

Supplementary Information

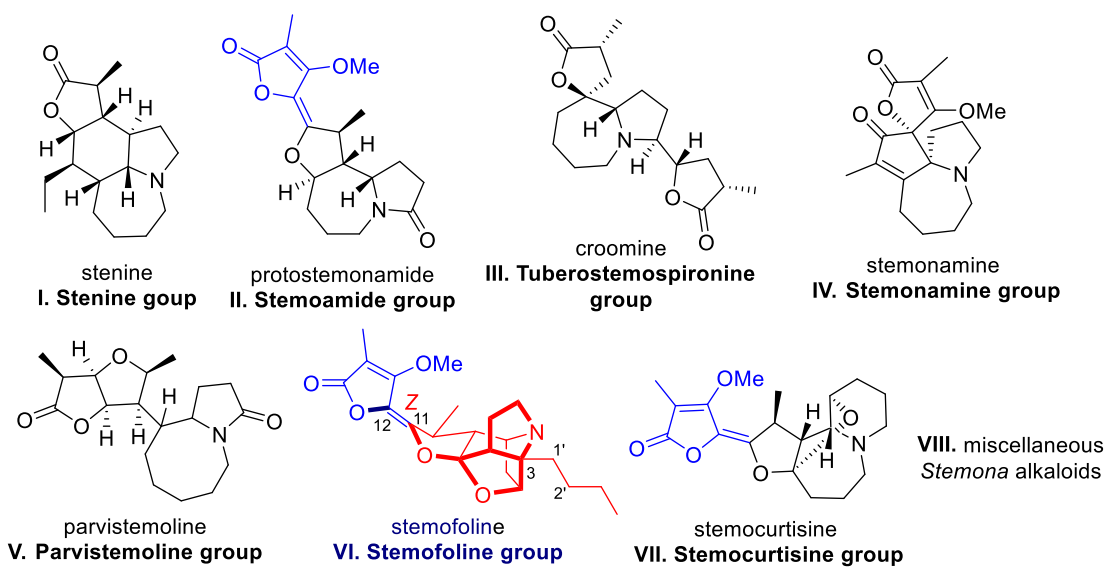
Enantioselective Total Syntheses of (+)-Stemofoline and Three Congeners Based on a Biogenetic Hypothesis

Huang *et al.*

Table of Contents

Eight Structural Groups of <i>Stemona</i> Alkaloids	2
General Information	3
Experimental Procedures	4
Comparison of ¹ H and ¹³ C NMR Data of Our Synthetic Compounds (1 , 2 , 7 - 9) with Those of Reported Data	29
NOESY Spectra of Compounds 24 , 13 , 12 , and 31	38
Single-Crystal X-Ray Diffraction Analysis of 30	45
NMR Spectra of the Synthesized Compounds in This Article	48
Supplementary References	104

Supplementary Note 1



Supplementary Figure 1. Eight structural groups of *Stemona* alkaloids

Supplementary Note 2

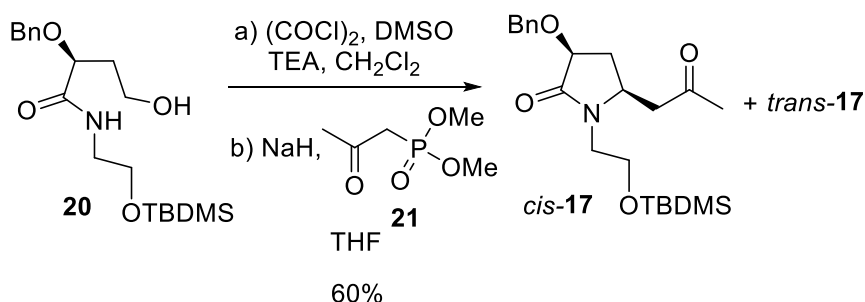
General Information

All reactions were carried out under a nitrogen atmosphere under anhydrous conditions and all reagents were purchased from commercial suppliers without further purification. Solvent purification was conducted according to Purification of Laboratory Chemicals (Peerrin, D. D.; Armarego, W. L. and Perrins, D. R., Pergamon Press: Oxford, 1980). Reactions were monitored by Thin Layer Chromatography on plates (GF254) supplied by Yantai Chemicals (China) visualized by ultraviolet or stained with ethanolic solution of phosphomolybdic acid and cerium sulfate or iodine vapour. Flash column chromatography was performed using Qindao Haiyang Chemicals silica gel (200-300 mesh), eluting (unless otherwise stated) with EtOAc/ *n*-hexane (Hex) or EtOAc/ petroleum ether mixture (bp. 60-90 °C) (PE). NMR spectra were recorded on Bruker AV III 400, Bruker AV III 500, Bruker AV III 850 instruments and calibrated by using tetramethyl silane (TMS) ($\delta\text{H} = 0.00$ p.p.m.) and CDCl_3 ($\delta\text{C} = 77.00$ p.p.m.) as internal references. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, dd = double doublet, td = triple doublet, dt = double triplet, dq = doubl quartet, m = multiplet. Infrared (IR) spectra were measured with Nicolet FT-380 spectrometer using film KBr pellet techniques. High-resolution mass spectra analyses were performed on Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer (Bruker Daltonics) with 7 T magnet (Magnetex) and electrospray ionization (ESI) source (Apollo II, Bruker Daltonics) in positive ion mode. Optical rotations were measured using Anton Paar MCP-500 polarimeter. Melting points were uncorrected.

Supplementary Note 3

Experimental procedures

Synthesis of Compound *cis*-17



To a cooled solution ($-78\text{ }^{\circ}\text{C}$) of oxalyl chloride (4.26 mL, 49.7 mmol) in CH_2Cl_2 (110 mL) under a nitrogen atmosphere was added dropwise a solution of DMSO (7.04 mL, 99.4 mmol) in CH_2Cl_2 (23 mL). After being stirred for 15 min at $-78\text{ }^{\circ}\text{C}$, a solution of compound **20** (16.57 g, 45.2 mmol) (compound **20** was prepared from the addition of commercially available (*S*)- α -benzyloxy- γ -lactone (*S*)-**18** with *O*-silylated β -aminoethanol **19**)^[1] in CH_2Cl_2 (45 mL) was added dropwise. After being stirred at the same temperature for 30 min, Et_3N (31.4 mL, 226 mmol) was added. The reaction was stirred for 2.5 h at $-78\text{ }^{\circ}\text{C}$ before being quenched with ice-water (50 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 ($3 \times 200\text{ mL}$). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The presumed mixture of aldehyde amide and its ring-opening tautomer **A** was directly used in the next step without further purification.

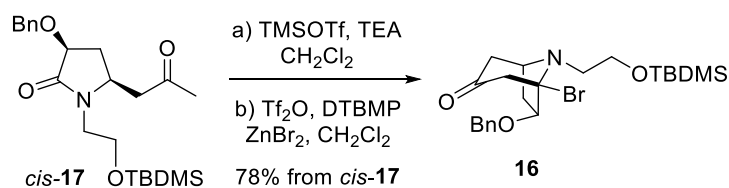
To a suspension of dimethyl acetylmethylphosphonate **21** (10.6 mL, 76.8 mmol) in THF (500 mL) at $0\text{ }^{\circ}\text{C}$ under a nitrogen atmosphere was added NaH (2.71 g, 67.8 mmol, 57-63% oil dispersion) and the mixture was stirred for 1 h. To the resulting mixture was added a solution of mixture **A** in THF (50 mL) at $0\text{ }^{\circ}\text{C}$. The reaction mixture was warmed to reflux and stirred overnight. Then the reaction was quenched with a saturated aqueous solution of NH_4Cl (100 mL). The organic layer was separated and

the aqueous layer was extracted with EtOAc (3 × 200 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and evaporated. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/2) to give compound *cis*-**17**^[1] (10.96 g, colorless oil, yield: 60% from **20**) and *trans*-**17**^[1] (3.85 g, colorless oil, yield: 21% from **20**).

Compound *cis*-**17**: [α]_D²⁰ −49.5 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 2953, 2929, 2857, 1697, 1454, 1421, 1376, 1255, 1098, 1027, 836, 778 cm^{−1}; **¹H NMR** (400 MHz, CDCl₃) δ 7.41–7.25 (m, 5H), 4.92 (d, *J* = 11.9 Hz, 1H), 4.72 (d, *J* = 11.9 Hz, 1H), 4.08–4.00 (m, 2H), 3.78–3.62 (m, 3H), 3.14 (dd, *J* = 17.6, 3.7 Hz, 1H), 3.11–3.05 (m, 1H), 2.62 (dd, *J* = 17.6, 9.8 Hz, 1H), 2.55 (dt, *J* = 13.7, 7.6 Hz, 1H), 2.14 (s, 3H), 1.63 (dt, *J* = 13.7, 5.0 Hz, 1H), 0.87 (s, 9H), 0.04 (d, *J* = 2.5 Hz, 6H); **¹³C NMR** (100 MHz, CDCl₃) δ 206.1, 172.8, 137.9, 128.3 (2C), 127.9 (2C), 127.7, 75.4, 72.0, 61.3, 52.5, 48.1, 43.5, 33.6, 30.6, 25.8 (3C), 18.1, −5.5 (2C); **HRMS** calcd for C₂₂H₃₅NO₄SiNa [M+Na⁺]: 428.2228; found: 428.2229.

Compound *trans*-**17**: [α]_D²⁰ −57.5 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 2950, 2928, 2857, 1715, 1459, 1253, 1098, 836, 775 cm^{−1}; **¹H NMR** (400 MHz, CDCl₃) δ 7.40–7.24 (m, 5H), 4.94 (d, *J* = 12.0 Hz, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.23–4.16 (m, 1H), 4.13 (t, *J* = 7.6 Hz, 1H), 3.80–3.70 (m, 2H), 3.62 (dt, *J* = 14.3, 4.8 Hz, 1H), 3.13–3.05 (m, 1H), 3.01 (dd, *J* = 17.4, 3.4 Hz, 1H), 2.41 (dd, *J* = 17.4, 9.6 Hz, 1H), 2.33–2.24 (m, 1H), 2.14 (s, 3H), 1.96 (ddd, *J* = 13.5, 7.6, 3.4 Hz, 1H), 0.88 (s, 9H), 0.05 (s, 6H); **¹³C NMR** (100 MHz, CDCl₃) δ 205.7, 172.9, 137.9, 128.3 (2C), 127.9 (2C), 127.6, 74.5, 71.9, 61.4, 52.4, 47.1, 43.6, 33.4, 30.5, 25.8 (3C), 18.2, −5.47, −5.52; **HRMS** calcd for C₂₂H₃₅NO₄SiNa [M+Na⁺]: 428.2228; found: 428.2232.

Synthesis of Compound 16



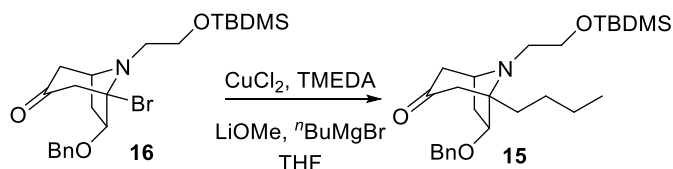
To a cooled solution (0 °C) of compound *cis*-**17** (4.98 g, 12.28 mmol) in anhydrous

CH₂Cl₂ (125 mL) under a nitrogen atmosphere were added Et₃N (4.27 mL, 30.7 mmol) and trimethylsilyl trifluoromethane sulfonate (TMSOTf) (4.44 mL, 24.56 mmol). After being stirred at 0 °C for 2 h, the reaction mixture was quenched with a saturated aqueous solution of NaHCO₃ (30 mL) and extracted with CH₂Cl₂ (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and evaporated to give an orange residue B, which was used in the next step without further purification.

To a cooled suspension (−78 °C) of the crude silyl enol ether B, 2,6-di-*tert*-butyl-4-methylpyridine (5.03 g, 24.56 mmol) and ZnBr₂ (5.53 g, 24.56 mmol) in anhydrous CH₂Cl₂ (250 mL) was added dropwise trifluoromethanesulfonic anhydride (Tf₂O) (2.43 mL, 14.73 mmol). After being stirred at −78 °C for 45 min, the mixture was warmed to room temperature slowly and then stirred for 1 h. The reaction was quenched with a saturated aqueous solution of NaHCO₃ (50 mL) and extracted with CH₂Cl₂ (3 × 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE = 1/10) to give bromide **16** (4.51 g, yield: 78% from *cis*-**17**) as a colorless oil.

Compound **16**: [α]_D²⁰ −53.5 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 2951, 2926, 2854, 1722, 1597, 1461, 1404, 1254, 1190, 1098, 893, 835, 775, 730, 693 cm^{−1}; **¹H NMR** (400 MHz, CDCl₃) δ 7.40–7.25 (m, 5H), 4.78 (d, *J* = 12.2 Hz, 1H), 4.68 (d, *J* = 12.2 Hz, 1H), 4.48 (dd, *J* = 10.4, 3.3 Hz, 1H), 3.90–3.76 (m, 3H), 3.34 (dt, *J* = 13.2, 5.0 Hz, 1H), 3.27 (d, *J* = 16.4 Hz, 1H), 2.95 (d, *J* = 16.4 Hz, 1H), 2.90–2.79 (m, 2H), 2.52–2.43 (m, 1H), 2.15 (d, *J* = 17.3 Hz, 1H), 1.36 (dd, *J* = 13.5, 3.3 Hz, 1H), 0.90 (s, 9H), 0.08 (s, 6H) ppm; **¹³C NMR** (100 MHz, CDCl₃) δ 204.5, 137.6, 128.3 (2C), 127.6, 127.4 (2C), 86.4, 85.4, 72.3, 63.1, 53.2, 50.1, 45.5, 40.9, 35.8, 25.8 (3C), 18.1, −5.45, −5.49 ppm; **HRMS** calcd for C₂₂H₃₄BrNO₃SiNa [M+Na⁺]: 490.1389 and 492.1369; found: 490.1381 and 492.1370.

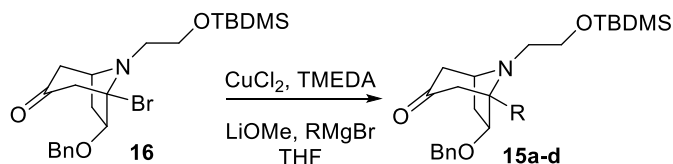
Synthesis of compound 15



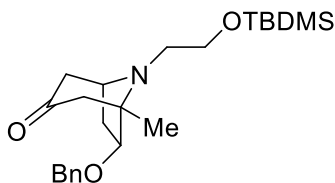
To a solution of the bromide **16** (2342 mg, 5.00 mmol), CuCl₂ (134 mg, 1.00 mmol), and LiOMe (228 mg, 6.00 mmol) in anhydrous THF (100 mL) under a nitrogen atmosphere was added *N,N,N',N'*-tetramethylethylenediamine (TMEDA) (0.32 mL, 2.00 mmol). After being stirred for 10 min, *n*-BuMgBr (14.7 mL, 12.5 mmol, 0.85 M in THF) was added dropwise, and the mixture was stirred for 30 min. The reaction was quenched with a saturated aqueous solution of NH₄Cl (50 mL), and the resulting mixture was stirred for 15 min under air until the aqueous phase turned blue. The mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE = 1/10) to give compound **15** (1810 mg, yield: 81%) as a colorless oil.

Compound **15**: [α]_D²⁰ +10.5 (*c* 1.0, CHCl₃); IR (film) ν_{max} : 2931, 2857, 1716, 1426, 1359, 1256, 1059, 835, 777, 697 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.34–7.22 (m, 5H), 4.56 (d, *J* = 12.1 Hz, 1H), 4.34 (d, *J* = 12.1 Hz, 1H), 3.80 (dd, *J* = 9.8, 3.5 Hz, 1H), 3.76–3.72 (m, 3H), 2.82–2.66 (m, 3H), 2.60 (d, *J* = 16.0 Hz, 1H), 2.32–2.23 (m, 1H), 2.10 (d, *J* = 16.4 Hz, 1H), 2.04 (d, *J* = 16.0 Hz, 1H), 1.55–1.48 (m, 1H), 1.39–1.31 (m, 2H), 1.28–1.19 (m, 3H), 1.14–1.06 (m, 1H), 0.89 (s, 9H), 0.85 (t, *J* = 7.0 Hz, 3H), 0.06 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ 209.0, 138.4, 128.2 (2C), 127.4 (3C), 80.4, 71.3, 67.1, 63.0, 55.4, 45.0, 44.0, 41.8, 35.6, 35.4, 25.9 (3C), 24.9, 23.3, 18.3, 14.0, –5.39, –5.41 ppm; HRMS calcd for C₂₆H₄₃NO₃SiNa [M+Na⁺]: 468.2904; found: 468.2905.

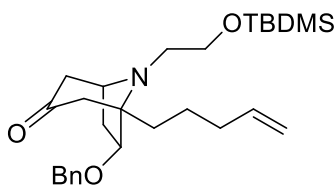
General Procedure for Synthesis of functionalized tropanone derivatives 15a-d



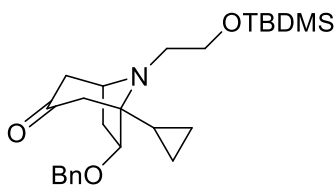
To a solution of the bromide **16** (0.30 mmol, 1.0 equiv), CuCl₂ (0.03 mmol, 0.10 equiv), and LiOMe (0.36 mmol, 1.2 equiv) in anhydrous THF (10 mL) under a nitrogen atmosphere was added *N,N,N',N'*-tetramethylethylenediamine (TMEDA) (0.06 mmol, 0.20 equiv). After being stirred for 10 min, an alkyl bromide (0.75 mmol, 2.5 equiv) was added dropwise, and the mixture was stirred for 30 min. The reaction was quenched with a saturated aqueous solution of NH₄Cl (5 mL), the resulting mixture was stirred for 15 min under air until the aqueous phase turned blue. The mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE = 1/10) to give an alkylated product **15a-d**.



Compound **15a**: (colorless oil, yield: 76%); [α]_D²⁰ −2.7 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 2955, 2929, 2856, 1716, 1426, 1256, 1100, 835, 777, 697 cm^{−1}; **¹H NMR** (500 MHz, CDCl₃) δ 7.35–7.24 (m, 5H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.39 (d, *J* = 12.1 Hz, 1H), 3.77–3.72 (m, 3H), 3.65 (dd, *J* = 9.8, 3.8 Hz, 1H), 2.79 (dd, *J* = 6.3, 6.3 Hz, 2H), 2.75 (dd, *J* = 16.3, 3.8 Hz, 1H), 2.57 (dd, *J* = 16.3, 1.2 Hz, 1H), 2.38–2.29 (m, 1H), 2.12 (d, *J* = 16.3 Hz, 1H), 2.08 (d, *J* = 16.3 Hz, 1H), 1.33 (dd, *J* = 13.6, 3.8 Hz, 1H), 1.17 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 208.9, 138.4, 128.3 (2C), 127.4, 127.3 (2C), 84.4, 71.7, 64.8, 63.4, 55.9, 45.4, 44.1, 41.7, 35.4, 25.9 (3C), 23.6, 18.3, −5.37, −5.40 ppm; **HRMS** calcd for C₂₃H₃₇NO₃SiNa [*M*+Na⁺]: 426.2435; found: 426.2440.

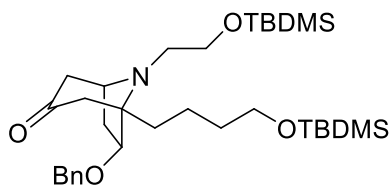


Compound **15b**: (colorless oil, yield: 75%); $[\alpha]_D^{20} +13.5$ (*c* 1.0, CHCl₃); **IR** (film) $\nu_{\max}$: 3065, 2930, 2857, 1716, 1640, 1471, 1257, 1100, 835, 777, 738, 698 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 7.34–7.24 (m, 5H), 5.71 (dddd, *J* = 16.9, 10.1, 6.8, 6.8 Hz, 1H), 5.00–4.92 (m, 2H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.33 (d, *J* = 12.1 Hz, 1H), 3.79 (dd, *J* = 9.7, 3.3 Hz, 1H), 3.77–3.72 (m, 3H), 2.79 (dd, *J* = 14.1, 3.3 Hz, 1H), 2.75 (dt, *J* = 12.7, 6.4 Hz, 1H), 2.69 (dt, *J* = 12.7, 6.0 Hz, 1H), 2.60 (d, *J* = 16.0 Hz, 1H), 2.32–2.24 (m, 1H), 2.11 (d, *J* = 16.6 Hz, 1H), 2.04 (d, *J* = 16.0 Hz, 1H), 1.98 (d, *J* = 6.8 Hz, 1H), 1.95 (d, *J* = 6.8 Hz, 1H), 1.56–1.48 (m, 1H), 1.41–1.32 (m, 3H), 1.28–1.20 (m, 1H) 0.89 (s, 9H), 0.06 (s, 6H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 208.9, 138.4, 138.3, 128.3 (2C), 127.5, 127.4 (2C), 114.8, 80.4, 71.3, 67.1, 63.0, 55.4, 45.0, 44.0, 41.8, 35.4, 35.3, 34.1, 25.9 (3C), 22.1, 18.3, –5.36, –5.38 ppm; **HRMS** calcd for C₂₇H₄₃NO₃SiNa [M+Na⁺]: 480.2904; found: 480.2905.



Compound **15c**: (colorless oil, yield: 78%); $[\alpha]_D^{20} -5.3$ (*c* 1.0, CHCl₃); **IR** (film) $\nu_{\max}$: 2954, 2928, 2856, 1717, 1462, 1360, 1255, 1098, 835, 777, 697 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 7.34–7.23 (m, 5H), 4.54 (d, *J* = 12.2 Hz, 1H), 4.38 (d, *J* = 12.2 Hz, 1H), 3.83–3.72 (m, 3H), 3.67 (dd, *J* = 8.8, 3.5 Hz, 1H), 3.08 (ddd, *J* = 12.7, 6.6, 6.3 Hz, 1H), 2.82 (dd, *J* = 13.3, 6.6 Hz, 1H), 2.80–2.74 (m, 1H), 2.37–2.30 (m, 1H), 2.29 (dd, *J* = 15.8, 1.5 Hz, 1H), 2.10 (dt, *J* = 16.4, 1.5 Hz, 1H), 1.93 (d, *J* = 15.8 Hz, 1H), 1.38–1.32 (m, 2H), 0.90 (s, 9H), 0.83–0.76 (m, 1H), 0.50–0.44 (m, 1H), 0.37–0.30 (m, 2H), 0.07 (s, 6H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 208.8, 138.4, 128.2 (2C), 127.3 (3C), 82.9, 71.5, 68.8, 63.5, 55.8, 45.9, 42.1, 39.4, 35.7, 25.9 (3C), 18.3, 17.3, –1.1, –1.0, –5.35, –5.36 ppm; **HRMS** calcd for C₂₅H₃₉NO₃SiNa [M+Na⁺]: 452.2591; found:

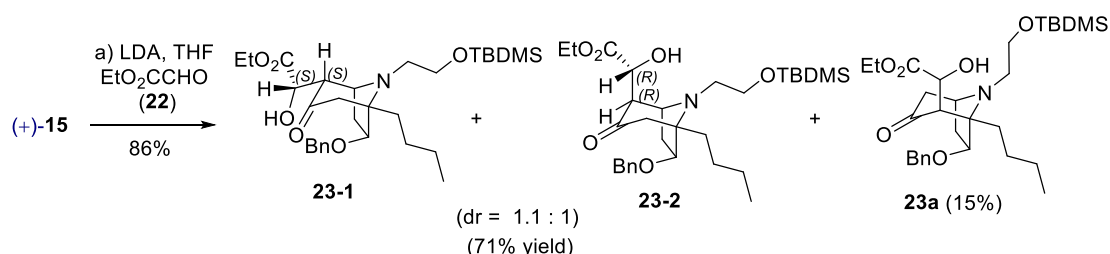
452.2594.



Compound **15d**: (colorless oil, yield: 85%); $[\alpha]_D^{20} +5.7$ (c 1.0, CHCl_3); **IR** (film) ν_{max} : 2953, 2929, 2857, 1716, 1463, 1361, 1256, 1100, 836, 776, 698 cm^{-1} ; **^1H NMR** (500 MHz, CDCl_3) δ 7.36–7.24 (m, 5H), 4.57 (d, $J = 12.1$ Hz, 1H), 4.37 (d, $J = 12.1$ Hz, 1H), 3.82 (dd, $J = 9.8, 3.5$ Hz, 1H), 3.79–3.75 (m, 3H), 3.57 (dd, $J = 6.5, 6.5$ Hz, 2H), 2.85–2.69 (m, 3H), 2.63 (d, $J = 16.1$ Hz, 1H), 2.34–2.25 (m, 1H), 2.12 (d, $J = 16.5$ Hz, 1H), 2.06 (d, $J = 16.1$ Hz, 1H), 1.57 (ddd, $J = 13.8, 12.3, 4.6$ Hz, 1H), 1.50–1.42 (m, 2H), 1.42–1.32 (m, 3H), 1.25–1.18 (m, 1H), 0.92 (s, 9H), 0.91 (s, 9H), 0.08 (s, 6H), 0.05 (s, 6H) ppm; **^{13}C NMR** (125 MHz, CDCl_3) δ 208.9, 138.4, 128.2 (2C), 127.4, 127.3 (2C), 80.7, 71.4, 67.1, 63.2, 62.9, 55.4, 45.0, 43.9, 41.8, 35.9, 35.5, 33.4, 26.0 (3C), 25.9 (3C), 19.2, 18.30, 18.26, -5.3 (2C), -5.38 , -5.41 ppm; **HRMS** calcd for $\text{C}_{32}\text{H}_{57}\text{NO}_4\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}^+]$: 598.3718; found: 598.3724.

Asymmetric Total Synthesis of Stemofoline alkaloids (+)-Stemoburkilline (7), (+)-(11*S*,12*R*)-Dihydrostemofoline (8), and unnatural diastereomer (+)-(11*S*,12*S*)-Dihydrostemofoline (9)

Synthesis of Compound 23-1 and 23-2



To a cooled solution (-78°C) of lithium diisopropylamide (LDA) (3.54 mL, 7.08 mmol, 2.0 M in THF) was added a solution of compound **15** (1050 mg, 2.36 mmol) in anhydrous THF (50 mL) under a nitrogen atmosphere. After being stirred at the same

temperature for 30 min, ethyl glyoxylate **22** (1.47 mL, 7.08 mmol, *ca.* 50% in toluene, v/v) was slowly added, and then mixture was stirred for 1.5 h at the same temperature. The reaction was quenched with a saturated aqueous solution of NH₄Cl (20 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/5) to give two diastereomers **23-1** (475 mg, colorless oil, yield: 37%) and **23-2** (440 mg, colorless oil, yield: 34%) as well as with regioisomer **23a** (single diastereomer, 193 mg, colorless oil, yield: 15%). The diastereomeric mixture **23-1** and **23-2** was used in the next step without separation.

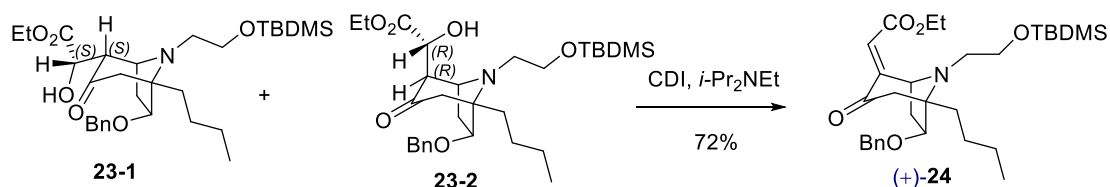
Compound **23-1**: [α]_D²⁰ -3.3 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 3508, 2955, 2930, 2857, 1738, 1714, 1463, 1257, 1009, 936, 836, 778, 737, 698 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 7.34–7.23 (m, 5H), 4.57 (d, *J* = 12.2 Hz, 1H), 4.32 (d, *J* = 12.2 Hz, 1H), 4.30–4.20 (m, 2H), 4.11–4.07 (m, 1H), 3.81–3.72 (m, 4H), 3.45 (d, *J* = 7.0 Hz, 1H), 3.34–3.31 (m, 1H), 2.84 (dt, *J* = 13.0, 6.3 Hz, 1H), 2.74 (dt, *J* = 13.0, 6.6 Hz, 1H), 2.62 (d, *J* = 15.5 Hz, 1H), 2.20–2.14 (m, 1H), 2.07 (dd, *J* = 13.8, 3.4 Hz, 1H), 2.04 (d, *J* = 15.5 Hz, 1H), 1.55–1.48 (m, 1H), 1.36–1.31 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.30–1.26 (m, 1H), 1.26–1.20 (m, 2H), 1.12–1.07 (m, 1H), 0.90 (s, 9H), 0.85 (t, *J* = 7.2 Hz, 3H), 0.07 (s, 6H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 208.7, 173.0, 138.4, 128.3 (2C), 127.4 (3C), 80.4, 71.5, 70.2, 68.2, 63.1, 61.7, 60.0, 50.6, 44.8, 44.2, 35.3, 32.3, 25.9 (3C), 25.0, 23.3, 18.4, 14.1, 13.9, -5.3 (2C) ppm; **HRMS** calcd for C₃₀H₄₉NO₆SiNa [*M*+Na⁺]: 570.3221; found: 570.3228.

Compound **23-2**: [α]_D²⁰ +2.4 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 3460, 2929, 2857, 1714, 1463, 1258, 1098, 1029, 856, 778, 698 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 7.34–7.23 (m, 5H), 4.79 (t, *J* = 4.9 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 4.30 (d, *J* = 12.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.78 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.73–3.65 (m, 2H), 3.61 (dd, *J* = 7.3, 3.5 Hz, 1H), 3.22–3.18 (m, 1H), 2.82–2.71 (m, 2H), 2.68 (d, *J* = 4.9 Hz, 1H), 2.65 (d, *J* = 15.2 Hz, 1H), 2.20–2.12 (m, 1H), 2.09 (d, *J* = 15.2 Hz, 1H), 1.87 (dd, *J* = 13.9, 3.5 Hz, 1H), 1.56–1.48 (m, 1H), 1.40–1.34 (m, 1H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.26–1.20 (m, 3H), 1.13–1.04 (m, 1H), 0.90 (s, 9H), 0.85 (t, *J* = 7.1 Hz, 3H), 0.06 (s,

6H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 207.0, 173.2, 138.4, 128.2 (2C), 127.4 (3C), 80.4, 71.2, 68.6, 68.3, 62.4, 61.7, 57.4, 50.5, 45.1, 44.2, 35.4, 32.6, 25.9 (3C), 25.0, 23.2, 18.4, 14.2, 14.0, -5.31, -5.33 ppm; HRMS calcd for $\text{C}_{30}\text{H}_{49}\text{NO}_6\text{SiNa}$ $[\text{M}+\text{Na}^+]$: 570.3221; found: 570.3223.

Compound **23a**: $[\alpha]_{\text{D}}^{20} +1.1$ (*c* 1.0, CHCl_3); IR (film) ν_{max} : 3490, 2956, 2929, 2857, 1721, 1463, 1258, 1098, 1029, 854, 777, 698 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.23 (m, 5H), 4.61–4.56 (m, 2H), 4.35 (d, $J = 12.0$ Hz, 1H), 4.28–4.20 (m, 2H), 3.88 (dd, $J = 9.2, 2.2$ Hz, 1H), 3.79–3.68 (m, 3H), 2.27–2.25 (m, 1H), 2.98 (dt, $J = 12.5, 6.4$ Hz, 1H), 2.84–2.77 (m, 1H), 2.47–2.36 (m, 3H), 1.97–1.89 (m, 1H), 1.65–1.56 (m, 2H), 1.31 (t, $J = 7.3$ Hz, 3H), 1.31–1.24 (m, 5H), 0.90–0.86 (m, 12H), 0.06 (s, 6H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 207.0, 172.3, 137.5, 128.3 (2C), 127.7, 127.6 (2C), 84.4, 72.1, 71.0, 70.9, 63.0, 61.1, 57.3, 54.0, 49.6, 48.7, 34.8, 33.7, 25.9 (3C), 25.5, 23.4, 18.3, 14.2, 13.8, -5.43, -5.45 ppm; HRMS calcd for $\text{C}_{30}\text{H}_{49}\text{NO}_6\text{SiNa}$ $[\text{M}+\text{Na}^+]$: 570.3221; found: 570.3230.

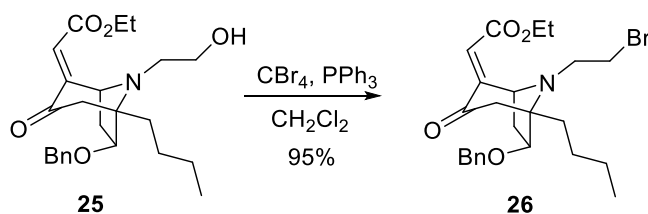
Synthesis of Compound 24



To a cooled solution (0 °C) of diastereomeric **23-1** and **23-2** (1090 mg, 2.00 mmol) in anhydrous CH_2Cl_2 (40 mL) were added successively *N,N*-4-(dimethylamino)pyridine (DMAP) (244 mg, 2.00 mmol), *i*-Pr₂NEt (2.31 mL, 14.0 mmol), and a solution of *N,N*-carbonyldiimidazole (CDI) (1620 mg, 10.0 mmol) in CH_2Cl_2 (10 mL) under a nitrogen atmosphere. After being stirred for 4 h, the reaction was quenched with a saturated aqueous solution of NaHCO_3 (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 $\times$ 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/10) to give compound **24** (762 mg, yield: 72%) as a colorless oil.

12.0 Hz, 1H), 4.37 (d, $J = 12.0$ Hz, 1H), 4.23 (dq, $J = 10.9, 7.1$ Hz, 1H), 4.21 (dq, $J = 10.9, 7.1$ Hz, 1H), 3.95 (dd, $J = 9.0, 2.5$ Hz, 1H), 3.69 (ddd, $J = 10.6, 10.6, 3.4$ Hz, 1H), 3.58–3.47 (m, 1H), 3.01 (d, $J = 18.2$ Hz, 1H), 2.83 (ddd, $J = 15.1, 10.6, 5.1$ Hz, 1H), 2.55–2.47 (m, 3H), 2.20 (d, $J = 18.2$ Hz, 1H), 1.62–1.54 (m, 2H), 1.43–1.35 (m, 1H), 1.29 (t, $J = 7.1$ Hz, 3H), 1.30–1.20 (m, 3H), 1.19–1.10 (m, 1H), 0.86 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 198.2, 165.8, 151.2, 137.8, 128.3 (2C), 127.6, 127.4 (2C), 122.6, 80.7, 71.4, 65.7, 60.9, 58.9, 55.2, 45.2, 43.1, 36.14, 36.10, 25.0, 23.1, 14.1, 13.9 ppm; HRMS calcd for $\text{C}_{24}\text{H}_{33}\text{NO}_5\text{Na}$ [$\text{M}+\text{Na}^+$]: 438.2251; found: 438.2249.

Synthesis of Compound 26

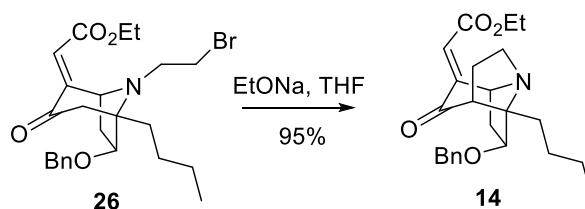


To a cooled solution (0 °C) of alcohol **25** (1910 mg, 4.60 mmol) in anhydrous CH_2Cl_2 (50 mL) were added CBr_4 (1980 mg, 5.98 mmol) and PPh_3 (2500 mg, 6.90 mmol) under a nitrogen atmosphere. The resulting mixture was stirred at 0 °C for 30 min and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel ($\text{EtOAc/PE} = 1/10$) to give bromide **26** (2080 mg, yield: 95%) as a colorless oil.

Compound **26**: $[\alpha]_{\text{D}}^{20} +87.9$ (c 1.0, CHCl_3); IR (film) ν_{max} : 3029, 2956, 2931, 2868, 1701, 1453, 1368, 1236, 1181, 1130, 1028, 883, 737, 698 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.22 (m, 5H), 6.58 (s, 1H), 5.22 (d, $J = 7.8$ Hz, 1H), 4.56 (d, $J = 12.1$ Hz, 1H), 4.36 (d, $J = 12.1$ Hz, 1H), 4.23 (dq, $J = 11.0, 7.1$ Hz, 1H), 4.21 (dq, $J = 11.0, 7.1$ Hz, 1H), 3.93 (dd, $J = 9.0, 2.8$ Hz, 1H), 3.44 (ddd, $J = 9.6, 9.6, 4.6$ Hz, 1H), 3.36 (ddd, $J = 9.6, 7.9, 7.9$ Hz, 1H), 3.00 (d, $J = 18.1$ Hz, 1H), 2.94 (ddd, $J = 13.1, 7.9, 4.6$ Hz, 1H), 2.78 (ddd, $J = 13.1, 9.6, 7.9$ Hz, 1H), 2.52 (ddd, $J = 13.8, 9.0, 7.8$ Hz, 1H), 2.18 (d, $J = 18.1$ Hz, 1H), 1.59–1.54 (m, 1H), 1.51 (dd, $J = 13.8, 2.8$ Hz, 1H), 1.43–1.35 (m, 1H), 1.31 (t, $J = 7.1$ Hz, 3H), 1.29–1.22 (m, 3H), 1.19–1.09 (m, 1H), 0.87 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 198.4, 165.9, 151.5, 137.9, 128.3

(2C), 127.6, 127.4 (2C), 122.3, 80.4, 71.4, 65.9, 60.9, 55.7, 45.9, 43.4, 36.0, 35.9, 30.4, 25.0, 23.2, 14.1, 13.9 ppm; **HRMS** calcd for C₂₄H₃₂BrNO₄Na [M+Na⁺]: 500.1407 and 502.1386; found: 500.1406 and 502.1384.

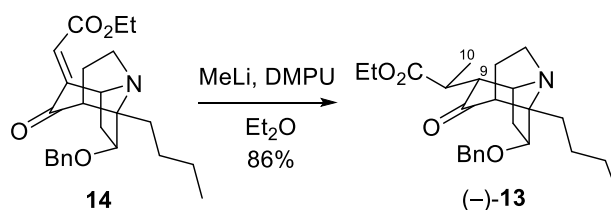
Synthesis of Compound 14



To a cooled solution (0 °C) of bromide **26** (2080 mg, 4.36 mmol) in anhydrous THF (100 mL) was added under a nitrogen atmosphere a freshly prepared NaOEt (10.5 mL, 5.23 mmol, 0.5 M in THF and EtOH). The resulting mixture was stirred at the same temperature for 20 min, then quenched with a saturated aqueous solution of NH₄Cl (40 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 2/1) to give compound **14** (1640 mg, yield: 95%) as a colorless oil.

Compound **14**: [α]_D²⁰ +27.3 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 3029, 2957, 2933, 1707, 1454, 1236, 1180, 1098, 1030, 975, 735, 697 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 7.35–7.21 (m, 5H), 6.63 (s, 1H), 5.01 (d, *J* = 6.1 Hz, 1H), 4.54 (d, *J* = 12.3 Hz, 1H), 4.37 (d, *J* = 12.3 Hz, 1H), 4.22 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.19 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.08 (d, *J* = 7.3 Hz, 1H), 3.06 (dd, *J* = 13.5, 3.6 Hz, 1H), 3.04 (d, *J* = 6.7 Hz, 1H), 2.95 (ddd, *J* = 13.5, 8.7, 6.7 Hz, 1H), 2.37 (ddd, *J* = 13.3, 6.7, 6.7 Hz, 1H), 2.32–2.23 (m, 1H), 1.83 (d, *J* = 13.4 Hz, 1H), 1.77 (ddd, *J* = 13.3, 8.7, 3.6 Hz, 1H), 1.57–1.50 (m, 1H), 1.40–1.20 (m, 5H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 198.8, 165.8, 153.3, 137.7, 128.3 (2C), 127.5, 127.3 (2C), 122.4, 82.0, 78.9, 71.6, 63.6, 60.7, 55.7, 46.1, 38.9, 33.9, 30.9, 26.1, 23.1, 14.1, 13.9 ppm; **HRMS** calcd for C₂₄H₃₁NO₄Na [M+Na⁺]: 420.2145; found: 420.2139.

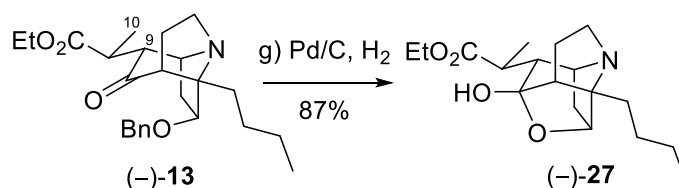
Synthesis of Compound 13



To a cooled solution ($-40\text{ }^{\circ}\text{C}$) of compound **14** (1640 mg, 4.13 mmol) in anhydrous ether (50 mL) under nitrogen atmosphere was added 1,3-dimethyl-tetrahydropyrimidin-2(1*H*)-one (DMPU) (0.55 mL, 4.54 mmol). After being stirred for 10 min, methyllithium (MeLi) (3.25 mL, 4.54 mmol, 1.4 M in ether) was added dropwise. The reaction mixture was stirred at the same temperature for 20 min, then quenched with a saturated aqueous solution of NH_4Cl (40 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc ($3 \times 50\text{ mL}$). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hex. = 2/1) to give compound **13** (1460 mg, yield: 86%) as a colorless oil (single diastereomer as seen for NMR spectra).

Compound **13**: $[\alpha]_{\text{D}}^{20} -24.9$ (c 1.0, CHCl_3); **IR** (film) ν_{max} : 3036, 2935, 1716, 1673, 1455, 1378, 1262, 1183, 1102, 1072, 1029, 973, 736, 698 cm^{-1} ; **^1H NMR** (500 MHz, CDCl_3) δ 7.35–7.24 (m, 5H), 4.52 (d, $J = 12.2\text{ Hz}$, 1H), 4.38 (d, $J = 12.2\text{ Hz}$, 1H), 4.24 (dq, $J = 10.8, 7.1\text{ Hz}$, 1H), 4.16 (dq, $J = 10.8, 7.1\text{ Hz}$, 1H), 4.00 (d, $J = 8.3\text{ Hz}$, 1H), 3.48 (t, $J = 5.9\text{ Hz}$, 1H), 3.18 (ddd, $J = 13.7, 8.6, 5.5\text{ Hz}$, 1H), 3.11 (ddd, $J = 13.7, 9.9, 4.3\text{ Hz}$, 1H), 2.92 (dd, $J = 10.5, 5.6\text{ Hz}$, 1H), 2.76 (d, $J = 6.5\text{ Hz}$, 1H), 2.54 (ddd, $J = 14.3, 10.5, 7.3\text{ Hz}$, 1H), 2.20–2.10 (m, 1H), 2.07–2.00 (m, 1H), 1.75 (ddd, $J = 13.9, 8.6, 4.3\text{ Hz}$, 1H), 1.60 (d, $J = 13.9\text{ Hz}$, 1H), 1.52–1.45 (m, 1H), 1.31 (t, $J = 7.1\text{ Hz}$, 3H), 1.28–1.15 (m, 5H), 1.05 (d, $J = 7.1\text{ Hz}$, 3H), 0.85 (t, $J = 7.1\text{ Hz}$, 3H) ppm; **^{13}C NMR** (125 MHz, CDCl_3) δ 207.3, 176.5, 138.0, 128.2 (2C), 127.42 (2C), 127.40, 81.5, 79.0, 71.7, 62.4, 60.5, 54.8, 48.4, 45.7, 37.6, 33.7, 32.5, 31.0, 25.9, 23.1, 14.4, 14.1, 13.9 ppm; **HRMS** calcd for $\text{C}_{25}\text{H}_{35}\text{NO}_4\text{Na}$ [$\text{M}+\text{Na}^+$]: 436.2458; found: 436.2457.

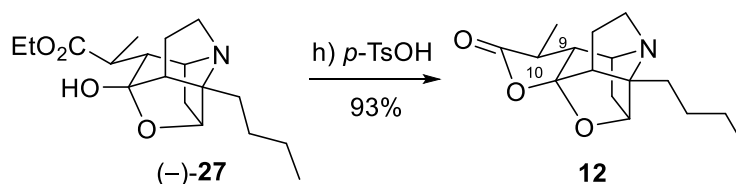
Synthesis of Compound 27



A suspension of compound **13** (1460 mg, 3.54 mmol) and 10% Pd/C (730 mg) in ethanol (50 mL) was stirred under an atmosphere of H₂ for 2 days at room temperature. The mixture was filtered through a Celite pad by washing with methanol. The solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 4/1) to afford compound **27** (995 mg, yield: 87%) as a colorless oil.

Compound **27**: $[\alpha]_{\text{D}}^{20} -0.8$ (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 3373, 2957, 2931, 1733, 1463, 1377, 1319, 1290, 1262, 1175, 1140, 1086, 1032, 979, 948, 912, 819, 757, 656 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.29 (br s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.27 (br s, 1H), 3.10-2.97 (m, 2H), 2.82-2.74 (m, 1H), 2.20 (dd, *J* = 9.8, 3.6 Hz, 1H), 2.14 (d, *J* = 6.0 Hz, 1H), 1.91-1.85 (m, 2H), 1.82 (d, *J* = 12.0 Hz, 1H), 1.68-1.60 (m, 1H), 1.55-1.48 (m, 2H), 1.42-1.30 (m, 3H), 1.28-1.21 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.13 (d, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 178.0, 105.5, 82.0, 79.9, 62.5, 60.6, 55.8, 47.3, 41.2, 36.9, 33.6, 31.5, 27.3, 26.2, 23.2, 15.0, 14.04, 13.99 ppm; **HRMS** calcd for C₁₈H₂₉NO₄ [M+Na⁺]: 346.1989; found: 346.1986.

Synthesis of Compound **12** (two-step manner from Compound **13**)



A solution of compound **27** (995 mg, 3.08 mmol) and *p*-toluenesulfonic acid (PTSA) monohydrate (879 mg, 4.62 mmol) in toluene (30 mL) was stirred at 85 °C for 2 h. After being cooled down to room temperature, a saturated aqueous NaHCO₃ was added till pH = 8. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was

purified by flash chromatography on silica gel (CH₂Cl₂/MeOH= 20/1) to give compound **12** (775 mg, yield: 91%) as a colorless oil.

¹H NMR and ¹³C NMR data of **12** matched by-product by Kende's total synthesis of isostemofoline^[2] and semi-synthesis compound by Pyne and Ung^[3].

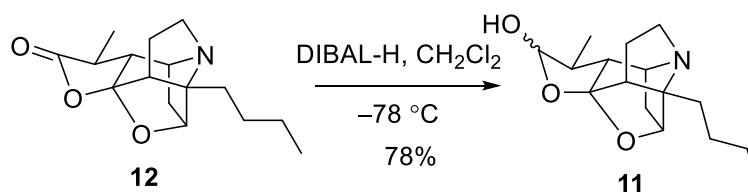
Compound **12**: [α]_D²⁰ +24.4 (*c* 1.0, CHCl₃) {lit^[3] [α]_D²⁰ +26.3 (*c* 0.21, CHCl₃) (semi-synthetic compound by Pyne and Ung)}; **IR** (film) ν_{max} : 2955, 2933, 2869, 1799, 1458, 1235, 1133, 1081, 1021, 980, 831, 751 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.33 (br s, 1H), 3.41 (br s, 1H), 3.15 (ddd, *J* = 13.6, 10.4, 5.4 Hz, 1H), 3.02 (ddd, *J* = 13.6, 8.5, 4.6 Hz, 1H), 2.81–2.73 (m, 1H), 2.65 (d, *J* = 6.2 Hz, 1H), 1.98 (d, *J* = 12.7 Hz, 1H), 1.96 (d, *J* = 12.7 Hz, 1H), 1.95–1.89 (m, 1H), 1.82 (ddd, *J* = 13.9, 8.5, 5.4 Hz, 1H), 1.78–1.72 (m, 1H), 1.63–1.50 (m, 2H), 1.45–1.39 (m, 1H), 1.38–1.30 (m, 2H), 1.25 (d, *J* = 7.0 Hz, 3H), 1.29–1.21 (m, 1H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 178.3, 109.1, 83.0, 78.8, 61.1, 50.1, 47.6, 45.6, 35.7, 32.8, 31.8, 27.2, 26.5, 23.1, 14.0, 13.2 ppm; **HRMS** calcd for C₁₆H₂₄NO₄ [*M*+H⁺]: 278.1751; found: 278.1747.

Synthesis of Compound **12** from Compound **13** without further purification

A suspension of compound **13** (1145 mg, 2.77 mmol) and 10% Pd/C (580 mg) in ethanol (50 mL) was stirred under an atmosphere of H₂ for 2 days at room temperature. The mixture was filtered through a Celite pad, and washed with ethanol. The solvent was removed under reduced pressure. The residue C was directly used in the next synthetic step without further purification.

A solution of the residue C and *p*-toluenesulfonic acid (PTSA) monohydrate (791 mg, 4.16 mmol) in toluene (30 mL) was stirred at 85 °C for 2 h. After being cooled down to room temperature, the resulting mixture was quenched with saturated aqueous solution of NaHCO₃ till pH reached 8. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (CH₂Cl₂/MeOH= 20/1) to give compound **12** (637 mg, yield: 83%, from compound **13**) as a colorless oil.

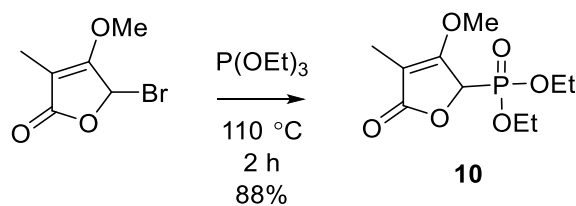
Synthesis of Compound 11



To a cooled solution ($-78\text{ }^{\circ}\text{C}$) of compound **12** (775 mg, 2.80 mmol) in anhydrous CH₂Cl₂ (50 mL) was added diisobutyl aluminium hydride (DIBAL-H) (3.10 mL, 3.10 mmol, 1.0 M in toluene) dropwise under a nitrogen atmosphere. After being stirred at the same temperature for 30 min, the reaction was quenched with a saturated aqueous solution of NH₄Cl (40 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ ($3 \times 50\text{ mL}$). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH = 10/1) to give lactol **11** (609 mg, yield: 78%) as an inseparable diastereoisomeric mixture (*d.r.* = 2.6: 1), which was used in the next step as it was.

Compound **11**: **IR** (film) ν_{max} : 3357, 2957, 2931, 2873, 1720, 1456, 1338, 1119, 1031, 931, 754, 687 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃, data of the diastereomeric mixture) δ 5.47 (d, J = 5.5 Hz, 0.3H), 5.01 (br s, 0.7H), 4.26 (s, 0.7H), 4.18 (br s, 0.3H), 4.18 (br s, 0.3H), 3.38 (br s, 0.3H), 3.33 (br s, 0.7H), 3.15–3.06 (m, 1H), 3.04–2.93 (m, 1H), 2.50–2.36 (m, 1.3H), 2.22–2.14 (m, 0.7H), 1.99 (t, J = 11.7 Hz, 0.7H), 1.91 (t, J = 12.0 Hz, 0.3H), 1.89–1.70 (m, 2H), 1.69–1.60 (m, 2H), 1.60–1.48 (m, 2H), 1.44–1.30 (m, 3H), 1.30–1.20 (m, 1H), 1.14 (t, J = 6.4 Hz, 2H), 1.03 (t, J = 6.9 Hz, 1H), 0.91 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (125 MHz, CDCl₃, data of the diastereomeric mixture) δ 112.3, 112.0, 108.4, 101.1, 82.4, 82.1, 78.8, 78.1, 61.0, 50.4, 50.2, 47.6, 47.5, 47.3, 43.0, 41.0, 38.9, 33.4, 33.0, 31.7, 27.4, 27.3, 26.6, 26.3, 23.2, 14.8, 14.0, 11.1 ppm; **HRMS** calcd for C₁₆H₂₆NO₃ [$\text{M}+\text{H}^+$]: 280.1907; found: 280.1915.

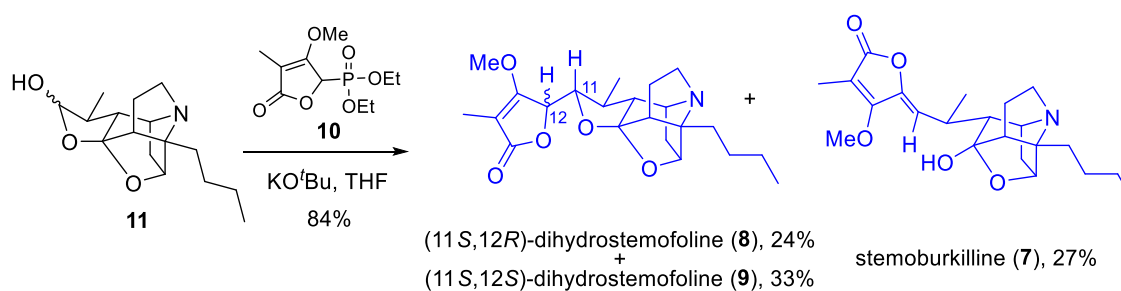
Synthesis of Compound 10



The mixture of the known compound 5-bromo-4-methoxy-3-methylfuran-2(5*H*)-one^[4] (2050 mg, 10.0 mmol) and P(OEt)_3 (2.2 mL, 13.0 mmol) was stirred at 110 °C for 2 h. The mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (EtOAc/PE = 4/1) to give compound **10** (2320 mg, yield: 88%) as a pale yellow oil.

Compound **10**: **IR** (film) ν_{max} : 2986, 2914, 1763, 1662, 1455, 1396, 1337, 1263, 1023, 977 cm^{-1} ; **^1H NMR** (400 MHz, CDCl_3) δ 4.91 (d, $J_{\text{P-H}} = 10.7$ Hz, 1H), 4.29–4.16 (m, 4H), 4.15 (s, 3H), 1.97 (d, $J = 2.8$ Hz, 3H), 1.36 (t, $J = 7.1$ Hz, 3H), 1.31 (t, $J = 7.1$ Hz, 3H) ppm; **^{13}C NMR** (100 MHz, CDCl_3) δ 173.9, 169.4 (d, $J_{\text{P-C}} = 5.2$ Hz, 1C), 99.7 (d, $J_{\text{P-C}} = 5.2$ Hz, 1C), 73.3 (d, $J_{\text{P-C}} = 162.2$ Hz, 1C), 64.3 (d, $J_{\text{P-C}} = 6.4$ Hz, 1C), 63.9 (d, $J_{\text{P-C}} = 6.4$ Hz, 1C), 59.4, 16.4 (d, $J_{\text{P-C}} = 5.6$ Hz, 2C), 8.3 ppm; **HRMS** calcd for $\text{C}_{10}\text{H}_{17}\text{O}_6\text{PNa}$ [$\text{M}+\text{Na}^+$]: 287.0660; found: 287.0655.

Completion of the total synthesis of (+)-Stemoburkilline (**7**), (+)-(11*S*,12*R*)-Dihydrostemofoline (**8**), and (+)-(11*S*,12*S*)-Dihydrostemofoline (**9**)



To a cooled suspension (0 °C) of compound **10** (1440 mg, 5.45 mmol) in anhydrous THF (20 mL) was added KO^tBu (665 mg, 5.45 mmol) under a nitrogen atmosphere. The suspension was stirred for 30 min. To the resulting mixture was added dropwise a solution of compound **11** (305 mg, 1.09 mmol) in THF (10 mL). After being stirred at the same temperature for 1 h, the reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL). The organic layer was separated and the aqueous layer was

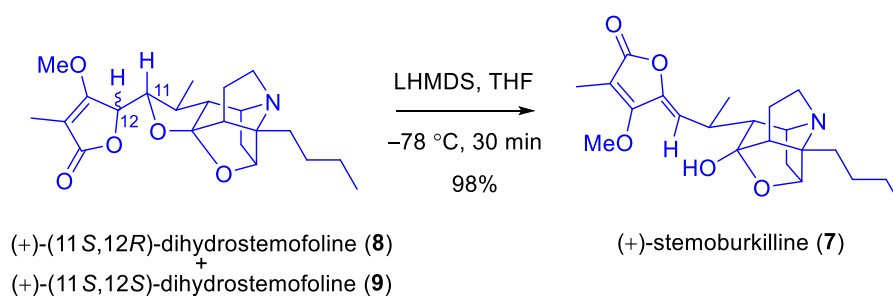
extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/MeOH = 5/1) to give (+)-stemoburkilline (**7**) (114 mg, colorless oil, yield: 27%), (+)-(11*S*,12*R*)-dihydrostemofoline (**8**) (101 mg, colorless oil, yield: 24%), and (+)-(11*S*,12*S*)-dihydrostemofoline (**9**) (140 mg, colorless oil, yield: 33%), combined yield: 84%. The mixture of the three products (**7**, **8**, and **9**) was used without separation in the total synthesis of stemofoline (**1**).

(+)-Stemoburkilline (**7**): $[\alpha]_{\text{D}}^{20} +5.1$ (*c* 1.0, CHCl₃) {lit.^[6] $[\alpha]_{\text{D}}^{24} +7.6$ (*c* 0.64, CHCl₃) (semi-synthetic compound by Pyne); lit.^[5] $[\alpha]_{\text{D}}^{26} +37.5$ (*c* 0.28, CHCl₃) (natural product)}; **IR** (film) ν_{max} : 3331, 2958, 2929, 2873, 1755, 1633, 1454, 1355, 1032, 987, 756, 666 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 5.47 (d, *J* = 10.0 Hz, 1H), 4.32 (br s, 1H), 4.11 (s, 3H), 3.34 (br s, 1H), 3.20–3.12 (m, 1H), 3.12–3.05 (m, 1H), 3.01–2.94 (m, 1H), 2.19 (d, *J* = 5.5 Hz, 1H), 2.05 (s, 3H), 1.96–1.91 (m, 1H), 1.90–1.82 (m, 2H), 1.76 (dd, *J* = 9.2, 3.5 Hz, 1H), 1.67–1.61 (m, 1H), 1.55–1.50 (m, 2H), 1.44–1.37 (m, 1H), 1.36–1.30 (m, 2H), 1.28–1.21 (m, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 170.5, 161.8, 142.0, 114.7, 105.9, 99.3, 82.2, 80.3, 63.6, 58.9, 55.6, 47.3, 44.7, 33.4, 31.3, 28.3, 27.3, 26.2, 23.1, 18.5, 14.0, 8.6 ppm; **HRMS** calcd for C₂₂H₃₂NO₅ [M+H⁺]: 390.2275; found: 390.2271.

(+)-(11*S*,12*R*)-Dihydrostemofoline (**8**): $[\alpha]_{\text{D}}^{20} +28.3$ (*c* 1.0, CHCl₃) {lit.^[5] $[\alpha]_{\text{D}}^{26} +38.9$ (*c* 0.35, CHCl₃) (natural product)}; **IR** (film) ν_{max} : 2957, 2930, 2873, 1756, 1671, 1458, 1353, 1031, 961, 756 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.59 (br s, 1H), 4.23 (br s, 1H), 4.11 (s, 3H), 3.79 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.48 (br s, 1H), 3.18–3.13 (m, 1H), 3.03–2.99 (m, 1H), 2.64–2.59 (m, 1H), 2.47 (d, *J* = 6.0 Hz, 1H), 2.01 (br s, 3H), 2.02–1.98 (m, 1H), 1.89–1.84 (m, 1H), 1.74–1.70 (m, 1H), 1.64 (dd, *J* = 12.0, 3.0 Hz, 1H), 1.67–1.62 (m, 1H), 1.56 (t, *J* = 8.0 Hz, 2H), 1.41–1.37 (m, 1H), 1.35–1.29 (m, 2H), 1.25–1.20 (m, 1H), 1.08 (d, *J* = 6.5 Hz, 3H), 0.89 (t, *J* = 7.0 Hz, 3H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 174.6, 170.3, 111.8, 98.6, 86.3, 82.6, 78.1, 76.5, 61.2, 58.9, 50.5, 47.4, 47.3, 33.4, 33.1, 31.3, 27.2, 26.4, 23.1, 14.8, 13.9, 8.7 ppm; **HRMS** calcd for C₂₂H₃₁NO₅Na [M+Na⁺]: 412.2094; found: 412.2091.

(+)-(11*S*,12*S*)-Dihydrostemofoline (**9**): $[\alpha]_D^{20} +18.7$ (c 1.0, CHCl_3) {lit.^[5] $[\alpha]_D^{26} +35.9$ (c 0.22, CHCl_3) (semi-synthetic compound by Pyne)}; **IR** (film) ν_{max} : 2957, 2876, 1758, 1666, 1461, 1339, 1030, 957, 757, 666 cm^{-1} ; **^1H NMR** (500 MHz, CDCl_3) δ 4.75 (d, $J = 6.5$ Hz, 1H), 4.21 (br s, 1H), 4.10 (s, 3H), 3.69 (t, $J = 7.0$ Hz, 1H), 3.40 (br s, 1H), 3.16–3.07 (m, 1H), 3.02–2.94 (m, 1H), 2.55–2.45 (m, 1H), 2.47 (d, $J = 6.0$ Hz, 1H), 1.98–1.94 (m, 1H), 1.95 (br s, 3H), 1.89–1.83 (m, 1H), 1.76–1.70 (m, 1H), 1.65–1.59 (m, 2H), 1.56–1.51 (m, 2H), 1.44–1.37 (m, 1H), 1.34 (q, $J = 6.8$ Hz, 2H), 1.26–1.21 (m, 1H), 1.12 (d, $J = 6.3$ Hz, 3H), 0.91 (t, $J = 6.8$ Hz, 3H) ppm; **^{13}C NMR** (125 MHz, CDCl_3) δ 174.3, 173.1, 112.8, 98.8, 87.8, 82.3, 78.7, 78.6, 61.1, 59.3, 50.5, 47.5, 47.3, 35.0, 33.4, 31.7, 27.3, 26.7, 23.3, 16.5, 14.0, 8.3 ppm; **HRMS** calcd for $\text{C}_{22}\text{H}_{31}\text{NO}_5\text{Na}$ $[\text{M}+\text{Na}^+]$: 412.2094; found: 412.2085.

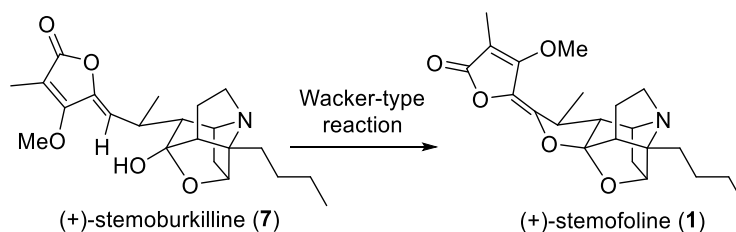
Synthesis of (+)-Stemoburkilline (**7**)



To a cooled solution (-78 °C) of a mixture of diastereomers (+)-(11*S*,12*R*)-dihydrostemofoline **8** and (+)-(11*S*,12*S*)-dihydrostemofoline **9** (89.5 mg, 0.23 mmol) in anhydrous THF (5 mL) was added lithium bis(trimethylsilyl)amide (LiHMDS) (0.28 mL, 0.28 mmol, 1.0 M in THF) under a nitrogen atmosphere. After being stirred at the same temperature for 30 min, the reaction was quenched with a saturated aqueous solution of NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 20/1$) to give (+)-stemoburkilline **7** (87.7 mg, yield: 98%) as a colorless oil.

Asymmetric Total Synthesis of (+)-Stemofoline (1), (+)-Isostemofoline (2):

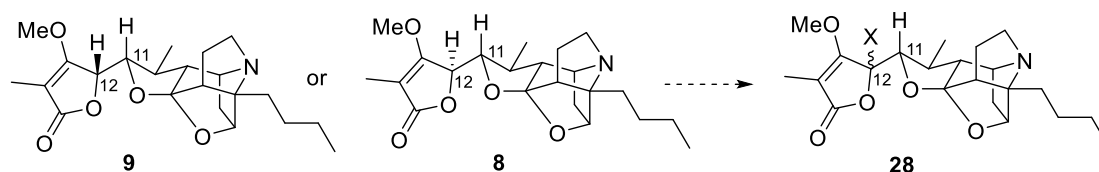
Supplementary Table 1. Attempted conversion of 7 into 1 by Wacker-type reaction



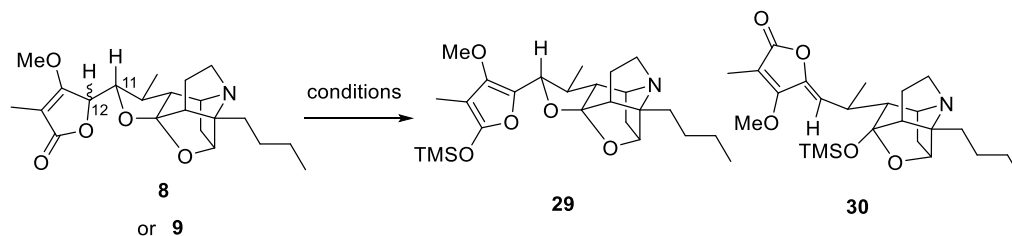
entry	Conditions	yield
1	Na ₂ PdCl ₄ , TBHP, NaOAc, AcOH, <i>t</i> -BuOH/H ₂ O, rt	ND ^a
2	Na ₂ PdCl ₄ , TBHP, NaOAc, AcOH, dioxane/H ₂ O, rt	ND
3	PdCl ₂ , CuCl, O ₂ , Na ₂ HPO ₄ , DME, 85 °C	NR ^b
4 ^c	PdCl ₂ , CuCl, O ₂ , Na ₂ HPO ₄ , DME, 85 °C	NR
5 ^c	Pd(TFA) ₂ ^d , MeCN, rt to 65 °C	NR
6 ^c	Pd(TFA) ₂ , IMes, DMAP, Na ₂ CO ₃ , toluene, rt	decomp.

^aND = Not detected. ^bNR = No reaction. ^cHydrochloride salt of stemoburkilline (7) used as the starting material. ^d2.0 equiv of Pd used.

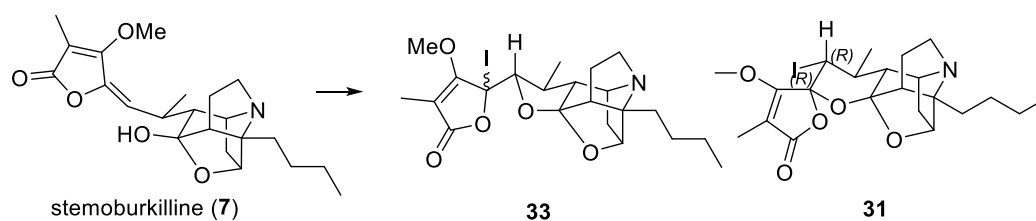
Supplementary Table 2. Attempted transformations of 8/9 to 28



Entry	Conditions	Products/Yield
1	IBX, DMSO	NR ^a
2	O ₂ , DBU, MeCN, reflux	Mixture of 7, 8, 9
3	LDA, NIS, THF, -78 °C to rt	Mixture of 7, 8, 9
4	DBU, NIS, THF, rt to 60 °C	Mixture of 7, 8, 9
5	LDA, NBS, THF, -78 °C to rt	Only 7
6	DBU, NBS, THF, rt to 60 °C	Mixture of 7, 8, 9

^aNR = No reaction.**Supplementary Table 3. Attempted transformations of 8/9 to 29**

Entry	Conditions	Yield
1	Et ₃ N, TMSOTf, CH ₂ Cl ₂ , -20 °C to rt	58% for SM and 30% for 30
2	LHMDS, TMSCl, THF, -78 °C	93% for 30
3	HMDS, TMSI, CH ₂ Cl ₂ , 0 °C to rt	27% for SM and 55% for 30
4	DBU, TMSOTf, CH ₂ Cl ₂ , -20 °C to rt	11% for SM and 71% for 30
5	TMSI, CH ₃ CN, reflux	NR ^a

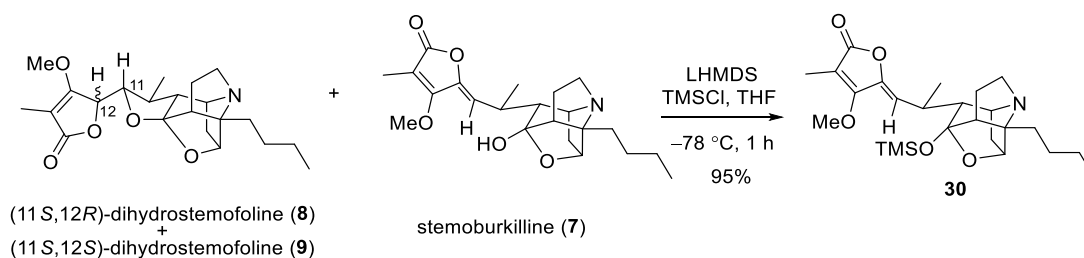
^aNR = No reaction.**Supplementary Table 4. Attempted transformations of 7 to 33**

Entry	Conditions	Yield
1	NIS, CH ₂ Cl ₂ , rt to reflux	NR ^a
2	NIS, CH ₃ CN, rt to reflux	NR
3	NIS, THF, rt to reflux	NR
4	NIS, Et ₃ N, CH ₂ Cl ₂ , rt to reflux	Mixture of 7 , 8 , 9
5	NIS, DBU, CH ₂ Cl ₂ , rt to 35 °C	Mixture of 7 , 8 , 9
6	NIS, DBU, THF, rt to 60 °C	Mixture of 7 , 8 , 9
7	NIS, NaOEt, THF, 60 °C	Mixture of 7 , 8 , 9
8	NIS, NaH, THF, 60 °C	Mixture of 7 , 8 , 9
9	NIS, LDA, THF, -78 °C	Only 7

10	NIS, ^t BuOK, THF, rt	decomposed
11	PhSeCl, K ₂ CO ₃ , THF, 60°C	ND ^b
12	I ₂ , NaHCO ₃ , THF, rt	86% for 31

^aNR = No reaction. ^bND = Not detected.

Synthesis of Compound 30

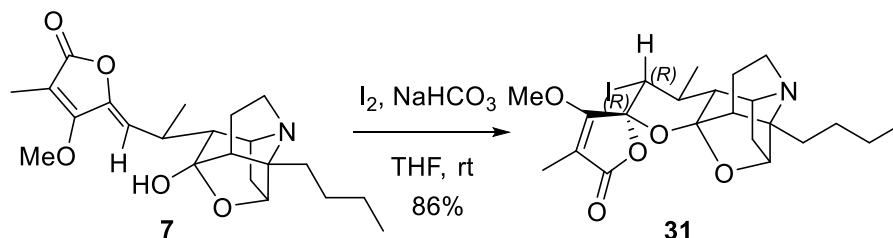


To a cooled solution (−78 °C) of the mixture of the products obtained from the HWE reaction of **11**: **7**, **8** and **9** (59.2 mg, 0.15 mmol) in anhydrous THF (5 mL), was added lithium bis(trimethylsilyl)amide (LiHMDS) (0.23 mL, 0.23 mmol, 1.0 M in THF) under a nitrogen atmosphere. The mixture was stirred for 30 min before addition of trimethyl chlorosilane (TMSCl) (0.029 mg, 0.23 mmol). After being stirred at −78 °C for 1 h, the reaction was quenched with a saturated aqueous solution of NH₄Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH = 20/1) to give compound **30** (65.6 mg, yield: 95%) as a colorless oil.

Compound **30**: **M.p.**: 141~142 °C; [α]_D²⁰ −10.5 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 2956, 2875, 1760, 1635, 1455, 1356, 1248, 1037, 977, 844, 755 cm^{−1}; **¹H NMR** (500 MHz, CDCl₃) δ 5.33 (d, *J* = 9.0 Hz, 1H), 4.27 (br s, 1H), 4.10 (s, 3H), 3.31 (br s, 1H), 3.09 (ddd, *J* = 13.4, 8.0, 8.0 Hz, 1H), 3.02–2.98 (m, 1H), 2.96 (dd, *J* = 13.4, 6.8, 6.8 Hz, 1H), 2.20 (dd, *J* = 3.3, 3.3 Hz, 1H), 2.05 (s, 3H), 1.90 (d, *J* = 11.9 Hz, 1H), 1.87–1.82 (m, 2H), 1.70 (dd, *J* = 9.5, 3.3 Hz, 1H), 1.60 (ddd, *J* = 12.0, 3.3, 3.3 Hz, 1H), 1.64–1.57 (m, 1H), 1.55–1.46 (m, 2H), 1.38–1.31 (m, 3H), 1.24–1.19 (m, 1H), 1.00 (d, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 3H), 0.01 (s, 9H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 171.1, 162.4, 140.0, 118.4, 107.2, 98.2, 81.9, 79.7, 63.3, 58.7, 55.6, 47.3, 45.4, 33.3, 31.2, 28.4,

27.3, 26.1, 23.1, 18.1, 13.9, 8.6, 1.5 (3C) ppm; **HRMS** calcd for C₂₅H₄₀NO₅Si [M+H⁺]: 462.2670; found: 462.2677.

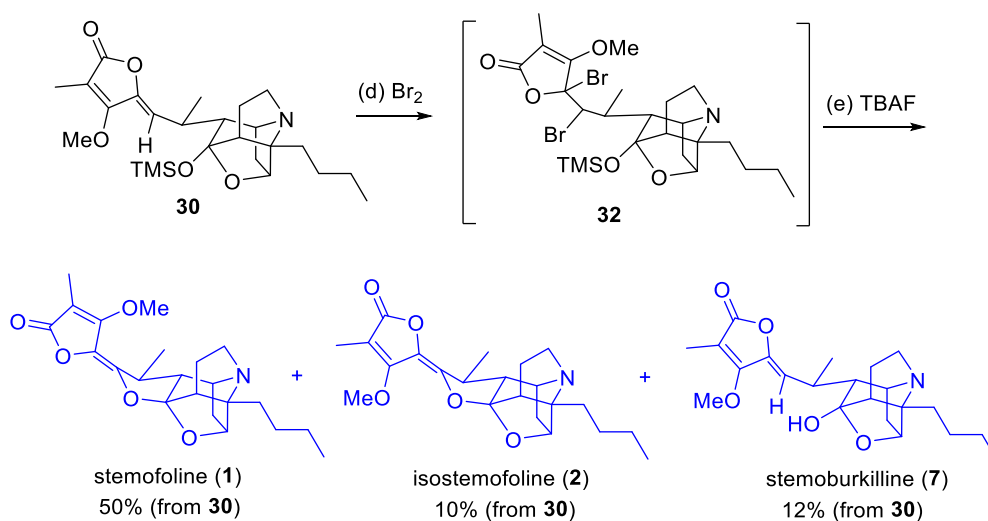
Synthesis of Compound 31



A solution of (+)-stemoburkilline **7** (24.0 mg, 0.062 mmol) in THF (2 mL) was added NaHCO₃ (26.0 mg, 0.31 mmol), and the suspension was stirred for 5 min. To the resulting mixture was added I₂ (78.0 mg, 0.31 mmol), and the reaction was stirred overnight before being quenched with a saturated aqueous Na₂S₂O₃ (3 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (MeOH/CH₂Cl₂ = 1/20) to give compound **31** (27.1 mg, yield: 86%) as a pale yellow oil.

Compound **31**: [α]_D²⁰ +33.5 (*c* 1.0, CHCl₃); **IR** (film) ν_{max} : 2959, 2926, 2854, 1748, 1634, 1260, 1074, 1015, 799, 755, 665 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.46 (br s, 1H), 4.15 (d, *J* = 13.0 Hz, 1H), 4.13 (br s, 3H), 3.44 (s, 1H), 3.15 (ddd, *J* = 13.5, 10.6, 5.4 Hz, 1H), 2.99 (ddd, *J* = 13.5, 8.6, 5.1 Hz, 1H), 2.67–2.54 (m, 1H), 2.36 (d, *J* = 6.2 Hz, 1H), 2.02 (s, 3H), 2.01 (d, *J* = 9.2 Hz, 1H), 1.93–1.87 (m, 1H), 1.84 (ddd, *J* = 13.9, 10.6, 5.1 Hz, 1H), 1.67 (dd, *J* = 13.0, 3.1 Hz, 1H), 1.59–1.50 (m, 3H), 1.45–1.36 (m, 1H), 1.32 (dd, *J* = 14.3, 7.2 Hz, 2H), 1.24–1.17 (m, 1H), 1.14 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H) ppm; **¹³C NMR** (125 MHz, CDCl₃) δ 171.6, 168.2, 105.5, 101.5, 100.3, 81.2, 81.1, 63.1, 59.4, 54.4, 47.2, 43.6, 37.3, 33.0, 32.2, 31.4, 27.2, 26.6, 23.1, 20.6, 13.9, 8.0 ppm; **HRMS** calcd for C₂₂H₃₀INO₅ [M+Na⁺]: 538.1061; found: 538.1062.

Synthesis of (+)-Stemofoline (1), (+)-Isostemofoline (2), and (+)-Stemoburkilline (7)



To a solution of compound **30** (40.0 mg, 0.087 mmol) in CH_2Cl_2 (10 mL) was added dropwise Br_2 (0.022 mL, 0.43 mmol). After being stirred for 30 min, the reaction was quenched with a saturated aqueous solution of NaS_2O_3 (3 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The presumed dibromination product **32** was directly used in the next step without further purification.

To a solution of the crude **32** in THF (5 mL) at 0 °C was added dropwise tetrabutylammonium fluoride (TBAF) (0.45 mL, 0.45 mmol, 1.0 M in THF) under a nitrogen atmosphere. The mixture was stirred for 1 h before being quenched with a saturated aqueous solution of NH_4Cl (3 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 20/1$) to give (+)-stemofoline (**1**) (16.6 mg, colorless oil, yield: 50%), (+)-isostemofoline (**2**) (3.4 mg, colorless oil, yield: 10%) and (+)-stemoburkilline (**7**) (3.9 mg, colorless oil, yield: 12%).

(+)-Stemofoline (**1**): $[\alpha]_{\text{D}}^{20} +276$ (c 1.0, MeOH) {lit.^[7] $[\alpha]_{\text{D}} +273$ (MeOH); lit.^[8] $[\alpha]_{\text{D}}^{20} +270$ (c 0.8, MeOH)}; **IR** (film) ν_{max} : 2956, 2928, 2855, 1746, 1621, 1365, 1141, 1006, 754, 677 cm^{-1} ; **^1H NMR** (850 MHz, CDCl_3) δ 4.25 (br s, 1H), 4.13 (s, 3H), 3.46 (br s,

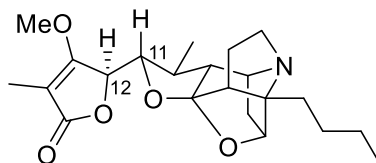
1H), 3.13 (ddd, $J = 13.6, 10.0, 5.1$ Hz, 1H), 3.09 (dd, $J = 10.0, 6.6$ Hz, 1H), 2.99 (ddd, $J = 13.6, 8.8, 4.7$ Hz, 1H), 2.69 (d, $J = 6.3$ Hz, 1H), 2.07 (s, 3H), 1.95 (d, $J = 12.1$ Hz, 1H), 1.93–1.88 (m, 1H), 1.84–1.82 (m, 1H), 1.81 (dd, $J = 10.0, 3.6$ Hz, 1H), 1.72–1.69 (m, 1H), 1.58–1.52 (m, 2H), 1.44–1.39 (m, 1H), 1.37 (d, $J = 6.5$ Hz, 3H), 1.36–1.32 (m, 2H), 1.28–1.22 (m, 1H), 0.91 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (216 MHz, CDCl_3) δ 169.7, 162.8, 148.4, 127.9, 112.7, 98.5, 82.8, 78.5, 60.9, 58.8, 49.9, 47.6, 47.5, 34.5, 33.3, 31.6, 27.3, 26.7, 23.1, 18.3, 14.0, 9.2 ppm; HRMS calcd for $\text{C}_{22}\text{H}_{30}\text{NO}_5$ [$\text{M}+\text{H}^+$]: 388.2118; found: 388.2126.

(+)-Isostemofoline (**2**): colorless oil. $[\alpha]_{\text{D}}^{20} +102.1$ (c 0.5, CHCl_3) (the optical rotation of this alkaloid has not been reported previously); IR (film) ν_{max} : 2957, 2929, 2857, 1747, 1620, 1446, 1396, 1157, 1025, 752, 674 cm^{-1} ; ^1H NMR (850 MHz, CDCl_3) δ 4.29 (br s, 1H), 4.13 (s, 3H), 3.50–3.48 (m, 1H), 3.24–3.19 (m, 1H), 3.15 (ddd, $J = 13.9, 10.4, 5.0$ Hz, 1H), 3.02 (ddd, $J = 13.9, 8.8, 4.6$ Hz, 1H), 2.71 (d, $J = 6.2$ Hz, 1H), 2.06 (s, 3H), 1.99 (d, $J = 12.2$ Hz, 1H), 1.96–1.91 (m, 1H), 1.84 (ddd, $J = 13.9, 8.8, 5.3$ Hz, 1H), 1.75 (dd, $J = 10.8, 3.6$ Hz, 1H), 1.72 (dt, $J = 12.3, 3.3$ Hz, 1H), 1.63–1.55 (m, 2H), 1.46–1.41 (m, 1H), 1.47 (d, $J = 6.5$ Hz, 3H), 1.37 (q, $J = 7.0$ Hz, 2H), 1.30–1.26 (m, 1H), 0.94 (t, $J = 7.0$ Hz, 3H) ppm; ^{13}C NMR (216 MHz, CDCl_3) δ 169.7, 162.8, 148.4, 127.9, 112.7, 98.5, 82.8, 78.5, 60.9, 58.8, 49.9, 47.6, 47.5, 34.5, 33.3, 31.6, 27.3, 26.7, 23.1, 18.3, 14.0, 9.2 ppm; HRMS calcd for $\text{C}_{22}\text{H}_{30}\text{NO}_5$ [$\text{M}+\text{H}^+$]: 388.2118; found: 388.2122.

^1H NMR and ^{13}C NMR data of (+)-stemoburkilline (**7**) matched those described in page S21.

Supplementary Note 4

Comparison of ^1H and ^{13}C NMR Data of Our Synthetic Compounds (1, 2, 7-9) with Those of Reported Data

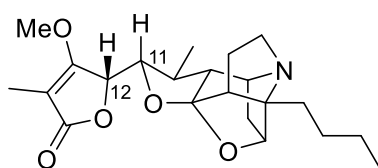


Supplementary Table 5. Comparison of ^1H NMR Spectral Data of (11*S*,12*R*)-dihydrostemofoline (**8**)

^1H NMR	
Our synthetic compound (500 MHz, CDCl_3)	Natural product ^[5] (500 MHz, CDCl_3)
4.59 (br s, 1H)	4.60 (br s, 1H)
4.23 (br s, 1H)	4.22 (br s, 1H)
4.11 (s, 3H)	4.11 (s, 3H)
3.79 (dd, $J = 9.0, 3.0$ Hz, 1H)	3.79 (dd, $J = 9, 3$ Hz, 1H)
3.48 (br s, 1H)	3.44 (br s, 1H)
3.18–3.13 (m, 1H)	3.14 (m, 1H)
3.03–2.99 (m, 1H)	3.01 (m, 1H)
2.64–2.59 (m, 1H)	2.61 (m, 1H)
2.47 (d, $J = 6.0$ Hz, 1H)	2.45 (d, $J = 6$ Hz, 1H)
2.01 (br s, 3H)	2.01 (br s, 3H)
2.02–1.98 (m, 1H)	1.99 (m, 1H)
1.89–1.84 (m, 1H)	1.82 (m, 1H)
1.74–1.70 (m, 1H)	1.72 (m, 1H)
1.64 (dd, $J = 12.0, 3.0$ Hz, 1H)	1.64 (dd, $J = 12, 3$ Hz, 1H)
1.67–1.62 (m, 1H)	1.63 (dd, $J = 7.5, 3$ Hz, 1H)
1.56 (t, $J = 8.0$ Hz, 2H)	1.56 (t, $J = 8$ Hz, 2H)
1.41–1.37 (m, 1H)	1.40 (m, 1H)
1.35–1.29 (m, 2H)	1.33 (m, 2H)
1.25–1.20 (m, 1H)	1.23 (m, 1H)
1.08 (d, $J = 6.5$ Hz, 3H)	1.08 (d, $J = 6.5$ Hz, 3H)
0.89 (t, $J = 7.0$ Hz, 3H)	0.87 (t, $J = 7$ Hz, 3H)

Supplementary Table 6. Comparison of ^{13}C NMR Spectral Data of (11*S*,12*R*)-dihydrostemofoline (**8**)

^{13}C NMR	
Our synthetic compound (125 MHz, CDCl_3)	Natural product ^[5] (125 MHz, CDCl_3)
174.6	174.5
170.3	170.3
111.8	111.8
98.6	98.5
86.3	86.3
82.6	82.2
78.1	78.2
76.5	76.5
61.2	61.0
58.9	58.8
50.5	50.5
47.4	47.4
47.3	47.3
33.4	33.4
33.1	33.1
31.3	31.5
27.2	27.2
26.4	26.5
23.1	23.2
14.8	14.8
13.9	13.9
8.7	8.7

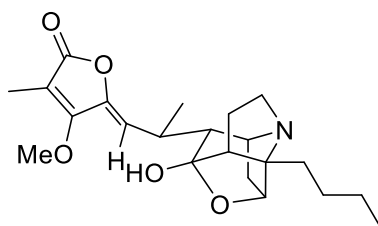


Supplementary Table 7. Comparison of ^1H NMR Spectral Data of (11*S*,12*S*)-dihydrostemofoline (**9**)

^1H NMR	
Our synthetic compound (500 MHz, CDCl_3)	Semi-synthetic compound ^[5] (500 MHz, CDCl_3)
4.75 (d, $J = 6.5$ Hz, 1H)	4.75 (d, $J = 6.5$ Hz, 1H)
4.21 (br s, 1H)	4.21 (br s, 1H)
4.10 (s, 3H)	4.10 (s, 3H)
3.69 (t, $J = 7.0$ Hz, 1H)	3.69 (t, $J = 7$ Hz, 1H)
3.40 (br s, 1H)	3.38 (br s, 1H)
3.16–3.07 (m, 1H)	3.09 (m, 1H)
3.02–2.94 (m, 1H)	2.96 (m, 1H)
2.55–2.45 (m, 1H)	2.48 (m, 1H)
2.47 (d, $J = 6.0$ Hz, 1H)	2.47 (d, $J = 6$ Hz, 1H)
1.98–1.94 (m, 1H)	1.97 (m, 1H)
1.95 (br s, 3H)	1.95 (br s, 3H)
1.89–1.83 (m, 1H)	1.85 (m, 1H)
1.76–1.70 (m, 1H)	1.73 (m, 1H)
1.65–1.59 (m, 2H)	1.62 (m, 1H)
	1.60 (m, 1H)
1.56–1.51 (m, 2H)	1.54 (m, 2H)
1.44–1.37 (m, 1H)	1.40 (m, 1H)
1.34 (q, $J = 6.8$ Hz, 2H)	1.35 (q, $J = 6.8$ Hz, 2H)
1.26–1.21 (m, 1H)	1.23 (m, 1H)
1.12 (d, $J = 6.3$ Hz, 3H)	1.12 (d, $J = 6.3$ Hz, 3H)
0.91 (t, $J = 6.8$ Hz, 3H)	0.92 (t, $J = 6.8$ Hz, 3H)

Supplementary Table 8. Comparison of ^{13}C NMR Spectral Data of (11*S*,12*S*)-dihydrostemofoline (**9**)

^{13}C NMR	
Our synthetic compound (125 MHz, CDCl_3)	Semi-synthetic compound ^[5] (125 MHz, CDCl_3)
174.3	174.3
173.1	173.3
112.8	112.8
98.8	98.8
87.8	87.8
82.3	82.1
78.7	78.7
78.6	78.6
61.1	61.1
59.3	59.4
50.5	50.5
47.5	47.5
47.3	47.2
35.0	35.1
33.4	33.4
31.7	31.8
27.3	27.4
26.7	26.8
23.3	23.4
16.5	16.9
14.0	14.1
8.3	8.2

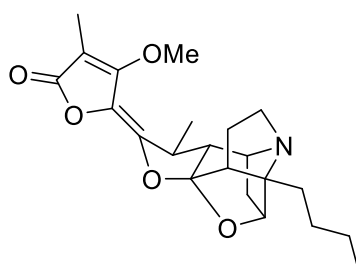


Supplementary Table 9. Comparison of ^1H NMR Spectral Data of Stemoburkilline (7)

^1H NMR		
Our synthetic compound (500 MHz, CDCl_3)	Natural product ^[5] (500 MHz, CDCl_3)	Semi-synthetic compound ^[6] (500 MHz, CDCl_3)
5.47 (d, $J = 10.0$ Hz, 1H)	5.50 (d, $J = 10$ Hz, 1H)	5.48 (d, $J = 10$ Hz, 1H)
4.32 (br s, 1H)	4.38 (br s, 1H)	4.30 (br s, 1H)
4.11 (s, 3H)	4.13 (s, 3H)	4.10 (s, 3H)
3.34 (br s, 1H)	3.60 (br s, 1H)	3.28 (br s, 1H)
3.20–3.12 (m, 1H)	3.27 (m, 1H)	3.13 (m, 1H)
3.12–3.05 (m, 1H)	3.18 (m, 1H)	3.05 (m, 1H)
3.01–2.94 (m, 1H)	3.09 (m, 1H)	2.94 (m, 1H)
2.19 (d, $J = 5.5$ Hz, 1H)	2.34 (d, $J = 5.9$ Hz, 1H)	2.15 (d, $J = 5.0$ Hz, 1H)
2.05 (s, 3H)	2.07 (s, 3H)	2.05 (s, 3H)
1.96–1.91 (m, 1H)	1.99 (m, 1H)	1.91 (m, 1H)
1.90–1.82 (m, 2H)	1.93 (m, 2H)	1.83 (m, 2H)
1.76 (dd, $J = 9.2, 3.5$ Hz, 1H)	1.85 (m, 1H)	1.74 (m, 1H)
1.67–1.61 (m, 1H)	1.80 (m, 1H)	1.59 (m, 1H)
1.55–1.50 (m, 2H)	1.67 (m, 1H)	1.48 (m, 2H)
	1.60 (m, 1H)	
1.44–1.37 (m, 1H)	1.39 (m, 1H)	1.38 (m, 1H)
1.36–1.30 (m, 2H)	1.36 (m, 2H)	1.32 (m, 2H)
1.28–1.21 (m, 1H)	1.29 (m, 1H)	1.24 (m, 1H)
1.05 (d, $J = 6.9$ Hz, 3H)	1.08 (d, $J = 6.8$ Hz, 3H)	1.05 (d, $J = 6.5$ Hz, 3H)
0.90 (t, $J = 7.2$ Hz, 3H)	0.92 (t, $J = 6.8$ Hz, 3H)	0.90 (t, $J = 7.5$ Hz, 3H)

Supplementary Table 10. Comparison of ^{13}C NMR Spectral Data of Stemoburkilline (7)

^{13}C NMR		
Our synthetic compound (125 MHz, CDCl_3)	Natural product ^[5] (125 MHz, CDCl_3)	Semi-synthetic compound ^[6] (125 MHz, CDCl_3)
170.5	170.5	170.8
161.8	161.8	162.1
142.0	141.9	142.1
114.7	114.7	115.2
105.9	105.7	106.2
99.3	99.1	99.5
82.2	82.9	82.1
80.3	79.8	80.6
63.6	63.4	63.8
58.9	59.3	59.1
55.6	55.4	55.9
47.3	46.5	47.5
44.7	44.2	45.0
33.4	32.9	33.7
31.3	30.2	31.7
28.3	28.4	28.6
27.3	27.5	27.5
26.2	25.3	26.7
23.1	23.7	23.4
18.5	18.7	18.8
14.0	14.1	14.2
8.6	8.7	8.8

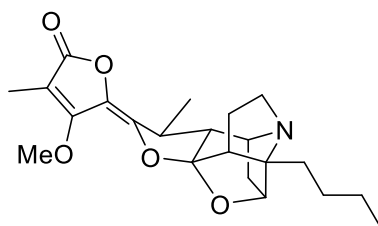


Supplementary Table 11. Comparison of ^1H NMR Spectral Data of stemofoline (**1**)

^1H NMR		
Our synthetic compound (850 MHz, CDCl_3)	Natural product ^[9] (CDCl_3)	Natural product ^[8] (CDCl_3)
4.25 (br s, 1H)	4.28 (br s, 1H)	4.25 (br s, 1H)
4.13 (s, 3H)	4.15 (s, 3H)	4.13 (s, 3H)
3.46 (br s, 1H)	3.53 (br s, 1H)	3.46 (br s, 1H)
3.13 (ddd, $J = 13.6, 10.0, 5.1$ Hz, 1H)	3.18 (ddd, 1H)	3.13 (ddd, $J = 13.6, 9.8, 5.1$ Hz, 1H)
3.09 (dd, $J = 10.0, 6.6$ Hz, 1H)	3.10 (dd, $J = 9.9, 6.6$ Hz, 1H)	3.08 (dd, $J = 10.4, 6.6$ Hz, 1H)
2.99 (ddd, $J = 13.6, 8.8, 4.7$ Hz, 1H)	3.04 (ddd, 1H)	2.99 (ddd, $J = 13.6, 8.6, 5.1$ Hz, 1H)
2.69 (d, $J = 6.3$ Hz, 1H)	2.72 (d, $J = 6.0$ Hz, 1H)	2.69 (d, $J = 6.3$ Hz, 1H)
2.07 (s, 3H)	2.07 (s, 3H)	2.07 (s, 3H)
1.95 (d, $J = 12.1$ Hz, 1H)	1.98 (d, $J = 12.2$ Hz, 1H)	1.95 (d, $J = 12.1$ Hz, 1H)
1.93–1.88 (m, 1H)	1.89 (m, 2H)	1.87 (m, 2H)
1.84–1.82 (m, 1H)		
1.81 (dd, $J = 10.0, 3.6$ Hz, 1H)	1.83 (dd, $J = 10.0, 3.6$ Hz, 1H)	1.81 (dd, $J = 10.4, 2.7$ Hz, 1H)
1.72–1.69 (m, 1H)	1.75 (m, 1H)	1.69 (m, 1H)
1.58–1.52 (m, 2H)	1.59 (m, 2H)	1.55 (m, 2H)
1.44–1.39 (m, 1H)	1.44 (m, 1H)	1.42 (m, 1H)
1.37 (d, $J = 6.5$ Hz, 3H)	1.38 (d, $J = 6.5$ Hz, 3H)	1.37 (d, 3H)
1.36–1.32 (m, 2H)	1.34 (m, 2H)	1.33 (m, 2H)
1.28–1.22 (m, 1H)	1.25 (m, 1H)	1.24 (m, 1H)
0.91 (t, $J = 7.1$ Hz, 3H)	0.93 (t, $J = 6.9$ Hz, 3H)	0.91 (t, 3H)

Supplementary Table 12. Comparison of ^{13}C NMR Spectral Data of stemofoline (**1**)

^{13}C NMR		
Our synthetic compound (216 MHz, CDCl_3)	Natural product ^[9] (CDCl_3)	Natural product ^[8] (CDCl_3)
169.7	169.7	169.7
162.8	162.8	162.8
148.4	148.3	148.4
127.9	127.9	127.9
112.7	112.6	112.7
98.5	98.6	98.6
82.8	83.2	82.8
78.5	78.4	78.6
60.9	61.1	60.9
58.8	58.9	58.8
49.9	49.8	49.9
47.6	47.5	47.6
47.5	47.4	47.6
34.5	34.5	34.6
33.3	33.2	33.3
31.6	31.4	31.6
27.3	27.3	27.3
26.7	26.4	26.7
23.1	23.1	23.1
18.3	18.3	18.3
14.0	13.9	14.0
9.2	9.2	9.2

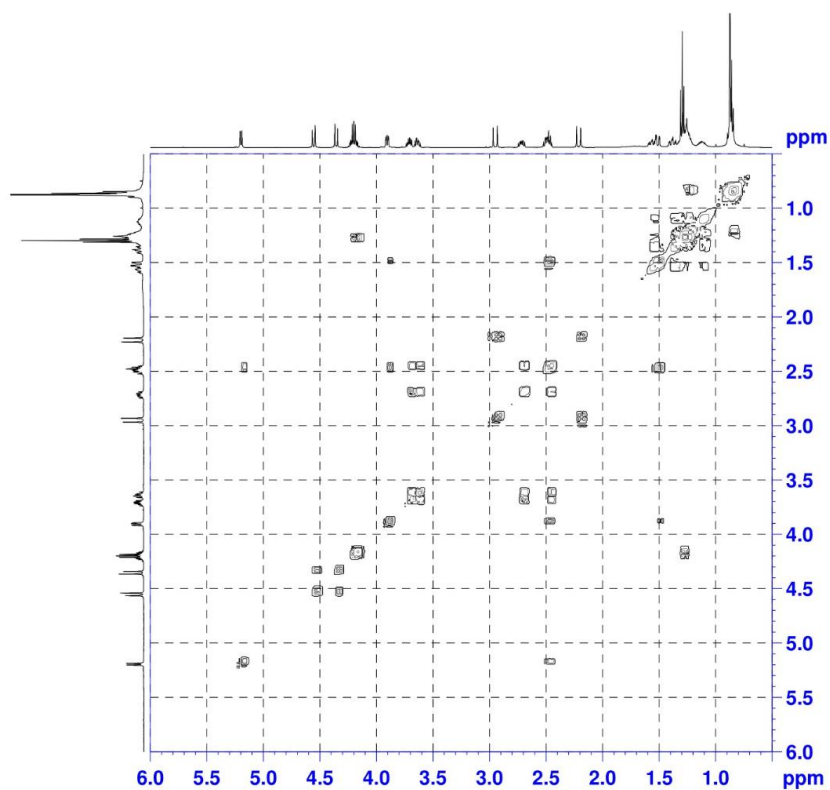


Supplementary Table 13. Comparison of ^1H NMR Spectral Data of isostemofoline (**2**)

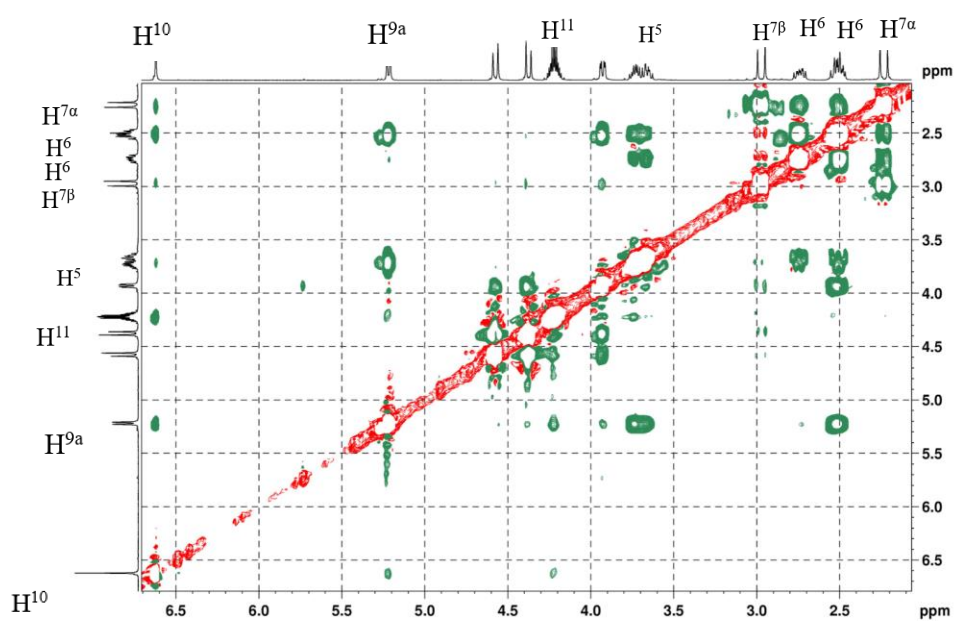
^1H NMR (only ^1H NMR data is available)	
Our synthetic compound (850 MHz, CDCl_3)	Kende's synthetic compound ^[3] (400 MHz, CDCl_3)
4.29 (s, 1H)	4.29 (s, 1H)
4.13 (s, 3H)	4.12 (s, 3H)
3.50–3.48 (m, 1H)	3.49 (m, 1H)
3.24–3.19 (m, 1H)	3.20 (m, 2H)
3.15 (ddd, $J = 13.9, 10.4, 5.0$ Hz, 1H)	3.03 (m, 1H)
3.02 (ddd, $J = 13.9, 8.8, 4.6$ Hz, 1H)	
2.71 (d, $J = 6.2$ Hz, 1H)	2.73 (d, $J = 5.2$ Hz, 1H)
2.06 (s, 3H)	2.05 (s, 3H)
1.99 (d, $J = 12.2$ Hz, 1H)	2.00 (m, 2H)
1.96–1.91 (m, 1H)	1.74 (dd, $J = 10.8, 3.6$ Hz, 2H)
1.84 (ddd, $J = 13.9, 8.8, 5.3$ Hz, 1H)	
1.75 (dd, $J = 10.8, 3.6$ Hz, 1H)	
1.72 (dt, $J = 12.3, 3.3$ Hz, 1H)	1.58 (m, 3H)
1.63–1.55 (m, 2H)	
1.46–1.41 (m, 1H)	
1.47 (d, $J = 6.5$ Hz, 3H)	1.46 (d, $J = 6.4$ Hz, 3H)
1.37 (q, $J = 7.0$ Hz, 2H)	1.36 (q, $J = 6.8$ Hz, 2H)
1.30–1.26 (m, 1H)	1.28 (m, 1H)
0.94 (t, $J = 7.0$ Hz, 3H)	0.92 (t, $J = 6.8$ Hz, 3H)

Supplementary Note 5

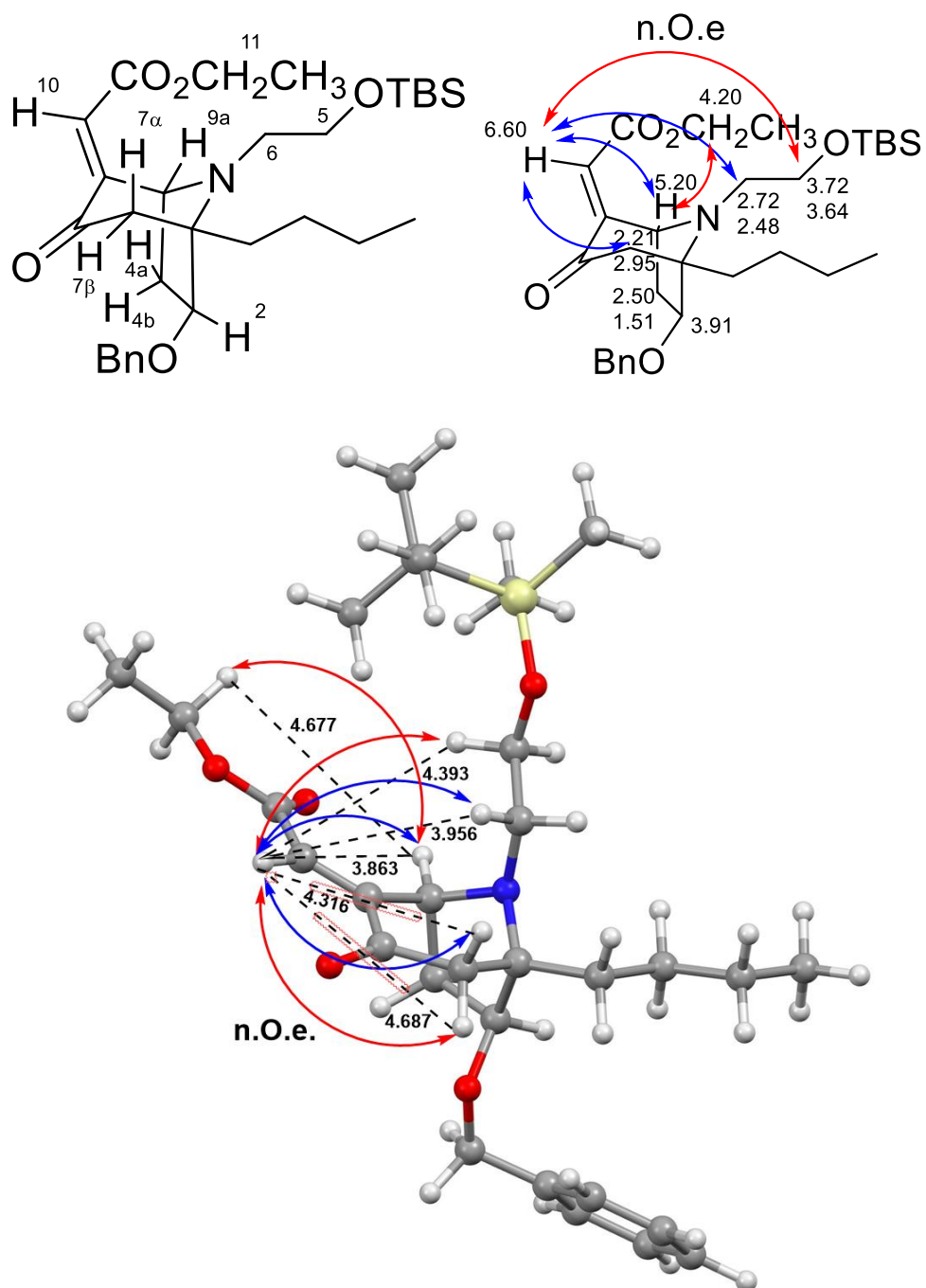
NOESY spectra of compounds 24, 13, 12 and 31



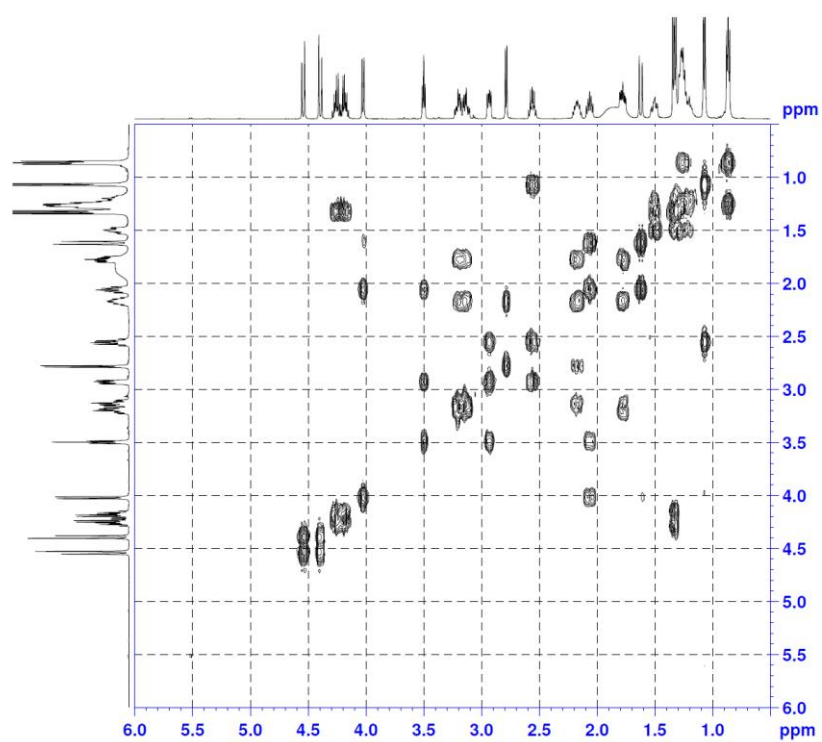
Supplementary Figure 2. ¹H-¹H COSY spectrum of compound 24



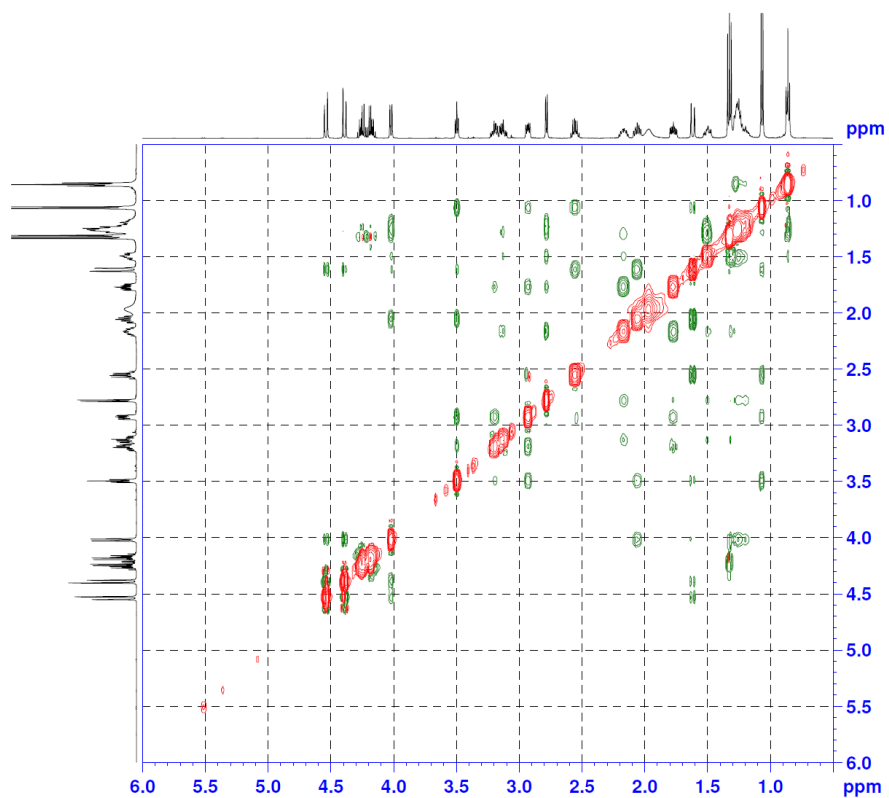
Supplementary Figure 3. NOESY spectrum of compound 24



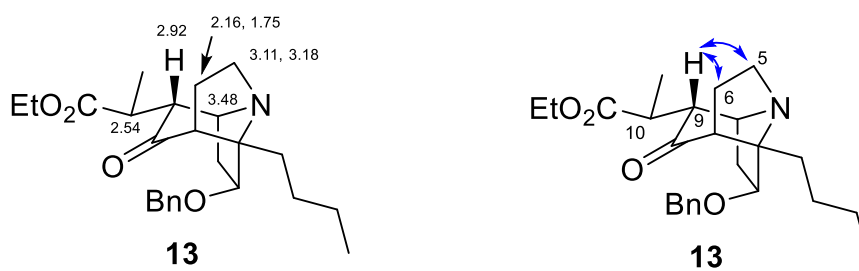
Supplementary Figure 4. Geometry of **24** optimized at b3lyp/6-31G* level and key correlations shown in NOESY spectrum



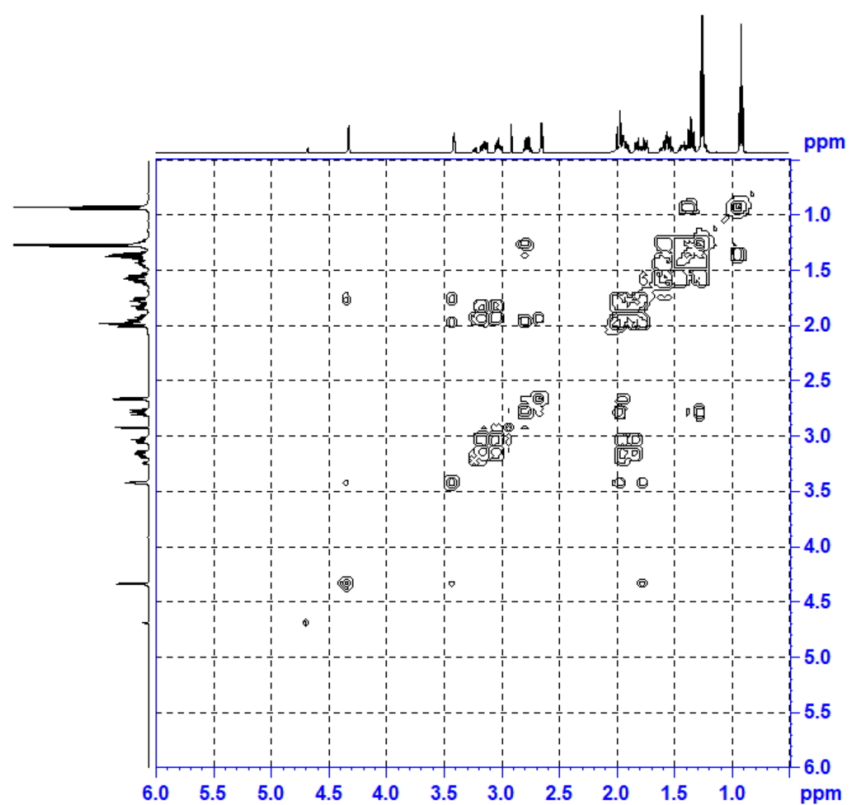
Supplementary Figure 5. ^1H - ^1H COSY spectrum of compound **13**



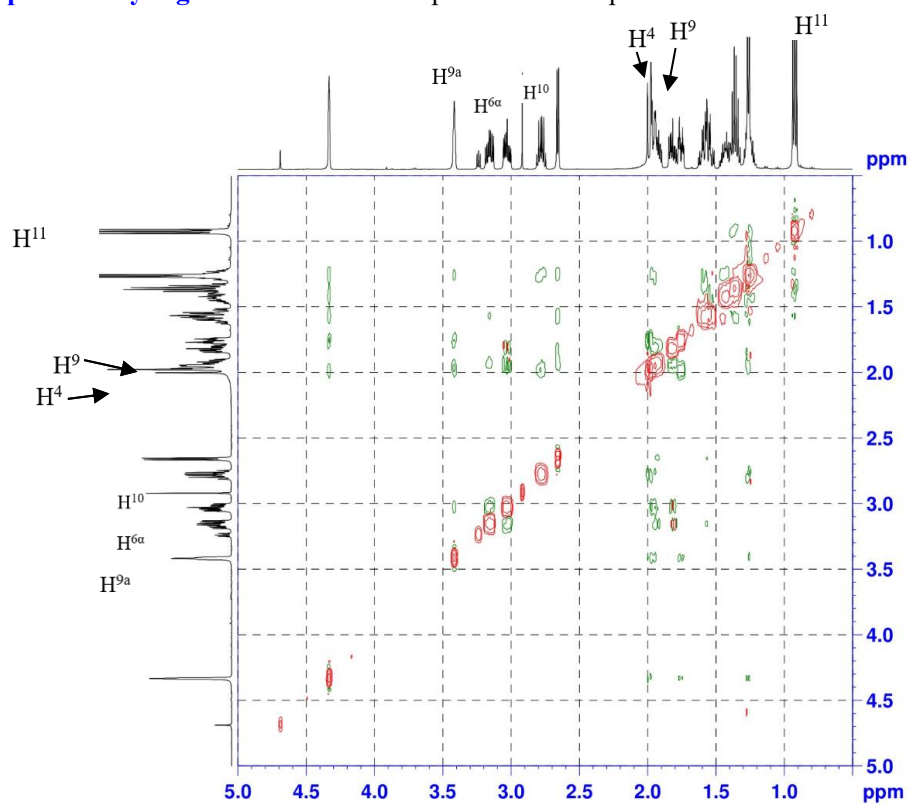
Supplementary Figure 6. NOESY spectrum of compound **13**



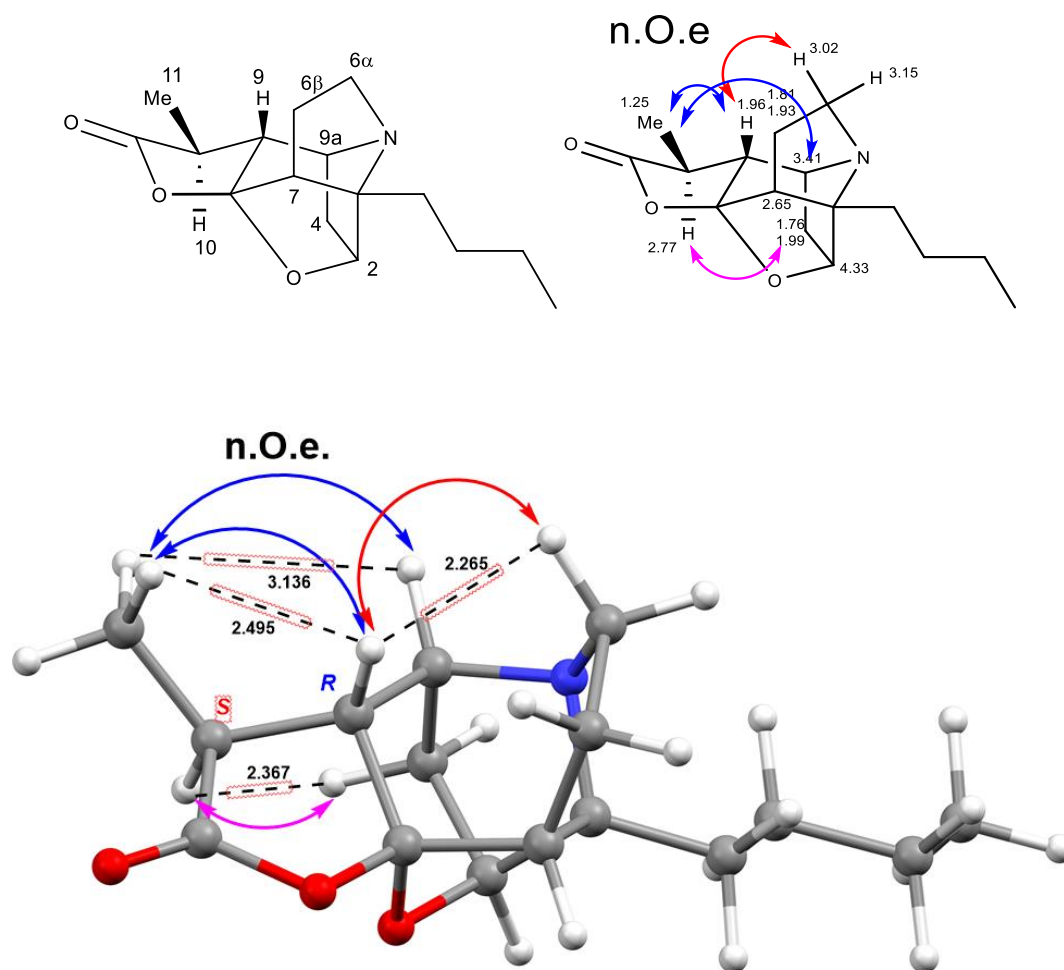
Supplementary Figure 7. Key correlations of compound **13** shown in NOESY spectrum



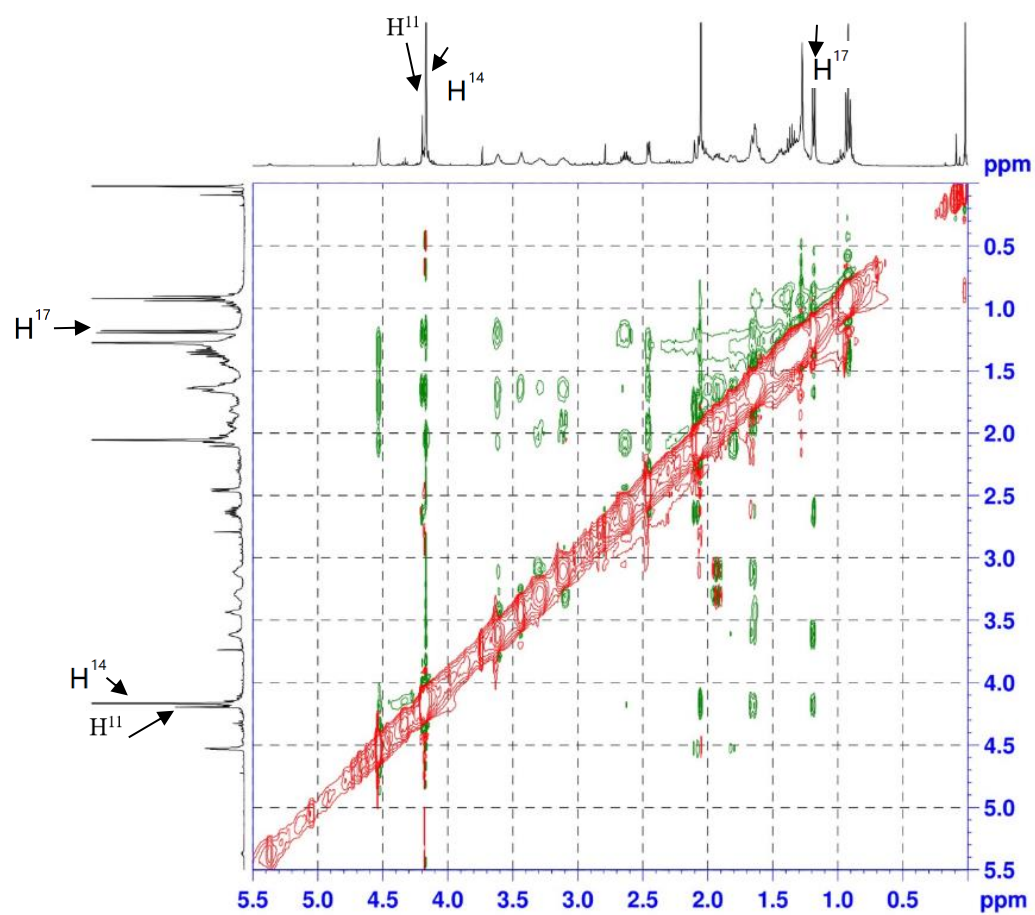
Supplementary Figure 8. ^1H - ^1H COSY spectrum of compound **12**



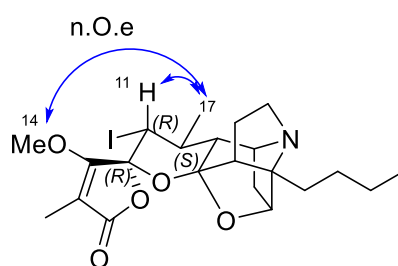
Supplementary Figure 9. NOESY spectrum of compound **12**



Supplementary Figure 10. Geometry of **12** optimized at b3lyp/6-31G* level and key correlations shown in NOESY spectrum



Supplementary Figure 11. NOESY spectrum of compound **31**



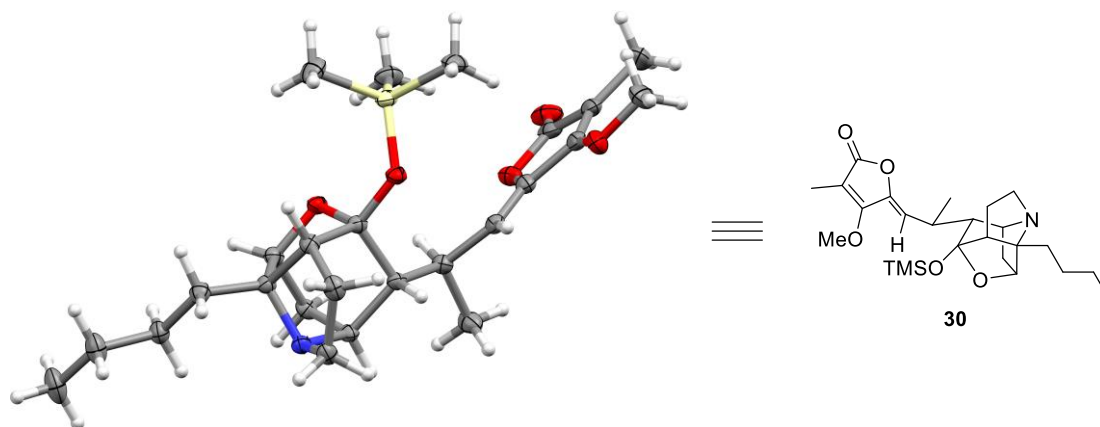
Supplementary Figure 12. The key correlations shown in NOESY spectrum

Supplementary Note 6

Single-Crystal X-Ray Diffraction Analysis of 30

X-Ray Crystallographic Data

CCDC 1962403 contains the crystallographic data for compound **30**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.



Supplementary Figure 13. X-ray crystal structure of **30**
(Thermal ellipsoids are shown with 50% probability.)

Supplementary Table 14. Crystal data and structure refinement for compound **30**.

Identification code	hxzh-1
Empirical formula	C ₂₅ H ₃₉ NO ₅ Si
Formula weight	461.66
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	P2 ₁
a/Å	9.74827(11)
b/Å	10.52493(10)
c/Å	12.70946(12)
α /°	90
β /°	93.2925(9)
γ /°	90
Volume/Å ³	1301.84(2)
Z	2
ρ_{calc} /cm ³	1.178
μ /mm ⁻¹	1.066
F(000)	500.0
Crystal size/mm ³	1.091 × 0.518 × 0.424

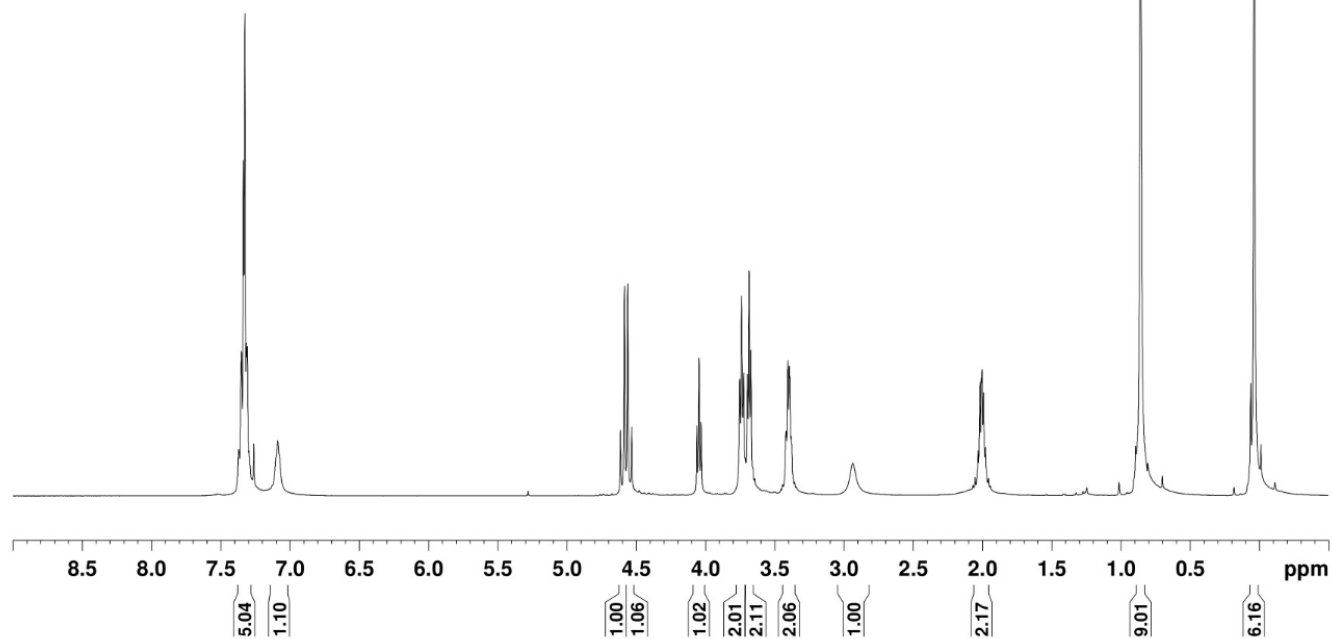
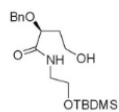
Radiation	CuK α (λ = 1.54184)
2 Θ range for data collection/ $^{\circ}$	6.966 to 134.898
Index ranges	-11 $\leq$ h $\leq$ 11, -12 $\leq$ k $\leq$ 12, -15 $\leq$ l $\leq$ 15
Reflections collected	18255
Independent reflections	4677 [R_{int} = 0.0209, R_{sigma} = 0.0138]
Data/restraints/parameters	4677/1/296
Goodness-of-fit on F^2	1.064
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0280, wR_2 = 0.0774
Final R indexes [all data]	R_1 = 0.0281, wR_2 = 0.0775
Largest diff. peak/hole / e $\text{\AA}^{-3}$	0.21/-0.18
Flack parameter	0.008(8)

Supplementary Table 15. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for compound 30. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	x	y	z	U_{eq}
Si01	3710.5(5)	7457.1(5)	6695.8(4)	21.21(14)
O002	4525.4(14)	6682.7(13)	7686.8(10)	19.0(3)
O003	7963.9(15)	6223.4(14)	5688.2(12)	24.6(3)
O004	3936.8(14)	4668.6(13)	7084.4(10)	19.4(3)
O005	8104.6(16)	9100.1(15)	7120.9(12)	30.3(3)
O006	8682.2(17)	6610.9(19)	4067.3(12)	35.3(4)
N007	4496.2(17)	3286.6(16)	9354.1(12)	18.4(3)
C008	7807(2)	6958(2)	6584.4(16)	21.6(4)
C009	4434.1(19)	5417.1(17)	7977.0(14)	17.1(4)
C00A	5859.4(19)	4896.2(17)	8368.1(14)	16.8(4)
C00B	5648.5(19)	3472.2(18)	8659.2(15)	17.6(4)
C00C	3279.3(19)	3689.3(18)	8672.1(14)	17.9(4)
C00D	6957.7(19)	5085.9(18)	7556.4(15)	19.6(4)
C00E	5075(2)	2743.3(18)	7687.9(15)	20.4(4)
C00F	3348(2)	5144.3(18)	8778.6(15)	19.2(4)
C00G	7338.7(19)	6464.7(19)	7456.5(15)	20.2(4)
C00H	4539(2)	4133(2)	10277.3(15)	22.6(4)
C00I	3698(2)	3426.0(19)	7526.9(14)	19.4(4)
C00J	8440(2)	7027(2)	4925.2(16)	26.7(5)
C00K	1956(2)	1622(2)	8861.6(16)	23.1(4)
C00L	1967(2)	3059.5(19)	8996.5(16)	22.7(4)
C00M	8195(2)	8257(2)	6342.6(17)	24.2(4)
C00N	8567(2)	8310(2)	5334.0(17)	27.7(5)

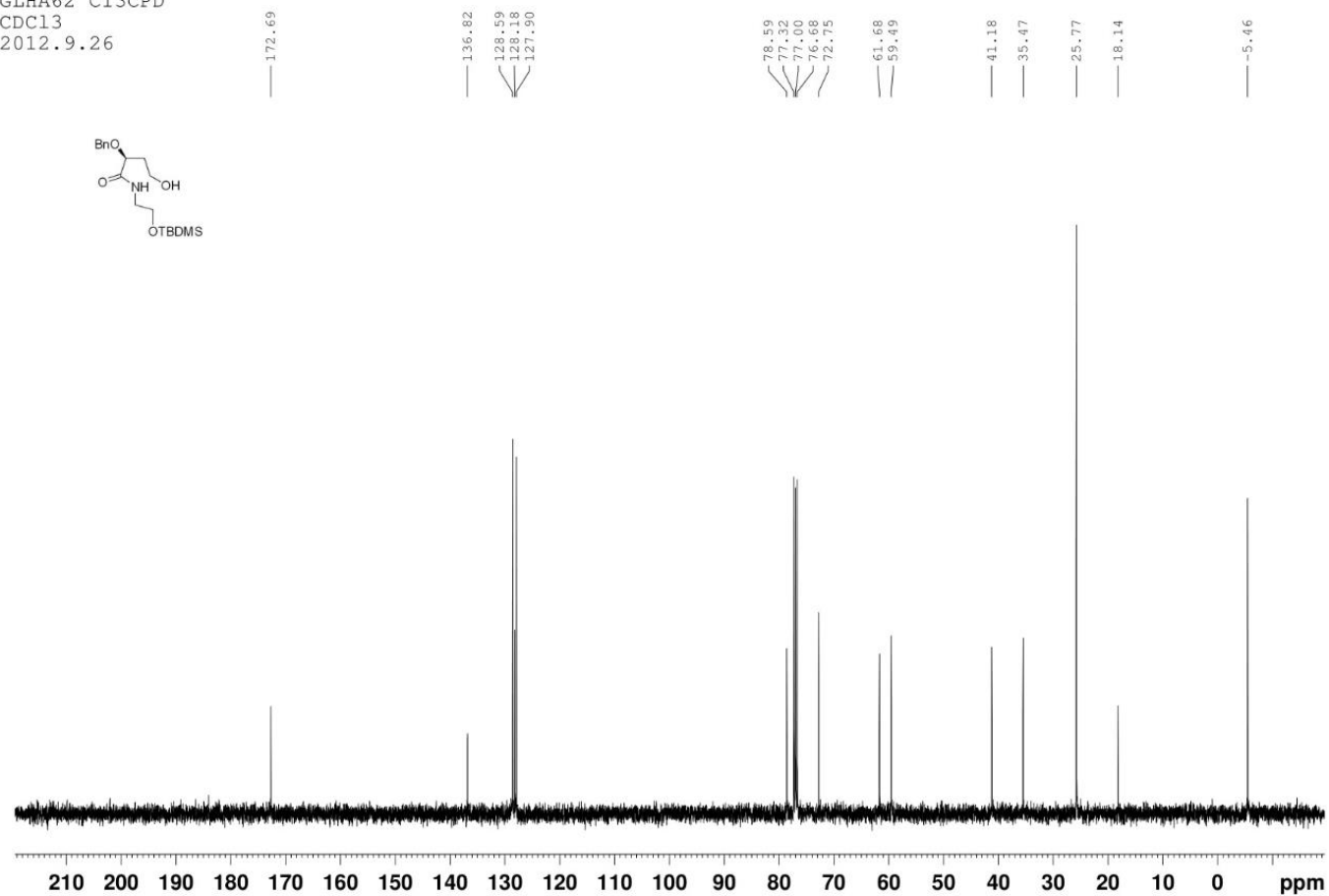
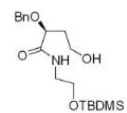
C00O	4273(3)	9135(2)	6879.8(18)	31.2(5)
C00P	8274(2)	4316(2)	7827.5(18)	29.3(5)
C00Q	3802(2)	5386.8(19)	9932.5(15)	22.7(4)
C00R	4228(3)	6875(2)	5395.2(17)	32.3(5)
C00S	1813(2)	7363(2)	6779.4(19)	34.1(5)
C00T	737(2)	985(2)	9336(2)	33.4(5)
C00U	9080(3)	9347(3)	4649(2)	40.4(6)
C00V	727(3)	-445(2)	9133(2)	41.0(6)
C00W	8327(3)	10420(2)	6901(2)	42.8(6)

GLHA62 PROTON256
CDCl3
2012.9.26



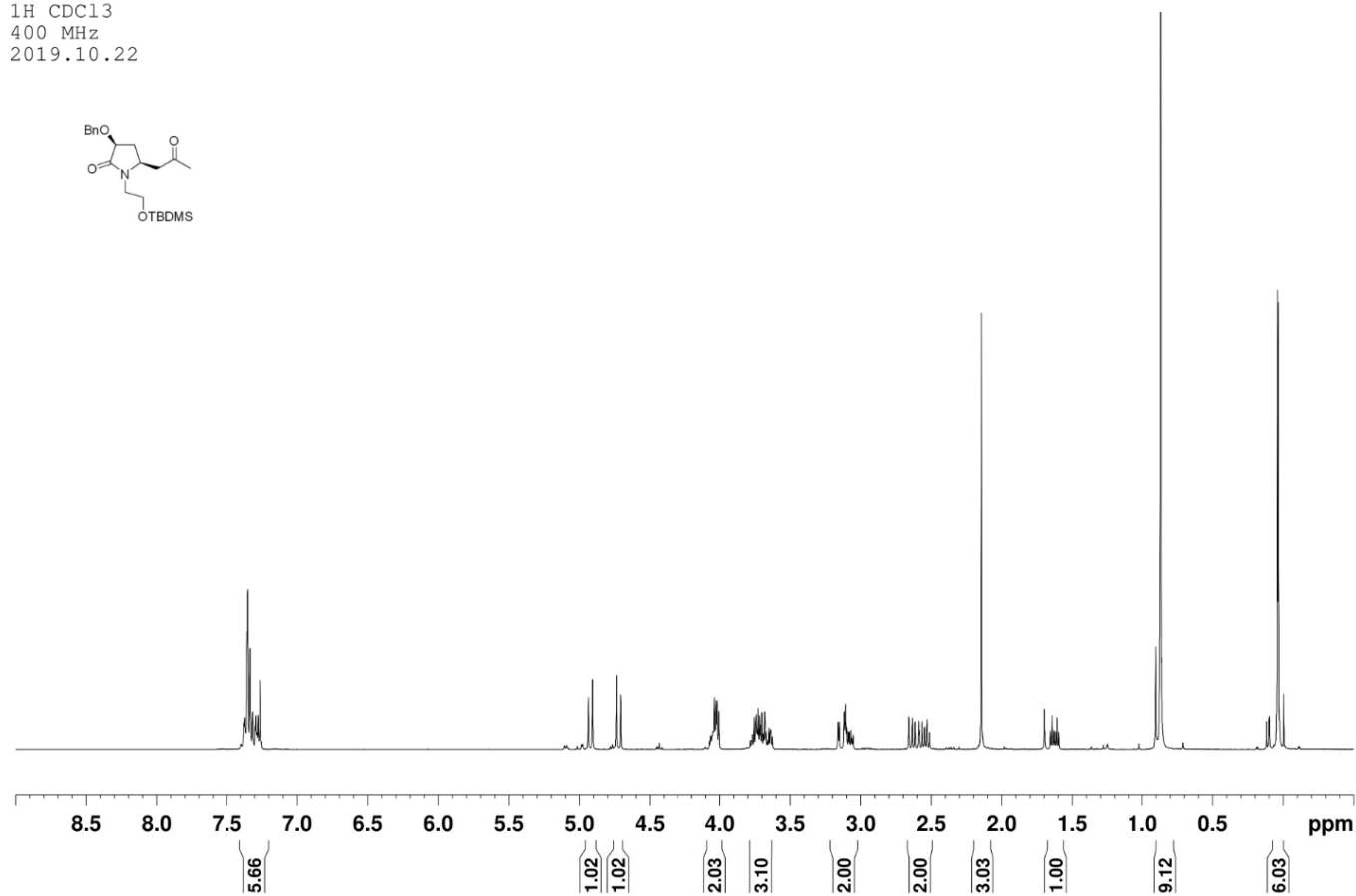
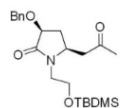
Supplementary Figure 14. ¹H NMR spectrum of compound **20**

GLHA62 C13CPD
 CDC13
 2012.9.26

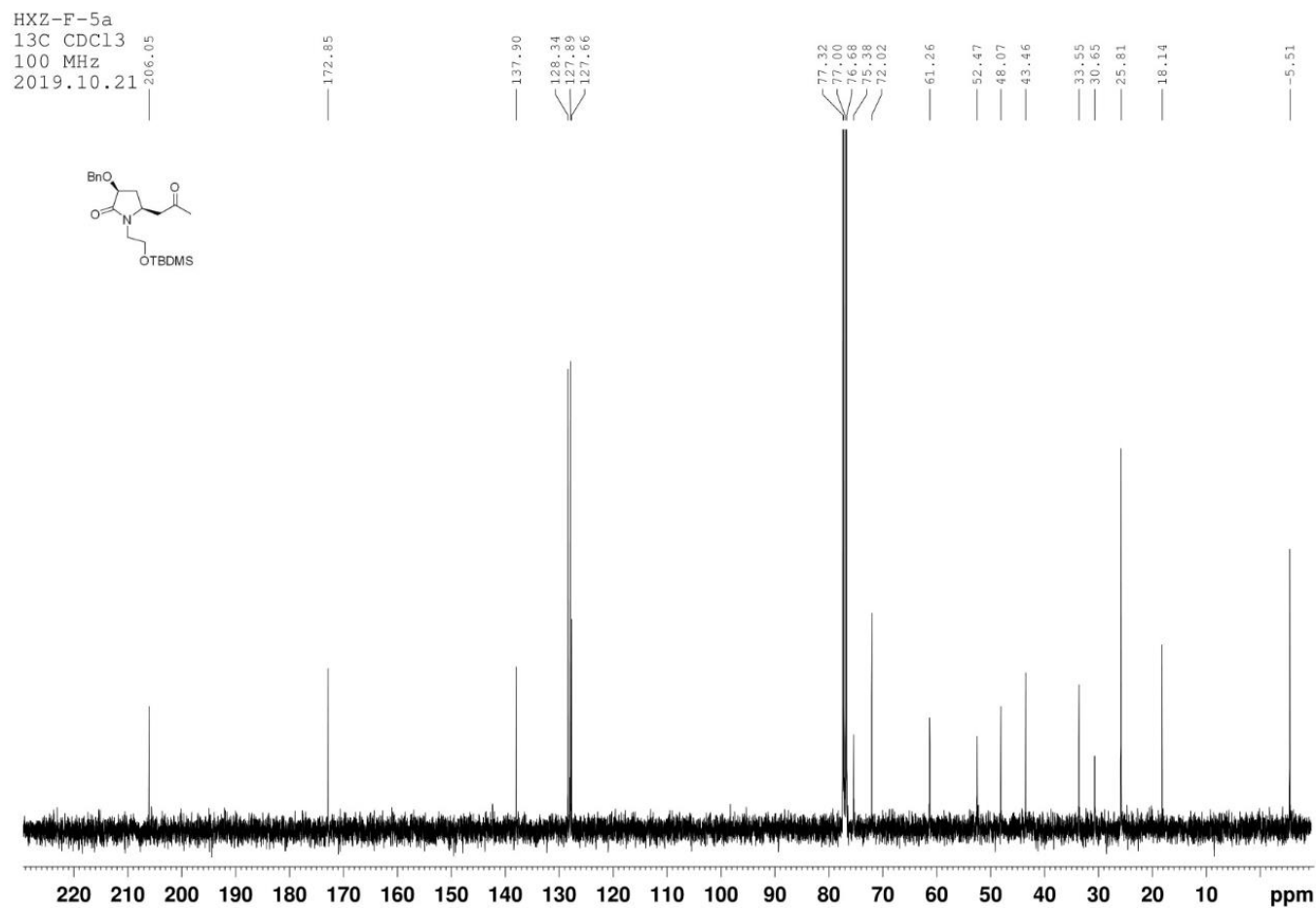


Supplementary Figure 15. ¹³C NMR spectrum of compound 20

HXZ-F-5a
1H CDCl3
400 MHz
2019.10.22

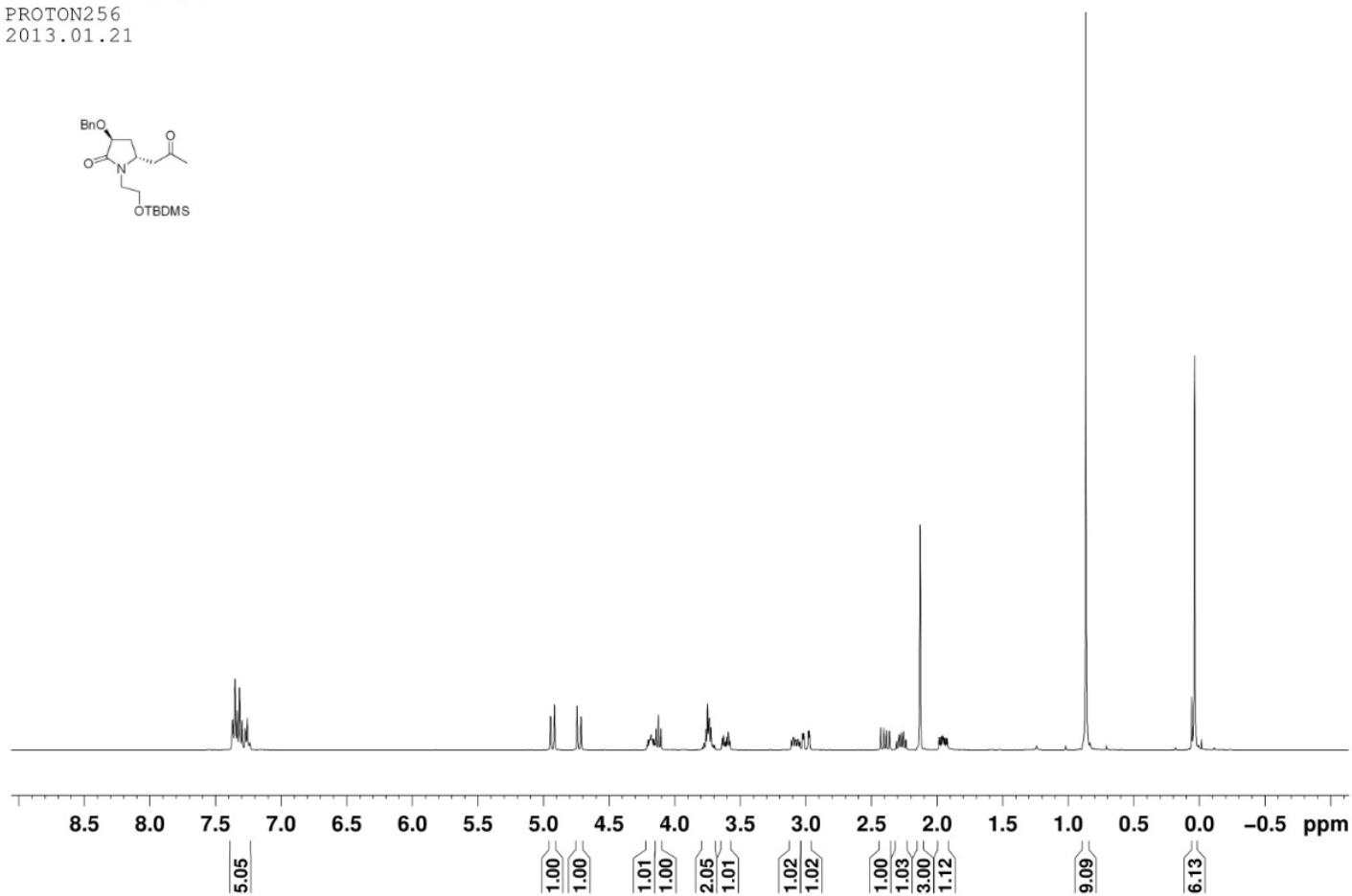
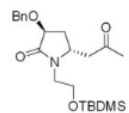


Supplementary Figure 16. ^1H NMR spectrum of compound *cis*-17



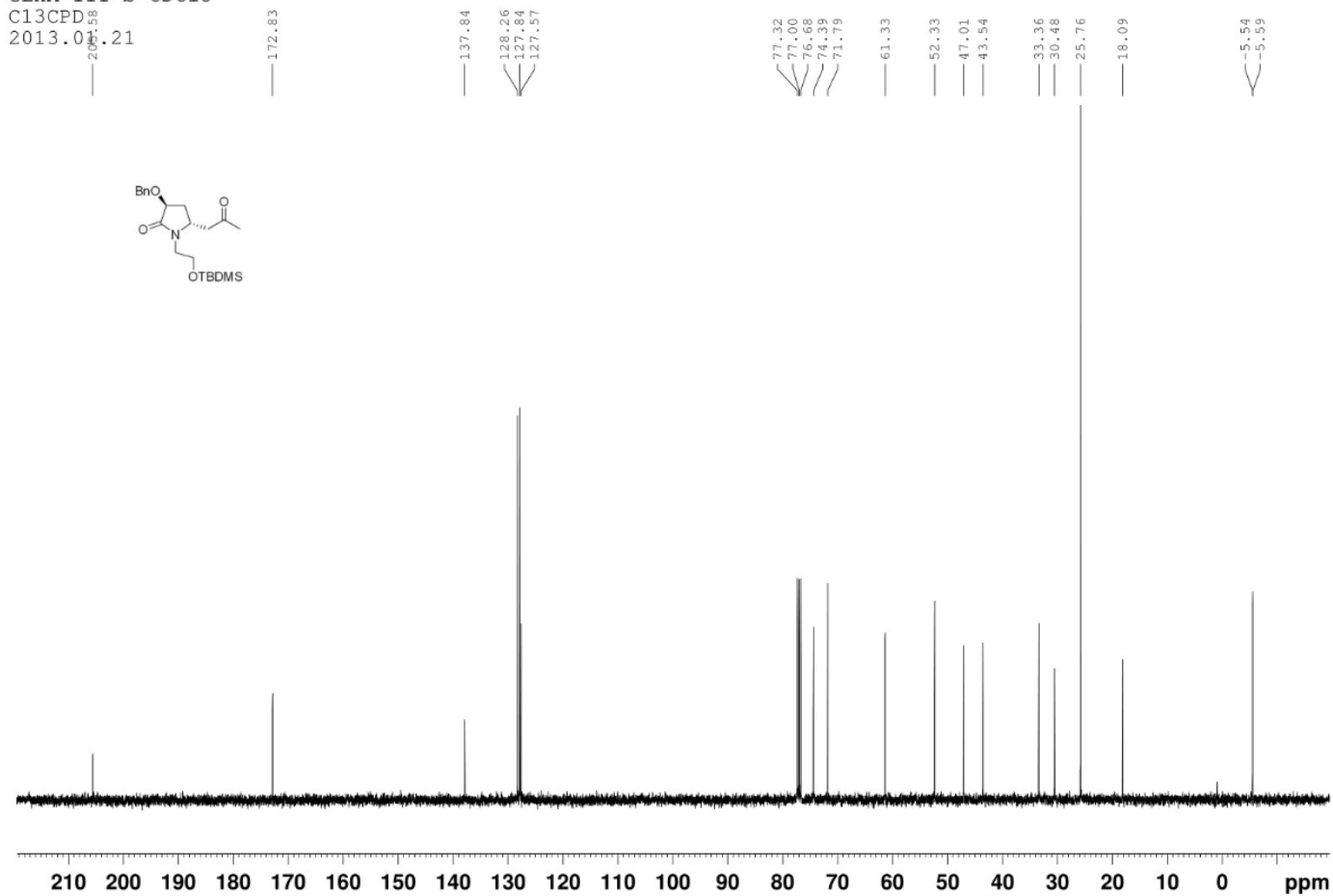
Supplementary Figure 17. ¹³C NMR spectrum of compound *cis*-17

GLHA-111 b CDC13
PROTON256
2013.01.21



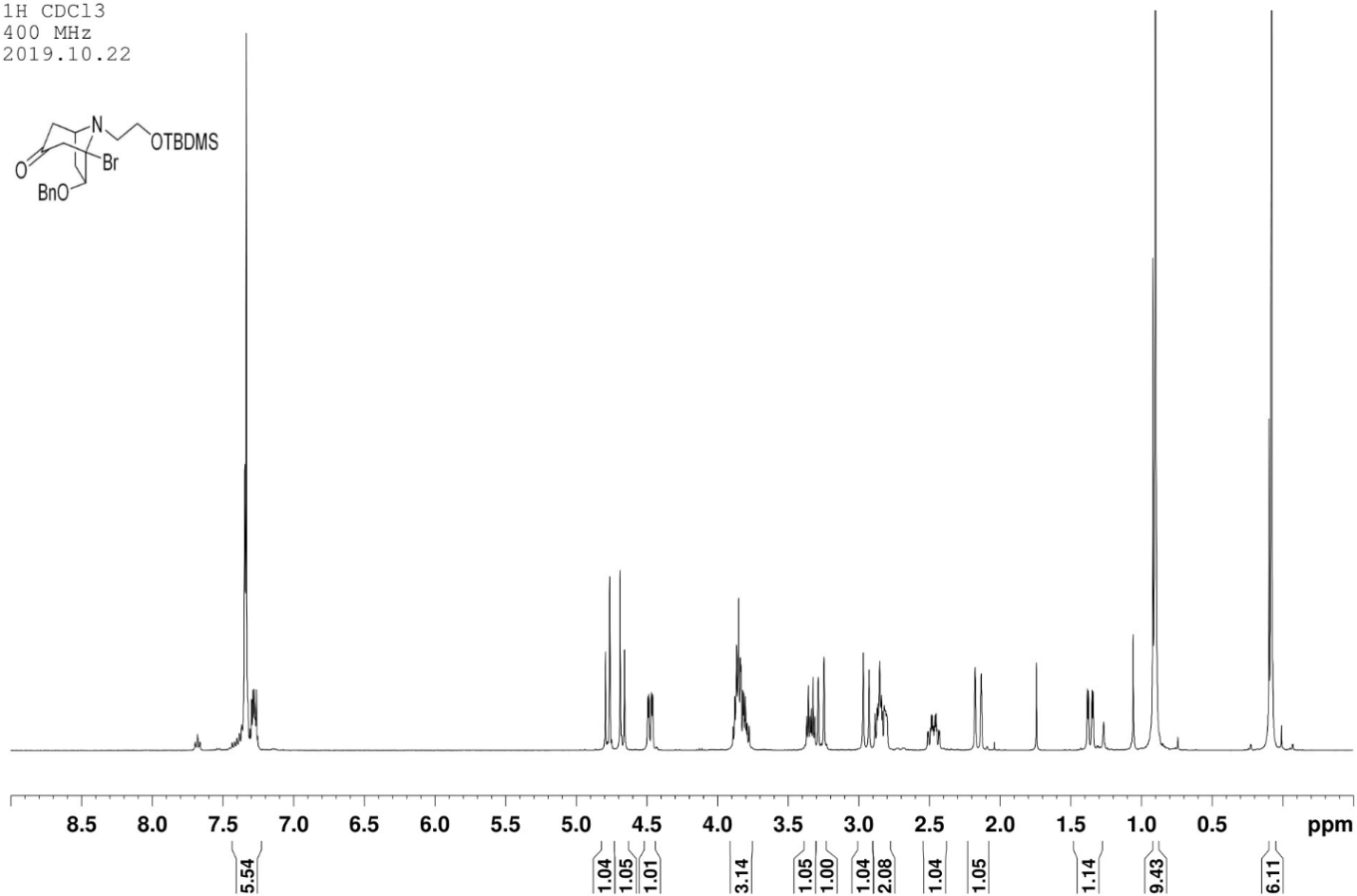
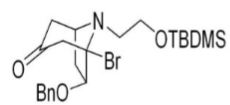
Supplementary Figure 18. ¹H NMR spectrum of compound *trans*-17

GLHA-111 b CDCl₃
 C13CPD
 2013.04.21



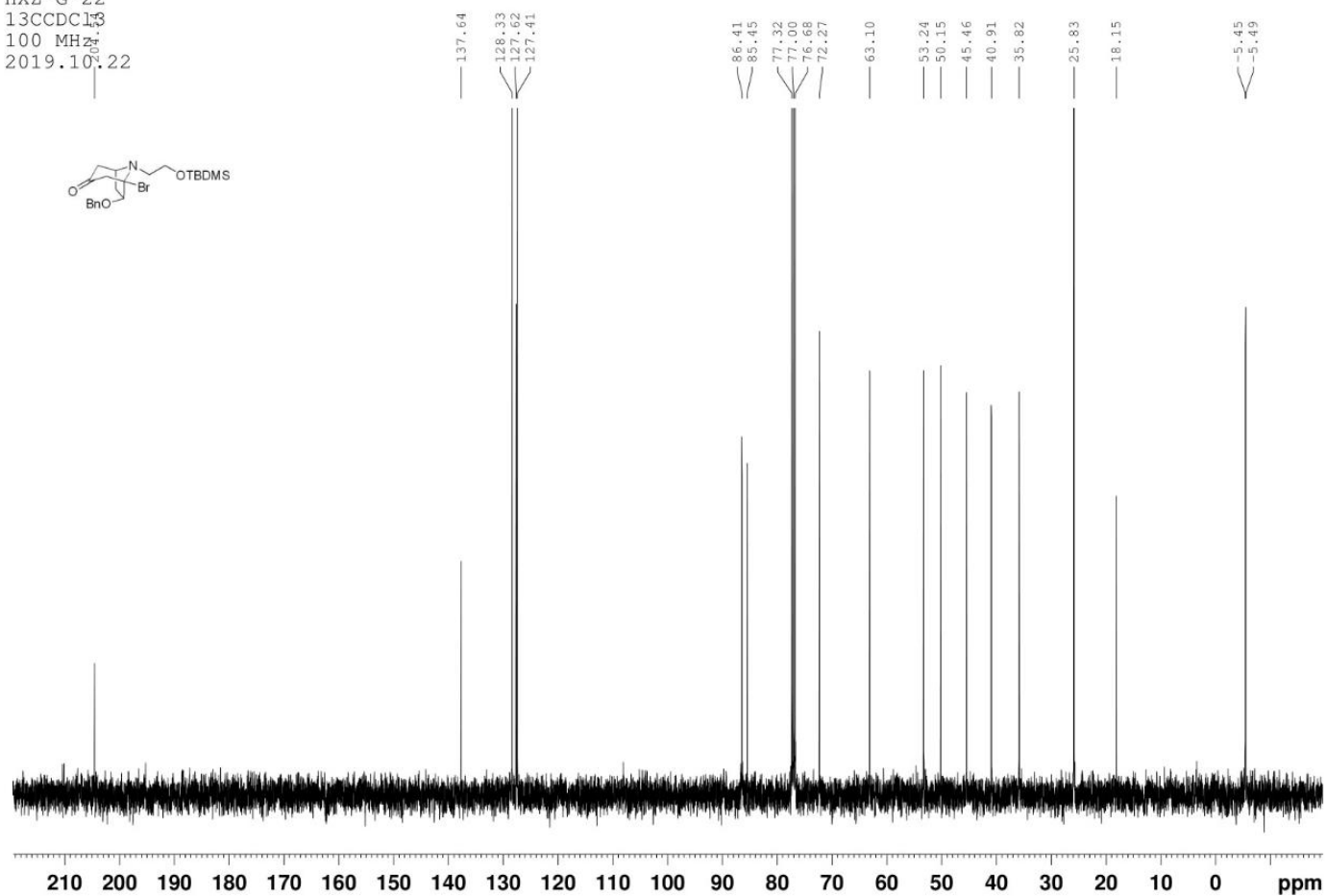
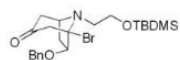
Supplementary Figure 19. ¹³C NMR spectrum of compound *trans*-17

HXZ-G-22
1H CDCl3
400 MHz
2019.10.22



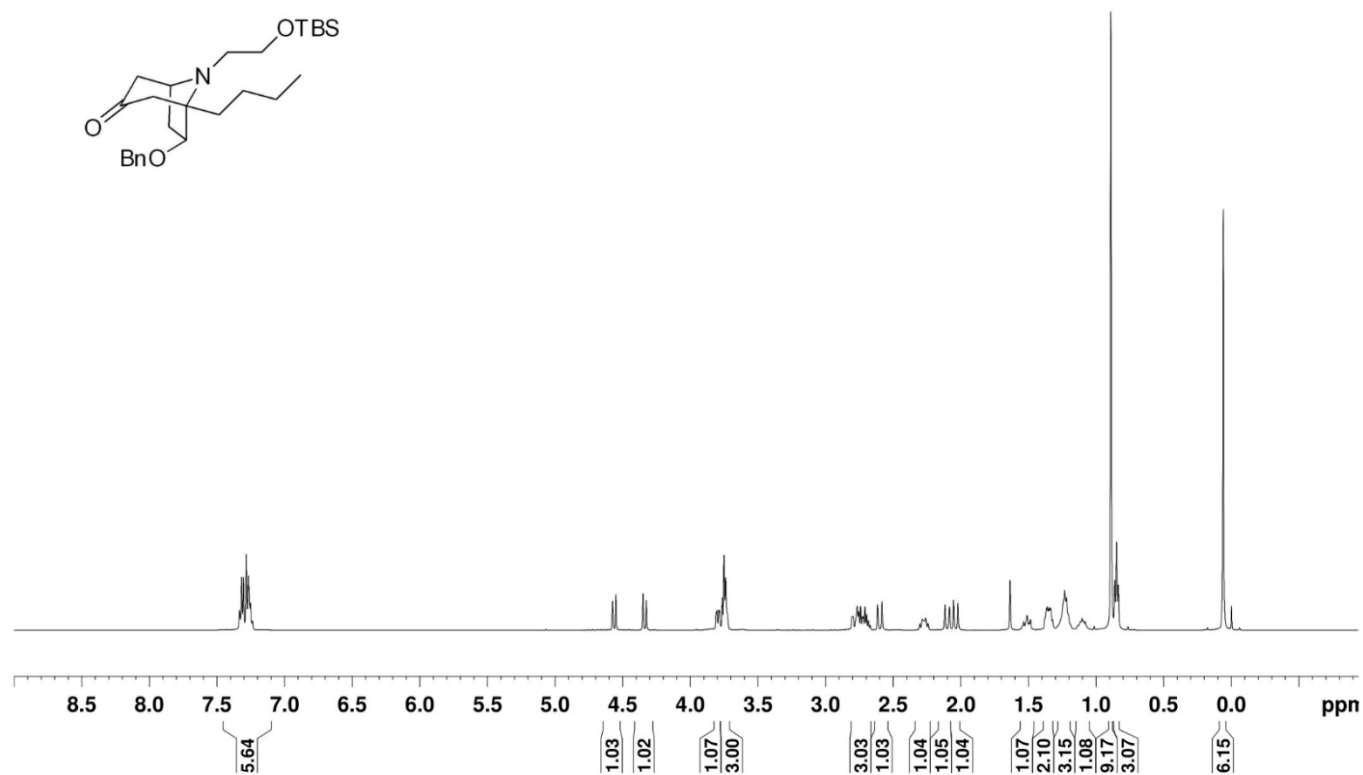
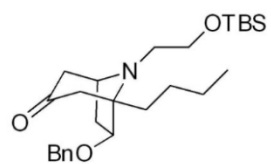
Supplementary Figure 20. ¹H NMR spectrum of compound 16

HXZ-G-22
 13CCDC153
 100 MHz
 2019.10.22



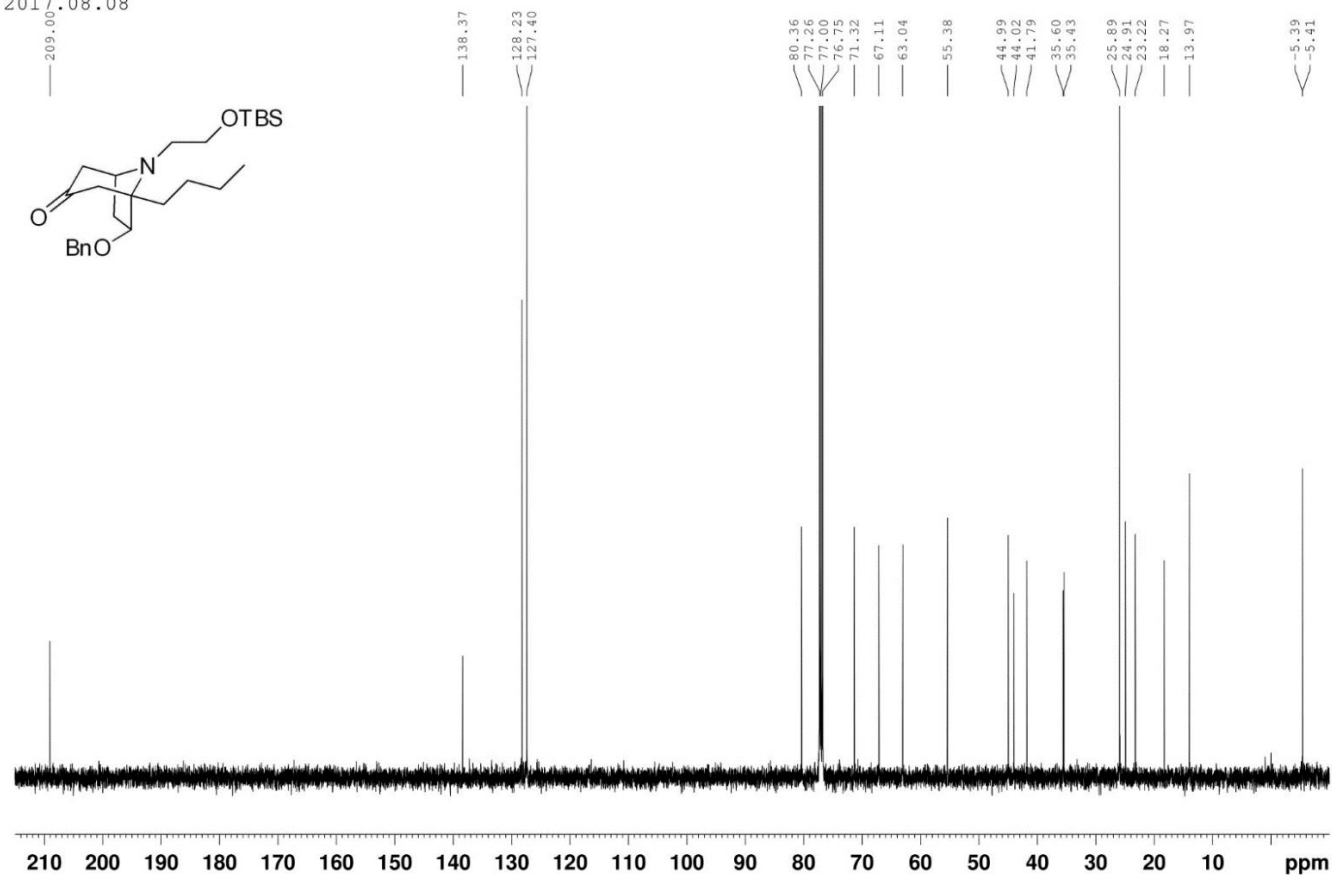
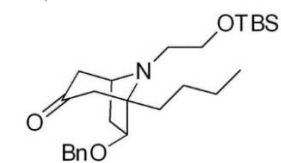
Supplementary Figure 21. ¹³C NMR spectrum of compound 16

HXZ-H-16 PROTON256
CDCl3 500MHz
2017.08.08



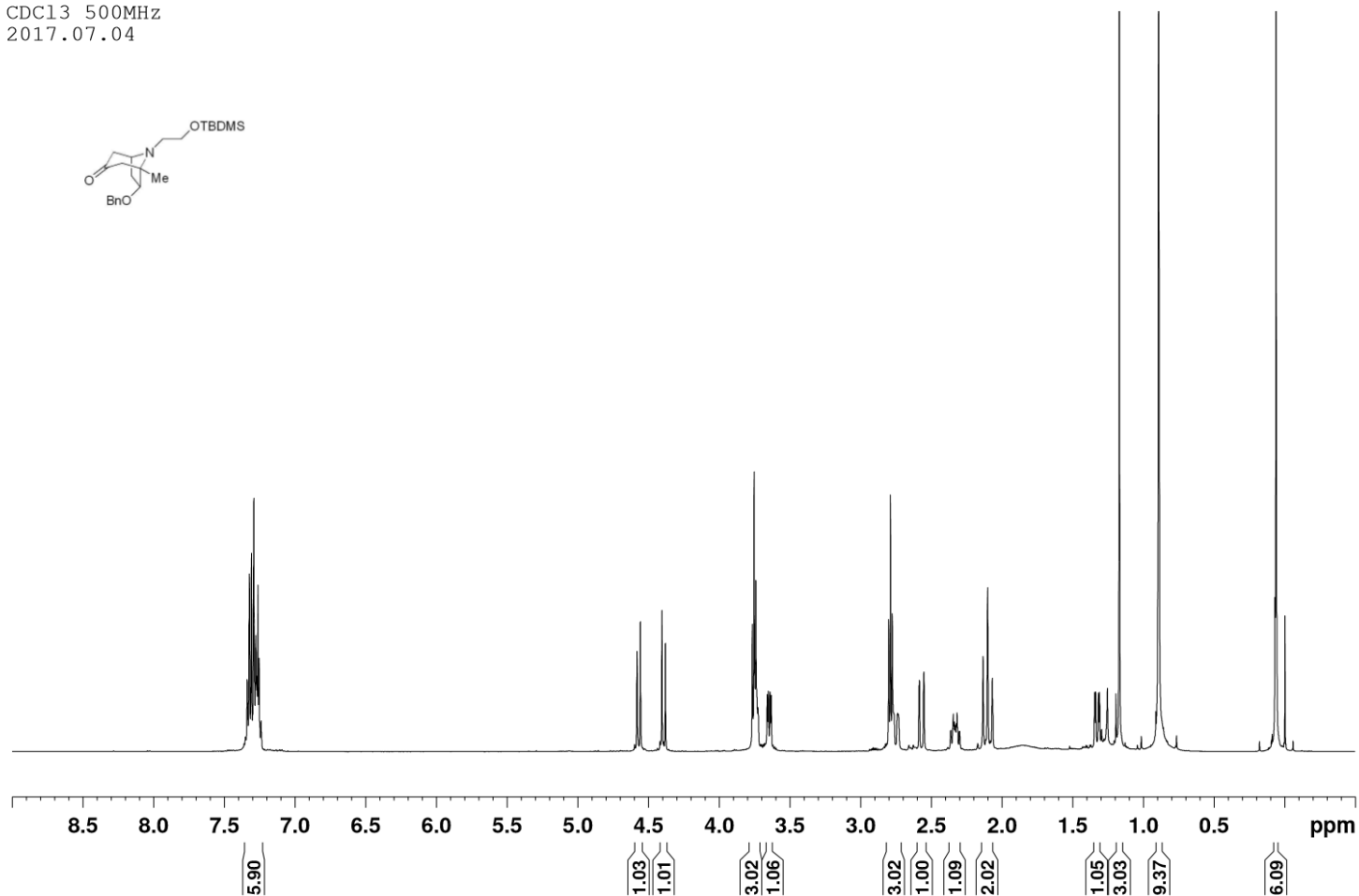
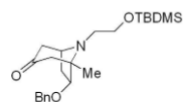
Supplementary Figure 22. ¹H NMR spectrum of compound 15

HXZ-H-16 C13CPD
 CDC13 125MHz
 2017.08.08



Supplementary Figure 23. ¹³C NMR spectrum of compound 15

HXZ-G-119 PROTON256
CDCl3 500MHz
2017.07.04



Supplementary Figure 24. ¹H NMR spectrum of compound 15a

201

— 138.39

$$\begin{array}{r} 128.27 \\ 127.40 \\ 127.28 \end{array}$$

—84.43

77.26
77.00
76.75
71.66

— 71.66

64.79

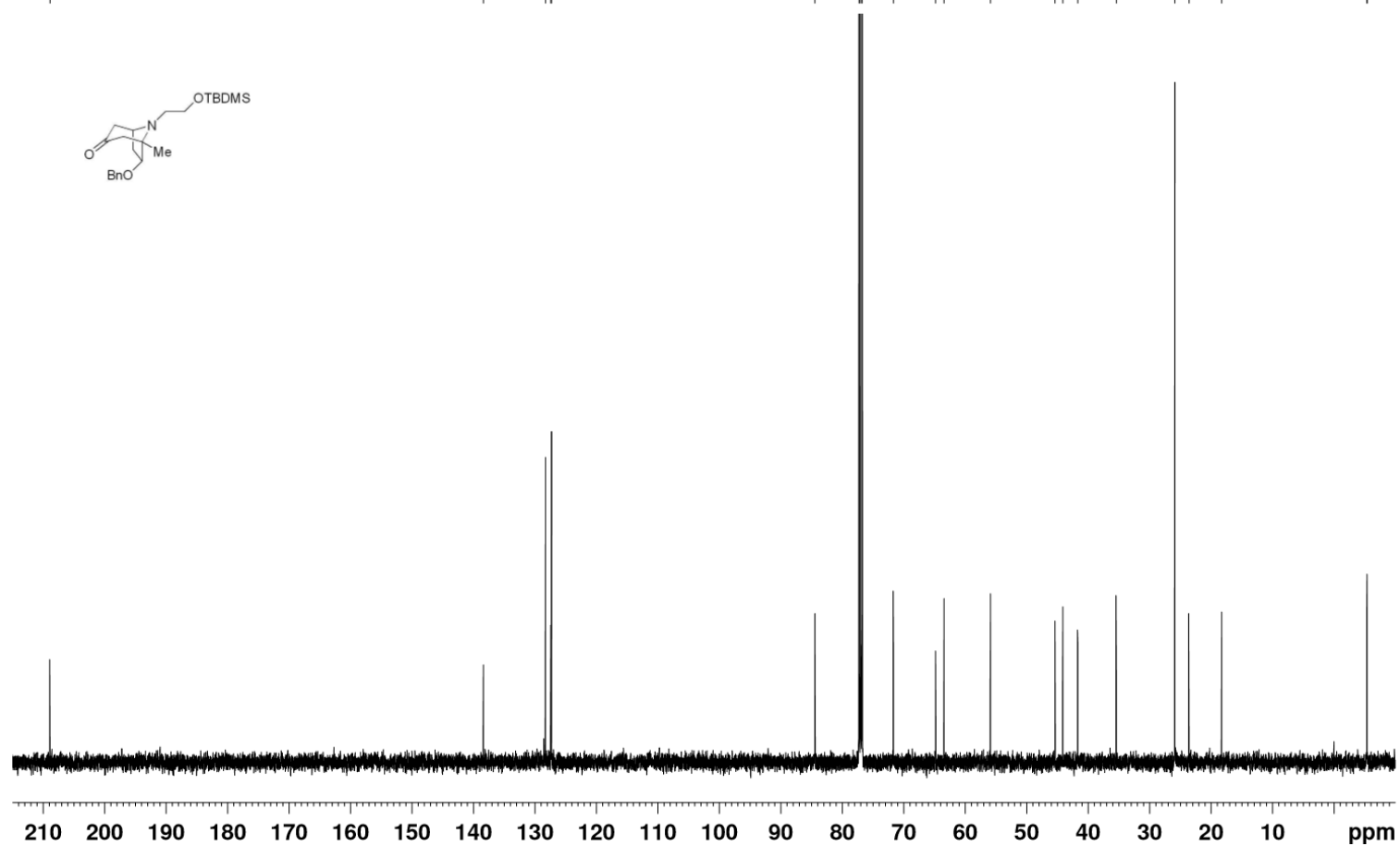
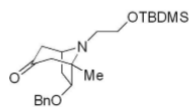
C
 C
 L
 L

45.56
44.11

1

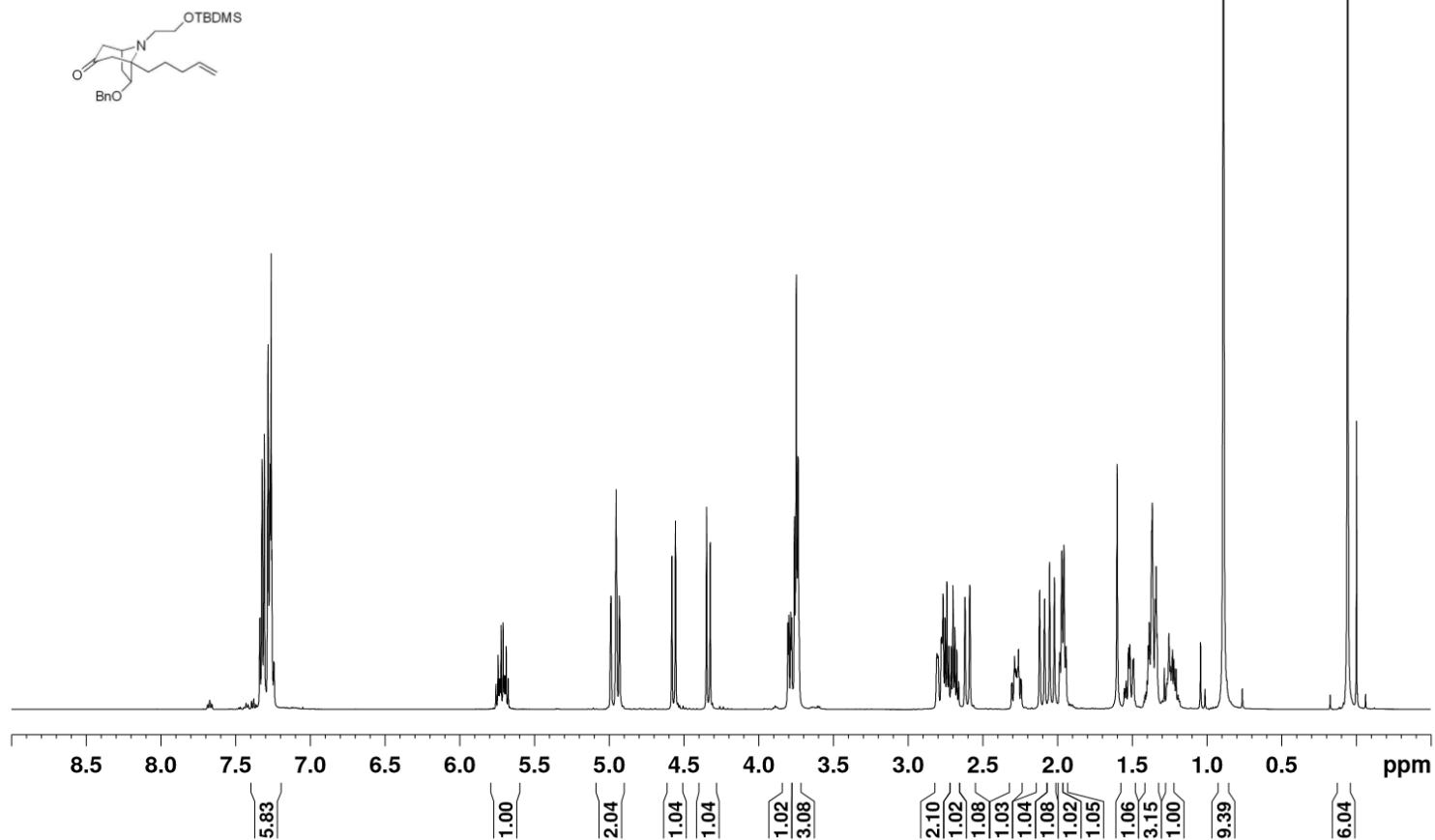
— 25.88
— 23.59

— 18.26

$$\begin{array}{r} 5.37 \\ 5.40 \end{array}$$


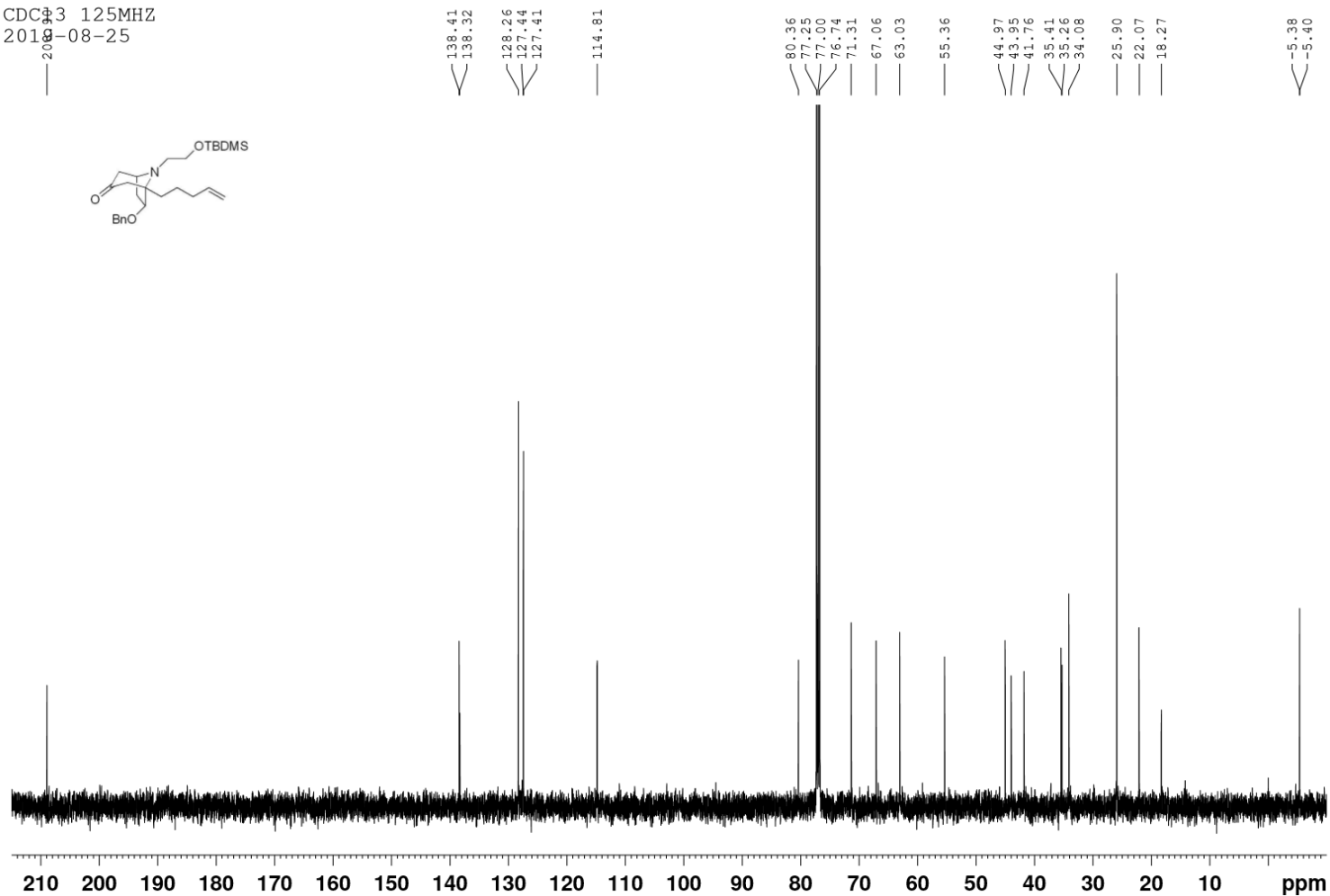
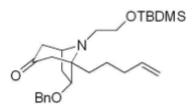
Supplementary Figure 25. ^{13}C NMR spectrum of compound **15a**

HXZ-J-6 PROTON256
CDC13 500MHZ
2019-08-25



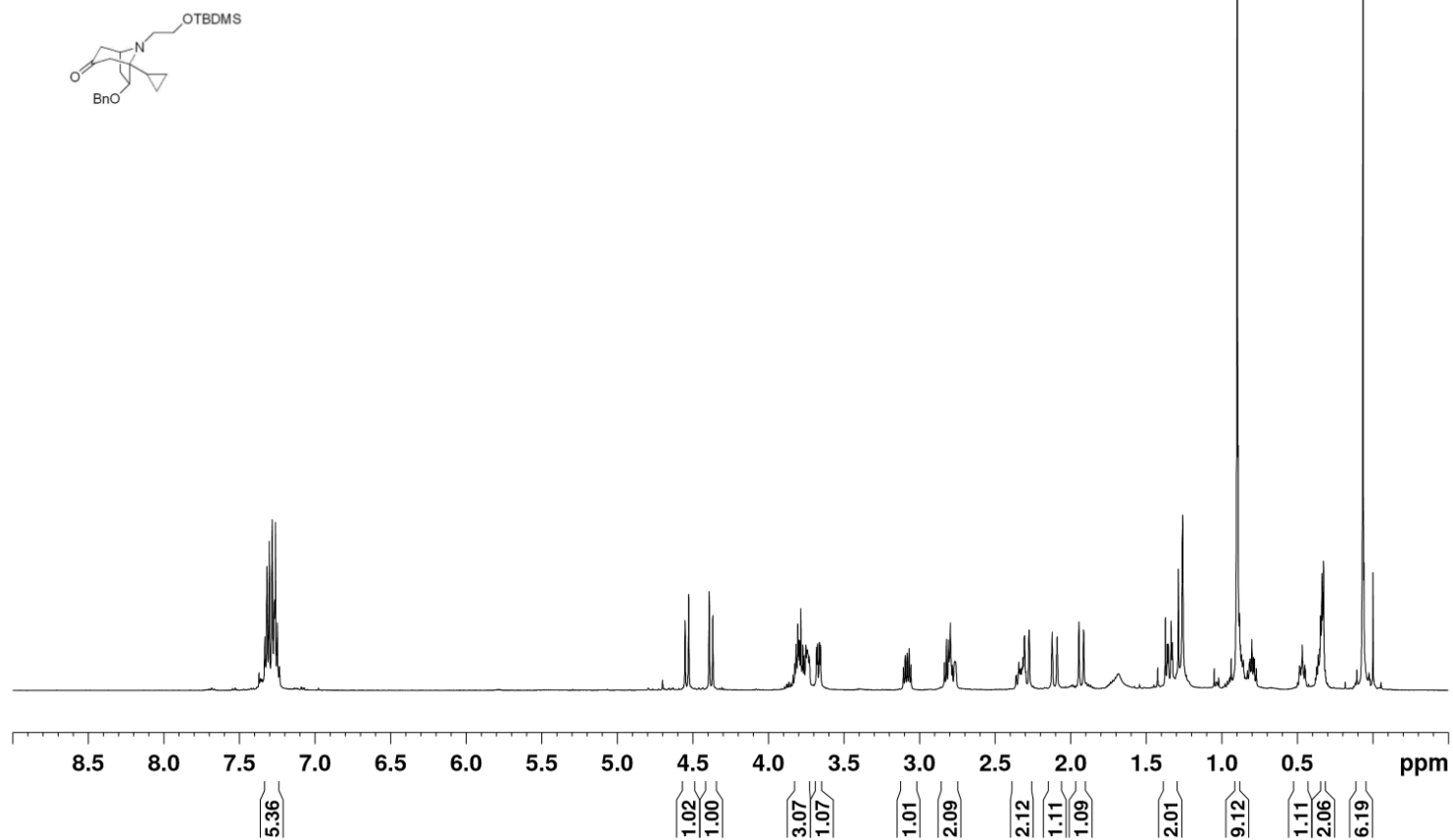
Supplementary Figure 26. ¹H NMR spectrum of compound 15b

HXZ-J-6 C13CPD
 CDCCl3 125MHZ
 2019-08-25



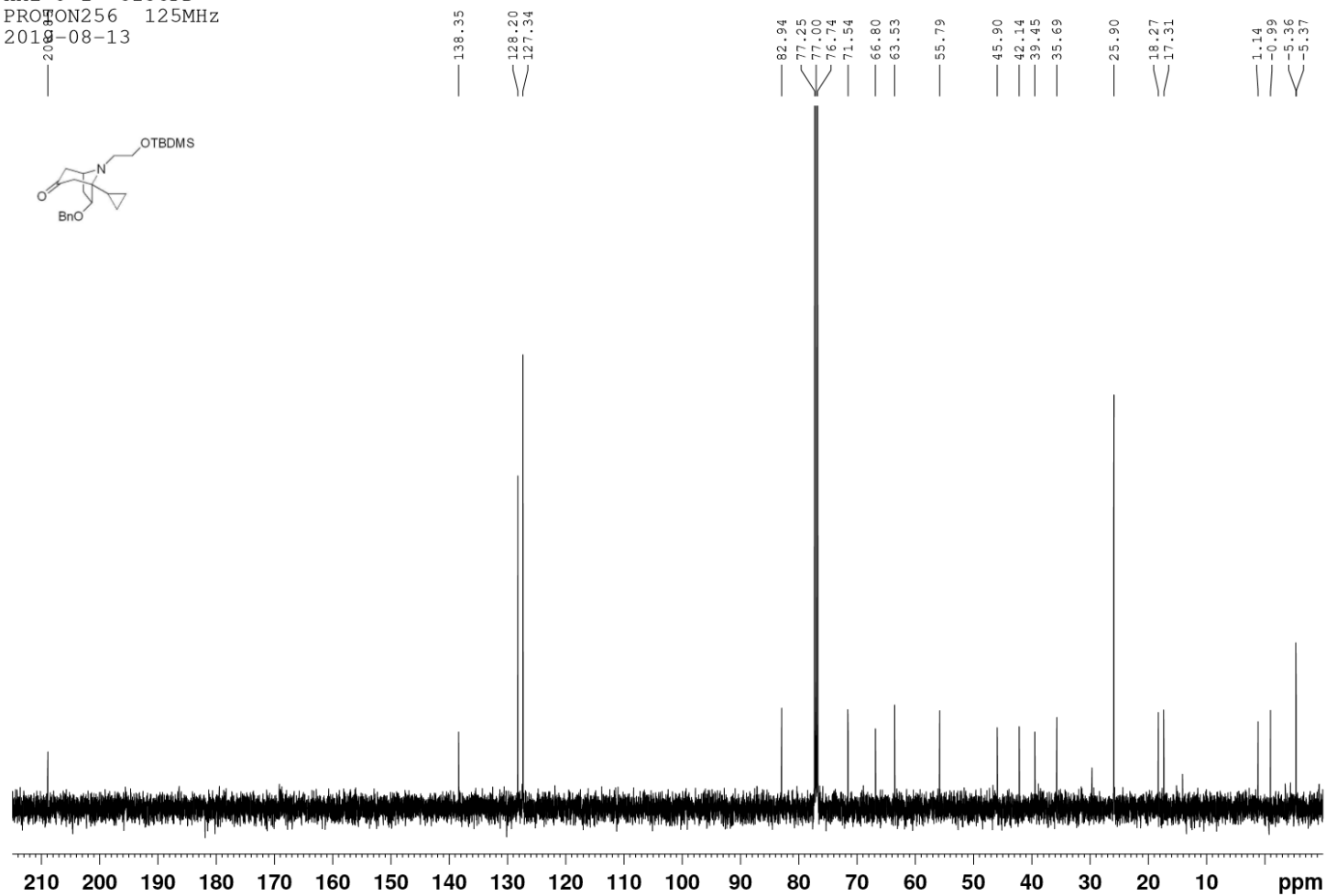
Supplementary Figure 27. ^{13}C NMR spectrum of compound **15b**

HXZ-J-1 PROTON256
 PROTON256 500MHz
 2019-08-13



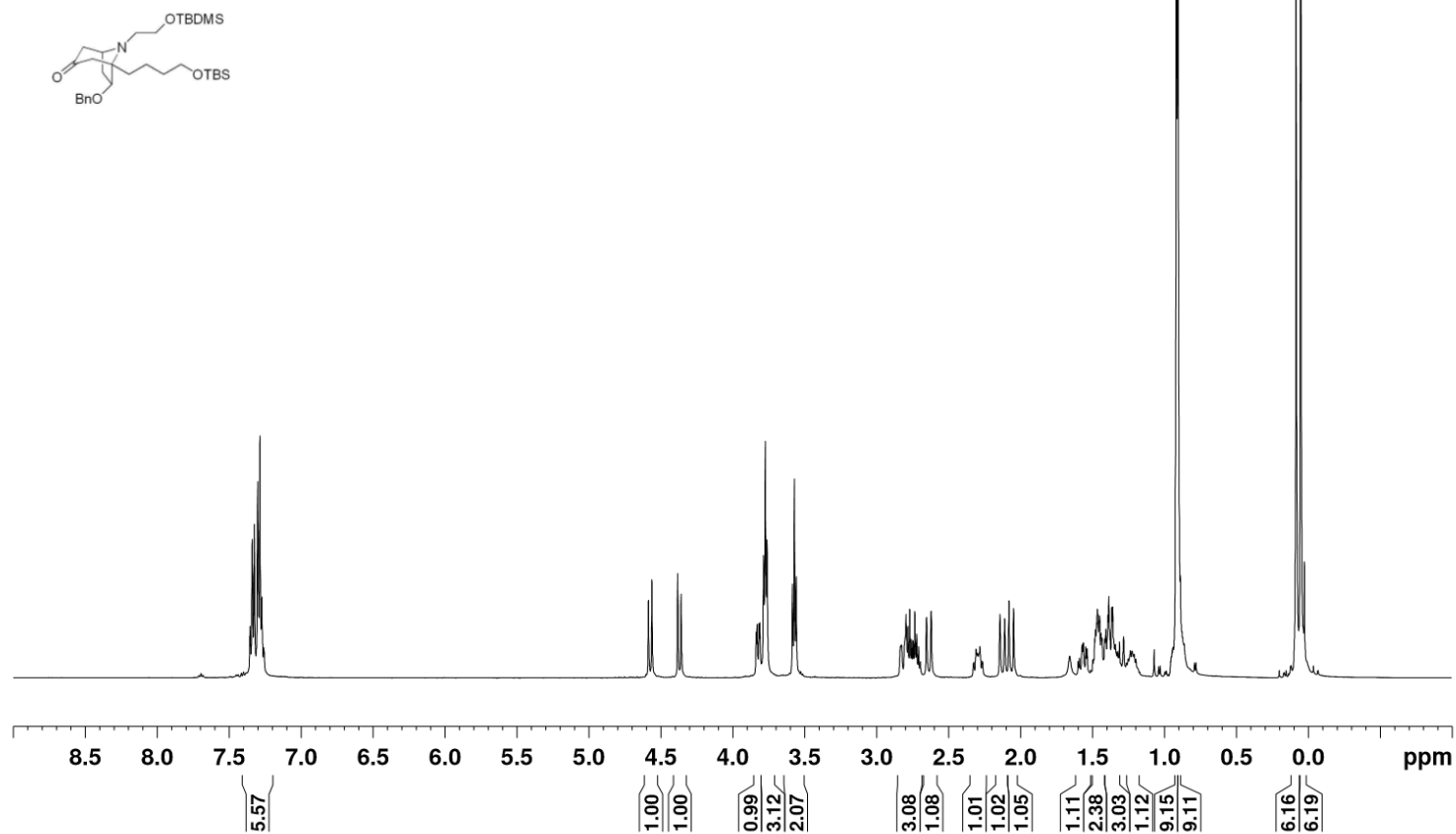
Supplementary Figure 28. ¹H NMR spectrum of compound 15c

Chemical structure of compound 1: A bicyclic molecule featuring a benzylidene-protected ketone, a cyclopropyl group, and a tert-butyldimethylsilyl (OTBDMS) ether.



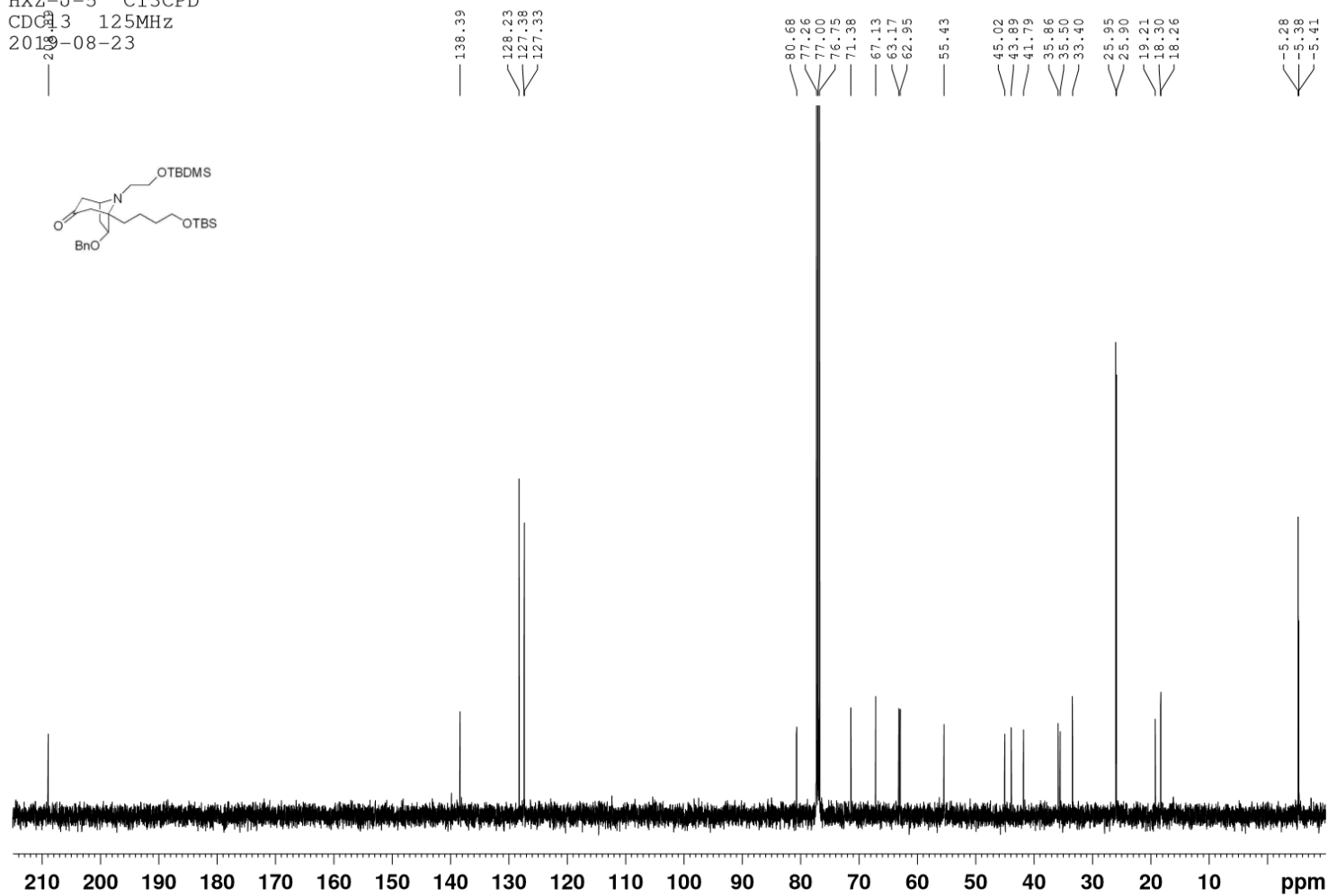
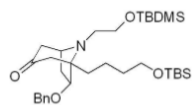
Supplementary Figure 29. ^{13}C NMR spectrum of compound **15c**

HXZ-J-5 PROTON256
PROTON256 500MHz
2019-08-23



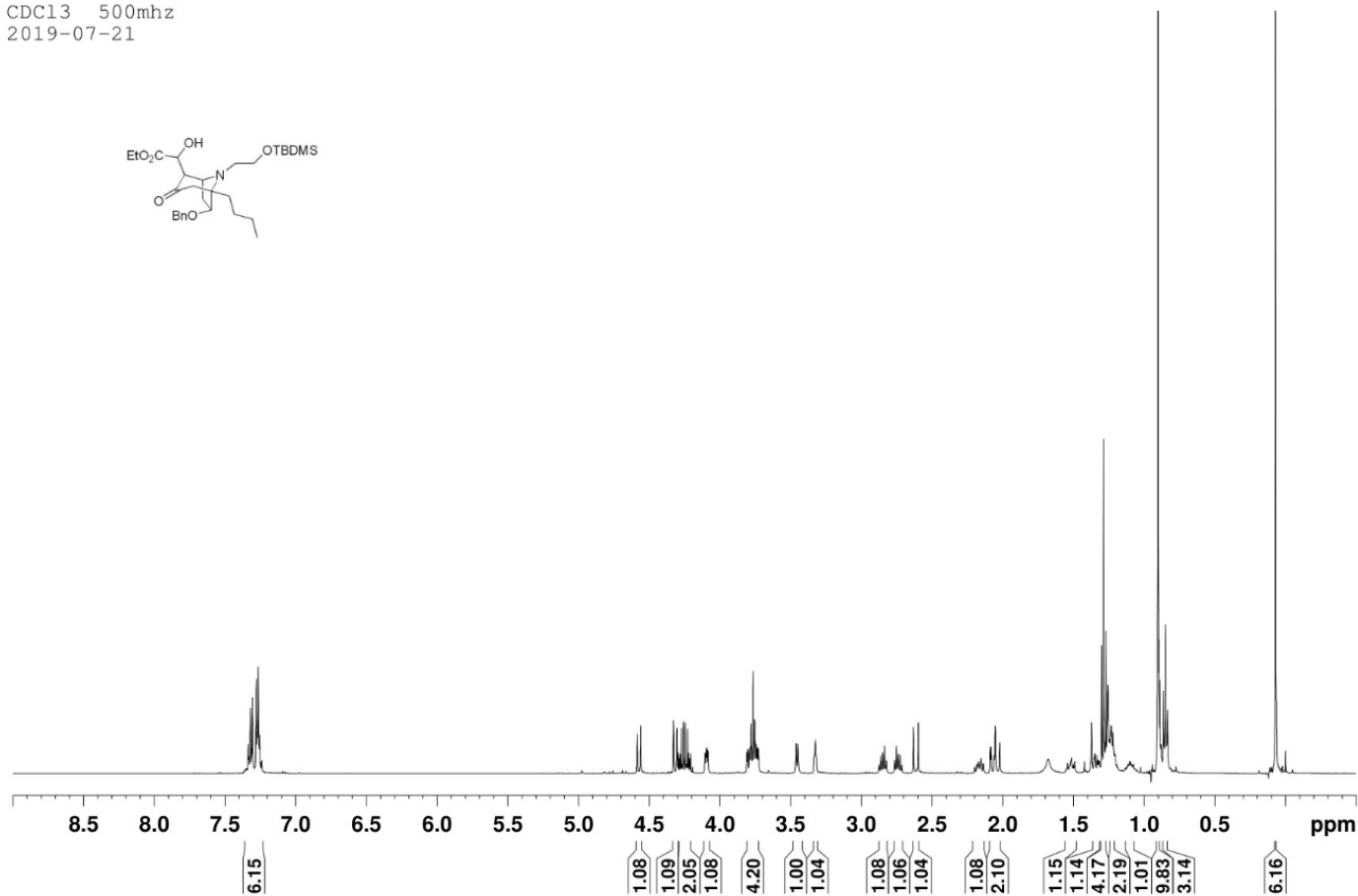
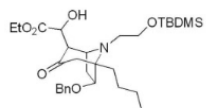
Supplementary Figure 30. ^1H NMR spectrum of compound 15d

HXZ-J-5 C13CPD
 CDCl₃ 125MHz
 2019-08-23



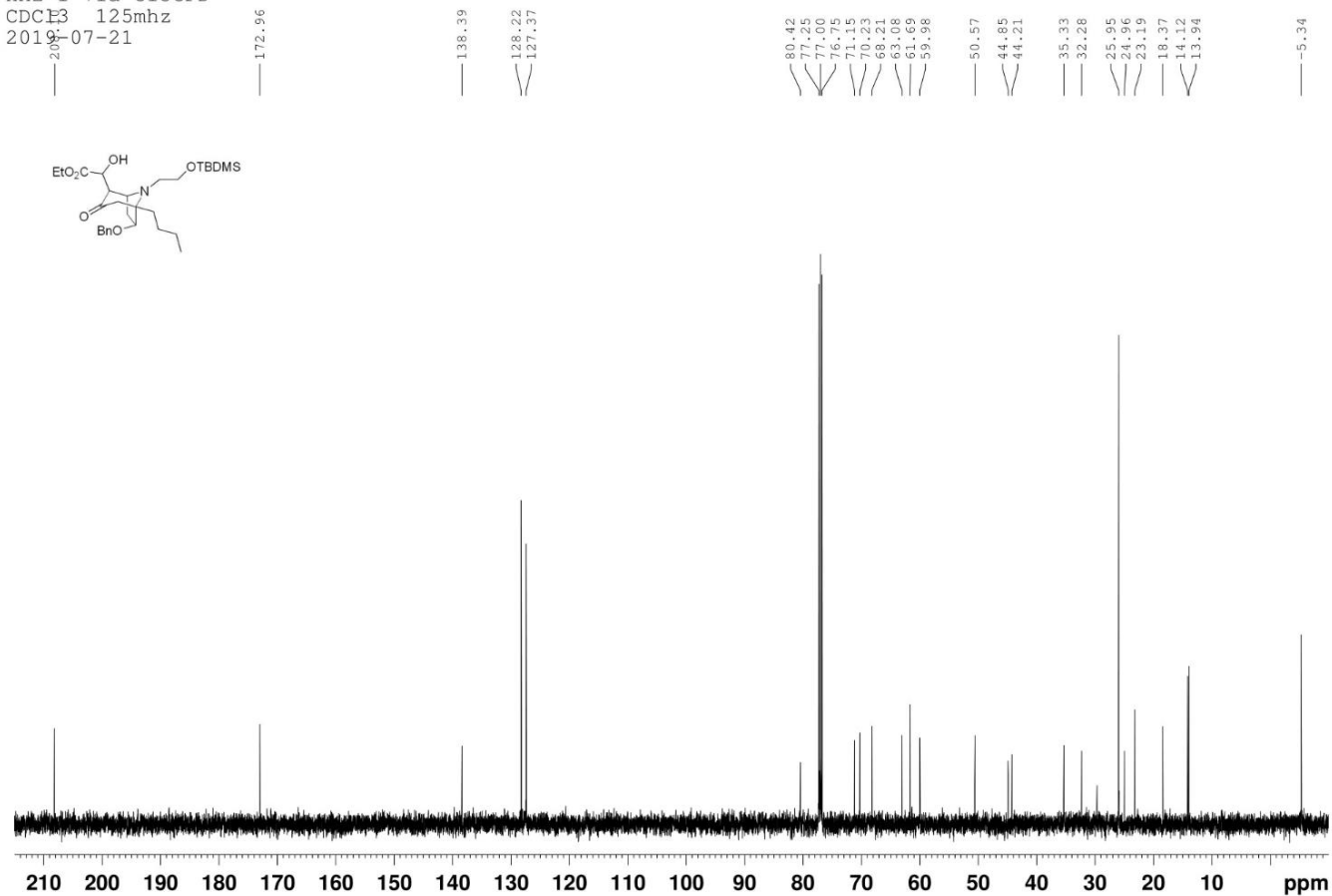
Supplementary Figure 31. ¹³C NMR spectrum of compound **15d**

HXZ-I-71a PROTON256
 CDCl3 500mhz
 2019-07-21



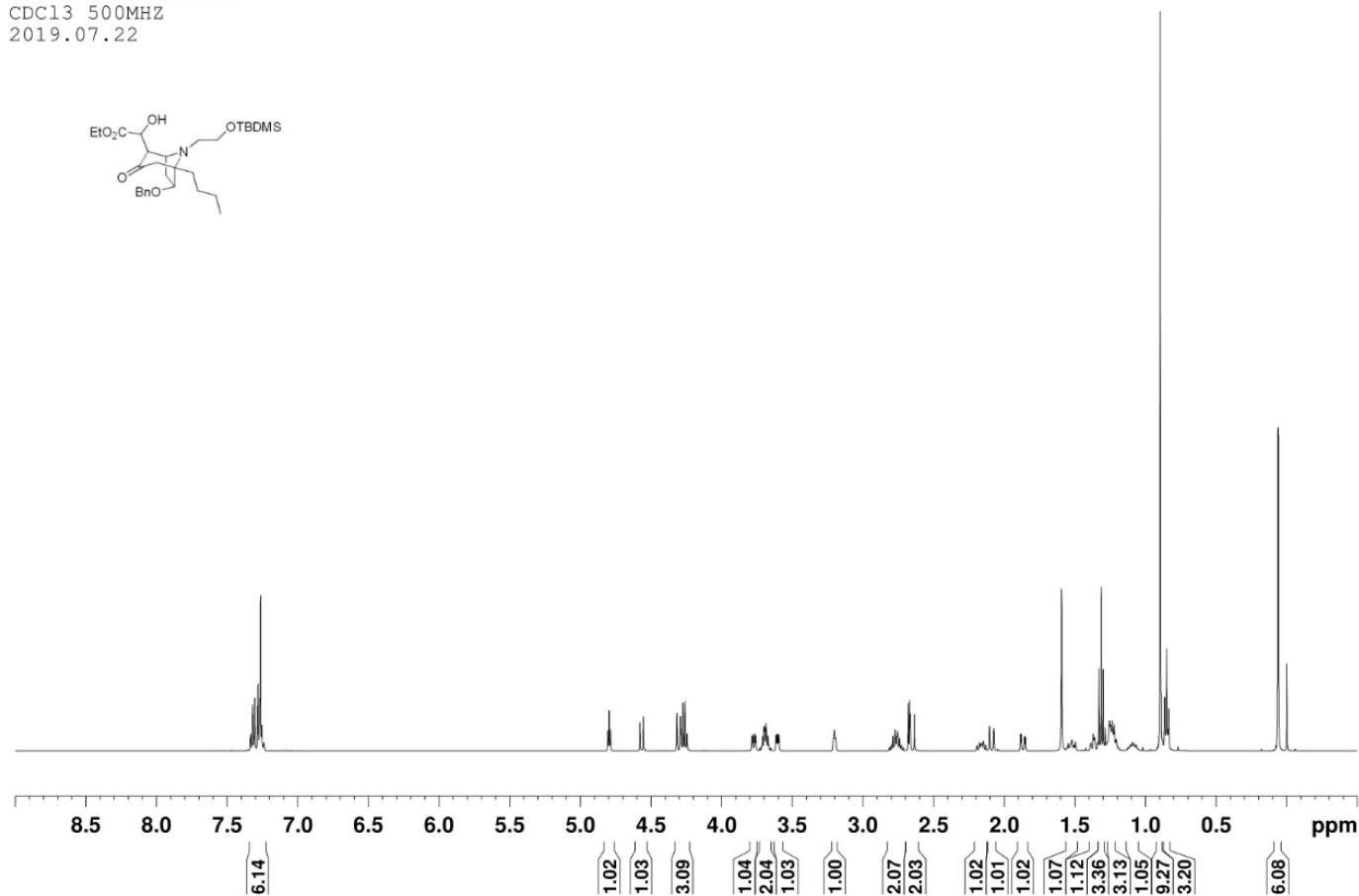
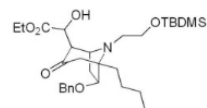
Supplementary Figure 32. ^1H NMR spectrum of compound 23-1 or 23-2

HXZ-I-71a C13CPD
 CDCl₃ 125mhz
 2019-07-21



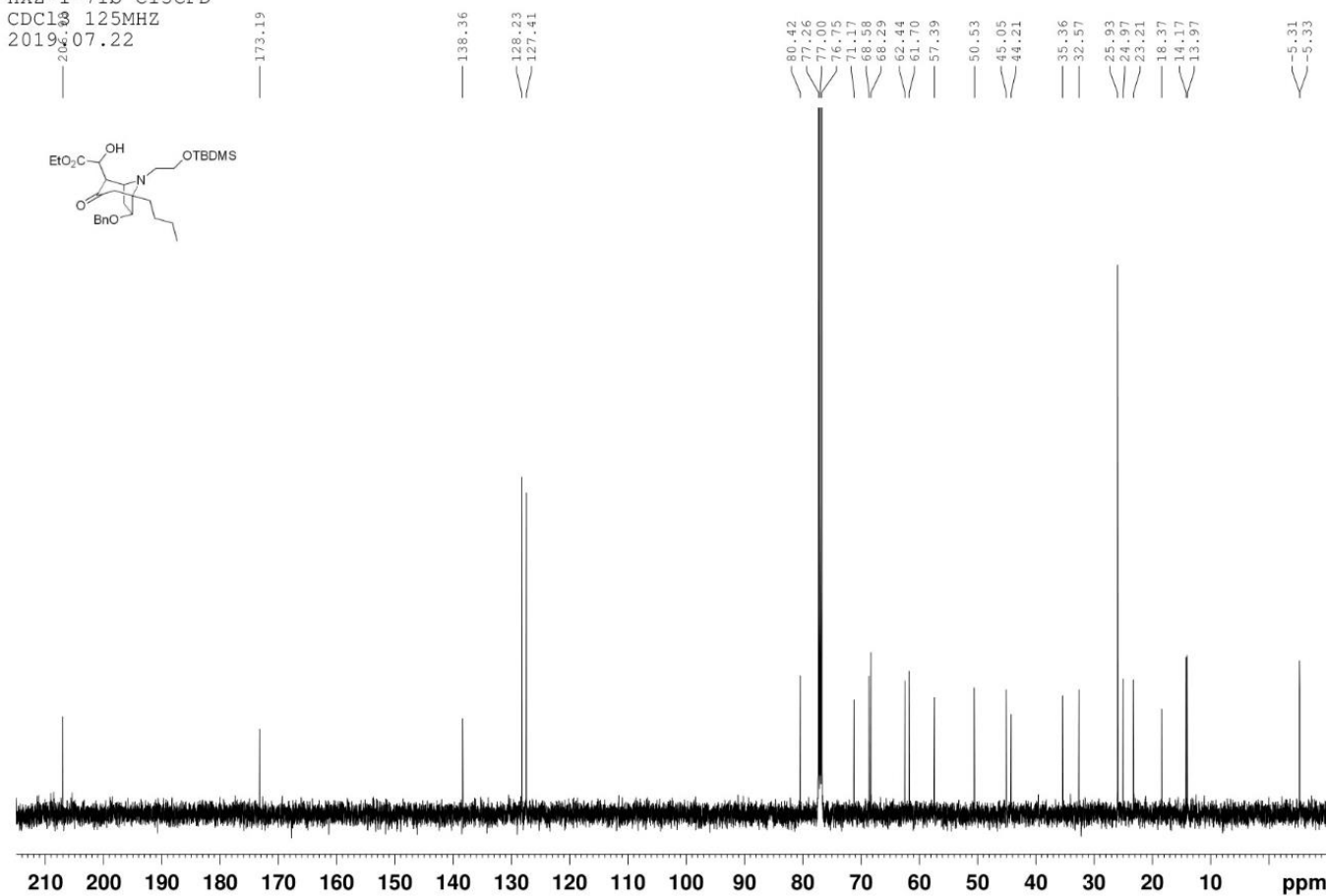
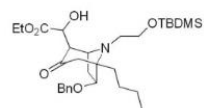
Supplementary Figure 33. ¹³C NMR spectrum of compound 23-1 or 23-2

HXZ-I-71b PROTON256
 CDC13 500MHZ
 2019.07.22



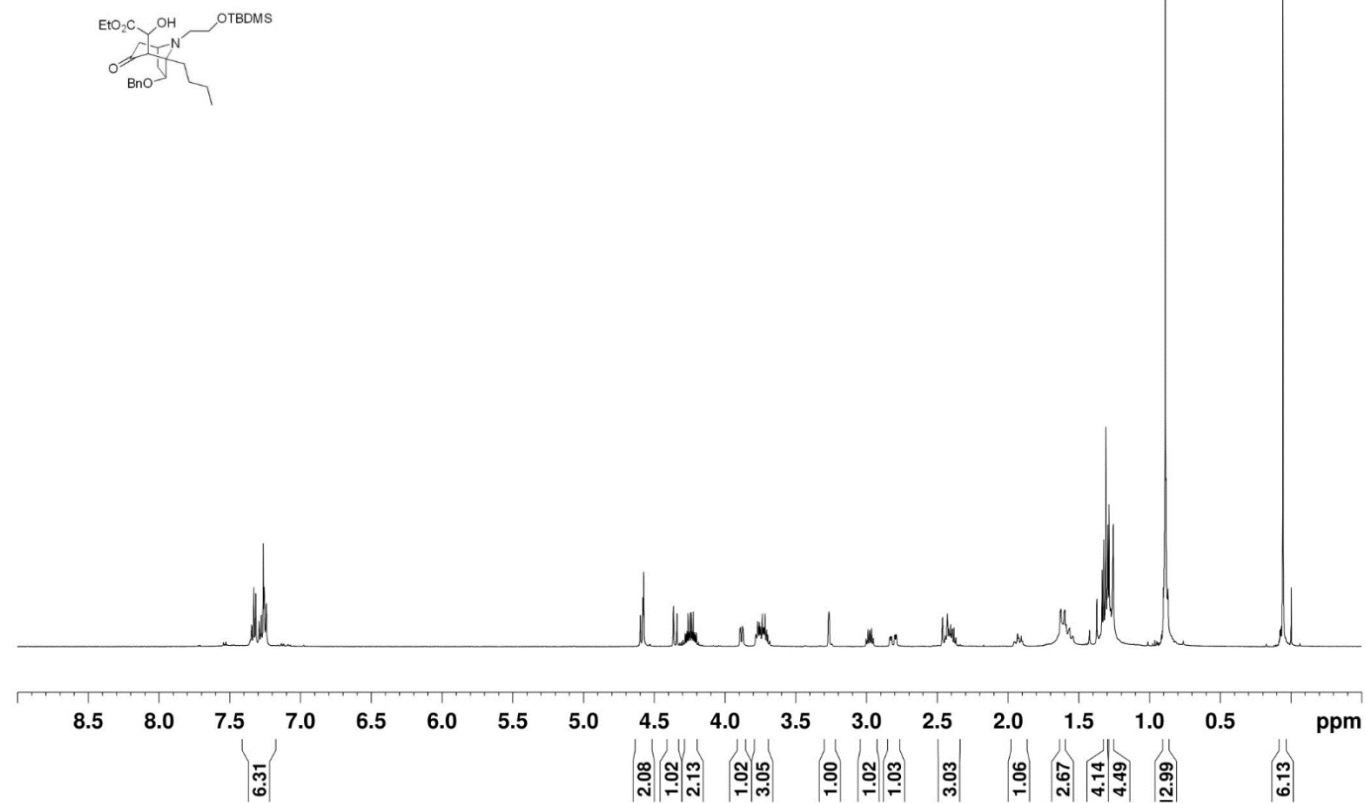
Supplementary Figure 34. ^1H NMR spectrum of compound 23-1 or 23-2

HX2-I-71b C13CPD
 CDC13 125MHZ
 201907.22



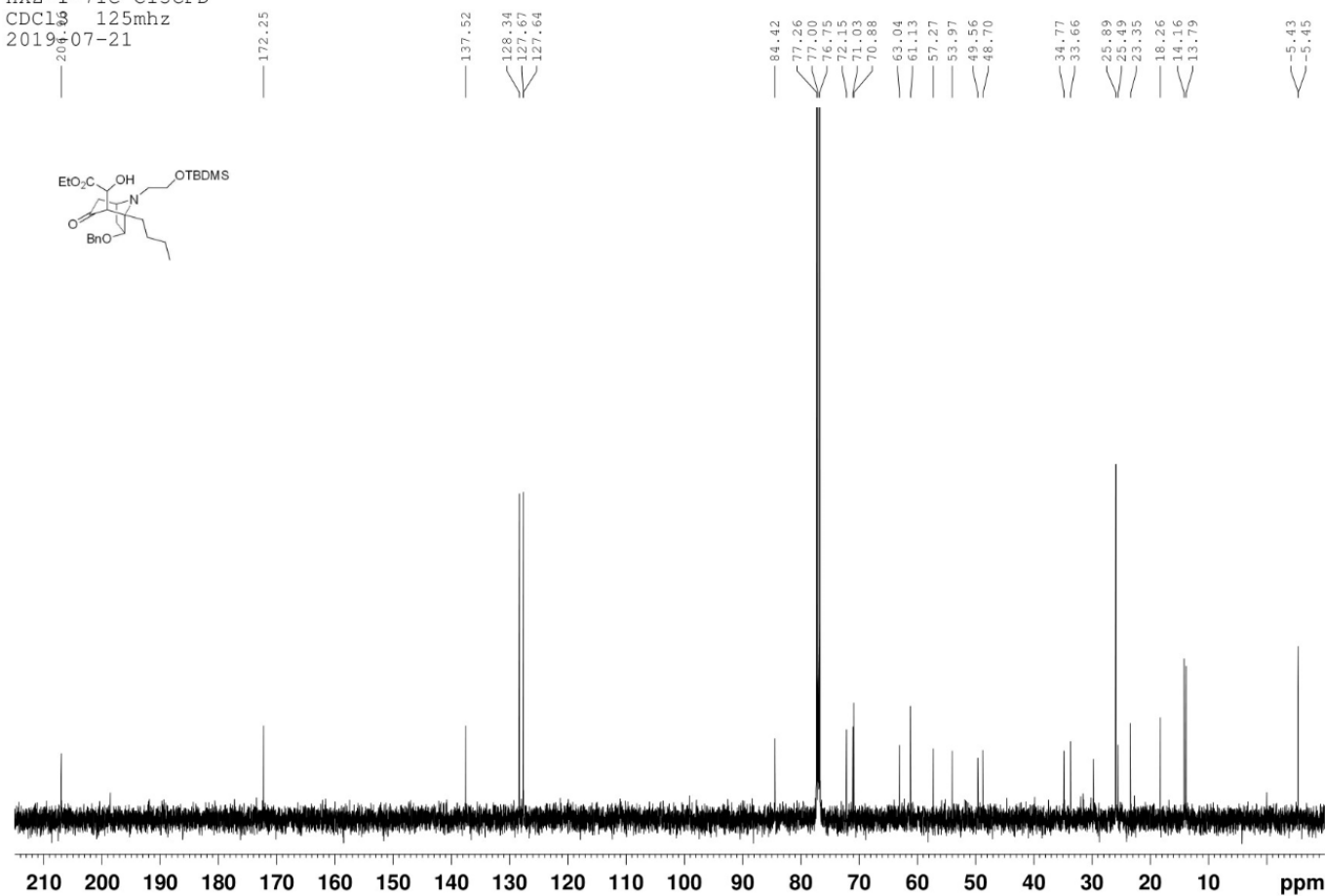
Supplementary Figure 35 ^{13}C NMR spectrum of compound 23-1 or 23-2

HXZ-I-71c PROTON256
CDCl3 500mhz
2019-07-21



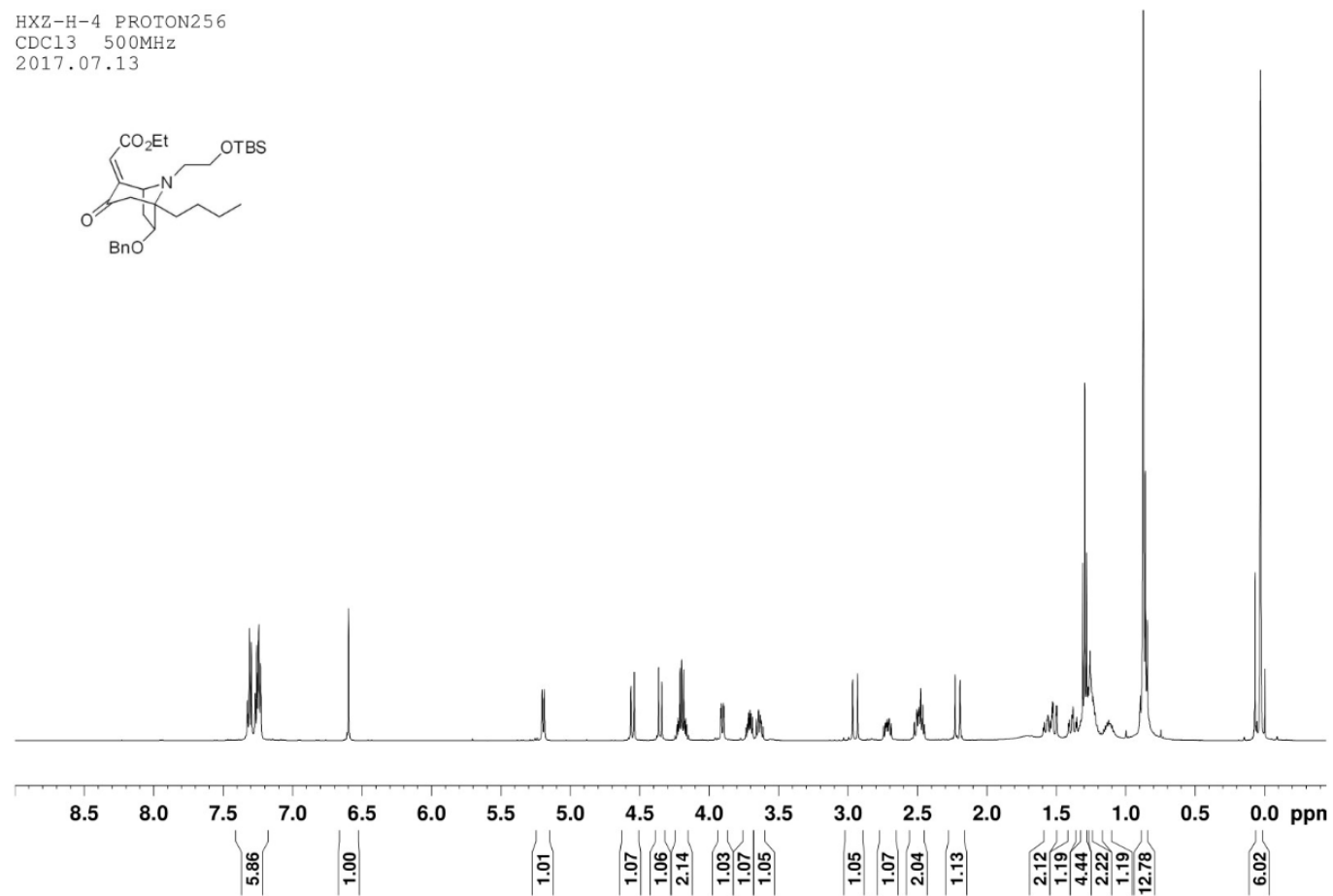
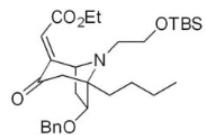
Supplementary Figure 36. ¹H NMR spectrum of compound 23a

HXZ-I-71c C13CPD
 CDC13 125mhz
 2019-07-21

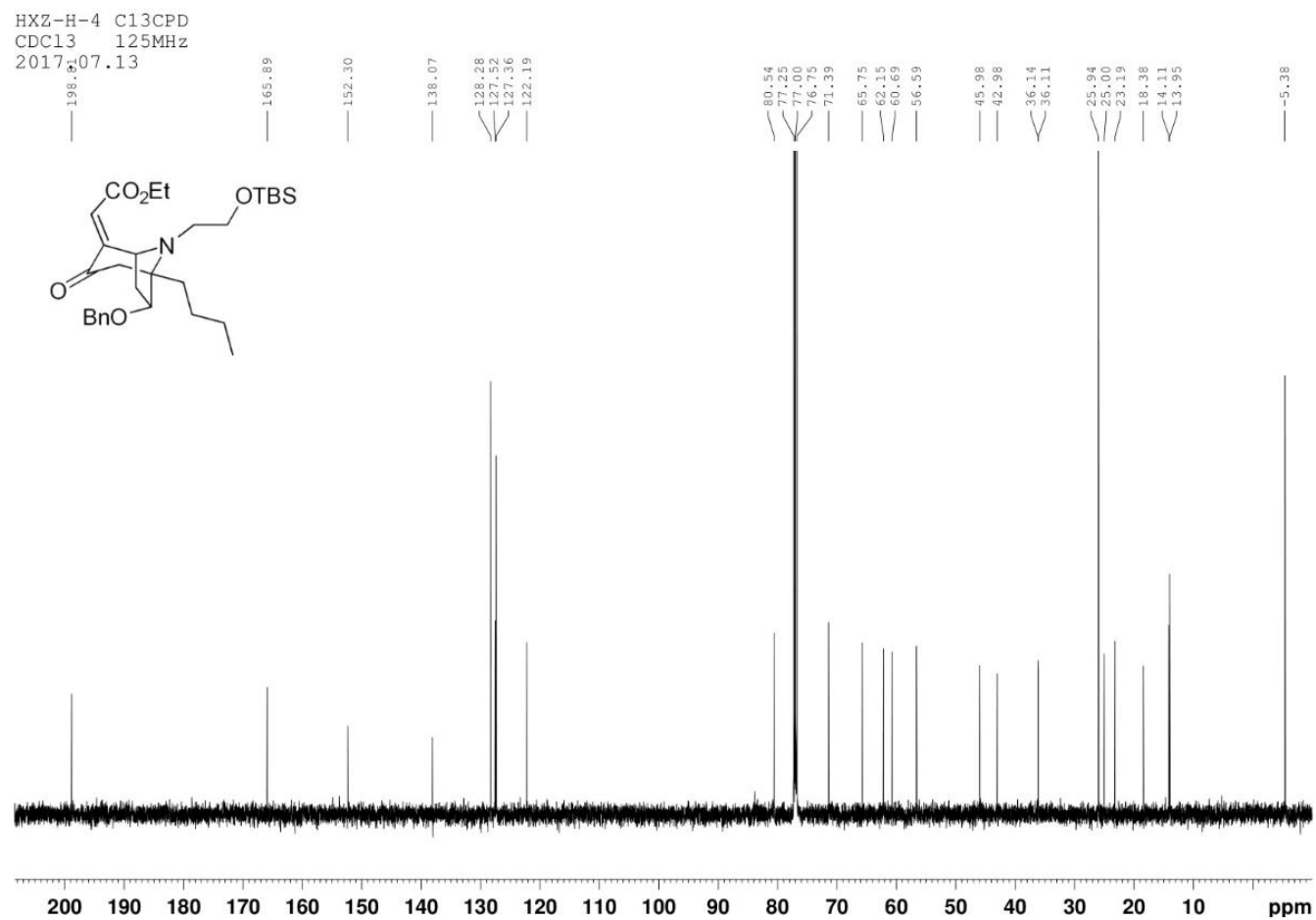


Supplementary Figure 37. ^{13}C NMR spectrum of compound 23a

HXZ-H-4 PROTON256
CDC13 500MHz
2017.07.13

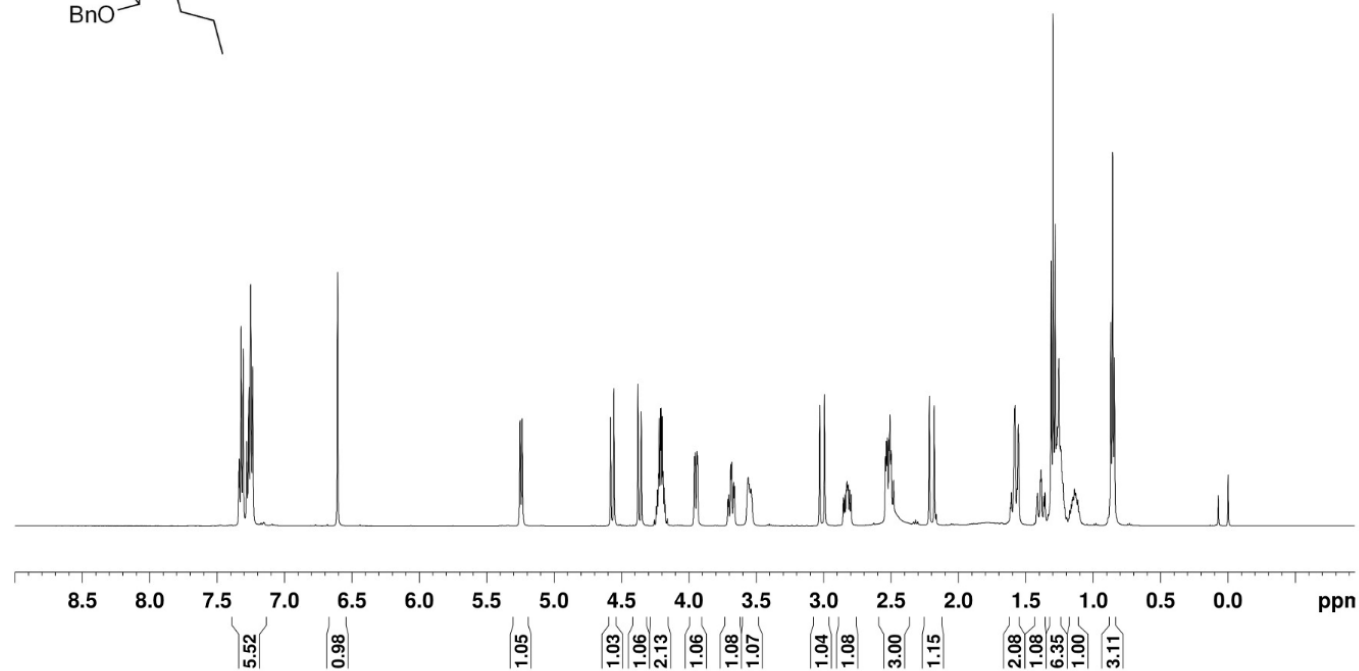
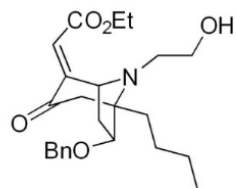


Supplementary Figure 38. ¹H NMR spectrum of compound 24



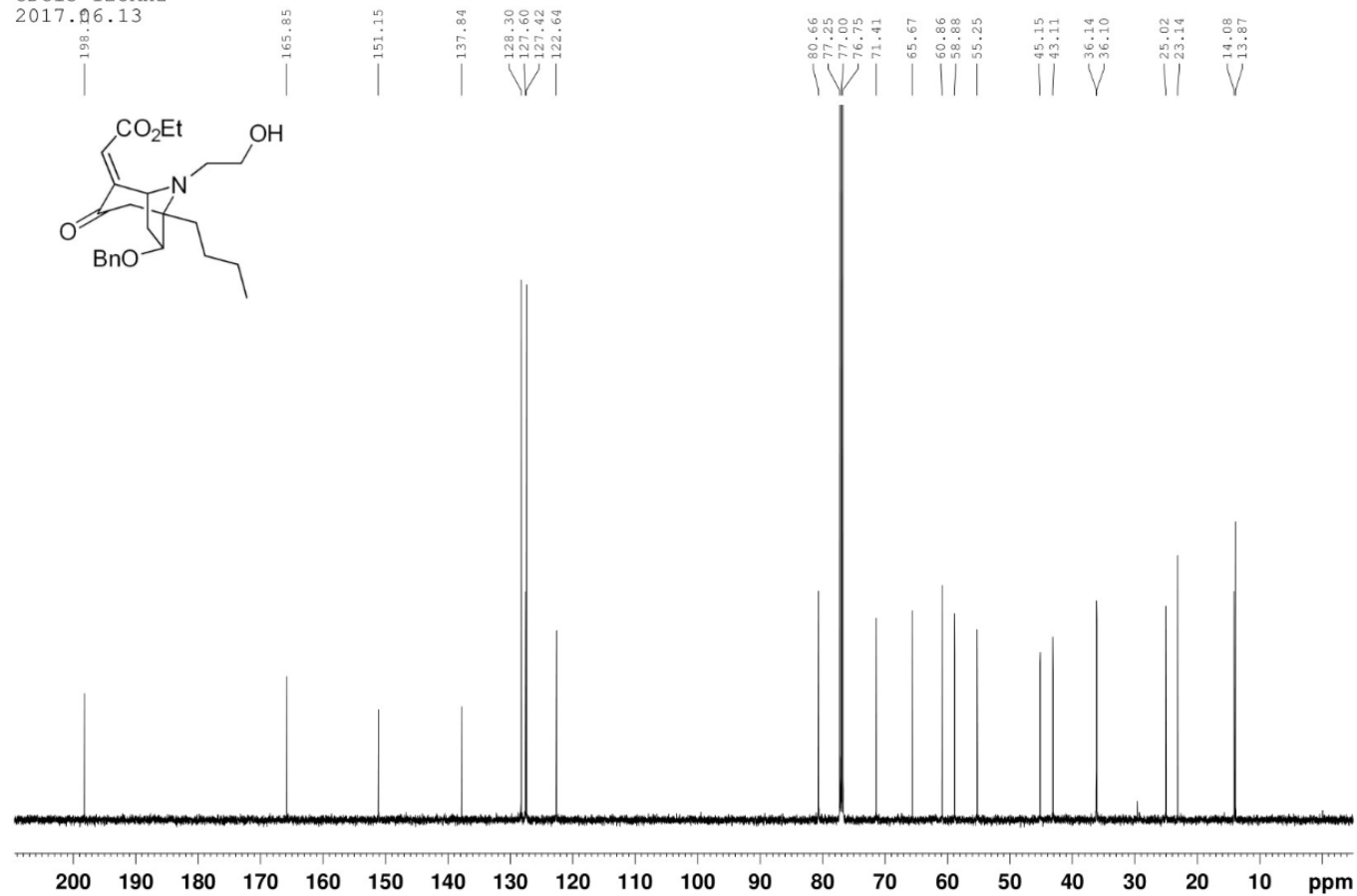
Supplementary Figure 39. ^{13}C NMR spectrum of compound 24

HXZ-G-100 PROTON256
CDCl3 500MHz
2017.06.13



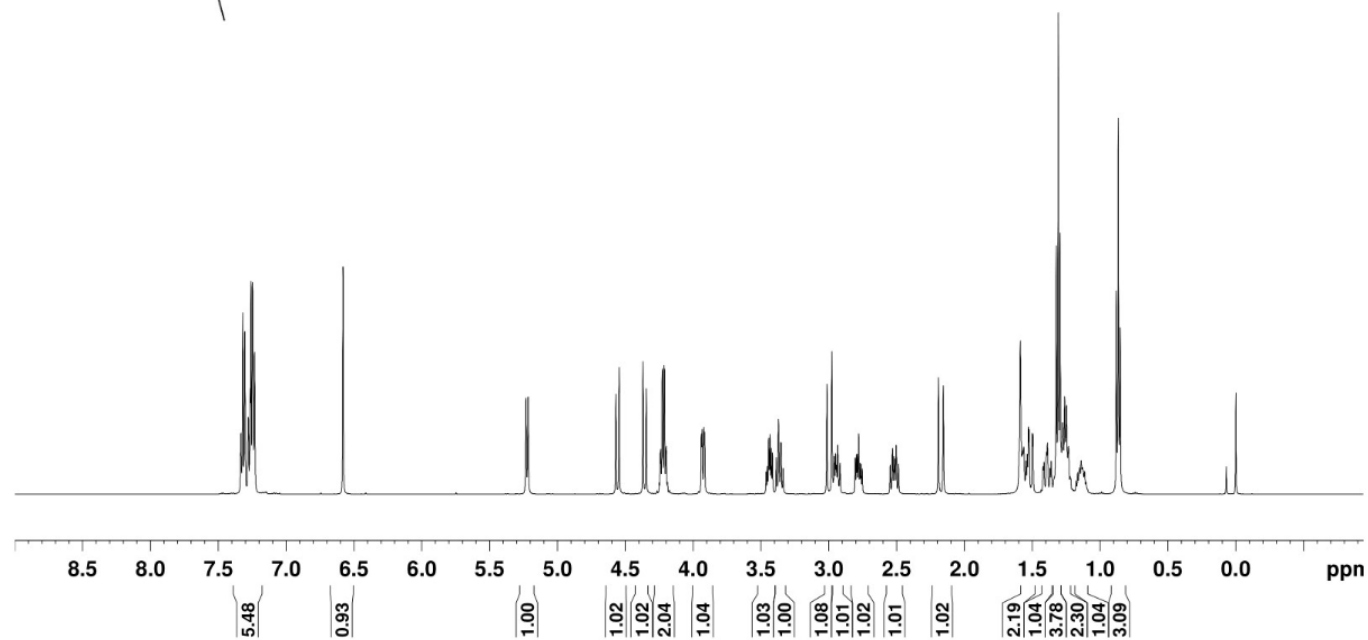
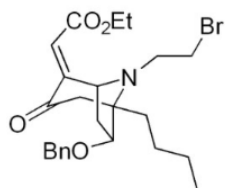
Supplementary Figure 40. ¹H NMR spectrum of compound 25

HXZ-G-100 C13CPD
 CDC13 125MHz
 2017.06.13



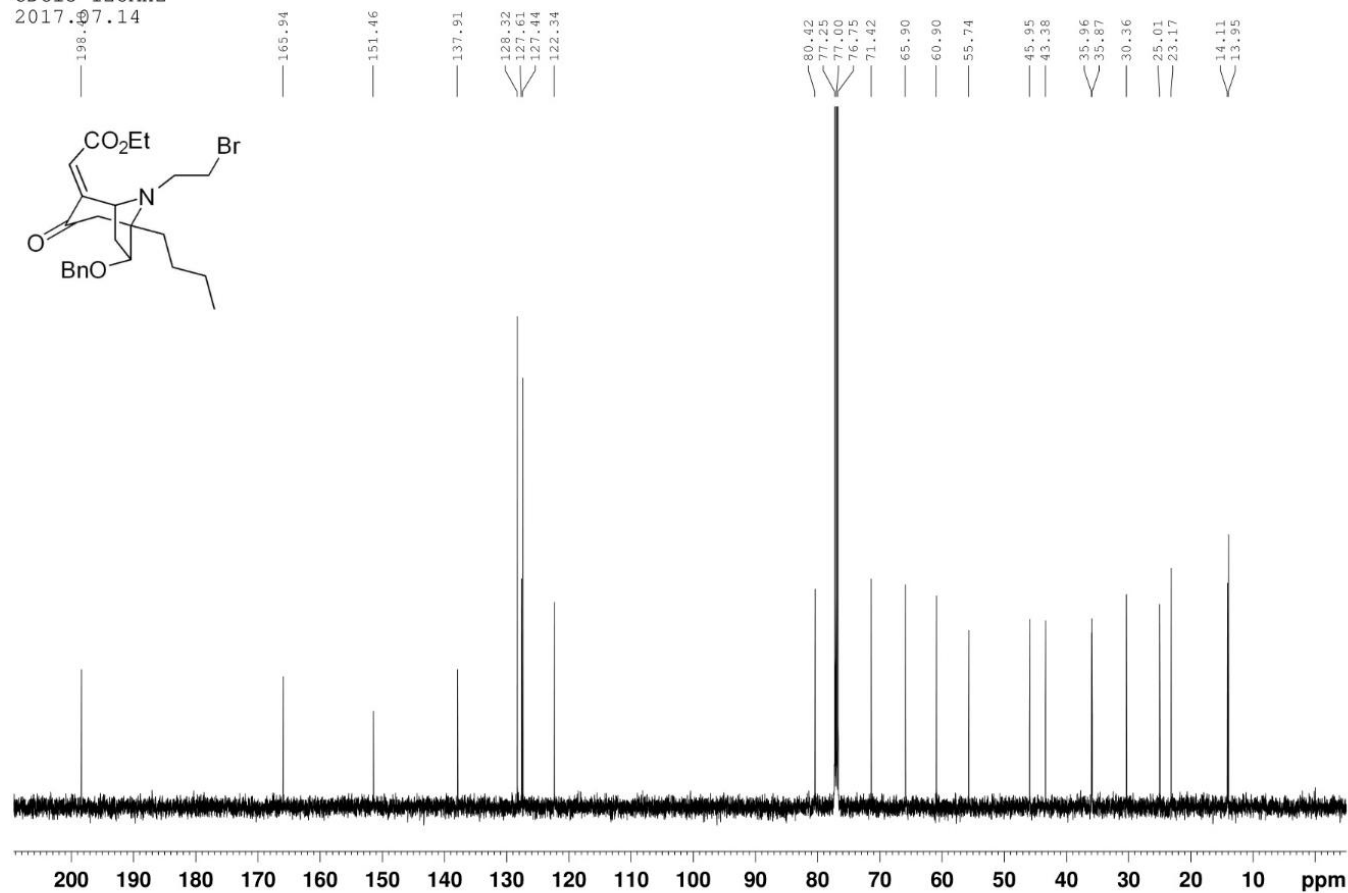
Supplementary Figure 41. ¹³C NMR spectrum of compound 25

HXZ-H-6 PROTON256
CDC13 500MHZ
2017.07.14



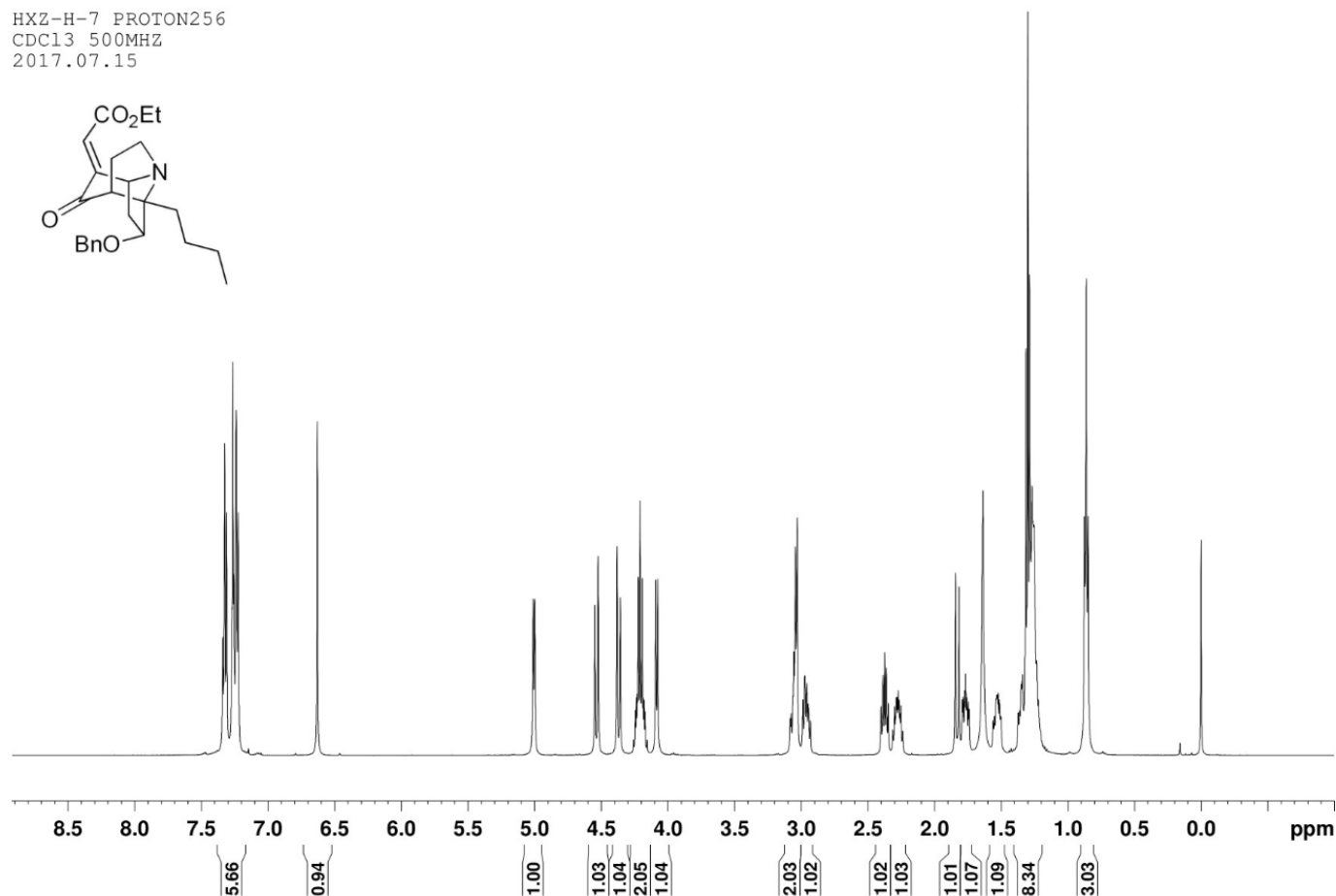
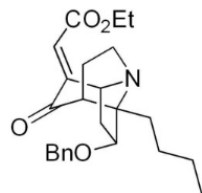
Supplementary Figure 42. ¹H NMR spectrum of compound 26

HXZ-H-6 C13CPD
 CDC13 125MHZ
 2017.07.14

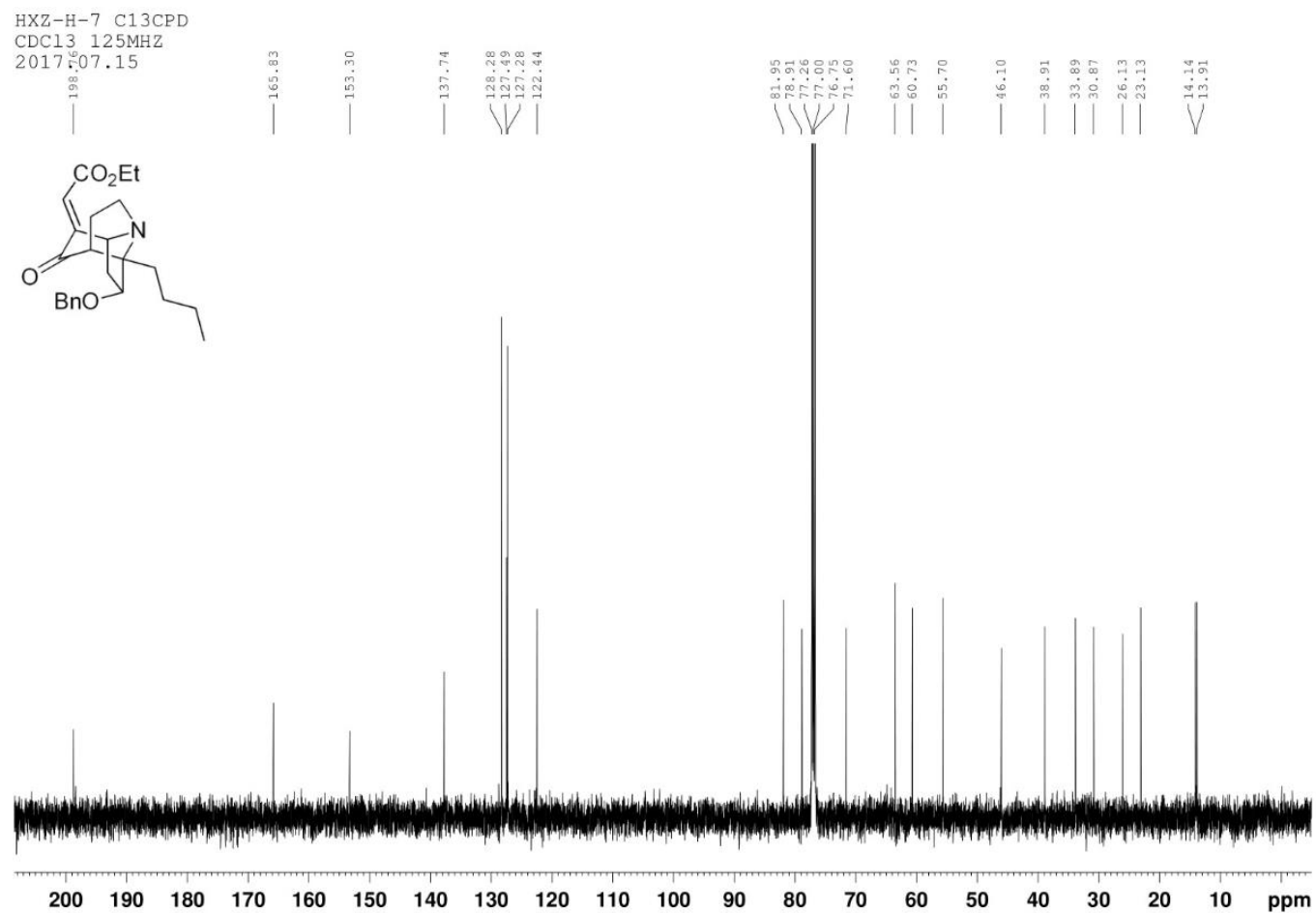


Supplementary Figure 43. ¹³C NMR spectrum of compound 26

HXZ-H-7 PROTON256
CDC13 500MHZ
2017.07.15

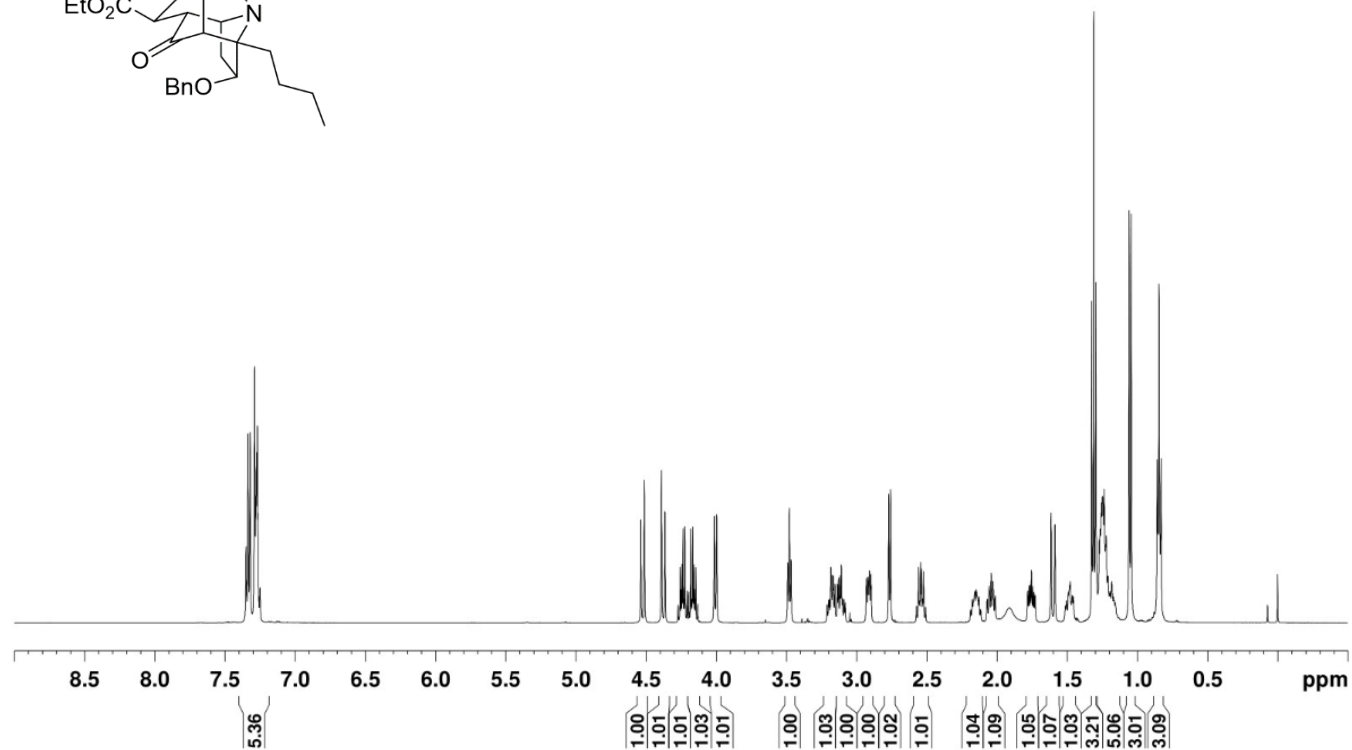
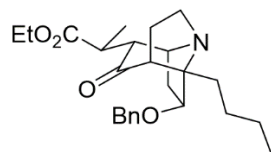


Supplementary Figure 44. ¹H NMR spectrum of compound 14

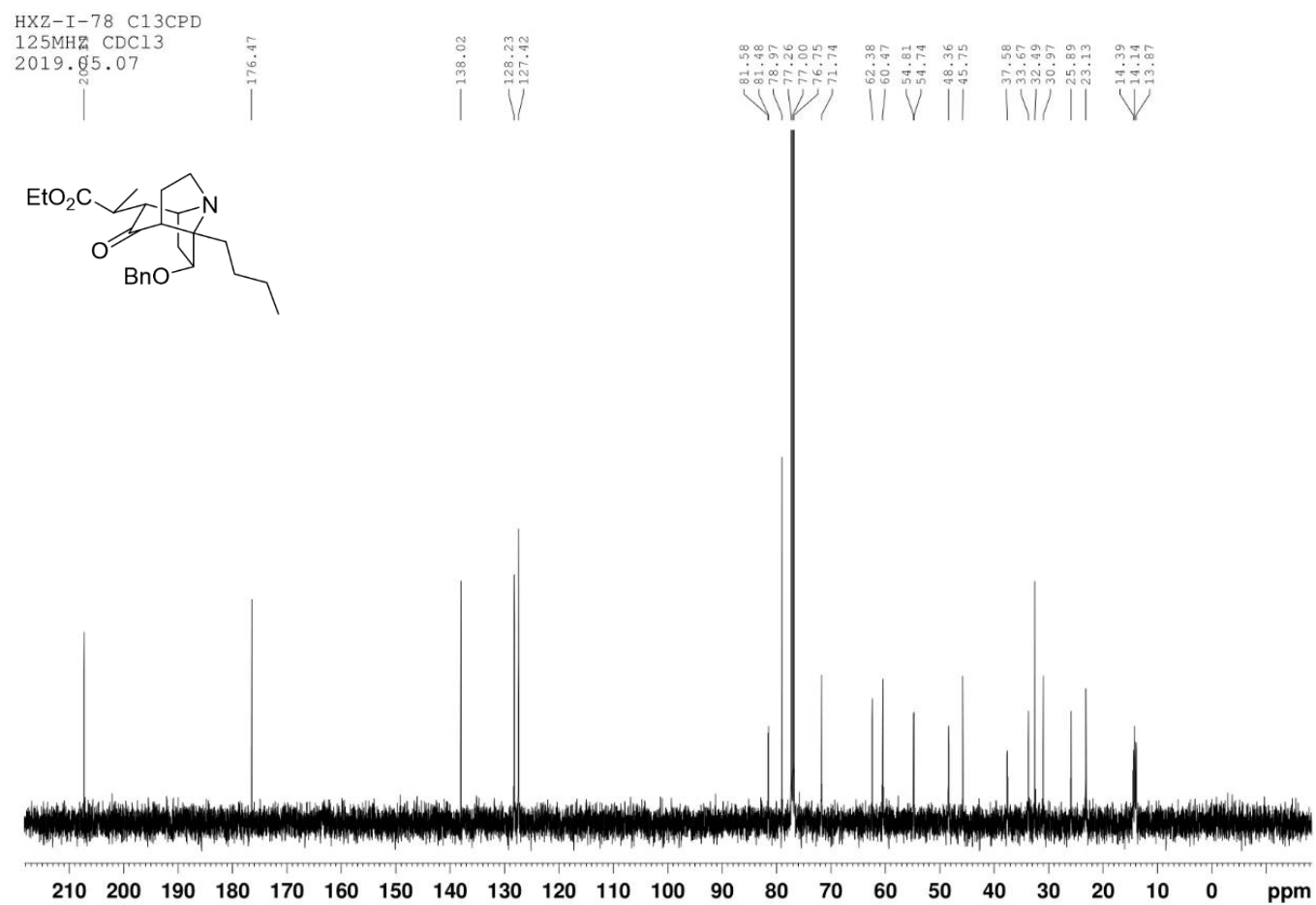


Supplementary Figure 45. ^{13}C NMR spectrum of compound 14

HXZ-I-78 PROTON 256
CDCl3 500MHz
2019.05.07

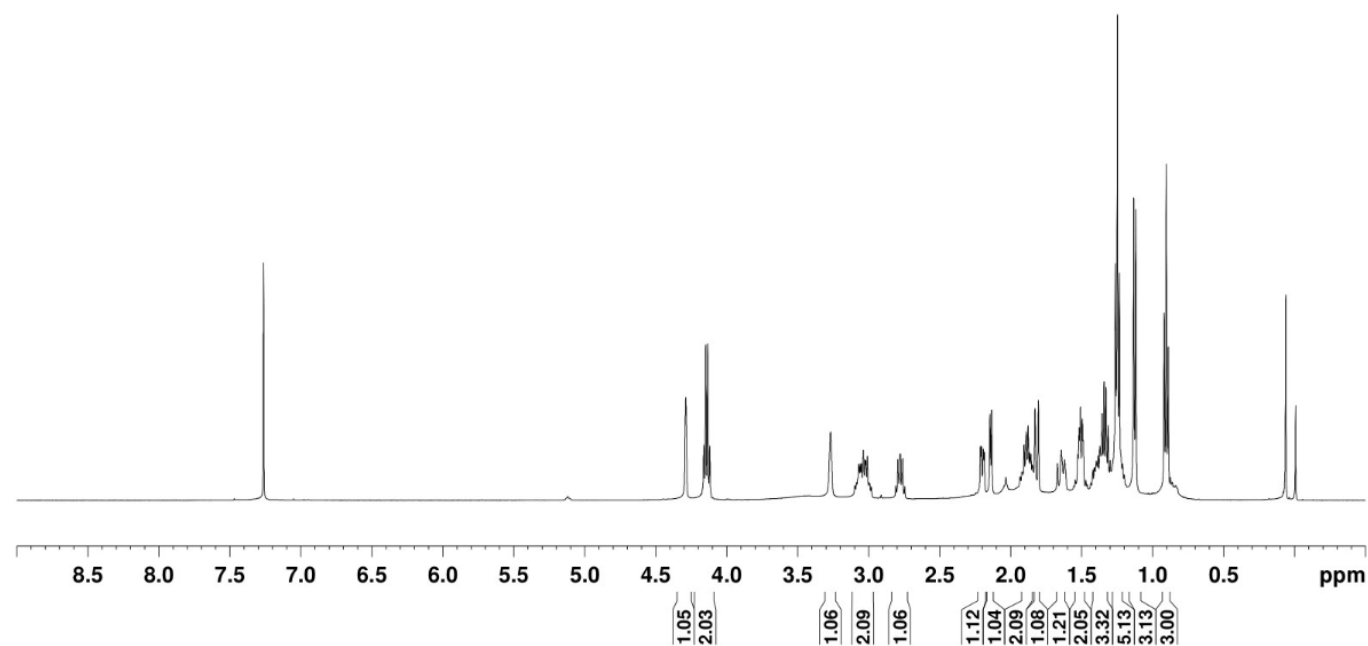
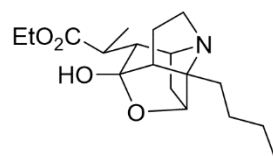


Supplementary Figure 46. ¹H NMR spectrum of compound 13



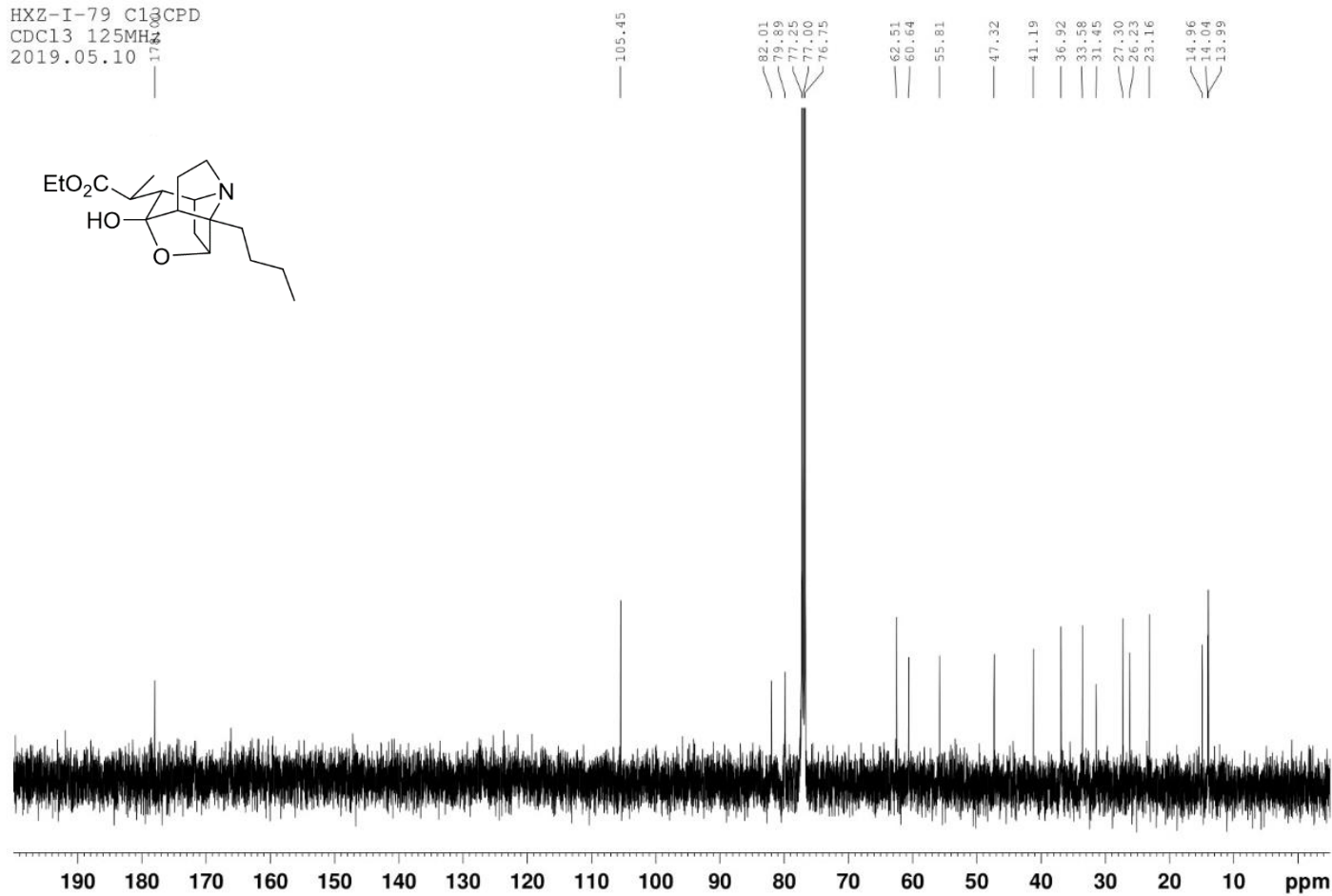
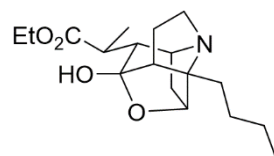
Supplementary Figure 47. ¹³C NMR spectrum of compound 13

HXZ-I-79 PROTON 256
CDC13 500MHz
2019.05.10



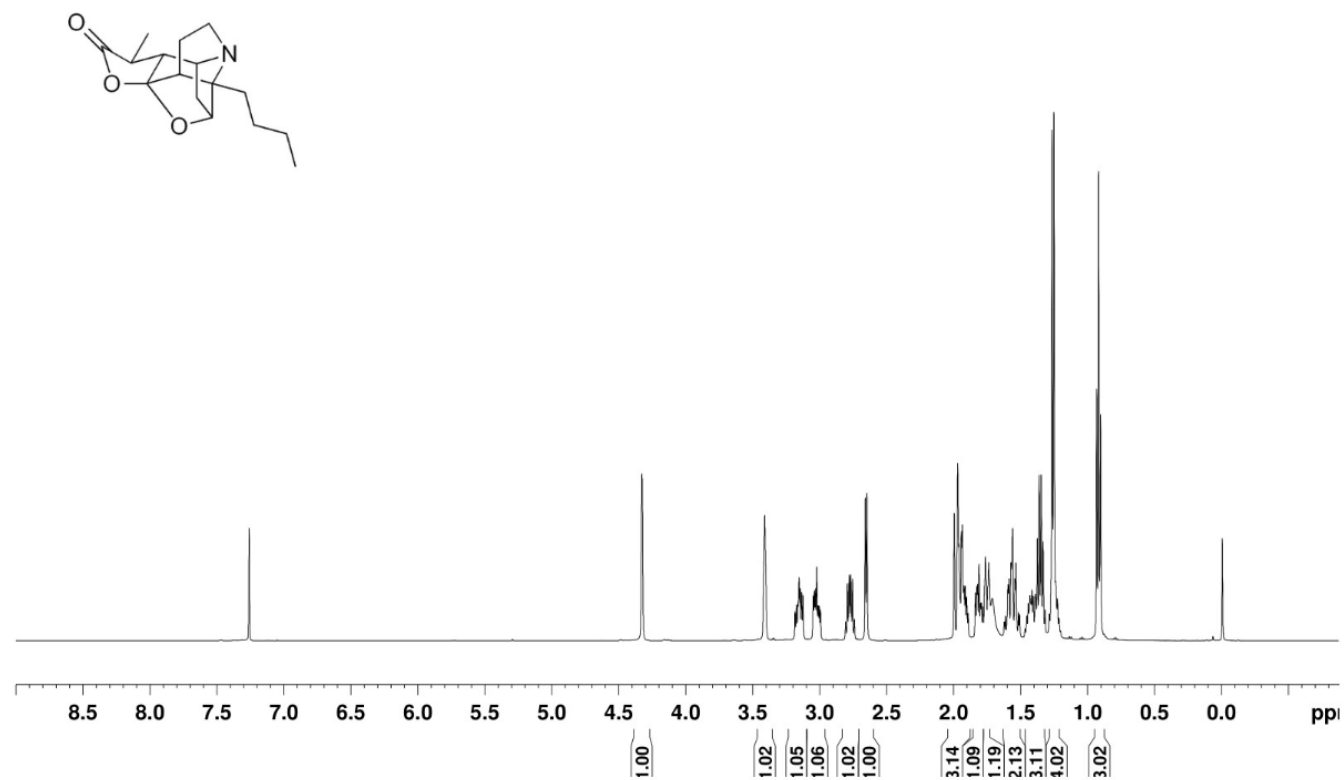
Supplementary Figure 48. ¹H NMR spectrum of compound 27

HXZ-I-79 C13CPD
 CDC13 125MHz
 2019.05.10



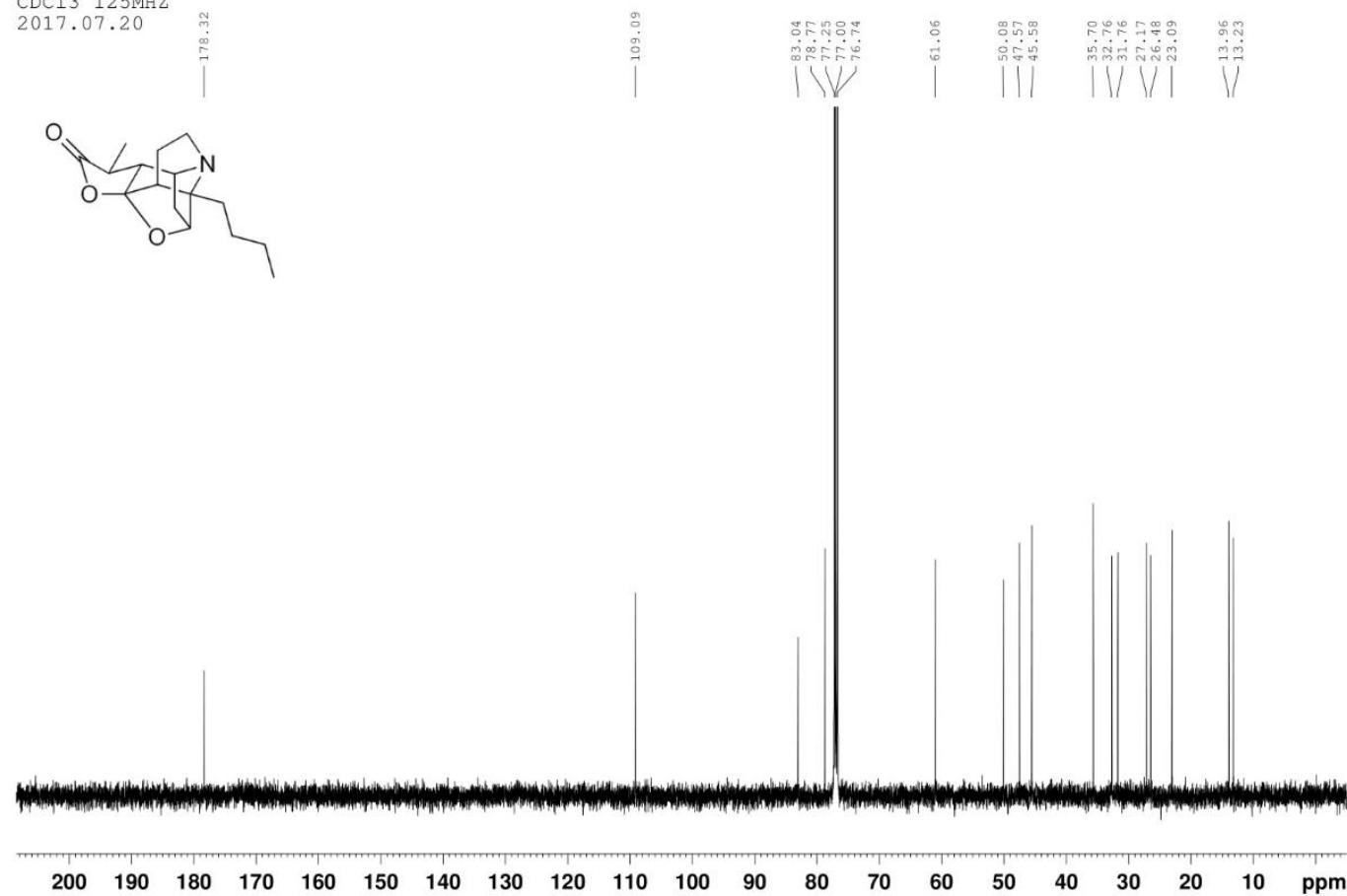
Supplementary Figure 49. ^{13}C NMR spectrum of compound 27

HXZ-H-10 PROTON256
CDCl3 500MHZ
2017.07.20



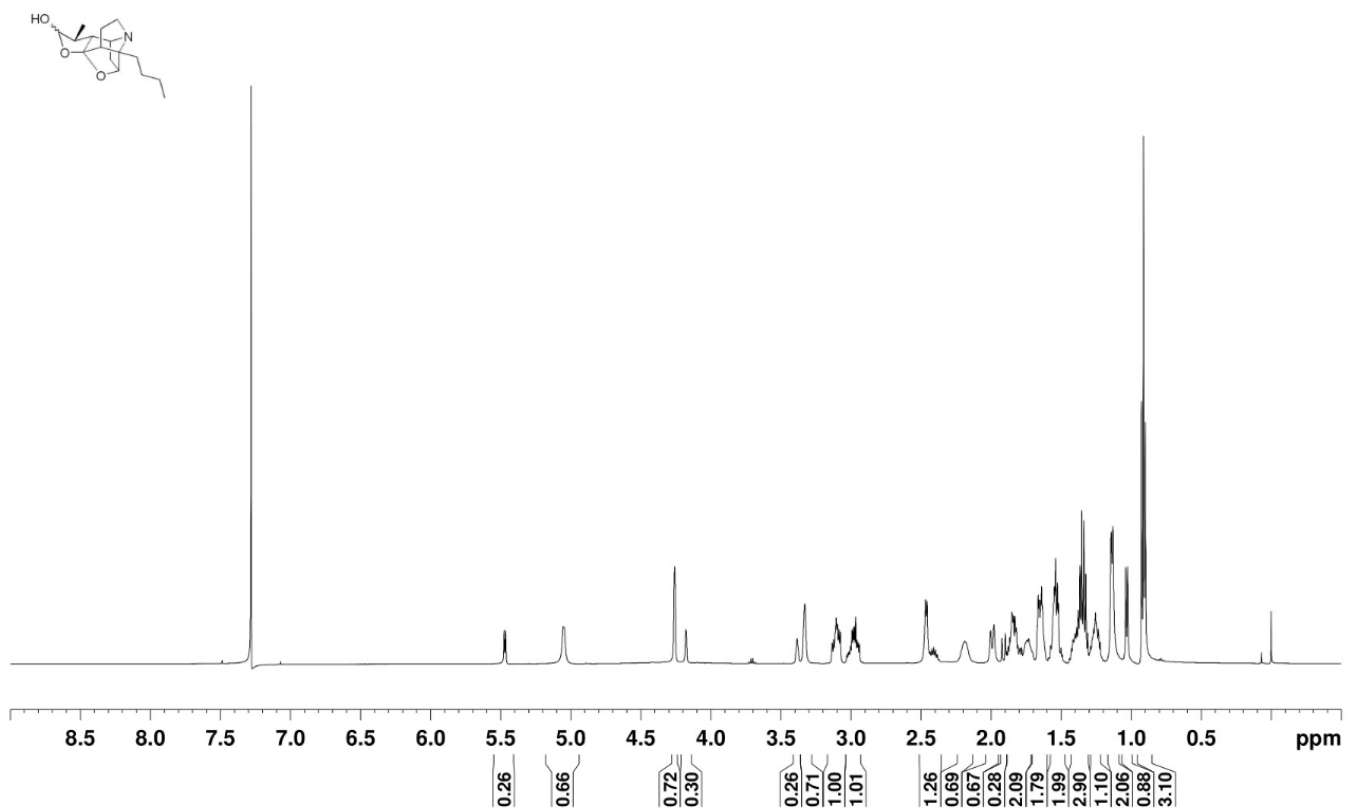
Supplementary Figure 50. ^1H NMR spectrum of compound **12**

HXZ-H-10 C13CPD
 CDC13 125MHZ
 2017.07.20



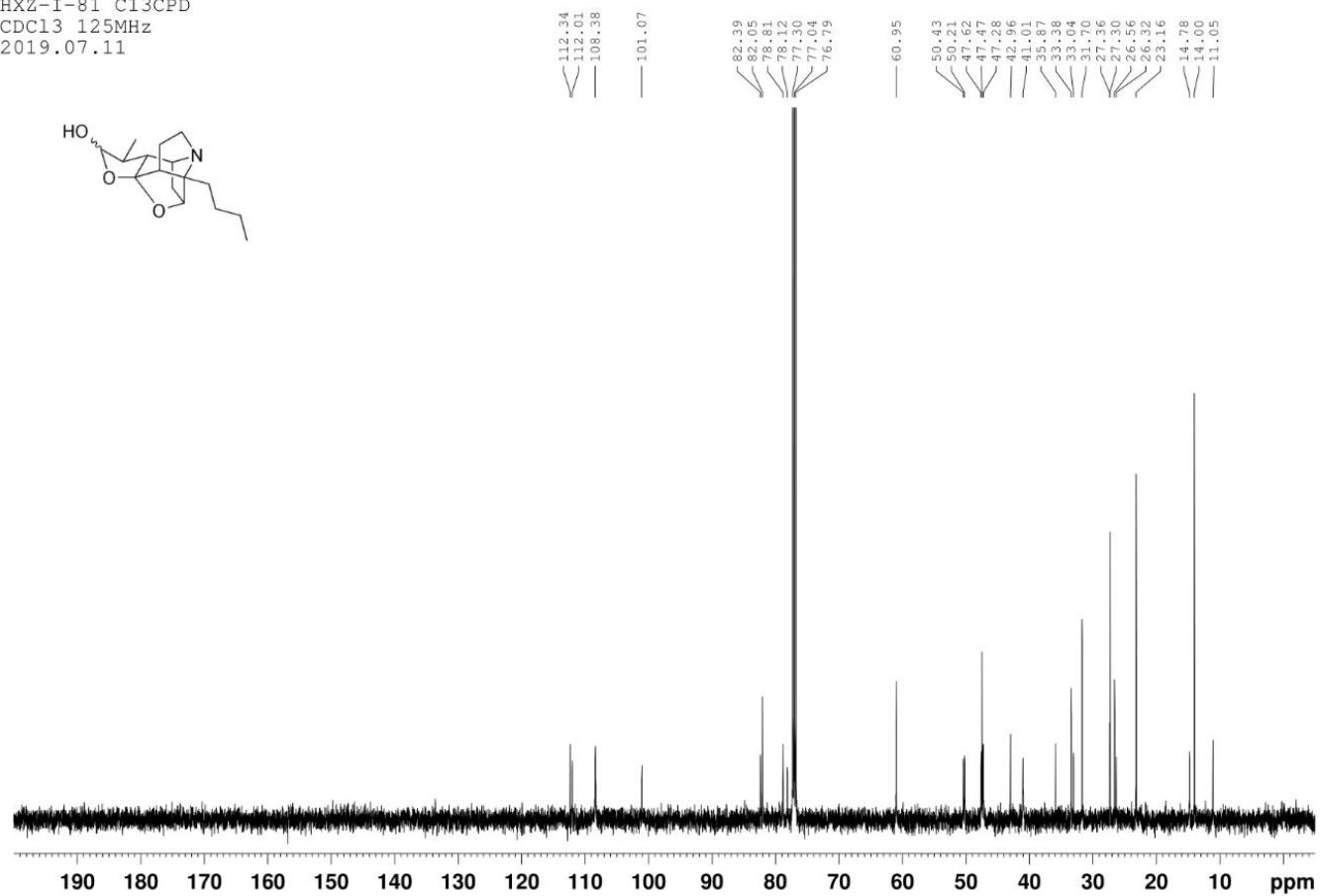
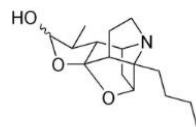
Supplementary Figure 51. ¹³C NMR spectrum of compound 12

HXZ-I-81 PROTON256
CDC13 500MHz
2019.07.11



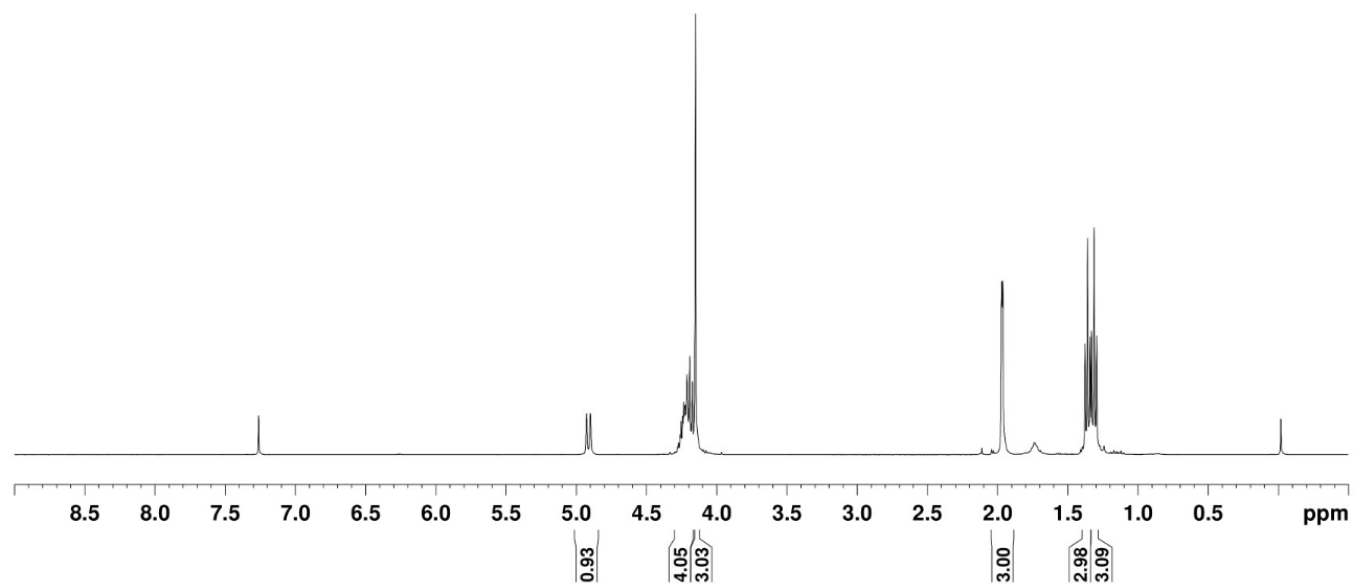
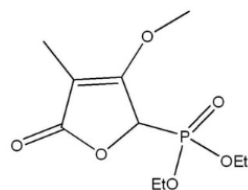
Supplementary Figure 52. ¹H NMR spectrum of compound 11

HXZ-I-81 C13CPD
CDCl3 125MHz
2019.07.11



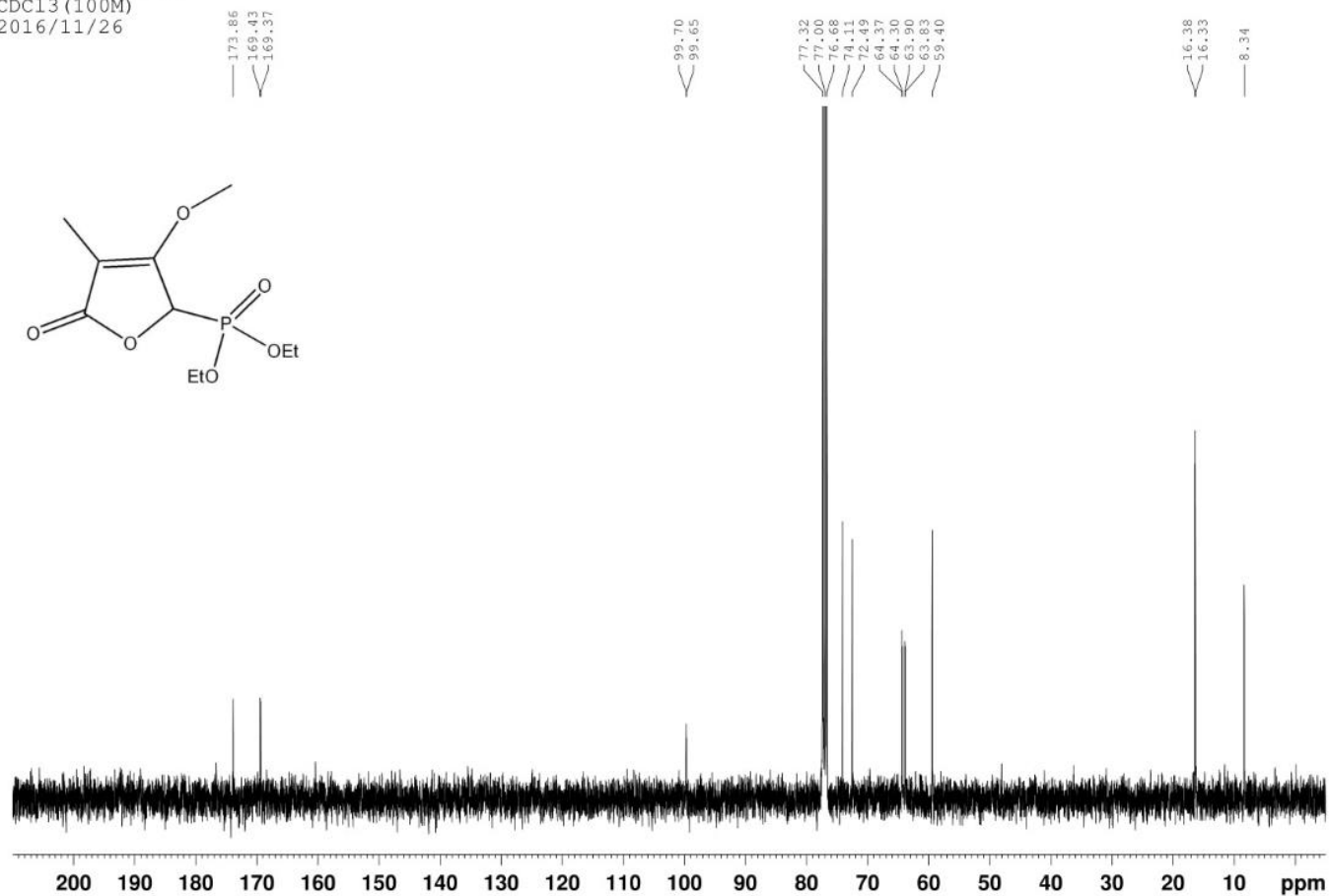
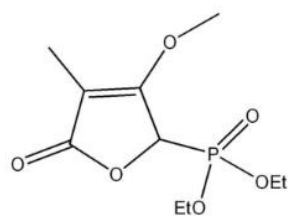
Supplementary Figure 53. ^{13}C NMR spectrum of compound **11**

HXZ-F-65 PROTON256
CDC13 (400M)
2016/11/26



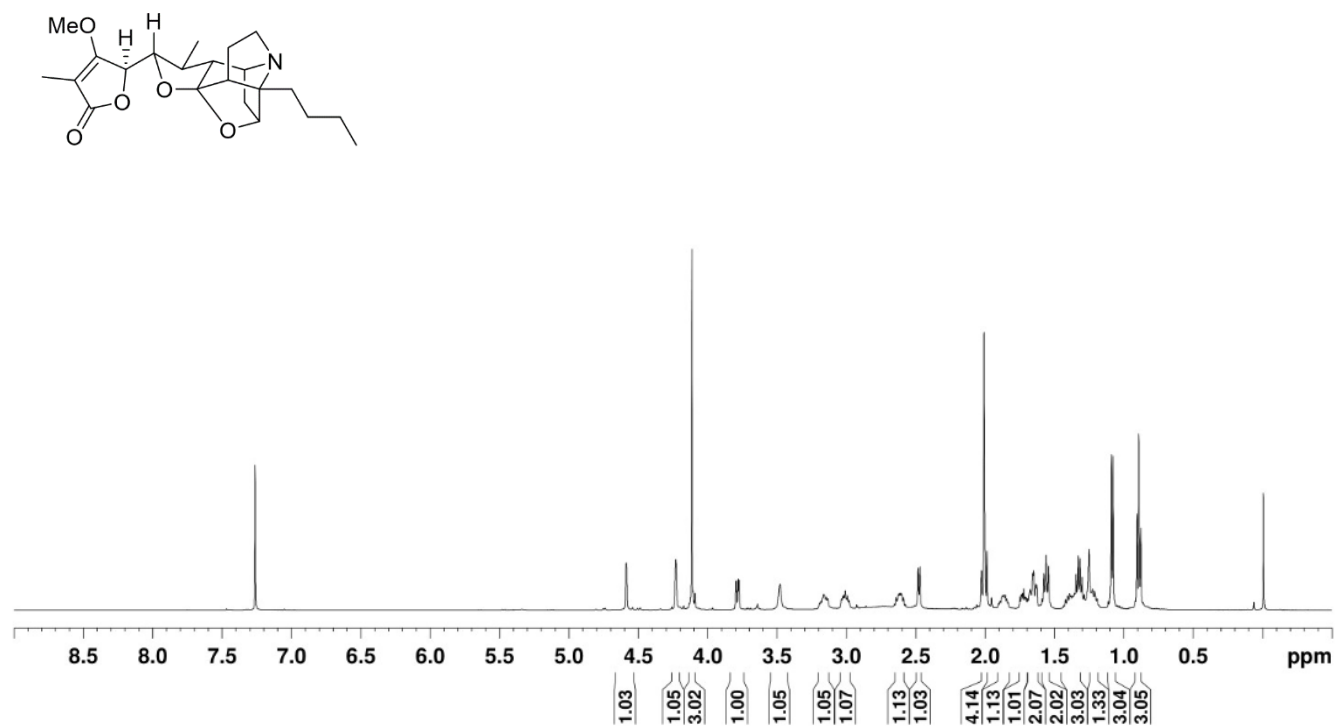
Supplementary Figure 54. ¹H NMR spectrum of compound **10**

HXZ-F-65 C13CPD
 CDC13 (100M)
 2016/11/26



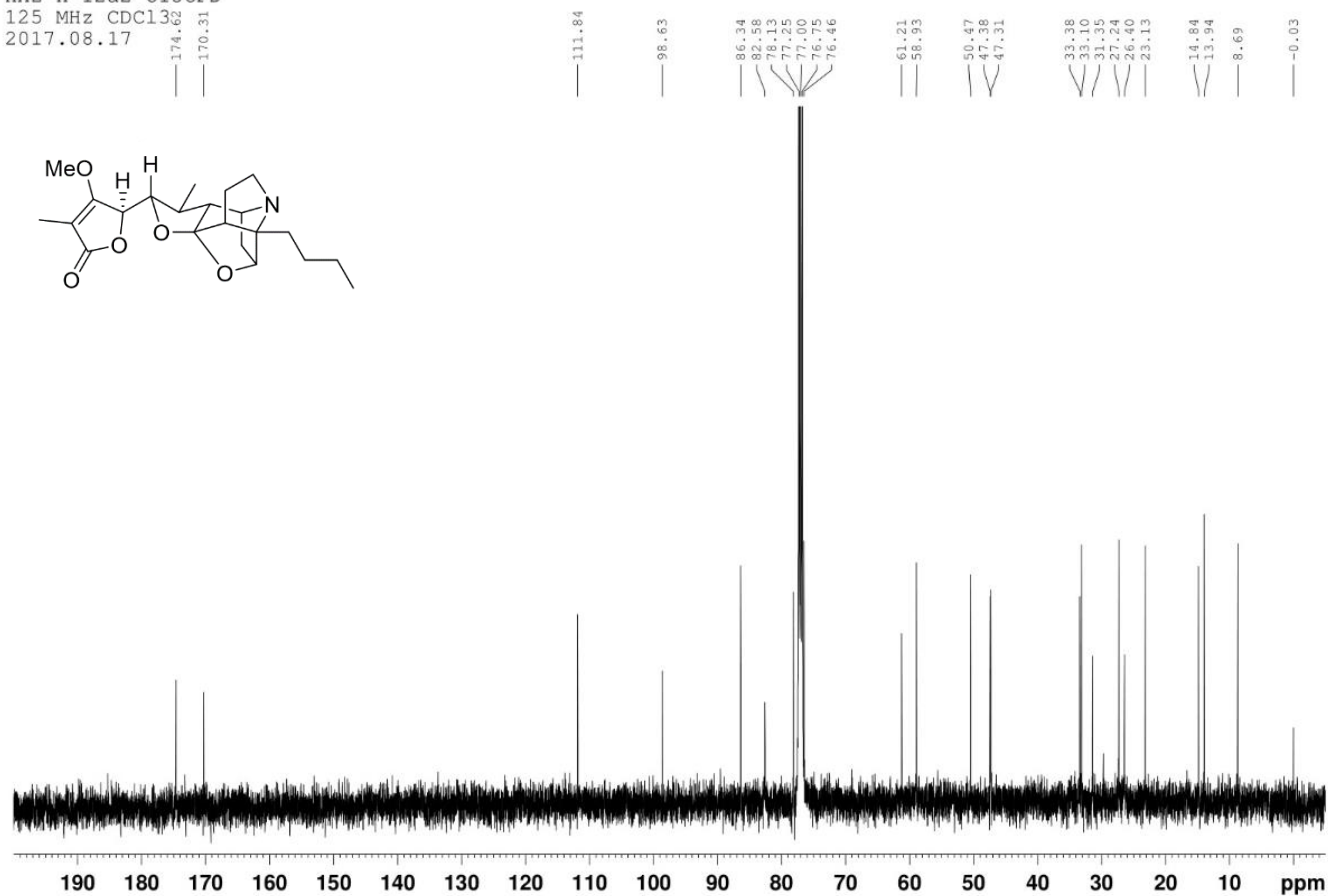
Supplementary Figure 55. ^{13}C NMR spectrum of compound **10**

HXZ-H-12a2 PROTON256
500 MHZ CDCl3
2017.07.27



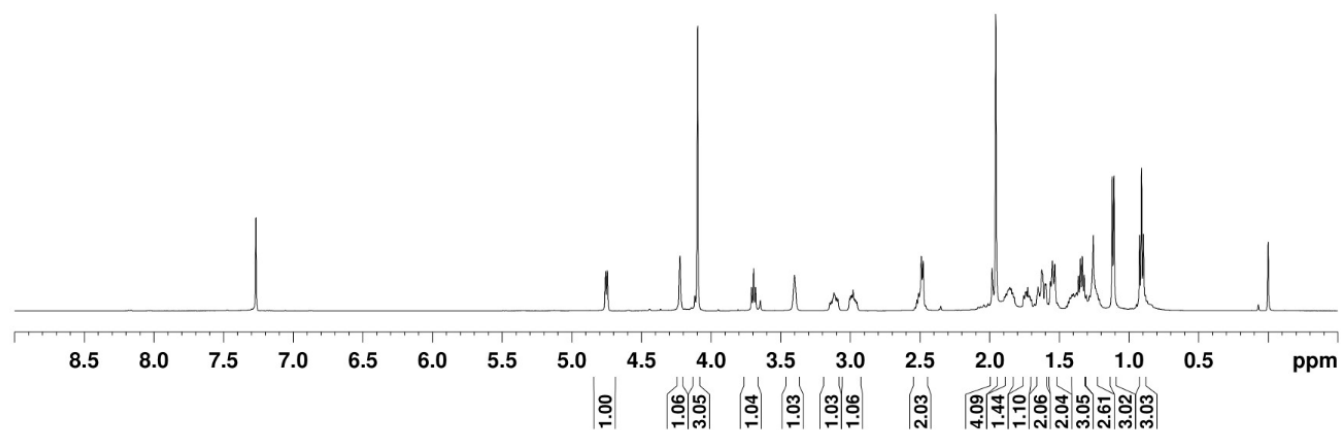
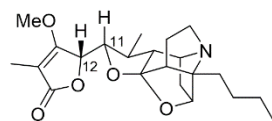
Supplementary Figure 56. ¹H NMR spectrum of compound (11*S*,12*R*)-dihydrostemofoline (**8**)

HXZ-H-12a2 C13CPD
125 MHz CDCl₃
2017.08.17



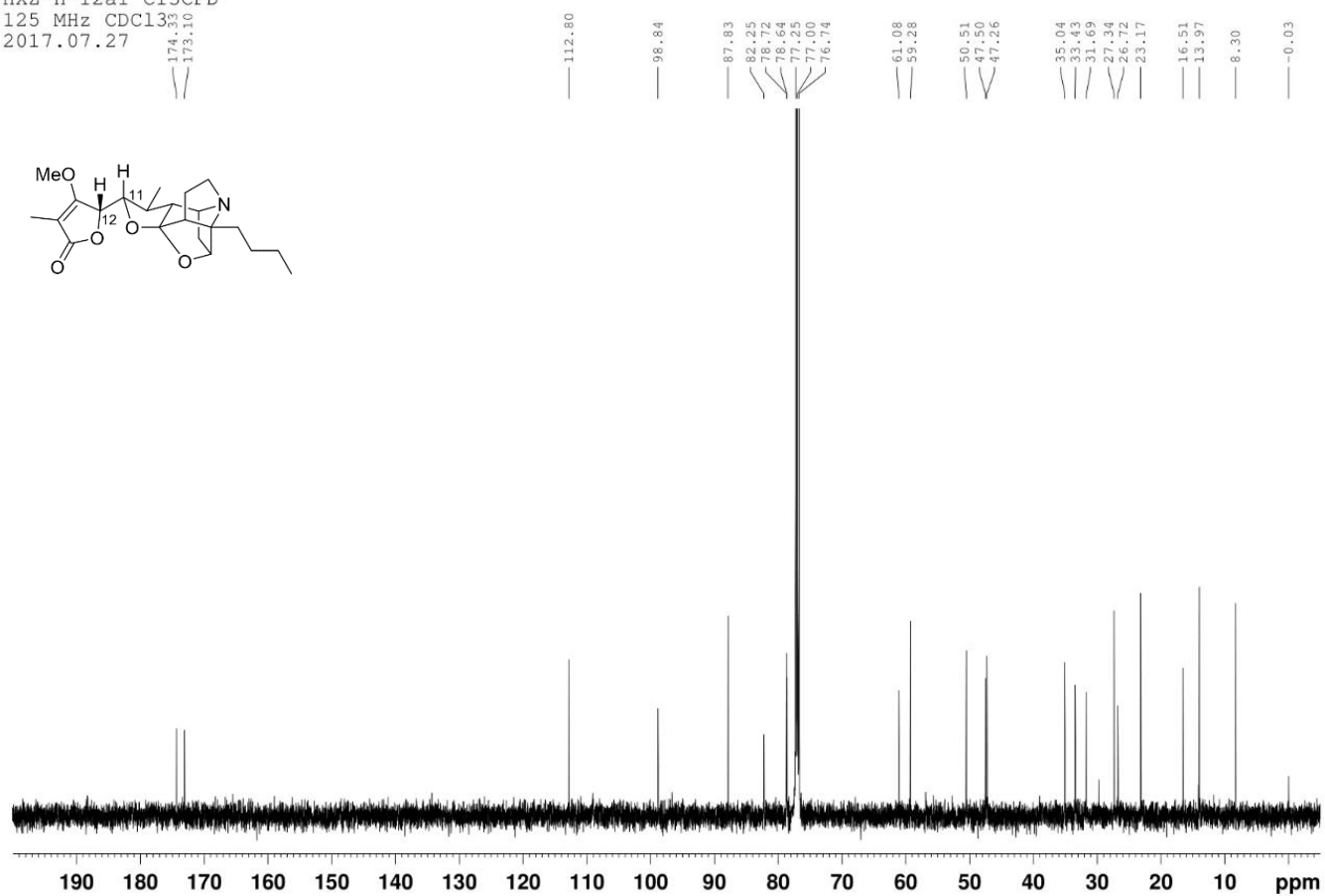
Supplementary Figure 57. ¹³C NMR spectrum of compound (11S,12R)-dihydrostemofoline (**8**)

HXZ-H-12a1 PROTON256
500 MHz CDCl₃
2017.07.27

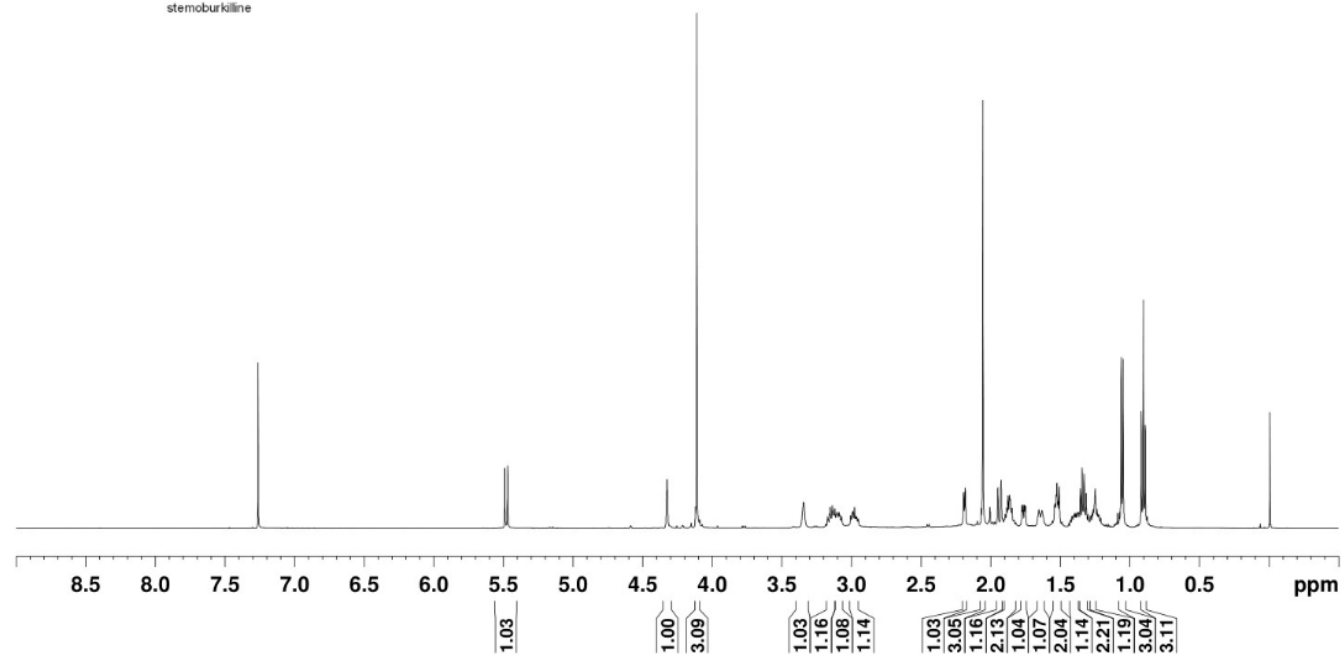


Supplementary Figure 58. ¹H NMR spectrum of compound (11S,12S)-dihydrostemofoline (**9**)

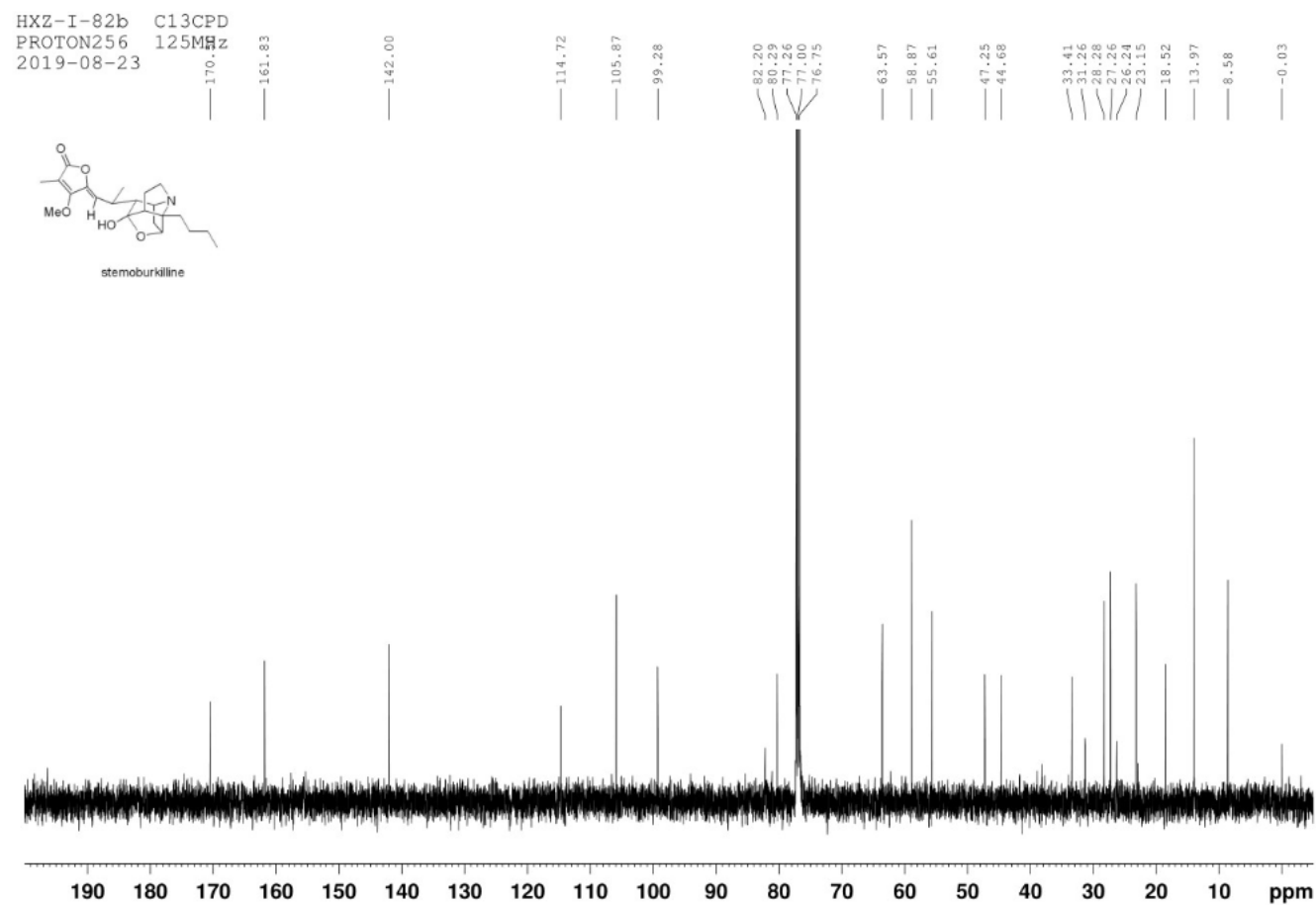
HXZ-H-12a1 C13CPD
125 MHz CDC13
2017.07.27



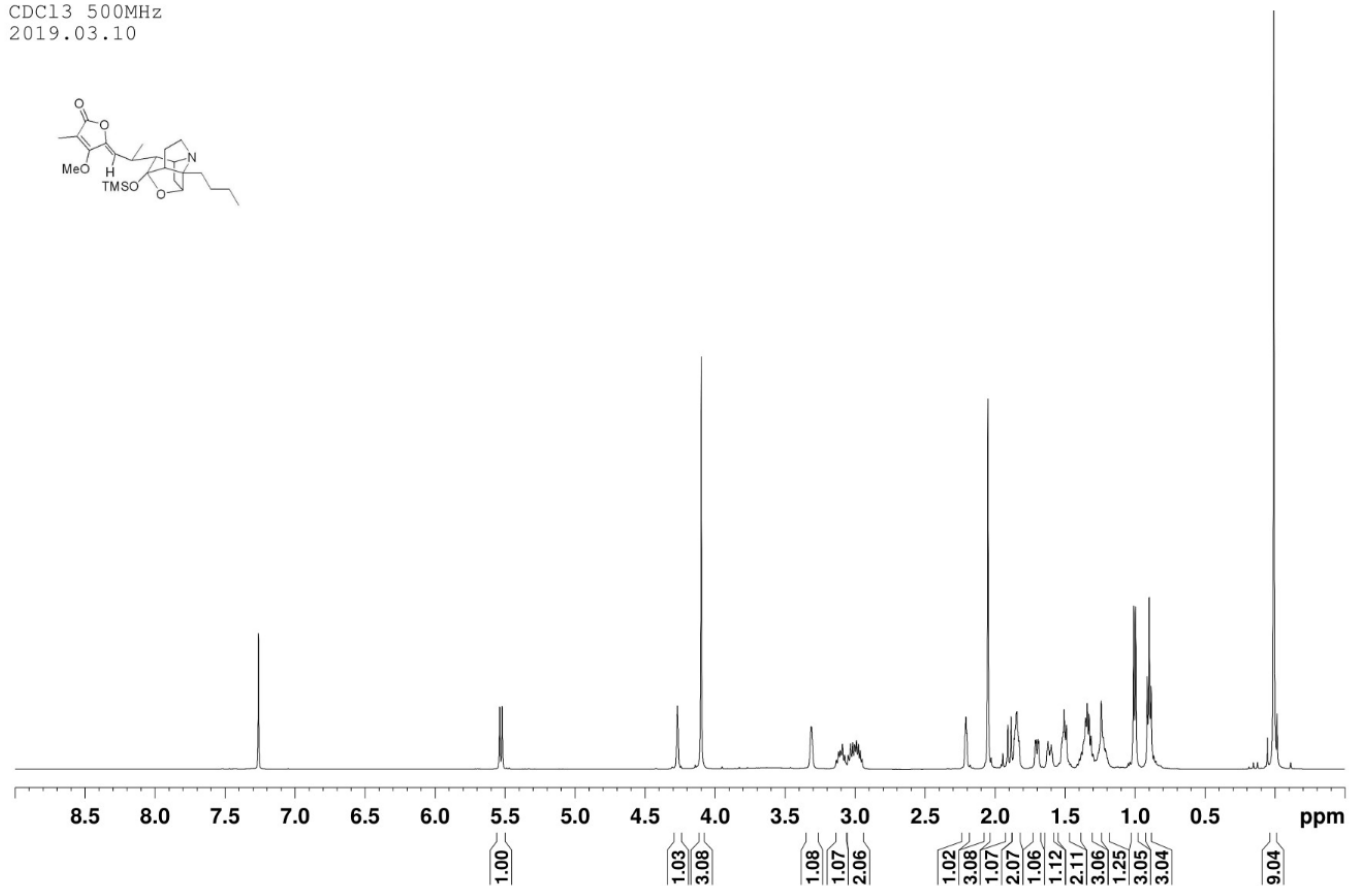
Supplementary Figure 59. ^{13}C NMR spectrum of compound (11S,12S)-dihydrostemofoline (9)

CC(C)C12C3C(C1)OC2C(C3)C4C(C(C4)OC5C(C(C5)OC6C(C(C6)OC7C(C(C7)OC8C(C(C8)OC9C(C(C9)OC10C(C(C10)OC11C(C(C11)OC12C(C(C12)OC13C(C(C13)OC14C(C(C14)OC15C(C(C15)OC16C(C(C16)OC17C(C(C17)OC18C(C(C18)OC19C(C(C19)OC20C(C(C20)OC21C(C(C21)OC22C(C(C22)OC23C(C(C23)OC24C(C(C24)OC25C(C(C25)OC26C(C(C26)OC27C(C(C27)OC28C(C(C28)OC29C(C(C29)OC30C(C(C30)OC31C(C(C31)OC32C(C(C32)OC33C(C(C33)OC34C(C(C34)OC35C(C(C35)OC36C(C(C36)OC37C(C(C37)OC38C(C(C38)OC39C(C(C39)OC40C(C(C40)OC41C(C(C41)OC42C(C(C42)OC43C(C(C43)OC44C(C(C44)OC45C(C(C45)OC46C(C(C46)OC47C(C(C47)OC48C(C(C48)OC49C(C(C49)OC50C(C(C50)OC51C(C(C51)OC52C(C(C52)OC53C(C(C53)OC54C(C(C54)OC55C(C(C55)OC56C(C(C56)OC57C(C(C57)OC58C(C(C58)OC59C(C(C59)OC60C(C(C60)OC61C(C(C61)OC62C(C(C62)OC63C(C(C63)OC64C(C(C64)OC65C(C(C65)OC66C(C(C66)OC67C(C(C67)OC68C(C(C68)OC69C(C(C69)OC70C(C(C70)OC71C(C(C71)OC72C(C(C72)OC73C(C(C73)OC74C(C(C74)OC75C(C(C75)OC76C(C(C76)OC77C(C(C77)OC78C(C(C78)OC79C(C(C79)OC80C(C(C80)OC81C(C(C81)OC82C(C(C82)OC83C(C(C83)OC84C(C(C84)OC85C(C(C85)OC86C(C(C86)OC87C(C(C87)OC88C(C(C88)OC89C(C(C89)OC90C(C(C90)OC91C(C(C91)OC92C(C(C92)OC93C(C(C93)OC94C(C(C94)OC95C(C(C95)OC96C(C(C96)OC97C(C(C97)OC98C(C(C98)OC99C(C(C99)OC100C(C(C100)OC101C(C(C101)OC102C(C(C102)OC103C(C(C103)OC104C(C(C104)OC105C(C(C105)OC106C(C(C106)OC107C(C(C107)OC108C(C(C108)OC109C(C(C109)OC110C(C(C110)OC111C(C(C111)OC112C(C(C112)OC113C(C(C113)OC114C(C(C114)OC115C(C(C115)OC116C(C(C116)OC117C(C(C117)OC118C(C(C118)OC119C(C(C119)OC120C(C(C120)OC121C(C(C121)OC122C(C(C122)OC123C(C(C123)OC124C(C(C124)OC125C(C(C125)OC126C(C(C126)OC127C(C(C127)OC128C(C(C128)OC129C(C(C129)OC130C(C(C130)OC131C(C(C131)OC132C(C(C132)OC133C(C(C133)OC134C(C(C134)OC135C(C(C135)OC136C(C(C136)OC137C(C(C137)OC138C(C(C138)OC139C(C(C139)OC140C(C(C140)OC141C(C(C141)OC142C(C(C142)OC143C(C(C143)OC144C(C(C144)OC145C(C(C145)OC146C(C(C146)OC147C(C(C147)OC148C(C(C148)OC149C(C(C149)OC150C(C(C150)OC151C(C(C151)OC152C(C(C152)OC153C(C(C153)OC154C(C(C154)OC155C(C(C155)OC156C(C(C156)OC157C(C(C157)OC158C(C(C158)OC159C(C(C159)OC160C(C(C160)OC161C(C(C161)OC162C(C(C162)OC163C(C(C163)OC164C(C(C164)OC165C(C(C165)OC166C(C(C166)OC167C(C(C167)OC168C(C(C168)OC169C(C(C169)OC170C(C(C170)OC171C(C(C171)OC172C(C(C172)OC173C(C(C173)OC174C(C(C174)OC175C(C(C175)OC176C(C(C176)OC177C(C(C177)OC178C(C(C178)OC179C(C(C179)OC180C(C(C180)OC181C(C(C181)OC182C(C(C182)OC183C(C(C183)OC184C(C(C184)OC185C(C(C185)OC186C(C(C186)OC187C(C(C187)OC188C(C(C188)OC189C(C(C189)OC190C(C(C190)OC191C(C(C191)OC192C(C(C192)OC193C(C(C193)OC194C(C(C194)OC195C(C(C195)OC196C(C(C196)OC197C(C(C197)OC198C(C(C198)OC199C(C(C199)OC200C(C(C200)OC201C(C(C201)OC202C(C(C202)OC203C(C(C203)OC204C(C(C204)OC205C(C(C205)OC206C(C(C206)OC207C(C(C207)OC208C(C(C208)OC209C(C(C209)OC210C(C(C210)OC211C(C(C211)OC212C(C(C212)OC213C(C(C213)OC214C(C(C214)OC215C(C(C215)OC216C(C(C216)OC217C(C(C217)OC218C(C(C218)OC219C(C(C219)OC220C(C(C220)OC221C(C(C221)OC222C(C(C222)OC223C(C(C223)OC224C(C(C224)OC225C(C(C225)OC226C(C(C226)OC227C(C(C227)OC228C(C(C228)OC229C(C(C229)OC230C(C(C230)OC231C(C(C231)OC232C(C(C232)OC233C(C(C233)OC234C(C(C234)OC235C(C(C235)OC236C(C(C236)OC237C(C(C237)OC238C(C(C238)OC239C(C(C239)OC240C(C(C240)OC241C(C(C241)OC242C(C(C242)OC243C(C(C243)OC244C(C(C244)OC245C(C(C245)OC246C(C(C246)OC247C(C(C247)OC248C(C(C248)OC249C(C(C249)OC250C(C(C250)OC251C(C(C251)OC252C(C(C252)OC253C(C(C253)OC254C(C(C254)OC255C(C(C255)OC256C(C(C256)OC257C(C(C257)OC258C(C(C258)OC259C(C(C259)OC260C(C(C260)OC261C(C(C261)OC262C(C(C262)OC263C(C(C263)OC264C(C(C264)OC265C(C(C265)OC266C(C(C266)OC267C(C(C267)OC268C(C(C268)OC269C(C(C269)OC270C(C(C270)OC271C(C(C271)OC272C(C(C272)OC273C(C(C273)OC274C(C(C274)OC275C(C(C275)OC276C(C(C276)OC277C(C(C277)OC278C(C(C278)OC279C(C(C279)OC280C(C(C280)OC281C(C(C281)OC282C(C(C282)OC283C(C(C283)OC284C(C(C284)OC285C(C(C285)OC286C(C(C286)OC287C(C(C287)OC288C(C(C288)OC289C(C(C289)OC290C(C(C290)OC291C(C(C291)OC292C(C(C292)OC293C(C(C293)OC294C(C(C294)OC295C(C(C295)OC296C(C(C296)OC297C(C(C297)OC298C(C(C298)OC299C(C(C299)OC300C(C(C300)OC301C(C(C301)OC302C(C(C302)OC303C(C(C303)OC304C(C(C304)OC305C(C(C305)OC306C(C(C306)OC307C(C(C307)OC308C(C(C308)OC309C(C(C309)OC310C(C(C310)OC311C(C(C311)OC312C(C(C312)OC313C(C(C313)OC314C(C(C314)OC315C(C(C315)OC316C(C(C316)OC317C(C(C317)OC318C(C(C318)OC319C(C(C319)OC320C(C(C320)OC321C(C(C321)OC322C(C(C322)OC323C(C(C323)OC324C(C(C324)OC325C(C(C325)OC326C(C(C326)OC327C(C(C327)OC328C(C(C328)OC329C(C(C329)OC330C(C(C330)OC331C(C(C331)OC332C(C(C332)OC333C(C(C333)OC334C(C(C334)OC335C(C(C335)OC336C(C(C336)OC337C(C(C337)OC338C(C(C338)OC339C(C(C339)OC340C(C(C340)OC341C(C(C341)OC342C(C(C342)OC343C(C(C343)OC344C(C(C344)OC345C(C(C345)OC346C(C(C346)OC347C(C(C347)OC348C(C(C348)OC349C(C(C349)OC350C(C(C350)OC351C(C(C351)OC352C(C(C352)OC353C(C(C353)OC354C(C(C354)OC355C(C(C355)OC356C(C(C356)OC357C(C(C357)OC358C(C(C358)OC359C(C(C359)OC360C(C(C360)OC361C(C(C361)OC362C(C(C362)OC363C(C(C363)OC364C(C(C364)OC365C(C(C365)OC366C(C(C366)OC367C(C(C367)OC368C(C(C368)OC369C(C(C369)OC370C(C(C370)OC371C(C(C371)OC372C(C(C372)OC373C(C(C373)OC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94

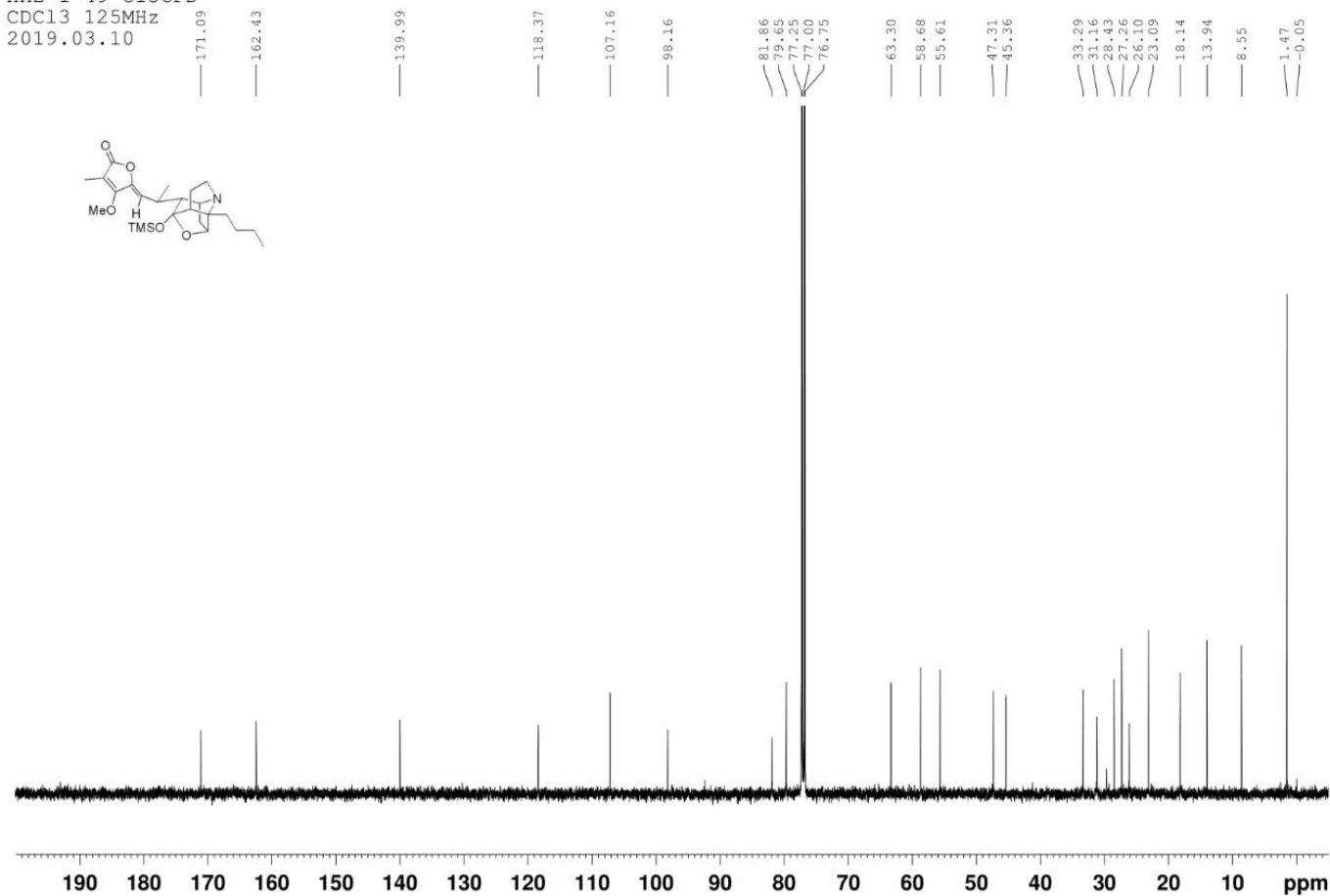
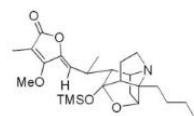


Supplementary Figure 61. ^{13}C NMR spectrum of compound stemoburkilline (7)



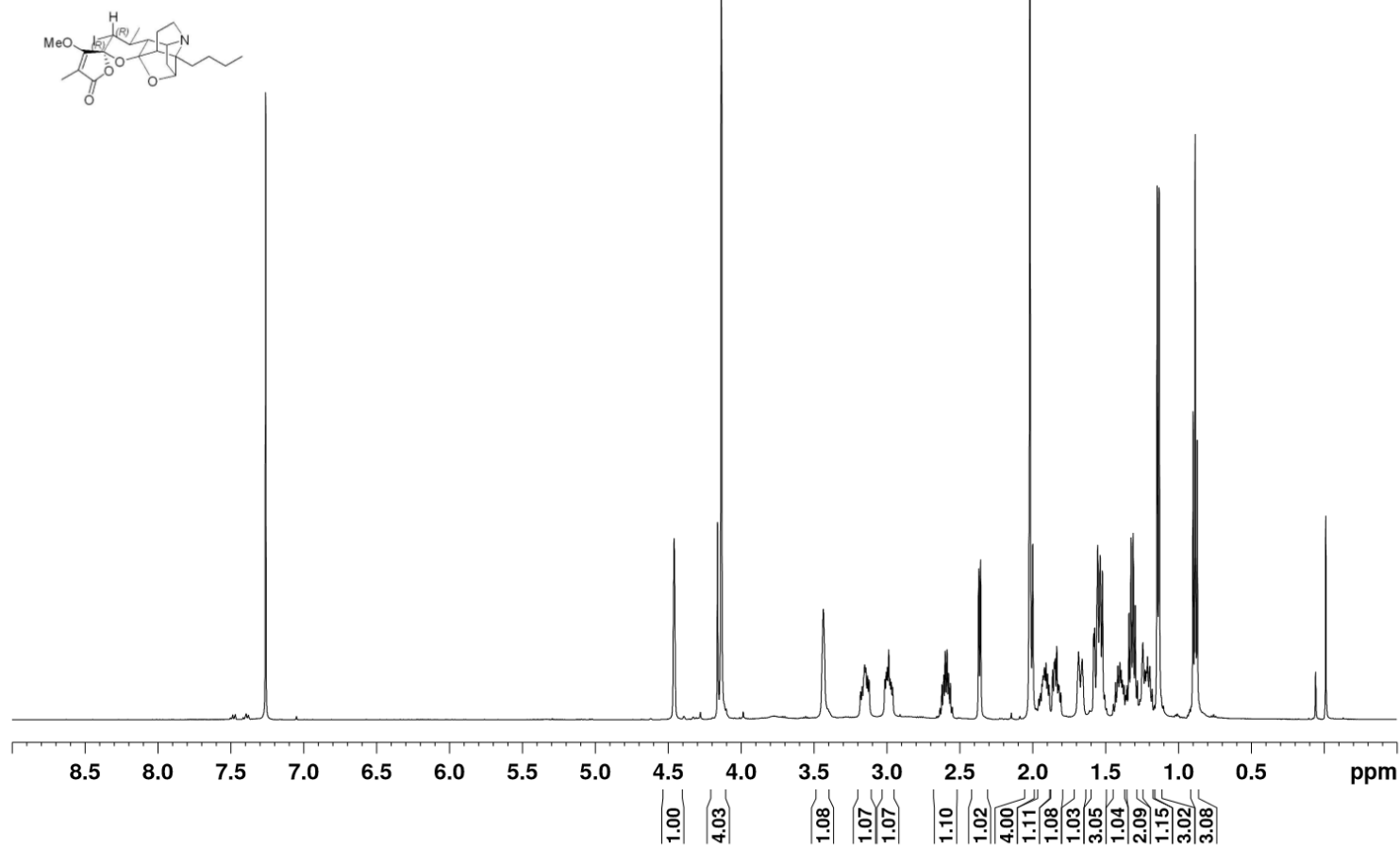
Supplementary Figure 62. ^1H NMR spectrum of compound **30**

HXZ-I-49 C13CPD
 CDCl3 125MHz
 2019.03.10



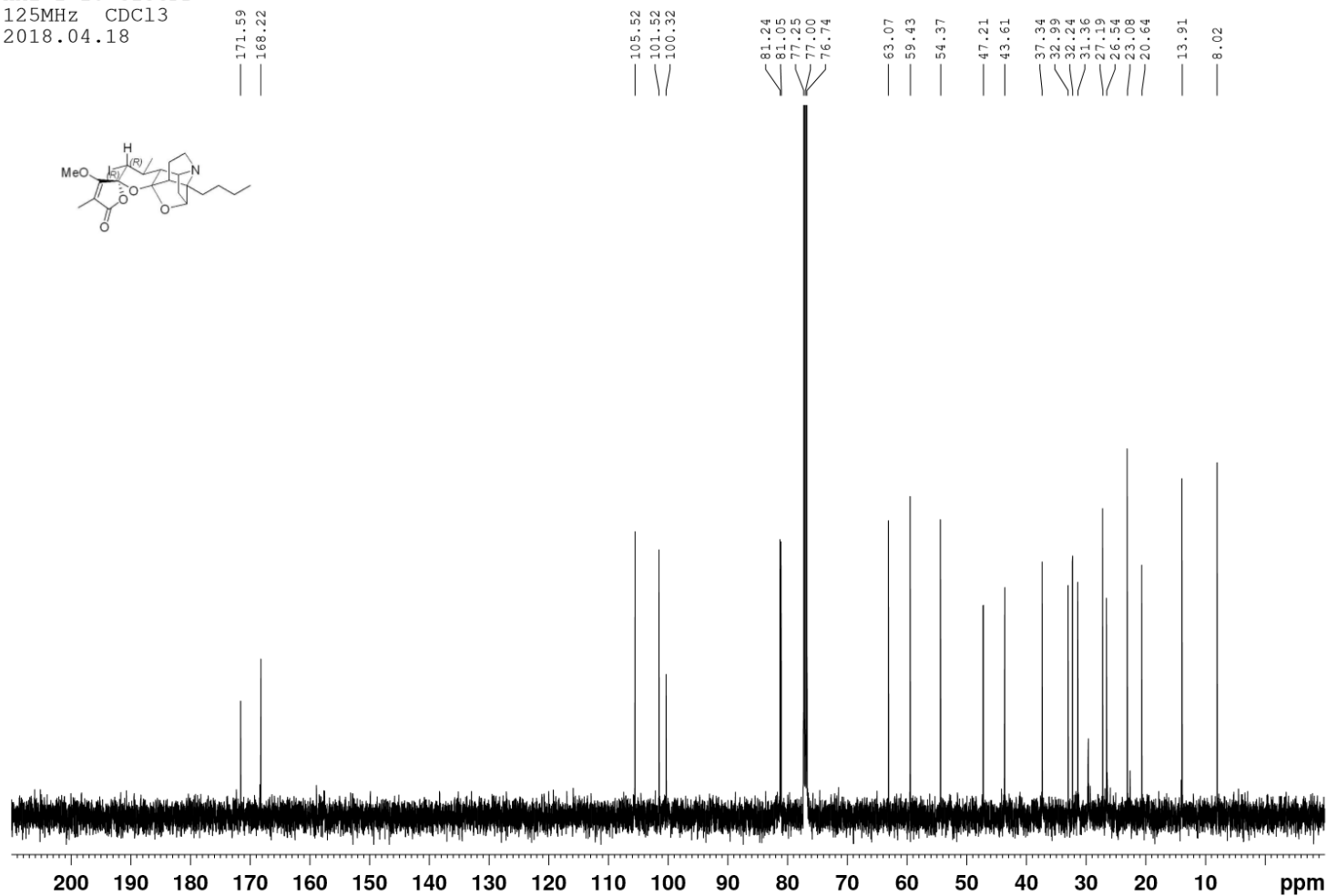
Supplementary Figure 63. ¹³C NMR spectrum of compound 30

HXZ-I-10 PROTON256
500MHz CDCl3
2018.04.18



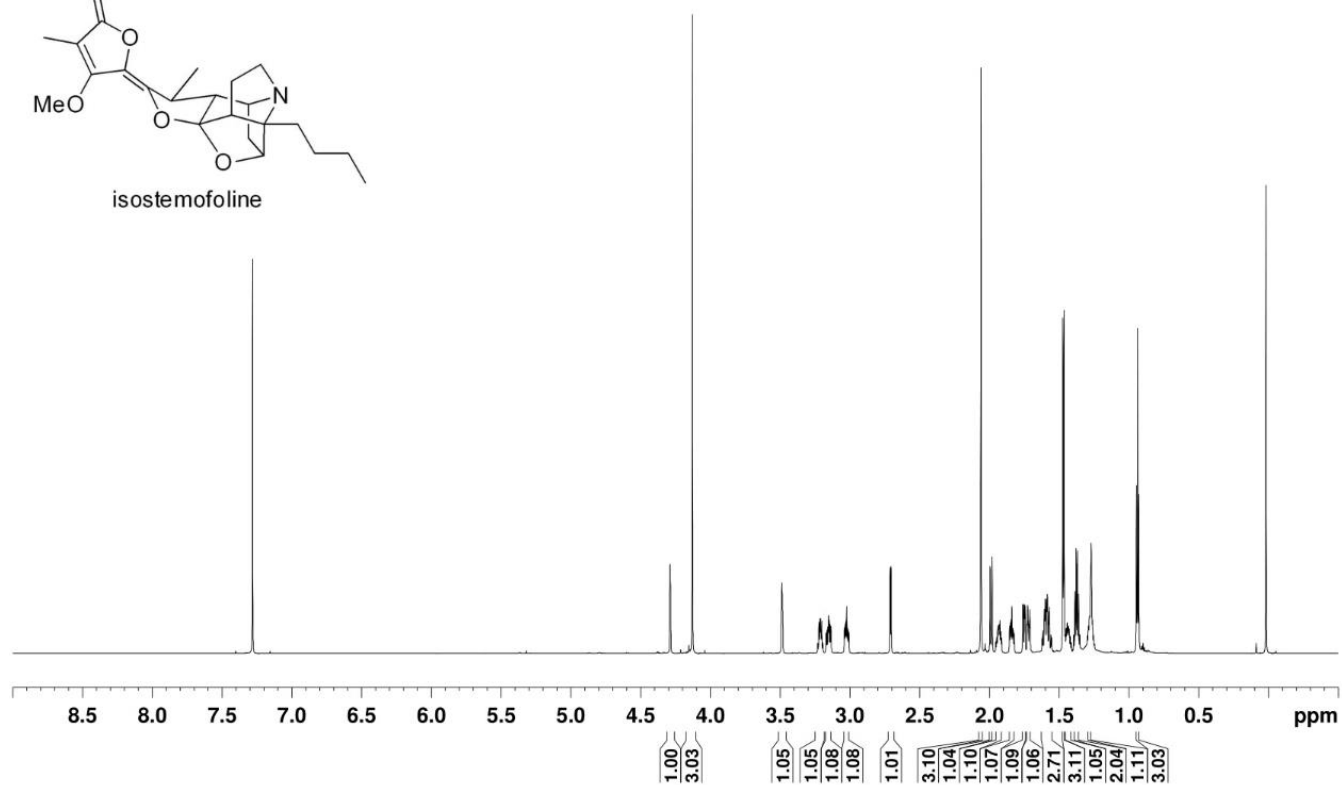
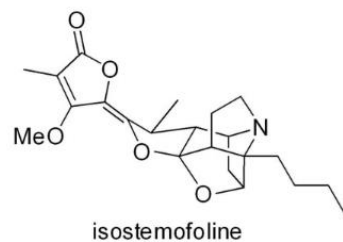
Supplementary Figure 64. ¹H NMR spectrum of compound 31

HXZ-I-10 C13CPD
125MHz CDCl3
2018.04.18



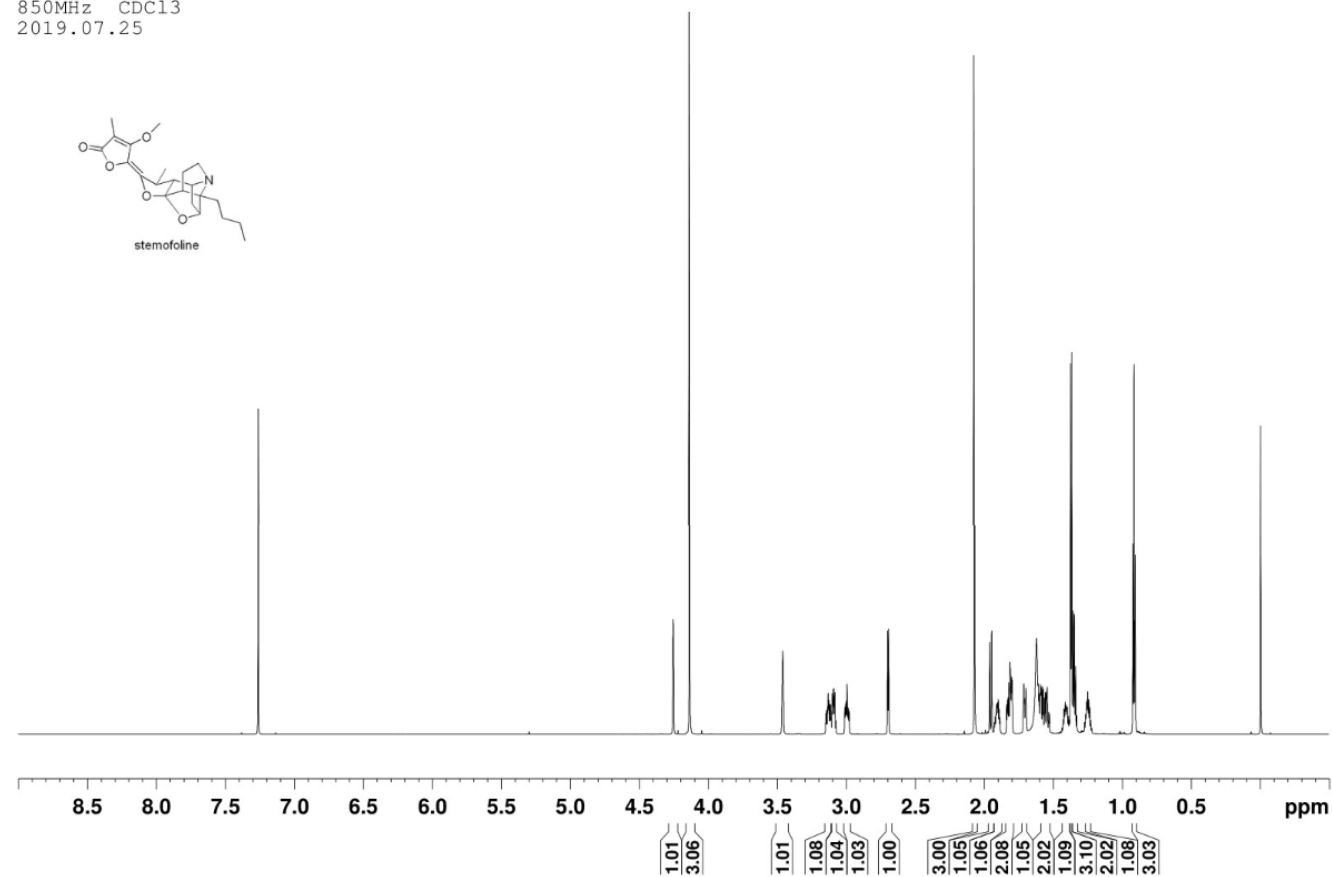
Supplementary Figure 65. ¹³C NMR spectrum of compound 31

HXZ-I-84a-HPLC PROTON256
850MHz CDCl3
2019.07.25

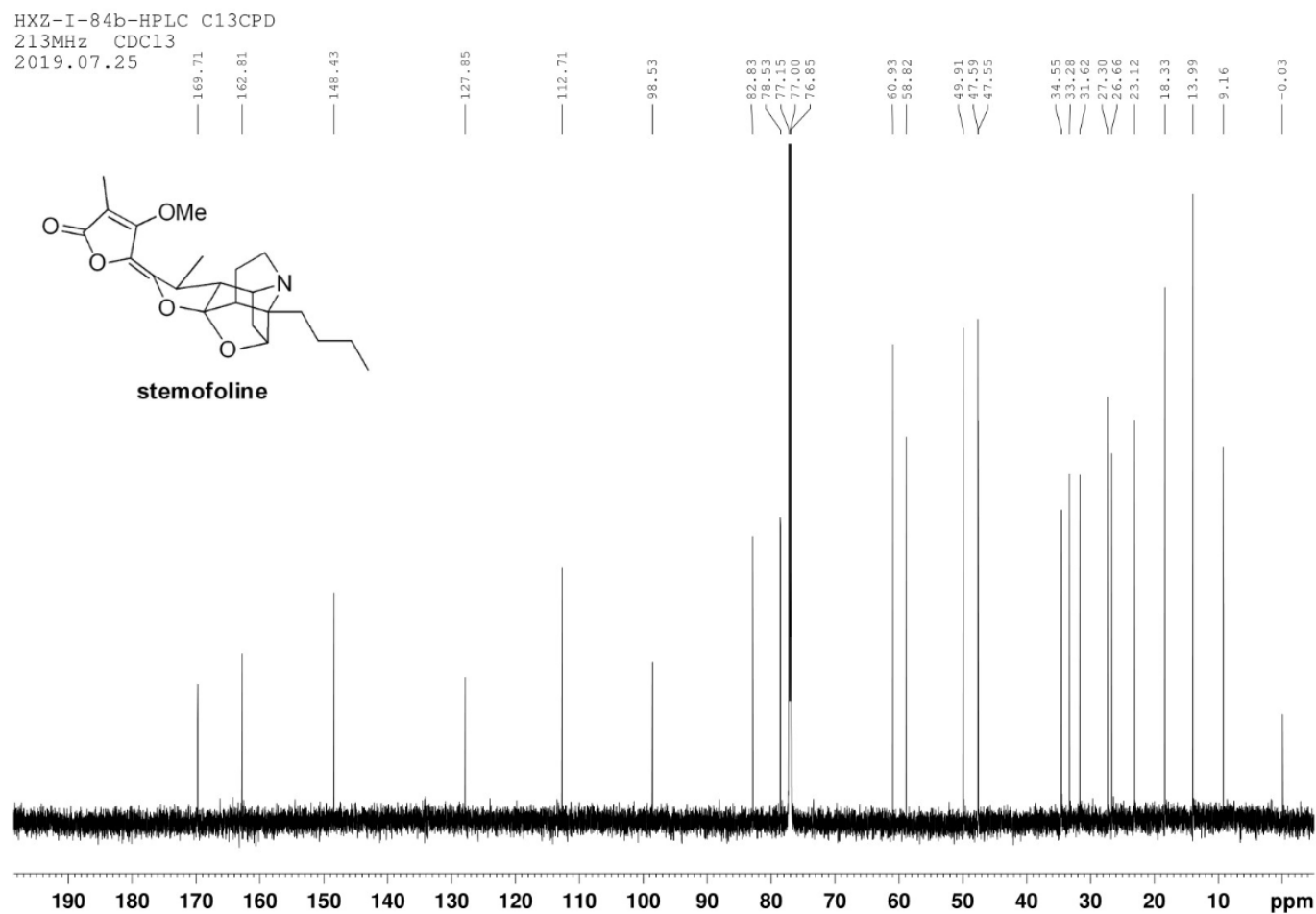


Supplementary Figure 66. ^1H NMR spectrum of compound isostemofoline (2)

HXZ-I-84b-HPLC PROTON256
850MHz CDC13
2019.07.25



Supplementary Figure 68. ¹H NMR spectrum of compound stemofoline (**1**)



Supplementary Figure 69. ^{13}C NMR spectrum of compound stemofoline (1)

Supplementary References

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