Total Synthesis of (±)-Vertine with Z-Selective RCM as a Key Step

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Supplementary Information

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1. General

Solvents were purified on Al_2O_3 drying columns using a Solvtek system or by following standard procedures. Reactions and manipulations involving organometallic or moisture sensitive compounds were carried out under dry nitrogen and glassware was heated under vacuum prior use.

Analytical thin layer chromatography (TLC) was performed with Merck SIL G/UV_{254} plates visualized with UV light. Flash column chromatography was performed in air with silicagel 60 (Fluka).

Microwave reactions were performed on a Biotage Initiator, SW version 1.2 build 5637.

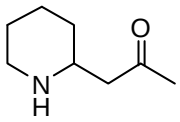
NMR spectra were recorded on Bruker ARX-500, AMX-400 spectrometers in the solvent indicated. ^{1}H- and ^{13}C-NMR chemical shifts (δ) are quoted in parts per million (ppm) relative to the TMS scale ($CDCl_3$: $\delta_C \equiv 77.05$ ppm; residual $CHCl_3$: $\delta_H \equiv 7.26$ ppm). Coupling constants *J* are quoted in Hz.

Infrared spectra (bands in cm^{-1}) were recorded on a Perkin–Elmer Spectrum 100 spectrophotometer using a diamond ATR Golden Gate accessory.

Electron impact (EI) HRMS mass spectra were obtained using a *Finningan MAT 95* spectrometer operating at 70eV. Electrospray ionization (ESI) HRMS analyses were measured on a VG analytical 7070E spectrometer. Melting points were determined on a Büchi 540 spectrometer and are uncorrected.

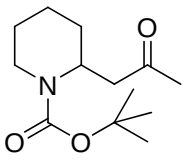
2. Specific procedures

(±) Pelletierine



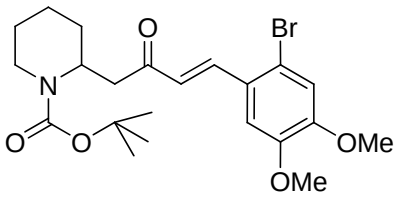
According to a procedure adapted from that described by Quick.[1] Freshly distilled Piperidine (10 ml, 100 mmol) was added dropwise to a rapidly stirred suspension of NCS (15.120 g, 111.6 mmol) in ether (500 ml). After stirring for 4 h at room temperature, the mixture was filtered through celite® and the filtrate concentrated to ~80 ml behind a safety screen. The crude chloroamine was added dropwise into an ice-cold solution of KOH (5.600 g, 100 mmol) in absolute ethanol (50 ml). The mixture was allowed to stir overnight, with a white precipitate forming which was removed by filtration. In parallel, the sodium salt of ethyl acetoacetate was prepared from NaOH (6 g, 150 mmol) and ethyl acetoacetate (12.800 ml, 100 mmol) in water, heating to 50°C for 4 h and then stirring overnight at room temperature. The crude piperidine and the enolate solutions were combined and refluxed for 4h. The resulting yellow solution was cooled to room temperature, and most of the organic solvent (ether, EtOH) removed under reduced pressure. The aqueous mixture was extracted with CH_2Cl_2 (3×75ml), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting oil was purified by silica gel column chromatography eluting with $CHCl_3$:MeOH:aq.NH_3, (85:15:1) affording racemic pelletierine (7 g, 50%) as yellow oil. Spectral data matches literature values.[1] **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.03-2.87 (2H, m), 2.71-2.59 (1H, m), 2.48 (2H, d, *J* 6.4, C<u>H</u>$_2$C(O)CH$_3$), 2.12 (3H, s, C<u>H</u>$_3$), 2.10 (1H, br s, N<u>H</u>), 1.79-1.70 (1H, m), 1.64-1.89 (2H, m), 1.46-1.26 (2H, m), 1.20-1.06 (1H, m). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 67.68, 52.19, 50.12, 46.45 32.03 30.38 25.59 25.40 24.31

[Tert-butyl-2-(2-oxopropyl)piperidine-1-carboxylate] (7)



A solution of Pelletierine (1.500 g, 10.6 mmol), di-*tert*butyldicarbonate (3.140 g, 14.84 mmol) and $NaHCO_3$ (2.700 g) in EtOH (53 ml) was stirred under ultrasound for 30 mn. The reaction mixture was then filtered through Celite® and evaporated *in vacuo*. The residue was then purified by flash chromatography on silica gel eluting with EtOAc:Cyclohexane (1:3) to yield colourless oil (1.540 g, 60%). Spectral data matches literature values.[2] **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.75 (1H, s, NC<u>H</u>), 4 (1H, s, NC<u>H</u>), 2.85 (1H, t, J Hz), 2.69 (2H, C<u>H</u>$_2$CO, dd J 2, 6.8 Hz), 2.22 (1H, s, C<u>H</u>$_2$CO), 1.6 (6H, C<u>H</u>$_2$, m), 1.48 (9H, C<u>H</u>$_3$, s). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.6, 79.5, 47.2, 44.2, 30.1, 28.4, 27.3, 26.8, 25.3, 18.8.

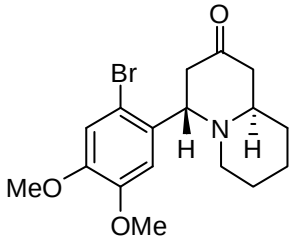
[(R, E)-tert-butyl 2-(4-(2-bromo-4,5-dimethoxyphenyl)-2-oxobut-3-enyl)piperidine-1-carboxylate] (8)



A solution of compound **7** (2.300 g, 9.54 mmol), 6-Bromo veratraldehyde (2.660 g, 10.97 mmol) and NaOH 6M (2.380 ml, 14.3 mmol) in MeOH (160 ml) was heated at 55°C during 16h. The reaction mixture was cooled down and evaporated *in vacuo*. Water was added (50 ml) then the aq. layer was extracted with CH_2Cl_2 (3×75 ml). The combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The residue was then purified by flash chromatography on silica gel eluting Et_2O:Cyclohexane (6:4) to yield yellow oil (4 g, 91 %). **IR** (neat): 2934, 1679, 1503, 1592, 1262, 1162, 1058, 910, 727. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (1H, d, J 16 Hz, C<u>H</u>), 7.03 (1H, s, Ar<u>H</u>), 6.97 (1H, s, Ar<u>H</u>), 6.5 (1H, d, J 16 Hz, C<u>H</u>), 4.7 (1H, s, C<u>H</u>), 3.9 (1H, s, C<u>H</u>), 3.8 (6H, s, C<u>H</u>$_3$), 2.83 (2H, d, J 7.2 Hz, C<u>H</u>$_2$), 2.7 (1H, m, C<u>H</u>), 1.57-1.55 (6H, m, C<u>H</u>$_2$), 1.3 (9H, s, C<u>H</u>$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 199.6, 156.1,

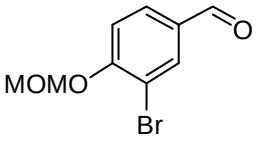
152.8, 150.5, 142.5, 128.1, 127.6, 119.1, 116.9, 110.5, 80.9, 57.6, 57.4, 54.8, 42.4, 29.7, 26.7, 20.3. **HR-MS** (ESI) for $C_{22}H_{31}NO_5$ $[M+H]^+$: calcd. 468.1385, found 468.1380.

[(4S,9aR)-hexahydro-4-(2-bromo-4,5-dimethoxyphenyl)-1H-quinolizin-2(6H)-one] (4)



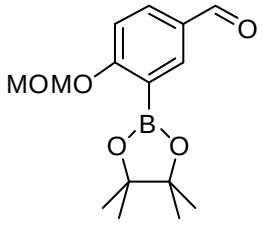
To a solution of compound **8** (1.940 g, 4.15 mmol) in CH_2Cl_2 (14 ml) was added TFA (17 ml, 220 mmol) dropwise at 0°C. The reaction was then stirred at this temperature for 1h. The reaction mixture was evaporated *in vacuo* then taken up in THF (40 ml) and cooled to 0°C. A solution of 1M NaOH (8.310 ml) was added dropwise. The reaction mixture was stirred at room temperature for 4h then extracted with EtOAc (100 ml); the combined organic layers were washed with brine (3× 100 ml) and dried over $MgSO_4$. The product was then purified by flash chromatography on silica gel eluting with EtOAc to yield yellow solid (1.100 g, 72%). **m.p.** 102-104°C. **IR** (neat): 3463, 3025, 2945, 2970, 1738, 1506, 1445, 1366, 1217, 853.9. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.95 (1H, s, ArH), 6.81 (1H, s, ArH), 4.77 (1H, dd, *J* 5.6, 6.8 Hz, NCHAr), 3.82 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 3.24-3.20 (1H, m, NCHalkyl), 2.93 (1H, d, *J* 12.8 Hz, Nalkyl-H), 2.68-2.65 (2H, m, COalkyl-H), 2.40-2.33 (3H, m, COalkyl-H+ Nalkyl-H), 1.76-1.73 (1H, m, alkyl-H), 1.60-1.25 (5H, m, alkyl-H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 209.2, 148.9, 148.7, 131.9, 115.4, 114.3, 111.1, 59.4, 56.9, 56.3, 56.2, 50.1, 47.5, 47.2, 29.0, 24.4, 21.8**.** **HR-MS** (ESI) for $C_{17}H_{23}Br_1O_3N$ $[M+H]^+$: calcd. 368.0855, found 368.0859.

[3-bromo-4-(methoxymethoxy)benzaldehyde]



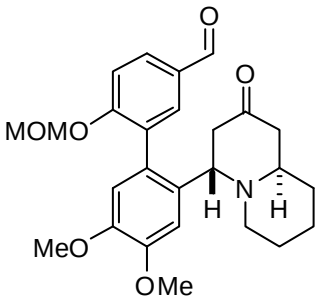
A suspension of 3-Bromo-4-hydroxy-benzaldehyde (15 g, 74.6 mmol) in CH_2Cl_2 (155 ml) was cooled with an ice bath before addition of Hunig's base (20.440 ml, 119 mol); dissolution occurs upon addition of the base. MOMCl (7.360 ml, 97 mmol) was added dropwise, and the reaction mixture was stirred for 16h at room temperature then quenched with sat. aq. NH_4Cl (50 ml). The aq. layer was extracted with EtOAc (3× 75 ml); the combined organic layers were washed with brine (3× 100 ml) and dried over $MgSO_4$. The residue was passed through a pad of silica, eluting with EtOAc:cyclohexane (1:3) to yield yellow solid (18.600 g, 98%). **m.p.** 54-56°C. **IR** (neat): 2965, 2832, 1691, 1591, 1488, 1142, 915. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.9 (1H, s, C<u>H</u>O), 8.13 (1H, d, *J* 2.0 Hz, Ar<u>H</u>), 7.83 (1H, dd, *J* 2.0, 8.4 Hz, Ar<u>H</u>), 7.16 (1H, d, *J* 8.4 Hz, Ar<u>H</u>), 5.39 (2H, s, OC<u>H</u>$_2$O), 3.57 (3H, s, CH_2OC<u>H</u>$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 189.7, 158.5, 134.7, 131.5, 130.8, 115.1, 113.4, 94.8, 56.6. **HR-MS** (ESI) for $C_9H_{10}Br_1O_3$ $[M+H]^+$: calcd. 244.9820, found 244.9807.

[4-(methoxymethoxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde] (11)



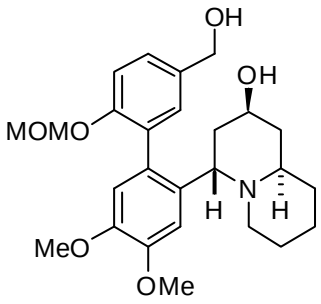
To a 20 mL microwave vial equipped with magnetic stirring bar were added 3-bromo-4-MOM-benzaldehyde (0.600 g, 2.45 mmol), bis(pinacolato)diboron (0.687 g, 2.7 mmol), Pd(dppf)Cl_2 (0.059 g, 3 mol%) and KOAc (0.600 g, 2 mmol, dried by heating at 130^{o}C under vacuum for 16h). Then the vial was sealed, degassed, and purged with N_2. Degassed Dioxane (17 ml) was added. The reaction mixture was subjected to microwave irradiation for 40 minutes at 140^{o}C (pre-stirring 30 seconds, normal absorption level). Then the reaction mixture was filtered over celite® and washed with EtOAc (100 ml). The filtrate was evaporated in *vacuo*, the residue was purified by flash chromatography on silica gel eluting with Et_2O: pentane (1:2) to yield colourless oil (0.600 g, 87%). **IR** (neat): 2977, 1691, 1344, 1141, 915. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.82 (1, s, C<u>H</u>O), 8.13 (1H, d, *J* 2.2 Hz, Ar<u>H</u>), 7.83 (1H, dd, *J* 2 2.,8.6Hz, Ar<u>H</u>), 7.06 (1H, d, *J* 8.6 Hz, Ar<u>H</u>), 5.2 (2H, s, OC<u>H</u>$_2$O), 3.42 (3H, s, OC<u>H</u>$_3$), 1.28 (12H, s, C<u>H</u>$_3$).**^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.1,166.3, 139.8, 133.7, 130.1, 114.2, 94.2, 83.9, 56.3, 24.8**.**

[(4S,9aR)-hexahydro-4-(2-(2'-methoxymethoxy-5'-carboxaldehyphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2(6H)-one] (12)



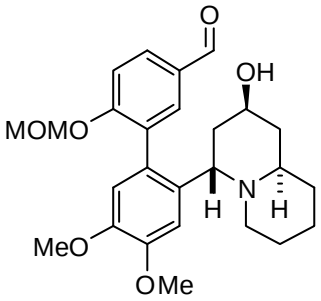
Degassed dimethoxyethane (90 ml) was added under N_2 to a mixture of quinolizidinone **4** (1.170 g, 2.8 mmol), 4-methoxymethoxy-3-(4,4,5,5-tetramethyl-[1.3.2]dioxaborolan-2-yl)-benzaldehyde **11** (0.900 g, 3 mmol), CsF (1.280 g, 8.4 mmol) and $Pd(PPh_3)_4$ (0.220 g, 5 mol). The reaction mixture was heated at 95 C for 18 h. The resulting white suspension was filtered through a pad of celite® and washed with EtOAc (200 ml). After evaporation *in vacuo*, the residue was purified by flash chromatography on silica gel eluting with EtOAc to yield yellow oil (1.010 g, ~80%, contaminated with triphenylphosphineoxyde). Appears as an 80:20 mixture of rotamers about the biaryl axis (variable with concentration). **IR** (neat): 2931, 1712, 1511, 1244, 987. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.92 (0.8H, s, C<u>H</u>O), 9.89 (0.2H, s, C<u>H</u>O), 7.92 (1H, dd, *J* 2.2, 8.6 Hz, Ar<u>H</u>), 7.72 (0.8H, d, 2.2 Hz, Ar<u>H</u>), 7.32 (1H, d, *J* 8.6 Hz, Ar<u>H</u>), 6.87 (0.20H, s, Ar<u>H</u>), 6.72 (0.8H, s, Ar<u>H</u>), 6.63 (0.20H, s, Ar<u>H</u>), 6.60 (0.8H, s, Ar<u>H</u>), 5.25 (0.2H, d, *J* 7 Hz, OC<u>H</u>$_2$O, <u>A</u>B), 5.18 (0.8H, d, *J* 7 Hz, OC<u>H</u>$_2$O, <u>A</u>B), 5.10 (0.8H, d, *J* 7, OC<u>H</u>$_2$O, A<u>B</u>), 5.04 (0.2H, d, *J* 7, OC<u>H</u>$_2$O, A<u>B</u>), 4.30 (0.2H, dd, *J* 5.6, 5.7 Hz, NC<u>H</u>Ar), 4.10 (0.8H, dd, *J 5.1, 5.3* Hz, NC<u>H</u>Ar), 3.88 (3H, s, OC<u>H</u>$_3$), 3.83 (2.4H, s, OC<u>H</u>$_3$), 3.79 (0.6H, s, OC<u>H</u>$_3$), 3.39 (0.6H, s, C<u>H</u>$_3$OCH$_2$), 3.02 (2.4H, s, C<u>H</u>$_3$OCH$_2$), 3.07 (1H, m, NC<u>H</u>Alkyl),2.81-2.76 (0.8H, dd, *J 5.3 14* Hz, C<u>H</u>$_2$CO), 2.71-2.66 (0.2H, dd, *J 5 14* Hz, CHC<u>H</u>$_2$CO, <u>A</u>BX), 2.63-2.52 (2H, m, COC<u>H</u>$_2$, <u>A</u>BX), 2.41-2.38 (1H, d, *J* 12.4, NC<u>H</u>$_2$, A<u>B</u>X), 2.32-2.26 (1H, m, COC<u>H</u>$_2$, A<u>B</u>X), 2.14-2.01 (1H, m, NC<u>H</u>$_2$, A<u>B</u>X), 1.74-1.16 (6H, m, alkyl-C<u>H</u>$_2$). **^{13}C NMR** (100 MHz, $CDCl_3$): *major isomer* – δ 210.6, 190.1, 159.9, 159.8, 148.7, 147.9, 133.2, 132.2, 131.9, 130.7, 129.8, 128.6, 114.6, 113.3, 110.3, 95.1, 59.3, 56.8, 56.1, 56.1, 55.7, 50.3 , 47.5, 47.0, 31.0, 23.7, 23.4; **HR-MS** (ESI) for $C_{26}H_{32}NO_6$ $[M+H]^+$: calcd. 454.2212, found 454.2224.

[(4S,9aR)-hexahydro-4-(2-(2'-methoxymethoxy-5'-methanolphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2(6H)-ol]



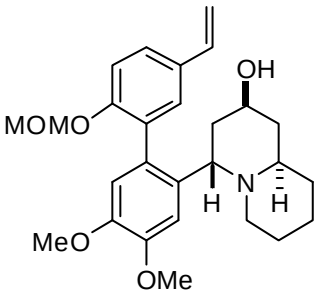
A solution of compound **12** (1.340 g, 2.95 mmol) in THF (100 ml) was cooled to –78 C before dropwise addition of L-Selectride (1.0M in THF, 6.500ml, 6.5 mmol). After 1 h, the reaction was quenched by addition of MeOH (50 ml). The reaction mixture was concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with EtOAc to yield pale brown foam (0.820 g, 62%). Appears as a 60:40 mixture of rotamers about the biaryl axis. **m.p.**: 79-82°C. **IR** (neat): 3361, 2930, 2853, 1606, 1514, 1494, 1463, 1244, 1205, 1078, 996. **^{1}H NMR** (400 MHz, C_6D_6): δ 7.48 (0.6H, d, *J* 2.0 Hz, ArH), 7.41 (0.6H, br s, ArH), 7.37 (0.4H, d, *J* 1.8 Hz, ArH), 7.31 (0.4H, br s, ArH), 7.27-7.18 (1.4H, m, ArH), 7.12 (0.6H, dd, *J* 8.6, 2.0 Hz, ArH), 6.86 (0.6H, s, ArH), 6.76 (0.4H, s, ArH), 4.97 (0.4H, d, *J* 6.6 Hz, OCH_2O, AB), 4.92 (0.6H, d, *J* 6.6 Hz, OCH_2O, AB), 4.83 (0.4H, d, *J* 6.6 Hz, OCH_2O, AB), 4.78 (0.6H, d, *J* 6.6 Hz, OCH_2O, AB), 4.66 (0.6H, d, *J* 12.6 Hz, CH_2OH, AB), 4.60-4.52 (2H, m, 1.4H CH_2O and 0.6H CHOH), 4.42-4.37 (0.4H, m, CHOH), 4.34-4.27 (0.4H, m, NCHAr), 4.18-4.12 (0.6H, m, NCHAr), 3.66 (1.8H, s, CH_3), 3.62 (1.2H, s, CH_3), 3.48 (1.8H, s, CH_3), 3.42 (1.2H, s, CH_3), 3.12-3.07 (3.4H, m, 3H CH_3 and 0.4H NCH), 3.06-2.98 (1H, m, alkyl-H), 2.76-2.73 (0.4H, m, alkyl-H), 2.58-2.52 (0.6H, m, alkyl-H), 2.53 (0.6H, m, alkyl-H), 2.13-1.09 (10H, m, alkyl-H). **^{13}C NMR** (100 MHz, C_6D_6): *cannot distinguish isomers, nor see doubling of all carbons as some signals are broad* –Major isomer δ 154.5, 150.1, 148.5, 135.3, 132.5, 131.8, 131.0, 128.3, 127.9, 95.4, 115.6, 115.3,112.5, 65.5, 64.8, 57.2, 56.1, 56.0, 55.4, 53.4, 51.5, 42.9, 40 (br), 30.9 (br), 26.3, 22.9 (br). **HR-MS** (ESI) for $C_{26}H_{36}NO_6$ $[M+H]^+$: calcd. 458.2542, found 454.2537**.**

[(4S,9aR)-hexahydro-4-(2-(2'-methoxymethoxy-5'-carboxaldehyphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2(6H)-ol] (13)



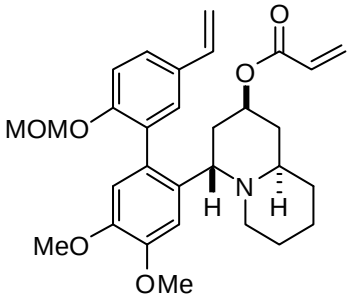
To a solution of the diol (0.780 g, 1.7 mmol) in Et_2O/acetone (6:1, 120/20 ml) was added MnO_2 (4 g, 5 wt eq). Starting material was consumed within 20 min. The mixture was filtered through celite® (washing extensively with EtOAc, 600 ml), and the filtrate was concentrated *in vacuo* to yield brown solid (0.766 g, 98%). Appears as a 60:40 mixture of rotamers about the biaryl axis (variable with concentration). **m.p.**: 84-86°C. **IR** (neat):3386, 2930, 1692, 1597, 1513, 1245, 1205, 1081, 978. **^{1}H NMR** (400 MHz, C_6D_6): δ 9.74 (0.6H, s, CHO), 9.71 (0.4H, s, CHO), 7.87 (0.6H, d, *J* 2.0 Hz, ArH), 7.82 (0.4H, d, *J* 2.0 Hz, ArH), 7.55 (0.6H, dd, *J* 8.6, 2.3 Hz, ArH), 7.51 (0.4H, dd, *J* 8.6, 2.3 Hz, ArH), 7.29-7.26 (1H, m, ArH), 7.11 (0.6H, d, *J* 8.6 Hz, ArH), 7.06 (0.4H, d, *J* 8.6 Hz, ArH), 6.65 (0.4H, s, ArH), 6.61 (0.6H, s, ArH), 4.90 (0.6H, d, *J* 6.8 Hz, OCH_2O, AB), 4.78 (0.4H, d, *J* 6.8 Hz, OCH_2O, AB), 4.73 (0.6H, *J* 6.8 Hz, OCH_2O, AB), 4.64 (0.4H, d, *J* 6.8 Hz, OCH_2O, AB), 4.35 (0.4H, dd, *J* 5.5, 5.5 Hz, CHOH), 4.22-4.17 (1.2H, m, NCHAr and CHOH), 4.04-4.02 (0.4H, m, NCHAr), 3.58 (1.2H, s, CH_3), 3.57 (1.8H, s, CH_3), 3.44 (1.2H, s, CH_3), 3.37 (1.8H, s, CH_3), 3.11-3.04 (0.6H, m, NCH), 2.99 (1.8H, s, CH_3), 3.00 (1.2H, s, CH_3), 2.98-2.89 (1H, m, 0.4H NCH and 0.6H alkyl-CH_2), 2.70-2.67 (0.6H, m, alkyl-CH2), 2.51 (0.4H, ddd, *J* 12.4, 12.4, 2.3, alkyl-CH_2, ABX), 2.32-2.26 (0.6H, ddd, *J* 12.1, 12.1, 2.5, alkyl-CH_2, ABX), 2.23-2.17 (0.6H, m, alkyl-CH_2), 2.11-2.04 (0.6H, m, alkyl-CH_2), 1.99-1.90 (1.8H, m, alkyl-CH_2), 1.68-1.06 (7H, m, alkyl-CH_2). **^{13}C NMR** (100 MHz, C_6D_6): *cannot fully distinguish isomers* – δ Major isomer 190.5, 160.6, 150.2, 149.0, 133.3, 133.2, 131.8, 132.3, 131.5, 130.7, 115.2, 114.7, 112.9, 95.3, 65.6, 56.7, 56.4, 56.4, 55.9, 55.4, 51.6, 42.9, 41, 32, 25.8, 24. **HR-MS** (ESI) for $C_{26}H_{34}NO_6$ $[M+H]^+$: calcd. 456.2388, found 456.2380.

[(4S,9aR)-hexahydro-4-(2-(2'-methoxymethoxy-5'-vinylphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2(6H)-ol] (14)



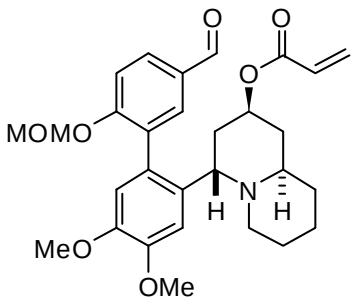
A 1.6M solution of *n*BuLi 1.6M (7.530 ml, 12 mmol) in hexane was added dropwise under N_2 to a cooled solution (0°C) of $(Ph_3)_3PCH_3Br$ (4.480 g, 12.5 mmol) in dry THF (11 ml). The mixture was stirred at 0°C during 30mn and 30mn at room temperature. The reaction mixture was cooled to –78°C and compound **13** (1.100 g, 2.4 mmol) was added slowly. The reaction mixture was stirred 16 h until room temperature. The reaction was quenched with sat. aq. NH_4Cl (20 ml) then the aq. layer was extracted with EtOAc (3×50 ml). The combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with EtOAc:MeOH:NEt_3 (1:0.1:0.05) to yield yellow solid (0.530 g, 65%). Appears as a 60:40 mixture of rotamers about the biaryl axis (variable with concentration). **m.p.**: 100-104°C. **IR** (neat): 3600, 2929, 1631, 1511, 1462, 1242, 987. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (1H, ddd, *J* 2.04, 8.32, 9.34 Hz, ArH), 7.16-7.08 (2H, m, ArH), 6.99 (1H, s, ArH), 6.68-6.59 (1H, s ArH, 1H, dd, *J* 10.8, 17.6 Hz, CHCH$_2$), 5.59 (1H, d, *J* 17.6 Hz, CHCH$_2$), 5.15-5.18 (2H, m, 1H CHCH$_2$, 1H OCH$_2$), 4.98 (H, d, *J* 6.8 Hz, OCH$_2$), 4.28-4.24 (0.7H, m, CHOH), 4.20-4.07 (1.3H, m, 1H ArCHN, 0.3H CHOH), 3.91 (3H, s, OCH$_3$), 3.82 (2.1H, s, OCH$_3$), 3.80 (0.9H, s, OCH$_3$), 3.32 (3H, s, CH$_3$OCH$_2$), 3.08 (0.4H, m, NCH-Alkyl), 2.95 (0.6H, m, NCH-Alkyl), 2.64-2.61 (0.4H, d, *J* 12.8 Hz, CH$_2$N, ABX), 2.47-2.44 (0.6H, d, *J* 12.8 Hz, CH$_2$N, ABX), 2.10-1.16 (11H, m, CH$_2$CO,CH$_2$N alkyl-CH$_2$). **^{13}C NMR** (100 MHz, $CDCl_3$): *cannot fully distinguish isomers* – δ Major isomer 154.8, 148.3, 146.9, 136.2, 131.6, 131.3, 131.2, 131, 129.6, 126.8, 114.8, 113.4, 112.7, 111.0, 95.1, 65.3, 56.3, 56.2, 56.2, 56.0, 55.5, 51.0, 41.6, 40.9, 35.8, 25.0, 23.9. **HR-MS** (ESI) for $C_{27}H_{36}NO_5$ $[M+H]^+$: calcd. 454.2598, found 454.2588.

[(4S,9aR)-hexahydro-4-(2-(2'-methoxymethoxy-5'-vinylphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2yl-acrylate] (15)



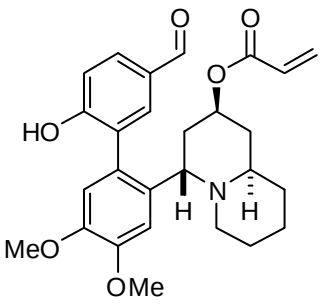
A solution of compound **14** (0.669 g, 1.47 mmol), NEt_3 (0.825 ml, 5.9 mmol), acrylic acid (0.172 ml, 2.5 mmol) in CH_2Cl_2 (2 ml) was stirred during 5mn at 0°C then cannulated to a solution of Mukayama salt (0.679 g, 2.65 mmol) in DCM (2ml). The reaction mixture was stirred 1 hour at 0°C and 1h at room temperature. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (10 ml) then the aq. layer was extracted with EtOAc (3×10 ml). The combined organic layers were washed with brine (3× 20ml), dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with EtOAc:MeOH (1:0.05) to yield yellow solid (0.560 g, 84 %). Appears as a 70:30 mixture of rotamers about the biaryl axis (variable with concentration). **m.p.**: 95-98°C**. IR** (neat, cm^{-1}): 2930, 1716, 1634, 1605, 1497, 1247, 1184, 982, 809. **^{1}H NMR** (400 MHz, C_6D_6) δ 7.42-7.36 (1.7H, m, ArH), 7.26-7.31 (1.3H, m, ArH), 7.17-7.12 (1H, m, ArH), 6.69-6.62 (2H, m 1H ArH, 1H $CHCH_2$), 6.25-6.19 (1H, m, $CHCH_2$), 6.01-5.90 (1H, dd, *J*.10.4, 17.2 Hz, $CHCH_2$), 5.63-5.55 (1H, dd, *J* 1.2 17.6 Hz, $CHCH_2$), 5.40-5.29 (2H, m, 1H $CHCH_2$, 1H CHOH), 5.09-5.04 (1H, dd, *J* 1.2 10.4, $CHCH_2$), 6.8 (0.7H, d, *J* 6.8 Hz, OCH_2 ABX), 6.72 (0.3H, d, *J* 6.8 Hz, OCH_2, ABX), 4.76-4.71 (1H, d, *J* 6.8 Hz OCH_2 ABX), 3.4-3.37 (0.3H, m, ArCHN), 3.25-3.23 (0.7H, m, ArCHN), 3.61 (3H, s, CH_3O), 3.43 (0.9H, s, OCH_3), 3.38 (2.1H, s, OCH_3), 3.08 (0.9H, s, OCH_3), 3.02 (2.1H, s, OCH_3), 2.92-2.89 (1H, m, NCH-alkyl), 2.48-2.36 (1.7H, m, CH_2N), 2.09-1.99 (2.3H, m, 0.3H CH_2N and 2 alkyl-CH_2), 1.73-0.95 (8H, m, alkyl-CH_2). **^{13}C NMR** (100 MHz, $CDCl_3$): *cannot fully distinguish isomers* – δ Major isomer 165.6, 154.9, 148.8, 147.3, 136.2, 133.8, 131.4, 130.8, 130.7, 130.5, 129.4, 129.3, 126.8, 115.1, 113.0, 112.6, 110.1, 95.0, 69.0, 56.4, 56.2, 55.9, 55.8, 52.1, 50.6, 38.0, 35.7, 29.0, 25.8, 21.9. **HR-MS** (ESI) for $C_{30}H_{38}NO_6$ $[M+H]^+$: calcd. 508.2689, found 508.2693.

[(4S,9aR)-hexahydro-4-(2-(2'-methoxymethoxy-5'-carboxaldehyphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2yl-acrylate] (16)



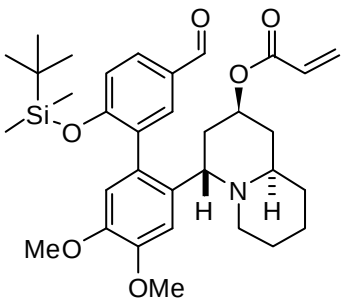
A solution of coumpond **13** (0.700 g, 1.53 mmol), NEt_3 (0.429 ml, 3.07 mmol), 4-DMAP (0.034 g, 0.3 mmol) in CH_2Cl_2 (15 ml) was stirred during 15mn at 0°C then acryloyl chloride (0.250 ml, 3.07 mmol) was added. The reaction mixture was stirred 1 hour at 0°C and 2h at room temperature. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (20 ml) then the aq. layer was extracted with CH_2Cl_2 (3×30 ml). The combined organic layers were washed with brine (3× 80ml), dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with EtOAc: MeOH (1:0.05) to yield yellow solid (0.640 g, 84%). Appears as a 70:30 mixture of rotamers about the biaryl axis (variable with concentration). **m.p.**:63-66°C. **IR** (neat, cm^{-1}):2932, 2852, 1716, 1690, 1597, 1244, 1189, 974. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.88 (0.7H, s, C<u>H</u>O), 9.78, (0.3H, s, C<u>H</u>O), 7.83-7.79 (1H, m, Ar<u>H</u>), 7.66 (0.7H, d, *J 2.1* Hz, Ar<u>H</u>), 7.50 (0.3H, d, J 2.1, Ar<u>H</u>), 7.31-7.28 (0.3H, d, J 8.6 Hz, ArH), 7.24-7.22 (0.7H, d, J 8.6, Ar<u>H</u>), 7.11 (1H, s, Ar<u>H</u>), 6.59 (0.3H, s, Ar<u>H</u>), 6.56 (0.7H, s, Ar<u>H</u>), 6.2-6.15 (1H, dd, *J.1.2, 17.3* Hz, CHC<u>H</u>$_2$, <u>A</u>BX), 5.98-5.84 (1H, dd, *J 10.4, 17.2* Hz, C<u>H</u>CH$_2$), 5.77-5.69 (1H, dd, *J 1.2, 10.4* Hz, CHC<u>H</u>$_2$, A<u>B</u>X), 5.23-5.15 (2H, m, C<u>H</u>OH, OC<u>H</u>$_2$O A<u>B</u>X), 5.02 (0.3H, d, *J* 6.9 Hz, OC<u>H</u>$_2$O, <u>A</u>BX), 4.95 (0.7H, d, *J* 6.9 Hz, OC<u>H</u>$_2$O <u>A</u>BX), 4.07 (0.3H, m, ArC<u>H</u>N), 3.92 (3.7H, s, OC<u>H</u>$_3$, m, ArC<u>H</u>N), 3.79 (2.1H, s, OC<u>H</u>$_3$), 3.76 (0.9H, s, OC<u>H</u>$_3$), 3.36 (0.9H, s, C<u>H</u>$_3$OCH$_2$), 3.23 (2.1H, s, C<u>H</u>$_3$OCH$_2$), 3.05 (1H, m, C<u>H</u>N), 2.73-2.6 (1, d, *J 12.4* Hz, C<u>H</u>$_2$N <u>A</u>BX), 2.33 (1, m, C<u>H</u>$_2$N A<u>B</u>X), 2.-1.97 (3H, m, C<u>H</u>$_2$CHO), 1.62-1.47 (3H, m, C<u>H</u>$_2$CHO, alkyl-C<u>H</u>$_2$), 1.24-1.01 (5H, m, alkyl-C<u>H</u>$_2$). **^{13}C NMR** (100 MHz, $CDCl_3$): *cannot fully distinguish isomers* – δ Major isomer 191.1, 165.4, 160.1, 149.2, 147.6, 133.2, 132.2, 131.3, 131.2, 130.7, 130.4, 130.0, 128.8, 114.5, 112.8, 110.1, 94.6, 68.8, 56.5, 56.3, 56.0, 55.9, 52.6, 50.3, .37.5, 35.3, 28.9, 21.9, 20.0. **HR-MS** (ESI) for $C_{29}H_{36}NO_7[M+H]^+$: calcd. 510.2499, found 510.2486.

[(4S,9aR)-hexahydro-4-(2-(2'-hydroxy-5'-carboxaldehyphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2yl-acrylate] (17)



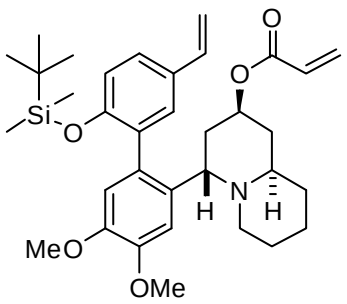
To a stirred solution of compound **16** (0.546 g, 1.07 mmol), in CH_2Cl_2 (8 ml) was added TFA (8 ml, 107 mmol) at 0°C. The reaction mixture was stirred 1 hour at 0°C and 2h at room temperature. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (100 ml) then the aq. layer was extracted with CH_2Cl_2 (3×100 ml). The combined organic layers were washed with brine (3× 120ml), dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with EtOAc:MeOH:Et_3N (1:0.1:0.02) to yield yellow solid (0.430 g, 87%). Appears as a 70/30 mixture of rotamers about the biaryl axis (variable with concentration). **m.p.:** 102-105°C. **IR** (neat, cm^{-1}): 2932, 2851, 1716, 1681, 1582, 1246, 1179, 983. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.78-9.76 (1H, s, C<u>H</u>O), 7.73 (0.7H, dd, *J 2, 8.3* Hz, Ar<u>H</u>), 7.67 (0.3H, dd, *J 2.3, 8.3* Hz Ar<u>H</u>), 7.57 (1H, d, *J 2* Hz, Ar<u>H</u>), 7.28 (0.7H, s, Ar<u>H</u>), 7.27 (0.3H, s, Ar<u>H</u>), 7.03 (0.7H, d, *J 8.3* Hz, Ar<u>H</u>), 6.88 (0.7H, d, *J 8.3* Hz, Ar<u>H</u>), 6.79 (0.3H, s, Ar<u>H</u>), 6.67 (0.3H, s, Ar<u>H</u>), 6.64 (0.7H, s, Ar<u>H</u>), 6.40-6.28 (1H, d, *J. 17.4* Hz, CHC<u>H$_2$</u> <u>A</u>BX), 6.14-6.07 (1H, dd, *J 10.3, 17.4* Hz, C<u>H</u>CH$_2$), 5.87-5.8 (1H, dd, *J 10.3* Hz, CHC<u>H$_2$</u> A<u>B</u>X), 5.71 (1H, m, C<u>H</u>O), 3.98 (2.1H, s, OC<u>H$_3$</u>), 3.89 (1.6H, s, OC<u>H$_3$</u>, ArC<u>H</u>N), 3.80 (3H, s, OC<u>H$_3$</u>), 3.26-3.27 (1H, m, C<u>H</u>N), 3.03-3.97 (0.7H, C<u>H$_2$</u>N <u>A</u>BX), 2.84-2.81 (0.3H, m, C<u>H$_2$</u>N <u>A</u>BX), 2.53 (0.3H, m, C<u>H$_2$</u>N <u>A</u>B<u>X</u>), 2.27-2.11 (2.7H, m, C<u>H$_2$</u>CHO, C<u>H$_2$</u>N A<u>B</u>X), 1.99-1.91 (1.7H, m, C<u>H$_2$</u>CHO), 1.77-1.37 (6.3H, m, alkyl-C<u>H$_2$</u>). **^{13}C NMR** (100 MHz, $CDCl_3$): *cannot fully distinguish isomers* – Major isomer δ 191.1, 165.9, 165.3, 148.6, 148.4, 133.6, 132.6, 132.0, 131.6, 130.9, 128.7, 127.9, 120.1, 114.9, 111.1, 69.5, 56.5, 56.2, 55.4, 49.3, 47.0, .32.2, 29.3, 28.9, 27.9, 23.9, 18.5. ; 1xC not observed for each isomer. **HR-MS** (ESI) for $C_{27}H_{31}NO_6$ $[M+H]^+$: calcd. 465.2233, found 456.2380.

[(4S,9aR)-hexahydro-4-(2-(2'-tert-butyldimethylsiloxy-5'-carboxaldehyphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2yl-acrylate] (18)



A solution of coumpond **17** (0.311 g, 0.668 mmol), NEt_3 (0.168 ml, 1.2 mmol), 4-DMAP (0.015 g, 0.13 mmol) in CH_2Cl_2 (7 ml) was stirred during 5mn at 0°C then TBDMSCl (0.150 g, 1.01 mmol) was added. The reaction mixture was stirred 1 hour at 0°C and 2h at room temperature. The reaction mixture was quenched with sat. aq. NH_4Cl (20 ml) then the aq. layer was extracted with CH_2Cl_2 (3×50 ml). The combined organic layers were washed with brine (3× 70ml), dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with EtOAc:MeOH (1:0.02) to yield yellow solid (0.320 g, 83%). Appears as a 60:40 mixture of rotamers about the biaryl axis (variable with concentration). **m.p.** 85-88°C. **IR** (neat, cm^{-1}): 2937, 2855, 1718, 1692, 1595, 1249, 1182, 1047, 834. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.88 (0.6H, s, C<u>H</u>O), 9.77 (0.4H, s, C<u>H</u>O), 7.78-7.79 (1H, dd, J 2.2, 8.3 Hz, Ar<u>H</u>), 7.69 (0.6H, d, J 2.2 Hz, Ar<u>H</u>), 7.51 (0.4H, d, J 2.2 Hz, Ar<u>H</u>), 7.07 (1H, s, Ar<u>H</u>), 6.96 (0.4H, d, J 8.3 Hz, Ar<u>H</u>), 6.88 (0.6H, d, J 8.3 Hz, Ar<u>H</u>), 6.60 (0.4H, s, Ar<u>H</u>), 6.57 (0.6H, s, Ar<u>H</u>), 6.18 (0.4H, dd, *J*. 1.5 17.2 Hz, CHC<u>H</u>$_2$), 6.13 (0.6H, dd, *J*. 1.5 17.2 Hz, CHC<u>H</u>$_2$), 5.96-5.86 (1H, dd, *J* 10.3, 17.2 Hz, C<u>H</u>CH$_2$), 5.73-5.69 (1H, dd, *J* 1.5 10.3, Hz, CHC<u>H</u>$_2$), 5.18-5.15 (1H, m, C<u>H</u>O), 4.04-4.01 (0.4H, m, NC<u>H</u>Ar), 3.91 (3.6H, s, 3H OC<u>H</u>$_3$ and 0.6H NC<u>H</u>Ar), 3.78 (1.2H, s, OC<u>H</u>$_3$), 3.77 (1.8H, s, OC<u>H</u>$_3$), 3.06-2.95 (1H, m, NC<u>H</u>-alkyl,), 2.77-2.65 (1H, t, J 13.38 Hz, NC<u>H</u>$_2$-alkyl, <u>A</u>BX), 2.30-2.24 (1H, q, J 13.13 Hz, NC<u>H</u>$_2$-alkyl, <u>A</u>BX), 2.03-1.85 (3H, m, C<u>H</u>$_2$CHO), 1.63-1.44 (3H, m, 1H C<u>H</u>$_2$CHO, 2H alkyl-C<u>H</u>$_2$), 1.16-1.01 (4H, m, alkyl-C<u>H</u>$_2$), 0.72 (3.6H, s, (C<u>H</u>$_3$)$_3$CSi), 0.64 (5.4H, s, (C<u>H</u>$_3$)$_3$CSi), 0.14 (1.8H, s, C<u>H</u>$_3$Si), 0.04 (3H, s, C<u>H</u>$_3$Si), -0.09 (1.2H, s, C<u>H</u>$_3$Si). **^{13}C NMR** (100 MHz, $CDCl_3$): *cannot fully distinguish isomers* – δ Major isomer 191.1, 165.4, 159.5, 149.0, 147.3, 134.1, 133.7, 132.9, 130.4, 129.9, 129.5, 129.2, 119.8, 113.2, 110.6, 68.6, 56.5, 56.0, 55.8, 52.8, 50.2, 38.8, 35.9, 29.8, 29.1, 25.8, 25.5, 25.4, 22.5, 18.2, -4.2, -4.4. **HR-MS** (ESI) for $C_{33}H_{46}NO_6Si[M+H]^+$: calcd. 580.3087, found 580.3088.

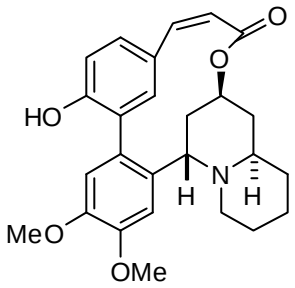
[(4S,9aR)-hexahydro-4-(2-(2'-tert-butyldimethylsiloxy-5'-vinylphenyl)-4,5-dimethoxyphenyl)-1H-quinolizin-2yl-acrylate] (19)



Into a flame-dried flask and under N_2 was placed a 20% suspension of the Nysted reagent in THF (0.458 ml, 0.238 mmol) an additional THF was added (0.5 ml): The suspension was cooled to 0 ^oC and neat titanium tetrachloride (26 μL, 0.238 mmol) was introduced dropwise followed by the addition of a solution of compound **18** (0.115 g, 0.198 mmol) in THF (0.5 ml). The reaction mixture was stirred at 0^oC for 1 h. The reaction was quenched by addition of 1M HCl (5 ml) then the aq. layer was extracted with CH_2Cl_2 (3×20 ml). The combined organic layers were washed with sat. aq. NH_4Cl solution (3× 20 ml) dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with EtOAc:MeOH (1:0.02) to yield yellow oil (0.070 g, 60%). Appears as a 60:40 mixture of rotamers about the biaryl axis (variable with concentration).

IR (neat, cm^{-1}): 2928, 2855, 1723, 1603, 1490, 1248, 1034, 905 **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26-7.96 3(H, m, ArH), 6.82 (0.4H, d, *J 8.4* Hz, ArH), 6.72 (0.6H, d, *J 8.4* Hz, ArH), 6.67-6.51 (2H, m, 1H ArH and 1H CHCH$_2$), 6.2-6.15 (1H, d, *J 17.3* Hz, CHCH$_2$, ABX), 5.98-5.91 (1H, m, CHCH$_2$), 5.75-5.67 (1H, d, *J 10.4* Hz, CHCH$_2$, ABX), 5.59-5.5 (1H, d, J 17.6 Hz, CHCH$_2$, ABX), 5.19 (1H, m, CHCO), 5.12-5.03 (1H, d, *J 10.9* Hz, CHCH$_2$, ABX), 4.5 (0.6H, m, ArCHN), 3.92 (3.4H, m, 3H CH$_3$ and 0.4H ArCHN), 3.79, 3.77 (3H, s, CH$_3$), 3.37 (1H, m, NCH$_2$), 3.11 (1H, m, NCH$_2$), 2.75-2.71 (1H, m, CH$_2$-alkyl), 2.37-1.39 (10H, m, CH$_2$-alkyl), 0.72 (3.6H, s, (CH$_3$)$_3$Si), 0.64 (5.4H, s, (CH$_3$)$_3$Si), 0.11 (0.9H, s, CH$_3$Si), 0.08 (0.9H, s, CH$_3$Si), -0.01 (1.8H, s, CH$_3$Si), -0.17 (1.8H, s, CH$_3$Si). **^{13}C NMR** (100 MHz, $CDCl_3$): *cannot fully distinguish isomers* – δ Major isomer 165.3, 153.7, 149.0, 147.4, 136.3, 130.9, 130.7, 130.5, 130.2, 130.0, 129.1, 128.9, 126.6, 119.0, 113.3, 112.2, 110.5, 70.8, 56.0, 55.8, 52.5, 50.8, 50.2, 38.8, 37.4, 29.2, 26.7, 25.6, 25.5, 22.9, 18.2, -4.1, -4.4. **HR-MS** (ESI) for $C_{34}H_{48}NO_5Si$ $[M+H]^+$: calcd. 578.3270, found 578.3296.

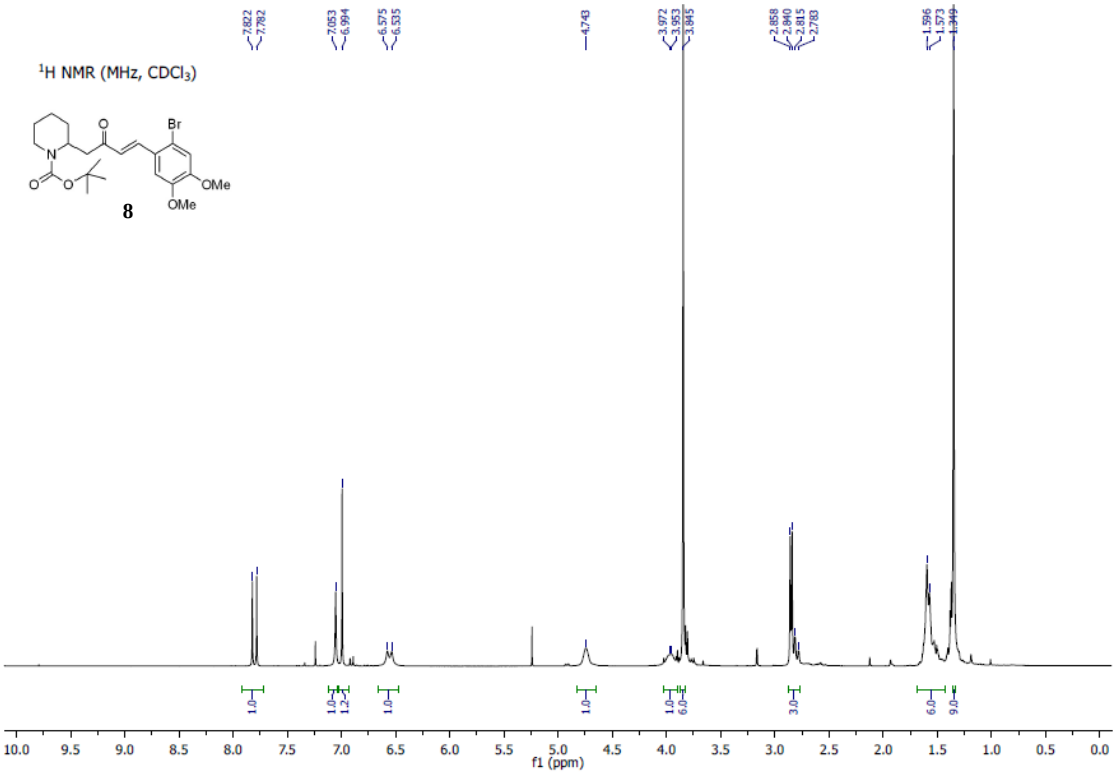
(±)-Vertine

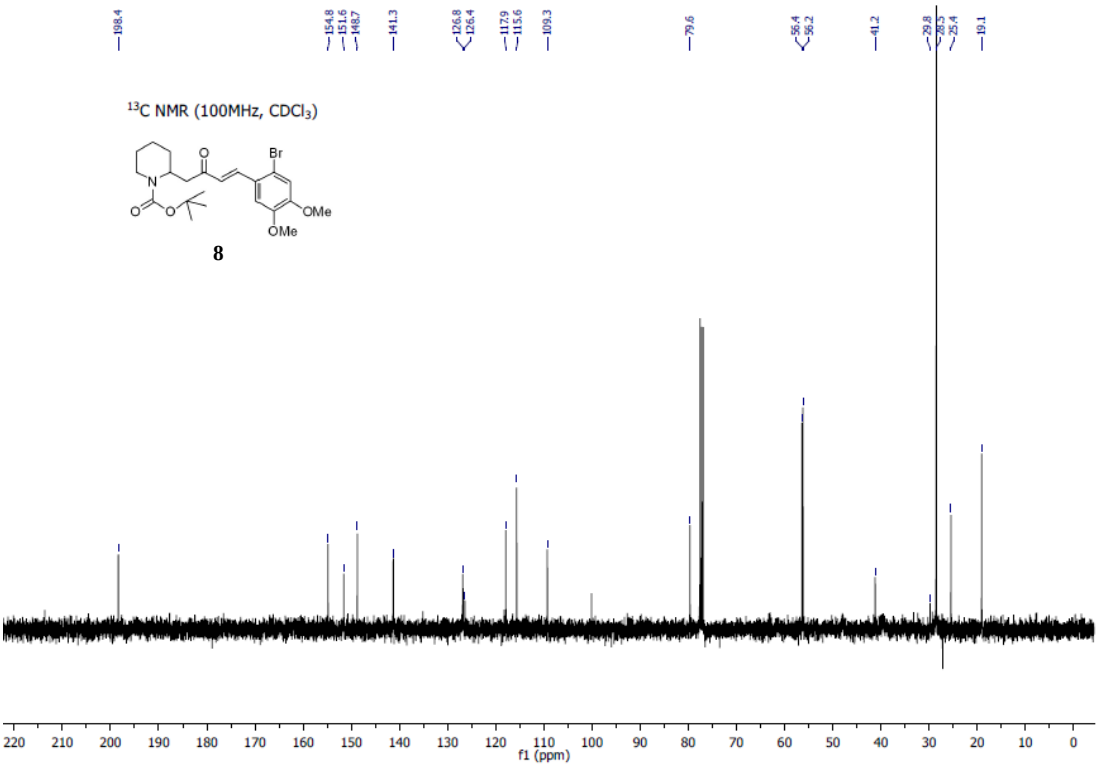


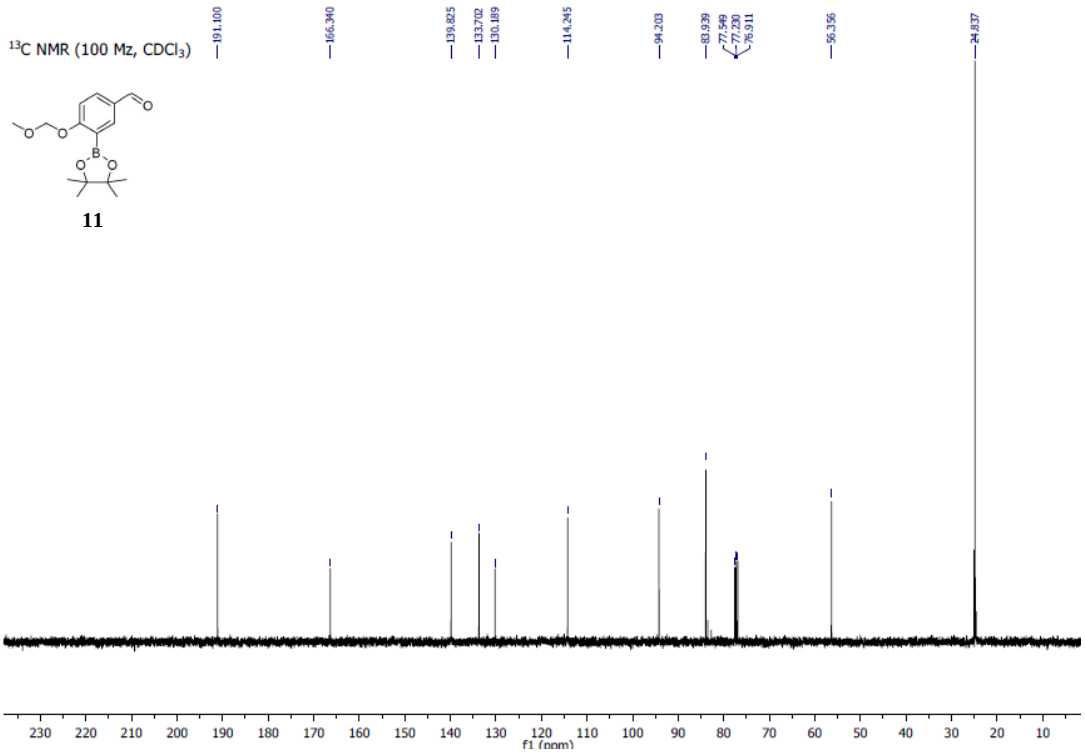
Into a flame-dried flask and under N_2 was placed compound **19** (0.025 g, 0.04 mmol) and the Hoveyda Grubb's catalyst (0.005 g, 20%) then degassed toluene (9 ml) was added. The reaction mixture was heated at 110°C during 16 h. The reaction mixture was cooled down filtered through celite® and evaporated *in vacuo*. The residue was passed through a short silica gel pad, eluting with DCM:MeOH (9:1) to remove most of the impurities. The product was then dissolved in THF (5ml) and TBAF (0.012 g, 0.047 mmol) was added at -30°C. The reaction mixture was stirred at this temperature for 1h. The reaction mixture was quenched by addition of sat. aq. NH_4Cl solution (3× 20 ml) then the aq. layer was extracted with CH_2Cl_2 (3×20 ml). The combined organic layers were washed with brine (3× 30 ml), dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography on neutral alumina eluting with benzene:MeOH (9:1) to yield pale brown foam (0.007 g, 37%) Spectral data match literature values.[3]

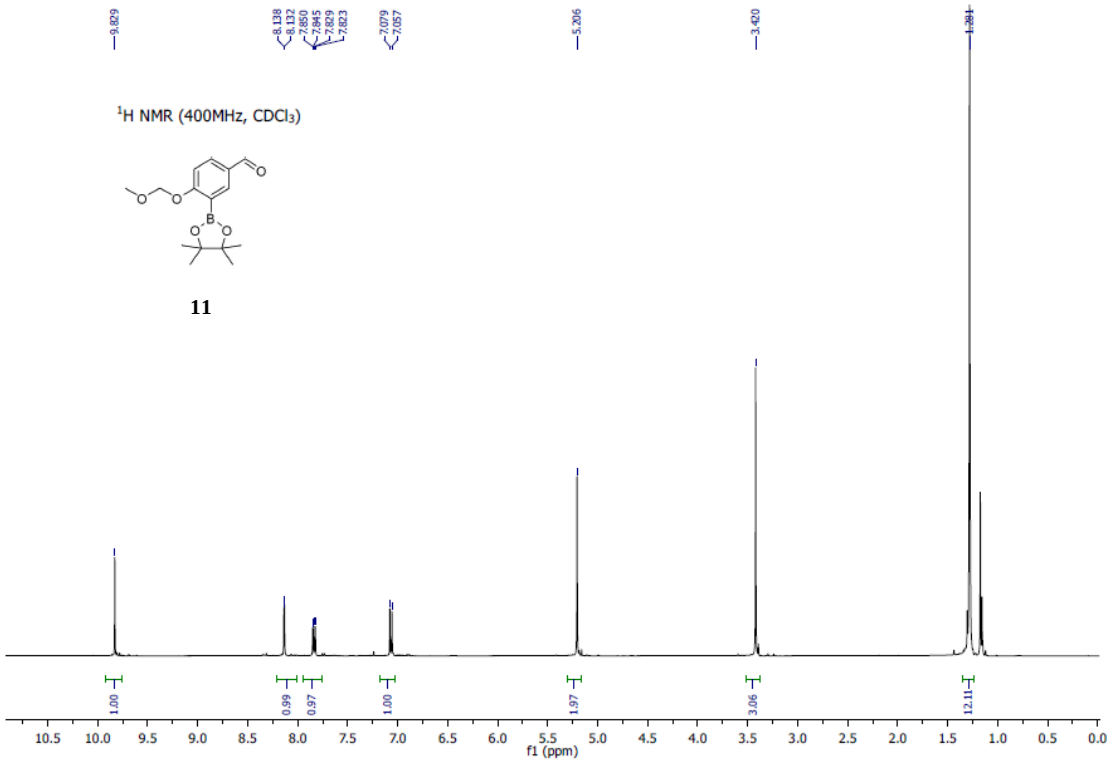
^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (1H, dd, *J 2.3, 8.4* Hz, ArH), 7.02 (1H, s, ArH), 6.98 (1H, s, ArH), 6.94 (1H, d, *J 2.3* Hz, ArH), 6.85 (1H, d, *J 8.4* Hz, ArH), 6.72 (1H, d, *J 12.6* Hz, ArCH), 5.70 (1H, d, *J 12.6* Hz, CHCH), 5.20 (1H, m, CH0), 4.65 (1H, d, *J 11.*3 Hz, ArCHN), 3.77 (3H, s, OCH_3), 3.74 (3H, s, CH_3O), 3.02-3.01 (1H, m, NCH-Alkyl), 2.75 (1H, d, *J 14* Hz, NCH_2, ABX), 2.36-2.29 (1H, td, *J 3 13.4* Hz, NCH_2, ABX), 2.16-2.04 (1H, m, CH_2CHO), 1.93-1.86 (1H, m, CH_2CHO) 1.65-1.58 (2H, m, 1H for CH_2-alkyl and 1H for CH_2CHO), 1.27-1.05 (2H, m, CH_2-alkyl), 0.98-0.94 (1H, d, *J 14.4* Hz, CH_2-alkyl), 0.70-0.56 (2H, m, CH_2-alkyl) **^{13}C NMR** (125 HMHz, CD_3O_D) δ 170.1, 157.3, 150.9, 148.9, 137.3, 132.6, 131.7, 131.0, 126.6, 126.5, 119.3, 117.4, 115.85, 110.0, 72.7, 59.0, 56.7, 56.3, 51.3, 49.0, 40.5, 35.3, 27.3, 25.1, 20.5 (one quaternary carbon was not detected). **HR-MS** (ESI) for $C_{26}H_{30}NO_5$ $[M+H]^+$: calcd. 436.2119, found 436.2118.

3. Spectroscopic data

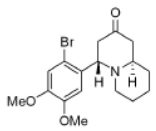




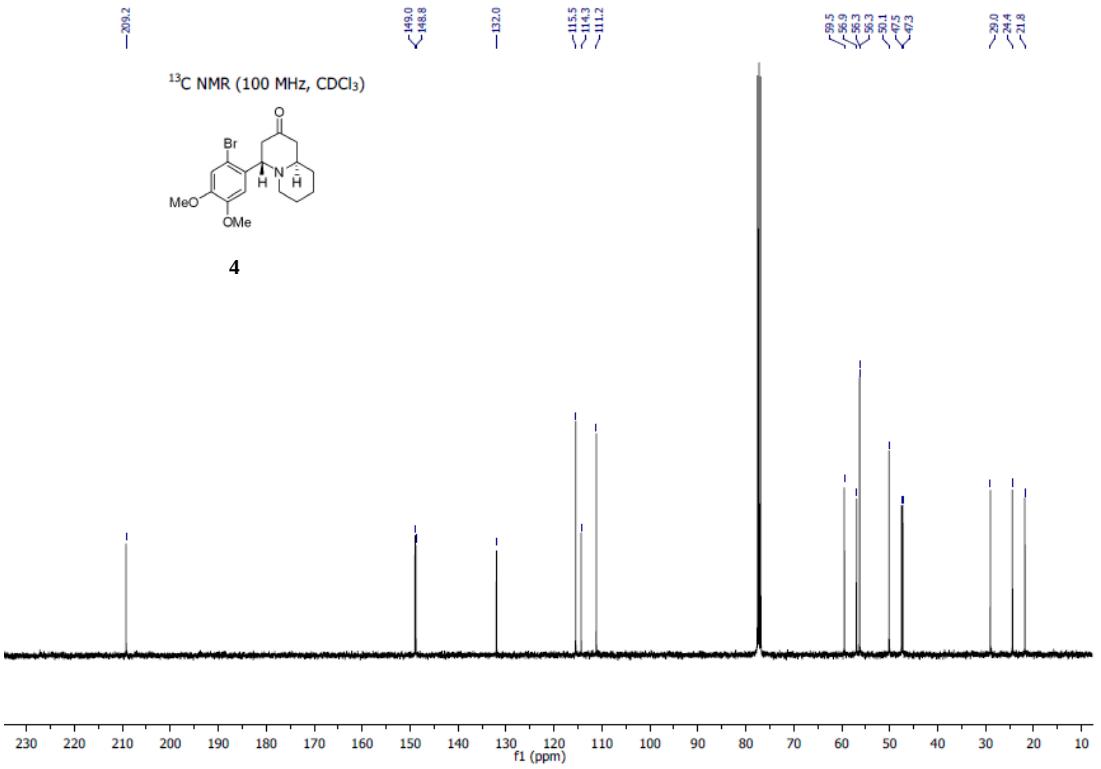

13C NMR (100 Mz, CDCl3)
191.100
166.340
139.825
133.702
130.189
114.245
94.203
83.939
77.569
77.230
76.911
56.356
24.837
11
f1 (ppm)


1H NMR (400MHz, CDCl3)
9.829
8.138
8.132
7.850
7.845
7.829
7.823
7.079
7.057
5.206
3.420
1.284
11
1.00
0.99
0.97
1.00
1.97
3.06
12.11
f1 (ppm)

^{1}H, NMR (400 MHz, $CDCl_3$)

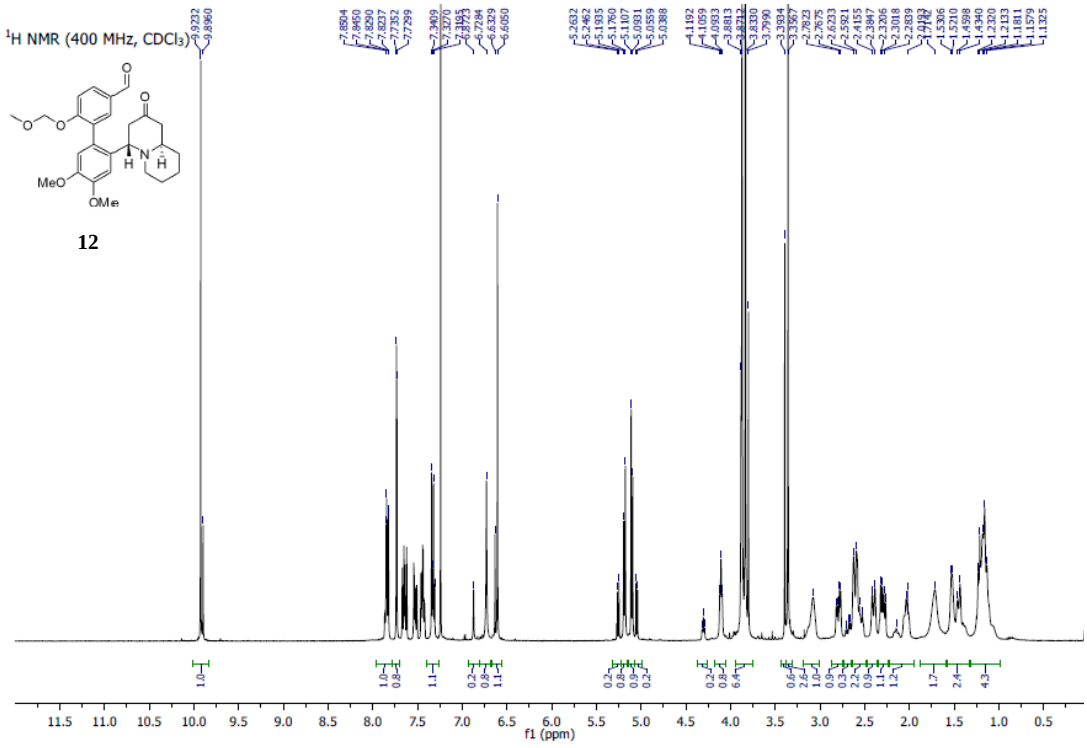


4

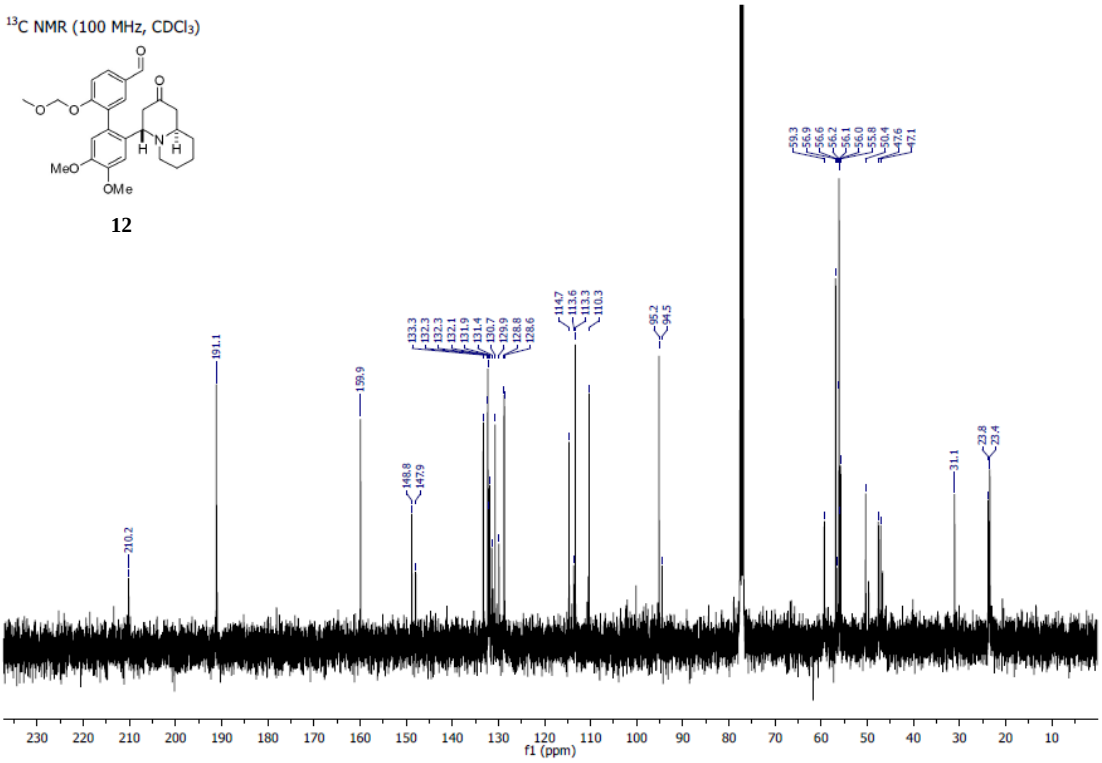


^{13}C NMR (100 MHz, $CDCl_3$)

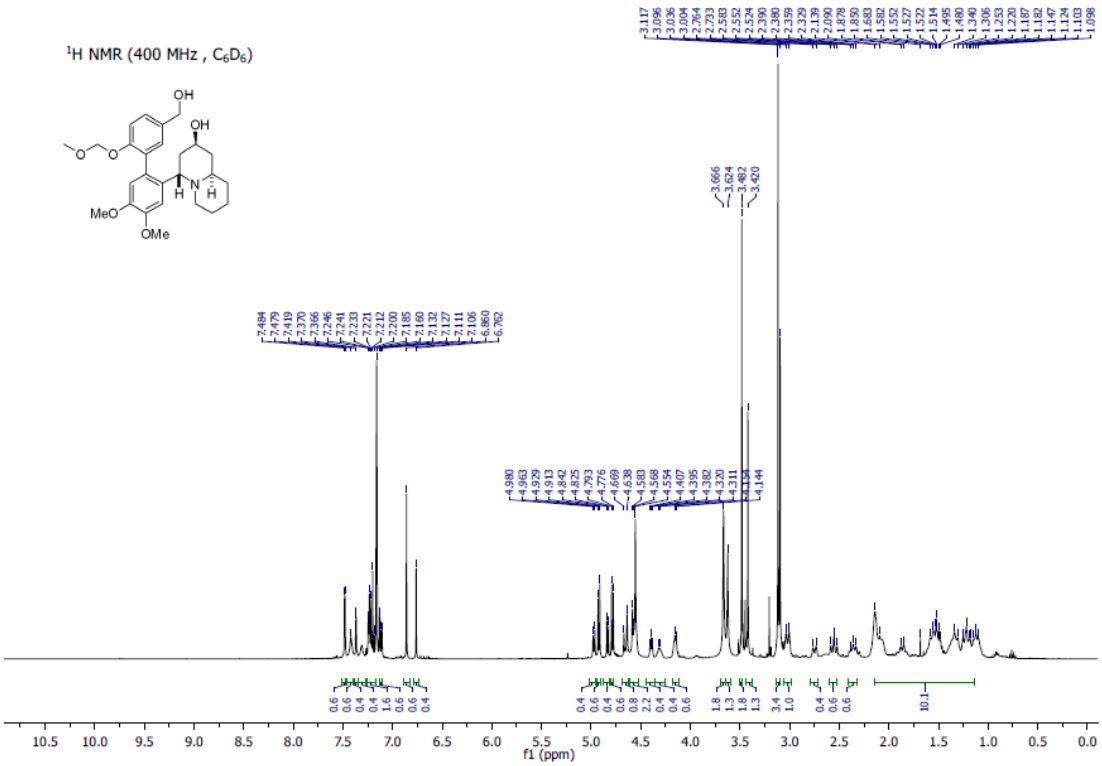
4

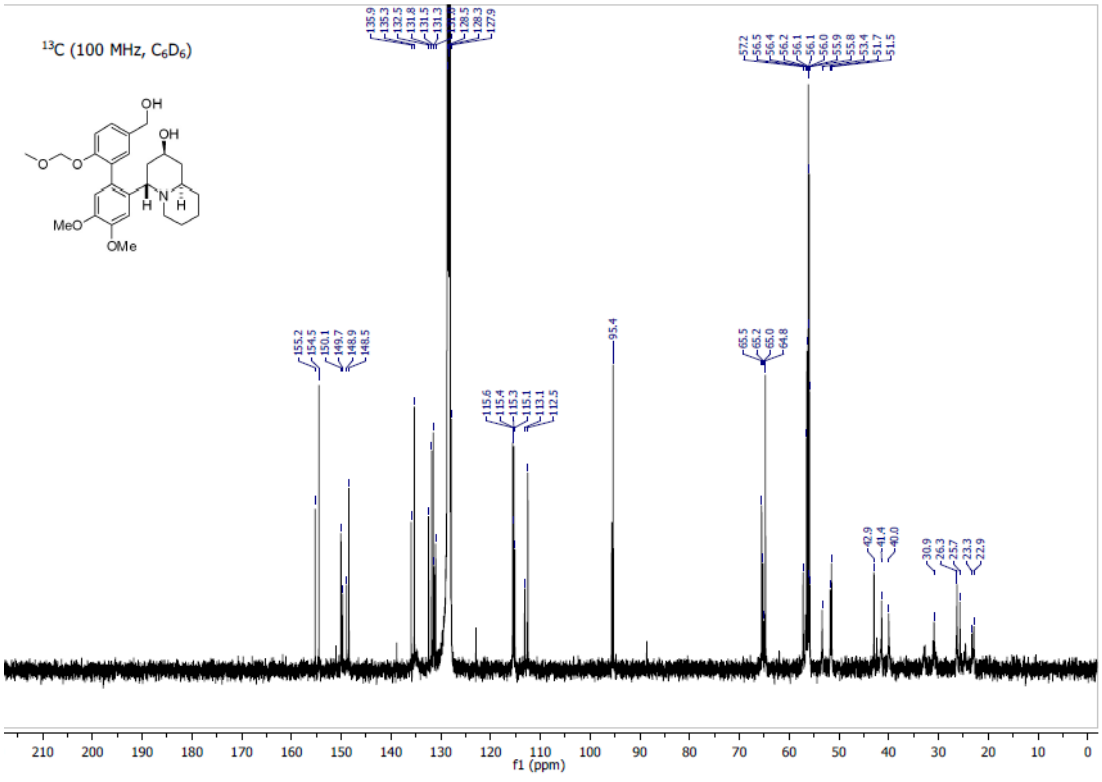

^{1}H NMR (400 MHz, CDCl$_3$)
MeO
OMe
f1 (ppm)

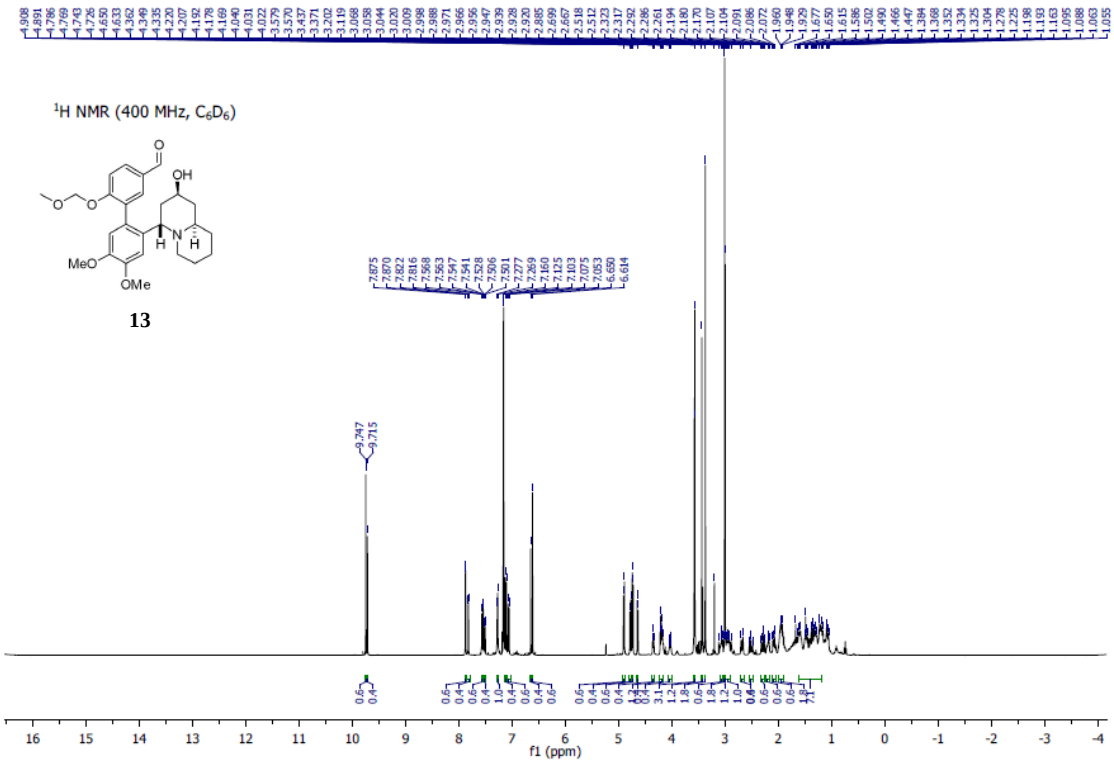
12


^{13}C NMR (100 MHz, CDCl$_3$)
MeO
OMe
f1 (ppm)

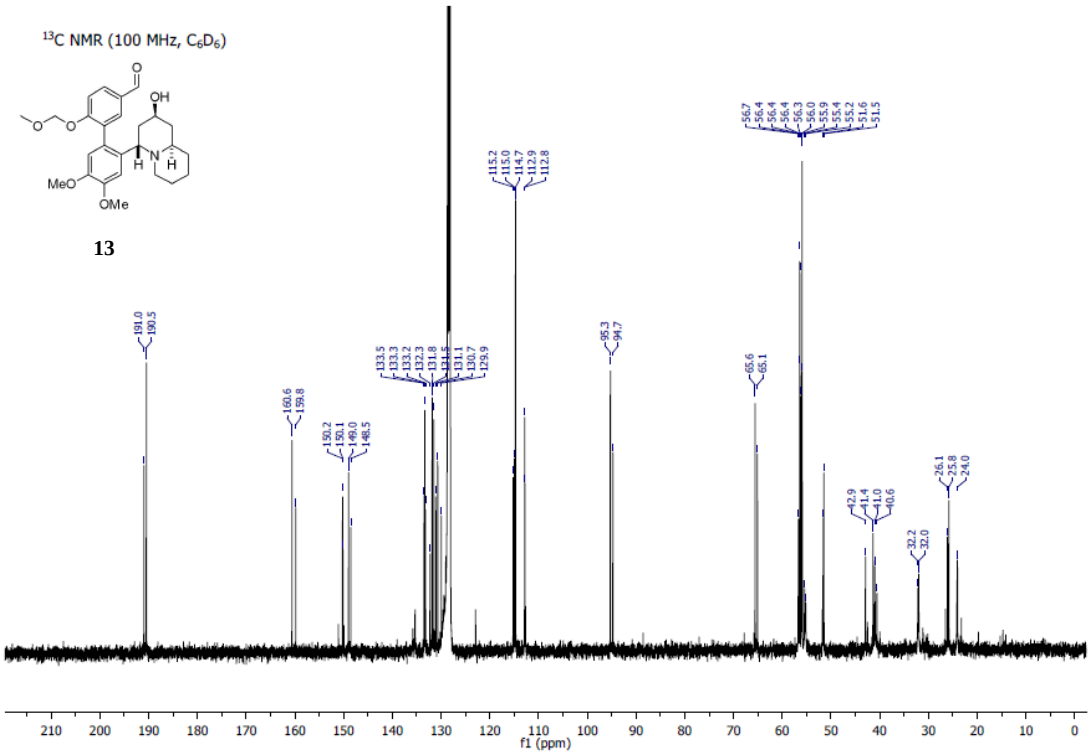
12


^{1}H NMR (400 MHz , C_6D_6)
OH
OH
MeO
OMe
f1 (ppm)


^{13}C (100 MHz, C_6D_6)
OH
OH
MeO
OMe
f1 (ppm)

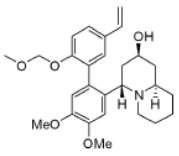

^{1}H NMR (400 MHz, C_6D_6)
OH
O
MeO
OMe
H
N
H
f1 (ppm)

13


^{13}C NMR (100 MHz, C_6D_6)
OH
O
MeO
OMe
H
N
H
f1 (ppm)

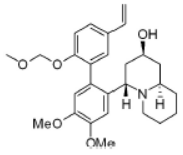
13

^{1}H NMR (400 MHz, $CDCl_3$)



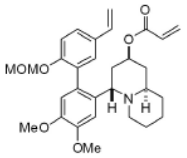
14

^{13}C NMR (100 MHz, $CDCl_3$)



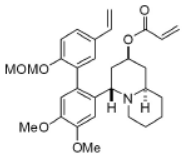
14

^{1}H NMR (400 MHz, C_6D_6)



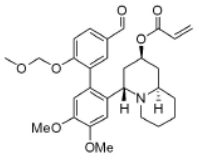
15

^{13}C NMR (100 MHz, $CDCl_3$)



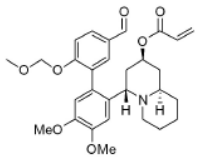
15

^{1H} NMR (400 MHz, $CDCl_3$)



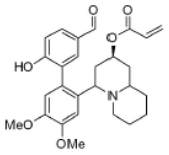
16

^{13}C NMR (100MHz, $CDCl_3$)



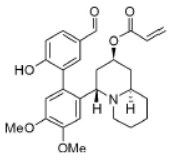
16

^{1}H NMR (400 MHz, $CDCl_3$)



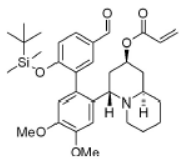
17

^{13}C NMR (100 MHz, $CDCl_3$)



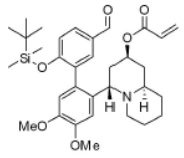
17

^{1}H NMR (400 MHz, $CDCl_3$)



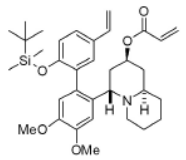
18

^{13}C NMR (100 MHz, $CDCl_3$)



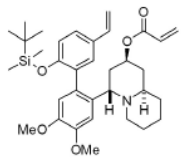
18

^{1}H NMR (400 MHz, $CDCl_3$)



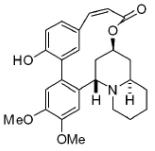
19

^{13}C NMR (100 MHz, $CDCl_3$)



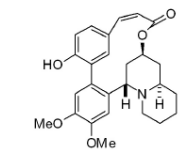
19

^{1}H NMR (400 MHz, MeOD)



Vertine

^{13}C NMR (125 MHz, MeOD)



Vertine

4. References

1. J. Quick and R. Oterson, *Synthesis*, 1976, 745-746.

2. S. G. Davies, A. M. Fletcher, P. M. Roberts and A. D. Smith, *Tetrahedron*, 2009, **65**, 10192-10213.

3. C. S. Rumalla, A. N. Jadhav, T. Smillie, F. R. Fronczek and I. A. Khan, *Phytochemistry*, 2008, **69**, 1756-1762.