Supporting Information For

Enantioselective Total Syntheses of Pentacyclic Homoproaporphine Alkaloids

Liu-Yang Pu, Fan Yang, Ji-Qiang Chen, Ying Xiong, Huai-Yu Bin, Jian-Hua Xie*, Qi-Lin Zhou,*

State Key Laboratory and Institute of Elemento-organic Chemistry, College of Chemistry, Nankai University, Tianjin 300071, China

Email: jhxie@nankai.edu.cn; qlzhou@nankai.edu.cn

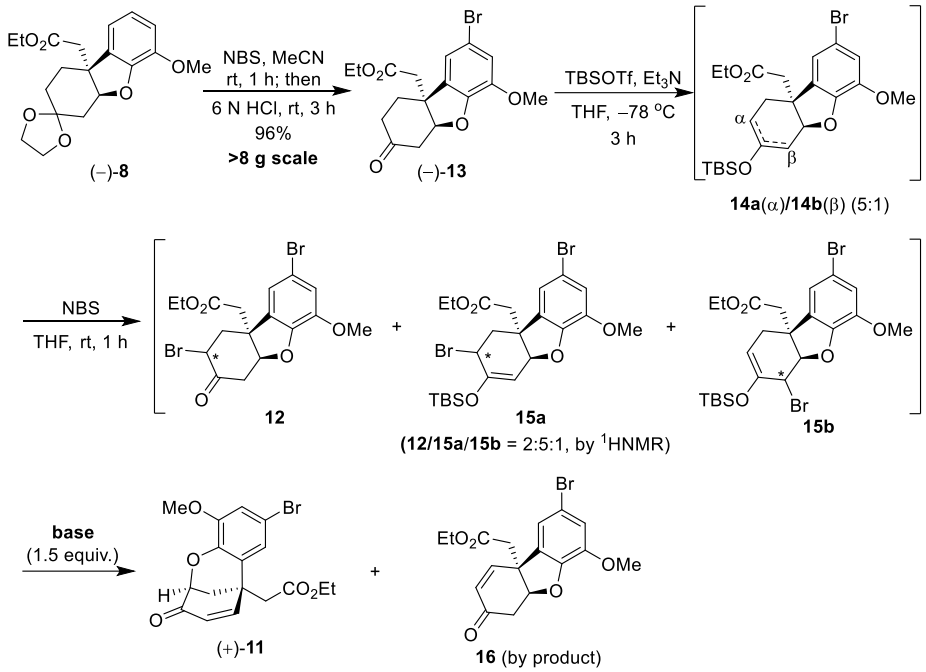
Table of Contents

A) General Information

All reactions and manipulations which are sensitive to moisture or air were performed under inert atmosphere of argon. All chemicals were purchased from J&K, TCI and Aldrich, and were used as received. Tianjin. Petroleum ether (PE) refers to the fraction boiling in the 60–90 °C range. Anhydrous THF, Et_2O was distilled from sodium benzophenone ketyl. Anhydrous CH_2Cl_2, Et_3N, DMSO and *i*PrOH were distilled from calcium hydride. NMR spectra were recorded on a Bruker AV 400 spectrometer at 400 MHz (^{1}H NMR), 101 MHz (^{13}C NMR). Chemical shifts were reported in ppm relative to internal TMS for ^{1}H NMR data, deuterated solvent for ^{13}C NMR data, respectively. Data are presented in the following space: chemical shift, multiplicity, coupling constant in hertz (Hz), and signal area integration in natural numbers. Optical rotations were determined using a Perkin Elmer 341 polarimeter. HRMS were recorded on APEXII and ZAB-HS spectrometer. High-resolution mass spectra were recorded on an IonSpec FT-ICR mass spectrometer. HPLC analyses were determined using a Hewlett Packard Model HP 1100 Series chromatography.

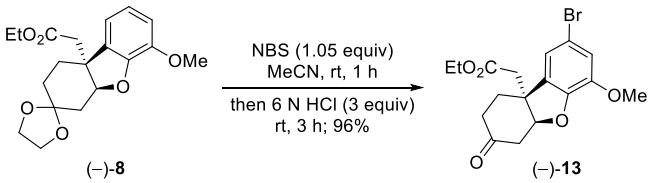
B) Synthesis of Enone Intermediate (+)-11

Enone intermediate (+)-**11** was synthesized from tricyclic benzofuran (–)-**8** by the following procedure.



Tricyclic benzofuran (–)-**8** was synthesized according to our previously developed method in five steps in around 70% overall yields and 93% ee on a multi-gram scale from commercially available 7-bromo-1,4-dioxaspiro[4.5]decan-8-one and 2-iodo-6-methoxyphenol.[1]

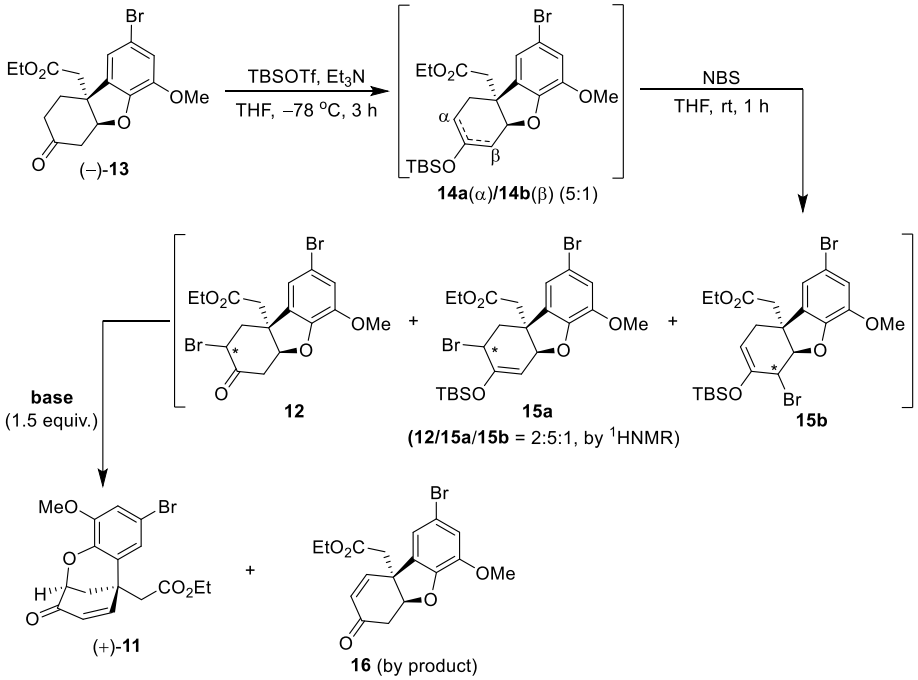
Synthesis of compound (–)-13



To a solution of compound (–)-**8** (8.60 g, 24.7 mmol) in 100 mL MeCN was added NBS (4.76 g, 25.9 mmol) slowly in small portions at room temperature, and the resulting mixture was stirred for 1 h to complete the reaction. Then saturated aqueous solution of $Na_2S_2O_3$ (20 mL) was added to quench the reaction. Subsequently, aqueous 6N HCl solution (12 mL) was added to the mixture and stirred at room temperature for another 3 h. After neutralization with saturated aqueous $NaHCO_3$ solution (150 mL), the mixture was extracted with EtOAc (3 × 60 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (3:1) to give the product (–)-**13** (8.90 g, 96% yield) as a white solid. 6.70 g white crystal was yielded after recrystallization from Et_2O, 72% recrystallization yield, mp 99–101 °C, 99.5% ee; HPLC conditions: column, Chiralcel OJ-3; eluent, 2-propanol/hexane 20:80; temp, 25 °C; flow rate, 1.0 mL/min; detection, 210 nm light; R_f 0.5 (petroleum ether/ethyl acetate = 2:1); $[\alpha]_D^{25}$ –162.6 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 2936, 1723, 1616, 1486, 1444, 1202, 1026, 838, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 6.88 (d, *J* = 1.6 Hz, 1H), 6.86 (d, *J* = 1.6 Hz, 1H), 5.26 (t, *J* = 3.2 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.03 (dd, *J* = 17.2, 3.2 Hz, 1H), 2.97 (dd, *J* = 17.2, 3.2 Hz, 1H),

2.86 (d, J = 16.0 Hz, 1H), 2.81 (d, J = 16.0 Hz, 1H), 2.34–2.25 (m, 2H), 1.98–1.87 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 208.4, 170.4, 146.6, 144.9, 133.8, 118.3, 115.5, 112. 9, 86.9, 61.0, 56.2, 46.6, 44.2, 42.2, 35.6, 31.2, 14.2; HRMS (*m/z*): calcd for $C_{17}H_{20}BrO_5$ ([M + H]$^+$) 383.0489, found 383.0478.

Synthesis of enone intermediate (+)-11 in a one-pot procedure



1. Screening of the bases

To a solution of compound (–)-**13** (0.19 g, 0.50 mmol) in THF (1.5 mL) at –78 °C was added Et_3N (0.23 mL, 1.70 mmol), then TBSOTf (0.25 mL, 1.10 mmol) was added dropwise within 5 min. The mixture was stirred at –78 °C for 3 h to complete the reaction and then concentrated in high vacuo. The resulting colorless oil was dissolved in THF (1.5 mL) and treated with a solution of NBS (0.11 g, 0.60 mmol) in THF (1.5 mL) dropwise. The mixture was stirred at room temperature for another 1 h. Then to the mixture was added base (0.80 mmol) in THF (0.80 mL) dropwise. The resulting mixture was stirred at room temperature for 2–20 h and quenched with saturated aqueous $NaHCO_3$ solution (5 mL) and extracted with Et_2O (3 × 5 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (3:1) to give a mixture of product (+)-**11** (R_f 0.37) and by-product **16** (R_f 0.37) as a white solid. The results are summarized in Table S1.

Table S1. The results of enantioselective synthesis of (+)-**11** in a one-pot procedure.[a]

Entry	Base	Temp (°C)	Time (h)	(+)-**11**/**16**[b]	Yield (%)[c]
1	DBU	rt	15	94:6	58
2	*t*BuOK	rt	20	97:3	37
3	DABCO	50	10	96:4	41
4	Et_3N	50	10	99:1	27
5	TBAF	rt	2	>99:1	69
6[d]	TBAF	rt	2	>99:1	70

[a] Reaction conditions: (–)-**13** (0.19 g, 0.50 mmol), 1.5 equivalent of base.

[b] The ratio of (+)-**11** to **16** was ditermind by ^{1}H NMR.

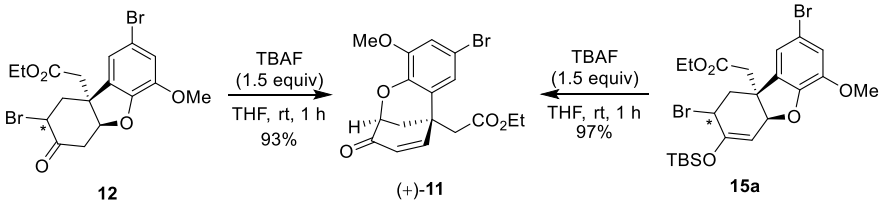
[c] The yield of (+)-**11** was caculated from the combined isolated yield of (+)-**11** and **16** over 3 steps.

[d] Performed on a gram-scale ((–)-**13**, 1.15 g, 3.00 mmol).

2. Gram-scale synthesis with TBAF as a base

To a solution of compound (–)-**13** (1.15 g, 3.00 mmol) in THF (9.0 mL) at –78 °C was added Et_3N (1.37 mL, 9.90 mmol), TBSOTf (1.52 mL, 6.60 mmol) was added dropwise within 15 min. The mixture was stirred at –78 °C for 3 h to complete the reaction and then concentrated in high vacuo. The resulting colorless oil was dissolved in THF (9.0 mL) and treated with a solution of NBS (0.58 g, 3.15 mmol) in THF (9.0 mL) dropwise. The mixture was stirred at room temperature for another 1 h. Then to the mixture was added TBAF (4.70 mL, 4.70 mmol, 1.0 M in THF) dropwise. The resulting mixture was stirred at room temperature for 2 h and quenched with saturated aqueous $NaHCO_3$ solution (15 mL) and extracted with Et_2O (3 × 15 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (3:1) to give the product (+)-**11** (0.82 g, 70% yield) as a white solid. mp 77–79 °C; R_f 0.37 (petroleum ether/ethyl acetate = 3:1).

3. Treatment of the isolated intermediates 12, **15a, and 15b with TBAF**



General procedure: To a solution of the isolated bromide intermediate (27.0 μmol) THF (0.20 mL) was added TBAF (40.0 μL, 40.0 μmol, 1.0 M in THF) was added dropwise. The resulting mixture was stirred at room temperature for 1 h and quenched with saturated aqueous $NaHCO_3$ solution (3 mL) and extracted with Et_2O (3 × 3 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (3:1) to give the product as a white solid.

For intermediate **12**, the product (+)-**11** (9.6 mg) was obtained in 93% yield.

For intermediate **15a**, the product (+)-**11** (10.0 mg) was obtained in 97% yield.

For intermediate **15b**, only complex mixtures without any detectable (+)-**11** were obtained.

The data of the isolated intermediates (**14**, **12**, **15a,** and **15b)** and product (+)-**11** as below:

14a/14b (5:1): colorless oil (R_f 0.63, petroleum ether/ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.91 (d, *J* = 1.6 Hz, 0.17H), 6.86 (d, *J* = 1.6 Hz, 0.17H), 6.82 (d, *J* = 2.0 Hz, 0.83H), 6.81 (d, *J* = 2.0 Hz, 0.83H), 5.24 (d, *J* = 4.0 Hz, 0.17H), 5.18 (dd, *J* = 4.8, 3.2 Hz, 0.83H), 4.98 (d, *J* = 4.0 Hz, 0.17H), 4.74–4.70 (m, 0.83H), 4.10 (q, *J* = 7.2 Hz, 0.34H), 4.09 (q, *J* = 7.2 Hz, 1.66H), 3.84 (s, 0.51H), 3.82 (s, 2.49H), 2.69 (s, 1.66H), 2.63 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.57 (d, *J* = 5.6 Hz, 0.34H), 2.51 (dd, *J* = 16.0, 3.2 Hz, 1H), 2.36 (dd, *J* = 15.2, 3.2 Hz, 1H), 2.27 (dd, *J* = 15.2, 2.4 Hz, 1H), 2.15–1.93 (m, 1H), 1.21 (t, *J* = 7.2 Hz, 0.51H), 1.20 (t, *J* = 7.2 Hz, 2.49H), 0.89–0.84 (m, 9H), 0.11–0.00 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.7, 170.5, 156.8, 150.3, 147.4, 146.3, 145.8, 144.6, 136.1, 135.0, 118.7, 118.3, 118.0, 115.0, 114.6, 111.8, 101.3, 100.2, 89.0, 86.8, 60.6, 56.2, 56.1, 48.3, 45.6, 44.2, 42.1, 34.9, 33.4, 29.2, 26.8, 25.6, 18.0, 14.1, –4.5(2), –4.6, –4.9; HRMS (*m/z*): calcd for $C_{23}H_{34}BrO_5Si$ ($[M + H]^+$) 498.5085, found 498.5082.

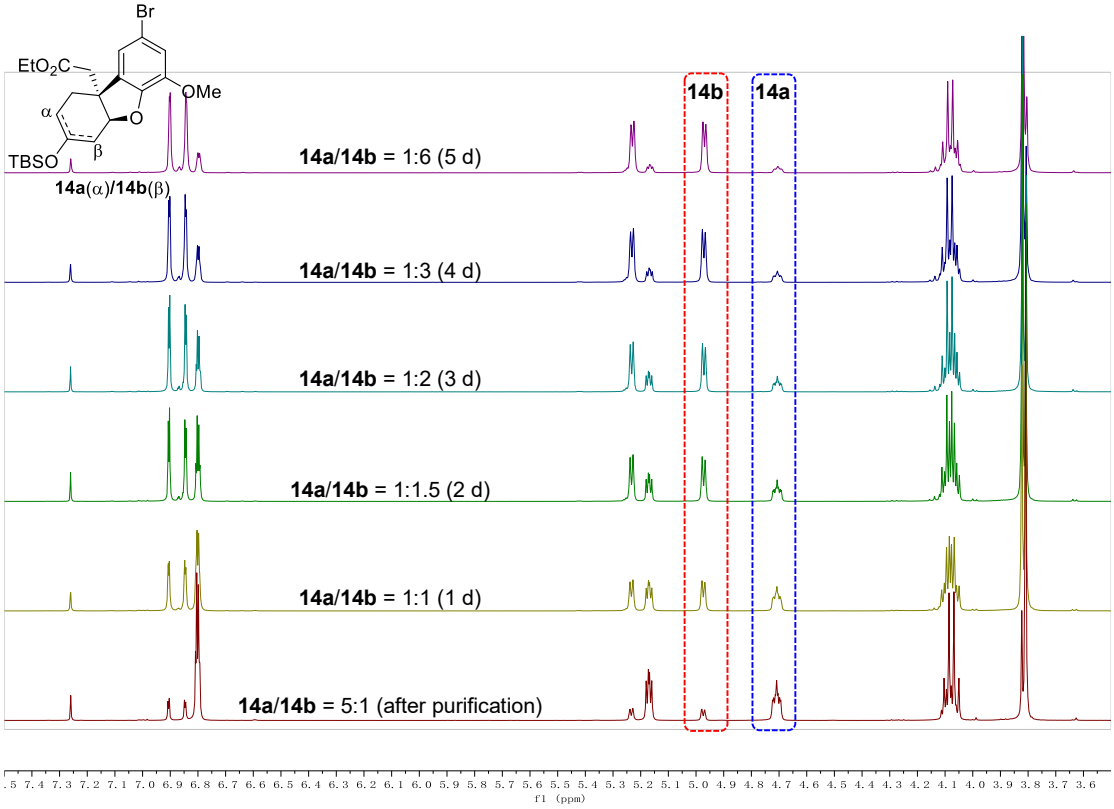
12 (unstable, with minor isomers or other impurities): yellow oil (R_f 0.4, petroleum ether/ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.93 (d, *J* = 1.6 Hz, 1H), 6.91 (d, *J* = 1.6 Hz, 1H), 5.24 (t, *J* = 3.2 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.11 (dd, *J* =14.0, 4.8 Hz, 1H), 3.85 (s, 3H), 3.27 (dd, *J* = 15.6, 3.2 Hz, 1H), 3.17 (dd, *J* = 15.6, 3.2 Hz, 1H), 2.90 (d, *J* = 16.4 Hz, 1H), 2.81 (d, *J* = 16.4 Hz, 1H), 2.77 (t, *J* = 14.0 Hz, 1H), 2.48 (dd, *J* = 15.6, 4.8 Hz, 1H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 200.6, 170.2, 146.2, 145.2, 132.8, 118.3, 116.0, 113.7, 86.4, 61.3, 56.4, 48.5, 46.9, 43.6, 42.6, 41.5, 14.2; HRMS (*m/z*): calcd for $C_{17}H_{19}Br_2O_5$ ($[M + H]^+$) 463.1415, found 463.1412.

15a: yellow oil (R_f 0.6, petroleum ether/ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.02 (d, *J* = 2.0 Hz, 1H), 6.88 (d, *J* = 2.0 Hz, 1H), 5.31 (dd, *J* = 4.4, 0.8 Hz, 1H), 5.11 (dd, *J* = 4.4, 0.8 Hz, 1H), 4.47 (t, *J* = 6.0 Hz, 1H), 4.17–4.07 (m, 2H), 3.84 (s, 3H), 2.82 (d, *J* = 16.0 Hz, 1H), 2.74 (d, *J* = 16.0 Hz, 1H), 2.69 (d, *J* = 6.0 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.18 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.2, 153.3, 145.8, 145.7, 134.5, 118.8, 115.3, 112.6, 102.9, 85.6, 60.7, 56.2, 45.9, 44.7, 41.5, 38.8, 25.5, 18.2, 14.2, –4.7, –4.8; HRMS (*m/z*): calcd for $C_{23}H_{33}Br_2O_5Si$ ($[M + H]^+$) 577.4045, found 577.4038.

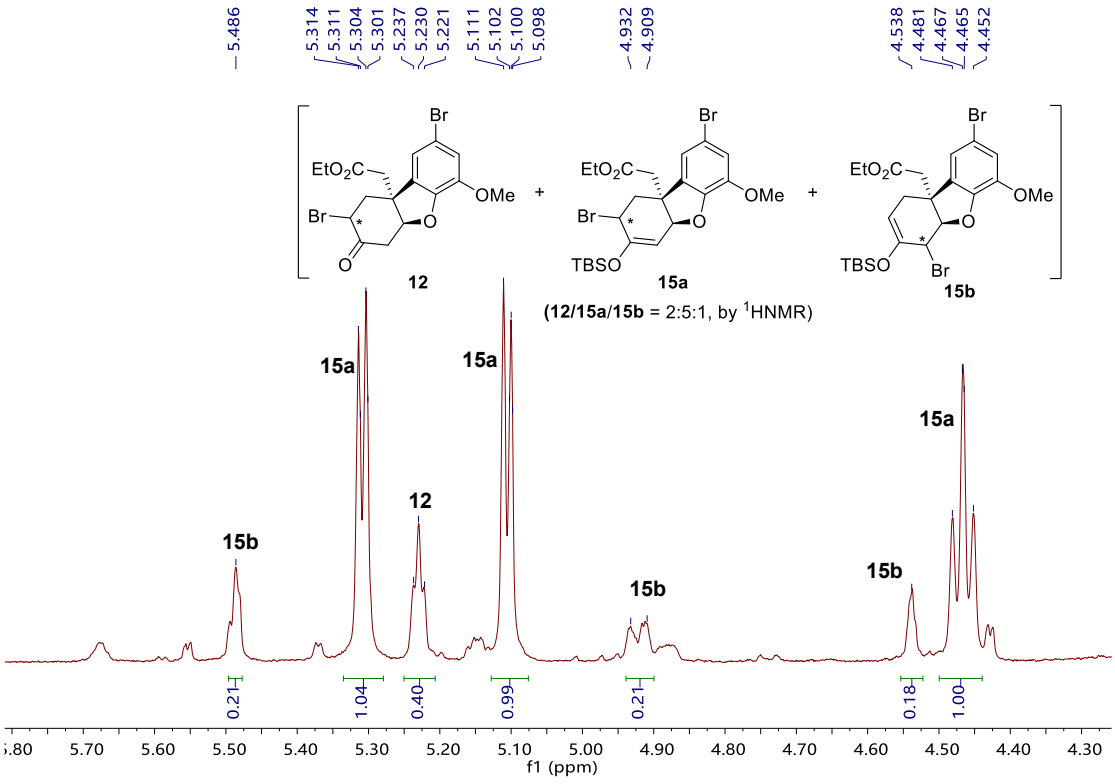
15b: yellow oil (R_f 0.65, petroleum ether/ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.86 (d, *J* = 1.6 Hz, 1H), 6.82 (d, *J* = 1.6 Hz, 1H), 5.49 (d, *J* = 2.0 Hz, 1H), 4.93 (d, *J* = 7.6 Hz, 1H), 4.58–4.53 (m, 1H), 4.09–4.01 (m, 2H), 3.82 (s, 3H), 2.85 (s, 2H), 2.64 (dd, *J* = 15.6, 2.8 Hz, 1H), 2.54 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.13 (t, *J* = 7.2 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 169.8, 150.5, 146.8, 144.2, 135.1, 118.1, 115.0, 112.4, 106.0, 91.5, 60.7, 56.1, 48.2, 46.8, 46.0, 33.9, 25.6, 18.0, 14.0, –4.7, –4.8; HRMS (*m/z*): calcd for $C_{23}H_{33}Br_2O_5Si$ ($[M + H]^+$) 577.4045, found 577.4040.

(+)-**11**: a white solid (R_f 0.37, petroleum ether/ethyl acetate = 3:1). mp 76–79 °C; $[\alpha]_D^{25}$ +250.0 (*c* 0.1, $CHCl_3$); IR (KBr): ν_{max} = 2978, 2939, 1729, 1688, 1573, 1472, 1445, 1268, 1207, 1037, 860, 822 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.01 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.95 (s, 2H), 6.14 (dd, *J* = 10.0, 0.8 Hz, 1H), 4.88–4.85 (m, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.17 (d, *J* = 15.2 Hz, 1H), 2.81 (d, *J* = 15.2 Hz, 1H), 2.59 (dd, *J* = 13.6, 1.6 Hz, 1H), 2.35 (ddd, *J* = 13.6, 4.0, 2.4 Hz, 1H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 191.2, 169.8, 156.9, 149.7, 141.1, 127.5, 126.3, 118.5, 114.6, 112.5, 74.9, 61.1, 56.3, 41.2, 35.1, 32.6, 14.2; HRMS (*m/z*): calcd for $C_{17}H_{18}BrO_5$ ($[M + H]^+$) 381.0332, found 381.0334.

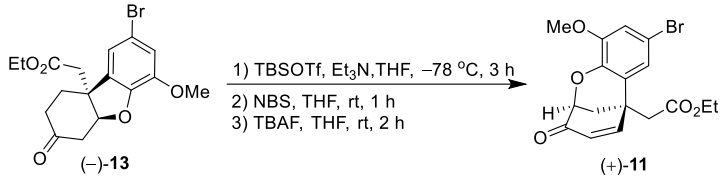
The ratio of **14a**/**14b** was determined by ^{1}H NMR and varied over time.



The ratio of **12**/**15a**/**15b** was determined by ^{1}H NMR.



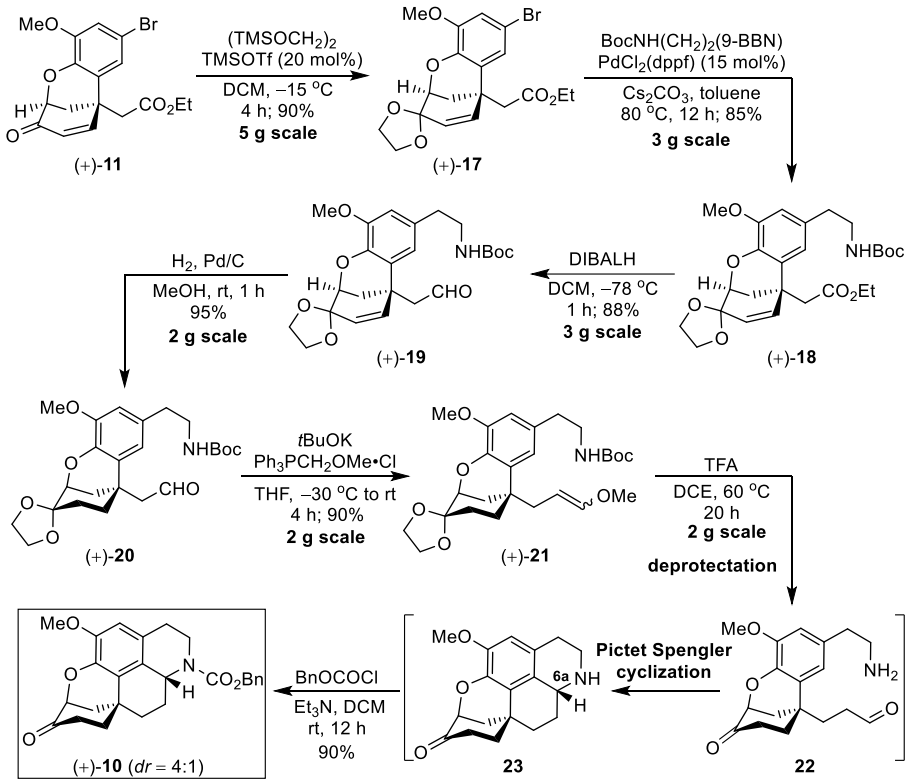
Synthesis of enone intermediate (+)-11 from purified intermediates



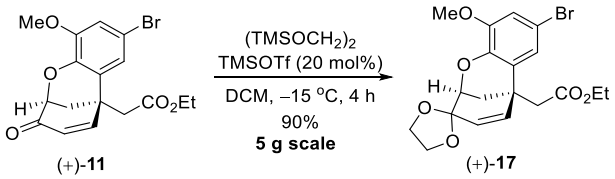
To a solution of compound (–)-**13** (5.90 g, 15.4 mmol) in THF (77 mL) at –78 °C was added Et_3N (7.03 mL, 50.8 mmol), and TBSOTf (7.78 mL, 33.9 mmol) was added dropwise within 10 min. The mixture was stirred at –78 °C for 3 h to complete the reaction. Water (50 mL) was added to quench the reaction and the mixture was extracted with Et_2O (3 × 40 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was flash chromatographed on silica-gel with petroleum ether/ethyl acetate (3:1) to give a colorless oil. The colorless oil was re-dissolved in THF (60 mL) and cooled to 0 °C with an ice-bath. A solution of NBS (2.97 g, 16.2 mmol) in THF (80 mL) was then added dropwise at 0 °C, and the resulting reaction mixture was stirred at room temperature for another 1 h. The reaction mixture was then quenched with saturated aqueous $Na_2S_2O_3$ solution (50 mL) and extracted with Et_2O (3 × 50 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was flash chromatographed on a silica-gel column with petroleum ether/ethyl acetate (3:1) to give a yellow oil. The yellow oil was re-dissolved in THF (60 mL), and TBAF (23.1 mL, 23.1 mmol, 1.0 M in THF) was added dropwise. The resulting mixture was stirred at room temperature for 2 h and quenched with saturated aqueous $NaHCO_3$ solution (30 mL) and extracted with Et_2O (3 × 60 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to give the product (+)-**11** (5.05 g, 86% yield) as a white solid.

C) Enantioselective Synthesis of Ketone Intermediate (+)-10

The ketone intermediate (+)-**10** was synthesized by the following procedure.

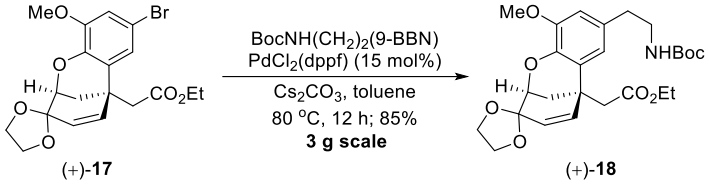


Synthesis of compound (+)-17



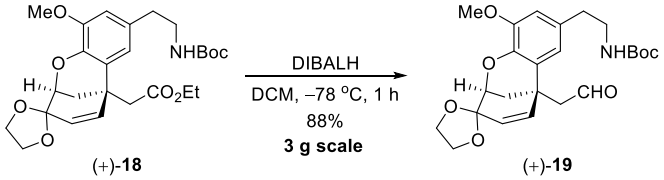
To a solution of compound (+)-**11** (5.20 g, 13.6 mmol) and 2,2,7,7-tetramethyl-3,6-dioxa-2,7-disilaoctane (10.0 mL, 40.9 mmol) in CH_2Cl_2 (60 mL) was added TMSOTf (0.49 mL, 2.73 mmol) dropwise at –15 °C. The mixture was stirred at the same temperature for 4 h, quenched with saturated aqueous $NaHCO_3$ solution (40 mL), and extracted with CH_2Cl_2 (3 × 40 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (2:1) to give the product (+)-**17** (5.20 g, 90% yield) as a white solid: mp 45–47 °C; R_f 0.5 (petroleum ether/ethyl acetate = 1:1); $[\alpha]_D^{25}$ +175.8 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 2979, 2940, 2891, 1731, 1574, 1475, 1445, 1416, 1265, 1212, 1149, 1122, 1016, 993, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 6.86 (d, *J* = 2.0 Hz, 1H), 6.85 (d, *J* = 2.0 Hz, 1H), 5.85 (dd, *J* = 9.6, 1.6 Hz, 1H), 5.58 (dd, *J* = 9.6, 1.6 Hz, 1H), 4.54–4.50 (m, 1H), 4.27–4.20 (m, 1H), 4.18–4.12 (m, 2H), 4.10–4.03 (m, 2H), 3.96–3.88 (m, 1H), 3.83 (s, 3H), 2.95 (d, *J* = 14.8 Hz, 1H), 2.79 (d, *J* = 14.8 Hz, 1H), 2.56 (d, *J* = 13.2 Hz, 1H), 2.21 (ddd, *J* = 13.2, 4.8, 2.0 Hz, 1H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.1, 149.1, 141.2, 138.7, 129.0, 125.6, 117.8, 113.5, 111.5, 104.3, 74.0, 65.8, 65.4, 60.7, 56.1, 41.1, 34.5, 30.8, 14.2; HRMS (*m/z*): calcd for $C_{19}H_{21}BrNaO_6$ ($[M + Na]^+$) 447.0414, found 447.0419.

Synthesis of compound (+)-18



The mixture of compound (+)-**17** (3.50 g, 8.23 mmol), $PdCl_2(dppf)•CH_2Cl_2$ (1.00 g, 1.23 mmol), and was dissolved in toluene (35 mL). A solution of Cs_2CO_3 (8.04 g, 24.7 mmol) in H_2O (8 mL) and a solution of $BocNH(CH_2)_2$(9-BBN), which was generated by *in situ* by the reaction of *tert*-butyl vinylcarbamate (1.77 g, 12.4 mmol) and $(9\text{-BBN})_2$ (1.51 g, 6.18 mmol) in THF (12 mL) at room temperature for 4 h, was added. The resulting mixture was stirred at 80 °C for 12 h, and then filtered through a pad of Florisil. The filtrate was washed with water (30 mL), and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1) to give the product (+)-**18** (3.43 g, 85% yield) as a light yellow-green solid: mp 44–46 °C; R_f 0.45 (petroleum ether/ethyl acetate = 2:3); $[\alpha]_D^{25}$ +142.6 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3374, 2977, 2937, 2897, 1710, 1589, 1484, 1366, 1158, 1051, 992, 950, 733 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 6.58 (s, 1H), 6.54 (s, 1H), 5.88 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.56 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.55 (brs, 1H), 4.53–4.50 (m, 1H), 4.28–4.20 (m, 1H), 4.19–4.10 (m, 2H), 4.10–4.01 (m, 2H), 3.97–3.89 (m, 1H), 3.84 (s, 3H), 3.38–3.25 (m, 2H), 3.00 (d, *J* = 14.8 Hz, 1H), 2.80 (d, *J* = 14.8 Hz, 1H), 2.69 (t, *J* = 6.8 Hz, 2H), 2.55 (d, *J* = 13.2 Hz, 1H), 2.19 (ddd, *J* = 13.2, 5.2, 2.4 Hz, 1H), 1.44 (s, 9H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.5, 155.9, 148.2, 140.4, 139.3, 129.8, 127.5, 125.1, 114.9, 110.7, 104.5, 79.2, 73.7, 65.7, 65.4, 60.6, 55.8, 41.9, 41.3, 36.0, 34.5, 31.0, 28.4, 14.2; HRMS (*m/z*): calcd for $C_{26}H_{35}NNaO_8$ $[M + Na]^+$) 512.2255, found 512.2258.

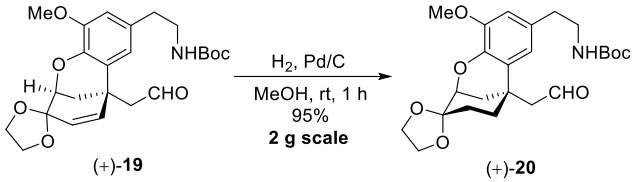
Synthesis of compound (+)-19



To a solution of compound (+)-**18** (3.40 g, 6.94 mmol) in CH_2Cl_2 (40 mL) at –78 °C was added DIBALH (13.9 mL, 1.0 M in hexane, 13.9 mmol) dropwise. The resulting mixture was stirred at –78 °C for 1 h and then quenched with saturated aqueous sodium-potassium tartrate solution (30 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 30 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1) to give the product (+)-**19** (2.72 g, 88% yield) as a white solid: mp 75–77 °C; R_f 0.34 (petroleum ether/ethyl acetate = 2:3); $[\alpha]_D^{25}$ +155.7 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3599, 3354, 2966, 2932, 2897, 1708, 1589, 1516, 1483, 1366, 1273, 1166, 1144, 950, 844, 733 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.82 (s, 1H), 6.61 (s, 1H), 6.50 (s, 1H), 5.90 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.62 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.59–4.48 (m, 2H), 4.31–4.23 (m, 1H), 4.14–4.03 (m, 2H), 3.97–3.91 (m, 1H), 3.85 (s, 3H), 3.33–3.25 (m, 2H), 2.97–2.91 (m, 2H), 2.70 (t, *J* = 6.8 Hz, 2H), 2.47 (d, *J* = 13.2 Hz, 1H), 2.18 (ddd, *J* = 13.2, 4.8, 2.0 Hz, 1H), 1.44 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 200.6, 155.9, 148.5, 140.4, 138.7, 130.3, 126.8, 126.0, 115.0, 110.9, 104.3, 79.3, 73.5, 65.8, 65.4, 55.9, 49.3, 41.9, 36.0,

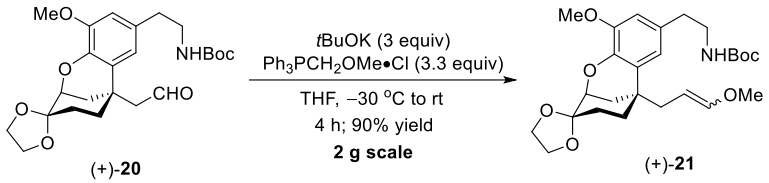
33.9, 31.5, 28.4; HRMS (*m/z*): calcd for $C_{24}H_{31}NNaO_7$ ([M + Na]$^+$) 468.1993, found 468.1998.

Synthesis of compound (+)-20



The mixture of compound (+)-**19** (2.67 g, 6.00 mmol) and 10% Pd/C (0.27 g) in MeOH (30 mL) was charged with H_2 balloon, and the mixture was stirred at room temperature for 1 h. The mixture was then filtered through a pad of Florisil and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1) to give the product (+)-**20** (2.57 g, 95% yield) as a white solid: mp 123–125 °C; R_f 0.55 (petroleum ether/ethyl acetate, 1:2); $[\alpha]_D^{25}$ +25.2 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3727, 3703, 3626, 3602, 3369, 2934, 2890, 1714, 1588, 1517, 1482, 1365, 1272, 1220, 1169, 1146, 1110, 1037, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.66 (t, *J* = 2.8 Hz, 1H), 6.61 (s, 1H), 6.55 (s, 1H), 4.64 (brs, 1H), 4.33 (t, *J* = 2.8 Hz, 1H), 4.09–3.99 (m, 3H), 3.95–3.90 (m, 1H), 3.86 (s, 3H), 3.39–3.21 (m, 2H), 3.02 (dd, *J* = 16.0, 2.0 Hz, 1H), 2.75–2.66 (m, 2H), 2.60 (dd, *J* = 16.0, 2.4 Hz, 1H), 2.16–2.13 (m, 2H), 1.95–1.85 (m, 1H), 1.66–1.61 (m, 1H), 1.61–1.53 (m, 2H), 1.44 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 201.5, 155.9, 148.1, 141.9, 130.5, 126.2, 116.6, 110.5, 107.8, 79.2, 73.3, 65.0 (2), 55.8, 51.4, 41.9, 38.2, 36.0, 33.1, 31.7, 28.6, 28.4; HRMS (*m/z*): calcd for $C_{24}H_{34}NO_7^+$ ([M + H]$^+$) 448.2330, found 448.2327.

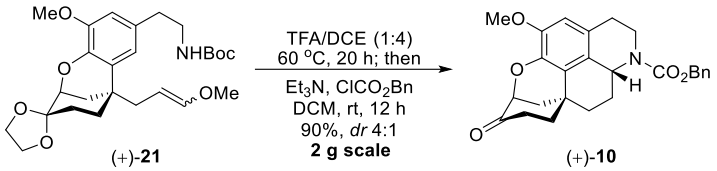
Synthesis of compound (+)-21



To a solution of (methoxymethyl)triphenylphosphonium chloride (6.86 g, 20.0 mmol) in THF (20 mL) was added *t*BuOK (2.08 g, 18.0 mmol) in portions at –30 °C, and the resulting suspension solution was stirred at the same temperature for 0.5 h. The solution of compound (+)-**20** (2.69 g, 6.00 mmol) in 15 mL THF was then added, and the resulting mixture was stirred at room temperature for another 4 h. The reaction mixture was quenched with H_2O (30 mL) and extracted with ethyl acetate (4 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (2:1 to 1:1) to give the product (+)-**21** as a mixture of *Z* and *E* isomers (44:56, 2.57 g, 90% yield): mp 46–51 °C; R_f 0.53 (petroleum ether/ethyl acetate = 1:1); $[\alpha]_D^{25}$ +33.8 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3632, 3359, 2932, 1708, 1587, 1516, 1480, 1365, 1250, 1145, 1022, 949, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.62 (s, 0.44H), 6.60 (s, 0.56H), 6.56 (s, 1H), 6.30 (d, *J* = 12.8 Hz, 0.56H), 5.93 (d, *J* = 6.4 Hz, 0.44H), 4.65–4.54 (m, 1.56H), 4.30 (m, 1.2H), 4.24 (q, *J* = 7.2 Hz, 0.56H), 4.09–3.95 (m, 3.7H), 3.95–3.86 (m, 1.0H), 3.85 (s, 1.68H), 3.84 (s, 1.32H), 3.59 (s, 1.32H), 3.45 (s, 1.56H), 3.37–3.25 (m, 2.0H), 2.75–2.66 (m, 2.0H), 2.60–2.43 (m, 1.44H), 2.22 (dd, *J* = 14.0, 8.8 Hz, 0.56H), 1.96–1.75 (m, 4H), 1.57–1.50 (m, 2H), 1.44 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.9, 149.0, 147.8, 147.7, 142.1, 129.8, 129.6, 128.1 (2), 117.2, 116.8, 109.8 (2), 108.4 (2), 101.7, 97.8, 79.1, 73.7

(2), 65.0, 64.9, 59.4 (2), 56.0, 55.8, 42.1, 42.0, 37.9, 37.7, 36.9, 36.0, 35.9, 34.3, 34.1, 32.7, 30.8, 29.0, 28.4; HRMS (*m/z*): calcd for $C_{26}H_{41}N_2O_7$ ($[M + NH_4]^+$) 493.2908, found 493.2905.

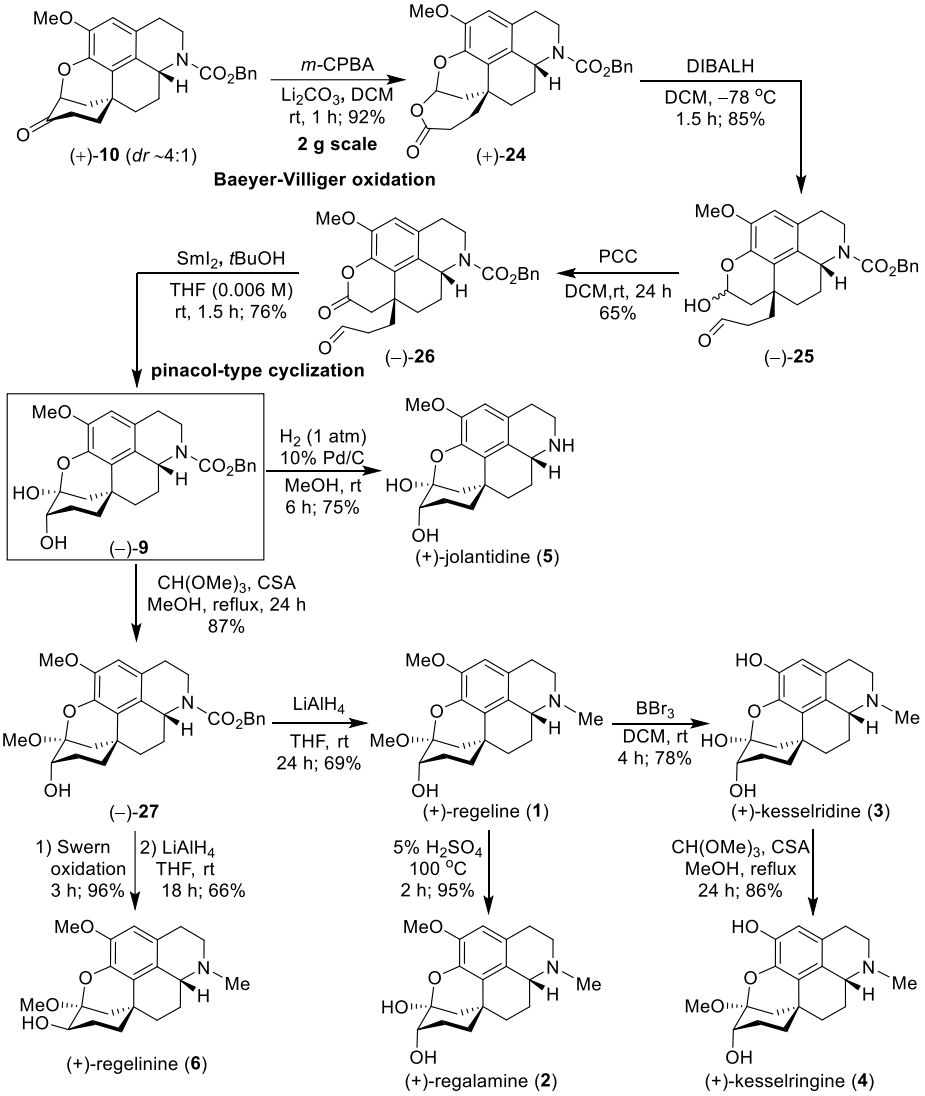
Synthesis of compound (+)-10



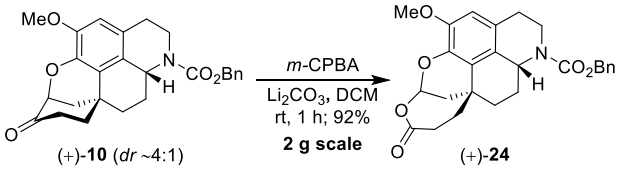
To a solution of (+)-**21** (2.80 g, 5.89 mmol) in DCE (55 mL) was added 14 mL TFA dropwise. The resulting reaction mixture was stirred at 60 °C for 20 h and then concentrated in vacuo. The residue was re-dissolved with CH_2Cl_2 (40 mL), and Et_3N (6.09 mL, 44.0 mmol) and $ClCO_2Bn$ (3.43 mL, 23.6 mmol) were added dropwise successively at room temperature. The reaction mixture was stirred for 12 h, quenched with H_2O (40 mL), and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1) to give the product (+)-**10** as a mixture of two diastereoisomers (*dr* = 4:1, 2.30 g, 90% yield): white solid, mp 62–67 °C; R_f 0.46 (petroleum ether/ethyl acetate = 1:1); $[\alpha]_D^{25}$ +149.0 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 2938, 2866, 1725, 1695, 1600, 1486, 1423, 1280, 1195, 1101, 990, 735, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.53–7.28 (m, 5H), 6.61 (s, 1H), 5.27–5.18 (m, 2H), 4.94–4.82 (m, 0.85H), 4.75 (d, *J* = 4. 8 Hz, 0.15 H), 4.71–4.69 (m, 0.85H), 4.58–4.56 (m, 1.5H), 4.48–4.39 (m, 1H), 3.87 (s, 3H), 2.99–2.76 (m, 2H), 2.65–2.56 (m, 1H), 2.47–2.18 (m, 4H), 2.15–2.03 (m, 2H), 1.97–1.83 (m, 2H), 1.73 (m, 1H), 1.64–1.49 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 206.0, 155.2, 146.4, 140.2, 136.8, 128.5, 128.0, 127.8, 127.8, 125.9, 123.7, 110.2, 78.5, 67.1, 56.0, 49.4, 40.2, 39.2, 39.1, 36.6, 32.2, 31.2, 30.7, 29.9; HRMS (*m/z*): calcd for $C_{26}H_{28}NO_5$ ($[M + H]^+$) 434.1962, found 434.1957.

D) Enantioselective Synthesis of Pentacyclic Homoproaporphine Alkaloids

The advanced chiral intermediate (−)-**9** and the members of pentacyclic homoproaphine alkaloid family were synthesized by the following procedure.



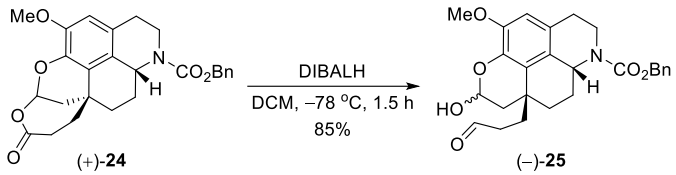
Synthesis of compound (+)-24



To a solution of compound (+)-**10** (2.30 g, 5.31 mmol) in CH_2Cl_2 (35 mL) was added Li_2CO_3 (0.12 g, 1.60 mmol) and *m*-CPBA (1.47 g, 6.80 mmol). The resulting mixture was stirred at room temperature for 1 h, and quenched with saturated Na_2CO_3 solution (30 mL), and extracted with CH_2Cl_2 (3 × 40 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (2:1) to give the product (+)-**24** (2.20 g, 92% yield) as a white solid, mp 83–85 °C; R_f 0.47 (petroleum ether/ethyl acetate = 1:1); $[\alpha]_D^{25}$ +55.8 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 2930, 2871, 1740, 1695, 1423, 1266, 1099, 1036, 737, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.29 (m, 5H), 6.64 (s, 1H), 5.97 (dd, *J* = 5.2,

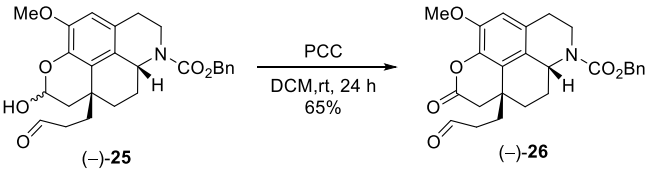
0.8 Hz, 1H), 5.30–5.14 (m, 2H), 4.76 (dd, *J* = 12.0, 4.4 Hz, 1H), 4.47–4.37 (m, 1H), 3.88 (s, 3H), 2.93–2.80 (m, 2H), 2.66–2.58 (m, 1H), 2.57–2.49 (m, 1H), 2.48–2.37 (m, 1H), 2.34–2.20 (m, 2H), 2.16–2.08 (m, 1H), 2.03–1.95 (m, 1H), 1.93–1.83 (m, 1H), 1.79–1.70 (m, 1H), 1.61–1.48 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 172.8, 155.1, 145.9, 140.3, 136.8, 128. 6, 128.1, 127.8, 127.4, 125.1, 123.3, 110.6, 94.7, 67.2, 56.1(2), 49.8, 40.9, 39.1, 36.1, 35.5, 33.2, 32.4, 31.9, 30.1; HRMS (*m/z*): calcd for $C_{26}H_{28}NO_6$ ($[M + H]^+$) 450.1911, found 450.1904.

Synthesis of compound (–)-25



To a solution of compound (+)-**24** (0.66 g, 1.47 mmol) in CH_2Cl_2 (15 mL) at –78 °C was added DIBALH (2.20 mL, 1.0 M in hexane, 2.20 mmol) dropwise. The mixture was stirred at –78 °C for 1.5 h, quenched with saturated aqueous solution of sodium-potassium tartrate (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1 to 100% ethyl acetate) to give the product (–)-**25** (0.56 g, 85% yield) as a mixture of diastereoisomers (not stable). R_f 0.58 (100% ethyl acetate); $[\alpha]_D^{25}$ –123.0 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3744, 3479, 2930, 1695, 1424, 1358, 1269, 1195, 1101, 735, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.71 (s, 1H), 7.49–7.32 (m, 5H), 6.59 (s, 1H), 5.87–5.69 (m, 1H), 5.26–5.18 (m, 2H), 4.84 (dd, *J* = 10.4, 5.6 Hz, 1H), 4.46–4.35 (m, 1H), 3.86 (s, 3H), 2.90–2.83 (m, 2H), 2.64–2.56 (m, 1H), 2.53–2.45 (m, 1H), 2.44–2.26 (m, 2H), 2.22 (dd, *J* = 13.9, 4.0 Hz, 1H), 2.16–2.05 (m, 1H), 1.97–1.84 (m, 2H), 1.68 (dd, *J* = 13.9, 8.8 Hz, 2H), 1.55–1.48 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 201.2, 155.3, 147.1, 139.9, 136.8, 128.6, 128.5, 128.1, 128.0, 127.8, 126.8, 110.3, 92.7, 67.2, 55.9, 42.1, 39.8, 39.5, 39.2, 34.6, 33.0, 32.4, 30.4, 29.3; HRMS (*m/z*): calcd for $C_{26}H_{30}NO_6$ ($[M + H]^+$) 452.2068, found 452.2074.

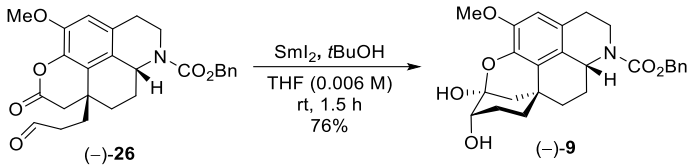
Synthesis of compound (–)-26



To a solution of compound (–)-**25** (0.35 g, 0.77 mmol) in CH_2Cl_2 (15 mL) was added pyridinium chlorochromate (PCC, 0.26 g, 1.20 mmol), and the mixture was stirred at room temperature for 1.5 h. The reaction mixture was filtrated through a short plug of silica gel and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1) to give the product (–)-**26** (0.23 g, 65% yield) as a white solid (with a minor diastereoisomer): mp 59–62 °C; R_f 0.4 (petroleum ether/ethyl acetate = 1:1); $[\alpha]_D^{25}$ –36.6 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3733, 3625, 2939, 1769, 1696, 1488,1447, 1268, 1229, 1195, 1126,1100, 904, 737, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.68 (s, 1H), 7.52–7.33 (m, 5H), 6.69 (s, 1H), 5.28–5.21 (m, 2H), 4.75 (dd, *J* = 11.2, 4.4 Hz, 1H), 4.47–4.45 (m, 1H), 3.90 (s, 3H), 2.94–2.82 (m, 2H), 2.77 (d, *J* = 16.0 Hz, 1H), 2.71–2.59 (m, 2H), 2.55–2.46 (m, 1H), 2.45–2.28 (m, 2H), 2.05–1.99 (m, 1H), 1.99–1.89 (m, 2H), 1.75–1.68 (m, 1H),

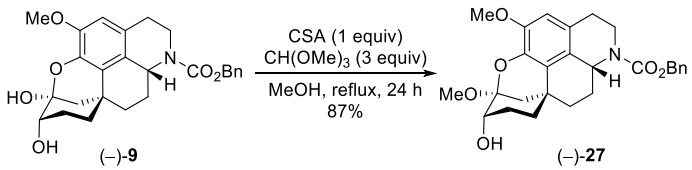
1.57–1.48 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 200.1, 167.0, 155.2, 146.3, 138.8, 136.6, 130.8, 128.6, 128.1, 128.1, 127.9, 125.7, 125.1, 111.4, 67.3, 56.1, 50.5, 42.3, 39.2, 38.9, 35.1, 32.5, 31.7, 30.6; HRMS (*m/z*): calcd for $C_{26}H_{28}NO_6$ ([M + H]$^+$) 450.1911, found 450.1916.

Synthesis of compound (–)-9



To a solution of compound (–)-**26** (0.23 g, 0.50 mmol) in THF (83 mL) were added *t*BuOH (0.23 mL, 2.50 mmol) and SmI_2 (25.0 mL, 2.50 mmol, 0.1 M in THF) at room temperature. The mixture was stirred at room temperature for 1.5 h, quenched with saturated aqueous NH_4Cl solution (50 mL), and extracted with Et_2O (3 × 50 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1 to 100% ethyl acetate) to give the product (–)-**9** (0.17 g, 76% yield) as a white solid: mp 98–100 °C; R_f 0.41 (100% ethyl acetate); $[\alpha]_D^{25}$ –86.4 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3463, 2930, 2866, 1695, 1601, 1427, 1358, 1267, 1173, 1095, 1053, 736, 700 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ: 7.48–7.21 (m, 5H), 6.60 (s, 1H), 5.22–5.12 (m, 2H), 4.71 (dd, *J* = 11.6, 4.8 Hz, 1H), 4.37–4.23 (m, 1H), 3.76 (s, 3H), 3.73–3.67 (m, 1H), 2.84 (t, *J* = 12.0 Hz, 1H), 2.70 (td, *J* = 12.0, 4.0 Hz, 1H), 2.55 (d, *J* = 15.2 Hz, 1H), 2.21–2.14 (m, 2H), 1.90–1.82 (m, 1H), 1.72 (td, *J* = 13.2, 3.6 Hz, 1H), 1.66–1.58 (m, 2H), 1.57–1.43 (m, 3H), 1.35 (tt, *J* = 14.4, 4.0 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ: 155.5, 145.7, 142.5, 136.8, 127.8, 127.5, 127.5, 124.8, 124.5, 123.9, 110.3, 99.3, 70.6, 66.9, 55.1, 49.7, 38.9, 38.7, 34.6, 33.4, 32.9, 29.2, 27.1; HRMS (*m/z*): calcd for $C_{26}H_{30}NO_6$ ([M + H]$^+$) 452.2068, found 452.2065.

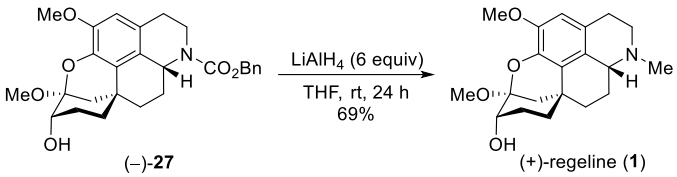
Synthesis of compound (–)-27



To a solution of compound (–)-**9** (0.19 g, 0.42 mmol) in MeOH (10 mL) were added $CH(OMe)_3$ (0.14 mL, 1.25 mmol) and (+)-10-camphorsulfonic acid (CSA, 0.10 g, 0.42 mmol). The reaction mixture was heated to reflux for 24 h, diluted with saturated aqueous solution of $NaHCO_3$ (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (1:1) to give the product (–)-**27** (0.17 g, 87% yield) as a white solid (with a minor diastereoisomer), mp 75–77 °C; R_f 0.36 (petroleum ether/ethyl acetate = 1:1); $[\alpha]_D^{25}$ –35.5 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3483, 2938, 2838, 1695, 1425, 1267, 1198, 1097, 1061, 736 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41–7.29 (m, 5H), 6.56 (s, 1H), 5.23–5.18 (m, 2H), 4.81 (dd, *J* = 11.2, 5.2 Hz, 0.8H), 4.53 (dd, *J* = 10.4, 5.6 Hz, 0.2H), 4.48–4.32 (m, 1H), 3.80–3.88 (m, 4H), 3.43 (s, 3H), 2.97–2.77 (m, 2H), 2.57 (d, *J* = 14.0 Hz, 1H), 2.43 (s, 1H), 2.34–2.28 (m, 1H), 2.07–2.01 (m, 1H), 1.99–1.82 (m, 2H), 1.78–1.63 (m, 4H), 1.44–1.38 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$, rotamer mixture) δ:

156.4, 146.0, 142.5, 136.9, 128.5, 128.0, 127.8, 124.3, 124.3, 122.4, 110.2, 102.2, 71.3, 70.6, 67.0, 56.0, 49.2, 39.1, 35.4, 34.9, 34.6, 33.7, 33.0, 29.9, 26.6; HRMS (*m/z*): calcd for $C_{27}H_{32}NO_6$ ([M + H]$^+$) 466.2224, found 466.2222.

Synthesis of (+)-regeline (1)



To a solution of (–)-**27** (87.0 mg, 0.19 mmol) in THF (6 mL) was added $LiAlH_4$ (43.0 mg, 1.12 mmol), and the resulting mixture was stirred at room temperature for 24 h. The reaction was then quenched by slow addition of H_2O (8 mL), and the mixture was extracted with EtOAc (3 × 6 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with ethyl acetate/triethylamine (30:1) to give the product (+)-regeline (**1**) (45.0 mg, 69% yield) as a white solid: mp 201–203 °C (lit.[2] 198–200 °C); R_f 0.26 (ethyl acetate/triethylamine = 30:1); $[\alpha]_D^{25}$ +92.0 (*c* 1.5, MeOH) (lit.[2] +93 (*c* 1.5, MeOH)); IR (KBr): ν_{max} = 3175, 2945, 2877, 2833, 1598, 1485, 1463, 1374, 1259, 1225, 1159, 1061, 1004, 872, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.52 (s, 1H), 3.84–3.83 (m, 1H), 3.83 (s, 3H), 3.43 (s, 3H), 3.12–3.03 (m, 1H), 3.03–2.98 (m, 1H), 2.94 (dd, *J* = 9.7, 5.5 Hz, 1H), 2.62 (dd, *J* = 15.6, 3.8 Hz, 1H), 2.53–2.47 (m, 1H), 2.45 (s, 3H), 2.31–2.25 (m, 1H), 2.01 (d, *J* = 12.3 Hz, 1H), 1.86–1.78 (m, 2H), 1.77–1.69 (m, 1H), 1.73–1.66 (m, 2H), 1.59–1,53 (m, 1H), 1.48–1.33 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 146.0, 142.1, 126.2, 124.6, 123.9, 109.8, 102.0, 70.8, 60.0, 55.9, 537, 49.2, 43.7, 34.7, 34.3, 34.2, 33.1, 28.9, 27.1, 26.4; HRMS (*m/z*): calcd for $C_{20}H_{28}NO_4$ ([M + H]$^+$) 346.2013, found 346.2011.

The product (+)-**1** (20.0 mg) was re-dissolved in a mixed solvent of ethyl acetate (1 mL) and *n*-hexane (1 mL). After slowly evaporating the solvents at ambient temperautre, the fine crystals were obtained amd their structure was analyzed by X-ray diffraction.

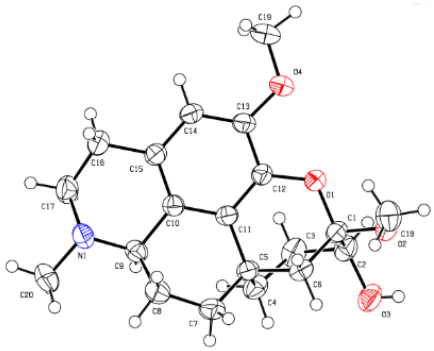
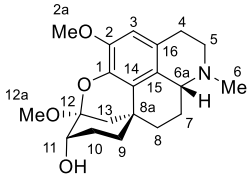


Table S2. Crystal data and structure refinement for (+)-regeline (**1**) (CCDC 2003662)

Empirical formula	$C_{20}H_{27}NO_4$
Formula weight	345.42
Temperature/K	294.15
Crystal system	trigonal
Space group	$P3_2$
a/Å	11.34890(10)
b/Å	11.34890(10)
c/Å	12.20100(10)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	1360.92(3)
Z	3
ρ_{calc}g/cm^3	1.264
μ/mm^{-1}	0.706
F(000)	558.0
Crystal size/mm^3	0.34 × 0.26 × 0.24
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.998 to 158.73
Index ranges	$-14 \leq h \leq 14$, $-13 \leq k \leq 13$, $-15 \leq l \leq 15$
Reflections collected	11417
Independent reflections	3640 [R_{int} = 0.0195, R_{sigma} = 0.0157]
Data/restraints/parameters	3640/1/234
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0302, wR_2 = 0.0869
Final R indexes [all data]	R_1 = 0.0304, wR_2 = 0.0871
Largest diff. peak/hole / e Å^{-3}	0.24/-0.15
Flack parameter	0.04(6)

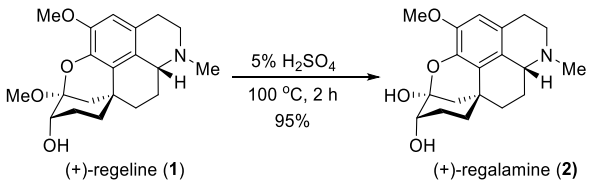
Table S3. Comparison of NMR data of natural and synthetic (+)-regeline



(+)-regeline

No.	^{1}H NMR ($CDCl_3$) δ:	
	Natural[2]	Synthetic (400 MHz)
3	6.42 (s)	6.52 (s)
6a	——	2.94 (dd, *J* = 9.7, 5.5 Hz)
11	——	3.84–3.83 (m)
O-Me	3.74 (s)	3.83 (s)
O-Me	3.34 (s)	3.43 (s)
N-Me	2.36 (s)	2.45 (s)
	^{13}C NMR ($CDCl_3$) δ:	
	Natural[2]	Synthetic (101 MHz)
1	145.0	146.0
2	142.1	142.1
14	126.4	126.2
15	124.6	124.6
16	123.8	123.9
3	110.2	109.8
12	101.9	102.0
11	70.5	70.8
6a	60.0	60.0
2a	56.0	55.9
5	53.6	53.7
12a	48.9	49.2
6	43.6	43.7
8a	34.6	34.7
4, 13, 10, 9, 8, 7	34.2, 34.2, 33.0, 28.8, 27.0, 26.4	34.3, 34.2, 33.1, 28.9, 27.1, 26.4

Synthesis of (+)-regalamine (2)



(+)-regeline (**1**) (+)-regalamine (**2**)

The mixture of (+)-**1** (44.0 mg, 0.13 mmol) and 2 mL of 5% H_2SO_4 was heated to 100 °C and stirred at the same temperature for 2 h. The reaction mixture was then cooled to room temperature, and a saturated aqueous solution of Na_2CO_3 (4 mL) was added to quench the reaction. The mixture was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with ethyl acetate/

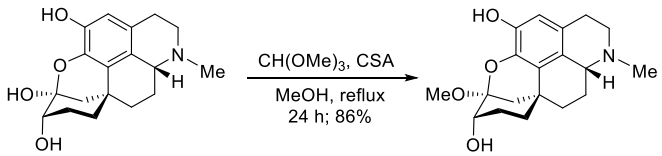
triethylamine (20:1) to give the product (+)-regalamine (**2**) (41.0 mg, 95% yield) as a white solid: mp 220–222 °C (lit.[3] 225–226 °C); R_f 0.15 (ethyl acetate/triethylamine = 30:1); $[\alpha]_D^{25}$ +43.8 (*c* 1.92, MeOH) (lit.[3] +33 (*c* 1.93, MeOH)); IR (KBr): ν_{max} = 3464, 3370, 2938, 2858, 2794, 1599, 1485, 1446, 1373, 1265, 1224, 1174, 1138, 1055, 1013, 875, 734, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 6.45 (s, 1H), 3.83–3.82 (m, 1H), 3.81 (s, 3H), 3.13–3.09 (m, 1H), 3.00–2.98 (m, 1H), 2.94 (dd, *J* = 10.0, 5.6 Hz, 1 H), 2.59 (dd, *J* = 16.4, 3.2 Hz, 1 H), 2.49 (td, *J* = 11.6, 3.6 Hz, 1 H), 2.44 (s, 3 H), 2.29–2.26 (m, 1 H), 2.20 (d, *J* = 12.4 Hz, 1 H), 1.72–1.69 (m, 4 H), 1.52–1.48 (m, 1 H), 1.48–1.45 (m, 1 H), 1.38–1.35 (m, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 145.6, 141.4, 126.2, 124.7, 123.6, 109.5, 99.4, 71.4, 60.1, 55.8, 53.6, 43.6, 39.0, 34.9, 33.9, 32.8, 28.7, 26.9, 26.5; HRMS (*m/z*): calcd for $C_{19}H_{26}NO_4$ ($[M + H]^+$) 332.1856, found 332.1863.

Synthesis of (+)-kesselridine (3)

(+)-regeline (**1**) (+)-kesselridine (**3**)

To a solution of (+)-regeline (20.0 mg, 57.9 μmol) in CH_2Cl_2 (3 mL) was added BBr_3 (0.17 mL, 1.0 M, 0.17 mmol) in CH_2Cl_2, and the resulting mixture was stirred at room temperature for 4 h. The reaction mixture was diluted with saturated aqueous solution of $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (3 × 8 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with ethyl acetate/triethylamine (20:1) to give the product (+)-kesselridine (**3**) (14.0 mg, 78% yield) as a white solid: mp 205–206 °C (lit.[4] 232–234 °C); R_f 0.22 (ethyl acetate/triethylamine = 30:1); $[\alpha]_D^{25}$ +200.0 (*c* 0.1, pyridine) (lit.[4] –50 (pyridine)); IR (KBr): ν_{max} = 3737, 3651, 3626, 2955, 2918, 2850, 1461, 1377, 1237, 1131, 992, 966, 895, 853 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ: 6.45 (s, 1H), 3.71–3.70 (m, 1H), 3.07–3.01 (m, 2H), 3.01–2.92 (m, 1H), 2.63–2.54 (m, 2H), 2.46 (s, 3H), 2.34–2.26 (m, 1H), 2.16 (d, *J* = 12.8 Hz, 1H), 1.80–1.68 (m, 3H), 1.65–1.58 (m, 1H), 1.56 (d, *J* = 12.4 Hz, 1H), 1.46–1.42 (m, 1H), 1.40–1.33 (m, 1H), 1.32–1.27 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ: 144.5, 142.4, 125.0, 124.8, 123.9, 114.2, 100.8, 72.1, 61.7, 54.5, 42.6, 39.6, 35.8, 34.8, 34.3, 28.2(2), 27.1; HRMS (*m/z*): calcd for $C_{19}H_{26}NO_4$ ($[M + H]^+$) 318.1700, found 318.1699.

Synthesis of (+)-kesselringine (4)

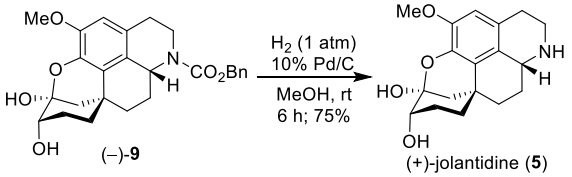


(+)-kesselridine (**3**) (+)-kesselringine (**4**)

To a solution of (+)-**3** (28.0 mg, 88.2 μmol) in MeOH (5 mL) were added $CH(OMe)_3$ (30.0 μL, 0.27 mmol) and (+)-10-camphorsulfonic acid (CSA, 30.0 mg, 0.13 mmol). The reaction mixture was heated to reflux for 24 h, diluted with saturated aqueous $NaHCO_3$ solution (10 mL), and extracted with EtOAc (3 × 6 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with ethyl acetate/triethylamine (20:1) to give the product (+)-kesselringine (**4**) (25.0 mg, 86% yield) as a white solid: mp 197–198 °C (lit.[5]

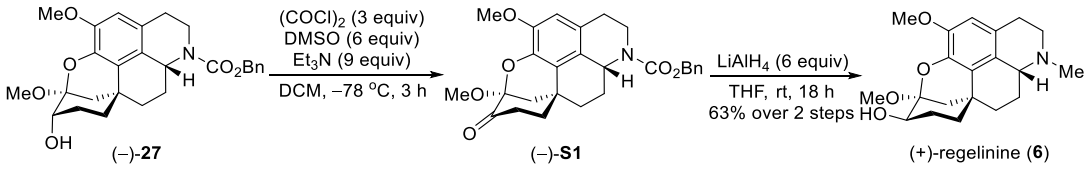
194–196 °C); R_f 0.25 (ethyl acetate/triethylamine = 30:1); $[\alpha]_D^{25}$ +79.0 (*c* 1.0, $CHCl_3$) (lit.[6] +93 (*c* 1.0, $CHCl_3$)); IR (KBr): ν_{max} = 3473, 2953, 2928, 2868, 1595, 1503, 1462, 1377, 1272, 1189, 1059, 813, 723, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 6.56 (s, 1H), 5.51 (brs, 1H), 3.75 (m, 1H), 3.42 (s, 3H), 3.13–2.89 (m, 3H), 2.65–2.50 (m, 2H), 2.46 (s, 3H), 2.36–2.23 (m, 2H), 2.02 (d, *J* = 12.4 Hz, 1H), 1.88–1.68 (m, 5H), 1.57–1.49 (m, 1H), 1.46–1.31 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.2, 139.9, 125.4, 123.2, 112.5, 102.8, 77.2, 70.9, 60.2, 53.6, 49.4, 43.5, 34.6, 34.1, 34.0, 33.3, 28.4, 27.1, 26.3; HRMS (*m/z*): calcd for $C_{19}H_{26}NO_4$ ($[M + H]^+$) 332.1856, found 332.1859.

Synthesis of compound (+)-jolantidine (5)



To a solution of compound (–)-**9** (41.0 mg, 91.8 μmol) in MeOH (5 mL) was added Pd/C (9.0 mg), and the suspension mixture was stirred at room temperature under ambient H_2 pressure for 6 h. The mixture was then filtered through a pad of Florisil and concentrated in vacuo. The residue was chromatographed on silica-gel column with dichloromethane/methanol (3:1) to give the product (+)-jolantidine (**5**) (21.0 mg, 75% yield) as a white solid: mp 269–270 °C (lit.[7] 275–277 °C); R_f 0.53 (dichloromethane/methanol = 3:1); $[\alpha]_D^{25}$ +90.5 (*c* 0.4, MeOH) (lit.[7] +102 (*c* 0.4, MeOH)); IR (KBr): ν_{max} = 3454, 3298, 2925, 2853, 1598, 1484, 1445, 1368, 1265, 1173, 1051, 1013, 737, 702 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ: 6.61 (s, 1H), 3.77 (s, 3H), 3.75–3.72 (m, 1H), 3.72–3.70 (m, 1H), 3.26–3.19 (m, 1H), 3.02 (td, *J* = 11.2, 4.4 Hz, 1H), 2.98–2.88 (m, 1H), 2.71–2.65 (m, 1H), 2.18 (d, *J* = 12.4 Hz, 1H), 2.15–2.09 (m, 1H), 1.83–1.67 (m, 3H), 1.65–1.58 (m, 1H), 1.54 (d, *J* = 12.4 Hz, 1H), 1.47–1.35 (m, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ: 147.4, 143.6, 127.6, 125.8, 124.8, 111.9, 100.7, 72.1, 56.5, 52.5, 44.0, 39.5, 36.0, 34.8, 34.5, 29.2, 28.8, 28.2; HRMS (*m/z*): calcd for $C_{18}H_{24}NO_4$ ($[M + H]^+$) 318.1700, found 318.1697.

Synthesis of (+)-regelinine (6)



To a solution of oxalyl chloride (0.10 mL, 1.10 mmol) in CH_2Cl_2 (1 mL) was added slowly the solution of DMSO (0.16 mL, 2.20 mmol) in CH_2Cl_2 (1 mL) at –78 °C. A solution of (–)-**27** (0.17 g, 0.37 mmol) in CH_2Cl_2 (3 mL) was added dropwise at the same temperature and the reaction mixture was stirred for 2 h. Subsequently, triethylamine (0.46 mL, 3.30 mmol) was added dropwise at –78 °C. The reaction mixture was stirred for 1 h, warmed to room temperature naturally, and quenched with water (5 mL), extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phase was dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica-gel column with petroleum ether/ethyl acetate (2:1) to give the product (–)-**S1** (0.16 g, 96% yield) as a white solid, mp 75–77 °C; R_f 0.43 (petroleum ether/ethyl acetate = 1:1); $[\alpha]_D^{25}$ +150 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 2945, 2840, 1734, 1697, 1488, 1424, 1278, 1206, 1085, 983, 735, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.44–

7.30 (m, 5H), 6.67 (dd, *J* = 10.0, 3.2 Hz, 0.2), 6.66□6.57 (m, 1H), 5.88 (m, 0.2H), 5.30–5.09 (m, 2H), 4.95 (m, 0.2H), 4.82 (m, 0.6H), 4.57 (m, 0.13H), 4.43 (d, *J* = 12.4 Hz, 0.69H), 3.85 (m, 3H), 3.62 (m, 3H), 3.49□3.28 (m, 0.65H), 2.97–2.74 (m, 2H), 2.66–2.56 (m, 0.8H), 2.46–2.12 (m, 5.1H), 2.00–1.72 (m, 3.5H), 1.63–1.46 (m, 0.9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 202.1, 156.4, 146.6, 141.1, 136.8, 128.6, 128.1(2), 123.8, 121.6, 112.6, 111.1, 99.3, 67.2, 56.2, 51.2, 42.7, 40.0, 39.1, 37.1, 36.3, 34.9, 34.5, 32.6, 29.9; HRMS (*m/z*): calcd for $C_{27}H_{30}NO_6$ ([M + H]$^+$) 464.2068, found 464.2066.

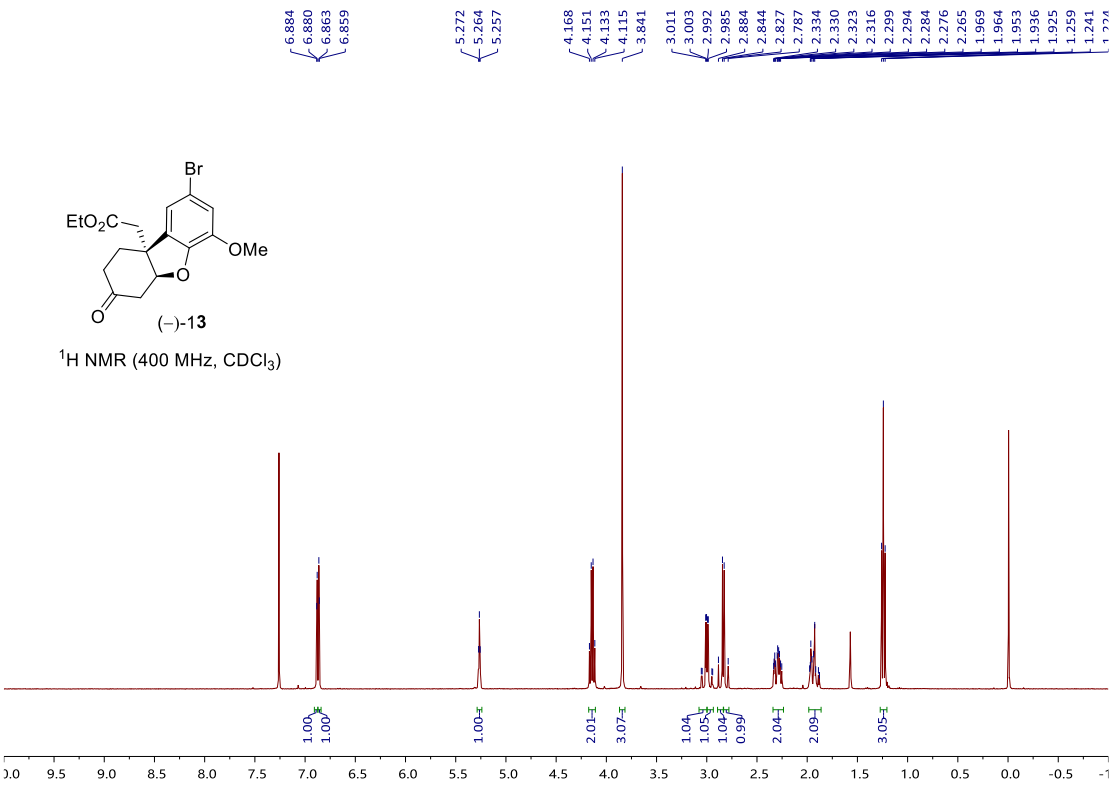
To the solution of (−)-**S1** in THF (8 mL) was added $LiAlH_4$ (83.5 mg, 2.20 mmol), and the resulting mixture was stirred at room temperature for 24 h. The reaction was then quenched by slow addition of H_2O (8 mL), and the mixture was extracted with EtOAc (3 × 8 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica-gel column with ethyl acetate/triethylamine (30:1) to give (+)-regelinine (**6**) (80.0 mg, 63% yield over 2 steps) as a white solid: mp 252–253 °C (lit.[8] 253–254 °C); R_f 0.32 (ethyl acetate/triethylamine = 20:1); $[\alpha]_D^{25}$ +110.4 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} = 3348, 2942, 2844, 1599, 1486, 1454, 1244, 1076, 976, 889, 730 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.51 (s, 1H), 3.83 (s, 3H), 3.72 (dd, *J* = 11.2, 5.2 Hz, 1H), 3.41 (s, 3H), 3.12–2.96 (m, 2H), 2.90 (dd, *J* = 10.0, 5.2 Hz, 1H), 2.73–2.56 (m, 2H), 2.50 (td, *J* = 11.2, 4.0 Hz, 1H), 2.44 (s, 3H), 2.30–2.23 (m, 1H), 2.15 (dd, *J* = 12.8, 2.8 Hz, 1H), 1.92–1.83 (m, 1H), 1.82–1.68 (m, 3H), 1.59–1.47 (m, 2H), 1.44–1.27 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 146.0, 142.4, 126.0, 124.6, 123.5, 110.0, 100.8, 75.5, 60.2, 55.9, 53.7, 49.4, 43.7, 37.6, 37.4, 34.9, 34.0, 28.9, 28.1, 27.2; HRMS (*m/z*): calcd for $C_{20}H_{28}NO_4$ ([M + H]$^+$) 346.2013, found 346.2013.

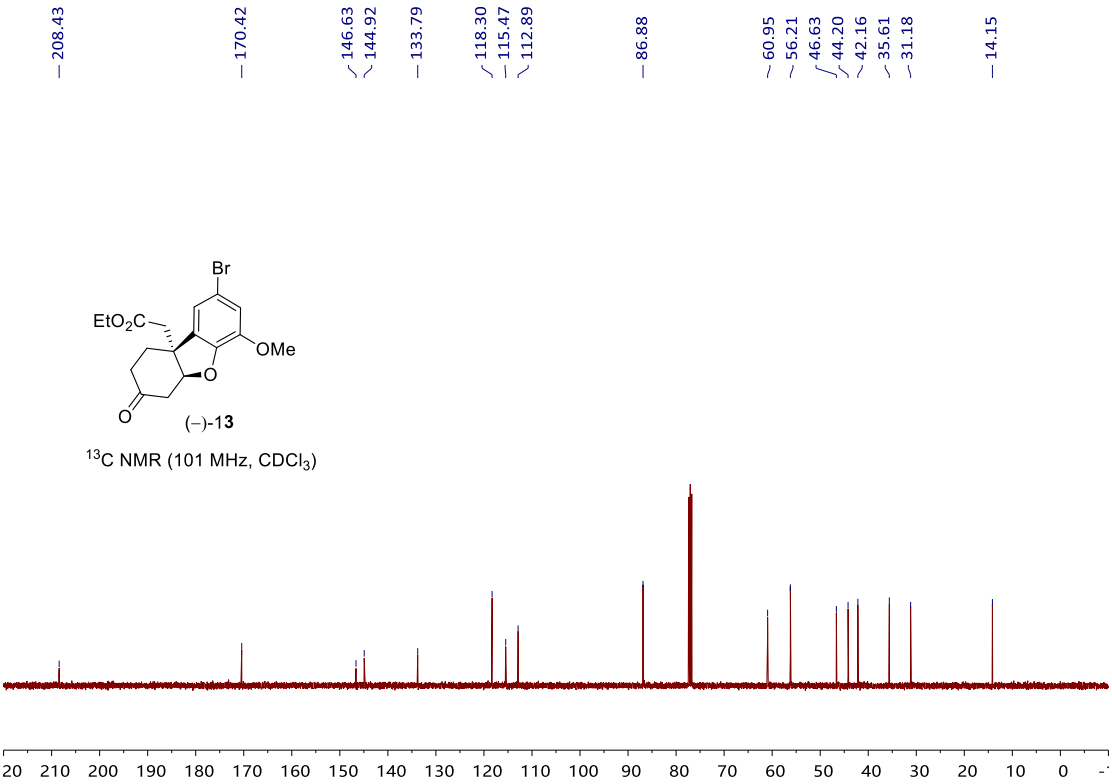
References

1. Chen, J.-Q.; Xie, J.-H.; Bao, D.-H.; Liu, S.; Zhou, Q.-L. Total synthesis of (−)-galanthamine and (−)-lycoramine via catalytic asymmetric hydrogenation and intramolecular reductive Heck cyclization. *Org. Lett.* **2012**, *14*, 2714–2717.
2. Abdullaeva, D. A.; Yusupov M. K.; Aslanov, K. A. The structure of regeline. *Chem. Nat. Comp.* **1976**, *12*, 702–705.
3. Yusupov, M. K.; Abdullaeva, D. A.; Aslanov, K. A.; Sadykov, A. S. The structure of regalamine. *Chem. Nat. Comp.* **1975**, *11*, 395–397.
4. Kasimov, K.; Yusupov, M. K.; Timbekov É. K.; Aslanov, K. A. Structure of kesselridine. *Chem. Nat. Comp.* **1975**, *11*, 202–205.
5. Yusupov, M. K.; Sadykov, A. S. The structure of kesselringine. *Chem. Nat. Comp.* **1976**, *12*, 305–308.
6. Yusupov, M. K.; Mukhamedyarova, N. L.; Sadykov, A. S.; Dolejš, L.; Sedmera P.; Šantavý, F. Constitution of the alkaloid kesselringine. *Collect. Czech. Chem. Commun.* **1977**, *42*, 1581–1587.
7. Chommadov, B.; Usmanov, A. M.; Yusupov, M. K. Jolantidine — A new base from Merendera jolantae. *Chem. Nat. Comp*. **1983**, *19*, 755.
8. Yusupov, M. K.; Chommadov B.; Aslanov, K. A. The structure of regelinine. *Chem. Nat. Comp.* **1985**, *21*, 396–397.

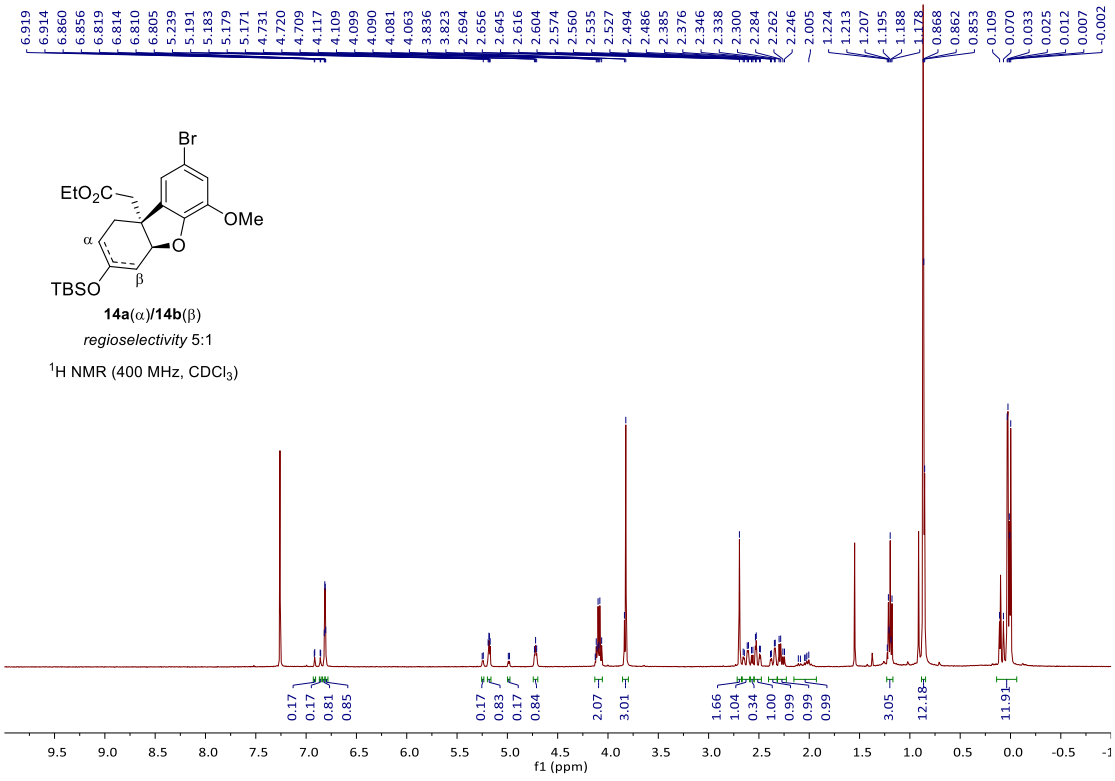
E) NMR Spectra of New Compounds and Pentacyclic Homoproaporphine Alkaloids

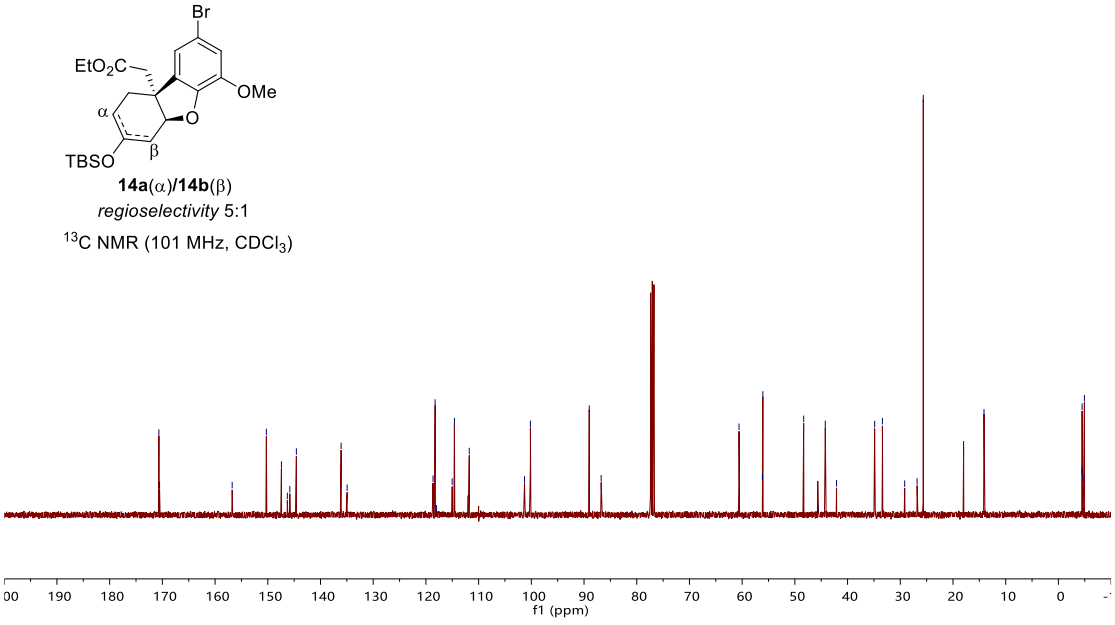
Compound (–)-13



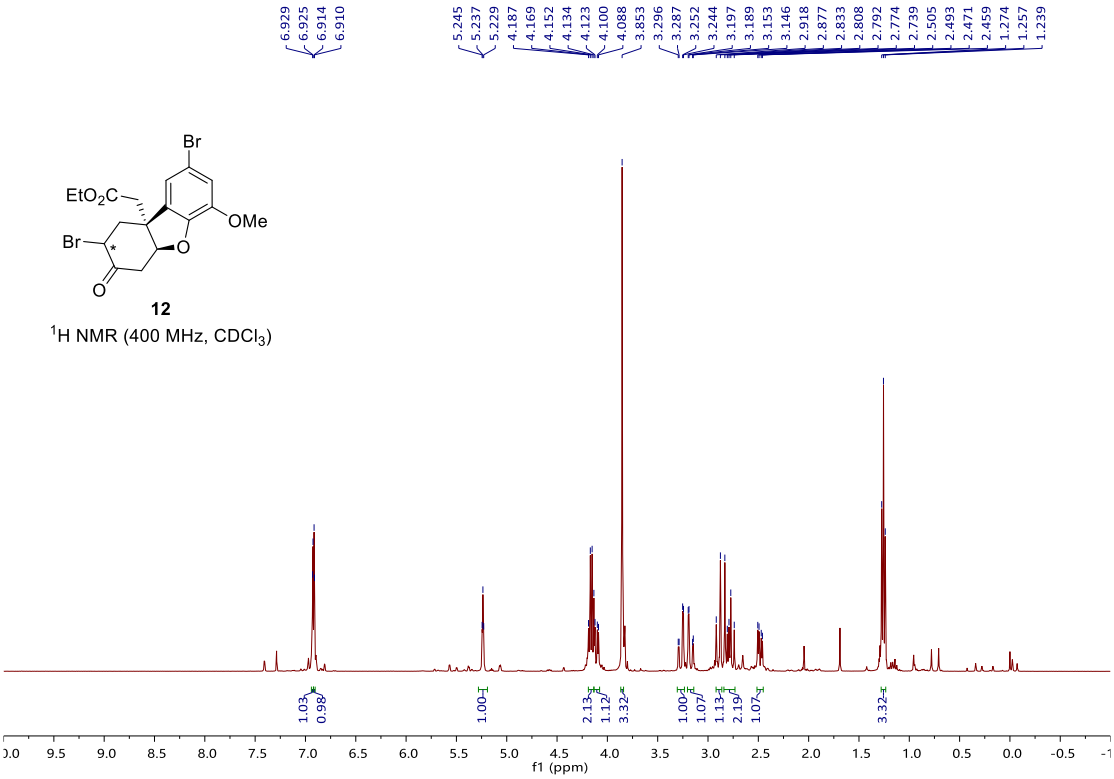


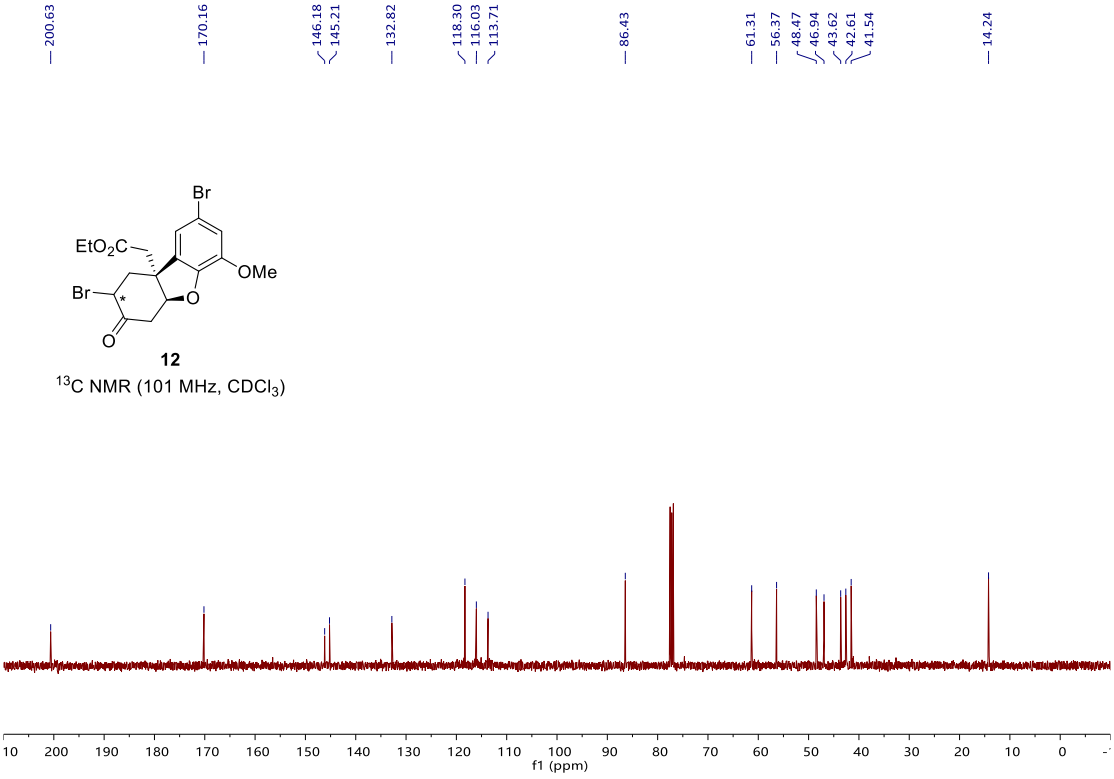
Compound 14


Br
EtO2C
OMe
α
O
TBSO
β
14a(α)/14b(β)
regioselectivity 5:1
1H NMR (400 MHz, CDCl3)
f1 (ppm)

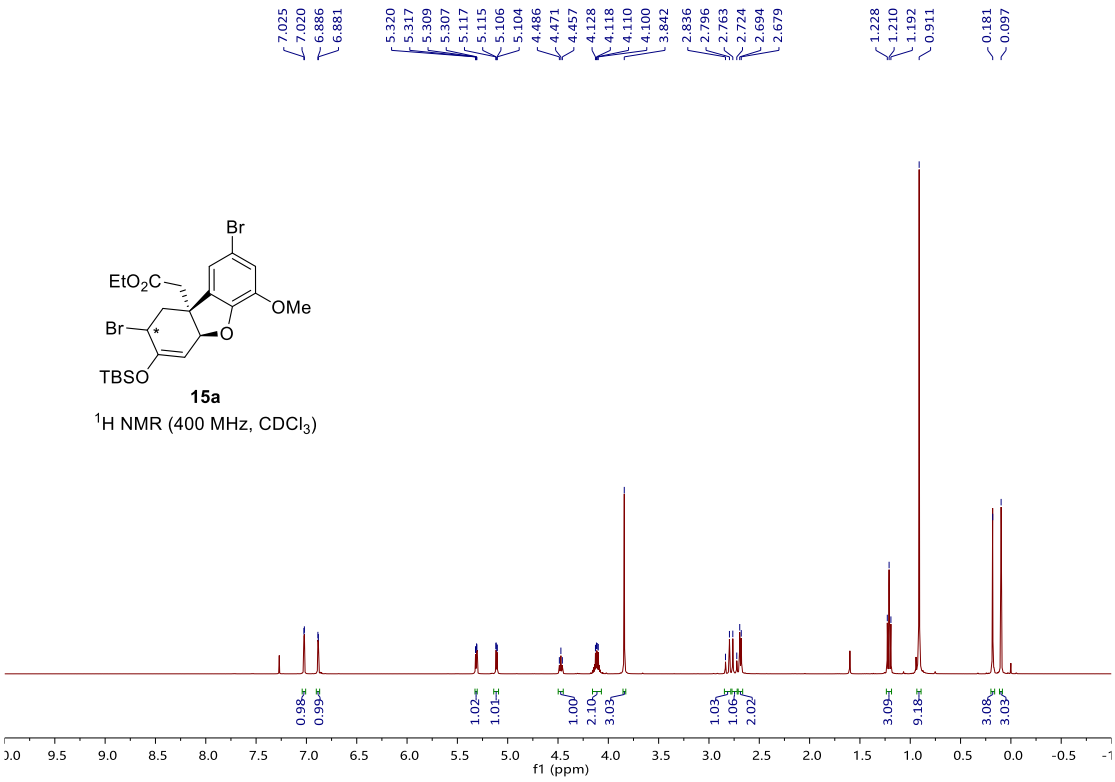

Br
EtO2C
OMe
α
O
TBSO
β
14a(α)/14b(β)
regioselectivity 5:1
13C NMR (101 MHz, CDCl3)
f1 (ppm)

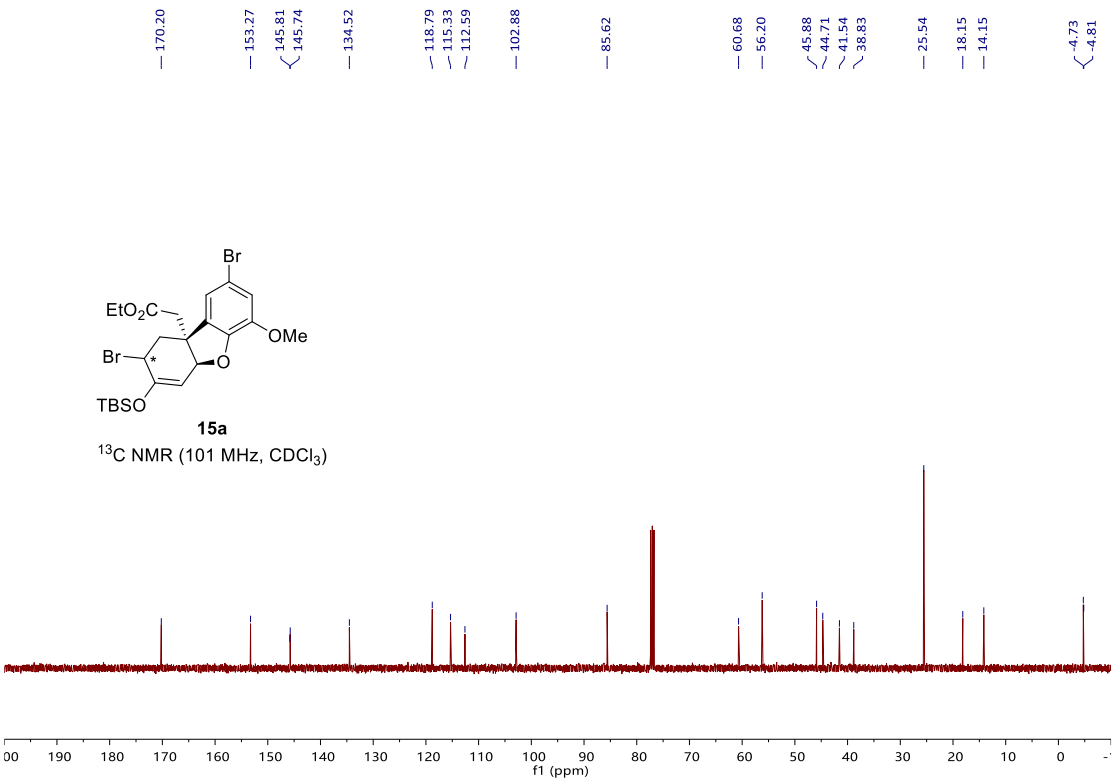
Compound 12 (not stable)



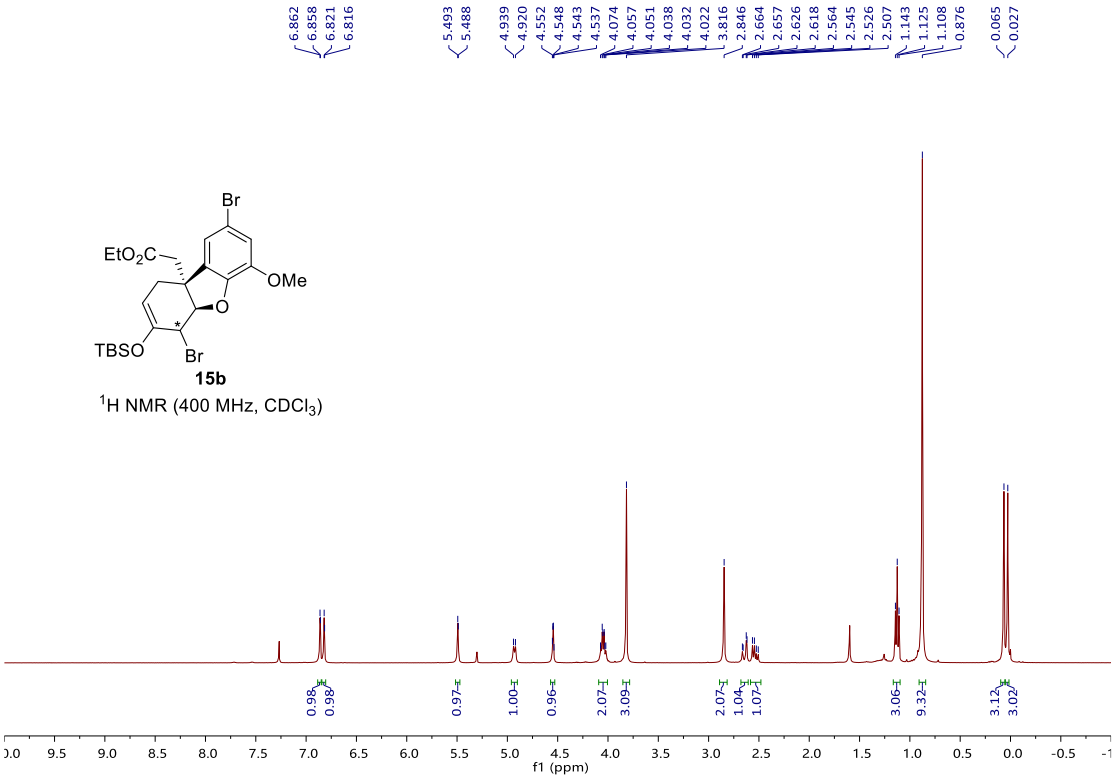


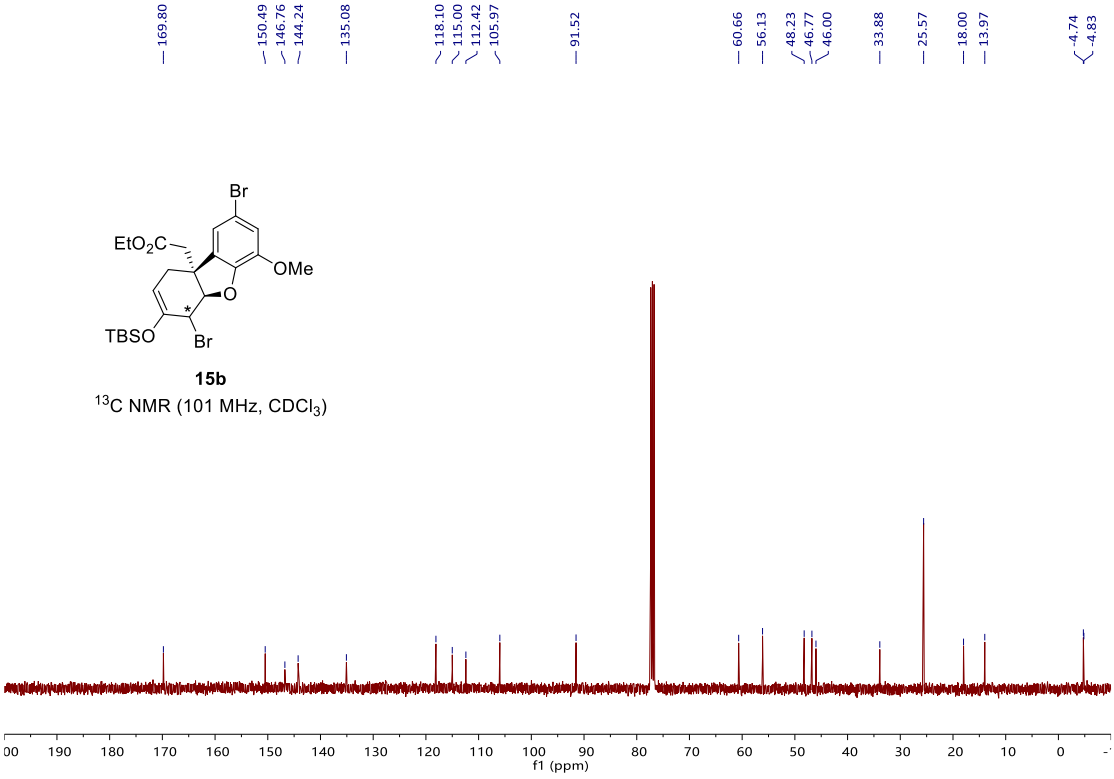
Compound 15a



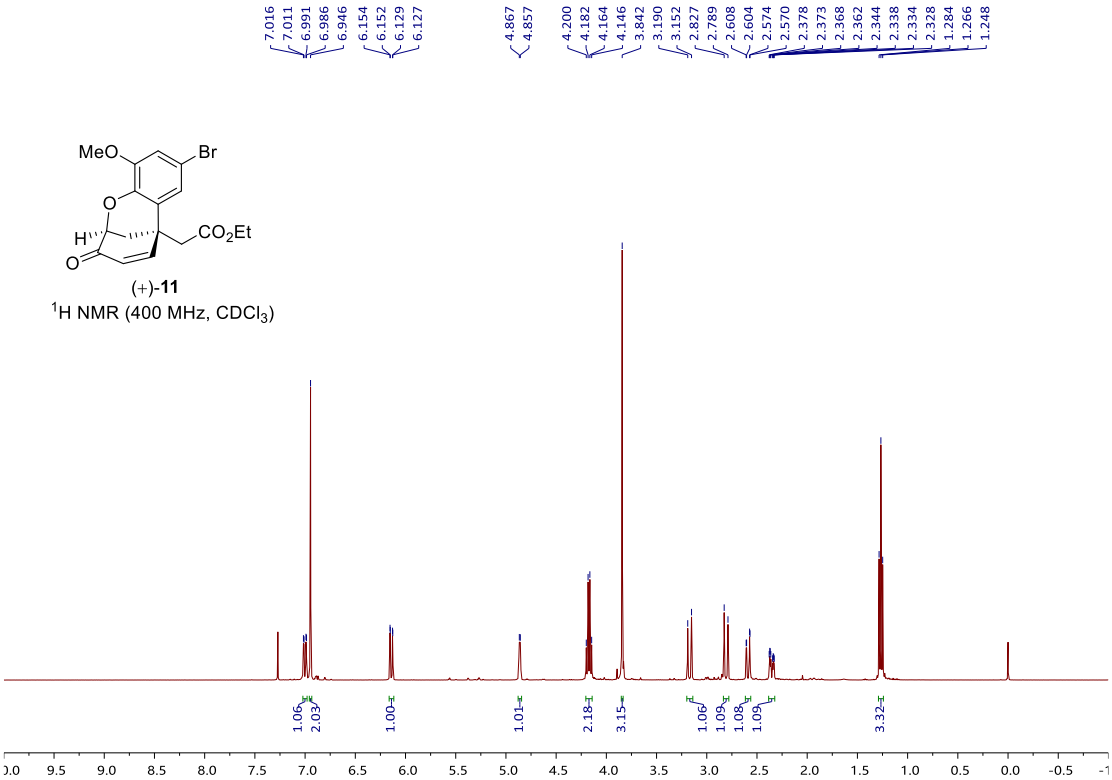


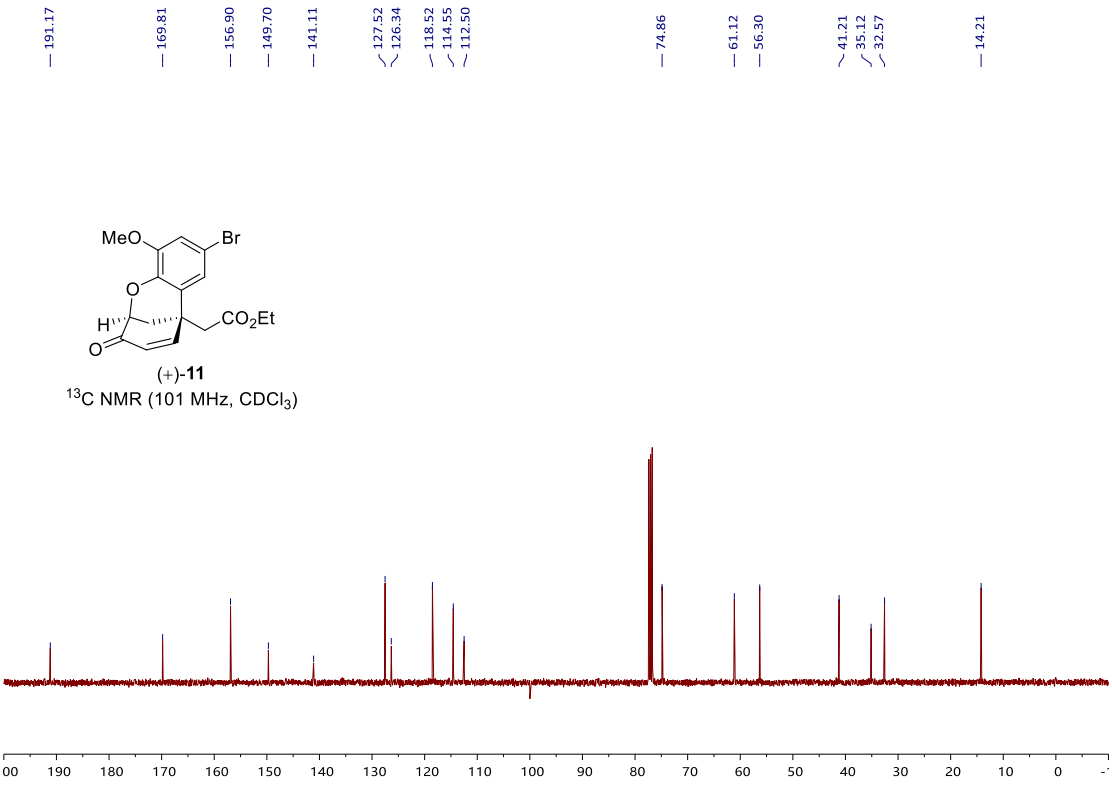
Compound 15b



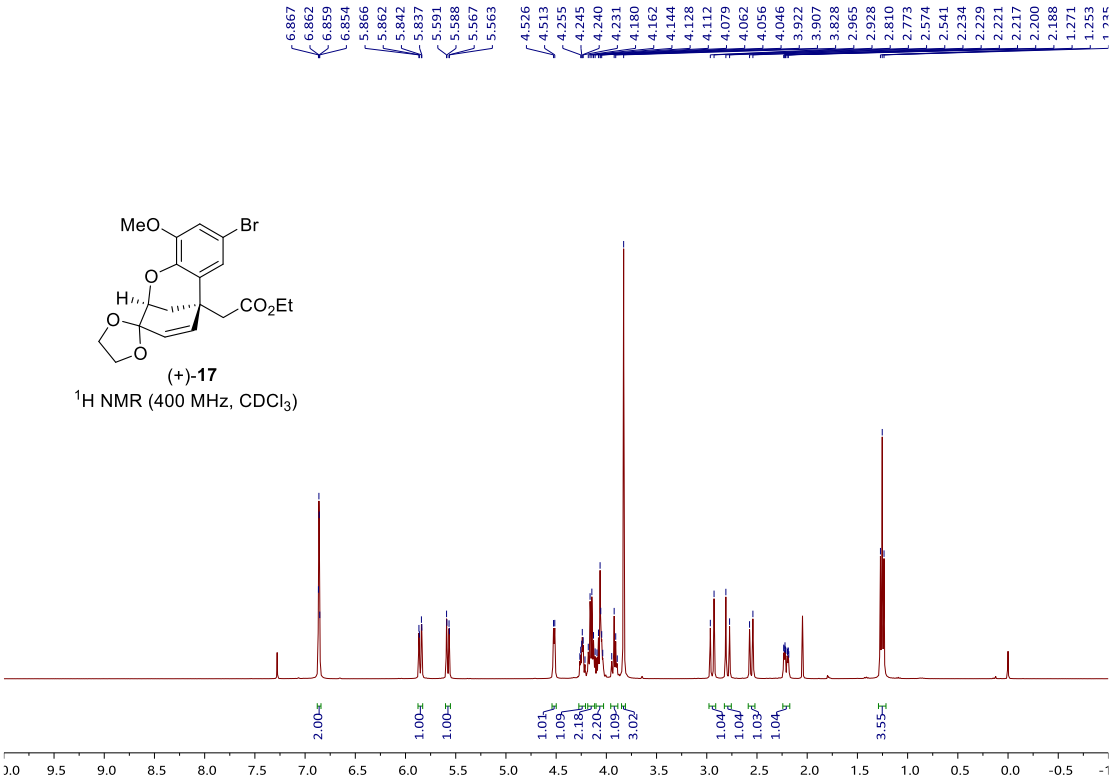


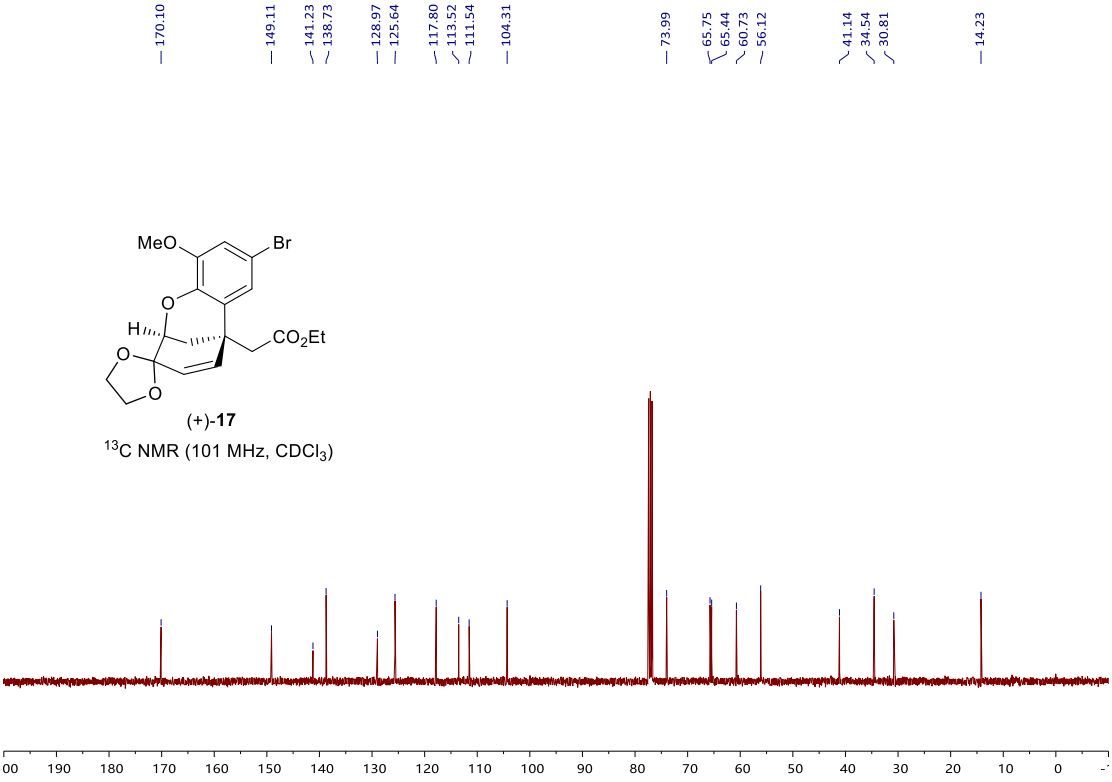
Compound (+)-11


7.016
7.011
6.991
6.986
6.946
6.154
6.152
6.129
6.127
4.867
4.857
4.200
4.182
4.164
4.146
3.842
3.190
3.152
2.827
2.789
2.608
2.604
2.574
2.570
2.378
2.373
2.368
2.362
2.344
2.338
2.334
2.328
1.284
1.266
1.248
MeO
Br
O
H
O
CO2Et
(+)-11
1H NMR (400 MHz, CDCl3)
1.06
2.03
1.00
1.01
2.18
3.15
1.06
1.09
1.08
1.09
3.32
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

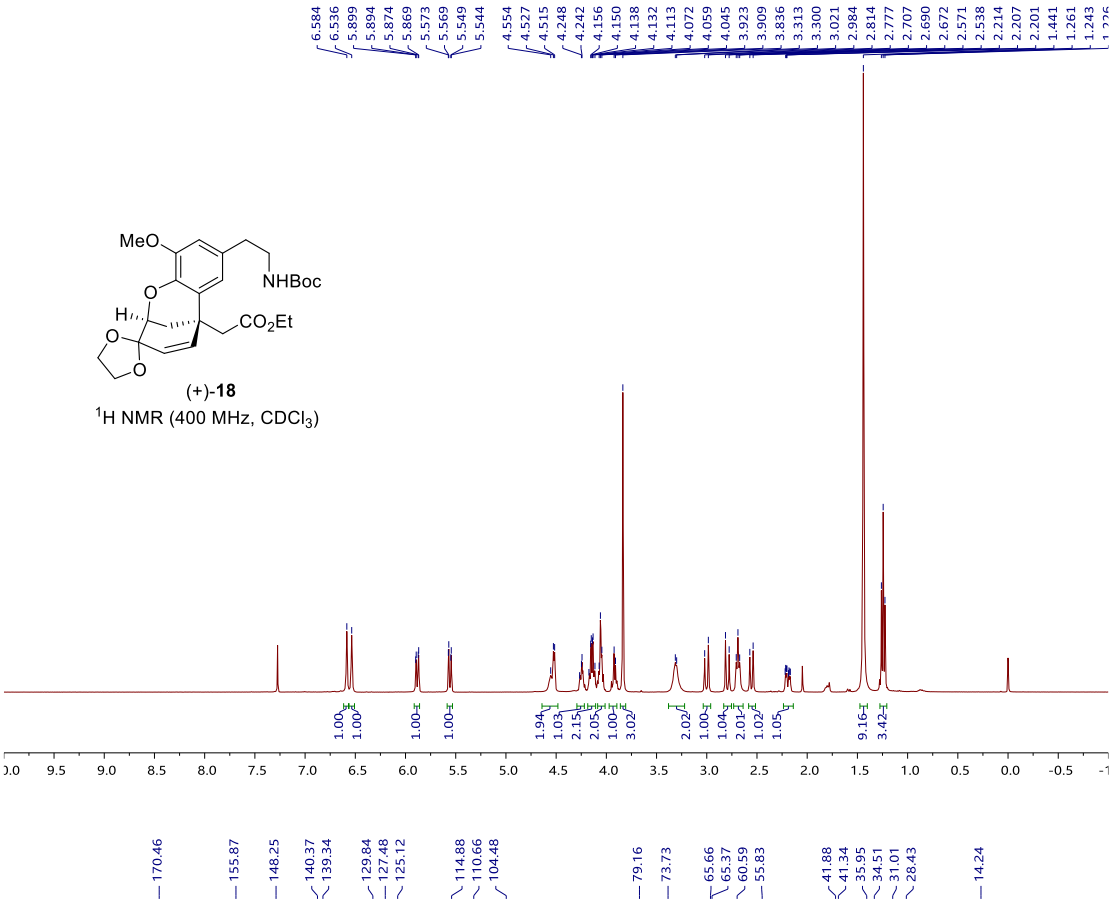

191.17
169.81
156.90
149.70
141.11
127.52
126.34
118.52
114.55
112.50
74.86
61.12
56.30
41.21
35.12
32.57
14.21
MeO
Br
O
H
O
CO2Et
(+)-11
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

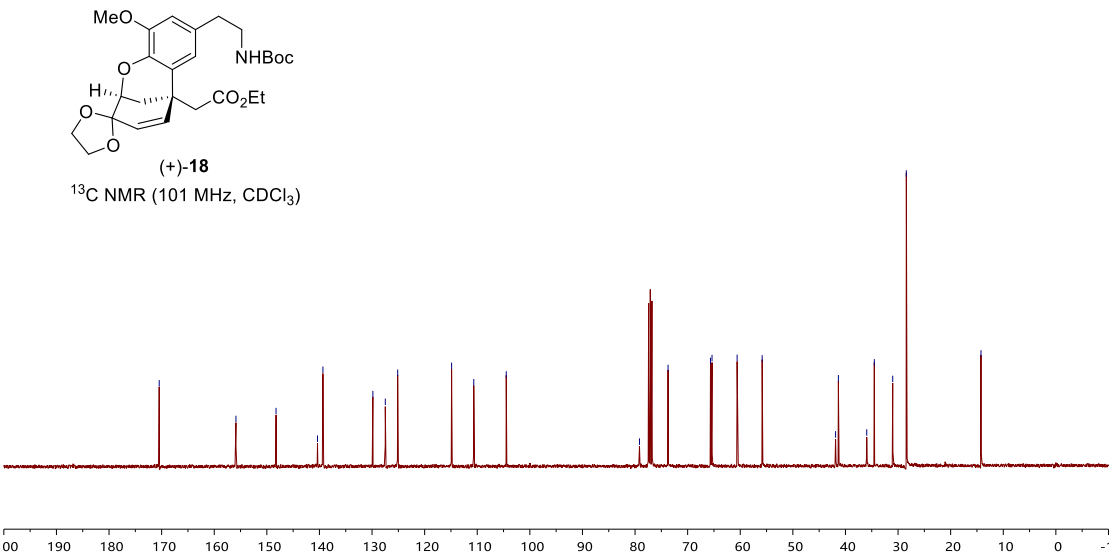
Compound (+)-17


6.867
6.862
6.859
6.854
5.866
5.862
5.842
5.837
5.591
5.588
5.567
5.563
4.526
4.513
4.255
4.245
4.240
4.231
4.180
4.162
4.144
4.128
4.112
4.079
4.062
4.056
4.046
3.922
3.907
3.828
2.965
2.928
2.810
2.773
2.574
2.541
2.234
2.229
2.221
2.217
2.200
2.188
1.271
1.253
MeO
Br
O
H
O
CO2Et
O
(+)-17
1H NMR (400 MHz, CDCl3)
2.00
1.00
1.00
1.01
1.09
2.18
2.20
1.09
3.02
1.04
1.04
1.03
1.04
3.55
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

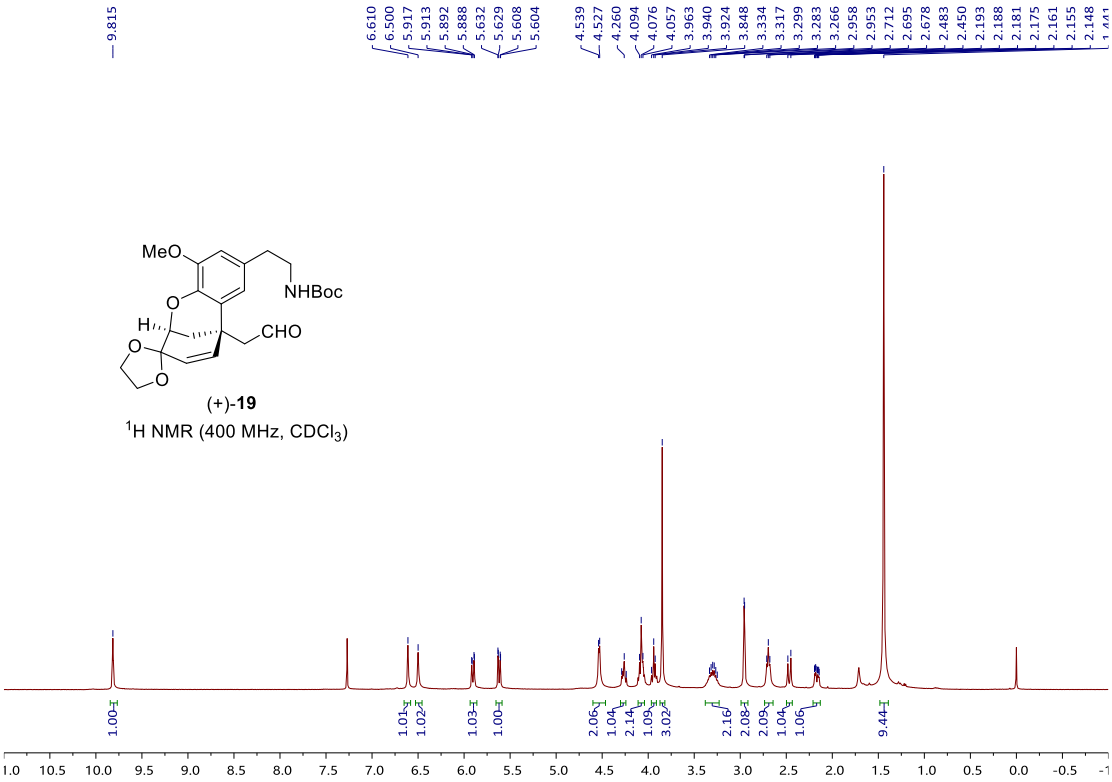

170.10
149.11
141.23
138.73
128.97
125.64
117.80
113.52
111.54
104.31
73.99
65.75
65.44
60.73
56.12
41.14
34.54
30.81
14.23
MeO
Br
O
H
O
CO2Et
O
(+)-17
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

Compound (+)-18


MeO
NHBoc
O
H
CO2Et
O
O
(+)-18
1H NMR (400 MHz, CDCl3)

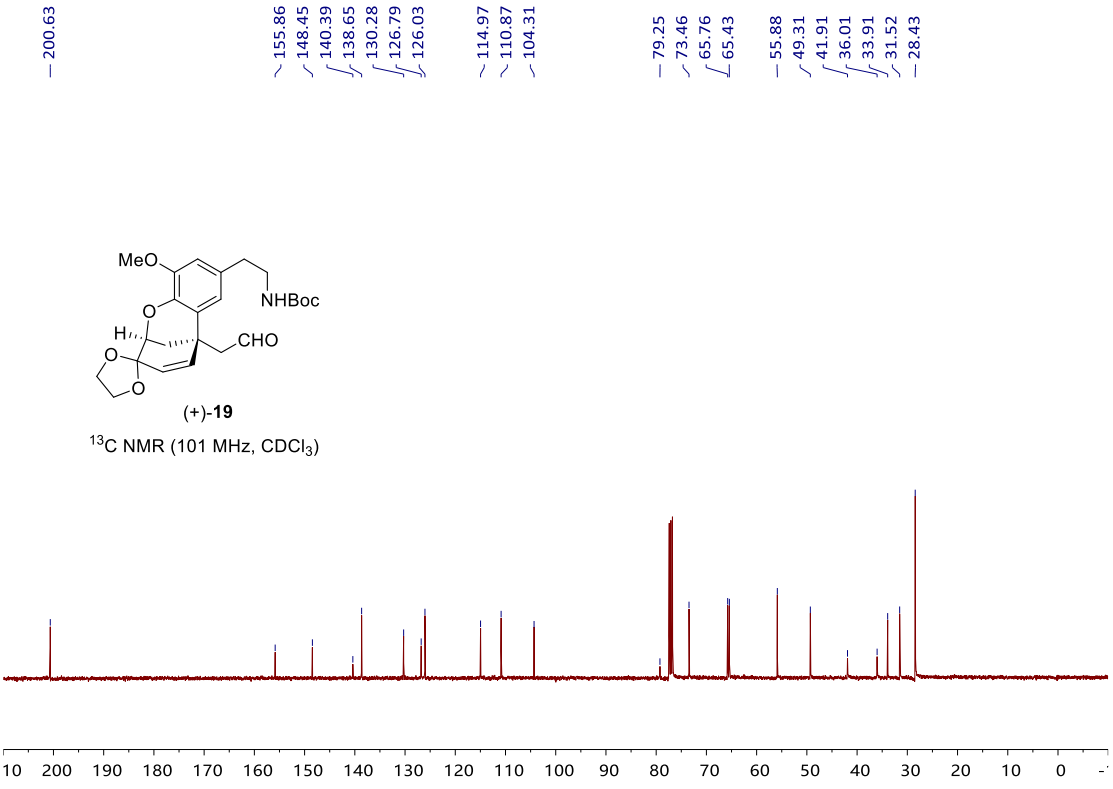

MeO
NHBoc
O
H
CO2Et
O
O
(+)-18
13C NMR (101 MHz, CDCl3)

Compound (+)-19



(+)-**19**

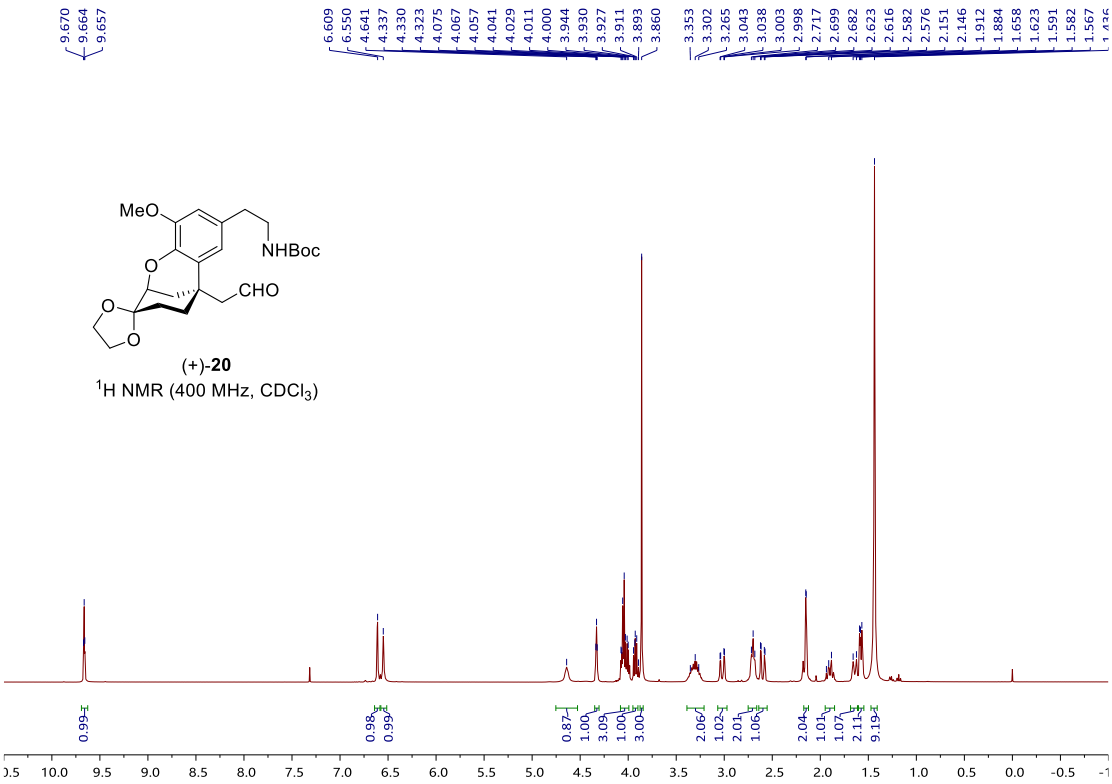
^{1}H NMR (400 MHz, $CDCl_3$)

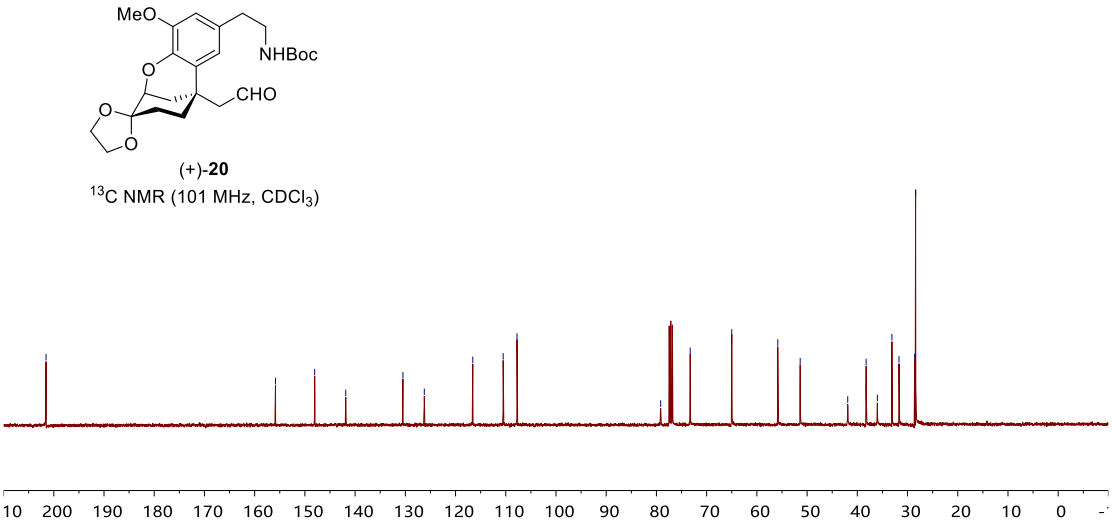


(+)-**19**

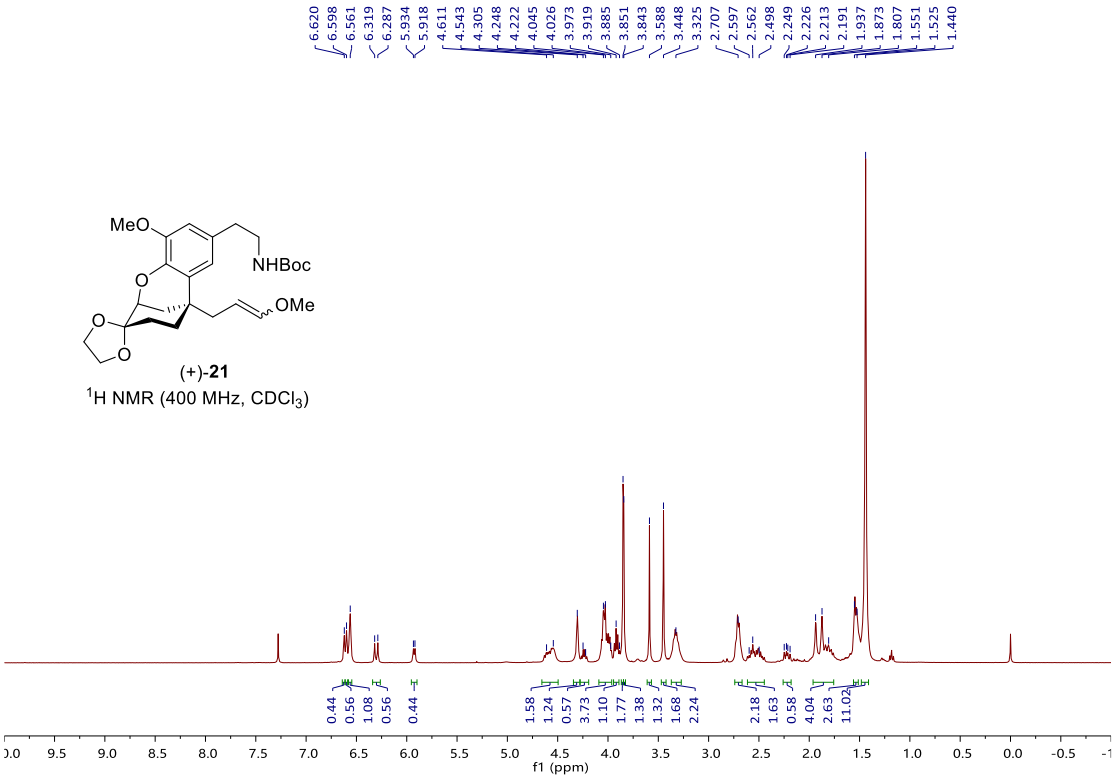
^{13}C NMR (101 MHz, $CDCl_3$)

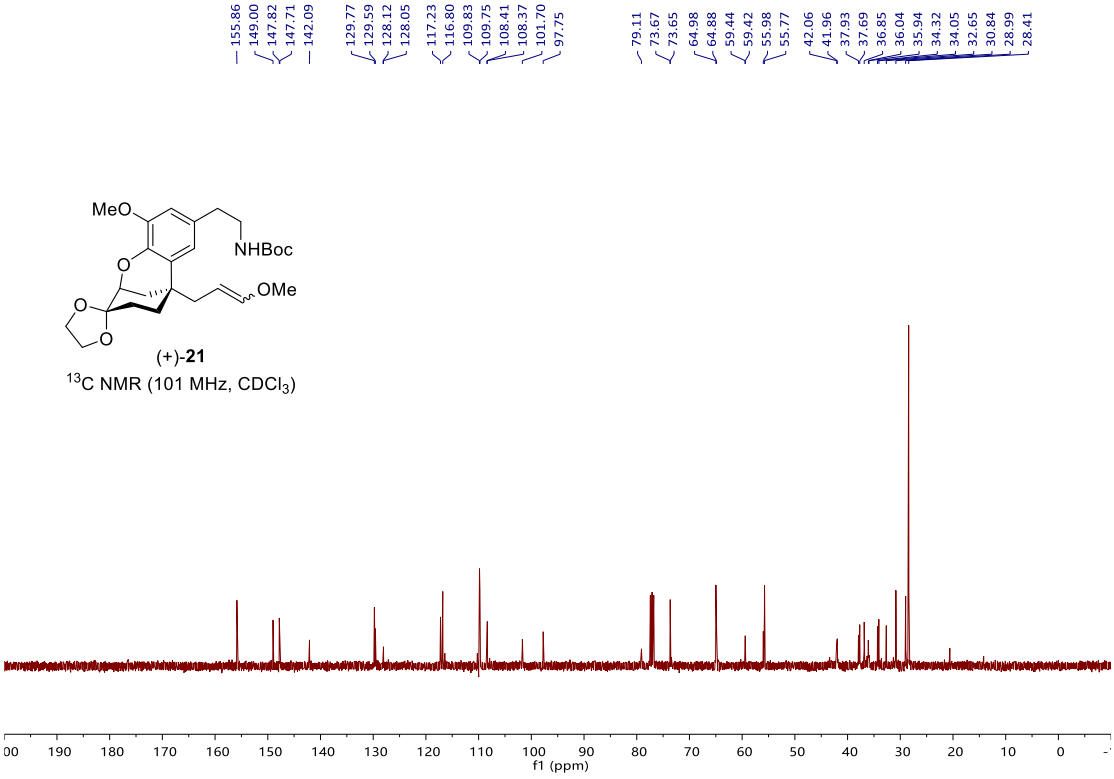
Compound (+)-20


MeO
NHBoc
CHO
O
O
O
(+)-20
1H NMR (400 MHz, CDCl3)

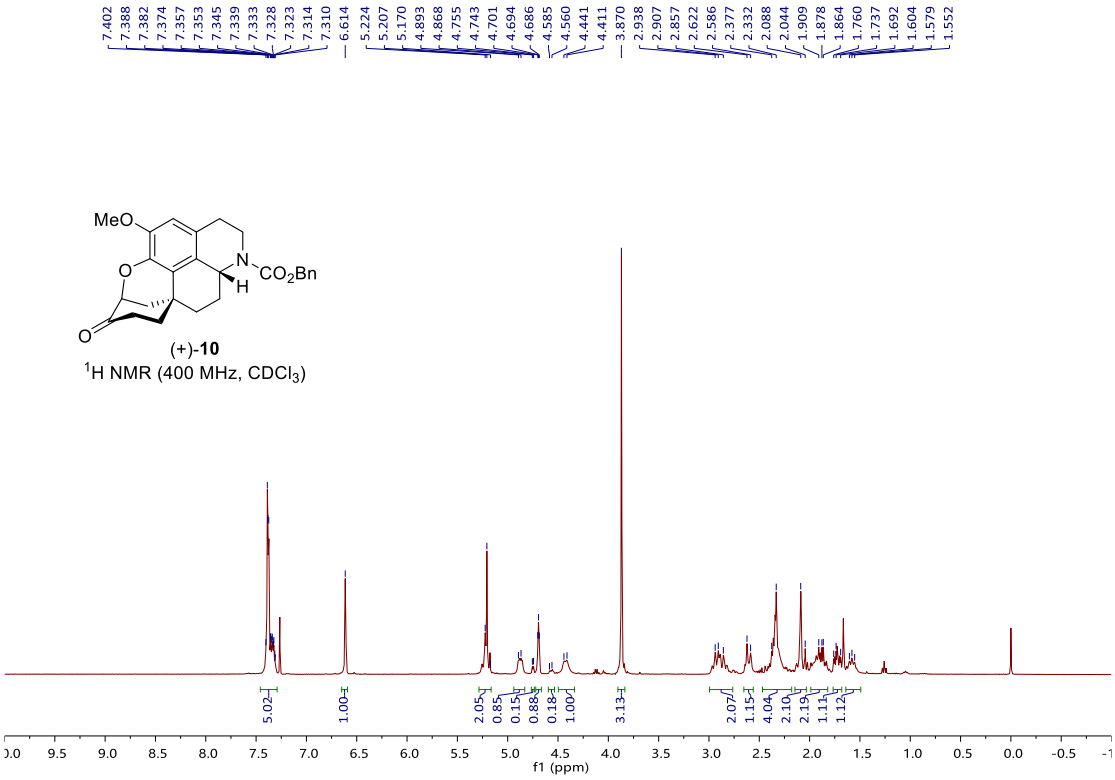

MeO
NHBoc
CHO
O
O
O
(+)-20
13C NMR (101 MHz, CDCl3)

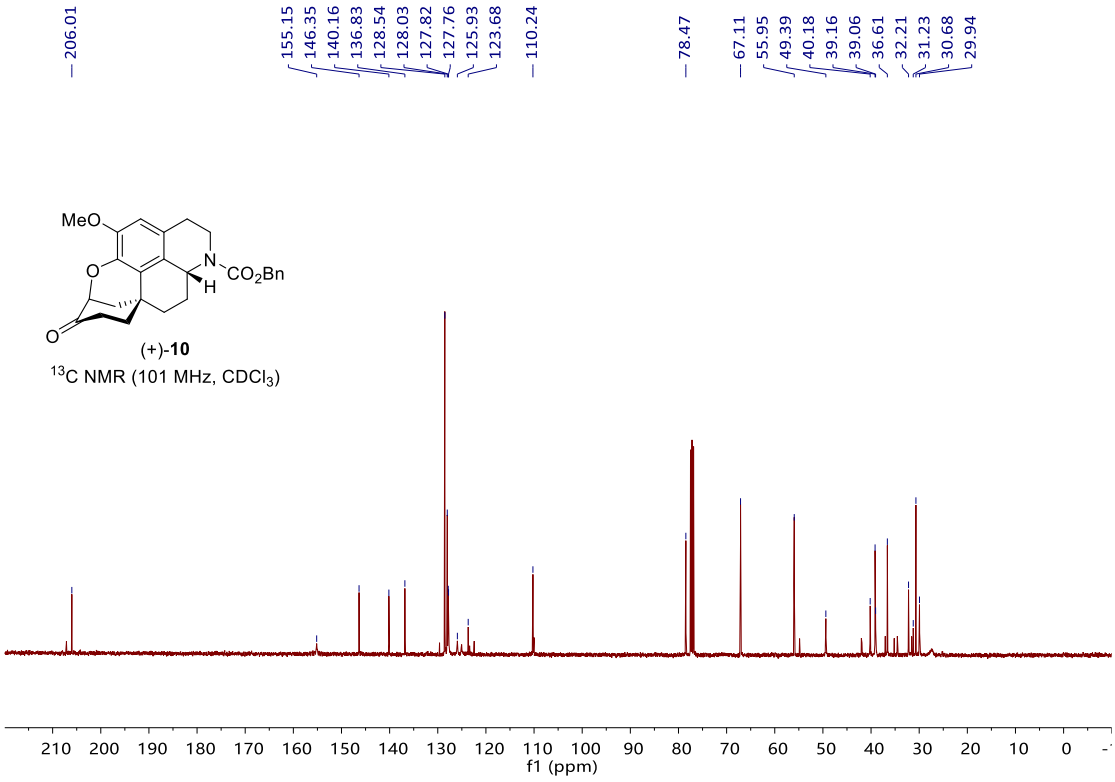
Compound (+)-21 (a mixture of *Z* and *E* isomers in a ratio of 44:56)



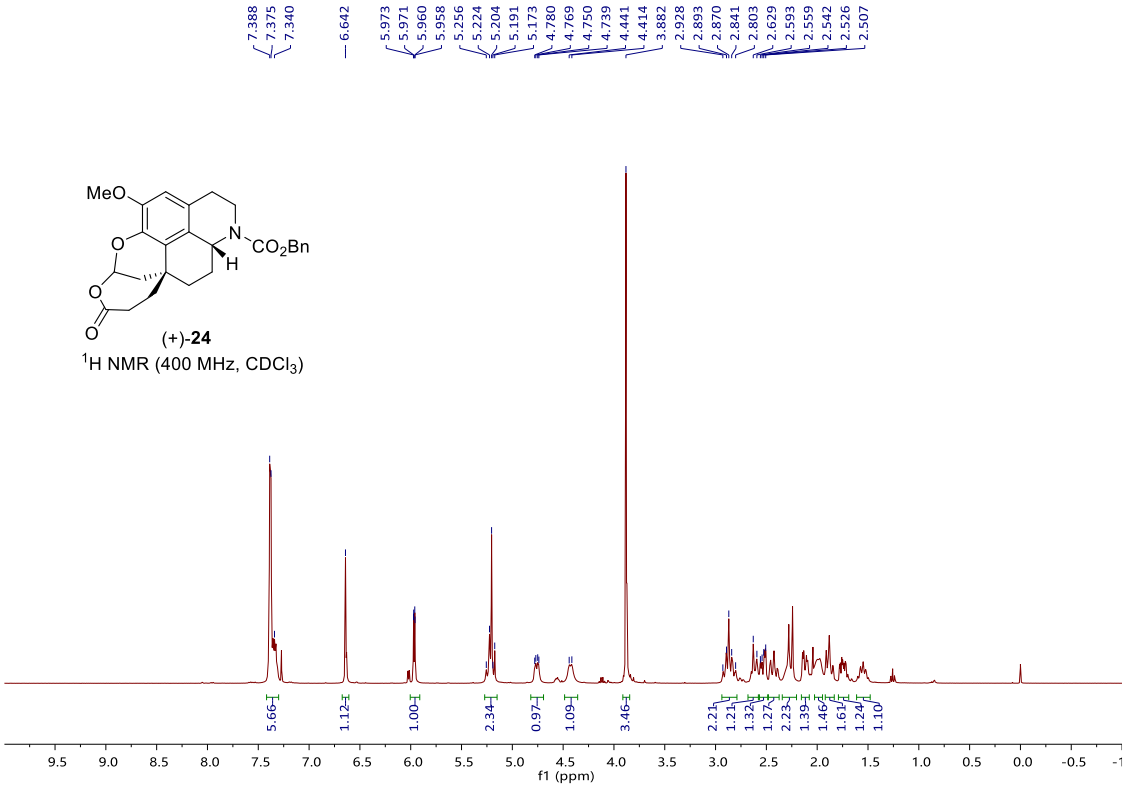


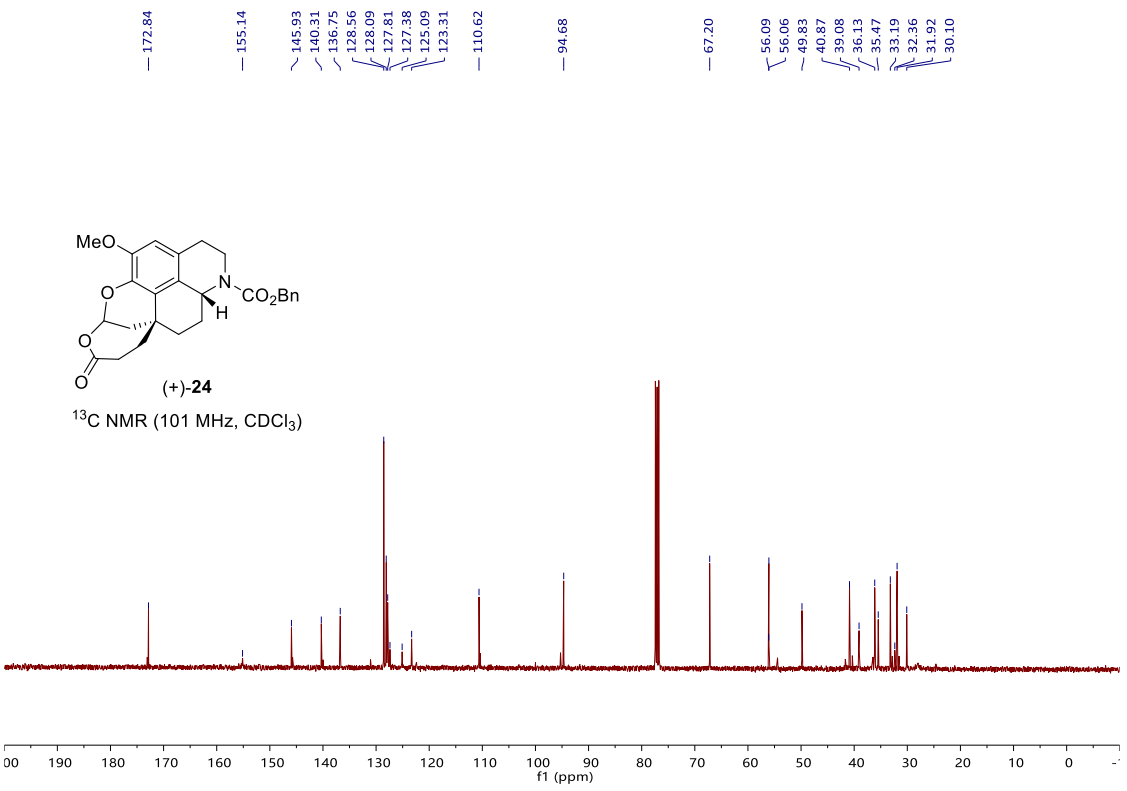
Compound (+)-10 (with a minor diastereoisomer)



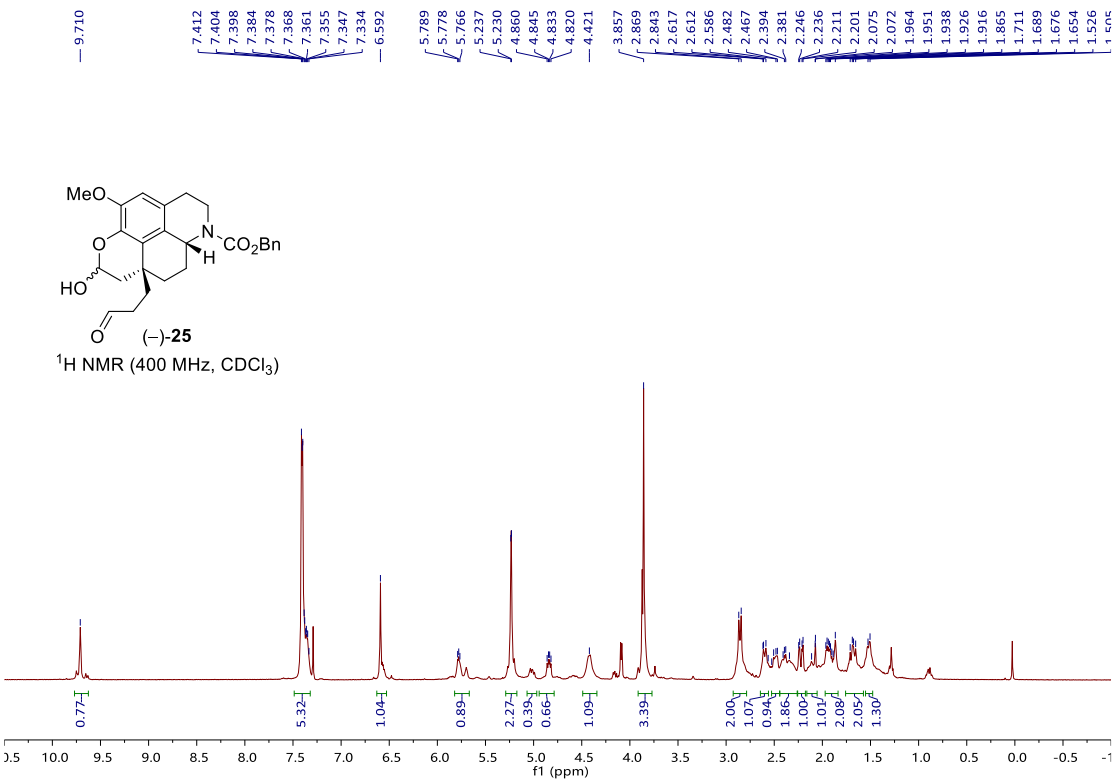


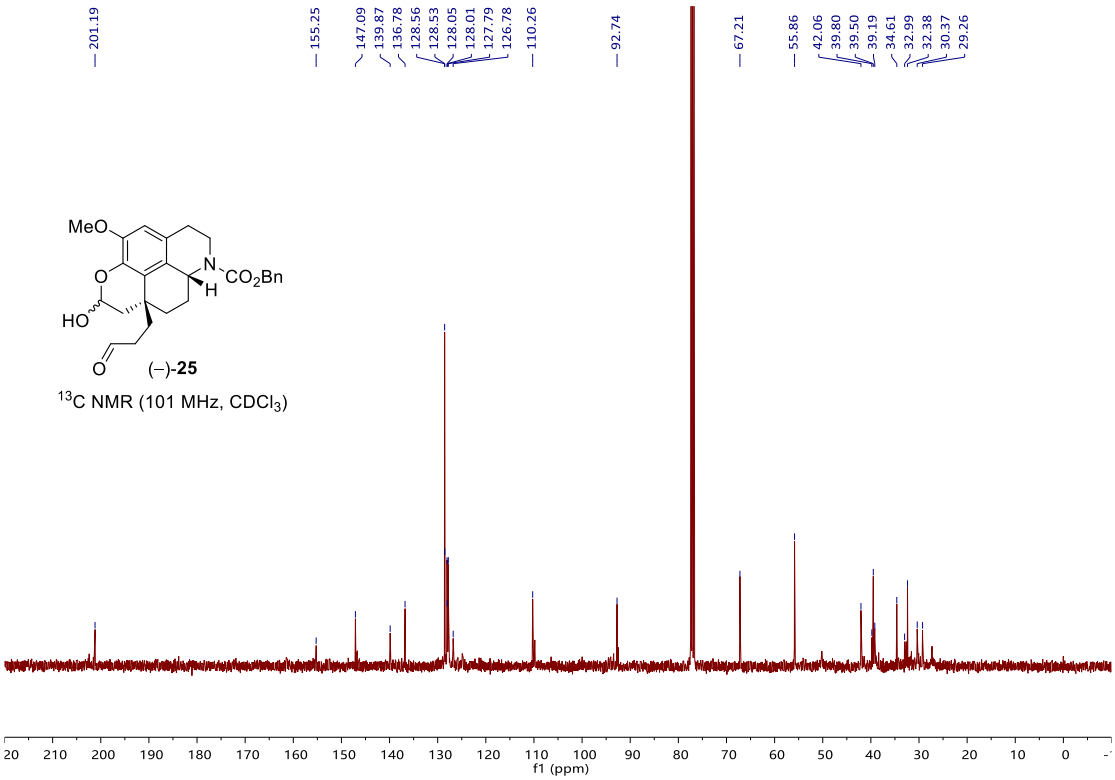
Compound (+)-24 (with a minor diastereoisomer)



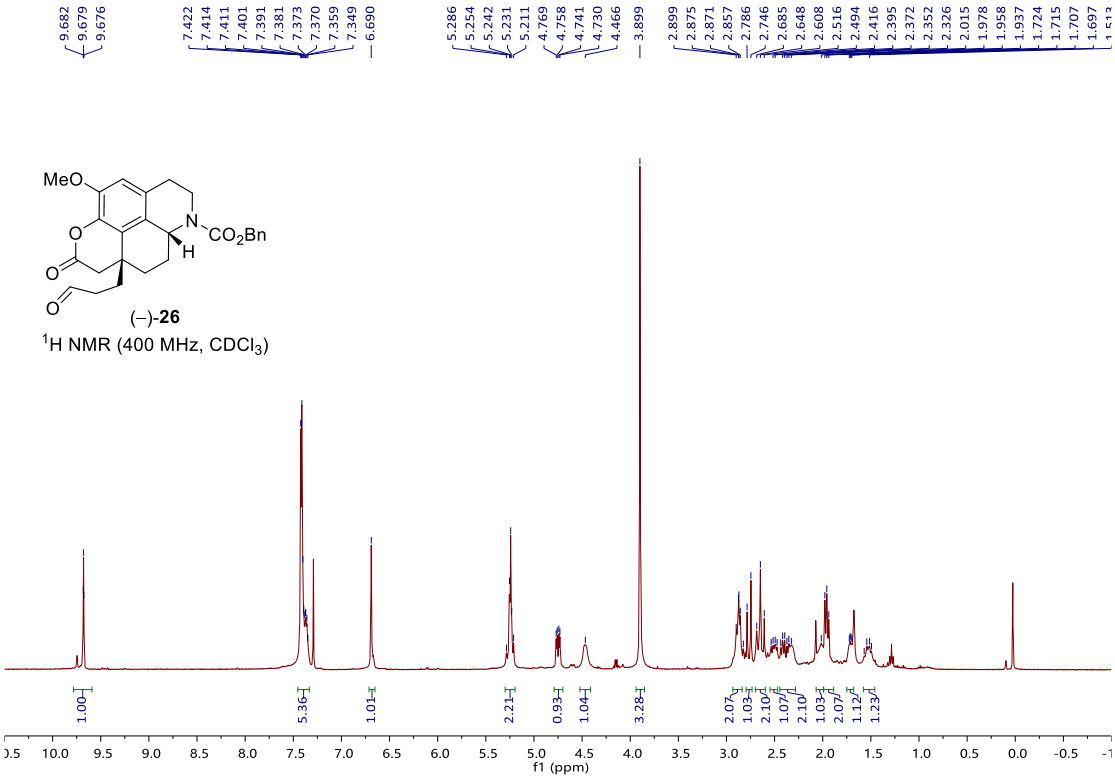


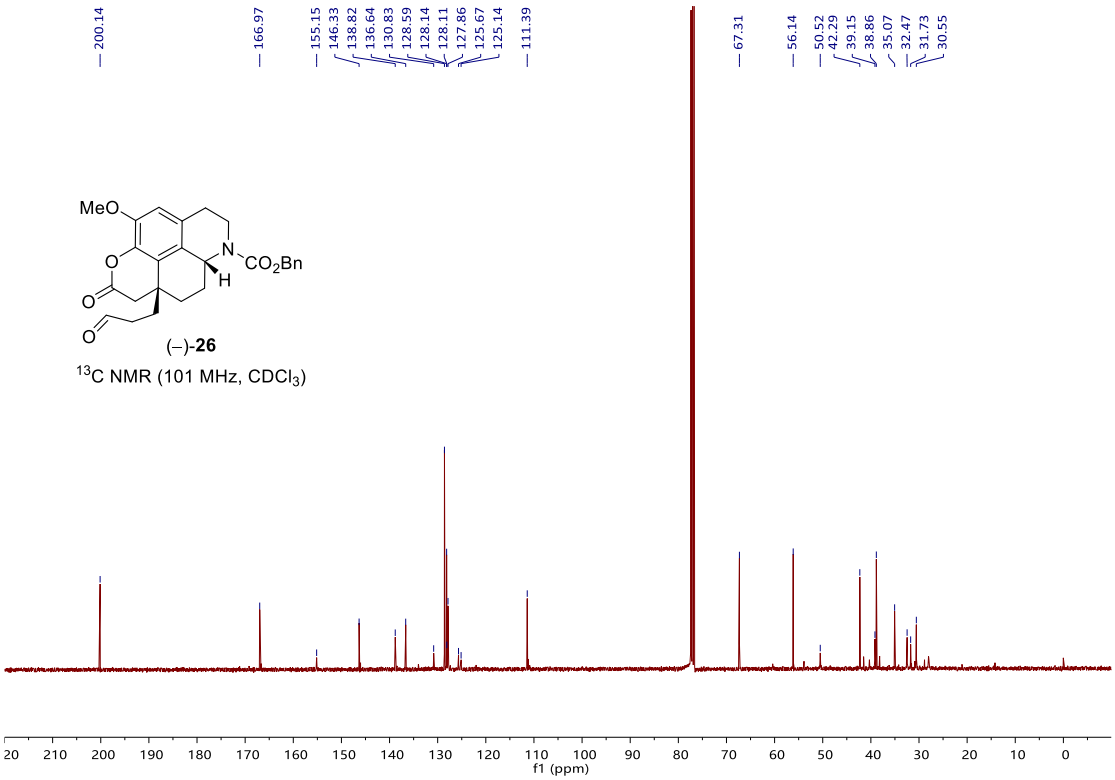
Compound (–)-25 (not stable, with minor diastereoisomers)



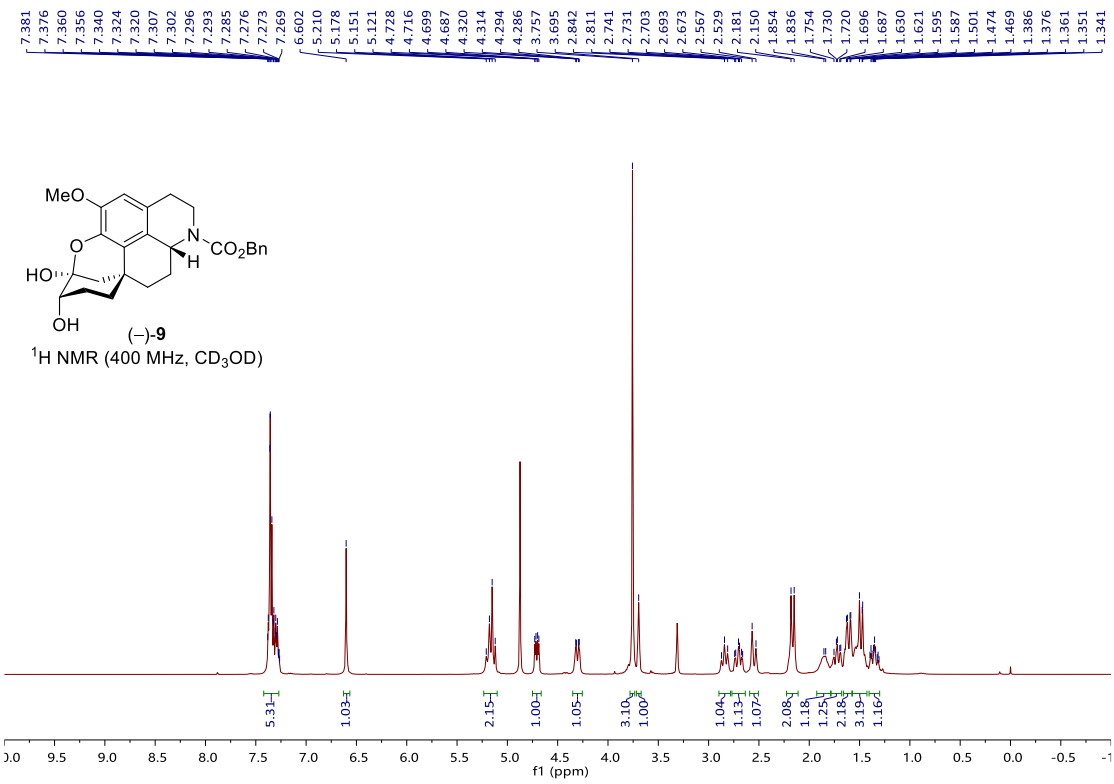


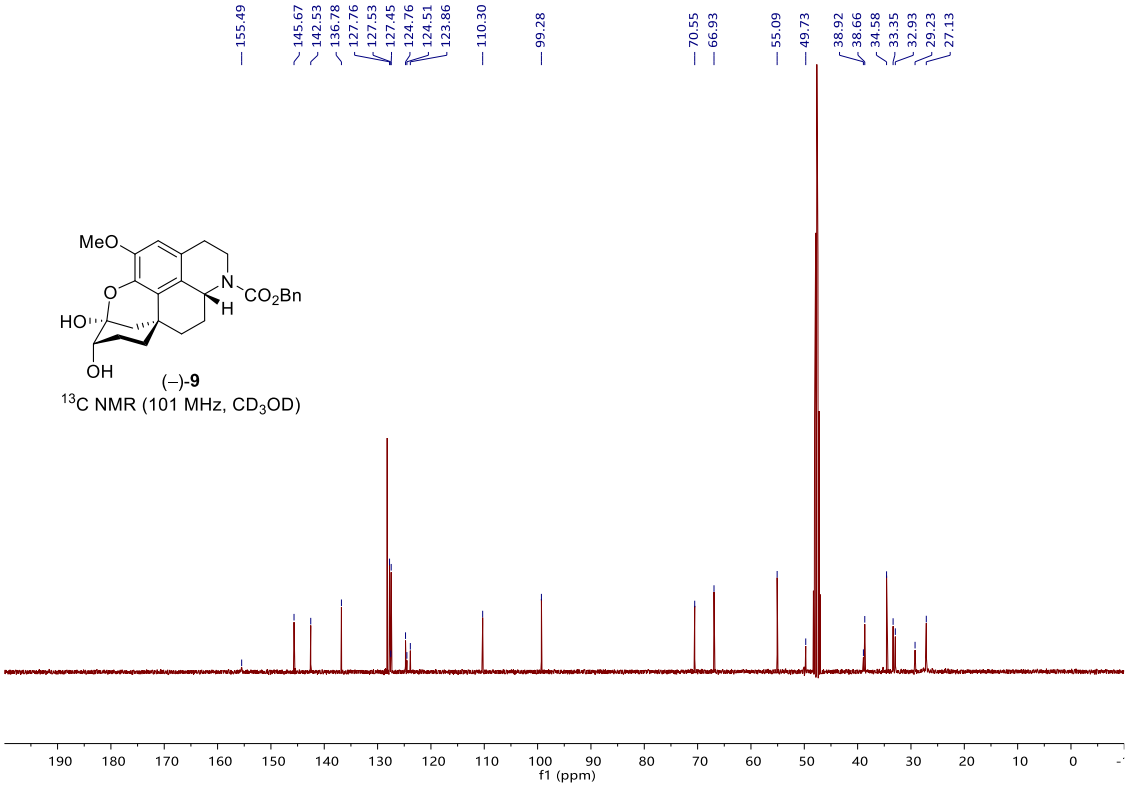
Compound (–)-26 (with a minor diastereoisomer)



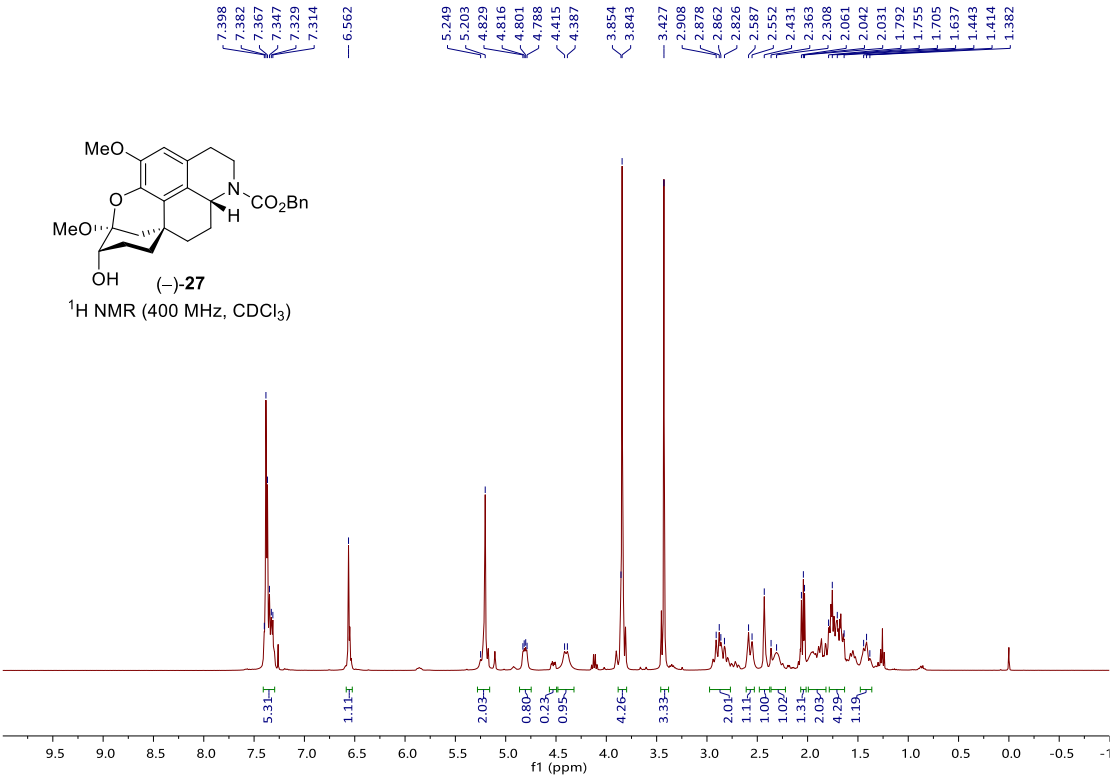


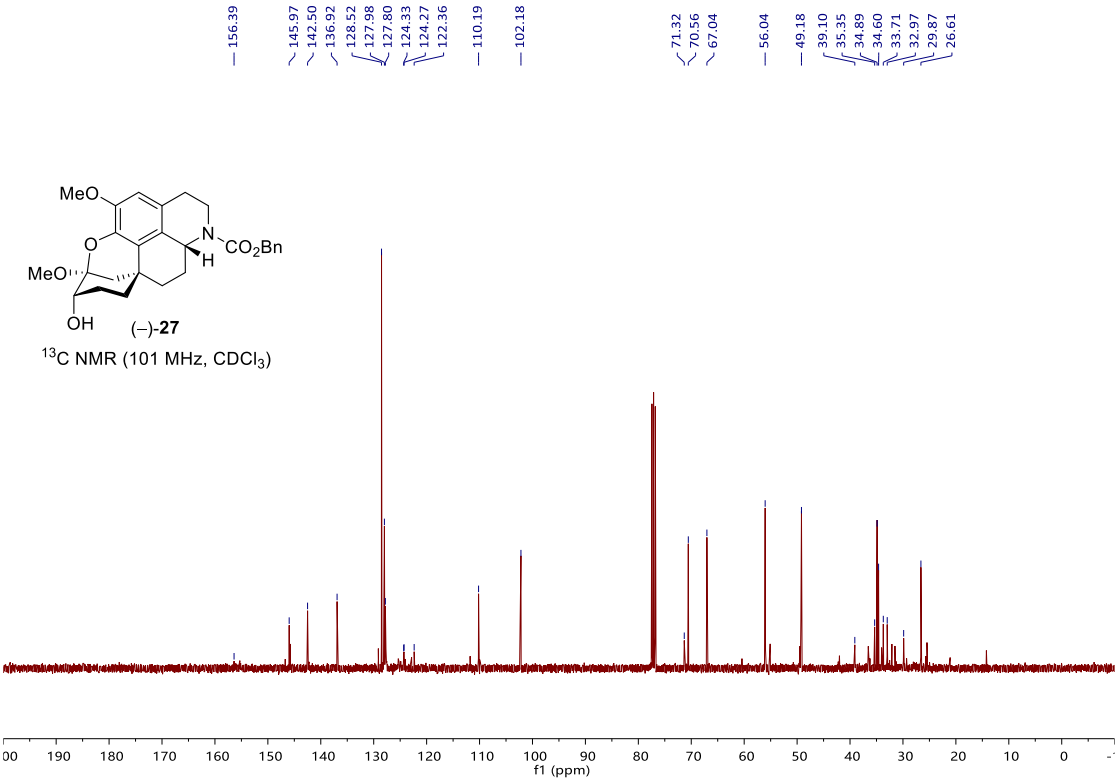
Compound (–)-9


MeO
O
HO
OH
N
H
CO2Bn
(–)-9
1H NMR (400 MHz, CD3OD)
f1 (ppm)

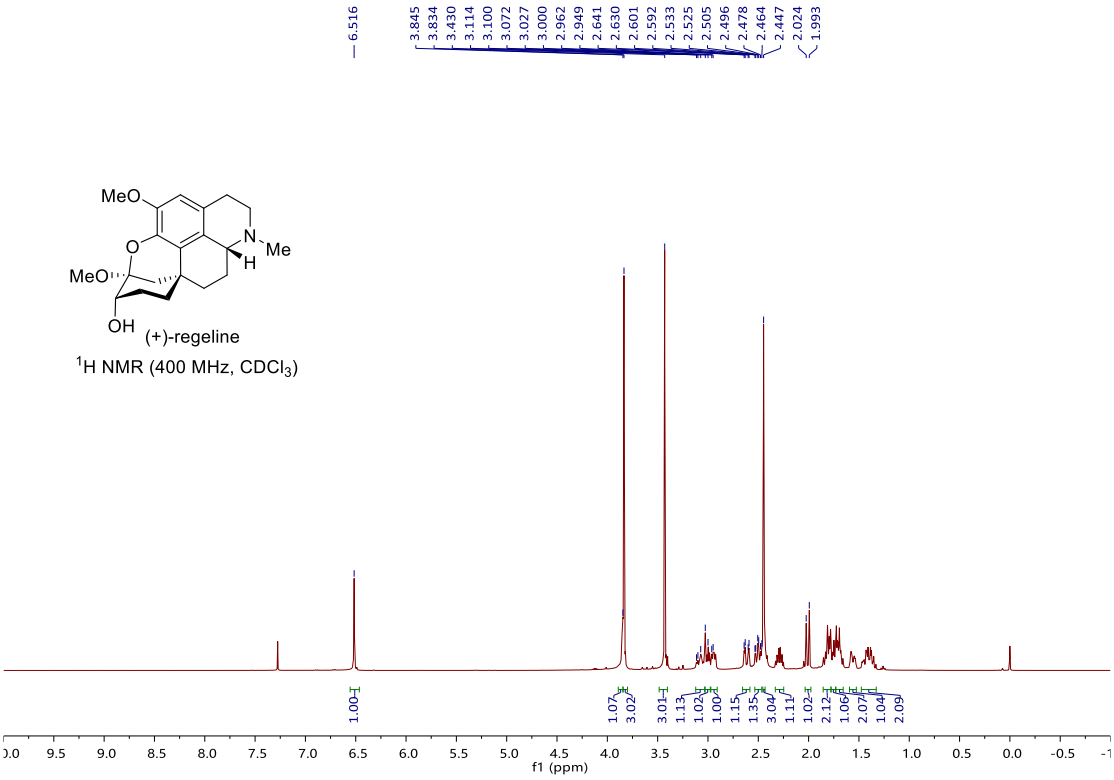

MeO
O
HO
OH
N
H
CO2Bn
(–)-9
13C NMR (101 MHz, CD3OD)
f1 (ppm)

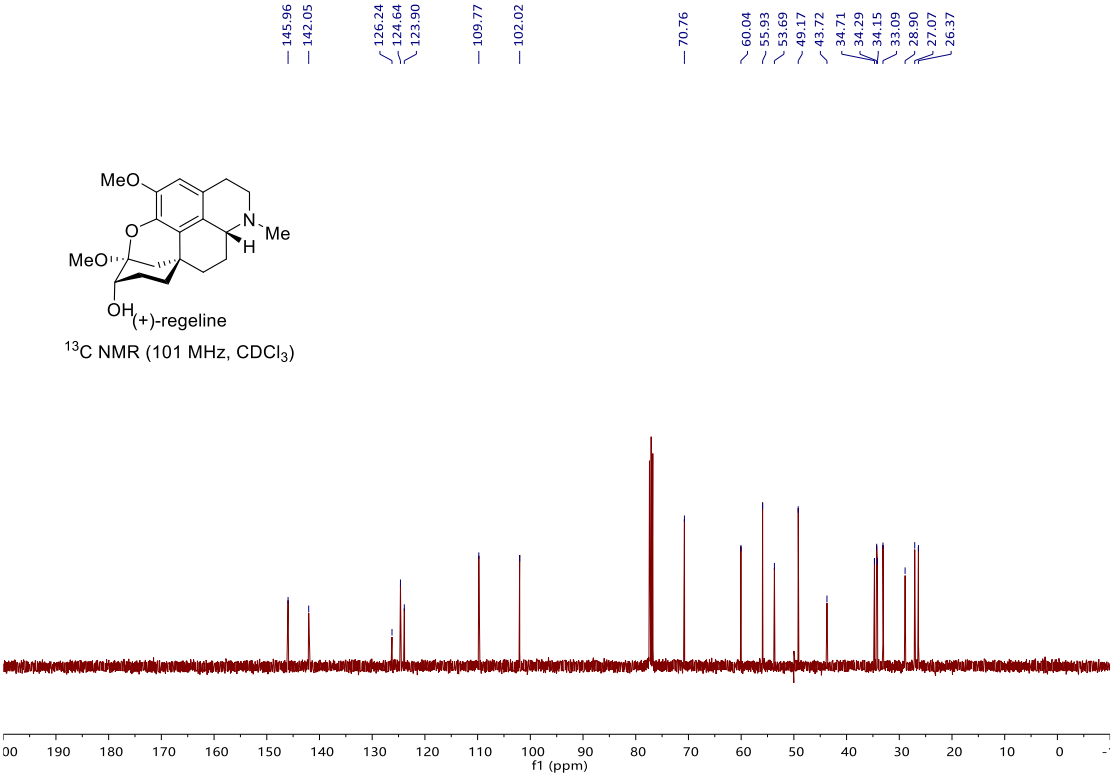
Compound (–)-27 (with a minor diastereoisomer)



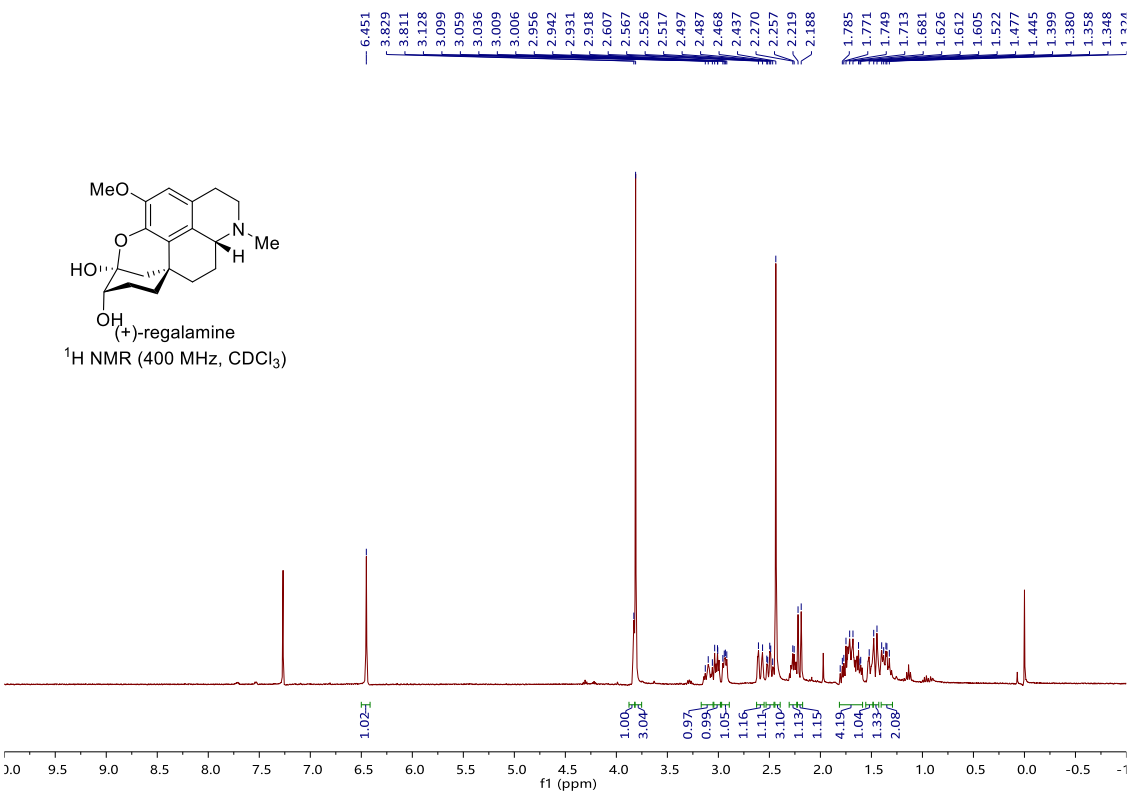


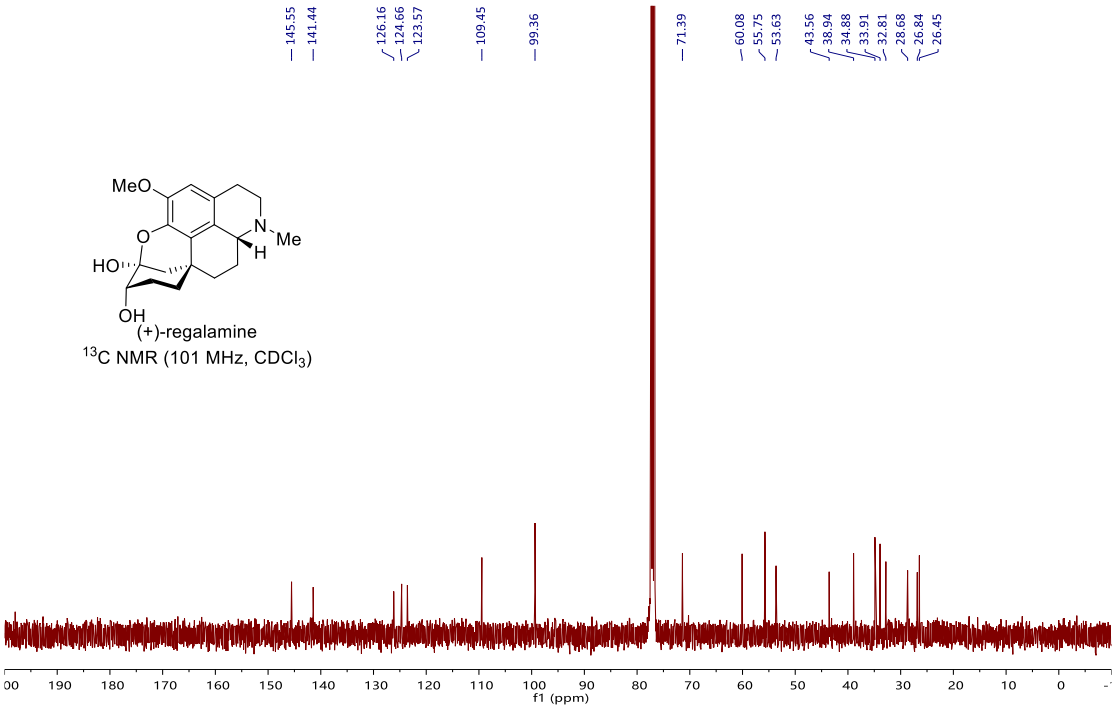
(+)-Regeline (1)


6.516
3.845
3.834
3.430
3.114
3.100
3.072
3.027
3.000
2.962
2.949
2.641
2.630
2.601
2.592
2.533
2.525
2.505
2.496
2.478
2.464
2.447
2.024
1.993
MeO
O
MeO
N
Me
H
OH
(+)-regeline
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
1.07
3.02
3.01
1.13
1.02
1.00
1.15
1.35
3.04
1.11
1.02
2.12
1.06
2.07
1.04
2.09
f1 (ppm)

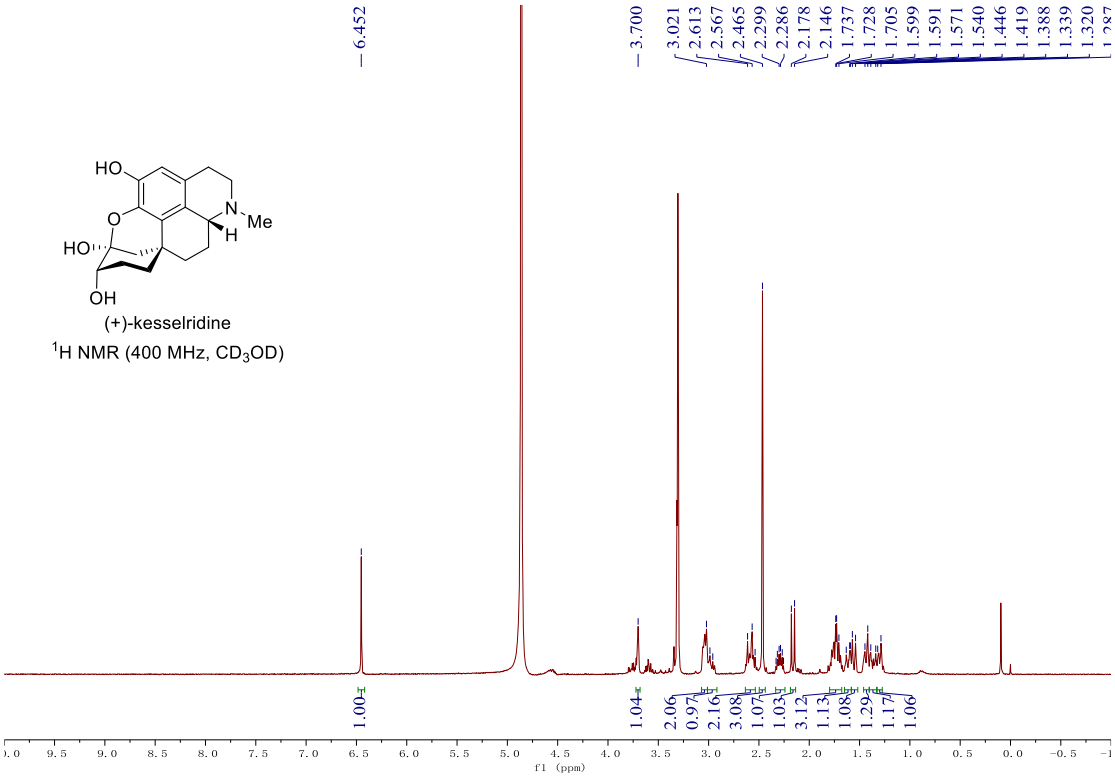

145.96
142.05
126.24
124.64
123.90
109.77
102.02
70.76
60.04
55.93
53.69
49.17
43.72
34.71
34.29
34.15
33.09
28.90
27.07
26.37
MeO
O
MeO
N
Me
H
OH
(+)-regeline
^{13}C NMR (101 MHz, CDCl$_3$)
f1 (ppm)

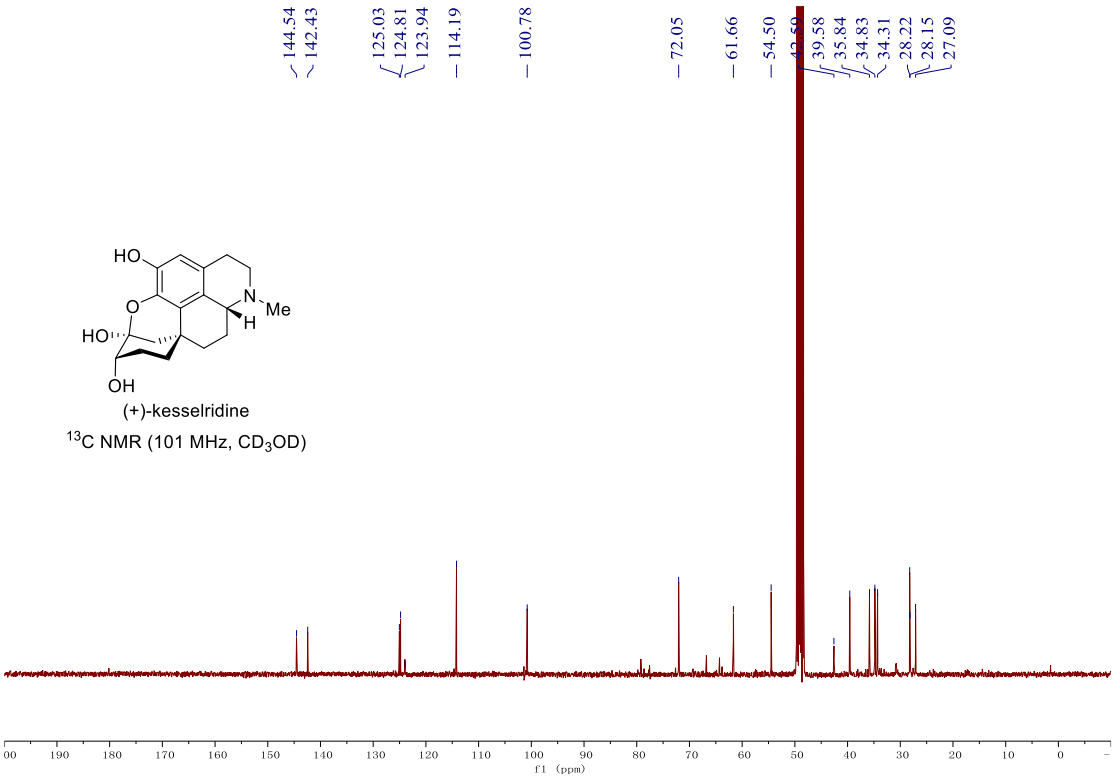
(+)-Regalamine (2)



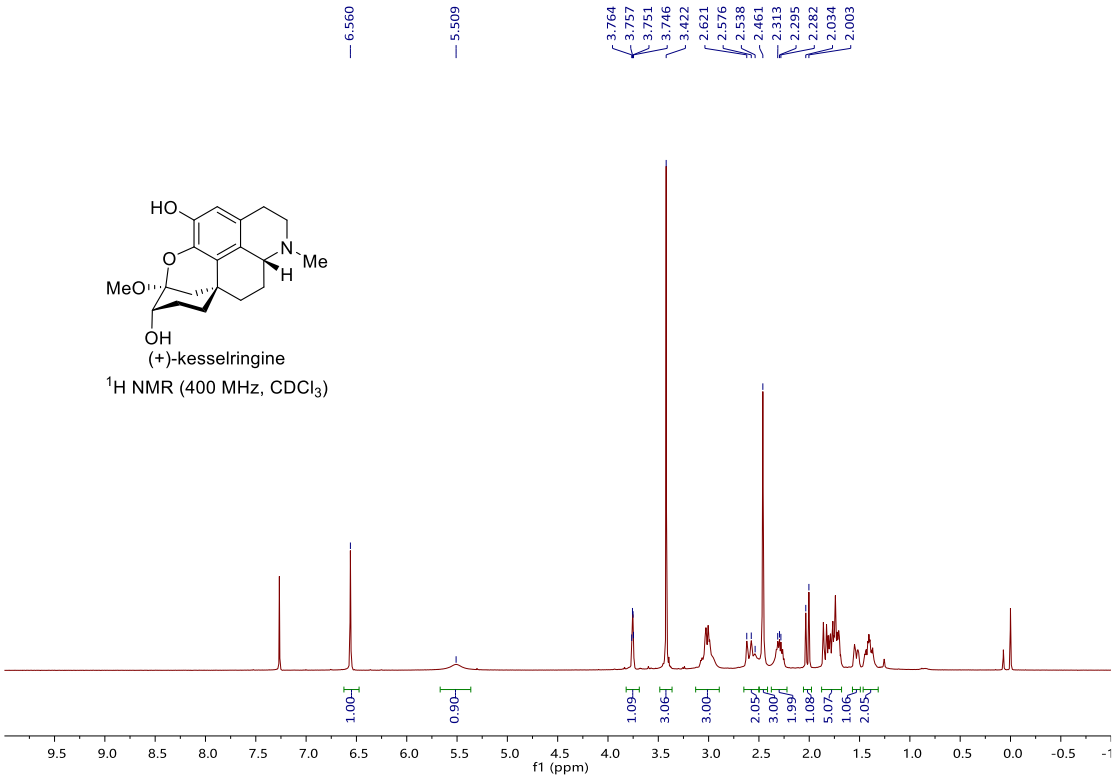


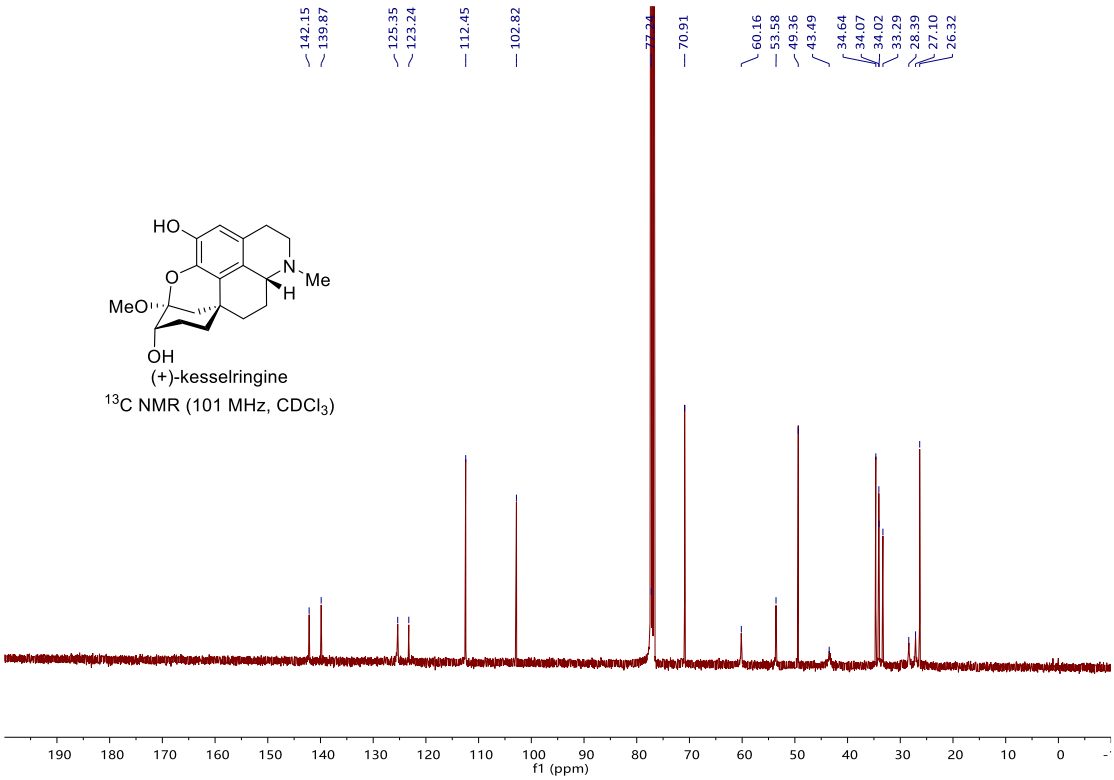
(+)-Kesselridine (3)



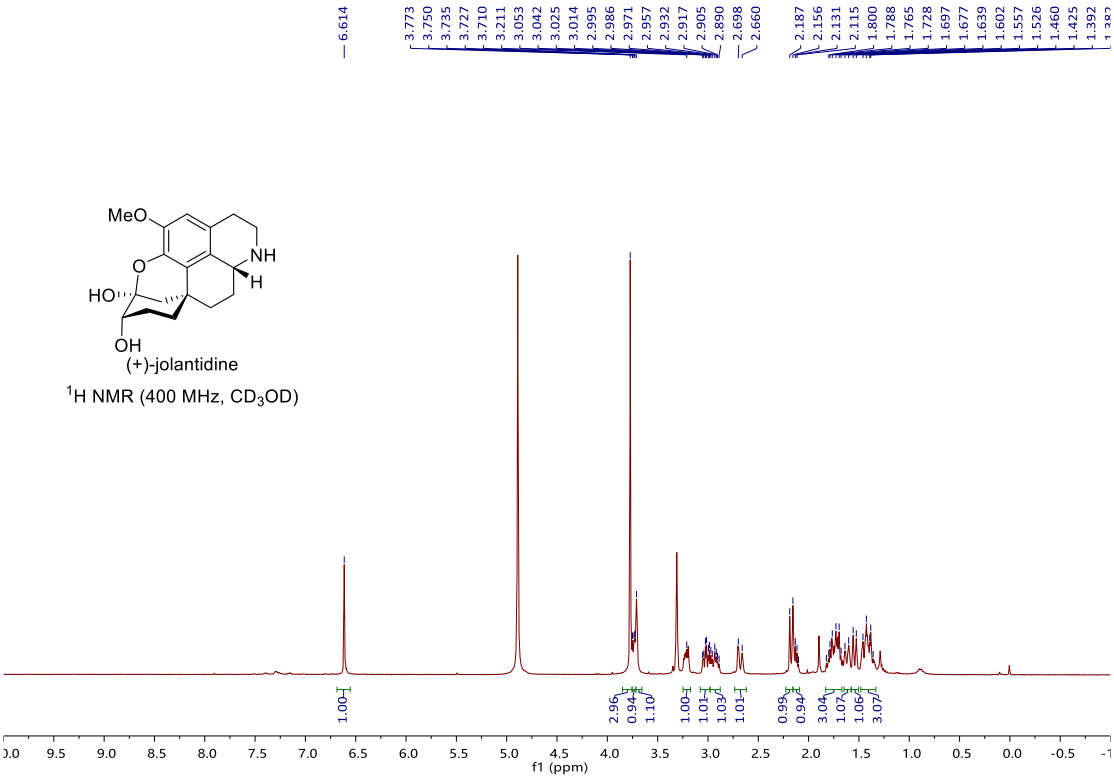


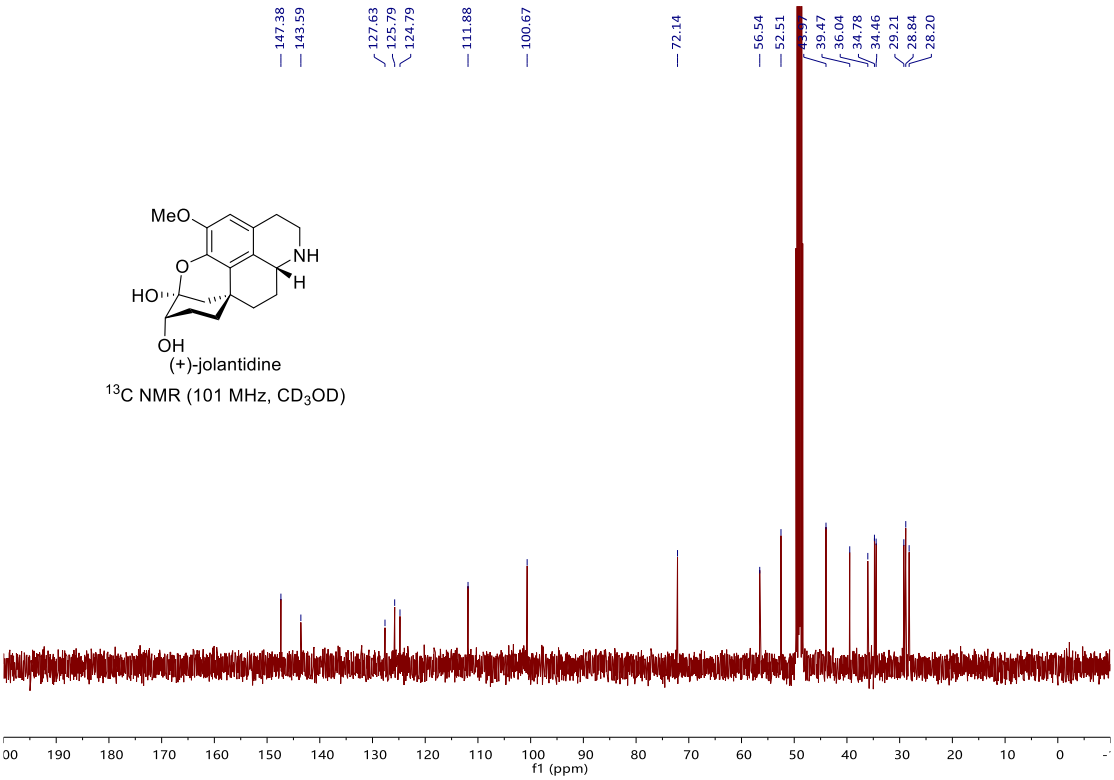
(+)-Kesselringine (4)



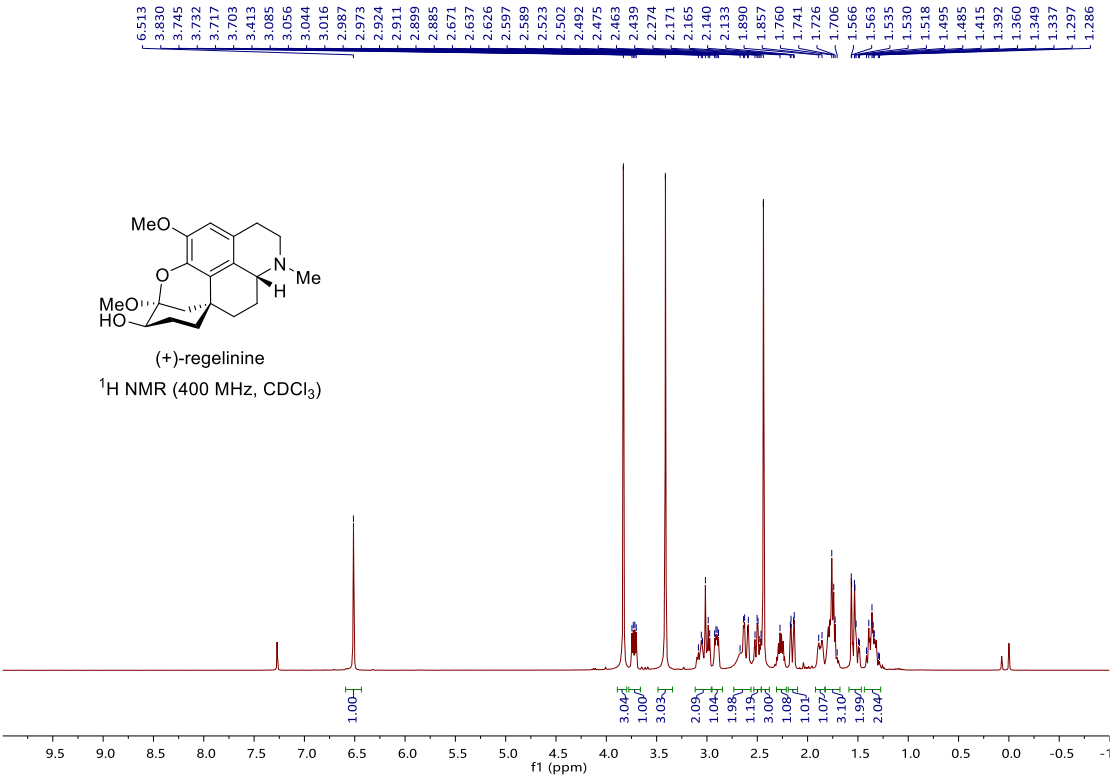


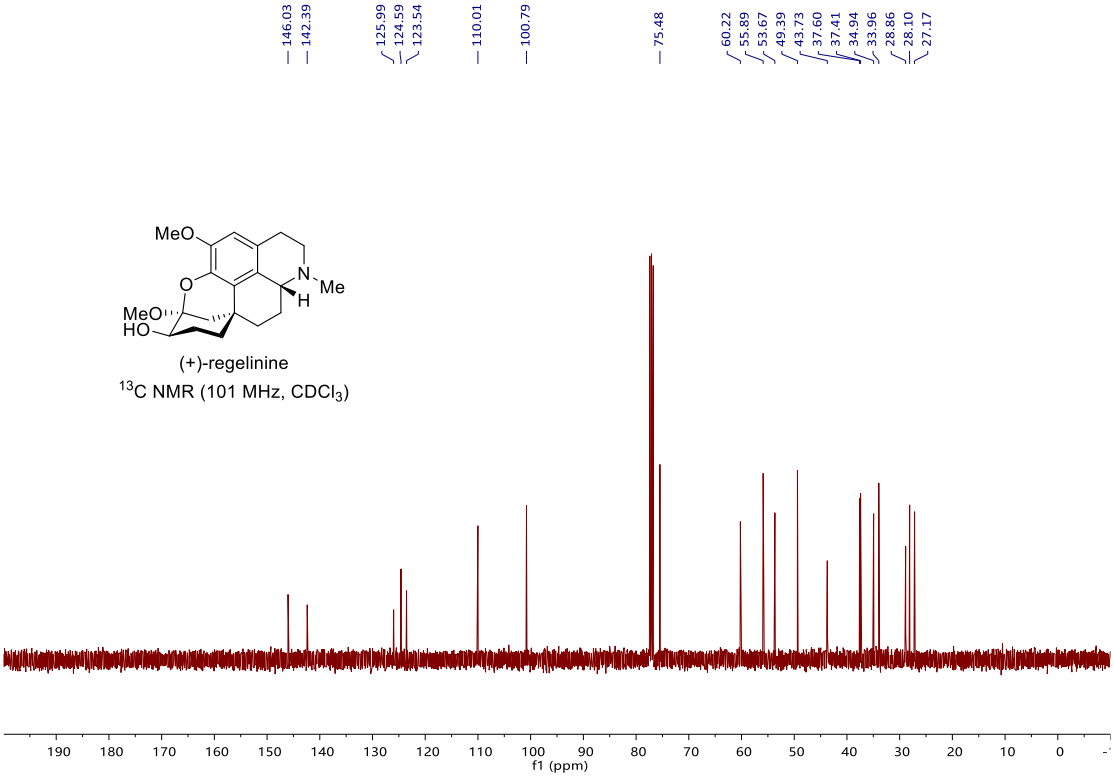
(+)-Jolantidine (5)



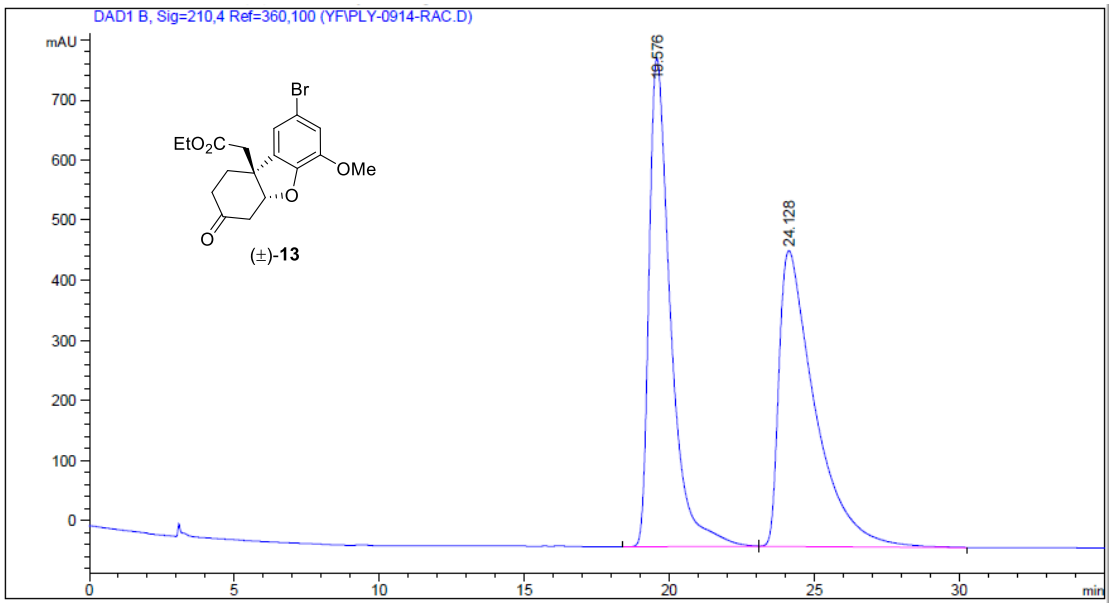


(+)-Regelinine (6)

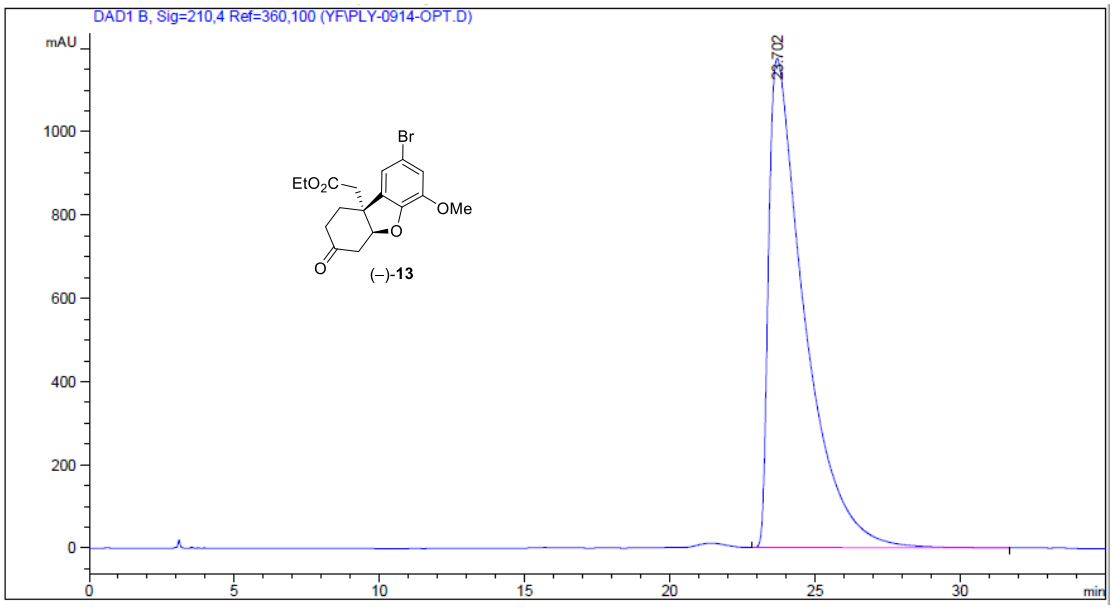




F) HPLC Charts for (–)-13



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.576	BB	0.7724	4.18316e4	812.86902	49.8041
2	24.128	BB	1.2077	4.21606e4	492.00912	50.1959



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.702	BB	1.2485	1.00802e5	1175.42114	100.0000