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Supporting Information

# Bio-inspired Construction of Tetracyclic Ring System with an Avarane Skeleton: Total Synthesis of Dactyloquinone A †

**Yumeng Wu, § [a] Xuanxuan Du, § [a] Xianyang Wang,[a] Hainan Liu, [a] Luning Zhou, [a] Yu Tang*[ab] and Dehai Li*[ab]**

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## 1. General Methods

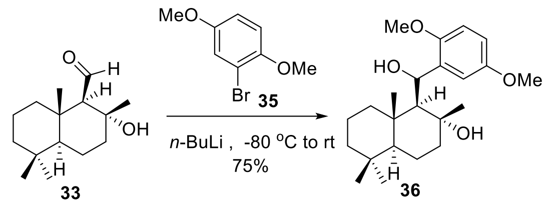
All reactions were carried out under an argon atmosphere with dry solvent under anhydrous conditions, unless otherwise noted. Dry dichloromethane ($CH_2Cl_2$) and tetrahydrofuran (THF) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Anhydrous acetone, dimethylformamide (DMF), 1, 4-dioxane, ethyl acetate (EtOAc), and toluene were purchased from commercial suppliers and stored under argon. Yields refer to chromatographically and spectroscopically ($^1$H NMR) homogenous material, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise noted.

Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm silica gel plates (GF254, Qingdao) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid (PMA) as developing agents. Silica gel (200-400 mesh, Qingdao) was used for column chromatography.

NMR spectra were recorded on Bruker AV 400, Agilent AV 500 or JEOL AV 400 instruments and calibrated using residual undeuterated solvent ($CDCl_3$, $\delta_H$ = 7.26 ppm, $\delta_C$ = 77.1 ppm; DMSO, $\delta_H$ = 2.50 ppm, $\delta_C$ = 39.6 ppm;) as an internal reference. The information in parentheses report fine structures (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad), scalar coupling constants (*J*, given in Hz), relative integration of signals and the signal assignment. HRESIMS data were measured on UHD Accurate Mass Q-TOF LC/MS G6540A. X-ray data were obtained by a Bruker D8 Venture diffractometer using graphite monochromated Cu-Kα radiation. Semi-preparative HPLC (Hitachi chromaster).

## 2. Experimental Procedures and Physical Data of Compounds

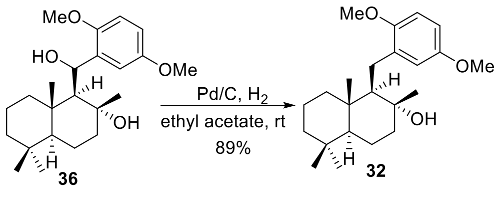
### 2.1 Synthesis of benzylic alcohol 36



Aldehyde **33** was prepared in 53% by 3 steps of the process reported in literature.[1] To a solution of **35** 1-bromo-2,5-dimethoxy benzene (23.6 g, 109.0 mmol, 3.0 eq) in anhydrous THF (250 mL) under $N_2$ atmosphere at -80 °C was added *n*-BuLi (54.5 ml, 2 M in hexane, 109.0 mmol, 3.0 eq) dropwise. The reaction was stirred at -80 °C for 1.5 h and a solution of aldehyde **21** (8.7 g, 36.3 mmol, 1.0 eq) in anhydrous THF (50 mL) was added dropwise. The resultant mixture was stirred at -80 °C for 30 min, then allowed to warm to rt. The mixture was quenched with saturated $NH_4Cl$ solution (50 mL) and extracted with EtOAc (3 × 100 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 50:1) to give Benzylic alcohol **36** as brown oil (8.8 g, 37.0 mmol, 75%).

**Characterization of benzylic alcohol 36: TLC:** $R_f$ = 0.30 (petrol ether/EtOAc = 2:1); **$^1$H NMR (400 MHz, DMSO-*d*$_6$):** δ 7.01 (d, *J* = 3.0 Hz, 1H ), 6.81 (d, *J* = 8.9 Hz, 1H ), 6.71 (dd, *J* = 8.8, 3.0 Hz, 1H ), 5.92 (d, *J* = 5.2 Hz, 1H ), 5.47 (s, 1H), 5.24–5.21 (m, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 1.89 (d, *J* = 8.1 Hz, 1H ), 1.69–1.66 (m, 1H), 1.53–1.44 (m, 2H), 1.39 (s, 3H), 1.01–0.98 (m, 5H), 0.96 (s, 3H), 0.93–0.86 (m, 1H), 0.83–0.80 (m, 1H), 0.77 (s, 3H), 0.72 (s, 3H) ppm; **$^{13}$C NMR (100 MHz, DMSO-*d*$_6$):** δ 153.9, 149.8, 139.2, 115.4, 112.6, 112.1, 74.0, 65.4, 63.8, 56.6, 56.2, 55.8, 44.6, 41.7, 39.3, 38.8, 33.9, 33.4, 26.3, 22.0, 20.1, 18.6, 16.2 ppm; **HRMS (ESI-TOF):** calcd for $C_{23}H_{36}NaO_4^+$ $[M+Na]^+$ 399.2506, found 399.2508.

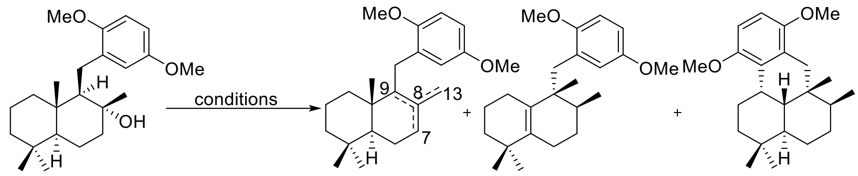
### 2.2 Synthesis of alcohol 32



To a stirred solution of benzylic alcohol **36** (3.8 g, 10.0 mmol, 1.0 eq) in EtOAc (20 mL) was added 10% Pd/C (2.36 g, 1.0 mmol, wetted with ca.55% water, 0.1 eq) at rt. The resulting mixture was stirred at this temperature for 14 h under $H_2$. The reaction mixture was filtered through diatomite and the solvent was concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 40:1) to give alcohol **32** as white solid (3.2g, 8.9 mmol, 89%).

**Characterization of alcohol 20: M.P.:**102.6-104.6°C; **TLC:** $R_f$ = 0.51 (petrol ether/EtOAc = 4:1); **$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.80 (d, *J* = 3.0 Hz, 1H ), 6.74 (d, *J* = 8.9 Hz, 1H ), 6.58 (dd, *J* = 8.8, 3.0 Hz, 1H ), 3.80 (s, 3H), 3.74 (s, 3H), 2.85 (dd, *J* = 14.8, 5.2 Hz, 1H ), 2.52 (dd, *J* = 14.8, 4.4 Hz, 1H ), 1.86–1.80 (m, 2H), 1.65–1.52 (m, 3H), 1.46–1.35 (m, 3H), 1.27 (s, 3H), 1.24–1.20 (m, 1H), 1.13–1.05 (m, 1H), 0.94–0.91 (m, 1H), 0.89 (s, 3H), 0.84 (s, 3H), 0.84–0.81 (m, 1H), 0.79 (s, 3H) ppm; **$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 153.8, 150.8, 134.1, 117.7, 111.6, 110.5, 73.8, 62.6, 56.2, 56.0, 55.7, 43.6, 41.9, 40.5, 39.5, 33.6, 33.4, 25.4, 24.5, 21.6, 20.4, 18.7, 15.6 ppm; **HRMS (ESI-TOF):** calcd for $C_{23}H_{36}NaO_3^+$ $[M+Na]^+$ 383.2557, found 383.2559.

### 2.3 Table S1. Preliminary lewis acidic conditions screened for the formation of 37 and by product.[a]



**32** **39**: $\Delta^{8,13}$ **40**: $\Delta^{7,8}$ **41**: $\Delta^{8,9}$ **37** **42**

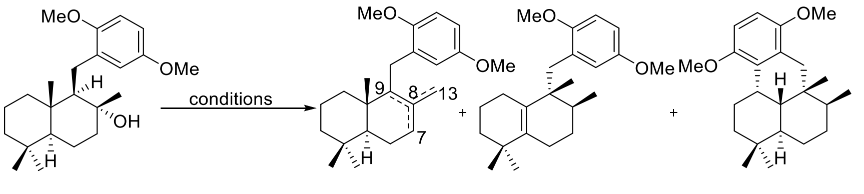
| Entry | LA | t (h) | Yield (%)[b] | | | | |
|---|---|---|---|---|---|---|---|
| | | | **39** | **40** | **41** | **37** | **42** |
| 1 | $Sn(OTf)_2$ | 4 | 27 | 64 | 0 | 0 | 0 |
| 2 | $TiCl_4$ | 0.02 | 0 | 0 | 0 | 0 | 89 |
| 3 | $Ho(OTf)_3$ | 4 | 41 | 34 | 14 | 0 | 0 |
| 4 | $Hg(OTf)_2$ | 0.25 | 0 | 0 | 33 | 45 | 0 |
| 5 | $Lu(OTf)_3$ | 2.5 | 43 | 39 | 0 | 0 | 0 |
| 6 | $Dy(OTf)_3$ | 13 | 27 | 21 | 0 | 0 | 0 |
| 7 | $Er(OTf)_3$ | 5 | 42 | 42 | 0 | 0 | 0 |
| 8 | $Sc(OTf)_3$ | 0.5 | 0 | 0 | 92 | 0 | 0 |
| 9 | LiCl | 12 | 0 | 0 | 0 | 0 | 0 |
| 10 | $SnCl_2$ | 7 | 9 | 70 | 10 | 0 | 0 |
| 11 | $BF_3.OEt_2$ | 0.15 | 0 | 0 | 15 | 62 | 15 |
| 12 | $MgBr_2$ | 1 | 0 | 0 | 0 | 0 | 0 |
| 13 | BPA | 3 | 0 | 0 | 0 | 0 | 0 |
| 14 | $Yb(OTf)_3$ | 3 | 0 | 0 | 0 | 0 | 0 |
| 15 | $Mg(OTf)_3$ | 2.5 | 6 | 62 | 18 | 0 | 0 |
| 16 | AgF | 1 | 0 | 0 | 0 | 0 | 0 |
| 17 | $Fe(OAc)_2$ | 1 | 0 | 0 | 0 | 0 | 0 |
| 18 | $LiBF_4$ | 1 | 0 | 0 | 0 | 0 | 0 |
| 19 | $La(OTf)_3$ | 1 | 0 | 0 | 0 | 0 | 0 |
| 20 | $ZnBr_2$ | 4 | 4 | 9 | 4 | 37 | 33 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 21 | $LiPF_6$ | 0.30 | 0 | 0 | 35 | 42 | 14 |
| 22 | PTSA | 12 | 41 | 41 | 0 | 0 | 0 |
| 23 | $SnCl_4$ | 0.08 | 0 | 0 | 0 | 0 | 89 |
| 24 | CSA | 12 | 28 | 28 | 0 | 0 | 0 |
| 25 | $Cu(OAc)_2$ | 4 | 0 | 0 | 0 | 0 | 0 |
| 26 | $CoBr_2$ | 5 | 0 | 0 | 0 | 0 | 0 |
| 27 | LiI | 4 | 0 | 0 | 0 | 0 | 0 |
| 28 | $In(OTf)_3$ | 0.5 | 26 | 61 | 0 | 0 | 0 |
| 29 | $Gd(OTf)_3$ | 1.2 | 25 | 6 | 0 | 0 | 0 |
| 30 | $AlCl_3$ | 0.5 | 0 | 0 | 0 | 0 | 96 |
| 31 | $Bi(OTf)_3$ | 0.12 | 0 | 0 | 82 | 10 | 0 |
| 32 | $Fe(OTf)_3$ | 1 | 4 | 42 | 17 | 0 | 0 |
| 33 | $Sm(OTf)_3$ | 15 | 53 | 25 | 12 | 0 | 0 |
| 34 | TfOH | 0.25 | 0 | 0 | 0 | 0 | 91 |

[a] To a solution of alcohol **32** (0.1mmol, 1.0 eq) in DCM (5ml) at rt was added Lewis Acid (3.0 eq).

[b] Total yields were deter mined by $^1H$ NMR analysis of the crude reaction mixtures.

## 2.4 Table S2. Optimization of the lewis acid rearrangement reaction for compound 37.[a]



**32** **39**: Δ8,13 **40**: Δ7,8 **41**: Δ8,9 **37** **42**

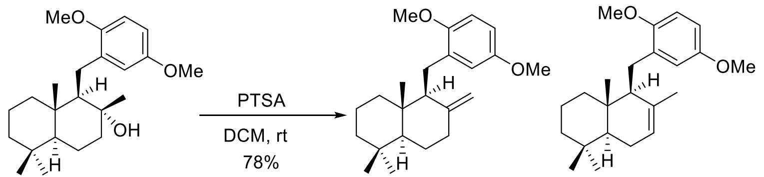
| Entry | LA | Eq | Temp (°C) | T (h) | **Yield (%)[b]** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | **39** | **40** | **41** | **37** | **42** |
| 1 | $Bi(OTf)_3$ | 3 | rt | 0.1 | 0 | 0 | 82 | 10 | 0 |
| 2 | $Bi(OTf)_3$ | 3 | rt | 1.2 | 0 | 0 | 17 | 57 | 20 |
| 3 | $Bi(OTf)_3$ | 2.5 | rt | 1.2 | 0 | 0 | 85 | 4 | 0 |
| 4 | $Bi(OTf)_3$ | 2 | rt | 6.6 | 0 | 0 | 0 | 42 | 48 |
| 5 | $Bi(OTf)_3$ | 2 | rt | 2 | 0 | 0 | 34 | 44 | 12 |
| 6 | $Bi(OTf)_3$ | 1 | rt | 2 | 0 | 0 | 64 | 21 | 6 |
| 7 | $Bi(OTf)_3$ | 3 | rt | 1.3 | 0 | 0 | 0 | 33 | 57 |
| 8 | $Bi(OTf)_3$ | 3 | rt | 2 | 0 | 0 | 0 | 32 | 58 |
| 9 | $Sc(OTf)_3$ | 3 | rt | 11 | 0 | 0 | 70 | 13 | 6 |
| 10 | $Sn(OTf)_2$ | 3 | rt | 4 | 27 | 64 | 0 | 0 | 0 |
| 11 | $Sn(OTf)_2$ | 3 | rt | 9.4 | 23 | 68 | 0 | 0 | 0 |
| 12 | $Sn(OTf)_2$ | 3 | rt | 18.5 | 7 | 81 | 0 | 0 | 0 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 13 | $Fe(OTf)_3$ | 3 | rt | 0.9 | 4 | 69 | 16 | 0 | 0 |
| 14 | $BF_3.OEt_2$ | 3 | rt | 9 | 0 | 0 | 0 | 0 | 91 |
| 15 | $BF_3.OEt_2$ | 8 | -50 | 2.3 | 0 | 0 | 49 | 42 | 0 |
| 16 | $BF_3.OEt_2$ | 8 | -50 | 2.5 | 0 | 0 | 47 | 43 | 0 |
| 17 | $BF_3.OEt_2$ | 17 | -50 | 3 | 0 | 0 | 36 | 54 | 0 |
| 18 | $BF_3.OEt_2$ | 17 | -50 | 6 | 0 | 0 | 25 | 65 | 0 |
| 19 | $BF_3.OEt_2$ | 17 | -80 | 1 | 14 | 22 | 4 | 0 | 0 |
| 20 | $BF_3.OEt_2$ | 17 | -50 | 15.5 | 0 | 0 | 26 | 64 | 0 |
| 21 | $BF_3.OEt_2$ | 17 | -40 | 11 | 0 | 0 | 0 | 84 | 8 |
| 21 | $SnCl_4$ | 3 | -20 | 0.3 | 0 | 0 | 0 | 0 | 89 |
| 22 | TfOH | 1 | -40 | 0.17 | 0 | 0 | 0 | 0 | 90 |
| 23 | $Eu(OTf)_3$ | 3 | rt-reflux | 9 | 24 | 31 | 7 | 12 | 10 |

[a] Reactions were performed on a 0.1 mmol scale in $CH_2Cl_2$.

[b] Total yields were determined by $^1$H NMR analysis of the crude reaction mixtures.

## 2.5 Synthesis of compound 39 and 40



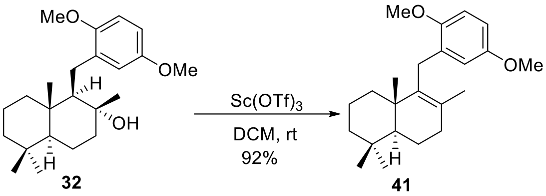
**32** **39** **40**

To a solution of **32** (21.0 mg, 0.06 mmol, 1.0 eq) in DCM (3 mL) at rt was added p-Toluenesulfonic acid monohydrate (31.0 mg, 0.18 mmol, 3.0 eq). The resulting mixture was stirred at this temperature for 12 h . The mixture was quenched with $H_2O$ (10 mL) and extracted with DCM (3 × 5 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 100:1) to give 39 (8.2 mg, 0.023 mmol, 39%) as a colorless oil and 40 (8.2 mg, 0.023 mmol, 39%) as a colorless oil. The NMR data of compound **39** were consistent with reference 2.[2]

**Characterization of compound 39: TLC:** $R_f$ = 0.51 (petrol ether/EtOAc = 20:1); **$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.74–6.62 (m, 3H), 4.74 (br. s, 1H), 4.60 (br. s, 1H), 3.79 (s, 3H), 3.74 (s, 3 H), 2.74 (d, *J* = 6.8 Hz, 2 H), 2.37–2.32 (m, 1H), 2.20 (t, *J* = 6.7 Hz, 1H), 2.04–1.96 (m, 1H), 1.89–1.86 (m, 1H), 1.76–1.33 (m, 1H), 1.21–1.17 (m, 1H), 0.89 (s, 3H), 0.83 (s, 3 H), 0.81 (s, 3 H) ppm;**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 153.3, 151.8, 148.4, 132.2, 116.3, 110.9, 109.7, 107.7, 56.0, 55.8, 55.7, 42.3, 40.0, 39.2, 38.3, 33.8, 33.7, 29.8, 24.5, 23.3, 21.9, 19.6, 14.7 ppm; **HRMS (ESI-TOF):** calcd for $C_{23}H_{33}O_2^-$ $[M-H]^-$ 341.2486, found 341.2478.

**Characterization of compound 40: TLC:** $R_f$ = 0.50 (petrol ether/EtOAc = 20:1); **$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.84 (d, *J* = 3.0 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 1H), 6.65 (dd, *J* = 8.8, 3.0 Hz, 1H), 5.36 (br. s, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 2.74–2.54 (m, 2H), 1.97–1.89 (m, 2H), 1.57–1.41 (m, 7H), 1.22–1.06 (m, 3H), 0.91 (s, 3 H), 0.89 (s, 3 H), 0.88 (s, 3 H) ppm; **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 153.5, 151.6, 136.0, 133.8, 122.1, 116.2, 111.2, 110.0, 56.0, 55.8, 54.5, 50.4, 42.4, 39.6, 37.0, 33.4, 33.2, 26.3, 23.9, 22.4, 22.1, 19.1, 14.0 ppm; **HRMS (ESI-TOF):** calcd for $C_{23}H_{34}NaO_2^+$ $[M+Na]^+$ 365.2451, found 365.2452.

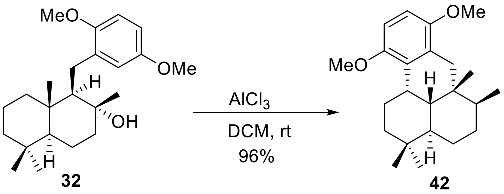
## 2.6 Synthesis of compound 41



To a solution of **32** (300.0 mg, 0.8 mmol, 1.0 eq) in DCM (40 mL) at rt was added Sc(OTf)$_3$ (1.2 g, 2.4 mmol, 3.0 eq). The resulting mixture was stirred at this temperature for 0.5 h. The mixture was quenched with $H_2O$ (20 mL) and extracted with DCM (3 × 20 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure to give **41** (252.0 mg, 0.7 mmol, 92%) as a colorless oil**.** The NMR data are consistent with reference 1.[1]

**Characterization of compound 41:TLC:** $R_f$ = 0.50 (petrol ether/EtOAc = 20:1); **$^1$H NMR (400 MHz, CDCl$_3$):** δ 6.74 (d, *J* = 8.4 Hz, 1H), 6.66–6.63 (m, 2 H), 3.82 (s, 3 H), 3.75 (s, 3 H), 3.37 (d, *J* = 17.8 Hz, 1 H), 3.22 (d, *J* = 17.8 Hz, 1 H), 2.17 (dd, *J* = 10.8, 7.4 Hz, 1 H), 2.06 (dd, *J* = 17.6,6.2 Hz, 1 H), 1.72 (dd, *J* = 12.4, 6.9 Hz, 1 H), 1.56–1.51 (m, 2 H), 1.48 (s, 3 H), 1.35–1.31 (m, 2 H), 1.26 (d, *J* = 6.0 Hz, 2 H), 1.10 (dd, *J* = 13.0, 3.7 Hz, 1 H), 1.01 (s, 3 H), 0.97–0.93 (m, 1 H), 0.90 (s, 3 H), 0.84 (s, 3 H) ppm; **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 153.4, 151.2, 137.2, 131.3, 129.1, 116.2, 110.1, 109.0, 55.9, 55.7, 51.2, 41.8, 39.0, 36.0, 33.6, 33.4, 33.3, 27.0, 21.8, 20.3, 20.3, 19.2, 19.0 ppm; **HRMS (ESI-TOF):** calcd for $C_{23}H_{34}NaO_2^+$ $[M+Na]^+$ 365.2451, found 365.2448.

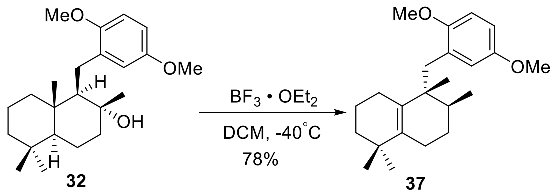
## 2.7 Synthesis of compound 42



To a solution of **32** (61.0 mg, 0.17 mmol, 1.0 eq) in DCM (10 mL) at rt was added AlCl$_3$ (68.0 mg, 0.51 mmol, 3.0 eq). The resulting mixture was stirred at this temperature for 0.5 h. The mixture was quenched with $H_2O$ (10 mL) and extracted with DCM (3 × 10 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure to give **42** (54.8 mg, 0.16 mmol, 96%) as a colorless oil**.** The NMR data are consistent with reference 3 and 4.[3-4]

**Characterization of compound 42:TLC:** $R_f$ = 0.50 (petrol ether/EtOAc = 20:1); **$^1$H NMR (400 MHz, CDCl$_3$):** δ 6.68–6.63 (m, 2H), 3.80 (s, 3H), 3.75 (s, 3H), 3.09–3.01 (m, 3H), 2.14–2.05 (m, 2H), 1.63–1.07 (m, 9H), 1.02 (d, *J* = 7.2 Hz, 3H), 0.86 (s, 3H), 0.79 (s, 3H), 0.75 (s, 3H); **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 153.2, 151.9, 128.5, 128.4, 108.5, 106.6, 55.8, 55.5, 42.4, 39.1, 38.4, 38.2, 34.6, 33.6, 32.8, 32.6, 30.6, 29.0, 25.1, 24.1, 21.6, 20.5, 14.7; **HRMS (ESI-TOF):** calcd for $C_{23}H_{34}NaO_2^+$ [M+Na]$^+$ 365.2451, found 365.2442.

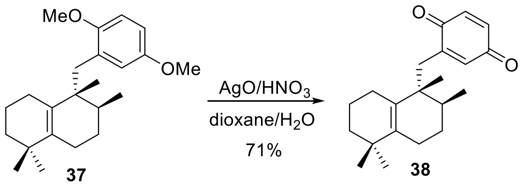
### 2.8 Synthesis of compound 25



To a solution of **3**2 (500 mg, 1.39 mmol, 1.0 eq) in DCM (30 mL) at -40°C was added boron trifluoride etherate (3.0 ml, 23.68 mmol, 17.0 eq). The mixture was stirred at -40°C for 11 h.The mixture was quenched with $H_2O$ (30 mL) and extracted with DCM (3 × 20 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 200:1) to give **37** (371 mg, 1.08 mmol, 78%) as a colorless oil , NMR yield is 84%. The NMR data are consistent with reference 4 and 5. [4-5]

**Characterization of compound 37: TLC:** $R_f$ = 0.49 (petrol ether/EtOAc = 20:1); **$^1$H NMR (400 MHz, CDCl$_3$):** δ 6.86 (m, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 6.67 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 2.93 (d, *J* = 15.3 Hz, 1H), 2.62 (d, *J* = 15.2 Hz, 1H), 2.09–2.01 (m, 4H), 1.94–1.90 (m, 1H), 1.68–1.60 (m, 4H), 1.47–1.44 (m, 2H), 1.01 (s, 3H), 1.00 (s, 3H), 0.92 (s, 3H), 0.78 (d, *J* = 6.5 Hz, 3H) ppm; **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 153.2, 152.5, 136.0, 132.9, 130.0, 116.7, 111.1, 111.0, 56.0, 55.8, 41.7, 40.0, 34.7, 34.5, 33.6, 28.5, 28.3, 26.9, 26.5, 23.8, 22.2, 20.1, 16.2 ppm; **HRMS (ESI-TOF):** calcd for $C_{23}H_{34}NaO_2^+$ [M+Na]$^+$ 365.2451, found 365.2450.

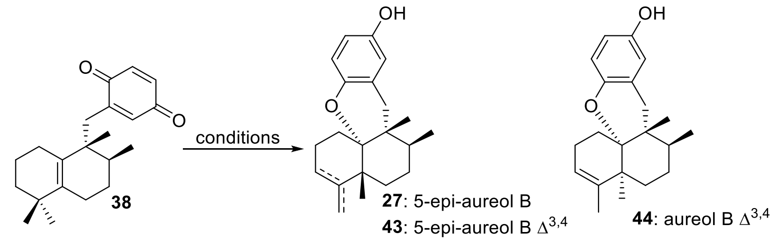
### 2.9 Synthesis of quinone 38



To a solution of **37** (164.1 mg, 0.5 mmol, 1.0 eq) in dioxane (30 mL) was added AgO (125.0 mg, 1.0 mmol, 2.0 eq) and 6 N $HNO_3$ (0.47 mL, 1.5 mmol, 3.0 eq). The mixture was stirred at rt for 10 min. After the reaction is complete, The mixture was quenched with saturated $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 15 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 50:1) to give quinone **38**(110.9 mg, 0.355 mmol, 71%) as a yellow oil.

**Characterization of compound 38: TLC:** $R_f$ = 0.65 (petrol ether/EtOAc = 20:1); **$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.76–6.67 (m, 3H), 2.77 (d, *J* = 16.6 Hz, 1H), 2.38 (d, *J* = 16.6 Hz, 1H), 2.09–1.78 (m, 4H), 1.60–1.54 (m, 3H), 1.47–1.31 (m, 4H), 1.00 (s, 3H), 0.98 (s, 3H), 0.93 (s, 3H) 0.81 (d, *J* = 6.7 Hz, 3H) ppm; **$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 187.9, 187.8, 147.3, 138.2, 137.0, 136.1, 133.9, 131.2, 41.8, 39.7, 34.7, 34.1, 33.4, 28.6, 28.0, 26.9, 26.4, 24.2, 22.3, 19.9, 16.5 ppm; **HRMS (ESI-TOF):** calcd for $C_{21}H_{29}O_2^+$ $[M+H]^+$ 313.2162, found 313.2157.

## 2.10 Table S3 Optimization of the construction of a tetracyclic ring system with an avarane skeleton.[a]



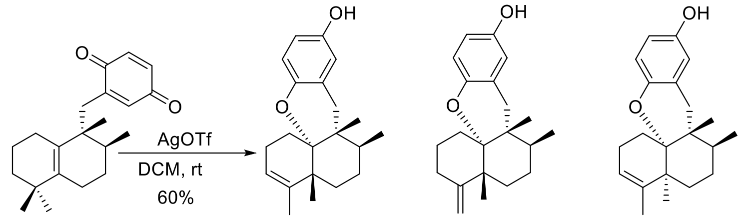
| Entry | LA | Eq | T (°C) | Solvent | yield (%)[b] | | |
|---|---|---|---|---|---|---|---|
| | | | | | **18** | **17** | **14** |
| 1 | TMSOTf | 0.2 | rt | DCM | 41 | 0 | 5 |
| 2 | TfOH | 0.3 | rt | DCM | 0 | 0 | 0 |
| 3 | AgOTf | 1.0 | rt | DCM | 42 | 14 | 8 |
| 4 | $Fe(OTf)_2$ | 1.0 | rt | DCM | 23 | 0 | 0 |
| 5 | $Bi(OTf)_3$ | 1.0 | rt | DCM | 20 | 0 | 0 |
| 6 | $Zn(OTf)_2$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 7 | $Fe(OTf)_3$ | 1.0 | rt | DCM | 13 | 0 | 0 |
| 8 | $La(OTf)_3$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 9 | $In(OTf)_3$ | 1.0 | rt | DCM | 25 | 4 | 0 |
| 10 | $Dy(OTf)_3$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 11 | $Eu(OTf)_3$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 12 | $Ho(OTf)_3$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 13 | $Lu(OTf)_3$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 14 | $Sn(OTf)_2$ | 1.0 | rt | DCM | 14 | 0 | trace |
| 15 | p-TsOH | 1.0 | rt | DCM | 11 | 0 | trace |
| 16 | CSA | 1.0 | rt | DCM | trace | 0 | 0 |
| 17 | $CF_3COOAg$ | 1.0 | rt | DCM | 0 | 0 | 0 |
| 18 | $F_6LiP$ | 1.0 | rt | DCM | 30 | 0 | trace |
| 19 | $FeBr_3$ | 1.0 | rt | DCM | 0 | 0 | 0 |
| 20 | $AlCl_3$ | 1.0 | rt | DCM | 32 | trace | trace |
| 21 | TMSOTf | 1.0 | -80 | DCM | 28 | 0 | 16 |
| 22 | TfOH | 1.0 | -80 | DCM | 29 | 0 | 10 |
| 23 | $FeCl_3$ | 1.5 | -80 | DCM | 58 | 0 | 0 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 24 | $BCl_3$ | 1.0 | -80 | DCM | 22 | 0 | 0 |
| 25 | $BF_3$ .$OEt_2$ | 1.0 | -80 | DCM | 50 | 0 | 15 |
| 26 | $BBr_3$ | 1.0 | -80 | DCM | 0 | 0 | 0 |
| 27 | $MgBr_2$ | 1.0 | -80 | DCM | 0 | 0 | 0 |
| 28 | $AuCl_3$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 29 | $Cu(OTf)_2$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 30 | $Hg(OTf)_2$ | 1.0 | rt | DCM | trace | 0 | 0 |
| 31 | $B(C_6F_6)_3$ | 1.0 | rt | DCM | 0 | 0 | 0 |
| 32 | $In(OTf)_3$ | 1.0 | -78 | $CHCl_3$ | 34 | 0 | 19 |
| 33 | $In(OTf)_3$ | 1.0 | -78-rt | toluene | 24 | 0 | 12 |
| 34 | $In(OTf)_3$ | 1.0 | -78-rt | DCM | 40 | 0 | 16 |
| 35 | TMSOTf | 0.2 | -78 | DCM | 43 | 3 | 27 |
| 36 | $In(OTf)_3$ | 1.0 | -78-rt | THF | 0 | 0 | 0 |

[a] Reactions were performed on a 0.1 mmol scale.

[b] yields were deter mined by $^1$H NMR analysis of the crude reaction mixtures.

**2.11 Synthesis of aureol B $\Delta^{3,4}$ (44) and 5-epi-aureol B (27) and 5-epi-aureol B $\Delta^{3,4}$ (43)**



**38** **43**: 5-epi-aureol B $\Delta^{3,4}$ **27**: 5-epi-aureol B **44**: aureol B $\Delta^{3,4}$

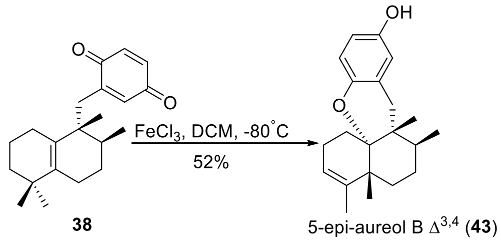
To a solution of quinone **38** (2.5 g, 8.3 mmol, 1.0 eq) in DCM (50 mL) at rt was added AgOTf (2.0 g, 8.0 mmol, 1.0 eq). The mixture was stirred at rt for 2 h. After the reaction is complete, The mixture was quenched with $H_2O$ (20 mL) and extracted with DCM (3 × 25 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 30:1) to give a mixture of compounds **43** and **27** and **44** (1.5 g, 4.8 mmol, 60%) as white solid, aureol B $\Delta^{3,4}$ (**44**) : 5-epi-aureol B (**27**) : 5-epi-aureol B $\Delta^{3,4}$ (**43**) = 0.6:1:3 in $^1$H NMR. we finally obtained these compounds by HPLC purification.

**Characterization of 5-epi-aureol B $\Delta^{3,4}$ (43): M.P.:** 56.8-59.2°C; **TLC:** $R_f$ = 0.50 (petrol ether/EtOAc = 3:1); **$[\alpha]^{21.7}_D$** (c =0.0240 g/100ml, MeOH) : -75; **$^1$H NMR (500 MHz, $CDCl_3$):** δ 6.64 (d, $J$ = 8.7 Hz, 1H), 6.55 (dd, $J$ = 8.7, 3.0 Hz, 1H), δ = 6.49 (d, $J$ = 3.0 Hz, 1H), 5.26 (br. s, 1H), 2.60 (d, $J$ = 17.7 Hz, 1H), 2.56 (d, $J$ = 17.7 Hz, 1H), 1.99 (td, $J$ = 12.6, 5.1 Hz, 1H),1.92–1.83 (m, 3H), 1.77–1.69 (m, 1H), 1.65 (s, 3H), 1.52–1.37 (m, 5H), 1.18 (s, 3H), 0.95 (s, 3H), 0.80 (d, $J$ = 6.8 Hz, 3H) ppm; **$^{13}$C NMR (125 MHz, $CDCl_3$):** δ 148.4, 147.6, 140.0, 121.9, 119.5, 117.4, 114.8, 114.2, 82.3, 42.4, 37.4, 35.3, 31.9, 29.6, 26.9, 23.6, 23.0, 21.0, 19.5, 18.5, 16.1 ppm; **HRMS (ESI-TOF):** calcd for $C_{21}H_{29}O_2^+$ $[M+H]^+$ 313.2162, found 313.2155.

**Characterization of 5-epi-aureol B (27): M.P.:** 91.6-92.7°C; **TLC:** $R_f$ = 0.50 (petrol ether/EtOAc = 3:1); **$[\alpha]^{22.4}_D$** (c =0.0192 g/100ml, MeOH) : -45; **$^1$H NMR (500 MHz, $CDCl_3$):** δ 6.62 (d, *J* = 8.7 Hz, 1H), 6.56 (dd, *J* = 8.5, 3.0 Hz, 1H), δ = 6.54 (d, *J* = 3.0 Hz, 1H), 4.67 (s, 1H), 4.60 (s, 1H), 2.53 (s, 2H), 2.38 (td, *J* = 13.7, 7.5 Hz, 1H), 2.21–2.15 (m, 2H), 1.84 (td, *J* = 13.8, 4.9 Hz, 1H), 1.72–1.45 (m, 7H), 1.35 (dt, *J* = 12.9, 3.0 Hz, 1H), 1.26 (s, 3H), 0.96 (s, 3H), 0.79 (d, *J* = 6.8 Hz, 3H) ppm; **$^{13}$C NMR (125 MHz, $CDCl_3$):** δ 157.2, 148.5, 146.5, 122.2, 117.4, 115.0, 114.2, 104.5, 83.4, 44.0, 37.4, 35.1, 32.1, 31.9, 31.0, 27.1, 24.2, 23.9, 22.2, 19.2, 16.2 ppm; **HRMS (ESI-TOF):** calcd for $C_{21}H_{29}O_2^+$ $[M+H]^+$ 313.2162, found 313.2158.

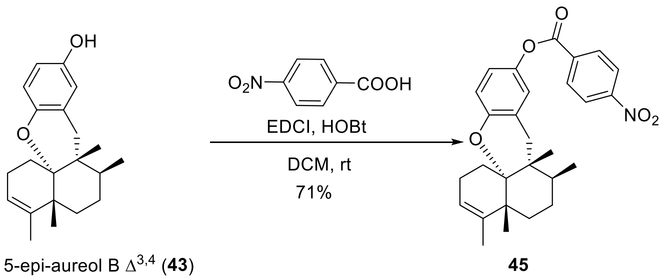
**Characterization of aureol B $\Delta^{3,4}$ (44): M.P.:** 52.1-52.9°C; **TLC:** $R_f$ = 0.50 (petrol ether/EtOAc = 3:1); **$[\alpha]^{25}_D$** (c =0.0340 g/100ml, MeOH) : -3; **$^1$H NMR (500 MHz, $CDCl_3$):** δ 6.63 (d, *J* = 8.7 Hz, 1H), 6.57 (dd, *J* = 8.5, 2.5 Hz, 1H), δ = 6.49 (d, *J* = 2.2 Hz, 1H), 5.26 (s, 1H), 2.70 (d, *J* = 17.6 Hz, 1H), 2.57 (d, *J* = 17.7 Hz, 1H), 2.21–2.19 (m, 2H), 2.03–1.88 (m, 2H), 1.78 (s, 3H), 1.74–1.63 (m, 3H), 1.31–1.26 (m, 3H), 1.18 (s, 3H), 0.98 (s, 3H), 0.74 (d, *J* = 6.8 Hz, 3H) ppm; **$^{13}$C NMR (125 MHz, $CDCl_3$):** δ 148.3, 147.3, 140.3, 122.2, 121.7, 117.0, 114.9, 114.1, 81.8, 41.8, 38.4, 34.7, 32.5, 31.7, 28.8, 27.4, 25.3, 24.7, 19.3, 17.9, 16.1 ppm; **HRMS (ESI-TOF):** calcd for $C_{21}H_{29}O_2^+$ $[M+H]^+$ 313.2162, found 313.2157.

### 2.12 Synthesis of 5-epi-aureol B $\Delta^{3,4}$ (43)



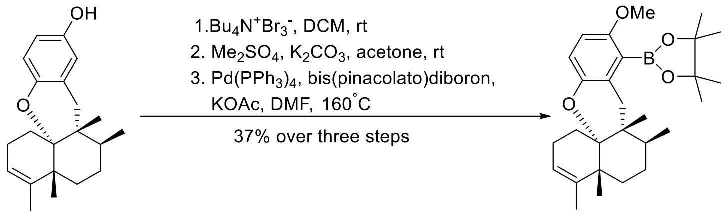
To a solution of **38** (3.8 g, 12.3 mmol, 1.0 eq) in DCM (60 mL) at -80°C was added $FeCl_3$ (3.0 g, 18.5 mmol, 1.5 eq). The mixture was stirred at -80°C for 10 h. After the reaction is complete, The mixture was quenched with $H_2O$ (20 mL) and extracted with DCM (3 × 15 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 30:1) to give 5-epi-aureol B $\Delta^{3,4}$ (**43**) (2.0 g, 6.4 mmol, 52%) as white solid. For data of 5-epi-aureol B $\Delta^{3,4}$, see 2.11.

### 2.13 Synthesis of ester 45



To a solution of **43** (39 mg, 0.13 mmol, 1.0 eq) in DCM (10 mL) at rt was added EDCI (36 mg, 0.19 mmol, 1.5 eq) and HOBt (25 mg, 0.19 mmol, 1.5 eq) and p-nitrobenzoic acid (25 mg, 0.15 mmol, 1.2 eq). The mixture was stirred at rt for 12 h. After the reaction is complete, The mixture was quenched with $H_2O$ (10 mL) and extracted with DCM (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether: EtOAc = 60:1) to give **45** (110.9 mg, 0.355 mmol, 71%) as yellow solid, The structure of ester **45** was determined by X-ray crystallographic analysis.

## 2.14 Synthesis of boron ester 47



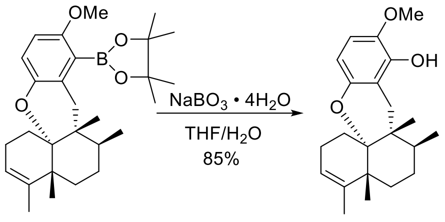
**43**: 5-epi-aureol B $\Delta^{3,4}$

**47**

To a solution of phenol **43** (448 mg, 1.43 mmol, 1.0 eq) in DCM (10 ml) at rt was added $Bu_4N^+Br_3^-$ (68.9 mg, 1.43 mmol, 1.0 eq). The reaction was stirred at rt until the reaction is complete. The mixture was quenched with saturated $H_2O$ (10 mL) and extracted with DCM (3 × 10 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude material was then used directly in the next step without further purification. $K_2CO_3$ (895 mg, 6.53 mmol, 3.5 eq) and $Me_2SO_4$ (0.4ml, 4.68 mmol, 2.5 eq) were added to acetone (10 mL) solution of step 1: oily liquid (368 mg, 0.91 mmol, 1.0 eq) at rt. Stirring at rt, TLC analysis until the reaction is complete. The mixture was quenched with saturated $H_2O$ (10 mL) and extracted with EtOAc (3 × 10 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude material was then used directly in the next step without further purification. bis(pinacolato)diboron (447 mg, 1.76mmol, 1.5 eq) and $Pd(PPh_3)_4$ (135.2 mg, 0.117 mmol, 0.1 eq) and KOAc (689 mg, 7.02 mmol, 6.0 eq) were added to DMF (15 mL) solution of step 2: oily liquid (476 mg, 1.17 mmol, 1 eq) under Ar atmosphere at rt. The resultant mixture was allowed to warm to 160°C and stirred overnight. The mixture was quenched with saturated $H_2O$ (50 mL) and extracted with EtOAc (3 × 20 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 100:1) to give boron ester **47** (171 mg, 0.525 mmol, 37% over three steps) as white solid.

**Characterization of boron ester 47: M.P.:** 44.4-47.3°C; **TLC:** $R_f$ = 0.50 (petrol ether/EtOAc = 8:1); **$^1$H NMR (400 MHz, CDCl$_3$):** δ 6.70 (d, $J$ = 8.8 Hz, 1H), 6.58 (d, $J$ = 8.6 Hz, 1H), 5.25 (s, 1H), 3.70 (s, 3H), 2.67 (d, $J$ = 17.0 Hz, 1H), 2.59 (d, $J$ = 17.9 Hz, 1H), 2.22–1.68 (m, 7H), 1.64 (s, 3H), 1.38 (s, 12H), 1.27–1.26 (m, 2H), 1.16 (s, 3H), 0.93 (s, 3H), 0.78 (d, $J$ = 6.6 Hz, 3H) ppm; **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 156.3, 147.5, 140.1, 125.2, 119.7, 118.5, 110.1, 83.8, 81.9, 56.5, 42.5, 37.4, 35.5, 32.0, 29.7, 27.0, 25.0, 24.7, 23.7, 23.0, 21.1, 19.8, 18.7, 16.2 ppm; **HRMS (ESI-TOF):** calcd for $C_{28}H_{42}BO_4^+$ $[M+H]^+$ 453.3171, found 453.3169.

### 2.15 Synthesis of phenol 48

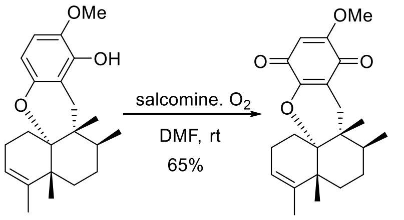


**47** **48**

To a solution of boron ester **47** (100 mg, 0.22 mmol, 1.0 eq) in THF (10 mL) was added water (5 mL) and $NaBO_3.4H_2O$ (102 mg, 0.66 mmol, 3.0 eq). The mixture was stirred at 40°C for 4 hours. After the reaction is complete, add $H_2O$ (20 ml) and extracted with EtOAc (3 × 25 mL). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 500:1) to give phenol **48** (65 mg, 0.19mmol, 85%) as white solid .

**Characterization of phenol 33: M.P.:** 65.4-67.3°C; **TLC:** $R_f$ = 0.30 (petrol ether/EtOAc = 4:1); **$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.65 (d, $J$ = 8.6 Hz, 1H), δ = 6.31 (d, $J$ = 8.9 Hz, 1H), 5.66 (br. s, 1H), 5.26 (s, 1H), 3.82 (s, 3H), 2.77 (d, $J$ = 18.0 Hz, 1H), 2.39 (d, $J$ = 17.9 Hz, 1H), 2.00 (td, $J$ = 12.7,5.4 Hz, 1H), 1.91–1.70 (m, 4H), 1.66 (s, 3H), 1.54–1.38 (m, 4H), 1.19 (s, 3H), 1.01 (s, 3H), 0.82 (d, $J$ = 3.3Hz, 3H) ppm; **$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 148.5, 143.2, 140.2, 139.5, 119.7, 109.6, 109.0, 106.6, 82.3, 56.7, 42.5, 36.9, 32.2, 29.9, 29.7, 27.1, 23.7, 23.1, 21.1, 19.8, 18.7, 16.3 ppm; **HRMS (ESI-TOF):** calcd for $C_{22}H_{31}O_3^+$ $[M+H]^+$ 343.2268, found 343.2261.

### 2.16 Synthesis of dactyloquinone A $\Delta^{3,4}$ (49)

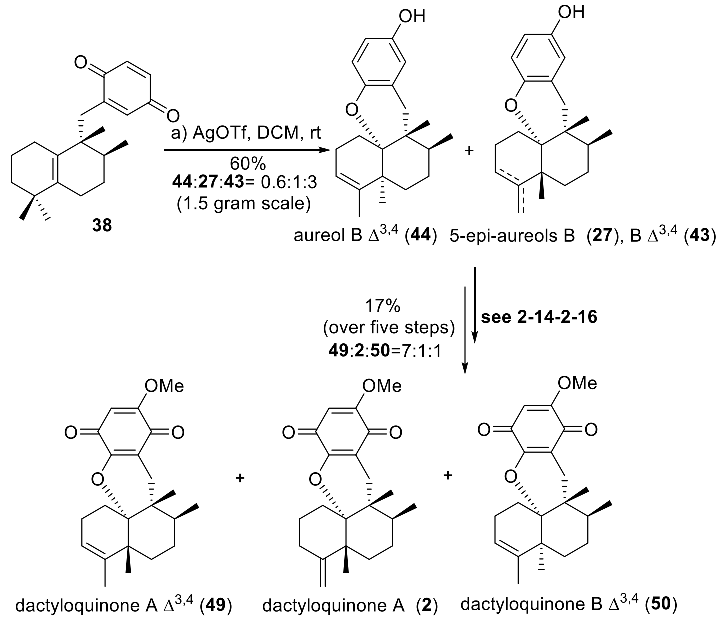


**48** **49:** dactyloquinone A $\Delta^{3,4}$

*N*, *N′*-Bis(salicylidene)ethylenediaminocobalt(II) (28 mg, 0.08 mmol, 0.5 eq) was added to a solution of phenol **48** (50 mg, 0.15 mmol, 1.0 eq) in DMF (10 mL) at rt and oxygen was bubbled through the reaction mixture for 30 min. After 30 min, water (15 mL) was added and the mixture was extracted with EtOAc (3×10 ml). the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, petrol ether : EtOAc = 50:1) to give dactyloquinone A $\Delta^{3,4}$ **49** (36 mg, 0.10mmol, 65%) as pale yellow solid.

**Characterization of dactyloquinone A $\Delta^{3,4}$ (49): M.P.:** 74.2-76.5°C; **TLC:** $R_f$ = 0.33 (petrol ether/EtOAc = 3:1); **$[\alpha]^{22.9}_D$** (c =0.0262 g/100ml, MeOH) : -181; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 5.71 (s, 1H), 5.28 (s, 1H), 3.79 (s, 3H), 2.52 (d, $J$ = 19.1 Hz, 1H), 2.10 (d, $J$ = 19.0 Hz, 1H), 2.00–1.87 (m, 3H), 1.82–1.73 (m, 1H), 1.67 (s, 3H), 1.64–1.61 (m, 1H), 1.46–1.43 (m, 4H), 1.18 (s, 3H), 1.00 (s, 3H), 0.80 (d, *J* = 5.7 Hz, 3H) ppm; **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 181.6, 181.3, 159.4, 153.0, 139.6, 119.3, 114.8, 105.0, 88.4, 56.5, 42.2, 37.4, 32.4, 29.5, 28.7, 26.7, 23.7, 22.9, 21.7, 19.5, 18.6, 16.2 ppm; **HRMS (ESI-TOF):** calcd for $C_{22}H_{29}O_4^+$ [M+H]$^+$ 357.2060, found 357.2057.

### 2.17 Synthesis of dactyloquinone A (2) and dactyloquinone A $\Delta^{3,4}$ (49) and dactyloquinone B $\Delta^{3,4}$ (50)



Synthesis of aureol B $\Delta^{3,4}$ (**14**) and 5-epi-aureol B (**17**) and 5-epi-aureol B $\Delta^{3,4}$ (**18**), for details, see 2.11. The mixture of dactyloquinone A (**2**) and dactyloquinone A $\Delta^{3,4}$ (**49**) and dactyloquinone B $\Delta^{3,4}$ (**50**) was obtained by the same operation and method as dactyloquinone A $\Delta^{3,4}$, the last step crude product was purified by flash column chromatography (silica gel, petrol ether:EtOAc = 30:1) to give a mixture of compounds **2** and **49** and **50** as pale yellow solid (139 mg, 0.39 mmol, 17%, over five steps). Dactyloquinone A (**2**) and dactyloquinone A $\Delta^{3,4}$ (**49**) are still inseparable mixtures after HPLC purification.

**Characterization of dactyloquinone B $\Delta^{3,4}$ (50): M.P.:** 170.0-171.9°C; **TLC:** *R*$_f$ = 0.33 (petrol ether/EtOAc = 3:1); **$[\alpha]^{22.7}_D$** (c =0.0158g/100ml, MeOH) : -81; **$^1$H NMR (400 MHz, CDCl$_3$):** δ 5.73 (s, 1H), 5.28 (s, 1H), 3.81 (s, 3H), 2.61 (d, *J* = 19.0 Hz, 1H), 2.27–2.22 (m, 1H), 2.18 (d, *J* = 19.0 Hz, 1H), 1.99–1.95 (m, 2H), 1.76 (s, 3H), 1.68–1.64 (m, 1H), 1.42–1.29 (m, 5H), 1.26 (s, 3H), 1.02 (s, 3H), 0.75 (d, *J* = 6.7 Hz, 3H) ppm; **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 181.8, 181.4, 159.5, 153.0, 139.8, 122.4, 114.2, 104.8, 87.7, 56.5, 42.0, 38.4, 33.0, 31.8, 28.5, 27.7, 27.4, 25.7, 24.7, 19.2, 17.8, 16.3 ppm; **HRMS (ESI-TOF):** calcd for $C_{22}H_{29}O_4^+$ [M+H]$^+$ 357.2060, found 357.2054.

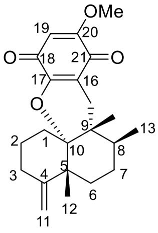
For data of dactyloquinone A $\Delta^{3,4}$**(49)**, see 2.16.

**Characterization of dactyloquinone A (2): TLC:** *R*$_f$ = 0.33 (petrol ether/EtOAc = 3:1); **$^1$H NMR (400 MHz, CDCl$_3$):** δ 5.70 (s, 1H), 4.79 (s, 1H), 4.69 (s, 1H), 3.79 (s overlap, 3H), 2.50 (d, *J* = 19.3 Hz, 1H), 2.03 (d, *J* = 19.1 Hz, 1H), 2.38 ( br t, 13.5Hz, 1H), 2.38 ( br d, 14.0 Hz, 1H), 2.09 (overlap, 1H ), 1.90 (overlap, 1H ), 1.57-1.55 (m, 1H), 1.52-1.51(m, 2H), 1.50-1.49 (m, 2H), 1.44 (overlap, 1H), 1.35-1.33 (m, 1H), 1.26 (s, 3H), 1.01 (s, 3H), 0.80 (d overlap,

$J$ = 5.7 Hz, 3H) ppm; **$^{13}$C NMR (100 MHz, CDCl$_3$):** δ 181.3, 181.0, 159.3, 155.0, 152.3, 115.3, 106.0, 104.9 (overlap), 89.0, 56.4 (overlap), 43.8, 37.3, 32.6, 31.4, 31.0, 28.4, 26.8, 25.0, 24.0, 22.1, 19.1, 16.3 ppm. *Data is for a mixture of dactyloquinone A and dactyloquinone A $\Delta^{3,4}$. Isolation of isomers proved to be difficult. Due to the peak overlap, multiplicity cannot be accurately determined for dactyloquinone A.

## 2.18 Natural Product Spectral Comparisons

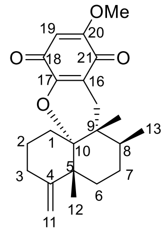
**Table S4**. Comparison of $^1$H NMR spectroscopic data (CDCl$_3$) of natural[6] and synthetic dactyloquinone A.



dactyloquinone A

| | **Natural dactyloquinone A** | **Synthetic dactyloquinone A** | **Deviation** |
|---|---|---|---|
| No. | δ $^1$H [ppm; mult; $J$ (Hz)] | δ $^1$H [ppm; mult; $J$ (Hz)] | (synthetic-natural) |
| | CDCl$_3$, 500 MHz | CDCl$_3$, 400 MHz | Δδ (ppm) |
| 1 | 1.57; m | 1.57-1.55; m | - |
| | 1.90; td; 4.7, 14.0 | 1.90; (overlap) | - |
| 2 | 1.51; m | 1.52-1.51; m | - |
| 3 | 2.22; br d; 13.8 | 2.22; br d; 14.0 | 0 |
| | 2.38; br t; 13.8 | 2.38; br t; 13.5 | 0 |
| 6 | 1.35; m | 1.35-1.33; m | 0 |
| | 2.09; dt; 5.6; 13.0 | 2.09; (overlap) | - |
| 7 | 1.49; m | 1.50-1.49; m | - |
| 8 | 1.44; m | 1.44; (overlap) | - |
| 11 | 4.69; s | 4.69; s | 0 |
| | 4.79; s | 4.79; s | 0 |
| 12 | 1.27; s | 1.26; s | -0.01 |
| 13 | 0.81; d; 6.6 | 0.80; d; 5.7; (overlap) | -0.01 |
| 14 | 1.01; s | 1.01; s | 0 |
| 15 | 2.03; d; 19.1 | 2.03; d; 19.1 | 0 |
| | 2.51; d; 19.1 | 2.50; d; 19.3 | -0.01 |
| 19 | 5.70; s | 5.70; s | 0 |
| 20-OMe | 3.79; s | 3.79; s; (overlap) | 0 |

**Table S5**. Comparison of $^{13}$C NMR spectroscopic data (CDCl$_3$) of natural[6] and synthetic dactyloquinone A.



dactyloquinone A

| | **Natural dactyloquinone A** | **Synthetic dactyloquinone A** | **Deviation** |
|---|---|---|---|
| No. | δ $^{1}$H [ppm; mult; *J* (Hz)] | δ $^{1}$H [ppm; mult; *J* (Hz)] | (synthetic-natural) |
| | CDCl$_3$, 500 MHz | CDCl$_3$, 400 MHz | Δδ (ppm) |
| 1 | 25.0 | 25.0 | 0 |
| 2 | 22.1 | 22.1 | 0 |
| 3 | 31.4 | 31.4 | 0 |
| 4 | 155.0 | 155.0 | 0 |
| 5 | 43.8 | 43.8 | 0 |
| 6 | 31.0 | 31.0 | 0 |
| 7 | 26.8 | 26.8 | 0 |
| 8 | 32.6 | 32.6 | 0 |
| 9 | 37.4 | 37.3 | -0.1 |
| 10 | 89.1 | 89.0 | -0.1 |
| 11 | 106.0 | 106.0 | 0 |
| 12 | 23.9 | 24.0 | 0.01 |
| 13 | 16.2 | 16.3 | 0.01 |
| 14 | 19.1 | 19.1 | 0 |
| 15 | 28.4 | 28.4 | 0 |
| 16 | 115.4 | 115.3 | -0.1 |
| 17 | 152.3 | 152.3 | 0 |
| 18 | 181.0 | 181.0 | 0 |
| 19 | 104.9 | 104.9 | 0 |
| 20 | 159.3 | 159.3 | 0 |
| 21 | 181.3 | 181.3 | 0 |
| 20-OMe | 56.3 | 56.4 | 0.1 |

## 3. References

[1] H. S. Wang, H. J. Li, Z. G. Zhang and Y. C. Wu, Divergent Synthesis of Bioactive Marine Meroterpenoids by Palladium-Catalyzed Tandem Carbene Migratory Insertion, *Eur. J. Org. Chem*., 2018, **7**, 915-925.

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[4] A. R. Martínez, L. Enríquez, M. Jaraíz , L. P. Morales, I. Rodríguez-García and E. D. Ojeda, A Concise Route for the Synthesis of Tetracyclic Meroterpenoids: (±)-Aureol Preparation and Mechanistic Interpretation, *Mar. Drugs*., 2020, **18**, 441.

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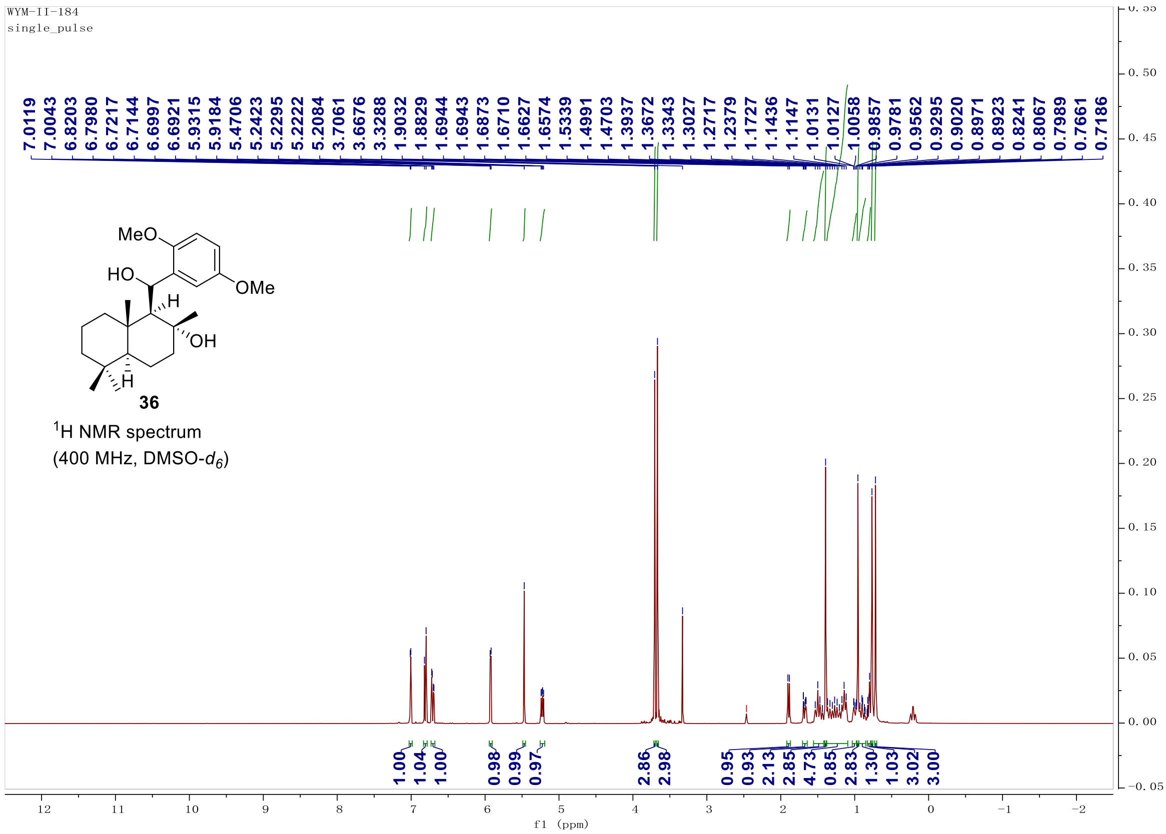
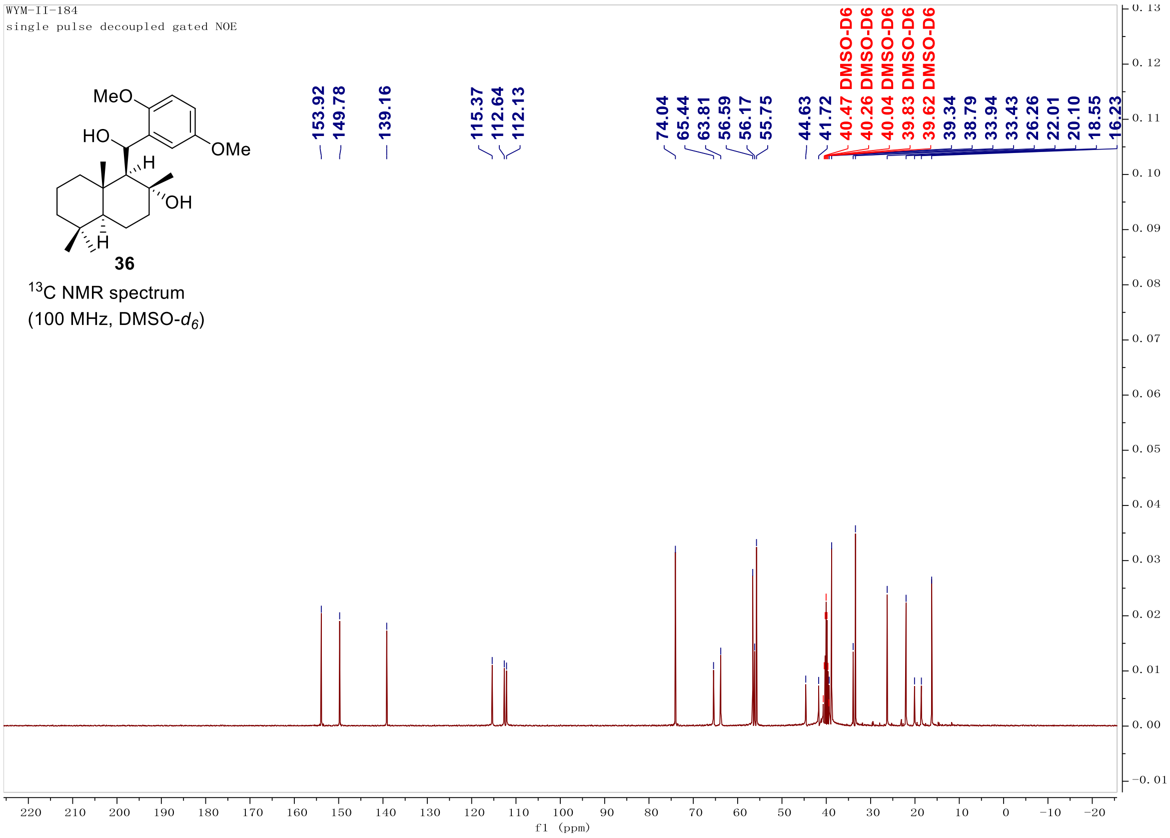
[6] H. Mitome, T. Nagasawa, H. Miyaoka, Y. Yamada and R. W. M. van Soest, Dactyloquinones A and B, New Sesquiterpenoid Quinones from the Okinawan Marine Sponge Dactylospongiaelegans, *J. Nat. Prod.*, 2001. **64**, 1506-1508.

## 4. NMR Spectra



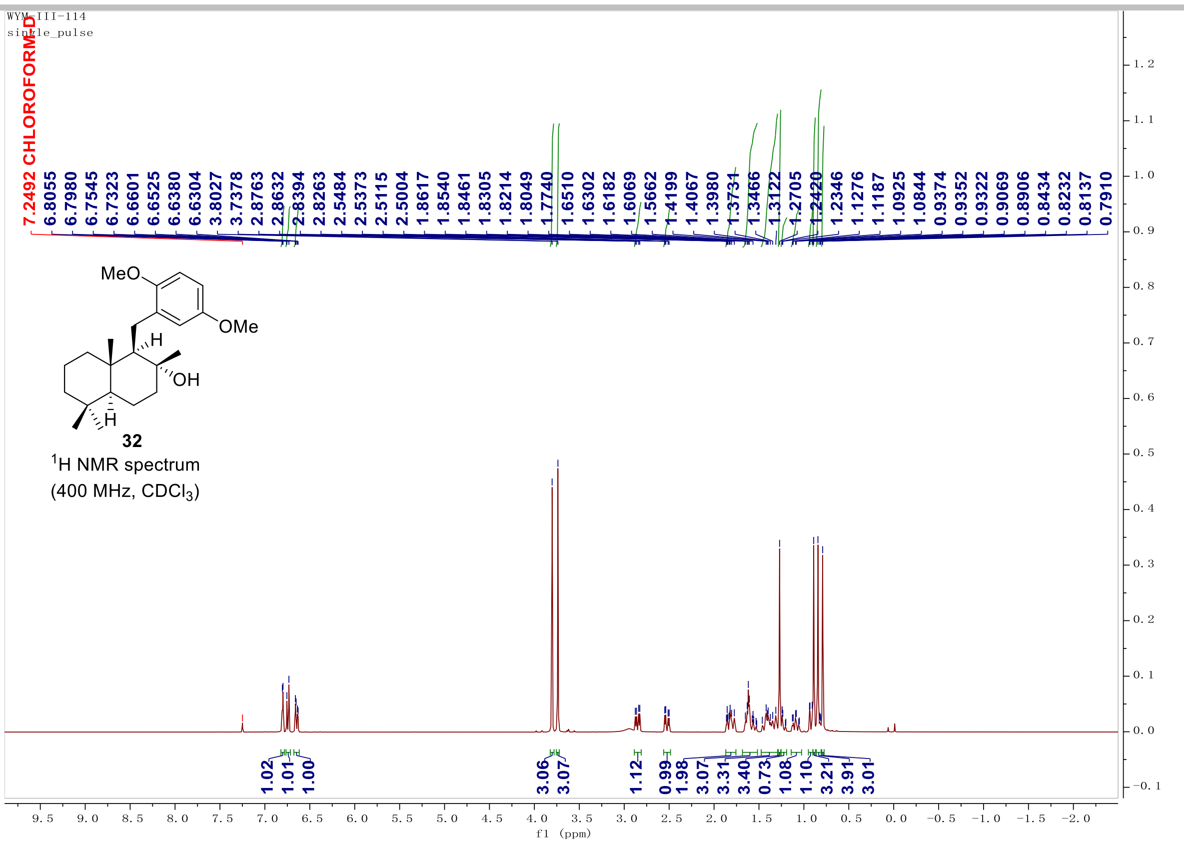
**36**

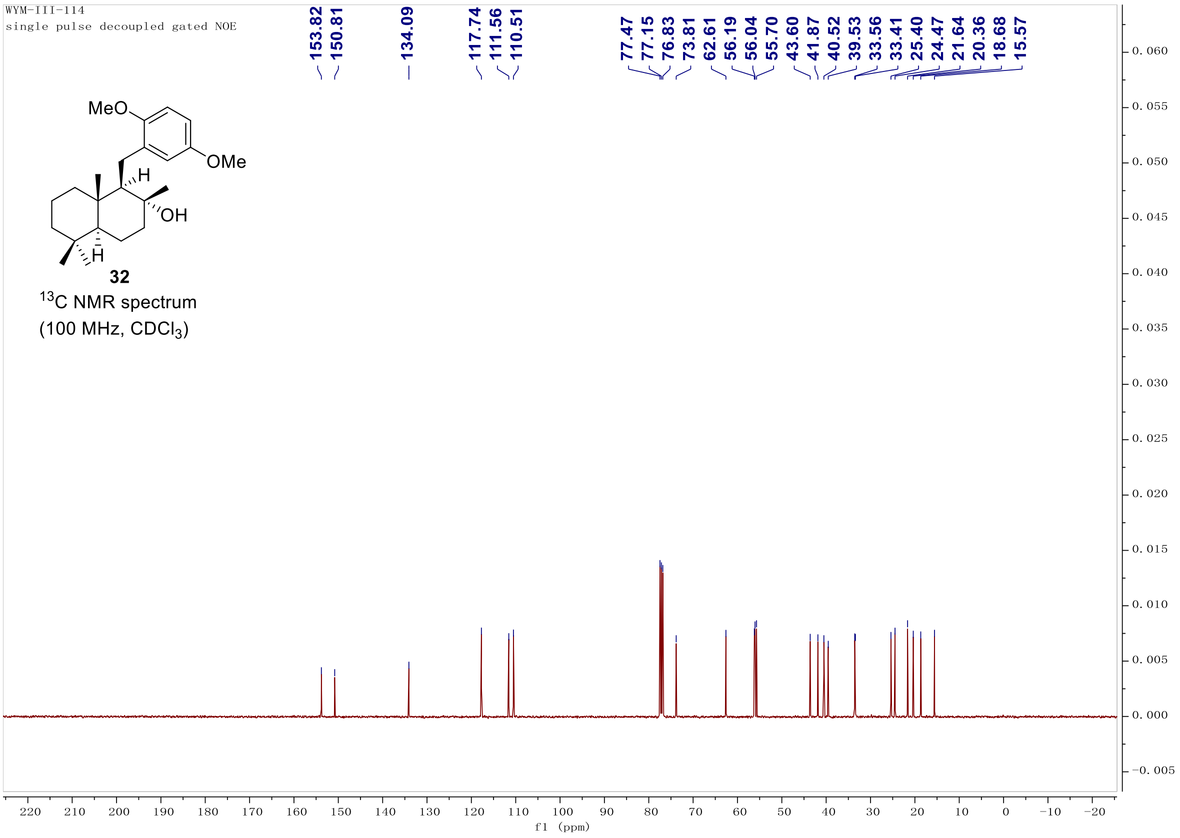
$^1$H NMR spectrum
(400 MHz, DMSO-$d_6$)

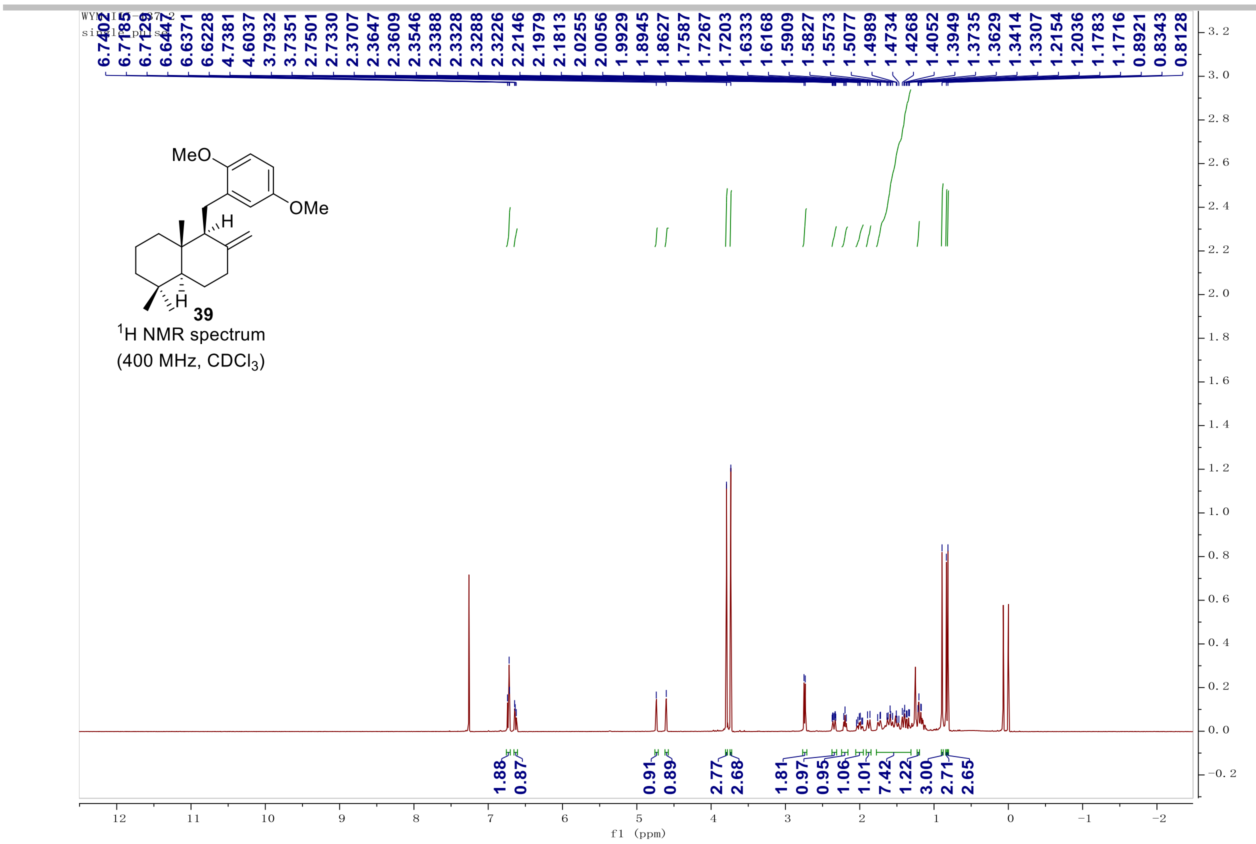


**36**

$^{13}$C NMR spectrum
(100 MHz, DMSO-$d_6$)

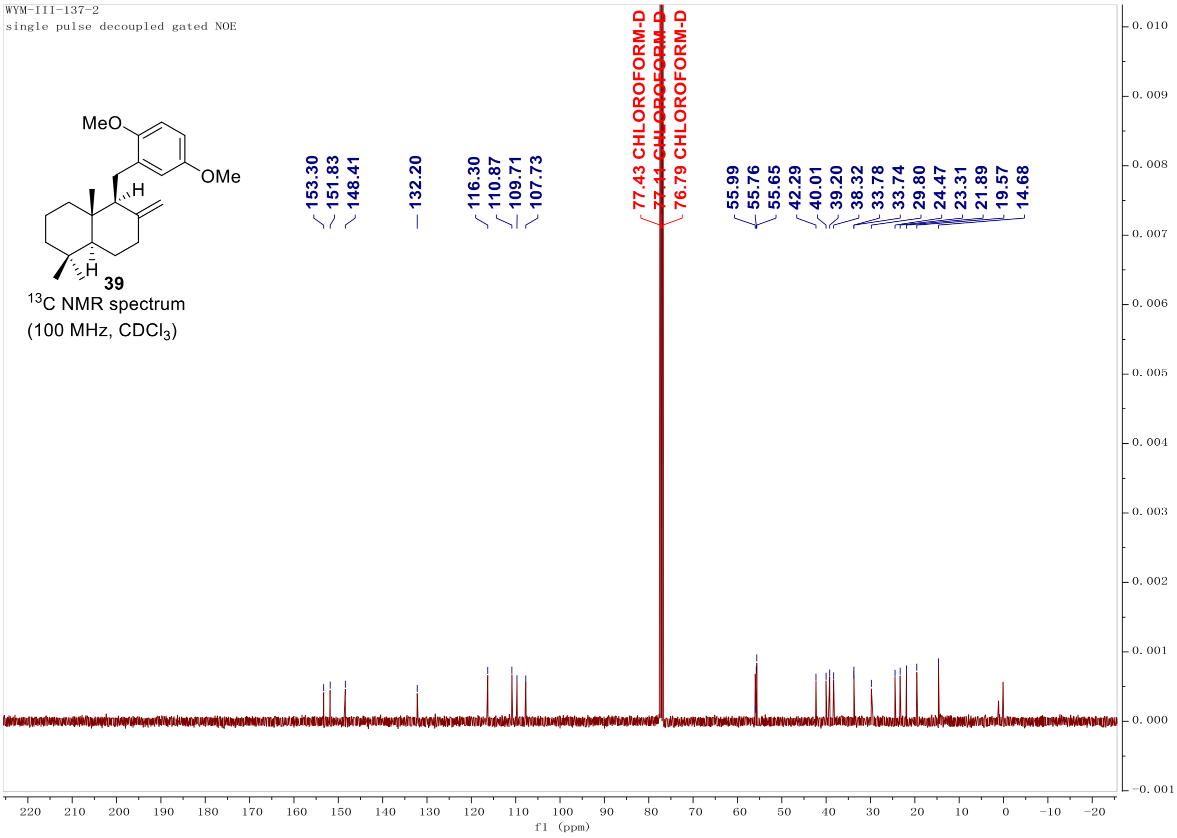

WYM-III-114
single_pulse
7.2492 CHLOROFORM-D
6.8055
6.7980
6.7545
6.7323
6.6601
6.6525
6.6380
6.6304
3.8027
3.7378
2.8763
2.8632
2.8394
2.8263
2.5484
2.5373
2.5115
2.5004
1.8617
1.8540
1.8461
1.8305
1.8214
1.8049
1.7740
1.6510
1.6302
1.6182
1.6069
1.5662
1.4199
1.4067
1.3980
1.3731
1.3466
1.3122
1.2705
1.2420
1.2346
1.1276
1.1187
1.0925
1.0844
0.9374
0.9352
0.9322
0.9069
0.8906
0.8434
0.8232
0.8137
0.7910
MeO
OMe
H
OH
H
32
$^1$H NMR spectrum
(400 MHz, $CDCl_3$)
1.02
1.01
1.00
3.06
3.07
1.12
0.99
1.98
3.07
3.31
3.40
0.73
1.08
1.10
3.21
3.91
3.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
−1.5
−2.0
f1 (ppm)
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
−0.1


WYM-III-114
single pulse decoupled gated NOE
153.82
150.81
134.09
117.74
111.56
110.51
77.47
77.15
76.83
73.81
62.61
56.19
56.04
55.70
43.60
41.87
40.52
39.53
33.56
33.41
25.40
24.47
21.64
20.36
18.68
15.57
MeO
OMe
H
OH
H
32
$^{13}$C NMR spectrum
(100 MHz, $CDCl_3$)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
f1 (ppm)
0.060
0.055
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
−0.005



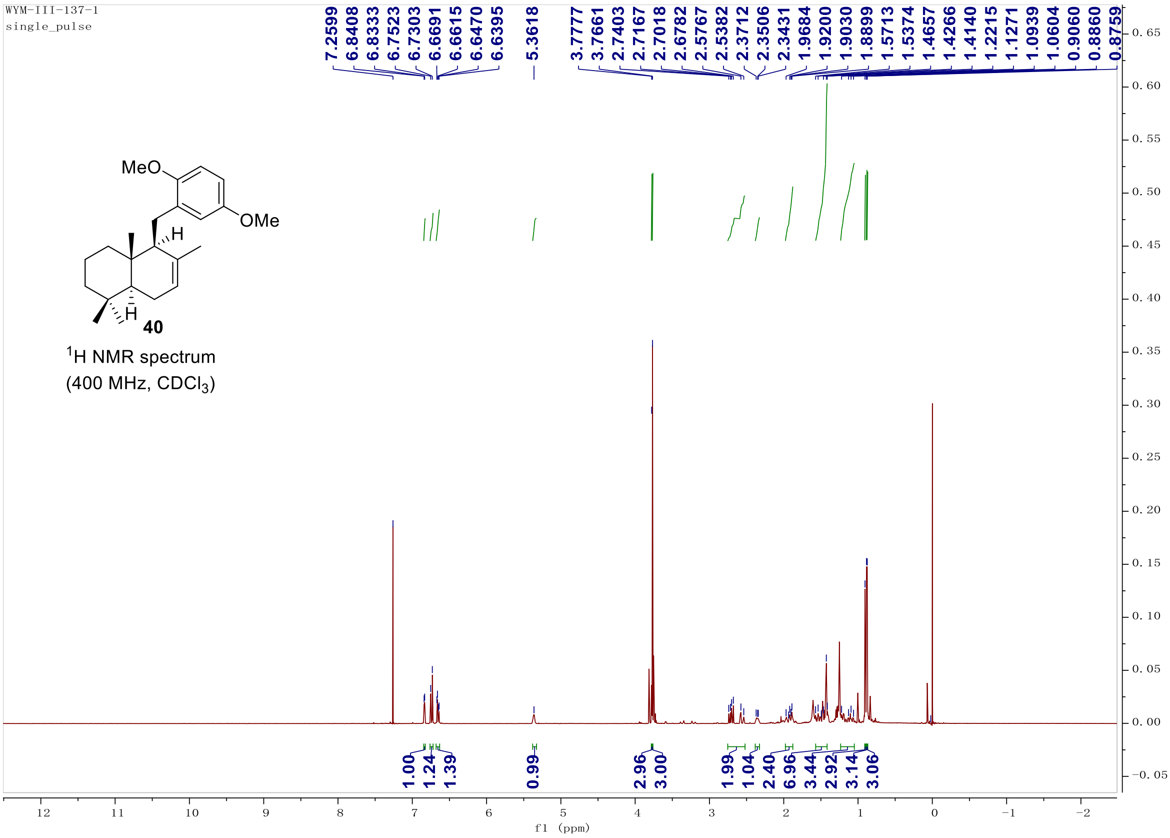
**39**

$^1$H NMR spectrum
(400 MHz, $CDCl_3$)

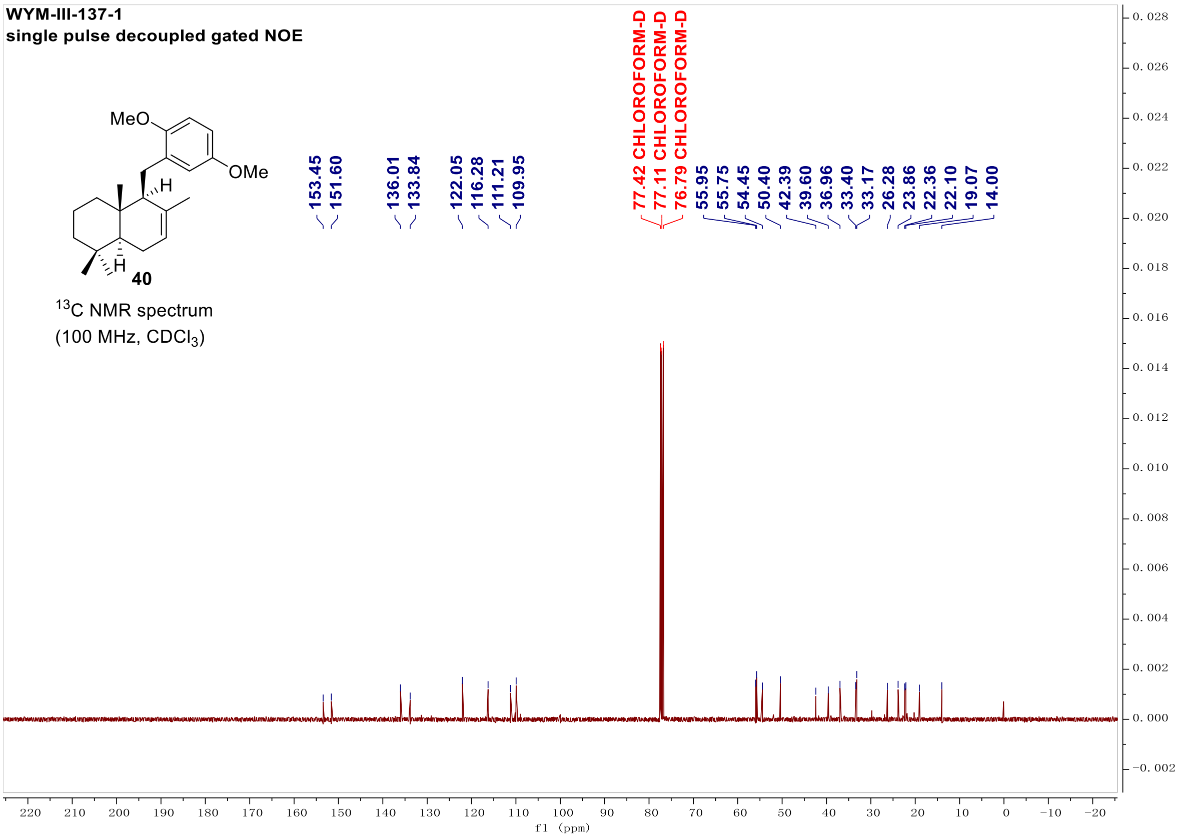


**39**

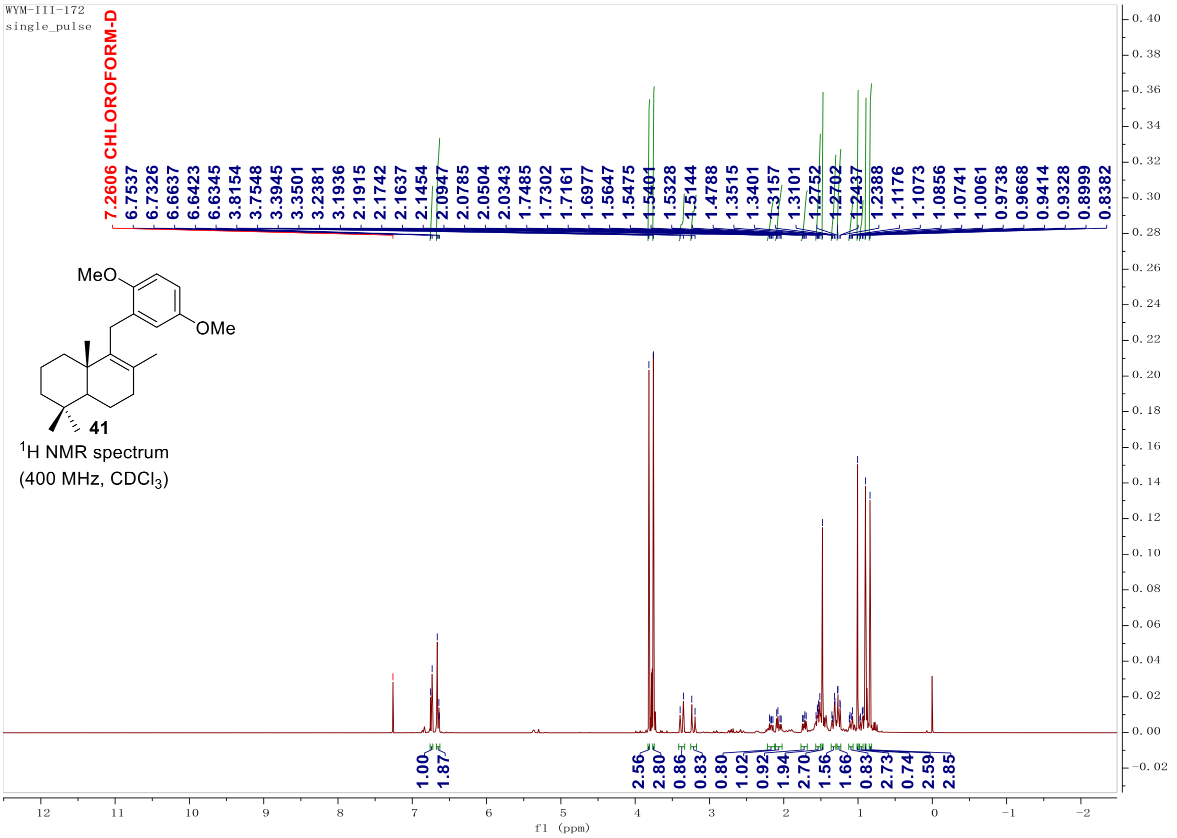
$^{13}$C NMR spectrum
(100 MHz, $CDCl_3$)



$^1$H NMR spectrum (400 MHz, CDCl$_3$)

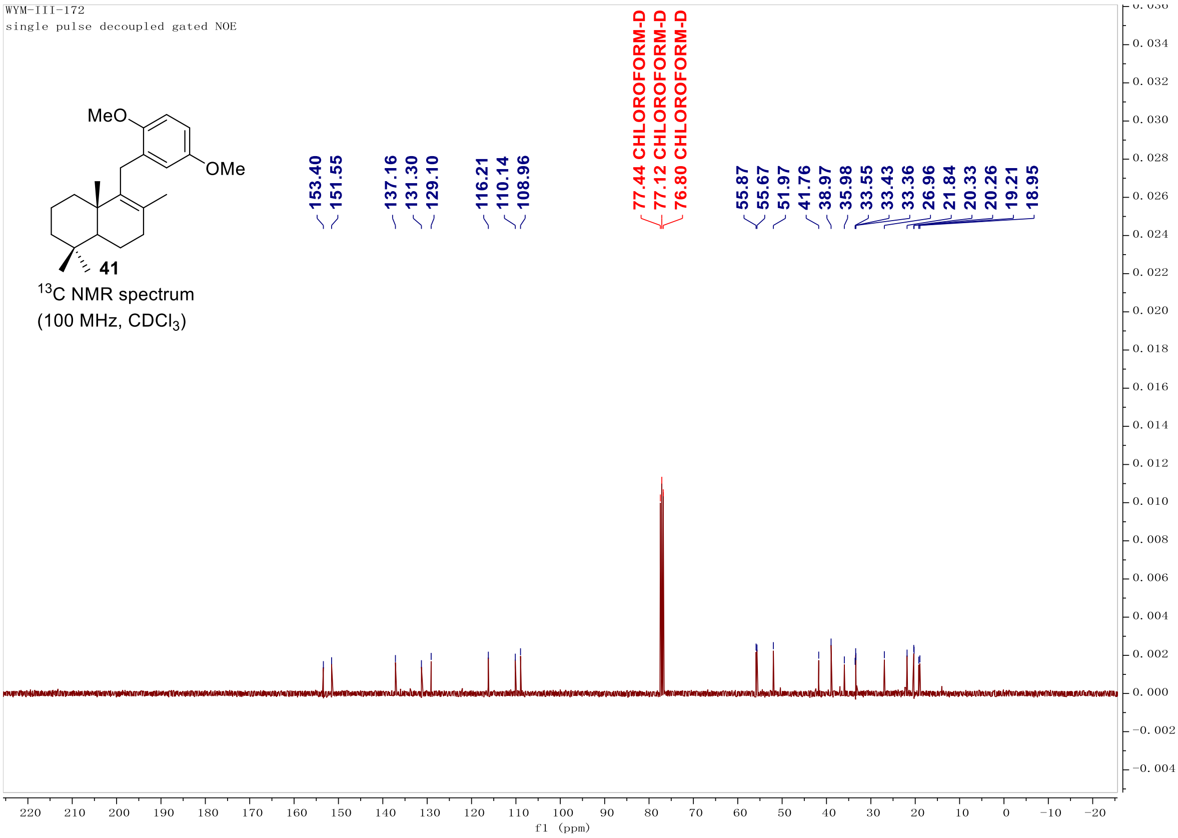


$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)



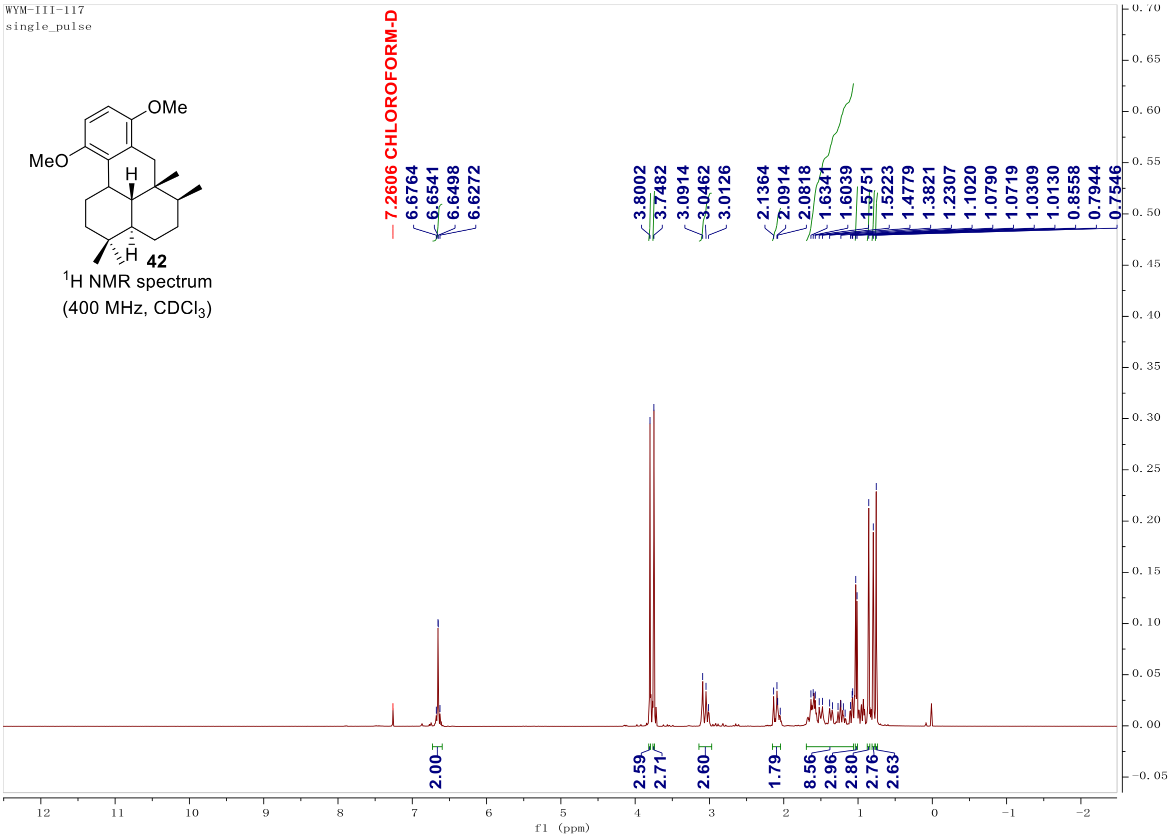
**41**

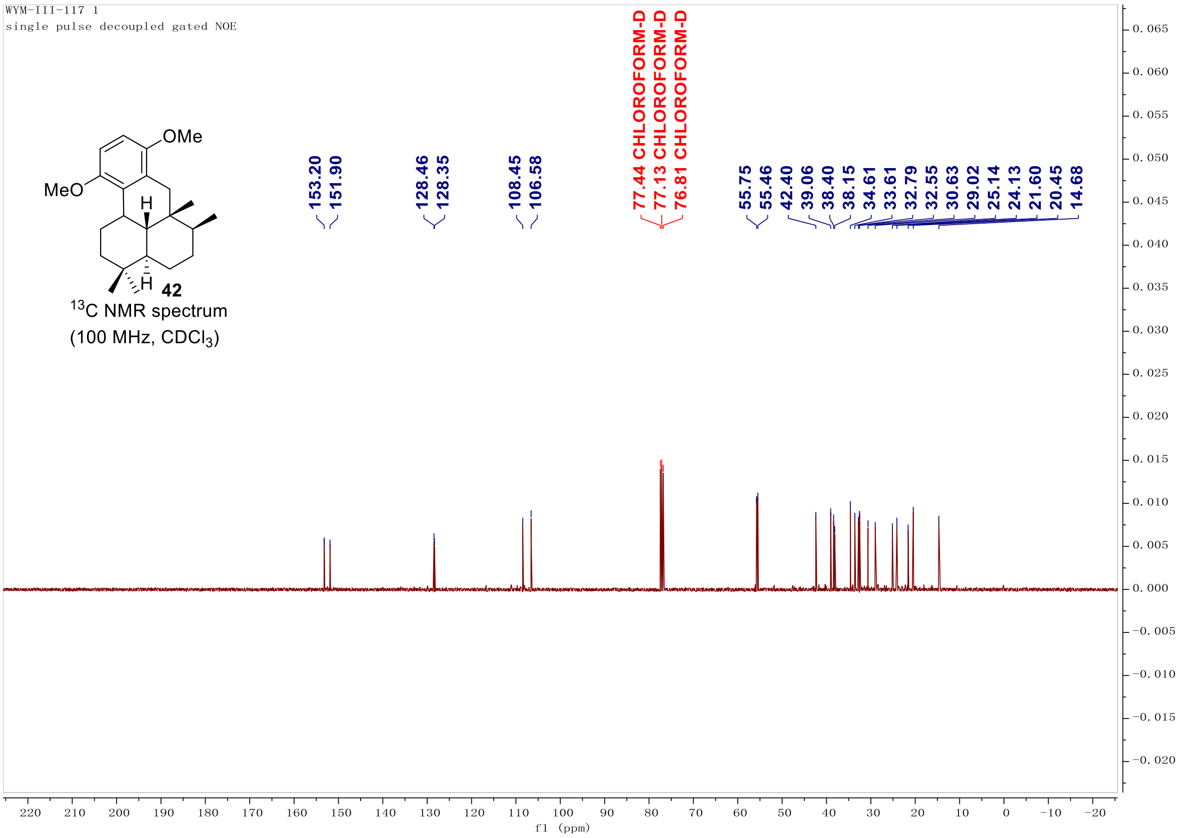
$^1$H NMR spectrum
(400 MHz, $CDCl_3$)

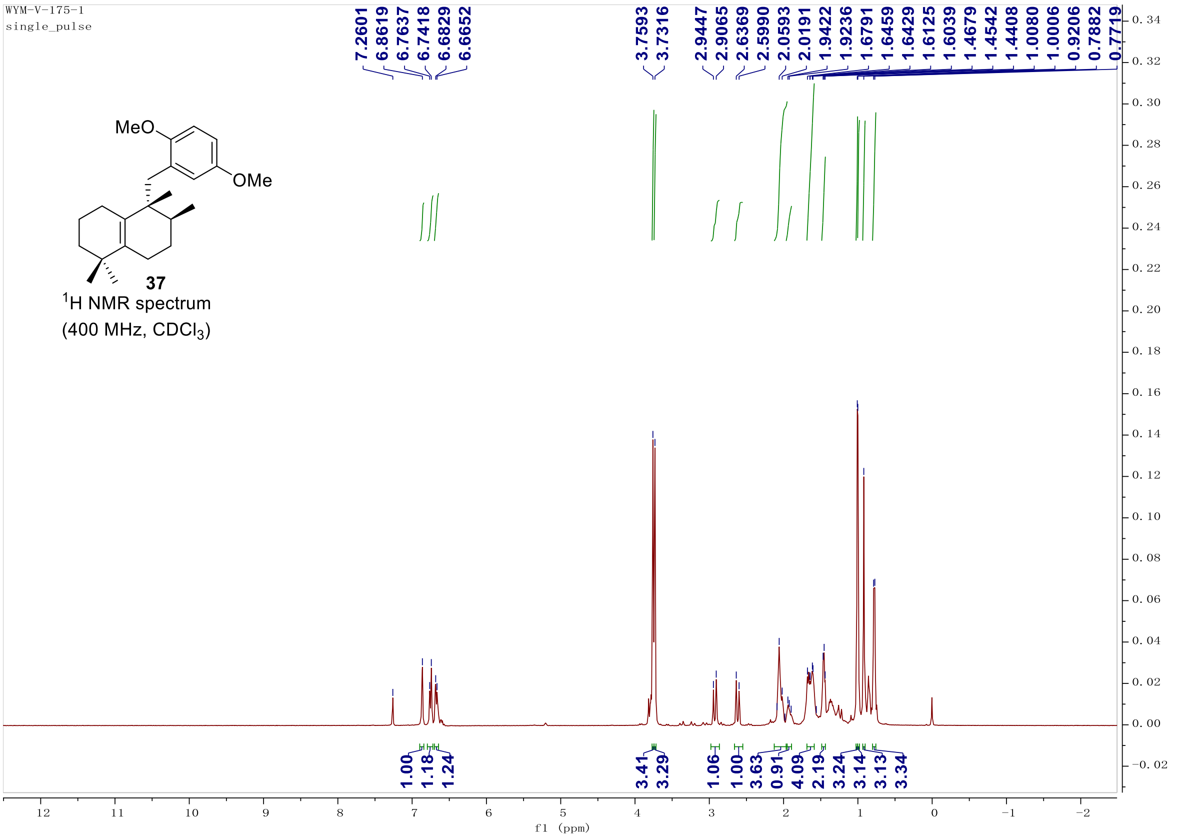


**41**

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


WYM-III-117
single_pulse
OMe
MeO
H
H
42
$^{1}$H NMR spectrum
(400 MHz, $CDCl_3$)
7.2606 CHLOROFORM-D
6.6764
6.6541
6.6498
6.6272
3.8002
3.7482
3.0914
3.0462
3.0126
2.1364
2.0914
2.0818
1.6341
1.6039
1.5751
1.5223
1.4779
1.3821
1.2307
1.1020
1.0790
1.0719
1.0309
1.0130
0.8558
0.7944
0.7546
2.00
2.59
2.71
2.60
1.79
8.56
2.96
2.80
2.76
2.63
12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2
f1 (ppm)
0.70 0.65 0.60 0.55 0.50 0.45 0.40 0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00 −0.05

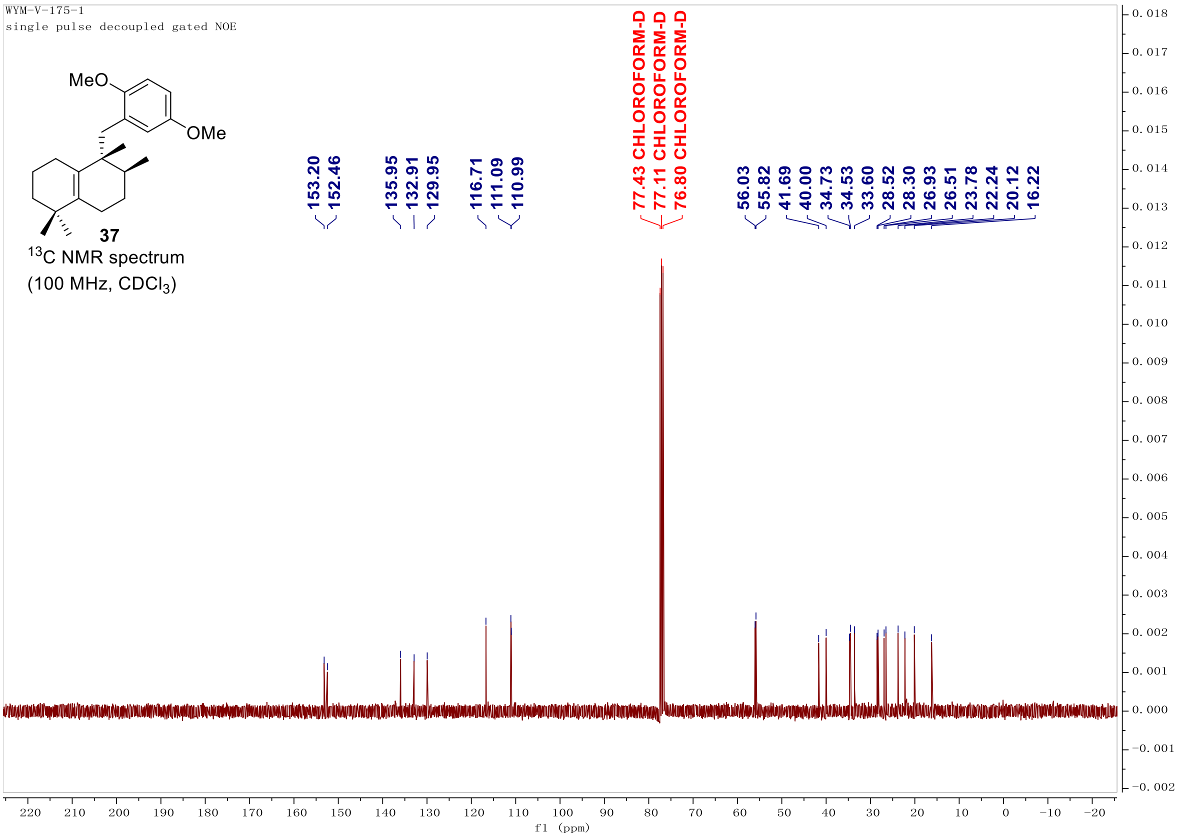

WYM-III-117 1
single pulse decoupled gated NOE
OMe
MeO
H
H
42
$^{13}$C NMR spectrum
(100 MHz, $CDCl_3$)
153.20
151.90
128.46
128.35
108.45
106.58
77.44 CHLOROFORM-D
77.13 CHLOROFORM-D
76.81 CHLOROFORM-D
55.75
55.46
42.40
39.06
38.40
38.15
34.61
33.61
32.79
32.55
30.63
29.02
25.14
24.13
21.60
20.45
14.68
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
f1 (ppm)
0.065 0.060 0.055 0.050 0.045 0.040 0.035 0.030 0.025 0.020 0.015 0.010 0.005 0.000 −0.005 −0.010 −0.015 −0.020



**37**

$^1$H NMR spectrum

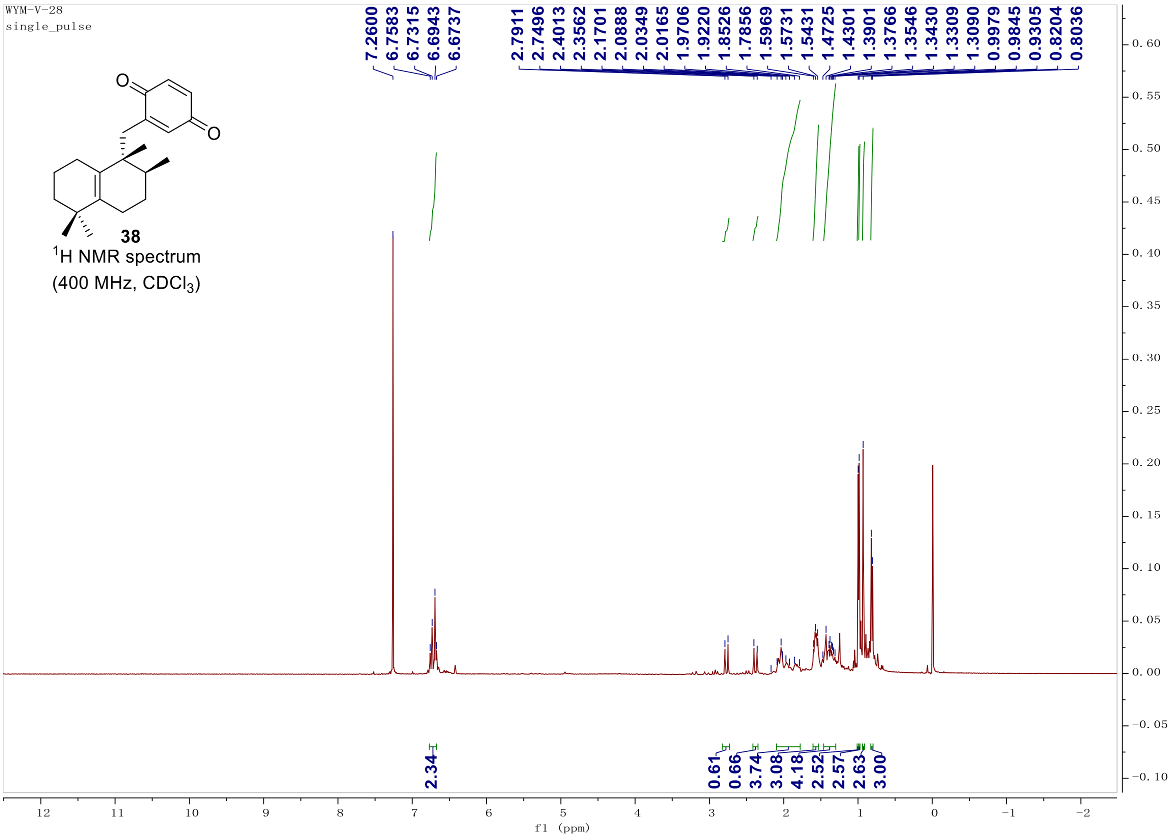
(400 MHz, $CDCl_3$)

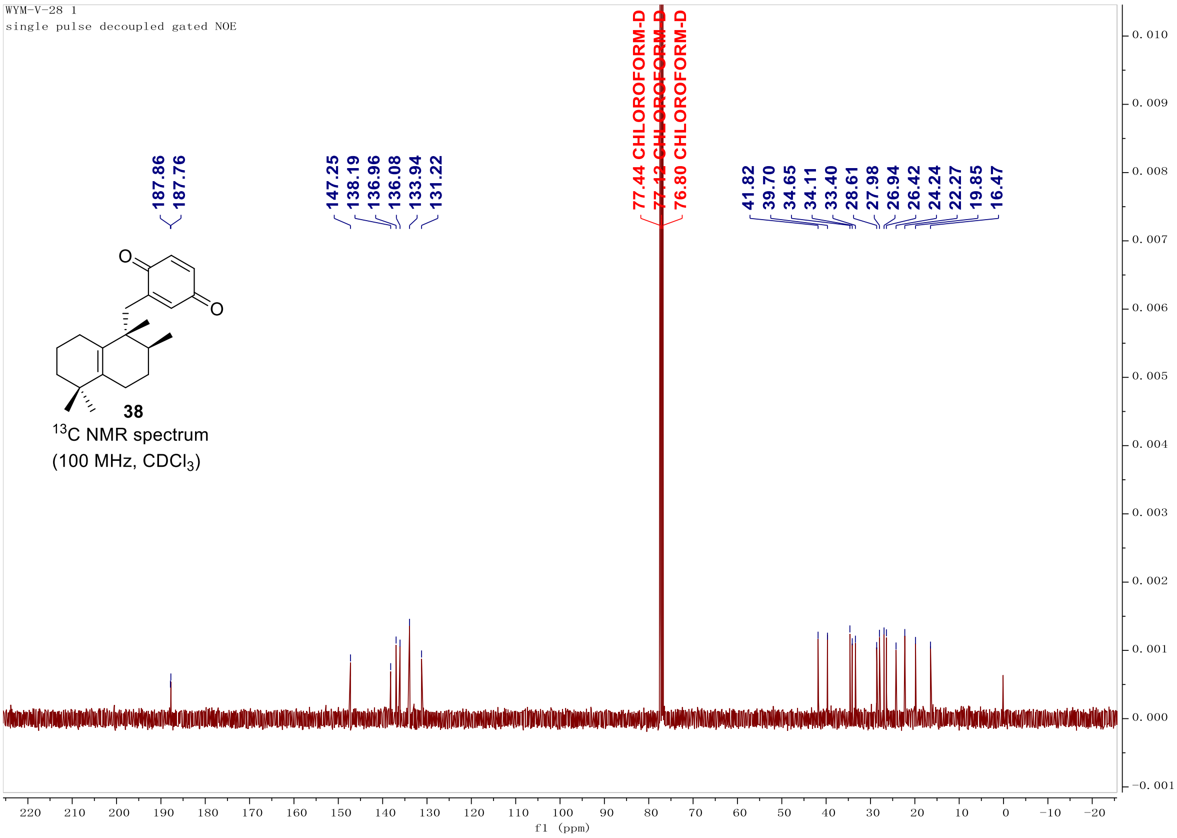


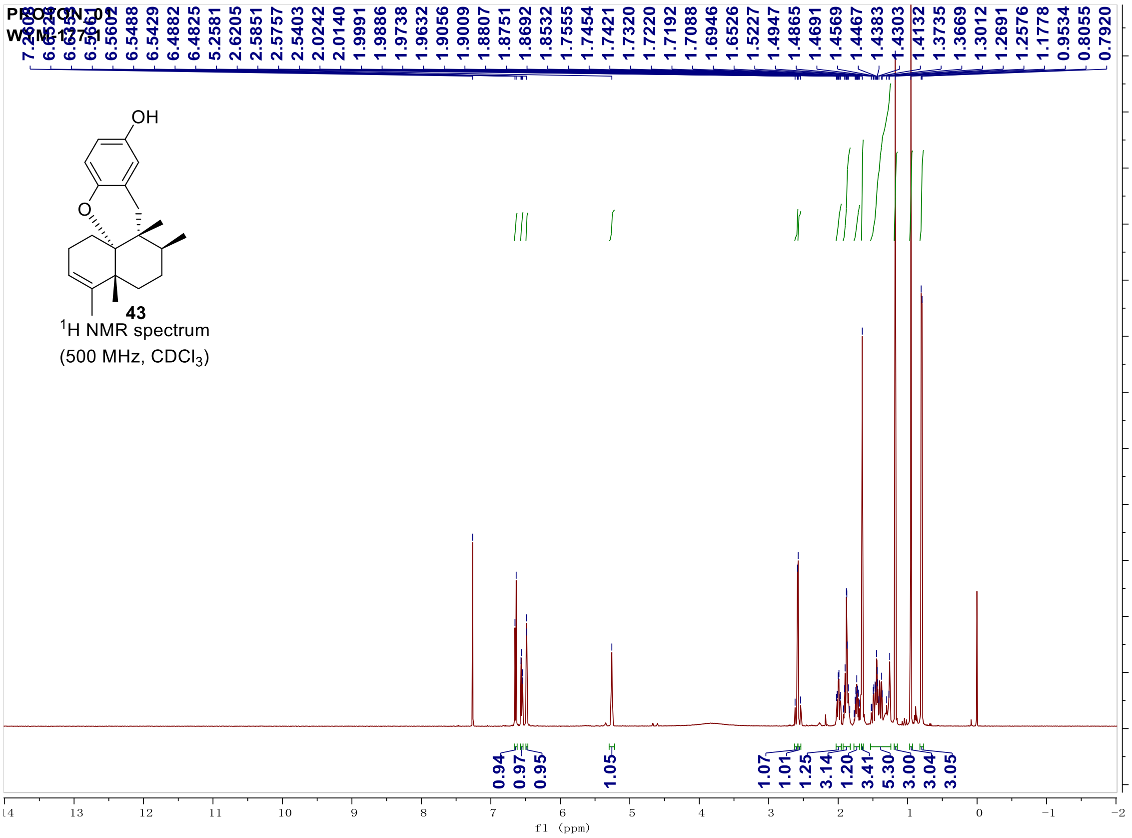
**37**

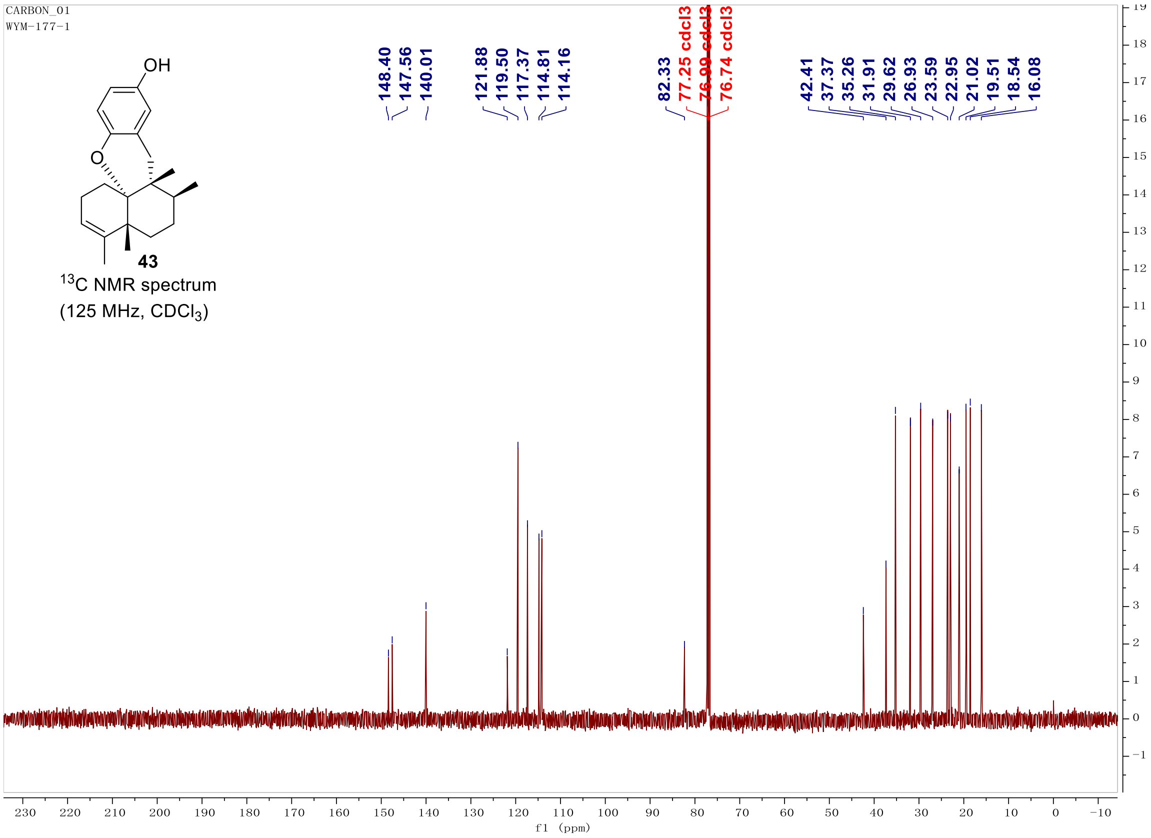
$^{13}$C NMR spectrum

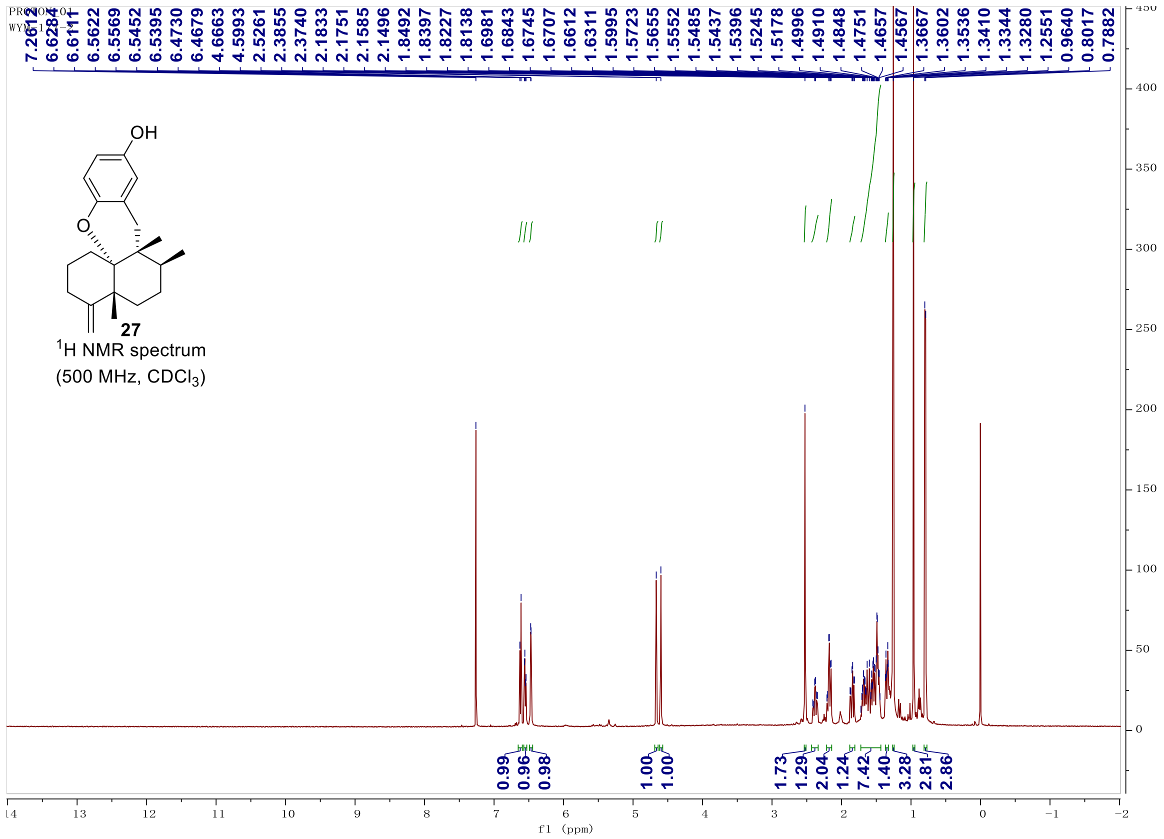
(100 MHz, $CDCl_3$)

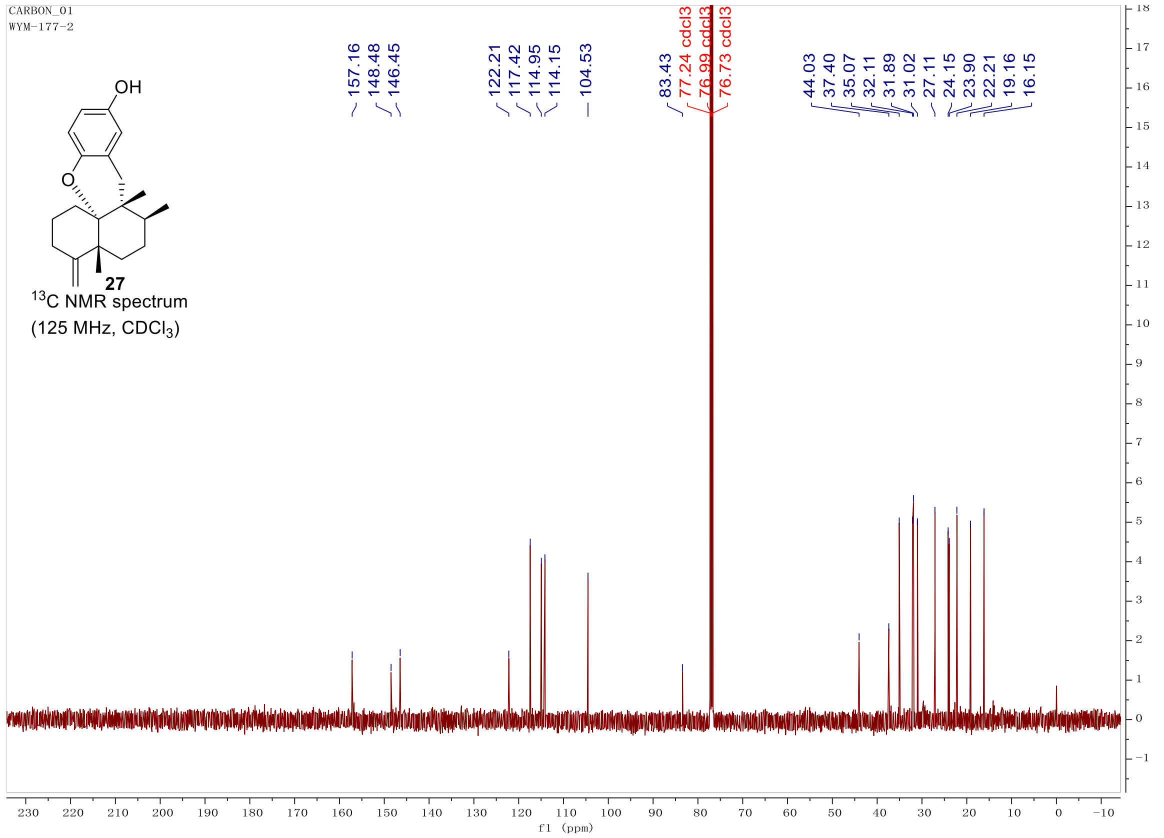

WYM-V-28
single_pulse
38
$^1$H NMR spectrum
(400 MHz, CDCl$_3$)
7.2600
6.7583
6.7315
6.6943
6.6737
2.7911
2.7496
2.4013
2.3562
2.1701
2.0888
2.0349
2.0165
1.9706
1.9220
1.8526
1.7856
1.5969
1.5731
1.5431
1.4725
1.4301
1.3901
1.3766
1.3546
1.3430
1.3309
1.3090
0.9979
0.9845
0.9305
0.8204
0.8036
2.34
0.61
0.66
3.74
3.08
4.18
2.52
2.57
2.63
3.00
f1 (ppm)

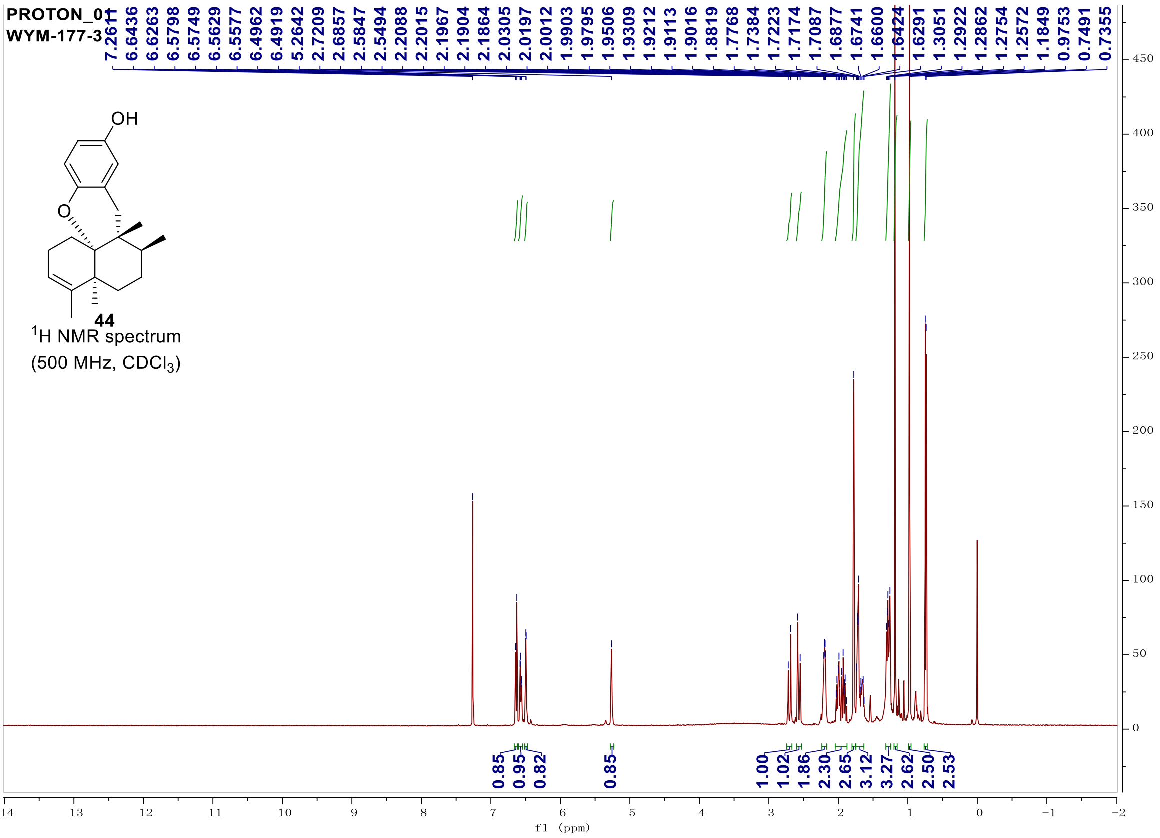

WYM-V-28 1
single pulse decoupled gated NOE
38
$^{13}$C NMR spectrum
(100 MHz, CDCl$_3$)
187.86
187.76
147.25
138.19
136.96
136.08
133.94
131.22
77.44 CHLOROFORM-D
77.12 CHLOROFORM-D
76.80 CHLOROFORM-D
41.82
39.70
34.65
34.11
33.40
28.61
27.98
26.94
26.42
24.24
22.27
19.85
16.47
f1 (ppm)

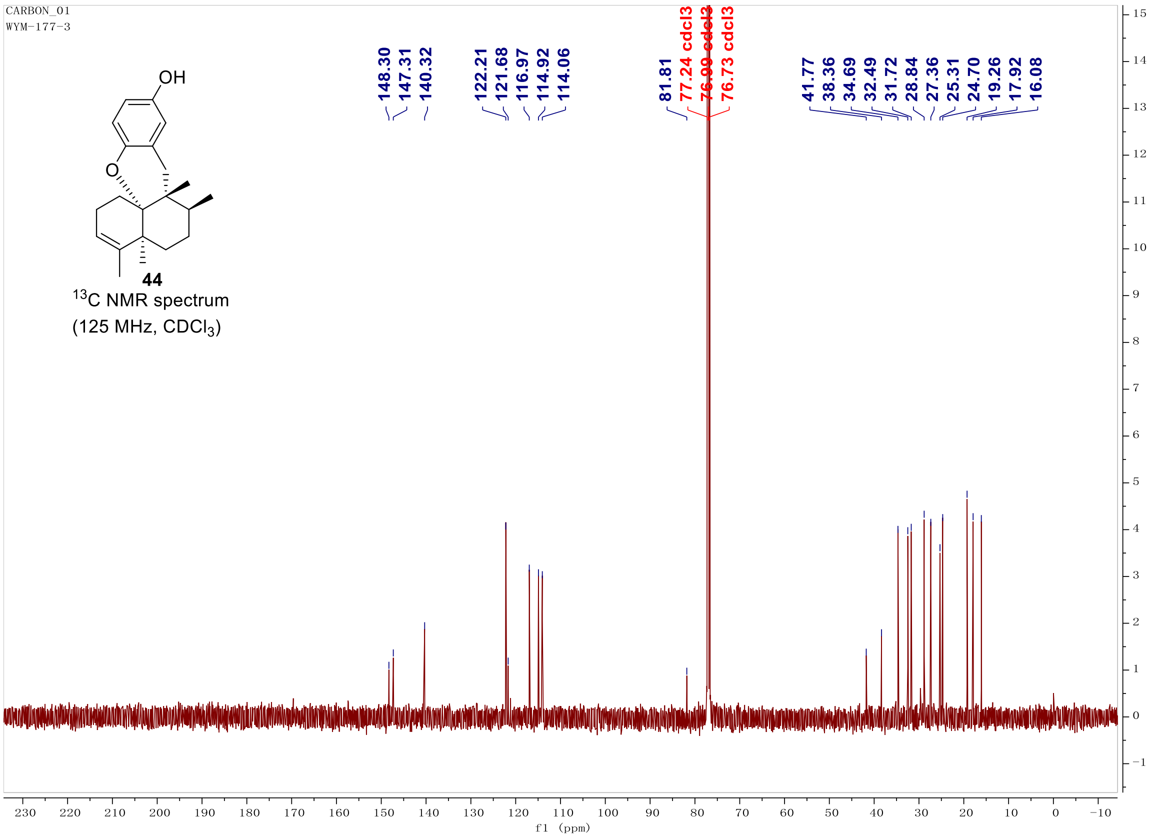

PROTON_01
WYM-177-1
7.2608
6.6524
6.6353
6.5661
6.5602
6.5488
6.5429
6.4882
6.4825
5.2581
2.6205
2.5851
2.5757
2.5403
2.0242
2.0140
1.9991
1.9886
1.9738
1.9632
1.9056
1.9009
1.8807
1.8751
1.8692
1.8532
1.7555
1.7454
1.7421
1.7320
1.7220
1.7192
1.7088
1.6946
1.6526
1.5227
1.4947
1.4865
1.4691
1.4569
1.4467
1.4383
1.4303
1.4132
1.3735
1.3669
1.3012
1.2691
1.2576
1.1778
0.9534
0.8055
0.7920
OH
O
43
$^1$H NMR spectrum
(500 MHz, CDCl$_3$)
0.94
0.97
0.95
1.05
1.07
1.01
1.25
3.14
1.20
3.41
5.30
3.00
3.04
3.05
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)
600
550
500
450
400
350
300
250
200
150
100
50
0
−50

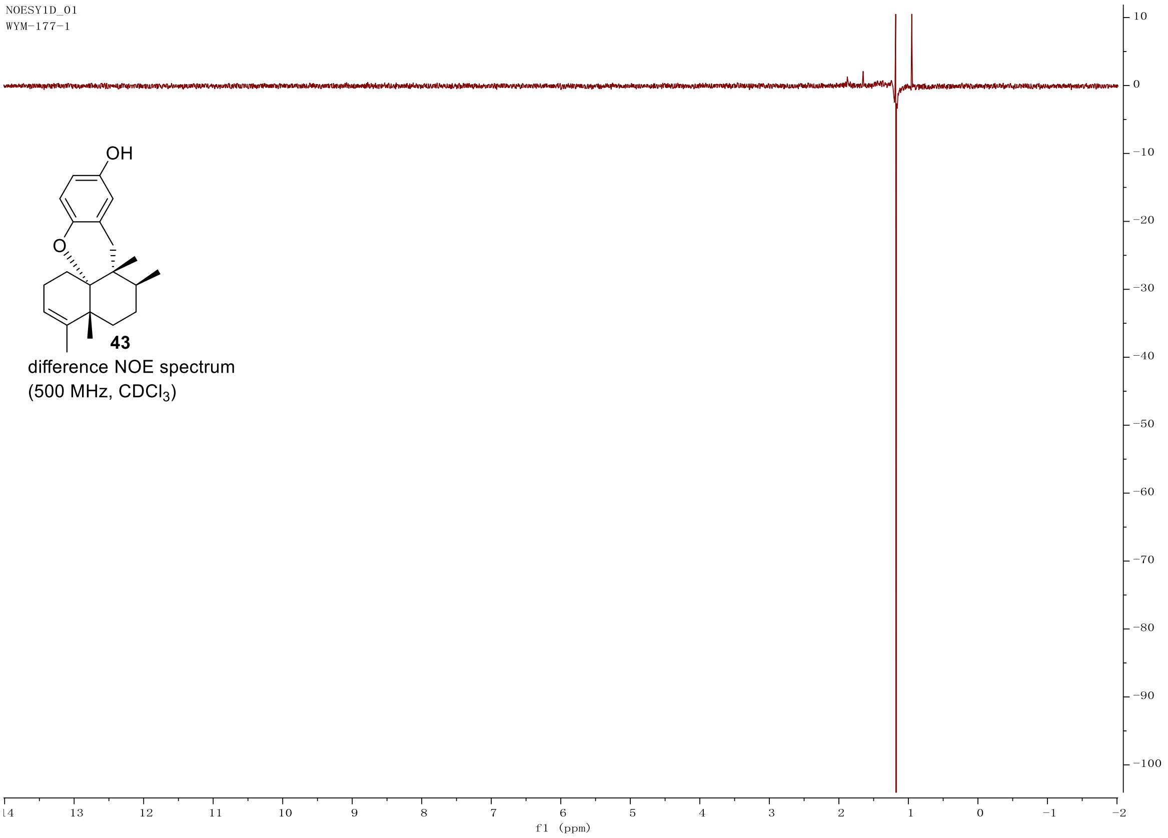

CARBON_01
WYM-177-1
OH
O
43
$^{13}$C NMR spectrum
(125 MHz, CDCl$_3$)
148.40
147.56
140.01
121.88
119.50
117.37
114.81
114.16
82.33
77.25 cdcl3
76.99 cdcl3
76.74 cdcl3
42.41
37.37
35.26
31.91
29.62
26.93
23.59
22.95
21.02
19.51
18.54
16.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1


PROTON_01
WYM-177-2
7.2612
6.6284
6.6111
6.5622
6.5569
6.5452
6.5395
6.4730
6.4679
4.6663
4.5993
2.5261
2.3855
2.3740
2.1833
2.1751
2.1585
2.1496
1.8492
1.8397
1.8227
1.8138
1.6981
1.6843
1.6745
1.6707
1.6612
1.6311
1.5995
1.5723
1.5655
1.5552
1.5485
1.5437
1.5396
1.5245
1.5178
1.4996
1.4910
1.4848
1.4751
1.4657
1.4567
1.3667
1.3602
1.3536
1.3410
1.3344
1.3280
1.2551
0.9640
0.8017
0.7882
OH
O
27
$^1$H NMR spectrum
(500 MHz, $CDCl_3$)
0.99
0.96
0.98
1.00
1.00
1.73
1.29
2.04
1.24
7.42
1.40
3.28
2.81
2.86
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
450
400
350
300
250
200
150
100
50
0


CARBON_01
WYM-177-2
157.16
148.48
146.45
122.21
117.42
114.95
114.15
104.53
83.43
77.24 cdcl3
76.99 cdcl3
76.73 cdcl3
44.03
37.40
35.07
32.11
31.89
31.02
27.11
24.15
23.90
22.21
19.16
16.15
OH
O
27
$^{13}$C NMR spectrum
(125 MHz, $CDCl_3$)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

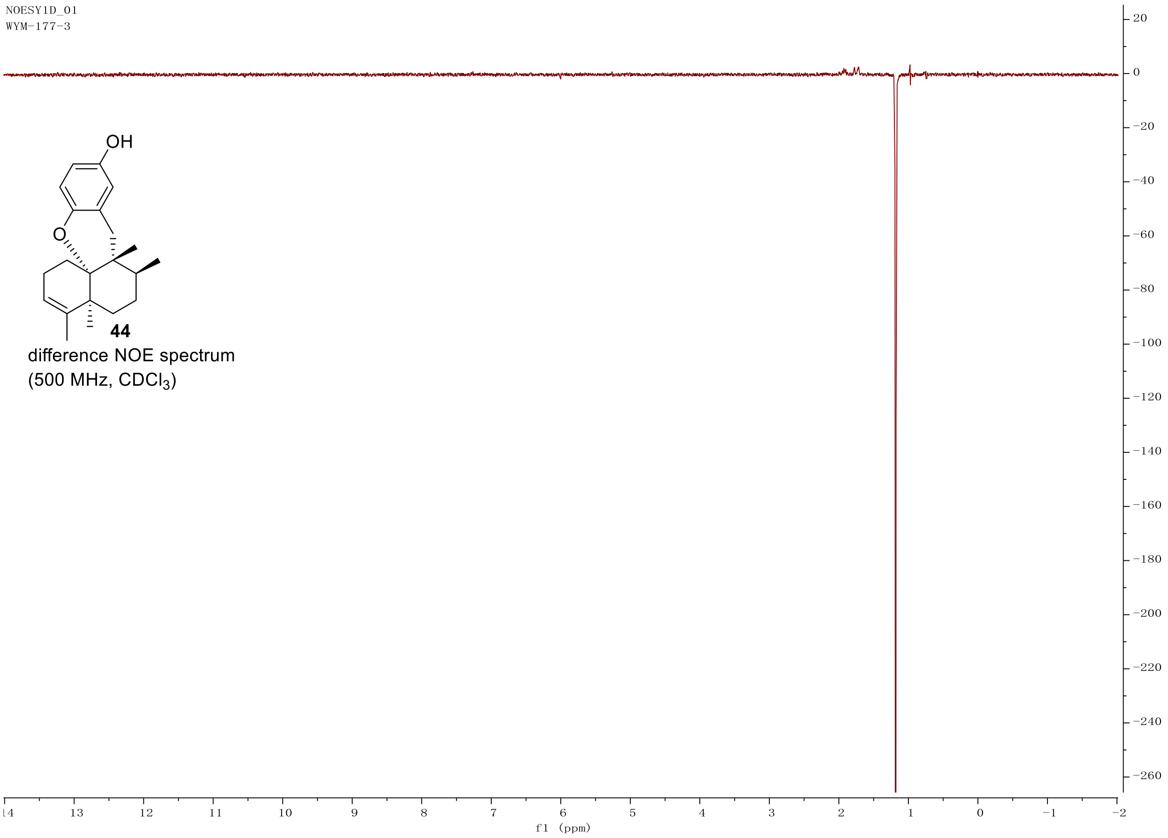

PROTON_01
WYM-177-3
7.2611
6.6436
6.6263
6.5798
6.5749
6.5629
6.5577
6.4962
6.4919
5.2642
2.7209
2.6857
2.5847
2.5494
2.2088
2.2015
2.1967
2.1904
2.1864
2.0305
2.0197
2.0012
1.9903
1.9795
1.9506
1.9309
1.9212
1.9113
1.9016
1.8819
1.7768
1.7384
1.7223
1.7174
1.7087
1.6877
1.6741
1.6600
1.6424
1.6291
1.3051
1.2922
1.2862
1.2754
1.2572
1.1849
0.9753
0.7491
0.7355
OH
O
44
$^1$H NMR spectrum
(500 MHz, $CDCl_3$)
0.85
0.95
0.82
0.85
1.00
1.02
1.86
2.30
2.65
3.12
3.27
2.62
2.50
2.53
450
400
350
300
250
200
150
100
50
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)


CARBON_01
WYM-177-3
148.30
147.31
140.32
122.21
121.68
116.97
114.92
114.06
81.81
77.24 cdcl3
76.99 cdcl3
76.73 cdcl3
41.77
38.36
34.69
32.49
31.72
28.84
27.36
25.31
24.70
19.26
17.92
16.08
OH
O
44
$^{13}$C NMR spectrum
(125 MHz, $CDCl_3$)
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)



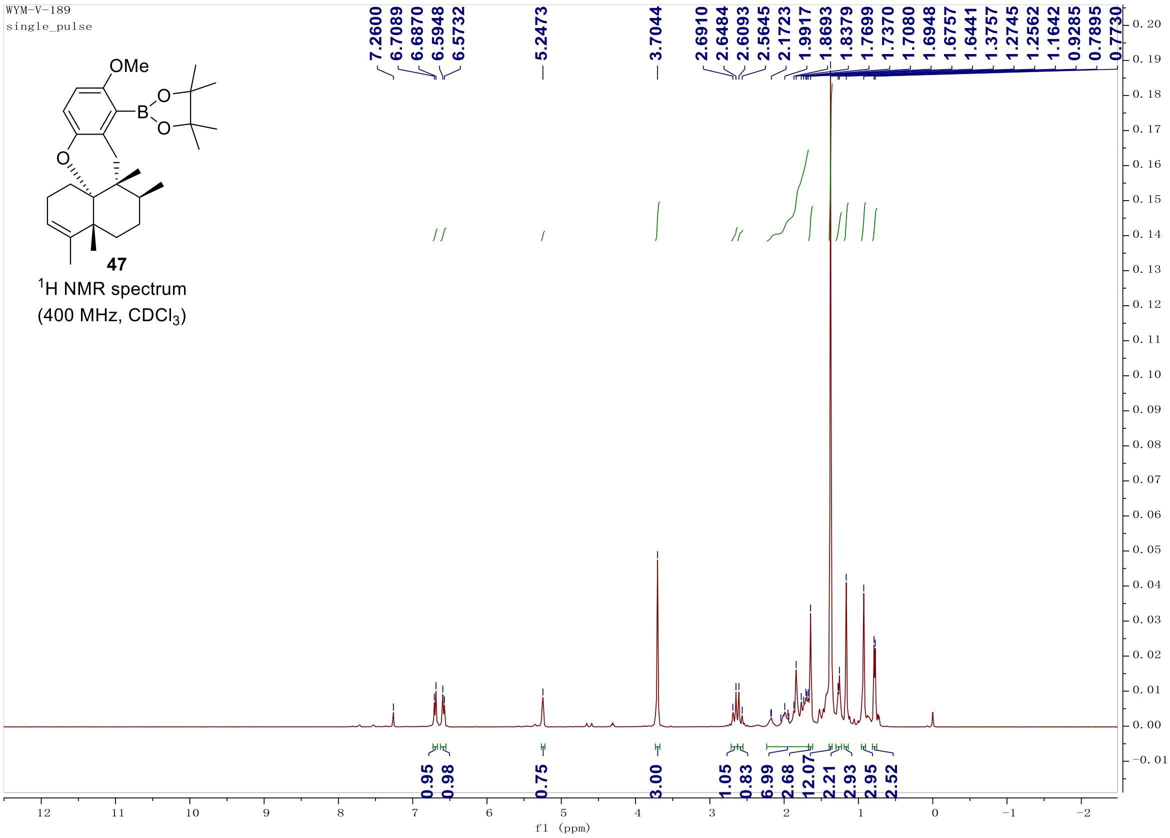
**43**

difference NOE spectrum
(500 MHz, $CDCl_3$)



**44**

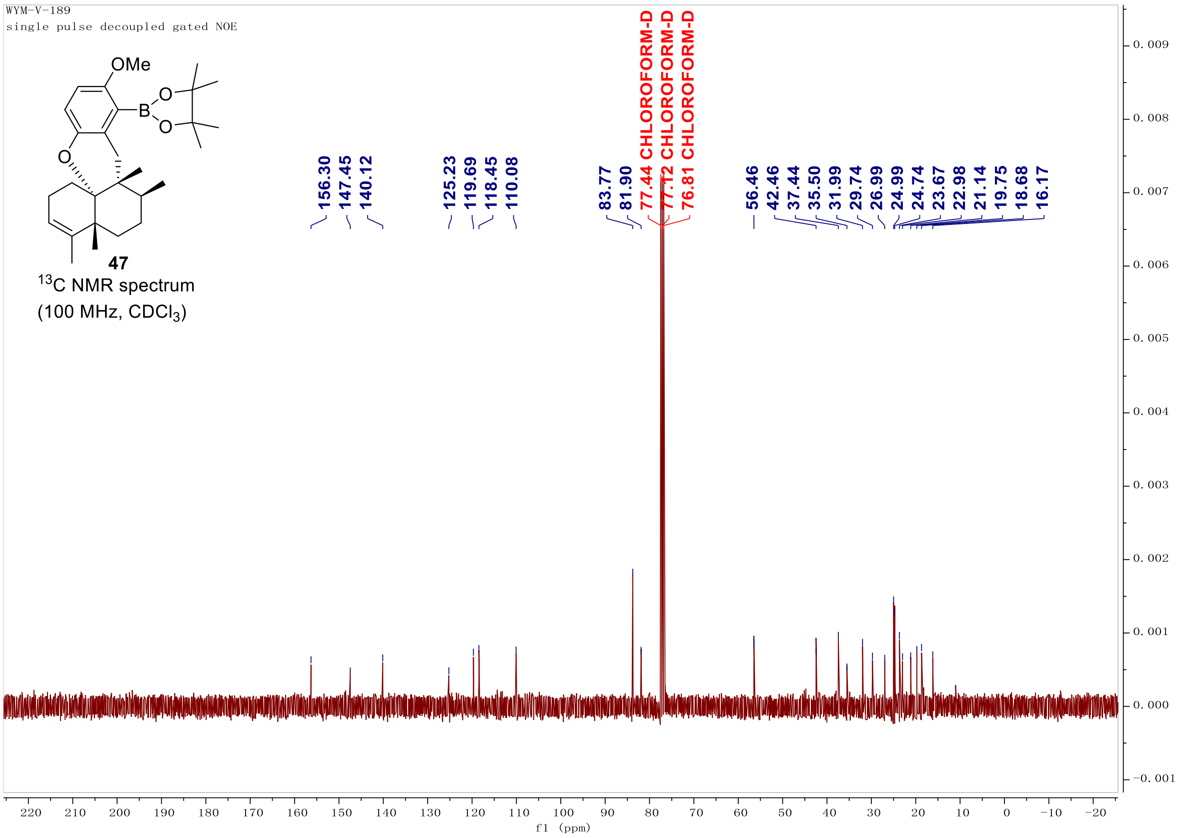
difference NOE spectrum
(500 MHz, $CDCl_3$)



**47**

$^1$H NMR spectrum

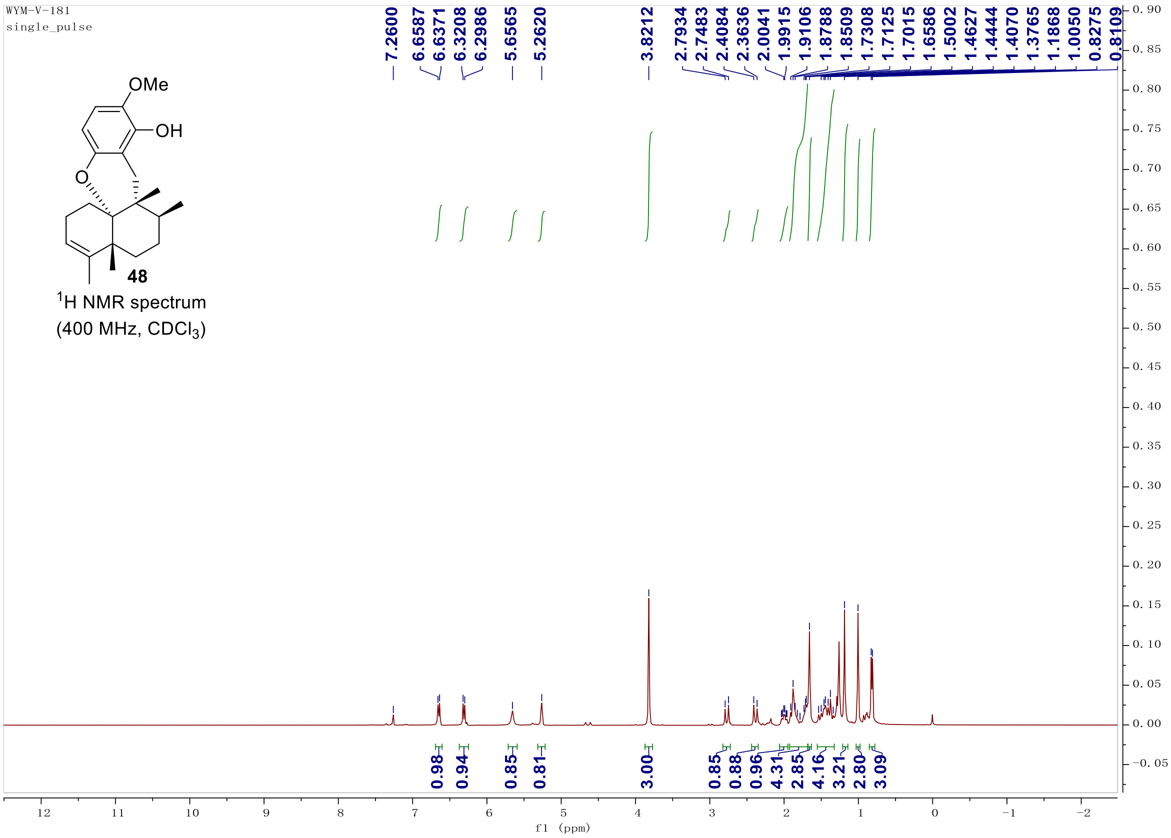
(400 MHz, $CDCl_3$)

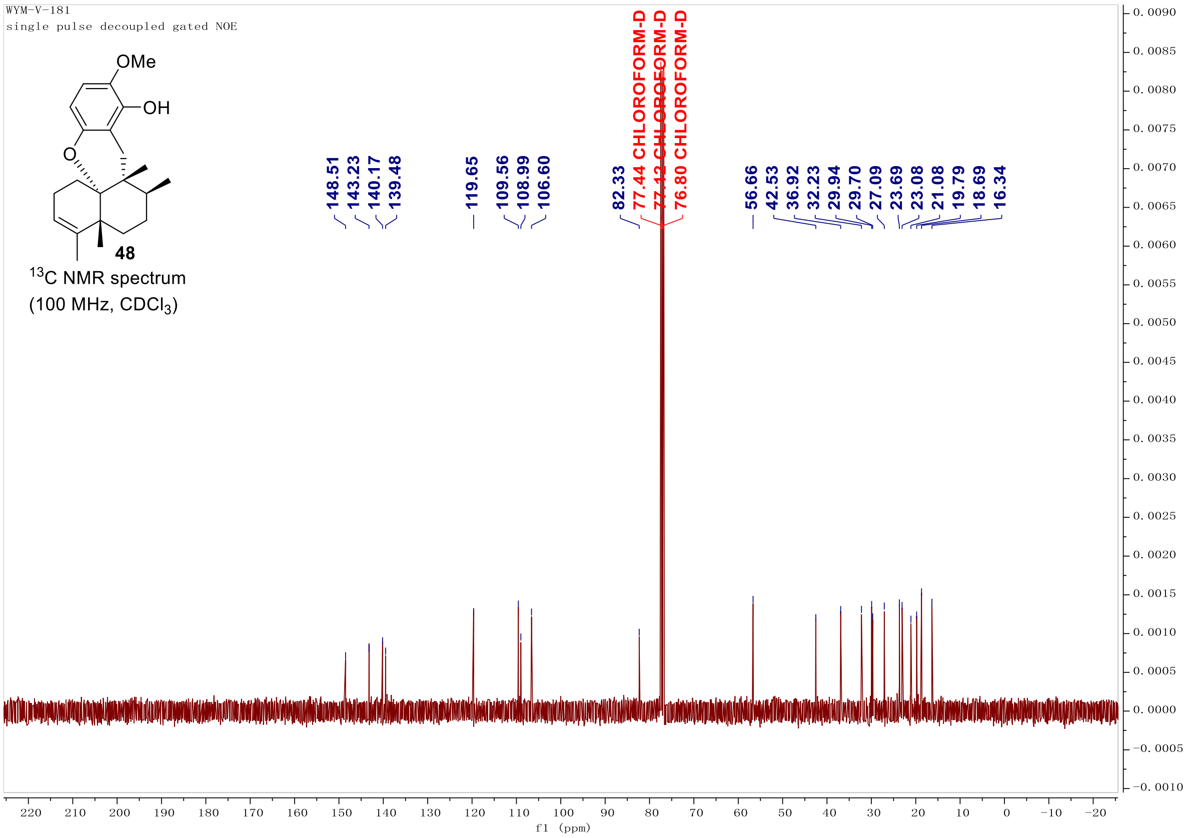


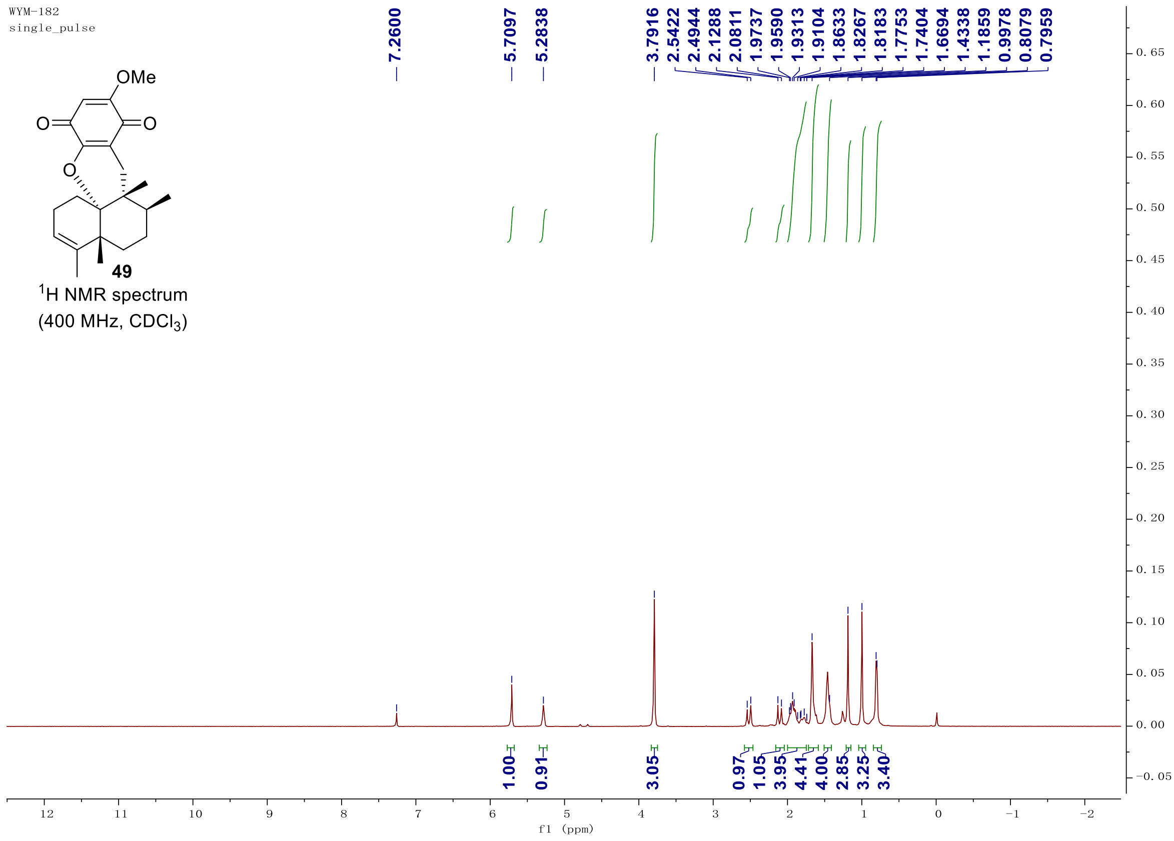
**47**

$^{13}$C NMR spectrum

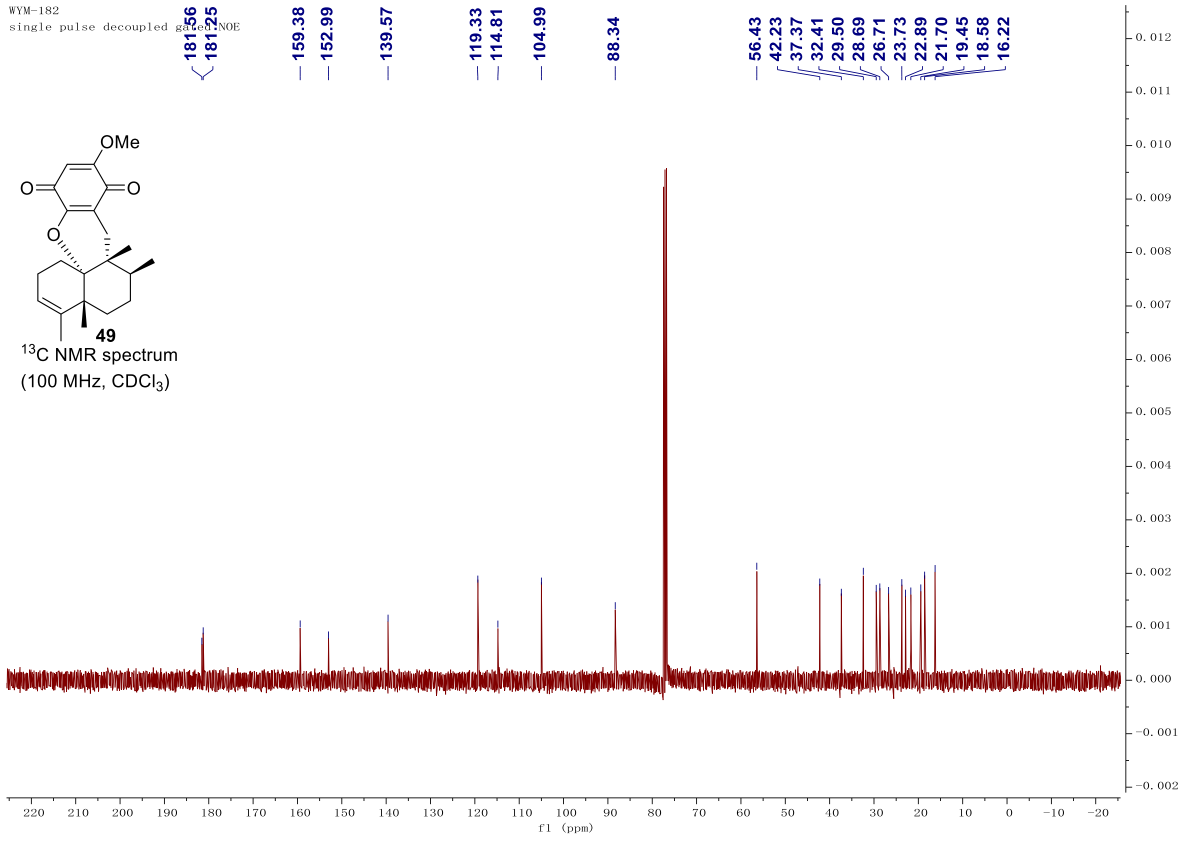
(100 MHz, $CDCl_3$)


WYM-V-181
single_pulse
OMe
OH
O
48
1H NMR spectrum
(400 MHz, CDCl3)
7.2600
6.6587
6.6371
6.3208
6.2986
5.6565
5.2620
3.8212
2.7934
2.7483
2.4084
2.3636
2.0041
1.9915
1.9106
1.8788
1.8509
1.7308
1.7125
1.7015
1.6586
1.5002
1.4627
1.4444
1.4070
1.3765
1.1868
1.0050
0.8275
0.8109
0.98
0.94
0.85
0.81
3.00
0.85
0.88
0.96
4.31
2.85
4.16
3.21
2.80
3.09
f1 (ppm)

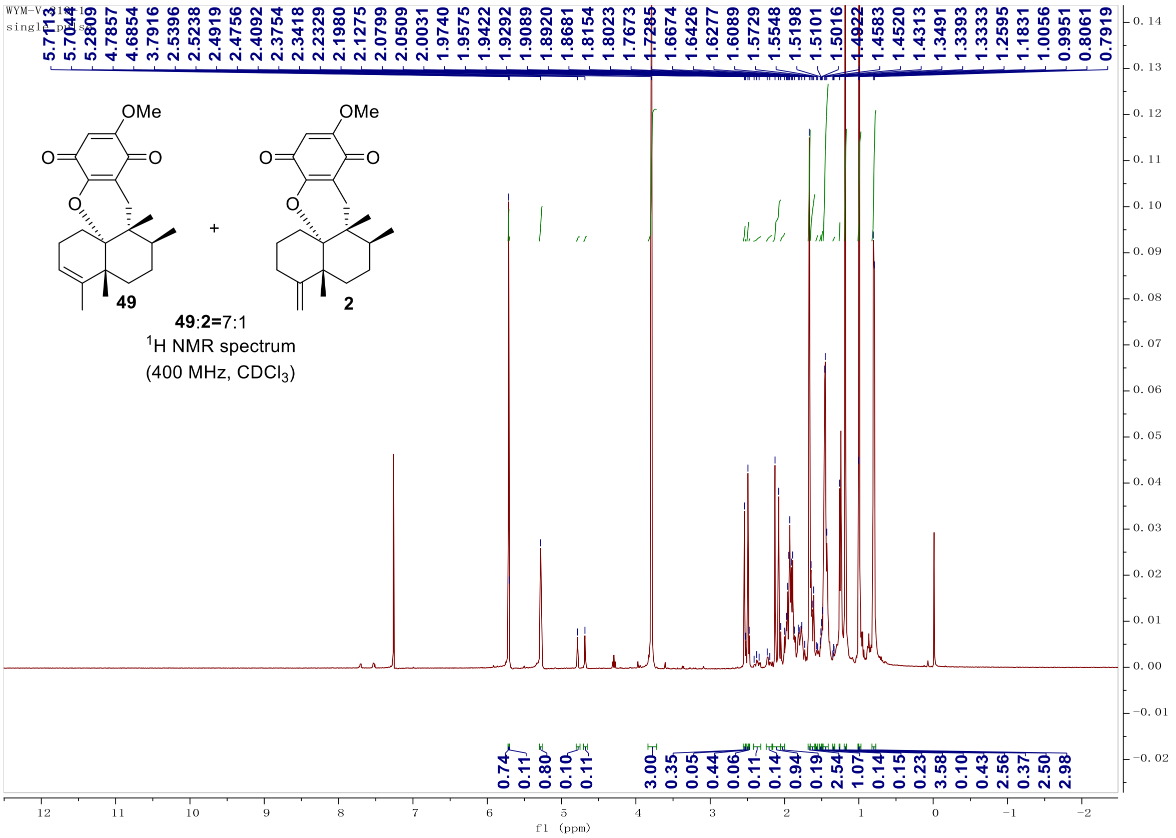

WYM-V-181
single pulse decoupled gated NOE
OMe
OH
O
48
13C NMR spectrum
(100 MHz, CDCl3)
148.51
143.23
140.17
139.48
119.65
109.56
108.99
106.60
82.33
77.44 CHLOROFORM-D
77.12 CHLOROFORM-D
76.80 CHLOROFORM-D
56.66
42.53
36.92
32.23
29.94
29.70
27.09
23.69
23.08
21.08
19.79
18.69
16.34
f1 (ppm)

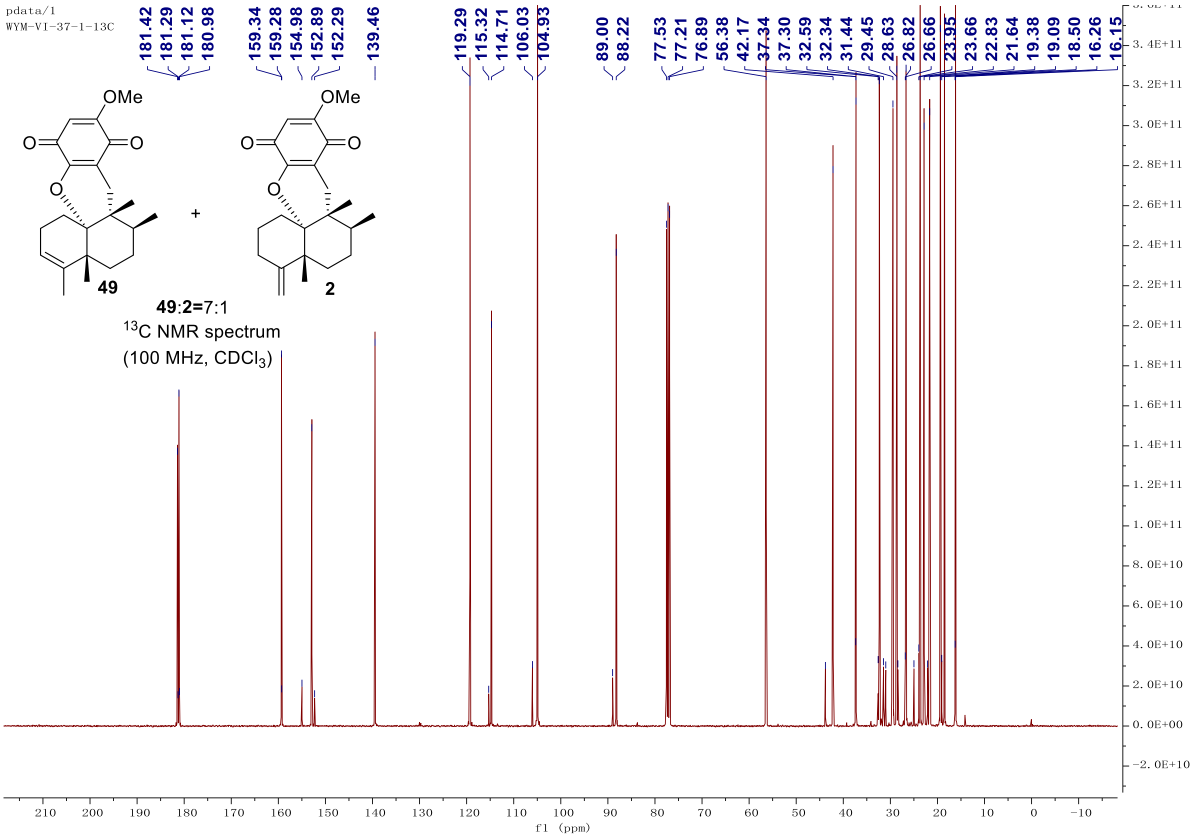


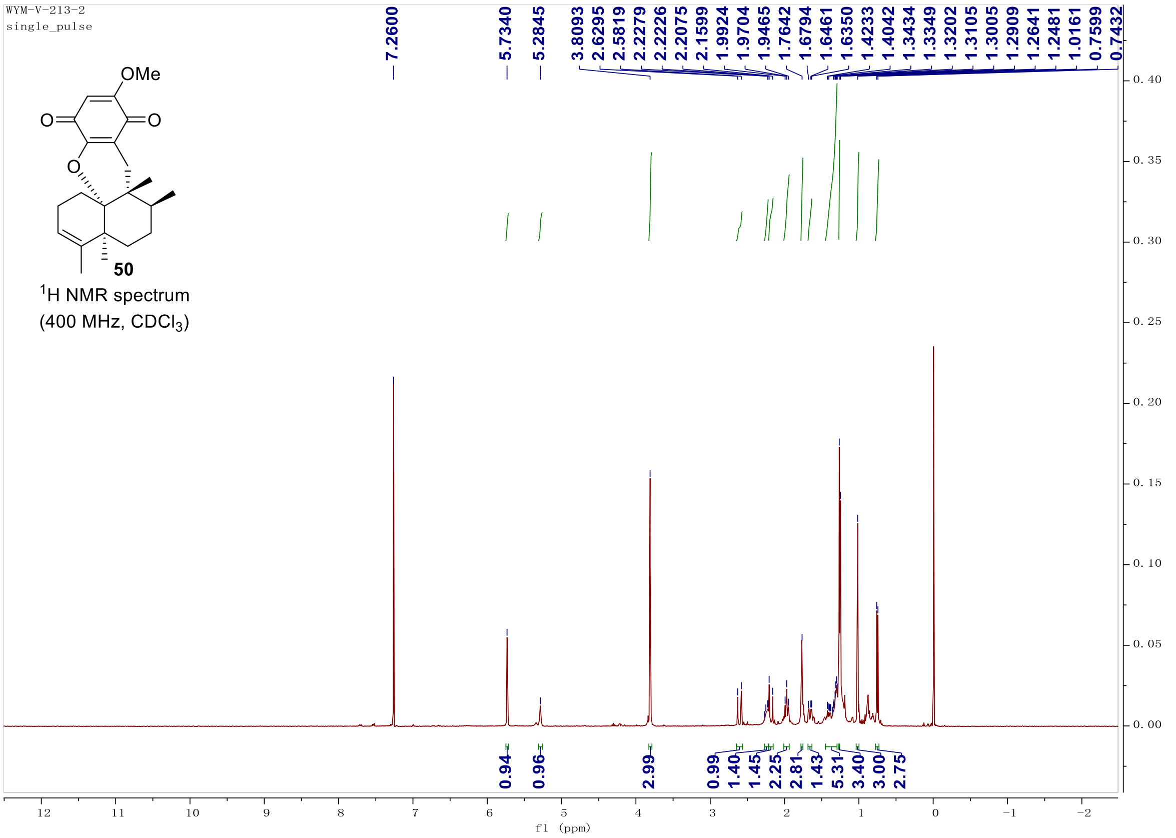
$^{1}$H NMR spectrum (400 MHz, CDCl$_3$)

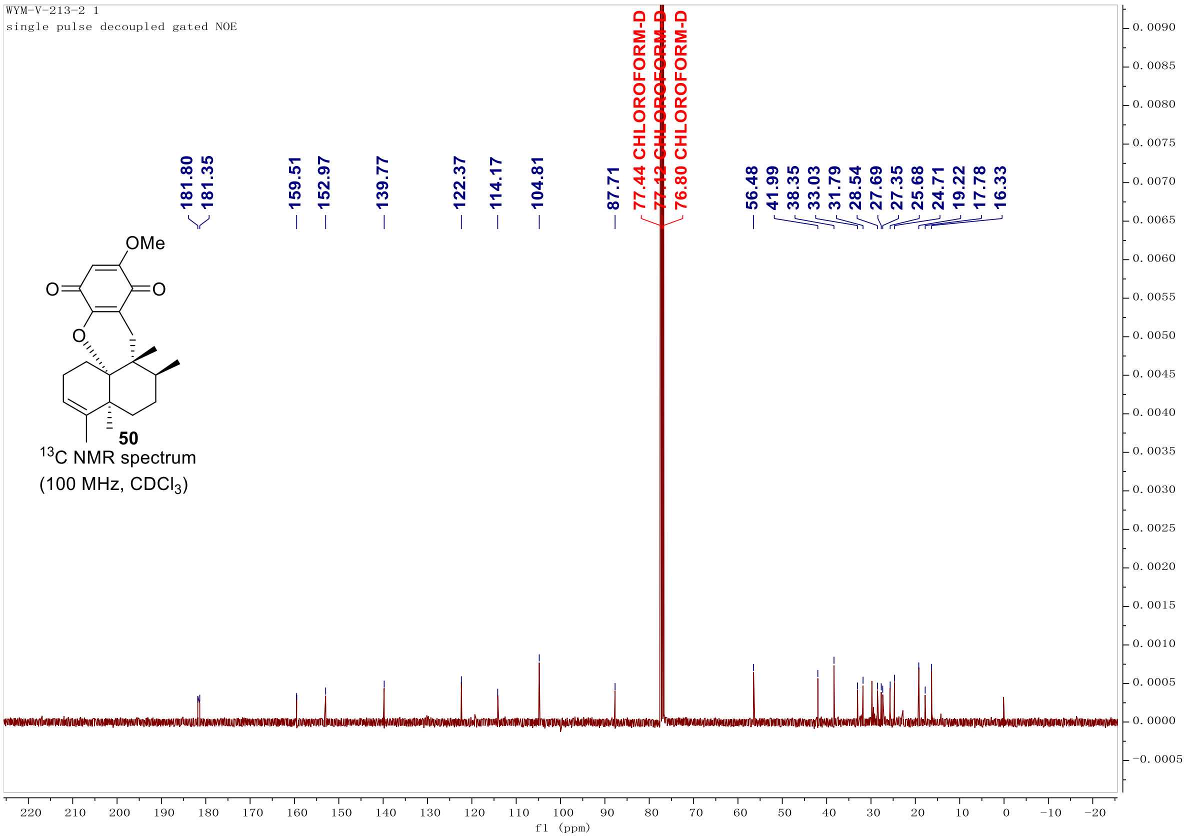


$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)


WYM-V
singl
5.7113 5.7044 5.2809 4.7857 4.6854 3.7916 2.5396 2.5238 2.4919 2.4756 2.4092 2.3754 2.3418 2.2329 2.1980 2.1275 2.0799 2.0509 2.0031 1.9740 1.9575 1.9422 1.9292 1.9089 1.8920 1.8681 1.8154 1.8023 1.7673 1.7285 1.6674 1.6426 1.6277 1.6089 1.5729 1.5548 1.5198 1.5101 1.5016 1.4922 1.4583 1.4520 1.4313 1.3491 1.3393 1.3333 1.2595 1.1831 1.0056 0.9951 0.8061 0.7919
OMe
O
O
O
49
2
+
49:2=7:1
$^1$H NMR spectrum
(400 MHz, CDCl$_3$)
0.74 0.11 0.80 0.10 0.11 3.00 0.35 0.05 0.44 0.06 0.11 0.14 0.94 0.19 2.54 1.07 0.14 0.15 0.23 3.58 0.10 0.43 2.56 0.37 2.50 2.98
f1 (ppm)

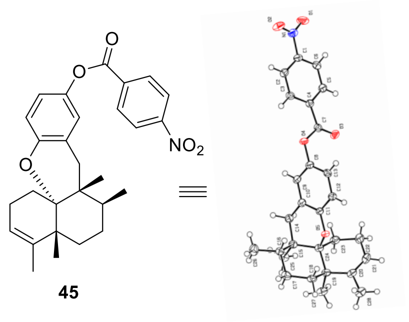

pdata/1
WYM-VI-37-1-13C
181.42 181.29 181.12 180.98 159.34 159.28 154.98 152.89 152.29 139.46 119.29 115.32 114.71 106.03 104.93 89.00 88.22 77.53 77.21 76.89 56.38 42.17 37.34 37.30 32.59 32.34 31.44 29.45 28.63 26.82 26.66 23.95 23.66 22.83 21.64 19.38 19.09 18.50 16.26 16.15
OMe
O
O
O
49
2
+
49:2=7:1
$^{13}$C NMR spectrum
(100 MHz, CDCl$_3$)
f1 (ppm)


WYM-V-213-2
single_pulse
OMe
O
O
O
50
$^1$H NMR spectrum
(400 MHz, CDCl$_3$)
7.2600
5.7340
5.2845
3.8093
2.6295
2.5819
2.2279
2.2226
2.2075
2.1599
1.9924
1.9704
1.9465
1.7642
1.6794
1.6461
1.6350
1.4233
1.4042
1.3434
1.3349
1.3202
1.3105
1.3005
1.2909
1.2641
1.2481
1.0161
0.7599
0.7432
0.94
0.96
2.99
0.99
1.40
1.45
2.25
2.81
1.43
5.31
3.40
3.00
2.75
f1 (ppm)


WYM-V-213-2 1
single pulse decoupled gated NOE
181.80
181.35
159.51
152.97
139.77
122.37
114.17
104.81
87.71
77.44 CHLOROFORM-D
77.12 CHLOROFORM-D
76.80 CHLOROFORM-D
56.48
41.99
38.35
33.03
31.79
28.54
27.69
27.35
25.68
24.71
19.22
17.78
16.33
OMe
O
O
O
50
$^{13}$C NMR spectrum
(100 MHz, CDCl$_3$)
f1 (ppm)

## 5. X-ray Crystallographic Data of Compounds

**Table S6**. Crystal data and structure refinement for CCDC 2150432


45

| | |
|---|---|
| Identification code | CCDC 2150432 |
| Empirical formula | $C_{28}H_{31}NO_5$ |
| Formula weight | 461.54 |
| Temperature | 293(2) K |
| Wavelength | 1.54184 A |
| Crystal system | Orthorhombic |
| space group | P2(1)2(1)2(1) |
| Unit cell dimensions | a = 7.6357(4) A alpha = 90 deg. |
| | b = 17.5288(11) A beta = 90 deg. |
| | c = 17.6701(9) A gamma = 90 deg. |
| Volume | 2365.1(2) A^$^{3}$ |
| Z | 4 |
| Calculated density | 1.296 Mg/m^$^{3}$ |
| Absorption coefficient | 0.716 mm^-1 |
| F(000) | 984 |
| Crystal size | 0.120 x 0.120 x 0.110 mm |
| Theta range for data collection | 3.552 to 67.233 deg. |
| Limiting indices | -5<=h<=9, -18<=k<=20, -18<=l<=21 |
| Reflections collected / unique | 5563 / 3703 [R(int) = 0.0334] |
| Completeness to theta = 67.233 | 99.9 % |
| Refinement method | Full-matrix least-squares on F^$^{2}$ |
| Data / restraints / parameters | 3703 / 0 / 311 |
| Goodness-of-fit on F^2 | 1.026 |
| Final R indices [I>2sigma(I)] | R1 = 0.0430, wR2 = 0.0968 |
| R indices (all data) | R1 = 0.0505, wR2 = 0.1021 |
| Absolute structure parameter | 0.1(2) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.158 and -0.191 e.A^$^{-3}$ |