Supporting Information

Concise Total Synthesis of (±)-Pileamartines A and B

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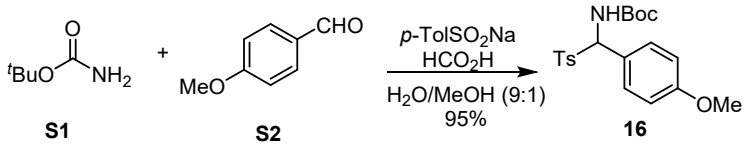
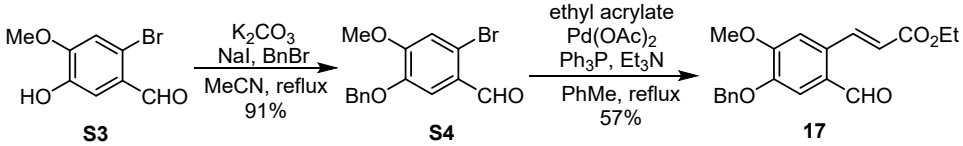
Part 1. Experimental Procedure and Spectral Data

General Methods. All reactions involving air or moisture sensitive reagents or intermediates were performed under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Anhydrous THF was distilled over sodium benzophenone ketyl under argon; CH_2Cl_2 and dimethyl formamide were refluxed with CaH_2 and freshly distilled prior to use. All other solvents and reagents were used as obtained from commercial sources without further purification. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on gel F254 plates. The silica gel (200-300 mesh) was used for column chromatography, and the distillation range of petroleum was 60-90 °C. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a *JEOL-400YH (400 MHz)* instrument. Chemical shifts were denoted in ppm (δ), and calibrated by using tetramethylsilane (TMS, $\delta = 0.00$ ppm) as internal standard for ^{1}H NMR and the deuterated solvent $CDCl_3$ (77.00 ppm) for ^{13}C NMR. Signal splitting patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) or broad (br), and coupling constants (*J*) are reported in Hz. High resolution mass spectra (HRMS) were performed by Analytical Instrument Center at the State Key Laboratory of Chemical Oncogenomics of Peking University Shenzhen Graduate School on an Electron Spray Injection (ESI) mass spectrometer. Melting point was recorded on an SGW® X-4A melting point apparatus.



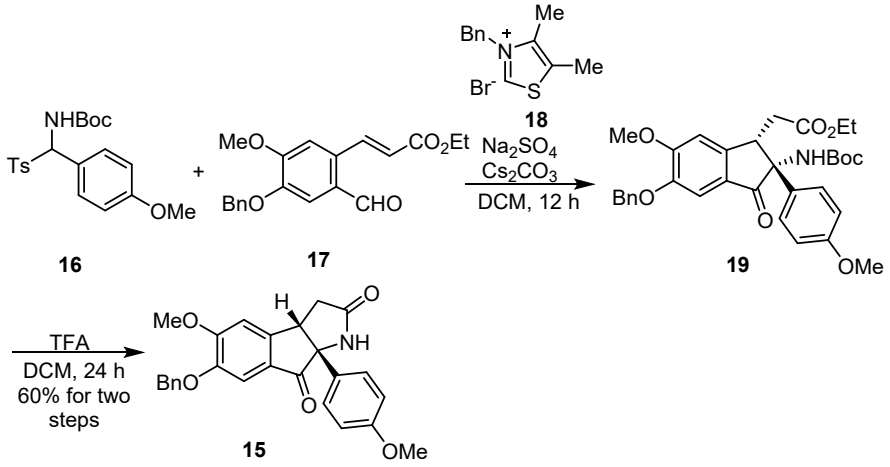
Synthesis of phenyl(tosyl)methylcarbamate 16. $BocNH_2$ (10.0 g, 86 mmol) and sodium *p*-toluenesulfinate (19.8 g, 111 mmol) were dissolved in a mixture consisting of water (90 mL) and MeOH (10 mL). Then *p*-anisaldehyde (12.4 mL, 103 mmol) and formic acid (15 mL) were successively added. The solution was stirred overnight at room temperature and a mass of white precipitate was formed. The resulting mixture was filtered, washed with water (20 mL × 3) and then Et_2O (20 mL × 3), dried *in vacuo* to give phenyl(tosyl)methylcarbamate **16** (31.7 g, 95%) as a white powder. The spectra data are in accord with these reported previously.[1]



Synthesis of 3-(2-formylphenyl)acrylate 17. To a solution of hydroxybenzaldehyde **S3** (7.1 g, 31 mmol) in MeCN (200 mL) were added K_2CO_3 (8.5 g, 62 mmol), NaI (4.6

g, 31 mmol) and benzyl bromide (5.5 mL, 46 mmol) at room temperature, and the resulting mixture was warmed to reflux. Then the mixture was cooled to room temperature after stirring for 5 h, and then filtered, washed with EtOAc (50 mL × 3), and the filtrate was concentrated *in vacuo*. The resulting residue was purified through column chromatography (petroleum ether /ethyl acetate = 5:1) to give benzyl phenyl ether **S4** (9.0 g, 91%) as a pale powder.

Under N_2 atmosphere, bromobenzaldehyde **S4** (9.0 g, 28 mmol) was dissolved in dry toluene (200 mL), then palladium acetate (629 mg, 2.8 mmol), triphenylphosphine (1.5 g, 5.6 mmol), triethylamine (19.5 mL, 140 mmol) and ethyl acrylate (15.2 mL, 140 mmol) were added. The mixture was warmed to reflux overnight before it was cooled to room temperature, and then it was filtered, washed with EtOAc (50 mL × 3). The filtrate was concentrated *in vacuo* to give a dark residue, which was purified through column chromatography (petroleum ether /ethyl acetate = 3:1) to afford 3-(2-formylphenyl)acrylate **17** (5.5 g, 57%) as a yellow amorphous solid. The spectra data are in accord with these reported previously.[2]

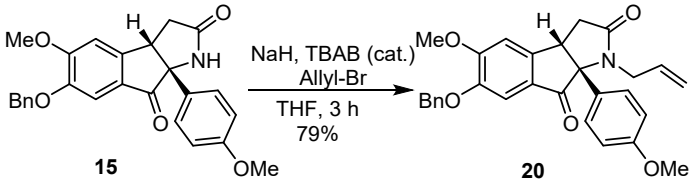


Synthesis of polyhydroindenopyrrole 15. The known thiazolium salt **18**[3] was synthesized from commercially available materials following the procedures reported previously.

To a solution of phenyl(tosyl)methylcarbamate **16** (2.30 g, 5.88 mmol) in dichloromethane (40 mL) was added anhydrous Na_2SO_4 (8.35 g, 58.8 mmol), and the mixture was vigorously stirred for 10 min before the addition of Cs_2CO_3 (4.22 g, 12.9 mmol), thiazolium salt **18** (166 mg, 0.585 mmol) and 3-(2-formylphenyl)acrylate **17** (4.00 g, 11.8 mmol). The resulting mixture was stirred at room temperature overnight, and then water (*ca*. 50 mL) was added to dissolve the suspended solids. The mixture was separated, and the aqueous phase was extracted with dichloromethane (100 mL × 3). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* until *ca.* 50 mL residue remained.

Trifluoroacetic acid (8.7 mL, 118 mmol) was added and then the resulting dark mixture was stirred for 24 h before saturated Na_2CO_3 (aq., *ca*. 50 mL) was slowly added to quench the reaction. Then the mixture was diluted with water (30 mL) and separated, and the aqueous phase was extracted with dichloromethane (100 mL × 3). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified through column chromatography (petroleum ether /ethyl acetate = 1:1 and then dichloromethane/MeOH = 50:1) to give polyhydroindenopyrrole **15** (1.50 g, 60% over two steps) as a light yellow powder.

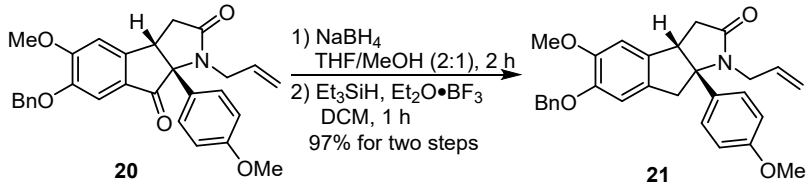
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.44 (m, 2H), 7.44–7.37 (m, 2H), 7.37–7.32 (m, 1H), 7.30 (s, 1H), 7.16 (d, J = 8.8 Hz, 2H), 6.90 (s, 1H), 6.88 (d, J = 9.0 Hz, 2H), 6.56 (br s, 1H), 5.20 (s, 2H), 4.01 (s, 3H), 3.84 (dd, J = 10.6, 2.9 Hz, 1H), 3.80 (s, 3H), 3.09 (dd, J = 17.6, 10.6 Hz, 1H), 2.48 (dd, J = 17.6, 3.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 201.3, 175.1, 159.5, 157.8, 150.4, 149.8, 135.9, 131.6, 128.7, 128.2, 127.4, 126.8, 126.4, 114.3, 106.9, 106.8, 71.8, 70.9, 56.5, 55.3, 48.1, 36.1; **HRMS** (ESI) *m/z*: calcd for $C_{26}H_{24}NO_5^+$ $[M+H]^+$, 430.1649; found, 430.1650; **M. p.** > 255 °C (decomposed).



***N*-allylation of 15**. To a solution of **15** (986 mg, 2.3 mmol) in anhydrous THF (20 mL) were added sodium hydride (dispersed in mineral oil, 60 wt%, 276 mg, 6.9 mmol) and tetrabutylammonium bromide (TBAB, 74 mg, 0.2 mmol). Allyl bromide (360 μL, 4.1 mmol) was added via a syringe after stirring for 20 min and the mixture was stirred for another 3 h before the careful addition of water (*ca*. 10 mL) to quench the reaction. Then the mixture was diluted with EtOAc (10 mL) and separated, and the aqueous phase was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified through column chromatography (petroleum ether /ethyl acetate = 1:1) to give **20** as a white powder (851 mg, 79%).

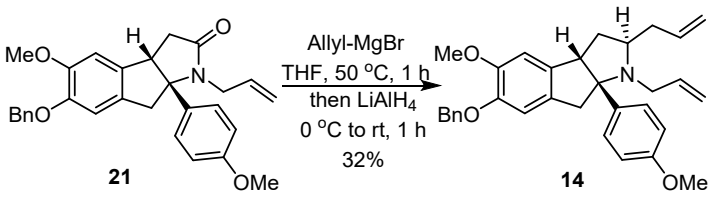
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.42 (m, 2H), 7.42–7.36 (m, 2H), 7.36–7.32 (m, 1H), 7.30 (s, 1H), 7.15–7.06 (m, 2H), 6.94–6.87 (m, 2H), 6.86 (s, 1H), 5.70–5.56 (m, 1H), 5.19 (s, 2H), 4.97–4.86 (m, 2H), 4.18 (ddt, J = 15.5, 5.9, 1.6 Hz, 1H), 3.98 (s, 3H), 3.80 (s, 3H), 3.79–3.72 (m, 1H), 3.68 (dd, J = 10.2, 2.3 Hz, 1H), 3.11 (dd, J = 17.4,

10.4 Hz, 1H), 2.62 (dd, *J* = 17.4, 2.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 199.9, 173.1, 159.4, 157.5, 149.6, 149.4, 135.8, 132.1, 130.1, 128.6, 128.1, 127.8, 127.4, 127.3, 116.9, 114.3, 106.7, 106.6, 75.5, 70.8, 56.4, 55.2, 46.9, 44.1, 35.7; **HRMS** (ESI) *m/z*: calcd for $C_{29}H_{28}NO_5^+$ $[M+H]^+$, 470.1962; found, 470.1960; **M. p.** = 152–154 °C.



Synthesis of dihydroindene 21. Ketone **20** (851 mg, 1.8 mmol) was dissolved in a mixture of THF (12 mL) and MeOH (6 mL) and then $NaBH_4$ (207 mg, 5.4 mmol) was added in one portion. TLC (DCM/MeOH = 50:1) showed that the starting material was completely consumed after 2 h stirring. Acetone (3 mL) was added to consume the remaining $NaBH_4$ before the addition of silica gel (*ca*. 3 g). After stirring for another 10 min, the mixture was filtered and washed with DCM (20 mL × 3). Volatile in the filtrate was removed *in vacuo* and the residue was redissolved in anhydrous DCM (20 mL) under N_2. Then Et_3SiH (870 μL, 5.4 mmol) was added, followed by the addition of $Et_2O•BF_3$ (670 μL, 5.4 mmol) after 10 min stirring. The resulting mixture was stirred for 1h and TLC (DCM/MeOH = 50:1) showed the full consumption of the alcohol intermediate. Saturated Na_2CO_3 (aq., *ca*. 10 mL) was added to quench the reaction and the mixture was separated. The aqueous phase was extracted with DCM (20 mL×3) and the combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 2:1 to 1:1) to give dihydroindene **21** (801 mg, 97% for two steps) as a white powder.

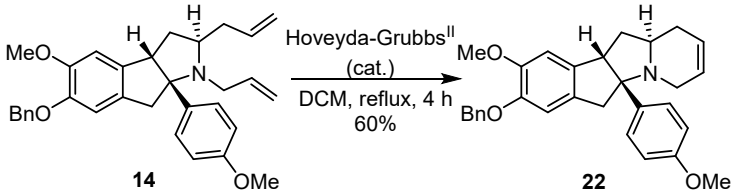
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.41 (m, 2H), 7.40–7.34 (m, 2H), 7.33–7.27 (m, 1H), 7.18 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.71 (d, *J* = 6.8 Hz, 2H), 5.72–5.58 (m, 1H), 5.15 (s, 2H), 4.84 (ddd, *J* = 10.4, 3.2, 1.2 Hz, 1H), 4.73 (ddd, *J* = 17.2, 3.2, 2.0 Hz, 1H), 4.37–4.28 (m, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 3.63 (d, *J* = 8.2 Hz, 1H), 3.56 (d, 16.8 Hz, 1H), 3.41 (ddt, *J* = 16.8, 5.6, 1.6 Hz, 1H), 3.34 (d, *J* = 16.8 Hz, 1H), 2.87 (dd, *J* = 17.0, 8.4 Hz, 1H), 2.60 (dd, *J* = 16.9 Hz, 1.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 174.2, 158.9, 149.8, 148.2, 137.1, 135.8, 134.2, 133.2, 131.8, 128.5, 127.8, 127.2, 127.0, 115.7, 114.2, 110.6, 107.7, 78.1, 71.2, 56.2, 55.3, 53.0, 43.8, 41.9, 36.0; **HRMS** (ESI) *m/z*: calcd for $C_{29}H_{30}NO_4^+$ $[M+H]^+$, 456.2169; found, 456.2170; **M. p.** = 102–104 °C.



Reductive allylation of lactam 21. Lactam **21** (90 mg, 0.20 mmol) was dissolved in anhydrous THF (5 mL) under N_2 and a solution of allyl magnesium bromide in Et_2O (1 M, 400 μL, 0.40 mmol) was added at room temperature. Then the mixture was warmed to 50 °C and stirred for 1 h before it was cooled to 0 °C. A solution of $LiAlH_4$ in THF (2.5 M, 160 μL, 0.40 mmol) was slowly added via a syringe and the resulting mixture was slowly warmed to room temperature and stirred for 1 h. Then water (*ca*. 1 mL) was carefully added to quench the reaction, followed by the addition of saturated seignette salt (aq., 5 mL), and the resulting mixture was vigorously stirred until it turned clear. Then the mixture was separated. The aqueous phase was extracted with DCM (10 mL×3) and the combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 20:1) to give diene **14** (30 mg, 32%) as a colorless oil.

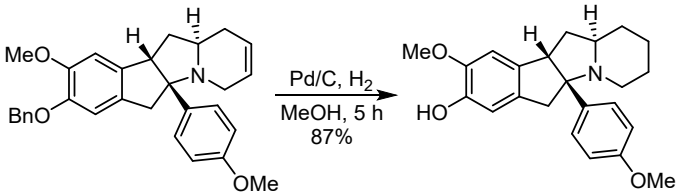
A slightly lower yield (86 mg, 29%) was obtained in a scaled-up reaction (**21**, 276 mg, 0.61 mmol).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.44 (m, 2H), 7.44–7.34 (m, 4H), 7.34–7.28 (m, 1H), 6.81 (s, 1H), 6.78 (d, J = 4.0 Hz, 2H), 6.63 (s, 1H), 5.94–5.75 (m, 2H), 5.14 (s, 2H), 5.12–4.92 (m, 4H), 3.83 (s, 3H), 3.77 (s, 3H), 3.38 (d, J = 16.9 Hz, 1H), 3.35–3.24 (m, 2H), 3.15 (dd, J = 15.6, 6.6 Hz, 1H), 3.07 (d, J = 16.7 Hz, 1H), 2.94–2.82 (m, 1H), 2.59–2.49 (m, 1H), 2.20–2.08 (m, 1H), 1.99–1.87 (m, 1H), 1.87–1.78 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.0, 149.4, 147.7, 141.0, 138.7, 138.1, 137.5, 136.0, 134.0, 128.5, 127.7, 127.3, 126.9, 116.2, 114.8, 113.2, 109.9, 108.0, 80.1, 71.4, 62.4, 58.3, 56.1, 55.2, 52.0, 39.7, 39.5, 38.1; **HRMS** (ESI) *m/z*: calcd for $C_{32}H_{36}NO_3^+$ $[M+H]^+$, 482.2690; found, 482.2688.



Synthesis of 22. To a solution of diene **14** (86 mg, 0.18 mmol) in anhydrous DCM (18 mL) was added Hoveyda-Grubbs' catalyst (the 2nd generation, 11 mg, 0.02 mmol) under N_2 and the mixture was warmed to reflux. The dark mixture was cooled to room temperature and concentrated *in vacuo* after it was stirred for 4 h and monitored by TLC (PE/EA = 10:1) for the complete consumption of the diene. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 20:1) to give tetrahydropyridine **22** (49 mg, 60%) as a colorless oil.

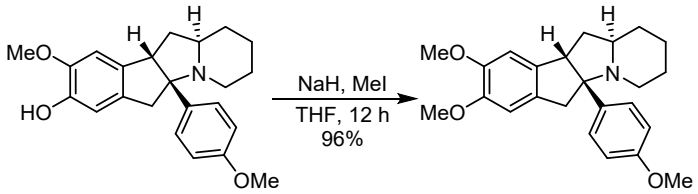
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.44 (m, 2H), 7.42–7.35 (m, 4H), 7.35–7.28 (m, 1H), 6.84–6.76 (m, 3H), 6.66 (s, 1H), 5.79–5.68 (m, 2H), 5.15 (dd, J = 14.4, 12.0 Hz, 2H), 3.84 (s, 3H), 3.77 (s, 3H), 3.38 (d, J = 16.8 Hz, 1H), 3.32 (dd, J = 9.9, 2.1 Hz, 1H), 3.17 (dt, J = 15.8, 2.8 Hz, 1H), 3.01 (d, J = 16.8 Hz, 1H), 3.02–2.94 (m, 1H), 2.79–2.68 (m, 1H), 2.33–2.21 (m, 1H), 2.15–2.02 (m, 1H), 1.98 (ddd, J = 12.0, 6.0, 2.1 Hz, 1H), 1.93–1.83 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.0, 149.4, 147.7, 139.8, 137.8, 137.4, 134.1, 128.5, 127.7, 127.3, 126.7, 125.7, 124.2, 113.4, 109.7, 108.1, 77.6, 71.3, 58.6, 56.1, 55.4, 55.2, 45.5, 40.2, 37.8, 33.6; **HRMS** (ESI) *m/z*: calcd for $C_{30}H_{32}NO_3^+$ $[M+H]^+$, 454.2377; found, 454.2374.



22 pileamartine B (**2**)

Synthesis of pileamartine B (2). To a solution of tetrahydropyridine **22** (49 mg, 0.11 mmol) in methanol (2 mL) was added 10% Pd/C (5 mg) and the mixture was stirred for 5 h under hydrogen atmosphere (vacuumized and refilled with hydrogen three times) at room temperature until complete consumption of **22**, which was monitored by TLC (PE/EA = 10:1). Then Pd/C was filtered off and washed with methanol (5 mL ×3). The filtrate was concentrated *in vacuo* to give a residue, which was purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give pileamartine B (**2**) (34 mg, 87%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.35 (m, 2H), 6.84–6.80 (m, 2H), 6.80 (s, 1H), 6.60 (s, 1H), 5.55 (s, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.46 (d, J = 17.1 Hz, 1H), 3.24 (dd, J = 9.0, 2.4 Hz, 1H), 2.91 (d, J = 17.2 Hz, 1H), 2.75 (d, J = 10.9 Hz, 1H), 2.45–2.35 (m, 1H), 2.17 (td, J = 11.1, 3.5 Hz, 1H), 1.84–1.73 (m, 4H), 1.68–1.59 (m, 2H), 1.29–1.17 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.8, 146.1, 144.8, 141.0, 136.8, 135.5, 126.4, 113.3, 109.5, 106.8, 77.0, 59.5, 58.9, 56.0, 55.2, 46.5, 40.2, 37.5, 32.3, 25.9, 24.4; **HRMS** (ESI) *m/z*: calcd for $C_{23}H_{28}NO_3^+$ $[M+H]^+$, 366.2064; found, 366.2061.

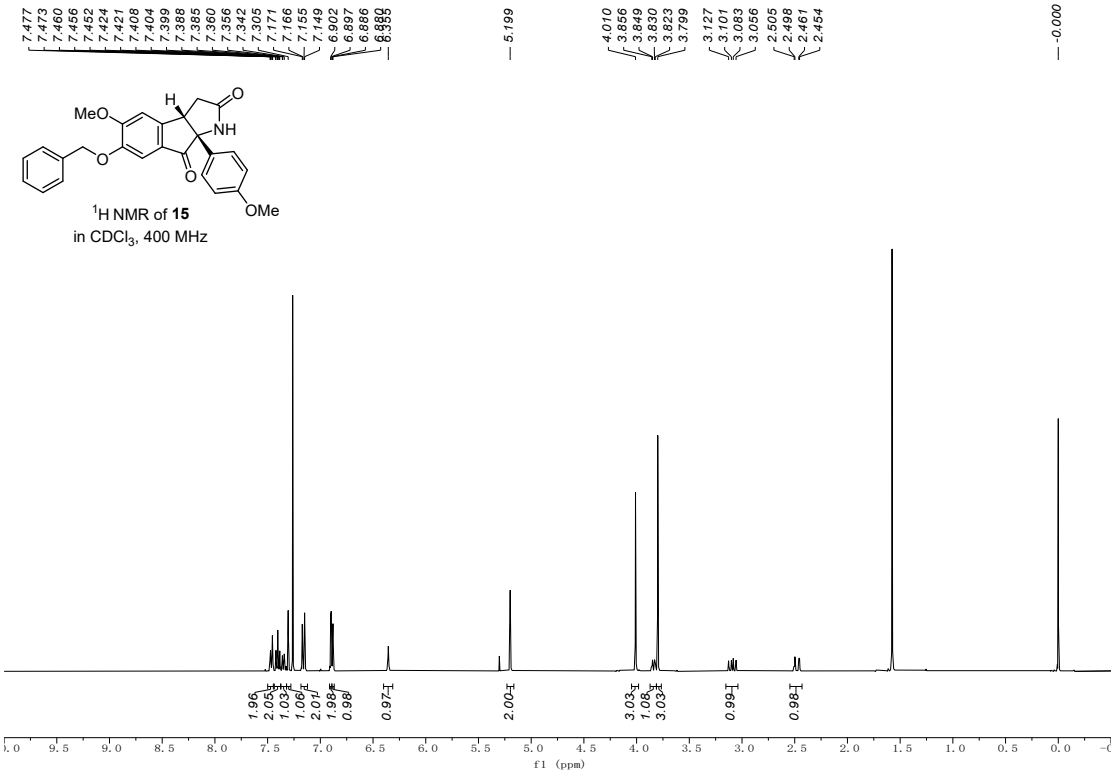


pileamartine B (**2**) pileamartine A (**1**)

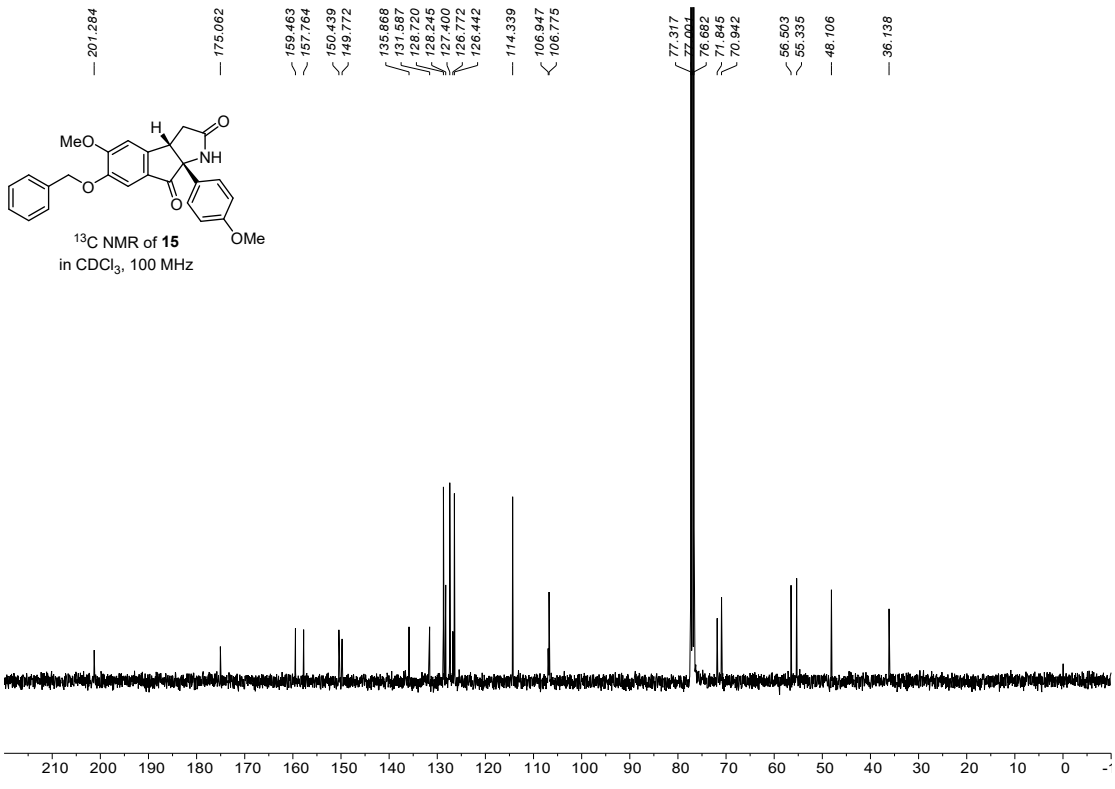
Synthesis of pileamartine A (1). To a solution of pileamartine B (**2**) (15.7 mg, 0.04 mmol) in anhydrous THF (1 mL) was added NaH (60% in mineral oil, 8.6 mg, 0.22 mmol), followed by MeI (3 μL, 0.05 mmol) and the mixture was stirred at room temperature for 12 h. TLC (PE/EA = 10:1) showed the complete consumption of pileamartine B (**2**) and water (*ca*. 1 mL) was added dropwise to quench the reaction. Then the resulting mixture was diluted with EtOAc (2 mL) and separated. The aqueous phase was extracted with EtOAc (5 mL×3) and the combined organic layers were washed with brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give pileamartine A (**1**) (15.6 mg, 96%) as an off-white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.34 (m, 2H), 6.85–6.79 (m, 2H), 6.76 (s, 1H), 6.63 (s, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.78 (s, 3H), 3.50 (d, J = 17.0 Hz, 1H), 3.27 (dd, J = 8.3, 3.1 Hz, 1H), 2.94 (d, J = 17.0 Hz, 1H), 2.82–2.72 (m, 1H), 2.45–2.34 (m, 1H), 2.19 (td, J = 10.9, 3.6 Hz, 1H), 1.87–1.72 (m, 4H), 1.69–1.59 (m, 2H), 1.33–1.16 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.9, 148.7, 148.4, 141.0, 137.3, 134.6, 126.4, 113.4, 107.4, 106.7, 77.2, 59.5, 59.0, 56.0(2C), 55.2, 46.5, 40.0, 37.8, 32.4, 25.9, 24.4; **HRMS** (ESI) *m/z*: calcd for $C_{24}H_{30}NO_3^+$ $[M+H]^+$, 380.2220; found, 380.2218; **M. p.** = 146–147 °C.

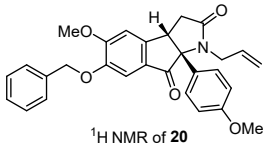
Part 2. NMR Spectra of New Compounds



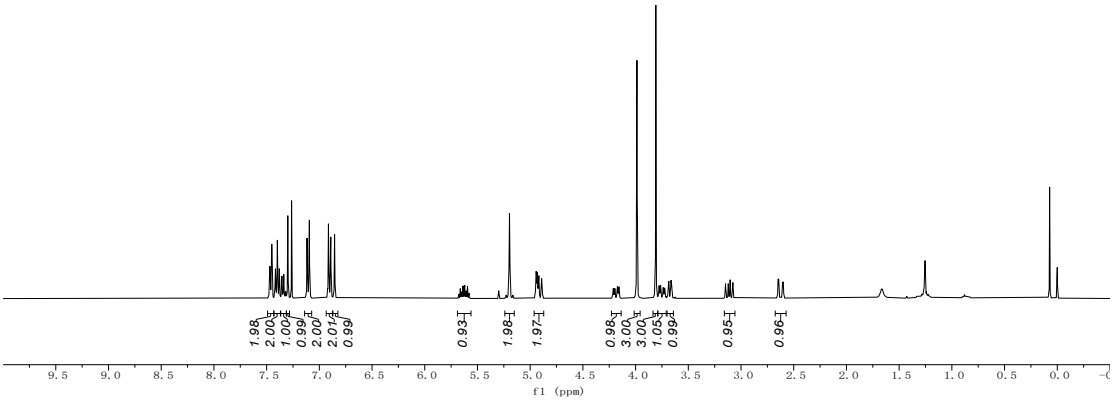
^{1}H NMR of **15**
in $CDCl_3$, 400 MHz

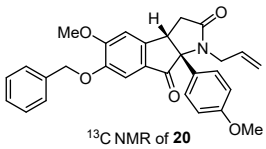


^{13}C NMR of **15**
in $CDCl_3$, 100 MHz

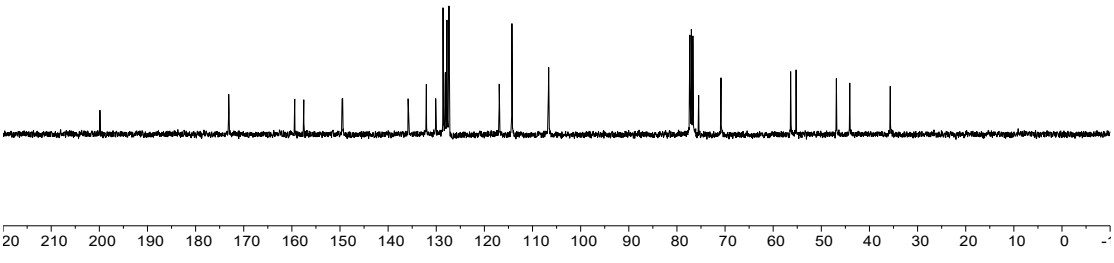


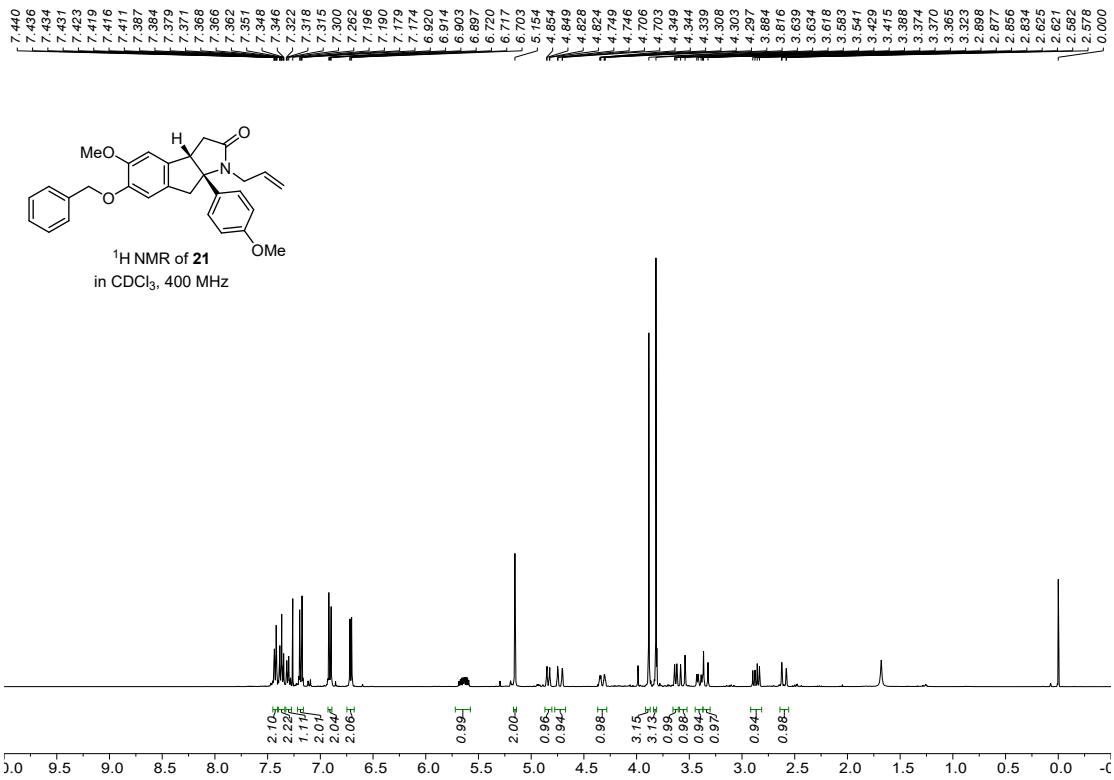
^{1}H NMR of **20**
in $CDCl_3$, 400 MHz



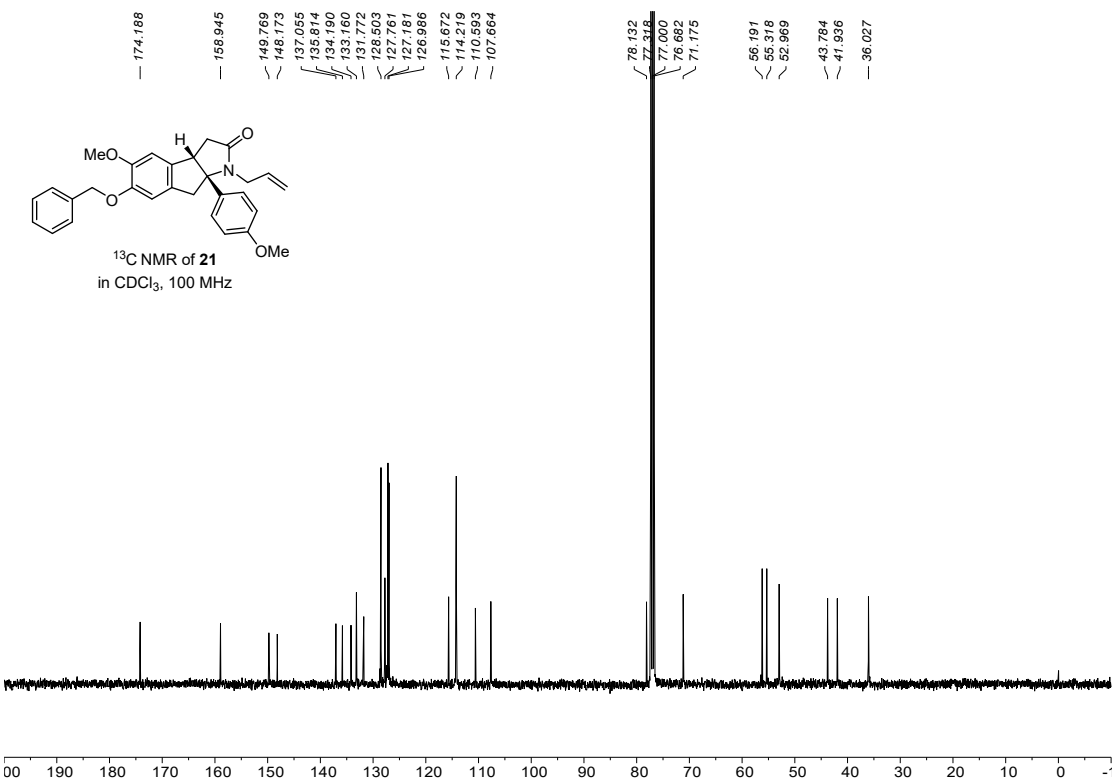


^{13}C NMR of **20**
in $CDCl_3$, 100 MHz

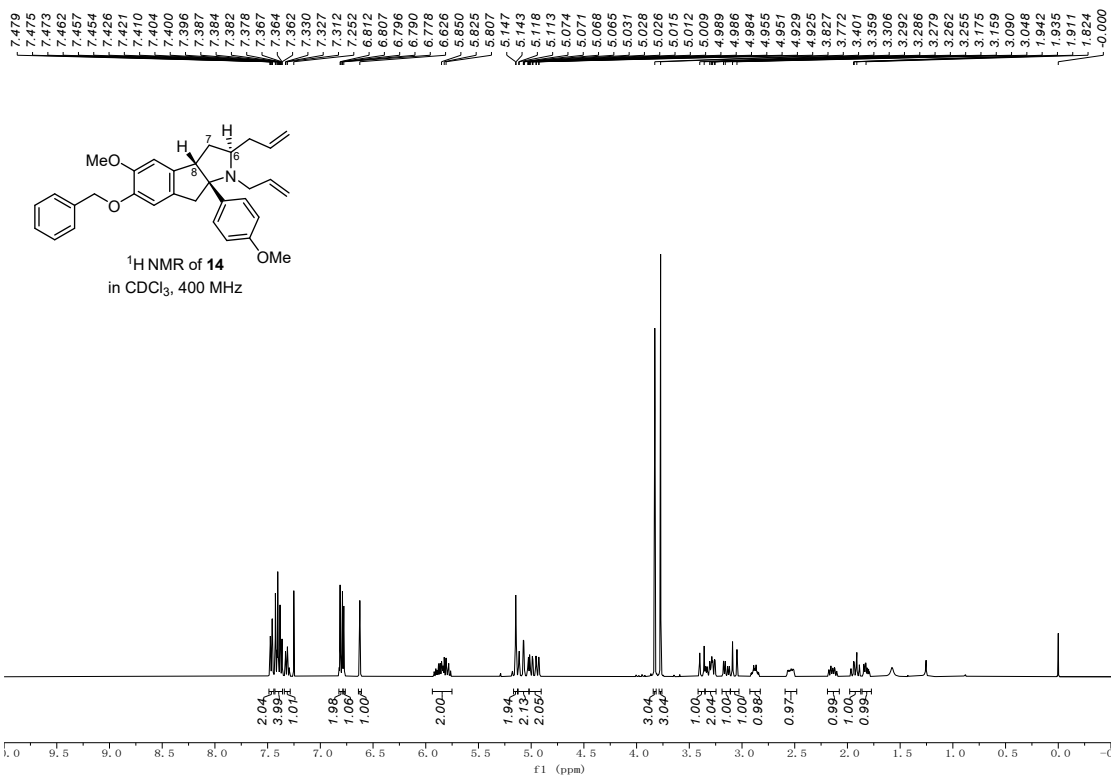




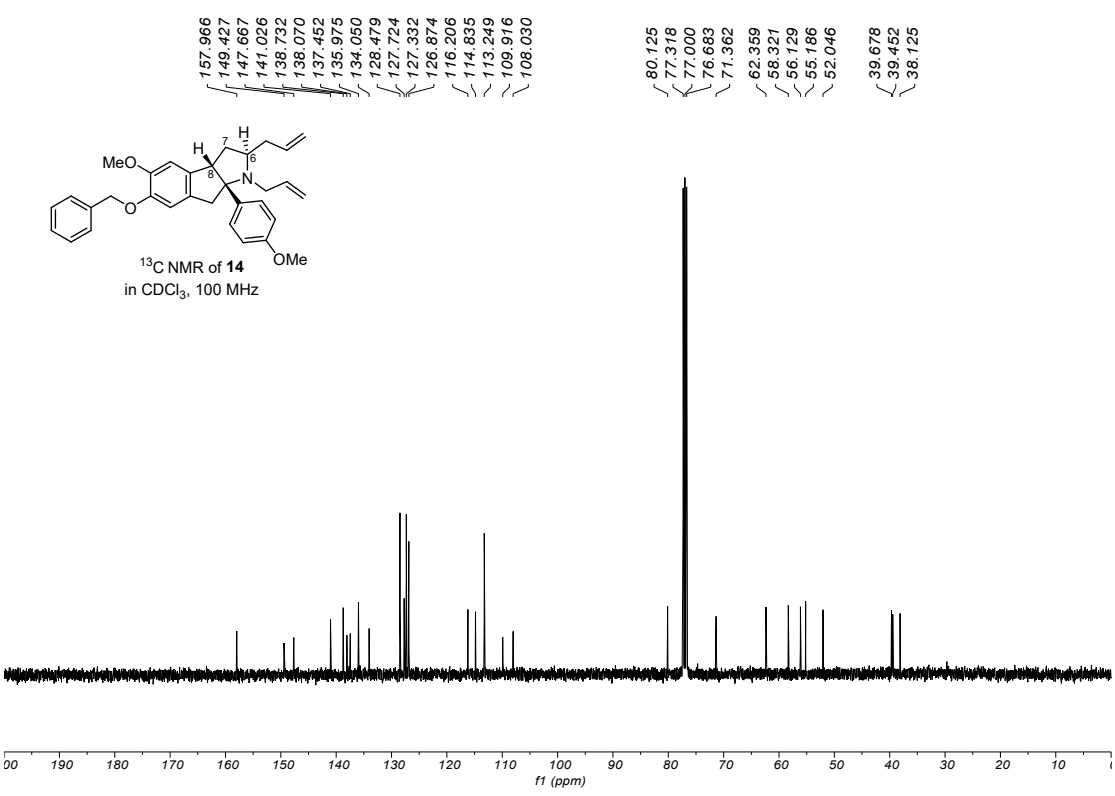
^{1}H NMR of **21**
in $CDCl_3$, 400 MHz



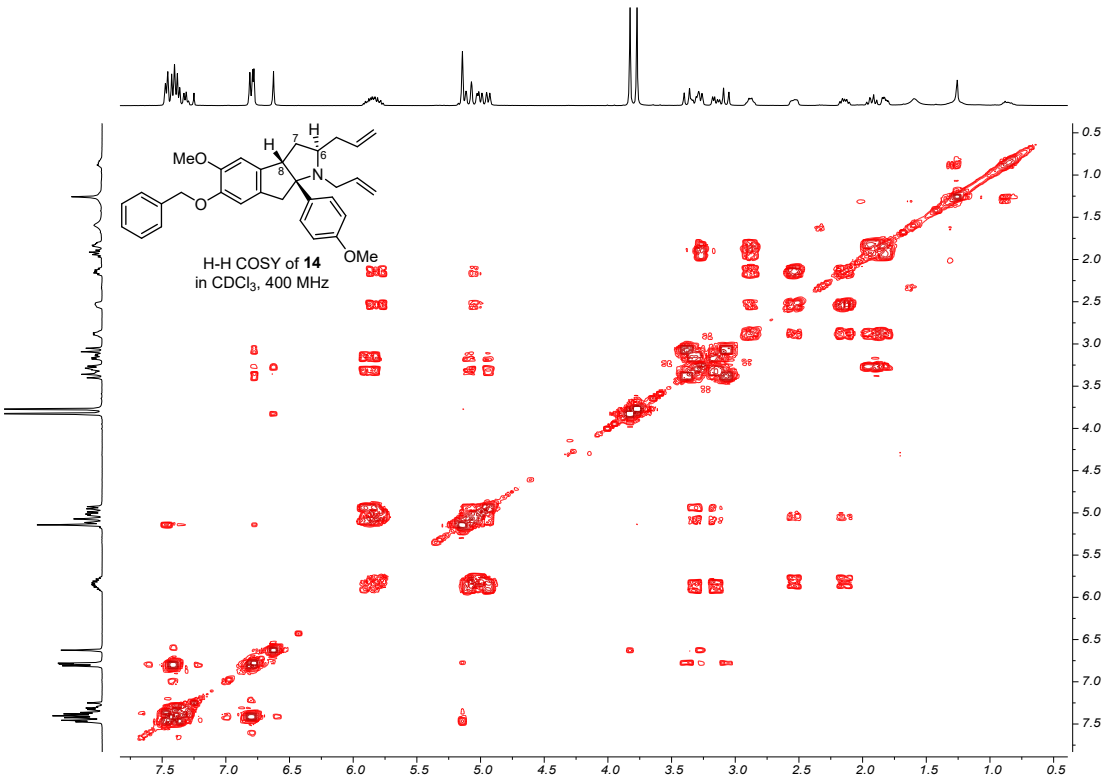
^{13}C NMR of **21**
in $CDCl_3$, 100 MHz

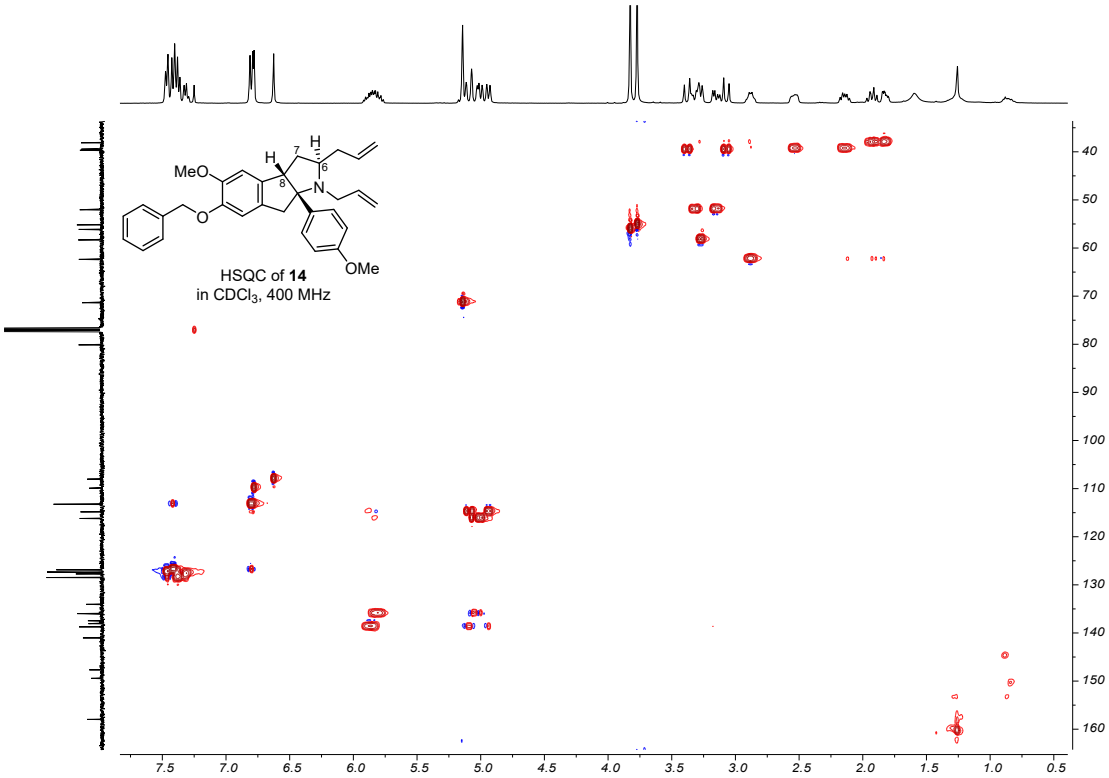


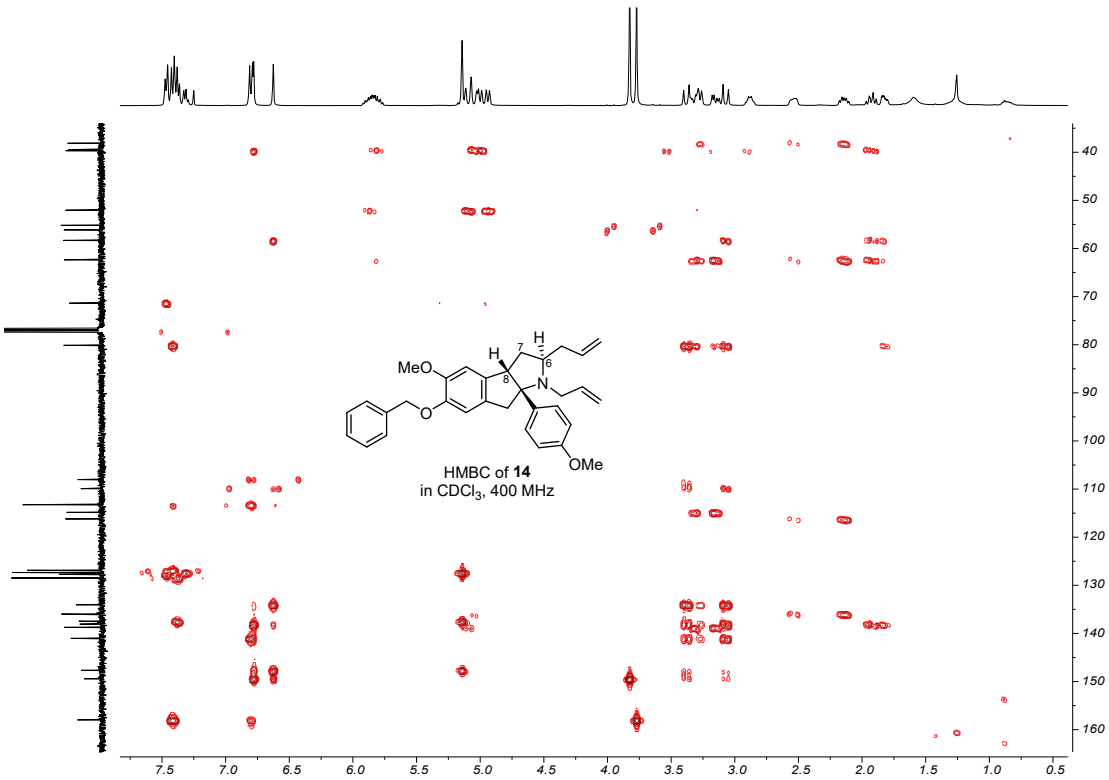
^{1}H NMR of **14**
in $CDCl_3$, 400 MHz



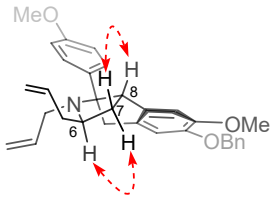
^{13}C NMR of **14**
in $CDCl_3$, 100 MHz


MeO
O
H
H
N
OMe
H-H COSY of 14
in CDCl3, 400 MHz

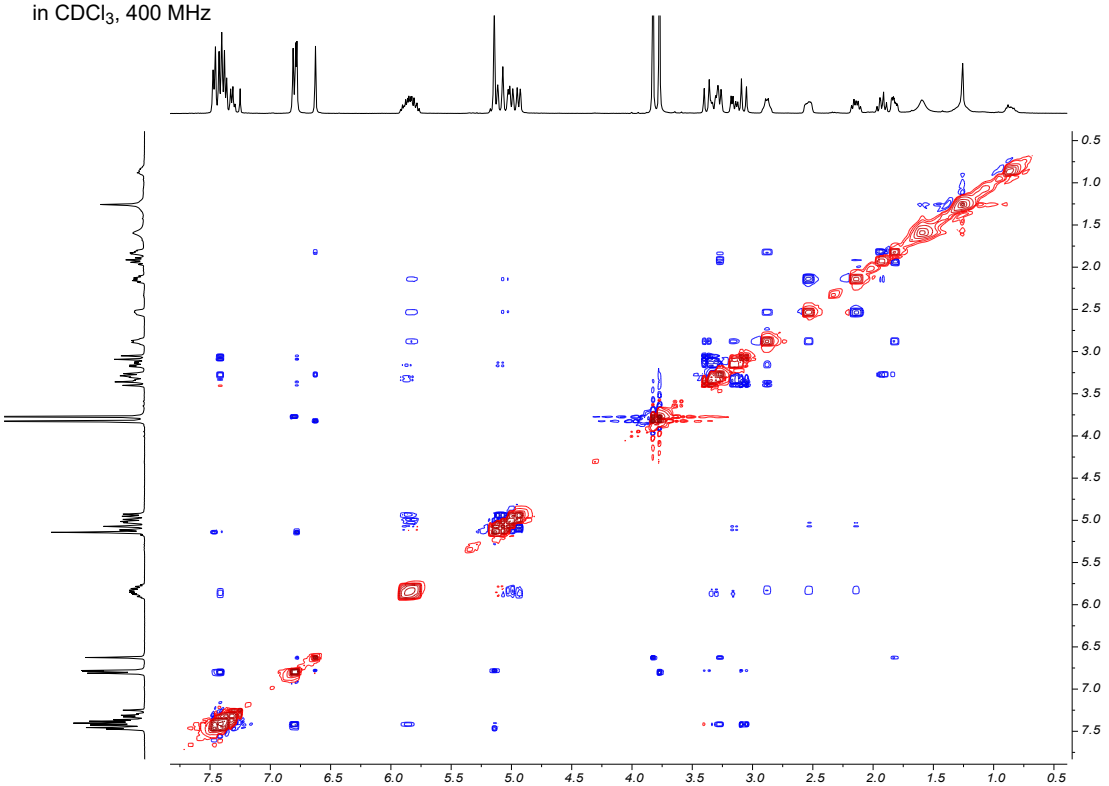

MeO
O
H
H
N
OMe
HSQC of 14
in CDCl3, 400 MHz

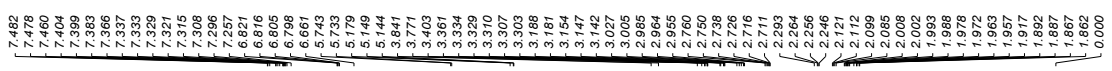


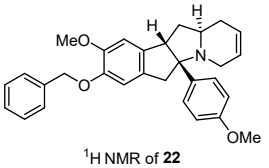
HMBC of **14**
in $CDCl_3$, 400 MHz



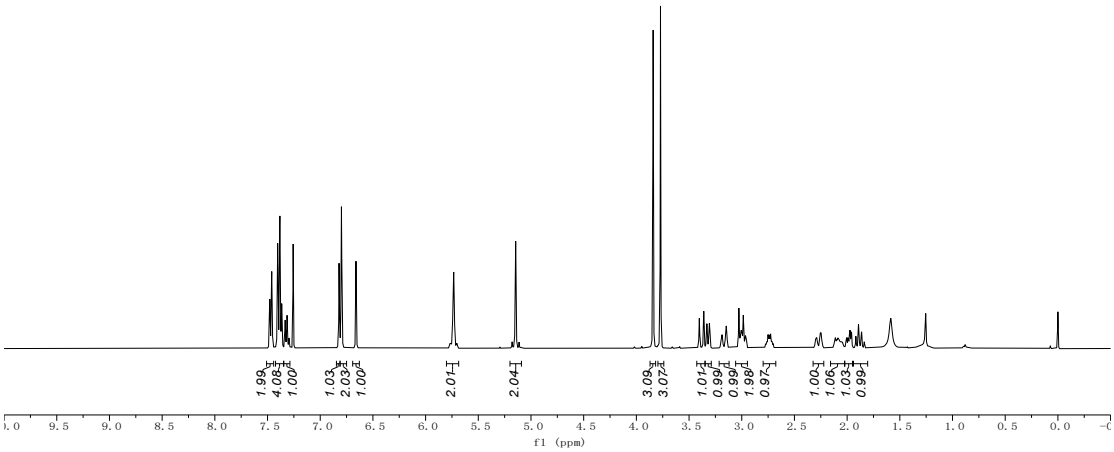
NOESY of **14**
in $CDCl_3$, 400 MHz

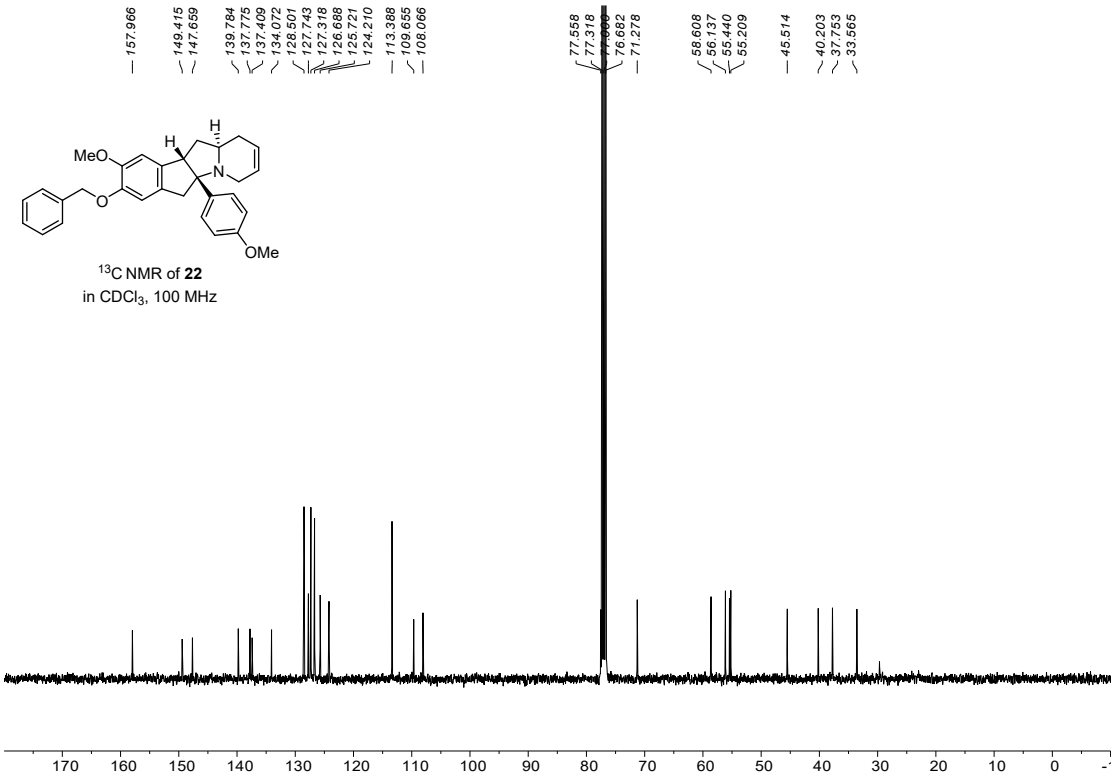




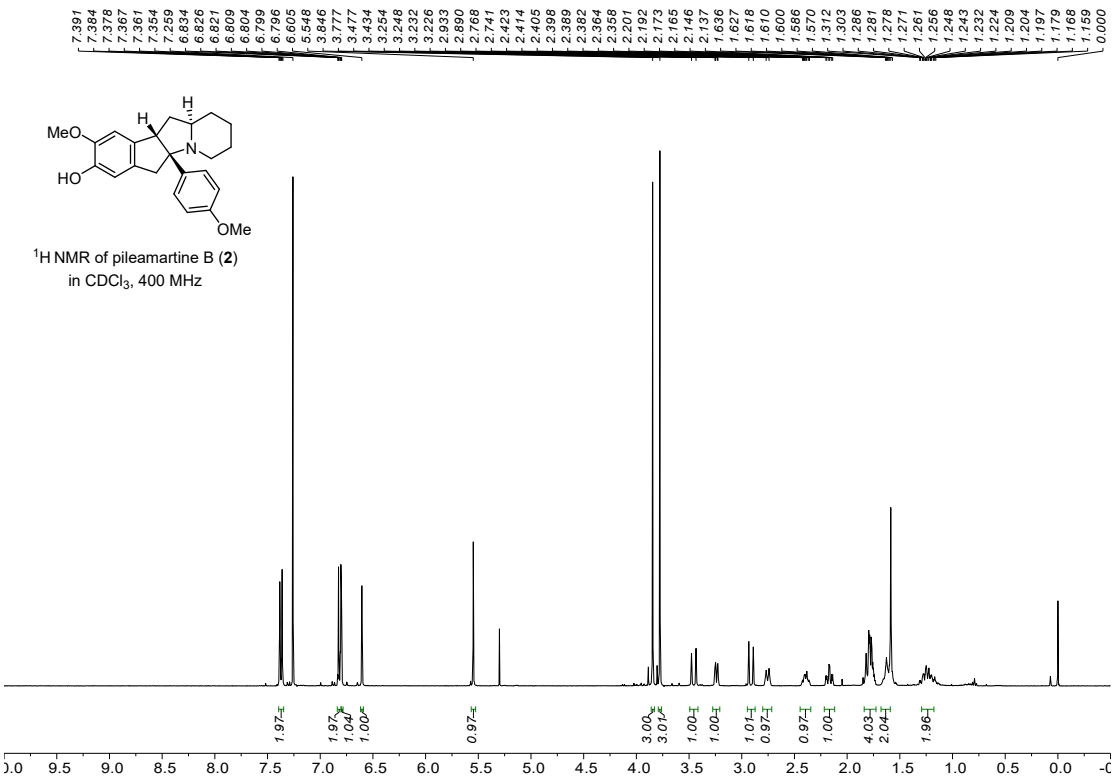


^{1}H NMR of **22**
in $CDCl_3$, 400 MHz

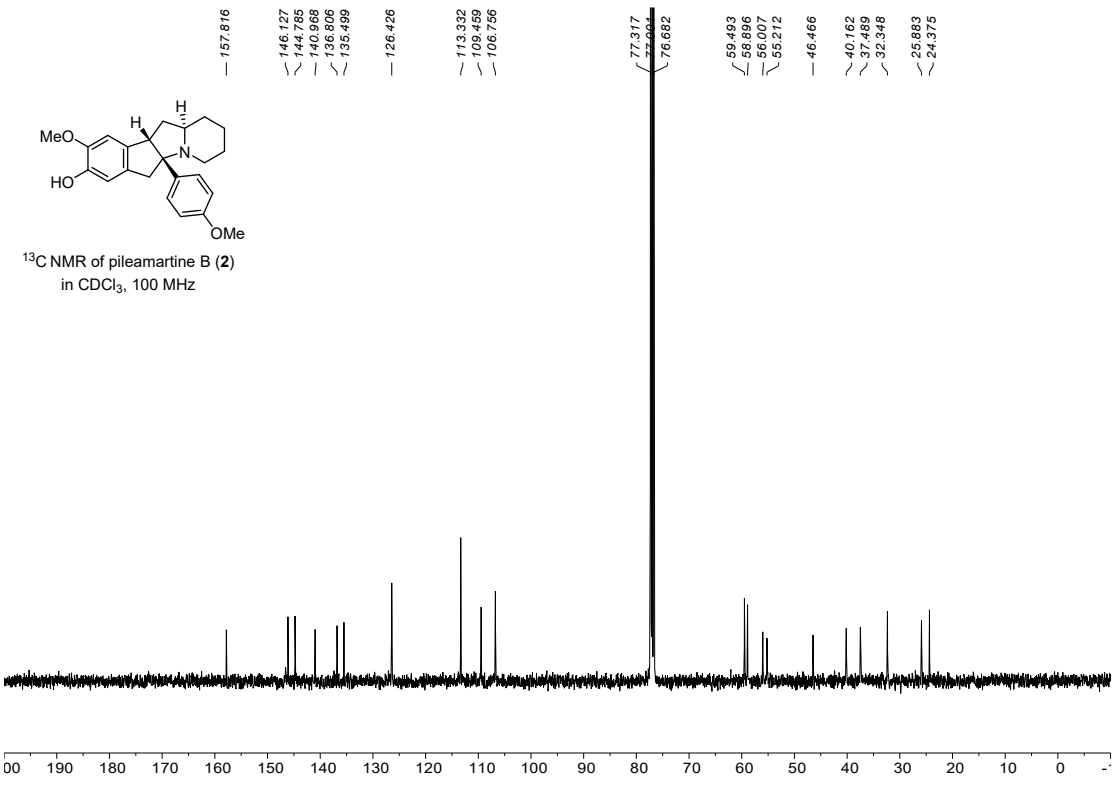




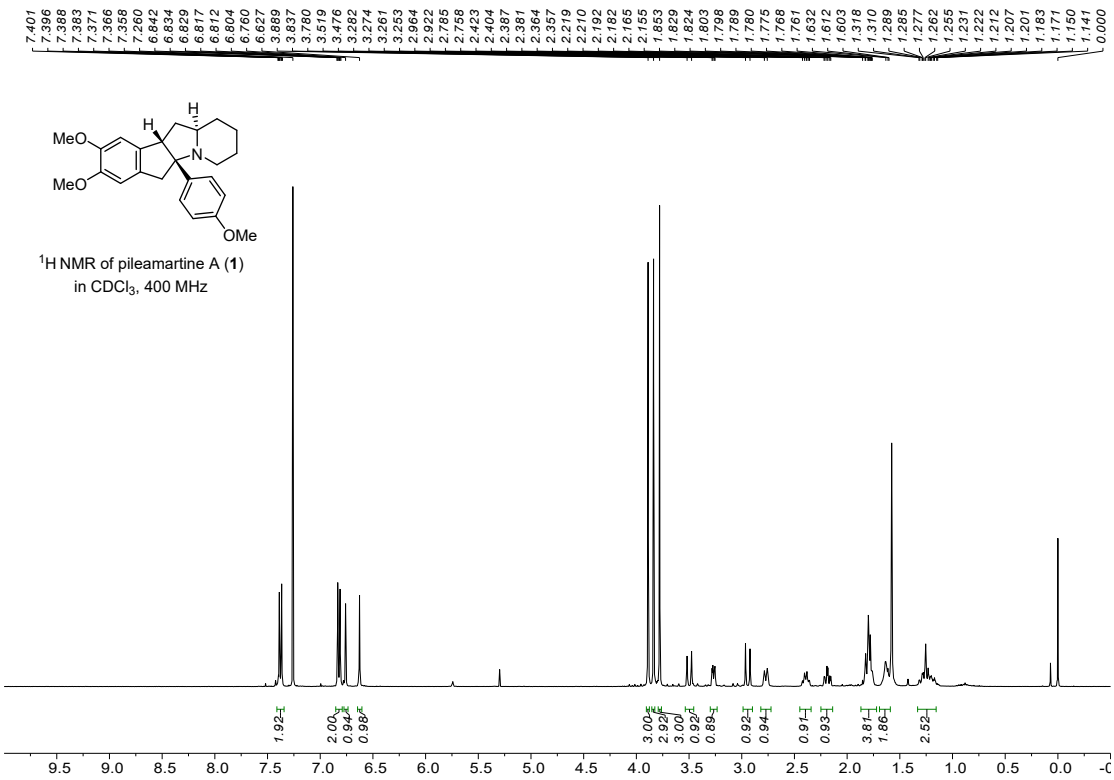
^{13}C NMR of **22**
in $CDCl_3$, 100 MHz



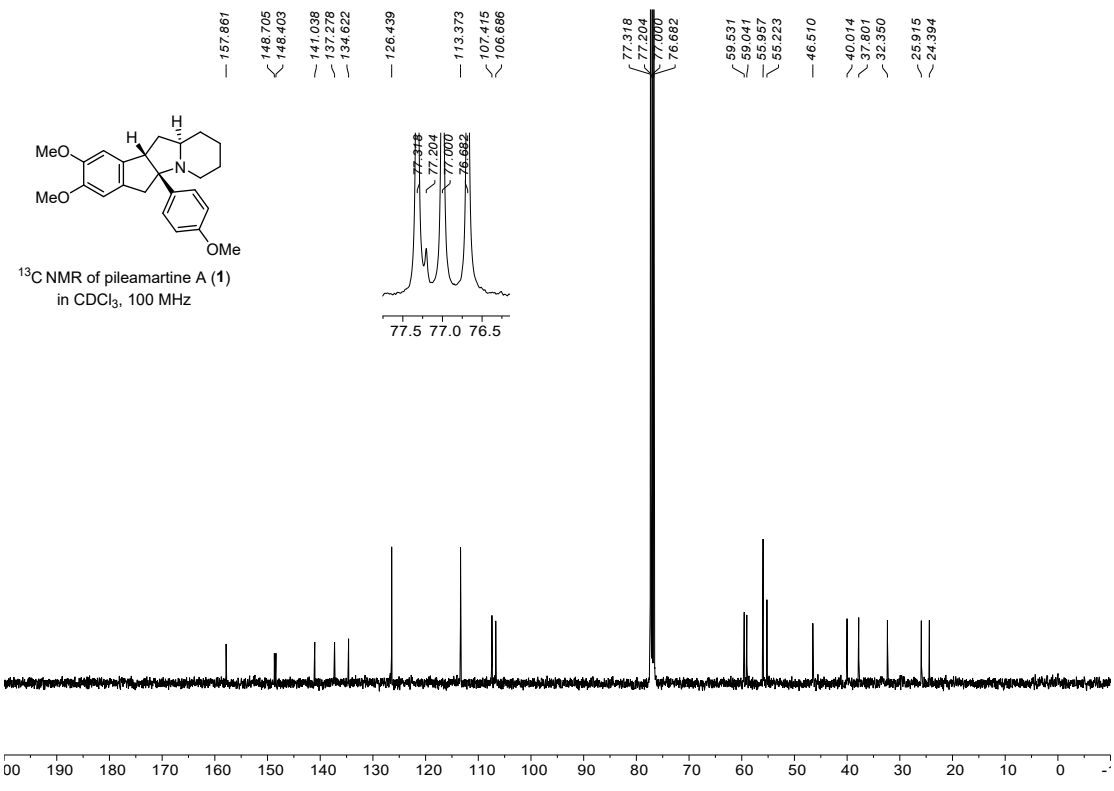
^{1}H NMR of pileamartine B (**2**)
in $CDCl_3$, 400 MHz



^{13}C NMR of pileamartine B (**2**)
in $CDCl_3$, 100 MHz

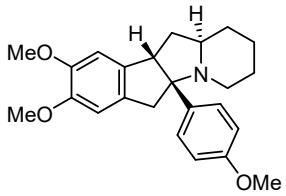


^{1}H NMR of pileamartine A (**1**)
in $CDCl_3$, 400 MHz



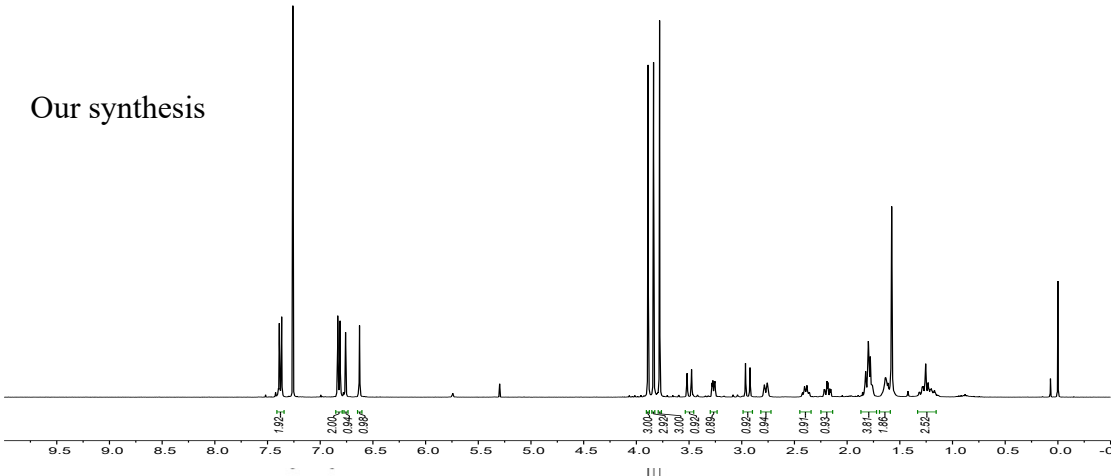
^{13}C NMR of pileamartine A (**1**)
in $CDCl_3$, 100 MHz

Part 3. Comparison of the Spectroscopic Data of Authentic and Synthetic pileamartines

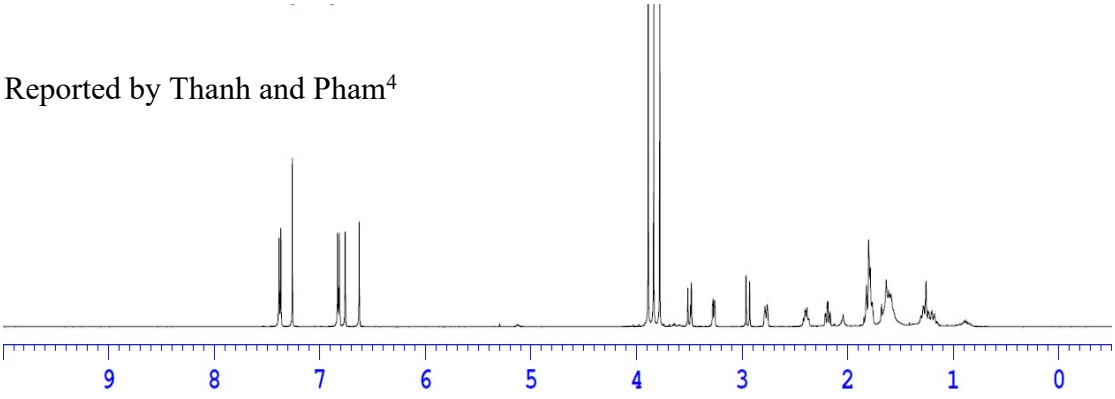


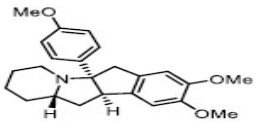
^{1}H NMR of pileamartine A (**1**)

Our synthesis

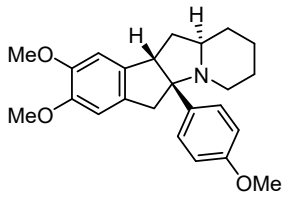


Reported by Thanh and Pham[4]



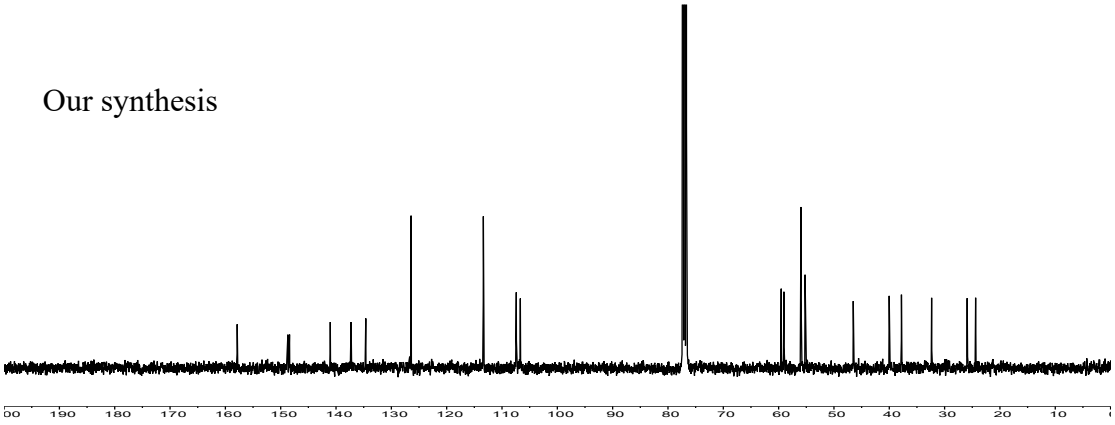


Reported by Bower[5]

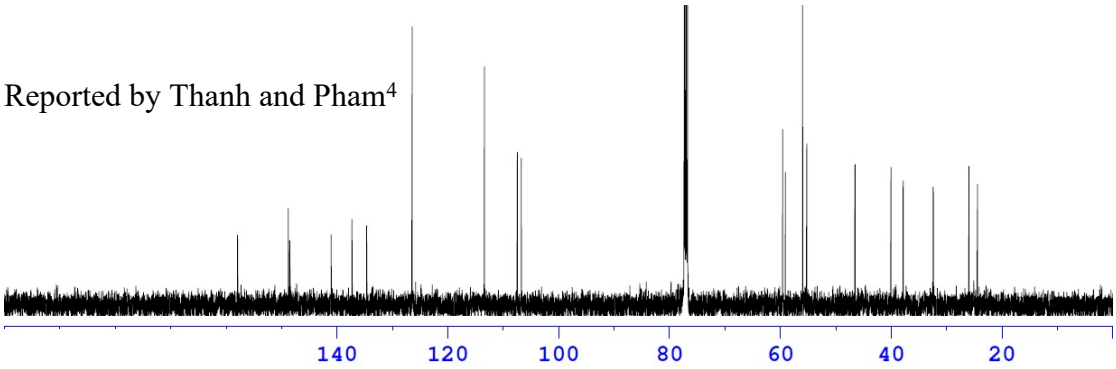


^{13}C NMR of pileamartine A (**1**)

Our synthesis



Reported by Thanh and Pham[4]



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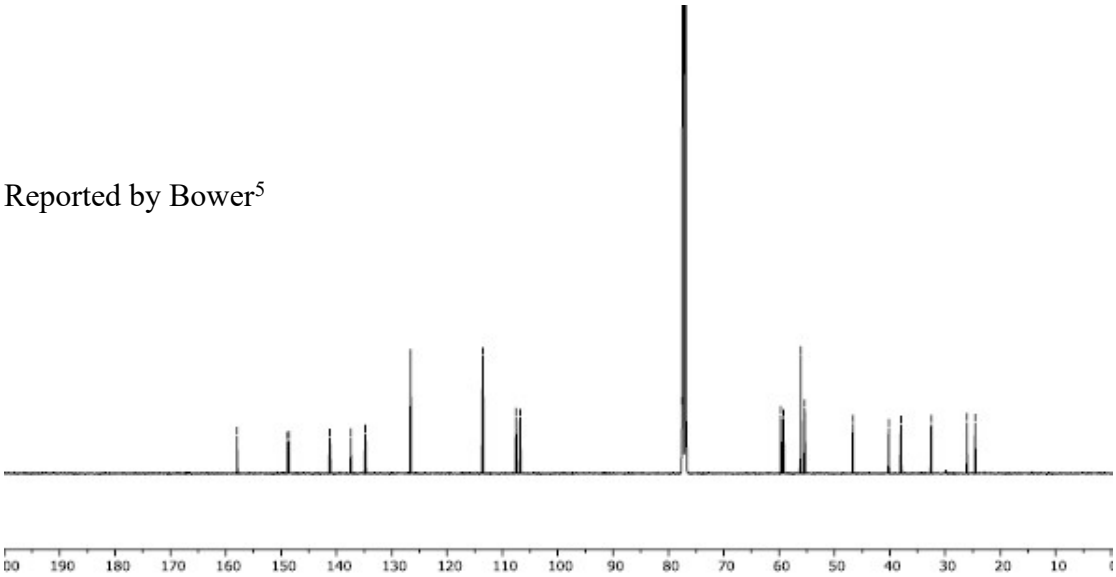
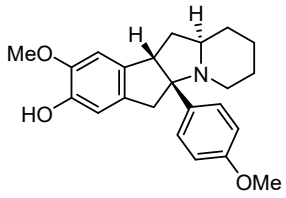
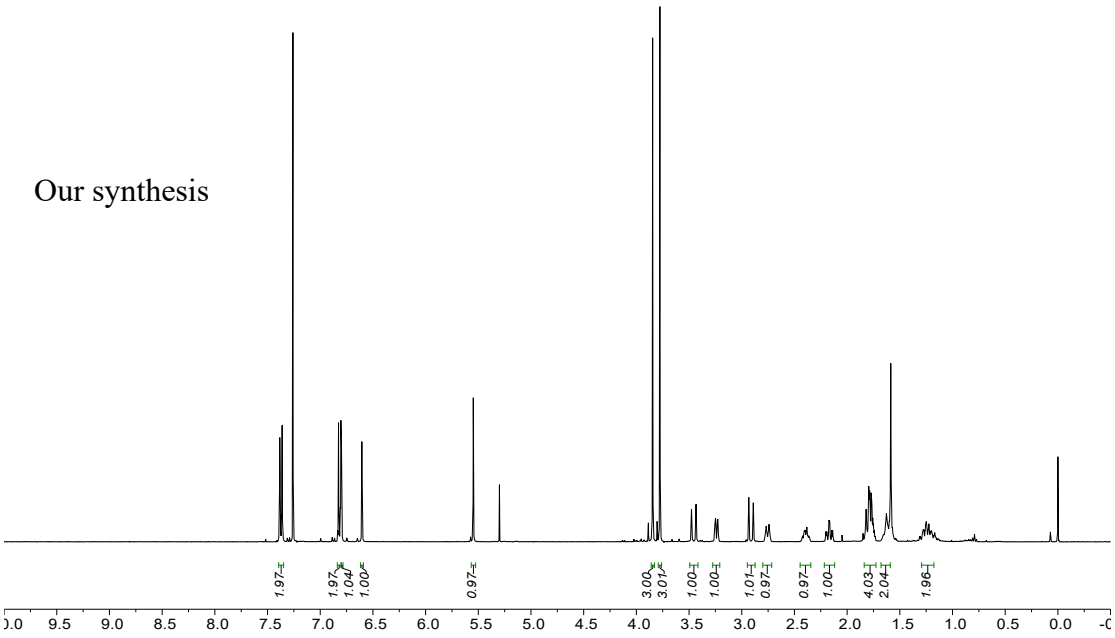
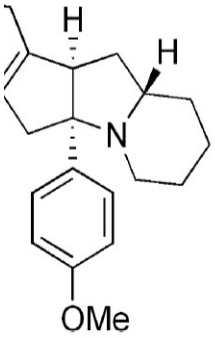




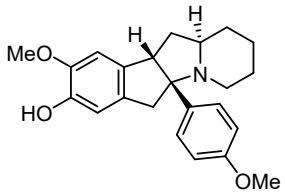
^{1}H NMR of pileamartine B (**2**)

Our synthesis



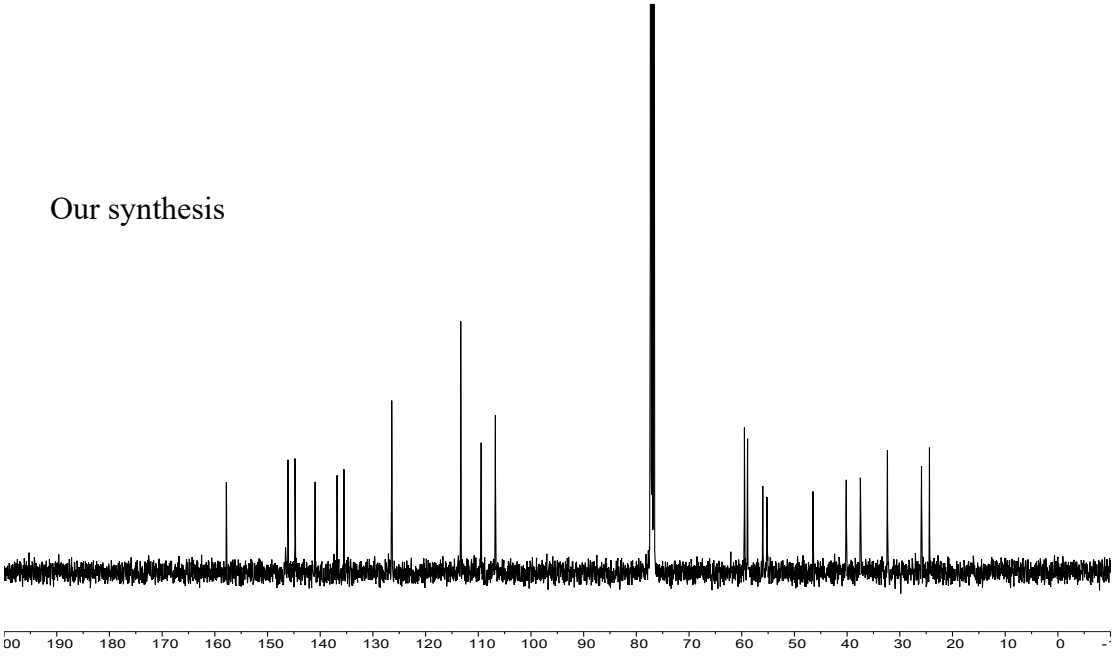


Reported by
Thanh and Pham[4]



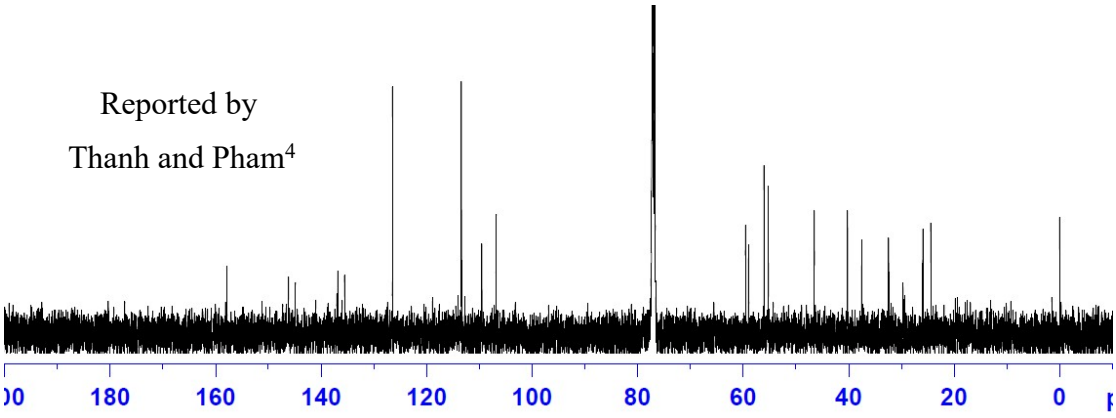
^{13}C NMR of pileamartine B (**2**)

Our synthesis



Reported by

Thanh and Pham[4]



Part 4. References

1. (a) A. G. Wenzel and E. N. Jacobsen, Asymmetric catalytic Mannich reactions catalyzed by urea derivatives: enantioselective synthesis of beta-aryl-beta-amino acids, *J. Am. Chem. Soc.*, 2002, **124**, 12964-12965; (b) C. Rampalakos and W. D. Wulff, A Novel Bis-Thiourea Organocatalyst for the Asymmetric Aza-Henry Reaction, *Adv. Synth. Catal.*, 2008, **350**, 1785-1790.
2. G. Satyanarayana, H. Madhurima and J. Krishna, Concise Three-Step Strategy for the Synthesis of 2-Benzoxepin-3(1H)-ones, *Synthesis*, 2015, **47**, 1245-1254.
3. J. Rehbein, S. M. Ruser and J. Phan, NHC-catalysed benzoin condensation - is it all down to the Breslow intermediate?, *Chem. Sci.*, 2015, **6**, 6013-6018.
4. A. D. T. Thuy, V. T. T. Thanh, H. D. T. Mai, H. T. Le, M. Litaudon, V. M. Chau and V. C. Pham, Pileamartines A and B: Alkaloids from Pilea aff. martinii with a new carbon skeleton, *Tetrahedron Lett.*, 2018, **59**, 1909-1912.
5. B. T. Jones, J. Garcia-Carceles, L. Caiger, I. R. Hazelden, R. J. Lewis, T. Langer and J. F. Bower, Complex Polyheterocycles and the Stereochemical Reassignment of Pileamartine A via Aza-Heck Triggered Aryl C-H Functionalization Cascades, *J. Am. Chem. Soc.*, 2021, **143**, 15593-15598.