Supporting Information

Synthetic Studies on the Ambiguine Family of Alkaloids: Construction of the ABCD Ring System

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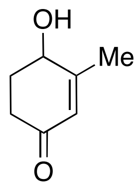
Materials and Methods

^{1}H and ^{13}C NMR spectra were recorded on Varian DPX-300 spectrometer. Low-resolution mass spectra (MS) were obtained at 50-70 eV by electron impact (EI). Chemical ionization mass spectra (CIMS) were obtained using isobutane as a carrier gas. Infrared spectra were obtained using a Perkin-Elmer 1600 FTIR. Intensities of signals were estimated as vs = very strong, s = strong, m =medium, w = weak, b = broad. Chemical shifts (ppm) are relative to TMS used as an internal standard. The multiplicity were marked as s =singlet, d = dublet, t = triplet, q = quartet, qu quintet, m = multiplet. Melting points are uncorrected. Flash column chromatography was carried out using Sorbent Technologies stand grade silica gel (230 x 400 mesh). Analytical and preparative thin-layer chromatography (TLC) were performed on EM Science silica gel 60 PF$_{254}$ plates. All non-aqueous reactions were performed under an inert atmosphere of argon in flame-dried glassware, containing a stir bar, unless otherwise noted. Anhydrous diethyl ether (Et_2O), toluene (PhMe), *N*,*N*-dimethylforamide (DMF), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), dimethylsulfoxide (DMSO), methanol (MeOH), benzene, triethylamine (TEA), diisopropylamine, acetonitrile and tetrahydrofuran (THF) were obtained via a dual column solvent purification system (J.C. Meyer of Glass Contour). All other solvents and reagents were used as obtained from commercial sources without further purification unless noted. Organic extracts were dried with Na_2SO_4 (unless otherwise noted) before filtration and concentration under reduced pressure.

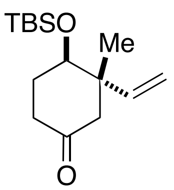
4-hydroxy-3-methylcyclohex-2-enone (7):



A 500 mL 3-necked round bottom flask equipped with a dry-ice condenser was purged with argon and cooled to -78°C after which ammonia (193 mL, 7728 mmol, 120 eq.) was condensed into. m-Methylanisole (8.11 mL, 64.4 mmol, 1 eq.) in ether (80.2 mL, 772.8 mmol, 12 eq.) was added to the flask followed by t-butanol (82 ml, 869 mmol, 13.5 eq.) and left to stir at -78°C for 10 min. Lithium wire (2.2 g, 322 mmol, 5 eq.) was added to the solution over a 30 min period and left to stir at -78°C for 4 h. The reaction was quenched with solid ammonium chloride and stirred for 2 h. Gentle heating, 33°C, of the reaction evaporated the ammonia. Once the ammonia was removed, the resulting solution was diluted with 150 mL of pentane and then poured onto 200 mL of 1:1 water:pentane. The pentane layer was washed with water (3 x 50 mL), dried with anhydrous MgSO$_4$ and concentrated to afford product. Oxalic acid (64 mg, 0.704 mmol, 0.044 eq.) was added to 32 mL of 3:1 methanol:water and stirred at rt for 5 min. The crude product (2 g, 16 mmol, 1 eq.) was added and left to stir at rt. After 1 h the reaction was diluted with water and extracted with DCM (3 x 20 mL), washed with water, dried over anhydrous MgSO4 and concentrated. The resulting oil was used without purification. The crude product was added to DCM (190 mL) then mCPBA (5.11 g, 22.87 mmol, 1.2 eq.) and stirred at rt for 3 h. The reaction is quenched with 100 mL of a NaHCO3 (sat) solution. The organic layer was separated and placed back into the same round bottom flask and triethyl amine (5.3 mL, 38.12 mmol, 2 eq.) was added and stirred at rt for 3.5 h. The reaction was quenched with brine (50 mL) and extracted with DCM (2 x 50 mL). The organic layers were combined and dried over anhydrous MgSO4, concentrated and purified by flash silica gel chromatography (1:1 EtOAc:hexane) to afford product in a 93% yield (3 steps).

^{1}**HNMR:** (300 MHz, CDCl$_3$) δ 5.845 (s, 1H), 4.379 (t, 3.6, 1H), 2.990 (bs, 1H), 2.613-2.516 (m, 1H), 2.339-2.245 (m, 2H), 2.051 (s, 3H), 2.023-1.944 (m, 1H);^{13}**CNMR:** (75 MHz, CDCl$_3$) δ 199.3, 163.9, 127.1, 68.9, 35.1, 32.1, 20.9; **IR:** (NaCl Film) 3321, 1660 cm^{-1}; **HMRS-FAB:** [M] calcd for $C_7H_{10}O_2$, 126.07; found, 126.0812.

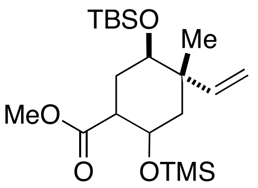
(3S,4R)-4-((tert-nutyldimethylsilyl)oxy)-3-methyl-3-vinylcyclohexanone (5):



To a DMF (125 mL), (7) (2.38 g, 19.06 mmol, 1 eq.), imidazole (1.6 g, 22.87 mmol, 1.2 eq.) and TBSCl (3.4 g, 22.87 mmol, 1.2 eq.) was added. The reaction was left to stir until the disappearance of all starting material, monitored by TLC (typically between 20 and 22 h). The reaction was quenched with brine and extracted with hexane (3 x 75 mL), dried over anhydrous $MgSO_4$ and concentrated. The crude oil was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product. Solid $CuBr•Me_2S$ (3.13 g, 12.48 mmol, 1.5 eq.) was added to a solution of THF (80 mL) and stirred while cooling to -78°C. Vinylmagnesium bromide (24.96 mL, 24.96 mmol, 1.5 eq.) was added over a 20 minute peiod and left to stir for an additional hour at the same temperature. TMEDA (2.89 mL, 24.96 mmol, 3 eq.), TMSCl (3.17 mL, 24.96 mmol, 3 eq.) and the product (2 g, 8.32 mmol, 1 eq.) in THF (8mL) was added. The reaction was left to stir at -78°C for a 4 h period, no additional dry-ice was added to the bath to allow the reaction to reach rt over this period. The reaction was diluted with hexane, washed with sat'd $NaHCO_3$ and water until the aqueous layer was no longer blue in color, dried over anhydrous $MgSO_4$ and concentrated. The crude oil was added to a pre-mixed solution (80 mL) of THF:H_2O:HOAc (2:1:1) and stirred at rt for 1 h. The reaction was diluted with EtOAc, washed with sat'd $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated. The crude oil was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 92% yield (3 steps).

^{1}HNMR: (300 MHz, CDCl3) δ 5.672 (dd, 17.4, 11.2 Hz, 1H), 5.018 (dd, 3, 14 Hz, 2H), 3.673 (t, 3.6 Hz, 1H), 2.594-1.772 (comp, 6H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 211.6, 143.9, 114.4, 72.8, 46.7, 35.9, 29.9, 26.0, 24.9, 18.3, -4.2; **IR:** (NaCl Film) 1623 cm^{-1}; **HMRS-FAB:** [M+H]+ calcd for $C_{15}H_{28}O_2Si$, 269.19; found, 269.1979.

(4S,5R)-methyl 5-((TBS)oxy)-4-methyl-2-((TMS)oxy)-4-vinylcyclohexanecarboxylate (6):

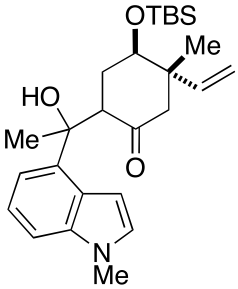


To solution of THF (37 mL) compound (**5**) (1.0 g, 3.72 mmol, 1.0 eq.) was added and cooled to -78 °C. To the cooled solution was added LiHMDS (4.10 mL, 4.09 mL, 1.1 eq.) and left to stir for 1 h to which methylcyanoformate (0.44 mL, 5.58 mmol, 1.5 eq.) was added. Once added the reaction was allowed to warm to RT gradually at which point NH_4Cl was added to quench and extracted with hexanes. The organic layers were combined, washed with brine and water, dried and concentrated. Purification by flash silica gel chromatography (5% EtOAc in Hexane) afforded product. The product (100 mg, 0.306 mmol) was added to THF (3 mL) and cooled to 0 °C, to which $NaBH_4$ (23 mg, 0.61 mmol, 2 eq.) added in one portion. The reaction was concentrated after 1 h and purified by flash silica gel chromatography (1:4 EtOAc:Hexane). NaH (44 mg, 1.09 mmol, 1.2 eq.) was added to THF (10 mL) and cooled to

0 °C, to which the product (300 mg, 0.91 mmol) was added dropwise over 10 min and left to stir for 30 min. The reaction was brought to rt and TMSCl (0.16 mL, 1.27 mmol, 1.4 eq.) was added and left to stir for 1 h. The reaction was quenched with brine and extracted with hexanes (x2). The organic layers were combined washed with water and brine, dried and concentrated. The crude oil was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 73% yield (3 steps).

^{1}HNMR: (300 MHz, $CDCl_3$) δ 12.130 (s, 1H), 5.758 (dd, 17.7 Hz, 1H), 4.997 (dd, 3.1 Hz, 2H), 3.742 (s, 3H), 3.581 (t,4.8 Hz, 3H), 2.402-2.182 (m, 6H), 1.020 (s, 3H), 0.849 (s, 9H), 0.038 (s, 6H), 0.025 (s, 9H); **^{13}CNMR:** (75 MHz, $CDCl_3$) δ 170.9, 144.0, 112.8, 78.1, 72.2, 51.7, 46.3, 41.6, 36.9, 29.5, 26.0, 21,4, 18.2, 4.6, 3.9; **IR:** (NaCl Film) 1632, 1243 cm^{-1}; **HMRS-FAB**: [M] calcd for $C_{20}H_{40}O_4Si_2$, 400.25; found, **Need**. SEE 4-017

(4R,5S)-4-((tert-butyldimethylsilyl)oxy)-2-(1-hydroxy-1-(1-methyl-1H-indol-4-yl)ethyl)-5-methyl-5-vinylcyclohexanone (7):

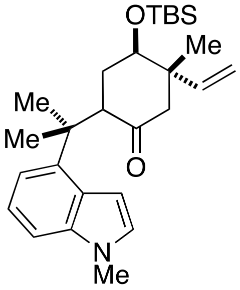


To a solution of *N*-methoxy-methylamine hydrochloride (59 mg, 0.6 mmol, 2 eq.) in CH_2Cl_2 (4 mL) at -78 °C, dimethyl aluminium chloride (0.04 mL, 0.36 mmol, 1.2 eq.) was added and the mixture was stirred for 1 h. Compound **6** (121 mg, 0.30 mmol) was added and the mixture was stirred at -78 °C for 30 min. The reaction mixture was then stirred at rt for 4 h. The reaction was quenched with excess HCl (1 M) and diluted with EtOAc. The mixture was filtered through celite, washed with HCl (1 M), $NaHCO_3$ $_{(sat'd)}$, and extracted with EtOAc (x2). The organic layers were combined, dried over $MgSO_4$ and concentrated. The crude material was taken up in THF (8 mL), cooled to -78 °C and then MeLi (1.6 M in Et_2O 0.23 mL, 0.36 mmol, 1.2 eq.) was added and left to stir for 1 h. The reaction was quenched with NH_4Cl and extracted with hexane (x2). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product. To THF (10 mL) was added the product (100 mg, 0.19 mmol), cooled to 0 °C and AcOH (0.02 mL, 0.29 mmol, 1.5 eq.) was added. The reaction was quenched with brine after 45 min and concentrated. The crude material was taken up in THF (4 mL) and DMP (322 mg, 0.76 mmol, 4 eq.) was added and left to stir for 2 h. To the reaction was added $Na_2S_2O_3$ $_{(sat'd)}$, left to stir for 30 min, washed with $Na_2S_2O_3$ $_{(sat'd)}$ (x2), $NaHCO_3$ $_{(sat'd)}$ then brine, dried over $MgSO_4$ and concentrated. The crude material was purifed by flash silica gel chromatography

(1:3 EtOAc:hexane) to afford product **7** in a 59% yield (4 steps).

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.245-7.232 (m, 4H), 6.831 (s, 1H), 6.091 (dd, 17.2, 10.5 Hz, 1H), 5.079 (dd, 21.5, 10.6 Hz, 2H), 5.018 (dd, 3, 14 Hz, 2H), 3.740 (s, 3H), 3.673 (t, 3.6 Hz, 1H), 3.569 (s, 1H), 2.792 (t, 3.6 Hz, 1H), 2.594-1.872 (comp, 5H), 1.354 (s, 3H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 198.6, 145.3, 144.2, 141.3, 123.8, 120.8, 115.1, 114.4, 107.3, 99.2, 73.2, 72.8, 71.6, 46.7, 38.8, 35.9, 31.2, 28.4, 26.0, 23.7, 18.2, -3.0; **IR:** (NaCl Film) 3297, 1654 cm^{-1}; **HMRS-FAB**: $[M+H]^+$ calcd for $C_{26}H_{39}NO_3Si$, 442.27; found, 442.2742.

(4R,5S)-4-((tert-butyldimethylsilyl)oxy)-5-methyl-2-(2-(1-methyl-1H-indol-4-yl)propan-2-yl)-5-vinylcyclohexanone (8):

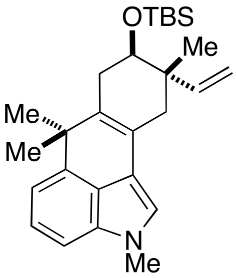


To a solution of THF (8 mL) and **7** (300 mg, 0.68 mmol) was added TsOH (cat'l) and refluxed for 1 h. The reaction was concentrated and purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford the exo-cyclic enone. Solid $CuBr•Me_2S$ (49 mg, 0.18 mmol, 0.2 eq.) was added to a solution of THF (40 mL) and stirred while cooling to -78°C. Methylmagnesium bromide (1M in THF, 2.82 mL, 2.82 mmol, 3 eq.) was added over a 20 minute peiod and left to stir for an additional hour at the same temperature. TMEDA (0.44 mL, 3.76 mmol, 4 eq.), TMSCl (0.36 mL, 2.82 mmol, 3 eq.) and the product (400 mg, 0.944 mmol, 1 eq.) in THF (10 mL) was added. The reaction was left to stir at -78°C for a 4 h period, no additional dry-ice was added to the bath to allow the reaction to reach rt over this period. The reaction was diluted with hexane, washed with sat'd $NaHCO_3$ and water until the aqueous layer was no longer blue in color, dried over anhydrous $MgSO_4$ and concentrated. The crude oil was added to a pre-mixed solution (10 mL) of $THF:H_2O:HOAc$ (2:1:1) and stirred at rt for 1 h. The reaction was diluted with EtOAc, washed with sat'd $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated. The crude oil was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product **8** in 67% yield (3 steps).

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.245-7.232 (m, 4H), 6.831 (s, 1H), 6.091 (dd, 17.2, 10.5 Hz, 1H), 5.079 (dd, 21.5, 10.6 Hz, 2H), 5.018 (dd, 3, 14 Hz, 2H), 3.740 (s, 3H), 3.673 (t, 3.6 Hz, 1H), 2.712 (t, 3.6 Hz, 1H), 2.594-1.872 (comp, 5H), 1.555 (s, 6H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 198.6, 145.3, 144.2, 141.3, 123.8, 120.8, 115.1, 114.4, 107.3, 99.2, 73.2, 72.8, 46.7, 38.8, 35.9, 32.2, 31.2, 28.4, 26.0, 25.1, 18.2, -3.0;

IR: (NaCl Film) 1654 cm^{-1}; **HMRS-FAB**: $[M+H]^+$ calcd for $C_{27}H_{41}NO_2Si$, 440.29; found, 440.2895.

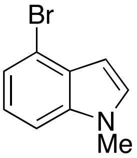
(8R,9S)-8-((tert-butyldimethylsilyl)oxy)-2,6,6,9-tetramethyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indole (9):



To a solution of THF (**ADD**) and **8** (350 mg, 0.80 mmol) was added BF_3-etherate (0.10 mL, 0.84 mmol, 1.05 eq.) and left to stir at rt for 2 h. The reaction was concentrated and purified via flash silica gel chromatography (1:4 EtOAc:hexane) to afford product **9** in a 92% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.245-7.232 (m, 4H), 6.831 (s, 1H), 6.091 (dd, 17.2, 10.5 Hz, 1H), 5.079 (dd, 21.5, 10.6 Hz, 2H), 5.018 (dd, 3, 14 Hz, 2H), 3.740 (s, 3H), 3.673 (t, 3.6 Hz, 1H), 2.594-1.872 (comp, 5H), 1.555 (s, 6H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 145.3, 144.2, 141.3, 123.8, 121.7, 120.8, 115.1, 114.4, 107.3, 99.2, 73.2, 72.8, 46.7, 38.8, 35.9, 32.2, 31.2, 28.4, 26.0, 25.1, 18.2, -3.0; **IR:** (NaCl Film); **HMRS-FAB**: [M] calcd for $C_{27}H_{39}NOSi$, 421.28; found, 421.2785.

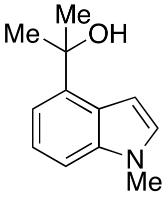
4-bromo-1-methyl-1H-indole (15):



To a solution of THF (50 mL) was added NaH (263 mg, 6.58 mmol, 1.2 eq.) at rt, to which compound **14** (0.7 mL, 5.48 mmol) was added drop wise and allowed to stir. After 30 min, methyl iodide (0.48 mL, 7.67 mmol, 1.4 eq.) was added and allowed to stir for 5 h. The reaction was quenched with brine and extracted with hexane (x2). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 97% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.327 (dd, 0.03, 0.8 Hz, 1H), 7.282 (dt, 8.2, 0.8 Hz, 1H), 7.109 (m, 2H), 6.569 (dd, 0.04, 0.8 Hz, 2H), 3.778 (s, 3H); **^{13}CNMR:** (75 MHz, $CDCl_3$) δ 141.2, 131.3, 128.4, 124.6, 122.6, 113.3, 108.9, 101.9, 34.1; **IR:** (NaCl Film) Need; **HMRS-FAB**: $[M+H]^+$ calcd for C_9H_8BrN, 208.98; found, Need.

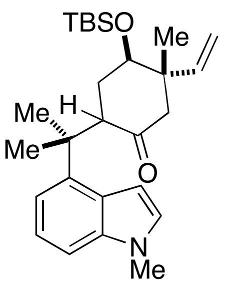
2-(1-methyl-1H-indol-4-yl)propan-2-ol (16):



To a stirring solution of **15** (300 mg, 1.43 mmol) in Et_2O (28 mL) at -78 °C was slowly added *t*BuLi (1.7 M in pentane, 1.68 mL, 2.86 mmol, 2 eq.) and left to stir for 15 min. Acetone (0.12 mL, 1.57 mmol, 1.1 eq.) in Et_2O (14 mL) was added, and the resultant mixture was allowed to stir for 1h. The reaction was quenched with NH_4Cl $_{(sat'd)}$ and extracted with hexanes (x3). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 91% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.291-7.166 (m, 3H), 7.087 (d, 3.2 Hz, 1H), 6.801 (d, 3.2 Hz, 1H), 3.808 (s, 3H), 2.049 (s, 1H), 1.774 (s, 3H); **^{13}CNMR:** (75 MHz, $CDCl_3$) δ 128.4, 125.1, 121.5, 114.9, 108.8, 102.0, 73.8, 33.2, 31.1; **IR:** (NaCl Film) Need; **HMRS-FAB**: $[M+H]^+$ calcd for $C_{12}H_{15}NO$, 189.12; found, Need.

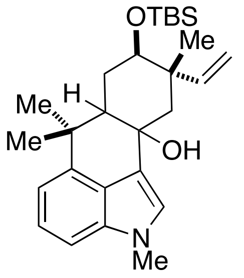
(4R,5S)-4-((tert-butyldimethylsilyl)oxy)-5-methyl-2-(2-(1-methyl-1H-indol-4-yl)propan-2-yl)-5-vinylcyclohexanone (18a):



Compound **5** (200 mg, 0.75 mmol) was added to THF (7 mL) and cooled to -78 °C, to which LHMDS (1 M in THF, 0.82 mL, 0.82 mL, 1.1 eq.) was added. After 45 min at -78 °C, TMSCl (0.11 mL, 0.89 mL, 1.2 eq.) was added and left to stir for 45 min at the same temperature. The reaction was quenched with brine, poured onto a brine:hexane (1:1) mixture and extracted with hexanes (x2). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated to afford product **17** that was used without further purification. To a solution of **17** (150 mg, 0.44 mmol, 1.2 eq.) in DCM (2 mL) was added **16** (69 mg, 0.37 mmol), cooled to -78 °C, and after stirring for 5 min was added 1 M tin (IV) chloride in DCM (0.41 mL, 0.41 mmol, 1.1 eq.) and left to stir for 15 min. The reaction was quenched with $NaHCO_3$ $_{(sat'd)}$ at the same temperature and extracted with DCM (x3). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 83% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.245-7.232 (m, 4H), 6.831 (s, 1H), 6.091 (dd, 17.2, 10.5 Hz, 1H), 5.079 (dd, 21.5, 10.6 Hz, 2H), 5.018 (dd, 3, 14 Hz, 2H), 3.740 (s, 3H), 3.673 (t, 3.6 Hz, 1H), 2.712 (t, 3.6 Hz, 1H), 2.594-1.872 (comp, 5H), 1.555 (s, 6H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 198.6, 145.3, 144.2, 141.3, 123.8, 120.8, 115.1, 114.4, 107.3, 99.2, 73.2, 72.8, 46.7, 38.8, 35.9, 32.2, 31.2, 28.4, 26.0, 25.1, 18.2, -3.0; **IR:** (NaCl Film) 1654 cm^{-1}; **HMRS-FAB**: $[M+H]^+$ calcd for $C_{27}H_{41}NO_2Si$, 440.29; found, 440.2895.

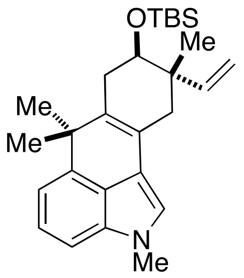
(8R,9S)-8-((tert-butyldimethylsilyl)oxy)-2,6,6,9-tetramethyl-9-vinyl-2,6,6a,7,8,9,10,10a-octahydronaphtho[1,2,3-cd]indol-10a-ol (18b):



Compound **5** **(**200 mg, 0.75 mmol) was added to THF (7 mL) and cooled to -78 °C, to which LHMDS (1 M in THF, 0.82 mL, 0.82 mL, 1.1 eq.) was added. After 45 min at -78 °C, TMSCl (0.11 mL, 0.89 mL, 1.2 eq.) was added and left to stir for 45 min at the same temperature. The reaction was quenched with brine, poured onto a brine:hexane (1:1) mixture and extracted with hexanes (x2). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated to afford product **17** that was used without further purification. To a solution of **17** (150 mg, 0.44 mmol, 1.2 eq.) in DCM (2 mL) was added **16** (69 mg, 0.37 mmol), cooled to -78 °C, and after stirring for 5 min was added fuming tin (IV) chloride in DCM (0.41 mmol, 1.1 eq.) and left to stir for 15 min. The reaction was quenched with $NaHCO_{3\ (sat'd)}$ at the same temperature and extracted with DCM (x3). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 83% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.245-7.232 (m, 4H), 6.972 (s, 1H), 6.091 (dd, 17.2, 10.5 Hz, 1H), 5.032 (dd, 21.5, 10.6 Hz, 2H), 4.976 (dd, 3, 14 Hz, 2H), 3.740 (s, 3H), 3.673 (t, 3.6 Hz, 1H), 2.734 (m, 1H), 2.594-1.872 (comp, 5H), 1.731 (s, 6H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 145.3, 144.2, 141.3, 123.8, 121.7, 120.8, 115.1, 114.4, 107.3, 99.2, 75.3, 73.6, 46.2, 38.8, 35.9, 33.2, 31.5, 28.4, 26.0, 25.1, 18.2, -3.0; **IR:** (NaCl Film) 3389 cm^{-1}; **HMRS-FAB**: $[M+H]^+$ calcd for $C_{27}H_{41}NO_2Si$, 440.29; found, 440.2904.

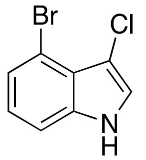
(8R,9S)-8-((tert-butyldimethylsilyl)oxy)-2,6,6,9-tetramethyl-9-vinyl-2,6,7,8,9,10-hexahydronaphtho[1,2,3-cd]indole (18c):



Compound **5** **(**200 mg, 0.75 mmol) was added to THF (7 mL) and cooled to -78 °C, to which LHMDS (1 M in THF, 0.82 mL, 0.82 mL, 1.1 eq.) was added. After 45 min at -78 °C, TMSCl (0.11 mL, 0.89 mL, 1.2 eq.) was added and left to stir for 45 min at the same temperature. The reaction was quenched with brine, poured onto a brine:hexane (1:1) mixture and extracted with hexanes (x2). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated to afford product **17** that was used without further purification. To a solution of **17** (150 mg, 0.44 mmol, 1.2 eq.) in DCM (2 mL) was added **16** (69 mg, 0.37 mmol), cooled to -44 °C, and after stirring for 5 min was added fuming tin (IV) chloride in DCM (0.41 mmol, 1.1 eq.) and left to stir for 15 min. The reaction was quenched with $NaHCO_3$ $_{(sat'd)}$ at the same temperature and extracted with DCM (x3). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 83% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 8.231 (s, 1H), 7.245-7.232 (m, 4H), 6.091 (dd, 17.2, 10.5 Hz, 1H), 5.079 (dd, 21.5, 10.6 Hz, 2H), 5.018 (dd, 3, 14 Hz, 2H), 3.740 (s, 3H), 3.673 (t, 3.6 Hz, 1H), 2.594-1.872 (comp, 5H), 1.555 (s, 6H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 145.3, 144.2, 141.3, 123.8, 121.7, 120.8, 115.1, 114.4, 107.3, 99.2, 73.2, 72.8, 46.7, 38.8, 35.9, 32.2, 31.2, 28.4, 26.0, 25.1, 18.2, -3.0; **IR:** (NaCl Film); **HMRS-FAB**: [M] calcd for $C_{27}H_{39}NOSi$, 421.28; found, 421.2785.

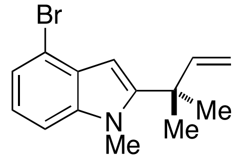
4-bromo-3-chloro-1H-indole (20):



To DMF (20 mL) was added **14** (0.5 mL, 3.97 mmol) and stirred vigorously at rt till the indole was completely dissolved, then NCS (530 mg, 3.97 mmol, 1 eq.) was added. The reaction was left to stir at rt for 12 h and then quenched with brine and extracted with ethyl acetate (3 x 30 mL). The organic layers were combined, washed with brine and water, dried over $MgSO_4$ and concentrated. The crude oil obtained was purified by flash silica gel chromatography (1:9 EtOAc:hexane) to afford the product **20** in a 97%.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.18 (s, 1H), 7.20 (m, 2H), 7.37 (dd, 1H), 7.67 (dd, 1H), 8.05 (br. s, 1H); **^{13}CNMR**: (75 MHz, $CDCl_3$) δ 133.38, 125.75, 123.33, 121.34, 118.04, 111.01, 104.05; **IR:** (Thin Film) Need; **HMRS-FAB**: $[M+H]^+$ calcd for C_8H_5BrClN, 228.93; found, 228.9217.

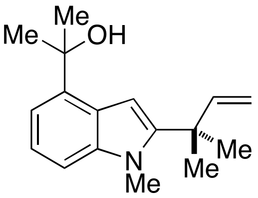
4-bromo-1-methyl-2-(2-methylbut-3-en-2-yl)-1H-indole (21):



To THF (8 mL) was added **20** (200 mg, 0.867 mmol) and cooled to 0 °C, to which Et_3N (0.42 mL, 3.03 mmol, 3.5 eq.) was added then a preformed solution of 2-methyl-2,3-butadiene (1.31 mL, 13.2 mmol, 2.0 eq.) in THF and 9-BBN (0.5 M in THF, 1.8 mL, 13.2 mmol, 2.0 eq.). The reaction was left to stir for 2 h and then poured onto 1 M NaOH:Et_2O (1:1) and washed with water (x2) and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product. To a solution of THF (4 mL) was added NaH (18 mg, 0.45 mmol, 1.2 eq.) at rt, to which the product (100 mg, 0.378 mmol) was added drop wise and allowed to stir. After 30 min, methyl iodide (0.03 mL, 0.53 mmol, 1.4 eq.) was added and allowed to stir for 5 h. The reaction was quenched with brine and extracted with hexane (x2). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 78% yield (2 steps).

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.281-7.199 (m, 2H), 7.042 (t, 7.5 Hz, 1H), 6.440 (s, 1H), 6.069 (dd, 17.4, 10.6 Hz, 1H), 5.082 (dd, 30.1, 10.6, 2H), 3.732 (s, 3H), 1.561 (s, 6H); **^{13}CNMR:** (75 MHz, $CDCl_3$) δ 147.6, 145.9, 139.0, 127.9, 122.3, 122.0, 114.4, 113.1, 108.1, 99.4, 38.9, 32.6, 28.5; **IR:** (NaCl Film); **HMRS-FAB**: $[M+H]^+$ calcd for $C_{14}H_{16}BrN$, 277.05; found, 277.0493.

2-(1-methyl-2-(2-methylbut-3-en-2-yl)-1H-indol-4-yl)propan-2-ol (22):

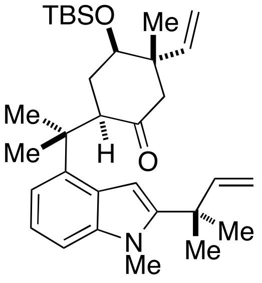


To a stirring solution of **21** (81 mg, 0.29 mmol) in Et_2O (2 mL) at -78 °C was slowly added *t*BuLi (1.7 M in pentane, 0.34 mL, 0.58 mmol, 2 eq.) and left to stir for 15 min. Acetone (0.02 mL, 0.29 mmol, 1 eq.) in Et_2O (2 mL) was added, and the resultant mixture was allowed to stir for 1h. The reaction was quenched with $NH_4Cl_{\text{(sat'd)}}$ and extracted with hexanes (x3). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product in 98% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.227-7.140 (m, 3H), 6.690 (s, 1H), 6.086 (dd, 17.4, 10.6 Hz, 1H), 5.077 (dd, 21.7, 10.6 Hz, 2H) 3.740 (s, 3H), 2.055 (s, 1H), 1.775 (s, 6H), 1.555 (s, 6H); **^{13}CNMR:** (75 MHz, $CDCl_3$) δ 146.4, 145.9, 140.5, 123.9, 120.9, 115.1, 112.7, 108.4, 99.7, 73.8, 38.8, 32.2, 28.6; **IR:** (NaCl Film) 3306 cm^{-1}; **HMRS-FAB**: $[M+H]^+$ calcd for

$C_{17}H_{23}NO$, 258.18; found, 258.1802.

(2R,4R,5S)-4-((tert-butyldimethylsilyl)oxy)-5-methyl-2-(2-(1-methyl-2-(2-methylbut-3-en-2-yl)-1H-indol-4-yl)propan-2-yl)-5-vinylcyclohexanone (23):



Compound **5** **(**530 mg, 4.34 mmol) was added to THF (40 mL) and cooled to -78 °C, to which LHMDS (4.77 mL, 4.77 mmol, 1.1 eq.) was added. After 45 min at -78 °C, TMSCl (0.66 mL, 5.21 mmol, 1.2 eq.) was added and left to stir for 45 min at the same temperature. The reaction was quenched with brine, poured onto a brine:hexane (1:1) mixture and extracted with hexanes (x2). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated to afford product **17** that was used without further purification. To a solution of **17** (69 mg, 0.326 mmol, 2.1 eq.) in DCM (2 mL) was added **22** (40 mg, 0.155 mmol), cooled to -78 °C, and after stirring for 5 min was added fuming tin (IV) chloride in DCM (0.16 mL, 1.05 eq.) and left to stir for 15 min. The reaction was quenched with $NaHCO_{3\ (sat'd)}$ at the same temperature and extracted with DCM (x3). The organic layers were combined, washed with water and brine, dried over $MgSO_4$ and concentrated. The crude material was purified by flash silica gel chromatography (1:4 EtOAc:hexane) to afford product **23** in 61% yield.

^{1}HNMR: (300 MHz, $CDCl_3$) δ 7.245-7.232 (m, 3H), 6.701 (s, 1H), 6.092 (dd, 17.3, 10.5 Hz, 1H), 6.710 (dd, 17.2, 10.9 Hz, 1H), 6.091 (dd, 17.2, 10.5 Hz, 1H), 5.079 (dd, 21.5, 10.6 Hz, 2H), 5.018 (dd, 3, 14 Hz, 2H), 3.740 (s, 3H), 3.673 (t, 3.6 Hz, 1H), 2.712 (t, 3.6 Hz, 1H), 2.594-1.872 (comp, 5H), 1.775 (s, 6H), 1.555 (s, 6H), 1.046 (s, 3H), 0.925 (s, 9H), 0.108 (s, 6H); **^{13}CNMR:** (75 MHz, CDCl3) δ 198.6, 145.3, 145.1, 144.2, 141.3, 123.8, 120.8, 115.1, 114.4, 112.6, 107.3, 99.2, 73.2, 72.8, 46.7, 38.8, 35.9, 32.2, 31.2, 28.4, 26.0, 25.1, 18.2, -3.0; **IR:** (NaCl Film) 1654 cm^{-1}; **HMRS-FAB**: $[M+H]^+$ calcd for $C_{32}H_{49}NO_2Si$, 507.35; found, 507.3546.