Supporting Information

TOTAL SYNTHESIS OF (–)-ZEPHYRANTHINE

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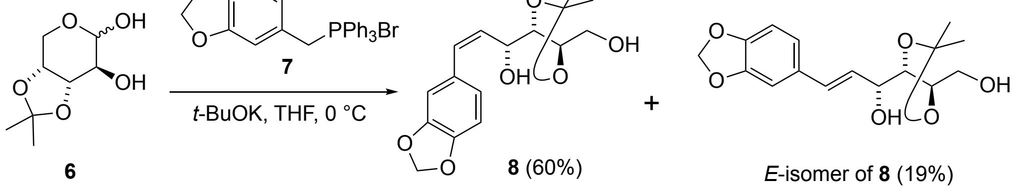
Experimental Procedures

General Details. Reactions were performed in oven-dried glassware fitted with rubber septa under an argon atmosphere. Toluene, *o*-xylene, *t*-BuPh and DMSO were distilled from CaH_2. Acetone, and MeOH were distilled from $CaSO_4$. Toluene, *o*-xylene, *t*-BuPh, DMSO, acetone, MeOH, CH_2Cl_2 and $(CH_2Cl)_2$ were dried over activated 3Å molecular sieves. THF (dehydrated, stabilizer free) was purchased from KANTO CHEMICAL CO., INC. Commercial reagents were used without further purification. Thin-layer chromatography was performed on Merck 60 F_{254} precoated silica gel plates, which were visualized by exposure to UV (254 nm) or stained by submersion in *p*-anisaldehyde solution or ethanolic phosphomolybdic acid solution followed by heating on a hot plate. Flash column chromatography was performed on silica gel (Silica Gel 60 N; 63–210 or 40–50 mesh, KANTO CHEMICAL CO., INC.). Preparative layer chromatography was performed on Merck PLC silica gel 60 F_{254}. ^{1}H NMR spectra were recorded at 500 MHz with JEOL ECA-500 spectrometer or 400 MHz with JEOL ECS-400 spectrometer. ^{13}C NMR spectra were recorded at 125 MHz with JEOL ECA-500 spectrometer. Chemical shifts are reported in ppm with reference to solvent signals [^{1}H NMR: $CDCl_3$ (7.26); ^{13}C NMR: $CDCl_3$ (77.16)]. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. MPLC (medium pressure liquid chromatography) was performed on Yamazen, YFLC AI-580. Infrared spectra were recorded using BRUKER ALPHA FT-IR spectrometer. Mass spectra were measured with Waters, LCT Premier XE (ESI-TOF). Optical rotations were measured with a JASCO P-2100 polarimeter. Melting points were measured with a Yanaco MODEL MP-S3.

Preparation of Alkene 8 and *E*-isomer of 8



Potassium *t*-butoxide (85%, 7.05 g, 53.4 mmol) was added to a mixture of phosphonium salt **7**[1] (28.4 g, 59.5 mmol) and THF (140 mL) at 50 °C. The mixture was stirred for 10 min at 50 °C. The resulting mixture was cooled to 0 °C. After stirring for 15 min at 0 °C, lactol **6**[2] (2.75 g, 14.5 mmol) was added to the mixture of the ylide. After stirring for 20 h at 0 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl (70 mL) and H_2O (70 mL), and extracted with EtOAc (5x 150 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc 1:1) and MPLC (Yamazen Ultra Pack Column D, 50×300 mm, EtOAc/hexane 40:60 to 60:40, 45 mL/min, alkene **8**: T_R = 64.0 min, ***E*-isomer of 8**: T_R = 80 min) to give alkene **8** (2.68 g, 60%) and its *E*-isomer (864 mg, 19%). **8**: a colorless oil; $[\alpha]^{28}_D$ +153.2 (*c* 1.01, $CHCl_3$); IR (film) 3404, 2985, 2925, 1489, 1443, 1240, 1039 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (d, *J* = 1.5 Hz, 1H), 6.86 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.60 (d, *J* = 11.5 Hz, 1H), 5.97 (s, 2H), 5.63 (dd,

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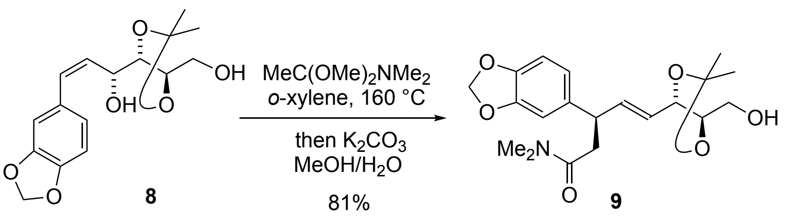
[1] L. W. Rotherham and J. E. Semple, *J. Org. Chem.*, 1998, **63**, 6667.

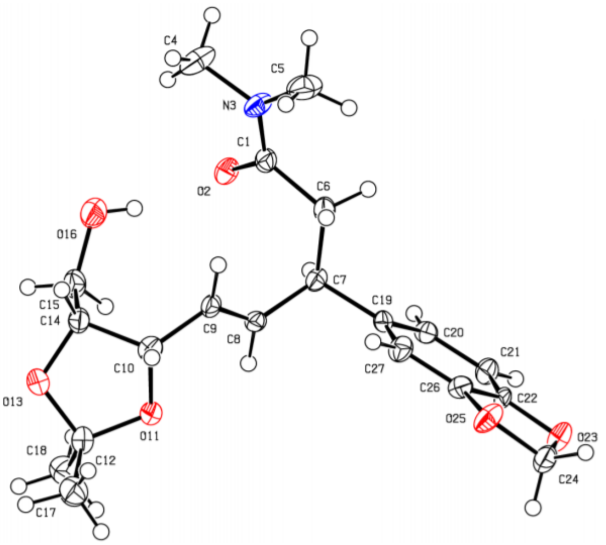
[2] J. Gelas and D. Horton, *Carbohydr. Res.*, 1975, **45**, 181.

J = 11.5, 9.5 Hz, 1H), 4.55 (ddd, *J* = 9.5, 5.5, 4.6 Hz, 1H), 4.21 (ddd, *J* = 6.3, 6.3, 4.3 Hz, 1H), 4.15 (dd, *J* = 6.3, 5.5 Hz, 1H), 3.62–3.52 (m, 2H), 2.86 (brd, 1H), 2.39 (brt, 1H), 1.51 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9 (C), 147.4 (C), 134.3 (CH), 130.1 (C), 127.7 (CH), 123.0 (CH), 109.1 (CH), 108.9 (C), 108.5 (CH), 101.3 (CH_2), 80.0 (CH), 77.4 (CH), 65.8 (CH), 61.2 (CH_2), 27.6 (CH_3), 25.3 (CH_3); HRMS (ESI), calcd for $C_{16}H_{20}O_6Na^+$ $(M+Na)^+$ 331.1158, found 331.1152. ***E*-isomer of 8**: white crystals; mp 102.0–103.0 °C; $[\alpha]^{26}_{D}$ +8.2 (*c* 1.00, $CHCl_3$); IR (film) 3403, 2985, 2895, 1490, 1446, 1251, 1038 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, *J* = 1.7 Hz, 1H), 6.82 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.62 (d, *J* = 15.8 Hz, 1H), 6.08 (dd, *J* = 15.8, 6.9 Hz, 1H), 5.95 (s, 2H), 4.40 (ddd, *J* = 6.9, 5.2, 4.9 Hz, 1H), 4.27 (ddd, *J* = 6.6, 5.5, 4.9 Hz, 1H), 4.20 (dd, *J* = 6.6, 4.9 Hz, 1H), 3.82 (dd, *J* = 5.5, 4.9 Hz, 2H), 2.77 (brs, 1H), 2.41 (brt, 1H), 1.54 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.2 (C), 147.7 (C), 132.7 (CH), 130.8 (C), 126.0 (CH), 121.7 (CH), 108.7 (C), 108.4 (CH), 105.9 (CH), 101.3 (CH_2), 79.7 (CH), 77.4 (CH), 70.6 (CH), 61.3 (CH_2), 27.5 (CH_3), 25.2 (CH_3); HRMS (ESI), calcd for $C_{16}H_{20}O_6Na^+$ $(M+Na)^+$ 331.1158, found 331.1142.

Preparation of 9 by the Claisen Rearrangement of 8



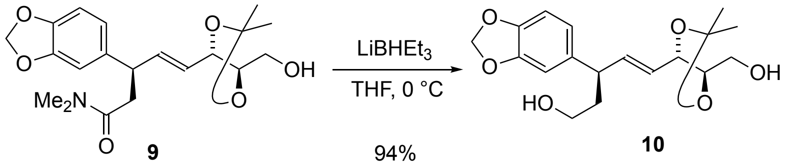
A sealed tube was charged with alkene **8** (2.68 g, 8.69 mmol), *N*,*N*-dimethylacetamide dimethyl acetal (2.5 mL, 17 mmol) and *o*-xylene (29 mL). The solution was heated to 160 °C, and maintained at 160 °C for 23 h. After cooling to room temperature, K_2CO_3 (300 mg, 2.17 mmol), MeOH (15 mL) and H_2O (15 mL) were added to the solution. The resulting mixture was stirred for 1 h, and quenched with saturated aqueous NH_4Cl (15 mL). The mixture was concentrated and extracted with EtOAc (5x 30 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/MeOH 1:0 to 9:1) to give amide **9** (2.67 g, 81%): white crystals; mp 136.0–137.0 °C; $[\alpha]^{27}_{D}$ –46.0 (*c* 1.01, $CHCl_3$); IR (film) 3423, 2985, 2934, 1631, 1488, 1245, 1039 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 1.7 Hz, 1H), 6.67 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.92 (s, 2H), 5.91 (ddd, *J* = 15.5, 7.7, 0.9 Hz, 1H), 5.59 (ddd, *J* = 15.5, 8.0, 0.9 Hz, 1H), 4.65 (ddd, *J* = 8.0, 6.6, 0.9 Hz, 1H), 4.21 (ddd, *J* = 7.8, 6.6, 4.9 Hz, 1H), 3.87 (dddd, *J* = 8.3, 7.7, 6.3, 0.9 Hz, 1H), 3.65 (dd, *J* = 11.5, 7.8 Hz, 1H), 3.53 (dd, *J* = 11.5, 4.9 Hz, 1H), 3.05 (bs, 1H), 2.97 (s, 3H), 2.92 (s, 3H), 2.69 (dd, *J* = 15.8, 8.3 Hz, 1H), 2.65 (dd, *J* = 15.8, 6.3 Hz, 1H), 1.44 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5 (C), 147.9 (C), 146.3 (C), 137.2 (CH), 137.0 (C), 125.7 (CH), 120.4 (CH), 108.5 (CH), 108.5 (C), 108.0 (CH), 101.1 (CH_2), 78.5 (CH), 78.0 (CH), 61.2 (CH_2), 44.3 (CH), 39.5 (CH_2), 37.4 (CH_3), 35.7 (CH_3), 27.9 (CH_3), 25.2 (CH_3); HRMS (ESI), calcd for $C_{20}H_{27}NO_6Na^+$ $(M+Na)^+$ 400.1736, found 400.1731.



Crystal structure of **9**

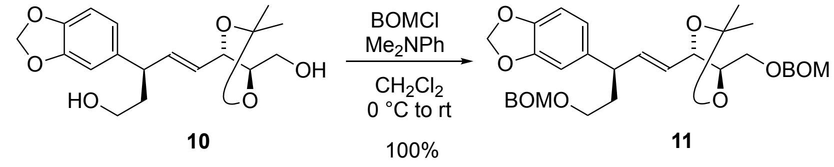
CCDC reference: 1842600. For the detailed results of X-ray crystallographic analysis of **9**, see: T. Oishi, K. Ishii, M. Ishibashi, T. Sato, and N. Chida, *Acta Cryst*. 2018, **E73**, 983.

Preparation of Diol 10



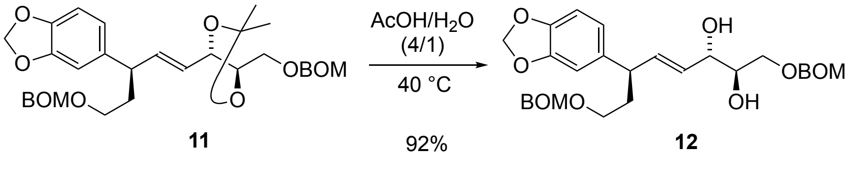
Lithium triethylborohydride (1.0 M in THF, 51 mL, 51 mmol) was added dropwise over 25 min to a solution of amide **9** (2.42 g, 6.39 mmol) and THF (64 mL) at 0 °C. After maintaining for 10 min, MeOH (32 mL) was added dropwise over 15 min to the solution. The resulting solution was maintained for 15 min, and quenched with saturated aqueous NH_4Cl (32 mL). The mixture was concentrated and extracted with EtOAc (3x 30 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 3:1) to give diol **10** (2.03 g, 94%): a colorless oil; $[\alpha]^{22}_{D}$ –16.6 (*c* 0.95, $CHCl_3$); IR (film) 3397, 2934, 2882, 1487, 1244, 1039 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 1.7 Hz, 1H), 6.64 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.92 (s, 2H), 5.91 (ddd, *J* = 15.5, 7.7, 0.9 Hz, 1H), 5.56 (ddd, *J* = 15.5, 8.0, 1.2 Hz, 1H), 4.64 (ddd, *J* = 8.0, 6.6, 0.9 Hz, 1H), 4.21 (ddd, *J* = 6.6, 6.6, 4.9 Hz, 1H), 3.65–3.54 (m, 4H), 3.47 (dtd, *J* = 7.7, 7.5, 1.2 Hz, 1H), 1.98 (brs, 1H), 1.92 (dt, *J* = 7.5, 6.3 Hz, 2H), 1.61 (brs, 1H), 1.48 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9 (C), 146.1 (C), 138.8 (CH), 137.3 (C), 124.9 (CH), 120.5 (CH), 108.7 (C), 108.4 (CH), 107.9 (CH), 101.0 (CH_2), 78.5 (CH), 78.1 (CH), 61.9 (CH_2), 60.5 (CH_2), 44.8 (CH), 38.1 (CH_2), 27.9 (CH_3), 25.3 (CH_3); HRMS (ESI), calcd for $C_{18}H_{24}O_6Na^+$ $(M+Na)^+$ 359.1471, found 359.1461.

Preparation of Di-*O*-BOM Ether 11



Benzyl chloromethyl ether (BOMCl) (6.1 mL, 45 mmol) was added to a solution of diol **10** (2.50 g, 7.43 mmol), *N*,*N*-dimethyl aniline (9.0 mL, 67 mmol) and CH_2Cl_2 (50 mL) at 0 °C. This solution was allowed to warm to room temperature, maintained for 17 h at room temperature, quenched with saturated aqueous NH_4Cl (32 mL), and extracted with $CHCl_3$ (4x 25 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:5) to give BOM ether **11** (4.30 g, 100%): a colorless oil; $[\alpha]^{22}_D$ –3.5 (*c* 0.99, $CHCl_3$); IR (film) 2934, 2879, 1487, 1245, 1041, 737, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.27 (m, 10H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.61 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.92–5.87 (m, 1H), 5.90 (d, *J* = 1.5 Hz, 1H), 5.89 (d, *J* = 1.5 Hz, 1H), 5.43 (ddd, *J* = 15.5, 7.7, 1.2 Hz, 1H), 4.75 (s, 2H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.68 (d, *J* = 6.6 Hz, 1H), 4.61 (d, *J* = 11.7 Hz, 1H), 4.59 (dd, *J* = 7.7, 6.9 Hz, 1H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.54 (s, 2H), 4.30 (td, *J* = 6.9, 5.2 Hz, 1H), 3.56–3.40 (m, 5H), 2.00 (ddt, *J* = 13.5, 6.6, 6.6 Hz, 1H), 1.90 (ddt, *J* = 13.5, 8.6, 6.0 Hz, 1H), 1.48 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9 (C), 146.2 (C), 138.6 (CH), 137.97 (C), 137.96 (C), 136.9 (C), 128.55 (CH), 128.53 (CH), 128.00 (CH), 127.98 (CH), 127.84 (CH), 127.80 (CH), 124.7 (CH), 120.9 (CH), 109.0 (C), 108.4 (CH), 108.1 (CH), 101.0 (CH_2), 95.1 (CH_2), 94.8 (CH_2), 78.1 (CH), 77.2–77.1 (CH), 69.6 (CH_2), 69.4 (CH_2), 67.6 (CH_2), 65.7 (CH_2), 44.5 (CH), 35.4 (CH_2), 28.0 (CH_3), 25.4 (CH_3); HRMS (ESI), calcd for $C_{34}H_{40}O_8K^+$ $(M+K)^+$ 615.2360, found 615.2361.

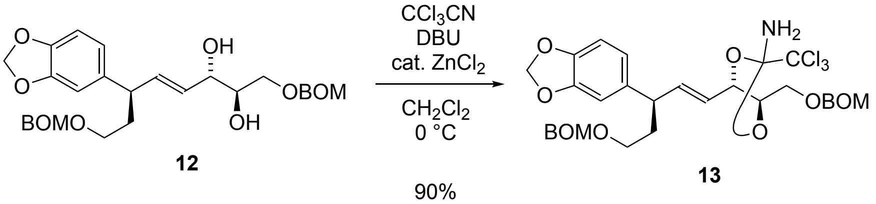
Preparation of Diol 12



A flask was charged with BOM ether **11** (4.28 g, 7.42 mmol) and $AcOH/H_2O$ (4:1, 74 mL). The solution was heated at 40 °C for 12 h. The resulting solution was cooled to room temperature, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 3:1) to give allylic 1,2-diol **12** (3.68 g, 92%): a colorless oil; $[\alpha]^{28}_D$ –9.3 (*c* 1.00, $CHCl_3$); IR (film) 3439, 2933, 2882, 1486, 1244, 1112, 1039, 739, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.26 (m, 10H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 1.7 Hz, 1H), 6.63 (dd, *J* = 8.0 1.7 Hz, 1H), 5.90 (d, *J* = 1.4 Hz, 1H), 5.88 (d, *J* = 1.4 Hz, 1H), 5.87 (ddd, *J* = 15.5, 7.5, 1.2 Hz, 1H), 5.54 (ddd, *J* = 15.5, 6.6, 1.2 Hz, 1H), 4.75 (s, 2H), 4.72 (d, *J* = 6.6 Hz, 1H), 4.69 (d, *J* = 6.6 Hz, 1H), 4.58 (s, 2H), 4.56 (s, 2H), 4.19 (ddd, *J* = 6.6, 5.2, 5.2 Hz, 1H), 3.74–3.63 (m, 3H), 3.56–3.45 (m, 2H), 3.44 (ddd, *J* = 7.8, 7.5, 7.2 Hz, 1H), 2.77 (brd, 1H), 2.28 (brd, 1H), 1.98 (ddt, *J* = 13.8, 7.2, 6.6 Hz, 1H), 1.91 (ddt, *J* = 13.8, 7.8, 6.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9 (C), 146.1 (C), 137.9 (C), 137.6 (C), 137.3 (C), 137.1 (CH), 128.6 (CH), 128.5 (CH), 128.1 (CH), 128.0 (CH), 127.97 (CH), 127.95

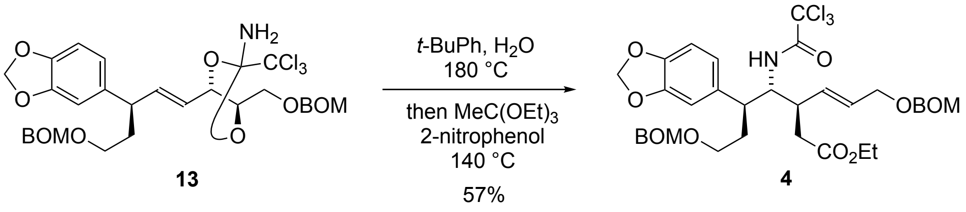
(CH), 127.8 (CH), 120.7 (CH), 108.4 (CH), 108.0 (CH), 101.0 (CH_2), 95.3 (CH_2), 94.8 (CH_2), 73.7 (CH), 72.8 (CH), 69.8 (CH_2), 69.7 (CH_2), 69.4 (CH_2), 65.8 (CH_2), 44.8 (CH), 35.6 (CH_2); HRMS (ESI), calcd for $C_{31}H_{36}O_8Na^+$ $(M+Na)^+$ 559.2308, found 559.2308.

Preparation of Cyclic Orthoamide 13



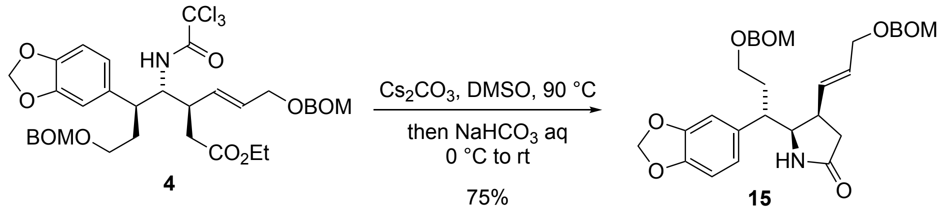
1,8-Diazabicyclo[5.4.0]undec-7-ene (370 μL, 2.5 mmol) was added dropwise to a solution of allylic 1,2-diol **12** (2.64 g, 4.92 mmol), CCl_3CN (640 μL, 6.4 mmol), $ZnCl_2$ (67.1 mg, 492 μmol) and CH_2Cl_2 (98 mL) at 0 °C. The solution was maintained at 0 °C for 64 h, allowed to warm to room temperature, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:6) to give orthoamide **13** (3.00 g, 90%): a colorless oil; $[\alpha]^{22}_{D}$ +8.2 (*c* 0.97, $CHCl_3$); IR (film) 3414, 3335, 2932, 2883, 1486, 1244, 1200, 1109, 1040, 804, 738, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.27 (m, 10H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 1.7 Hz, 1H), 6.61 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.98 (ddd, *J* = 15.5, 7.2, 0.6 Hz, 1H), 5.91 (d, *J* = 1.4 Hz, 1H), 5.89 (d, *J* = 1.4 Hz, 1H), 5.53 (ddd, *J* = 15.5, 8.3, 1.2 Hz, 1H), 5.04 (dd, *J* = 8.3, 7.6 Hz, 1H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.73–4.69 (m, 1H), 4.70 (d, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.54 (s, 2H), 3.75 (dd, *J* = 10.9, 8.3 Hz, 1H), 3.54 (dd, *J* = 10.9, 4.3 Hz, 1H), 3.52–3.41 (m, 3H), 2.52 (s, 2H), 2.01 (dddd, *J* = 13.8, 7.2, 6.6, 6.3 Hz, 1H), 1.89 (ddt, *J* = 13.8, 8.9, 5.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9 (C), 146.3 (C), 140.2 (CH), 137.9 (C), 137.8 (C), 136.4 (C), 128.52 (CH), 128.50 (CH), 128.0 (CH), 127.9 (CH), 127.83 (CH), 127.78 (CH), 122.6 (CH), 120.9 (CH), 114.2 (C), 108.4 (CH), 108.0 (CH), 102.6 (C), 101.0 (CH_2), 94.9 (CH_2), 94.7 (CH_2), 80.2 (CH), 79.3 (CH), 69.6 (CH_2), 69.4 (CH_2), 66.4 (CH_2), 65.6 (CH_2), 44.5 (CH), 35.3 (CH_2); HRMS (ESI), calcd for $C_{33}H_{36}NO_8Cl_3K^+$ $(M+K)^+$ 718.1144, found 718.1149.

Preparation of 4 by the Overman/Claisen Rearrangement of 13



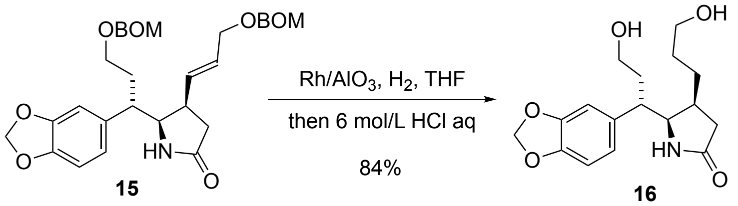
A sealed tube was charged with orthoamide **13** (189 mg, 278 μmol), H_2O (12 μL, 670 μmol) and *t*-BuPh (28 mL). The mixture was heated to 180 ºC, and maintained for 5 d. After cooling to room temperature, $MeC(OEt)_3$ (2.5 mL, 14 mmol) and 2-nitrophenol (58.0 mg, 417 μmol) were added to the same reaction vessel. The mixture was then heated to 140 ºC, and maintained for 8 h. After cooling to room temperature, the mixture was directly purified by silica gel column chromatography (EtOAc/hexane 1:7) and MPLC (Yamazen Ultra Pack Column B, 26×300 mm, EtOAc/hexane 20:80 to 41:59, 20 mL/min, **4**: T_R = 31.5 min) to afford trichloroacetamide **4** (118 mg, 57%): a yellow oil; $[\alpha]^{22}_{D}$ +2.6 (*c* 1.05, $CHCl_3$); IR (film) 3413, 2930, 2881, 1718, 1505, 1488, 1244, 1164, 1111, 1040, 817, 740, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.27 (m, 10H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 1.7 Hz, 1H), 6.59 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.22 (d, *J* = 10.1 Hz, 1H), 5.90 (d, *J* = 1.4 Hz, 1H), 5.87 (d, *J* = 1.4 Hz, 1H), 5.68 (dt, *J* = 15.5, 5.5 Hz, 1H), 5.54 (dddd, *J* = 15.5, 8.6, 1.5, 1.2 Hz, 1H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 6.6 Hz, 1H), 4.62 (d, *J* = 6.6 Hz, 1H), 4.58 (s, 2H), 4.51 (s, 2H), 4.21 (ddd, *J* = 10.1, 8.0, 4.6 Hz, 1H), 4.17–4.12 (m, 2H), 4.06 (dd, *J* = 5.5, 1.2 Hz, 2H), 3.49 (ddd, *J* = 9.5, 6.1, 4.6 Hz, 1H), 3.31 (ddd, *J* = 9.5, 9.2, 5.2 Hz, 1H), 3.07–2.96 (m, 2H), 2.60 (dd, *J* = 15.8, 6.0 Hz, 1H), 2.39 (dd, *J* = 15.8, 8.3 Hz, 1H), 2.18 (dddd, *J* = 14.1, 9.2, 6.1, 4.3 Hz, 1H), 1.85 (dddd, *J* = 14.1, 10.6, 5.2, 4.6 Hz, 1H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6 (C), 161.7 (C), 148.3 (C), 147.0 (C), 137.94 (C), 137.86 (C), 133.2 (C), 131.2 (CH), 129.5 (CH), 128.6 (CH), 128.5 (CH), 128.00 (CH), 127.95 (CH), 127.92 (CH), 127.8 (CH), 121.9 (CH), 108.6 (CH), 108.5 (CH), 101.2 (CH_2), 94.8 (CH_2), 93.7 (CH_2), 92.9 (C), 69.5 (CH_2), 69.4 (CH_2), 67.4 (CH_2), 65.2 (CH_2), 60.8 (CH_2), 57.2 (CH), 44.5 (CH), 40.9 (CH), 37.3 (CH_2), 33.1 (CH_2), 14.4 (CH_3); HRMS (ESI), calcd for $C_{37}H_{42}NO_9Cl_3Na^+$ $(M+Na)^+$ 772.1823, found 772.1815.

Preparation of γ-Lactam 15



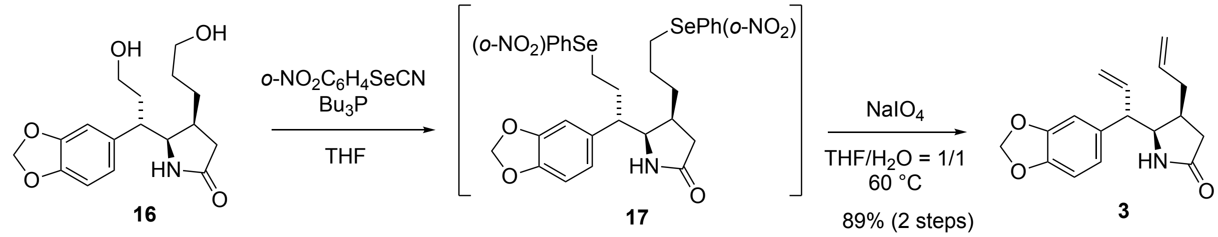
Cesium carbonate (280 mg, 344 μmol) was added to a solution of trichloroacetamide **4** (258 mg, 344 μmol) and DMSO (11 mL). The resulting mixture was heated to 90 ºC, and stirred for 3 h. After cooling to room temperature, the resulting mixture was poured into ice-cold saturated aqueous $NaHCO_3/H_2O$ (1:1, 11 mL). This mixture was stirred for 15 min at 0 °C, and then allowed to warm to room temperature. The mixture was stirred for 12 h at room temperature, and extracted with EtOAc/THF (1:1, 7x 30 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc / hexane 4:1 to 1:0) to give lactam **15** (145 mg, 75%): a colorless oil; $[\alpha]^{22}_{D}$ –52.9 (*c* 1.01, $CHCl_3$); IR (film) 3212, 2927, 2883, 1698, 1501, 1246, 1111, 1039, 743, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.22 (m, 10H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.60 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.95 (d, *J* = 1.4 Hz, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 5.87 (ddt, *J* = 15.5, 9.8, 1.2 Hz, 1H), 5.75 (dt, *J* = 15.5, 5.7 Hz, 1H), 5.01 (s, 1H), 4.78 (d, *J* = 6.6 Hz, 1H), 4.77 (d, *J* = 6.6 Hz, 1H), 4.62 (d, *J* = 6.9 Hz, 1H), 4.61 (s, 2H), 4.57 (d, *J* = 6.9 Hz, 1H), 4.47 (d, *J* = 11.8 Hz, 1H), 4.44 (d, *J* = 11.8 Hz, 1H), 4.15 (dd, *J* = 5.7, 1.2 Hz, 2H), 3.77 (dd, *J* = 10.6, 5.4 Hz, 1H), 3.38 (ddd, *J* = 10.1, 7.5, 3.7 Hz, 1H), 3.25 (ddd, *J* = 10.1, 8.9, 6.3 Hz, 1H), 3.18–3.12 (m, 1H), 2.68 (ddd, *J* = 11.8, 10.6, 3.5 Hz, 1H), 2.65 (dd, *J* = 16.6, 7.7 Hz, 1H), 2.16 (dd, *J* = 16.6, 1.8 Hz, 1H), 2.08–2.01 (m, 1H), 1.64–1.53 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1 (C), 148.5 (C), 147.0 (C), 137.95 (C), 137.92 (C), 134.3 (C), 130.1 (CH), 129.5 (CH), 128.59 (CH), 128.52 (CH), 128.0 (CH), 127.89 (CH), 127.88 (CH), 127.81 (br, CH), 121.7 (CH), 108.8 (CH), 107.9 (br, CH), 101.3 (CH_2), 94.6 (CH_2), 93.9 (CH_2), 69.6 (CH_2), 69.3 (CH_2), 67.5 (CH_2), 65.0 (CH_2), 62.4 (CH), 43.1 (CH), 41.1 (CH), 38.7 (CH_2), 31.4 (CH_2); HRMS (ESI), calcd for $C_{33}H_{37}NO_7Na^+$ $(M+Na)^+$ 582.2468, found 582.2471.

Preparation of Diol 16



Rhodium-Alumina (10 wt%, 14.5 mg) was added to a solution of lactam **15** (145 mg, 259 μmol) and THF (5.2 mL) at room temperature. The flask was purged with hydrogen. The mixture was stirred under hydrogen atmosphere (1 atm) at room temperature for 26 h. Aqueous HCl (6M, 5.2 mL) was then added to the mixture. The resulting mixture was stirred for 11 h, poured into aqueous NaOH (1M, 31 mL), and extracted with EtOAc/THF (1:1, 7x 50 mL). The combined organic extracts were washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/MeOH 1:0 to 4:1) to give diol **16** (69.5 mg, 84%): a colorless oil; $[\alpha]^{26}_{D}$ –37.4 (*c* 1.00, $CHCl_3$); IR (film) 3315, 2934, 2878, 1681, 1488, 1442, 1245, 1037, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.76 (d, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 1.7 Hz, 1H), 6.67 (dd, *J* = 7.7, 1.7 Hz, 1H), 5.96 (d, *J* = 1.7 Hz, 1H), 5.96 (d, *J* = 1.7 Hz, 1H), 5.04 (s, 1H), 3.79 (dd, *J* = 10.6, 5.5 Hz, 1H), 3.71 (dd, *J* = 6.1, 5.7 Hz, 2H), 3.59 (ddd, *J* = 10.3, 6.0, 4.0 Hz, 1H), 3.40 (ddd, *J* = 10.3, 9.5, 5.2 Hz, 1H), 2.89 (ddd, *J* = 11.5, 10.6, 2.9 Hz, 1H), 2.53–2.42 (m, 2H), 2.16 (d, *J* = 14.9 Hz, 1H), 1.93 (dddd, *J* = 14.0, 9.5, 6.0, 2.9 Hz, 1H), 1.85–1.77 (m, 1H), 1.77–1.64 (m, 2H), 1.55–1.46 (m, 1H), 1.45–1.36 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0 (C), 148.5 (C), 147.0 (C), 134.7 (C), 121.9 (CH), 108.8 (CH), 107.9 (CH), 101.3 (CH_2), 62.4 (CH_2), 62.3 (CH), 59.7 (CH_2), 41.9 (CH), 37.5 (CH_2), 36.9 (CH), 35.0 (CH_2), 30.1 (CH_2), 23.4 (CH_2); HRMS (ESI), calcd for $C_{17}H_{24}NO_5^+$ $(M+H)^+$ 322.1654, found 322.1654.

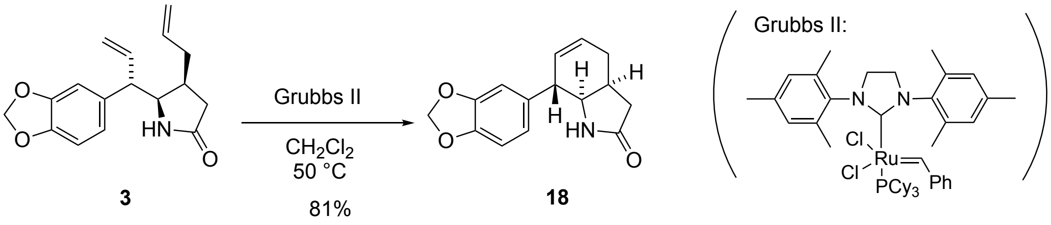
Preparation of Diene 3



Tributylphosphine (490 μL, 2.0 mmol) was added to a solution of diol **16** (31.9 mg, 99.3 μmol), *o*-nitrophenyl selenocyanate (282 mg, 1.24 mmol) and THF (5.0 mL) at room temperature. This solution was maintained for 30 min at room temperature, quenched with brine/H_2O (1:1, 5.0 mL) and extracted with EtOAc (3x 10 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated to give di-selenide **17**, which was used in the next step without further purification.

Sodium periodate (426 mg, 1.99 mmol) was added to a solution of the above selenide **17** and THF/H_2O (1:1, 10 mL) at room temperature. The solution was heated to 60 °C, and maintained at 60 °C for 45 min. After cooling to room temperature, the resulting solution was quenched with 10wt% aqueous sodium thiosulfate (5.0 mL) and extracted with EtOAc (3x 10 mL). The combined organic extracts were washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 3:1) to give diene **3** (25.2 mg, 89% for 2 steps): a brown oil; $[\alpha]^{22}_{D}$ –36.1 (*c* 1.00, $CHCl_3$); IR (film) 3259, 2905, 1697, 1487, 1246, 1038, 919 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 1.7 Hz, 1H), 6.65 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.95 (s, 2H), 5.94 (ddd, *J* = 17.8, 10.9, 7.5 Hz, 1H), 5.70 (dddd, *J* = 16.6, 10.9, 8.6, 5.4 Hz, 1H), 5.21 (ddd, *J* = 10.9, 1.2, 0.9 Hz, 1H), 5.18 (ddd, *J* = 17.8, 1.2, 1.2 Hz, 1H), 5.13–5.08 (m, 2H), 5.01 (brs, 1H), 3.98 (dd, *J* = 10.9, 5.7 Hz, 1H), 3.34 (dd, *J* = 10.9, 7.5 Hz, 1H), 2.56–2.49 (m, 1H), 2.49–2.42 (m, 1H), 2.45 (dd, *J* = 16.3, 7.8 Hz, 1H), 2.24 (dd, *J* = 16.3, 1.4 Hz, 1H), 2.07 (ddd, *J* = 13.8, 11.5, 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4 (C), 148.5 (C), 147.0 (C), 137.3 (CH), 135.7 (CH), 134.7 (C), 121.3 (CH), 117.9 (CH_2), 117.2 (CH_2), 108.9 (CH), 108.1 (CH), 101.3 (CH_2), 60.7 (CH), 49.4 (CH), 36.8 (CH_2), 36.3 (CH), 32.3 (CH_2); HRMS (ESI), calcd for $C_{17}H_{20}NO_3^+$ $(M+H)^+$ 286.1443, found 286.1436.

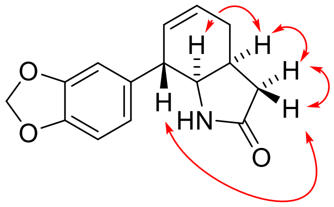
Synthesis of 18 by the RCM reaction of diene 3



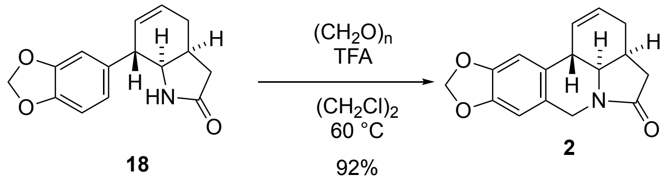
3 **18**

A solution of diene **3** (28.2 mg, 98.8 μmol) in CH_2Cl_2 (9.9 mL) was heated to reflux, and maintained for 1 h at that temperature for deoxygenation. Second-generation Grubbs catalyst (4.2 mg, 4.9 μmol) was then added to the solution at that temperature. The resulting solution was maintaining for 5 h. After cooling to room temperature, the resulting solution was quenched with ethyl vinyl ether (3.0 mL) and extracted with EtOAc (3x 10 mL). The combined organic extracts were washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 3:1) to give olefine **18** (20.5 mg, 81%): white crystals; mp 104.5–105.5 °C; $[\alpha]^{24}_{D}$ –96.1 (*c* 0.96, $CHCl_3$); IR (film) 3205, 2899, 1694, 1486, 1247, 1038 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.65 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.99 (dddd, *J* = 9.8, 5.8, 3.2, 2.9 Hz, 1H), 5.96 (s, 2H), 5.78 (dddd, *J* = 9.8, 2.9, 2.9, 0.6 Hz, 1H), 5.59 (brs, 1H), 3.43 (dd, *J* = 8.1, 8.0 Hz, 1H), 3.06 (dddd, *J* = 8.0, 4.3, 2.9, 2.9 Hz, 1H), 2.69 (ddddd, *J* = 8.9, 8.6, 8.3, 8.1, 6.0 Hz, 1H), 2.62–2.55 (m, 1H), 2.54 (dd, *J* = 16.6, 8.9 Hz, 1H), 2.21 (dd, *J* = 16.6, 8.6 Hz, 1H), 2.04 (ddddd, *J* = 17.2, 6.0, 3.2, 3.2, 2.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3 (C), 148.4 (C), 146.8 (C), 136.7 (C), 130.0 (CH), 128.2 (CH), 121.3 (CH), 108.6 (CH), 108.2 (CH), 101.2 (CH_2), 60.6 (CH), 46.6 (CH), 37.6 (CH_2), 31.7 (CH), 28.4 (CH_2); HRMS (ESI), calcd for $C_{15}H_{16}NO_3^+$ $(M+H)^+$ 258.1130, found 258.1129.

NOESY experiments of 18 (500 MHz, $CDCl_3$)

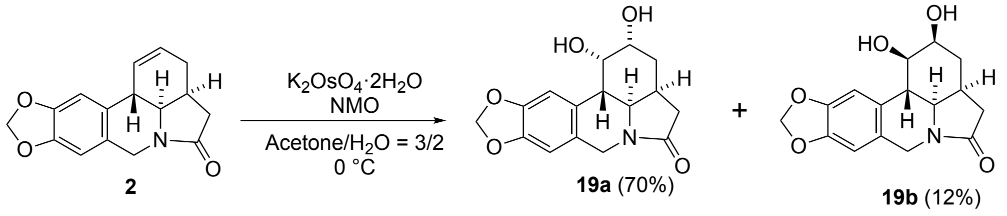


Preparation of ABCD-ring 2



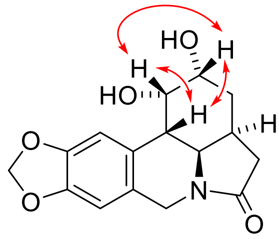
Trifluoroacetic acid (33 μL, 410 μmol) was added to a mixture of olefine **18** (10.6 mg, 41.2 μmol), paraformaldehyde (30.9 mg, 1.03 mmol) and 1,2-dichloroethane (4.1 mL) at room temperature. The mixture was heated to 60 °C, and stirred at 60 °C for 1 h. After cooling to room temperature, the resulting mixture was quenched with saturated aqueous $NaHCO_3$ (4.0 mL) and extracted with $CHCl_3$ (3x 10 mL). The combined organic extracts were washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 3:1) to give lactam **2** (10.2 mg, 92%): a colorless oil; $[\alpha]^{22}_{D}$ –121.4 (*c* 1.00, $CHCl_3$); IR (film) 2924, 1681, 1485, 1267, 1247, 1036, 933, 852 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.63 (s, 1H), 6.31 (ddd, *J* = 9.2, 3.4, 3.4 Hz, 1H), 6.12 (dddd, *J* = 9.2, 6.6, 3.2, 3.0 Hz, 1H), 5.95 (d, *J* = 1.4 Hz, 1H), 5.95 (d, *J* = 1.4 Hz, 1H), 4.95 (d, *J* = 17.2 Hz, 1H), 4.25 (d, *J* = 17.2 Hz, 1H), 3.28 (dd, *J* = 9.5, 9.3 Hz, 1H), 3.11–3.04 (m, 1H), 2.82 (ddd, *J* = 17.2, 10.3, 1.2 Hz, 1H), 2.75 (ddd, *J* = 15.3, 7.4, 6.6 Hz, 1H), 2.68 (ddddd, *J* = 10.3, 9.5, 7.8, 7.4, 6.6 Hz, 1H), 2.24 (dd, *J* = 17.2, 7.8 Hz, 1H), 1.99–1.91 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0 (C), 146.9 (C), 146.7 (C), 130.5 (CH), 129.6 (C), 128.6 (CH), 125.3 (C), 106.9 (CH), 105.8 (CH), 101.2 (CH_2), 60.5 (CH), 43.3 (CH_2), 39.2 (CH), 38.5 (CH_2), 30.4 (CH_2), 28.6 (CH); HRMS (ESI), calcd for $C_{16}H_{16}NO_3^+$ $(M+H)^+$ 270.1130, found 270.1125.

Diols 19a and 19b

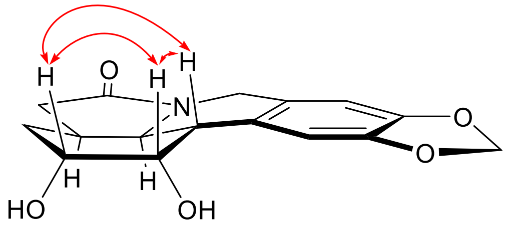


N-Methylmorpholine *N*-oxide (21.7 mg, 185 μmol) was added to a solution of lactam **2** (8.3 mg, 30.8 μmol), potassium osmate(VI) dihydrate (6.8 mg, 18.5 μmol) and acetone/H_2O (3:2, 6.2 mL) at 0 °C. After maintaining for 5 h at 0 °C, the reaction solution was quenched with 10wt% aqueous sodium thiosulfate (5 mL) and extracted with $CHCl_3$ (7x 15 mL). The combined organic extracts were washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/MeOH 1:0 to 5:1) and HPLC (PEGASIL Silica 120-5, 250×20 mm, UV 254 nm, EtOAc/MeOH 8:1, 10 mL/min, **19b**: T_R = 12.0 min, **19a**: T_R = 13.0 min) to give diol **19a** (6.5 mg, 70%) and diol **19b** (1.1 mg, 12%). **19a**: white crystals; mp 213.5–214.0 °C; $[\alpha]^{24}_{D}$ –53.0 (*c* 1.00, MeOH); IR (film) 3418, 2924, 2865, 1658, 1485, 1243, 1188, 1037, 932, 848, 731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.83 (s, 1H), 6.62 (s, 1H), 5.95 (d, *J* = 1.2 Hz, 1H), 5.94 (d, *J* = 1.2 Hz, 1H), 4.99 (d, *J* = 16.9 Hz, 1H), 4.53 (s, 1H), 4.19 (d, *J* = 16.9 Hz, 1H), 4.01–3.95 (m, 1H), 3.64 (dd, *J* = 10.7, 6.8 Hz, 1H), 2.79 (ddddd, *J* = 12.4, 8.9, 6.9, 6.8, 1.5 Hz, 1H), 2.53 (dd, *J* = 16.9, 8.9 Hz, 1H), 2.50 (d, *J* = 10.7 Hz, 1H), 2.22 (dd, *J* = 16.9, 12.4 Hz, 1H), 2.21–2.16 (m, 1H), 2.10 (ddd, *J* = 14.0, 11.2, 6.9 Hz, 1H), 2.08–2.00 (m, 1H), 1.98 (ddd, *J* = 14.0, 5.5, 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8 (C), 146.95 (C), 146.92 (C), 127.8 (C), 126.3 (C), 107.1 (CH), 104.9 (CH), 101.3 (CH_2), 69.0 (CH), 67.7 (CH), 54.9 (CH), 43.4 (CH_2), 41.4 (CH), 35.0 (CH_2), 30.4 (CH), 28.6 (CH_2); HRMS (ESI), calcd for $C_{16}H_{18}NO_5^+$ $(M+H)^+$ 304.1185, found 304.1172. Diastreomeric diol **19b**; a colorless oil; $[\alpha]^{24}_D$ –26.7 (*c* 0.23, MeOH); IR (film) 3410, 2925, 2859, 1658, 1503, 1484, 1238, 1037 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (s, 1H), 6.53 (s, 1H), 5.94 (d, *J* = 1.4 Hz, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 4.91 (d, *J* = 16.9 Hz, 1H), 4.13 (d, *J* = 16.9 Hz, 1H), 4.02 (dd, *J* = 9.8, 4.3 Hz, 1H), 4.01–3.95 (m, 1H), 3.39 (dd, *J* = 11.5, 7.7 Hz, 1H), 3.02 (brs, 1H), 2.76 (dd, *J* = 11.5, 9.8 Hz, 1H), 2.72–2.63 (m, 2H), 2.48–2.39 (m, 1H), 2.31 (brs, 1H), 2.01–1.93 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7 (C), 146.9 (C), 146.7 (C), 130.3 (C), 125.3 (C), 107.2 (CH), 106.2 (CH), 101.2 (CH_2), 70.9 (CH), 69.1 (CH), 56.6 (CH), 43.2 (CH_2), 42.2 (CH), 37.2 (CH_2), 31.2 (CH_2), 29.1 (CH); HRMS (ESI), calcd for $C_{16}H_{18}NO_5^+$ $(M+H)^+$ 304.1185, found 304.1186.

NOESY experiment for 19a (500 MHz, $CDCl_3$)

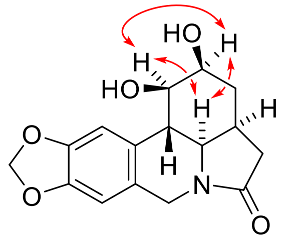


19a

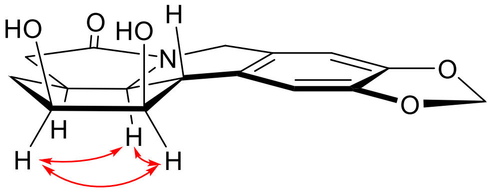


19a

NOESY experiment for 19b (500 MHz, $CDCl_3$)

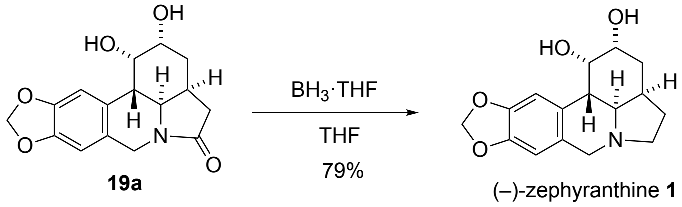


19b



19b

(−)-Zephyranthine 1



Borane-tetrahydrofuran complex (1.0 M in THF, 740 μL, 740 μmol) was added to a solution of diol **19a** (4.5 mg, 14.8 μmol) and THF (3.0 mL) at room temperature. This solution was maintained for 13 h at room temperature. After cooling to 0 °C, MeOH/AcCl (9:1, 2.0 mL) was added to the resulting solution via cannula. The solution was concentrated, quenched with saturated aqueous $NaHCO_3$ (2.0 mL), and extracted with $CHCl_3$ (20 mL x 10). The combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by preparative thin-layer chromatography (CH_2Cl_2/saturated NH_3 in MeOH 5:1) to give (−)-zephyranthine **1** (3.4 mg, 79%): white solid; mp 112.0–113.0 °C; $[\alpha]^{29}_{D}$ −30.4 (*c* 0.56, MeOH); IR (film) 3371, 2923, 1503, 1484, 1242, 1135, 1038, 932, 847 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.88 (s, 1H), 6.59 (s, 1H), 5.91 (d, *J* = 1.5 Hz, 1H), 5.90 (d, *J* = 1.5 Hz, 1H), 4.60 (dd, *J* = 3.2, 1.9 Hz, 1H), 4.21 (d, *J* = 16.4 Hz, 1H), 3.99 (ddd, *J* = 10.6, 5.2, 3.2 Hz, 1H), 3.74 (d, *J* = 16.4 Hz, 1H), 3.24 (ddd, *J* = 10.1, 8.9, 6.9 Hz, 1H), 3.06 (dd, *J* = 10.3, 6.0 Hz, 1H), 2.77 (ddd, *J* = 10.1, 10.1, 4.3 Hz, 1H), 2.63–2.55 (m, 1H), 2.48 (d, *J* = 10.3 Hz, 1H), 2.04 (ddd, *J* = 13.5, 10.6, 6.1 Hz, 1H), 1.99 (dddd, *J* = 13.2, 9.2, 8.9, 4.3 Hz, 1H), 1.90 (ddd, *J* = 13.5, 5.2, 2.9 Hz, 1H), 1.77–1.68 (m 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5 (C), 146.1 (C), 129.6 (C), 129.3 (C), 107.2 (CH), 104.5 (CH), 100.9 (CH_2), 69.1 (CH), 68.9 (CH), 57.6 (CH), 53.2 (CH_2), 53.0 (CH_2), 36.6 (CH), 35.1 (CH), 30.3 (CH_2), 27.4 (CH_2); HRMS (ESI), calcd for $C_{16}H_{20}NO_4^+$ $(M+H)^+$ 290.1392, found 290.1388.

Comparison of $[\alpha]_D$ values of 1

Chida (this study): $[\alpha]^{29}_{D}$ −30.4 (*c* 0.56, MeOH)

Oppolzer (*J. Am. Chem. Soc.*, 1994, **116**, 3139):

$[\alpha]^{29}_{D}$ +49.0 (*c* 0.26, $CHCl_3$) (for (+)-trianthine, an antipode of (−)-zephyranthine)

Sun (*Chem. Asian J.,* 2017, **12**, 1309):

$[\alpha]^{20}_{D}$ −28.9 (*c* 0.40, MeOH)

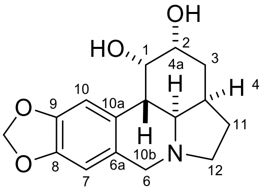
Ozeki (natural sample, *Chem. Pharm. Bull.*, 1964, **12**, 253):

$[\alpha]^{24}_{D}$ −43.2 (*c* 0.47, $CHCl_3$)

Bastida (natural sample, *Fitterapia,* 2001, **72**, 444):

$[\alpha]^{20}_{D}$ −30.6 (*c* 0.56, MeOH)

Comparison of ^{1}H NMR of zephyranthine



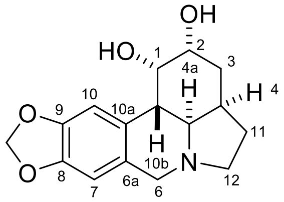
	our synthetic sample[1]	**Oppolzer**[2]	**Sun**[3]
Proton	^{1}H NMR (500 MHz, $CDCl_3$)	^{1}H NMR (400 MHz, $CDCl_3$)	^{1}H NMR (400 MHz, $CDCl_3$)
10	6.88 (s, 1H)	6.88 (s, 1H)	6.88 (s, 1H)
7	6.59 (s, 1H)	6.59 (s, 1H)	6.59 (s, 1H)
OCH_2O	5.92 (d, *J* = 1.5 Hz, 1H)	5.91 (d, *J* = 1.48 Hz, 1H)	5.92 (d, *J* = 1.2 Hz, 1H)
OCH_2O	5.91 (d, *J* = 1.5 Hz, 1H)	5.90 (d, *J* = 1.48 Hz, 1H)	5.90 (d, *J* = 1.2 Hz, 1H)
1	4.60 (dd, *J* = 3.2, 2.5 Hz, 1H)	4.59 (m, 1H)	4.59 (s, 1H)
6	4.21 (d, *J* = 16.4 Hz, 1H)	4.21 (d, *J* = 16.5 Hz, 1H)	4.22 (d, *J* = 16.5 Hz, 1H)
2	3.99 (ddd, *J* = 10.6, 5.2, 3.2 Hz, 1H)	4.00–3.96 (ddd, *J* = 10.7, 5.2, 3.3 Hz, 1H)	4.02–3.97 (m, 1H)
6	3.74 (d, *J* = 16.4 Hz, 1H)	3.74 (d, *J* = 16.5 Hz, 1H)	3.75 (d, *J* = 16.8 Hz, 1H)
12	3.24 (ddd, *J* = 10.1, 8.9, 6.9 Hz, 1H)	3.24 (td, *J* = 8.8, 8.1 Hz, 1H)	3.24 (td, *J* = 8.8, 7.2 Hz, 1H)
4a	3.06 (dd, *J* = 10.3, 6.0 Hz, 1H)	3.06 (dd, *J* = 10.7, 6.3 Hz, 1H)	3.06 (dd, *J* = 10.4, 6.4 Hz, 1H)
12	2.77 (ddd, *J* = 10.1, 10.1, 4.3 Hz, 1H)	2.77 (td, *J* = 9.9, 4.0 Hz, 1H)	2.77 (td, *J* = 10.0, 4.4 Hz, 1H)
4	2.63–2.55 (m, 1H)	2.65–2.55 (m, 1H)	2.64–2.54 (m, 1H)
10b	2.48 (d, *J* = 10.3 Hz, 1H)	2.47 (d, *J* = 10.3 Hz, 1H)	2.48 (d, *J* = 10.4 Hz, 1H)
3	2.04 (ddd, *J* = 13.5, 10.6, 6.1 Hz, 1H)	2.2–1.8 (m, 5H, 3-H_2, 11-H, and 2 x OH)	2.08–1.87 (m, 5H, 3-H_2, 11-H, and 2 x OH))
11	1.99 (dddd, *J* = 13.2, 9.2, 8.9, 4.3 Hz, 1H)		
3	1.90 (ddd, *J* = 13.5, 5.2, 2.9 Hz, 1H)		
11	1.77–1.68 (m, 1H)	1.8–1.6 (m, 1H)	1.77–1.69 (m, 1H)

1) Signals of OH protons were not assigned due to the overlap with singnal of residual H_2O in $CDCl_3$.

2) W. Oppolzer, A. C. Spivey, and C. G. Bochet, *J. Am. Chem. Soc.*, 1994, **116**, 3139.

3) Y.-J. Chen, S.-L. Cai, C.-C. Wang, J.-D. Cheng, S. Kramer, and Z.-W. Sun, *Chem. Asian J.*, 2017, **12**, 1309.

Comparison of ^{13}C NMR of zephyranthine

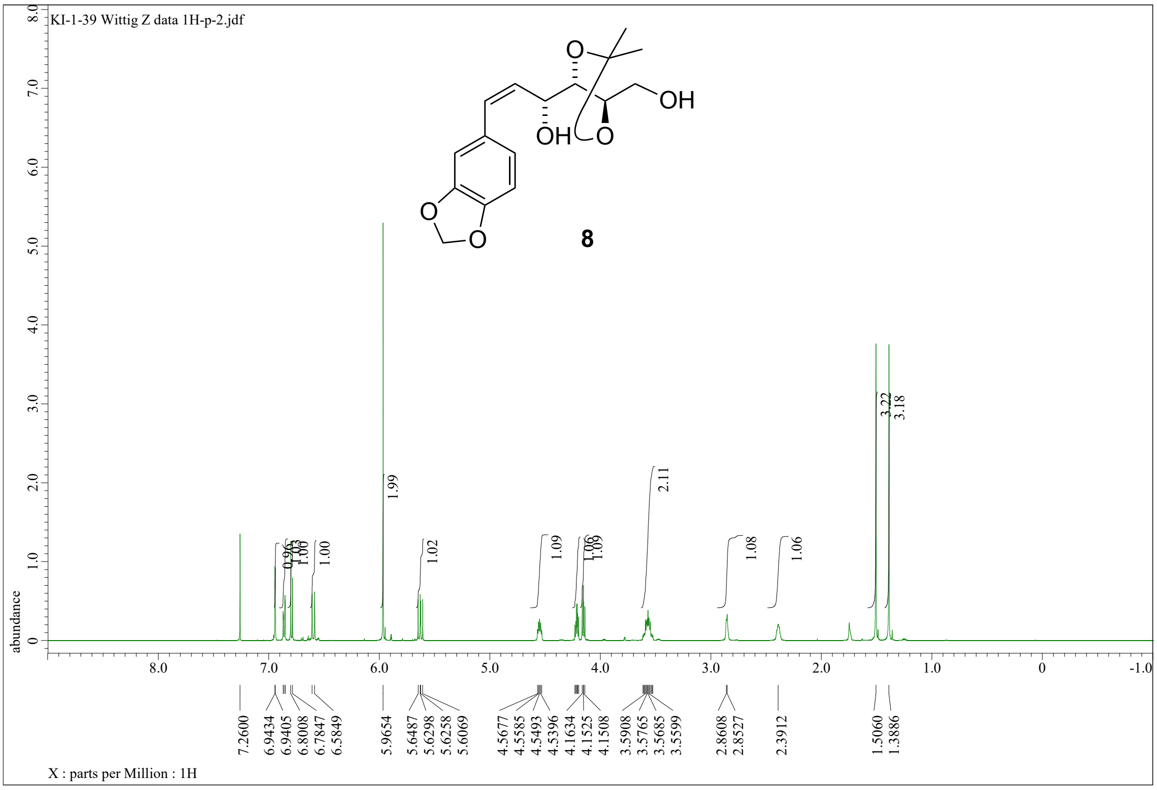


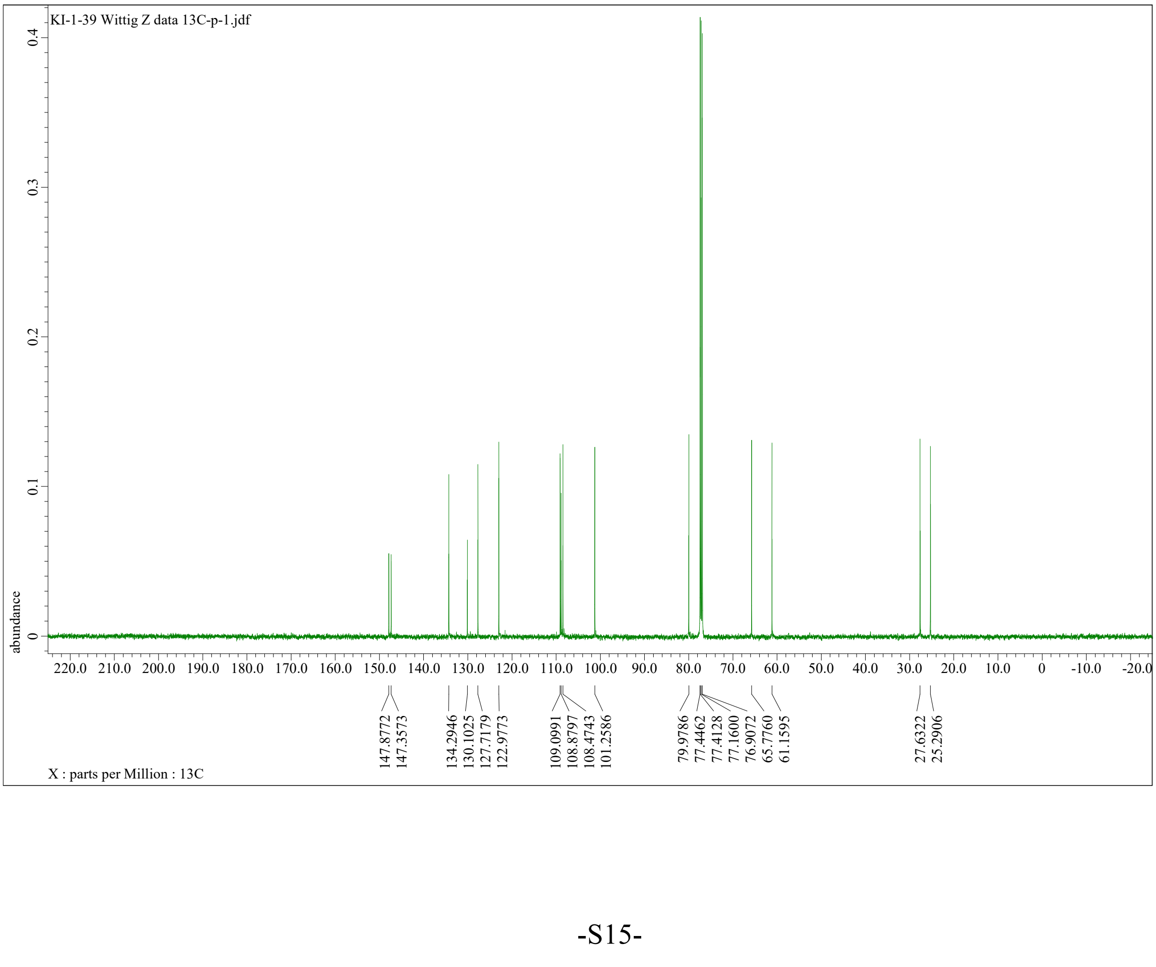
	our synthetic sample	**Oppolzer**[1]	**Sun**[2]
Carbon	^{13}C NMR (125 MHz, $CDCl_3$)	^{13}C NMR (100 MHz, $CDCl_3$)	^{13}C NMR (100 MHz, $CDCl_3$)
9	146.5 (C)	146.4 (C)	146.4
8	146.1 (C)	145.9 (C)	145.9
6a	129.6 (C)	129.5 (C)	129.4
10a	129.3 (C)	129.1 (C)	129.1
7	107.2 (CH)	107.1 (CH)	107.1
10	104.5 (CH)	104.4 (CH)	104.4
OCH_2O	100.9 (CH_2)	100.8 (CH_2)	100.8
2	69.1 (CH)	68.9 (CH)	68.9
1	68.9 (CH)	68.8 (CH)	68.8
4a	57.6 (CH)	57.5 (CH)	57.5
12	53.2 (CH_2)	53.1 (CH_2)	53.0
6	53.0 (CH_2)	52.9 (CH_2)	52.9
4	36.6 (CH)	36.4 (CH)	36.4
10b	35.1 (CH)	35.0 (CH)	35.0
3	30.3 (CH_2)	30.1 (CH_2)	30.1
11	27.4 (CH_2)	27.2 (CH_2)	27.2

1. W. Oppolzer, A. C. Spivey, and C. G. Bochet, *J. Am. Chem. Soc.*, 1994, **116**, 3139.
2. Y.-J. Chen, S.-L. Cai, C.-C. Wang, J.-D. Cheng, S. Kramer, and Z.-W. Sun, *Chem. Asian J.,* 2017, **12**, 1309.

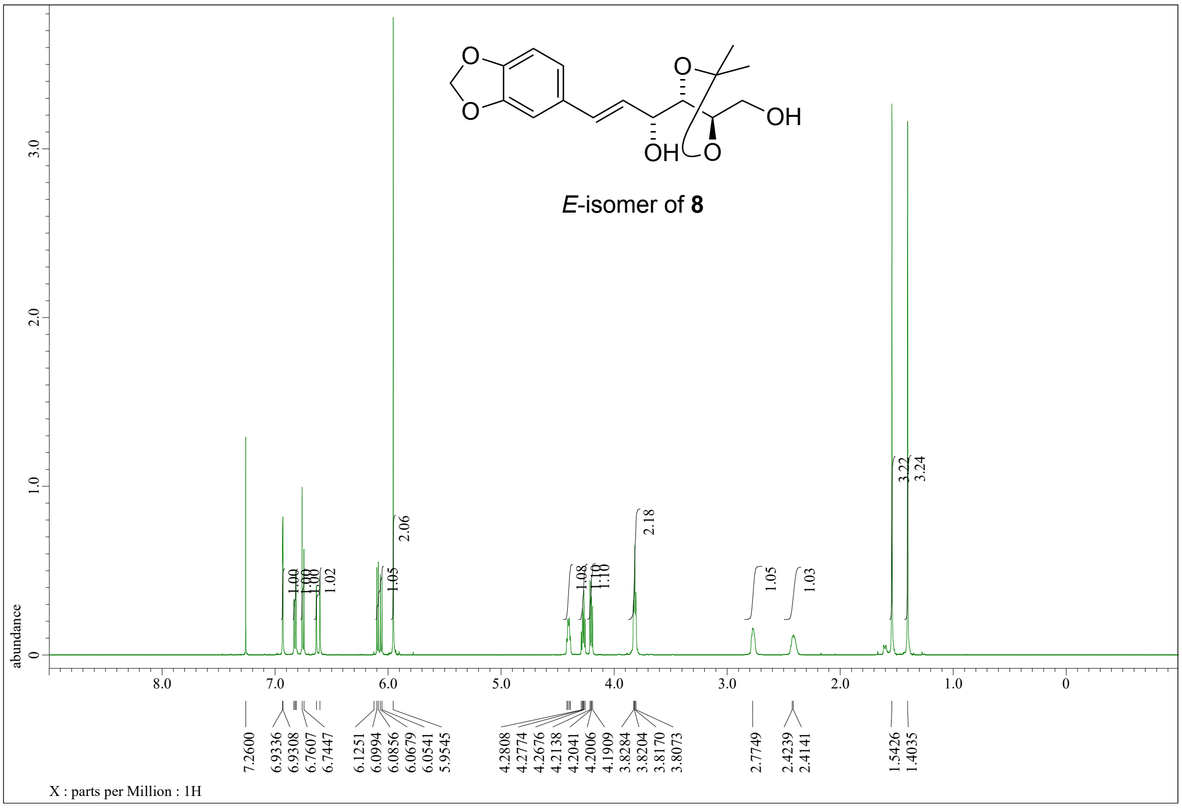
Spectral Charts

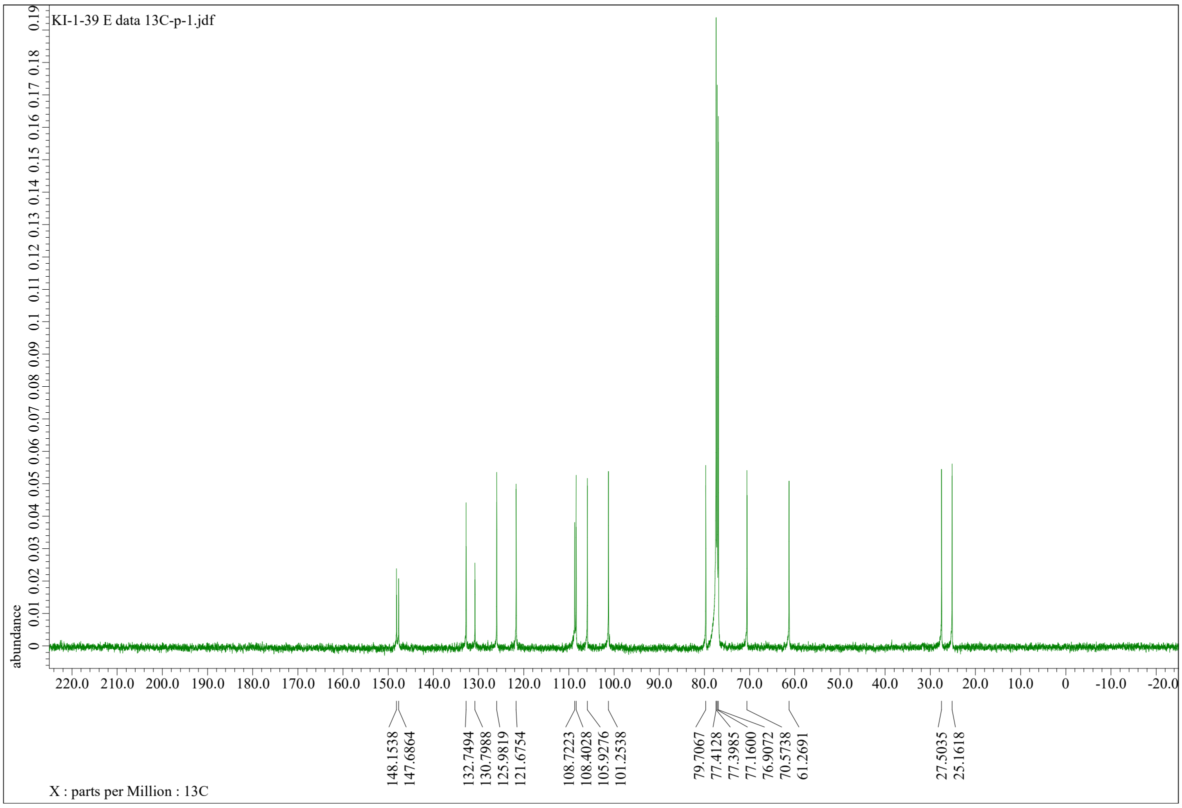
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **8**.



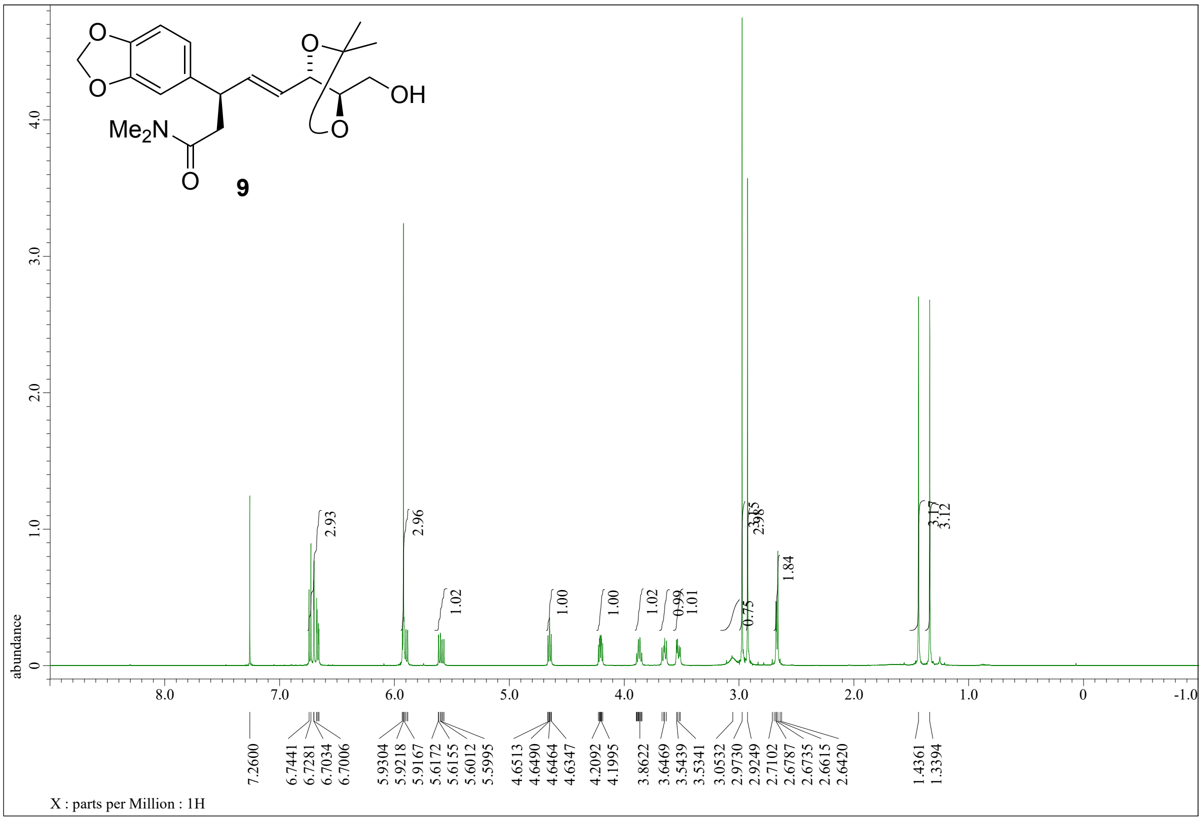


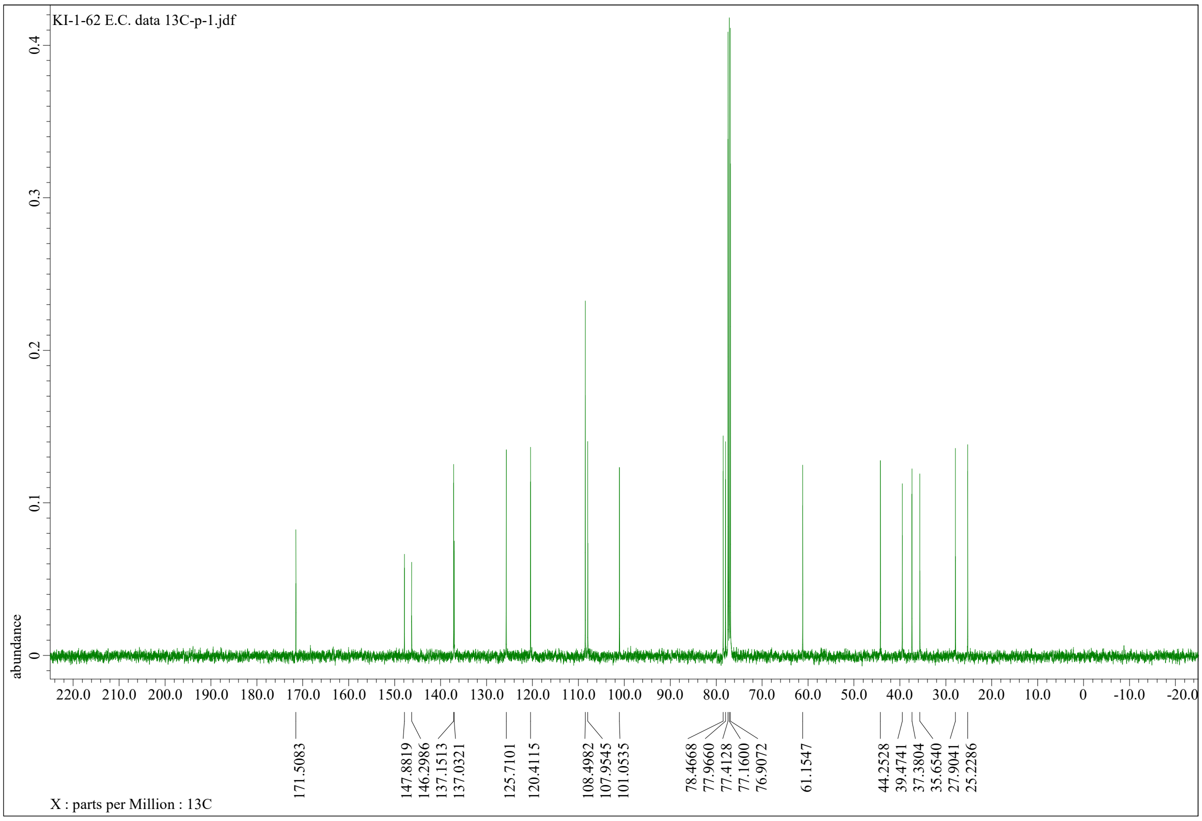
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of ***E*-isomer of 8**.



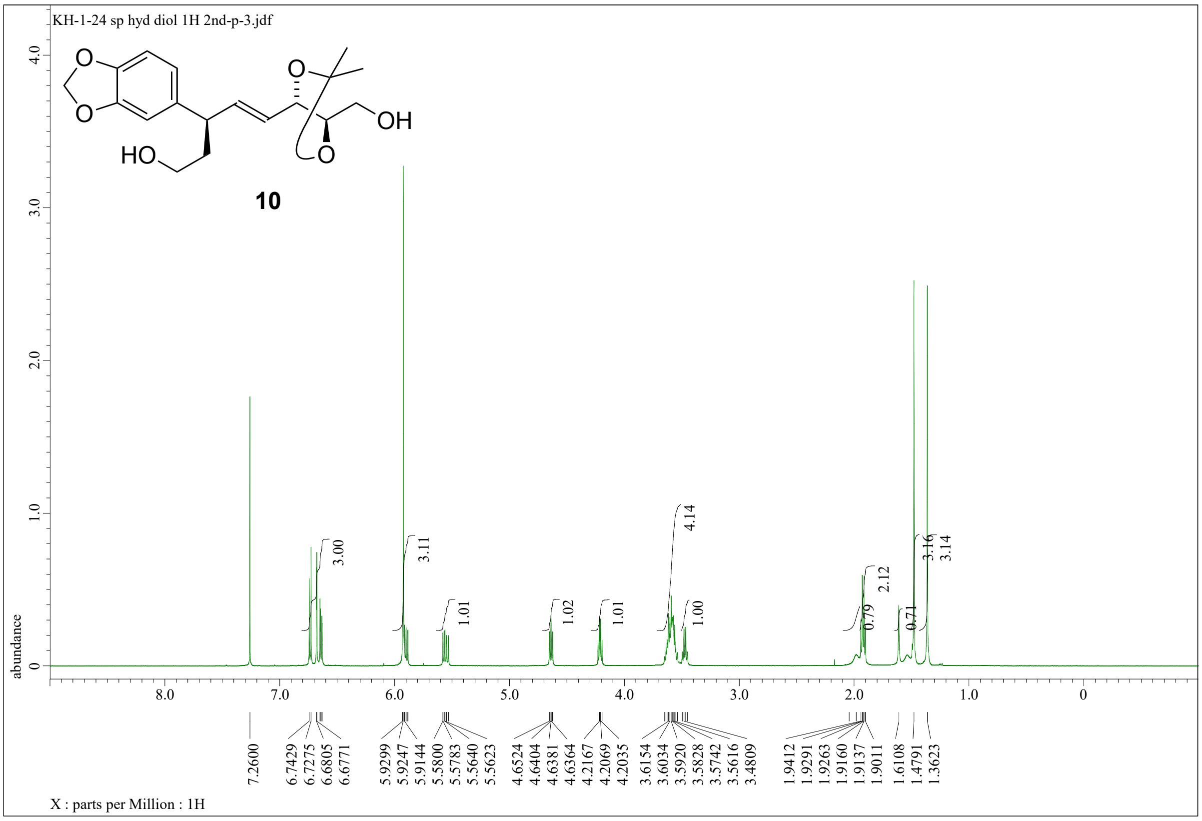


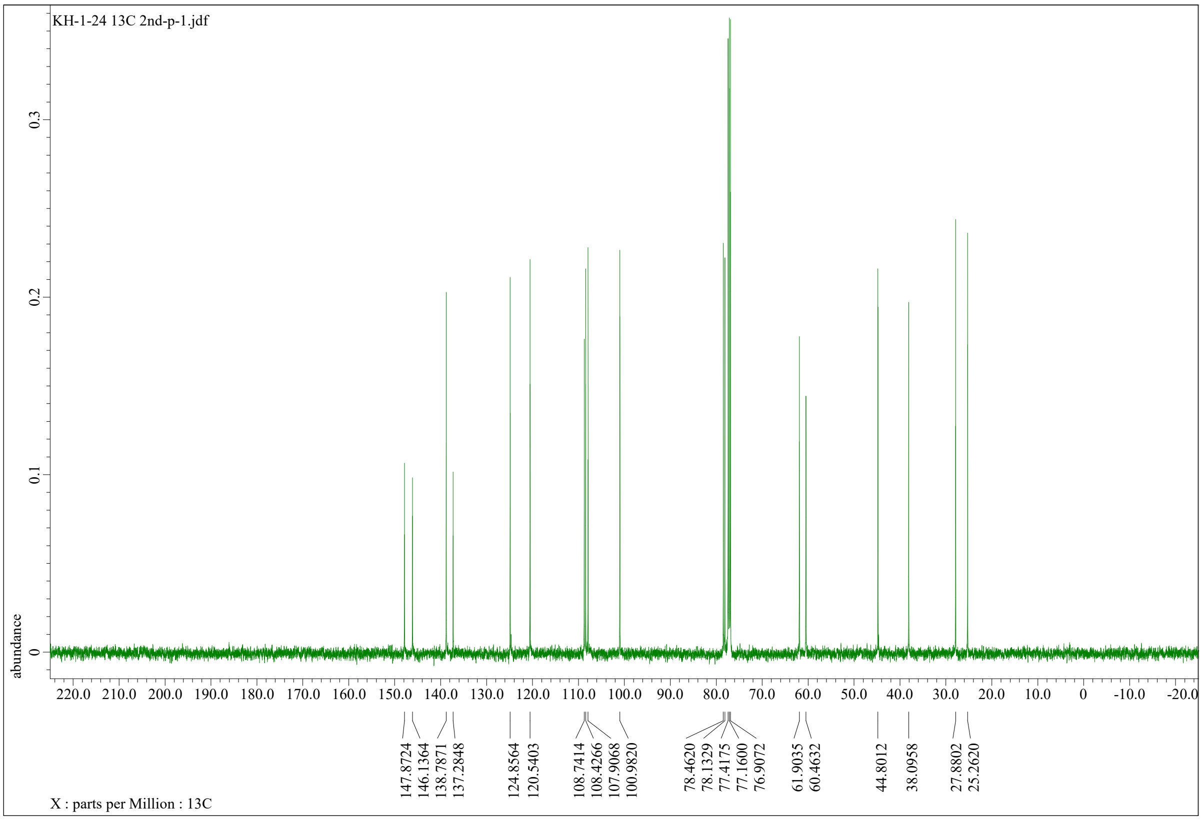
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **9.**



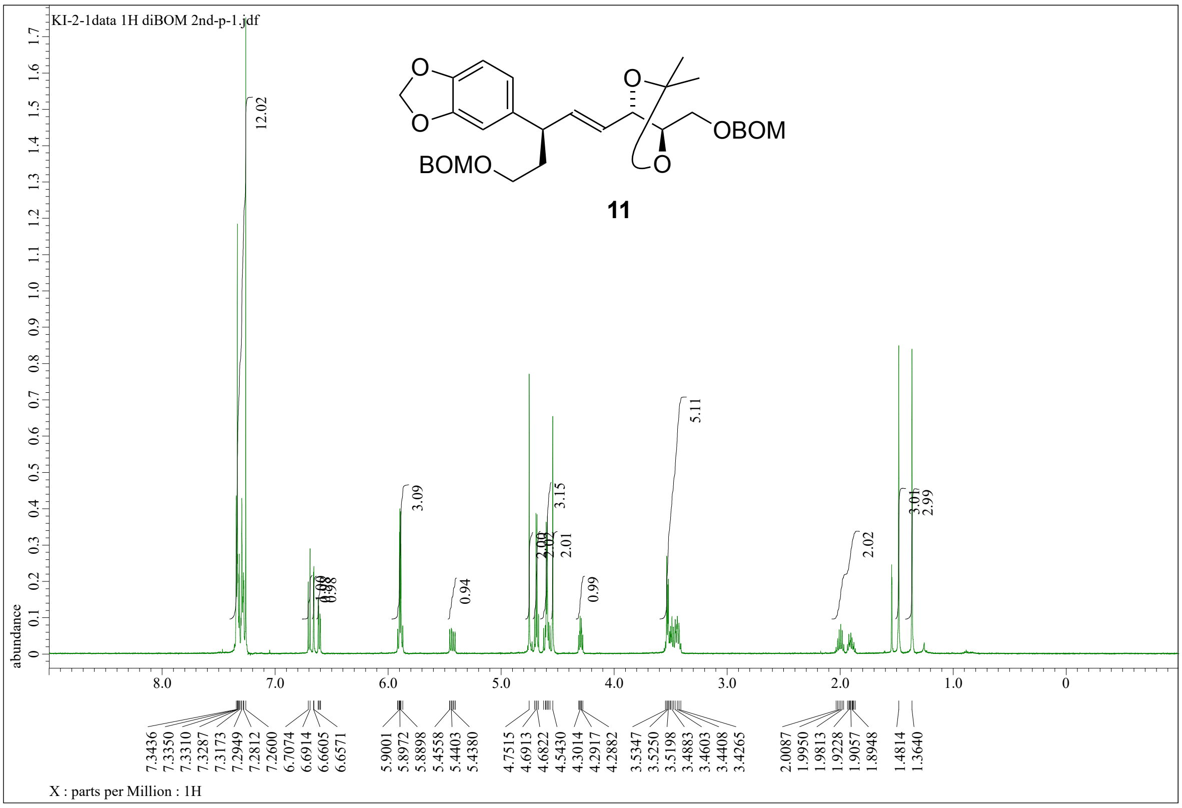


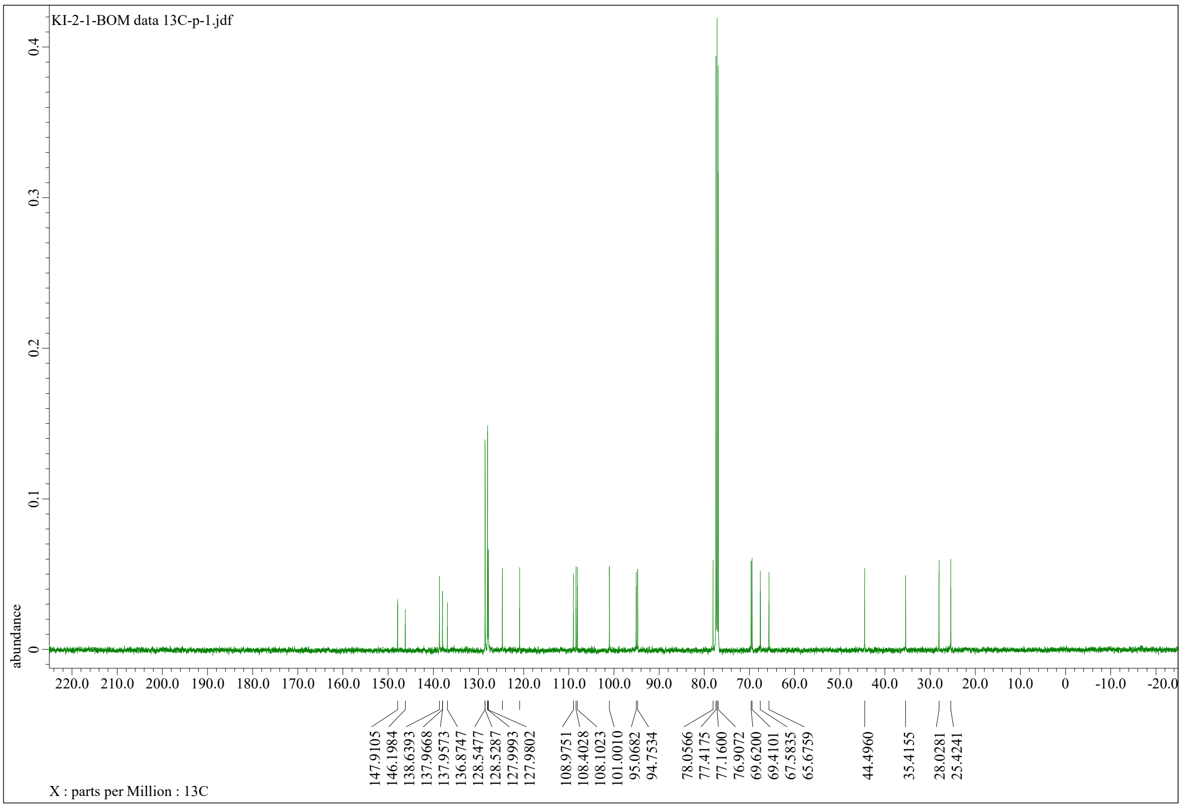
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **10**.



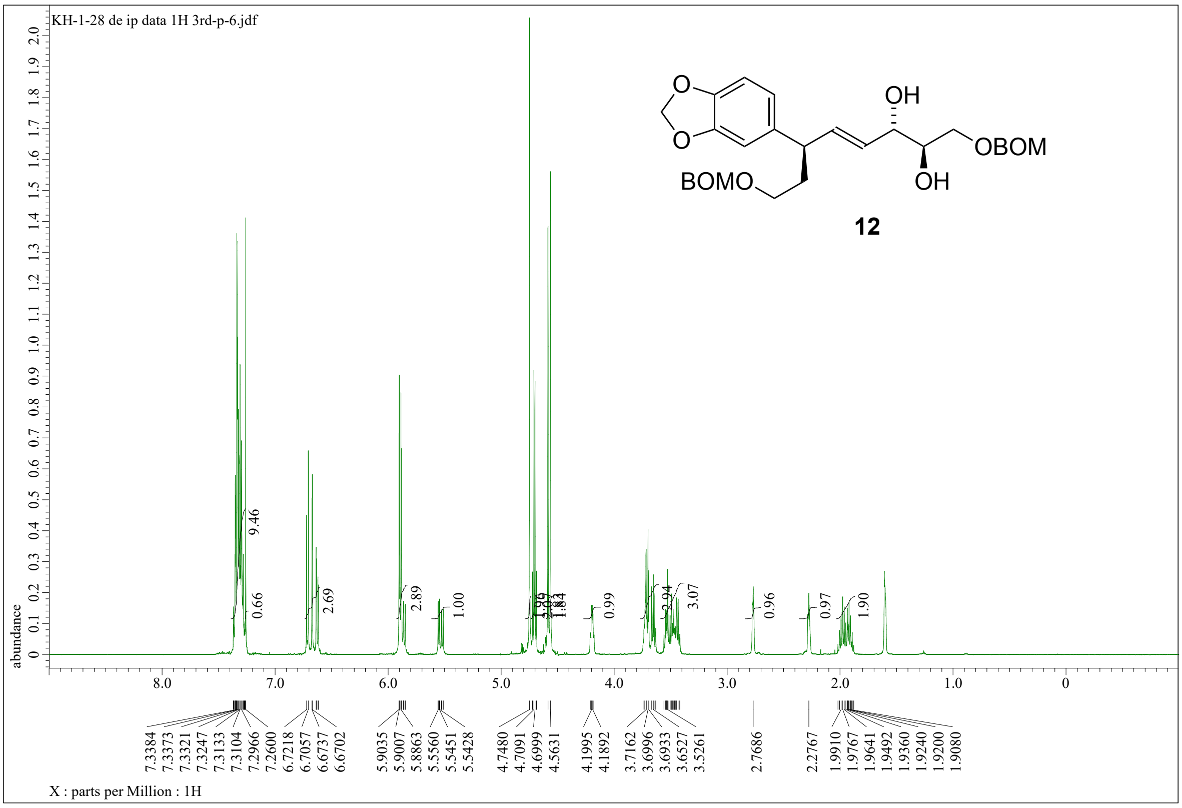


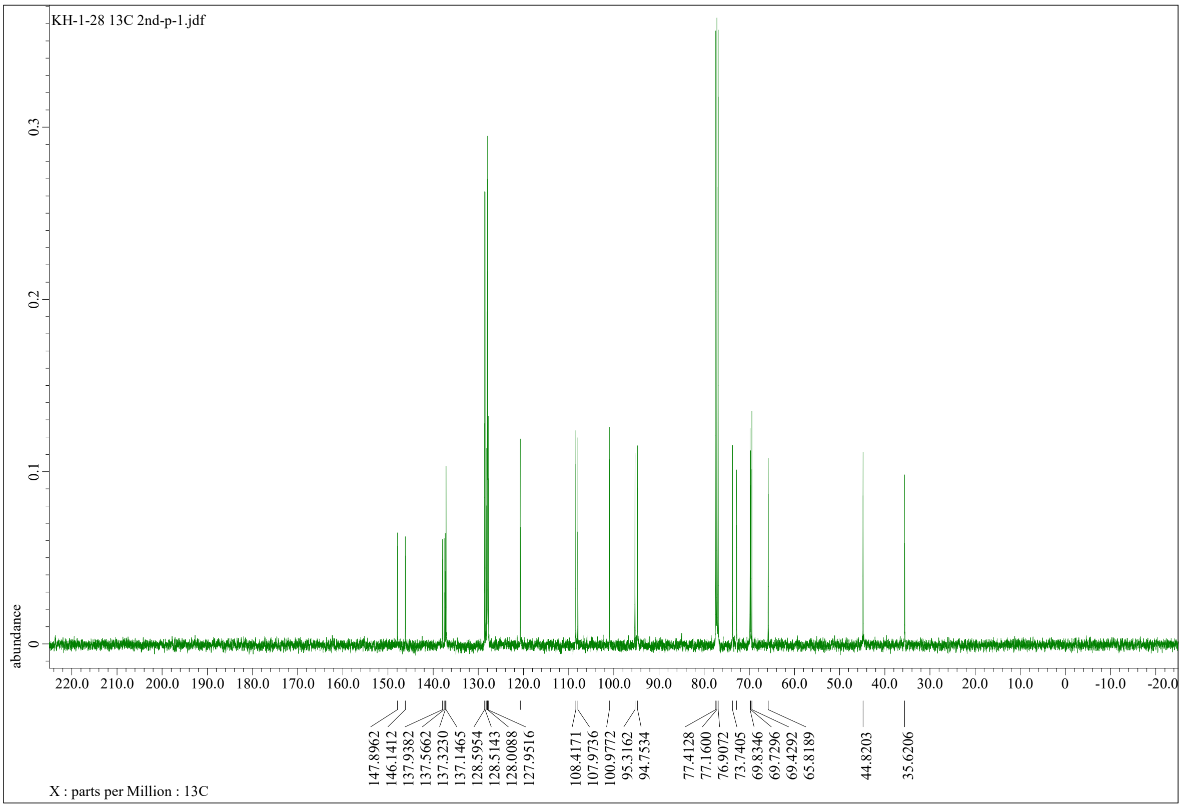
^{1}H (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) charts of compound **11**.



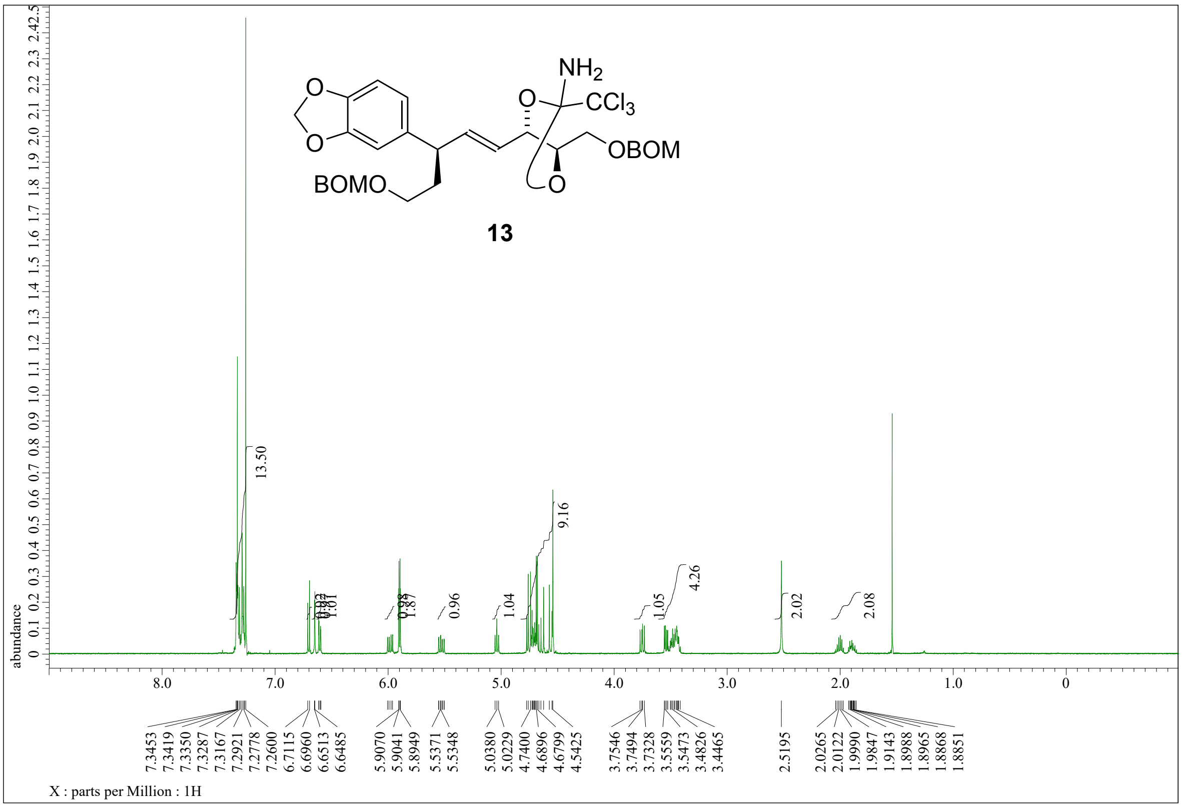


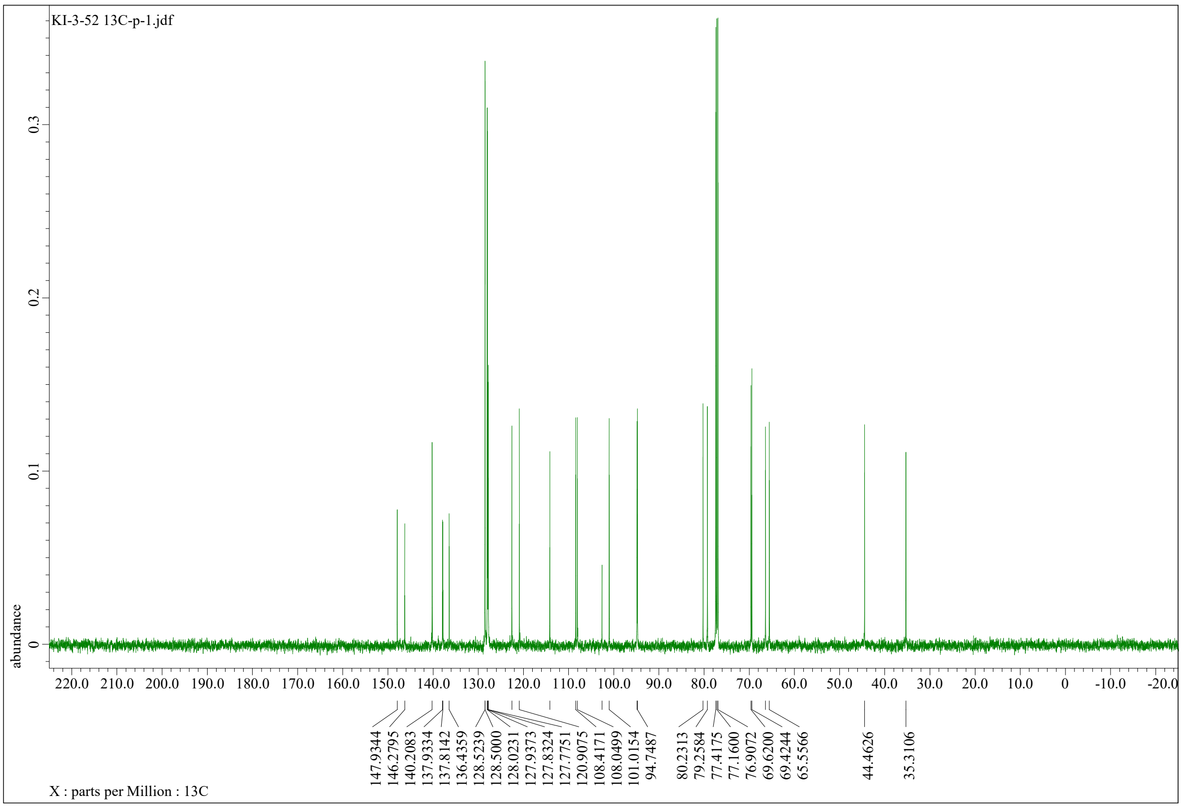
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **12**.



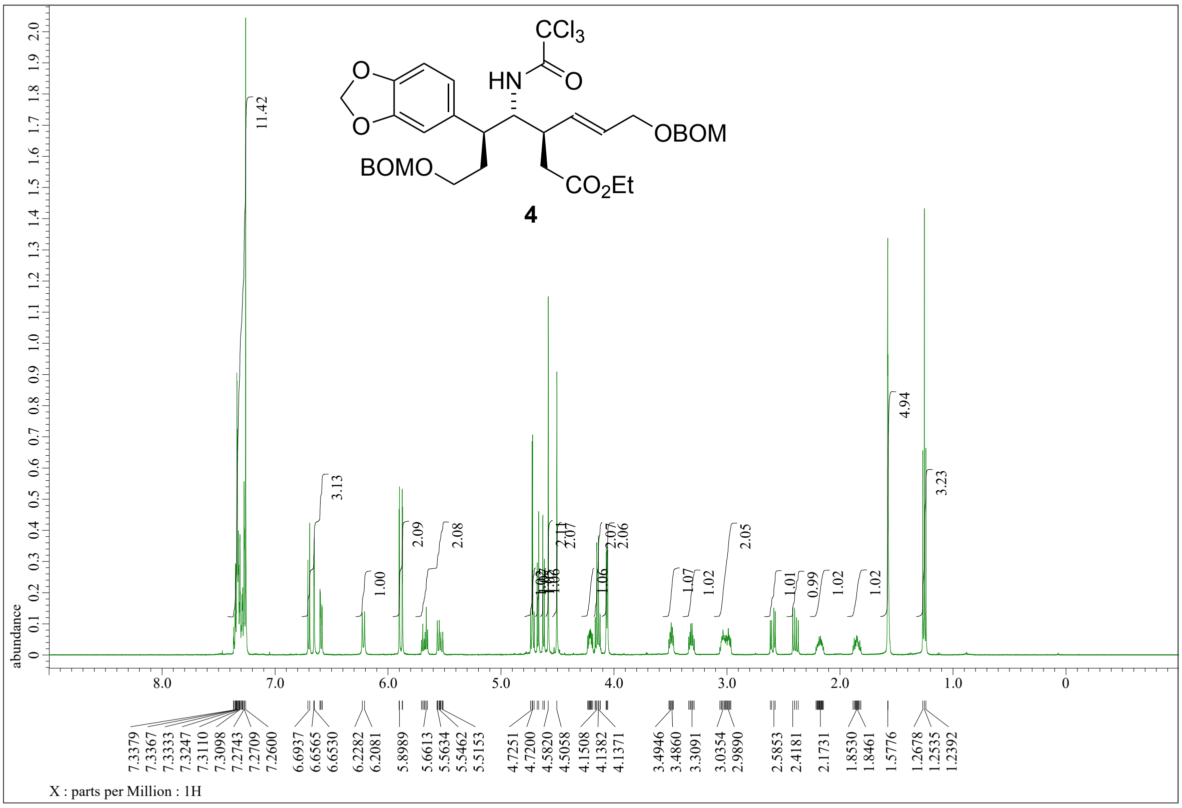


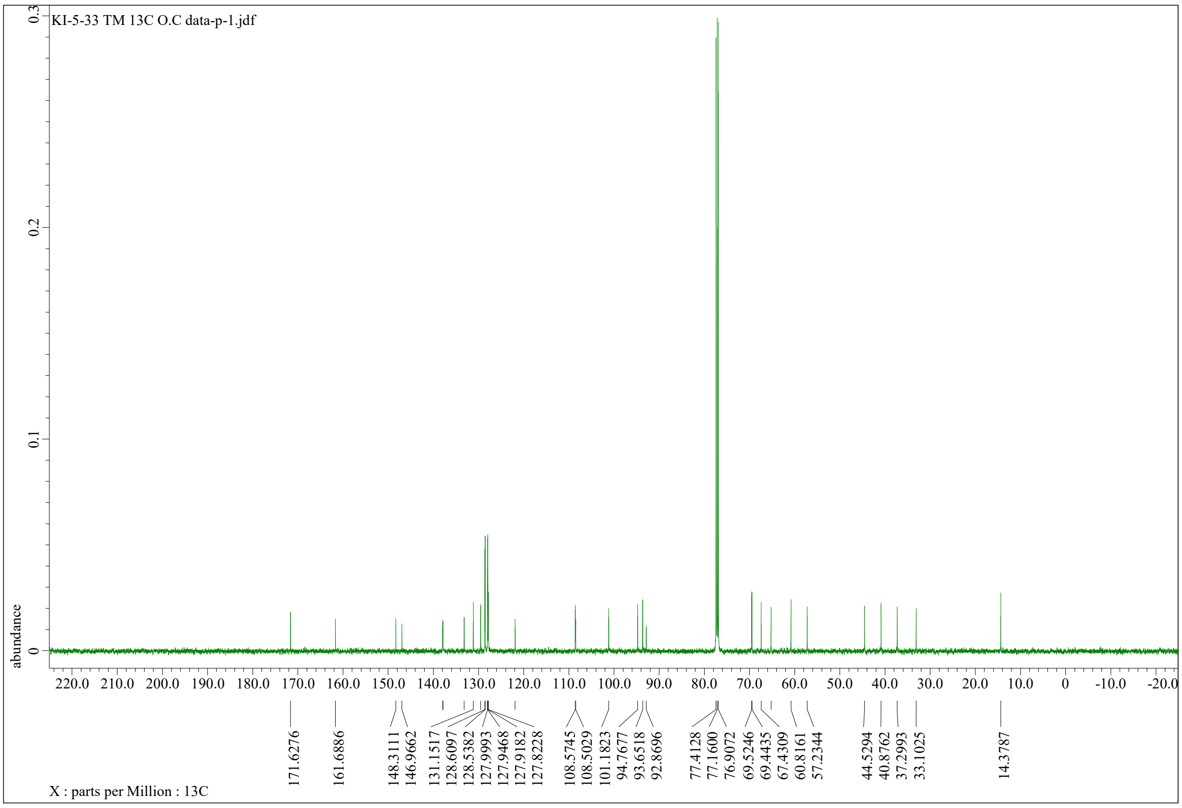
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **13**.



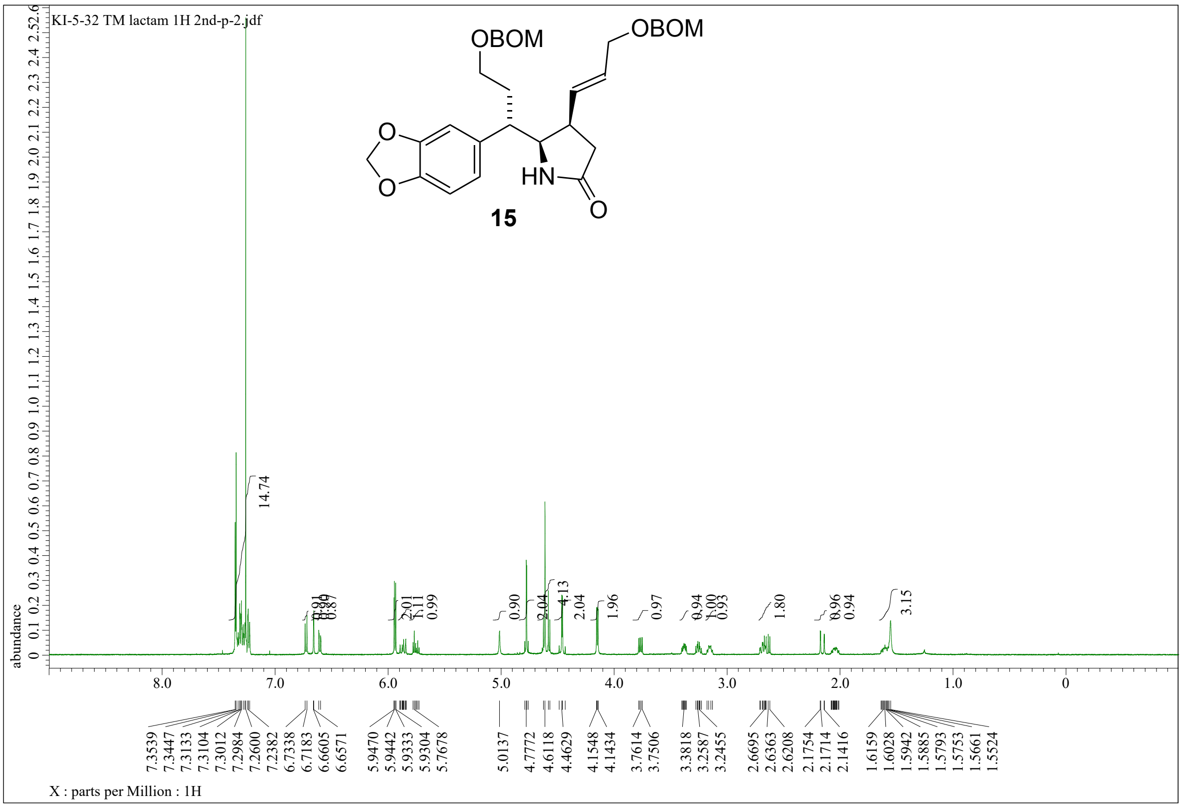


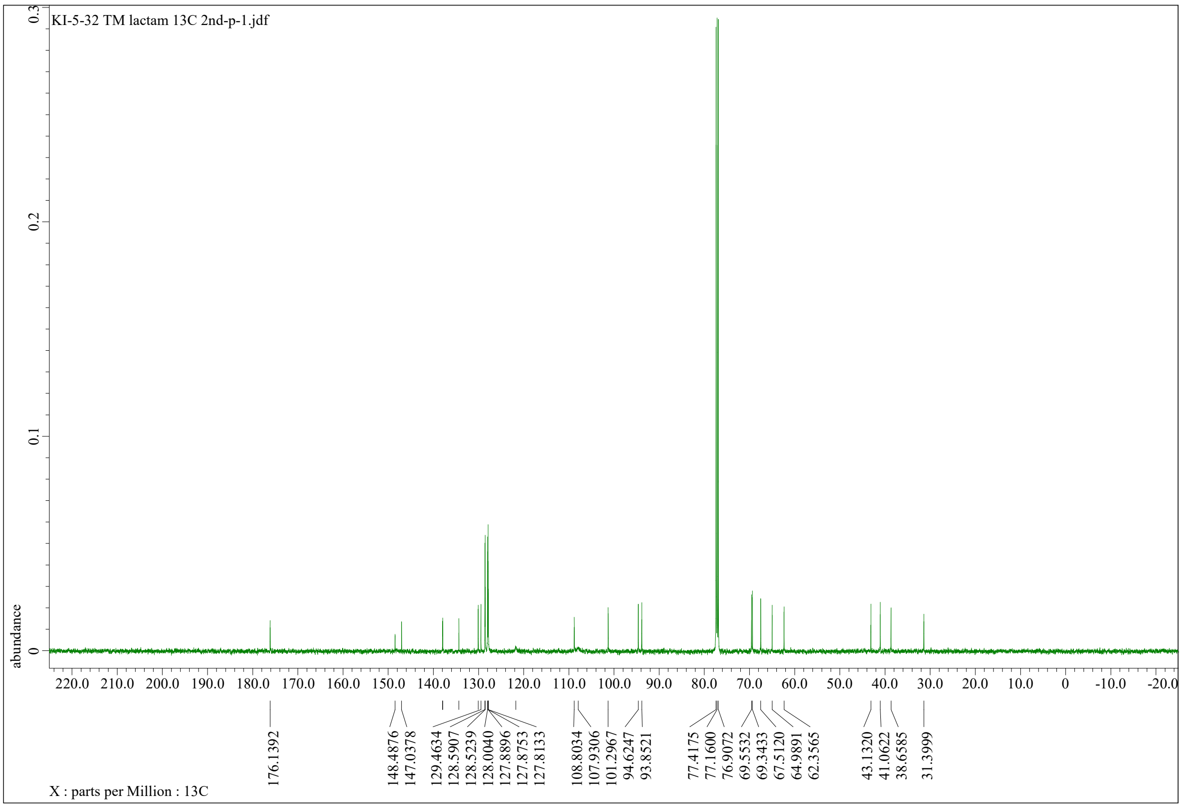
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **4**.



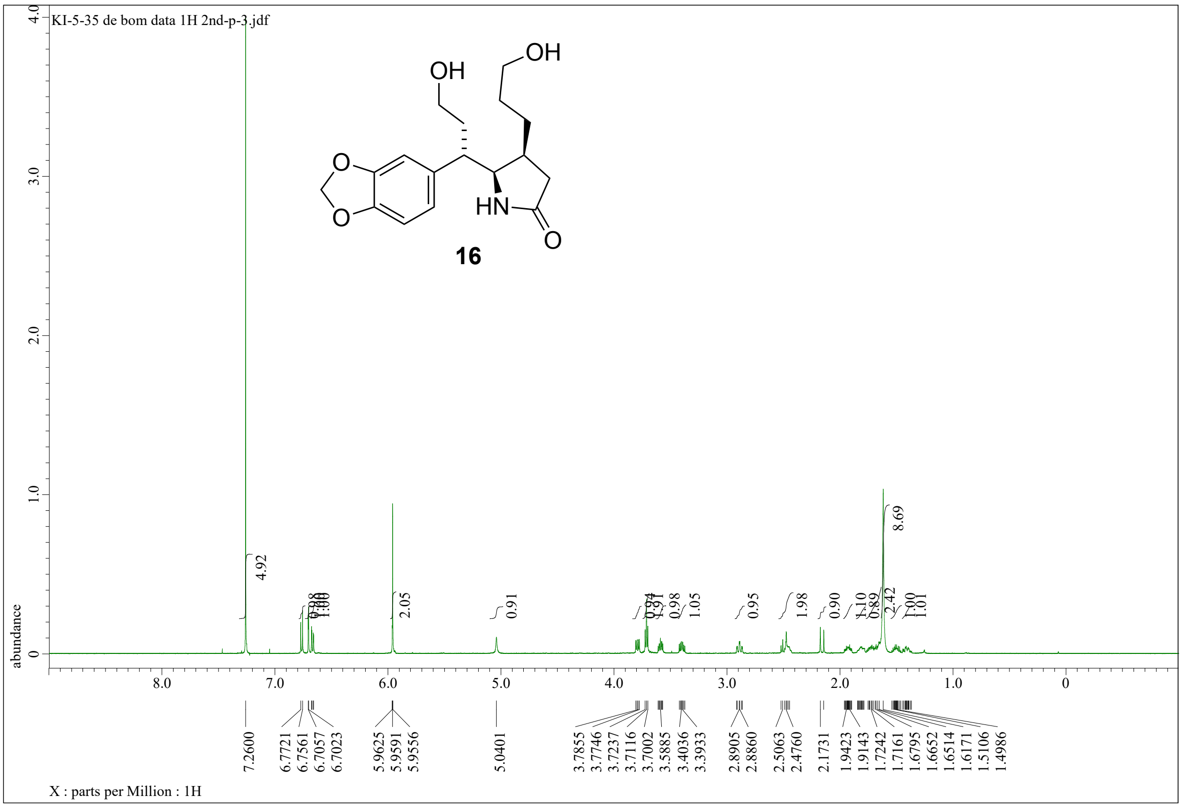


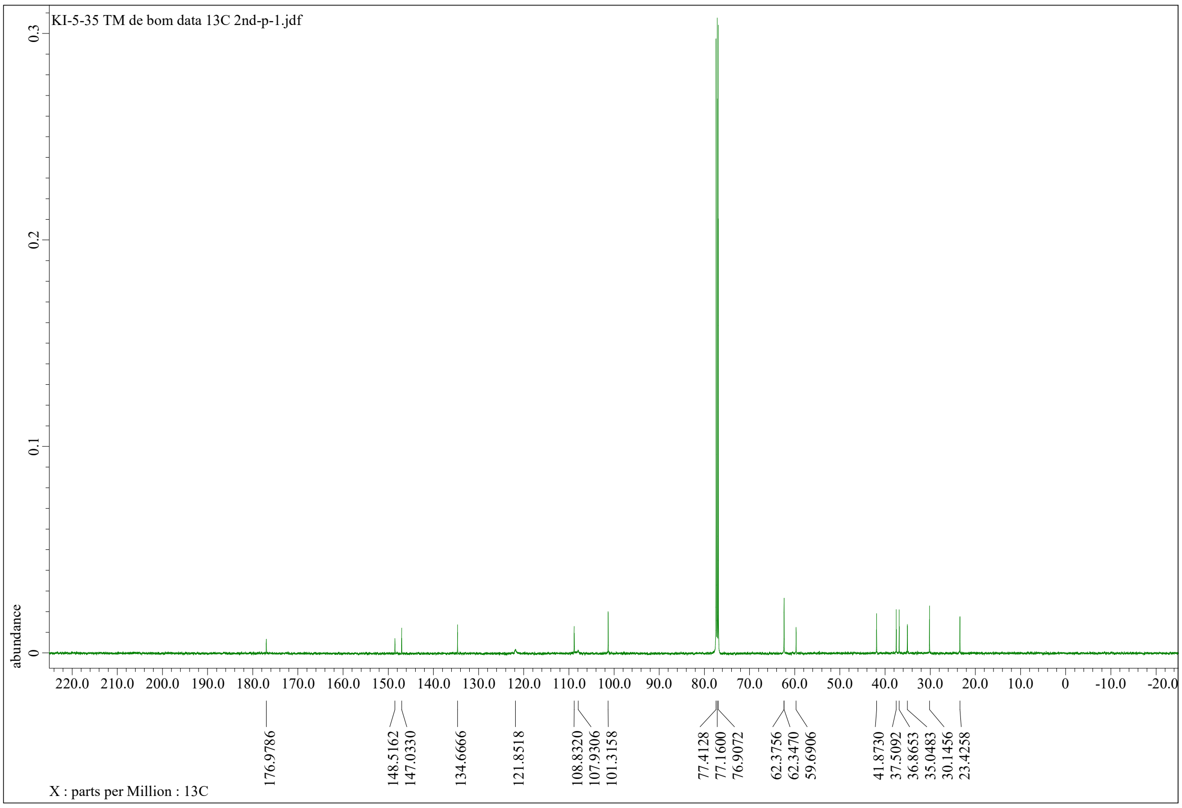
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **15**.



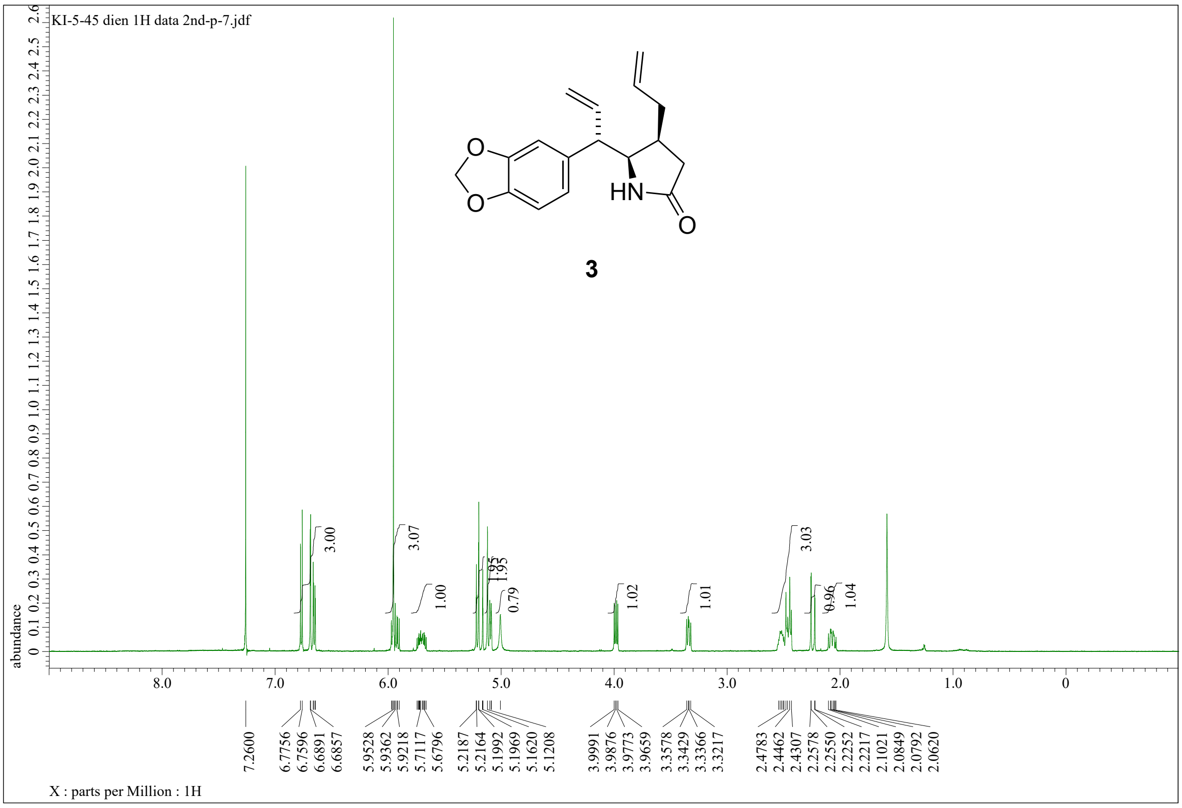


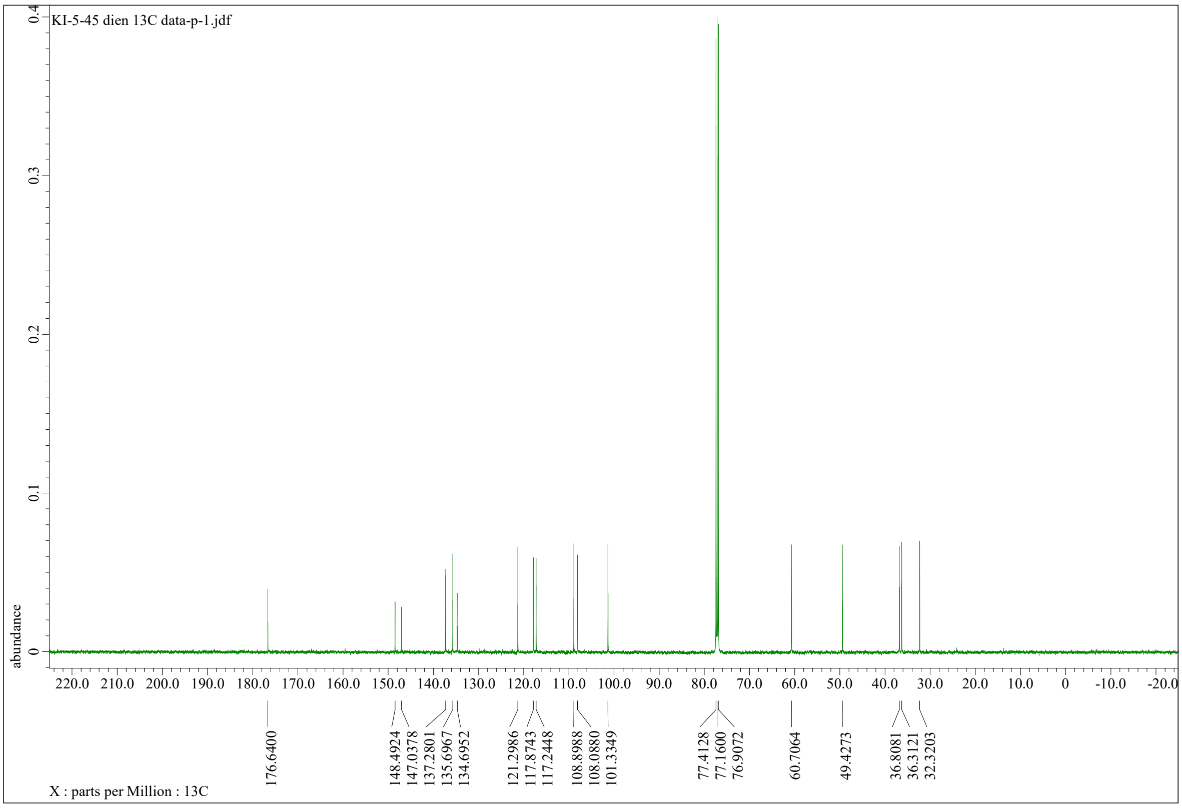
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **16**.



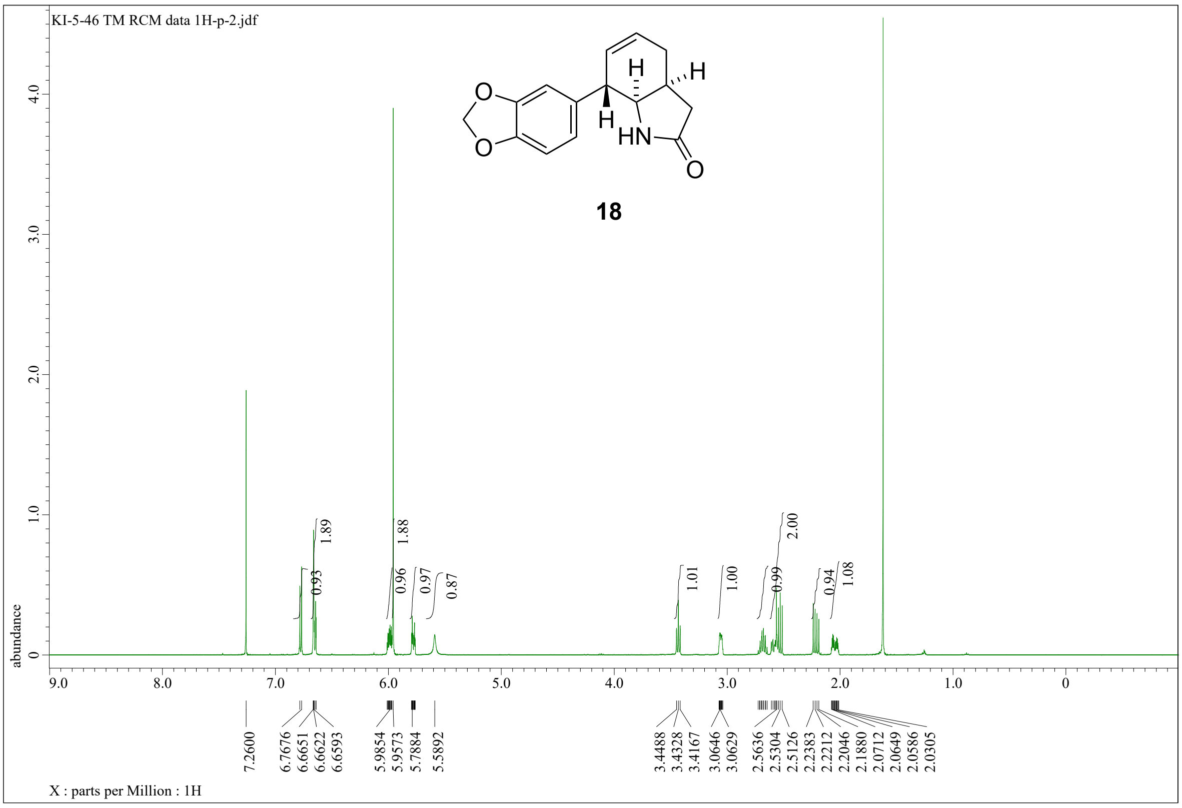


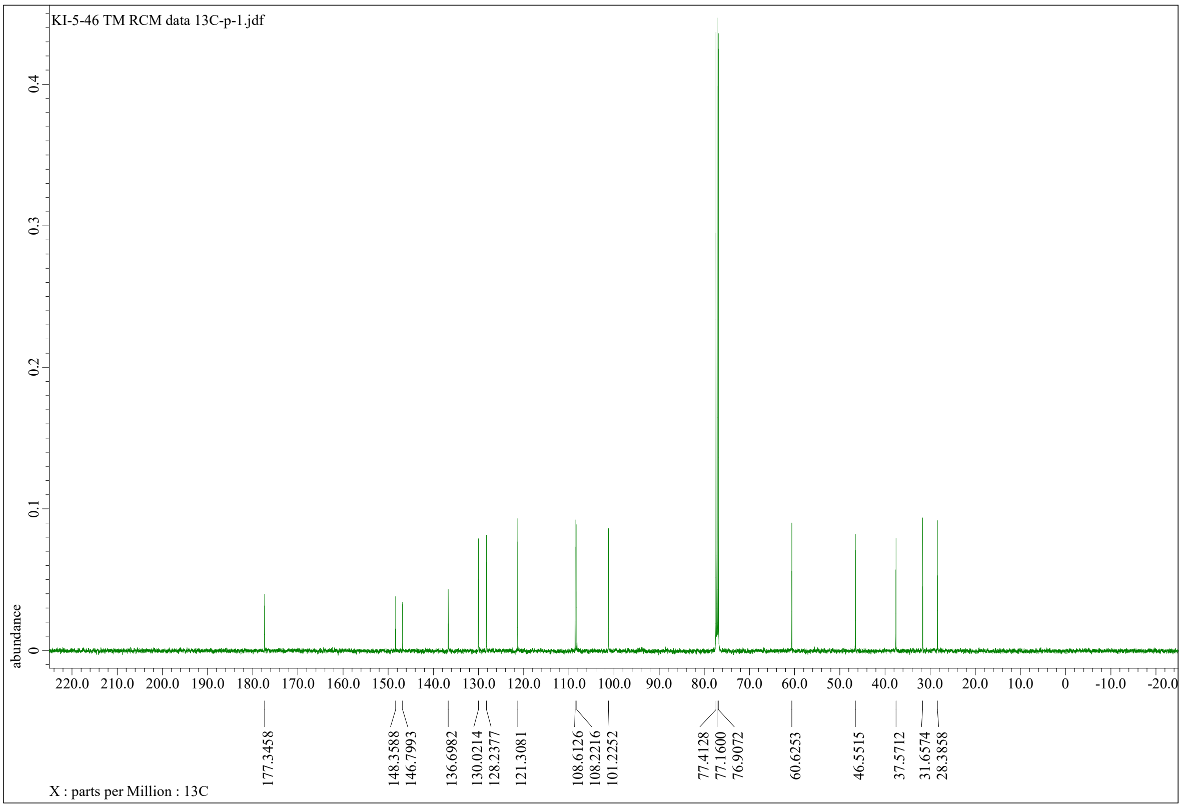
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **3**.



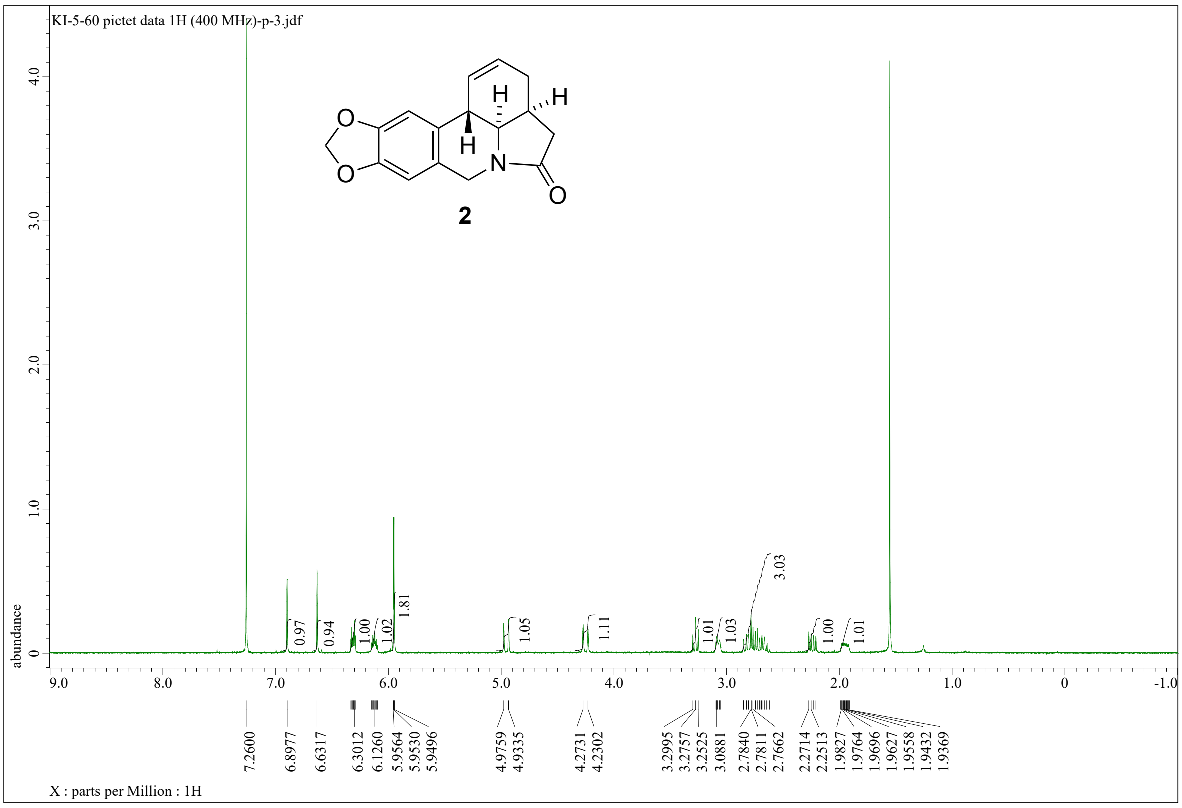


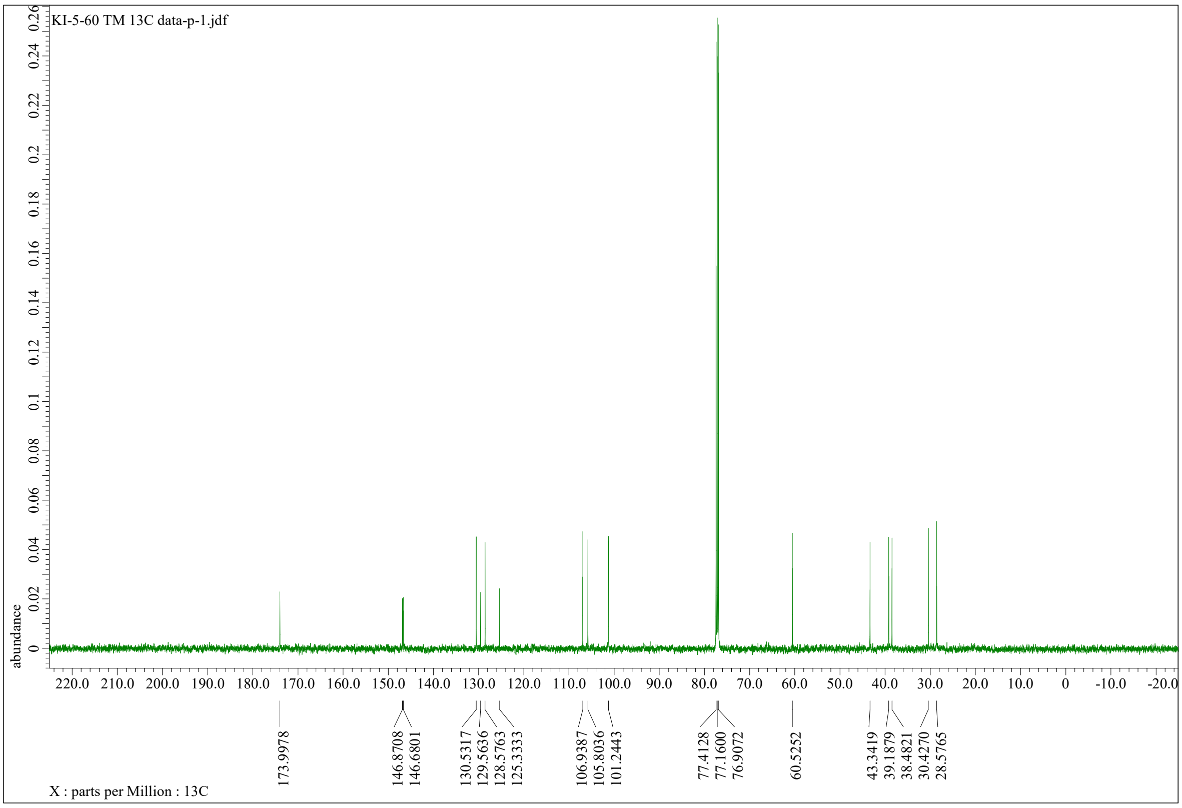
^{1}H (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) charts of compound **18**.



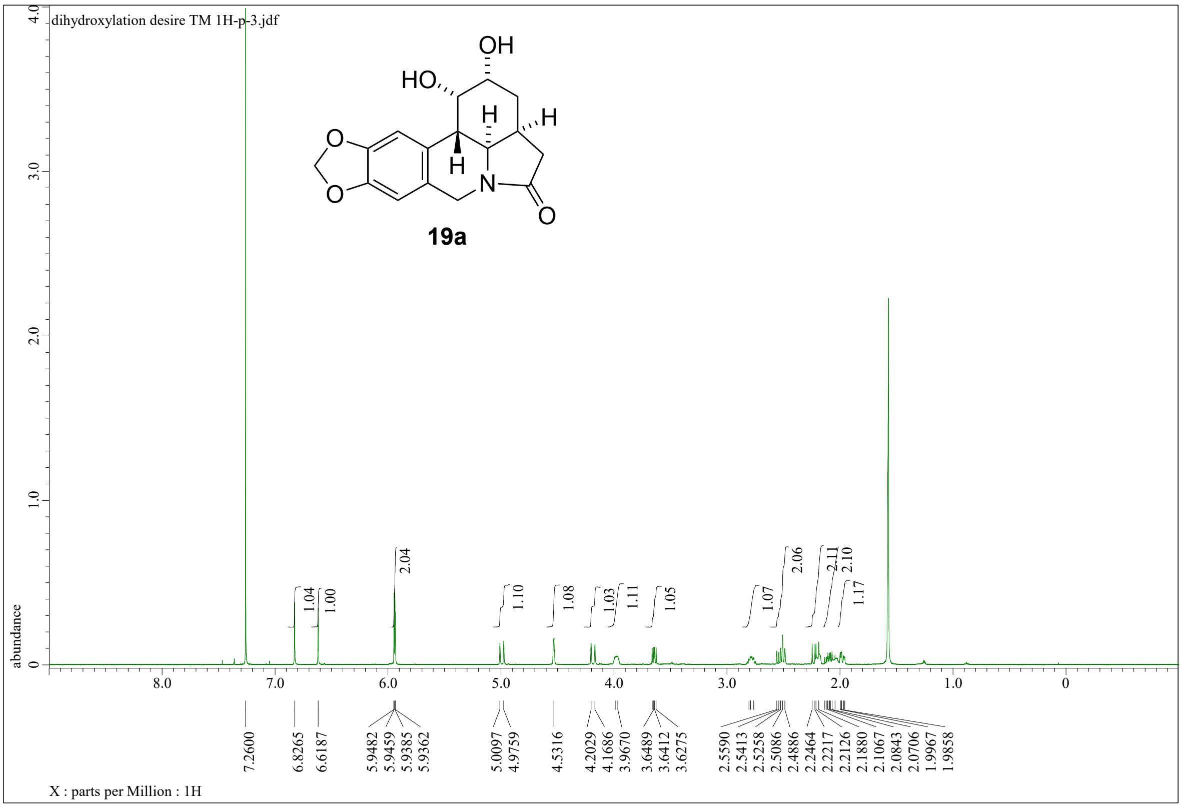


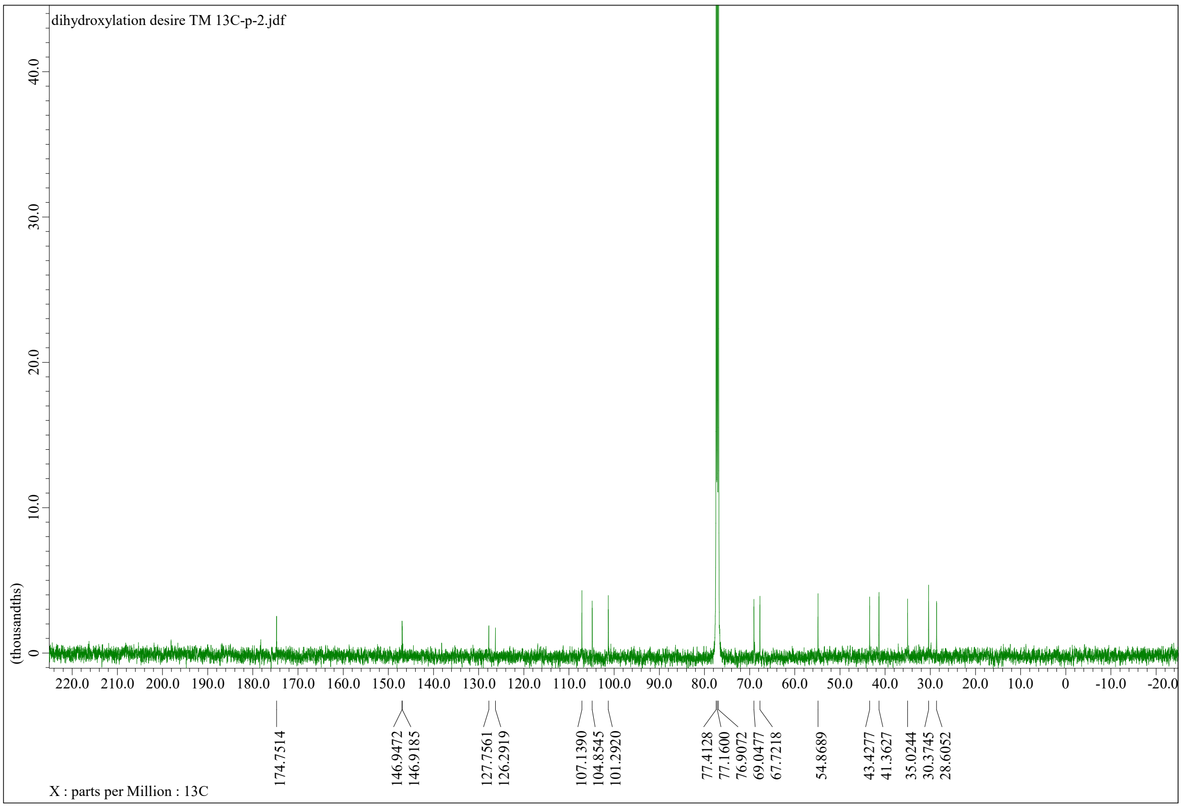
^{1}H (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) charts of compound **2**.



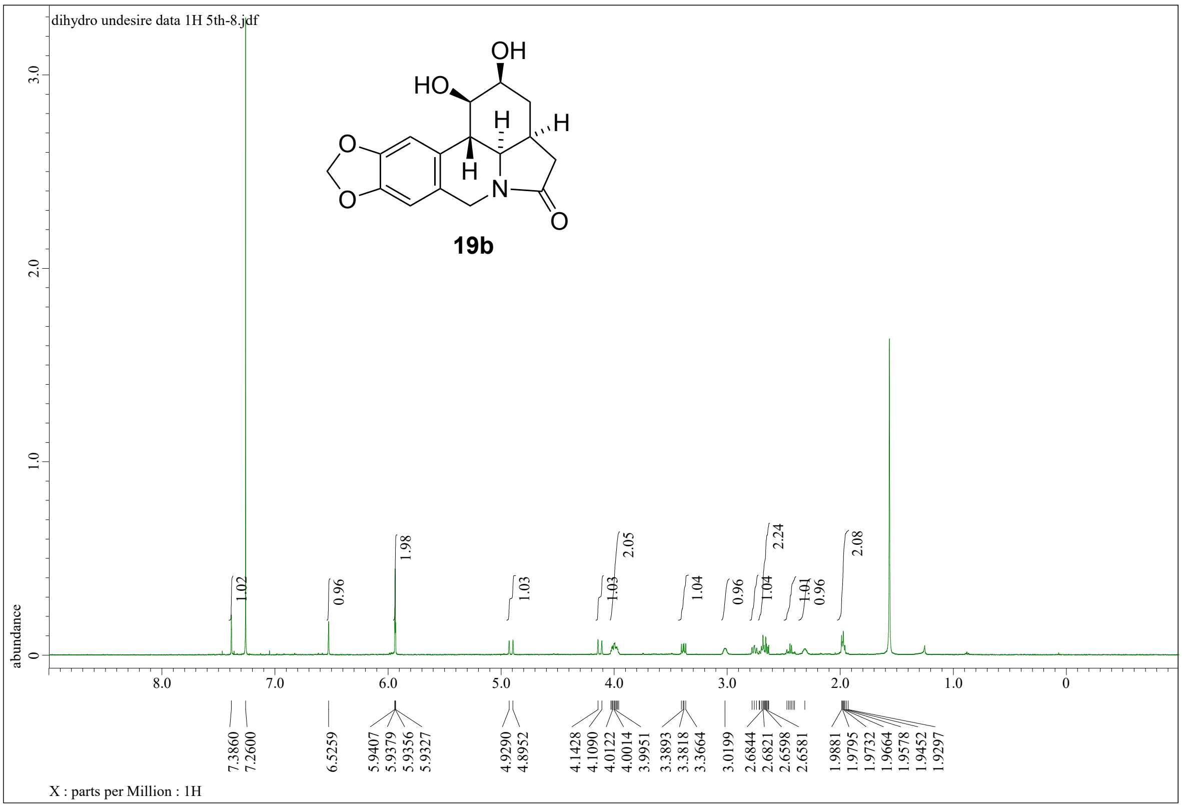


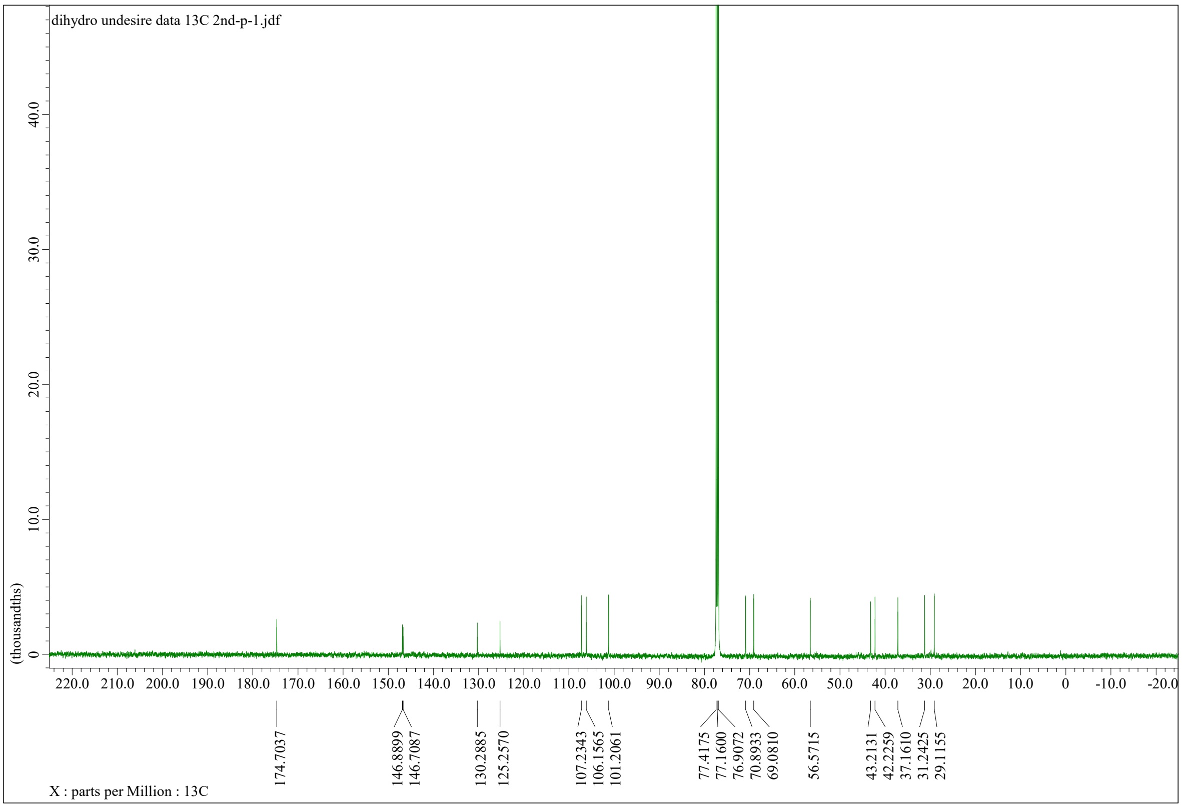
^{1}H (500 MHz, CDCl$_3$) and ^{13}C NMR (125 MHz, CDCl$_3$) charts of compound **19a**.





^{1}H (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) charts of compound **19b**.





^{1}H (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) charts of (–)-zephyranthine **1**.