nature chemistry

Supplementary information

https://doi.org/10.1038/s41557-024-01714-7

Efficient and modular synthesis of ibogaine and related alkaloids

In the format provided by the authors and unedited

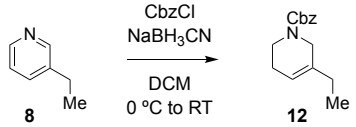
Table of Contents

1. General Information

All reagents were obtained from commercial sources and reactions were performed using oven-dried glassware (120°C) under an inert N_2 atmosphere unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless-steel cannula. Organic solutions were concentrated under reduced pressure (~5 Torr) by rotary evaporation. Solvents were purified by passage under 12 psi N_2 through activated alumina columns. Chromatography was performed using Fisher Chemical™ Silica Gel Sorbent (230–400 Mesh, Grade 60). Compounds purified by chromatography were typically applied to the adsorbent bed using the indicated solvent conditions with a minimum amount of added chloroform as needed for solubility. Thin layer chromatography (TLC) was performed on Merck silica gel 60 F254 plates (250 µm). Visualization of the developed chromatogram was accomplished by fluorescence quenching or by staining with iodine, butanolic ninhydrin, aqueous potassium permanganate, or aqueous ceric ammonium molybdate (CAM). Irradiation of photochemical reactions was carried out using 2 HIGROW LED Aquarium Light Blub, Wolezek 30W LED Plant Grow Light Bulb with 18x2W 450-460nm.

Nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker 400 operating at 400 and 100 MHz, a Varian 600 operating at 600 and 150 MHz, or a Bruker 600 operating at 600 and 150 MHz for ^{1}H and ^{13}C, respectively, and are referenced internally according to residual solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet), coupling constant (Hz), and integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Infrared (IR) spectra were recorded on a Nicolet iS10 FTIR Spectrometer. High-resolution mass spectra were obtained using a Thermo Fisher Scientific Q-Exactive HF Orbitrap.

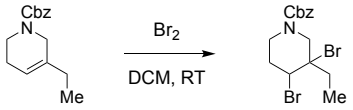
2. Detailed Synthesis Procedures and Experimental Data for all Compounds



benzyl 5-ethyl-3,6-dihydropyridine-1(2*H*)-carboxylate (12)
A stirred solution of 3-ethylpyridine (10.48 mL, 93.40 mmol, 1.00 equiv.) in DCM/AcOH (374 mL/187 mL, 0.166 M) was cooled to 0 °C and solid sodium cyanoborohydride (14.67 g, 233.00 mmol, 2.50 equiv.) was added in one portion. Benzyl chloroformate (17.26 mL, 121.00 mmol, 1.30 equiv.) was added dropwise over 15 min and the reaction mixture was slowly warmed to ambient temperature over the course of 16 h. The reaction mixture was quenched by the addition of aqueous saturated $NaHCO_3$ (150 mL) and the organic layers were separated. The aqueous layer was extracted further with DCM (2 x 200 mL) and the combined organic fractions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification via chromatography on silica gel (20:1 hexanes/ethyl acetate) afforded compound **12** (14.89 g, 65%) as a colorless oil.

R_f = 0.65 (7:3 hexanes/EtOAc)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.40 – 7.28 (m, 5H), 5.53 (s, 1H), 5.16 (s, 2H), 3.89 – 3.81 (m, 2H), 3.52 (t, *J* = 5.74 Hz, 2H), 2.12 (s, 2H), 1.98 (s, 2H), 1.03 (t, *J* = 7.4 Hz, 3H)

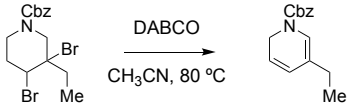
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 155.27, 137.04, 136.89, 128.41, 127.87, 127.83, 118.03, 117.60, 66.90, 66.80, 49.68, 45.92, 44.68, 40.66, 40.39, 30.51, 27.30, 24.91, 24.57, 12.11, 11.21
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. for $C_{15}H_{20}NO_2^+$, 246.1498; found, 246.1490



12 **S20**

benzyl 3,4-dibromo-3-ethylpiperidine-1-carboxylate (S20)
Compound **S20** was synthesized using a known procedure[1]. Compound **S20** (9.85 g, 96%) was isolated as a clear oil that crystallized into a white solid upon standing. Spectral data matched that reported in the literature.

R_f = 0.45 (7:3 hexanes/EtOAc)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.41 – 7.28 (m, 5H), 5.20 – 5.08 (m, 2H), 4.63 – 4.59 (s, 1H), 4.31 – 3.97 (m, 2H) 3.52 – 3.25 (m, 2H), 2.85 – 2.70 (m, 1H), 2.08 – 1.80 (m, 3H), 1.19 – 1.07 (m, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 155.42, 155.28, 137.19, 136.67, 128.58, 128.54, 128.15, 128.05, 127.95, 127.85, 71.54, 67.53, 66.96, 55.99, 50.96, 50.59, 49.83, 44.84, 39.52, 39.37, 33.83, 31.52, 31.19, 30.67, 11.38, 8.67

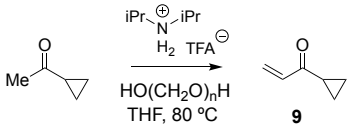


S20 **10**

benzyl 5-ethylpyridine-1(2*H*)-carboxylate (10)
A 2-neck flask was charged with compound **S20** (8.50 g, 20.98 mmol, 1.00 equiv.) and anhydrous DABCO (8.14 g, 72.59 mmol, 3.46 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous acetonitrile (159 mL, 0.13M) was added. The resulting solution was stirred and heated at reflux for 3 h after which the reaction was allowed to cool to ambient temperature and filtered. The reaction vessel and filter cake were washed with DCM (2 x 50 mL) and the filtrate was concentrated under reduced pressure to remove excess acetonitrile. The resulting residue was diluted in DCM (75 mL) and washed with brine (3 x 50 mL). The organic fractions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue (3.77 g, 74%) was used immediately in the Diels-Alder reaction without further purification.

Note: DABCO was recrystallized and dried prior to use. Dihydropyridine **10** is prone to isomerization and the rigorous omission of water is critical to maintaining reproducibility. Prolonged reaction times can also result in isomerization to the undesired diene. It is advised to monitor the reaction via TLC and LCMS.

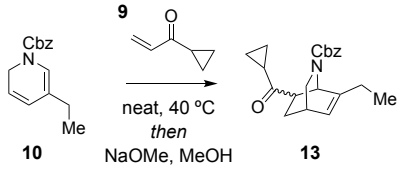
[1] Redding, M. T., Fukuyama, T. Stereocontrolled Total Synthesis of (±)-Catharanthine via Radical-Mediated Indole Formation. *Org. Lett.* **1** 973—976 (1999).



1-cyclopropylprop-2-en-1-one (9)
A Schlenk tube was sequentially charged with THF (100 mL, 0.70 M), cyclopropyl methyl ketone (7.00 mL, 70.65 mmol, 1 equiv.), diisopropylammonium trifluoroacetate (17.00 g, 78.99, 1.12 equiv.) and paraformaldehyde (5.00 g, 166.50 mmol, 2.35 equiv.) under a stream of nitrogen. The mixture was stirred and heated at 80 °C for 48 h, after which it was cooled to ambient temperature, diluted with DCM (200 mL) and filtered. The reaction vessel and filter cake were washed with additional DCM. The filtrate was poured into water (200 mL) and the layers were separated. The aqueous layer was further extracted with DCM (2 x 100 mL) and the combined organic fractions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification via chromatography on silica gel (3:2 hexanes/DCM) afforded compound **9** (5.50 g, 81%) as a light-yellow oil.

Note: Enone **9** is volatile (60°C at 60 torr) and very pungent. Extreme caution should be used when handling.

R_f = 0.35 (2:1 hexanes/DCM)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 6.43 (dd, *J* = 17.6, 10.5 Hz, 1H), 6.24 (dd, *J* = 17.6, 1.2 Hz, 1H), 5.77 (dd, *J* = 10.5, 1.2 Hz, 1H), 2.20 – 2.11 (m, 1H), 1.05 (td, *J* = 3.7, 1.0 Hz, 2H), 0.94 – 0.86 (m, 2H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 200.39, 136.57, 127.44, 18.14, 11.12
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_6H_9O^+$, 97.0658; found, 97.0655

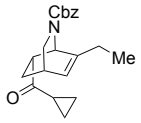


Benzyl(1*R*,4*S*,7*R*)-7-(cyclopropanecarbonyl)-6-ethyl-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (13)
A Schlenk flask was sequentially charged with compound **10** (3.77 g, 15.51 mmol, 1.00 equiv.) and compound **9** (2.98 g, 31.02 mmol, 2.00equiv.). The mixture was cooled to -78 °C after which it was evacuated and refilled with nitrogen. The mixture was warmed to ambient temperature and this process was repeated 2 times. The degassed mixture was stirred and heated at 40 °C for 72 h. The reaction vessel was cooled to ambient temperature, diluted with methanol (50 mL, 0.30 M) and solid sodium methoxide (0.25 g, 4.65 mmol, 0.30 equiv.) was added in small portions over 5 min. The resulting solution was stirred at ambient temperature for an additional 12 h after which it was concentrated under reduced pressure to remove methanol and any volatiles. The unpurified residue was diluted in DCM (100 mL), poured into water (50 mL) and the layers were separated. The aqueous layer was further extracted with DCM (2 x 50 mL) and the combined organic extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue

was purified via chromatography on silica gel (gradient elution 10:1→7:3 hexanes/EtOAc) to afford compound **13** (3.03 g, 64%) as a clear yellow oil and a 50:50 ratio of epimers.

Note: Purification is easiest when performed using the "dry-load" method. Separation of endo and exo epimers can be achieved by chromatography on silica gel using 10:1 DCM/EtOAc. Endo and exo epimers were originally assigned based on literature precedent for Diels-Alder endo selectivity. When NaOMe/MeOH is omitted from the reaction, a 9:1 ratio of **13a:13b** is isolated. Additional characterization data support this assignment. Endo and exo epimers of **13** were separated by column chromatography and were assigned using a combination of ^{1}H NMR, COSY, HSQC, and 1D selective gradient NOESY. Specifically, ^{1}H NMR, COSY, and HSQC were used to assign the signals corresponding to the olefin, cyclopropyl methylene, and cyclopropyl methine protons. From there, the methine proton peak in both endo/exo spectra were suppressed through a 1D selective gradient NOESY. For the endo epimer, a correlation was observed between the olefinic proton and the methine. This same correlation was absent in the 1D selective gradient NOESY of the exo epimer. To provide further evidence, the olefinic proton was then suppressed for both epimers. The endo epimer retained the correlation to the methine peak, while the exo epimer did not show a correlation to the methine peak. Taken together, these data suggest that for the endo epimer, a through-space interaction is possible between the methine proton and olefinic proton due to the presence of the cyclopropyl moiety under the ring. The exo epimer lacks this same through-space interaction.

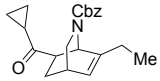
R_f = 0.40 (7:3 hexanes/ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 7.38 – 7.27 (m, 10H), 5.98 (dp, *J* = 7.0, 1.8 Hz, 1H), 5.94 (dt, *J* = 6.4, 1.9 Hz, 1H), 5.19 – 5.02 (m, 6H), 4.92 (dt, *J* = 8.4, 2.1 Hz, 1H), 3.38 – 3.24 (m, 3H), 3.02 – 2.91 (m, 2H), 2.89 – 2.66 (m, 3H), 2.33 – 2.19 (m, 2H), 2.19 – 2.02 (m, 5H), 1.99 – 1.80 (m, 2H), 1.70 – 1.61 (m, 2H), 1.39 (dddt, *J* = 16.5, 13.5, 10.7, 3.1 Hz, 1H), 1.14 – 1.02 (m, 3H), 1.02 – 0.80 (m, 8H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 209.47, 208.93, 208.79, 208.42, 155.14, 154.74, 154.61, 147.27, 146.76, 145.03, 144.77, 137.08, 136.86, 128.52, 128.46, 128.43, 128.38, 128.29, 127.95, 127.89, 127.81, 127.78, 127.64, 127.60, 127.48, 126.94, 125.59, 125.39, 125.04, 124.98, 66.89, 66.84, 66.81, 66.50, 65.34, 52.44, 52.35, 52.24, 51.71, 51.29, 51.04, 51.01, 48.20, 47.85, 47.75, 47.61, 30.61, 30.35, 30.17, 26.58, 26.32, 26.22, 25.90, 24.89, 24.80, 24.69, 19.99, 19.60, 19.44, 19.16, 12.40, 11.73, 11.72, 11.56, 11.45, 11.34, 11.25, 11.17, 11.06
HRMS (ESI) = *m/z* $[M + Na]^+$ calcd. for $C_{21}H_{25}NO_3Na^+$, 362.1728; found, 362.1722



13a

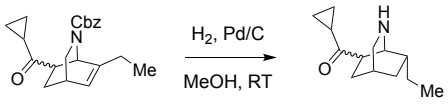
R_f = 0.40 (7:3 hexanes/ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.38 – 7.27 (m, 5H), 5.93 (dq, *J* = 6.8, 1.9 Hz, 1H), 5.19 – 5.07 (m, 3H), 3.39 – 3.21 (m, 2H), 2.97 (tt, *J* = 10.0, 2.6 Hz, 1H), 2.78 (ddt, *J* = 14.6, 6.4, 2.7 Hz, 1H), 2.19 – 2.02 (m, 3H), 1.98 – 1.79 (m, 2H), 1.64 (ddd, *J* = 12.3, 9.3, 2.5 Hz, 1H), 1.03 – 0.80 (m, 7H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed) = 208.65, 208.28, 155.02, 154.49, 144.93, 144.69, 136.82, 136.76, 128.36, 128.33, 127.84, 127.79, 127.71, 127.67, 124.94, 124.88,

66.78, 66.72, 52.34, 52.14, 50.93, 50.88, 47.75, 47.50, 30.52, 30.27, 26.48, 25.80, 24.82, 19.33, 19.05, 11.44, 11.34, 11.23, 11.15, 11.09
HRMS (ESI) = *m/z* [M + Na]$^+$ calcd. for $C_{21}H_{25}NO_3Na^+$, 362.1728; found, 362.1722



13b

R_f = 0.40 (7:3 hexanes/ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.39 – 7.28 (m, 5H), 6.00 (m, 1H), 5.10 – 5.02 (m, 3H), 3.31 (m, 1H), 3.03 – 2.93 (m, 1H), 2.90 – 2.71 (m, 2H), 2.35 – 2.16 (m, 3H), 2.12 – 1.94 (m, 1H), 1.48 – 1.35 (m, 1H), 1.14 – 1.03 (m, 4H), 0.99 – 0.84 (m, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed) = 209.49, 208.95, 155.18, 154.77, 147.31, 146.80, 137.13, 136.90, 128.42, 128.33, 127.98, 127.93, 127.68, 127.52, 125.63, 125.43, 66.87, 66.53, 52.47, 52.39, 51.75, 51.32, 48.24, 47.79, 30.39, 30.21, 26.36, 26.27, 24.84, 24.73, 20.03, 19.64, 12.44, 11.77, 11.76, 11.37, 11.23, 11.20, 11.10, 10.83
HRMS (ESI) = *m/z* [M + Na]$^+$ calcd. for $C_{21}H_{25}NO_3Na^+$, 362.1728; found, 362.1722



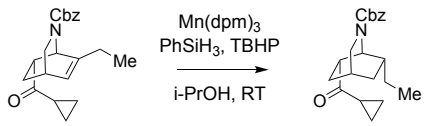
13 **14**

cyclopropyl((1*S*,4*R*,7*R*)-7-ethyl-2-azabicyclo[2.2.2]octan-6-yl)methanone (14)
A flask was charged with compound **13** (2.95 g, 8.69 mmol, 1.00 equiv.) and unreduced 10 wt % Pd/C (295 mg, 0.27 mmol, 0.03 equiv.). The flask was evacuated and refilled with nitrogen 3 times. MeOH (87 mL, 0.1 M) was added in one portion and hydrogen gas was bubbled through the resulting solution for 1 min. The reaction mixture was stirred under hydrogen atmosphere at ambient temperature for 1 h after which it was filtered through a pad of celite. The reaction vessel and filter cake were washed with DCM (3 x 50 mL). The filtrate was concentrated under reduced pressure and purified via chromatography on silica gel (10:1 DCM:MeOH, 1% NH_4OH) to afford compound **14** (1.64 g, 91%) as a yellow oil. The epimers were not separated nor characterized individually.

Note: The stereoconfiguration at C20 was determined retroactively upon completing the synthesis of epiibogaine. Based on TLC and LCMS analysis, it was clear that two compounds were present, and given that C16 can be readily epimerized (see above), we presume that a 50:50 ratio of C16 epimers is obtained. We noticed that using reduced Pd/C gave irreproducible results for carbamate removal.

R_f = 0.1(10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (epimers observed): 3.07 – 2.88 (m, 4H), 2.88 – 2.78 (m, 4H), 2.07 – 1.80 (m, 8H), 1.73 – 1.65 (m, 2H), 1.64 – 1.55 (m, 2H), 1.44 – 1.31 (m, 4H), 1.04 – 0.98 (m, 4H), 0.98 – 0.91 (m, 6H), 0.90 – 0.81 (m, 6H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (epimers observed) = 213.84, 212.84, 49.36, 49.03 47.43, 47.16, 46.34, 46.24, 39.07, 36.82, 35.08, 34.57, 34.05, 32.34, 27.50, 26.72, 25.06, 19.81, 18.97, 18.48, 11.90, 11.32, 11.25, 10.86, 10.79, 10.76

HRMS (ESI) = *m/z* $[M + H]^+$ calcd. for $C_{13}H_{22}NO^+$, 208.1698; found, 208.1699



13a **17a**

Benzyl(1*S*,4*R*,6*S*,7*R*)-6-(cyclopropanecarbonyl)-7-ethyl-2-azabicyclo[2.2.2]octane-2-carboxylate (17a)

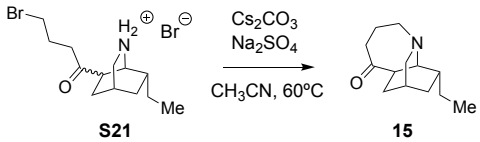
To a stirring solution of **13a** (1.50 g, 4.42 mmol, 1.00 equv.) in anhydrous iPrOH (8.84 mL, 0.50 M) was added phenylsilane (0.82 mL, 6.63 mmol, 1.50 equiv.) and a 5.5 M solution of tert-butyl hydroperoxide in decane (1.20 mL, 6.63 mmol, 1.50 equiv.). The resulting mixture was degassed by bubbling nitrogen through the solution for 10 min. Next, $Mn(dpm)_3$ (0.27 g, 0.44 mmol, 0.10 equiv.) was added in one portion and the reaction was further degassed for an additional 30 s. The mixture was stirred at ambient temperature for 2 h after which it was concentrated under reduced pressure. The residue was purified via chromatography on silica gel (gradient elution 10:1→7:3 hexanes/EtOAc) to afford compound **17a** (1.26 g, 84%) as a clear oil.

R_f = 0.37 (7:3 hexanes/ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.40 – 7.27 (m, 5H), 5.25 – 4.98 (m, 2H), 4.72 – 4.35 (m, 1H), 3.46 – 3.18 (m, 2H), 3.15 – 2.86 (m, 1H), 2.35 (d, 1H), 2.40 – 2.16 (m, 1H), 2.03 – 1.80 (m, 3H), 1.57 – 1.35 (m, 2H), 1.31 – 1.21 (m, 1H), 1.05 – 0.76 (m, 7H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed) = 210.06, 209.68, 155.15, 154.71, 137.27, 137.05, 128.64, 128.51, 128.09, 127.95, 127.84, 127.77, 127.56, 66.97, 51.62, 51.45, 50.11, 49.76, 48.06, 47.96, 46.38, 40.67, 40.54, 31.87, 31.85, 27.51, 27.48, 26.69, 26.55, 24.92, 24.77, 19.78, 19.57, 12.73, 12.63, 12.46, 12.26, 10.92
HRMS (ESI) = *m/z* $[M + Na]^+$ calcd. For $C_{21}H_{27}NO_3Na^+$, 364.1888; found, 364.1889

14 **S21**

(1*S*,4*R*,7*R*)-6-(4-bromobutanoyl)-7-ethyl-2-azabicyclo[2.2.2]octan-2-ium bromide (S21)

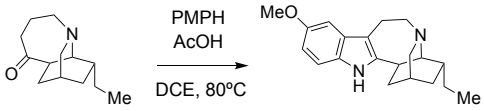
To a stirring solution of compound **14** (1.25 g, 6.03 mmol, 1.00 equiv.) in DCM (6.03 mL, 1.0 M) was added 33 wt % HBr/AcOH (3.12 mL, 18.08 mmol, 3.00 equiv.) in one portion. The solution was stirred at ambient temperature for 2 h after which it was concentrated under reduced pressure. The residue was dried under high vacuum for 1 h and then stirred vigorously in diethyl ether (30 mL). The diethyl ether was decanted and the residue was dried under high vacuum. Product **S21** (2.18 g, 98%) was isolated as an orange foam and was used in the next reaction without any further purification or characterization.



S21 15

1-ethyloctahydro-3,10-methanopyrido[1,2-*a*]azepin-9(6*H*)-one (15)
A flask was charged with compound **S21** (2.18 g, 5.90 mmol, 1.00 equiv.), anhydrous Cs_2CO_3 (2.88 g, 8.85 mmol, 1.5 equiv.), and anhydrous Na_2SO_3 (2.52 g, 17.71 mmol, 3.00 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous CH_3CN (59 mL, 0.10 M) was added in one portion. The reaction mixture was heated to 60 °C and stirred for 6 h. The heterogeneous mixture was cooled to ambient temperature and filtered. The reaction vessel and filter cake were washed with DCM (2 x 30 mL). The filtrate was concentrated under reduced pressure and the residue was purified via chromatography on silica gel (20:1 DCM/MeOH) to afford compound **15** (0.50 g, 41%) as a light brown oil.

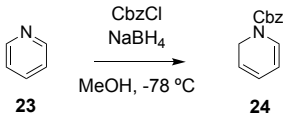
R_f = 0.43 (20:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 3.18 – 2.92 (m, 3H), 2.80 (dd, *J* = 13.2, 2.7 Hz, 1H), 2.66 – 2.51 (m, 3H), 2.06 – 1.75 (m, 7H), 1.61 – 1.49 (m, 1H), 1.39 – 1.19 (m, 2H), 1.08 (dd, *J* = 12.7, 2.6 Hz, 1H), 0.90 (t, *J* = 7.4 Hz, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 216.98, 54.88, 53.83, 50.10, 46.87, 43.79, 41.70, 31.40, 30.54, 27.92, 26.77, 21.24, 12.31
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{13}H_{22}NO^+$, 208.1698; found, 208.1694



15 Epiibogaine (16)

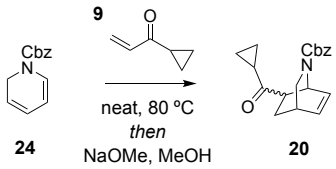
epiibogaine (16)
A flask was charged with compound **15** (0.20 g, 0.96 mmol, 1 equiv.) and para-methoxy phenylhydrazine (0.25 g, 1.44 mmol, 1.5 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous DCE (9.64 mL, 0.1 M) and AcOH (0.83 mL, 14.47 mmol, 15 equiv.) was added. The resulting mixture was degassed by bubbling nitrogen through the solution for 10 min. The flask was heated to 80 °C and stirred for 12 h after which it was cooled to ambient temperature and diluted with DCM (20 mL). Saturated aqueous $NaHCO_3$ was added to the reaction mixture until the pH was adjusted to 7-8. The organic layer was separated, and the aqueous layer was further extracted with DCM (2 x 50 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. Purification via chromatography on silica gel (gradient elution 20:1→10:1 DCM/MeOH, 0.25% NH_4OH) afforded **epiibogaine** (0.24 g, 81%) as a colorless oil.

R_f = 0.33 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, MeOD) δ (ppm) = 7.16 (d, *J* = 8.7 Hz, 1H), 6.95 (d, *J* = 2.4 Hz, 1H), 6.73 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.81 (s, 3H), 3.60 – 3.53 (m, 2H), 3.55 – 3.41 (m, 3H), 3.41 – 3.37 (m, 1H), 3.35 – 3.23 (m, 1H), 3.16 – 3.06 (m, 1H), 2.28 (d, *J* = 2.6 Hz, 1H), 2.22 – 2.01 (m, 3H), 1.75 – 1.63 (m, 1H), 1.56 (td, *J* = 7.3, 3.1 Hz, 2H), 1.38 – 1.19 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H)
^{13}C NMR (101 MHz, MeOD) δ (ppm) = 154.01, 139.67, 130.07, 128.55, 111.18, 111.01, 107.34, 99.39, 59.08, 56.25, 54.92, 50.37, 37.60, 32.16, 29.14, 28.18, 26.49, 24.11, 17.90, 10.58
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{20}H_{27}N_2O^+$, 311.2128; found, 311.2126



benzyl pyridine-1(2*H*)-carboxylate (24)
A flask was charged with methanol (500 mL, 0.50 M) and pyridine (20.36 mL, 252.84 mmol, 1.00 equiv.) and cooled to -78 °C after which sodium borohydride (11.47 g, 303.41 mmol, 1.20 equiv.) was added in one portion. Benzyl chloroformate (43.13 mL, 303.41 mmol, 1.20 equiv.) was added dropwise over 1 h to the reaction mixture. The reaction mixture was stirred at -78°C for an additional 3 h after which it was diluted in Et_2O (200 mL), poured into 1 M HCl (400 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 x 200 mL) and the combined organic extracts were washed with 1 M NaOH (100 mL) followed by brine (100 mL). The organic extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue (54.31 g, 98%) was immediately used without further purification or characterization.

Note: Intermediate **24** is prone to oxidation and must be used immediately upon isolation



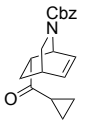
benzyl (1*S*,4*S*)-7-(cyclopropanecarbonyl)-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (20)
A Schlenk flask was sequentially charged with compound **24** (15.50 g, 72.00 mmol, 1.00 equiv.) and compound **9** (13.84 g, 144.01 mmol, 2.00 equiv.). The mixture was cooled to -78 °C after which the flask was evacuated and refilled with nitrogen 3 times. The mixture was stirred and heated at 80 °C for 72 h. The reaction vessel was cooled to ambient temperature, diluted with methanol (240 mL, 0.30 M) and solid sodium methoxide (1.16 g, 21.60 mmol, 0.30 equiv.) was added in small portions over 5 min. The resulting solution was stirred at ambient temperature for an additional 12 h after which it was concentrated under reduced pressure to remove methanol and any volatiles. The unpurified residue was diluted in DCM (200 mL), poured into water (100 mL) and the layers were separated. The aqueous layer was further extracted with DCM (2 x 100 mL) and the combined organic fractions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified via chromatography on silica gel (7:3 hexanes/EtOAc) to afford compound **17** (20.17 g, 90%) as a clear yellow oil. Compound **20** was isolated as a 50:50 mixture of exo:endo epimers.

Note: Separation of endo and exo epimers can be achieved by chromatography on silica gel using 10:1 DCM/EtOAc

R_f = 0.42 (7:3 hexanes:EtOAc)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 7.38 – 7.30 (m, 10H), 6.58 – 6.44 (m, 2H), 6.43 – 6.34 (m, 1H), 6.30 – 6.24 (m, 1H), 5.23 (d, *J* = 6.1 Hz, 1H), 5.18 – 5.02 (m, 4H), 4.70 (d, *J* = 5.7 Hz, 1H), 3.38 – 3.25 (m, 3H), 3.05 – 2.71 (m, 5H), 2.27 – 2.16 (m, 1H), 2.14 – 2.02 (m, 1H), 2.03 – 1.81 (m, 2H), 1.77 – 1.67 (1H), 1.48 – 1.41 (m, 1H), 1.06 – 0.81 (m, 8H)

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 209.36, 208.75, 208.49, 155.26, 154.76, 137.04, 136.85, 136.78, 135.52, 135.35, 134.90, 134.72, 132.28, 131.88, 130.42, 130.15, 128.53, 128.50, 128.43, 128.36, 128.18, 128.09, 127.99,127.84, 127.72, 127.57, 127.49, 66.93, 66.59, 52.49, 52.32, 52.29, 47.91, 47.62, 47.50, 47.19, 47.00, 30.78, 30.55, 30.31, 30.13, 24.28, 23.62, 23.50, 20.05, 19.73, 19.43, 19.27, 12.50, 11.82, 11.50, 11.36, 11.21, 10.86, 10.64

HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{19}H_{22}NO_3^+$, 312.1598; found, 312.1599



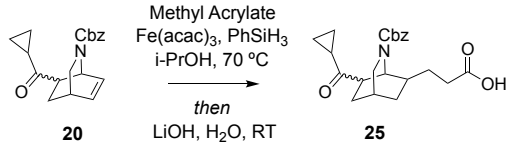
R_f = 0.35 (10:1 DCM:EtOAc)

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.39 – 7.30 (m, 5H), 6.41 – 6.37 (m, 1H), 6.30 – 6.25 (m, 1H), 5.29 (dt, *J* = 6.0, 2.0 Hz, 1H), 5.15 (d, *J* = 12.4 Hz, 2H), 3.41 – 3.22 (m, 2H), 3.02 (ddd, *J* = 10.2, 6.8, 4.1 Hz, 1H), 2.85 (d, *J* = 15.8 Hz, 1H), 2.05 – 1.68 (m, 3H), 1.07 – 0.81 (m, 4H)

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 208.48, 155.24, 136.81, 134.89, 134.69, 130.39, 130.11, 128.47, 127.95, 66.90, 52.62, 52.27, 47.18, 46.97, 30.75, 30.51, 25.18, 24.23, 19.41, 19.23, 11.49, 11.19, 10.85, 10.61

HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{19}H_{22}NO_3^+$, 312.1598; found, 312.1599

Note: The endo epimer was assigned based on the predominant isomer obtained following the Diels-Alder reaction prior to epimerization.



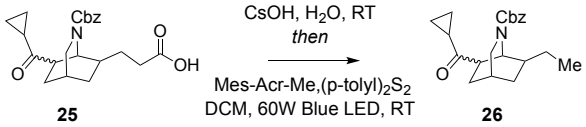
3-((1*S*,4*R*)-2-((benzyloxy)carbonyl)-7-(cyclopropanecarbonyl)-2-azabicyclo[2.2.2]octan-6-yl)propanoic acid (25)

A flask was sequentially charged with compound **20** (3.30 g, 10.59 mmol, 1.00 equiv.), isopropanol (53 mL, 0.2 M), methyl acrylate (5.76 mL, 63.58 mmol, 6.00 equiv.), and $Fe(acac)_3$ (1.12 g, 3.18 mmol, 0.30 equiv.). To this solution was added phenylsilane (3.91 mL, 31.79 mmol, 3.00 equiv.) in one portion. The mixture was stirred and heated at 70 °C under air atmosphere for 24 h, after which it was cooled to ambient temperature. The reaction mixture was diluted in H_2O (100 mL) and LiOH (2.53 g, 105.97 mmol, 10.00 equiv.) was added in one portion. The solution was stirred at ambient temperature for 12 h after which it was acidified with 1 M HCl (100 mL). The mixture was poured into DCM (200 mL) and the layers were separated. The aqueous layer was further extracted with DCM (2 x 100 mL) and the combined organic fractions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified via chromatography on silica gel (gradient elution 10:1→1:1 hexanes/EtOAc) to afford compound **25** (3.02 g, 74%) as a clear foam.

Note: The configuration at C20 was determined retroactively upon completing the total synthesis of ibogaine. Based on LCMS analysis, we presume that a 50:50 ratio of C16 epimers is obtained.

Vigorous bubbling is observed upon 5 min of heating. Purification of **25** can be challenging when using chromatography on silica gel as the compound streaks. Alternatively, the methyl ester can be chromatographed easily (gradient elution 10:1→7:3 hexanes/EtOAc) and then a subsequent hydrolysis can yield compound **25** with no purification needed.

R_f = 0.15 (7:3 hexanes/EtOAc)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 7.38 – 7.27 (m, 5H), 5.20 – 4.96 (m, 2H), 4.70 – 4.36 (m, 1H), 3.54 – 3.15 (m, 2H), 3.06 – 2.85 (m, 1H), 2.59 – 2.16 (m, 4H), 2.11 – 1.84 (m, 3H), 1.81 – 1.41 (m, 4H), 1.17 – 0.66 (m, 4H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 210.17, 209.45, 178.74, 156.21, 137.09, 128.62, 128.56, 128.52, 128.33, 128.20, 127.92, 127.69, 127.66, 127.62, 67.23, 66.86, 52.14, 48.95, 48.74, 37.79, 37.68, 33.64, 32.26, 31.99, 31.53, 31.39, 30.02, 29.88, 29.69, 26.06, 25.96, 24.14, 24.03, 19.99, 19.88, 19.62, 12.55, 11.66, 11.36, 11.20
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{22}H_{28}NO_5^+$, 387.1968; found, 387.1962



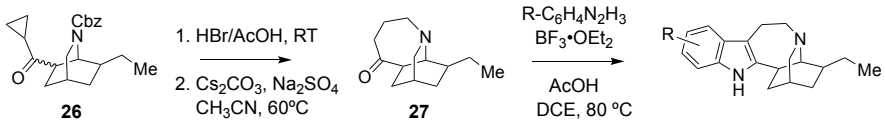
benzyl (1*S*,4*R*)-6-(cyclopropanecarbonyl)-7-ethyl-2-azabicyclo[2.2.2]octane-2-carboxylate (26)
A glass reaction tube was charged with compound **25** (1.85 g, 4.79 mmol, 1.00 equiv.). A solution of CsOH•H_2O (806 mg, 4.79 mmol, 1.00 equiv.) in H_2O (9.6 mL) was added and the milky white heterogeneous mixture was stirred vigorously for 1 h. In a separate flask, 9-mesityl-10-methylacridinium tetrafluoroborate (96 mg, 0.23 mmol, 0.05 equiv.) and p-tolyl disulfide (1.77 g, 7.19 mmol, 1.50 equiv.) was dissolved in DCM (38.4 mL). The acridinium/disulfide solution was added to compound **25** in one portion. The biphasic solution was tightly capped under air atmosphere and stirred (1000 rpm) between two 30 W blue LED lamps (8 cm distance between reaction vessel and lamp) for 24 h at ambient temperature. After 24 h, another portion of 9-mesityl-10-methylacridinium tetrafluoroborate (96 mg, 0.23 mmol, 0.05 equiv.) was added to the reaction mixture and the resulting solution was placed in the photoreactor for an additional 24 h. Upon reaction completion, the reaction mixture was poured into water (50 mL) and the layers were separated. The aqueous layer was further extracted with DCM (2 x 50 mL) and the combined organic extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified via chromatography on silica gel (7:3 hexanes/EtOAc) to afford compound **26** as an orange oil. Compound **26** was further purified by dissolution in ethyl acetate and subsequent addition of activated charcoal (50 mg). Heating the stirred solution at 50 °C for 30 min, followed by filtration and concentration under reduced pressure afforded compound **26** (1.16 g, 71%) as a light-yellow oil.

Note: Conversion rate is highly dependent on the diameter of the reaction vessel. We have observed the best results when using a reaction vessel to reaction volume ratio of 1.5 cm/15 mL. A fan was used to cool the reaction vessel during irradiation and it is advised to seal the reaction tube cap with electrical tape. It is essential that the biphasic reaction is stirred vigorously (>1000 rpm) so that the two layers mix properly. Inadequate mixing will result in poor transfer of the carboxylate salt into the organic layer and ultimately lead to poor reaction conversion. Heating compound **26** in excess activated charcoal for longer than 30 min will lead to reduced yields.

R_f = 0.65 (7:3 hexanes/EtOAc)

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 7.40 – 7.27 (m, 5H), 5.27 –4 .97 (m, 2H), 4.70 – 4.37 (m, 1H), 3.46 – 3.11 (m, 2H), 3.03 – 2.84 (m, 1H), 2.38 – 2.17 (m, 1H), 2.13 – 1.63 (m, 3H), 1.54 – 1.16 (m, 4H), 1.16 – 1.06 (m, 1H), 1.05 – 0.72 (m, 7H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers and epimers observed): 210.37, 209.65, 156.00, 155.72, 137.35, 136.94, 128.48, 128.21, 127.80, 127.73, 66.95, 66.55, 52.44, 51.78, 51.08, 50.30, 49.35, 49.03, 46.88, 46.41, 46.31, 43.78, 40.78, 40.59, 36.50, 36.34, 36.03, 35.96, 35.40, 35.16, 34.87, 34.72, 32.38, 32.23, 29.53, 28.28, 28.14, 27.90, 26.58, 26.43, 26.15, 26.05, 24.26, 24.15, 19.88, 19.57, 12.41, 11.77, 11.75, 11.24, 11.09
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{21}H_{28}NO_3^+$, 342.2068; found, 342.2065

General procedure for preparation of iboga derivatives

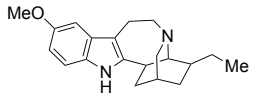


A solution of 33 wt % HBr/AcOH (3.00 equiv.) was added in one portion to compound **26** (1.00 equiv.) while stirring. The dark orange mixture was stirred at ambient temperature for 2 h after which it was concentrated under reduced pressure. The residue was dried under high vacuum for 1 h and then stirred vigorously in diethyl ether (30-50 mL). The diethyl ether was decanted, and the resulting alkyl bromide was dried under high vacuum. This process was repeated 3x to ensure all the benzyl bromide was removed. A flask was charged with alkyl bromide (1.00 equiv.), anhydrous Cs_2CO_3 (1.50 equiv.), and anhydrous Na_2SO_3 (3.00 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous CH_3CN (0.1 M) was added in one portion. The reaction mixture was heated to 60 °C and stirred for 6 h. The heterogeneous mixture was cooled to ambient temperature and filtered. The reaction vessel and filter cake were washed with DCM (2 x 10 mL). The filtrate was concentrated under reduced pressure and the resulting residue was dissolved in DCM (10 mL) and washed with sat. $NaHCO_3$ (3 x 5 mL). The organic extract was dried over sodium sulfate, filtered, and concentrated under reduced pressure to yield compound **27** as an unpurified brown oil.

A flask was charged with unpurified compound **27** (1.00 equiv.) and substituted phenylhydrazine (1.50 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous DCE (0.1 M) and AcOH (15.00 equiv.) was added. The resulting mixture was degassed by bubbling nitrogen through the solution for 10 min. The flask was heated to 80 °C and stirred for 1 h after which it was cooled to ambient temperature and BF_3•OEt_2 (1.20 equiv.) was added in one portion. The resulting mixture was heated at 80 °C for 12 h after which it was cooled to ambient temperature and diluted with DCM (10 mL). Saturated aqueous $NaHCO_3$ was added to the reaction mixture until the pH was adjusted to 7-8. The organic layer was separated, and the aqueous layer was further extracted with DCM (2 x 20 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. Purification via chromatography on silica gel (gradient elution 20:1→10:1 DCM/MeOH, 0.25% NH_4OH) afforded iboga derivates.

Note: The solvent volume for extraction and dilution are representative of a 200 mg scale for intermediate **26**. On larger scales, it was found that sonicating the alkyl bromide in diethyl ether allowed for more efficient benzyl bromide removal. We noticed a considerable decrease in yield (10-15%) when purifying compound **27** via chromatography on silica gel (20:1 DCM/MeOH). Instead, compound **27** was used as an unpurified mixture in the subsequent Fischer indole

reactions. For obtaining biologically pure iboga alkaloids, a second purification via chromatography on silica gel was used with an 8:2 EtOAc/MeOH mobile phase.



ibogaine (1)

Ibogaine (1) – 500 mg scale
Synthesized from compound **26** (500 mg, 1.46 mmol, 1.00 equiv.) following the general procedure for iboga derivative preparation. Para-methoxyphenylhydrazine • HCl (382 mg, 2.19 mmol, 1.50 equiv.) was used and $BF_3 \bullet OEt_2$ was omitted from the Fischer indole reaction. **Ibogaine** (140 mg, 31% over three steps) was isolated as an orange foam.

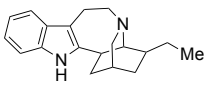
Ibogaine (1) – 1.33g scale
Synthesized from compound **26** (1.33 g, 3.86 mmol, 1 equiv.) following the general procedure for iboga derivative preparation. Para-methoxyphenylhydrazine • HCl (1.02 g, 5.84 mmol, 1.5 equiv.) was used and $BF_3 \bullet OEt_2$ was omitted from the Fischer indole reaction. **Ibogaine** (263 mg, 22% over three steps) was isolated as an orange foam.

Note: Para-methoxyphenylhydrazine • HCl (PMPH) is prone to decomposition and should be prepared fresh before use. Yields were diminished when using older bottles of PMPH.

R_f = 0.33 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.53 (s, 1H), 7.14 (d, *J* = 8.7 Hz, 1H), 6.93 (m, 1H), 6.77 (dd, *J* = 8.6, 2.4 Hz, 1H), 3.86 (s, 3H), 3.41 – 3.30 (m, 2H), 3.17–3.10 (m, 1H), 3.09 – 3.05 (m, 1H), 3.00 – 2.95 (m, 1H), 2.93 – 2.87 (m, 1H), 2.85 (s, 1H), 2.61 (dd, *J* = 17.3, 5.4 Hz, 1H), 2.09 – 2.00 (m, 1H), 1.85 (s, 1H), 1.83 – 1.77 (m, 1H), 1.65 (dq, *J* = 13.3, 3.5 Hz, 1H), 1.55 (q, *J* = 7.2 Hz, 2H), 1.48 – 1.43 (m, 1H), 1.24 – 1.18 (m, 1H), 0.90 (t, *J* = 7.1 Hz, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 153.98, 142.89, 130.13, 129.71, 110.75, 110.69, 109.17, 100.39, 57.48, 56.02, 54.19, 49.98, 41.97, 41.61, 34.22, 32.11, 27.84, 26.51, 20.71, 11.91
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{20}H_{27}N_2O^+$, 311.2128; found, 311.2128
IR (Smart iTX Diamond) = ν 3397, 3058 ,2917, 2854, 1624, 1585, 1452, 1433, 1361, 790 cm^{-1}

Note: Enantiopure (+)-ibogaine was synthesized from intermediate **(–)-S19**. Enantiopure (–)-ibogaine was synthesized from intermediate **(+)-S19.** Enantiopurity determined by HPLC (Section 5).

Specific Rotation for (+)-ibogaine = $[\alpha]_D^{20}$ = 50.1 (c = 0.01 in MeOH)
Enantomeric Excess (ee) = >99% (determined by chiral HPLC)

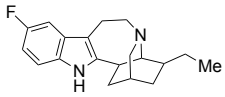


ibogamine (2)

Ibogamine (2)
Synthesized from compound **26** (500 mg, 1.46 mmol, 1 equiv.) following the general procedure for iboga derivative preparation. Phenylhydrazine • HCl (317 mg, 2.19 mmol, 1.50 equiv) was used in the Fischer indole reaction. **Ibogamine** (118 mg, 29% over 3 steps) was isolated as a yellow foam.

R_f = 0.37 (10:1 DCM/MeOH)

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.66 (br. s., 1H), 7.48 – 7.44 (dd, *J* = 6.95 Hz, 1.61 Hz, 1H), 7.27 – 7.24 (m, 1H), 7.14 – 7.05 (m, 2H), 3.47 – 3.28 (m, 2H), 3.22 – 3.12 (dt, *J* = 13.61 Hz, 3.71 Hz, 1H), 3.10 – 3.02 (m, 2H), 2.99 – 2.92 (m, 1H), 2.92 – 2.87 (m, 1H), 2.76 – 2.68 (m, 1H), 2.11 – 2.01 (m, 1H), 1.90 – 1.78 (m, 2H), 1.69 – 1.62 (m, 1H), 1.61 – 1.53 (m, 2H), 1.52 – 1.45 (m, 1H), 1.26 – 1.20 (m, 1H), 0.90 (t, *J* = 7.10 Hz, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 141.37, 134.67, 129.55, 121.10, 119.18, 117.89, 110.12, 109.04, 57.83, 54.35, 49.95, 41.76, 40.95, 33.97, 31.79, 27.59, 26.23, 20.44, 11.90
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{19}H_{25}N_2^+$, 281.2018; found, 281.2026
IR (Smart iTX Diamond) = ν 3399, 3052, 2920, 2850, 1671, 1602, 1494, 1461, 1362, 735 cm^{-1}



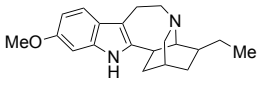
10-fluoroibogamine (29)

10-fluoroibogamine (29)
Synthesized from compound **26** (200 mg, 0.59 mmol, 1.00 equiv.) following the general procedure for iboga derivative preparation, with 4-fluorophenylhydrazine • HCl (143 mg, 0.88 mmol, 1.50 equiv.) being used in the Fischer indole reaction. **10-fluoroibogamine** (56 mg, 32% yield over 3 steps) was isolated as a clear orange oil.

R_f = 0.42 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.64 (s, 1H), 7.15 (dd, *J* = 8.7, 4.4 Hz, 1H), 7.10 (dd, *J* = 9.8, 2.5 Hz, 1H), 6.84 (td, *J* = 9.1, 2.5 Hz, 1H), 3.43 – 3.27 (m, 2H), 3.20 – 2.98 (m, 3H), 2.96 – 2.86 (m, 2H), 2.63 – 2.54 (m, 1H), 2.10 – 2.04 (m, 1H), 1.90 – 1.77 (m, 2H), 1.66 (m, 1H), 1.59 – 1.46 (m, 3H), 1.22 (m, 1H), 0.90 (t, *J* = 7.1 Hz, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 157.89 ($^1J_{CF}$ = 234.29 Hz), 143.72, 131.08, 130.11, 110.58 ($^1J_{CF}$ = 9.60 Hz), 109.53, 109.01 ($^1J_{CF}$ = 26.29 Hz), 103.03 ($^1J_{CF}$ = 22.72 Hz), 57.53, 54.19, 50.01, 41.89, 41.38, 34.08, 31.95, 27.77, 26.38, 20.59, 11.92
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{19}H_{24}N_2F^+$, 299.1928; found, 299.1925
IR (Smart iTX Diamond) = ν 3397, 3051, 2923, 2856, 1671, 1580, 1485, 1454, 1362, 734 cm^{-1}

Note: Enantiopure (+)-fluoroibogamine was synthesized from intermediate **(–)-S19**. Enantiopure (-)-fluoroibogamine was synthesized from intermediate **(+)-S19.**

Specific Rotation for (–)-fluoroibogamine = $[\alpha]_D^{20}$ = -35.3 (c = 0.01 in MeOH)
Specific Rotation for (+)-fluoroibogamine = $[\alpha]_D^{20}$ = 34.6 (c = 0.01 in MeOH)

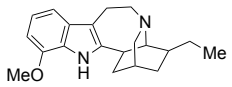


tabernanthine (4)

Tabernanthine (4)
Synthesized from compound **26** (200 mg, 0.59 mmol, 1.00 equiv.) following the general procedure for iboga derivative preparation, with 3-methoxyphenylhydrazine HCl (153 mg, 0.88 mmol, 1.5 equiv.) being used in the Fischer indole reaction. **Tabernanthine** (24 mg, 13.3% yield over 3 steps) was isolated as a clear orange oil.

R_f = 0.35

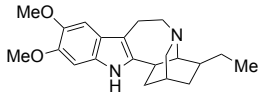
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.51 (s, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 6.77 (s, 1H) 6.76 (d, *J* = 8.5 Hz, 1H), 3.83 (s, 3H), 3.44 – 3.38 (m, 1H), 3.36 – 3.26 (m, 1H), 3.16 (td, *J* = 13.1, 3.7 Hz, 1H), 3.05 (d, *J* = 10.4 Hz, 2H), 2.95 – 2.87 (m, 2H), 2.66 (d, *J* = 16.3 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.87 – 1.77 (m, 2H), 1.67 – 1.51 (m, 4H), 1.24 – 1.20 (m, 1H), 0.90 (t, *J* = 7.1 Hz, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 155.86, 140.47, 135.35, 124.19, 118.46, 108.83, 108.48, 94.37, 57.77, 55.84, 54.11, 49.82, 41.88, 41.28, 34.19, 32.06, 27.67, 26.45, 20.72, 11.89
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{20}H_{27}N_2O^+$, 311.2128; found, 311.2127
IR (Smart iTX Diamond) = ν 3356, 2952, 2918, 2855, 1626, 1564, 1496, 1460, 1380, 735 cm^{-1}



12-methoxyibogamine (28)

12-methoxyibogamine (28)
Synthesized from compound **26** (200 mg, 0.59 mmol, 1.00 equiv.) following the general procedure for iboga derivative preparation, with 2-methoxyphenylhydrazine • HCl (153 mg, 0.88 mmol, 1.50 equiv.) was used in the Fischer indole reaction. **12-methoxyibogamine** (32 mg, 17.4% yield over 3 steps) was isolated as a clear yellow oil.

R_f = 0.31 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.85 (s, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.59 (dd, *J* = 7.7, 0.9 Hz, 1H), 3.94 (s, 3H), 3.41 – 3.31 (m, 2H), 3.19 – 3.05 (m, 2H), 3.02 – 2.92 (m, 2H), 2.86 (d, *J* = 2.0 Hz, 1H), 2.69 – 2.62 (m, 1H), 2.08 – 2.00 (m, 1H), 1.86 – 1.78 (m, 2H), 1.67 – 1.47 (m, 4H), 1.21 – 1.17 (m, 1H), 0.90 (t, *J* = 7.1 Hz, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 145.49, 141.51, 131.02, 124.72, 119.47, 110.89, 109.74, 101.25, 57.55, 55.33, 54.21, 49.97, 41.94, 41.47, 34.23, 32.10, 27.81, 26.51, 20.84, 11.89
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{20}H_{27}N_2O^+$, 311.2128; found, 311.2127
IR (Smart iTX Diamond) = ν 3398, 3049, 2919, 2854, 1684, 1577, 1499, 1456, 1386, 729 cm^{-1}



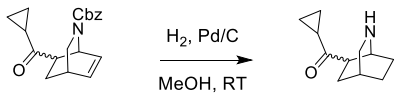
ibogaline (3)

Ibogaline (3)
Synthesized from compound **26** (200 mg, 0.59 mmol, 1.00 equiv.) following the general procedure for iboga derivative preparation, with 3,4-dimethoxyphenylhydrazine • HCl (179 mg, 0.88 mmol, 1.50 equiv.) being used in the Fischer indole reaction. **Ibogaline** (32 mg, 16.4% yield over 3 steps) was isolated as a brown oil.

R_f = 0.22 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.50 (s, 1H), 6.86 (s, 1H), 6.84 (s, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 3.47 – 3.35 (m, 3H), 3.22 – 2.93 (m, 5H), 2.38 – 2.26 (m, 1H), 2.00 – 1.83 (m, 3H), 1.77 – 1.68 (m, 1H), 1.57 – 1.37 (m, 3H), 0.89 (t, *J* = 7.24, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 147.19, 145.45, 137.15, 128.90, 120.90, 108.05, 99.82, 94.93, 60.54, 56.62, 56.45, 56.38, 47.28, 34.20, 33.36, 27.91, 26.93, 21.19, 18.64, 14.33, 11.93
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{21}H_{29}N_2O_2^+$, 341.2228; found, 341.2231
IR (Smart iTX Diamond) = ν 3339, 3053, 2931, 2874, 1631, 1566, 1484, 1463, 730 cm^{-1}

Note: We observed that ibogaline (**3**) is unstable and prolonged drying under high vacuum led to the presence of impurities in the ^{1}H NMR spectrum. We suspect that ibogaline is prone to

enhanced auto-oxidation due to the presence of two methoxy substituents on the indole ring system.[2]

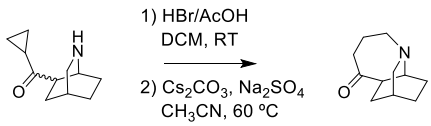


20 **S4**

((1*S*,4*R*)-2-azabicyclo[2.2.2]octan-6-yl)(cyclopropyl)methanone (S4)
A flask was charged with compound **20** (10.30 g, 33.07 mmol, 1.00 equiv.) and unreduced 10 wt % Pd/C (1.03 g, 0.96 mmol, 0.03 equiv.). The flask was evacuated and refilled with nitrogen 3 times. MeOH (330 mL, 0.1 M) was added in one portion and hydrogen gas was bubbled through the resulting solution for 1 min. The reaction mixture was stirred under hydrogen atmosphere at ambient temperature for 1 h after which it was filtered through a pad of celite. The reaction vessel and filter cake were washed with DCM (3 x 50 mL). The filtrate was concentrated under reduced pressure to afford compound **S4** (5.63 g, 95%) as a yellow oil. The epimers were not separated nor characterized individually.

Note: Based on LCMS analysis, we presume that a 50:50 ratio of C16 epimers is obtained. We observed that prolonged reaction times (>1.5 h) gave an over reduced product with a m/z of 182. We hypothesize that the cyclopropyl ketone is being reduced to the corresponding alcohol.

R_f = 0.10 (10:1 DCM/MeOH, 1% NH_4OH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (epimers observed) = 3.35 – 3.19 (m, 1H), 3.16 – 2.95 (m, 2H), 2.93 – 2.84 (m, 1H), 2.24 – 1.95 (m, 3H), 1.75 – 1.66 (m, 2H), 1.64 – 1.53 (m, 2H), 1.08 – 0.79 (m, 5H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (epimers observed) = 212.75, 210.44, 52.36, 51.28, 47.04, 46.74, 45.70, 45.41, 27.58, 26.71, 25.41, 24.49, 24.44, 24.23, 24.04, 23.52, 19.89, 19.73, 11.23, 10.86, 10.81, 10.67
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{11}H_{18}NO^+$, 180.1388; found, 180.1381



S4 **S3**

octahydro-3,10-methanopyrido[1,2-*a*]azepin-9(6*H*)-one (S3)
To a stirring solution of compound **S4** (5.63 g, 31.42 mmol, 1.00 equiv.) in DCM (31 mL, 1.0 M) was added 33 wt % HBr/AcOH (16.27 mL, 94.27 mmol, 3.00 equiv.) in one portion. The solution was stirred at ambient temperature for 2 h after which it was concentrated under reduced pressure. The residue was dried under high vacuum for 1 h and then stirred vigorously in diethyl ether (50 mL). The diethyl ether was decanted, and the residue was dried under high vacuum. The alkyl bromide (**S1** and **S2**) was isolated as a 1:1 mixture of diastereomers as an orange foam (10.71 g, 100% yield) and characterized by ^{1}H NMR.

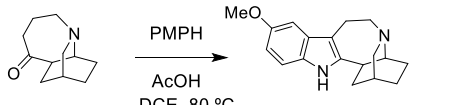
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 9.77 (b, 1 H), 9.26 (b, 2H), 7.71 (b, 1H), 4.01 (s, 1H), 3.93 (s, 1H), 3.62 – 3.24 (m, 8H), 2.92 – 2.41 (m, 6H), 2.27 – 2.00 (m, 8H), 1.98 – 1.85 (m, 2H), 1.79 – 1.54 (m, 8H)

[2] Taylor, W. I. The Iboga and Voacanga Alkaloids. *The Alkaloids: Chemistry and Physiology* , R. H. F. Manske Academic Press, 1965, vol. 8, pp. 203–235

Note: Attempts to obtain ^{13}C NMR data on the alkyl bromide were unsuccessful and decomposition was observed in $CDCl_3$. The compound can be stored for <10 days in a freezer under a N_2 atmosphere. Significant discoloration and decomposition were observed with prolonged storage.

A flask was charged with a 1:1 mixture of alkyl bromide diastereomers **S1** and **S2** (10.71 g, 31.41 mmol, 1.00 equiv.), anhydrous Cs_2CO_3 (15.35 g, 47.13 mmol, 1.50 equiv.), and anhydrous Na_2SO_4 (13.38 g, 94.26 mmol, 3.00 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous CH_3CN (314 mL, 0.1 M) was added in one portion. The reaction mixture was heated to 60 °C and stirred for 6 h. The heterogeneous mixture was cooled to ambient temperature and filtered. The reaction vessel and filter cake were washed with DCM. The filtrate was concentrated under reduced pressure and the residue was purified via chromatography on silica gel (20:1 DCM/MeOH) to afford compound **S3** (2.31 g, 41% over 2 steps) as a light brown oil.

R_f = 0.40 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 3.20 – 3.17 (m, 1H), 3.10 – 2.98 (m, 2H), 2.92 (dd, J = 9.6, 4.1 Hz, 1H), 2.88 – 2.81 (m, 1H), 2.59 (d, J = 9.7 Hz, 1H), 2.54 (dd, J = 12.5, 6.8 Hz, 1H), 2.49 (d, J = 12.5 Hz, 1H), 2.07 – 1.93 (m, 3H), 1.93 – 1.84 (m, 1H), 1.80 – 1.76 (m, 1H), 1.74 – 1.65 (m, 1H), 1.61 – 1.47 (m, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 216.49, 54.40, 51.61, 50.56, 50.37, 43.50, 29.56, 28.47, 25.82, 23.74, 20.80
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{11}H_{18}NO^+$, 180.1388; found, 180.1384

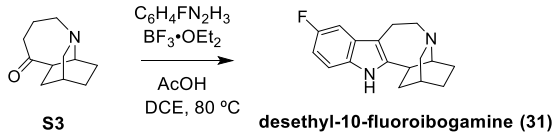


S3 **desethylibogaine (30)**

Desethylibogaine (30)
A flask was charged with compound **S3** (1.25 g, 6.97 mmol, 1.00 equiv.) and para-methoxyphenylhydrazine • HCl (1.82 g, 10.45 mmol, 1.50 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous DCE (69.70 mL, 0.10 M) and AcOH (5.98 mL, 104.59 mmol, 15.00 equiv.) was added. The resulting mixture was degassed by bubbling nitrogen through the solution for 10 min. The flask was heated to 80 °C and stirred for 12 h after which it was cooled to ambient temperature and diluted with DCM (30 mL). Saturated aqueous $NaHCO_3$ was added to the reaction mixture until the pH was adjusted to 7-8. The organic layer was separated, and the aqueous layer was further extracted with DCM (2 x 50 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. Purification via chromatography on silica gel (gradient elution 20:1→10:1 DCM/MeOH, 0.25% NH_4OH) afforded desethylibogaine **30** (1.65 g, 84%) as a yellow foam.

R_f = 0.38 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.61 (s, 1H), 7.14 (d, *J* = 8.6 Hz, 1H), 6.93 (s, 1H), 6.77 (d, *J* = 9.9 Hz, 1H), 3.86 (s, 3H), 3.42 – 3.33 (m, 1H), 3.32 – 3.19 (m, 3H), 3.17–3.09 (m, 2H), 2.98 (dd, *J* = 11.8, 4.7 Hz, 1H), 2.73–2.65 (m, 1H), 2.19 – 2.08 (m, 2H), 1.95 – 1.88 (m, 1H), 1.82 – 1.57 (m, 4H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 154.22, 142.34, 129.90, 129.75, 111.17, 111.13, 109.05, 100.33, 56.15, 54.48, 54.25, 50.18, 39.23, 34.58, 29.16, 25.32, 23.41, 20.05

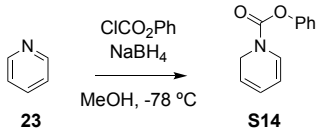
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{18}H_{23}N_2O^+$, 283.1808; found, 283.1815
IR (Smart iTX Diamond) = ν 3392, 3048, 2927, 2834, 1623, 1587, 1515, 1484, 1364, 731 cm^{-1}



S3 **desethyl-10-fluoroibogamine (31)**

Desethyl-10-fluoroibogamine (31)
A flask was charged with compound **S3** (1.10 g, 6.13 mmol, 1.00 equiv.) and para-fluorophenylhydrazine • HCl (1.49 g, 9.20 mmol, 1.50 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which anhydrous DCE (61.30 mL, 0.1 M) and AcOH (5.25 mL, 91.95 mmol, 15.00 equiv.) was added. The resulting mixture was degassed by bubbling nitrogen through the solution for 10 min. The flask was heated to 80 °C and stirred for 1 h after which it was cooled to ambient temperature and BF_3 • OEt_2 (0.907 mL, 7.35 mmol, 1.20 equiv.) was added in one portion. The resulting mixture was heated at 80 °C for 12 h after which it was cooled to ambient temperature and diluted with DCM (100 mL). Saturated aqueous $NaHCO_3$ was added to the reaction mixture until the pH was adjusted to 7-8. The organic layer was separated, and the aqueous layer was further extracted with DCM (2 x 50 mL). The combined organic fractions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification via chromatography on silica gel (gradient elution 20:1→10:1 DCM/MeOH, 0.25% NH_4OH) afforded **desethyl-10-fluoroibogamine** (1.33 g, 80%) as an orange foam.

R_f = 0.44 (10:1 DCM/MeOH)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.84 (s, 1H), 7.14 (dd, *J* = 8.7, 4.4 Hz, 1H), 7.09 (dd, *J* = 9.8, 2.5 Hz, 1H), 6.83 (ddd, *J* = 9.3, 8.7, 2.5 Hz, 1H), 3.39 – 3.22 (m, 3H), 3.13 (d, *J* = 2.5 Hz, 2H), 3.04 (dt, *J* = 3.7, 1.8 Hz, 1H), 2.96 (ddd, *J* = 11.6, 4.7, 1.7 Hz, 1H), 2.62 – 2.50 (m, 1H), 2.02 (ddt, *J* = 13.4, 9.9, 4.8 Hz, 2H), 1.89 (p, *J* = 2.9 Hz, 1H), 1.80 – 1.62 (m, 4H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 157.88 ($^1J_{CF}$ = 233.7 Hz), 143.87, 130.96, 130.09 ($^1J_{CF}$ = 9.3 Hz), 110.68 ($^1J_{CF}$ = 9.7 Hz), 109.67, 108.93 ($^1J_{CF}$ = 26.2 Hz), 102.91 ($^1J_{CF}$ = 23.4 Hz), 54.04, 53.76, 50.03, 40.04 (d, *J* = 3.4 Hz), 34.70, 29.88, 25.54, 23.64, 20.18
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{17}H_{20}FN_2^+$, 271.1608; found, 271.1609
IR (Smart iTX Diamond) = ν 3164, 3048, 2939, 2873, 1701, 1654, 1583, 1451, 1390, 732 cm^{-1}

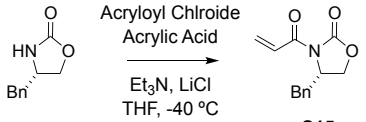


23 **S14**

phenyl pyridine-1(2*H*)-carboxylate (S14)
A flask was charged with methanol (200 mL, 0.5M) and pyridine (8.05 mL, 100 mmol, 1.00 equiv.) and cooled to -78 °C after which sodium borohydride (4.54 g, 120 mL, 120 mmol) was added in one portion. Phenyl chloroformate (15.05 mL, 120 mmol, 1.20 equiv.) was added dropwise over 1 h to the reaction mixture. The reaction mixture was stirred at -78°C for an additional 3 h after which it was diluted in Et_2O (100 mL), poured into 1 M HCl (200 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 x 100 mL) and the combined organic extracts were washed with 1 M NaOH (50 mL) followed by brine (50 mL). The organic extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue

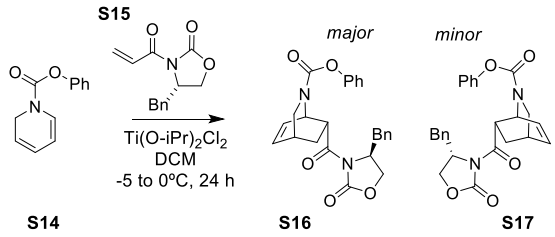
was recrystallized from ethanol to afford compound **S14** (18.71 g, 93%) as a crystalline white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.39 (t, *J* = 7.9 Hz, 2H), 7.28 – 7.21 (m, 1H), 7.20 – 7.12 (m, 2H), 6.95 – 6.79 (m, 1H), 5.91 (m, 1H), 5.66 – 5.53 (m, 1H), 5.33 – 5.21 (m, 1H), 4.60 (dd, *J* = 4.1, 2.1 Hz, 1H), 4.47 (dd, *J* = 4.1, 2.1 Hz, 1H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed) = 152.46, 151.43, 150.88, 150.70 (d, *J* = 10.0 Hz), 129.29, 125.99, 125.61 (d, *J* = 4.5 Hz), 125.29, 122.16, 121.77, 121.48, 119.39, 118.84, 105.94, 105.75, 44.21, 43.73
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{12}H_{12}NO_2^+$, 202.0868; found, 202.0866



(*S*)-3-acryloyl-4-benzyloxazolidin-2-one (S15)
A flask was sequentially charged with THF (250 mL, 0.20 M), acrylic acid (4.44 mL, 64.77 mmol, 1.30 equiv.) and triethylamine (17.36 mL, 124.57 mmol, 2.50 equiv.) under nitrogen atmosphere and cooled to -40 °C using a dry ice/acetonitrile cooling bath. Acryloyl chloride (4.83 mL, 59.78 mmol, 1.20 equiv.) was added dropwise to the reaction mixture and the resulting milky yellow solution was stirred at -40 °C for 1 h. Lithium chloride (2.64 g, 62.27 mmol, 1.25 equiv.) followed by (*S*)-4-benzyloxazolidin-2-one (8.83 g, 49.82 mmol, 1.00 equiv.) was added in one portion to the reaction mixture and the solution was slowly warmed to ambient temperature over the course of 24 h. The reaction mixture was then concentrated under reduced pressure and the resulting residue was dissolved in DCM (200 mL) and poured into a solution of 2 M HCl (100 mL). The layers were separated, and the aqueous layer was washed with DCM (2 x 100 mL). The organic extracts were combined, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified via chromatography on silica gel (gradient elution hexanes→7:3 hexanes/EtOAc) to afford compound **S15** (7.83 g, 68%) as a white solid.

R_f = 0.6 (7:3 hexanes/EtOAc)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.51 (dd, *J* = 17.0, 10.4 Hz, 1H), 7.40 – 7.17 (m, 5H), 6.61 (dd, *J* = 17.0, 1.8 Hz, 1H), 5.94 (dd, *J* = 10.4, 1.8 Hz, 1H), 4.74 (ddt, *J* = 9.5, 7.0, 3.4 Hz, 1H), 4.30 – 4.14 (m, 2H), 3.35 (dd, *J* = 13.4, 3.3 Hz, 1H), 2.81 (dd, *J* = 13.4, 9.5 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 164.91, 153.34, 135.23, 131.94, 129.46, 129.01, 127.41, 127.38, 66.29, 55.32, 37.82
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{13}H_{14}NO_3^+$, 232.0978; found, 232.0971



Phenyl (1*R*,4*R*,7*R*)-7-((*S*)-4-benzyl-2-oxooxazolidine-3-carbonyl)-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (S16)

A flask was sequentially charged with activated 4Å molecular sieves (16.00 g), compound **S15** (6.50 g, 28.10 mmol, 1.00 equiv.), and $Ti(O\text{-}iPr)_2Cl_2$ (11.78 g, 49.73 mmol, 1.77 equiv.). The flask was evacuated and refilled with nitrogen 3 times after which DCM (175 mL) was added and the resulting milky solution was stirred at ambient temperature for 1 h. The flask was then cooled to 0 °C in an ice bath and a solution of compound **S14** (11.31 mmol, 56.20 mmol, 2.00 equiv.) in DCM (175 mL) was added dropwise over 30 min. The reaction mixture was stirred at -10 °C to 0 °C for 48 h after which it was quenched with saturated aqueous $NaHCO_3$ (200 mL). The organic layer was separated, and the aqueous layer was washed with DCM (2 x 200 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The reside was purified via chromatography on silica gel (gradient elution 10:1→7:3 hexanes/EtOAc) to afford compound **S16** and **S17** (11.91 g, 98%, 77:23) as a white foam. The diastereomeric ratio of the unpurified residue is 77:23 (^{1}H NMR) and major diastereomer **S16** (9.17 g, 75%) can be separated via chromatography.

Note: The reaction was performed in a NaCl/ice bath placed in a cold room (~5 °C). Cooling bath temperatures ranged from -10 °C to 0 °C over the course of 48 hours. On larger scales, it is advised to filter the quenched reaction mixture over a bed of celite to remove the molecular sieves. The exact structure of diastereomer **S16** was assigned retroactively after completing the synthesis of (+)-ibogaine and comparing its chiral LCMS spectra with that of racemic ibogaine and natural (–)-ibogaine.

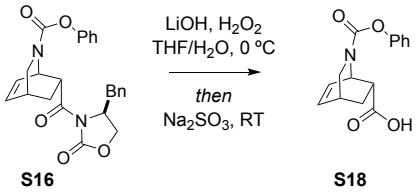
Major Isomer (S16)

R_f = 0.25 (7:3 hexanes/EtOAc)

^{1}H NMR (400 MHz, MeOD) δ (ppm) (rotamers observed) = 7.46 – 7.10 (m, 10H), 6.65 – 6.43 (m, 2H), 5.28 (ddd, *J* = 6.1, 2.8, 1.3 Hz, 0.5H), 5.12 (ddd, *J* = 5.8, 2.7, 1.5 Hz, 0.5H), 4.73 – 4.58 (m, 1H), 4.34 – 4.13 (m, 3H), 3.59 (dd, *J* = 10.3, 2.0 Hz, 0.5H), 3.38 (dd, *J* = 10.5, 2.0 Hz, 0.5H), 3.28 – 3.20 (m, 0.5H), 3.14 (dd, *J* = 13.5, 3.3 Hz, 1H), 3.07 – 3.01 (m, 0.5H), 2.92 (dtd, *J* = 15.0, 7.8, 4.1 Hz, 2H), 2.24 – 2.14 (m, 0.5H), 2.10 – 1.99 (m, 0.5H), 1.97 – 1.87 (m, 0.5H), 1.82 – 1.71 (m, 0.5H)

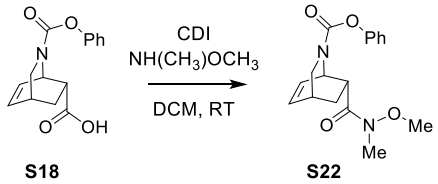
^{13}C NMR (101 MHz, MeOD) δ (ppm) (rotamers observed) = 173.93, 173.53, 155.26, 154.85, 154.71, 152.72, 152.68, 137.01, 136.95, 136.69, 135.83, 132.05, 130.84, 130.59, 130.57, 130.31, 130.29, 129.83, 129.78, 128.20, 126.46, 123.02, 122.92, 67.88, 67.81, 56.64, 56.56, 45.81, 45.39, 38.48, 38.33, 32.20, 31.95, 28.34, 27.44.

HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{25}H_{25}N_2O_5^+$, 433.1768; found, 433.1760



(1*R*,4*R*,6*R*)-2-(phenoxycarbonyl)-2-azabicyclo[2.2.2]oct-7-ene-6-carboxylic acid (S18)
A flask was sequentially charged with compound **S16** (8.50 g, 19.65 mmol, 1.00 equiv.), THF (260 mL) and 30% aqueous H_2O_2 (9.23 mL, 90.39 mmol , 4.60 equiv.) and cooled to 0 °C in an ice bath. A solution of LiOH (753 mg, 31.44 mmol, 1.60 equiv.) in H_2O (130 mL) was added via syringe pump (30 mL/hr) to the reaction and the resulting solution was slowly warmed to ambient temperature over 5 h. A solution of Na_2SO_3 (12.35 g, 98.05 mmol, 4.98 equiv.) in H_2O (50 mL) was added and the reaction mixture was stirred at ambient temperature for 1 h. A 5 M solution of aqueous NaOH (75 mL) was added and the resulting mixture was poured into DCM (100 mL) and the layers were separated. The aqueous layer was washed with DCM (2 x 50 mL) and then acidified to pH 3 with 4 M HCl (100 mL). The acidic aqueous layer was then extracted with DCM (3 x 150 mL) and the organic extracts were combined, dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford compound **S18** (5.21 g , 97%) as a white solid.

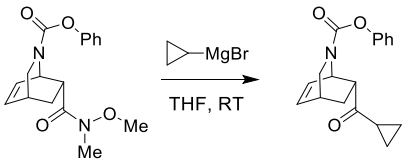
^{1}H NMR (400 MHz, MeOD) δ (ppm) (rotamers observed): 7.44 – 7.30 (m, 2H), 7.27 – 7.19 (m, 1H), 7.18 – 7.07 (m, 2H), 6.55 (ddd, *J* = 8.2, 6.6, 1.5 Hz, 1H), 6.43 (tdd, *J* = 8.0, 5.9, 1.5 Hz, 1H), 5.24 (ddd, *J* = 5.9, 3.3, 1.3 Hz, 0.5H), 5.11 (ddd, *J* = 5.9, 3.3, 1.4 Hz, 0.5H), 3.54 (dd, *J* = 10.3, 2.2 Hz, 1H), 3.29 – 3.10 (m, 2H), 3.09 – 2.88 (m, 2H), 2.06 – 1.80 (m, 2H)
^{13}C NMR (101 MHz, MeOD) δ (ppm) (rotamers observed) = 175.85, 155.52, 154.90, 152.68, 137.08, 137.00, 131.23, 131.10, 130.39, 130.33, 126.55, 126.51, 122.89, 44.89, 44.59, 32.09, 31.80, 26.95, 26.83
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{15}H_{16}NO_4^+$, 274.1078; found, 274.1071
Specific Rotation = $[\alpha]_D^{20}$ = 8.4 (c = 0.15 in MeOH)



Phenyl(1*R*,4*R*,7*R*)-7-(methoxy(methyl)carbamoyl)-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (S22)
To a stirring solution of compound **S18** (4.85 g, 17.74 mmol, 1.00 equiv.) in DCM (88 mL, 0.20 M) was added 1,1'-carbonyldiimidazole (CDI) (3.74 g, 23.06 mmol, 1.30 equiv.) in one portion. The resulting clear solution was stirred at ambient temperature for 1 h after which N,O-dimethylhydroxylamine hydrochloride (3.46 g, 35.48 mmol, 2.00 equiv.) was added in one portion. The mixture was stirred at ambient temperature for 12 h after which 4 M HCl (100 mL) was added, and the layers were separated. The aqueous layer was further extracted with DCM (2 x 100 mL) and the combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure to afford compound **S22** (5.55 g, 99%) as a white solid.

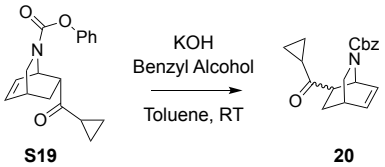
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.32 (ddd, *J* = 8.2, 7.2, 2.3 Hz, 2H), 7.19 – 7.07 (m, 3H), 6.54 – 6.38 (m, 2H), 5.20 – 5.03 (m, 1H), 3.70 (d, *J* = 4.4 Hz, 3H), 3.53 – 3.32

(m, 2H), 3.22 – 3.03 (m, 4H), 2.87 (dq, *J* = 5.1, 2.6 Hz, 1H), 1.97 (dddd, *J* = 12.5, 9.6, 5.6, 2.6 Hz, 1H), 1.77 (dddd, *J* = 12.3, 9.3, 4.7, 2.9 Hz, 1H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed) = 153.50, 152.92, 151.34, 134.66, 134.18, 130.96, 130.50, 129.28, 129.23, 125.19, 121.74, 121.63, 61.41, 61.30, 47.76, 47.36, 47.32, 47.05, 42.38, 41.82, 30.87, 30.60, 27.56, 27.34
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{17}H_{21}N_2O_4^+$, 317.1498; found, 317.1799
Specific Rotation = $[\alpha]_D^{20}$ = 18.4 (c = 0.10 in MeOH)



phenyl(1*R*,4*R*,7*R*)-7-(cyclopropanecarbonyl)-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (S19)
A flask was charged with compound **S22** (5.55 g, 17.56 mmol, 1.00 equiv.) after which THF (175 mL, 0.1 M) was added under a stream of nitrogen. A solution of 1.0 M cyclopropyl magnesium bromide (52.68 mL, 52.68 mmol, 3.00 equiv.) was added dropwise over 2 h to the reaction mixture at ambient temperature. The resulting solution was stirred at ambient temperature for 1 h after which it was quenched with saturated aqueous NH_4Cl (100 mL). The mixture was diluted in DCM (200 mL) and poured into water (100 mL). The layers were separated, and the aqueous layer was further washed with DCM (2 x 100 mL). The organic fractions were collected, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified via chromatography on silica gel (7:3 hexanes/EtOAc) to afford compound **S19** (5.01 g, 96%) as a white solid.

R_f = 0.45 (7:3 hexanes/EtOAc)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) (rotamers observed): 7.36 (tt, *J* = 6.9, 2.1 Hz, 2H), 7.19 (td, *J* = 7.2, 1.3 Hz, 1H), 7.16 – 7.09 (m, 2H), 6.50 – 6.27 (m, 2H), 5.32 (dq, *J* = 3.0, 1.3 Hz, 1H), 3.56 – 3.36 (m, 2H), 3.23 – 3.06 (m, 1H), 2.92 (s, 1H), 2.10 – 1.77 (m, 3H), 1.08 – 0.84 (m, 4H)
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) (rotamers observed) = 208.72, 208.37, 151.33, 135.03, 130.13, 129.29, 129.25, 125.28, 121.73, 52.69, 52.17, 47.67, 47.17, 30.83, 30.54, 25.12, 24.32, 19.45, 19.34, 11.52, 11.39, 10.97, 10.71
HRMS (ESI) = *m/z* $[M + H]^+$ calcd. For $C_{18}H_{20}NO_3^+$, 298.1438; found, 298.1433
Specific Rotation = $[\alpha]_D^{20}$ = 12.5 (c = 0.15 in MeOH)
Enantomeric Excess (ee) = 97.31%



benzyl (1*S*,4*S*)-7-(cyclopropanecarbonyl)-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (20)
A flask was sequentially charged with compound **S19** (5.00 g, 16.81 mmol, 1.00 equiv.), toluene (84 mL, 0.2 M) and benzyl alcohol (2.09 mL, 20.17 mmol, 1.20 equiv.). Powdered KOH (1.13 g, 20.17, 1.20 equiv.) was added to the reaction mixture in one portion and the resulting solution was stirred at ambient temperature for 12 h. The reaction was diluted in DCM (100 mL), poured into water (50 mL) and the layers were separated. The aqueous layer was washed with DCM (2

x 50 mL) and the combined organic extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified via chromatography on silica gel (7:3 hexanes/EtOAc) to afford compound **20** (4.92 g, 94%) as a light-yellow oil.

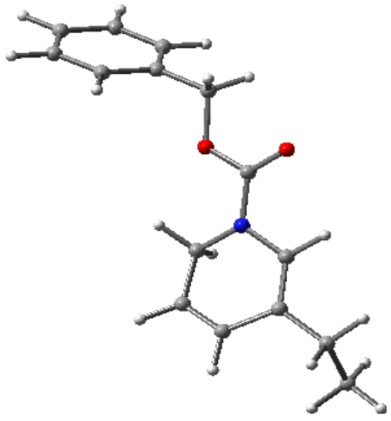
Note: Spectral data for compound **20** is in accordance with a previously noted procedure. Compound **20** was isolated as a 50:50 ratio of C16 epimers.

3. Quantum Chemical Calculations

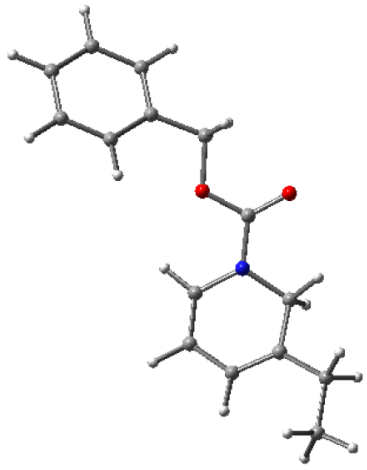
Structures were optimized at the M06-2X/6-31+G(d,p) level of theory, which is known to perform well for organic reactions.[3] Stationary points were characterized as minima via vibrational frequency analysis. Energies shown in the text are relative free energies at 298 K. All computations were carried out using Gaussian16.[4]

M06-2X/6-31+G(d,p)

Sum of electronic and thermal Free Energies=
-786.483725
+1.4 kcal/mol

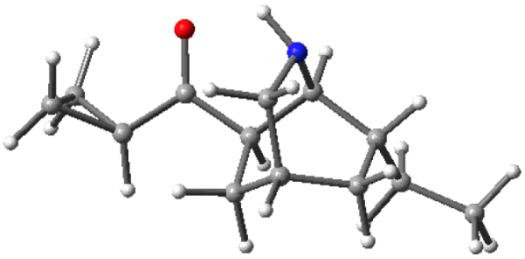


Sum of electronic and thermal Free Energies=
-786.485991
[0.0]

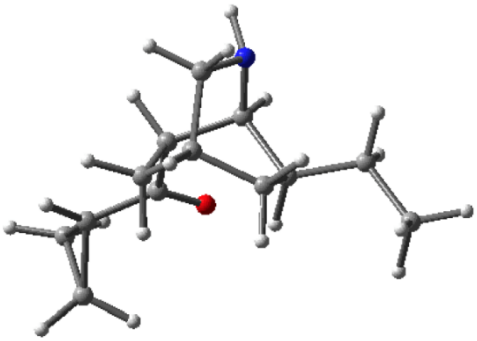


[3] (a) The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06 Functionals and Twelve Other Functionals. Zhao, Y. and Truhlar, D. G. Theor. Chem. Acc. 2008, 120, 215-241. (b) Density Functionals with Broad Applicability in Chemistry. Zhao, Y. and Truhlar, D. G. Acc. Chem. Res. 2008, 41, 157-167 (c) How Accurate Are the Minnesota Density Functionals for Noncovalent Interactions, Isomerization Energies, Thermochemistry, and Barrier Heights Involving Molecules Composed of Main-Group Elements? Mardirossian, N.; Head-Gordon, M. J. Chem. Theory Comput. 2016, 12, 4303-4325.

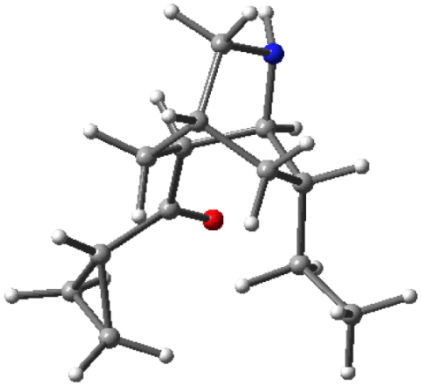
[4] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.



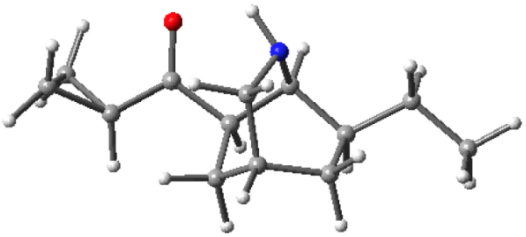
Sum of electronic and thermal Free Energies=
-637.446379
+0.6 kcal/mol



Sum of electronic and thermal Free Energies=
-637.445782
+1.0 kcal/mol



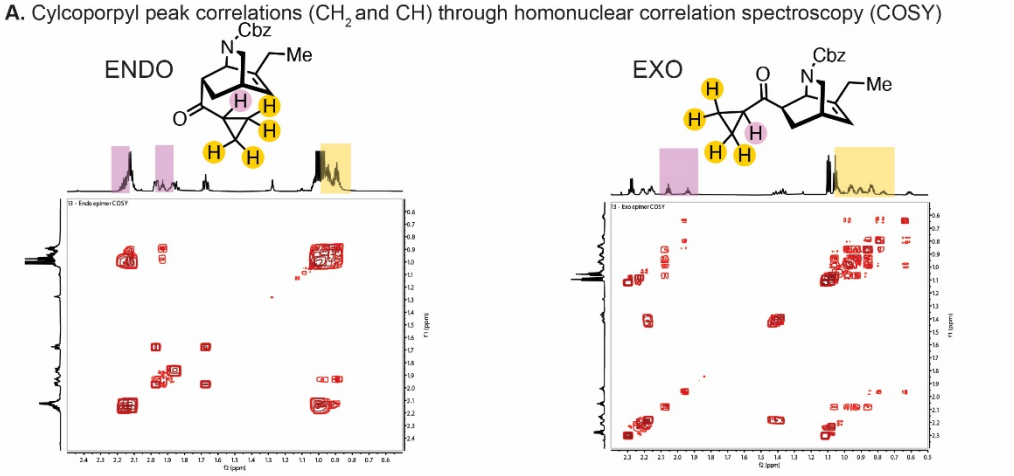
Sum of electronic and thermal Free Energies=
-637.442088
+3.3 kcal/mol



Sum of electronic and thermal Free Energies=
-637.447352
[0.0]

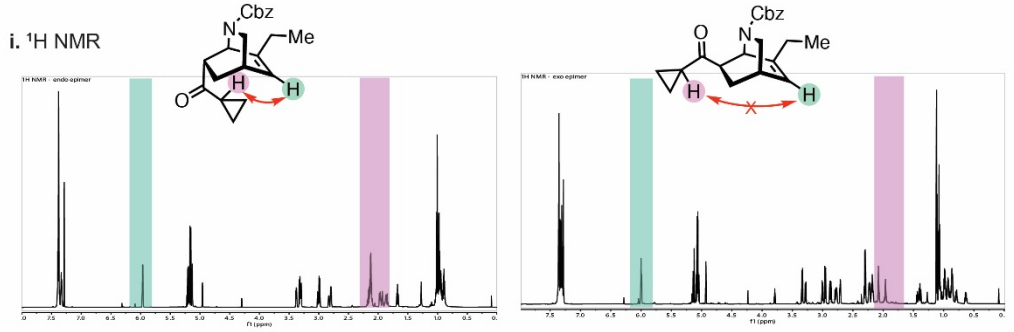
4. Characterization of Intermediate 13

A. Cylcoporpyl peak correlations (CH_2 and CH) through homonuclear correlation spectroscopy (COSY)

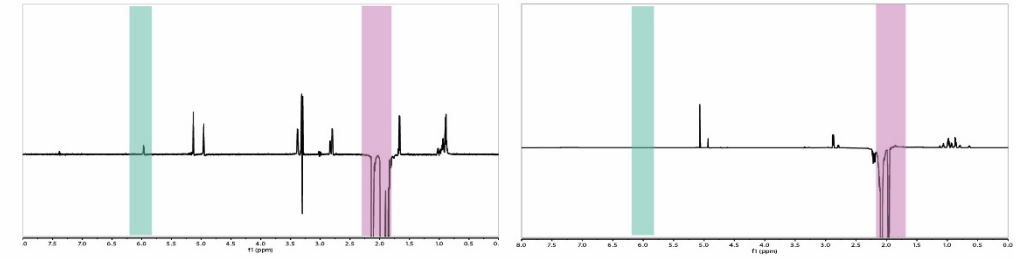


B. Observed correlations through 1D Selective NOESY shows correlations between methine of cyclopropyl in endo epimer, but not in exo epimer

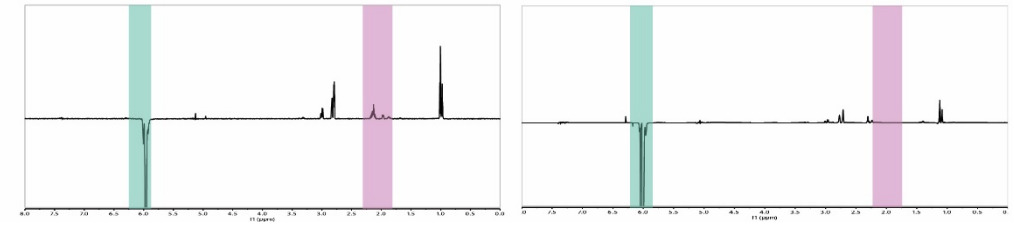
i. ^{1}H NMR



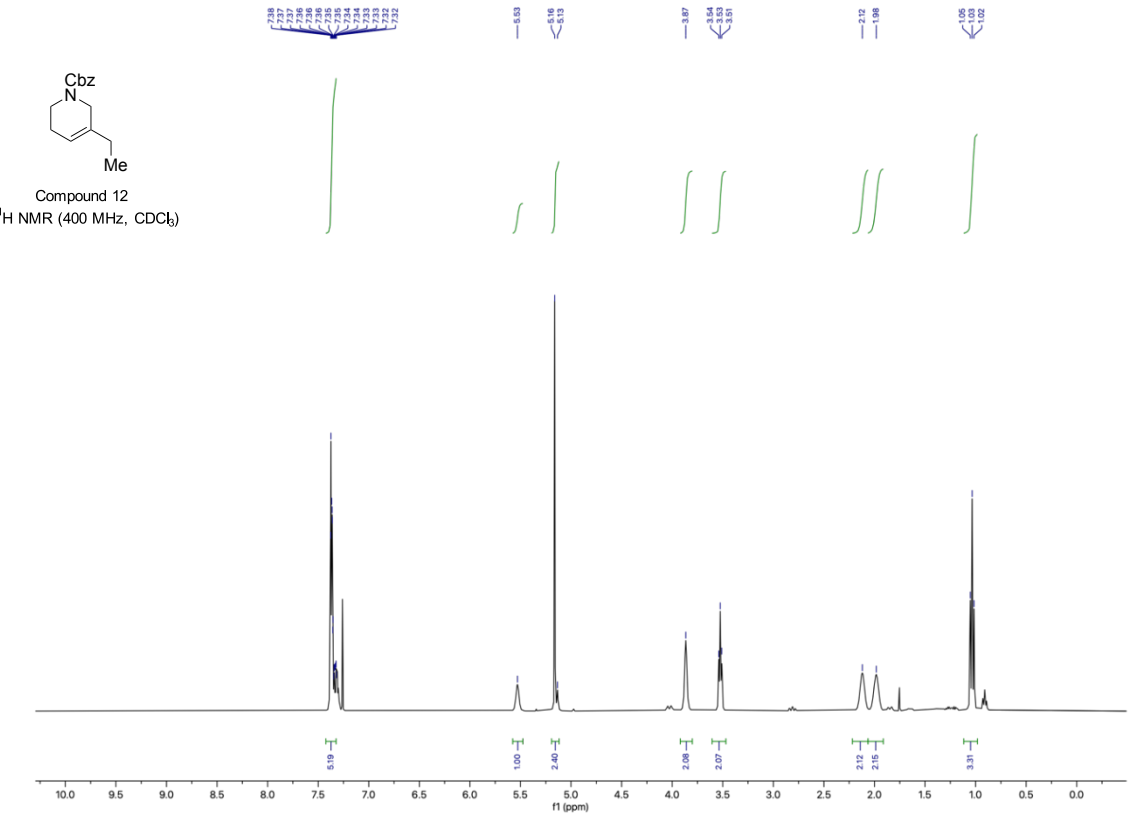
ii. 1D Selective NOESY - cyclopropyl methine proton suppressed



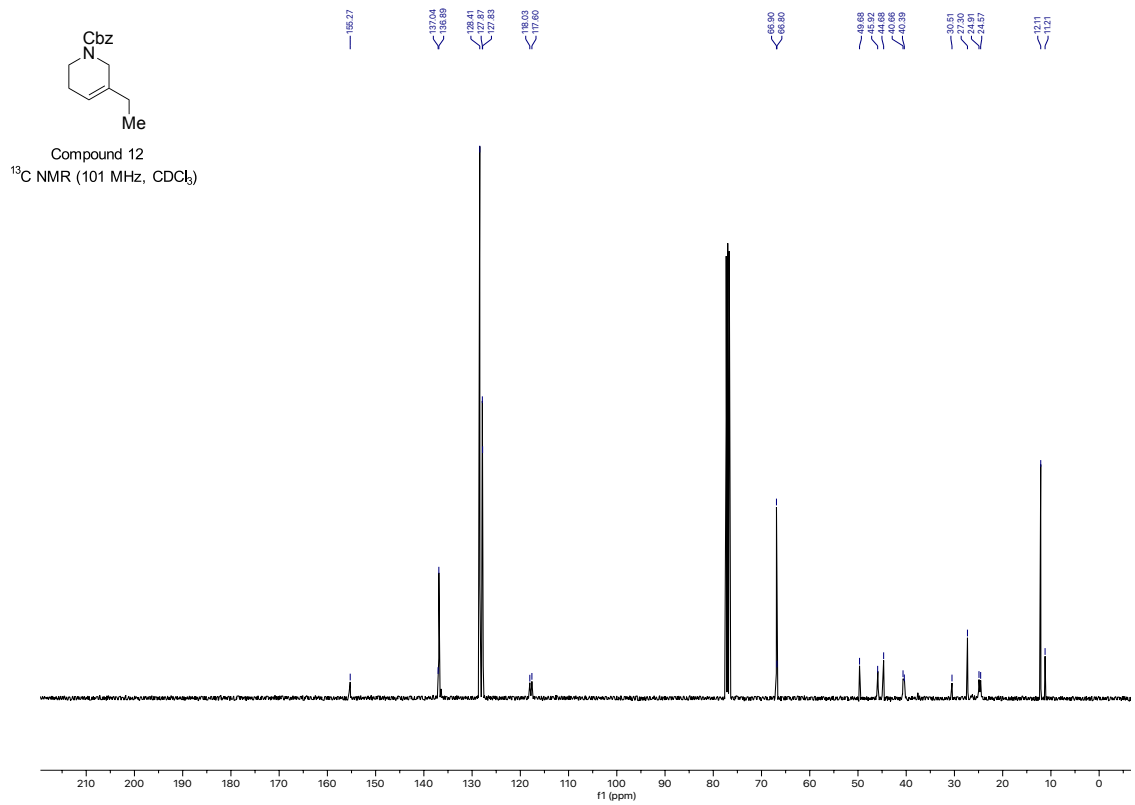
iii. 1D Selective NOESY - olefinic proton suppressed



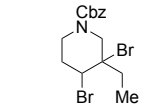
5. ^{1}H and ^{13}C Spectra



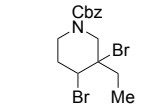
Compound 12
^{1}H NMR (400 MHz, $CDCl_3$)



Compound 12
^{13}C NMR (101 MHz, $CDCl_3$)



Compound S20
^{1}H NMR (400 MHz, $CDCl_3$)



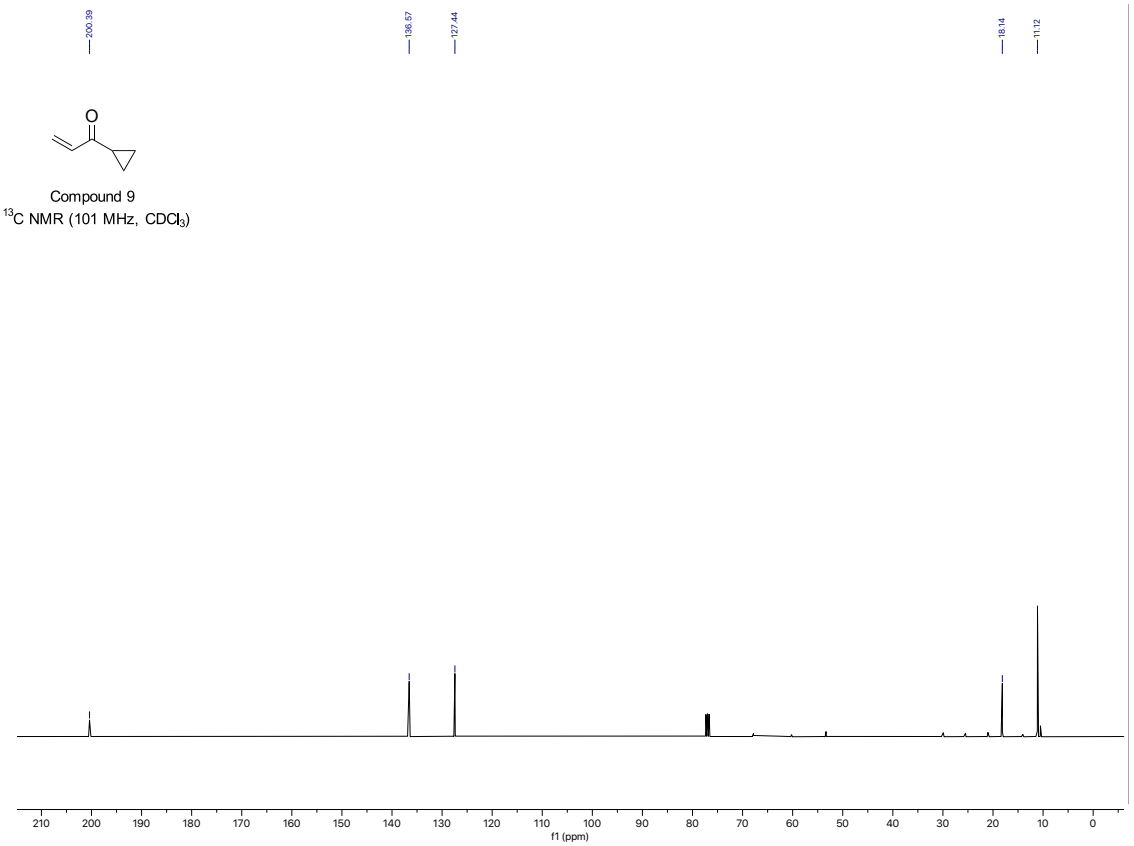
Compound S20
^{13}C NMR (101 MHz, $CDCl_3$)

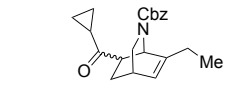
Compound 9

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

Compound 9

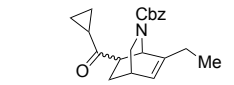
^{13}C NMR (101 MHz, $CDCl_3$)





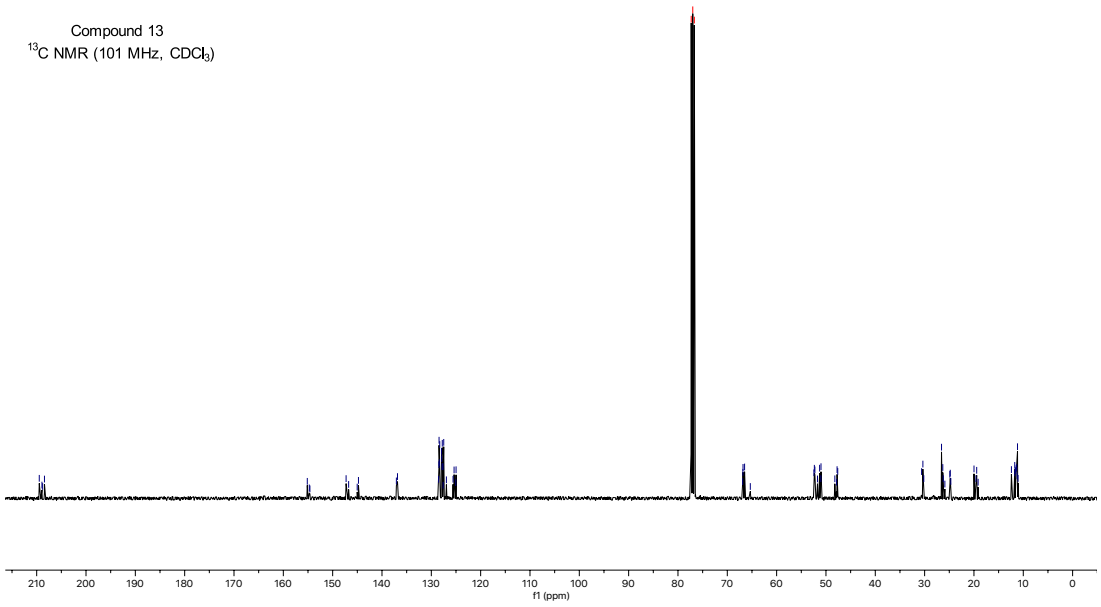
Compound 13

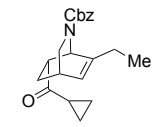
^{1}H NMR (400 MHz, $CDCl_3$)



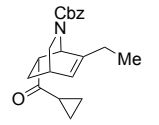
Compound 13

^{13}C NMR (101 MHz, $CDCl_3$)

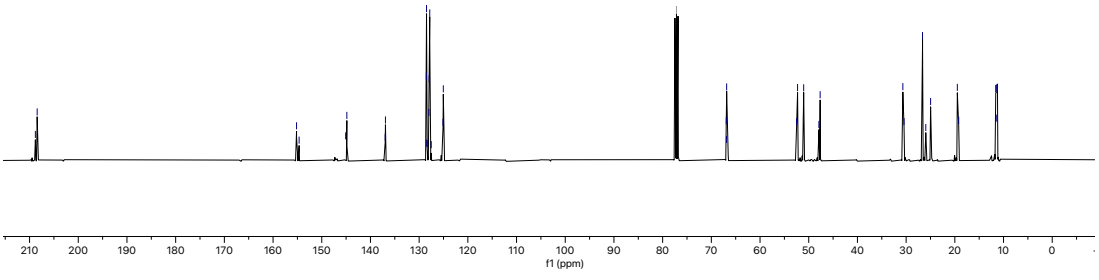


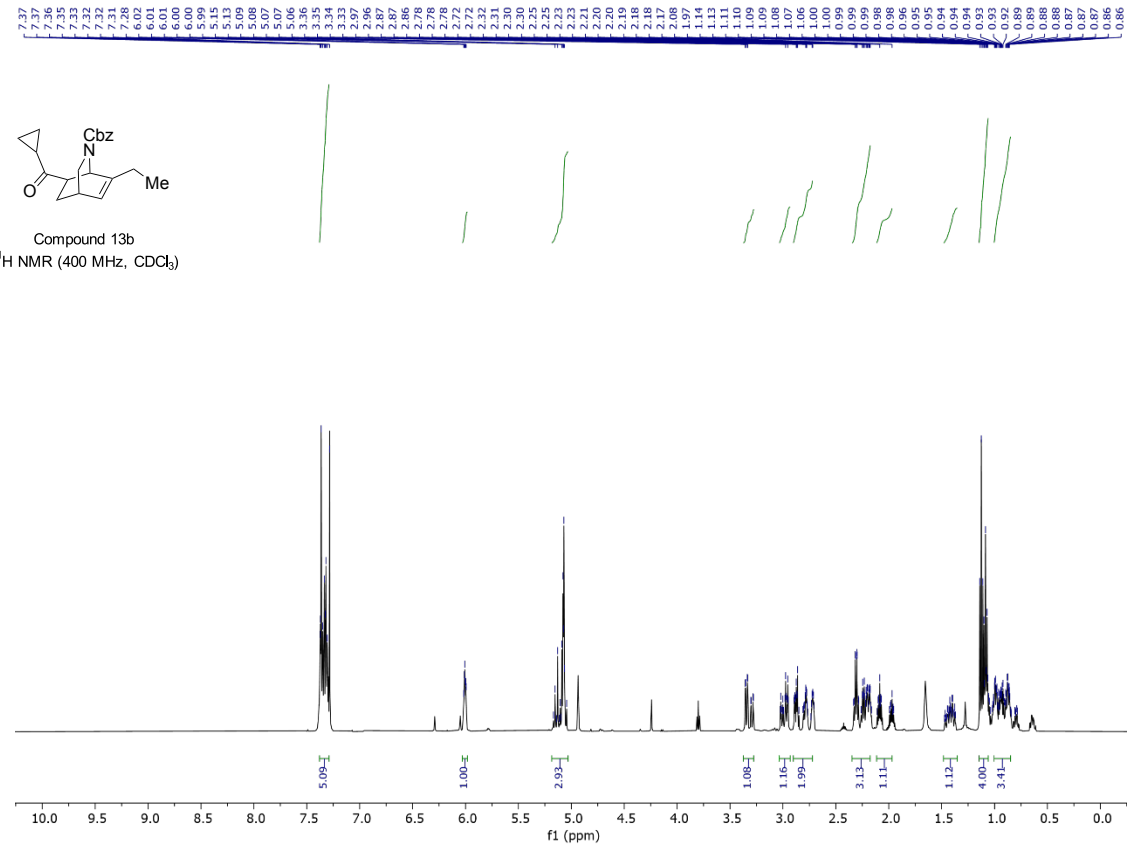


Compound 13a
^{1}H NMR (400 MHz, $CDCl_3$)

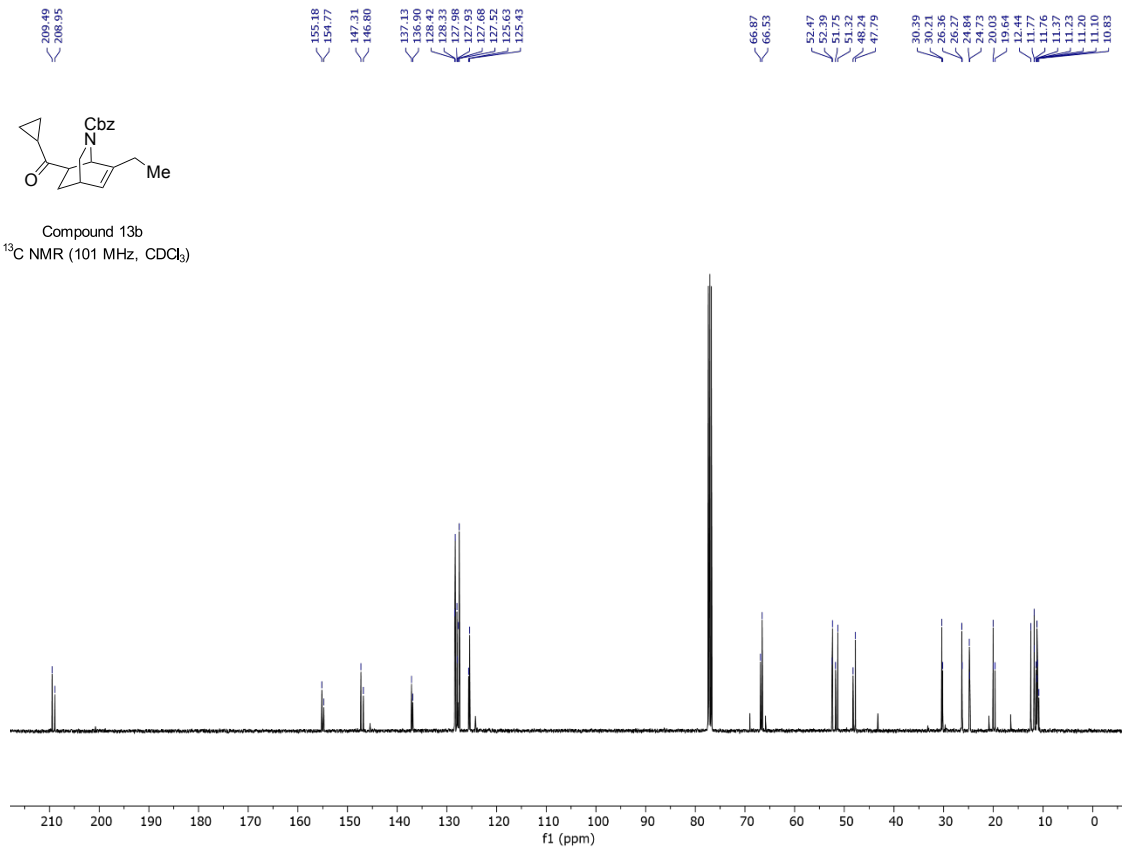


Compound 13a
^{13}C NMR (101 MHz, $CDCl_3$)

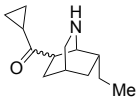




Compound 13b
^{1}H NMR (400 MHz, $CDCl_3$)

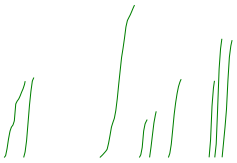


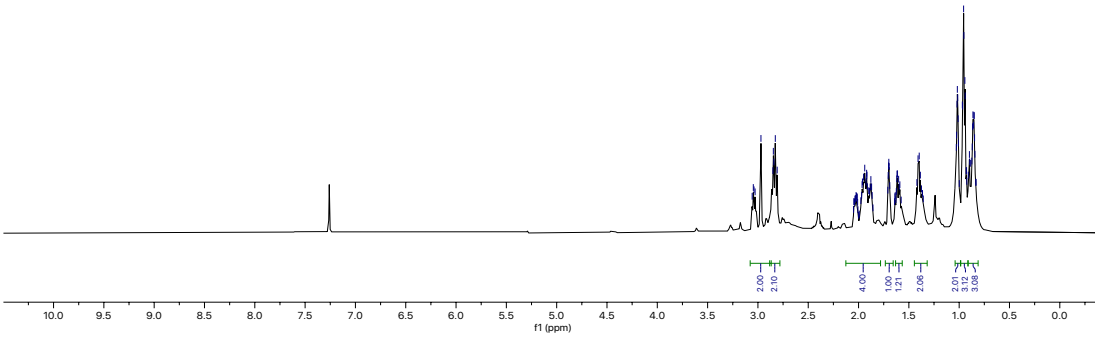
Compound 13b
^{13}C NMR (101 MHz, $CDCl_3$)

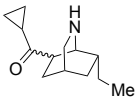


Compound 14

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

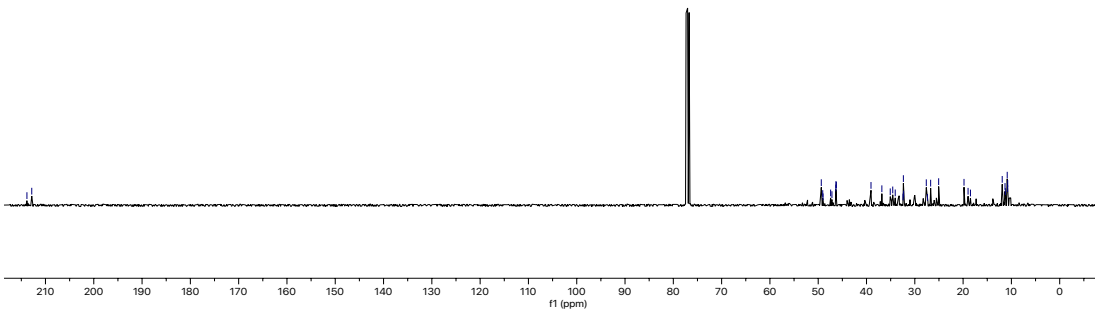


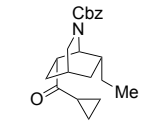




Compound 14

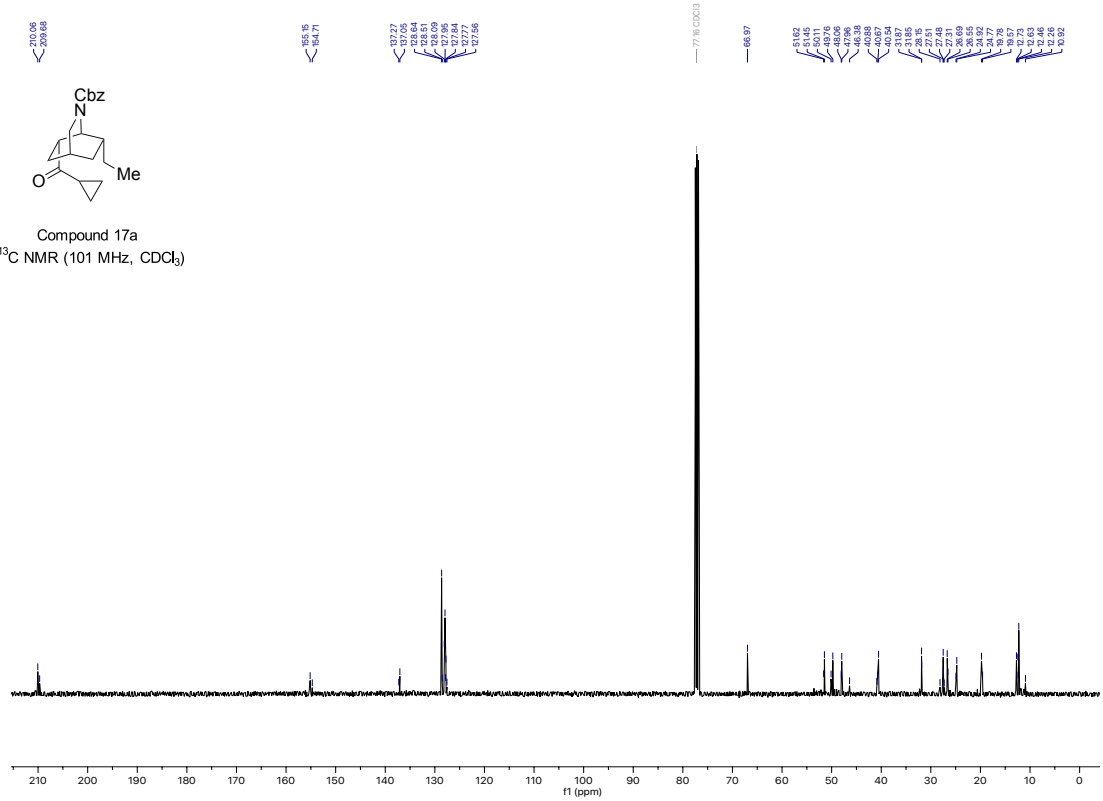
^{13}C NMR (101 MHz, $CDCl_3$)





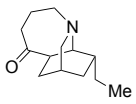
Compound 17a

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



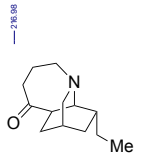
Compound 17a

^{13}C NMR (101 MHz, $CDCl_3$)



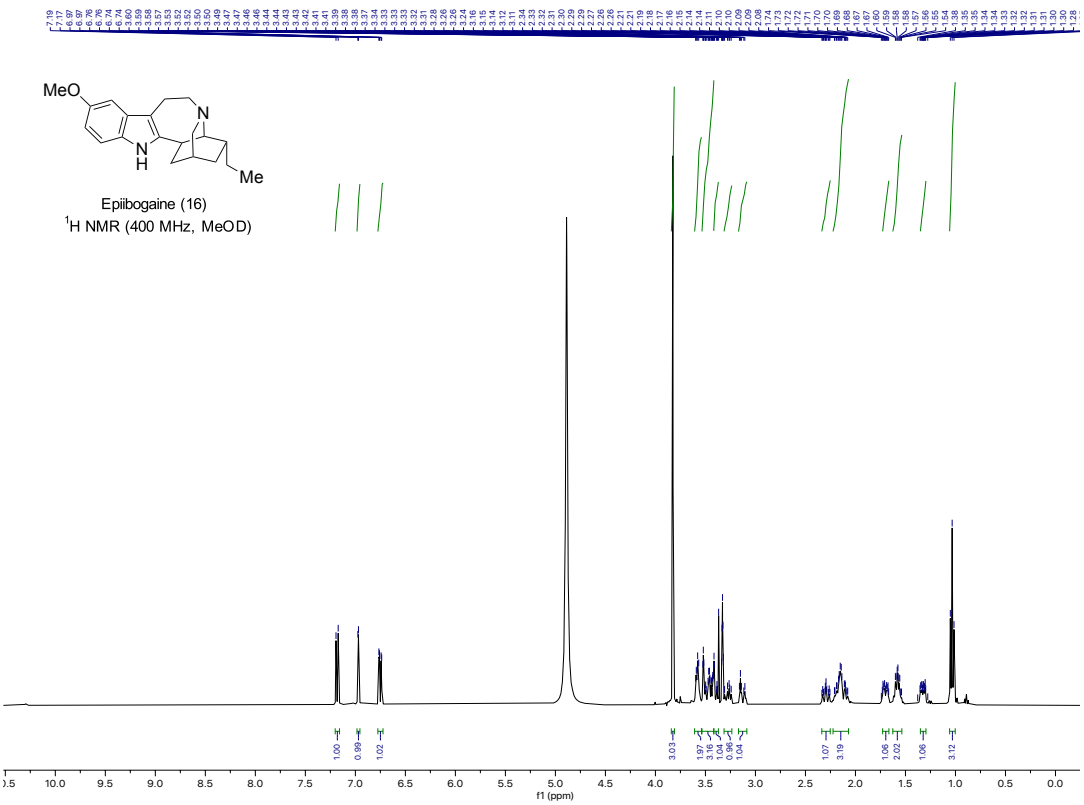
Compound 15

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

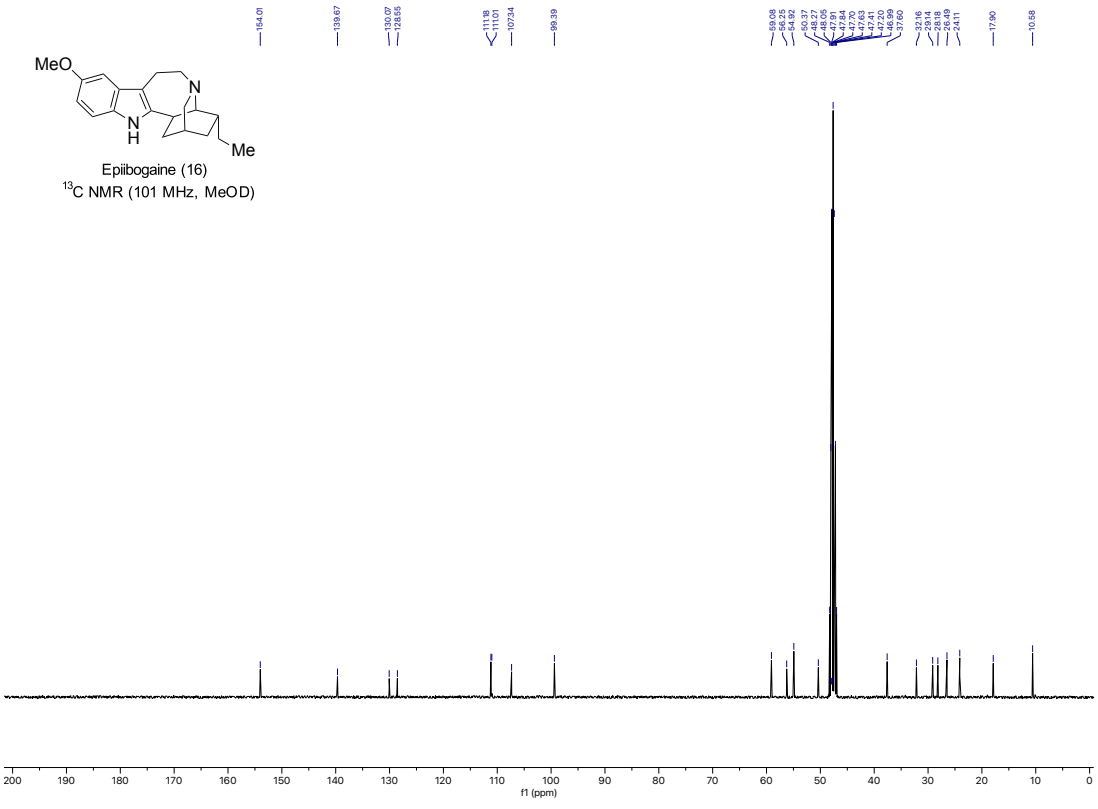


Compound 15

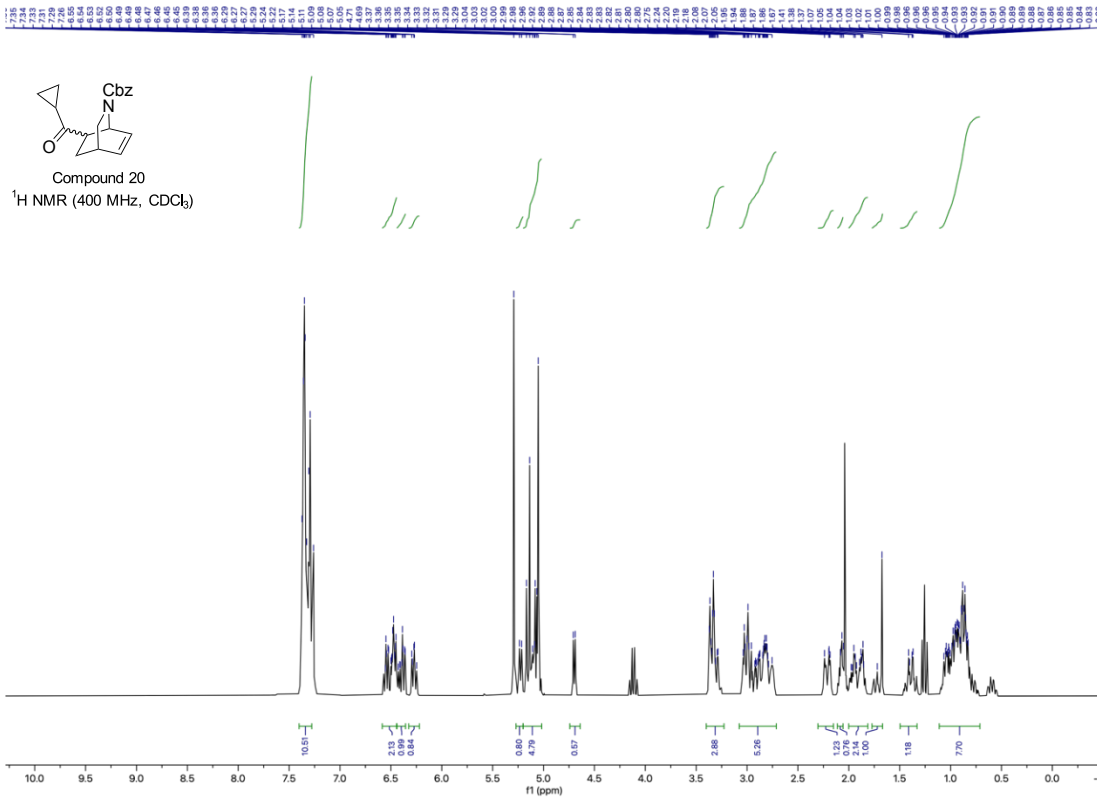
^{13}C NMR (101 MHz, $CDCl_3$)



Epiibogaine (16)
^{1}H NMR (400 MHz, MeOD)

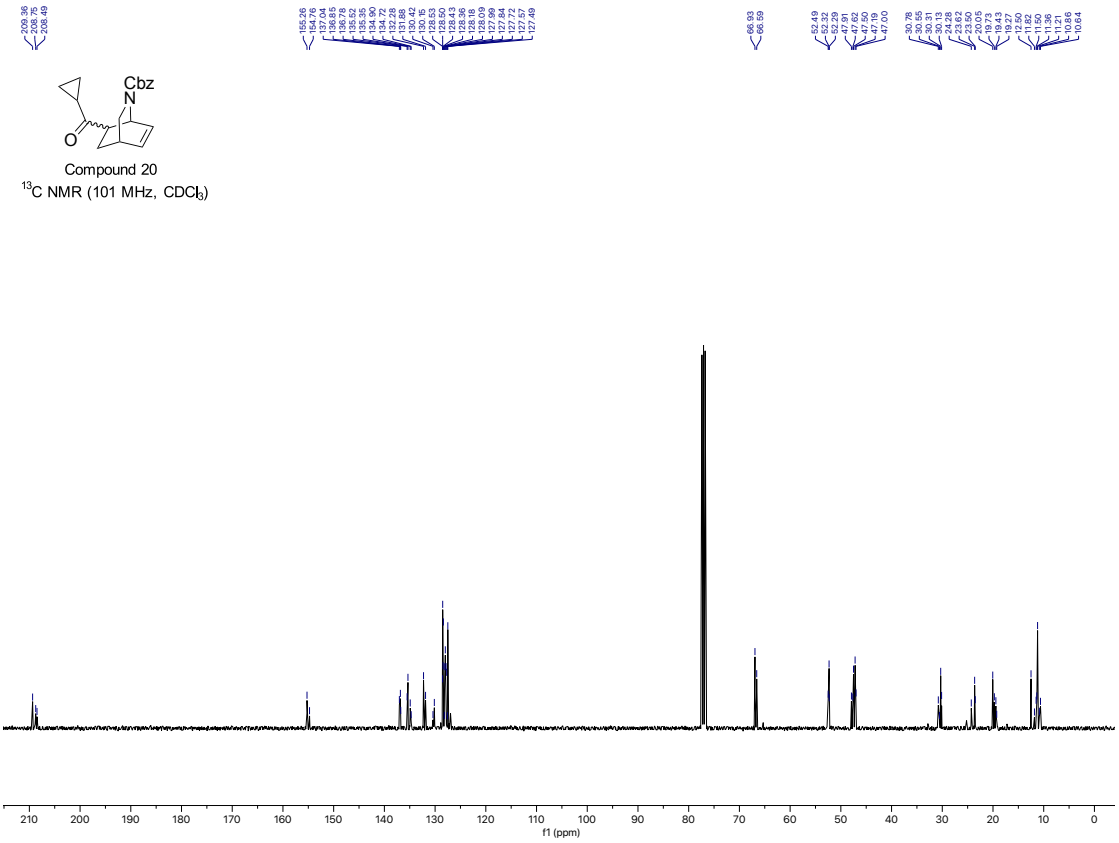


Epiibogaine (16)
^{13}C NMR (101 MHz, MeOD)



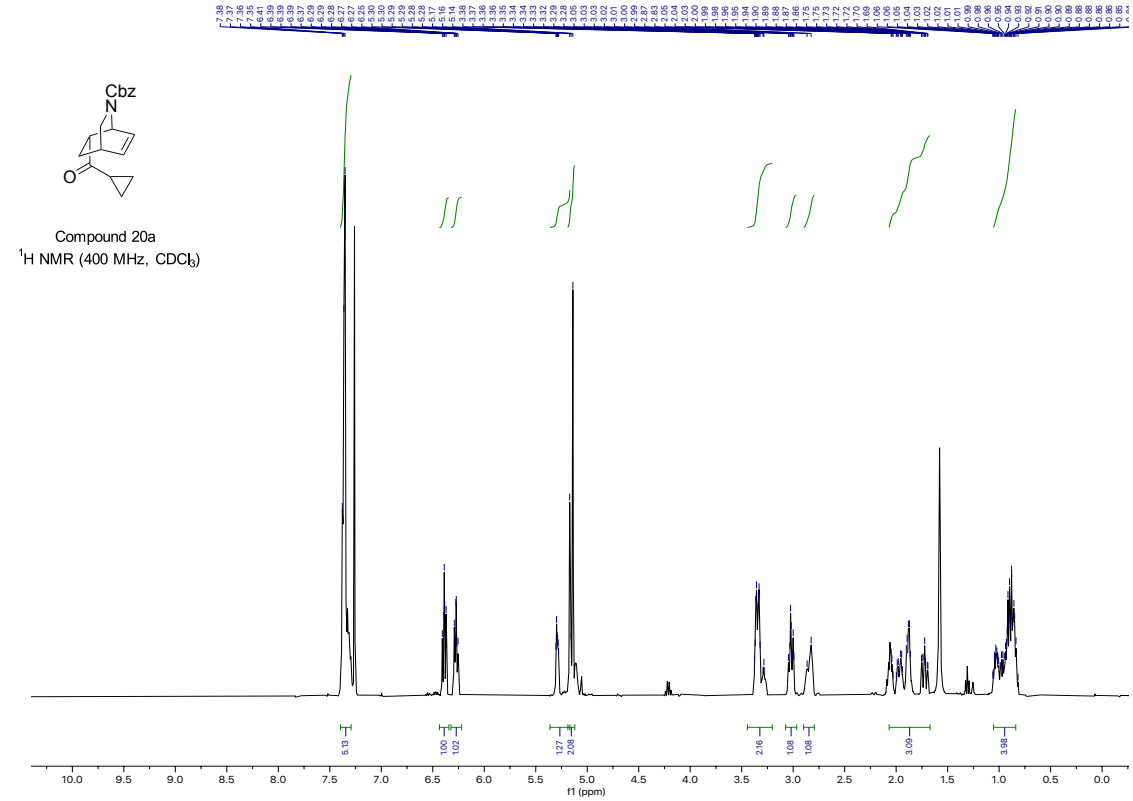
Compound 20

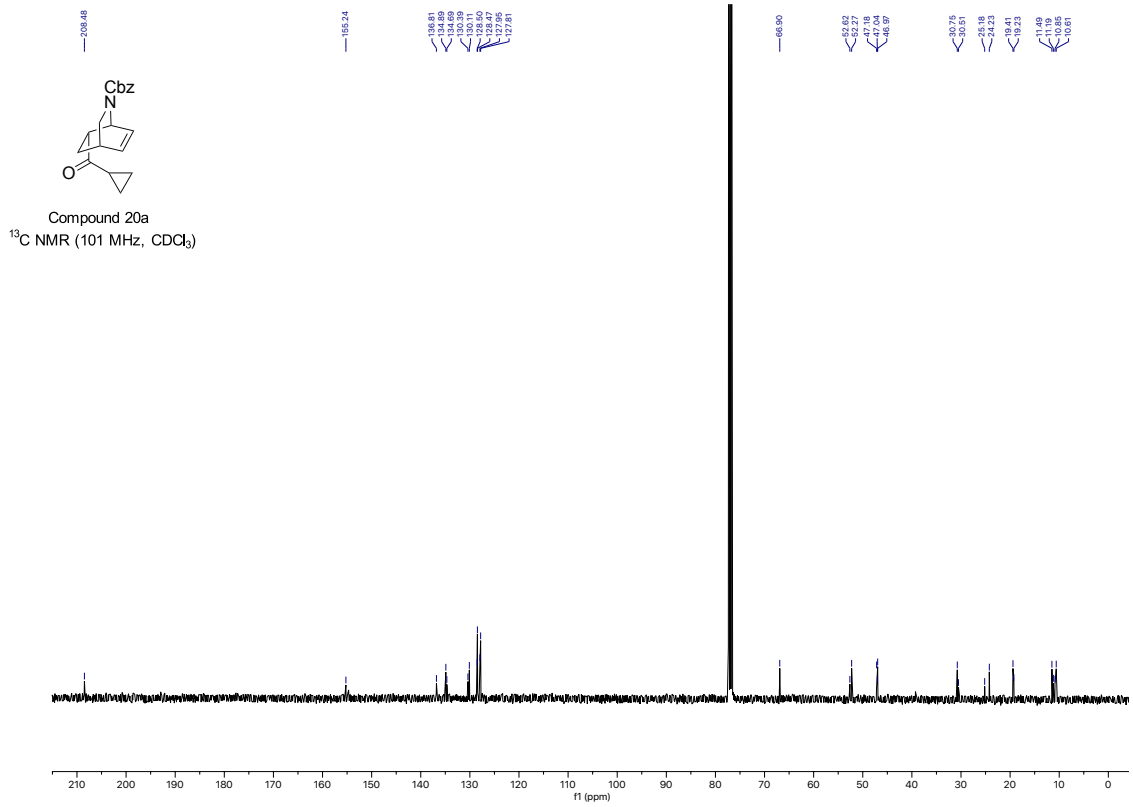
^{1}H NMR (400 MHz, $CDCl_3$)

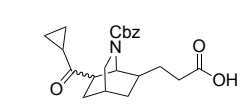


Compound 20

^{13}C NMR (101 MHz, $CDCl_3$)

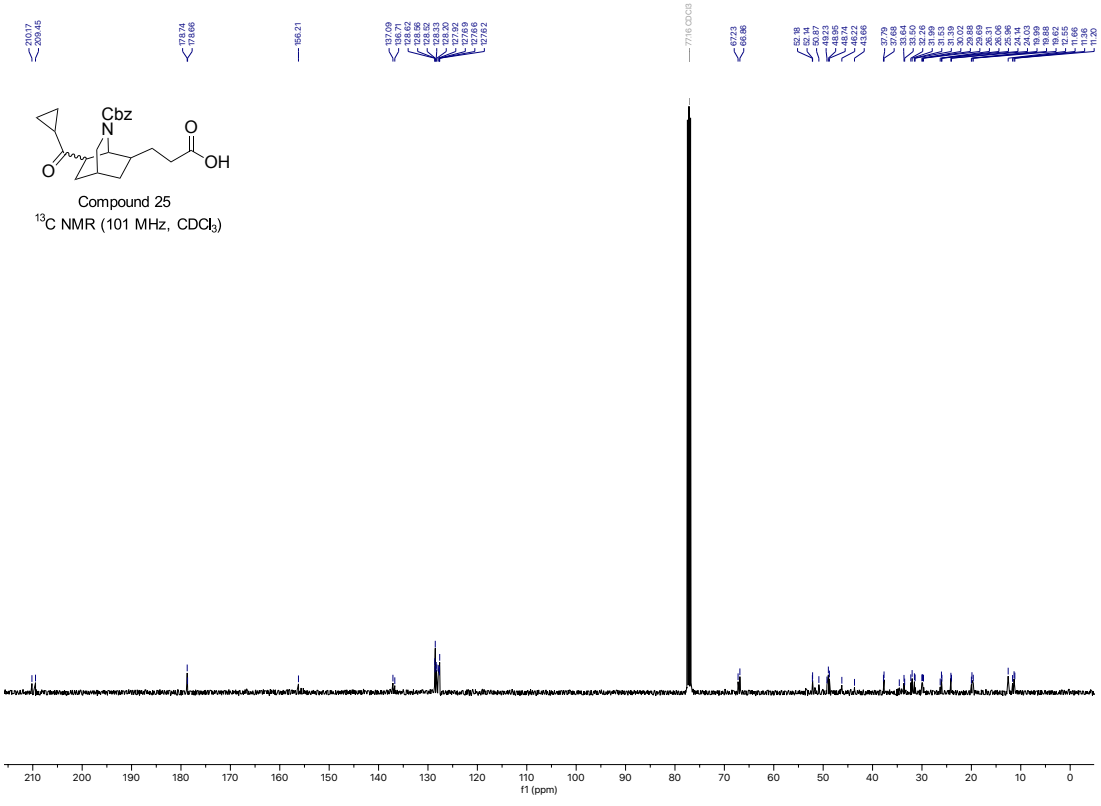

Cbz
N
O
Compound 20a
1H NMR (400 MHz, CDCl3)
5.13
1.00
1.02
1.27
2.08
2.16
1.08
1.08
3.09
3.98
f1 (ppm)


208.48
155.24
136.81
134.89
134.69
130.39
130.11
128.40
128.47
127.95
127.81
66.90
52.62
52.27
47.18
47.04
46.97
30.75
30.51
25.18
24.23
19.41
19.23
11.49
11.19
10.85
10.61
Cbz
N
O
Compound 20a
13C NMR (101 MHz, CDCl3)
f1 (ppm)



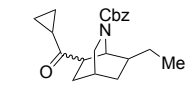
Compound 25

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



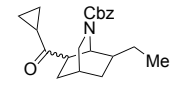
Compound 25

^{13}C NMR (101 MHz, $CDCl_3$)



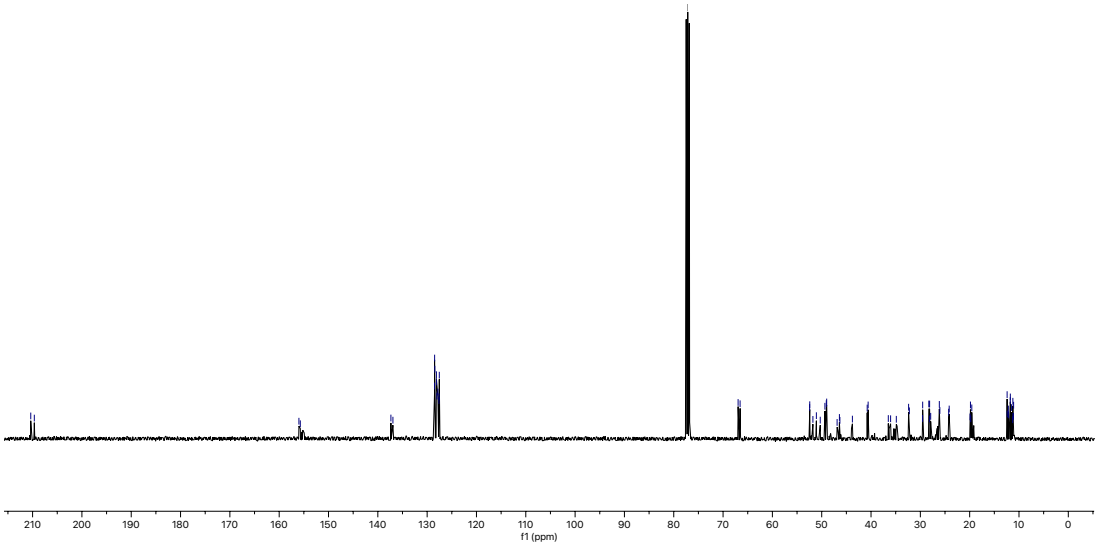
Compound 26

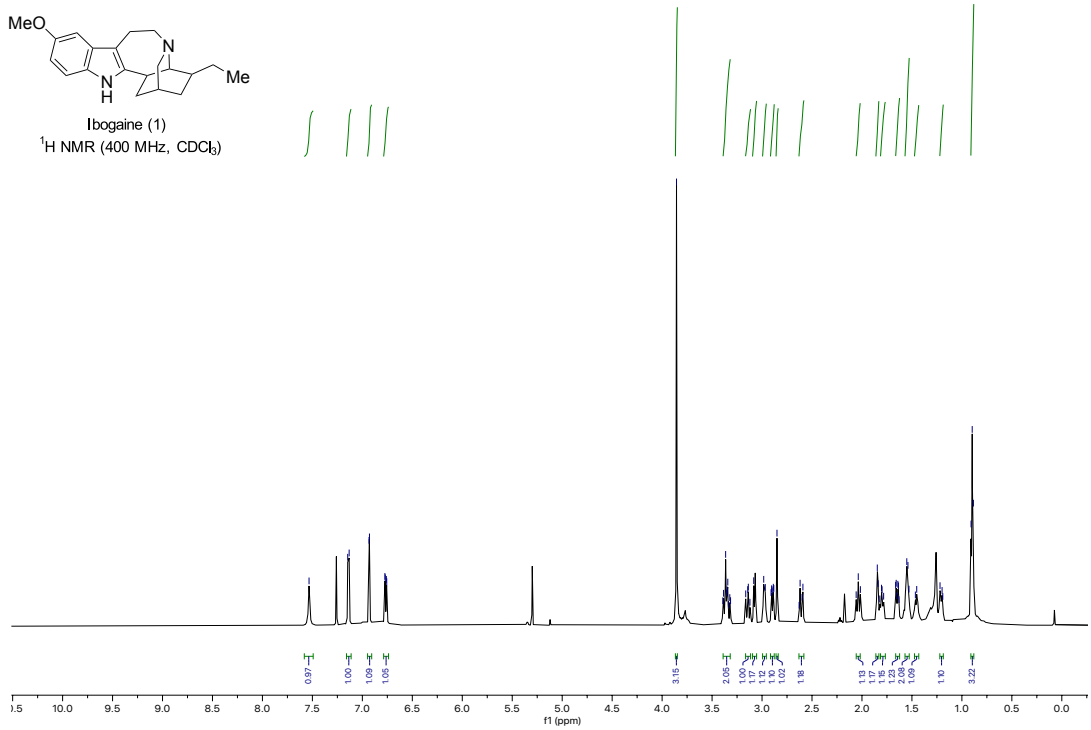
^{1}H NMR (400 MHz, $CDCl_3$)



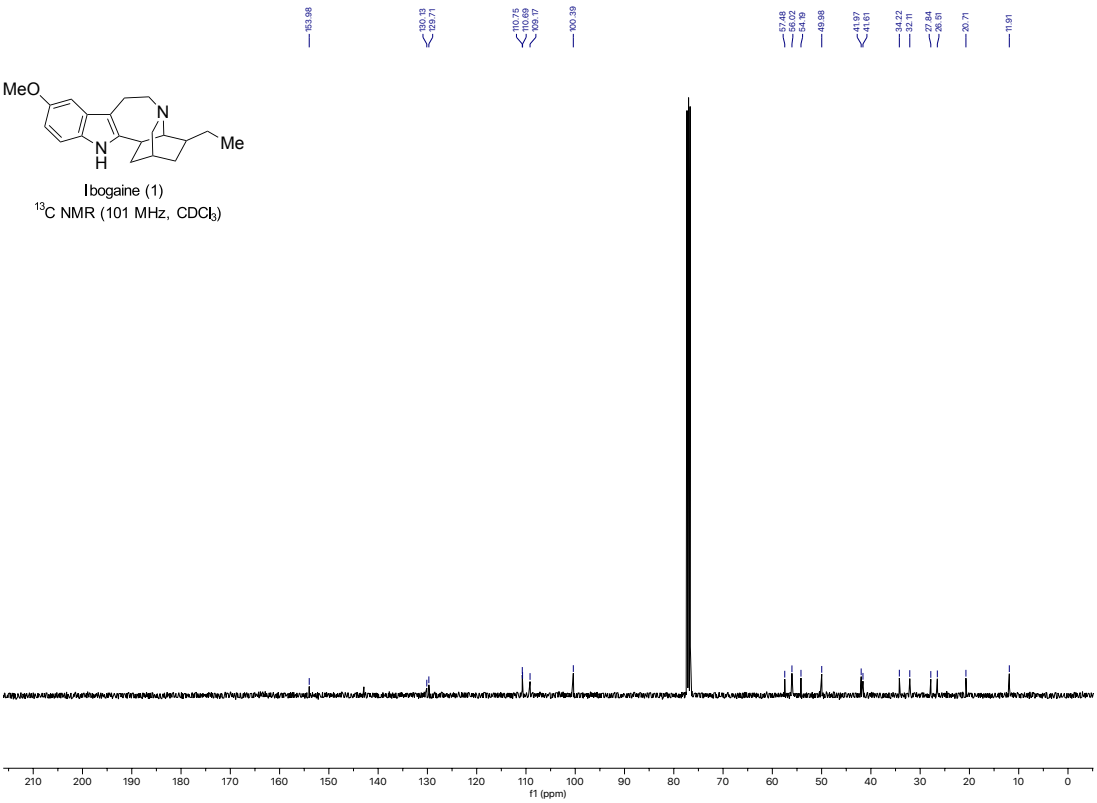
Compound 26

^{13}C NMR (101 MHz, $CDCl_3$)

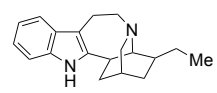




Ibogaine (1)
^{1}H NMR (400 MHz, $CDCl_3$)

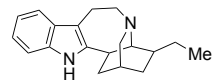


Ibogaine (1)
^{13}C NMR (101 MHz, $CDCl_3$)



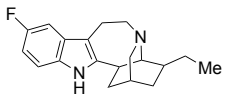
Ibogamine (2)

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

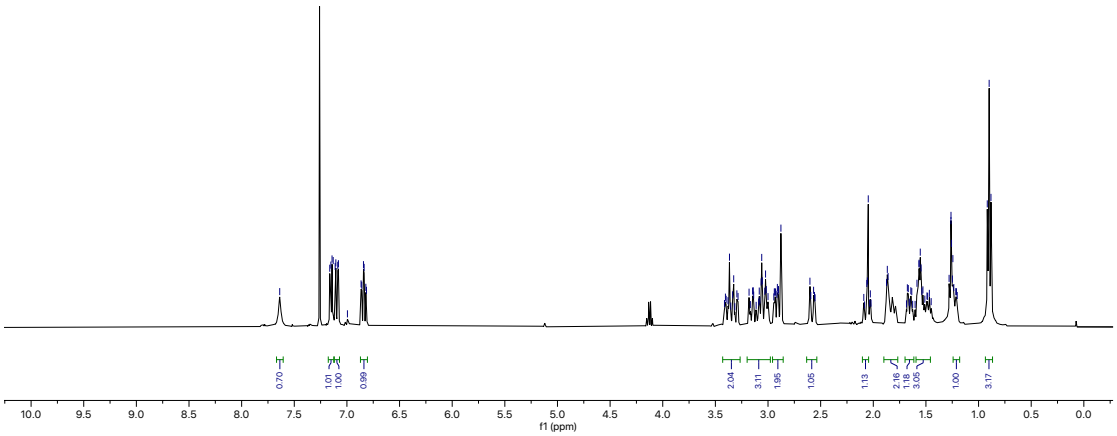


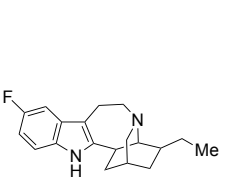
Ibogamine (2)

^{13}C NMR (101 MHz, $CDCl_3$)

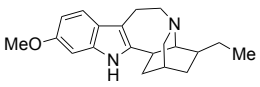


10-fluoroibogamine (29)
^{1}H NMR (400 MHz, $CDCl_3$)

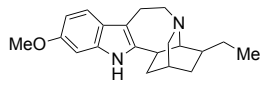




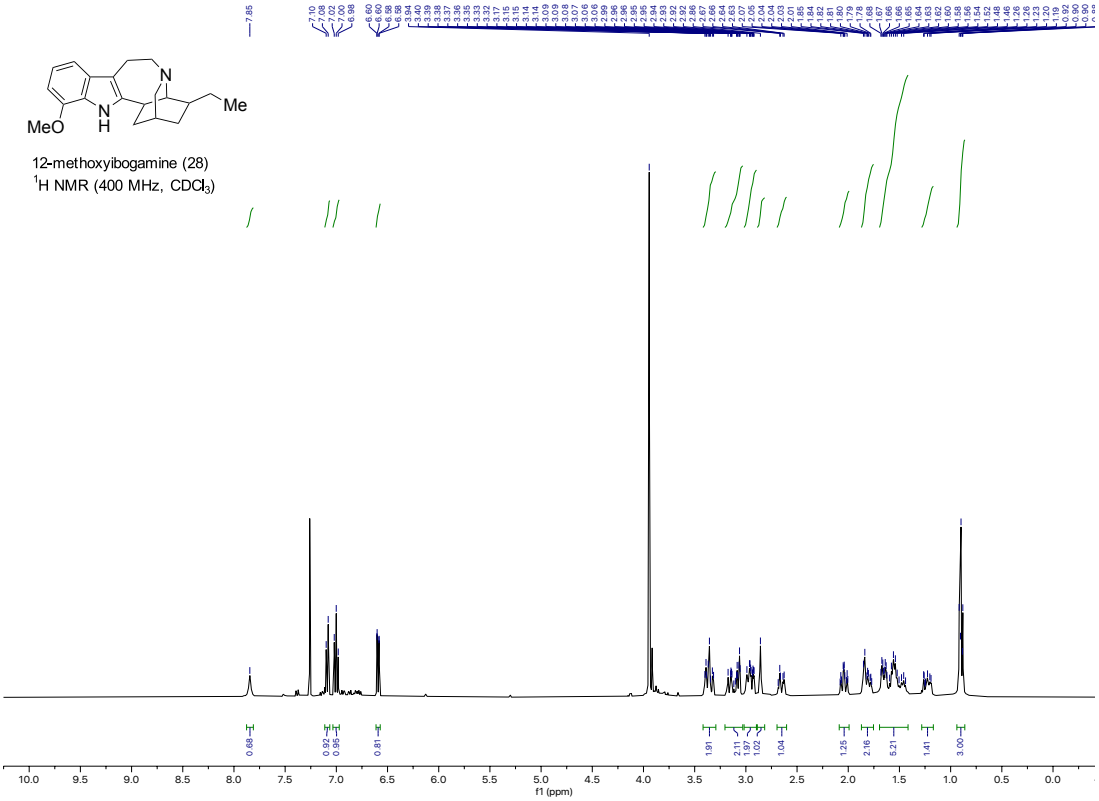
10-fluoroibogamine (29)
^{13}C NMR (101 MHz, $CDCl_3$)



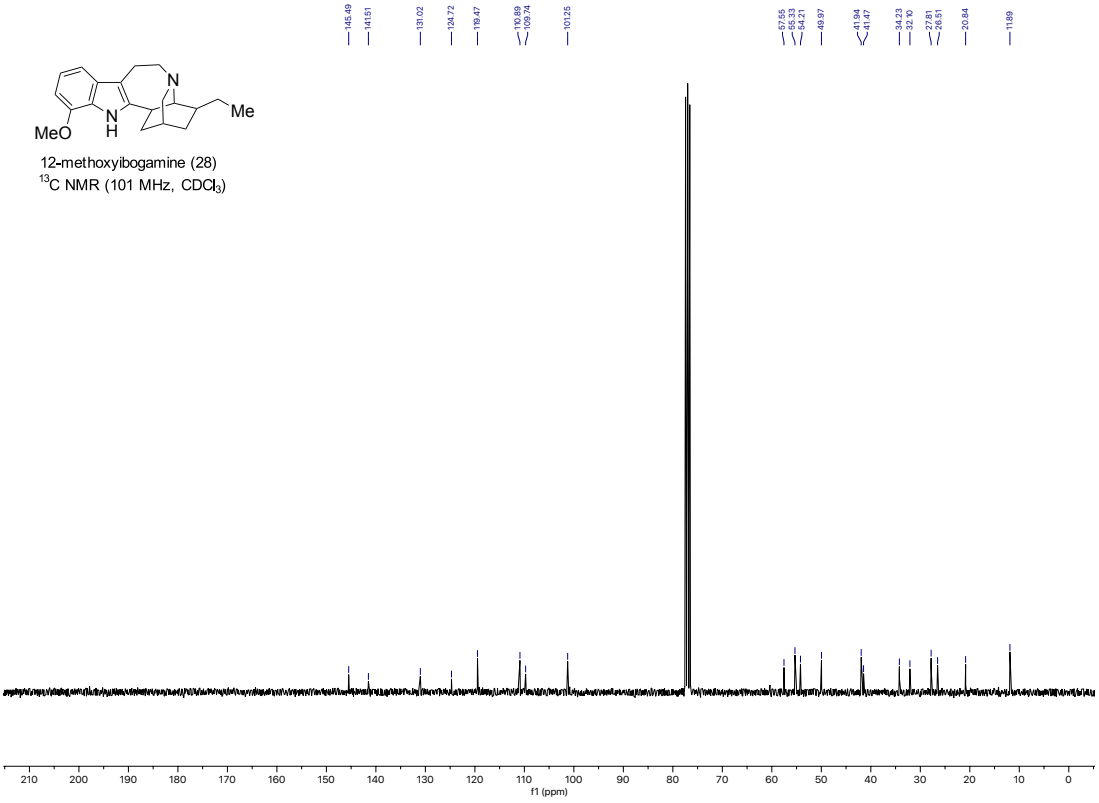
Tabernanthine (4)
^{1}H NMR (400 MHz, $CDCl_3$)



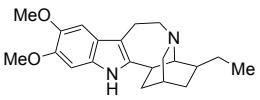
Tabernanthine (4)
^{13}C NMR (101 MHz, $CDCl_3$)



12-methoxyibogamine (28)
^{1}H NMR (400 MHz, $CDCl_3$)

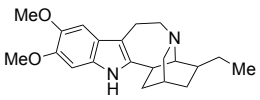


12-methoxyibogamine (28)
^{13}C NMR (101 MHz, $CDCl_3$)



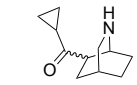
Ibogaline (3)

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



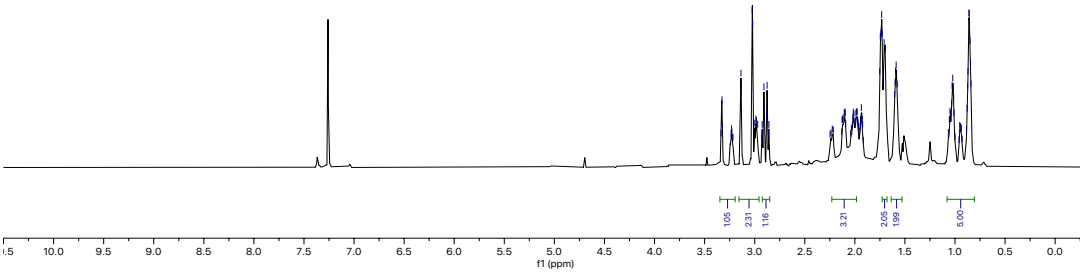
Ibogaline (3)

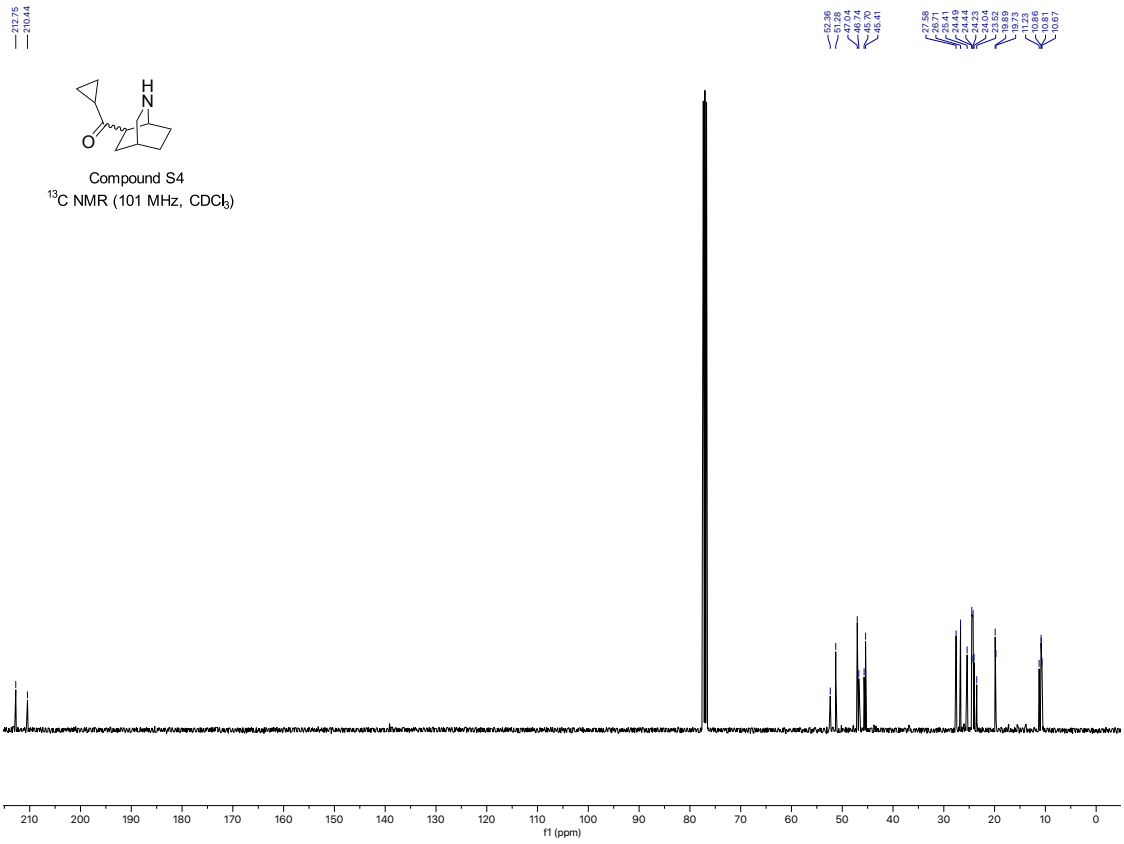
^{13}C NMR (101 MHz, $CDCl_3$)



Compound S4

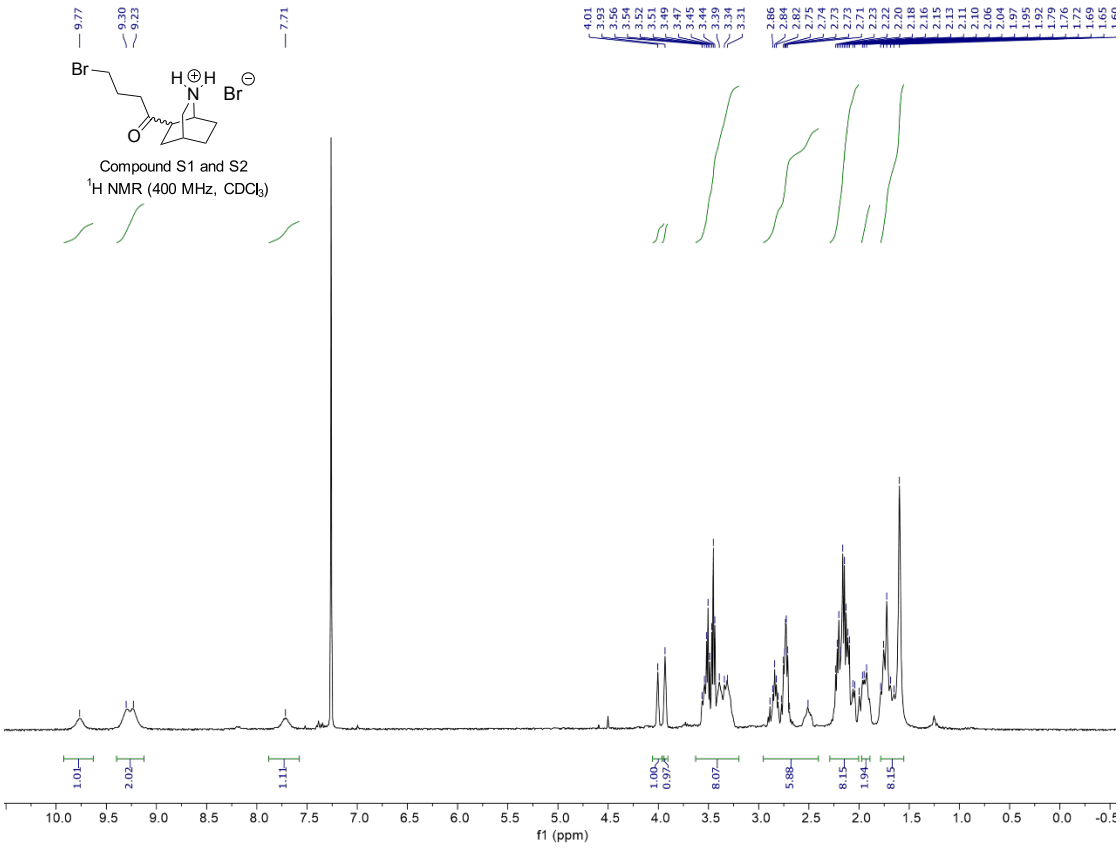
^{1}H NMR (400 MHz, $CDCl_3$)

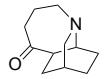




Compound S4

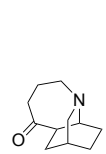
^{13}C NMR (101 MHz, $CDCl_3$)


Br
H
N
H
Br
O
Compound S1 and S2
1H NMR (400 MHz, CDCl3)
f1 (ppm)



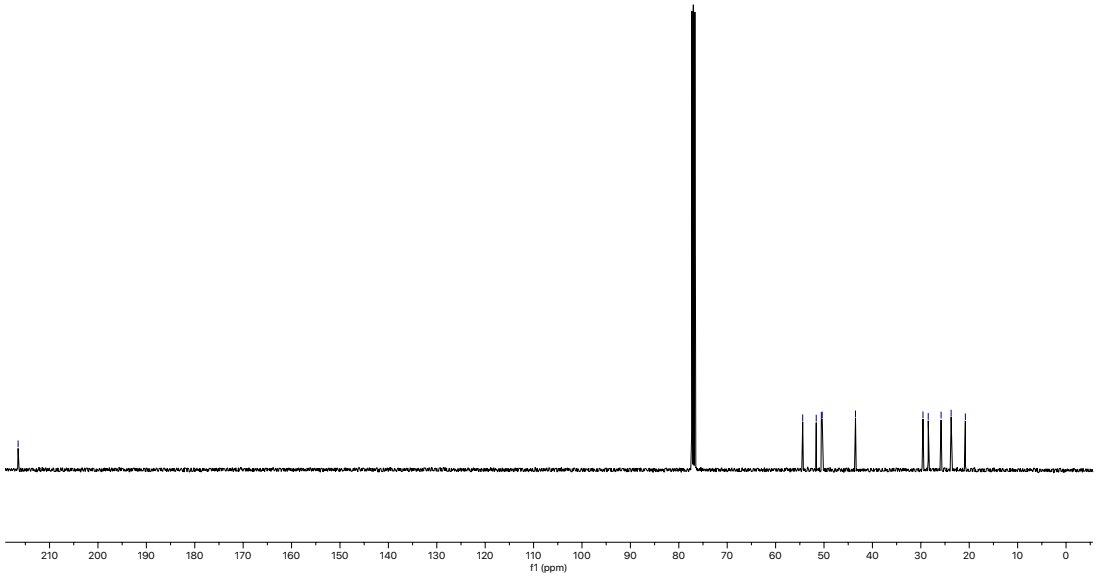
Compound S3

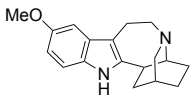
^{1}H NMR (400 MHz, $CDCl_3$)



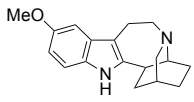
Compound S3

^{13}C NMR (101 MHz, $CDCl_3$)

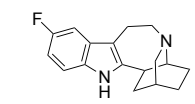




Desethylibogaine (30)
^{1}H NMR (400 MHz, $CDCl_3$)

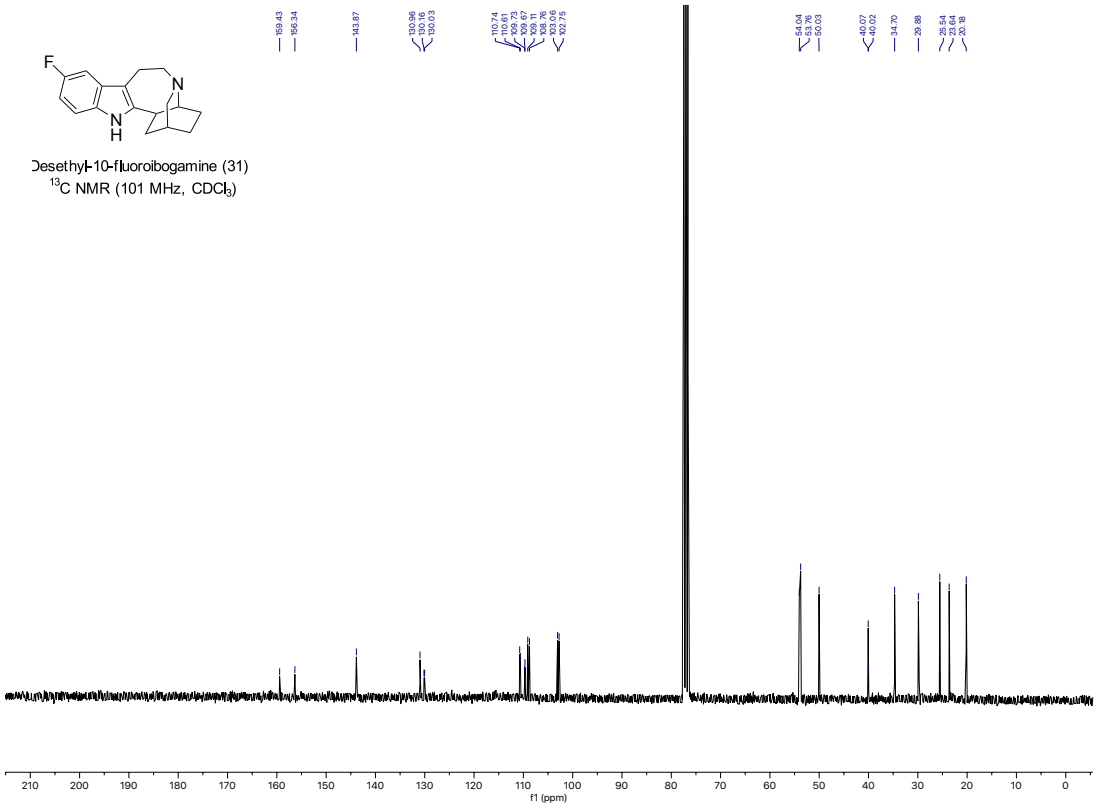


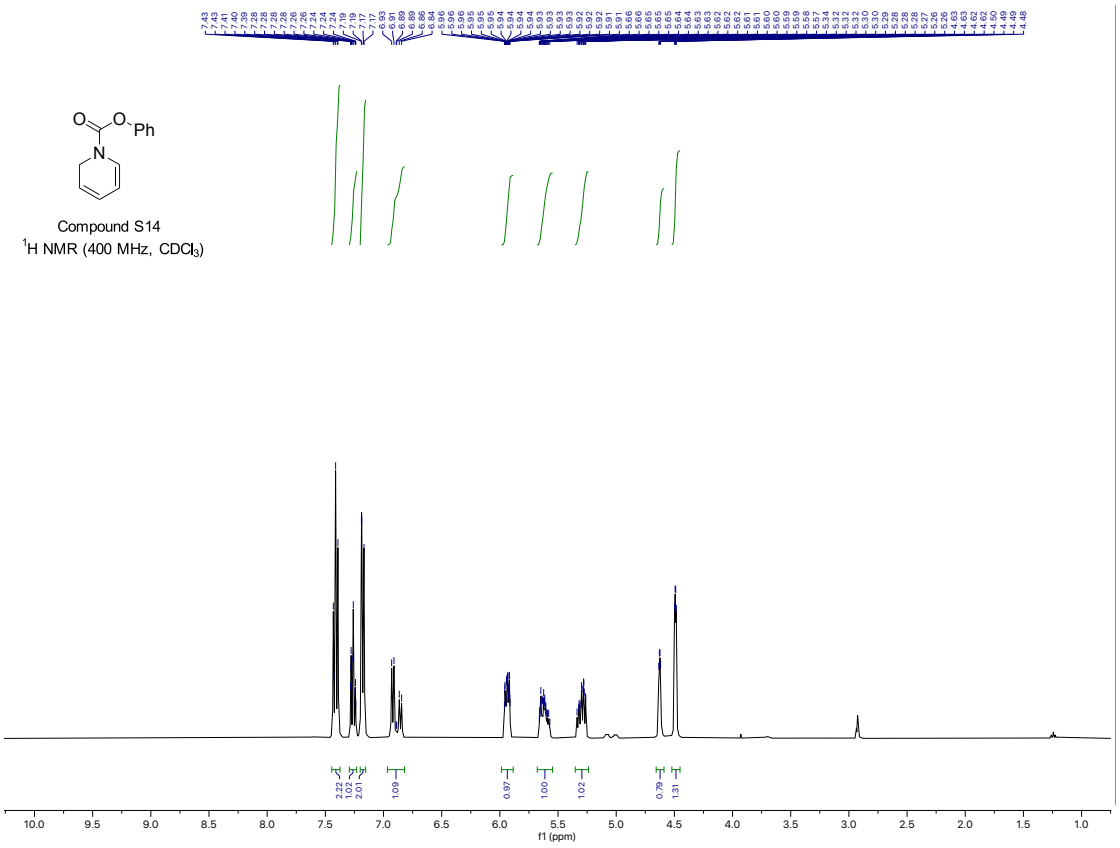
Desethylibogaine (30)
^{13}C NMR (101 MHz, $CDCl_3$)



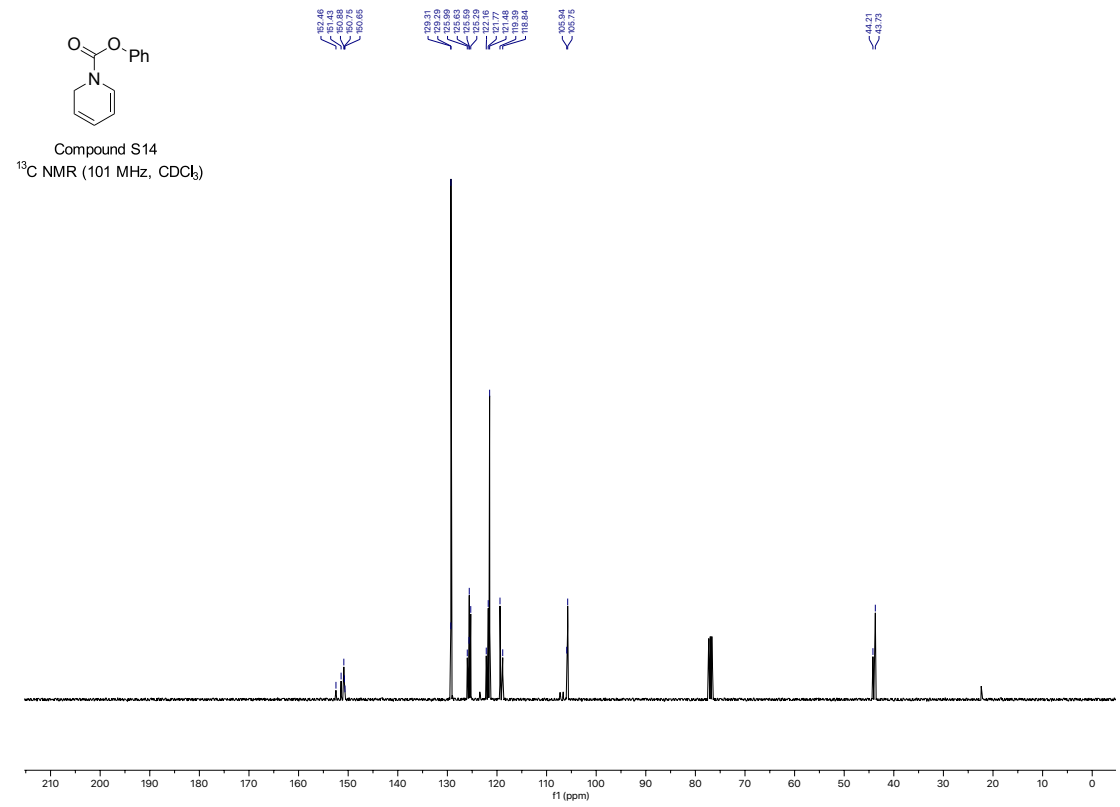
Desethyl-10-fluoroibogamine (31)
^{1}H NMR (400 MHz, $CDCl_3$)

Desethyl-10-fluoroibogamine (31)
^{13}C NMR (101 MHz, $CDCl_3$)

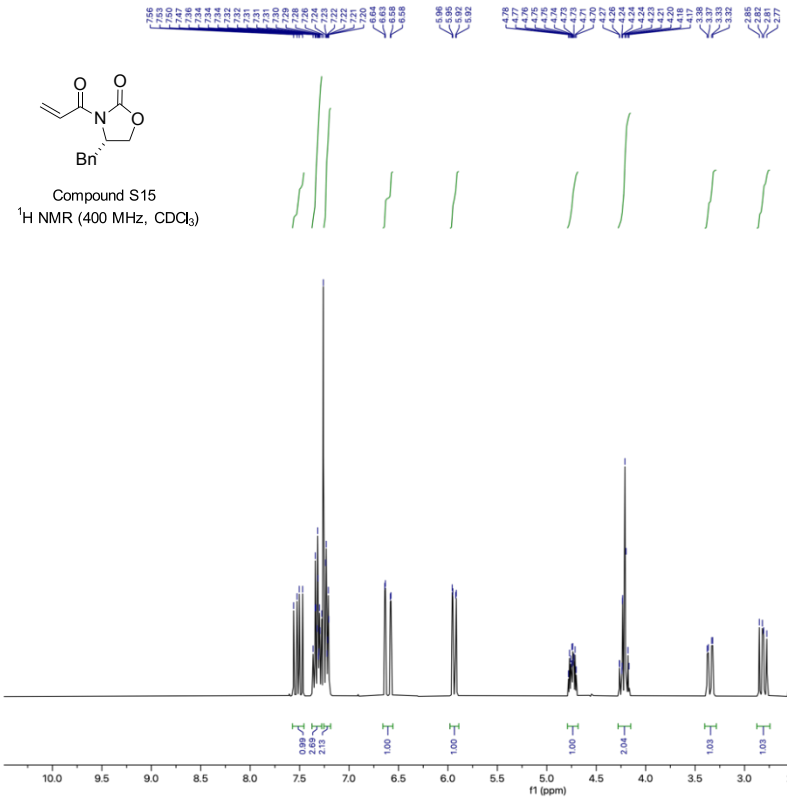




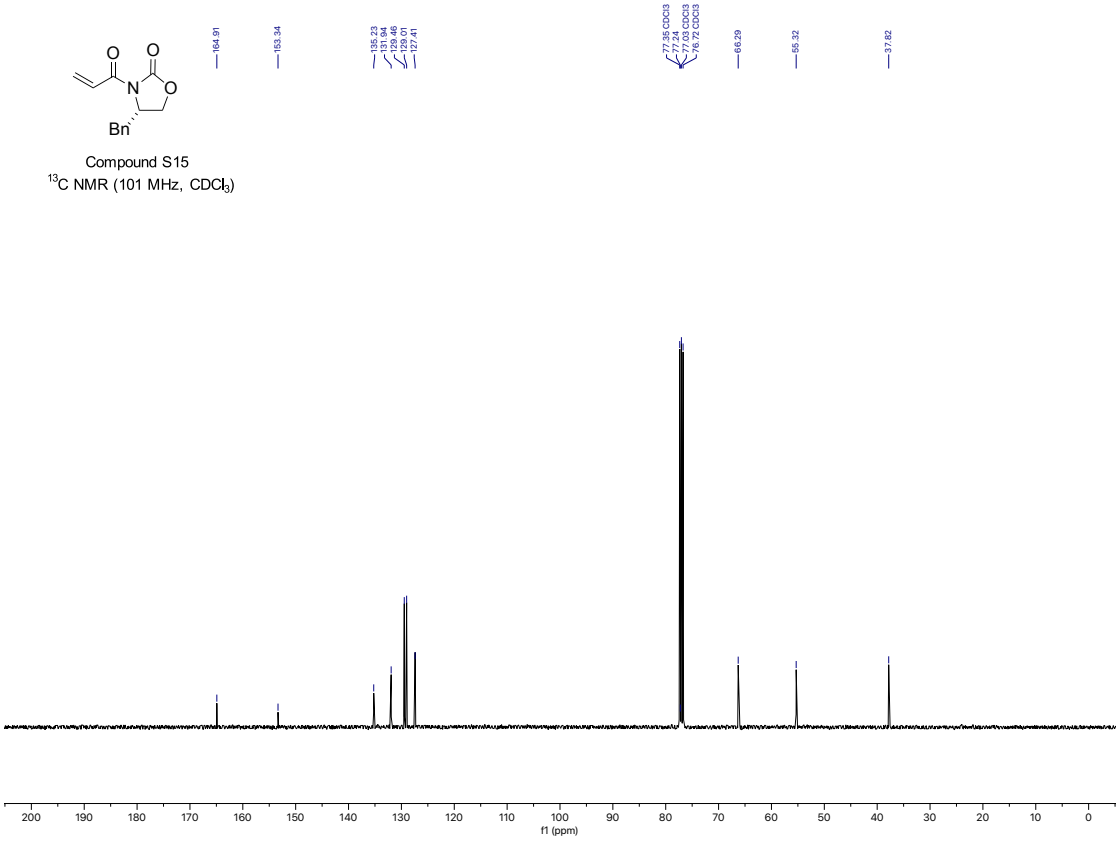
Compound S14
^{1}H NMR (400 MHz, $CDCl_3$)



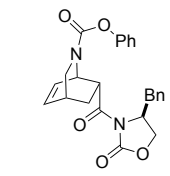
Compound S14
^{13}C NMR (101 MHz, $CDCl_3$)



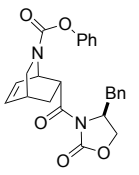
Compound S15
^{1}H NMR (400 MHz, $CDCl_3$)



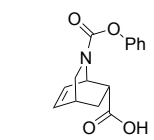
Compound S15
^{13}C NMR (101 MHz, $CDCl_3$)



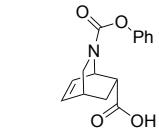
Compound S16
^{1}H NMR (400 MHz, MeOD)



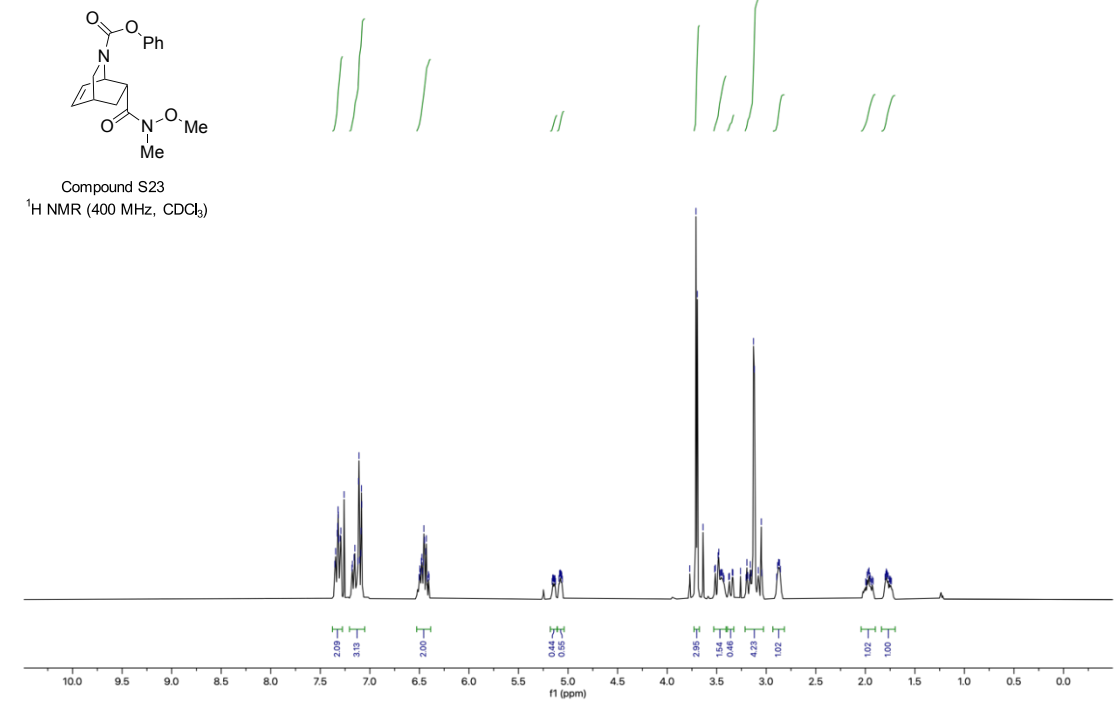
Compound S16
^{13}C NMR (101 MHz, MeOD)



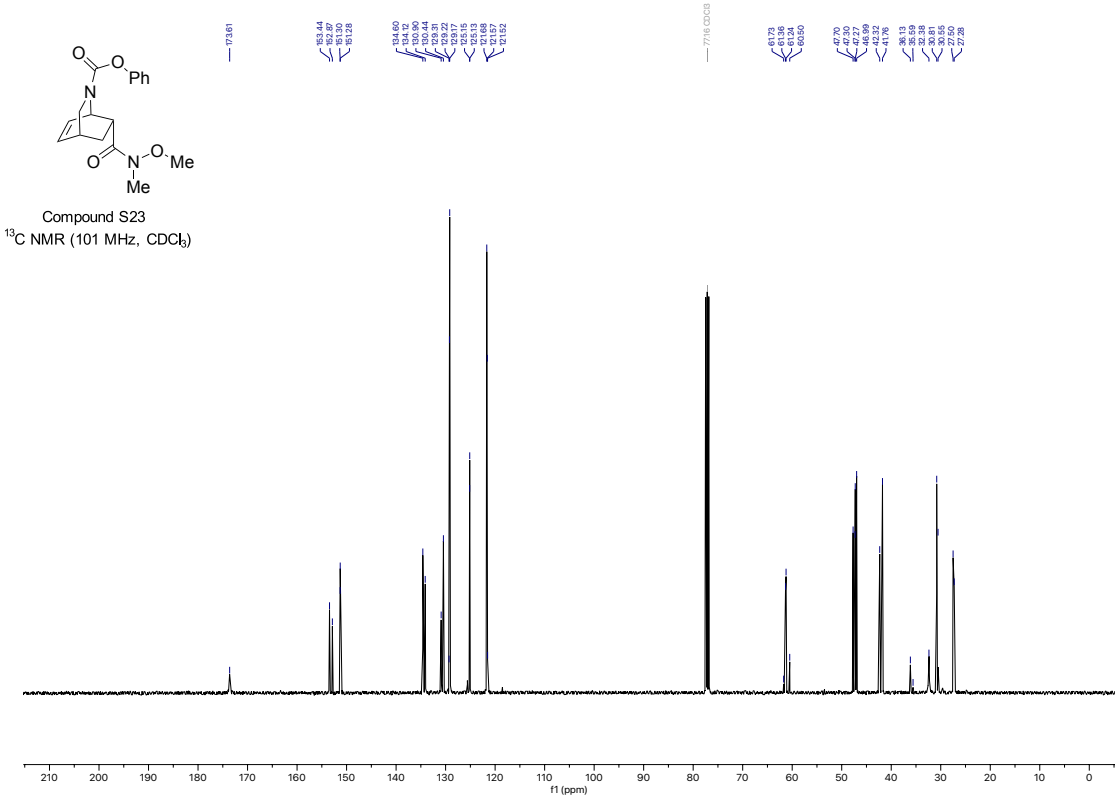
Compound S18
^{1}H NMR (400 MHz, MeOD)



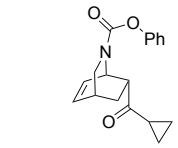
Compound S18
^{13}C NMR (101 MHz, MeOD)



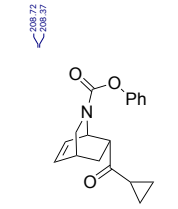
Compound S23
^{1}H NMR (400 MHz, $CDCl_3$)



Compound S23
^{13}C NMR (101 MHz, $CDCl_3$)

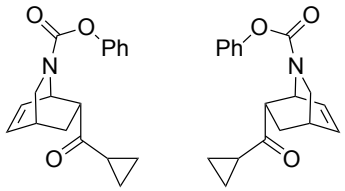


Compound S19
^{1}H NMR (400 MHz, $CDCl_3$)

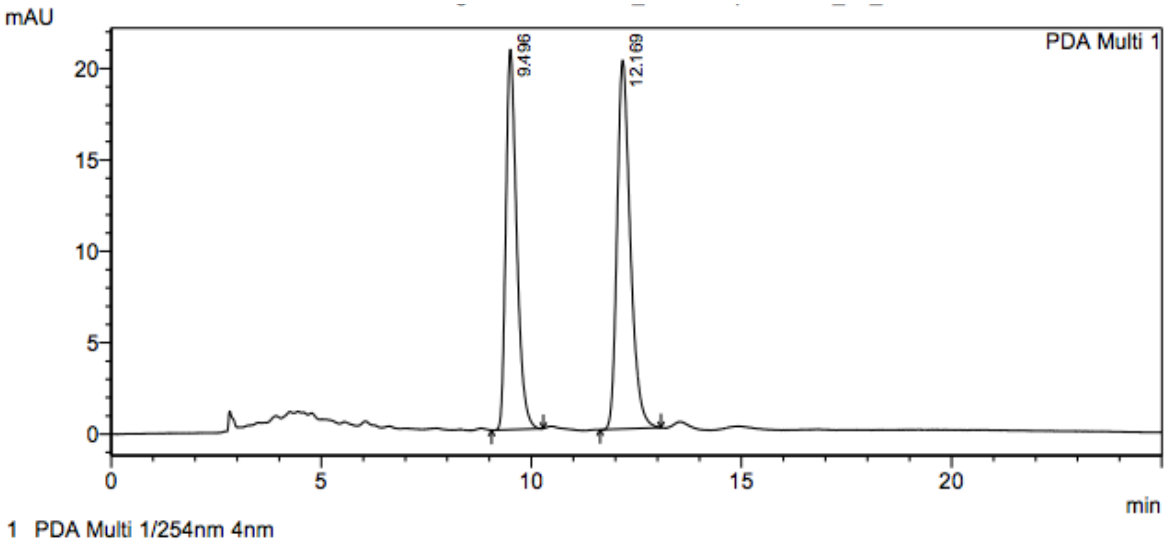


Compound S19
^{13}C NMR (101 MHz, $CDCl_3$)

6. Chiral HPLC Chromatograms



(±)-S19
(Chiralpak IA 90:10 Hexanes/i-PrOH, 1 mL/min, λ 254nm)
t_{R1} = 9.49 min, t_{R2} = 12.16 min



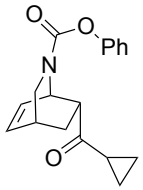
1 PDA Multi 1/254nm 4nm

< Peak Table >

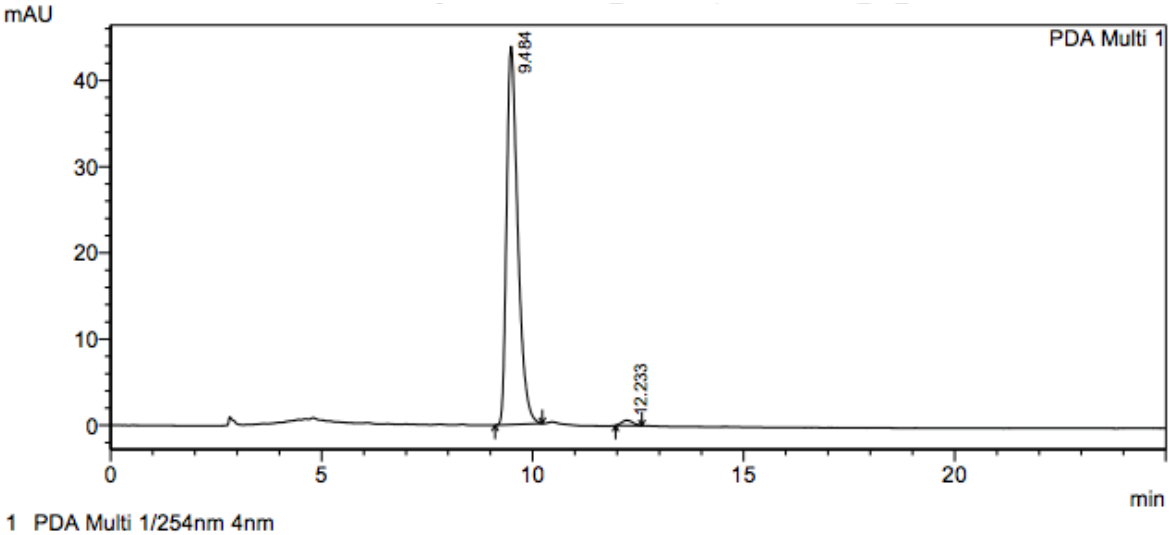
PeakTable C:\LabSolutions\Training1107\Rishab\OD_PhCarbCp-racemic_90_10.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.496	372120	20782	45.708	50.748
2	12.169	442011	20169	54.292	49.252
Total		814130	40951	100.000	100.000



(+)-S19
(Chiralpak IA 90:10 Hexanes/i-PrOH, 1 mL/min, λ 254nm)
t_{Rmajor} = 9.48 min, t_{Rminor} = 12.23 min



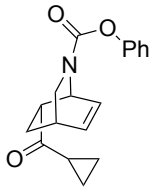
1 PDA Multi 1/254nm 4nm

< Peak Table >

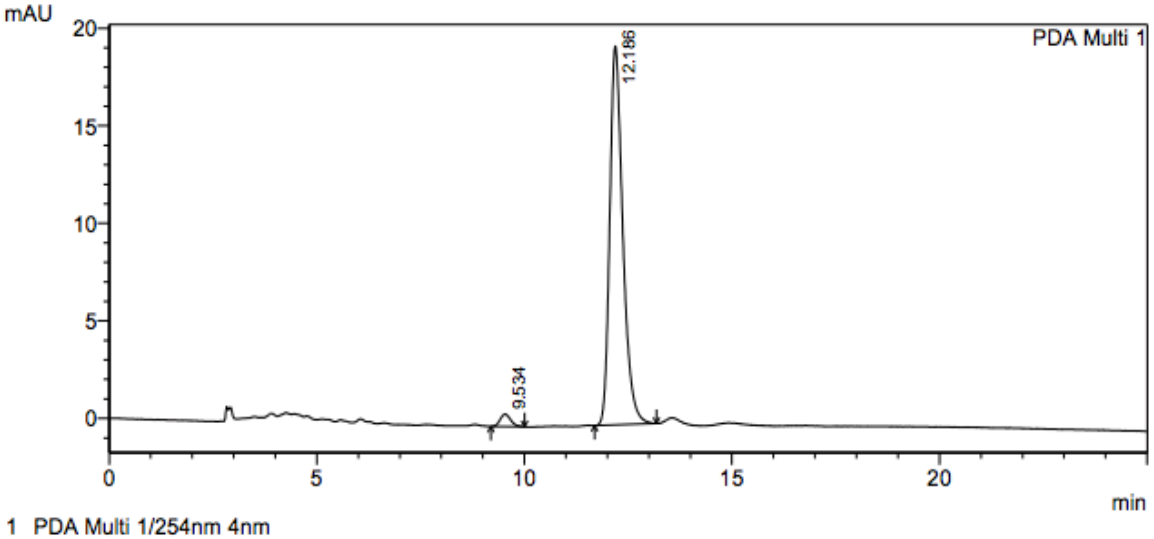
PeakTable C:\LabSolutions\Training1107\Rishab\OD_PhCarbCp-enantiomer2_90_10.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.484	807319	43854	98.657	98.645
2	12.233	10990	602	1.343	1.355
Total		818309	44456	100.000	100.000



(-)-S19
(Chiralpak IA 90:10 Hexanes/i-PrOH, 1 mL/min, λ 254nm)
t_{Rminor} = 9.53 min, t_{Rmajor} = 12.18 min

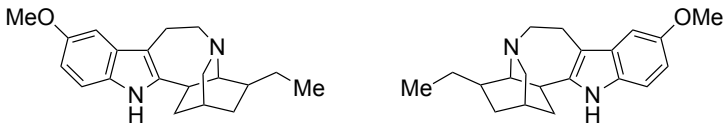


1 PDA Multi 1/254nm 4nm

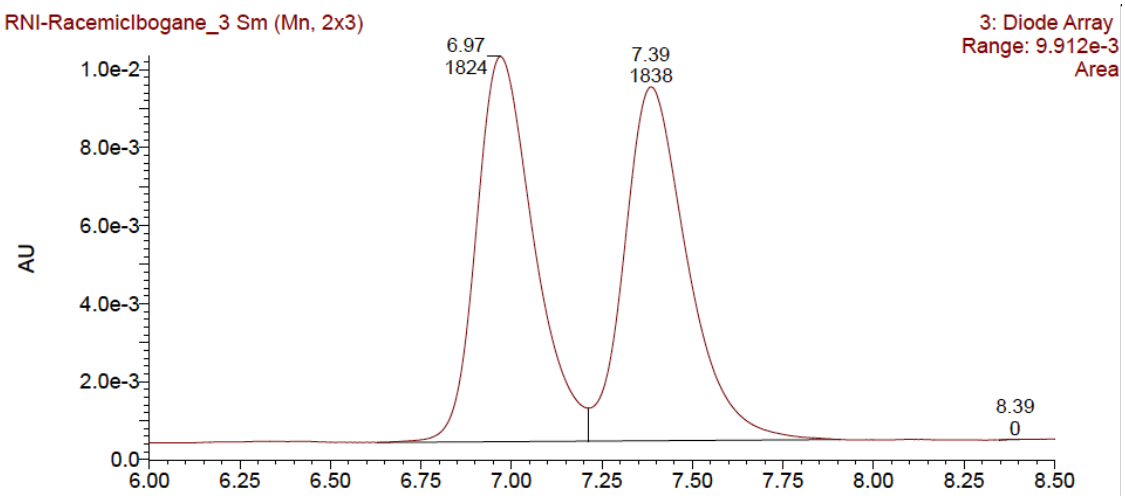
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Rishab\OD_PhCarbCp-enantiomer1_90_10.lcd
PDA Ch1 254nm 4nm

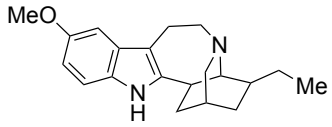
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.534	10892	633	2.502	3.157
2	12.186	424404	19418	97.498	96.843
Total		435296	20051	100.000	100.000



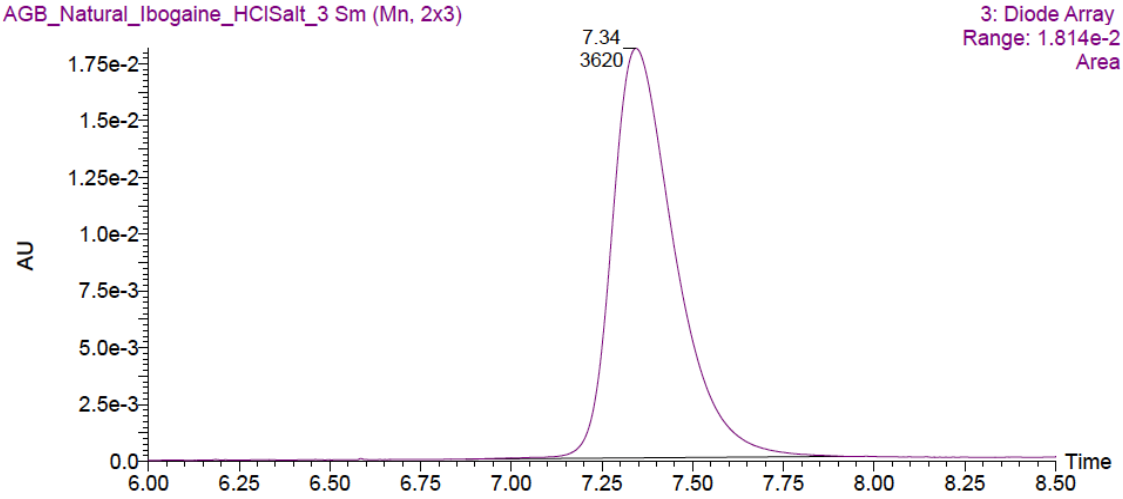
(±)-ibogaine
(Poroshell 120 Chiral-V MeOH/15mM NH_4HCO_2, 0.8 mL/min, 40 °C, λ 254nm)
Concentration: 0.9 mg/mL
t_{R1} = 6.97min, t_{R2} = 7.39 min



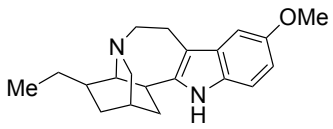
Peak	Ret. Time	Area	Area%
1	6.97	1824	49.808
2	7.39	1838	50.192
Total		3662	100.000



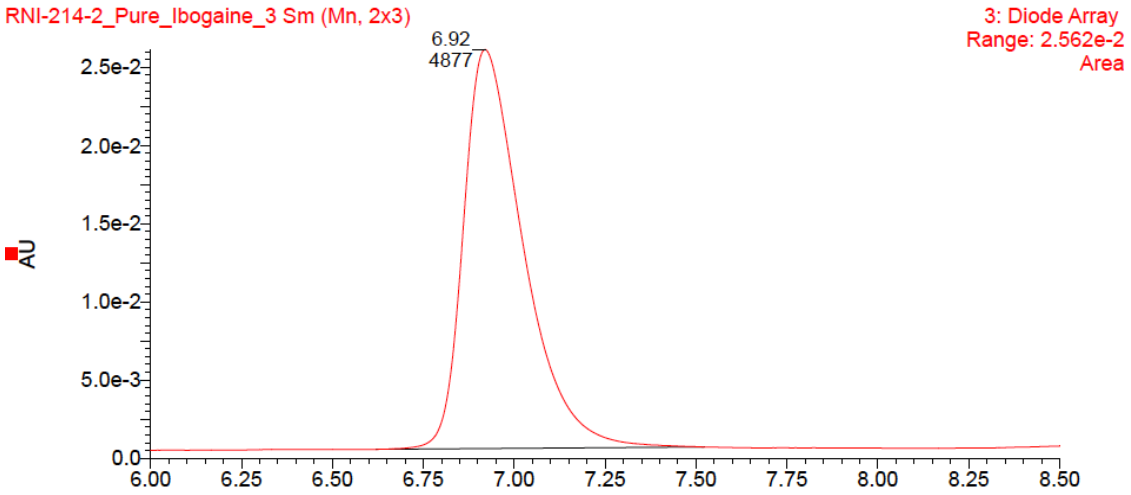
(–)-ibogaine
(Poroshell 120 Chiral-V MeOH/15mM NH_4HCO_2, 0.8 mL/min, 40 °C, λ 254nm)
Concentration: 0.5 mg/mL
t_{Rmajor} = 7.34min, t_{Rminor} = N/A



Peak	Ret. Time	Area	Area%
1	-	0	0
2	7.39	3620	100.000
Total		3620	100.000



(+)-ibogaine
(Poroshell 120 Chiral-V MeOH/15mM NH_4HCO_2, 0.8 mL/min, 40 °C, λ 254nm)
Concentration: 0.5 mg/mL
t_{Rmajor} = 7.34min, t_{Rminor} = N/A



Peak	Ret. Time	Area	Area%
1	6.92	4877	100.00
2	-	0	0
Total		4877	100.000