Supplementary Material S1

## **Supplementary Material**

## Stereoselective Approaches to 2,3,6-Trisubstituted Piperidines. An Enantiospecific Synthesis of Quinolizidine (-)-217A

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**Table of Contents** 

General information	S2
Synthesis	S2-S13
<sup>1</sup> H and <sup>13</sup> C spectra of intermediates towards (-)-217A	S14-S21
<sup>1</sup> H spectrum of (-)-217A	S22
NOESY of compound 22	S23

Supplementary Material S2

#### **General information**

<sup>1</sup>H NMR spectra were recorded on a Bruker AC-250 (250 MHz), AMX-400 (400 MHz) or DRX-500 (500MHz). Chemical shifts are reported in ppm from tetramethylsilane with the residual protic solvent resonance as the internal standard (CHCl<sub>3</sub>:  $\delta$  7.27). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, m = multiplet, app = apparent), coupling constants (Hz), assignements. <sup>13</sup>C NMR spectra were recorded on a Bruker AC-250 (62.9 MHz), AMX-400 (100.6 MHz) or DRX-500 (249.9 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference (CDCl<sub>3</sub>:  $\delta$  77.0). High-resolution mass spectra (HRMS) recorded for accurate mass analysis, were performed on Electrospray mode (TOF ES<sup>+</sup>) or a MicroMass Prospec operating in EI (EI+) mode. Elemental microanalysis was performed using a Perkin-Elmer 2400 CHNS / O Series II Elemental Analyser. Infrared (IR) Spectra were recorded on a Perkin Elmer Paragon 100 FTIR spectrophotometer, v<sub>max</sub> in cm<sup>-1</sup>. Samples were recorded as thin films using sodium chloride plates, as a DCM solution. Bands are characterised as broad (br), strong (s), medium (m), and weak (w). All solvents and reagents were purified using standard laboratory techniques according to methods published in "Purification of Laboratory Chemicals" by Perrin, Armarego, and Perrin (Pergamon Press, 1966).<sup>1</sup> Buchi Grignard, Flash chromatography was performed on silica gel (BDH Silica Gel 60 43-60). Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica (0.2 mm, Merck DC-alufolien Kieselgel 60 F254) which were developed using standard visualizing agents: Ultraviolet light or potassium permanganate.

X-ray crystallography data for compounds **17** & **18** have been submitted to Cambridge Crystallographic Data Centre, CCDC numbers are 823676 & 823677, respectively.

#### Synthesis of N-(3-hydroxy-1-hydroxymethyl-propyl)-4-methyl-benzenesulfonamide (6)



A flask was charged with diester **5** (5.80 g, 29.35 mmol, 1.0 eq) and THF (22 mL) and cooled to 0 °C. Distilled triethylamine (18 mL, 129.00 mmol, 4.4 eq) and then *p*-toluenesulfonylchloride (6.1 g, 32.23 mmol, 1.1 eq) were added and the mixture stirred at room temperature for 48 h. The reaction mixture was acidified with HCl (1M) to pH 3 and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaHCO<sub>3</sub> solution then dried over MgSO<sub>4</sub> and evaporated under reduce pressure to give a yellow solid (8.1 g, 87%). A solution of the residue (1 g, 3.17 mmol, 1.0 eq) in THF (15 mL) was added dropwise *via* cannula to a solution of lithium borohydride (152 mg, 6.80 mmol,

<sup>&</sup>lt;sup>1</sup> Perrin,D.D. and Armarego, W.L. Purification of Laboratory Chemicals; 3<sup>rd</sup> Ed., Permagon Press, Oxford 1988

2.2 eq) in THF (23 mL) at 0 °C and stirred for 48 h. The reaction mixture was quenched with an aqueous solution of K<sub>2</sub>CO<sub>3</sub>. The resulting mixture was extracted with EtOAc and the combined organic layers were dried over MgSO<sub>4</sub> and evaporated under reduced pressure providing **6** as a white powder (690 mg, 84%). M.p. 88 °C;  $[\alpha]^{23}_{D}$ =+10 (*c* 0.01, CHCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =1.59-1.77 (m, 2H), 1.91 (br, 1H), 2.43 (s, 3H), 3.37-3.87 (m, 5H), 7.36 (d, *J*=8.5 Hz, 2H), 7.66 (d, *J*=8.5 Hz, 2H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>):  $\delta$ =21.6, 34.4, 53.0, 58.7, 64.6, 127.1, 129.8, 140.5, 143.7. FTIR (film):  $v_{max}$ =3051 (b), 3339 (b), 3284 (b), 2843 (w), 2882 (w), 1599 (w), 1422 (m), 1323 (s), 1153 (s), 1061 (s) cm<sup>-1</sup>; HRMS (ES): *m/z* calcd for C<sub>11</sub>H<sub>18</sub>NO<sub>4</sub>S [MH<sup>+</sup>]: 260.0957; found: 260.0950.

Synthesis of (R)-2-(tert-butyl-diphenyl-silanoxyethyl)-1-(toluene-4-sulfonyl)-aziridine (7)



A 50 mL round-bottomed flask was charged with 6 (548 mg, 2.11 mmol, 1.0 eq), freshly distilled tributylphosphine (844  $\mu$ L, 3.38 mmol, 1.6 eq) and toluene (20 mL) at room temperature. The reaction mixture was cooled to 0 °C and 1,1'-azodicarbonyldipiperidine (ADDP) (800 mg, 3.17 mmol, 1.5 eq) was added in small portions. The reaction mixture was stirred for 2 h at 0 °C, then, allowed to reach room temperature overnight. The reaction mixture was evaporated under reduced pressure, dissolved in a mixture DCM/MeOH (10:1), dried on silica and purified by flash column chromatography (petroleum ether/EtOAc, 1:1) to provide 2-hydroxyethyl-1-(toluene-4-sulfonyl)-aziridine as a colourless oil (413 mg, 81%). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ=1.36-1.53 (m, 1H), 1.89-2.10 (m, 1H), 2.14 (d, J=4.5 Hz, 1H) 2.44 (s, 3H), 2.64 (d, J=7.0 Hz, 1H), 2.83-2.97 (m, 1H), 3.55-3.74 (m, 2H), 7.34 (d, J=8.0 Hz, 2H), 7.82 (d, J=8.0 Hz, 2H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>): δ=25.8, 29.6, 42.1, 55.3, 68.2, 128.3, 131.8, 132.0, 133.3;. FTIR (film): v<sub>max</sub>=3527 (br), 2925 (w), 1597 (w), 1320 (m), 1232 (w), 1160 (s), 1092 (w) cm<sup>-1</sup>; HRMS (ES): m/z calcd for C<sub>11</sub>H<sub>15</sub>NO<sub>3</sub>NaS [MNa<sup>+</sup>]: 264.0670; found: 264.0666. The aziridine (413 mg, 1.71 mmol) was dissolved in THF (2.5 mL) and the solution was cooled to 0 °C. TBDPSCI (556 µL, 2.14 mmol, 1.25 eq) and imidazole (350 mg, 5.13 mmol, 3.0 eq) were added. The reaction mixture was allowed to reach room temperature and stirred for 3 h. The reaction mixture was diluted with EtOAc and washed with brine. The organic layer was dried over MgSO<sub>4</sub> and concentrated in vacuo. Purification of the resulting oil by silica gel chromatography (petroleum/EtOAc, 10:1) provided 7 as a coulorless oil (739 mg, 90%). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ=0.96 (s, 9H), 1.42-1.74 (m, 2H), 2.05 (d, J=4.5 Hz, 1H), 2.32 (s, 3H), 2.60 (d, J=7.0 Hz, 1H), 2.76-2.88 (m, 1H), 3.49 (dd, J=5.5, 7.0 Hz, 2H), 7.18 (d, J=8.0 Hz, 2H), 7.25-7.41 (m, 6H), 7.48-7.57 (m, 4H), 7.74 (d, *J*=8.0 Hz, 2H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>): δ=19.1, 21.6, 26.8, 33.5, 34.4, 38.0, 61.2, 127.7, 128.0, 129.6, 129.7, 133.5, 135.5, 142.3, 144.4; FTIR (film): v<sub>max</sub>=3071 (w), 2930 (m), 2857 (m), 1598 (w), 1472 (w), 1428 (m), 1326 (s), 1164 (s), 1093 (s) cm<sup>-1</sup>; MS (ES): m/z: 502 [MNa<sup>+</sup>]; HRMS (ES): m/z calcd for C<sub>27</sub>H<sub>33</sub>NO<sub>3</sub>NaSiS: 502.1848; found: 502.1870.

## Synthesis of 2-(*tert*-butyl-diphenyl-silanoxyethyl)-5-methylene-1-(toluene-4-sulfonyl)-piperidine (9)



A solution of Grignard reagent 8<sup>2</sup> (0.14 M, 10 mL, 1.40 mmol, 2.5 eq) was added to 3-(*tert*-butyldiphenyl-silanyloxyethyl)-1-(toluene-4-sulfonyl)-aziridine 7 (270 mg, 0.56 mmol, 1.0 eq) in THF (6 mL). The reaction mixture was stirred at room temperature for 16 h. The reaction was quenched with saturated aqueous NH<sub>4</sub>Cl then extracted with EtOAc and the combined organic extracts were washed with brine. The solution was dried over MgSO<sub>4</sub> and solvent was removed in vacuo. The residue was purified by column chromatography (petroleum ether/EtOAc, 2:1) to give a clear oil (264 mg, 85%). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ=1.05 (s, 9H), 1.41-1.72 (m, 4H), 2.0-2.11 (m, 2H), 2.40 (s, 3H), 3.38-3.55 (m, 2H), 3.60-3.72 (m, 1H), 4.02 (s, 2H), 4.80 (br, 1H), 5.01 (1H, br), 5.42 (d, J=7.5 Hz, 1H), 7.22 (d, J=8.0 Hz, 2H), 7.32-7.50 (m, 6H), 7.54-7.62 (m, 4H), 7.70 (d, J=8.0 Hz, 2H); <sup>13</sup>C NMR (125 MHz in CDCl<sub>3</sub>): δ=19.0, 21.5, 26.9, 28.6, 29.3, 30.9, 52.4, 61.2, 66.0, 105.9, 109.8, 127.1, 129.9, 132.9, 133.0, 135.5, 135.6, 143.1, 148.2; FTIR (film): v<sub>max</sub>=3475 (br), 3276 (br), 2929 (s), 2851 (m), 1657 (w), 1423 (m), 1323 (m), 1157 (s), 1112 (s); HRMS (ES): m/z calcd for  $C_{31}H_{41}NO_4NaSiS$ [MNa<sup>+</sup>]: 574.2423; found: 574.2396. A solution of this compound (264 mg, 4.78 mmol, 1 eq) in toluene (3.9 mL) was transferred via cannula to a flask containing 4Å molecular sieves (115 mg), palladium acetate (11 mg, 0.048 mmol, 0.1 eq) and triphenylphosphine (50 mg, 0.19 mmol, 0.4 eq) in toluene (2.9 mL). The reaction mixture was placed under reflux for 16 h. The reaction was guenched with 1 M HCl from pH~6 to pH~2 and extracted with EtOAc. The aqueous layer were basified with 1 M NaOH from pH~2 to pH~6-7 and further extracted with EtOAc. The combined organic fractions were washed with brine, dried over MgSO4 and solvent was removed in vacuo. The residue was purified by column chromatography (petroleum ether/EtOAc, 20:1) to give 9 as a clear oil. (214 mg, 84%). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ=1.05 (s, 9H), 1.30-1.49 (m, 2H), 1.65-1.82 (m, 2H), 1.83-2.04 (m, 2H), 2.37 (s, 3H), 3.52 (d, J=15.0 Hz, 1H), 3.57-3.77 (m, 2H), 4.05-4.15 (m, 1H), 4.21 (d, J=15.0 Hz, 1H), 4.67 (br, 1H), 4.76 (br, 1H), 7.18 (d, J=8.0 Hz, 2H), 7.32-7.47 (m, 6H), 7.59-7.70 (m, 6H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>): δ=19.2, 21.5, 26.9, 27.3, 28.0, 32.9, 46.5, 50.0, 61.1, 110.3, 127.4, 127.7, 129.4, 129.6, 133.6, 135.6, 136.8, 142.3, 144.4; FTIR (film): v<sub>max</sub>=3060 (w), 2931 (m), 2847

<sup>&</sup>lt;sup>2</sup> J. C. R. Brioche, K. M. Goodenough, D. J. Whatrup, J. P. A. Harrity, J. Org. Chem. 2005, 73, 1946.

(m), 1466 (w), 1428 (m), 1341 (s), 1160 (s), 1111 (s) cm<sup>-1</sup>; MS (ES): m/z: 556 [MNa<sup>+</sup>]; HRMS (ES) m/z calcd for C<sub>31</sub>H<sub>39</sub>NO<sub>3</sub>NaSiS: 556.2318; found: 556.2330.

# Synthesisof2-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydro-pyridine (11)



A solution of CuBr.DMS (79 mg, 0.38 mmol, 0.4 eq) in DMS (2.3 mL) was added to a solution of the Büchi Grignard 10 (3 mL, 0.64 M, 1.91 mmol, 2.0 eq) at -78 °C. The resulting reaction mixture was stirred at this temperature for 1 h before a solution of 7 (458 mg, 0.95 mmol, 1 eq) in THF (2 mL) was added at -78 °C. The mixture was allowed to warm to room temperature overnight. The reaction was quenched with water. The aqueous layer was extracted with EtOAc and the combined organic layers washed with brine, dried over MgSO4 and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/EtOAc, 4:1) to give (R)-N-(1-[2-(tert-butyldiphenyl-silanyloxy)-ethyl]-4-[1,3]dioxolan-2-yl-butyl)-4-methyl-benzenesulfonamide as a colourless solid (478 mg, 86%). M.p. 79 °C;  $[\alpha]^{23}_{D}$  = +30 (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.02 (s, 9H), 1.20-1.69 (m, 8H), 2.39 (s, 3H), 3.31-3.55 (m, 2H), 3.59-3.72 (m, 1H), 3.76-3.99 (m, 4H), 4.76 (t, J=4.5 Hz, 1H), 5.30 (d, J=8.0 Hz 1H), 7.21 (d, J=8.0 Hz 2H), 7.32-7.49 (m, 6H), 7.54-7.63 (m, 4H), 7.70 (d, J=8.0 Hz, 2H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>): δ=19.0, 19.9, 21.5, 26.8, 33.5, 34.5, 35.4, 52.6, 61.2, 64.8, 104.3, 127.1, 127.8, 129.6, 129.9, 133.1, 135.5, 138.2, 142.9; FTIR (film): v<sub>max</sub>=3253 (br), 2929 (m), 2856 (m), 1472 (m), 1429 (m), 1319 (m), 1152 (s), 1113 (s), 1086 (s), 816 (m) cm<sup>-1</sup>; HRMS (ES) m/z calcd for C<sub>32</sub>H<sub>43</sub>NO<sub>5</sub>NaSiS [MNa<sup>+</sup>]: 604.2529; found: 604.2504. A solution of this compound (478 mg, 0.82 mmol, 1 eq) in anhydrous acetone (5 mL) was treated with trifluoroacetic acid (TFA; 305 µL, 4.11 mmol, 5 eq) at room temperature The reaction mixture was stirred overnight. Another 5 equivalents of TFA were added and the resulting mixture was stirred for a further 3 h. The reaction was quenched with a saturated aqueous solution of NaHCO<sub>3</sub>, extracted with EtOAc. The organic layers were combined, washed with brine, dried over MgSO4 and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 15:1) to give 11 as a clear oil (376 mg, 88%).  $[\alpha]^{23}_{D} = -120$  (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta = 1.00$  (s, 9H,), 1.37-1.89 (m, 6H), 2.34 (s, 3H), 3.58-3.80 (m, 2H), 4.03-4.16 (m, 1H), 4.87-4.98 (m, 1H), 6.48-6.56 (m, 1H), 7.20 (d, J=8.0 Hz, 2H), 7.26-7.40 (m, 6H), 7.55-7.66 (m, 6H); <sup>13</sup>C NMR (62.9 MHz,  $CDCl_3$ ):  $\delta = 17.2, 21.6, 22.6, 26.9, 29.0, 34.3, 50.0, 60.6, 109.0, 123.7, 127.1, 127.7, 129.6, 129.9,$ 135.5, 135.6, 138.2, 147.8; FTIR (film):  $v_{max}$ =3070 (w), 2929 (m), 2857 (m), 1645 (w), 1428 (m), 1344 (s), 1167 (s), 1111 (s), 823 (w), 705 (s) cm<sup>-1</sup>; HRMS (ES) m/z calcd for C<sub>30</sub>H<sub>38</sub>NO<sub>3</sub>SiS [MH<sup>+</sup>]: 520.2342; found: 520.2351.

Synthesis of 2-(*tert*-butyl-diphenyl-silanyloxyethyl)-5-methyl-1-(toluene-4-sulfonyl)-1,2,3,4tetrahydro-pyridine (12) and 2-(*tert*-butyl-diphenyl-silanyloxyethyl)-5-methyl-1-(toluene-4sulfonyl)-1,2,3,6-tetrahydro-pyridine (13)



A flask containing 4Å molecular sieves (190 mg) was flame dried under vaccum. Wilkinson's catalyst (17 mg, 0.019 mmol, 0.1 eq), DBU  $(9 \mu L, 0.06 \text{ mmol}, 0.3 \text{ eq})$  and ethanol (6 mL) were added. The resulting mixture was added to the substrate 9 (101 mg, 1. 89 mmol) via cannula. The reaction mixture was stirred at 40 °C for 16 hours. Solvent was removed in vacuo and the residue purified by flash chromatography (petroleum ether/EtOAc, 30:1) to give the product as an inseperable 2:1 mixture (12:13) (67 mg, 66%). 12:  $[\alpha]_{D}^{22}$ =-13.0 (c 1.2, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =1.05 (s, 9H), 1.17-1.34 (m, 4H), 1.54 (s, 3H), 1.87-1.99 (m, 2H), 2.40 (s, 3H), 3.73 (m, 2H), 3.93-4.05 (m, 1H), 6.29 (s, 1H), 7.24 (d, *J*=7.5 Hz, 2H), 7.32-7.49 (m, 6H), 7.56-7.69 (m, 6H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>): δ=19.2, 20.9, 21.6, 22.7, 22.8, 26.9, 34.4, 49.3, 60.7, 118.0, 118.2, 127.1, 127.7, 129.6, 135.5, 135.6, 142.0, 143.2, 144.5; HRMS (ES): *m/z* calcd for C<sub>31</sub>H<sub>39</sub>NO<sub>3</sub>NaSiS [MNa<sup>+</sup>]: 556.2161; found: 556.2138; **13**: <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ=1.01 (s, 9H), 1.46-1.66 (m, 5H), 1.69 (dd, J=5.0, 17.0 Hz, 1H), 2.02-2.20 (m, 1H,), 2.36 (s, 3H,), 3.16 (d, J=18.0 Hz, 1H), 3.48-3.71 (m, 2H) 3.86 (d, J=18.0 Hz, 1H), 4.13-4.25 (m, 1H), 5.19-5.31 (m, 1H), 7.15 (d, J=8.0 Hz, 2H), 7.33-7.46 (m, 6H), 7.54-7.66 (m, 6H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>): δ=19.3, 19.7, 20.5, 21.4, 21.9, 22.3, 44.6, 51.5, 62.3, 118.3, 120.3, 121.2, 126.9, 127.7, 129.5, 129.7, 133.4, 135.6, 143.9; HRMS (ES): m/z calcd for C<sub>31</sub>H<sub>39</sub>NO<sub>3</sub>NaSiS [MNa<sup>+</sup>]: 556.2161; found: 556.2138.

#### Synthesis of 8-bromo-8-methyl-9-(toluene-4-sulfonyl)-2-oxa-9-aza-bicyclo [3.3.1] nonane (14)



Sodium metal (2 mg, 0.081 mmol, 1.2 eq) was dissolved in MeOH (1 mL). To the resulting mixture, piperidine **12** (36 mg, 0.067 mmol, 1.0 eq) in MeOH (1 mL) was added *via* cannula followed by bromine (4  $\mu$ L, 0.081 mmol, 1.2 eq). After concentration of the reaction mixture in vacuo, Et<sub>2</sub>O was added. The organic layer was washed with water and then extracted with Et<sub>2</sub>O. The combined organic fractions were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 5:1) to give **14** as a yellow oil (24 mg,

95%). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =1.41-1.63 (m, 3H), 1.85 (s, 3H), 1.95-2.15 (m, 3H), 2.42 (s, 3H), 3.62-3.90 (m, 2H), 4.01-4.12 (m, 1H), 5.43 (br, 1H), 7.28 (d, *J*=8.5 Hz, 2H), 7.84 (d, *J*=8.5 Hz, 2H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>):  $\delta$ =21.6, 28.2, 30.9, 33.4, 30.8, 38.2, 45.9, 59.9, 84.7, 127.7, 129.4, 142.3, 144.4; FTIR (film):  $v_{max}$ =2928 (m), 1598 (w), 1449 (w), 1342 (m), 1164 (s), 1141 (m), 1093 (m), 1048 (m), 1018 (m), 998 (m) cm<sup>-1</sup>; HRMS (ES): *m/z* calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>3</sub>NaS<sup>79</sup>Br [MNa<sup>+</sup>]: 396.0245; found: 396.0245.

#### Synthesis of 8-methyl-9-(toluene-4-sulfonyl)-2-oxa-9-aza-bicyclo[3.3.1]nonane (15)



AIBN (20 mg, 0.13 mmol, 1.0 eq) was added to a solution of **14** (47 mg, 0.13 mmol, 1.0 eq) in benzene (2.3 mL). The solution was purged with nitrogen for 15 min then tributyltin hydride (100  $\mu$ L, 0.38 mmol, 3.0 eq) was added and the resulting mixture was stirred under reflux for 16 h. The reaction mixture was cooled to room temperature and benzene was removed in vacuo to give an oil. Purification by flash chromatography (petroleum ether/EtOAc, 5:1) afforded the product **15** as a colourless solid (34 mg, 92%). M.p. 142-144 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ = 0.96 (d, *J*=6.5 Hz, 3H), 1.22-1.35 (m, 1H), 1.58-1.97 (m, 6H), 2.35 (s, 3H), 3.33-3.45 (m, 1H), 3.84-3.97 (m, 1H), 3.97-4.06 (m, 1H), 5.22 (d, *J*=2.5 Hz, 1H), 7.22 (d, *J*=8.5 Hz, 2H), 7.72 (d, *J*=8.5 Hz, 2H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>):  $\delta$ =17.8, 21.6, 26.8, 26.9, 30.9, 36.6, 46.0, 60.6, 81.6, 127.4, 129.6, 140.1, 144.3; HRMS (ES): *m/z* calcd for C<sub>15</sub>H<sub>22</sub>NO<sub>3</sub>S [MH<sup>+</sup>]: 296.1320; found: 296.1326.

Synthesis of 2-allyl-6-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-1-(toluene-4-sulfonyl)-piperidin-3-ol (16a) and 2-allyl-6-(2-hydroxy-ethyl)-1-(toluene-4-sulfonyl)-piperidin-3-ol (16b)



A 0.06 M solution of dimethyldioxirane in acetone (5 mL, 0.30 mmol, 2.5 eq.) was added to a solution of **11** (63 mg, 0.12 mmol, 1 eq) in CH<sub>2</sub>Cl<sub>2</sub> (12 mL) at 0 °C *via* syringe. The reaction was stirred at 0 °C for 1 h and then allowed to warm to room temperature overnight. The reaction mixture was then concentrated in vacuo to provide the crude epoxide as colourless oil. No further purification was carried out. To a solution of the crude epoxide (65 mg, 0.16 mmol, 1.0 eq.) in DCM (6 mL) at -78 °C was slowly added BF<sub>3</sub>.OEt<sub>2</sub> (61  $\mu$ L, 0.48 mmol, 4.0 eq). The resulting solution was stirred for 15 min before allyltrimethylsilane (116  $\mu$ L, 0.73 mmol, 6.0 eq) was added slowly at the same temperature.

The reaction mixture was stirred at room temperature overnight and quenched with NH<sub>4</sub>Cl. The aqueous layer was extracted with EtOAc and the organic layer was washed with a saturated aqueous solution of NaHCO<sub>3</sub> and brine. The organic layer was dried over MgSO<sub>4</sub>, concentrated in vacuo and purified by silica gel chromatography (petroleum ether/EtOAc, 4:1) to give 16a (49 mg, 70%) and 16b (4 mg, 10%) as oils. **16a**:  $[\alpha]^{21}_{D}$ =-6.4 (c 1.1, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ =1.08 (s, 9H), 1.35-1.40 (m, 1H), 1.48-1.52 (m, 1H), 1.75-1.87 (m, 3H), 1.95-2.03 (m, 1H), 2.21-2.36 (m, 2H), 2.41 (s, 3H), 3.65-3.74 (m, 2H), 3.80 (br, 1H), 3.97-4.02 (m, 1H), 4.14-4.19 (m, 1H), 4.99-5.07 (m, 2H), 5.68-5.78 (m, 1H), 7.20 (d, J=8.0 Hz, 2H), 7.26-7.40 (m, 6H), 7.55-7.66 (m, 6H,); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>): δ=19.2, 20.1, 21.2, 21.5, 26.9, 37.3, 39.3, 49.4, 58.9, 61.7, 65.5, 117.8, 127.4, 127.7, 129.5, 133.2, 133.6, 135.5, 135.6, 136.3, 143.7. FTIR (film): v<sub>max</sub>=3530 (s), 3080 (m), 2960 (s), 2860 (s), 1670 (w), 1470 (w), 1430 (m), 1330 (m), 1260 (s), 1160 (s), 1110 (s), 939 (m), 816 (w) cm<sup>-1</sup>; HRMS (ES): m/z calcd for C<sub>33</sub>H<sub>44</sub>NO<sub>4</sub>SiS [MH<sup>+</sup>]: 578.2760; found: 578.2756; **16b**:  $[\alpha]^{21}_{D}$ =+50 (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ=1.11-1.34 (m, 2H), 1.42-1.53 (m, 1H), 1.57-2.0 (m, 3H), 2.21-2.54 (m. 5H), 3.09 (br. 1H), 3.57-3.72 (m.1H), 3.73-3.81 (m. 2H), 4.14-4.27 (m. 1H), 4.98-5.16 (m, 2H), 5.72-5.91 (m, 1H), 7.29 (d, J=8.5 Hz, 2H), 7.79 (d, J=8.5 Hz, 2H); <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>):  $\delta$ =21.3, 21.6, 29.7, 37.7, 39.7, 48.5, 58.7, 59.4, 65.3, 118.0, 127.3, 129.6, 134.8, 137.6, 143.5; FTIR (film):  $v_{max}$ =3407 (s), 2938 (m), 1721 (w), 1638 (w), 1441 (w), 1400 (w), 1319 (m), 1157 (s), 1098 (m), 924 (m), 816 (w) cm<sup>-1</sup>; HRMS (ES): m/z calcd for C<sub>17</sub>H<sub>26</sub>NO<sub>4</sub>S [MH<sup>+</sup>]: 340.1583; found: 340.1589.

Synthesisof(-)-(1R,3S,6S)-3-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-2-tosyl-2-aza-bicyclo[4.1.0]heptane (17)



To a solution of **11** (0.90 mg, 0.17 mmol, 1.0 eq) in toluene (3 mL) was added Et<sub>2</sub>Zn (1.04 mL, 1.0 M in hexanes, 1.04 mmol, 6.0 eq) and CH<sub>2</sub>I<sub>2</sub> (0.17 mL, 2.08 mmol, 12.0 eq) at 0 °C. After 60 hours the reaction was quenched with saturated aqueous NH<sub>4</sub>Cl solution and extracted with EtOAc. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub> and concentrated in vacuo. Purification by silica gel chromatography (petroleum ether/EtOAc, 10:1) provided **17** as a clear oil (89 mg, 96%, dr > 95 : 5).  $[\alpha]_D^{21} = -30.0$  (*c* 1.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ =-0.01 (ddd, *J* = 7.0, 6.0, 3.5 Hz, 1H), 0.61 (dt, *J*=9.0, 6.0 Hz, 1H), 0.99-1.07 (m, 1H), 1.09 (s, 9H), 1.15 (m, 1H), 1.45 (m, 1H), 1.54 (dd, *J*=14.0, 4.0 Hz, 1H), 1.63-1.82 (m, 2H), 1.87-1.98 (m, 1H), 2.43 (s, 3H), 2.72 (ddd, *J*=9.0, 6.5, 3.5 Hz, 1H), 3.70-3.83 (m, 2H), 3.93 (m, 1H), 7.26 (d, *J*=8.0 Hz, 2H), 7.38-7.48 (m, 6H), 7.68 – 7.76 (m, 6H); <sup>13</sup>C (100 MHz, CDCl<sub>3</sub>):  $\delta$ =8.7, 10.1, 14.6, 19.2, 21.5, 23.8, 26.1, 26.9, 34.6, 48.3, 61.4, 127.3, 127.6, 129.4, 129.6, 133.8, 135.6, 138.0, 142.8; FTIR (film.):  $v_{max}$ =2930 (m), 2855 (m),

1342 (m), 1163 (s), 1111 (s) cm<sup>-1</sup>; HRMS (ES): m/z calcd for C<sub>31</sub>H<sub>40</sub>NO<sub>3</sub>SiS [MH<sup>+</sup>]: 534.2498; found: 534.2483.

Synthesis of (+)-(1S,2R,5S)-2-bromo-2-(bromomethyl)-9-tosyl-8-oxa-9-aza-bicyclo[3.3.1]nonane (18)



To a solution of **17** (72 mg, 0.13 mmol, 1.0 eq) in MeOH (6 mL) was added *N*-bromosuccinimide (168 mg, 0.94 mmol, 7.0 eq) at room temperature. After 17 hours the reaction mixture was concentrated in vacuo. The residue was dissolved in DCM and filtered. The filtrate was washed sequentially with saturated aqueous Na<sub>2</sub>SO<sub>3</sub> solution and brine before drying over MgSO<sub>4</sub> and concentrating in vacuo. Purification by silica gel chromatography (petroleum ether/EtOAc, 5:1) provided **18** as a colourless solid (46 mg, 75%). M.p. 175 - 177 °C;  $[\alpha]_D^{20} = + 11.0$  (*c* 1.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ =1.48 -1.70 (m, 2H), 1.92- 2.17 (m, 3H), 2.23- 2.34 (m, 1H), 2.45 (s, 3H), 3.62-3.92 (m, 4H), 4.15 (m, 1H), 5.64 (s, 1H), 7.32 (d, *J*=8.5 Hz, 2H), 7.86 (d, *J*=8.5 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ =21.6, 28.0, 28.3, 30.1, 42.4, 45.4, 59.8, 67.4, 82.9, 127.7, 129.5, 137.1, 143.8; FTIR (film,):  $\nu_{max}$ =2961 (w), 2927 (m), 2850 (w), 1341 (s), 1165 (s) cm<sup>-1</sup>; HRMS (ES): *m/z* calcd for C<sub>15</sub>H<sub>19</sub>NO<sub>3</sub>S<sup>79</sup>Br<sub>2</sub>Na [MH<sup>+</sup>]: 473.9350; found: 473.9345.

#### Synthesis of (-)-2-((1R,3S,6S)-2-tosyl-2-aza-bicyclo[4.1.0]heptan-3-yl)ethanol (19)



To a solution of **17** (66 mg, 0.12 mmol, 1.0 eq) in THF (4 mL) was added TBAF solution (0.19 mL, 1.0 M in THF, 0.19 mmol, 1.5 eq) at room temperature. After 17 hours the reaction was quenched with water and extracted with EtOAc. The combined organic layers were washed with brine before drying over MgSO<sub>4</sub> and concentrating in vacuo. Purification by silica gel chromatography (petroleum ether/EtOAc, 10:1 to petroleum ether/EtOAc, 1:1) provided **19** as a pale yellow oil (36 mg, 99%, dr > 98 : 2).  $[\alpha]_D^{21}$  =-15.7 (*c* 0.7, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ =-0.16 (ddd, *J*=6.5, 6.0, 3.5 Hz 1H), 0.58 (dt, *J*=9.5, 6.0 Hz, 1H), 1.05 (tt, *J*=14.0, 5.0 Hz, 1H) 1.21 (m, 1H), 1.40 (m, 1H), 1.49 (m, 1H), 1.58 (dd, *J*= 14.0, 4.0 Hz, 1H), 1.76-1.88 (m, 2H), 2.45 (s, 3H), 2.86 (ddd, *J*=9.5, 6.5, 3.5 Hz, 1H), 3.13 (m, 1H,), 3.75 (m, 1H), 3.91-4.01 (m, 2H), 7.31 (d, *J*=8.5 Hz, 2H), 7.76 (d, *J*=8.5 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ = 7.6, 9.9, 14.5, 21.6, 24.6, 25.9, 33.9, 47.5, 58.5, 127.3, 129.6, 137.4,

143.4. FTIR (film) :  $v_{max}$ =3413 (s), 2936 (m), 2874 (m), 1336 (m), 1159 (s), 1094 (m) cm<sup>-1</sup>; HRMS (EI): m/z calcd for C<sub>15</sub>H<sub>21</sub>NO<sub>3</sub>S [M<sup>+</sup>]: 295.1242; found: 295.1253.

Synthesis of (2S,3R,6S)-6-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-3-(iodomethyl)-2-methoxy-1tosylpiperidine (20)



To a solution of cyclopropane **17** (200 mg, 0.37 mmol, 1.0 eq) in MeOH (20 mL) was added NIS (590 mg, 2.62 mmol, 7.0 eq) at room temperature under nitrogen. The reaction was stirred for 3 hours before quenching with saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>. The reaction mixture was extracted with DCM, washed with brine and dried over MgSO<sub>4</sub>. The reaction mixture was concentrated in vacuo to provide crude **20** (259 mg, 100%). The product was characterised by <sup>1</sup>H NMR spectroscopy before being employed directly in the next step. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ =1.10 (s, 9H), 1.24-1.45 (m, 4H), 1.90- 2.23 (m, 3H), 2.44 (s, 3H), 2.86-2.98 (m, 2H), 3.38 (s, 3H), 3.57-3.72 (m, 2H), 4.10 (m, 1H), 5.22 (br, 1H), 7.26 (d, *J*=8.0 Hz, 2H), 7.36-7.50 (m, 6H), 7.64-7.77 (m, 4H), 7.80 (d, *J*=8.0 Hz, 2H).

Synthesis of (-)-(*E*)-methyl 4-((2S,3R,6S)-6-(2-(tert-butyldiphenylsilyloxy)ethyl)-3-methyl-1-tosylpiperidin-2-yl)but-2-enoate (22)



To a solution of crude **20** (259 mg, 0.37 mmol, 1.0 eq) in toluene (14.7 mL) was added AIBN (12 mg, 0.07 mmol, 0.2 eq). The reaction mixture was purged with nitrogen for 15 minutes before HSnBu<sub>3</sub> (0.15 mL, 0.56 mmol, 1.5 eq) was added. The reaction was heated at reflux for 1  $\frac{1}{2}$  hours before cooling to room temperature and concentrating in vacuo. Purification by column chromatography on Fluorosil<sup>®</sup> (petroleum ether to petroleum ether/EtOAc 20:1) provided the crude product as a yellow oil. The product was contaminated by residual HSnBu<sub>3</sub> and was therefore used directly in the next step. A solution of the crude material (212 mg, 0.37 mmol, 1.0 eq) in DCM (10 mL) was cooled to -85 °C. To this was added a solution of **21**<sup>3</sup> (387 mg, 2.25 mmol, 6.0 eq) in DCM (3 mL) followed by BF<sub>3</sub>·OEt<sub>2</sub> (0.19 mL, 1.50 mmol, 4.0 eq) dropwise. The reaction was held at -85 °C for 1 hour before quenching with saturated aqueous NaHCO<sub>3</sub> solution. The reaction mixture was extracted with DCM,

<sup>&</sup>lt;sup>3</sup> J. R. Grunwell, A. Karipides, C. T. Wigal, S.W. Heinzman, J. Parlow, J. A. Surso, L. Clayton, F. J. Fleitz, M. Daffner, J. E. Stevens, J. Org. Chem. 1991, 56, 91.

washed with brine, dried over MgSO<sub>4</sub> and concentrated in vacuo. Purification by silica gel chromatography (petroleum ether/EtOAc, 90:10) provided **22** as a colourless oil (173 mg, 73% over three steps, dr > 98 : 2).  $[\alpha]_D{}^{21}$ =- 6.6 (*c* 1.05, CHCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =0.73 (d, *J*=7.0 Hz, 3H), 0.92 (t, *J*=7.5 Hz, 1H), 1.07 (s, 9H), 1.24-1.98 (m, 6H), 2.38 (s, 3H), 2.48 (t, *J*=7.5 Hz, 2H), 3.65 (t, *J*=6.5 Hz, 2H), 3.75 (m, 4H), 4.15 (m, 1H), 5.82 (d, *J*=15.5 Hz, 1H), 6.89 (dt, *J*=15.5, 7.5 Hz, 1H), 7.20 (d, *J*=8.0 Hz, 2H), 7.34-7.46 (m, 6H), 7.61-7.73 (m, 6H); <sup>13</sup>C NMR (62 MHz, CDCl<sub>3</sub>):  $\delta$ =18.7, 19.2, 20.3, 21.4, 21.5, 26.9, 29.4, 37.9, 39.4, 49.9, 51.6, 57.2, 61.8, 123.2, 127.1, 127.7, 129.5, 129.7, 133.7, 135.6, 138.5, 142.8, 146.1, 166.6. FTIR (film): *v*<sub>max</sub>=2952 (m), 2858 (m), 1724 (s), 1657 (m), 1428 (w), 1327 (m), 1162 (s) cm<sup>-1</sup>; HRMS (ES): *m/z* calcd for C<sub>36</sub>H<sub>48</sub>NO<sub>5</sub>SiS [MH<sup>+</sup>]: 634.3022; found: 634.2996.

Synthesis of 4-((2S,3R,6S)-6-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-3-methyl-1-tosylpiperidin-2yl)butan-1-ol (23)



A solution of 22 (60 mg, 0.09 mmol, 1.0 eq) in EtOAc (1.28 mL) was passed through a 10% palladium on carbon CatCart<sup>™</sup> cartridge under 1 bar of hydrogen at 20 °C on an H-cube<sup>™</sup> reactor. The reaction mixture was placed on a continual loop at a flow rate of 1 mL / min for 1 h. The reaction mixture was concentrated under reduced pressure to provide the reduced ester as a colourless oil (60 mg, 100%).  $[\alpha]_{D}^{20}=-2.0$  (c 1.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta=0.73$  (d, J=7.0 Hz, 3H), 0.90-0.99 (m, 1H), 1.06 (s, 9H), 1.24-1.33 (m, 1H), 1.53-1.75 (m, 7H), 1.81 (m, 1H), 1.98 (m, 1H), 2.34 (q, J=6.5 Hz, 2H), 2.39 (s, 3H), 3.57-3.70 (m, 6H), 4.10 (m, 1H), 7.21 (d, J=8.0 Hz, 2H), 7.35-7.47 (m, 6H), 7.63-.72 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ=19.2, 19.3, 21.1, 21.5, 21.8, 22.8, 26.9, 30.7, 33.8, 36.4, 38.0, 50.1, 51.5, 58.5, 61.7, 127.2, 127.7, 129.4, 129.6, 133.7, 135.6, 138.7, 142.6, 173.9. FTIR (film):  $v_{max}$  = 3048 (m), 2931 (s), 2858 (m), 1738 (s), 1462 (m), 1428 (m), 1328 (m), 1162 (s), 1109 (s), 1090 (s) cm<sup>-1</sup>; HRMS (ES): m/z calcd for C<sub>36</sub>H<sub>50</sub>NO<sub>5</sub>SiS [MH<sup>+</sup>]: 636.3179; found: 636.3162. To a solution of the reduced product (59 mg, 0.09 mmol, 1.0 eq) in THF (6 mL) was added LiAlH<sub>4</sub> (7 mg, 0.18 mmol, 2.0 eq) at 0 °C. After 10 minutes the reaction was allowed to warm to room temperature, stirred for 2 h, quenched with  $K_2CO_3$  solution and extracted with DCM. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub> and concentrated in vacuo to provide 23 as a colourless oil (57 mg, 100%).  $[\alpha]_D^{22}$ =-4.0 (c 1.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =0.75 (d, J=7.0 Hz, 3H), 0.88-0.99 (m, 2H), 1.09 (s, 9H), 1.20-2.11 (m, 11H), 2.41 (s, 3H), 3.57-3.74 (m, 5H), 4.12 (m, 1H), 7.23 (d, J=8.0 Hz, 2H), 7.35-7.51 (m, 6H), 7.62-7.76 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta=19.6$ , 19.8, 21.6, 21.9, 22.3, 24.0, 27.3, 31.1, 32.9, 37.2, 38.5, 50.5, 59.2, 62.2, 63.2, 127.6, 128.1, 129.7, 130.1, 134.1, 136.0, 139.2, 143.0; FTIR (film):  $v_{max}$ = 3359 (m), 2922 (s), 2853 (m), 1470 (m), 1428 (m), 1324 (m), 1160 (s), 1111 (s) cm<sup>-1</sup>; HRMS (ES): m/z calcd for C<sub>35</sub>H<sub>50</sub>NO<sub>4</sub>SiS [MH<sup>+</sup>]: 608.3230; found: 608.3215.

### Synthesis of 4-((2S,3R,6S)-6-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-3-methylpiperidin-2-yl)butan-1-ol (24)



Sodium metal (101 mg, 4.41 mmol, 47.0 eq) was washed with petroleum ether and added to a solution of naphthalene (481 mg, 3.75 mmol, 40.0 eq) in 1,2-dimethoxyethane (2 mL). The dark green mixture was stirred for 45 min before addition to a solution of alcohol **23** (57 mg, 0.09 mmol, 1.0 eq) in 1,2-dimethoxyethane (1 mL) at -78 °C. After 2 hours the reaction was quenched at -78 °C with saturated NH<sub>4</sub>Cl solution. The reaction was extracted with DCM, washed with brine, dried over MgSO<sub>4</sub> and concentrated in vacuo. Purification by silica gel chromatography (petroleum ether/EtOAc to DCM/MeOH gradient) provided **24** as a pale yellow oil (34 mg, 79%). [ $\alpha$ ]<sub>D</sub><sup>20</sup>=- 12.5 (*c* 1.3, CHCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$ =0.87 (d, *J*=6.5 Hz, 3H), 1.04 (s, 9H), 1.08-1.90 (m, 13H), 2.25 (br, 1H), 2.80 (br, 1H), 3.58 (m, 3H), 3.77 (m, 2H), 7.32-7.48 (m, 6H), 7.65 (m, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ =18.5, 19.2, 21.6, 26.9, 32.3, 32.7, 32.8, 34.1, 35.7, 38.8, 55.3, 61.8, 62.4, 63.0, 127.7, 129.7, 133.7, 135.5. FTIR (film):  $v_{max}$ =3356 (m), 2929 (s), 2856 (s), 1589 (w), 1455 (w), 1427 (m), 1111 (s) cm<sup>-1</sup>; HRMS (ES): *m/z* calcd for C<sub>28</sub>H<sub>44</sub>NO<sub>2</sub>Si [MH<sup>+</sup>]: 454.3141; found: 454.3127.

## Synthesis of (1R,4S,9aS)-4-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-1-methyl-octahydro-1Hquinolizine (25)



To a solution of amino alcohol **24** (33 mg, 0.07 mmol, 1.0 eq) in DCM (1.8 mL) was added triphenylphosphine (57 mg, 0.21 mmol, 3.0 eq), iodine (37 mg, 0.14 mmol, 2.0 eq) and imidazole (15 mg, 0.21 mmol, 3.0 eq) at – 10 °C. The reaction was allowed to warm to room temperature overnight. After 16 hours the reaction was quenched with saturated NaHCO<sub>3</sub> and extracted with DCM. The combined organic layers were washed with brine, dried with MgSO<sub>4</sub> and concentrated in vacuo. Purification by silica gel chromatography (petroleum ether/EtOAc, 1:1) provided **25** as a yellow oil (25 mg, 79%). [ $\alpha$ ]<sub>D</sub><sup>21</sup>=-35.8 (*c* 1.2, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ =0.83 (d, *J* = 6.5 Hz, 3H), 0.98 (m, 1H), 1.04 (s, 9H), 1.10-1.74 (m, 12H), 1.83-2.04 (m, 3H), 3.07 (br, 1H), 3.71 (t, *J*=7.0 Hz,

2H), 7.34-7.45 (m, 6H), 7.64-7.69 (m, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ =19.6, 19.7, 24.9, 26.5, 27.3, 30.4, 32.3, 34.2, 36.3, 37.4, 52.0, 61.3, 62.1, 70.2, 128.0, 129.9, 134.4, 136.0. FTIR (film):  $v_{max}$  = 3071 (w), 2930 (s), 2856 (m), 2787 (w), 1472 (w), 1428 (m), 1389 (w), 1361 (w), 1112 (s), 1086 (m) cm<sup>-1</sup>; HRMS (ES): *m/z* calcd for C<sub>28</sub>H<sub>42</sub>NO<sub>2</sub>Si [MH<sup>+</sup>]: 436.3036; found: 436.3040.

#### Synthesis of 2-((1R,4S,9aS)-1-methyl-octahydro-1H-quinolizin-4-yl)ethanol (26)<sup>4</sup>



To a solution of **25** (17 mg, 0.04 mmol, 1.0 eq) in THF (2 mL) was added TBAF (0.06 mL, 1.0 M solution in THF, 0.06 mmol, 1.5 eq) at room temperature. After 13 hours the reaction mixture was concentrated in vacuo. Purification by column chromatography on Fluorosil<sup>®</sup> (petroleum ether/EtOAc gradient to DCM/MeOH 3.3:1 with 2% NEt<sub>3</sub>) provided **26** as a colourless oil (7 mg, 100%).  $[\alpha]_D^{21}=-34.8 (c \ 0.7, CHCl_3)$ ; Lit<sup>4</sup>.  $[\alpha]_D^{20}=-32.8 (c \ 1.0, CHCl_3)$ ; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta=0.85$  (d, *J*=6.5 Hz, 3H), 0.96-1.96 (m, 15H), 2.21-2.46 (2H, m), 3.53 (br, 1H), 3.67 (ddd, *J*=11.0, 5.5, 3.0 Hz, 1H), 4.06 (td, *J*=11.0, 3.5 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta=8.4$ , 19.2, 24.4, 25.9, 29.4, 30.1, 32.0, 33.3, 59.1, 60.3, 61.7, 69.8; FTIR (film):  $v_{max}=3358$  (m), 2921 (s), 2851 (m), 1658 (w), 1632 (w), 1469 (w), 1378 (w), 1042 (w) cm<sup>-1</sup>; HRMS (ES): *m*/*z* calcd for C<sub>12</sub>H<sub>24</sub>NO: 198.1858 [MH<sup>+</sup>]; found: 198.1864.

<sup>&</sup>lt;sup>4</sup> M. Fellah, M. Santarem, G. Lhommet, V. Mouriès-Mansuy, J. Org. Chem. 2010, 75, 7803.



















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### <sup>1</sup>H spectra of compound (-)- 217A



<sup>1</sup>H spectra of compound (-)- 217A, J. Org. Chem., 2010, 75, 7803



## <sup>1</sup>H-<sup>1</sup>H NOESY spectrum of compound 22



