Supporting Information

A General Efficient Strategy for *cis*-3a-Aryloctahydroindole Alkaloids via Stereocontrolled $ZnBr_2$-Catalyzed Rearrangement of 2,3-Aziridino Alcohols

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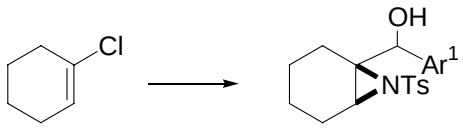
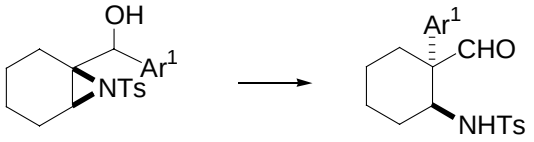


7 **8**

1-[1-Hydroxy-1-[3,4-(methylenedioxy)phenyl]methyl]-1,2-[N-(*p*-tolysulfonyl)aziridino]cyclohexane (8). Cyclohexenyl chloride **7** (10 g, 70%, 60 mmol) was diluted with 10 mL of dry Et_2O. This solution was added slowly to 50 mL of dry Et_2O containing lithium (1.05 g, 150 mmol). After the addition was completed, this mixture was stirred at room temperature for 4 h and then was cooled to –20^{o}C. A solution of piperonal (10 g, 66 mmol) in 20 mL of dry Et_2O was added dropwise. The reaction mixture was quenched with 40 mL water. The phases were separated and the aqueous phase was extracted with additional portions of Et_2O (3×50 mL). The combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue via silica gel column chromatography (petroleum/ethyl acetate = 6:1) provided 13 g (95%) of the allylic alcohol as a colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.56 (m, 4H), 1.81 (m, 2H), 2.06 (m, 2H), 4.95 (s, 1H), 5.83 (m, 1H), 5.92 (s, 2H), 6.76 (d, *J* = 1 Hz, 1H), 6.79 (d, *J* = 1 Hz, 1H), 6.83 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 22.4, 22.5, 24.1, 24.9, 77.8, 100.8, 106.9, 107.8, 119.7, 123.0, 136.7, 139.5, 146.7, 147.5; MS (EI) *m/z* 232 (M^+), 149 (base peak); HRMS (ESI) Calcd for $C_{14}H_{15}O_2$ (M^+-OH): 215.1067, found: 215.1069.

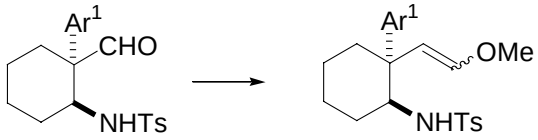
Allylic alcohol (232 mg, 1 mmol) was dissolved in 5 mL of dry CH_3CN. This solution was cooled to 0^{o}C. Then TsNClNa (273 mg, 1.2 mmol) and PTAB (76 mg, 0.2 mmol) were added. After stirring at room temperature for 24 h, the reaction mixture was diluted with 20 mL ethyl acetate and filtered through a plug of Al_2O_3 column (2-3cm). The Al_2O_3 column then washed with additional portions of 100 mL ethyl acetate. The filtrates was concentrated *in vacuo* and the residue was purified via Al_2O_3 column (petroleum/ethyl acetate = 4:1) to give 140 mg of a white solid **8** as a single isomer (35%); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00-1.05 (m, 1H), 1.26 (m, 1H), 1.48-1.62 (m, 5H), 2.10-2.13 (m, 1H), 2.45 (s, 3H), 3.89 (m, 1H), 4.15 (d, *J* = 5.8 Hz, 1H), 4.96 (d, *J* = 5.8 Hz, 1H), 5.96 (s, 2H), 6.73 (d, *J* = 8 Hz, 1H), 6.81 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H), 7.07 (d, *J* = 1.4 Hz, 1H), 7.36 (d, *J* = 8.0 Hz,

2H), 7.80 (d, J = 8.0 Hz, 2H); ^{13}C NMR (50MHz, $CDCl_3$): δ 19.2, 21.0, 21.5, 27.0, 32.7, 55.3, 74.4, 77.9, 100.9, 106.9, 109.4, 122.2, 127.2, 130.0, 132.8, 136.2, 144.3, 146.9, 147.1; MS (EI) *m/z* 401 (M^+), 91 (base peak); HRMS (ESI) Calcd for $C_{21}H_{23}NO_5SNa$ (M^++Na): 424.1189,found: 424.1191.



8 **11**

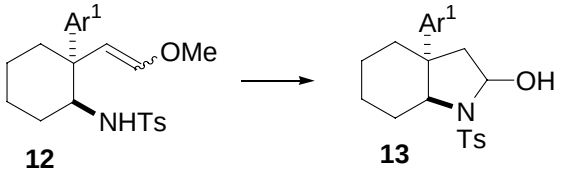
2-[3,4-(Methylenedioxy)phenyl]-2-formacyl-1-[N-(*p*-tolysulfonyl)]cyclohexane (11). To the solution of **8** (800 mg, 2 mmol) in 10 mL of dry CH_2Cl_2 was added $ZnBr_2$ (45 mg, 0.2 mmol). The reaction mixture was stirred at room temperature under Ar for 1 h and then was quenched with 5 mL water. The organic phase was washed with 5 mL brine, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography (petroleum/ethyl acetate/CH_2Cl_2 = 5:1:0.5) provided 770 mg (96%) of **11** as a colorless crystal; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19-1.22 (m, 1H), 1.39-1.44 (m, 1H), 1.70-1.78 (m, 3H), 1.94-2.03 (m, 2H), 2.12-2.16 (m, 1H), 2.38 (s, 3H), 3.42 (m, 1H), 5.43 (d, J = 10.3 Hz, 1H), 5.92 (d, J = 4.3 Hz, 2H), 6.47 (dd, J = 1.5 Hz, 8.2 Hz, 1H), 6.53 (s, 1H), 6.57 (d, J = 8.1 Hz, 1H), 7.09 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 9.35 (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 22.5, 24.8, 31.5, 32.2, 58.1, 58.5, 101.1, 107.5, 108.2, 121.1, 126.6, 129.1, 130.8, 138.1, 142.5, 147.0, 148.0, 203.3; MS (EI) *m/z* 401 (M^+), 135 (base peak); HRMS (ESI) Calcd for $C_{21}H_{24}NO_5S$ (M^++H): 402.1370, found: 402.1367.



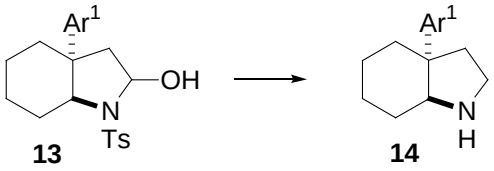
11 **12** (*E/Z*=1:1)

2-[3,4-(Methylenedioxy)phenyl]-2-methoxyethylene-1-[N-(*p*-tolysulfonyl)]cyclohexane (12). Methyoxymethyltriphenyl phosphonium chloride (1.37 g, 4 mmol) was suspended in 8 mL of dry THF and cooled to 0^{o}C. *n*-BuLi (1.5M in hexane, 2.5 mL, 3.75 mmol) was added slowly and the bright orange mixture was stirred at room temperature for 1h. **11** (400 mg, 1 mmol) was dissolved in 4 mL of dry THF and added to the phosphorane solution via syringe at 0^{o}C. After stirring at room temperature for 0.5 h, the reaction mixture was quenched with 10 mL water and extracted with additional portions ethyl acetate (3×10 mL). The combined organic phases were washed with 5 mL brine, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography (petroleum/ethyl acetate = 7:1) provided 395 mg (92%) of *E/Z* mixture (1/1) **12** as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16-1.79 (m, 12H), 1.94-2.37 (m, 4H), 2.40 (s, 3H), 2.42 (s, 3H), 3.18 (m, 1H), 3.38 (m, 1H), 3.57 (s, 3H), 3.59 (s, 3H), 4.27 (d, J = 7.2 Hz, 1H), 4.42 (d, J = 4.8 Hz, 1H), 4.74 (d, J = 13.2 Hz, 1H), 5.33 (d, J = 6.0 Hz, 1H), 5.87-5.91 (m, 4H), 6.10 (d, J = 7.2 Hz, 1H), 6.28 (d, J = 13.5 Hz, 1H), 6.45-6.68 (m, 6H), 7.12 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75MHz, $CDCl_3$): δ 21.5, 22.4,

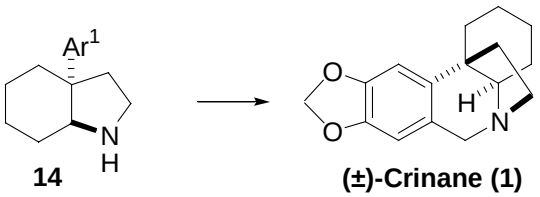
24.3, 25.1, 29.4, 31.0, 37.1, 39.6, 46.7, 49.2, 56.1, 59.6, 59.9, 60.7, 100.7, 100.9, 103.7, 106.2, 107.3, 107.5, 107.6, 119.8, 120.2, 126.8, 127.0, 129.1, 129.4, 136.8, 137.4, 138.4, 139.8, 142.4, 143.1, 145.6, 145.8, 147.1, 147.3, 147.5, 150.8; MS (EI) *m/z* 429 (M^+), 242 (base peak); HRMS (ESI) Calcd for $C_{23}H_{28}NO_5S$ (M^++H): 430.1683, found: 430.1680.



1-(*p*-Tolylsulfonyl)-2-hydroxy-3a-[3,4-(methylenedioxy)phenyl]-2,3,3a,4,5,6,7,7a-octahydroindole (13). To the solution of **12** (430 mg, 1 mmol) in 10 mL Et_2O was added 0.25 mL $HClO_4$ (70%). The reaction mixture was then stirred at room temperature for 8 h. After the reaction was completed, and then cooled to 0°C, 15 mL of saturated aqueous solution of $NaHCO_3$ was added. The phases were separated and the aqueous phase was extracted with ethyl acetate (3×10 mL). The combined organic phases were washed with 10 mL brine, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography (petroleum/ethyl acetate = 6:1) provided 360 mg (87%) of **13** as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26-1.33 (m, 2H), 1.48-1.52 (m, 2H), 1.60-1.68 (m, 2H), 1.77-1.97 (m, 2H), 2.18-2.22 (m, 1H), 2.33-2.38 (m, 11H), 2.39 (s, 3H), 3.60 (s, 1H), 3.71 (dd, *J* = 6.0 Hz, 9.2 Hz, 1H), 5.43 (t, *J* = 6.0 Hz, 1H), 5.89 (d, *J* = 17.8 Hz, 2H), 6.46 (s, 1H), 6.50-6.52 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ 21.4, 21.9, 23.1, 31.6, 36.7, 39.9, 48.2, 65.3, 83.5, 100.9, 106.7, 107.7, 118.62, 126.7, 129.2, 135.5, 139.9, 143.0, 145.8, 147.4; MS (EI) *m/z* 415 (M^+), 138 (base peak); HRMS (ESI) Calcd for $C_{22}H_{24}NO_4S$ (M^+-OH): 398.1421, found: 398.1423.

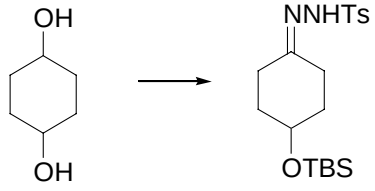


3a-[3,4-(Methylenedioxy)phenyl]-2,3,3a,4,5,6,7,7a-octahydroindole (14). To the solution of **13** (95 mg, 0.23 mmol) in 2 mL dry *o*-xylene was added dropwise Red-Al (3.5M in toluene, 0.4 mL, 1.38 mmol) at 0°C. Then the reaction mixture was refluxed under Ar for 6-8 h and cooled to 0°C. Aqueous solution of NaOH (3N, 2 mL) was added slowly. The mixture was extracted with additional portions of $CHCl_3$ (3×10 mL), dried over Na_2SO_4 and concentrated. Purification of the residue via a short silica gel (4-5 g) column chromatography ($CHCl_3$/CH_3OH/NEt_3 = 20:1:1) provided 40 mg (70%) of **14** as a colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.14-2.30 (m, 10H), 3.05-3.25 (m, 3H), 3.47 (s, 1H), 5.94 (s, 2H), 6.78 (s, 1H), 6.80 (d, *J* = 1.6 Hz, 1H), 6.87 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.9, 21.9, 25.9, 33.6, 41.1, 42.8, 47.8, 60.9, 100.8, 107.4, 107.8, 119.3, 140.3, 145.3, 147.6; MS (EI) *m/z* 244 (M^+-H), 84 (base peak); HRMS (ESI) Calcd for $C_{15}H_{20}NO_2$ (M^++H): 246.1489, found: 246.1491.



14 **(±)-Crinane (1)**

(±)-Crinane (1). A solution of **14** (25 mg, 0.1 mmol) in 8 mL THF was treated with Eschenmoser's salt (30 mg, 0.15 mmol) and heated to 40°C for 24 h. The THF was removed *in vacuo* and ethyl acetate (20 mL) was added. 1 N NaOH was added until the solution was basic. The organic phases were combined and washed with water (5 mL) and brine (5 mL), then dried over Na_2SO_4 and concentrated. Purification of the residue via silica gel column chromatography ($CHCl_3/CH_3OH$ = 10:1) provided 22 mg (86%) of the desired (±)-crinane (**1**) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20-1.31(m, 2H), 1.50-1.54 (m, 1H), 1.61-1.68 (m, 1H), 1.76-1.84 (m, 3H), 1.94-1.98 (m, 1H), 2.31 (m, 1H), 2.98 (m, 1H), 3.52 (m, 1H), 3.85, 4.46 (AB_q, J_{AB} = 16.5 Hz, 2H), 5.91 (s, 1H), 6,48 (s, 1H), 6.72 (s, 1H); ^{13}C NMR (50MHz, $CDCl_3$): δ 21.5, 24.1, 27.1, 28.8, 37.4, 42.9, 51.7, 61.6, 67.4, 100.7, 103.3, 106.2, 124.9, 141.6, 145.7, 146.4; MS (EI) *m/z* 257 (M^+), 41 (base peak); HRMS (ESI) Calcd for $C_{16}H_{20}NO_2$ (M^++H): 258.1489, found: 258.1487.



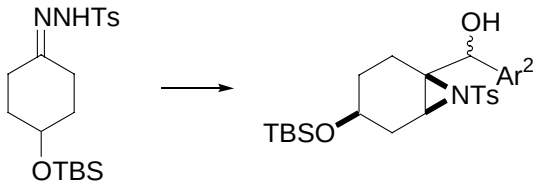
15 **16**

4-(*tert*-Butyldimethylsilyloxy)-1-cyclohexanone (*p*-tolysulfonyl)hydrazone (16). To the solution of cyclohexane-1, 4-diol (10 g, 86 mmol) and imidazole (14.7 g, 215 mmol) in 15 mL of dry DMF and 20 mL of THF was added dropwise the solution of TBDMSCl (16.2 g, 107 mmol) in 20 mL of dry DMF at 0°C. After the dropping was completed, the reaction mixture was quenched with 100 mL brine and extracted with ethyl acetate (3×100 mL). The organic phases were combined and dried over Na_2SO_4 and concentrated. Purification of the residue via silica gel column chromatography (petroleum/ethyl acetate = 4:1) provided 12.3 g (62%) of the alcohol mixtures (1/1) as a colorless oil; The little polar one: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.03 (s, 6H), 0.88 (s, 9H), 1.45-1.80 (m, 8H), 3.66 (m, 1H), 3.80 (m, 1H), ^{13}C NMR (50 MHz, $CDCl_3$): δ -4.9, 18.0, 25.7, 30.1, 31.3, 66.8, 68.9; HRMS (ESI) Calcd for $C_{12}H_{27}O_2Si$ (M^++H): 231.1775, found: 231.1771. The large polar one: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.04 (s, 6H), 0.86 (s, 9H), 1.32-1.40 (m, 4H), 1.81-1.95 (m, 4H), 3.62 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ -4.8, 18.1, 25.8, 32.6, 32.7, 69.4, 70.0; MS (EI) *m/z* 230 (M^+), 97 (base peak); HRMS (ESI) Calcd for $C_{12}H_{27}O_2Si$ (M^++H): 231.1775, found: 231.1774.

A mixture containing the alcohol mixtures (10 g, 43.5 mmol) and PCC (15 g, 65 mmol) in 200 mL of CH_2Cl_2 was stirred at room temperature for 6 h and quenched with 100 mL Et_2O. The suspension was filtered through an Al_2O_3 column. The filtered was concentrate *in vacuo* and the residue was purified via silica gel column chromatography (petroleum/ethyl acetate = 20:1) to give 9.7 g (98%)

of the ketone as colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.07 (s, 6H), 0.89 (s, 9H), 1.87-1.93 (m, 4H), 2.15-2.24 (m, 2H), 2.57-2.73 (m, 2H), 4.11 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ –5.0, 18.0, 25.7, 34.1, 36.8, 65.8, 211.7; MS (EI) *m/z* 213 (M^+-Me), 75 (base peak); HRMS (ESI) Calcd for $C_{12}H_{25}O_2Si$ (M^++H): 229.1618, found: 229.1623.

A solution of the ketone (10 g, 43.8 mmol) and *p*-tolysulfonyl hydrazine (8.2 g, 43.8 mmol) in 70 mL of dry THF was stirred at room temperature for 2 h. After removing the THF *in vacuo*, the residue was purified via a short silica gel column chromatograph (petroleum/ethyl acetate = 3:1) to give 17.0 g (98%) of **16** as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.008 (s, 6H), 0.84 (s, 9H), 1.64 (m, 4H), 2.17-2.35 (m, 3H), 2.40 (s, 3H), 2.44-2.46 (m, 1H), 3.93 (m, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ –5.0, 18.0, 21.6, 22.2, 25.7, 30.1, 33.1 34.2, 66.7, 128.0, 129.5, 143.8, 162.1; MS (EI) *m/z* 339 (M^+-^{t}Bu), 75 (base peak); HRMS (ESI) Calcd for $C_{19}H_{33}N_2O_3SiS$ (M^++H): 397.1976, found: 397.1979.

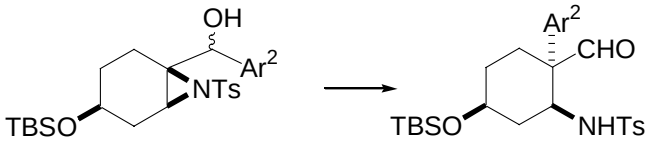


16 **17**

4-(*tert*-Butyldimethylsilyloxy)-1-[1-hydroxy-1-[3,4-(dimethoxy)phenyl]methyl]-1,2-[N-(*p*-tolysulfonyl)aziridino]cyclohexane (17). To a cold (-78^{o}C) suspension of **16** (4 g, 11 mmol) in 20 mL of dry tetramethylethlenediamine (TMEDA) was added dropwise under Ar during 15 min *n*-BuLi (1.5M in hexane, 23 mL, 35 mmol). The reaction mixture stirred at room temperature for 4 h and then cooled to -78^{o}C again. The solution of 3,4-dimethyoxybenzalehyde (3.6 g, 2.0 mmol) in 10 mL of TMEDA was added dropwise. The mixture was poured into 100 mL saturated aqueous solution of NH_4Cl. The layers were separated, and the aqueous layer was extracted with Et_2O (3×100 mL). The combined organic phases were washed with 100 mL of brine, dried over Na_2SO_4 and concentrated. Purification of the residue via silica gel column chromatography (petroleum/ethyl acetate = 4:1) provided 3.2 g (85%) of the allylic alcohol mixtures as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.035 (s, 6H), 0.86 (s, 9H), 1.55-1.63 (m, 1H), 1.78-2.03 (m, 4H), 2.28 (m, 1H), 3.858 (s, 3H), 3.863 (s, 3H), 3.93 (m, 1H), 5.02 (brs, 1H), 5.72 (brs, 1H), 6.82 (s, 1H), 6.84 (d, *J* = 1.6 Hz, 1H), 6.88 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ -4.8, 18.1, 22.9, 23.0, 25.8, 31.3, 31.4, 34.8, 55.7, 67.7, 67.8, 77.2, 109.3, 109.4, 110.6, 118.5, 118.7, 120.5, 134.9, 139.0, 139.2, 148.2, 148.7; MS (EI) *m/z* 378 (M^+), 229 (base peak); HRMS (ESI) Calcd for $C_{21}H_{34}O_4SiNa$ (M^++Na): 401.2119, found: 401.2114.

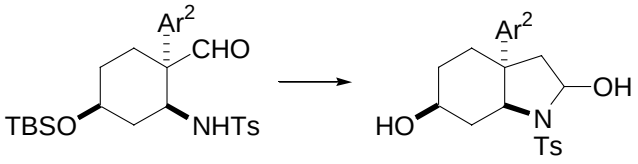
Allylic alcohols (380 mg, 1 mmol) were dissolved in 5 mL of dry CH_3CN. This solution was cooled to 0^{o}C. Then TsNClNa (273 mg, 1.2 mmol) and PTAB (76 mg, 0.2 mmol) were added. After stirring at room temperature for 24 h, the reaction mixture was diluted with 30 mL of ethyl acetate and filtered through a plug of Al_2O_3 column (3-4cm). The Al_2O_3 column then was washed with additional portions of 150 mL ethyl acetate. The filtrates was concentrated *in vacuo* and the residue was purified via silica gel column chromatography (petroleum/ethyl acetate = 7:1) to give 164 mg

(30%) of **17**[*] as two isomers (2:1) as colorless oils; the spectral properties of one of them: ^{1}H NMR (400 MHz, $CDCl_3$): δ -1.56 (s, 3H), -1.20 (s, 3H), 0.70 (s, 9H), 1.10-1.15 (m, 1H), 1.40-1.45 (m, 1H), 1.68-1.74 (m, 1H), 1.87-1.91 (m, 1H), 2.00-2.07 (m, 2H), 2.46 (s, 3H), 3.54 (m, 1H), 3.62 (m, 1H), 3.79 (d, *J* = 2.7 Hz, 1H), 3.87 (s, 3H), 3.91 (s, 3H), 5.23 (d, *J* = 2.8 Hz, 1H), 6.63 (d, *J* = 8.3 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 7.09 (s, 1H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ -5.2, -5.1, 17.8, 18.9, 21.5, 25.5, 27.6, 32.4, 46.4, 55.8, 60.3, 63.9, 74.4, 109.4, 111.0, 118.1, 126.7, 129.6, 132.3, 138.4, 143.9, 148.3, 148.9; MS (EI) *m/z* 547 (M^+), 192 (base peak); HRMS (ESI) Calcd for $C_{28}H_{42}NO_6SiS$ (M^++H): 548.2497, found: 548.2506.



17 **18**

3-(*tert*-Butyldimethylsilyloxy)-6-[3,4-(dimethoxy)phenyl]-6-formacyl-1-[N-(*p*-tolysulfonyl)]cyclohexane (18) To the solution of **17** (550 mg, 1 mmol) in 8 mL of dry CH_2Cl_2 was added $ZnBr_2$ (25 mg, 0.1 mmol). The reaction mixture was stirred at room temperature under Ar for 0.5 h and then was quenched with 3 mL water. The organic phase was washed with 3 mL brine, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography (petroleum/ethyl acetate = 6:1) provided 540 mg (98%) of **18** as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.057 (s, 3H), 0.098 (s, 3H), 0.96 (s, 9H), 1.19-1.32 (m, 1H), 1.64-1.72 (m, 1H), 1.80-1.94 (m, 2H), 2.07-2.10 (m, 1H), 2.36 (s, 3H), 2.52-2.59 (m, 1H), 3.70 (s, 3H), 3.74 (m, 1H), 3.87 (s, 3H), 4.10 (m, 1H), 5.41 (d, *J* = 10.6 Hz, 1H), 6.43 (s, 1H), 6.54 (d, *J* = 8.3 Hz, 1H), 6.68 (d, *J* = 8.3 Hz, 1H), 6.99 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 9.47 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ -5.0, 18.0, 21.3, 25.8, 26.4, 30.1, 38.9, 53.6, 55.2, 55.6, 58.0, 109.7, 110.5, 119.4, 126.8, 128.9, 130.0, 137.4, 142.5, 148.5, 149.0, 204.1; MS (EI) *m/z* 547 (M^+), 192 (base peak); HRMS (ESI) Calcd for $C_{28}H_{45}N_2O_6SiS$ (M^++NH_4): 565.2762, found: 565.2769.



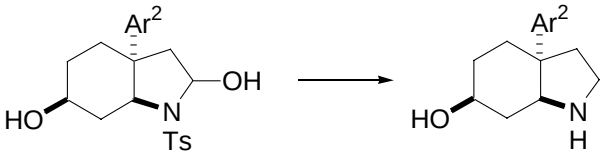
18 **19**

1-(*p*-Tolylsulfonyl)-2,6-dihydroxy-3a-[3,4-(dimethyoxy)phenyl]-2,3,3a,4,5,6,7,7a-octahydroindole (19). Methyoxymethyltriphenyl phosphonium chloride (1.37g, 4 mmol) was suspended in 8 mL of dry THF and cooled to 0^{o}C. *n*-BuLi (1.5M in hexane, 2.5 mL, 3.75 mmol) was added slowly and the bright orange mixture was stirred at room temperature for 1 h. **18** (550 mg, 1 mmol) was dissolved in 5 mL of dry THF and added to the phosphorane solution via syringe at 0^{o}C. After stirring at room temperature for 0.5 h, the reaction mixture was quenched with 10 mL water and extracted with

* In this step, two isomers were obtained. Due to the difficulty of isolation, we only reported the spectral properties of one of them.

additional portions ethyl acetate (3×10 mL). The combined organic phases were washed with 5 mL brine, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography provided 400 mg (70%) of *E* isomer (petroleum/ethyl acetate = 5:1) and 145 mg (25%) of *Z* isomer (petroleum/ethyl acetate = 3:1) as colorless oils; *E* isomer of the vinyl ethers: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.052 (s, 3H), 0.11 (s, 3H), 0.94 (s, 9H), 1.50-1.60 (m, 2H), 1.70-1.76 (m, 2H), 2.22-2.27 (m, 2H), 2.42 (s, 3H), 3.62 (s, 3H), 3.64 (s, 3H), 3.75-3.78 (m, 1H), 3.88 (s, 3H), 4.08 (m, 1H), 4.27 (d, *J* = 4.1 Hz, 1H), 4.85 (d, *J* = 13.3 Hz, 1H), 6.46 (d, *J* = 13.3 Hz, 1H), 6.56 (d, *J* = 2.0 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.78 (dd, *J* = 2.0 Hz, 8.4 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ -4.99, -5.00, 18.0, 21.4, 25.9, 30.0, 32.0, 37.2, 46.5, 55.0, 55.4, 55.8, 56.3, 66.8, 109.2, 110.2, 119.5, 127.1, 129.2, 129.5, 136.3, 138.7, 143.0, 147.7, 148.7, 151.0; MS (EI) *m/z* 575 (M^+), 171 (base peak); HRMS (ESI) Calcd for $C_{30}H_{49}N_2O_6SiS$ (M^++NH_4): 593.3075, found: 593.3068. *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.056 (s, 3H), 0.13 (s, 3H), 0.95 (s, 9H), 1.49-1.53 (m, 1H), 1.62-1.69 (m, 1H), 1.74-1.80 (m, 1H), 1.85-1.89 (m, 1H), 2.15-2.22 (m, 1H), 2.29-2.32 (m, 1H), 2.41 (s, 3H), 3.59 (s, 6H), 3.61 (m, 1H), 3.88 (s, 3H), 4.09 (m, 1H), 4.36 (d, *J* = 7.3H, 1H), 4.94 (d, *J* = 5.0 Hz, 1H), 6.17 (d, *J* = 7.3 Hz, 1H), 6.52 (d, *J* = 2.1 Hz, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 6.76 (dd, *J* = 2.2 Hz, 8.5 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ -4.99, -4.94, 18.0, 21.4, 25.9, 30.2, 32.1 37.9, 48.8, 54.8, 55.5, 55.8, 60.0, 66.8, 104.8, 109.1, 110.0, 119.0, 127.0, 129.0, 129.2, 136.5, 142.5, 147.4, 147.9, 148.5; MS (EI) *m/z* 575 (M^+), 171 (base peak); HRMS (ESI) Calcd for $C_{30}H_{49}N_2O_6SiS$ (M^++NH_4): 593.3075, found: 593.3078.

To the solution of the vinyl ethers (575 mg, 1 mmol) in 15 mL Et_2O was added 0.75 mL $HClO_4$ (70%). The reaction mixture was then stirred at room temperature for 8 h. After the reaction was completed, and then cooled to 0^{o}C, 25 mL saturated solution of $NaHCO_3$ was added. The phases were separated and the aqueous phase was extracted with ethyl acetate (3×15 mL). The combined organic phases were washed with 20 mL brine, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography (petroleum/ethyl acetate = 1:1) provided 406 mg (91%) of **19** as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.57-1.60 (m, 1H), 1.72-1.90 (m, 3H), 2.10-2.18 (m, 1H), 2.22-2.30 (m, 2H), 2.37 (s, 3H), 2.40 (m, 1H), 3.70 (s, 1H), 3.73 (s, 3H), 3.83 (s, 3H), 3.99 (t, *J* = 7.0 Hz, 1H), 4.21 (m, 1H), 5.48 (t, *J* = 5.1 Hz, 1H), 6.54 (d, *J* = 2.0 Hz, 1H), 6.56 (s, 1H), 6.66 (dd, *J* = 2.0 Hz, *J* = 8.3 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 28.9, 31.2, 37.6, 40.3, 47.2, 55.4, 55.6, 63.5, 65.9, 83.8, 109.4, 110.2, 117.4, 126.6, 129.2, 134.8, 137.8, 147.6, 148.5; MS (EI) *m/z* 447 (M^+), 91 (base peak); HRMS (ESI) Calcd for $C_{23}H_{29}NO_6SNa$ (M^++Na): 470.1608, found: 470.1604.



19 **20**

6-hydroxy-3a-[3,4-(dimethyoxy)phenyl]-2,3,3a,4,5,6,7,7a-octahydroindole (20). Route A: To the solution of **19** (90 mg, 0.2 mmol) in 2 mL of dry *o*-xylene was added dropwise Red-Al (3.5 M in toluene, 0.46 mL, 1.6 mmol) at 0^{o}C. Then the reaction mixture was refluxed under Ar for 6-8 h and

cooled to 0°C. Aqueous solution of NaOH (3N, 3 mL) was added slowly. The mixture was extracted with additional portions of $CHCl_3$ (3×10 mL), dried over Na_2SO_4 and concentrated. Purification of the residue via a short silica gel (4-5 g) column chromatography ($CHCl_3/CH_3OH/NEt_3$ = 2:1:0.5) provided 26 mg (50%) of **20** as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.20-1.33 (m, 1H), 1.66-1.83 (m, 3H), 1.88-2.08 (m, 3H), 213-2.18 (m, 1H), 2.97-3.17 (m, 2H), 3.25-3.39 (m, 2H), 3.66 (s, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.00 (m, 1H), 6.81 (d, *J* = 11.0 Hz, 1H), 6.87 (s, 1H), 6.89 (d, *J* = 11.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.7, 32.2, 35.5, 41.7, 43.2, 46.3, 56.0, 56.1, 62.1, 6.3, 110.5, 110.9, 138.5, 147.3, 148.9. MS (EI) *m/z* 276 (M^+-H), 56 (base peak); HRMS (ESI) Calcd for $C_{16}H_{24}NO_3$ (M^++H): 278.1751, found: 278.1753.

Route B: To the solution **19** (45 mg, 0.1 mmol) in 2 mL of dry CH_2Cl_2 was added $NaBH_3CN$ (30 mg, 0.5 mmol) and $TiCl_4$ (16 µl, 0.15 mmol) at -78°C. After 5 minutes, the mixture was quenched with aqueous solution of NaOH (0.1 N, 5 mL), then extracted with additional portions of CH_2Cl_2 (3×10 mL), dried over Na_2SO_4 and concentrated. Then, 41 mg (96%) of the amino alcohol **19'** was obtained as a colorless oil after purification by silica gel column chromatography (petroleum/ethyl acetate = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37-1.53 (m, 2H), 1.78-1.82 (m, 3H), 1.91-2.12 (m, 3H), 2.36 (s, 3H), 3.38 (m, 1H), 3.59 (m, 1H), 3.79 (s, 3H), 3.84 (s, 3H), 3.99 (t, *J* = 5 Hz, 1H), 4.14 (m, 1H), 6.63 (d, *J* = 4 Hz, 1H), 6.68 (d, *J* = 4 Hz, 1H), 6.71 (s, 1H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.60 (d, *J* = 8 Hz, 2H); ^{13}C NMR (75 MHz, CD_3COCD_3): δ 20.7, 29.9, 31.5, 34.2, 37.3, 46.5, 48.1, 55.3, 63.6, 65.4, 110.7, 111.5, 118.2, 127.3, 129.5, 135.5, 138.2, 143.1, 148.2, 149.3; MS (EI) *m/z* 431 (M^+), 91 (base peak); HRMS (ESI) Calcd for $C_{23}H_{30}NO_5S$ (M^++H): 432.1839, found: 432.1836.

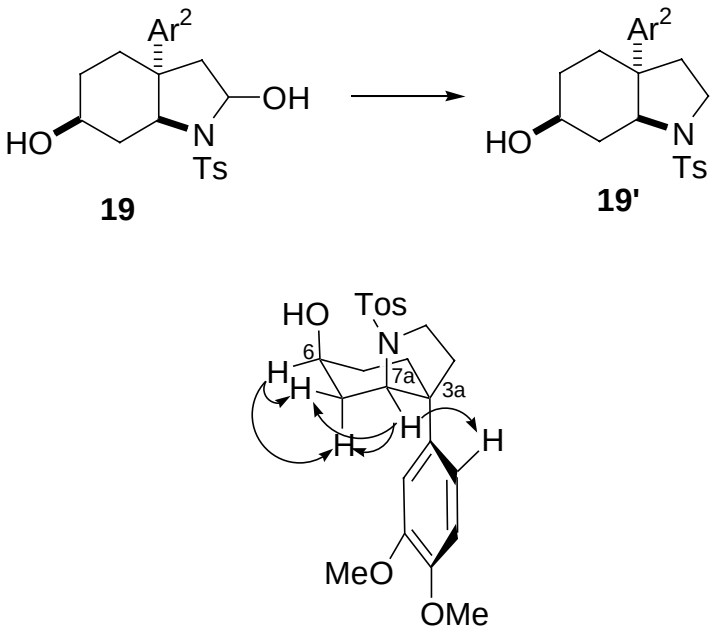
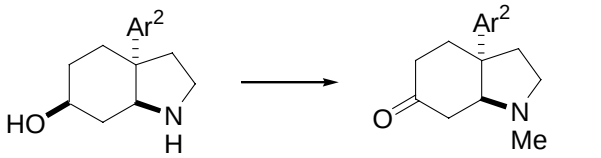


Figure. Diagnostic NOEs for **19'**.

To a solution of naphthalene (260 mg, 2 mmol) in DME (3 mL) was added sodium (42 mg, 1.8 mmol). The mixture was stirred at room temperature for 2 h. Then the solution of the product of the

reaction above (90 mg, 0.2 mmol) in DME (2 mL) was added dropwise at –78°C. The reaction was quenched with additional of saturated $NaHCO_3$ (0.5 mL), dried over Na_2SO_4 and concentrated. Purification of the residue via a short silica gel (4-5 g) column chromatography ($CHCl_3/CH_3OH/NEt_3$ = 2:1:0.5) provided 54 mg (97%) of **20** as a colorless oil.



20 **(±)-Mesembrine (2)**

(±)-Mesembrine (2). To a stirred solution of **20** (30 mg, 0.1 mmol) in CH_3OH (2 mL) containing 37% aqueous HCHO (25 μl, 0.3 mmol) at room temperature was added $NaBH_3CN$ (8 mg, 0.13 mmol) and $ZnCl_2$ (7 mg, 0.05 mmol). After 5 minutes, the reaction mixture was taken up in aqueous solution of NaOH (0.1 N, 2 mL). Removal of the most of methanol, the mixture was extracted with additional portions of ethyl acetate (3×10 mL), dried over Na_2SO_4 and concentrated. Purification of the residue via silica gel column chromatography ($CHCl_3/CH_3OH$ = 8:1) provided 30 mg (96%) of the amino alcohol as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.17-1.27 (m, 1H), 1.48-1.57 (m, 1H), 1.73-1.94 (m, 4H), 2.01-2.05 (m, 2H), 2.14-2.32 (m, 2H), 2.36 (s, 3H), 2.75 (m, 1H), 3.21 (ddd, *J* = 4.8 Hz, 9.0 Hz, 9.0 Hz, 1H), 3.87 (s, 3H), 3.88 (s, 3H), 3.99 (m, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.86 (d, *J* = 1.8 Hz, 1H), 6.90 (dd, *J* = 1.8 Hz, 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.8, 33.0, 34.8, 40.1, 40.5, 46.9, 54.3, 55.8, 55.9, 66.7, 70.0, 110.4, 110.7, 118.7, 139.0, 147.0, 148.7; MS (EI) *m/z* 290 (M^+-H, base peak); HRMS (ESI) Calcd for $C_{17}H_{26}NO_3$ (M^++H): 292.1907, found: 292.1901.

To a stirred solution of the amino alcohol (30 mg, 0.1 mmol) in 5 mL dry CH_2Cl_2 at room temperature was added PDC (56 mg, 0.15 mmol). The reaction mixture was quenched by aqueous solution of NaOH (0.1 N, 2 mL) after 2 h, and extracted with additional portions of CH_2Cl_2 (3×10 mL), then dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography ($CHCl_3/CH_3COCH_3$ = 6:1) provided 28 mg (93%) of (±)-mesembrine (**2**) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11-2.24 (m, 5H), 2.32 (s, 3H), 2.34 (m, 1H), 2.42 (m, 1H), 2.61 (m, 1H), 3.00 (m, 1H), 3.15 (m, 1H), 3.89 (s, 3H), 3.91 (s, 3H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.90 (s, 1H), 6.93 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.2, 36.2, 38.8, 40.1, 40.5, 47.5, 54.8, 55.9, 60.0, 70.3, 109.9, 110.9, 117.9, 140.1, 147.5, 149.0, 2121.5; MS (EI) *m/z* 289 (M^+), 70 (base peak); HRMS (ESI) Calcd for $C_{17}H_{24}NO_3$ (M^++H): 290.1751, found: 290.1758.