Supporting Information

Asymmetric Simmons-Smith Cyclopropanation of Allylic Amines

Varinder K. Aggarwal,^{*,†} Guang yu Fang,[†] Graham Meek[‡]

Department of Chemistry, University of Bristol, Cantock's Close, Bristol and Dowpharma,
Chiretech Technology Ltd., A Subsidiary of the Dow Chemical Company, Cambridge
Science Park, Milton Road, Cambridge, UK.

e-mail: V.Aggarwal@bristol.ac.uk

Experimental Procedures and spectral data

General procedures

All air and water sensitive reactions were carried out in oven dried glassware under an argon atmosphere. Solvents were dried by standard methods.¹ NMR spectra were recorded on Jeol 270 MHz or Jeol 400 MHz spectrometers using tetramethylsilane as the internal standard (0.00 ppm). CDCl₃ was used as the internal standard for ¹³C NMR spectra. CI mass spectra were obtained using a VG Platform mass spectrometer. IR spectra were obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. Flash chromatography was performed using silica gel (Merck Kieselgel 60). Melting points were determined with a Kofler hot stage apparatus and were not corrected. Optical rotations were determined using a Perkin-Elmer 241MC polarimeter.

(*S*)-*N*-(2-Hydroxy-1-phenyl-ethyl)-formamide², (*S*)-*N*-methyl-2-phenylglycinol³ and compounds (**9**)⁴ and (**10**)⁵ were prepared by literature methods.

General Procedures for 3a-h, 5a-f and 7

The 1,2-aminoalcohol (15.0 mmol) was mixed with NaHCO₃ (30.0 mmol) in DMF (15 mL) and then heated to 70 °C. The allylic bromide (15.7 mmol) in DMF (5 mL) was added to this solution over 3 hours. After the addition was complete the reactants were stirred for another 2 hours and the reaction was then quenched with water (100 mL). The mixture was extracted with petrol (2 x 30 mL). The organic solution was dried over Na₂SO₄ and concentrated under reduced pressure. The crude products were used in the next transformation without further purification.

(2*S*)-2-{Methyl[(*E*)-3-phenyl-2-propenyl]amino}-2-phenylethan-1-ol (**3a**)

The compound was obtained as a pale yellow oil (1.430 g, 89%), [α]_D²⁰ +91 (*c* = 0.005 g/mL, CHCl₃). ν_{max} /cm⁻¹ (neat) 3409, 3026, 2938, 2794, 1599, 1450. ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.20 (10H, m, ArH), 6.48 (1H, d, *J*=15.8 Hz, PhCHCH), 6.22 (1H, ddd, *J*=15.8, 7.3, 6.2 Hz, PhCHCH), 4.01 (1H, dd, *J*=10.6, 9.6 Hz, OCHHCH), 3.85 (1H, dd, *J*=9.6, 5.2 Hz, PhCHN), 3.69 (1H, dd, *J*=10.6, 5.2 Hz, OCHHCH), 3.26 (1H, ddd, *J*=13.7, 6.2, 1.3 Hz, NCHHCH), 3.06 (1H, dd, *J*=13.7, 7.3 Hz, NCHHCH), 2.20 (3H, s, NCH₃). ¹³C NMR (101 MHz, CDCl₃) δ 137.0, 135.7, 132.7, 129.1, 128.6, 128.4, 128.0, 127.7, 127.6, 126.4, 68.1, 61.0, 56.8, 37.2. *m/z* (CI) 268 (*M*+1, 8), 250 (11), 117 (100). HRMS found: 268.1689, C₁₈H₂₂NO required: 268.1701.

(2*S*)-2-Phenyl-2-[[(*E*)-3-phenyl-2-propenyl]amino]ethan-1-ol (**3b**)

The compound was obtained as pale yellow oil (2.873 g, 84%), $[\alpha]_D^{20} +66$ ($c = 0.013$ g/mL, CHCl_3). $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3325, 3060, 3026, 2835, 1599, 1449. ^1H NMR (270 MHz, CDCl_3) δ 7.34-7.21 (10H, m, ArH), 6.44 (1H, d, $J=15.9$ Hz, PhCHCH), 6.23 (1H, dt, $J=15.9$, 6.3 Hz, NCH₂CH), 3.84 (1H, dd, $J=8.6$, 4.3 Hz, PhCHN), 3.72 (1H, dd, $J=10.3$, 4.3 Hz, OCHHCH), 3.58 (1H, dd, $J=10.3$, 8.6 Hz, OCHHCH), 3.35 (1H, ddd, $J=14.2$, 6.0, 1.6 Hz, NCHHCH), 3.22 (1H, ddd, $J=14.2$, 6.6, 1.0 Hz, NCHHCH). ^{13}C NMR (68 MHz, CDCl_3) δ 140.6, 137.1, 131.6, 128.8, 128.6, 128.2, 127.7, 127.5, 127.4, 126.4, 66.8, 64.0, 49.4. m/z (CI) 254 (M+1, 91), 222 (52), 117 (100). HRMS found: 254.2539, $\text{C}_{17}\text{H}_{20}\text{NO}$ required: 254.1544.

(2S)-2-[Methyl[(E)-3-phenyl-2-propenyl]amino]-2-phenylethan-1-ol (3c)

The compound was obtained as white solid (0.943 g, 93%), $[\alpha]_D^{20} +170$ ($c = 0.007$ g/mL, CHCl_3). M.p.: 93-5 °C. $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3348, 2926, 2778, 1456. ^1H NMR (400 MHz, CDCl_3) δ 7.21-7.43 (15H, m, ArH), 6.51 (1H, d, $J=15.6$ Hz, PhCHCH), 6.19 (1H, ddd, $J=15.6$, 8.3, 4.9 Hz, PhCHCH), 4.17-4.08 (2H, m, PhCHN+ OCHHCH), 4.04 (1H, d, $J=13.7$ Hz, PhCHHN), 3.52-3.78 (2H, br, OCHHCH + NCHHCH), 3.21 (1H, d, 13.7 Hz, PhCHHN), 3.00 (1H, dd, $J=14.2$, 8.3 Hz, NCHHCH). ^{13}C NMR (101 MHz, CDCl_3) δ 138.6, 136.8, 135.4, 129.4, 128.2, 128.0, 127.6, 127.4, 127.3, 126.4, 125.1, 64.2, 60.7, 53.9, 52.2, 20.4, 17.3, 12.0. m/z (CI) 344 (M+1, 53), 326 (31), 312 (52), 117 (100). HRMS found: 344.2026, $\text{C}_{24}\text{H}_{26}\text{NO}$ required: 344.2014.

(2S)-2-[(Z)-2-Hexenyl(methyl)amino]-2-phenylethan-1-ol (3d)

The compound was obtained as a colourless oil (1.052 g, 78%), $[\alpha]_D^{20} +56$ ($c = 0.008$ g/mL, CHCl_3). $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3418, 2957, 2871, 1452. ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.29 (3H, m, ArH), 7.21-7.15 (2H, m, ArH), 5.55 (1H, ddd, $J=7.5$, 6.2, 5.5 Hz,

NCH₂CH), 5.47 (1H, dt, *J*=7.5, 7.0 Hz, CHCH₂CH₂), 3.97 (1H, dd, *J*=10.8, 10.0 Hz, OCHHCH), 3.82 (1H, dd, *J*= 10.0 Hz, 4.9 Hz, PhCHN), 3.65 (1H, dd, *J*=10.8, 4.9 Hz, OCHHCH), 3.07 (1H, dd, *J*=13.9, 5.5 Hz, NCHHCH), 2.96 (1H, dd, *J*=13.9, 6.2 Hz, NCHHCH), 2.15 (3H, s, NCH₃), 1.97 (2H, tdd, *J*=7.0, 7.3, 2.5 Hz, CHCH₂CH₂), 1.36 (2H, sextet, *J*=7.3 Hz, CH₃CH₂), 0.87 (3H, t, *J*=7.3 Hz, CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 135.8, 134.2, 129.1, 128.3, 127.9, 127.7, 67.5, 60.8, 56.6, 36.9, 34.6, 22.6, 13.8. *m/z* (CI) 234 (M+1, 74), 216 (39), 202 (100). HRMS found: 234.1849, C₁₅H₂₄NO required: 234.1858.

(2S)-2-[(E)-2-Hexenyl(methyl)amino]-2-phenylethan-1-ol (3e)

The compound was obtained as a colourless oil (1.266 g, 81%), [α]_D²⁰ +63 (*c* = 0.006 g/mL, CHCl₃). $\nu_{\max}/\text{cm}^{-1}$ (neat) 3418, 2957, 2872, 1452. ¹H NMR (400 MHz, CDCl₃) δ 7.37-7.31 (3H, m, ArH), 7.21-7.17 (2H, m, ArH), 5.55 (1H, dt, *J*=15.4, 6.6 Hz, NCH₂CH), 5.46 (1H, dt, *J*=15.4, 7.3 Hz, CHCH₂CH₂), 3.97 (1H, t, *J*=10.2 Hz, OCHHCH), 3.82 (1H, dd, *J*=10.2, 5.1 Hz, PhCHN), 3.64 (1H, dd, *J*=10.2, 5.1 Hz, OCHHCH), 3.06 (1H, dd, *J*=13.2, 5.5 Hz, NCHHCH), 2.83 (1H, dd, *J*=13.2, 7.0 Hz, NCHHCH), 2.13 (3H, s, NCH₃), 2.01 (2H, q, *J*=7.3 Hz, CHCH₂CH₂), 1.39 (2H, sextet, *J*=7.3 Hz, CH₂CH₃), 0.90 (3H, t, *J*=7.3 Hz, CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 135.7, 134.1, 129.1, 128.2, 127.8, 127.6, 67.5, 60.8, 56.5, 36.8, 34.5, 22.5, 13.7. *m/z* (CI) 234 (M+1, 88), 216 (67), 202 (100). HRMS found: 234.1857, C₁₅H₂₄NO required: 234.1858.

(2S)-2-[Methyl(3-methyl-2-butenyl)amino]-2-phenylethan-1-ol (3f)

The compound was obtained as a colourless oil (1.540 g, 97%), [α]_D²⁰ +72 (*c* = 0.007 g/mL, CHCl₃). $\nu_{\max}/\text{cm}^{-1}$ (neat) 3408, 3060, 3029, 2969, 2792, 1673, 1451. ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.33 (3H, m, ArH), 7.21-7.15 (2H, m, ArH), 5.24 (1H, t, *J*=6.6 Hz, CH₂CH), 3.97 (1H, t, *J*=10.0 Hz, OCHHCH), 3.81 (1H, dd, *J*=10.0, 4.8 Hz, PhCHN), 3.62 (1H, dd, *J*=10.0, 5.1 Hz, OCHHCH), 3.02 (1H, dd, *J*=13.6, 6.2 Hz, NCHHCH), 2.88 (1H, dd,

$J=13.6$, 7.7 Hz $NCHHCH$), 2.12 (3H, s, NCH_3), 1.71 (3H, s, $CHC(CH_3)CH_3$), 1.59 (3H, s, $CHC(CH_3)CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.8, 135.1, 129.1, 128.2, 127.8, 122.0, 67.6, 60.8, 51.9, 36.9, 25.9, 18.2. m/z (CI) 220 ($M+1$, 19), 202 (39), 188 (47), 134 (50), 121 (54), 105 (62), 69 (100). HRMS found: 220.1694, $C_{14}H_{22}NO$ required: 220.1701.

(E)-4-[[*(1S)*-2-Hydroxy-1-phenylethyl](methyl)amino]-2-buten-1-ol (3g)

The compound was obtained as a colourless oil (0.762 g, 75%), $[\alpha]_D^{20} +34$ ($c = 0.008$ g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3332, 2850, 1452. 1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.31 (3H, ArH), 7.22-7.16 (2H, m, ArH), 5.81-5.72 (2H, m, $CHCH$), 4.14 (2H, d, $J=5.2$ Hz, OCH_2CH), 3.97 (1H, t, $J=9.6$ Hz, $OCHHCH$), 3.81 (1H, dd, $J=9.6$, 4.8 Hz, $PhCHN$), 3.65 (1H, dd, $J=9.6$, 4.8 Hz, $OCHHCH$), 3.12 (1H, dd, $J=13.3$, 4.8 Hz, $NCHHCH$), 2.92 (1H, dd, $J=13.3$, 6.4 Hz, $NCHHCH$), 2.16 (3H, s, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 132.6, 129.2, 129.1, 128.3, 128.0, 67.7, 63.1, 60.9, 55.9, 37.1. m/z (CI) 222 ($M+1$, 82), 204 (100), 190 (95). HRMS found: 222.1490, $C_{13}H_{20}NO_2$ required: 222.1494.

Methyl (E)-4-[[*(1S)*-2-hydroxy-1-phenyl-ethyl](methyl)amino]-2-buten-1-ol (3h)

The compound was obtained as a colourless oil (1.827 g, 89%), $[\alpha]_D^{20} +47$ ($c = 0.015$ g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3425, 3029, 2950, 2797, 1721, 1658, 1436. 1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (3H, m, ArH), 7.24-7.18 (2H, m, ArH), 6.36 (1H, dt, $J=11.4$, 6.2 Hz, NCH_2CH), 5.97 (1H, d, $J=11.4$ Hz, $CHCO_2Me$), 3.95 (1H, dd, $J=8.4$, 6.7 Hz, $PhCHN$), 3.74 (1H, dd, $J=12.5$, 8.4 Hz, $OCHHCH$), 3.73 (3H, s, CO_2CH_3), 3.68 (1H, dd, $J=12.5$, 6.7 Hz, $OCHHCH$), 3.23 (1H, dd, $J=13.8$, 6.3 Hz, $NCHHCH$), 3.06 (1H, dd, $J=13.8$, 7.3 Hz, $NCHHCH$), 2.19 (3H, s, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 146.4, 136.3, 128.9, 128.4, 128.0, 122.6, 69.0, 61.6, 55.3, 51.2, 38.0. m/z (CI) 250 ($M+1$, 100), 232 (47), 218 (60), 130 (77). HRMS found: 250.1441, $C_{14}H_{20}NO_3$ required: 250.1443.

(1*R*, 2*R*)-2-[Methyl-[(*E*)-3-phenyl-2-propenyl]amino]-1-phenylpropan-1-ol (5a)

The compound was obtained as a white solid (2.548 g, 92%), $[\alpha]_D^{20}$ -130 ($c = 0.021$ g/mL, CHCl_3). M.p.: 60-2 °C. $\nu_{\text{max}}/\text{cm}^{-1}$ (CH_2Cl_2) 3381, 3062, 3031, 2975, 2844, 1604, 1448. ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.27 (10H, m, ArH), 6.54 (1H, d, $J=16.1$ Hz, PhCH=), 6.27 (1H, dt, $J=16.1, 6.4$ Hz, NCH_2CH), 4.27 (1H, d, $J=9.8$ Hz, PhCHOH), 3.39 (1H, dd, $J=13.7, 6.4$ Hz, NCHHCH), 3.17 (1H, dd, $J=13.7, 6.4$ Hz, NCHHCH), 2.77-2.73 (1H, m, CH_3CHN), 2.30 (3H, s, NCH_3), 0.77 (3H, d, $J=6.4$ Hz, CH_3CHN). ^{13}C NMR (101 MHz, CDCl_3) δ 142.2, 137.1, 132.6, 128.7, 128.3, 127.7, 127.6, 127.5, 126.5, 75.0, 65.0, 56.5, 36.0, 7.6. m/z (CI) 282 ($M+1$, 17), 176 (56), 117 (85), 91 (100). HRMS found: 282.1859, $\text{C}_{19}\text{H}_{24}\text{NO}$ required: 282.1858.

***N*-[(1*R*, 2*R*)-2-Methoxy-1-methyl-2-phenylethyl]-*N*-methyl-*N*-[(*E*)-3-phenyl-2-propenyl]amine (5b)**

2-[Methyl-(3-phenyl-allyl)-amino]-1-phenyl-propan-1-ol (562 mg, 2.0 mmol) was dissolved in anhydrous THF (15 mL). To this solution was added NaH (60% in mineral oil, 120 mg, 3.0 mmol) at 0 °C. After 1 hour, methyl iodide (0.15 mL, 2.4 mmol) was added. The reactants were stirred at room temperature for 24 hours. The reaction was quenched with sat. NaHCO_3 (20 mL) and extracted with petrol. The organic solution was dried over Na_2SO_4 . After removing the solvent, the residue was further purified by chromatography (silica gel, 5% methanol in DCM, $R_f=0.12$) to yield the product as a pale yellow oil (529 mg, 90%), $[\alpha]_D^{20}$ -98 ($c = 0.013$ g/mL, CHCl_3). $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3060, 3026, 2970, 2933, 2874, 1600. ^1H NMR (270 MHz, CDCl_3) δ 7.37-7.24 (10H, m, ArH), 6.54 (1H, d, $J=15.9$ Hz, CH_2CH), 6.31 (1H, ddd, $J=15.9, 7.3, 6.0$ Hz, $=\text{CHPh}$), 4.08 (1H, d, $J=9.0$ Hz, PhCH), 3.48 (1H, dd, $J=14.0, 6.0$ Hz, NCHHCH), 3.28 (1H, dd, $J=14.0, 7.3$ Hz, NCHHCH), 3.19 (3H, s, OCH_3), 3.11-3.07 (1H, m, NCHCH_3), 2.38 (3H, s, NCH_3), 0.71 (3H, d, $J=7.0$ Hz, CHCH_3). ^{13}C NMR (101 MHz, CDCl_3) δ 140.9, 137.6, 131.6, 129.3, 128.5, 127.9, 127.7, 127.2, 126.4,

86.8, 62.4, 57.2, 56.5, 37.5, 11.7. m/z (CI) 296 (M+1, 47), 174 (88), 117 (100). HRMS found: 296.2017, C₂₀H₂₅NO required: 296.2014.

(1R, 2R)-2-[(E)-2-Hexenyl(methyl)amino]-1-phenylpropan-1-ol (5c)

The compound was obtained as a colourless oil (1.134 g, 85%), $[\alpha]_D^{20}$ - 63 (c = 0.007 g/mL, CHCl₃). $\nu_{\max}/\text{cm}^{-1}$ (neat) 3348, 2959, 2928, 2872, 1453. ^1H NMR (400 MHz, CDCl₃) δ 7.36-7.24 (5H, m, ArH), 5.62-5.54 (1H, m, CHCH), 5.52-5.43 (1H, m, CHCH), 4.22 (1H, d, J =9.6Hz, PhCHOH), 3.16 (1H, dd, J =13.2, 5.5 Hz, NCHHCH), 2.93 (1H, dd, J =13.2, 7.1Hz, NCHHCH), 2.70 (1H, dq, J =9.6, 6.6Hz, CH₃CHN), 2.23 (3H, s, NCH₃), 2.03 (2H, dt, J =7.0, 6.6Hz, CHCH₂CH₂), 1.40 (2H, tq, J =7.3, 7.0Hz, CHCH₂CH₂), 0.91 (3H, t, J =7.3Hz, CH₂CH₃), 0.72 (3H, d, J =6.6 Hz, CH₃CHN). ^{13}C NMR (101 MHz, CDCl₃) δ 142.4, 133.9, 128.2, 127.8, 127.7, 127.4, 74.8, 64.3, 56.2, 35.7, 34.4, 22.5, 13.7, 7.3. m/z (CI) 248 (M+1, 39), 230 (20), 140 (100). HRMS found: 248.2017, C₁₆H₂₅NO required: 248.2014.

(1R, 2R)-2-[(Z)-2-Hexenyl(methyl)amino]-1-phenylpropan-1-ol (5d)

The compound was obtained as a colourless oil (1.241 g, 87%), $[\alpha]_D^{20}$ - 42 (c =0.010 g/mL, CHCl₃). $\nu_{\max}/\text{cm}^{-1}$ (neat) 3362, 2960, 2871, 1453. ^1H NMR (400 MHz, CDCl₃) δ 7.42-7.24 (5H, m, ArH), 5.61-5.47 (2H, m, CHCH), 4.22 (1H, d, J =11.7Hz, PhCHOH), 3.17 (1H, dd, J =13.7, 5.8 Hz, NCHHCH), 3.08 (1H, dd, J =13.7, 6.9Hz, NCHHCH), 2.69 (1H, dq, J =11.7, 6.8Hz, CH₃CHN), 2.25 (3H, s, NCH₃), 2.04 (2H, dt, J =7.3, 6.9Hz, CHCH₂CH₂), 1.39 (2H, sextet, J =7.3Hz, CHCH₂CH₂), 0.90 (3H, t, J =7.3Hz, CH₂CH₃), 0.74 (3H, d, J =6.8 Hz, CH₃CHN). ^{13}C NMR (101 MHz, CDCl₃) δ 142.3, 133.0, 128.2, 127.7, 127.5, 127.3, 74.8, 64.3, 50.4, 35.8, 29.6, 22.8, 13.8, 7.3. m/z (CI) 248 (M+1, 36), 230 (20), 140 (94), 83 (100). HRMS found: 248.2014, C₁₆H₂₅NO required: 248.2014.

(1R, 2R)-2-[Methyl(3-methyl-2-butenyl)amino]-1-phenylpropan-1-ol (5e)

The compound was obtained as a pale yellow oil (1.036 g, 99%), $[\alpha]_D^{20} -76$ ($c = 0.007$ g/mL, CHCl_3), $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3333, 3030, 2970, 2853, 1451. ^1H NMR (400 MHz, CDCl_3) δ 7.42-7.24 (5H, m, ArH), 5.34-5.13 (1H, m, $\text{CHC}(\text{CH}_3)_2$), 4.21 (1H, d, $J=9.7\text{Hz}$, PhCHOH), 3.12 (1H, dd, $J=13.2, 6.4\text{ Hz}$, NCHHCH), 3.00 (1H, dd, $J=13.7, 7.3\text{Hz}$, NCHHCH), 2.68 (1H, dq, $J=9.7, 6.4\text{Hz}$, CH_3CHN), 2.23 (3H, s, NCH_3), 1.76 (3H, s, $\text{C}(\text{CH}_3)\text{CH}_3$), 1.65 (3H, s, $\text{C}(\text{CH}_3)\text{CH}_3$), 0.74 (3H, d, $J=6.4\text{ Hz}$, CH_3CHN). ^{13}C NMR (101 MHz, CDCl_3) δ 143.5, 136.3, 129.3, 128.7, 128.5, 123.2, 75.8, 65.2, 52.4, 36.7, 26.9, 19.1, 8.4. m/z (CI) 234 ($\text{M}+1$, 29), 216 (10), 178 (18), 148 (30), 126 (100). HRMS found: 234.1847, $\text{C}_{15}\text{H}_{23}\text{NO}$ required: 234.1858.

(1R, 2R)-2-[Methyl-(2-methyl-allyl)-amino]-1-phenylpropan-1-ol (5f)

The compound was obtained as a colourless oil (1.125 g, 96%), $[\alpha]_D^{20} 67$ ($c=0.007$ g/mL, CHCl_3). $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3351, 2970, 2850, 1450. ^1H NMR (400 MHz, CDCl_3) δ 7.37-7.25 (5H, m, ArH), 4.91-4.90 (2H, m, CCH_2), 4.26 (1H, d, $J=9.5\text{Hz}$, PhCHOH), 3.12 (1H, d, $J=13.2\text{Hz}$, NCHHC), 2.92 (1H, d, $J=13.2$, NCHHC), 2.67 (1H, dq, $J=9.5, 6.6\text{Hz}$, CH_3CHN), 2.20 (3H, s, NCH_3), 1.83 (3H, s, CH_3CCH_2), 0.73 (3H, d, $J=6.6\text{Hz}$, CH_3CHN). ^{13}C NMR (101 MHz, CDCl_3) δ 142.7, 142.2, 128.2, 127.7, 127.4, 113.6, 74.9, 64.7, 60.6, 35.6, 20.5, 7.1. m/z (CI) 220 ($\text{M}+1$, 43), 202 (50), 112 (100). HRMS found: 220.1700, $\text{C}_{14}\text{H}_{21}\text{NO}$ required: 220.1701.

(1R, 2S)-2-[Methyl-[(E)-3-phenyl-2-propenyl]amino]-1-phenylpropan-1-ol (7)

The compound was obtained as a white solid (1.356 g, 96%), $[\alpha]_D^{20} -108$ ($c = 0.007$ g/mL, CHCl_3). M.p.: 80-1°C. $\nu_{\text{max}}/\text{cm}^{-1}$ (CH_2Cl_2) 3210, 3058, 3031, 2828, 1450. ^1H NMR

(400 MHz, CDCl₃) δ 7.38-7.27 (10H, m, ArH), 6.50 (1H, d, J =16.1 Hz, PhCH=), 6.22 (1H, dt, J =16.1, 6.8 Hz, NCH₂CH), 4.87 (1H, d, J =3.9 Hz, PhCHOH), 3.34-3.24 (2H, m, NCH₂), 2.91 (1H, dq, J = 6.8, 3.9 Hz, CH₃CHN), 2.32 (3H, s, NCH₃), 0.92 (3H, d, J =6.8 Hz, CH₃CHN). ¹³C NMR (101 MHz, CDCl₃) δ 142.5, 137.1, 132.4, 128.6, 128.0, 127.5, 127.0, 126.4, 126.2, 73.2, 63.0, 57.2, 39.2, 10.1. m/z (CI) 282 (M+1, 28), 264 (20), 174 (75), 117 (100). HRMS found: 282.1861, C₁₉H₂₄NO required: 282.1858.

General Procedures for 4b-f and 6a-f

Et₂Zn (1M solution in hexane, 0.60 mL, 0.60 mmol for **4b-f**, and 0.50 mL, 0.50 mmol for **6a-f**) was diluted in anhydrous DCM (2.0 mL). Diiodomethane (182 μ L, 1.20 mmol for **4b-f**, and 81 μ L, 1.00 mmol for **6a-f**) was added to this solution at 0 °C. Twenty minutes after the addition, the allylic amine derivative (**4b-f** or **6a-f**, 0.46 mmol) in DCM (0.5 mL) was added. The mixture was allowed to stir for 48 hours. The reaction was quenched with 10% EDTA (5.0 mL) at room temperature and the product was extracted with DCM (2 $\times$ 30 mL). The organic solution was dried over Na₂SO₄ and concentrated to yield the crude product, which was further purified by chromatography on silica gel.

(2S)-2-(Methyl-[(1S, 2S)-2-phenyl-cyclopropyl](methyl)amino)-2-phenylethan-1-ol (4a)

The compound was obtained as a white solid (0.122 g, 95%) and a 21:1 mixture of diastereoisomers. ¹H NMR (400 MHz, CDCl₃) δ (major isomer) 7.38-7.03 (10H, m, ArH), 3.96 (1H, t, J =10.2 Hz, OCHHCH), 3.81 (1H, dd, J =10.2, 5.0 Hz, PhCHN), 3.65 (1H, dd, J =10.2, 5.0 Hz, OCHHCH), 2.51 (1H, dd, J =12.8, 6.2 Hz, NCHHCH), 2.32 (1H, dd, J =12.8, 6.8 Hz, NCHHCH), 2.30 (3H, s, NCH₃), 1.66 (1H, dt, J =9.3, 4.5 Hz, PhCHCH), 1.21 (1H, m, NCH₂CH), 0.97 (1H, dt, J =8.4, 4.5 Hz, PhCHCHH), 0.79 (1H, dt, J =8.4, 5.4 Hz, PhCHCHH). ¹³C NMR (101 MHz, CDCl₃) δ 142.8, 128.9, 128.4, 128.3, 127.9, 125.8, 125.6, 69.0, 60.8, 58.1, 37.8, 23.1, 22.1, 14.8. m/z (CI) 282 (M+1, 33), 250 (58), 131 (100). HRMS found: 282.1858 C₁₉H₂₄NO required: 282.1858.

(2S)-2-(Benzyl-[[[(1S, 2S)-2-phenylcyclopropyl](methyl)amino]-2-phenylethan-1-ol (4c)

The compound was obtained as a white solid (0.142 g, 87%) and a 12:1 mixture of diastereoisomers. ^1H NMR (400 MHz, CDCl_3) δ (major isomer) 7.40-6.96 (15H, m, ArH), 4.08-4.02 (2H, m, OCHHCH + PhCHN), 3.68-3.57 (3H, m, PhCH₂N + OCHHCH), 2.61 (1H, dd, $J=13.7$, 6.5 Hz, NCHHCH), 2.38 (1H, dd, $J=13.7$, 6.3 Hz, NCHHCH), 1.63 (1H, dt, $J=4.5$, 9.3 Hz, PhCHCH), 1.27-1.22 (1H, m, NCH₂CH), 0.89 (1H, dt, $J=8.4$, 4.5 Hz, PhCHCHH), 0.71 (1H, dt, $J=8.4$, 5.4 Hz, PhCHCHH). ^{13}C NMR (101 MHz, CDCl_3) δ 138.3, 138.0, 137.2, 135.7, 134.1, 132.5, 129.4, 128.3, 127.5, 127.2, 125.4, 64.1, 60.3, m/z (CI) 358 (M+1, 33), 340 (23), 326 (57), 131 (100). HRMS found: 358.2176, $\text{C}_{25}\text{H}_{27}\text{NO}$ required: 358.2171).

(2S)-2-(Methyl-[[[(1S, 2R)-2-propylcyclopropyl](methyl)amino]-2-phenylethan-1-ol (4d)

The compound was obtained as a colourless oil (0.104 g, 92%) and a 20:1 mixture of diastereoisomers. $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3422, 3060, 2927, 2871, 1453, 1025. ^1H NMR (400 MHz CDCl_3) δ (major isomer) 7.35 (3H, m, ArH), 7.20 (2H, m, ArH), 3.98 (1H, t, $J=10.2$ Hz, OCHHCH), 3.82 (1H, dd, $J=10.2$, 5.0 Hz, OCHHCH), 3.64 (1H, dd, $J=10.2$, 5.0 Hz, PhCHN), 2.51 (1H, dd, $J=12.8$, 6.2 Hz, NCHHCH), 2.32 (1H, dd, $J=12.8$, 7.7 Hz, NCHHCH), 2.24 (3H, s, NCH₃), 1.40 (4H, m, CH₂CH₂), 1.06 (1H, m, NCH₂CH), 0.92 (3H, t, $J=7.2$ Hz, CH₂CH₃), 0.80 (1H, m, CHCH₂CH₂), 0.72 (1H, dt, $J=8.6$, 4.4 Hz, CHCHHCH), -0.14 (1H, dd, $J=9.9$, 5.5 Hz, CHCHHCH). ^{13}C NMR (101 MHz, CDCl_3) δ 135.80, 129.1, 128.2, 127.8, 69.0, 60.6, 54.1, 36.5, 31.1, 23.3, 15.8, 14.3, 14.1, 10.9. m/z (CI) 248 (M+1, 88), 230 (57), 216 (100). HRMS found: 248.2011, $\text{C}_{16}\text{H}_{26}\text{NO}$ required: 248.2014.

(2S)-2-(Methyl-[[[(1S, 2S)-2-propylcyclopropyl](methyl)amino]-2-phenylethan-1-ol (4e)

The compound was obtained as a colourless oil (0.108 g, 96%) and as a single diastereoisomer, $[\alpha]_D^{20} +69$ ($c = 0.0059$ g/mL, CHCl_3). $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3418, 2955, 2872, 1453, 1026. ^1H NMR (400 MHz, CDCl_3) δ 7.32 (3H, m, ArH), 7.17 (2H, m, ArH), 3.95 (1H, t, $J=10.5$ Hz, CHHCH), 3.82 (1H, dd, $J=10.5$, 4.8 Hz, OCHHCH), 3.63 (1H, dd, $J=10.5$, 4.8 Hz, PhCHN), 2.34 (1H, dd, $J=12.4$, 6.8 Hz, NCHHCH), 2.25 (3H, m, NCH_3), 2.16 (1H, dd, $J=12.4$, 6.8 Hz, NCHHCH), 1.41 (2H, m, CHCH_2CH_2), 1.20 (2H, m, CHCH_2CH_2), 0.90 (3H, t, $J=7.2$ Hz, CH_2CH_3), 0.62 (1H, m, NCH_2CH), 0.48 (1H, m, CHCH_2CH_2), 0.24 (2H, m, CHCH_2CH). ^{13}C NMR (101 MHz, CDCl_3) δ 135.6, 129.0, 128.3, 127.9, 68.8, 60.6, 58.6, 37.4, 36.1, 22.6, 18.4, 17.1, 14.1, 11.0. m/z (CI) 248 ($\text{M}+1$, 40), 230 (52), 216 (68), 105 (100). HRMS found: 248.2009, $\text{C}_{16}\text{H}_{26}\text{NO}$ required: 248.2014).

(2S)-2-([(1S)-2,2-Dimethylcyclopropyl](methyl)amino)-2-phenylethan-1-ol (4f)

The compound was obtained as a colourless oil (0.100 g, 94%) and as a 12:1 mixture of diastereoisomers. $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3411, 3029, 2941, 2866, 1452, 1024. ^1H NMR (400 MHz, CDCl_3) δ (major isomer) 7.35 (3H, m, ArH), 7.20 (2H, m, ArH), 3.98 (1H, t, $J=10.2$ Hz, OCHHCH), 3.82 (1H, dd, $J=10.2$, 5.1 Hz, OCHHCH), 3.64 (1H, dd, $J=10.2$, 5.0 Hz, PhCHN), 2.51 (1H, dd, $J=12.8$, 6.2 Hz, NCHHCH), 2.32 (1H, dd, $J=12.8$, 6.8 Hz, NCHHCH), 2.23 (3H, s, NCH_3), 1.05 (3H, s, $\text{C}(\text{CH}_3)\text{CH}_3$), 1.02 (3H, s, $\text{C}(\text{CH}_3)\text{CH}_3$), 0.69 (1H, tt, $J=8.8$, 6.2 Hz, NCH_2CH), 0.48 (2H, dd, $J=8.8$, 4.4 Hz, CCHHCH), 0.00 (1H, m, CCHHCH). ^{13}C NMR (101 MHz, CDCl_3) δ 129.0, 128.3, 127.9, 69.1, 60.5, 54.3, 36.7, 27.3, 23.2, 20.3, 19.1, 15. m/z (CI) 234 ($\text{M}+1$, 15), 216 (23), 202 (50), 134 (72), 105 (100). HRMS found: 234.1852, $\text{C}_{15}\text{H}_{24}\text{NO}$ required: 234.1858.

(1R, 2R)-2-(Methyl{[(1R, 2R)-2-phenylcyclopropyl](methyl)}amino)-1-phenylpropan-1-ol (6a)

The compound was obtained as a white solid (0.128 g, 95%) and as a single diastereoisomer, $[\alpha]_D^{20}$ -141 ($c = 0.0123$ g/mL, CHCl_3). Mp: 60-2 °C. $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3331, 3060, 3028, 2969, 2797, 1604, 1452, 1036, 1026. ^1H NMR (400 MHz, CDCl_3) δ 7.19 (10H, m, ArH), 4.20 (1H, d, $J=9.3$ Hz, PhCHOH), 2.80 (1H, dq, $J=9.3, 6.8$ Hz, CHNCHH), 2.70 (1H, dd, $J=12.7, 5.9$ Hz, NCHH), 2.35 (1H, dd, $J=12.7, 7.3$ Hz, NCHH), 2.32 (3H, s, NCH_3), 1.68 (1H, dt, $J=8.8, 4.9$ Hz, PhCHCH_2), 1.23 (1H, m, NCH_2CH), 1.02 (1H, dt, $J=8.3, 4.9$ Hz, CHCHHCH), 0.85 (1H, $J=8.8, 5.3$ Hz, CHCHHCH) 0.71(3H, d, $J=6.8$ Hz, NCHCH_3) ^{13}C NMR (400 MHz, CDCl_3) δ 142.7, 142.3, 128.5, 127.7, 127.5, 125.9, 125.7, 74.8, 64.6, 58.2, 36.4, 23.5, 22.6, 14.2, 7.4. m/z (CI) 296 ($M+1$, 15), 188 (31), 148 (50), 131 (100). HRMS found: 296.2016, $\text{C}_{20}\text{H}_{25}\text{NO}$ required: 296.2014.

***N*-[(1*R*, 2*R*)-2-Methoxy-1-methyl-2-phenylethyl]-*N*-methyl-*N*-{[(1*R*, 2*R*)-2-phenylcyclopropyl](methyl)}amine (6b)**

The compound was obtained as a white solid (0.131 g, 93%) and as a 3:2 mixture of diastereoisomers. $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3062, 3027, 2976, 2817, 1604, 1452, 1091. ^1H NMR (400 MHz, CDCl_3) δ (major isomer) 7.20 (10H, m, ArH), 4.01 (1H, d, $J=8.9$ Hz, MeOCH), 3.15 (4H, m, $\text{OCH}_3 + \text{NCHCH}_3$), 2.76 (1H, dd, $J=12.6, 5.6$ Hz, NCHHCH), 2.53 (1H, dd, $J=12.6, 5.2$ Hz, NCHHCH), 2.42 (3H, s, NCH_3), 1.67 (1H, dt, $J=8.6, 5.0$ Hz, PhCHCH_2), 1.26 (1H, m, NCH_2CH), 0.97 (1H, dt, $J=8.7, 4.5$ Hz, CHCHHCH), 0.87 (1H, dt, $J=8.7, 4.0$ Hz, CHCHHCH). ^{13}C NMR (101 MHz, CDCl_3) δ (two diastereomers) 143.4, 141.0, 128.4, 128.2, 127.9, 127.6, 125.9, 125.4, 86.7, 62.7, 62.4, 58.8, 56.5, 37.9, 37.8, 23.3, 22.9, 22.7, 22.4, 15.6, 14.6, 12.0, 11.5. m/z (CI) 310 ($M+1$, 37), 188 (75), 148 (69), 131 (100). HRMS found: 310.2167, $\text{C}_{21}\text{H}_{27}\text{NO}$ required: 310.2171).

(1*R*, 2*R*)-2-(Methyl-{[(1*R*, 2*R*)-2-propylcyclopropyl](methyl)}amino)-1-phenyl-propan-1-ol (6c)

The compound was obtained as a colourless oil (0.114 g, 96%) and as a single diastereoisomer, $[\alpha]_D^{20}$ -85 ($c = 0.0179$ g/mL, CHCl_3). $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3345, 2958, 2924, 2878, 1453, 1027, 1037. ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.25 (5H, m, ArH), 4.21 (1H, d, $J=9.8$ Hz, PhCHOH), 2.73 (1H, dq, $J=9.8, 6.8$ Hz, NCHCH_3), 2.49 (1H, dd, $J=12.7, 6.3$ Hz, NCHH), 2.32 (3H, s, NCH_3), 2.22 (1H, dd, $J=12.7, 9.1$ Hz, NCHH), 1.42 (2H, sextet, $J=7.1$ Hz, CH_2CH_3), 1.34-1.28 (1H, m, CHCHHCH_2), 1.24-1.19 (1H, m, CHCHHCH_2), 0.92 (3H, t, $J=7.1$ Hz, CH_2CH_3), 0.71 (3H, d, $J=6.8$ Hz, NCHCH_3), 0.69-0.64 (1H, m, NCH_2CH), 0.56-0.52 (1H, m, CHCH_2CH_2), 0.32 (2H, dd, $J=6.3, 3.9$ Hz, CHCH_2CH). ^{13}C NMR (101 MHz, CDCl_3) δ 142.4, 128.2, 127.7, 127.4, 74.7, 64.8, 58.4, 36.1, 22.7, 18.6, 17.6, 14.0, 10.7, 7.3. m/z (CI) 262 ($\text{M}+1$, 30), 244 (15), 154 (100). HRMS found: 262.2176, $\text{C}_{17}\text{H}_{27}\text{NO}$ required: 262.2171.

(1R, 2R)-2-((Methyl-[(1R, 2S)-2-propylcyclopropyl](methyl))amino)-1-phenylpropan-1-ol (6d)

The compound was obtained as a colourless oil (0.113 g, 95%) and as an 8:1 mixture of diastereoisomers. $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3331, 3060, 3028, 2969, 2797, 1604, 1452, 1036, 1026. ^1H NMR (400 MHz, CDCl_3) δ (major isomer) 7.43-7.29 (5H, m, ArH), 4.56 (1H, d, $J=9.9$ Hz, PhCHOH), 3.67-3.59 (1H, m, CH_3CHN), 3.16 (1H, dd, $J=12.5, 5.5$ Hz, NCHH), 2.99 (1H, dd, $J=12.5, 9.1$ Hz, NCHH), 2.82 (3H, s, NCH_3), 1.49-1.39 (3H, m, $\text{CH}_2\text{CHHCH}_3$), 1.38-1.10 (2H, m, $\text{CHHCH}_3 + \text{NCH}_2\text{CH}$), 1.08-0.90 (8H, m, $\text{NCHCH}_3 + \text{CH}_2\text{CH}_3 + \text{CHCH}_2\text{CH}_2 + \text{CHCHHCH}$), 0.34 (1H, dt, $J=5.5, 5.1$ Hz, CHCHHCH). ^{13}C NMR (101 MHz, CDCl_3) δ 140.7, 128.7, 128.4, 127.4, 74.1, 65.0, 53.9, 36.1, 30.8, 23.0, 16.7, 13.9, 11.8, 11.2, 9.5. m/z (CI) 262 ($\text{M}+1$, 42), 244 (15), 154 (100). HRMS found: 262.2166, $\text{C}_{17}\text{H}_{27}\text{NO}$ required: 262.2171.

(1R, 2R)-2-[[1-(1R, 2S)-2-propylcyclopropyl]methyl(methyl)amino]-1-phenylpropan-1-ol (6e)

The compound was obtained as a colourless oil (0.106 g, 94%) and as a 13:1 mixture of diastereoisomers. $\nu_{\max}/\text{cm}^{-1}$ (neat) 3331, 3060, 3028, 2969, 2797, 1604, 1452, 1036, 1026. ^1H NMR (400 MHz, CDCl_3) δ (major isomer) 7.45-7.23 (5H, m, ArH), 4.21 (1H, d, $J=9.8$ Hz, PhCHOH), 2.75-2.66 (1H, m, CH_3CHN), 2.63 (1H, dd, $J=12.7, 5.9$ Hz, NCHH), 2.38 (1H, dd, $J=12.7, 7.8$ Hz, NCHH), 2.31 (3H, s, NCH_3), 1.10 (3H, s, $\text{C}(\text{CH}_3)\text{CH}_3$), 1.05 (3H, s, $\text{C}(\text{CH}_3)\text{CH}_3$), 0.73 (3H, d, $J=6.3$ Hz, NCHCH_3), 0.54-0.49 (1H, m, NCH_2CH), 0.05-0.02 (2H, m, $\text{CHCH}_2\text{C}(\text{CH}_3)_2$). ^{13}C NMR (101 MHz, CDCl_3) δ 142.5, 128.2, 127.6, 127.4, 74.7, 64.4, 54.2, 35.6, 27.3, 23.8, 20.3, 18.6, 16.2, 7.5. m/z (CI) 248 ($M+1$, 25), 178 (18), 140 (100). HRMS found: 248.2010, $\text{C}_{16}\text{H}_{27}\text{NO}$ required: 248.2014.

(1R, 2R)-2-{Methyl[(1-methylcyclopropyl)methyl]amino}-1-phenylpropan-1-ol (6f)

The compound was obtained as a colourless oil (99 mg, 93%) and as a single diastereoisomer, $[\alpha]_{\text{D}}^{20} -63$ ($c = 0.0082$ g/mL, CHCl_3). $\nu_{\max}/\text{cm}^{-1}$ (neat) 3353, 2963, 2872, 1452, 1037, 1027. ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.25 (5H, m, ArH), 4.27 (1H, d, $J=9.8$ Hz, PhCHOH), 2.96-2.76 (1H, m, NCHCH_3), 2.47 (1H, d, $J=12.2$, NCHH), 2.29 (3H, s, NCH_3), 2.16 (1H, d, $J=12.2$ Hz, NCHH), 1.17 (3H, s, CH_3C), 0.69 (3H, d, $J=6.8$ Hz, NCHCH_3), 0.39-0.31 (2H, m, CH_2CH_2), 0.31-0.25 (2H, m, CH_2CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 142.4, 128.2, 127.7, 127.4, 74.9, 65.5, 62.4, 36.1, 21.5, 13.8, 12.4, 11.8, 7.1. m/z (CI) 234 ($M+1$, 42), 216 (14), 148 (21), 126 (100). HRMS found: 234.1859, $\text{C}_{15}\text{H}_{24}\text{NO}$ required: 234.1858.

(1R, 2S)-2-(Methyl{[(1R, 2R)-2-phenylcyclopropyl](methyl)}amino)-1-phenylpropan-1-ol (8)

The compound was obtained as a white solid (0.126 g, 95%) and as a single diastereoisomer, $[\alpha]_D^{20}$ -123 ($c = 0.009$ g/mL, CHCl_3). M.p: 69-70 °C, $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3330, 3060, 2977, 1603, 1494, 1046, 1029. ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.04 (10H, m, ArH), 4.90 (1H, d, $J=4.0$ Hz, PhCHOH), 2.90 (1H, dq, $J=7.0, 4.0$ Hz, NCHCH_3), 2.71 (1H, dd, $J=13.2, 5.8$ Hz, NCHH), 2.53 (1H, dd, $J=13.2, 6.8$ Hz, NCHH), 2.36 (3H, s, NCH_3), 1.73 (1H, m, PhCHCH_2), 1.23-1.15 (1H, m, NCH_2CH), 0.97 (1H, dt, $J=8.8, 5.1$ Hz, CHCHHCH), 0.87 (3H, d, $J = 7.0$ Hz, NCH_3), 0.82 (1H, dt, $J=8.8, 5.1$ Hz, CHCHHCH). ^{13}C NMR (400 MHz, CDCl_3) δ 142.8, 142.4, 128.5, 128.1, 127.0, 126.2, 125.8, 125.7, 72.9, 63.5, 59.3, 39.0, 23.0, 21.5, 15.0, 9.8. m/z (CI) 296 ($M+1$, 26), 278 (87), 131 (100). HRMS found: 296.2022, $\text{C}_{20}\text{H}_{25}\text{NO}$ required: 296.2014.

Confirmation of 6a stereochemistry by chemical correlation

(*R, R*)-Pseudo-ephedrine (83 mg, 0.5 mmol) and sodium cyanoborohydride (20 mg, 0.3 mmol) were mixed in methanol (1.5 mL). Acetic acid (71 μL , 1.3 mmol) and compound **10** (80 mg, 0.6 mmol) in methanol (0.5 mL) were sequentially added. After addition, the reactants were stirred at room temperature for 24 hours and extracted with DCM. The DCM solution was dried over Na_2SO_4 and concentrated to furnish the crude product, which was further purified by chromatography (silica gel, 5% methanol in dichloromethane) to obtain **11a** (0.144 g, 97%) [or **11b** (0.140 g, 95%) in the case of (*S, S*)-pseudo-ephedrine]. **11a** is virtually compound **6a**. Spectrum data for compound **11b**: $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3321, 3062, 3027, 1604, 1452, 1035, 1026. ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.07 (10H, m, ArH), 4.24 (1H, d, $J=9.5$ Hz, PhCHOH), 2.76 (1H, dq, $J=9.5, 6.6$ Hz, NCHCH_3), 2.55 (2H, d, $J=6.6$ Hz, NCH_2), 2.36 (3H, s, NCH_3), 1.78 (1H, dt, $J=8.4, 5.2$ Hz, PhCHCH_2), 1.33-1.24 (1H, m, NCH_2CH), 1.07 (1H, dt, $J=8.4, 5.1$ Hz, CHCHHCH), 0.89 (1H, $J=8.8, 5.1$ Hz, CHCHHCH), 0.75 (3H, d, $J=6.6$ Hz, CH_3CHN). ^{13}C NMR (101 MHz, CDCl_3) δ 142.8, 142.3, 128.4, 128.3, 127.7, 127.5, 125.9, 125.7, 74.8, 65.2, 58.5, 36.1, 22.6, 22.5, 15.2, 7.4. m/z (CI) 296 ($M+1$, 84), 188 (100). HRMS found: 296.2024, $\text{C}_{20}\text{H}_{25}\text{NO}$ required: 296.2014.

Removal of auxiliary:

Compound **6a** (147 mg, 0.5 mmol) was dissolved in methyl iodide (5 mL), the mixture was stirred in the dark for 6 days and the excess methyl iodide was removed under reduced pressure. The residue was re-dissolved in anhydrous THF (10 mL). To this mixture was added sodium hydride (60% w/w, Aldrich, 24 mg, 0.6 mmol) and the solution was heated at reflux for 3.5 hours and then cooled to room temperature. The reactants were diluted in petrol (40 mL). The solution was extracted with 1N HCl (2 x 10 mL). The acidic solution was neutralized with 2N NaOH (30 mL) and extracted with petrol (2 x 40 mL). The petrol solution was dried over Na₂SO₄ and concentrated in vacuo to give compound **12** as a colourless oil (80 mg, 92%), $[\alpha]_D^{20}$ -110 (c = 0.018 g/mL, CHCl₃). $\nu_{\max}/\text{cm}^{-1}$ (neat) 3026, 2762, 1604, 1455, 1032. ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.04 (5H, m, ArH), 2.39 (1H, dd, J =12.4, 6.2 Hz, NCHH), 2.30-2.25 (7H, m, N(CH₃)₂+NCHH), 1.68 (1H, dt, J =8.4, 5.1 Hz, CHCHHCH), 1.26-1.18 (1H, m, NCH₂CH), 0.97 (1H, dt, J =8.4, 5.1 Hz, CHCHHCH), 0.83 (1H, dt, J =8.4, 5.5 Hz, PhCH). ¹³C NMR (101 MHz, CDCl₃) δ 143.0, 128.3, 125.8, 125.5, 64.1, 45.5, 22.7, 21.5, 15.0. m/z (CI) 176 (M+1, 55), 132 (100). HRMS found: 176.1439, C₁₂H₁₈N required: 176.1439.

The same procedure was applied to compounds **4a** and **8**.

Compound 6d

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. M.; Rosen, R. K.; Timmers, F. T.

Organometallics, **1996**, *15*, 1518.

² Kamer, P. C. J.; Cleij, M. C.; Roeland, J. M.; Harada, T.; Hezemans, H. M. F.; Drenth, W. J. *Am. Chem. Soc.* **1988**, *110*, 1581.

³ Huszthy, P.; et al. *J. Org. Chem.* **1992**, *57*, 5383.

⁴ Denmark, S. E.; O'Connor, S. P.; Wilson, S. R. *Angew. Chem. Int. Ed.* **1998**, *37*, 1149.

⁵ Reynolds, K. A.; Finn, M. G. *J. Org. Chem.* **1997**, *62*, 2574.