Supporting Information for

An efficient asymmetric synthesis of (−)-lupinine

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1. Experimental

1.1. General Experimental

All reactions involving organometallic or other moisture sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.\(^1\) Water was purified by an Elix® UV–10 system. BuLi was purchased as a solution in hexanes and titrated against diphenylacetic acid before use. All other reagents were used as supplied without prior purification. Organic layers were dried over MgSO\(_4\). Thin layer chromatography was performed on aluminium plates coated with 60 F\(_{254}\) silica. Plates were visualised using UV light (254 nm), iodine, 1% aq KMnO\(_4\), or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Optical rotations were recorded in a water-jacketed 10 cm cell. Specific rotations are reported in 10\(^{-1}\) deg cm\(^2\) g\(^{-1}\) and concentrations in g/100 mL. IR spectra were recorded using an ATR module. Selected characteristic peaks are reported in cm\(^{-1}\). NMR spectra were recorded in the deuterated solvent stated. Spectra were recorded at rt. The field was locked by external referencing to the relevant deuteron resonance. \(^1\)H–\(^1\)H COSY, \(^1\)H–\(^{13}\)C HMQ, and \(^1\)H–\(^{13}\)C HMBC analyses were used to establish atom connectivity. Accurate mass measurements were run on a TOF spectrometer internally calibrated with polyalanine.

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1.2. Experimental Data

tert-Butyl (R,R)-3-[N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amino]-7-hydroxyheptanoate 18

BuLi (2.2 M in hexanes, 0.60 mL, 1.3 mmol) was added dropwise to a stirred solution of (R)-N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amine\(^2\) (325 mg, 1.30 mmol, >99:1 er) in THF (4 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of 15\(^3\)-\(^4\) (100 mg, 0.50 mmol, >99:1 dr) in THF (4 mL) at −78 °C was then added via cannula, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq NH₄Cl (0.5 mL) was added and the reaction mixture was allowed to warm to rt, then concentrated in vacuo. The residue was partitioned between Et₂O (15 mL) and H₂O (10 mL), the aqueous layer was extracted with Et₂O (2 × 10 mL), and the combined organic extracts were washed sequentially with 10% aq citric acid (10 mL), satd aq NaHCO₃ with EtO (2 × 10 mL) at −78 °C, and the resultant mixture was washed with 10% aq citric acid (10 mL) and brine (10 mL), then dried and concentrated in vacuo to give 18 in >99:1 dr. Purification via flash column chromatography (eluent 30–40 °C petrol/Et₂O, 1:1) gave 18 as a colourless oil (102 mg, 43%, >99:1 dr); [α]\(^D\)\(^2\) +30.7 (c 1.0 in CHCl₃); \(\nu_{\text{max}}\) (ATR) 3433 (O–H), 2971, 2933, 2864, 2836 (C–H), 1720 (C=O); δ\(_H\) (400 MHz, CDCl₃) 1.23–1.70 (6H, m, C(4)H₂, C(5)H₂, C(6)H₂), 1.33 (3H, d, J 6.9, C(α)Me), 1.41 (9H, s, CMe₃) 1.87 (1H, dd, J 14.7, 9.4, C(2)H₃A), 1.95 (1H, dd, J 14.7, 3.5, C(2)H₃B), 2.37–3.34 (1H, m, C(3)H), 3.40 (1H, d, J 14.8, NCH₃H₃Ar), 3.63 (2H, t, C(7)H₂), 3.70 (1H, d, J 14.8, NCH₃H₃Ar), 3.75–3.80 (1H, q, J 6.9, C(α)H), 3.80 (3H, s, OMe), 3.82 (3H, s, OMe), 6.85 (2H, d, J, 8.6, C(3′)H, C(5′)H), 6.89 (2H, d, J, 8.6, C(3′)H, C(5′)H), 7.22 (2H, d, J, 8.6, C(2′)H, C(6′)H), 7.32 (2H, d, J, 8.6, C(2′)H, C(6′)H); \(\delta_\text{C}\) (100 MHz, CDCl₃) 20.5 (C(α)Me), 23.0, 32.7, 33.2 (C(4), C(5), C(6)), 28.1 (CMe₃), 37.8 (C(2)), 49.3 (NCH₃Ar), 53.3 (C(3)), 55.2, 55.3 (2 × OMe), 57.0 (C(α)), 62.9 (C(7)), 80.0 (CMe₃), 113.4, 113.6, 128.9, 129.1 (C(2′), C(3′), C(5′), C(6′), C(2″), C(3″), C(5″), C(6″)), 133.8, 135.1 (C(1′), C(1″)), 158.3, 158.5 (C(4′), C(4″)), 172.4 (C(1)); \(m/z\) (ESI\(^+\)) 472 ([M+H]\(^+\), 100%); HRMS (ESI\(^+\)) C₂₈H₄₀NO₅\(^+\) ([M+H]\(^+\)) requires 472.3057; found 472.3051.

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**tert-Butyl (R,R)-3-[N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amino]-7-chloroheptanoate 19**

BuLi (2.2 M in hexanes, 3.2 mL, 7.1 mmol) was added dropwise to a stirred solution of (R)-N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amine\(^5\) (1.98 g, 7.31 mmol, >99:1 er) in THF (40 mL) at −78 °C and the resultant mixture was stirred at −78 °C for 30 min. A solution of 16\(^6,7\) (1.00 g, 4.57 mmol, >99:1 dr) in THF (40 mL) at −78 °C was added via cannula, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq NH\(_4\)Cl (4 mL) was added and the reaction mixture was allowed to warm to rt, then concentrated in vacuo. The residue was partitioned between CH\(_2\)Cl\(_2\) (40 mL) and H\(_2\)O (20 mL), the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (2 × 20 mL), and the combined organic extracts were washed sequentially with 10% citric acid (40 mL), satd aq Na\(_2\)CO\(_3\) (40 mL) and brine (40 mL), then dried and concentrated in vacuo to give 19 in >99:1 dr.

Purification via flash column chromatography (eluent 30–40°C petrol/Et\(_2\)O, 15:1) gave 19 as a colourless oil (1.84 g, 82%, >99:1 dr); [α]\(_D\)\(^22\) +34.3 (c 1.0 in CHCl\(_3\)); \(\nu\)\(_{\max}\) (ATR) 2970, 2933, 2868, 2835 (C−H), 1720 (C=O); \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 1.20–1.55 (4H, m, C(4)\(_H\), C(5)\(_H\)), 1.33 (3H, d, J 7.1, C(α)Me), 1.42 (9H, s, CMe\(_3\)), 1.65–1.80 (2H, m, C(6)\(_H\)), 1.87 (1H, dd, J 14.7, 9.4, C(2)\(\_H\)\(_A\)), 1.96 (1H, dd, J 14.7, 3.0, C(2)\(\_H\)\(_B\)), 2.35–3.35 (1H, m, C(3)\(_H\)), 3.41 (1H, d, J 14.8, NCH\(_3\)H\(_B\)Ar), 3.53 (2H, t, J 6.3, C(7)\(_H\)), 3.71 (1H, d, J 14.8, NCH\(_3\)H\(_B\)Ar), 3.76–3.81 (1H, q, J 7.1, C(α)H), 3.81 (3H, s, OMe), 3.83 (3H, s, OMe), 6.86 (2H, d, J, 8.7, C(3')\(_H\), C(5')\(_H\)), 6.90 (2H, d, J, 8.6, C(3'')\(_H\), C(5'')\(_H\)), 7.23 (2H, d, J, 8.7, C(2')\(_H\), C(6')\(_H\)), 7.33 (2H, d, J, 8.6, C(2'')\(_H\), C(6'')\(_H\)); \(\delta\)\(_C\) (100 MHz, CDCl\(_3\)) 20.6 (C(α)Me), 24.2, 32.4, 32.7 (C(4), C(5), C(6)), 28.1 (CMe\(_3\)), 37.7 (C(2)), 45.1 (C(7)), 49.3 (NCH\(_2\)Ar), 53.2 (C(3)), 55.2, 55.3 (2 × OMe), 57.1 (C(α)), 80.0 (CMe\(_3\)), 113.4, 113.7, 128.9, 129.1 (C(2'), C(3'), C(5'), C(6'), C(2'')', C(3'')'), C(5'')'), 133.7, 135.0 (C(1'), C(1'')), 158.4, 158.5 (C(4'), C(4'')), 172.2 (C(1)); \(m/z\) (ESI\(^+\)) 514 ([M\(^{37}\)Cl]+Na\(^+\), 26%), 512 ([M\(^{35}\)Cl]+Na\(^+\), 66%), 492 ([M\(^{37}\)Cl]+H\(^+\), 35%), 490 ([M\(^{35}\)Cl]+H\(^+\), 100%); HRMS (ESI\(^+\)) C\(_{28}\)H\(_{41}\)\(^{37}\)ClNO\(_4\)\(^+\) ([M\(^{37}\)Cl]+H\(^+\)) requires 492.2689; found 492.2698; HRMS (ESI\(^+\)) C\(_{28}\)H\(_{41}\)\(^{35}\)ClNO\(_4\)\(^+\) ([M\(^{35}\)Cl]+H\(^+\)) requires 490.2719; found 490.2719.

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LiHMDS (1.0 M in THF, 2.00 mL, 2.00 mmol, >99:1 dr) was added to a stirred solution of 19 (100 mg, 0.31 mmol) in THF (4 mL) at −78 °C. The reaction mixture was left to stir at −78 °C for 1 h before 1-iodo-3-(tert-butylidimethylsilyloxy)propane\(^8\) (0.57 mL, 2.4 mmol) was added. The resultant mixture was allowed to warm to rt over 12 h, then partitioned between Et\(_2\)O (15 mL) and H\(_2\)O (10 mL). The aqueous layer was extracted with Et\(_2\)O (2 × 10 mL), and the combined organic extracts were washed with brine (10 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/acetone, 25:1) gave 20 as a yellow oil (88 mg, 97%, >99:1 dr); \([\alpha]_D^{20} -9.7\) (c 1.0 in CHCl\(_3\)); \(\nu\)\(_{\text{max}}\) (ATR) 2972, 2932, 2856, 2834 (C−H), 1722 (C=O); \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 0.95–1.08 (1H, m, C(4)\(H\)_A), 1.10–1.22 (1H, m, C(3)\(H\)_A), 1.24–1.35 (1H, m, C(5)\(H\)_A), 1.36 (3H, d, J 6.8, C(α)\(Me\)), 1.37–1.47 (1H, m, C(6)\(H\)_A), 1.48 (9H, s, C\((\text{Me}_3)\)), 2.23 (1H, app t, J 11.1, C(1)\(H\)), 3.02 (1H, app t, J 11.1, C(2)\(H\)), 3.16 (1H, d, J 16.6, N\(\text{CH}_{3}\)H\(_B\)Ar), 3.68 (6H, s, 2 × O\(Me\)), 4.03 (1H, q, J 6.8, C(α)\(H\)), 6.78–6.80 (4H, m, Ar), 7.20–7.22 (4H, m, Ar); \(\delta\)\(_C\) (100 MHz, CDCl\(_3\)) 19.1 (C(α)\(Me\)), 25.2 (C(4)), 25.8 (C(3)), 27.9 (C(5)), 28.2 (C\((\text{Me}_3)\)), 30.7 (C(6)), 48.5 (N\(\text{CH}_{3}\)Ar), 50.2 (C(1)), 55.2 (2 × O\(Me\)), 59.1 (C(α)), 60.1 (C(2)), 79.4 (C\((\text{Me}_3)\)), 113.0, 113.1, 128.9, 129.9 (C(2'), C(3'), C(5'), C(6'), C(2''), C(3''), C(5''), C(6'')), 134.0, 136.9 (C(1'), C(1'')), 158.1 (C(4'), C(4'')), 175.1 (CO\(_2\)\(_{\text{Bu}}\)); \(m/z\) (ESI\(^+\)) 454 ([M+H]\(^+\), 100%); HRMS (ESI\(^+\)) C\(_{28}\)H\(_{40}\)NO\(_4\)+ ([M+H]\(^+\)) requires 454.2952; found 454.2949.

**tert-Butyl (R)-2-[N(1')-(p-methoxybenzyl)piperidin-2'-yl]acetate 22**

**Method A:** I\(_2\) (464 mg, 1.83 mmol), imidazole (124 mg, 1.83 mmol) and PPh\(_3\) (480 mg, 1.83 mmol) were added to a stirred solution of 18 (173 mg, 0.367 mmol, >99:1 dr) in MeCN (7.5 mL). The resultant mixture was heated at 80 °C for 16 h then allowed to cool to rt and concentrated in vacuo. The residue was dissolved in CH\(_2\)Cl\(_2\) (20 mL) and the resultant solution was washed sequentially with satd aq Na\(_2\)S\(_2\)O\(_3\) (10 mL), H\(_2\)O (10 mL) and brine (10 mL), then concentrated in vacuo. Purification via flash column chromatography (eluent 30–80 °C petrol/acetone, 25:1) gave 22 as a yellow oil (138 mg, 91%, >99:1 dr); \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 0.95–1.08 (1H, m, C(4)\(H\)_A), 1.10–1.22 (1H, m, C(3)\(H\)_A), 1.24–1.35 (1H, m, C(5)\(H\)_A), 1.36 (3H, d, J 6.8, C(α)\(Me\)), 1.37–1.47 (1H, m, C(6)\(H\)_A), 1.48 (9H, s, C\((\text{Me}_3)\)), 2.23 (1H, app t, J 11.1, C(1)\(H\)), 3.02 (1H, app t, J 11.1, C(2)\(H\)), 3.16 (1H, d, J 16.6, N\(\text{CH}_{3}\)H\(_B\)Ar), 3.68 (6H, s, 2 × O\(Me\)), 4.03 (1H, q, J 6.8, C(α)\(H\)), 6.78–6.80 (4H, m, Ar), 7.20–7.22 (4H, m, Ar); \(\delta\)\(_C\) (100 MHz, CDCl\(_3\)) 19.1 (C(α)\(Me\)), 25.2 (C(4)), 25.8 (C(3)), 27.9 (C(5)), 28.2 (C\((\text{Me}_3)\)), 30.7 (C(6)), 48.5 (N\(\text{CH}_{3}\)Ar), 50.2 (C(1)), 55.2 (2 × O\(Me\)), 59.1 (C(α)), 60.1 (C(2)), 79.4 (C\((\text{Me}_3)\)), 113.0, 113.1, 128.9, 129.9 (C(2'), C(3'), C(5'), C(6'), C(2''), C(3''), C(5''), C(6'')), 134.0, 136.9 (C(1'), C(1'')), 158.1 (C(4'), C(4'')), 175.1 (CO\(_2\)\(_{\text{Bu}}\)); \(m/z\) (ESI\(^+\)) 454 ([M+H]\(^+\), 100%); HRMS (ESI\(^+\)) C\(_{28}\)H\(_{40}\)NO\(_4\)+ ([M+H]\(^+\)) requires 454.2952; found 454.2949.

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40 °C petrol) gave 4-methoxystyrene as a colourless oil (20 mg, 40%); δH (400 MHz, CDCl₃) 3.82 (3H, s, OMe), 5.14 (1H, d, J 10.9, CH=CH₂H₃), 5.62 (1H, d, J 17.6, CH=CH₂H₅), 6.67 (1H, dd, J 17.6, 10.9, \( CH=CH₂ \)), 6.87 (2H, J 8.6, C(3)H, C(5)H), 7.35 (2H, J 8.6, C(2)H, C(6)H). Further elution (eluent 30–40 °C petrol/NEt₃, 100:1, then 30–40 °C petrol/acetone/NEt₃, 100:4:1) gave 22 as a yellow oil (80 mg, 68%); [α]₁̂D +20.1 (c 1.0 in CHCl₃); νmax (ATR) 2976, 2932, 2857, 2835, 2797 (C–H), 1725 (C=O); δH (400 MHz, CDCl₃) 1.35–1.55 (4H, m, C(3′)H₃, C(4′)H₂, C(5′)H₃), 1.45 (9H, s, CMe₃), 1.58–1.65 (1H, m, C(5′)H₅), 1.75–1.80 (1H, m, C(3′)H₃), 2.11–2.18 (1H, m, C(6′)H₃), 2.33 (1H, dd, J 14.5, 8.0, C(2′)H₅), 2.55–2.70 (2H, m, C(2′)H₂, C(6′)H₃), 2.91 (1H, m, C(2′′)H), 3.30 (1H, d, J 13.5, NCH₂H₃Ar), 3.73 (1H, d, J 13.5, NCH₂H₃Ar), 3.80 (3H, s, OMe), 6.85 (2H, d, J 8.6, C(3′′)H, C(5′′)H), 7.23 (2H, d, J 8.6, C(2′′)H, C(6′′)H); δC (100 MHz, CDCl₃) 22.3, 25.3 (C(4′), C(5′)), 28.1 (CMe₃), 31.0 (C(3′)), 37.3 (C(2′)), 50.0 (C(6′)), 55.2 (C(2″)), 57.6 (NCH₂Ar), 57.8 (OMe), 80.2 (CMe₃), 113.5, 129.9 (C(2″), C(3′′), C(5′′), C(6″)), 131.4 (C(1″)), 158.5 (C(4″)), 172.3 (C(1)); m/z (ESI⁺) 320 ([M+H]*)¹, 100%, 264 ([M–C₄H₉]*)⁹, 90%; HRMS (ESI⁺) C₁₉H₂₀NO₃⁺ ([M+H]*) requires 320.2220; found 320.2220.

Method B: Nal (844 mg, 5.63 mmol) was added to a stirred solution of 19 (1.38 g, 2.82 mmol, >99:1 dr) in MeCN (65 mL) and the resultant mixture was heated at reflux for 24 h. The reaction mixture was then allowed to cool to rt and diluted with Et₂O (65 mL). The resultant mixture was washed with H₂O (50 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/acetone, 15:1) gave 4-methoxystyrene as a colourless oil (200 mg, 53%). Further elution (eluent 30–40 °C petrol/acetone, 3:1) gave 22 as a yellow oil (793 mg, 88%).

tert-Butyl (R,R)-2-[N(1′)-(p-methoxybenzyl)piperidin-2′-yl]-5-(tert-butyldimethylsiloxy)pentanoate 24

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\text{LiHMDS (1.0 M in THF, 5.15 mL, 5.15 mmol) was added to a stirred solution of 22 (235 mg, 0.736 mmol) in THF (10 mL) at } -78 \text{ °C and the resultant mixture was stirred at } -78 \text{ °C for 1 h. 1-Iodo-3-(tert-butyldimethylsilyloxy)propane}^{10} (1.10 g, 3.68 mmol) was then added and the resultant mixture was allowed to warm to rt and stirred at rt for 16 h. Satd aq NH₄Cl (5 mL) was then added and the reaction mixture was concentrated in vacuo. The residue was partitioned between CH₂Cl₂ (10 mL) and H₂O (5 mL), and the organic layer was then dried and concentrated in vacuo. Purification by flash column chromatography (eluent 30–40 °C petrol/acetone, 5:1) gave 24 as a white solid (162.6 mg, 40%).}

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°C petrol/acetone/NH$_2$OH, 100:5:1) gave 24 as a colourless oil (271 mg, 75%, >99:1 dr); [$\alpha$]$^\text{D}_{20}$ +24.9 (c 1.0 in CHCl$_3$); $\nu$$_\text{max}$ (ATR) 2930, 2857 (C–H), 1728 (C=O); $\delta$$_H$ (400 MHz, CDCl$_3$) 0.04 (6H, s, SiMe$_2$), 0.89 (9H, s, SiCMe$_3$), 1.26–1.70 (10H, m, C(3)H$_2$, C(4)H$_2$, C(3')H$_2$, C(4')H$_2$, C(5')H$_2$), 1.47 (9H, s, OCMMe$_3$), 2.07–2.14 (1H, m, C(6')H$_A$), 2.64–2.68 (1H, m, C(2')H), 2.82–2.87 (1H, m, C(6')H$_B$), 2.87–2.93 (1H, m, C(2)H), 3.38 (1H, d, J 13.1, NCH$_2$H$_B$Ar), 3.56–3.68 (2H, m, C(5)H$_2$), 3.80 (3H, s, OMe), 3.82 (1H, d, J 13.1, NCH$_2$H$_B$Ar), 6.83 (2H, d, J 8.5, C(3'')H, C(5'')H), 7.23 (2H, d, J 8.5, C(2'')H, C(6'')H); $\delta$$_C$ (100 MHz, CDCl$_3$) −5.1 (SiMe$_2$), 18.5 (SiCMe$_3$), 23.1, 23.3, 24.6 (C(4), C(4'), C(5')), 26.1 (SiCMe$_3$), 28.4 (OCMe$_3$), 31.7 (C(3), C(3'))), 47.6 (C(2)), 49.8 (C(6')), 55.4 (OMe), 56.5 (NCH$_2$Ar), 62.6 (C(2')), 63.5 (C(5)), 80.1 (OCMe$_3$), 113.5, 130.2 (C(2''), C(3''), C(5''), C(6'')), 131.7 (C(1'')), 158.6 (C(4'')), 174.4 (C(1)); $m/z$ (ESI$^+$) 492 ([M+H]$^+$, 100%), 436 ([M–C$_4$H$_8$]$^+$, 25%); HRMS (ESI$^+$) C$_{28}$H$_{58}$NO$_4$Si$^+$ ([M+H]$^+$) requires 492.3504; found 492.3498.

tert-Butyl (R,R)-2-[N(1')-(p-methoxybenzyl)piperidin-2'-yl]-5-hydroxypentanoate 25

TBAF (1.0 M in THF, 2.70 mL, 2.70 mmol) was added dropwise to a stirred solution of 24 (265 mg, 0.539 mmol, >99:1 dr) in THF (10 mL). The resultant solution was stirred at rt for 4 h, then partitioned between Et$_2$O (10 mL) and H$_2$O (10 mL). The aqueous layer was extracted with Et$_2$O (3 × 10 mL) and the combined organic extracts were washed with brine (30 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40°C petrol/acetone/NH$_2$OH, 100:20:1) gave 25 as a yellow oil (173 mg, 85%, >99:1 dr); [$\alpha$]$^\text{D}_{20}$ +30.3 (c 1.0 in CHCl$_3$); $\nu$$_\text{max}$ (ATR) 3414 (O–H), 3032, 2930, 2857 (C–H), 1725 (C=O); $\delta$$_H$ (400 MHz, CDCl$_3$) 1.25–1.45 (3H, m, C(3')H$_A$, C(4')H$_A$, C(5')H$_A$), 1.46 (9H, s, CMe$_3$), 1.47–1.61 (4H, m, C(3)H$_2$, C(4)H$_2$), 1.61–1.80 (3H, m, C(3')H$_B$, C(4')H$_B$, C(5')H$_B$), 2.03–2.10 (1H, m, C(6')H$_A$), 2.60–2.66 (1H, m, C(2')H), 2.80–2.92 (2H, m, C(2)H, C(6')H$_B$), 3.34 (1H, d, J 13.1, NCH$_2$H$_B$Ar), 3.54–3.65 (2H, m, C(5)H$_2$), 3.78 (3H, s, OMe), 3.83 (1H, d, J 13.1, NCH$_2$H$_B$Ar), 6.83 (2H, d, J 8.4, C(3'')H, C(5'')H), 7.22 (2H, d, J 8.4, C(2'')H, C(6'')H); $\delta$$_C$ (100 MHz, CDCl$_3$) 21.7, 23.4, 23.7 (C(3'), C(4'), C(5')), 24.9 (C(3)), 28.1 (CMe$_3$), 31.6 (C(4)), 47.5 (C(2)), 50.5 (C(6')), 55.2 (OMe), 56.6 (NCH$_2$Ar), 62.4 (C(5)), 62.6 (C(2')), 80.3 (CMe$_3$), 113.4, 130.1 (C(2''), C(3''), C(5''), C(6'')), 131.2 (C(1'')), 158.5 (C(4'')), 174.5 (C(1)); $m/z$ (ESI$^+$) 378 ([M+H]$^+$, 100%), 322 ([M–C$_4$H$_8$]$^+$, 25%); HRMS (ESI$^+$) C$_{22}$H$_{36}$NO$_4$Si$^+$ ([M+H]$^+$) requires 378.2639; found 378.2633.
(R,R)-1-(Hydroxymethyl)octahydro-1H-quinolizine [(-)-lupinine] 1

Method A – Step 1: I$_2$ (548 mg, 2.16 mmol), imidazole (147 mg, 2.16 mmol) and polymer-supported PPh$_3$ (720 mg, ~3.2 mmol/g,) were added to a solution of 25 (163 mg, 0.432 mmol, >99:1 dr) in PhMe/MeCN (4:1, 5 mL). The resultant mixture was heated at 65 °C for 16 h, then allowed to cool to rt and concentrated in vacuo. The residue was dissolved in CH$_2$Cl$_2$ (10 mL) and the resultant solution was washed with satd aq Na$_2$S$_2$O$_3$ (10 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 10 mL) and the combined organic extracts were then concentrated in vacuo to give 26 as a brown oil (175 mg, >99:1 dr).

Method A – Step 2: LiAlH$_4$ (1.0 M in THF, 0.59 mL, 0.59 mmol) was added to a stirred solution of 26 (95 mg, >99:1 dr) in THF (4 mL) at 0 °C. The resultant mixture was heated at reflux for 48 h then allowed to cool to rt. 2.0 M aq NaOH (0.5 mL) was then added and the resultant mixture was heated at reflux for 3 h. The reaction mixture was then allowed to cool to rt and filtered through Celite$^\circledR$ (eluent CH$_2$Cl$_2$), then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl$_3$/MeOH/NH$_4$OH, 200:25:2) gave (-)-lupinine 1 as a pale yellow oil (26 mg, 66% from 25, >99:1 dr);$^{11,12}$ [α]$_D^{20}$ −12.0 (c 0.4 in EtOH); {lit.$^{11}$ for ent-1 [α]$_D^{20}$ +12.7 (c 0.35 in EtOH)}; ν$_{max}$ (ATR) 3323 (O–H), 2933, 2857, 2807, 2763 (C–H); δ$_H$ (400 MHz, C$_6$D$_6$) 0.94–1.06 (1H, m, C(8)H$_A$), 1.15–1.25 (2H, m, C(1)H, C(9)H$_A$), 1.25–1.44 (4H, m, C(2)H$_A$, C(3)H$_A$, C(7)H$_2$), 1.49–1.58 (2H, m, C(6)H$_A$, C(8)H$_B$), 1.63–1.80 (4H, m, C(2)H$_B$, C(4)H$_A$, C(9)H$_B$, C(9a)H), 2.23–2.37 (1H, m, C(3)H$_B$), 2.44–2.56 (2H, m, C(4)H$_B$, C(6)H$_B$), 3.75 (1H, app d, J 10.7, CH$_A$H$_B$OH), 4.18 (1H, dd, J 10.7, 4.8, CH$_A$H$_B$OH); δ$_H$ (400 MHz, CDCl$_3$) 1.21–1.34 (1H, m, CH$_2$), 1.49–1.64 (6H, m, C(1)H, CH$_2$), 1.71–1.91 (4H, m, CH$_2$), 1.98–2.08 (1H, m, CH$_2$), 2.10–2.23 (2H, m, C(9a)H, CH$_2$), 2.79–2.88 (2H, m, C(4)H$_A$, C(6)H$_A$), 3.70 (1H, d, J 10.8, CH$_A$H$_B$OH), 4.17 (1H, ddd, J 10.8, 4.6, 1.2, CH$_A$H$_B$OH); δ$_C$ (100 MHz, C$_6$D$_6$) 23.3 (C(3)), 25.0 (C(8)), 25.9 (C(7)), 29.9 (C(9)), 31.6 (C(2)), 38.9 (C(1)), 57.3 (C(6)), 57.4 (C(4)), 65.2 (C(9a)), 65.7 (CH$_2$OH); m/z (ESI$^+$) 170 ([M+H]$^+$, 100%); HRMS (ESI$^+$) C$_{10}$H$_{20}$NO$^+$ ([M+H]$^+$) requires 170.1539; found 170.1541.

Method B – Step 1: I$_2$ (343 mg, 1.35 mmol), imidazole (92 mg, 1.35 mmol) and polymer-supported PPh$_3$ (450 mg, ~3.2 mmol/g) were added to a solution of 25 (102 mg, 0.27 mmol, >99:1 dr) in PhMe/MeCN (4:1, 5 mL). The resultant mixture was heated at 65 °C for 60 h, then allowed to cool to rt and concentrated in vacuo. The residue was dissolved in CH$_2$Cl$_2$ (5 mL) and the resultant solution was washed sequentially with satd aq Na$_2$S$_2$O$_3$ (5 mL) and satd aq NaHCO$_3$ (5 mL). The combined aqueous layers were extracted with CH$_2$Cl$_2$ (3 × 5 mL).
mL) and the combined organic extracts were then concentrated in vacuo to give 27 as a brown oil (118 mg, >99:1 dr).

Method B – Step 2: LiAlH₄ (1.0 M in THF, 0.81 mL, 0.81 mmol) was added to a stirred solution of 27 (118 mg, >99:1 dr) in THF (2.5 mL) at 0 °C. The resultant mixture was heated at reflux for 16 h then allowed to cool to rt. 2.0 M aq NaOH (0.8 mL) was then added and the resultant mixture was heated at reflux for 3 h. The reaction mixture was then allowed to cool to rt and filtered through Celite® (eluent CH₂Cl₂), then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl₃/MeOH/NH₄OH, 200:25:2) gave (−)-lupinine 1 as a pale yellow oil (23 mg, 50% from 25, >99:1 dr); [α]₀D −9.5 (c 0.4 in EtOH); [lit.][13] for ent-1 [α]₀D +12.7 (c 0.35 in EtOH).

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2. Copies of $^1$H and $^{13}$C NMR spectra

*tert*-Butyl (R,R)-3-[N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amino]-7-hydroxyheptanoate 18 (400 MHz $^1$H, CDCl$_3$)
** tert-Butyl (R,R)-3-[N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amino]-7-hydroxyheptanoate 18 (100 MHz $^{13}$C, CDCl$_3$) **
**tert-Butyl (R,R)-3-[N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amino]-7-chloroheptanoate 19 (400 MHz $^1$H, CDCl$_3$)**

![NMR spectrum](image)
tert-Butyl (R,R)-3-[N-(p-methoxybenzyl)-N-(α-methyl-p-methoxybenzyl)amino]-7-chloroheptanoate 19 (100 MHz $^{13}$C, CDCl$_3$)
*tert*-Butyl \((R,R,R)\)-2-\([N-(p\text{-methoxybenzyl})-N-(\alpha\text{-methyl}-p\text{-methoxybenzyl})\text{amino}]\text{cyclohexane-1-carboxylate}\) 20 (400 MHz \(^1\text{H}, \text{CDCl}_3\))
tert-Butyl \((R,R,R)\)-2-[\(N-(p\text{-methoxybenzyl})-N-(\alpha\text{-methyl}-p\text{-methoxybenzyl})\text{amino}\)]cyclohexane-1-carboxylate 20 (100 MHz \(^{13}\text{C}, \text{CDCl}_3\))
tert-Butyl (R)-2-[N(1')-(p-methoxybenzyl)piperidin-2'-yl]acetate 22 (400 MHz $^1$H, CDCl$_3$)
tert-Butyl (R)-2-[N(1')-(p-methoxybenzyl)piperidin-2'-yl]acetate 22 (100 MHz $^{13}$C, CDCl$_3$)
*tert*-Butyl \((R,R)\)-2-\([N(1')-(p\text{-methoxybenzyl})\text{piperidin}-2'\text{-yl}]-5\text{-}(\text{tert-butyl}d)\text{imethylsiloxy})\text{pentanoate} 24 (400 MHz \(^1\text{H}, \text{CDCl}_3\))
tert-Butyl (R,R)-2-[N(1')-(p-methoxybenzyl)piperidin-2'-yl]-5-(tert-butyldimethylsiloxy)pentanoate 24 (100 MHz $^{13}$C, CDCl$_3$)
tert-Butyl (R,R)-2-[N(1')-(p-methoxybenzyl)piperidin-2'-yl]-5-hydroxypentanoate 25 (400 MHz $^1$H, CDCl$_3$)
*tert*-Butyl \((R,R)\)-2-\(\text{[N(1')(p-methoxybenzyl)piperidin-2'-yl]}\)-5-hydroxypentanoate 25 (100 MHz \(^{13}\text{C}, \text{CDCl}_3\))
(R,R)-1-(Hydroxymethyl)octahydro-1H-quinolizine [(-)-lupinine] 1 (400 MHz $^1$H, CDCl$_3$)
(R,R)-1-(Hydroxymethyl)octahydro-1H-quinolizine [(-)-lupinine] 1 (100 MHz $^{13}$C, C$_6$D$_6$)