 119.4 (CH), 118.0 (CH), 110.8 (CH), 108.2 (C), 104.4 (CH), 64.8 (two CH$_2$), 52.7 (CH$_3$), 51.2 (CH), 38.6 (CH$_2$), 34.2 (CH$_2$), 33.2 (CH$_2$), 21.0 (CH$_2$), 20.4 (CH$_2$); MS (m/z, relative intensity): 344 (M$^+$, 9), 299 (3), 245 (3), 229 (100),

$^6$ For best results, the aldehyde was used immediately after purification.
169 (8), 149 (4), 97 (4); exact mass calculated for C_{19}H_{24}N_{2}O_{4} (M^+) : 344.1736; found: 344.1739.

Preparation of 4.

To a solution of 3 (30 mg, 0.087 mmol) in THF (1 mL) was added LiAlH₄ (8.3 mg, 0.22 mmol, 2.5 equiv) at 0 °C, and the reaction mixture was stirred for 12 h and gradually warm up to room temperature. The reaction was quenched by the addition of EtOAc, followed by the addition of water (1 mL) and 15 aqueous NaOH solution (1 mL), and the solution was stirred at room temperature for 20 min. The mixture was extracted with EtOAc (2 x 5 mL), and the combined organic solution was washed with brine (4 mL) and dried over MgSO₄. The solution was concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 2-5% MeOH-CH₂Cl₂ (Rf = 0.36 in 2% MeOH-CH₂Cl₂) to afford product 4 (22 mg, 84% yield) as a colorless oil. Selected spectroscopic data for 4: [α]D²⁷ = +54.5 (c 1, CHCl₃); IR (neat): 3337, 2961, 2927, 1454, 1260, 1092, 1024, 800 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.99 (br s, 1 H), 7.46 (d, J = 7.5 Hz, 1 H), 7.28 (d, J = 8.0 Hz, 1 H), 7.12 (dd, J = 7.5, 8.0 Hz, 1 H), 7.07 (dd, J = 7.5, 8.0 Hz, 1 H), 4.83 (t, J = 4.5 Hz, 1 H), 3.99 – 3.93 (m, 2 H), 3.89 – 3.81 (m, 2 H), 3.51 (t, J = 5.5 Hz, 1 H), 3.18 – 3.12 (m, 1 H), 2.82 – 2.68 (m, 3 H), 2.46 (s, 3 H), 1.95 – 1.59 (m, 5 H), 1.52 – 1.44 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 136.0 (C), 134.8 (C), 127.3 (C), 121.3 (CH), 119.2 (CH), 118.0 (CH), 110.7 (CH), 108.3 (C), 104.7 (CH), 64.84 (CH₂), 64.80 (CH₂), 59.8 (CH), 49.6 (CH₂), 41.9 (CH₃), 33.4 (CH₂), 32.5 (CH₂), 19.9 (CH₂), 19.0 (CH₂); MS (m/z, relative intensity): 300 (M⁺, 2), 299 (M⁺-1, 1), 255 (1), 200 (1), 186 (14), 185 (100), 144 (6), 129 (3), 73 (8); exact mass calculated for C_{18}H_{24}N_{2}O_{2} (M⁺): 300.1838; found: 300.1837.
Preparation of 5

To a solution of 4 (10 mg, 0.033 mmol) in THF (0.34 mL) was added an aqueous solution of 2N HCl (0.34 mL), and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was diluted with the addition of water (2 mL), and the reaction was quenched by the addition of saturated aqueous NaHCO₃ solution (2 mL). The reaction mixture was stirred for 10 min, followed by the extraction with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine, dried over MgSO₄ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 7% MeOH–CH₂Cl₂ (Rf = 0.45 in 15% MeOH–CH₂Cl₂) to afford product 5 (6.8 mg, 80% yield) as a white solid. The enantiomeric excess was determined to be 78 % by HPLC analysis with chiral column CHIRALCEL® OD-H, 10% (10% MeOH–EtOAc) / 90% Hexane, flow rate 1.0 mL, λ = 280 nm (t_major = 12.5 min, t_minor = 19.5 min).
Preparation of adduct 8.

To a solution of tryptamine (40 mg, 0.25 mmol) in CH$_2$Cl$_2$ (6 mL) was added a solution of aldehyde 2c (32.5 mg, 0.25 mmol in CH$_2$Cl$_2$ (3 mL), followed by the addition of Et$_2$O (3 mL). The solution was stirred at room temperature for 2 h, prior to the addition of Na$_2$SO$_4$ (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was filtered by cannula transfer to a flame dried 25 mL round-bottomed flask, and the remaining was rinsed twice with dichloromethane (2 x 5 mL). The combined solution was concentrated in vacuo to give the crude imine as a pale yellow oil, which was immediately dissolved in Et$_2$O (15 mL) for the next step reaction. To this solution was added catalyst IX (6.5 mg, 0.0125 mmol, 5 mol %) and 2,6-lutidine (20 µL, 0.25 mmol, 1.0 equiv) at −78 °C, and the solution was stirred for 5 min. To the reaction mixture was added acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at −78 °C for 10 min, followed by warming to −60 °C and stirred at the same temperature for 32 h. The resulting heterogeneous mixture was then allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 50 to 60% EtOAc-hexane ($R_f = 0.38$ in 80% EtOAc-hexane) to afford product 8 (58 mg, 74% yield) as a white solid. M.p. 187–188 °C; $[\alpha]_D^{27} +94$ (c 1, CHCl$_3$). The enantiomeric excess was determined to be 92 % by HPLC with chiral column CHIRALPAK® IA, 12% i-PrOH/n-hexane, flow rate 1.0 mL, $\lambda = 275$ nm (t$_{major} = 25.1$ min, t$_{minor} = 32.1$ min). IR (neat): 3274, 2965, 2924, 2888, 1619, 1439, 1137, 1026, 800, 745 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): the compound exists as a 3:1 mixture of amide rotamers, signals corresponding to the major rotamer: $\delta$ 8.56 (br s, 1 H), 7.43 (d, $J = 7.5$ Hz, 1 H), 7.30 (d, $J = 7.5$ Hz, 1 H), 7.18 – 7.03 (m, 2 H), 5.81 (t, $J = 7.0$ Hz, 1 H), 4.98 (brs, 1 H), 5.04 – 4.89 (m, 1 H), 4.13 – 3.82 (m, 4 H), 3.56 – 3.46 (m, 1 H), 2.89 – 2.65 (m, 2 H), 2.19 (s, 3 H), 2.08 – 1.73 (m, 4 H).; $^{13}$C NMR (125 MHz, CDCl$_3$) signals corresponding to the major rotamer: $\delta$ 169.4 (C), 135.9 (C), 134.3 (C), 126.6 (C), 121.7 (CH), 119.3 (CH), 117.9 (CH), 111.0 (CH), 107.4 (C), 104.1 (CH), 65.1 (CH$_2$), 64.8 (CH$_2$) 48.2 (CH), 40.8 (CH$_2$), 28.9 (CH$_2$), 28.2 (CH$_2$), 22.0 (CH$_3$), 21.8 (CH$_3$); MS (m/z, relative intensity): 314 (M$^+$, 10), 271 (10), 226 (55), 213 (90), 183 (11), 171 (100), 169 (17), 144 (6), 115 (3), 73 (6); exact mass calculated for C$_{18}$H$_{22}$N$_2$O$_3$ (M$^+$): 314.1630; found: 314.1631.
Preparation of amine 17.

To a solution of diisopropylamine (0.513 mL, 3.66 mmol, 7.2 equiv) in THF (3.6 mL) was added a solution of n-butyllithium (1.46 mL, 2.5 M in hexane, 3.65 mmol, 7.2 equiv) at –78 °C and stirred at the same temperature for 10 min, followed by warming up to 0 °C and stirred for 15 min. To this solution was added borane-ammonia complex (98 mg, 90% purity, 2.86 mmol, 5.6 equiv), and the suspension solution was stirred at 0 °C for 15 min, followed by warming up to room temperature and stirred for additional 10 min. To the solution was added 8 (160 mg, 0.50 mmol) at 0 °C and stirred for 2 min, followed by heating up to 60 °C and stirred for 4 h. The resulting suspension was cooled to 0°C and the reaction was quenched by dropwise addition of 2N aqueous HCl solution (10 mL), followed by stirring for 30 min. The pH value of the solution was adjusted to 8 by the addition of saturated aqueous NaHCO₃. The reaction mixture was extracted five times with ethyl acetate (5 x 10 mL), and the combined organic extracts were dried over sodium sulfate and concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 5 to 10% MeOH-CH₂Cl₂ (Rf = 0.3 in 20% MeOH-CH₂Cl₂) to afford product 17 (85 mg, 61% yield) as a colorless oil. Selected spectroscopic data for 17: [α]D²⁷ –19.9 (c 1, MeOH); IR (neat): 3400, 3311, 3055, 2927, 2888, 1452, 1301, 1139, 1028, 945, 743 cm⁻¹; H NMR (500 MHz, CDCl₃): δ 8.08 (br s, 1 H), 7.46 (d, J = 8.0 Hz, 1 H), 7.29 (d, J = 8.0 Hz, 1 H), 7.12 (dd, J = 7.5, 7.5 Hz, 1 H), 7.07 (dd, J = 7.5, 7.5 Hz, 1 H), 4.93 (t, J = 4.0 Hz, 1 H), 4.15 – 4.07 (m, 1 H), 4.03 – 3.94 (m, 2 H), 3.90 – 3.83 (m, 2 H), 3.35 – 3.28 (m, 1 H), 3.06 – 3.00 (m, 1 H), 2.77 – 2.66 (m, 2 H), 2.05 – 1.73 (m, 5 H); C NMR (125 MHz, CDCl₃): δ 136.0 (C), 135.7 (C), 127.5 (C), 121.5 (CH), 119.3 (CH), 118.0 (CH), 110.7 (CH), 109.1 (C), 104.3 (CH), 65.0 (two CH₂), 52.0 (CH), 42.2 (CH₂), 29.6 (CH₂), 28.8 (CH₂), 22.7 (CH₂); MS (m/z, relative intensity): 272 (M⁺, 5), 271 (M⁺-1, 2), 184 (3), 172 (10), 171 (100), 169 (5), 144 (3), 115 (1), 99 (2); exact mass calculated for C₁₆H₂₀N₂O₂ (M⁺): 272.1525; found: 272.1526.
Preparation of 18 and 19.

To a solution of 17 (80 mg, 0.29 mmol) in methanol (3.0 mL) was added NaCNBH₃ (46 mg, 0.73 mmol, 2.5 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 5 min followed by the addition of 37% aqueous HCHO solution (3 mL). The solution was stirred at room temperature for 12 h until the completion of the reaction, as monitored by TLC. The solution was concentrated in vacuo to give the residue, and the residue. To the solution of the above residue in THF (3 mL) was added an aqueous solution of 2N HCl (3 mL), and the reaction mixture was stirred for 3 h at room temperature. The reaction was quenched with NaHCO₃ and the pH value of the solution was adjusted to 8. The reaction mixture was extracted with EtOAc (3 x 15 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 7% MeOH–CH₂Cl₂ (For 18: Rf = 0.45; for 19: Rf = 0.42 in 8% MeOH–CH₂Cl₂, twice developing) to afford product 18 (28 mg, 39% yield) and 19 (22 mg, 31% yield) as white solids.

Selected data for 18: M.p. 187–189 °C. Lit.7 184–186 °C. [α]D²⁷ +12.7 (c 1, CHCl₃); IR (neat): 3343, 3050, 2956, 2852, 1457, 1375, 1310, 1266, 1086, 1015, 802, 746 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.66 (d, J = 7.0 Hz, 1 H), 7.44 (d, J = 7.0 Hz, 1 H), 7.18 – 7.05 (m, 2 H), 5.48 (dd, J = 9.0, 5.5 Hz, 1 H), 3.18 – 3.02 (m, 2 H), 2.95 – 2.83 (m, 1 H), 2.73 – 2.66 (m, 1 H), 2.65 – 2.57 (m, 1 H), 2.55 – 2.48 (m, 1 H), 2.43 (s, 3 H), 2.23 – 2.18 (m, 1 H), 1.80 – 1.70 (m, 2 H), 1.35 – 1.24 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 137.9 (C), 135.1 (C), 128.2 (C), 121.6 (CH), 120.3 (CH), 118.1 (CH), 111.9 (CH), 107.1 (C), 78.8 (CH), 60.1 (CH), 54.3 (CH₂), 42.3 (CH₃), 33.3 (CH₂), 26.1 (CH₂), 21.5 (CH₂); MS (m/z, relative intensity): 242 (M⁺, 26), 241 (M⁺⁻, 19), 213 (9), 199 (100), 180 (25), 171 (17), 156 (17), 143 (27), 58 (38); exact mass calculated for C₁₅H₁₈N₂O (M⁺): 242.1419; found: 242.1420.

Selected data for 19: M.p. 175–176 °C. Lit.7 174–176 °C. [α]D²⁷ –7.5 (c 1, CHCl₃); IR (neat): 3327, 3050, 2956, 2924, 2852, 1456, 1310, 1263, 1086, 1015, 801, 745 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.47 (d, J = 7.5 Hz, 1 H), 7.41 (d, J = 7.5 Hz, 1 H), 7.15 (dd, J = 7.5, 7.5 Hz, 1 H), 7.09 (dd, J = 7.5, 7.5 Hz, 1 H), 5.81 (d, J = 2.5 Hz, 1 H), 3.05 – 3.00 (m, 1 H), 2.97 – 2.82 (m, 2 H), 2.71 – 2.63 (m, 1 H), 2.54 – 2.44 (m, 1 H), 2.13 – 2.05 (m, 1 H), 2.02 (s, 3 H), 2.00 – 1.93 (m, 1 H), 1.58 – 1.48 (m, 1 H), 1.05 – 0.95 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 135.9 (C), 133.2 (C), 128.0 (C), 121.2 (CH), 119.9 (CH), 118.1 (CH), 111.2 (CH),

106.0 (C), 74.4 (CH), 60.6 (CH) 54.8 (CH2), 41.9 (CH3), 31.3 (CH2), 21.2 (CH2), 20.1 (CH2).

Preparation of 20.

To a solution of 18 and 19 (25 mg, 0.103 mmol) and Et3N (44 µL, 0.32 mmol) in CH2Cl2 (3.2 mL) was added methanesulfonyl chloride (12 µL, 0.155 mmol) at 0 °C. The resulting solution was stirred at 0 °C to room temperature for 2 h. The reaction was quenched by the addition of water (2 mL), and the mixture was extracted with CH2Cl2 (3 x 5 mL). The organic solution was washed with saturated aqueous NaHCO3 solution, brine, dried over Na2SO4, and the solution was concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 7% MeOH–CH2Cl2 (Rf = 0.5 in 10% MeOH–CH2Cl2) to afford product 20 (18 mg, 78% yield) as a colorless oil. Selected spectroscopic data for 20: [α]D27 +47.0 (c 1, CHCl3); IR (neat): 3050, 2923, 2848, 1644, 1462, 1304, 1263, 1060, 806, 739, 721 cm⁻¹; ¹H NMR (500 MHz, CDCl3): δ 7.45 (d, J = 7.5 Hz, 1 H), 7.30 (d, J = 7.5 Hz, 1 H), 7.16 (dd, J = 7.5, 7.5 Hz, 1 H), 7.09 (dd, J = 7.5, 7.5 Hz, 1 H), 7.02 – 7.00 (m, 1 H), 5.24 – 5.19 (m, 1 H), 3.44 – 3.40 (m, 1 H), 3.20 – 3.16 (m, 1 H), 3.04 – 2.98 (m, 1 H), 2.78 – 2.60 (m, 3 H), 2.49 (s, 3 H), 2.20 – 2.12 (m, 1 H); ¹³C NMR (125 MHz, CDCl3): δ 134.7 (C), 131.9 (C), 127.7 (C), 122.3 (CH), 121.7 (CH), 120.0 (CH), 118.6 (CH), 108.6 (CH), 107.8 (C), 105.4 (CH), 57.2 (CH), 55.0 (CH2), 42.5 (CH3), 26.4 (CH2), 21.5 (CH2); MS (m/z, relative intensity): 224 (M⁺, 23), 223 (M⁺-1, 18), 181 (36), 180 (100), 167 (2), 152 (2); exact mass calculated for C13H16N2 (M⁺): 224.1313; found: 224.1315.

General procedure for the two-pot synthesis of (+)-5:

POT-1, 70% yield; 93% ee

POT-1 as previously described:

To a solution of tryptamine (40 mg, 0.25 mmol) in CH₂Cl₂ (6 mL) was added dropwise a solution of aldehyde 2a (36 mg, 0.25 mmol) in CH₂Cl₂ (3 mL), followed by the addition of Na₂SO₄ (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was carefully concentrated in vacuo and applied in high vacuum for the complete removal of solvent. The crude imine, as a pale yellow oil, was diluted with Et₂O (5 mL). To this solution was added catalyst IX (6.5 mg, 0.013 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at –78 °C, and the solution was stirred for 5 min. To the reaction mixture was added acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at –78 °C for 10 min, followed by warming to –60 °C and stirred at the same temperature for 20 h. The resulting heterogeneous mixture was allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 50 to 60% EtOAc-hexane \((R_f = 0.40\) in 80% EtOAc-hexane) to afford product 6 (52 mg, 63% yield) as a white solid. The enantiomeric excess was determined to be 93 % by chiral HPLC with chiral column CHIRALPAK® IA.

POT-2:

To a solution of diisopropylamine (0.18 mL, 1.28 mmol, 7.0 equiv) in THF (1.3 mL) was added a solution of n-butyllithium (0.52 mL, 2.5 M in hexane, 1.3 mmol, 7.1 equiv) at –78 °C and stirred at the same temperature for 10 min, followed by warm up to 0 °C and stirred for 15 min. To this solution was added borane-ammonia complex (35 mg, 90% purity, 1.02 mmol, 5.6 equiv), and the suspension solution was stirred at 0 °C for 15 min, followed by warm up to room temperature and stirred for additional 10 min. To this solution was added 6 (60 mg, 0.183 mmol) at 0 °C and stirred for 2 min, followed by heating up to 60 °C and stirred for 4 h. The resulting suspension was cooled to 0°C and the reaction was quenched by dropwise addition of 6N aqueous HCl solution until the pH value of the reaction mixture reached to 1-2, followed by stirring for 30 min. The pH value of the solution was adjusted to 8 by the addition of NaHCO₃. The reaction mixture was then carefully concentrated in
vacuo with a rotary evaporator, followed by connecting to high vacuum pump for 30 min. The crude mixture was then dissolved in MeOH (1.8 mL), and the reaction mixture was cooled to 0 °C for 5 min. To this solution was added NaCNBH₃ (46 mg, 0.753 mmol), followed by the addition of 37% aqueous HCHO solution (1.8 mL). The solution was stirred at room temperature for 12 h until the completion of the reaction, as monitored by TLC. The methanol was removed in vacuo, and the crude mixture was dissolved in THF (1.8 mL). To this solution was added an aqueous solution of 2N HCl (4 mL), and the reaction mixture was stirred for 3 h at room temperature. The reaction was quenched with the addition of solid NaHCO₃ and the pH value of the solution was adjusted to 8. The reaction mixture was extracted with EtOAc (3 x 15 mL), and the combined organic extracts were dried over Na₂SO₄ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 7% MeOH–CH₂Cl₂ (Rf = 0.45 in 15% MeOH–CH₂Cl₂) to afford the product (+)-5 as a white solid (21 mg, 45% yield from 6, and 33% yield from the starting tryptamine). The enantiomeric excess was determined to be 94 % by HPLC analysis with chiral column CHIRALCEL® OD-H, 10% (10% MeOH–EtOAc)/90% Hexane.

**General procedure for the one-pot synthesis of (+)-5:**

![Diagram](Image)

In a flame-dried 20-mL pear-shaped flask, a solution of tryptamine (40 mg, 0.25 mmol, 1.0 eq) in CH₂Cl₂ (6 mL) was prepared. To this solution was added dropwise via syringe a solution of aldehyde 2a (36 mg, 0.25 mmol) in CH₂Cl₂ (3 mL) at room temperature, followed by the addition of Et₂O (3 mL). The solution was stirred at room temperature for 2 h, followed by the addition of 4 Å molecular sieves (purchased from Aldrich®, beads, 4-8 mesh, ca.500 mg, around 10-12 beads), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The molecular sieve beads were removed by forceps, which were rinsed before removing from the flask (ca. 3 mL CH₂Cl₂ for rinsing). The resulting solution was concentrated in vacuo, yielding the imine as a pale yellow oil, which was immediately dissolved in Et₂O (5 mL) for the next-step reaction. To this solution was
added catalyst IX (6.5 mg, 0.013 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at –78 °C, and the solution was stirred for 5 min. To the reaction mixture was added dropwise acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at –78 °C for 10 min, followed by warming to –60 °C and stirred at the same temperature for 20 h. The resulting heterogeneous mixture was allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo, furnishing crude 6.

In a separated round-bottom flask, to a solution of diisopropylamine (0.25 mL, 1.78 mmol, 7.1 equiv) in THF (0.5 mL) was added a solution of n-butyllithium (0.72 mL, 2.5 M in hexane, 1.8 mmol, 7.2 equiv) at –78 °C and stirred at the same temperature for 10 min, followed by warm up to 0 °C and stirred for 15 min. To this solution was added borane-ammonia complex (48 mg, 90% purity, 1.40 mmol, 5.6 equiv), and the suspension solution was stirred at 0 °C for 15 min, followed by warm up to room temperature and stirred for additional 20 min. The lithium amidotrihydroborate (LiH2NBH3) solution was carefully transferred under nitrogen pressure (rinsed with 0.5 mL THF) to pre-cooled flask containing a solution of crude 6 in THF (0.5 mL) at 0 °C. The resulting solution was stirred for 2 min, followed by heating up to 60 °C and stirred for 4 h. Subsequently, the resulting suspension was cooled to 0°C, and the reaction was quenched by dropwise addition of 6N aqueous HCl solution until the pH value of the reaction mixture reached to 1-2, followed by stirring for 30 min. Later, the pH value of the solution was adjusted to 8 by the addition of solid NaHCO3. The reaction mixture was then carefully concentrated in vacuo with a rotary evaporator, followed by connecting to high vacuum pump for 30 min. The crude mixture was then dissolved in MeOH (1.6 mL), and the reaction mixture was cooled to 0 °C for 5 min. To this solution was added NaCNBH3 (47 mg, 0.75 mmol), followed by the addition of 37% aqueous HCHO solution (1.6 mL). The solution was stirred at room temperature for 12 h until the completion of the reaction, as monitored by TLC. The methanol was removed in vacuo, and the crude mixture was dissolved in THF (1 mL). To this solution was added an aqueous solution of 2N HCl (3 mL), and the reaction mixture was stirred for 3 h at room temperature. The reaction was quenched with the addition of solid NaHCO3 and the pH value of the solution was adjusted to 8. The reaction mixture was extracted with EtOAc (3 x 15 mL), and the combined organic extracts were dried over MgSO4 and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 7% MeOH–CH2Cl2 (Rf = 0.45 in 15% MeOH–CH2Cl2) to afford the product (+)-5 as a white solid (12 mg, 19% yield from the starting tryptamine). The enantiomeric excess was determined to be 91 % by HPLC analysis with chiral column CHIRALCEL® OD-H, 10% (10% MeOH–EtOAc)/90% Hexane.
Preparation of 13.

To a solution of 6-bromotryptamine (59.5 mg, 0.25 mmol) in CH₂Cl₂ (6 mL) was added a solution of aldehyde 2a (36 mg, 0.25 mmol) in CH₂Cl₂ (3 mL), followed by the addition of Na₂SO₄ (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was filtered by cannula transfer, and the remaining was rinsed twice with dichloromethane (2 × 5 mL). The combined solution was concentrated in vacuo to give the crude imine as a pale yellow oil, which was immediately dissolved in Et₂O (4.5 mL) and CH₂Cl₂ (0.5 mL) for the next step reaction. To this solution was added catalyst IX (6.5 mg, 0.013 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at −78 °C, and the solution was stirred for 5 min. To the reaction mixture was added acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at −78 °C for 10 min, followed by warming to −60 °C and stirred at the same temperature for 26 h. The resulting heterogeneous mixture was allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 50 to 60% EtOAc-hexane (Rₛ = 0.42 in 90% EtOAc-hexane) to afford product 13 (55 mg, 54% yield) as a white solid. M.p. 143–144 °C; [α]D 27° +20.3 (c 1, CHCl₃).

The enantiomeric excess was determined to be 83 % by HPLC analysis with chiral column CHIRALPAK® IA, 12% i-PrOH/n-hexane, flow rate 1.0 mL, λ = 254 nm (t_major = 29.9 min, t_minor = 22.6 min). IR (neat): 3281, 2961, 2924, 2854, 1630, 1614, 1446, 1262, 1095, 1022, 800 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): the compound exists as a 5:1 mixture of amide rotamers, signals corresponding to the major rotamer: δ 8.66 (br s, 1 H), 7.42 (d, J = 1.7 Hz, 1 H), 7.26 (d, J = 8.5 Hz, 1 H), 7.15 (dd, J = 8.5, 1.7 Hz, 1 H), 5.75 (t, J = 7.5 Hz, 1 H), 4.85 (t, J = 4.5 Hz, 1 H), 4.02 – 3.81 (m, 5 H), 3.52 – 3.44 (m, 1 H), 2.80 – 2.71 (m, 2 H), 2.20 (s, 3 H), 2.00 – 1.52 (m, 6 H), ¹³C NMR (125 MHz, CDCl₃) signals corresponding to the major rotamer: δ 169.6 (C), 136.8 (C), 135.2 (C), 125.5 (C), 122.6 (CH), 119.1 (CH), 113.8 (CH), 107.6 (C), 104.4 (CH), 64.9 (CH₂), 64.8 (CH₂), 48.4 (CH), 41.0 (CH₂), 33.8 (CH₂), 33.1 (CH₂), 22.0 (CH₂), 21.9 (CH₃), 20.4 (CH₂); MS (m/z, relative intensity): 408 (M⁺+2, 22), 406 (M⁺, 22), 365 (22), 363 (27), 293 (96), 291 (100), 251 (78), 250 (17), 249 (90), 212 (8), 170 (15), 168 (11), 143 (9), 99 (6), 73 (24); exact mass calculated for C₁₉H₂₃BrN₂O₃ (M⁺): 406.0892; found: 406.0898.
Preparation of Bromoindole 14.

To a solution of diisopropylamine (0.125 mL, 0.892 mmol, 6.6 equiv) in THF (1.2 mL) was added a solution of n-butyllithium (0.35 mL, 2.5 M in hexane, 0.875 mmol, 6.5 equiv) at –78 °C, and the solution was stirred at the same temperature for 10 min, followed by warm up to 0 °C and stirred for 15 min. To this solution was added borane-ammonia complex (24 mg, 90% purity, 0.63 mmol, 4.7 equiv), and the suspension solution was stirred at 0 °C for 15 min, followed by warm up to room temperature and stirred for additional 10 min. To the solution was added 13 (50 mg, 0.123 mmol) at 0 °C and stirred for 2 min, followed by heating up to 60 °C and stirred for 4 h. The resulting suspension was cooled to 0°C and the reaction was quenched by dropwise addition of 2N aqueous HCl solution (10 mL), followed by stirring for 30 min. The pH value of the solution was adjusted to 8 by the addition of saturated aqueous NaHCO3. The reaction mixture was extracted five times with ethyl acetate (5 x 10 mL), and the combined organic extracts were dried over MgSO4 and concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 5 to 10% MeOH-CH2Cl2 (Rf = 0.36 in 20% MeOH-CH2Cl2) to afford product 14 (30 mg, 67% yield) as a colorless oil. Selected spectroscopic data for 14: [α]D^27 –13.1 (c 1, MeOH); IR (neat): 3416, 3267, 2923, 2852, 2783, 1619, 1558, 1463, 1436, 1364, 1140, 1047, 800, 755 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 8.07 (br s, 1 H), 7.42 (s, 1 H), 7.29 (d, J = 8.5 Hz, 1 H), 7.16 (d, J = 8.5 Hz, 1 H), 4.87 (t, J = 4.5 Hz, 1 H), 4.05 – 4.02 (m, 1 H), 4.00 – 3.95 (m, 1 H), 3.88 – 3.82 (m, 2 H), 3.34 – 3.27 (m, 1 H), 3.03 – 2.96 (m, 1 H), 2.74 – 2.62 (m, 2 H), 1.90 – 1.55 (m, 7 H); ¹³C NMR (125 MHz, CDCl₃): δ 136.8 (C), 136.5 (C), 126.4 (C), 122.5 (CH), 119.2 (CH), 114.7 (C), 113.6 (CH), 109.2 (C), 104.4 (CH), 64.89 (CH₂), 64.87 (CH₂) 52.2 (CH) 42.2 (CH₂), 34.4 (CH₂), 33.3 (CH₂), 22.5 (CH₂), 20.2 (CH₂); MS (m/z, relative intensity): 366 (M⁺+2, 7), 364 (M⁺, 7), 264 (3), 262 (3), 251 (93), 249 (100), 234 (4), 170 (8), 143 (4), 99 (2), 73 (5); exact mass calculated for C₁₇H₂₁BrN₂O₂ (M⁺): 364.0786; found: 364.0779.
Preparation of arborescidine C (15).

To a solution of 14 (20 mg, 0.055 mmol) in methanol (0.55 mL) was added NaCNBH$_3$ (9 mg, 0.143 mmol, 2.6 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 5 min followed by the addition of 37% aqueous HCHO solution (0.55 mL, excess). The solution was stirred at room temperature for 12 h until the completion of the reaction, as monitored by TLC. The solution was concentrated in vacuo to give the residue. The residue was dissolved in THF (0.55 mL), followed by the addition of an aqueous solution of 2N HCl (0.55 mL), and the reaction mixture was stirred for 3 h at room temperature. The reaction was quenched with the addition of solid NaHCO$_3$ and the pH value of the solution was adjusted to 8. The reaction mixture was extracted with EtOAc (3 x 5 mL), and the combined organic extracts were dried over MgSO$_4$ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 8% MeOH–CH$_2$Cl$_2$ ($R_f$ = 0.47 in 15% MeOH–CH$_2$Cl$_2$) to afford product 15 (14 mg, 76% yield) as a white solid. M.p. 173–174 °C, lit.$^9$ 172–173 °C. Selected spectroscopic data for 15: $[\alpha]_D^{27}$ +3.1 (c 1, CHCl$_3$), lit.$^9$ $[\alpha]_D^{25}$ +3.0. lit.$^{10}$ $[\alpha]_D +3.3$ (c 1, CHCl$_3$). The enantiomeric excess was determined to be 86 % by HPLC analysis with chiral column CHIRALCEL® OD-H, 10% (10% MeOH–EtOAc) / 90% Hexane, flow rate 0.5 mL, $\lambda = 280$ nm (t$_{major} = 17.2$ min, t$_{minor} = 19.5$ min). IR (neat): 3319, 2924, 2852, 1609, 1514, 1106, 799, 756 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.42 (d, $J = 1.5$ Hz, 1 H), 7.25 (d, $J = 8.0$ Hz, 1 H), 7.15 (dd, $J = 8.0$, 1.5 Hz, 1 H), 6.07 (dd, $J = 4.8$, 1.5 Hz, 1 H), 3.59 (d, $J = 10.5$ Hz, 1 H), 2.98 – 2.93 (m, 1 H), 2.70 – 2.63 (m, 3 H), 2.44 (s, 3 H), 2.34 – 2.26 (m, 1 H), 2.24 – 2.17 (m, 1 H), 2.15 – 2.05 (m, 1 H), 1.82 – 1.74 (m, 1 H), 1.62 – 1.54 (m, 1 H), 1.44 – 1.34 (m, 1 H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 138.2 (C), 136.8 (C), 125.6 (C), 122.5 (CH), 119.4 (CH), 114.8 (C), 111.6 (CH), 108.9 (C), 76.6 (CH), 61.2 (CH), 50.4 (CH$_2$) 42.7 (CH$_3$), 34.3 (CH$_2$), 31.8 (CH$_2$), 20.2 (CH$_2$), 20.1 (CH$_2$); MS (m/z, relative intensity): 336 (M$^+$+2, 16), 334 (M$^+$, 16), 317 (15), 291 (17), 265 (85), 263 (100), 184 (8), 154 (9); exact mass calculated for C$_{16}$H$_{19}$BrN$_2$O (M$^+$): 334.0681; found: 334.0674.

Table S2. $^{13}$C NMR chemical shift comparison of the synthetic 15 with the natural product reported.

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Preparation of 16

![Preparation Diagram]

To a solution of 15 (20 mg, 0.06 mmol) and Et$_3$N (25 µL, 0.18 mmol) in CH$_2$Cl$_2$ (0.6 mL) was added methanesulfonyl chloride (6.8 µL, 0.088 mmol) at 0 °C. The resulting solution was stirred at 0 °C to room temperature for 2h. The reaction was quenched by the addition of water (1 mL), and the mixture was extracted with CH$_2$Cl$_2$ (2 x 5 mL). The organic solution was washed with saturated aqueous NaHCO$_3$ solution (5 mL), brine (5 mL), dried
over MgSO₄, and the solution was concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 3 to 5% MeOH–CH₂Cl₂ ($R_f = 0.46$ in 10% MeOH–CH₂Cl₂) to afford product 16 (15 mg, 79% yield) as a colorless oil. Selected spectroscopic data for 16: $[\alpha]_D^{27} +63$ (c 1, CHCl₃), lit.¹¹ $[\alpha]_D +70$ (c 0.6, CHCl₃); lit.¹² $[\alpha]_D –70$ (c 0.6, CHCl₃) for its enantiomer. IR (neat): 2924, 2852, 1608, 1468, 1314, 1222, 1106, 799, 756 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.48 (d, $J = 1.5$ Hz, 1 H), 7.32 (d, $J = 8.5$ Hz, 1 H), 7.22 (dd, $J = 8.5$, 1.5 Hz, 1 H), 6.82 (dt, $J = 9.8$, 2.0 Hz, 1 H), 5.13 – 5.07 (m, 1 H), 3.38 (d, $J = 10.0$ Hz, 1 H), 3.17 – 3.10 (m, 1 H), 2.92 – 2.85 (m, 1 H), 2.75 – 2.65 (m, 2 H), 2.54 (s, 3 H), 2.58 – 2.50 (m, 1 H), 2.45 – 2.39 (m, 1 H), 2.38 – 2.32 (m, 1 H), 1.92 – 1.83 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 138.0 (C), 136.9 (C), 125.8 (C), 123.3 (CH), 121.7 (CH), 119.3 (CH), 115.3 (C), 112.4 (CH), 111.2 (CH), 109.3 (C), 62.4 (CH), 52.6 (CH₂), 42.4 (CH₁), 29.9 (CH₂), 27.9 (CH₂), 20.6 (CH₂); MS (m/z, relative intensity): 318 (M⁺+2, 97), 317 (M⁺, 100), 316 (99), 315 (89), 289 (34), 287 (34), 275 (80), 274 (55), 273 (83), 272 (41), 260 (23); exact mass calculated for C₁₆H₁₇BrN₂ (M⁺): 316.0575; found: 316.0582.

Preparation of 7

To a solution of tryptamine (40 mg, 0.25 mmol) in CH₂Cl₂ (6 mL) was added a solution of aldehyde 2b (29 mg, 0.25 mmol)¹³ in CH₂Cl₂ (3 mL), followed by the addition of Et₂O (3 mL). The solution was stirred at room temperature for 2 h, prior to the addition of Na₂SO₄ (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was filtered by cannula transfer to a flame dried 25 mL round-bottomed flask, and the remaining was rinsed twice with CH₂Cl₂ (2 x 5 mL). The combined solution was concentrated in vacuo to give the crude imine as a pale yellow oil, which was immediately dissolved in Et₂O (10 mL) for the next step reaction. To this solution was added catalyst IX (6.5 mg, 0.0125 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at -78 °C, and the solution was stirred for 5 min. To the reaction mixture was added acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at -78 °C for 10 min, followed by warming to -60 °C and stirred at the same temperature for 28 h. The resulting heterogeneous mixture was then allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 50 to 60% EtOAc-hexane (Rᶠ = 0.35 in 80% EtOAc-hexane) to afford product 7 (48 mg, 64% yield) as a white solid. M.p. 197–198 °C; [α]D²⁷ +125 (c 1, CHCl₃). The enantiomeric excess was determined to be 86 % by HPLC with chiral column CHIRALPAK® IA, 12% i-PrOH/n-hexane, flow rate 1.0 mL, λ = 280 nm (tₒ_major = 27.1 min, tₒ_minor = 37.8 min). IR (neat): 3395, 3271, 2956, 2924, 2893, 2852, 1620, 1426, 1233, 1136, 1031, 746 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): the compound exists as a 2:1 mixture of amide rotamers, signals corresponding to the major rotamer: δ 8.74 (br s, 1 H), 7.44 (d, J = 7.5 Hz, 1 H), 7.32 (d, J = 8.0 Hz, 1 H), 7.18 – 7.12 (m, 1 H), 7.11 – 7.05 (m, 1 H), 5.85 (t, J = 6.5 Hz, 1 H), 5.16 (t, J = 5.0 Hz, 1 H), 5.11 – 5.04 (m, 1 H), 4.14 – 3.88 (m, 4 H), 3.49 – 3.41 (m, 1 H), 2.93 – 2.66 (m, 2 H), 2.19 (s, 3 H), 2.30 – 2.14 (m, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 169.1 (C), 136.0 (C), 134.0 (C), 126.5 (C), 121.7 (CH), 119.3 (CH), 117.9 (CH), 111.0 (CH), 107.5 (C), 102.7 (CH), 64.9 (OCH₂), 64.9 (OCH₂), 45.3 (CH), 41.5 (CH₂), 39.0 (CH₂), 22.0 (CH₂), 21.8 (CH₃); ¹³C NMR (125 MHz, CDCl₃), signals corresponding to the major rotamer: δ 169.1 (C), 136.0 (C), 134.0 (C), 126.5 (C), 121.7 (CH), 119.3 (CH),

¹³ For best results, the aldehyde was used immediately after purification.
117.9 (CH), 111.0 (CH), 107.5 (C), 102.7 (CH), 45.3 (CH), 41.6 (CH₂), 39.0 (CH₂), 22.0 (CH₂), 21.8 (CH₃); MS (m/z, relative intensity): 300 (M⁺, 77), 239 (7), 225 (10), 213 (100), 203 (31), 171 (94), 161 (40), 144 (38), 135 (75), 127 (39), 77 (38), 73 (42); exact mass calculated for C₁₇H₂₀N₂O₃ (M⁺): 300.1474; found: 300.1480.

**Figure S2.** ORTEP and Stereo plots for X-ray crystal structures of (+)-7.

CCDC 1523959 contains the supplementary crystallographic data for (+)-7. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).
Table S3. Crystal data and structure refinement for (+)-7, ic17656.

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Preparation of 7

To a solution of diisopropylamine (0.2 mL, 1.43 mmol, 7.1 equiv) in THF (2 mL) was added a solution of \( n \)-butyllithium (0.57 mL, 2.5 M in hexane, 1.43 mmol, 7.1 equiv) at \(-78^\circ\text{C}\) and stirred at the same temperature for 10 min, followed by warming up to 0 \(^\circ\text{C}\) and stirred for 15 min. To this solution was added borane-ammonia complex (38 mg, 90% purity, 1.0 mmol, 5.0 equiv), and the suspension solution was stirred at 0 \(^\circ\text{C}\) for 15 min, followed by warming up to room temperature and stirred for additional 10 min. Subsequently, the solution was cooled to 0 \(^\circ\text{C}\). To the solution was added 7 (60 mg, 0.20 mmol) at 0 \(^\circ\text{C}\) and stirred for 2 min, followed by heating up to 60 \(^\circ\text{C}\) and stirred for 4 h. The resulting suspension was cooled to 0 \(^\circ\text{C}\) and the reaction was quenched by dropwise addition of 2N aqueous HCl solution (5 mL), followed by stirring for 30 min. The pH value of the solution was adjusted to 8 by the addition of saturated aqueous NaHCO\(_3\). The reaction mixture was extracted five times with ethyl acetate (5 x 10 mL), and the combined organic extracts were dried over sodium sulfate and concentrated \textit{in vacuo} to give the residue. The crude product was purified by flash column chromatography with 5 to 10\% MeOH-CH\(_2\)Cl\(_2\) (\(R_f = 0.4\) in 20\% MeOH-CH\(_2\)Cl\(_2\)) to afford product 21 (33 mg, 64\% yield) as a pale yellow oil. Selected spectroscopic data for 21:

\([\alpha]_D^{27} = -25.9\ (c\ 1,\ \text{MeOH})\); IR (neat): 3390, 2961, 2924, 2890, 1603, 1453, 1260, 1137, 1113, 1017, 799, 743 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 8.75 (br, s, 1 H), 7.46 (d, \(J = 8.0\ \text{Hz}, 1\ \text{H}\)), 7.30 (d, \(J = 8.0\ \text{Hz}, 1\ \text{H}\)), 7.12 (dd, \(J = 7.5, 7.5\ \text{Hz}, 1\ \text{H}\)), 7.06 (dd, \(J = 7.5, 7.5\ \text{Hz}, 1\ \text{H}\)), 5.10 (t, \(J = 3.8\ \text{Hz}, 1\ \text{H}\)), 4.30 (br, s, 1 H), 4.11 – 4.02 (m, 2 H), 3.98 – 3.90 (m, 2 H), 3.36 – 3.31 (m, 1 H), 3.08 – 3.00 (m, 1 H), 2.80 – 2.68 (m, 2 H), 2.38 – 2.15 (m, 3 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 135.6 (C), 135.5 (C), 127.3 (C), 121.4 (CH), 119.1 (CH), 118.0 (CH), 110.9 (CH), 108.5 (C), 102.8 (CH), 65.1 (CH\(_2\)), 65.0 (CH\(_2\)), 48.7 (CH) 42.9 (CH\(_2\)), 39.1 (CH\(_2\)), 22.4 (CH\(_2\)); MS (m/z, relative intensity): 258 (M\(^+\), 23), 213 (5), 172 (13), 171 (100), 156 (10), 144 (9), 135 (7), 115 (4), 73 (10); exact mass calculated for C\(_{15}\)H\(_{18}\)N\(_2\)O\(_2\) (M\(^+\)): 258.1368; found: 258.1364.
Preparation of 22

To a solution of 21 (100 mg, 0.387 mmol) in methanol (3.8 mL) was added NaCNBH₃ (61 mg, 0.97 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 5 min followed by the addition of 37% aqueous HCHO solution (3 mL, excess). The solution was stirred at room temperature for 12 h until the completion of the reaction, as monitored by TLC. The solution was concentrated in vacuo to remove MeOH, and the residue was diluted with water. The mixture was extracted with EtOAc (15 mL x 3), and the combined organic extracts were dried over MgSO₄ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 10% MeOH–CH₂Cl₂ (Rf = 0.45 in 15% MeOH–CH₂Cl₂) to afford product 22 (75 mg, 71% yield) as a colorless oil. Selected spectroscopic data for 22: [α]D²⁷ +43.3 (c 1, CHCl₃); IR (neat): 3397, 3053, 2933, 2889, 1453, 1324, 1136, 1064, 1025, 944, 742 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 8.75 (br s, 1 H), 7.47 (d, J = 8.0 Hz, 1 H), 7.31 (d, J = 8.0 Hz, 1 H), 7.14 – 7.04 (m, 2 H), 5.09 (dd, J = 5.0, 3.0 Hz, 1 H), 4.14 – 4.06 (m, 2 H), 3.98 – 3.95 (m, 2 H), 3.68 – 3.65 (m, 1 H), 3.16 – 3.11 (m, 1 H), 2.80 – 2.72 (m, 3 H), 2.48 (s, 3 H) 2.39 – 2.35 (m, 1 H), 2.14 – 2.09 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 135.8 (C), 135.4 (C), 126.9 (C), 121.2 (CH), 119.0 (CH), 118.0 (CH), 110.8 (CH), 107.3 (C), 103.0 (CH), 65.2 (CH₂), 65.1 (CH₂) 55.4 (CH), 50.9 (CH₂), 42.1 (CH₃), 37.6 (CH₂), 19.7 (CH₂); MS (m/z, relative intensity): 272 (M⁺, 4), 229 (1), 186 (10), 185 (100), 156 (4), 144 (2), 73 (7); exact mass calculated for C₁₆H₂₀N₂O₂ (M⁺): 272.1525; found: 272.1522.

(Treatment of 22 with 2N HCl did not proceed the cyclization process as observed in the prior examples, probably due to the difficulty in the ring-strain formation. Hence, the product at this stage was isolated and characterized.)
Preparation of 9

To a solution of tryptamine (40 mg, 0.25 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (6 mL) was added a solution of aldehyde 2d\textsuperscript{14} (40 mg, 0.25 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (3 mL), followed by the addition of Et\textsubscript{2}O (3 mL). The solution was stirred at room temperature for 2 h, prior to the addition of sodium sulfate (500 mg), and the mixture was vigorously stirred at the same temperature for an additional 30 min. The resulting solution was filtered by cannula transfer, and the remaining was rinsed twice with dichloromethane (2 x 5 mL). The combined solution was concentrated in vacuo to give the crude imine as a pale yellow oil, which was immediately dissolved in Et\textsubscript{2}O (15 mL) for the next step reaction. To this solution was added catalyst IX (6.5 mg, 0.013 mmol, 5 mol %) and 2,6-lutidine (29 µL, 0.25 mmol, 1.0 equiv) at –78 °C, and the solution was stirred for 5 min. To the reaction mixture was added acetyl chloride (18 µL, 0.25 mmol, 1.0 equiv), and the resulting solution was stirred at –78 °C for 10 min, followed by warming to –60 °C and stirred at the same temperature for 34 h. The resulting heterogeneous mixture was allowed to warm to room temperature and stirred for 30 mins followed by concentration in vacuo. The crude product was purified by flash column chromatography with 50 to 60% EtOAc-hexane (R\texttextsubscript{f} = 0.30 in 80% EtOAc-hexane) to afford product 9 (60 mg, 70% yield) as a white solid. M.p. 154–155 °C; [\textgreek{a}]\textsubscript{25} = 100.7 (c 1, CHCl\textsubscript{3}). The enantiomeric excess was determined to be 92 % by HPLC with chiral column CHIRALPAK\texttextsuperscript{\textregistered} IA, 12% i-PrOH/n-hexane, flow rate 1.0 mL, \(\lambda = 254\) nm (t\textsubscript{major} = 22.8 min, t\textsubscript{minor} = 31.5 min). IR (neat): 3278, 3008, 2950, 2886, 1619, 1447, 1231, 1140, 1031, 945, 746 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) the compound exists as a 5:1 mixture of amide rotamers, signals corresponding to the major rotamer: \(\delta 8.47\) (s, 1 H), 7.43 (d, \(J = 7.8\) Hz, 1 H), 7.29 (d, \(J = 8.0\) Hz, 1 H), 7.17 – 7.03 (m, 2 H), 5.76 (dd, \(J = 8.7, 5.6\) Hz, 1 H), 4.81 (t, \(J = 4.8\) Hz, 1 H), 4.01 – 3.78 (m, 5 H), 3.53 – 3.44 (m, 1 H), 2.87 – 2.64 (m, 2 H), 2.21 (s, 3 H), 1.94 – 1.40 (m, 8 H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) signals corresponding to the major rotamer: \(\delta 169.6\) (C), 136.0 (C), 134.7 (C), 126.6 (C), 121.6 (CH), 119.4 (CH), 117.8 (CH), 110.9 (CH), 107.3 (C), 104.4 (CH), 64.8 (two CH\textsubscript{2}), 48.9 (CH), 41.0 (CH\textsubscript{2}), 34.3 (CH\textsubscript{2}), 33.5 (CH\textsubscript{2}), 26.0 (CH\textsubscript{2}), 23.9

\textsuperscript{14} For best results, the aldehyde was used immediately after purification.
(CH₂), 22.0 (CH₂), 21.9 (CH₃); MS (m/z, relative intensity): 342 (M⁺, 23), 299 (4), 297 (3), 255 (5), 214 (11), 213 (100), 171 (65), 169 (10), 144 (5), 115 (5), 97 (7), 73 (11); exact mass calculated for C₂₀H₂₆N₂O₃ (M⁺): 342.1943; found: 342.1944.

Preparation of 23.

To a solution of diisopropylamine (0.50 mL, 3.57 mmol, 7.2 equiv) in THF (3.5 mL) was added a solution of n-butyllithium (1.42 mL, 2.5 M in hexane, 3.55 mmol, 7.2 equiv) at −78 °C and stirred at the same temperature for 10 min, followed by warm up to 0 °C and stirred for 15 min. To this solution was added borane-ammonia complex (95.5 mg, 90% pure, 2.78 mmol, 5.6 equiv), and the suspension solution was stirred at 0 °C for 15 min, followed by warm up to room temperature and stirred for additional 10 min. To the solution was added 9 (170 mg, 0.496 mmol) at 0 °C and stirred for 2 min, followed by heating up to 60 °C and stirred for 4 h. The resulting suspension was cooled to 0°C and the reaction was quenched by dropwise addition of 2N aqueous HCl solution (10 mL), followed by stirring for 30 min. The pH value of the solution was adjusted to 8 by the addition of saturated aqueous NaHCO₃. The reaction mixture was extracted five times with ethyl acetate (5 x 20 mL), and the combined organic extracts were dried over sodium sulfate and concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 5 to 10% MeOH-CH₂Cl₂ (Rf = 0.4 in 20% MeOH-CH₂Cl₂) to afford product 23 (90 mg, 60% yield) as a colorless oil. Selected spectroscopic data for 23: [α]D²⁷ 27 –29.8 (c 1, MeOH); IR (neat): 3404, 3329, 2941, 1453, 1139, 1027, 945, 803, 743 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.98 (br, s, 1 H), 7.46 (d, J = 8.0 Hz, 1 H), 7.28 (d, J = 8.0 Hz, 1 H), 7.15 – 7.05 (m, 2 H), 4.85 (t, J = 4.7 Hz, 1 H), 4.06 – 4.01 (m, 1 H), 3.98 – 3.95 (m, 2 H), 3.86 – 3.82 (m, 2 H), 3.36 – 3.30 (m, 1 H), 3.04 – 2.96 (m, 1 H), 2.75 – 2.67 (m, 2 H), 1.96 – 1.80 (m, 2 H), 1.73 – 1.64 (m, 3 H), 1.60 – 1.45 (m, 4 H); ¹³C NMR (125 MHz, CDCl₃): δ 136.2 (C), 135.6 (C), 127.4 (C), 121.4 (CH), 119.2 (CH), 118.0 (CH), 110.7 (CH), 108.9 (C), 104.4 (CH), 64.8 (two CH₂), 52.4 (CH) 42.5 (CH₂), 34.7 (CH₂), 33.5 (CH₂), 25.6 (CH₂), 24.0 (CH₂), 22.6 (CH₂); MS (m/z,
Preparation of indole 24.

To a solution of 23 (90 mg, 0.3 mmol) in methanol (3.0 mL) was added NaCNBH$_3$ (50 mg, 0.796 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 5 min followed by the addition of 37% aqueous HCHO solution (3 mL, excess). The solution was stirred at room temperature for 12 h until the completion of the reaction, as monitored by TLC. The solution was concentrated in vacuo to remove MeOH. The residue was diluted with water, and the reaction mixture was extracted with EtOAc (3 x 15 mL), and the combined organic extracts were dried over Na$_2$SO$_4$ and concentrated in vacuo to give a residue. The crude product was purified by flash column chromatography with 5 to 10% MeOH–CH$_2$Cl$_2$ ($R_f = 0.4$ in 15% MeOH–CH$_2$Cl$_2$) to afford product 24 (68 mg, 72% yield) as a colorless oil. Selected spectroscopic data for 24: $[\alpha]_D^{25} +4$ (c 1, CHCl$_3$); IR (neat): 3250, 3056, 2927, 2859, 1678, 1463, 1453, 1140, 1031, 745 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.86 (br s, 1 H), 7.47 (d, $J = 8.0$ Hz, 1 H), 7.29 (d, $J = 8.0$ Hz, 1 H), 7.15 – 7.06 (m, 2 H), 4.84 (t, $J = 4.5$ Hz, 1H), 3.98 – 3.92 (m, 2 H), 3.87 – 3.80 (m, 2 H), 3.49 (t, $J = 5.0$ Hz, 1H), 3.19 – 3.10 (m, 1 H), 2.80 – 2.70 (m, 3 H), 2.45 (s, 3 H), 1.95 – 1.84 (m, 1 H), 1.79 – 1.62 (m, 3 H), 1.56 – 1.30 (m, 4 H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 135.9 (C), 134.9 (C), 127.3 (C), 121.2 (CH), 119.2 (CH), 118.0 (CH), 110.6 (CH), 108.3 (C), 104.5 (CH), 64.80 (CH$_2$), 64.79 (CH$_2$), 59.9 (CH), 49.9 (CH$_2$), 42.0 (CH$_3$), 33.5 (CH$_2$), 32.7 (CH$_2$), 25.0 (CH$_2$), 24.1 (CH$_2$), 19.2 (CH$_2$); exact mass calculated for C$_{19}$H$_{26}$N$_2$O$_2$ (M$^+$):314.1994; found: 314.1987.

(Treatment of 24 with 2N HCl did not proceed the cyclization process as observed in the prior examples, probably due to the difficulty in the formation of medium-size macrocycles. Hence, the product at this stage was isolated and characterized.)
Fig S36. 1H NMR (CDCl₃, 500 MHz) of compound 3.
Fig S37. 13C NMR (CDCl₃, 125 MHz) of compound 3.
Fig S38. DEPT of compound 3.
Fig S39. COSY of compound 3.
Fig S40. NOESY of compound 3.
Fig S41. HSQC of compound 3.
Fig S42. 1H NMR (CDCl3, 500 MHz) of compound 4.
Fig S43. 13C NMR (CDCl3, 125 MHz) of compound 4.
Fig S44. DEPT of compound 4.
Fig S45. COSY of compound 4.
Fig S46. NOESY of compound 4.
Fig S47. HSQC of compound 4.
Fig S48. 1H NMR (CDCl3, 500 MHz) of compound 5.
Fig S49. 13C NMR (CDCl3, 125 MHz) of compound 5.
Fig S50. DEPT of compound 5.
Fig S51. HSQC of compound 5.
Fig S52. COSY of compound 5.
Fig S53. NOESY of compound 5.
Fig S54 1H NMR (CDCl₃, 500 MHz) of compound 6.
Fig S55. 13C NMR (CDCl3, 125 MHz) of compound 6.
Fig S56. DEPT of compound 6.
Fig S57. COSY of compound 6.
Fig S58. NOESY of compound 6.
Fig S59. HSQC of compound 6.
Fig S60. 1H NMR (CDCl3, 500 MHz) of compound 7.
Fig S61. 13C NMR (CDCl3, 125 MHz) of compound 7.
Fig S62. DEPT of compound 7.
Fig S63 COSY of compound 7.
Fig S64. NOESY of compound 7.
Fig S65. HSQC of compound 7.
Fig S66. 1H NMR (CDCl₃, 500 MHz) of compound 8.
Fig S67. 13C NMR (CDCl3, 125 MHz) of compound 8.
Fig S68. DEPT of compound 8.
Fig S69. COSY of compound 8.
Fig S70. NOESY of compound 8.
Fig S71. HSQC of compound 8.

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Plot date: 2015-12-28
Fig S72. 1H NMR (CDCl₃, 500 MHz) of compound 9.
Fig S73. 13C NMR (CDCl3, 125 MHz) of compound 9.
Fig S74. DEPT of compound 9.
Fig S75. HSQC of compound 9.
Fig S76. COSY of compound 9.
Fig S77. NOESY of compound 9.
Fig S78. 1H NMR (CDCl3, 500 MHz) of compound 10.
Fig S79. 13C NMR (CDCl₃, 125 MHz) of compound 10.
Fig S80. DEPT of compound 10.
Fig S81. HSQC of compound 10.
Fig S82. COSY of compound 10.
Fig S83. NOESY of compound 10.
Fig S84. 1H NMR (CDCl₃, 500 MHz) of compound 11.
Fig S85. 13C NMR (CDCl3, 125 MHz) of compound 11.
Fig S86. DEPT of compound 11.
Fig S87. HSQC of compound 11.
Fig S88. COSY of compound 11.
Fig S89. NOESY of compound 11.
Fig S90. 1H NMR (CDCl3, 500 MHz) of compound 13.
Fig S91. 13C NMR (CDCl3, 125 MHz) of compound 13.
Fig S92. DEPT of compound 13.
Fig S93. HSQC of compound 13.
Fig S94. COSY of compound 13.
Fig S95. NOESY of compound 13.
Fig S96. 1H NMR (CDCl3, 500 MHz) of compound 14.
Fig S97. 13C NMR (CDCl₃, 125 MHz) of compound 14.
Fig S98. DEPT of compound 14.
Fig S99. HSQC of compound 14.
Fig S100. COSY of compound 14.
Fig S101. NOESY of compound 14.
Fig S102. 1H NMR (CDCl₃, 500 MHz) of compound 15.
Fig S103. 13C NMR (CDCl3, 125 MHz) of compound 15.
Fig S104. DEPT of compound 15.
Fig S105. HSQC of compound 15.
Fig S106. COSY of compound 15.
Fig S107. NOESY of compound 15.
Fig S108. 1H NMR (CDCl₃, 500 Hz) of compound 16.
Fig S109. 13C NMR (CDCl3, 125 MHz) of compound 16.
Fig S110. DEPT of compound 16.
Fig S111. HSQC of compound 16.
Fig S112. COSY of compound 16.
Fig S113. NOESY of compound 16.
Fig S114. 1H NMR (CDCl₃, 500 MHz) of compound 17.
Fig S115. 13C NMR (CDCl3, 125 MHz) of compound 17.
Fig S116. DEPT of compound 17.
Fig S117. HSQC of compound 17.
Fig S118. COSY of compound 17.
Fig S119. NOESY of compound 17.
Fig S120. 1H NMR (CDCl3, 500 MHz) of compound 18.
Fig S121. 13C NMR (CDCl3, 125 MHz) of compound 18.
Fig S122. DEPT of compound 18.
Fig S123. HSQC of compound 18.
Fig S124. COSY of compound 18.
Fig S125. NOESY of compound 18.
Fig S126. 1H NMR (CDCl₃, 500 MHz) of compound 19.
Fig S127. 13C NMR (CDCl₃, 125 MHz) of compound 19.
Fig S128. DEPT of compound 19.
Fig S129. HSQC of compound 19.
Fig S130. COSY of compound 19.
Fig S131. NOESY of compound 19.
Fig S132. 1H NMR (CDCl3, 500 MHz) of compound 20.
Fig S133. 13C NMR (CDCl₃, 125 MHz) of compound 20.
Fig S134. DEPT of compound 20.
Fig S135. HSQC of compound 20.
Fig S136. COSY of compound 20.
Fig S137. NOESY of compound 20.
Fig S138. 1H NMR (CDCl₃, 500 MHz) of compound 21.
Fig S139. 13C NMR (CDCl₃, 125 MHz) of compound 21.
Fig S140. DEPT of compound 21.
Fig S141. HSQC of compound 21.
Fig S142. COSY of compound 21.
Fig S143. NOESY of compound 21.
Fig S144. 1H NMR (CDCl3, 500 MHz) of compound 22.
Fig S145. 13C NMR (CDCl3, 125 MHz) of compound 22.
Fig S146. DEPT of compound 22.
Fig S147. HSQC of compound 22.
Fig S148. COSY of compound 22.
Fig S149. NOESY of compound 22.
Fig S150. 1H NMR (CDCl3, 500 MHz) of compound 23.
Fig S151. 13C NMR (CDCl3, 125 MHz) of compound 23.
Fig S152. DEPT of compound 23.
Fig S153. HSQC of compound 23.
Fig S154. COSY of compound 23.
Fig S155. NOESY of compound 23.
Fig S156. 1H NMR (CDCl₃, 500 MHz) of compound 24.
Fig S157. 13C NMR (CDCl3, 125 MHz) of compound 24.
Fig S158. DEPT of compound 24.
Fig S159. HSQC of compound 24.
Fig S160. COSY of compound 24.
Fig S161. NOESY of compound 24.
Fig S162. 1H NMR (CDCl3, 500 MHz) of catalyst IX.
Fig S163. 13C NMR (CDCl3, 125 MHz) of catalyst IX.
Fig S164. DEPT of catalyst IX.
Fig S165. HSQC of catalyst IX.
Fig S166. COSY of catalyst IX.
Fig S167. NOESY of catalyst IX.
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2014/06/13 04:00 下午
Processed Date and Time: 2014/06/13 04:48 下午
Reported Date and Time: 2014/06/13 04:48 下午

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Application(data): Vishal  
Sample Name: VMS-02-118 (Racemic)  
Injection from this vial: 1 of 1  
Vial Number: 1  
Vial Type: UNK  
Volume: 20.0 ul  
Sample Description: 15%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 1  
Column Type: IA  
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Method Description:

Chrom Type: Fixed WL Chromatogram, 254 nm

Peak Quantitation: AREA  
Calculation Method: EXT-STD  
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Peak rejection level: 200000

Fig S168. HPLC analysis of the racemic compound 3, for comparison (Table 1).
Fig S169. HPLC analysis of the chiral compound 3 obtained, (Table 1, entry 1).
Fig S170. HPLC analysis of the chiral compound 3 obtained, (Table 1, entry 2).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2014/08/12 03:31 下午
Reported Date and Time: 2014/08/12 04:15 下午
Processed Date and Time: 2014/08/12 04:15 下午

Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0015\DATA

Processing Method: test-IPA/Hx 1
System (acquisition): Sys 1 Series: 0015
Application(data): Vishal Vial Number: 1
Sample Name: VMS-02-140 (Chiral) Vial Type: UNK
Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 15%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 1
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Method Description:
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Peak Quantitation: AREA
Calculation Method: EXT-STD
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Peak rejection level: 200000

Fig S171. HPLC analysis of the chiral compound 3 obtained, (Table 1, entry 3).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2014/10/23 03:43 下午
Reported Date and Time: 2014/10/23 05:09 下午

Processed Date and Time: 2014/10/23 05:08 下午
Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0025\nProcessing Method: test-IPA/Hx 2

System (acquisition): Sys 1 Series: 0025
Application(data): Vishal Vial Number: 2
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Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

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Peak rejection level: 200000

Fig S172. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 1).
Fig S173. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 2).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2014/11/11 12:07 下午
Processed Date and Time: 2014/11/11 05:11 下午
Reported Date and Time: 2014/11/11 05:11 下午

Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0028\n
Processing Method: test-IPA/Hx 2
System (acquisition): Sys 1 Series: 0028
Application (data): Vishal Vial Number: 1
Sample Name: VMS-02-177 (chiral) Vial Type: UNK
Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 12%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Retention Time (min)

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Peak rejection level: 200000

Fig S174. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 3)
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2014/11/11 02:13 下午
Reported Date and Time: 2014/11/11 05:17 下午
Processed Date and Time: 2014/11/11 05:16 下午

Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0029\nProcessing Method: test-IPA/Hx 2

System (acquisition): Sys 1  Series: 0029
Application (data): Vishal  Vial Number: 1
Sample Name: VMS-02-178 (chiral)  Vial Type: UNK
Injection from this vial: 1 of 1  Volume: 20.0 ul
Sample Description: 12%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA  Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 254 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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5081050  80812  100.000

Peak rejection level: 200000

Fig S175. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 4)
Fig S176. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 5)
Fig S177. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 10)
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2014/12/15 06:10 下午
Processed Date and Time: 2014/12/16 03:39 下午
Reported Date and Time: 2014/12/16 03:40 下午

Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0034\n
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Application(data): Vishal Vial Number: 1
Sample Name: VMS-02-189 (chiral) Vial Type: UNK
Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 12%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA Method Developer: Vishal
Method Description:

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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4585884  62533  100.000

Peak rejection level: 200000

Fig S178. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 11)
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2014/12/15 06:58 下午
Reported Date and Time: 2014/12/16 03:45 下午
Processed Date and Time: 2014/12/16 03:43 下午
Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0035\nProcessing Method: test-IPA/Hx 2

System (acquisition): Sys 1  Series: 0035
Application(data): Vishal  Vial Number: 1
Sample Name: VMS-02-190 (chiral)  Vial Type: UNK
Injection from this vial: 1 of 1  Volume: 20.0 ul
Sample Description: 12%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA  Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 254 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200000

Fig S179. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 12)
Fig S180. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 13)
**D-2000 Elite HPLC System Manager Report**

**Processed Date and Time:** 05/24/2016 11:35 AM

**Data Path:** D:\Vishal\DATA\0037\ 

**Processing Method:** test-IPA/Hx 2

**System (acquisition):** Sys 1  
**Series:** 0037

**Application(data):** Vishal  
**Vial Number:** 1

**Sample Name:** VMS-02-195 (chiral) -30 degree  
**Vial Type:** UNK

**Injection from this vial:** 1 of 1  
**Volume:** 20.0 ul

**Sample Description:** 12%IPA+HX 1.0mL/MIN COL-IA

**Retention Time (min)**

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**Scale Factor 1:** 1.000

**Peak rejection level:** 200

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**Fig S181. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 14)**
**Fig S182. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 15)**
Fig S183. HPLC analysis of the chiral compound 6 obtained (Table 2, entry 16).
Fig S184. HPLC analysis of the racemic compound 6 obtained, for comparison (Table 2, entry 16).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 05/14/2016
Reported Date and Time: 05/14/2016
02:40 AM
04:37 PM

Processed Date and Time: 05/14/2016
04:37 PM

Data Path: D:\Vishal\DATA\0109\n
Processing Method: test-IPA/Hx 2

System (acquisition): Sys 1
Series: 0109
Application(data): Vishal
Vial Number: 3
Sample Name: VMS-03-82 (Co)
Vial Type: UNK
Injection from this vial: 1 of 1
Volume: 20.0 ul
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA
Method Developer: Vishal

Method Description:
Chrom Type: Fixed WL Chromatogram, 254 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200

Fig S185. HPLC analysis of the co-injection of racemic and chiral compound 6 obtained, for comparison (Table 2, entry 16).
D-2000 Elite HPLC System Manager Report

Processed Date and Time: 02/19/2016 04:04 PM

Data Path: D:\Vishal\DATA\0010\n
Processing Method: test-IPA/Hx

System (acquisition): Sys 1  Series: 0010
Application(data): Vishal  Vial Number: 1
Sample Name: Vms-02-93 (racemic)  Vial Type: UNK
Injection from this vial: 1 of 1  Volume: 20.0 ul
Sample Description: 12% IPA+HX 1.0 mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test-IPA/Hx
Column Type: IA  Method Developer: Vishal
Method Description:
Chrom Type: Fixed WL Chromatogram, 280 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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8466073  56480  100.000

Peak rejection level: 200

Fig S186. HPLC analysis of the racemic compound 7, for comparison (Table 3, entry 1).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 02/15/2016 02:05 PM
Reported Date and Time: 02/19/2016 04:15 PM
Processed Date and Time: 02/19/2016 04:15 PM

Data Path: D:\Vishal\DATA\0011\processing_method: test-IPA/Hx

System (acquisition): Sys 1 Series: 0011
Application (data): Vishal Vial Number: 2
Sample Name: Vms-02-93 (Chiral) Vial Type: UNK
Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 12% IPA+HX 1.0 mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test-IPA/Hx
Column Type: IA Method Developer: Vishal
Method Description:
Chrom Type: Fixed WL Chromatogram, 280 nm
Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200

Fig S187. HPLC analysis of the chiral compound 7 obtained (Table 3, entry 1).
**D-2000 Elite HPLC System Manager Report**

Analyzed Date and Time: 02/15/2016 12:54 PM

Reported Date and Time: 02/19/2016 03:35 PM

Processed Date and Time: 02/19/2016 03:35 PM

Data Path: D:\Vishal\DATA\0012\  
Processing Method: test-IPA/Hx

System (acquisition): Sys 1 Series: 0012  
Application(data): Vishal Vial Number: 3

Sample Name: Vms-02-93 (Co) Vial Type: UNK

Injection from this vial: 1 of 1 Volume: 20.0 ul

Sample Description: 12% IPA+HX 1.0 mL/MIN COL-IA

---

Chrom Type: Fixed WL Chromatogram, 280 nm

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**Processing Method:** test-IPA/Hx  
**Column Type:** IA  
**Method Developer:** Vishal  
**Method Description:**

Chrom Type: Fixed WL Chromatogram, 280 nm

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**Peak Quantitation:** AREA

**Calculation Method:** EXT-STD

**Scale Factor 1:** 1.000

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**Peak rejection level:** 200

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**Fig S188.** HPLC analysis of the co-injection of racemic and chiral compound 7 obtained, for comparison (Table 3, entry 1).

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D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2015/12/23 03:54 下午
Processed Date and Time: 2015/12/24 03:08 下午
Reported Date and Time: 2015/12/24 03:08 下午

Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0090\DATA
Processing Method: test-IPA/Hx
System (acquisition): Sys 1 Series: 0090
Application (data): Vishal Vial Number: 1
Sample Name: VMS-03-77 (Racemic) Vial Type: UNK
Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 275 nm

Processing Method: test-IPA/Hx
Column Type: ODH Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 275 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200000

Fig S189. HPLC analysis of the racemic compound 8, for comparison (Table 3, entry 2).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2015/12/23 04:38 PM
Reported Date and Time: 2015/12/24 03:19 PM
Processed Date and Time: 2015/12/24 03:18 PM

Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0091\n
Processing Method: test-IPA/Hx

System (acquisition): Sys 1
Series: 0091
Application (data): Vishal
Vial Number: 2
Sample Name: VMS-03-77 (Chiral)
Injection from this vial: 1 of 1
Volume: 20.0 µl
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 275 nm

Processing Method: test-IPA/Hx
Column Type: ODH
Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 275 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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3105784  53368  100.000

Peak rejection level: 200

Fig S190. HPLC analysis of the chiral compound 8 obtained (Table 3, entry 2).
Fig S191. HPLC analysis of the co-injection of racemic and chiral compound 8 obtained, for comparison (Table 3, entry 2).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 05/14/2016
Processed Date and Time: 05/14/2016
Reported Date and Time: 05/14/2016

Data Path: D:\Vishal\DATA\0107\
Processing Method: test-IPA/Hx 2
System (acquisition): Sys 1 Series: 0107
Application(data): Vishal Vial Number: 1
Sample Name: VMS-03-82 (Racemic) Vial Type: UNK
Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA Method Developer: Vishal
Method Description:

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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| Total | 4040841 | 71997 | 100.000 |

Peak rejection level: 200

Fig S192. HPLC analysis of the racemic compound 6, for comparison (Table 3, entry 3).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 05/14/2016  02:07 AM
Processed Date and Time: 05/14/2016  04:28 PM
Data Path: D:\Vishal\DATA\0108\nProcessing Method: test-IPA/Hx 2

System (acquisition): Sys 1  Series: 0108
Application(data): Vishal  Vial Number: 2
Sample Name: VMS-03-82 (Chiral)  Vial Type: UNK
Injection from this vial: 1 of 1  Volume: 20.0 ul
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA  Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 254 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
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3895914  75013  100.000

Peak rejection level: 200

Fig S193. HPLC analysis of the chiral compound 6 obtained (Table 3, entry 3).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 05/14/2016 02:40 AM
Processed Date and Time: 05/14/2016 04:37 PM

Data Path: D:\Vishal\DATA\0109\nProcessing Method: test-IPA/Hx 2

System (acquisition): Sys 1
Application(data): Vishal
Sample Name: VMS-03-82 (Co)
Injection from this vial: 1 of 1
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
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Method Developer: Vishal
Method Description:

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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3138970  60472  100.000

Peak rejection level: 200

Fig S194. HPLC analysis of the co-injection of racemic and chiral compound 6 obtained, for comparison (Table 3, entry 3).
Fig S195. HPLC analysis of the racemic compound 9, for comparison (Table 3, entry 4).
Fig S196. HPLC analysis of the chiral compound 9 obtained (Table 3, entry 4).
Fig S197. HPLC analysis of the co-injection of racemic and chiral compound 9 obtained, for comparison (Table 3, entry 4).
Fig S198. HPLC analysis of the racemic compound 3, for comparison (Table 3, entry 5).
Fig S199. HPLC analysis of the chiral compound 3 obtained (Table 3, entry 5).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 06/04/2016 04:36 PM
Reported Date and Time: 06/04/2016 05:19 PM
Processed Date and Time: 06/04/2016 05:18 PM
Data Path: D:\Vishal\DATA\0128\
Processing Method: test-IPA/Hx 1

System (acquisition): Sys 1
Series: 0128
Application (data): Vishal
Vial Number: 3
Sample Name: VMS-03-126 (Co)
Vial Type: UNK
Injection from this vial: 1 of 1
Volume: 20.0 ul
Sample Description: 15%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 1
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Chrom Type: Fixed WL Chromatogram, 254 nm
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5738822 177463 100.000

Peak rejection level: 100000

Fig S200. HPLC analysis of the co-injection of racemic and chiral compound 3 obtained, for comparison (Table 3, entry 5).
Fig S201. HPLC analysis of the chiral compound 6 obtained, (Scheme 4A, two-pot).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 05/14/2016          Reported Date and Time: 05/14/2016
          01:34 AM                                      04:10 PM

Processed Date and Time: 05/14/2016
          04:08 PM

Data Path: D:\Vishal\DATA\0107\
Processing Method: test-IPA/Hx 2

System (acquisition): Sys 1                 Series: 0107
Application(data): Vishal                     Vial Number: 1
Sample Name: VMS-03-82 (Racemic)            Vial Type: UNK
Injection from this vial: 1 of 1             Volume: 20.0 ul
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA                               Method Developer: Vishal
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Chrom Type: Fixed WL Chromatogram, 254 nm

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4040841       71997      100.000

Peak rejection level: 200

Fig S202. HPLC analysis of the racemic compound 6, for comparison (Scheme 4A, two-pot).
Fig S203. HPLC analysis of the co-injection of racemic and chiral compound 6 obtained, for comparison (Scheme 4A, two-pot).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 02/23/2016 03:19 PM
Reported Date and Time: 02/23/2016 04:06 PM
Processed Date and Time: 02/23/2016 04:06 PM

Data Path: D:\Vishal\DATA\0101\nProcessing Method: test-IPA/Hx 2

System (acquisition): Sys 1  Series: 0101
Application(data): Vishal  Vial Number: 1
Sample Name: VMS-03-99 (Racemic)  Vial Type: UNK
Injection from this vial: 1 of 1  Volume: 20.0 ul
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

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3507853  46992  100.000

Peak rejection level: 200

Fig S204. HPLC analysis of the racemic compound 6, for comparison  (Scheme 4A, one-pot).
Fig S205. HPLC analysis of the chiral compound 6 obtained (Scheme 4A, one-pot).
Fig S206. HPLC analysis of the co-injection of racemic and chiral compound 6 obtained, for comparison (Scheme 4A, one-pot).
**D-2000 Elite HPLC System Manager Report**

Analyzed Date and Time: 08/26/2016 05:15 PM  
Reported Date and Time: 08/31/2016 05:20 PM  
Processed Date and Time: 08/31/2016 05:19 PM  

Data Path: D:\Vishal\DATA\0171\  
Processing Method: test- 10% MeOH/EA/Hx 7

System (acquisition): Sys 1  
Application(data): Vishal  
Sample Name: VMS-02-221 (Chiral)  
Injection from this vial: 1 of 1  
Volume: 20.0 ul  
Sample Description: 10%me/ea+HX 1mL/MIN COL-ODH

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test- 10% MeOH/EA/Hx 7  
Column Type: ODH  
Method Developer: Vishal

Method Description:

Chrom Type: Fixed WL Chromatogram, 280 nm

Peak Quantitation: AREA  
Calculation Method: EXT-STD  
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2818448 154728 100.000

Peak rejection level: 200

Fig S207. HPLC analysis of the chiral compound 5 obtained, (Scheme 4A).
Fig S208. HPLC analysis of the racemic compound 5, for comparison (Scheme 4A).
Fig S209. HPLC analysis of the co-injection of racemic compound 5 and chiral compound 5 obtained, for comparison (Scheme 4A).
Fig S210. HPLC analysis of the racemic compound 3, for comparison (Scheme 4B).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 06/04/2016 04:05 PM
Processed Date and Time: 06/04/2016 04:41 PM
Reported Date and Time: 06/04/2016 04:42 PM

Data Path: D:\Vishal\DATA\0127\ 
Processing Method: test-IPA/Hx 1

System (acquisition): Sys 1  
Application(data): Vishal
Sample Name: VMS-03-126 (Chiral)  
Injection from this vial: 1 of 1
Volume: 20.0 ul  
Sample Description: 15%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 1  
Column Type: IA  
Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 254 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 100000

Fig S211. HPLC analysis of the chiral compound 3 obtained (Scheme 4B).
Fig S212. HPLC analysis of the co-injection of racemic compound 3 and chiral compound 3, for comparison (Scheme 4B).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 10/25/2016 06:59 PM   Reported Date and Time: 10/25/2016 07:32 PM
Processed Date and Time: 10/25/2016 07:31 PM
Data Path: D:\Vishal\DATA\0174\   Processing Method: test- 10% MeOH/EA/Hx 7
System (acquisition): Sys 1   Series: 0174
Application(data): Vishal   Vial Number: 1
Sample Name: VMS-03-145 (Racemic)   Vial Type: UNK
Injection from this vial: 1 of 1   Volume: 20.0 ul
Sample Description: 10%me/ea+HX 1mL/MIN COL-ODH

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test- 10% MeOH/EA/Hx 7
Column Type: ODH   Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 280 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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5842968  285934  100.000

Peak rejection level: 200

Fig S213. HPLC analysis of the racemic compound 5, for comparison (Scheme 4B).
Fig S214. HPLC analysis of the chiral compound 5 obtained (Scheme 4B).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 10/25/2016 10:31 PM
Reported Date and Time: 10/25/2016 11:11 PM
Processed Date and Time: 10/25/2016 11:10 PM
Data Path: D:\Vishal\DATA\0177\nProcessing Method: test- 10% MeOH/EA/Hx 7
System (acquisition): Sys 1
Series: 0177
Application (data): Vishal
Sample Name: VMS-03-145 (Co)
Vial Number: 1
Volume: 20.0 ul
Injection from this vial: 1 of 1
Sample Description: 10%me/ea+HX 1mL/MIN COL-ODH

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test- 10% MeOH/EA/Hx 7
Column Type: ODH
Method Developer: Vishal
Method Description:

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200

Fig S215. HPLC analysis of the co-injection of racemic compound 5 and chiral compound 5, for comparison (Scheme 4B).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 07/14/2016 08:51 PM
Processed Date and Time: 07/15/2016 12:10 PM
Reported Date and Time: 07/15/2016 12:12 PM

Data Path: D:\Vishal\DATA\0129\Data Path: D:\Vishal\DATA\0129\ processed: test-IPA/Hx 2

System (acquisition): Sys 1, Series: 0129
Application (data): Vishal, Vial Number: 1
Sample Name: VMS-02-231 (Racemic), Vial Type: UNK
Injection from this vial: 1 of 1, Volume: 20.0 ul
Sample Description: 12%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA
Method Developer: Vishal
Method Description:
Chrom Type: Fixed WL Chromatogram, 254 nm
Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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| Total | 2906535 | 52086 | 100.000 |

Peak rejection level: 200

Fig S216. HPLC analysis of the racemic compound 13, for comparison (Scheme 4C).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 07/15/2016 04:19 PM
Processed Date and Time: 07/15/2016 05:00 PM
Reported Date and Time: 07/15/2016 05:01 PM

Data Path: D:\Vishal\DATA\0132\n
Processing Method: test-IPA/Hx 2
System (acquisition): Sys 1
Series: 0132
Application(data): Vishal
Vial Number: 1
Sample Name: VMS-03-131 (Chiral)
Vial Type: UNK
Injection from this vial: 1 of 1
Volume: 20.0 ul
Sample Description: 12%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA
Method Developer: Vishal
Method Description:
Chrom Type: Fixed WL Chromatogram, 254 nm
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Calculation Method: EXT-STD
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Peak rejection level: 200

Fig S217. HPLC analysis of the chiral compound 13 obtained (Scheme 4C).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 10/12/2016 09:41 PM
Reported Date and Time: 10/12/2016 10:35 PM
Processed Date and Time: 10/12/2016 10:35 PM
Data Path: D:\Vishal\DATA\0173\nProcessing Method: test-IPA/Hx 2

System (acquisition): Sys 1 Series: 0173
Application(data): Vishal Vial Number: 1
Sample Name: VMS-03-131 (Co) Vial Type: UNK
Injection from this vial: 1 of 1 Volume: 20.0 ul
Sample Description: 12%IPA+HX 1.0mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx 2
Column Type: IA Method Developer: Vishal
Method Description:

Chrom Type: Fixed WL Chromatogram, 254 nm
Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200

Fig S218. HPLC analysis of the co-injection of racemic and chiral compound 13 obtained, for comparison (Scheme 4C).
Fig S219. HPLC analysis of the racemic compound 15, for comparison (Scheme 4C).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 07/28/2016
Processed Date and Time: 07/29/2016
Reported Date and Time: 07/29/2016

Data Path: D:\Vishal\DATA\0157\nProcessing Method: test- 10% MeOH/EA/Hx 7
System (acquisition): Sys 1
Application(data): Vishal
Sample Name: VMS-03-137 (Chiral)
Injection from this vial: 1 of 1
Sample Description: 10%me/ea+HX 0.5mL/MIN COL-ODH

Chrom Type: Fixed WL Chromatogram, 300 nm

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6663878  251596  100.000

Peak rejection level: 200000

Fig S220. HPLC analysis of the chiral compound 15 obtained (Scheme 4C).
Fig S221. HPLC analysis of the co-injection of racemic compound 15 and chiral compound 15, for comparison (Scheme 4C).
Fig S222. HPLC analysis of the racemic compound 8, for comparison (Scheme 5).
Fig S223. HPLC analysis of the chiral compound 8 obtained (Scheme 5).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 2015/12/23 05:18 下午  
Processed Date and Time: 2015/12/24 03:21 下午  
Reported Date and Time: 2015/12/24 03:21 下午  
Data Path: C:\WIN32APP\D2000HSM\Vishal\DATA\0092\  
Processing Method: test-IPA/Hx

System (acquisition): Sys 1  
Application(data): Vishal  
Sample Name: VMS-03-77 (Co)  
Injection from this vial: 1 of 1  
Volume: 20.0 ul  
Sample Description: 12%IPA+HX 1mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 275 nm

Processing Method: test-IPA/Hx  
Column Type: ODH  
Method Developer: Vishal

Method Description:

Peak Quantitation: AREA  
Calculation Method: EXT-STD  
Scale Factor 1: 1.000

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8627022 134337 100.000

Peak rejection level: 200000

Fig S224. HPLC analysis of the co-injection of racemic compound 8 and chiral compound 8, for comparison (Scheme 5).
Fig S225. HPLC analysis of the racemic compound 7, for comparison (Scheme 5).
**D-2000 Elite HPLC System Manager Report**

Analyzed Date and Time: 02/15/2016
Reported Date and Time: 02/19/2016 04:15 PM

Processed Date and Time: 02/19/2016 04:15 PM

Data Path: D:\Vishal\DATA\0011\
Processing Method: test-IPA/Hx

System (acquisition): Sys 1  Series: 0011
Application(data): Vishal  Vial Number: 2
Sample Name: Vms-02-93 (Chiral)  Vial Type: UNK
Injection from this vial: 1 of 1  Volume: 20.0 ul
Sample Description: 12% IPA+HX 1.0 mL/Min COL-IA

Chrom Type: Fixed WL Chromatogram, 280 nm

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Peak rejection level: 200

**Fig S226.** HPLC analysis of the chiral compound 7 obtained (Scheme 5).
Fig S227. HPLC analysis of the co-injection of racemic compound 7 and chiral compound 7, for comparison (Scheme 5).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 01/18/2016
Processed Date and Time: 01/18/2016
Reported Date and Time: 01/18/2016

Data Path: D:\Vishal\DATA\0004\n
System (acquisition): Sys 1
Application (data): Vishal
Sample Name: Vms-02-86 (racemic)
Sample Description: 12% IPA+HX 1.0 mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx
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Method Description:
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Scale Factor 1: 1.000

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Peak rejection level: 200000

Fig S228. HPLC analysis of the racemic compound 9, for comparison (Scheme 5).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 01/18/2016
10:28 PM
Reported Date and Time: 01/18/2016
11:23 PM
Processed Date and Time: 01/18/2016
11:21 PM
Data Path: D:\Vishal\DATA\0005\
Processing Method: test-IPA/Hx
System (acquisition): Sys 1
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Application(data): Vishal
Series: 0005
Vial Number: 2
Sample Name: Vms-02-86 (Chiral)
Vial Type: UNK
Injection from this vial: 1 of 1
Volume: 20.0 ul
Sample Description: 12% IPA+HX 1.0 mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx
Column Type: IA
Method Developer: Vishal
Method Description:
Chrom Type: Fixed WL Chromatogram, 254 nm
Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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3887646  48141  100.000

Peak rejection level: 200

Fig S229. HPLC analysis of chiral compound 9 obtained (Scheme 5).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 01/18/2016 11:07 PM
Processed Date and Time: 01/18/2016 11:54 PM
Reported Date and Time: 01/18/2016 11:54 PM

Data Path: D:\Vishal\DATA\0006\nProcessing Method: test-IPA/Hx

System (acquisition): Sys 1
Application (data): Vishal
Sample Name: Vms-02-86 (Co)
Injection from this vial: 1 of 1
Sample Description: 12% IPA+HX 1.0 mL/MIN COL-IA

Chrom Type: Fixed WL Chromatogram, 254 nm

Processing Method: test-IPA/Hx
Column Type: IA
Method Developer: Vishal
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Chrom Type: Fixed WL Chromatogram, 254 nm
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3312611  39009  100.000

Peak rejection level: 200

Fig S230. HPLC analysis of the co-injection of racemic compound 9 and chiral compound 9, for comparison (Scheme 5).
Fig S231. HPLC analysis of the racemic compound 5, for comparison (Scheme 6, two-pot synthesis).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 01/21/2017 10:50 PM
Processed Date and Time: 01/21/2017 11:37 PM
Reported Date and Time: 01/21/2017 11:38 PM

Data Path: D:\Vishal\DATA\0183\ 
Processing Method: test- 10% MeOH/EA/Hx 7
System (acquisition): Sys 1 
Application(data): Vishal 
Sample Name: VMS-03-159 (Chiral) 
Injection from this vial: 1 of 1 
Volume: 20.0 ul
Sample Description: 10%me/ea+HX 0.5mL/MIN COL-ODH

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test- 10% MeOH/EA/Hx 7
Column Type: ODH 
Method Developer: Vishal
Method Description:
Chrom Type: Fixed WL Chromatogram, 280 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200

Fig S232. HPLC analysis of the chiral compound 5 obtained (Scheme 6, two-pot synthesis).
Fig S233. HPLC analysis of the co-injection of racemic compound 5 and chiral compound 5, for comparison (Scheme 6, two-pot synthesis).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 01/21/2017 09:12 PM
Processed Date and Time: 01/21/2017 10:31 PM
Reported Date and Time: 01/21/2017 10:32 PM

Data Path: D:\Vishal\DATA\0180\Series: 1
Processing Method: test- 10% MeOH/EA/Hx 7
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Application(data): Vishal
Sample Name: VMS-03-162 (Racemic)
Injection from this vial: 1 of 1
Vial Number: 1
Vial Type: UNK
Volume: 20.0 ul
Sample Description: 10%me/ea+HX 1mL/MIN COL-ODH

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test- 10% MeOH/EA/Hx 7
Column Type: ODH
Method Developer: Vishal
Method Description:
Chrom Type: Fixed WL Chromatogram, 280 nm
Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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Peak rejection level: 200

**Fig S234.** HPLC analysis of the racemic compound 5, for comparison (Scheme 6, one-pot synthesis).
Fig S235. HPLC analysis of the chiral compound 5 obtained (Scheme 6, one-pot synthesis).
D-2000 Elite HPLC System Manager Report

Analyzed Date and Time: 01/21/2017
Reported Date and Time: 01/21/2017
10:15 PM
11:14 PM

Processed Date and Time: 01/21/2017
11:13 PM

Data Path: D:\Vishal\DATA\0182\
Processing Method: test- 10% MeOH/EA/Hx 7

System (acquisition): Sys 1
Series: 0182
Application (data): Vishal
Vial Number: 3
Sample Name: VMS-03-162 (Co)
Vial Type: UNK
Injection from this vial: 1 of 1
Volume: 20.0 ul
Sample Description: 10%me/ea+HX 1mL/MIN COL-ODH

Chrom Type: Fixed WL Chromatogram, 280 nm

Processing Method: test- 10% MeOH/EA/Hx 7
Column Type: ODH
Method Developer: Vishal

Method Description:

Chrom Type: Fixed WL Chromatogram, 280 nm

Peak Quantitation: AREA
Calculation Method: EXT-STD
Scale Factor 1: 1.000

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4805246 230960 100.000

Peak rejection level: 200

Fig S236. HPLC analysis of the co-injection of racemic compound 5 and chiral compound 5, for comparison (Scheme 6, one-pot synthesis).