

Supporting Information for

Formal Synthesis of Chelamidine Alkaloid and Derivatives

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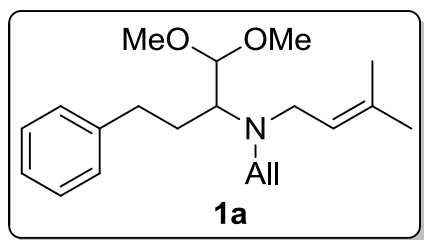
1. General Information

All reactions were carried out without exclusion of air or moisture unless otherwise stated. Molecular iodine, sodium percarbonate (avail. H₂O₂ 20-30%), and trifluoromethanesulfonic acid were purchased from commercial suppliers, and used directly as received. Commercial solvents and reagents were used without further purification. Secondary amines¹⁻⁴ and aldehydes⁵⁻⁸ were synthesized according to the literatures. Reactions were monitored through thin layer chromatography [Merck 60 F254 precoated silica gel plate (0.2 mm thickness)]. Subsequent to elution, spots were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible using basic solution of potassium permanganate or acidic solution of ceric molybdate as stain, followed by heating on a hot plate. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. Infrared spectra were recorded on a Shimadzu IR Prestige-21 FT-IR. Liquid samples were examined as film between NaCl salt plates. HRMS spectra were recorded on a Waters Q-ToF Premier Spectrometer. ¹H NMR and ¹³C NMR spectra were recorded using Bruker Avance 400 and 500 MHz spectrometers. Chemical shifts for ¹H NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-*d* (δ 7.260, singlet). Multiplicities were given as: s (singlet); brs (broad singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); ddd (doublets of doublets of doublet); td (triplet of doublet); m (multiplets); ddt (doublet of doublet of triplet) and etc. Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (¹³C NMR) are reported as δ in units of parts per million (ppm) downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-*d* (δ 77.00, triplet).

2. General Experimental Procedure for the Synthesis of α -Amino Acetals⁹⁻¹⁰ and Spectroscopic Information

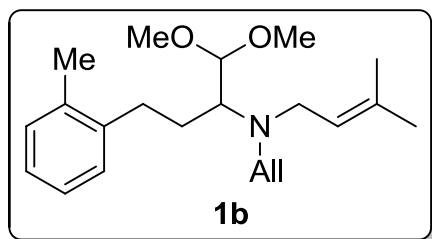
Iodine (25 mg, 0.1 mmol) was added to a mixture of sodium percarbonate (79 mg, 0.5 mmol), secondary amines (0.5 mmol), and aldehydes (0.60 mmol) in methanol (0.5 mL)/1,2-dichloroethane (2.0 mL) at room temperature. The mixture was stirred at 40 °C until secondary amine was completely converted by TLC detection. The resulting reaction mixture was mixed with a small amount of silica gel and concentrated. The crude product was purified by flash column chromatography (silica gel; ethyl acetate or diethyl ether/hexane = 1:100, v/v) to afford the corresponding desired product.

***N*-allyl-*N*-(1,1-dimethoxy-4-phenylbutan-2-yl)-3-methylbut-2-en-1-amine (1a):**



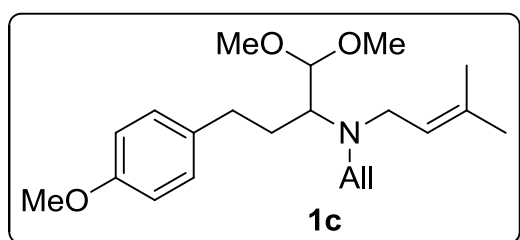
Light yellow oil; $R_f = 0.59$ (hexane: ethyl acetate = 5:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.27-7.12 (m, 5H), 5.85-5.76 (m, 1H), 5.19-5.03 (m, 3H), 4.27 (d, $J = 5.39$ Hz, 1H), 3.34 (s, 3H), 3.33 (s, 3H), 3.33-3.27 (m, 1H), 3.19-3.09 (m, 3H), 2.85-2.76 (m, 2H), 2.64-2.56 (m, 1H), 1.83-1.65 (m, 2H), 1.70 (s, 3H), 1.62 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 143.1, 138.4, 133.4, 128.5 (CH x 2), 128.1 (CH x 2), 125.4, 123.8, 115.6, 107.0, 58.6, 54.6, 54.4, 53.3, 48.0, 33.3, 28.6, 25.8, 17.9 ppm; **HRMS (ESI, m/z):** calcd for $\text{C}_{20}\text{H}_{32}\text{NO}_2^+ [\text{M}+\text{H}]^+$ 318.2433, found: 318.2436.

***N*-allyl-*N*-(1,1-dimethoxy-4-(*o*-tolyl)butan-2-yl)-3-methylbut-2-en-1-amine (1b):**



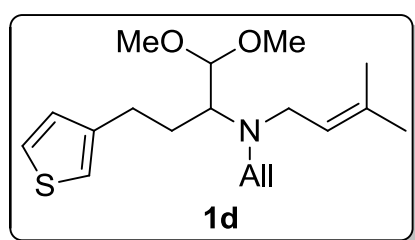
Light yellow oil; $R_f = 0.59$ (hexane: ethyl acetate = 5:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.18-7.06 (m, 4H), 5.89-5.79 (m, 1H), 5.23-5.06 (m, 3H), 4.31 (d, $J = 5.50$ Hz, 1H), 3.38 (s, 3H), 3.37 (s, 3H), 3.34-3.29 (m, 1H), 3.22-3.13 (m, 3H), 2.91-2.79 (m, 2H), 2.61-2.53 (m, 1H), 2.33 (s, 3H), 1.76-1.59 (m, 8H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 141.4, 138.4, 135.9, 133.6, 130.0, 128.8, 125.8, 125.6, 123.8, 115.8, 107.1, 59.2, 54.6, 54.5, 53.4, 48.0, 31.1, 27.5, 25.9, 19.3, 18.0 ppm; **HRMS (ESI, m/z):** calcd for $\text{C}_{21}\text{H}_{34}\text{NO}_2^+ [\text{M}+\text{H}]^+$ 332.2590, found: 332.2586.

***N*-allyl-*N*-(1,1-dimethoxy-4-(4-methoxyphenyl)butan-2-yl)-3-methylbut-2-en-1-amine (1c):**



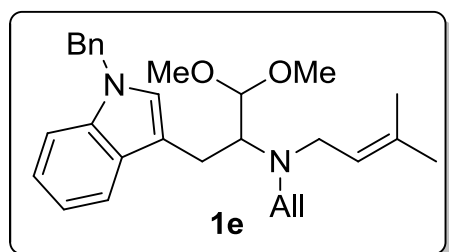
Light yellow oil; $R_f = 0.51$ (hexane: ethyl acetate = 5:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.12 (d, $J = 8.40$ Hz, 2H), 6.81 (d, $J = 8.45$ Hz, 2H), 5.86-5.76 (m, 1H), 5.18-5.03 (m, 3H), 4.27 (d, $J = 5.39$ Hz, 1H), 3.77 (s, 3H), 3.34 (s, 3H), 3.33 (s, 3H), 3.32-3.27 (m, 1H), 3.19-3.09 (m, 3H), 2.83-2.71 (m, 2H), 2.59-2.51 (m, 1H), 1.79-1.62 (m, 8H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 157.5, 138.4, 135.2, 133.4, 129.4 (CH x 2), 123.9, 115.6, 113.6 (CH x 2), 107.1, 58.6, 55.2, 54.6, 54.4, 53.4, 48.1, 32.3, 28.9, 25.9, 17.9 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{21}\text{H}_{34}\text{NO}_3^+ [\text{M}+\text{H}]^+$ 348.2539, found: 348.2537.

***N*-allyl-*N*-(1,1-dimethoxy-4-(thiophen-3-yl)butan-2-yl)-3-methylbut-2-en-1-amine (1d):**



Light yellow oil; $R_f = 0.59$ (hexane: ethyl acetate = 5:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.23-7.21 (m, 1H), 6.97-6.95 (m, 2H), 5.85-5.75 (m, 1H), 5.17-5.04 (m, 3H), 4.30 (d, $J = 5.31$ Hz, 1H), 3.36 (s, 3H), 3.35 (s, 3H), 3.34-3.29 (m, 1H), 3.20-3.09 (m, 3H), 2.86-2.79 (m, 2H), 2.70-2.62 (m, 1H), 1.85-1.67 (m, 5H), 1.63 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 143.4, 138.4, 133.5, 128.4, 124.8, 123.8, 123.8, 119.8, 115.6, 106.9, 58.5, 54.7, 54.3, 53.3, 48.0, 27.6, 27.5, 25.9, 17.9 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{18}\text{H}_{30}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$ 324.1997, found: 324.1992.

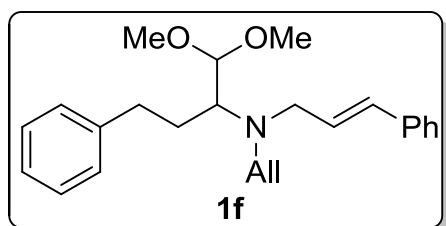
***N*-allyl-*N*-(3-(1-benzyl-1*H*-indol-3-yl)-1,1-dimethoxypropan-2-yl)-3-methylbut-2-en-1-amine (1e):**



Light yellow oil; $R_f = 0.44$ (hexane: ethyl acetate = 5:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.62 (d, $J = 7.71$ Hz, 1H), 7.28-7.20 (m, 4H), 7.15-7.05 (m, 4H), 6.99 (m, 1H), 5.71-5.61 (m, 1H), 5.26 (s, 2H), 5.02-4.90 (m, 3H), 4.33 (d, $J = 5.39$ Hz, 1H), 3.38 (s, 6H), 3.29-3.13 (m, 5H), 3.00-2.85 (m, 2H), 1.56 (s, 3H), 1.47 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz)

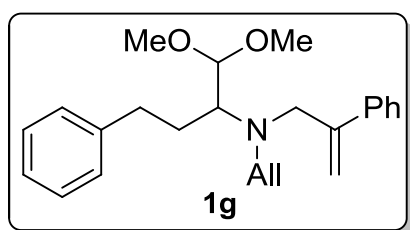
δ 138.5, 138.0, 136.4, 133.2, 128.60 (CH x 2), 128.57, 127.4, 126.8, 126.7 (CH x 2), 123.9, 121.3, 119.3, 118.6, 115.5, 114.0, 109.3, 107.2, 59.8, 54.9, 54.6, 53.6, 49.7, 48.2, 25.7, 22.0, 17.8 ppm; **HRMS (ESI, m/z)**: calcd for $C_{28}H_{37}N_2O_2^+$ $[M+H]^+$ 433.2855, found: 433.2856.

***N*-allyl-*N*-cinnamyl-1,1-dimethoxy-4-phenylbutan-2-amine (1f):**



Light yellow oil; R_f = 0.64 (hexane: ethyl acetate = 5:1); **1H NMR ($CDCl_3$, 400 MHz)** δ 7.36-7.19 (m, 9H), 7.17-7.13 (m, 1H), 6.46 (d, J = 15.89 Hz, 1H), 6.21-6.13 (m, 1H), 5.88-5.78 (m, 1H), 5.17 (d, J = 17.17 Hz, 1H), 5.07 (d, J = 10.16 Hz, 1H), 4.31 (d, J = 5.33 Hz, 1H), 3.48-3.31 (m, 9H), 3.23-3.18 (m, 1H), 2.90-2.82 (m, 2H), 2.67-2.59 (m, 1H), 1.87-1.69 (m, 2H) ppm; **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 143.0, 138.0, 137.4, 131.2, 129.9, 128.54 (CH x 2), 128.47 (CH x 2), 128.2 (CH x 2), 127.1, 126.2 (CH x 2), 125.5, 116.1, 107.1, 59.0, 54.8, 54.6, 53.6, 53.0, 33.3, 28.8 ppm; **HRMS (ESI, m/z)**: calcd for $C_{24}H_{32}NO_2^+$ $[M+H]^+$ 366.2433, found: 366.2431.

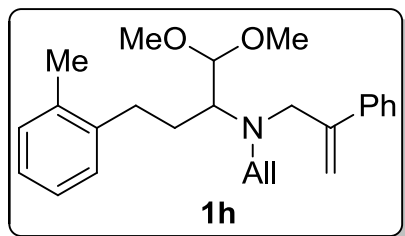
***N*-allyl-1,1-dimethoxy-4-phenyl-*N*-(2-phenylallyl)butan-2-amine (1g):**



Light yellow oil; R_f = 0.60 (hexane: ethyl acetate = 5:1); **1H NMR ($CDCl_3$, 400 MHz)** δ 7.43 (d, J = 7.83 Hz, 2H), 7.32-7.12 (m, 6H), 7.07 (d, J = 7.61 Hz, 2H), 5.82-5.72 (m, 1H), 5.35 (d, J = 29.55 Hz, 2H), 5.13 (d, J = 17.16 Hz, 1H), 5.06 (d, J = 9.83 Hz, 1H), 4.26 (d, J = 5.00 Hz, 1H), 3.67 (AB_q, J = 14.52 Hz, 2H), 3.36-3.30 (m, 7H), 3.20-3.14 (m, 1H), 2.88-2.84 (m, 1H), 2.58-2.50 (m, 1H), 2.31-2.23 (m, 1H), 1.80-1.60 (m, 2H) ppm; **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 146.9, 143.2, 140.6, 137.9, 128.4 (CH x 2), 128.1 (CH x 2), 128.0 (CH x 2), 127.3, 126.8 (CH x 2), 125.4, 116.5, 114.8, 107.3, 58.7, 54.97, 54.94, 54.7,

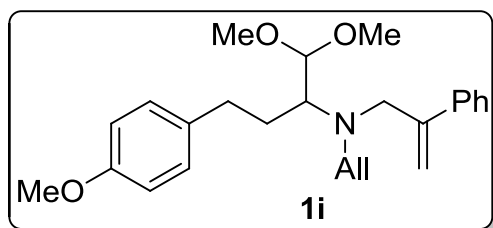
53.4, 33.1, 28.4 ppm; **HRMS (ESI, m/z)**: calcd for $C_{24}H_{32}NO_2^+ [M+H]^+$ 366.2433, found: 366.2432.

***N*-allyl-1,1-dimethoxy-*N*-(2-phenylallyl)-4-(*o*-tolyl)butan-2-amine (1h):**



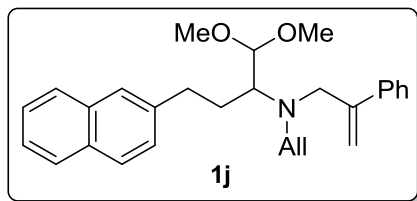
Light yellow oil; $R_f = 0.71$ (hexane: ethyl acetate = 5:1); **1H NMR ($CDCl_3$, 400 MHz)** δ 7.43 (d, $J = 7.51$ Hz, 2H), 7.30-7.20 (m, 3H), 7.08-7.01 (m, 4H), 5.86-5.76 (m, 1H), 5.37 (d, $J = 30.08$ Hz, 2H), 5.16 (d, $J = 17.17$ Hz, 1H), 5.09 (d, $J = 10.10$ Hz, 1H), 4.27 (d, $J = 5.15$ Hz, 1H), 3.69 (AB_q, $J = 14.50$ Hz, 2H), 3.38-3.30 (m, 7H), 3.19-3.13 (m, 1H), 2.94-2.89 (m, 1H), 2.54-2.46 (m, 1H), 2.26-2.17 (m, 1H), 2.15 (s, 3H), 1.72-1.53 (m, 2H) ppm; **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 146.8, 141.4, 140.5, 137.8, 135.8, 129.9, 128.5, 127.9 (CH x 2), 127.3, 126.7 (CH x 2), 125.7, 125.5, 116.5, 114.9, 107.1, 58.9, 55.0, 54.9, 54.7, 53.2, 30.7, 27.3, 19.2 ppm; **HRMS (ESI, m/z)**: calcd for $C_{25}H_{34}NO_2^+ [M+H]^+$ 380.2590, found: 380.2583.

***N*-allyl-1,1-dimethoxy-4-(4-methoxyphenyl)-*N*-(2-phenylallyl)butan-2-amine (1i):**



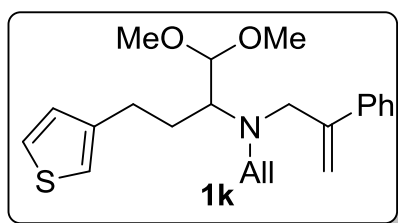
Light yellow oil; $R_f = 0.62$ (hexane: ethyl acetate = 5:1); **1H NMR ($CDCl_3$, 400 MHz)** δ 7.42 (d, $J = 7.25$ Hz, 2H), 7.32-7.22 (m, 3H), 6.98 (d, $J = 8.48$ Hz, 2H), 6.77 (d, $J = 8.47$ Hz, 2H), 5.82-5.71 (m, 1H), 5.35 (d, $J = 27.84$ Hz, 2H), 5.12 (d, $J = 17.00$ Hz, 1H), 5.06 (d, $J = 10.10$ Hz, 1H), 4.25 (d, $J = 5.04$ Hz, 1H), 3.75 (s, 3H), 3.66 (AB_q, $J = 14.56$ Hz, 2H), 3.35-3.31 (m, 7H), 3.20-3.15 (m, 1H), 2.87-2.82 (m, 1H), 2.52-2.45 (m, 1H), 2.27-2.19 (m, 1H), 1.77-1.57 (m, 2H) ppm; **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 157.5, 146.9, 140.6, 137.9, 135.2, 129.2 (CH x 2), 127.9 (CH x 2), 127.3, 126.7 (CH x 2), 116.4, 114.8, 113.5 (CH x 2), 107.3, 58.6, 55.2, 54.9 (CH₂ x 1), 54.9 (CH₃ x 1), 54.7, 53.4, 32.2, 28.6 ppm; **HRMS (ESI, m/z)**: calcd for $C_{25}H_{34}NO_3^+ [M+H]^+$ 396.2539, found: 396.2541.

***N*-allyl-1,1-dimethoxy-4-(naphthalen-2-yl)-*N*-(2-phenylallyl)butan-2-amine (1j):**



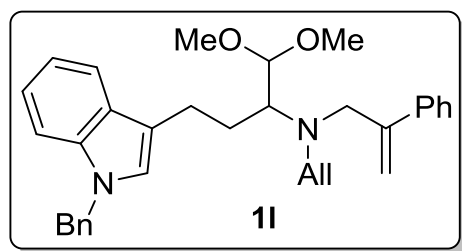
Light yellow oil; R_f = 0.60 (hexane: ethyl acetate = 10:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.80 – 7.71 (m, 3H), 7.51 (s, 1H), 7.48-7.37 (m, 4H), 7.36-7.27 (m, 3H), 7.26-7.20 (m, 1H), 5.90 – 5.71 (m, 1H), 5.41-5.33 (m, 2H), 5.18-5.06 (m, 2H), 4.31 (dd, J = 5.0, 1.8 Hz, 1H), 3.93 – 3.52 (m, 2H), 3.46 – 3.31 (m, 7H), 3.26 – 3.11 (m, 1H), 2.96-2.90 (m, 1H), 2.74-2.66 (m, 1H), 2.55 – 2.36 (m, 1H), 1.96 – 1.68 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 146.97, 140.76, 140.69, 138.00, 133.68, 131.92, 128.13, 127.95, 127.67, 127.49, 127.45, 126.90, 126.21, 125.81, 124.98, 116.71, 115.10, 107.23, 58.66, 55.18, 55.00, 54.85, 53.56, 33.30, 28.25 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 416.2590, found: 416.2586.

***N*-allyl-1,1-dimethoxy-*N*-(2-phenylallyl)-4-(thiophen-3-yl)butan-2-amine (1k):**



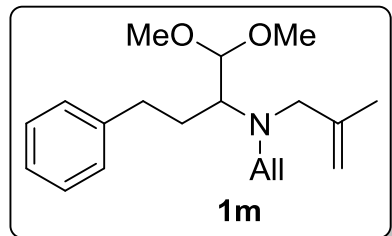
Light yellow oil; R_f = 0.70 (hexane: ethyl acetate = 5:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.40 (d, J = 7.13 Hz, 2H), 7.31-7.24 (m, 3H), 7.18-7.16 (m, 1H), 6.82-6.80 (m, 2H), 5.79-5.69 (m, 1H), 5.33 (d, J = 33.03 Hz, 2H), 5.12 (d, J = 17.18 Hz, 1H), 5.05 (d, J = 10.11 Hz, 1H), 4.26 (d, J = 4.94 Hz, 1H), 3.65 (AB_q, J = 14.49 Hz, 2H), 3.34-3.30 (m, 7H), 3.18-3.13 (m, 1H), 2.87-2.82 (m, 1H), 2.56-2.48 (m, 1H), 2.32-2.24 (m, 1H), 1.81-1.62 (m, 2H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 146.9, 143.3, 140.6, 137.8, 128.3, 127.9 (CH x 2), 127.3, 126.7 (CH x 2), 124.7, 119.5, 116.4, 114.8, 107.1, 58.4, 55.0, 54.9, 54.6, 53.4, 27.4, 27.2 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{22}\text{H}_{30}\text{NO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$ 372.1997, found: 372.1998.

***N*-allyl-4-(1-benzyl-1*H*-indol-3-yl)-1,1-dimethoxy-*N*-(2-phenylallyl)butan-2-amine (1l):**



Light yellow oil; R_f = 0.60 (hexane: ethyl acetate = 5:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.48 (d, J = 7.80 Hz, 1H), 7.44-7.41 (m, 2H), 7.30-7.04 (m, 11H), 6.79 (s, 1H), 5.83-5.73 (m, 1H), 5.34 (d, J = 26.11 Hz, 2H), 5.20 (s, 2H), 5.11 (d, J = 17.28 Hz, 1H), 5.03 (d, J = 10.28 Hz, 1H), 4.28 (d, J = 5.01 Hz, 1H), 3.68 (AB_q, J = 14.51 Hz, 2H), 3.38-3.33 (m, 4H), 3.31 (s, 3H), 3.20-3.15 (m, 1H), 2.98-2.93 (m, 1H), 2.73-2.66 (m, 1H), 2.46-2.35 (m, 1H), 1.90-1.73 (m, 2H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 146.9, 140.6, 138.0, 137.9, 136.6, 128.6 (CH x 2), 128.3, 128.0 (CH x 2), 127.4, 127.3, 126.8 (CH x 2), 126.7 (CH x 2), 125.1, 121.4, 119.3, 118.5, 116.5, 116.4, 114.8, 109.3, 107.3, 58.7, 54.98, 54.94, 54.6, 53.4, 49.7, 26.8, 22.4 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{33}\text{H}_{39}\text{N}_2\text{O}_2^+$ $[\text{M}+\text{H}]^+$ 495.3012, found: 495.3008.

***N*-allyl-1,1-dimethoxy-*N*-(2-methylallyl)-4-phenylbutan-2-amine (1m):**



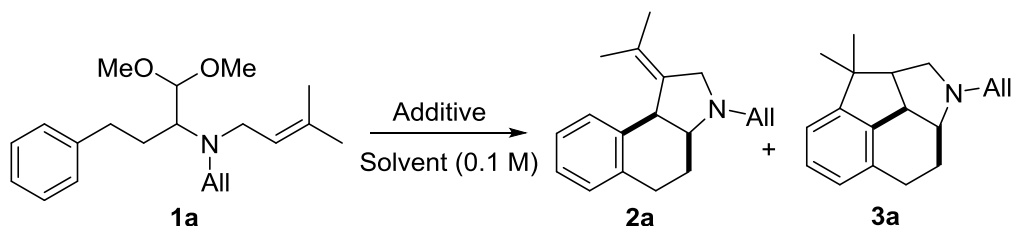
Light yellow oil; R_f = 0.75 (hexane: ethyl acetate = 5:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.27-7.13 (m, 5H), 5.84-5.74 (m, 1H), 5.12 (d, J = 17.19 Hz, 1H), 5.04 (d, J = 10.10 Hz, 1H), 4.86 (d, J = 30.56 Hz, 2H), 4.28 (d, J = 5.02 Hz, 1H), 3.35 (s, 6H), 3.27-3.03 (m, 4H), 2.90-2.82 (m, 2H), 2.62-2.55 (m, 1H), 1.85-1.64 (m, 5H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 144.6, 143.1, 138.1, 128.4 (CH x 2), 128.2 (CH x 2), 125.5, 116.1, 112.3, 107.0, 58.6, 56.8, 54.74, 54.65, 53.6, 33.5, 28.7, 20.6 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{19}\text{H}_{30}\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 304.2277, found: 304.2276.

3. Optimization Study for the Construction of Aza-Polycyclic Frameworks via Friedel-Crafts/Prins-type Cyclization Reaction

An optimization study was performed using the α -amino acetal **1a** as the model substrate to examine various reaction conditions. The reaction of the α -amino acetal **1a** without any

additive at 20 °C in dichloromethane did not afford any desired products after a 24 hour reaction time (Table S1, entry 1). This confirmed that the reaction could not proceed in the absence of Lewis or Brønsted acids. Various Lewis acids (AlCl_3 , FeCl_3 , and $\text{BF}_3\cdot\text{OEt}_2$) and Brønsted acids such as trifluoroacetic acid (TFA) and trifluoromethanesulfonic acid (TfOH) were then tested for this reaction. It was observed that TfOH was the most efficient additive, affording the desired product **2a** in 93% yield (Table S1, entries 2-6). After solvent screening (Table S1, entries 6-8), dichloromethane (DCM) was found to be the suitable solvent, furnishing the desired product **2a** in 93% yield at 20 °C. Under similar conditions, the use of acetonitrile did not afford any desired product, while nitromethane gave the product in a lower yield (80%). Gratifyingly, the different products **2a** or **3a** could be obtained in excellent or good yield by adjusting the stoichiometry of TfOH (Table S1). When 1.0 equivalent of TfOH was used, the yield of **2a** was significantly decreased (Table S1, entry 9). It was ascertained that when the amount of TfOH was increased to 4.0 and even 6.0 equivalents, the yield of **3a** could be increased to 81% (Table S1, entries 10-11).

Table S1. Optimization study on Friedel-Crafts/Prins-type cyclization reaction^a



entry	additive (equiv.)	solvent	T (°C)	t (h)	yield (%) ^b	
					2a	3a
1	—	DCM	20	24	0	0
2	AlCl_3 (2.0)	DCM	20	24	0	0
3	FeCl_3 (2.0)	DCM	20	24	trace	0
4	$\text{BF}_3\cdot\text{OEt}_2$ (2.0)	DCM	20	24	0	0
5	TFA (2.0)	DCM	20	24	0	0
6	TfOH (2.0)	DCM	20	12	93	trace
7	TfOH (2.0)	MeNO_2	20	12	80	0
8	TfOH (2.0)	MeCN	20	12	trace	0
9	TfOH (1.0)	DCM	20	24	trace	0
10	TfOH (4.0)	DCM	40	24	61	32
11	TfOH (6.0)	DCM	20	24	11	81

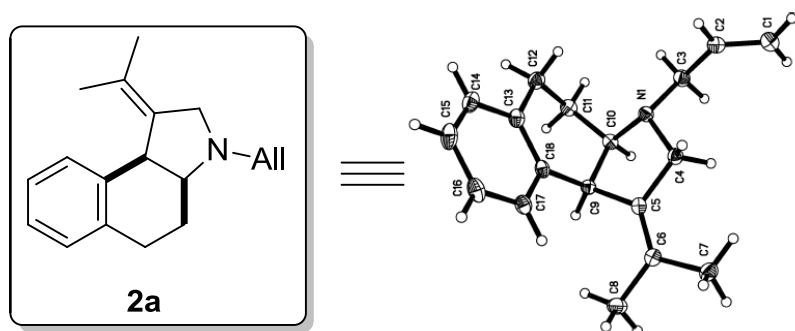
^aUnless otherwise noted, the reactions were carried out using α -amino acetal **1a** (0.1 mmol, 1.0 equiv.), additive (2.0 equiv.), solvent (1.0 mL). ^bIsolated yields based on α -amino acetal **1a**. All = allyl.

In a word, after our initial optimization studies, trifluoromethanesulfonic acid (TfOH) was identified as the optimal mediator for intramolecular Friedel-Crafts/Prins-type cyclization reaction of α -amino acetals at 20 °C in DCM, with the use of 2.0 equivalents for the selective formation of product **2a** in 93% yield and 6.0 equivalents for the formation of product **3a** in 81% yield.

4. General Experimental Procedure for the Construction of Aza-Polycyclic Frameworks with *endo* or *exo*-Cyclic Double Bond and Spectroscopic Information

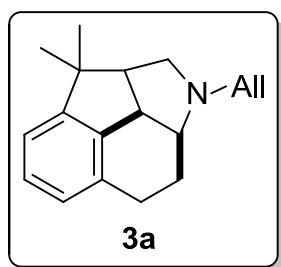
Typical procedure for intramolecular Friedel-Crafts/Prins-type cyclization reaction of α -amino acetals (*N*-allyl-*N*-(1,1-dimethoxy-4-phenylbutan-2-yl)-3-methylbut-2-en-1-amine **1a** as a model substrate): Trifluoromethanesulfonic acid (30 mg, 0.2 mmol, 2.0 equiv.) was added to α -amino acetal **1a** (31.7 mg, 0.1 mmol, 1.0 equiv.) in dry dichloromethane (1.0 ml) at 20 °C and was stirred at 20 °C for the specified time. The reaction mixture was quenched with saturated aqueous sodium bicarbonate (NaHCO₃). The aqueous layer was extracted with dichloromethane (2.0 ml \times 3) and the combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude oil was redissolved in a minimum amount of dichloromethane and was purified by flash column chromatography (silica gel; triethylamine/ethyl acetate/hexane = 0.1:1:10) to afford the desired product **2a** as the light yellow oil (23.6 mg, 93%). Then the product **2a** was dissolved in dichloromethane, hexane was added into it and solvent was evaporated to obtain the crystal (CCDC 965133).

3-allyl-1-(propan-2-ylidene)-2,3,3a,4,5,9b-hexahydro-1*H*-benzo[*e*]indole (2a**):**



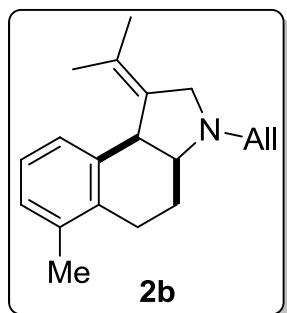
R_f = 0.60 (hexane: ethyl acetate = 3:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.20-7.09 (m, 4H), 5.94-5.84 (m, 1H), 5.18 (d, J = 17.19 Hz, 1H), 5.06 (d, J = 10.12 Hz, 1H), 3.68 (d, J = 5.75 Hz, 1H), 3.64 (d, J = 13.94 Hz, 1H), 3.48 (dd, J = 13.58, 5.17 Hz, 1H), 2.98-2.77 (m, 4H), 2.60-2.53 (m, 1H), 2.06-1.97 (m, 1H), 1.87 (s, 3H), 1.75-1.67 (m, 4H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 138.2, 137.7, 135.9, 133.4, 127.84, 127.77, 125.9, 125.6, 123.7, 116.5, 62.6, 56.7, 56.4, 44.8, 26.2, 25.3, 22.4, 20.6 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{18}\text{H}_{24}\text{N}^+$ $[\text{M}+\text{H}]^+$ 254.1909, found: 254.1909.

1-allyl-3,3-dimethyl-1,2,2a,2a¹,3,7,8,8a-octahydroindeno[2,1,7-*cde*]indole (3a):



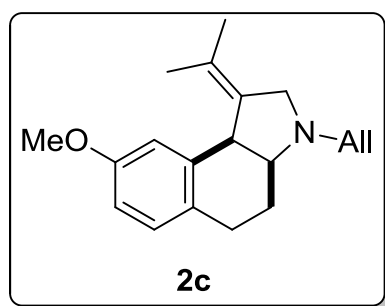
This compound was prepared by the general procedure described above except that trifluoromethanesulfonic acid (6.0 equiv.) was used in the reaction and was obtained as light yellow oil in 81% yield: R_f = 0.36 (hexane: ethyl acetate: triethylamine = 3:1:0.1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.16-7.12 (m, 1H), 6.95 (d, J = 7.43 Hz, 2H), 5.88-5.78 (m, 1H), 5.12 (d, J = 17.13 Hz, 1H), 5.04 (d, J = 10.14 Hz, 1H), 3.52-3.48 (m, 1H), 3.38-3.32 (m, 1H), 3.22-3.17 (m, 1H), 2.94-2.89 (m, 1H), 2.74-2.68 (m, 1H), 2.60-2.45 (m, 4H), 2.15-2.08 (m, 1H), 1.34 (s, 3H), 1.26 (s, 3H), 1.14-1.05 (m, 1H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 150.1, 141.8, 138.2, 136.6, 127.1, 123.1, 119.6, 116.3, 61.4, 55.8, 55.4, 53.6, 46.33, 46.27, 31.6, 27.9, 27.4, 23.5 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{18}\text{H}_{24}\text{N}^+$ $[\text{M}+\text{H}]^+$ 254.1909, found: 254.1912.

3-allyl-6-methyl-1-(propan-2-ylidene)-2,3,3a,4,5,9b-hexahydro-1*H*-benzo[*e*]indole (2b):



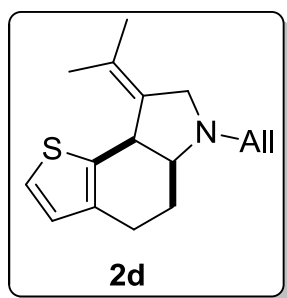
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 82% yield: R_f = 0.63 (hexane: ethyl acetate = 3:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.10-6.98 (m, 3H), 5.96-5.86 (m, 1H), 5.19 (d, J = 17.14 Hz, 1H), 5.07 (d, J = 10.14 Hz, 1H), 3.72 (d, J = 5.26 Hz, 1H), 3.61 (d, J = 13.74 Hz, 1H), 3.49 (dd, J = 13.59, 5.15 Hz, 1H), 3.95-3.92 (m, 2H), 2.86-2.74 (m, 2H), 2.53-2.47 (m, 1H), 2.27 (s, 3H), 2.00-1.81 (m, 4H), 1.68 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 137.6, 136.1, 136.0, 135.1, 134.2, 127.3, 125.9, 125.2, 123.2, 116.5, 62.2, 56.7, 56.5, 45.1, 24.3, 22.4, 22.2, 20.6, 19.8 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{19}\text{H}_{26}\text{N}^+$ $[\text{M}+\text{H}]^+$ 268.2056, found: 268.2064.

3-allyl-8-methoxy-1-(propan-2-ylidene)-2,3,3a,4,5,9b-hexahydro-1H-benzo[*e*]indole (2c):



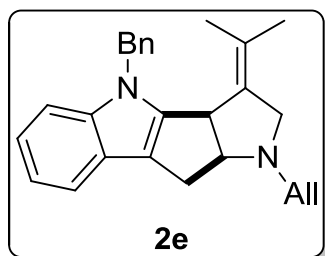
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 79% yield: R_f = 0.46 (hexane: ethyl acetate = 3:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.01 (d, J = 8.23 Hz, 1H), 6.77 (d, J = 2.44 Hz, 1H), 6.66 (dd, J = 8.22, 2.65 Hz, 1H), 5.94-5.84 (m, 1H), 5.18 (d, J = 18.01 Hz, 1H), 5.06 (d, J = 10.09 Hz, 1H), 3.76 (s, 3H), 3.64 (d, J = 6.97 Hz, 2H), 3.47 (dd, J = 13.58, 5.17 Hz, 1H), 3.65-3.63 (m, 2H), 3.49-3.44 (m, 1H), 2.96-2.90 (m, 2H), 2.83-2.76 (m, 2H), 2.54-2.47 (m, 1H), 2.04-1.96 (m, 1H), 1.87 (s, 3H), 1.71-1.63 (m, 4H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 157.9, 138.9, 135.8, 133.4, 130.5, 128.5, 123.8, 116.6, 113.8, 110.7, 62.6, 56.7, 56.5, 55.1, 45.0, 25.6, 25.4, 22.4, 20.6 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{19}\text{H}_{25}\text{NO}^+$ $[\text{M}+\text{H}]^+$ 284.2014, found: 284.2022.

6-allyl-8-(propan-2-ylidene)-5,5a,6,7,8,8a-hexahydro-4H-thieno[2,3-*e*]indole (2d):



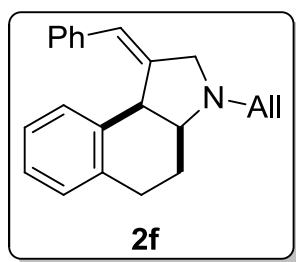
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 57% yield: R_f = 0.71 (hexane: ethyl acetate = 3:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.03 (d, J = 5.10 Hz, 1H), 6.71 (d, J = 5.12 Hz, 1H), 5.97-5.87 (m, 1H), 5.23-5.07 (m, 2H), 3.90 (s, 1H), 3.70-3.51 (m, 2H), 2.95-2.80 (m, 3H), 2.75-2.66 (m, 1H), 2.55-2.50 (m, 1H), 2.16-2.10 (m, 1H), 1.94 (s, 3H), 1.78-1.69 (m, 1H), 1.94 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 138.9, 135.9, 134.80, 134.76, 127.1, 123.0, 121.9, 116.6, 62.7, 56.9, 56.2, 43.1, 23.4, 22.5, 20.58, 20.56 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{16}\text{H}_{22}\text{NS}^+$ $[\text{M}+\text{H}]^+$ 260.1473, found: 260.1476.

1-allyl-4-benzyl-3-(propan-2-ylidene)-2,3,3a,4,9,9a-hexahydro-1H-pyrrolo[2',3':4,5]-cyclopenta[1,2-*b*]indole (2e):



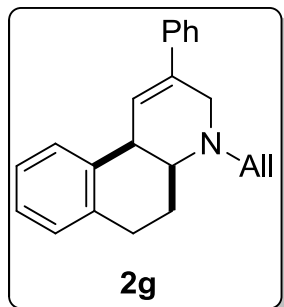
This compound was prepared by the general procedure described above except that the reaction was performed at 0 °C and was obtained as light yellow oil in 80% yield: R_f = 0.56 (hexane: ethyl acetate: triethylamine = 3:1:0.1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.47 (d, J = 7.79 Hz, 1H), 7.25-7.16 (m, 3H), 7.08-7.00 (m, 3H), 6.92 (d, J = 7.11 Hz, 2H), 6.00-5.90 (m, 1H), 5.31 (AB_q, J = 17.25 Hz, 2H), 5.21 (d, J = 17.12 Hz, 1H), 5.12 (d, J = 10.11 Hz, 1H), 4.34 (d, J = 5.47 Hz, 1H), 3.98-3.95 (m, 1H), 3.51-3.45 (m, 2H), 3.20-3.09 (m, 2H), 2.96 (s, 2H), 1.70 (s, 3H), 1.44 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 144.7, 141.3, 138.4, 135.9, 131.4, 128.4 (CH x 2), 126.8, 125.4 (CH x 2), 124.7 (C x 2), 120.5, 119.3, 118.8, 117.7, 117.1, 110.0, 73.8, 57.7, 55.9, 47.4, 47.0, 29.8, 22.4, 20.8 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{26}\text{H}_{29}\text{N}_2^+$ $[\text{M}+\text{H}]^+$ 369.2311, found: 369.2325.

3-allyl-1-benzylidene-2,3,3a,4,5,9b-hexahydro-1H-benzo[*e*]indole (2f):



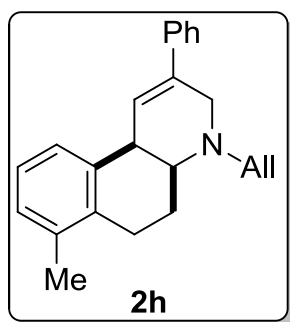
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 31% yield: R_f = 0.54 (hexane: ethyl acetate = 3:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.37 (d, J = 7.46 Hz, 1H), 7.32-7.29 (m, 2H), 7.23-7.12 (m, 6H), 7.32 (s, 1H), 6.01-5.91 (m, 1H), 5.27 (d, J = 17.14 Hz, 1H), 5.14 (d, J = 10.17 Hz, 1H), 3.96 (d, J = 6.30 Hz, 1H), 3.84-3.80 (m, 1H), 3.58-3.54 (m, 1H), 3.50-3.46 (m, 1H), 3.27-3.23 (m, 1H), 3.20-3.15 (m, 1H), 2.96-2.88 (m, 1H), 2.65-2.58 (m, 1H), 1.85-1.74 (m, 2H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 144.3, 137.7, 137.2, 135.9 (CH x 1 and C x 1), 129.7, 128.7, 128.3 (CH x 2), 128.2 (CH x 2), 126.3, 126.0, 125.7, 122.8, 116.8, 60.3, 55.8, 55.7, 48.8, 26.3, 22.8 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{22}\text{H}_{24}\text{N}^+$ $[\text{M}+\text{H}]^+$ 302.1909, found: 302.1916.

4-allyl-2-phenyl-3,4,4a,5,6,10b-hexahydrobenzo[f]quinoline (2g):



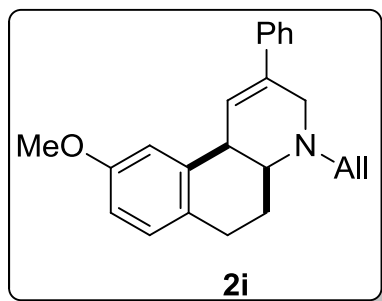
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 89% yield: R_f = 0.46 (hexane: ethyl acetate = 3:1); ^1H NMR (CDCl_3 , 400 MHz) δ 7.34-7.26 (m, 5H), 7.23-7.19 (m, 2H), 7.15-7.07 (m, 2H), 6.08 (s, 1H), 6.03-5.93 (m, 1H), 5.29 (d, J = 17.12 Hz, 1H), 5.18 (d, J = 10.09 Hz, 1H), 3.85 (s, 1H), 3.60-3.29 (m, 5H), 2.91-2.76 (m, 2H), 1.92-1.89 (m, 1H), 1.83-1.72 (m, 1H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 139.7, 139.1, 136.7, 136.1, 133.2, 129.3, 128.6, 128.3 (CH x 2), 127.4, 127.1, 126.3, 126.0, 125.1 (CH x 2), 117.6, 57.7, 55.4, 48.5, 40.0, 29.1, 17.6 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{22}\text{H}_{24}\text{N}^+$ $[\text{M}+\text{H}]^+$ 302.1909, found: 302.1905.

4-allyl-7-methyl-2-phenyl-3,4,4a,5,6,10b-hexahydrobenzo[f]quinoline (2h):



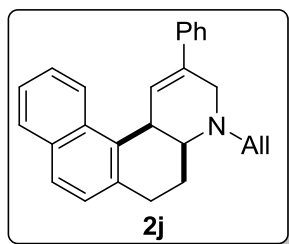
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 87% yield: R_f = 0.47 (hexane: ethyl acetate = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.35-7.33 (m, 2H), 7.29-7.25 (m, 2H), 7.23-7.12 (m, 3H), 7.02 (d, J = 7.07 Hz, 1H), 6.11 (s, 1H), 6.04-5.94 (m, 1H), 5.29 (d, J = 17.12 Hz, 1H), 5.18 (d, J = 10.11 Hz, 1H), 3.83 (s, 1H), 3.61-3.57 (m, 1H), 3.46-3.35 (m, 3H), 3.32-3.27 (m, 1H), 2.88-2.82 (m, 1H), 2.60-2.51 (m, 1H), 2.22 (s, 3H), 1.98-1.94 (m, 1H), 1.83-1.73 (m, 1H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 139.6, 139.1, 136.2, 136.0, 135.2, 133.1, 128.3 (CH x 2), 127.6, 127.5, 127.2, 127.1, 126.1, 125.1 (CH x 2), 117.6, 57.7, 54.9, 48.5, 40.2, 26.4, 19.7, 17.5 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{23}\text{H}_{26}\text{N}^+$ $[\text{M}+\text{H}]^+$ 316.2065, found: 316.2061.

4-allyl-9-methoxy-2-phenyl-3,4,4a,5,6,10b-hexahydrobenzo[f]quinoline (2i):



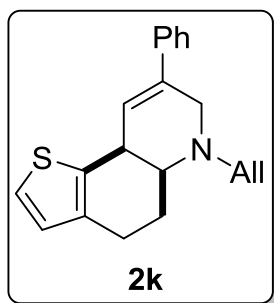
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 84% yield: R_f = 0.37 (hexane: ethyl acetate = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.35-7.19 (m, 5H), 6.99 (d, J = 8.41 Hz, 1H), 6.83 (d, J = 2.59 Hz, 1H), 6.71 (dd, J = 8.40, 2.66 Hz, 1H), 6.08 (s, 1H), 6.03-5.93 (m, 1H), 5.28 (d, J = 17.11 Hz, 1H), 5.18 (d, J = 10.11 Hz, 1H), 3.81 (s, 4H), 3.60-3.55 (m, 1H), 3.45-3.34 (m, 3H), 3.32-3.27 (m, 1H), 2.85-2.68 (m, 2H), 1.91-1.86 (m, 1H), 1.80-1.70 (m, 1H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 158.1, 140.3, 139.6, 136.0, 133.4, 129.5, 128.8, 128.3 (CH x 2), 127.2, 127.1, 125.1 (CH x 2), 117.6, 113.9, 112.3, 57.7, 55.4, 55.3, 48.5, 40.3, 28.3, 17.9 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{23}\text{H}_{26}\text{NO}^+$ $[\text{M}+\text{H}]^+$ 332.2014, found: 332.2018.

4-allyl-2-phenyl-3,4,4a,5,6,12c-hexahydronaphtho[1,2-f]quinoline (2j):



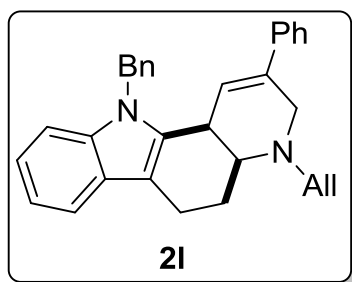
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 71% yield: R_f = 0.3 (hexane: ethyl acetate: triethylamine = 10:1:0.1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 8.13 (d, J = 8.5 Hz, 1H), 7.83 (dd, J = 8.1, 1.8 Hz, 1H), 7.65 (dd, J = 8.5, 1.7 Hz, 1H), 7.56-7.51 (m, 1H), 7.48-7.43 (m, 1H), 7.34 – 7.28 (m, 2H), 7.26 – 7.16 (m, 4H), 6.23 (t, J = 2.2 Hz, 1H), 6.09 – 5.93 (m, 1H), 5.36-5.30 (m, 1H), 5.23-5.19 (m, 1H), 4.52 (s, 1H), 3.77-3.71 (m, 1H), 3.57 – 3.35 (m, 4H), 3.15 – 2.93 (m, 2H), 2.05 – 1.81 (m, 2H).; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 139.61, 136.10, 133.96, 133.84, 133.04, 132.84, 131.77, 129.01, 128.40, 127.69, 127.34, 126.86, 126.39, 125.96, 125.32, 124.99, 123.36, 117.96, 58.09, 55.60, 49.16, 36.99, 30.17, 16.60 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{23}\text{H}_{26}\text{N}^+$ $[\text{M}+\text{H}]^+$ 352.2065, found: 352.2061.

6-allyl-8-phenyl-4,5,5a,6,7,9a-hexahydrothieno[2,3-*f*]quinoline (2k):



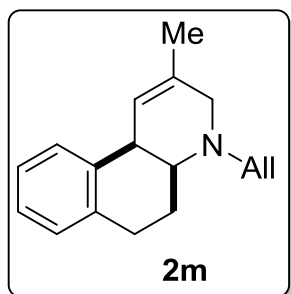
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 85% yield: R_f = 0.50 (hexane: ethyl acetate = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.35-7.21 (m, 5H), 6.92 (dd, J = 159.19, 5.07 Hz, 2H), 6.10 (s, 1H), 6.02-5.92 (m, 1H), 5.28 (d, J = 17.09 Hz, 1H), 5.18 (d, J = 10.08 Hz, 1H), 3.91 (s, 1H), 3.56-3.32 (m, 5H), 2.81-2.75 (m, 1H), 2.63-2.55 (m, 1H), 1.94-1.77 (m, 2H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 139.5, 137.9, 135.8, 135.4, 133.2, 128.3 (CH x 2), 127.3, 127.0, 126.0, 125.1 (CH x 2), 123.1, 117.7, 57.7, 55.9, 48.5, 36.5, 24.6, 18.6 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{20}\text{H}_{22}\text{NS}^+$ $[\text{M}+\text{H}]^+$ 308.1473, found: 308.1473.

4-allyl-11-benzyl-2-phenyl-4,4a,5,6,11,11b-hexahydro-3*H*-pyrido[3,2-*a*]carbazole (2l):



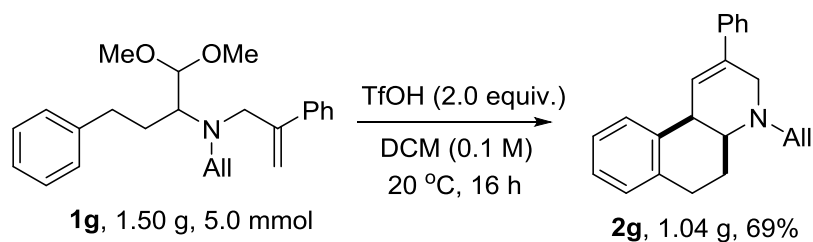
This compound was prepared by the general procedure described above except that the reaction was performed at 0 °C and was obtained as light yellow oil in 70% yield: R_f = 0.50 (hexane: ethyl acetate: triethylamine = 3:1:0.1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.51 (d, J = 6.94 Hz, 1H), 7.30-7.07 (m, 11H), 7.00 (d, J = 6.50 Hz, 2H), 6.01-5.91 (m, 1H), 5.88 (s, 1H), 5.42 (AB_q, J = 17.21 Hz, 2H), 5.27 (d, J = 17.08 Hz, 1H), 5.17 (d, J = 10.11 Hz, 1H), 3.91 (s, 1H), 3.64-3.60 (m, 1H), 3.48-3.34 (m, 4H), 2.98-2.93 (m, 1H), 2.74-2.66 (m, 1H), 2.04-2.00 (m, 1H), 1.91-1.80 (m, 1H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 139.0, 138.1, 137.5, 135.88, 135.86, 133.7, 128.8 (CH x 2), 128.2 (CH x 2), 127.24, 127.21, 126.8, 126.0 (CH x 2), 124.9 (C x 2), 122.4, 121.4, 119.2, 118.2, 117.8, 110.3, 109.4, 58.1, 56.3, 48.5, 46.4, 34.4, 20.0, 17.4 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{31}\text{H}_{31}\text{N}_2^+$ $[\text{M}+\text{H}]^+$ 431.2487, found: 431.2482.

4-allyl-2-methyl-3,4,4a,5,6,10b-hexahydrobenzo[f]quinoline (2m):



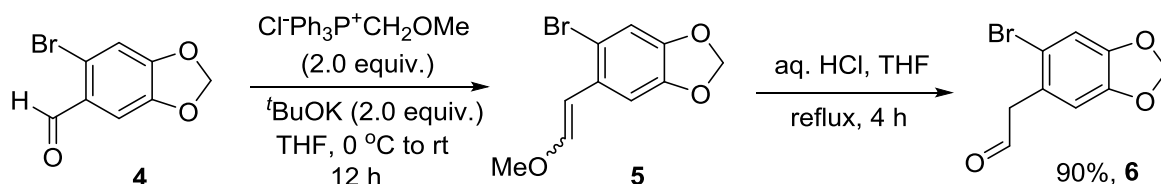
This compound was prepared by the general procedure described above and was obtained as light yellow oil in 65% yield: R_f = 0.39 (hexane: ethyl acetate = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.23-7.05 (m, 4H), 5.99-5.89 (m, 1H), 5.42 (s, 1H), 5.25 (d, J = 17.13 Hz, 1H), 5.15 (d, J = 10.09 Hz, 1H), 3.67 (s, 1H), 3.36-3.19 (m, 3H), 3.04-2.62 (m, 4H), 1.85-1.80 (m, 1H), 1.75-1.66 (m, 1H), 1.63 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 139.8, 136.4, 136.2, 130.3, 129.2, 128.5, 126.1, 125.8, 124.6, 117.3, 57.6, 55.4, 51.1, 39.8, 29.1, 20.6, 17.0 ppm; **HRMS (ESI, m/z)**: calcd for $\text{C}_{17}\text{H}_{22}\text{N}^+$ $[\text{M}+\text{H}]^+$ 240.1752, found: 240.1752.

5. General Experimental Procedure for Gram-Scale Reaction



Typical procedure for the gram scale reaction (*N*-allyl-1,1-dimethoxy-4-phenyl-*N*-(2-phenylallyl)butan-2-amine **1g** as a model example): Trifluoromethanesulfonic acid (10 mmol, 2.0 equiv.) was dropwise added to α -amino acetal **1g** (1.50 g, 5.0 mmol, 1.0 equiv.) in dry dichloromethane (50 ml) in 2 h at 20 °C and was then stirred at 20 °C for the specified time. The reaction mixture was quenched with saturated aqueous sodium bicarbonate (NaHCO₃). The aqueous layer was extracted with dichloromethane (20 ml \times 3) and the combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude oil was redissolved in a minimum amount of dichloromethane and was purified by flash column chromatography (silica gel; triethylamine/ethyl acetate/hexane = 0.1:1:10) to afford the desired product **2g** as the light yellow oil (1.04 g, 69%).

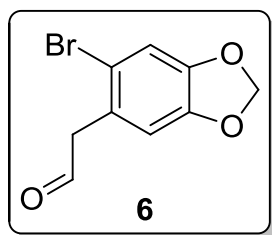
6. Experimental Procedure for Formal Synthesis of Homochelidonine and Chelamidine and Spectroscopic Information¹¹⁻¹²



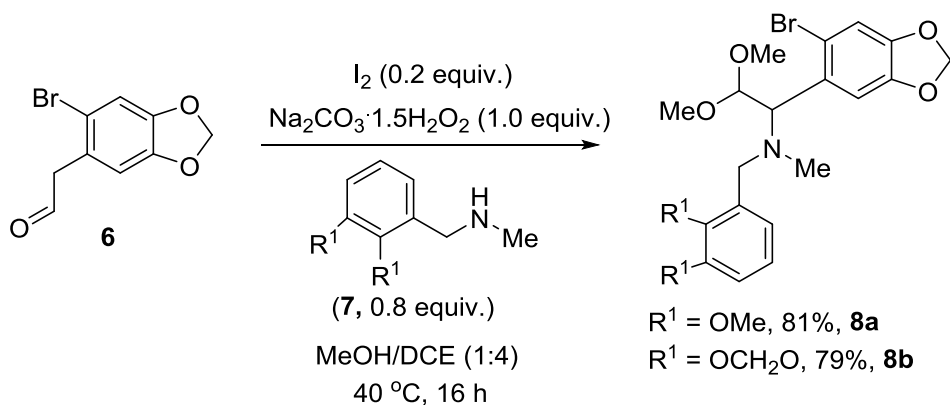
t-BuOK (3.07 g, 27.3 mmol) was added in portions to an ice-cooled and magnetically stirred suspension of methoxymethyltriphenylphosphonium chloride (4.49 g, 13.1 mmol) in anhydrous THF (25 mL) maintained under an atmosphere of nitrogen. The resulting dark-red suspension was then stirred for 0.5 h at ca. 0 °C. A solution of 6-bromopiperonal **4** (2.50 g, 10.9 mmol) in THF (25 mL) was then added slowly and the subsequent mixture was allowed to warm to 20 °C and stirred for 16 h. After that, NH₄Cl (25 mL of a saturated aqueous solution) then water (10 mL) were successively added. The reaction mixture was extracted with Et₂O (3 \times 40 mL) and the combined organic phases washed with brine (25 mL) before being dried (Na₂SO₄), filtered and concentrated to give a light orange-colored oil **5**.

Next, the mixture of the intermediate **5**, aqueous HCl (4 mL, 2 M), and THF (25 mL) was stirred and refluxed for 4 h and cooled and extracted with Et₂O (3 x 50 mL). The combined organic extracts were washed with water (20 mL) and NaHCO₃ (25 mL of a saturated aqueous solution), then dried (Na₂SO₄), filtered, concentrated, and subjected to flash chromatography (silica, 5:95 v/v ethyl acetate/hexane elution) to give the title compound **6** (2.38 g, 90%) as the light yellow oil.

2-(6-bromobenzo[d][1,3]dioxol-5-yl)acetaldehyde (**6**):

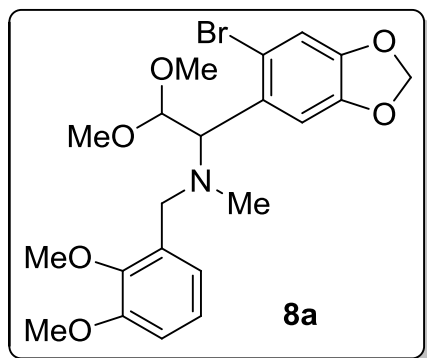


Light yellow oil; R_f = 0.60 (hexane: ethyl acetate = 4:1); ¹H NMR (CDCl₃, 500 MHz) δ 9.67 (t, J = 1.64 Hz, 1H), 7.02 (s, 1H), 6.68 (s, 1H), 5.96 (s, 2H), 3.73 (d, J = 1.68 Hz, 2H) ppm; ¹³C NMR (CDCl₃, 125 MHz) δ 198.2, 147.7, 147.4, 125.0, 115.0, 112.5, 110.8, 101.7, 50.0 ppm; HRMS (ESI, m/z): calcd for C₉H₈BrO₃⁺ [M+H]⁺ 242.9657, found: 242.9658.



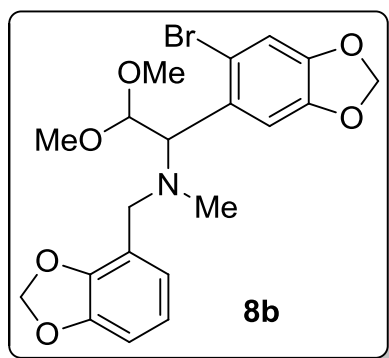
Iodine (25 mg, 0.1 mmol) was added to a mixture of sodium percarbonate (79 mg, 0.5 mmol), secondary amine **7** (0.5 mmol), and aldehyde **6** (0.625 mmol) in methanol (0.5 mL)/1,2-dichloroethane (2.0 mL) at room temperature. The mixture was stirred at 40 °C until secondary amine was completely converted by TLC detection. The resulting reaction mixture was mixed with a small amount of silica gel and concentrated. The crude product was purified by flash column chromatography (silica gel; ethyl acetate or diethyl ether/hexane = 1:100, v/v) to afford the corresponding desired product **8**.

1-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-*N*-(2,3-dimethoxybenzyl)-2,2-dimethoxy-*N*-methylethanamine (8a):

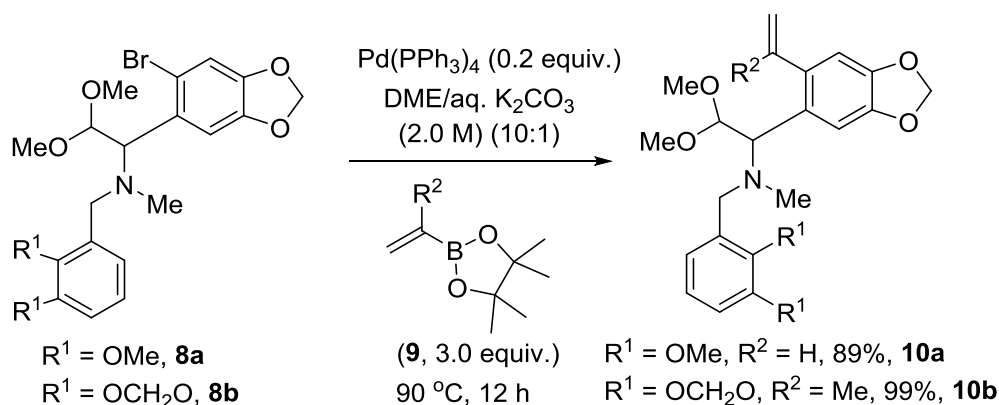


81% yield; Light yellow oil; R_f = 0.30 (hexane: ethyl acetate = 4:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.14 (s, 1H), 7.07-6.99 (m, 3H), 6.80-6.77 (m, 1H), 5.97-5.95 (m, 2H), 4.74 (d, J = 5.70 Hz, 1H), 4.34 (d, J = 5.70 Hz, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 3.66 (AB_q, J = 13.44 Hz, 2H), 3.50 (s, 3H), 3.33 (s, 3H), 2.22 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 152.4, 147.4, 147.2, 146.8, 133.4, 130.6, 123.6, 122.1, 116.7, 112.3, 110.6, 110.1, 105.2, 101.5, 67.4, 60.5, 55.6, 55.1, 54.2, 52.2, 38.7 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{21}\text{H}_{27}\text{BrNO}_6^+$ $[\text{M}+\text{H}]^+$ 468.1022, found: 468.1011.

***N*-(benzo[*d*][1,3]dioxol-4-ylmethyl)-1-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-2,2-dimethoxy-*N*-methylethanamine (8b):**

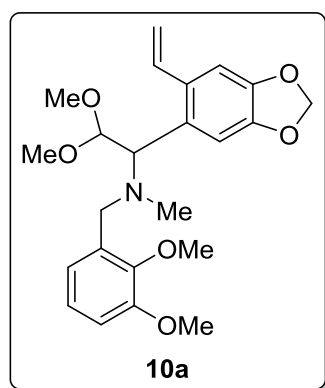


79% yield; Light yellow oil; R_f = 0.36 (hexane: ethyl acetate = 4:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.11 (s, 1H), 7.03 (s, 1H), 6.88-6.69 (m, 3H), 5.98-5.96 (m, 2H), 5.93-5.90 (m, 2H), 4.72 (d, J = 5.69 Hz, 1H), 4.33 (d, J = 5.68 Hz, 1H), 3.58 (AB_q, J = 13.41 Hz, 2H), 3.49 (s, 3H), 3.32 (s, 3H), 2.25 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 147.4, 147.0 (C x 2), 145.9, 130.3, 123.0, 121.2, 120.9, 116.8, 112.5, 110.2, 107.0, 105.2, 101.7, 100.5, 67.1, 55.3, 54.3, 52.3, 38.7 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{20}\text{H}_{23}\text{BrNO}_6^+$ $[\text{M}+\text{H}]^+$ 452.0709, found: 452.0703.



To a 50 mL round-bottom flask with a magnetic stirring bar was added aryl bromide **8** (0.5 mmol, 1.0 equiv.), boronic acid pinacol ester **9** (1.5 mmol, 3.0 equiv.), $\text{Pd(PPh}_3)_4$ (0.1 mmol, 0.2 equiv.), K_2CO_3 (2.5 mL, 2 M, 5.0 mmol, 10 equiv.) and 1,2-dimethoxyethane (25 mL). The reaction mixture was refluxed for 12 h. Then, water (20 mL) was added to quench the reaction and the aqueous layer was extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were washed with water (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4 . After being filtered and concentrated, the residual crude product was purified by flash column chromatography to afford the desired compound **10**.

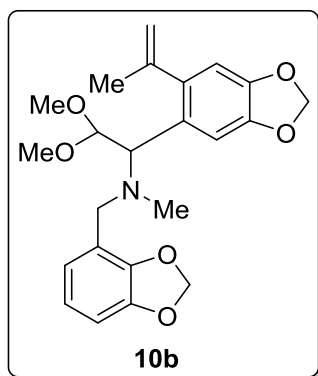
***N*-(2,3-dimethoxybenzyl)-2,2-dimethoxy-*N*-methyl-1-(6-vinylbenzo[*d*][1,3]dioxol-5-yl)ethanamine (10a):**



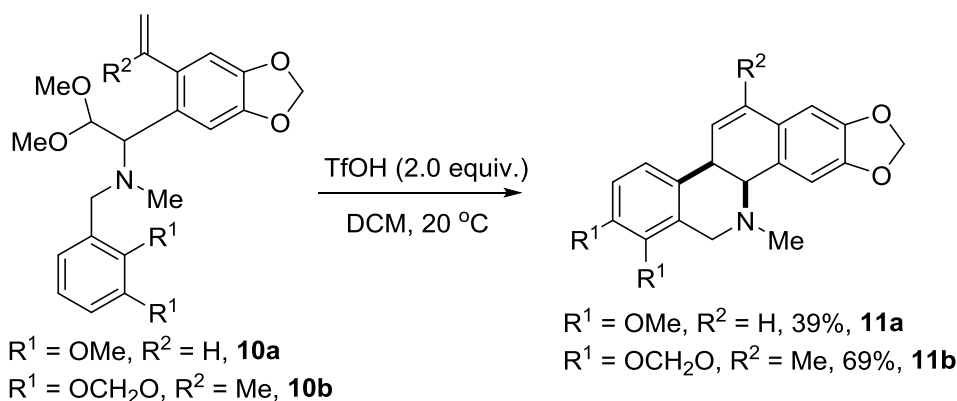
89% yield; Light yellow oil; R_f = 0.55 (hexane: ethyl acetate = 1:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.11-6.99 (m, 4H), 6.97 (s, 1H), 6.78 (dd, J = 7.30, 2.33 Hz, 1H), 5.95-5.93 (m, 2H), 5.48 (dd, J = 17.21, 1.33 Hz, 1H), 5.19 (dd, J = 10.88, 1.32 Hz, 1H), 4.79 (d, J = 5.97 Hz, 1H), 4.08 (d, J = 5.99 Hz, 1H), 3.84 (s, 3H), 3.75 (s, 3H), 3.62 (AB_q, J = 13.64 Hz, 2H), 3.47 (s, 3H), 3.28 (s, 3H), 2.20 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 152.5, 147.5, 146.8, 146.6, 135.2, 133.7, 132.6, 130.0, 123.7, 122.1, 114.7, 110.6, 109.0, 106.0,

105.5, 100.9, 64.5, 60.6, 55.7, 55.0, 54.4, 52.4, 38.9 ppm; **HRMS (ESI, m/z)**: calcd for $C_{23}H_{30}NO_6^+$ $[M+H]^+$ 416.2073, found: 416.2070.

***N*-(benzo[d][1,3]dioxol-4-ylmethyl)-2,2-dimethoxy-*N*-methyl-1-(6-(prop-1-en-2-yl)benzo[d][1,3]dioxol-5-yl)ethanamine (10b):**



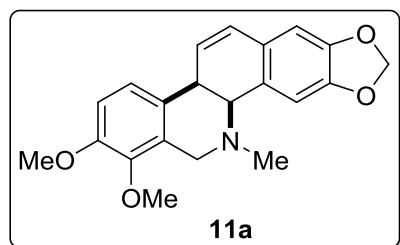
99% yield; Light yellow oil; R_f = 0.38 (hexane: ethyl acetate = 4:1); **1H NMR (CDCl₃, 400 MHz)** δ 7.08 (s, 1H), 6.88-6.68 (m, 3H), 6.63 (s, 1H), 5.95-5.90 (m, 4H), 5.05 (d, J = 121.68 Hz, 2H), 4.69 (d, J = 5.83 Hz, 1H), 4.16 (d, J = 5.84 Hz, 1H), 3.51 (AB_q, J = 13.28 Hz, 2H), 3.46 (s, 3H), 3.34 (s, 3H), 2.17 (s, 3H), 2.04 (s, 3H) ppm; **^{13}C NMR (CDCl₃, 100 MHz)** δ 146.9, 146.04, 146.00, 145.9, 145.2, 139.0, 128.1, 122.9, 121.5, 122.2, 116.3, 108.7, 108.0, 106.8, 106.2, 100.9, 100.5, 64.7, 56.1, 54.2, 52.3, 38.8, 25.6 ppm; **HRMS (ESI, m/z)**: calcd for $C_{23}H_{28}NO_6^+$ $[M+H]^+$ 414.1917, found: 414.1915.



Trifluoromethanesulfonic acid (30 mg, 0.2 mmol, 2.0 equiv.) was added to α -amino acetal **10** (0.1 mmol, 1.0 equiv.) in dry dichloromethane (1.0 ml) and was stirred at 20 °C for the specified time. The reaction mixture was quenched with saturated aqueous sodium bicarbonate (NaHCO₃). The aqueous layer was extracted with dichloromethane (2.0 ml \times 3) and the combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude oil was redissolved in a

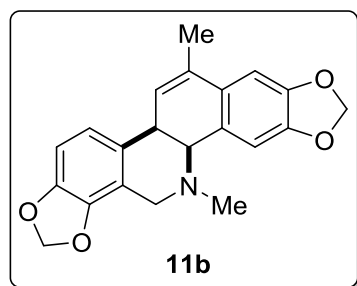
minimum amount of dichloromethane and was purified by flash column chromatography (silica gel; triethylamine/ethyl acetate/hexane = 0.1:1:10) to afford the desired product **11**.

1,2-dimethoxy-12-methyl-4b,11b,12,13-tetrahydro-[1,3]dioxolo[4',5':4,5]benzo[1,2-c]phenanthridine (11a):



39% yield; Light yellow oil; R_f = 0.38 (hexane: ethyl acetate = 1:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 6.98-6.85 (m, 2H), 6.79 (s, 1H), 6.64 (s, 1H), 6.36 (dd, J = 9.46, 3.01 Hz, 1H), 5.96-5.95 (m, 2H), 5.79 (d, J = 9.45 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 3.78 (AB_q, J = 16.26 Hz, 2H), 3.71 (s, 1H), 3.31 (d, J = 4.83 Hz, 1H), 2.17 (s, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 150.5, 147.4, 146.0, 144.9, 132.6, 129.5, 128.7, 128.2, 127.2, 125.3, 123.4, 111.4 (C x 2), 106.8, 101.0, 62.4, 60.1, 55.8, 53.7, 42.8, 39.0 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_4^+$ $[\text{M}+\text{H}]^+$ 352.1549, found: 352.1560.

7,13-dimethyl-5b,12b,13,14-tetrahydro-[1,3]dioxolo[4',5':4,5]benzo[1,2-c][1,3]dioxolo[4,5-*i*]phenanthridine (11b):



69% yield; Light yellow oil; R_f = 0.52 (hexane: ethyl acetate = 1:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 6.85 (s, 1H), 6.81 (s, 1H), 6.76-6.71 (m, 2H), 5.97-5.92 (m, 4H), 5.59 (s, 1H), 3.70 (AB_q, J = 15.74 Hz, 2H), 3.69-3.68 (m, 1H), 3.32 (d, J = 4.67 Hz, 1H), 2.16 (s, 3H), 2.04-2.03 (m, 3H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 147.6, 145.7, 145.1, 143.1, 131.0, 130.0, 129.8, 129.4, 127.7, 120.7, 116.9, 111.3, 107.3, 104.2, 101.1, 101.0, 63.0, 52.8, 42.7, 39.0, 19.4 ppm; HRMS (ESI, m/z): calcd for $\text{C}_{21}\text{H}_{20}\text{NO}_4^+$ $[\text{M}+\text{H}]^+$ 350.1392, found: 350.1382.

7. Reference:

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8. X-Ray Diffraction Analysis

8.1

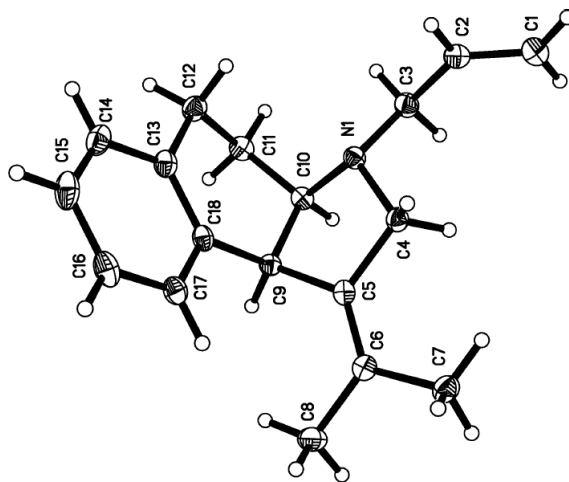


Figure S1. ORTEP drawing of **2a** showing 50% probability chosen for the ellipsoids.

8.2 Crystal data and structure refinement for 2a

CCDC number	965133	
Identification code	2a	
Empirical formula	C ₁₈ H ₂₃ N	
Formula weight	253.37	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.5072(6) Å	$\alpha = 88.049(3)^\circ$
	b = 9.2974(6) Å	$\beta = 78.840(3)^\circ$
	c = 9.7885(6) Å	$\gamma = 70.388(3)^\circ$
Volume	715.11(8) Å ³	
Z	2	
Density (calculated)	1.177 Mg/m ³	
Absorption coefficient	0.067 mm ⁻¹	
F(000)	276	
Crystal size	0.40 x 0.40 x 0.08 mm ³	
Theta range for data collection	2.84 to 29.08 °	
Index ranges	-11 ≤ h ≤ 11, -12 ≤ k ≤ 12, -12 ≤ l ≤ 13	
Reflections collected	10410	
Independent reflections	3781 [R(int) = 0.0447]	

Completeness to theta = 29.08 °	98.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9946 and 0.9735
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3781 / 0 / 174
Goodness-of-fit on F ²	1.026
Final R indices [I>2sigma(I)]	R1 = 0.0507, wR2 = 0.1190
R indices (all data)	R1 = 0.0738, wR2 = 0.1325
Largest diff. peak and hole	0.335 and -0.236 e.Å ⁻³

9. ^1H and ^{13}C NMR spectra

