Supporting Information

Biomimetic Total Syntheses of Renifolins F and Antiarone K

Jarish Ahamad and Faiz Ahmed Khan*
Department of Chemistry, Indian Institute of Technology Hyderabad, Kandi, Sangareddy, 502284
*Corresponding Author: Email address- faiz@chy.iith.ac.in (Faiz Ahmed Khan)

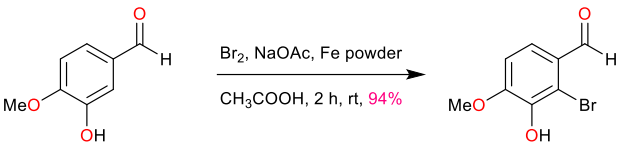
Contents

Part 1. General Information

All reactions that were sensitive to air and moisture were conducted using glassware that had been dried in an oven and under a nitrogen atmosphere. Dry and freshly distilled solvents were used unless otherwise specified. When heating was required, a heating mantle was used as the heat source. Non-aqueous reactions were performed using standard syringe and septa techniques. Commercially available reagents were used without further purification unless stated otherwise. THF, toluene, MeOH, EtOH, and diethyl ether (Et_2O) were dried by distillation over Na/benzophenone, while dichloromethane, dimethylformamide, acetonitrile, triethylamine, and diisopropylethylamine were distilled from CaH_2. TLC inspections were carried out on silica gel GF254 plates. Column and flash chromatography were performed using silica gel (60-120, 100-200, and 300–400 mesh). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 600 or 400 MHz instrument, respectively. For natural products, structural assignments were made with additional information from HSQC and HMBC experiments. Signal positions were reported in ppm, with the abbreviations s, d, t, m, and bs representing singlet, doublet, triplet, multiplet, and broad singlet, respectively. All NMR chemical shifts were referenced to residual solvent peaks or to $Si(CH_3)_4$ as an internal standard ($CDCl_3$ ^1H NMR = 7.26 ppm, 13C NMR = 77.16 ppm; $(CD_3)_2CO$ 1H NMR = 2.05 ppm, ^{13}C NMR = 206.68 and 29.92 ppm). All coupling constants J were reported in Hz. High-resolution mass spectra (HRMS) were obtained using a UHD accurate-mass Q-TOF LC/MS mass spectrometer with ESI ionization. FTIR spectra were obtained using a Bruker Alpha instrument. The X-ray single-crystal analysis was conducted using a Bruker D8 Venture instrument diffractometer equipped with graphite monochromated Cu Kα radiation. $InCl_3.4H_2O$ was purchased from BLD and used directly.

Part 2. Experimental Procedures and Spectroscopic Data

Synthesis of 2-bromo-3-hydroxy-4-methoxybenzaldehyde (10)



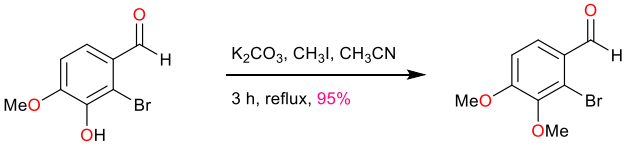
9 **10**

Procedure adapted from a literature procedure.

To a rapidly stirring suspension of 3-hydroxy-4-methoxybenzaldehyde **9** (12 g, 78.95 mmol), sodium acetate (7.8 g, 95.74 mmol, 1.5 eq.) and iron powder (0.45 g, 7.9 mmol, 0.1 eq.) in acetic acid (70 ml) at -10℃, was added dropwise a solution of bromine (15.2 g, 94.74 mmol, 1.2 eq.) in acetic acid (50 ml). After the addition was complete the thick suspension was stirred at room temperature for 2 h and then poured into ice-water (100 ml). The brownish precipitate was collected, washed with cold water, and dried overnight to afford **10** (17.08 g, 94 %) as a brownish solid. Exp. mp199-201℃ was matched with the reported mp 200-204 ℃.

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

Synthesis of 2-bromo-3,4-dimethoxybenzaldehyde (11)



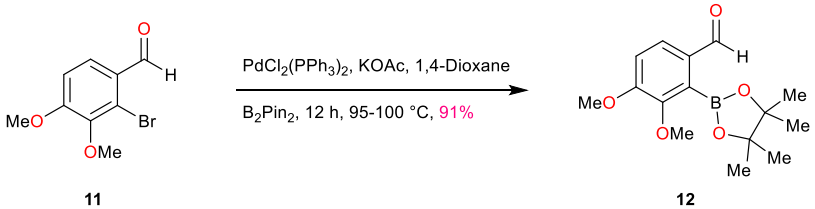
10 **11**

Procedure adapted from a literature procedure.

To a rapidly stirring suspension of 2-bromo-3-hydroxy-4-methoxybenzaldehyde, **10** (9 g, 38.96 mmol, 1 eq.), potassium carbonate (16 g, 116.88, mmol, 3 eq.) in acetonitrile (70 ml) at room temperature was added methyl iodide (11 g, 77.92 mmol, 2 eq.) dropwise. Thereafter, the reaction mixture was refluxed for 3 h, cooled, and then poured into ice water (70 ml). The white precipitate was collected, washed with cold water, and dried overnight to afford **11** (9.1 g, 95 %) as a white solid. Exp. mp 75-78 ℃ was matched with the reported mp 80 ℃.

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

Synthesis of 3,4-dimethoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (12)



11 **12**

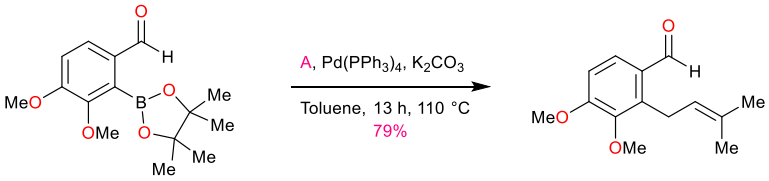
Procedure adapted from a literature procedure.

A solution of 2-bromo-3,4-dimethoxybenzaldehyde **11** (2.2 g, 8.98 mmol, 1 eq.), KOAc (1.8 g, 17.96 mmol, 2 eq.), and Pin_2B_2 (4.5 g, 17.96 mmol, 2 eq.) in dry 1,4-dioxane (30 mL) was stirred at rt under nitrogen. To the stirring solution, was added $Pd(PPh_3)_2Cl_2$ (0.19 g, 0.27 mmol, 0.03 eq.) under nitrogen, and the mixture was stirred overnight at 95-100 °C under nitrogen. The reaction was followed by TLC. After the completion of the reaction, the mixture was cooled and filtered. The solution was concentrated to afford the crude product. The residue was purified by column chromatography to give the title compound **12** as a white solid (2.386 g, 91%). ^{1}H NMR results of the synthetic compound **12** align with the data published previously.

Data for 12:

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.53 (d, *J* = 8.3 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 3.91 (s, 3H), 3.84 (s, 3H), 1.45 (s, 12H).

Synthesis of 3,4-dimethoxy-2-(3-methylbut-2-en-1-yl)benzaldehyde (13)



12 **13**

Procedure adapted from a literature procedure.

A solution of 3,4-dimethoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde **12** (0.735 g, 2.52 mmol, 1 eq.), compound (**A**) prenyl bromide (1.13 g, 7.56 mmol, 3 eq.) and K_2CO_3 (5.2 g, 37.8 mmol, 15 eq.) in dry toluene (20 mL) was stirred at rt under nitrogen. To the stirring solution was added $Pd(PPh_3)_4$ (0.09 g, 0.08 mmol, 0.03 eq.) under nitrogen, and the mixture was stirred overnight at 100 °C under nitrogen. The reaction was followed by TLC. After completion of the reaction, the mixture was cooled and filtered. The solution was concentrated to afford the crude product. The residue was purified by column chromatography to give the title compound **13** as a yellow oil (2.386 g, 79%). ^{1}H NMR results of the synthetic compound **13** align with the data published previously.

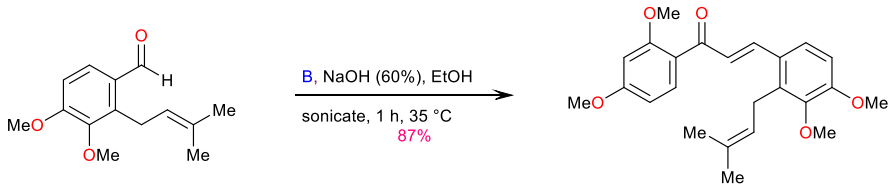
Data for 13:

^{1}H NMR (600 MHz, $CDCl_3$) δ 10.09 (s, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 1H), 5.12 (t, *J* = 6.8 Hz, 1H), 3.93 (s, 3H), 3.80 (s, 3H), 3.78 (d, *J* = 6.7 Hz, 2H), 1.79 (s, 3H), 1.66 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 191.20, 157.68, 147.09, 138.87, 132.25, 128.64, 128.02, 123.19, 109.70, 60.91, 55.94, 25.81, 24.06, 18.16.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{18}O_3$ 235.1329, found 235.1328.

Synthesis of (E)-3-(3,4-dimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)-1-(2,4-dimethoxyphenyl)prop-2-en-1-one (14)



13 **14**, *cis/trans* (0:100)

Procedure adapted from a literature procedure.

To a stirring solution of commercially available 2,4-dimethoxyacetophenone **B** (0.92 g, 5.12 mmol, 1.2 eq.) in EtOH (25 ml), a 60% NaOH solution (4 ml) was added. The reaction was stirred at room temperature for 30 min. Benzaldehyde **13** (1 g, 4.27 mmol, 1 eq.) was then added and the reaction was sonicated for 1 h at 35 °C. The progression of the reaction was monitored by TLC. The reaction mixture was extracted with EtOAc and H_2O. The combined organic layers were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **14** (14.7 g, 87%) as a yellow oil.

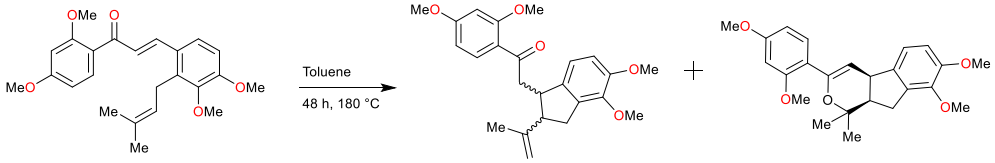
Data for 14:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 15.6 Hz, 1H), 7.66 (d, *J* = 8.6 Hz, 1H), 7.40 (d, *J* = 8.6 Hz, 1H), 7.22 (d, *J* = 4.2 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 1H), 6.50 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.44 (d, *J* = 2.3 Hz, 1H), 5.01 (t, *J* = 7.5 Hz, 1H), 3.83 (s, 4H), 3.82 (s, 3H), 3.81 (s, 3H), 3.75 (s, 3H), 3.46 (d, *J* = 9.2 Hz, 2H), 1.71 (s, 3H), 1.60 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 191.01, 163.97, 160.29, 154.21, 147.14, 140.51, 136.52, 132.75, 132.02, 127.90, 126.97, 123.05, 122.91, 122.56, 110.16, 105.11, 98.78, 60.82, 55.82, 55.80, 55.62, 25.80, 25.46, 18.04.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{24}H_{28}O_5$ 397.2010, found 397.2022.

Synthesis of 2-(4,5-dimethoxy-2-(prop-1-en-2-yl)-2,3-dihydro-1H-inden-1-yl)-1-(2,4-dimethoxyphenyl)ethan-1-one (15) and 3-(2,4-dimethoxyphenyl)-7,8-dimethoxy-1,1-dimethyl-1,4a,9,9a-tetrahydroindeno[2,1-c]pyran (16)



14, cis/trans (0:100) **15**, 70% (3:1) **16**, 22%

Procedure adapted from a literature procedure.

Compound **14** (0.424 g, 1.07 mmol) was dissolved in dry toluene (21 ml) in a sealed tube under a nitrogen atmosphere at room temperature. The reaction mixture was stirred at 180 °C until complete completion of the starting material. After cooling, the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **15** (0.287 g, 70%) yellow oil as a mixture of isomers (3:1) and **16** (0.094 g, 22%) as a solid compound (mp 158-160 °C).

Data for 15:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.8 Hz, 1H), 7.75 (d, *J* = 8.7 Hz, 0.24H), 6.86 (d, *J* = 8.1 Hz, 0.29H), 6.79 (d, *J* = 9.3 Hz, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 6.66 (d, *J* = 8.2 Hz, 0.24H), 6.54 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.50 (dd, *J* = 8.7, 2.3 Hz, 0.27H), 6.45 (d, *J* = 2.3 Hz, 1H), 6.40 (d, *J* = 2.2 Hz, 0.28H), 4.84 (d, *J* = 9.2 Hz, 0.58H), 4.77 (d, *J* = 16.1 Hz, 2H), 3.85 (d, *J* = 1.3 Hz, 7H), 3.84 (s, 3H), 3.83 (s, 1H), 3.82 (s, 3H), 3.81 (s, 1H), 3.80 (s, 1H), 3.76 – 3.68 (m, 1H), 3.29 (d, *J*=7.0 Hz, 0.11H), 3.24 (dd, *J* = 6.5, 3.3 Hz, 2H), 3.18 (s, 0.40H), 3.10 (dt, *J* = 15.7, 7.9 Hz, 1H), 3.04 – 2.91 (m, 1H), 2.87 – 2.73 (m, 2H), 1.74 (s, 3H), 1.66 (s, 0.29H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 199.92, 164.39, 164.24, 160.68, 151.15, 146.24, 145.54, 144.99, 140.80, 140.42, 135.49, 132.91, 132.61, 121.56, 119.63, 119.04, 112.00, 111.78, 111.20, 105.18, 105.10, 98.38, 60.37, 60.33, 56.21, 56.10, 55.62, 55.59, 55.49, 55.24, 51.33, 48.92, 44.30, 43.48, 41.99, 33.77, 31.59, 22.43, 19.66.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{24}H_{28}O_5$ 397.2010, found 397.2023.

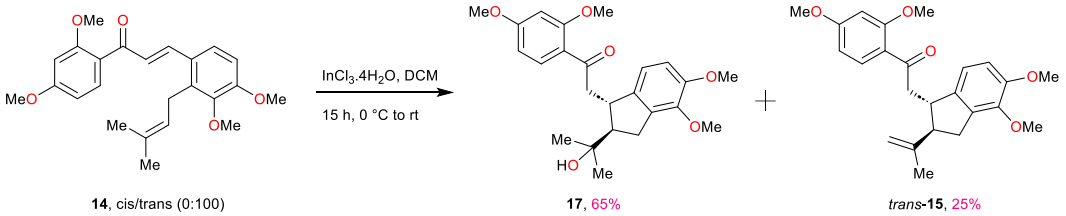
Data for 16:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.8 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.43 (d, *J* = 7.1 Hz, 2H), 5.26 (s, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.81 (dd, *J* = 7.4, 3.4 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.15 – 2.91 (m, 2H), 2.58 (q, *J* = 8.4 Hz, 1H), 1.46 (s, 3H), 1.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.44, 158.32, 151.25, 146.07, 145.54, 140.08, 135.37, 129.72, 119.18, 118.64, 111.20, 104.09, 102.62, 99.19, 75.21, 60.35, 56.21, 55.67, 55.45, 48.51, 40.89, 30.00, 26.58, 25.19.

HRMS: (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{24}H_{30}O_5$ 398.2088, found 398.2056.

Synthesis of 1-(2,4-dimethoxyphenyl)-2-((1S,2R)-2-(2-hydroxypropan-2-yl)-4,5-dimethoxy-2,3-dihydro-1H-inden-1-yl)ethan-1-one (17) and 2-((1S,2R)-4,5-dimethoxy-2-(prop-1-en-2-yl)-2,3-dihydro-1H-inden-1-yl)-1-(2,4-dimethoxyphenyl)ethan-1-one (*trans*-15)



14, cis/trans (0:100) → **17**, 65% + *trans*-**15**, 25%

Procedure:

To a well-stirred solution of compound **14** (0.164 g, 0.41 mmol, 1 eq.) in dichloromethane (CH_2Cl_2, 4 ml) was added $InCl_3.4H_2O$ (0.12 g, 0.41 mmol, 1 eq,) in a fraction at 0 °C. The reaction mixture was stirred at room temperature until complete completion of the starting material. The reaction mixture was extracted with DCM and H_2O. The combined organic layers were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **17** (0.11 g, 65%) as a yellow oil and *trans*-**15** (0.40 g, 25%) as an oil.

Data for 17:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.8 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.53 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.43 (d, *J* = 2.3 Hz, 1H), 4.08 – 3.64 (m, 14H), 3.28 (dd, *J* = 6.8, 4.9 Hz, 2H), 3.11 (d, *J* = 9.1 Hz, 1H), 2.80 (dd, *J* = 17.3, 3.3 Hz, 1H), 2.40 – 2.23 (m, 1H), 1.23 (s, 3H), 0.97 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 200.34, 164.81, 161.15, 151.09, 144.76, 140.71, 135.97, 133.09, 120.70, 118.91, 111.51, 105.28, 98.31, 72.85, 60.12, 56.18, 56.07, 55.58, 55.52, 51.57, 41.45, 31.32, 29.22, 24.38.

HRMS: (ESI-TOF) *m/z*: $[M+K]^+$ calcd for $C_{24}H_{30}O_6$ 453.1674, found 453.1691.

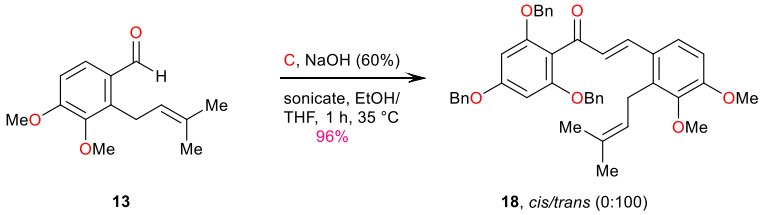
Data for *trans*-15:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.7 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 6.54 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.45 (d, *J* = 2.3 Hz, 1H), 4.76 (d, *J* = 17.5 Hz, 2H), 3.86 (d, *J* = 1.1 Hz, 6H), 3.84 (s, 3H), 3.82 (s, 3H), 3.75 – 3.68 (m, 1H), 3.23 (dd, *J* = 6.4, 3.4 Hz, 2H), 3.10 (dd, *J* = 15.0, 7.2 Hz, 1H), 2.98 – 2.72 (m, 2H), 1.74 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 199.95, 164.41, 160.69, 151.17, 146.27, 145.02, 140.45, 135.51, 132.93, 121.60, 119.05, 111.78, 111.25, 105.20, 98.41, 60.34, 56.23, 55.63, 55.51, 55.25, 48.93, 43.51, 33.79, 19.67.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{24}H_{28}O_5$ 397.2010, found 397.2023.

Synthesis of (E)-3-(3,4-dimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)-1-(2,4,6-tris(benzyloxy)phenyl)prop-2-en-1-one (18)



13 → **18**, *cis/trans* (0:100)

Procedure adapted from a literature procedure.

To a stirring solution of acetophenone **C** (0.474 g, 1.08 mmol, 1.1 eq.) in EtOH (5 ml), a 60% NaOH solution (2 ml) was added. The reaction was stirred at room temperature for 30 min. Benzaldehyde **13** (0.23 g, 0.98 mmol, 1 eq.) was then added and the reaction was sonicated for 1 h at 35 °C. The progression of the reaction was monitored by TLC. The reaction mixture was extracted with EtOAc and H_2O. The combined organic layers were dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **18** (0.615 g, 96%) as a yellow solid (mp 102-105 °C).

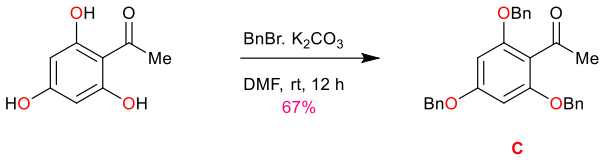
Data for 18:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 15.9 Hz, 1H), 7.44 – 7.32 (m, 5H), 7.31 – 7.21 (m, 10H), 6.84 (d, *J* = 15.8 Hz, 1H), 6.79 (d, *J* = 8.8 Hz, 1H), 6.26 (s, 2H), 5.02 (s, 4H), 4.99 (s, 2H), 4.89 (t, *J* = 6.7 Hz, 1H), 3.88 (s, 3H), 3.77 (s, 3H), 3.31 (d, *J* = 6.6 Hz, 2H), 1.49 (s, 3H), 1.46 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.62, 161.14, 157.67, 154.26, 146.95, 143.00, 136.67, 136.50, 136.15, 131.84, 128.99, 128.73, 128.52, 128.47, 128.23, 127.73, 127.56, 127.30, 126.97, 123.25, 122.64, 113.17, 110.14, 93.63, 77.10, 70.40, 70.30, 60.78, 55.74, 25.57, 25.28, 17.63.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{43}H_{42}O_6$ 655.3054, found 655.3067.

Synthesis of 1-(2,4,6-tris(benzyloxy)phenyl)ethan-1-one (C)



C

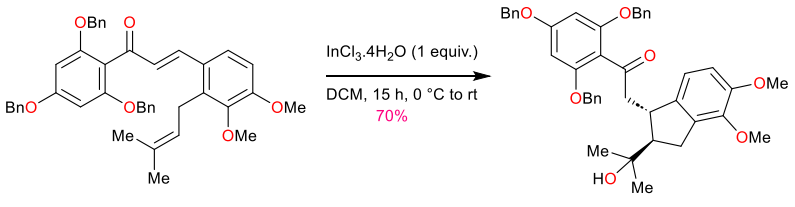
Procedure adapted from a literature procedure.

To a solution of 2,4,6-trihydroxy acetophenone (0.5 g, 2.97mmol, 1 eq.) in DMF (15 mL) was added K_2CO_3 (2.4 g, 17.82 mmol, 6 eq.), and the reaction was stirred for 30 min at room temperature; then benzyl bromide (3 g, 17.82 mmol, 6 eq.) was added to the solution. After 14 h, the reaction was quenched with a saturated solution of NH_4Cl, then extracted with ethyl acetate twice (50 mL each). The organic layer was washed three times with brine solution and then dried over anhydrous Na_2SO_4. The organic layer was evaporated to dryness and then subjected to a silica gel column using hexane−EtOAc. Fractions containing the product were pooled and dried to give the title compound **C** (0.875 g, 67%). ^{1}H NMR results of the synthetic compound **C** align with the data published previously.

Data for C:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 15H), 6.26 (s, 2H), 5.05 (s, 4H), 5.01 (s, 2H), 2.49 (s, 3H).

Synthesis of 2-((1S,2R)-2-(2-hydroxypropan-2-yl)-4,5-dimethoxy-2,3-dihydro-1H-inden-1-yl)-1-(2,4,6-tris(benzyloxy)phenyl)ethan-1-one (19)



18, *cis/trans* (0:100)

19

Procedure:

To a well-stirred solution of compound **18** (0.156 g, 0.24 mmol, 1 eq.) in dichloromethane (CH_2Cl_2, 4 ml) was added $InCl_3.4H_2O$ (0.12 g, 0.41 mmol, 1 eq.) in a fraction at 0 °C. The reaction mixture was stirred at room temperature until the complete completion of the starting material. The reaction mixture was extracted with DCM and H_2O. The combined organic layers were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **19** (0.112 g, 70%) as a yellow solid (mp 128-130 °C).

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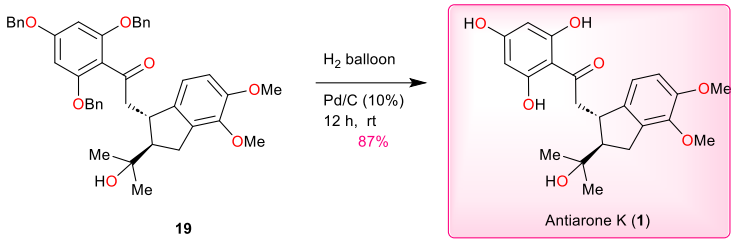
Data for 19:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.31 (m, 16H), 6.65 (d, *J* = 8.3 Hz, 1H), 6.49 (d, *J* = 8.2 Hz, 1H), 6.26 (s, 2H), 5.02 (s, 2H), 5.01 (s, 4H), 3.80 (s, 3H), 3.78 (s, 3H), 3.80 – 3.72 (m, 1H), 3.25 – 3.14 (m, 1H), 3.12 – 3.03 (m, 1H), 2.96 (s, 1H), 2.80 (dd, *J* = 17.2, 9.0 Hz, 1H), 2.64 (dd, *J* = 17.2, 4.2 Hz, 1H), 2.14 (dt, *J* = 8.8, 4.0 Hz, 1H), 1.10 (s, 3H), 0.92 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 204.58, 161.30, 157.14, 150.99, 144.70, 140.38, 136.40, 136.34, 135.68, 128.79, 128.74, 128.32, 128.23, 127.70, 127.60, 118.98, 114.46, 111.44, 93.43, 72.79, 70.84, 70.38, 60.14, 56.13, 55.84, 52.62, 40.62, 31.08, 29.12, 24.73.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{43}H_{44}O_7$ 673.3160, found 673.3152.

Synthesis of 2-((1S,2R)-2-(2-hydroxypropan-2-yl)-4,5-dimethoxy-2,3-dihydro-1H-inden-1-yl)-1-(2,4,6-trihydroxyphenyl)ethan-1-one {antiarone K (1)}



Procedure adapted from a literature procedure.

To a well-stirred solution of compound **19** (0.058 g, 0.09 mmol, 1 eq.) in EtOAc: MeOH (2 ml, 1:1) was added 10% Pd/C (0.055 g, 0.52 mmol, 6 eq.) under inert atmosphere. The reaction mixture was stirred at room temperature under a hydrogen atmosphere until the complete completion of the starting material. After completion, the reaction mixture was filtered through a short pad of elite, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give antiarone K (**1**) (0.031 g, 87%) as a white crystalline solid (mp 125-127 °C, Lit mp 117-119 °C). The NMR data pertaining to the synthetic antiarone K (**1**) aligns with the results documented in the isolation report.

Data for antiarone K (1):

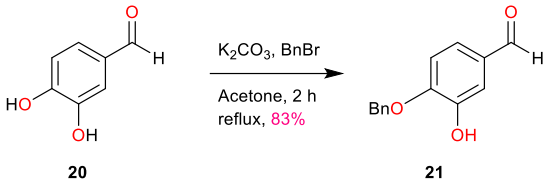
^{1}H NMR (600 MHz, acetone-d_6) δ 11.90 (s, 2H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 5.93 (s, 2H), 3.80 (dt, *J* = 6.5, 3.5 Hz, 1H), 3.77 (s, 6H), 3.65 (s, 1H), 3.46 (dd, *J* = 16.7, 6.3 Hz, 1H), 3.30 (dd, *J* = 16.8, 7.2 Hz, 1H), 3.05 (dd, *J* = 17.1, 9.0 Hz, 1H), 2.95 (dd, *J* = 17.1, 4.2 Hz, 1H), 2.34 (dt, *J* = 9.0, 4.1 Hz, 1H), 1.07 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (150 MHz, acetone-d_6) δ 205.61, 165.51, 152.06, 145.75, 142.06, 137.03, 119.75, 112.69, 105.62, 95.83, 72.62, 59.93, 56.34, 56.16, 52.58, 43.21, 31.09, 27.88, 27.10.

DEPT (151 MHz, acetone-d_6) δ 119.50, 112.44, 95.58, 59.68, 56.09, 55.91, 42.96, 27.63, 26.85.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$-(H_2O) calcd for $C_{22}H_{26}O_7$ 385.1645, found 385.1647.

Synthesis of 4-(benzyloxy)-3-hydroxybenzaldehyde (21)

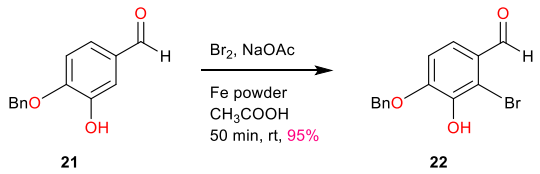


Procedure adapted from a literature procedure.

To a solution of **20** (7 g, 50.72mmol, 1 eq.) in acetone (50 mL) was added K_2CO_3 (7.7 g, 55.80 mmol, 1.1 eq.), and the reaction was stirred for 30 min at room temperature; then benzyl bromide (8.6 g, 50.72 mmol, 1 eq.) was added to the solution. After stirring at reflux for 2 h, the reaction was quenched with a saturated solution of NH_4Cl, then extracted with ethyl acetate twice (50 mL each). The organic layer was washed three times with brine solution and then dried over anhydrous Na_2SO_4. The organic layer was evaporated to dryness and then subjected to a silica gel column using hexanes-EtOAc. Fractions containing the product were pooled and dried to give the title compound **21** (9.59 g, 83%) as a white solid. (mp 114-116 °C, Lit mp 120 °C).

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

Synthesis of 4-(benzyloxy)-2-bromo-3-hydroxybenzaldehyde (22)

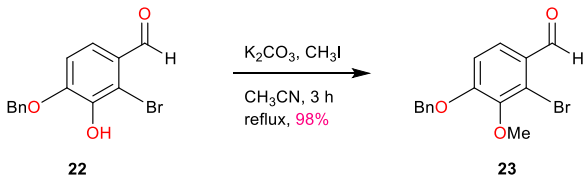


Procedure adapted from a literature procedure.

To a rapidly stirring suspension of **21** (7.74 g, 33.94 mmol, 1 eq.), sodium acetate (4.2 g, 50.91 mmol, 1.5 eq.) and iron powder (0.19 g, 3.4 mmol, 0.1 eq.) in acetic acid (60 ml) at -10°C, was added dropwise a solution of bromine (6.5 g, 40.73 mmol, 1.2 eq.) in acetic acid (40 ml). After the addition was complete the thick suspension was stirred at room temperature for 50 min and then poured into ice-water (100 ml). The brownish precipitate was collected, washed with cold water, and dried overnight to afford **22** (9.9 g, 95%) as a solid. (mp 111-113 °C, lit. mp 114-116 °C).

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

Synthesis of 4-(benzyloxy)-2-bromo-3-methoxybenzaldehyde(23)

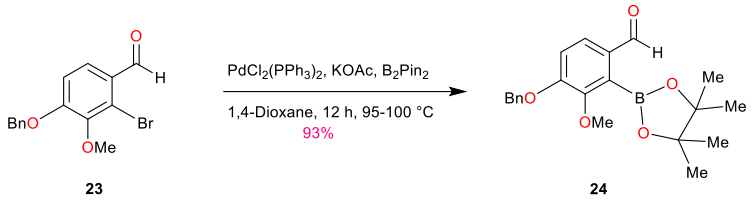


Procedure adapted from a literature procedure.

To a rapidly stirring suspension of **22** (9 g, 29.32 mmol, 1 eq.), potassium carbonate (12.2 g, 87.95, mmol, 3 eq.) in acetonitrile (70 ml) at room temperature was added dropwise methyl iodide (8.4 g, 58.63 mmol, 2 eq.). Thereafter, the reaction mixture was refluxed for 3 h, cooled, and then poured into ice water (70 ml). The white precipitate was collected, washed with cold water, and dried overnight to afford **23** (9.2 g, 98 %) as a white solid (mp 98-100 °C, Lit. mp 99-101 °C).

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

Synthesis of 4-(benzyloxy)-3-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (24)



Procedure adapted from a literature procedure.

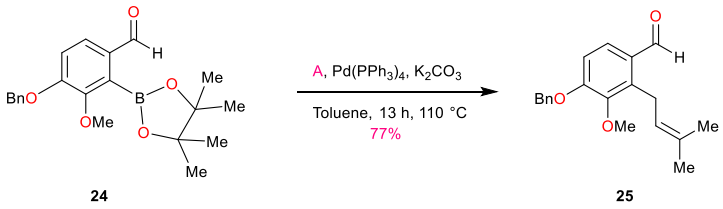
A solution of **23** (2.2 g, 6.86 mmol, 1 eq.), KOAc (1.35 g, 13.71 mmol, 2 eq.), and Pin_2B_2 (3.48 g, 13.71 mmol, 2 eq.) in 1,4-dioxane (30 mL) was stirred at rt under nitrogen. To the stirring solution was added $Pd(PPh_3)_2Cl_2$ (0.24 g, 0.34 mmol, 0.05 eq.) under nitrogen, and the mixture was stirred overnight at 95-100 °C under nitrogen. The reaction was followed by TLC. After completion of the reaction, the mixture was cooled and filtered. The solution was concentrated to afford the crude product. The residue was purified by column chromatography to give the title compound **24** (2.34 g, 93%) as a white solid; mp 138-140 °C. ^{1}H NMR results of the synthetic compound **24** align with the data published previously.

Data for 24:

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 7.39 (s, 1H), 7.35 – 7.23 (m, 5H), 6.94 (d, J = 9.2 Hz, 1H), 5.09 (d, J = 1.4 Hz, 2H), 3.80 (s, 3H), 1.38 (s, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 191.46, 156.45, 152.85, 136.08, 133.69, 130.40, 128.76, 128.27, 127.27, 113.84, 84.44, 70.55, 24.95.

Synthesis of 4-(benzyloxy)-3-methoxy-2-(3-methylbut-2-en-1-yl)benzaldehyde (25)



Procedure adapted from a literature procedure.

A solution of **24** (1 g, 2.72 mmol, 1 eq.), compound (**A**) prenyl bromide (1.2 g, 8.16 mmol, 3 eq.) and K_2CO_3 (5.6 g, 40.76 mmol, 15 eq.) in dry toluene (20 mL) was stirred at rt under nitrogen. To the stirring solution was added $Pd(PPh_3)_4$ (0.094 g, 0.08 mmol, 0.03 eq.) under nitrogen, and the mixture was stirred overnight at 100 °C under nitrogen. The reaction was followed by TLC. After completion of the reaction, the mixture was cooled and filtered. The solution was concentrated to afford the crude product. The residue was purified by column chromatography to give the title compound **25** (0.65 g, 77%) as a yellow oil.

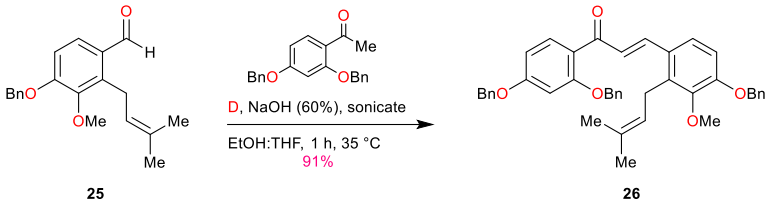
Data for 25:

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.48 – 7.33 (m, 5H), 6.94 (d, *J* = 8.6 Hz, 1H), 5.19 (s, 2H), 5.14 (t, *J* = 6.7 Hz, 1H), 3.85 (s, 3H), 3.80 (d, *J* = 7.9 Hz, 2H), 1.80 (s, 3H), 1.67 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 191.09, 156.64, 147.35, 138.96, 136.14, 132.14, 128.73, 128.33, 128.24, 128.14, 127.28, 123.10, 111.05, 70.52, 60.84, 25.73, 24.03, 18.08.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{20}H_{22}O_3$ 311.1642, found 311.1640.

Synthesis of (E)-3-(4-(benzyloxy)-3-methoxy-2-(3-methylbut-2-en-1-yl)phenyl)-1-(2,4-bis(benzyloxy)phenyl)prop-2-en-1-one (26)



25 26

Procedure adapted from a literature procedure.

To a stirring solution of acetophenone **D** (0.306 g, 0.92 mmol, 1.1 eq.) in EtOH (3 ml), a 60% NaOH solution (1 ml) was added. The reaction was stirred at room temperature for 30 min. Benzaldehyde **25** (0.26 g, 0.84 mmol, 1 eq.) was then added and the reaction was sonicated for 1 h at 35 °C. The progression of the reaction was monitored by TLC. The reaction mixture was extracted with EtOAc and H_2O. The combined organic layers were dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **26** (0.477 g, 91%) as a yellow gum.

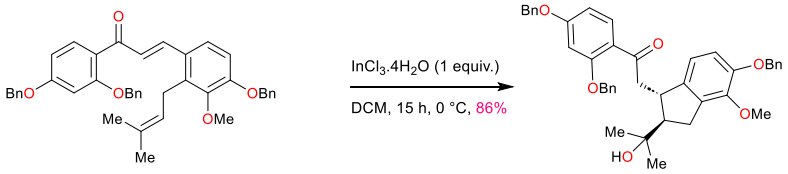
Data for 26:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 15.5 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.51 – 7.36 (m, 13H), 7.29 – 7.22 (m, 3H), 6.94 (d, *J* = 8.6 Hz, 1H), 6.69 – 6.62 (m, 3H), 5.16 (s, 2H), 5.12 (s, 2H), 5.09 (s, 2H), 5.08 – 5.04 (m, 1H), 3.86 (s, 3H), 3.53 (d, *J* = 6.7 Hz, 2H), 1.80 (s, 3H), 1.65 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 190.03, 163.21, 159.55, 153.00, 147.37, 139.91, 136.98, 136.55, 136.32, 136.06, 133.19, 131.88, 128.76, 128.69, 128.32, 128.16, 128.10, 128.04, 127.82, 127.62, 127.24, 127.19, 122.92, 122.82, 122.73, 111.87, 106.53, 100.58, 77.15, 70.82, 70.50, 70.32, 60.82, 25.78, 25.44, 18.05.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{42}H_{40}O_5$ 625.2942, found 625.2972.

Synthesis of 2-((1S,2R)-5-(benzyloxy)-2-(2-hydroxypropan-2-yl)-4-methoxy-2,3-dihydro-1H-inden-1-yl)-1-(2,4-bis(benzyloxy)phenyl)ethan-1-one (35)



26 27

Procedure:

To a well-stirred solution of compound **26** (0.2 g, 0.32 mmol, 1 eq.) in dichloromethane (CH_2Cl_2, 8 ml) was added $InCl_3.4H_2O$ (0.94 g, 0.32 mmol, 1 eq.) in a fraction at 0 °C. The reaction mixture was stirred at room temperature until the complete completion of the starting material. The reaction mixture was extracted with DCM and H_2O. The combined organic layers were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **27** (0.17 g, 86%) as an oil.

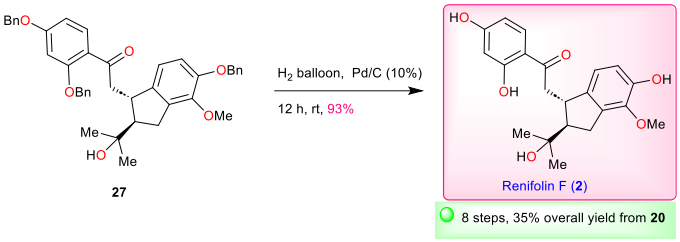
Data for 27:

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, *J* = 9.6 Hz, 1H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.35 – 7.12 (m, 13H), 6.65 (d, *J* = 8.2 Hz, 1H), 6.61 – 6.49 (m, 3H), 5.01 (d, *J* = 2.5 Hz, 4H), 4.97 (s, 2H), 3.79 (s, 3H), 3.71 (dd, *J* = 8.3, 4.9 Hz, 1H), 3.58 (s, 1H), 3.30 – 3.24 (m, 1H), 3.21 – 3.15 (m, 1H), 2.93 (dd, *J* = 17.3, 9.2 Hz, 1H), 2.67 (dd, *J* = 17.3, 3.5 Hz, 1H), 2.12 (dt, *J* = 9.1, 3.5 Hz, 1H), 1.13 (s, 3H), 0.88 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 200.49, 163.83, 160.22, 150.23, 145.46, 141.18, 137.65, 136.20, 136.06, 135.81, 133.09, 128.86, 128.74, 128.66, 128.45, 128.33, 127.94, 127.71, 127.68, 127.40, 121.45, 118.95, 114.01, 106.60, 100.51, 72.95, 71.38, 70.97, 70.43, 60.34, 56.04, 52.14, 41.42, 31.38, 29.42, 24.37.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+(-H_2O)$ calcd for $C_{42}H_{42}O_6$ 625.2948, found 625.2966.

Synthesis of 1-(2,4-dihydroxyphenyl)-2-((1S,2R)-5-hydroxy-2-(2-hydroxypropan-2-yl)-4-methoxy-2,3-dihydro-1H-inden-1-yl)ethan-1-one {renifolin F (2)}



Procedure adapted from a literature procedure.

To a well-stirred solution of compound **27** (0.085 g, 0.13 mmol, 1 eq.) in EtOAc: MeOH (4 ml, 1:1) was added 10% Pd/C (0.084 g, 0.80 mmol, 6 eq.) under inert atmosphere. The reaction mixture was stirred at room temperature under a hydrogen atmosphere until the complete completion of the starting material. After completion, the reaction mixture was filtered through a short pad of celite, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give renifolin F (**2**) (0.04 g, 93%) as a gum. The NMR data pertaining to the synthetic renifolin F (**2**) aligns with the results documented in the isolation report.

Data for renifolin F (2):

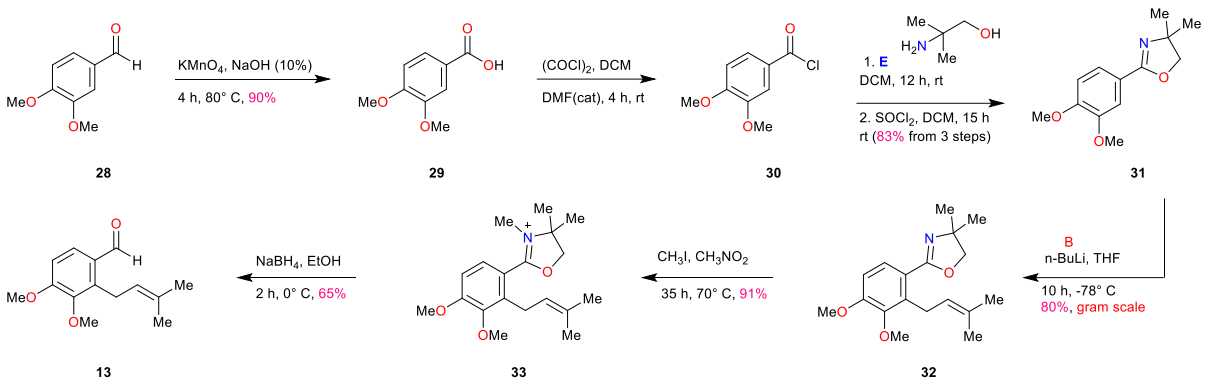
^{1}H NMR (600 MHz, acetone-d_6) δ 12.89 (s, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 6.70 (d, *J* = 9.0 Hz, 1H), 6.63 (d, *J* = 8.1 Hz, 1H), 6.42 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.34 (d, *J* = 2.4 Hz, 1H), 3.80 (s, 3H), 3.80 – 3.75 (m, 1H), 3.66 (s, 1H), 3.35 (dd, *J* = 16.3, 6.2 Hz, 1H), 3.21 (dd, *J* = 16.4, 7.2 Hz, 1H), 3.12 (dd, *J* = 16.8, 9.0 Hz, 1H), 2.94 (dd, *J* = 16.8, 5.0 Hz, 1H), 2.38 (dt, *J* = 9.3, 4.9 Hz, 1H), 1.13 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (150 MHz, acetone-d_6) δ 205.42, 166.36, 165.63, 149.02, 144.20, 139.98, 135.87, 133.91, 120.08, 115.72, 115.70, 114.25, 108.82, 108.79, 103.59, 72.61, 60.01, 59.99, 56.75, 46.50, 43.07, 31.50, 28.48, 26.66.

DEPT (150 MHz, acetone-d_6) δ 133.91, 120.08, 115.70, 108.82, 108.80, 103.59, 60.00, 56.75, 43.07, 28.48, 26.66.

HRMS (ESI-TOF) *m/z*: $[M+H]^+(-H_2O)$ calcd for $C_{21}H_{24}O_6$ 355.1540, found 355.1542.

Scheme S1. Synthesis of intermediate 13 via oxazoline-directed metalation



Synthesis of 3,4-dimethoxybenzoic acid (29)

Procedure adapted from a literature procedure.

Compound **28** (10 g, 60.24 mmol, 1 eq.) was placed into a round bottom flask followed by the addition of an aqueous NaOH (10%, 9.19g, 72.29 mmol, 1.2 eq.) solution. Subsequently, $KMnO_4$ in 90 ml of H_2O (11.4 g, 72.29 mmol, 1.2 eq.) was gradually introduced in an ice-water bath. The mixture was then heated to 80°C for 4 hours. Following the cooling of the reaction mixture, filtration was carried out, and the filtrate was acidified to pH=3 by the addition of concentrated HCl. The resulting precipitate was filtered, washed with water, and dried at room temperature to afford compound **29** (9.85 gm, 90%) in the form of a white solid. The melting point and the spectral data align with those reported in the literature.

Data for 29:

Exp. mp = 178-181 °C (Lit. mp = 179-182 °C)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.60 (d, *J* = 2.2 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 3.96 (s, 3H), 3.95 (s, 3H).

Synthesis of 2-(3,4-dimethoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (31)

Procedure adapted from a literature procedure.

To a solution of 3,4-dimethoxybenzoic acid, **29** (10.22 g, 56.15 mmol, 1eq.) in CH_2C1_2 (270 mL) was added oxalyl chloride (11.4 g, 89.76 mmol, 1.6 eq.) and DMF (1.22 g, 16.85 mmol, 0.3 eq.) under an inert atmosphere. The solution was stirred at r.t. for 4 h and then the solvent was removed in vacuo. The acid chloride **30** was redissolved in CH_2C1_2 (270 ml) and a solution of (A) 2-amino-2-methyl-l-propanol (10 g, 112.3 mmol, 2 eq.) dissolved in 10% NaOH (300 mL) was added dropwise, and the solution was stirred overnight. The layers were separated, and the organic layer was concentrated in vacuo. The resulting solid was dissolved in CH_2CI_2 (300 mL), and thionyl chloride (33.4 g, 280.75 mmol, 5 eq.) was added, and the reaction was stirred overnight. H_20 (150 mL) and 10% NaOH (350 mL) were then added to the solution which was stirred for 3 h. The layers were separated, and the aqueous layer was extracted with CH_2CI_2 (2 x 150 mL). The combined organic layers were dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give phenyloxazoline **31** (10.5 g, 83%) as a yellow oil. The spectral data aligns with those reported in the literature.

Data for 31:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.43 (d, *J* = 2.0 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 1H), 4.05 (s, 2H), 3.90 (s, 1H), 3.88 (s, 1H), 1.34 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.93, 151.56, 148.65, 121.69, 120.72, 110.82, 110.40, 79.10, 67.54, 56.10, 55.98, 28.50.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{17}NO_3$ 236.1281, found 236.1289.

Synthesis of 2-(3,4-dimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)-4,4-dimethyl-4,5-dihydrooxazole (32)

Procedure adapted from a literature procedure.

To a well-stirred solution of phenyloxazoline, **31** (4.3 g, 18.30 mmol, 1eq.) in dry tetrahydrofuran (36 mL) was added n-butyl lithium (34 ml, 54.90 mmol, 3 eq.) at -78 °C under an inert atmosphere. The reaction mixture was stirred for 1 h at the same temperature. Subsequently treated with (**A**) prenyl bromide (7.7 g, 51.23 mmol, 2.8 eq.) dropwise via syringe through rubber septa and stirred for 3 h at the same temperature. The cooling bath was removed, and the mixture was stirred at rt. until the completion of the reaction. After completion, the reaction mixture was quenched by NH_4Cl and H_2O and extracted with EtOAc (3x00 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give phenyloxazoline **32** (4.4 g, 80%) as a yellow oil.

Data for 32:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 1H), 6.75 (d, *J* = 8.7 Hz, 1H), 5.14 (t, *J* = 7.6 Hz, 1H), 4.01 (s, 2H), 3.85 (s, 3H), 3.76 (s, 3H), 3.73 (d, *J* = 6.8 Hz, 2H), 1.74 (s, 3H), 1.64 (s, 3H), 1.34 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.79, 154.65, 147.33, 136.51, 131.22, 126.56, 123.73, 121.09, 109.34, 78.80, 67.62, 60.61, 55.72, 28.43, 26.31, 25.83, 18.16.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{25}NO_3$ 304.1907, found 304.1917.

Synthesis of 2-(3,4-dimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)-3,4,4-trimethyl-4,5-dihydrooxazol-3-ium (33)

Procedure adapted from a literature procedure.

To a well-stirred solution of compound **32** (4 g, 13.18 mmol, 1 eq.) in nitromethane (CH_3NO_2, 50 ml) was added methyl iodide (5.6 g, 39.55 mmol, 3 eq.) at room temperature. The reaction mixture was stirred at 80 °C until complete completion of the starting material. The reaction was then cooled, and the solvent was removed in vacuo. The residue obtained was washed with ethanol to obtain **33** (5.45 g, 91%) as a brownish solid (mp = 118-120 °C).

Data for 33:

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.8 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 1H), 4.96 (s, 2H), 4.95 – 4.89 (m, 1H), 3.91 (s, 3H), 3.78 (s, 3H), 3.42 (s, 5H), 1.78 (s, 6H), 1.67 (s, 3H), 1.66 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.69, 157.74, 147.71, 136.75, 134.60, 129.23, 121.56, 111.76, 110.97, 82.27, 67.69, 61.02, 56.29, 32.06, 26.09, 25.85, 24.73, 18.34.

HRMS: (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{19}H_{28}NO_3$ 318.2058, found 318.2072.

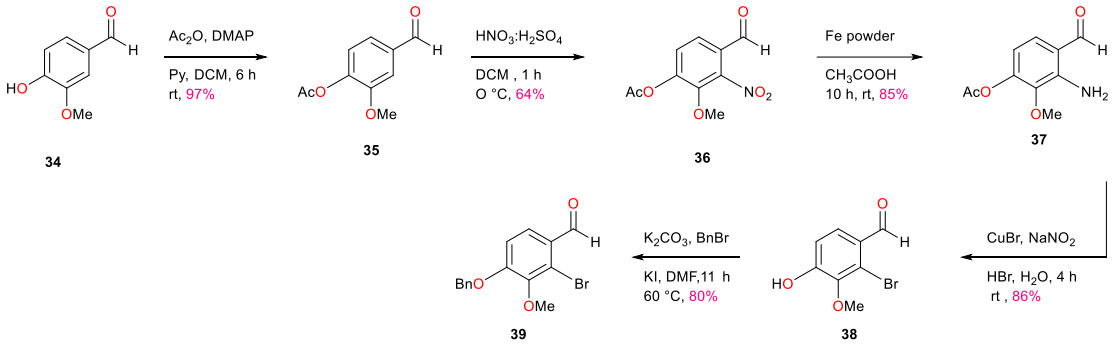
Synthesis of 3,4-dimethoxy-2-(3-methylbut-2-en-1-yl)benzaldehyde (13)

Procedure adapted from a literature procedure.

Sodium borohydride (0.9 g, 22.50 mmol, 2 eq) was added to a solution of **33** (5 g, 11.25 mmol, 1 eq.) in ethanol (50 ml) at ice bath temperature (0 °C) over a period of 1 h. the solution was then stirred at 0-5 °C for 2 h. and the resulting oxazoline was hydrolyzed with 5% aqueous HC1-THF and extracted with diethyl ether. The combined organic layers were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue obtained was purified by column chromatography to give **13** (1.7 g, 65%) as a yellow oil.

Data for 13: Page no. 4, SI.

Scheme S2. Synthesis of intermediate 23



Synthesis of 4-formyl-2-methoxyphenyl acetate (35)

Procedure adapted from a literature procedure.

Vanillin **34** (20 g, 131.58 mmol, 1 eq.) was suspended in methylene chloride (50 mL), and then acetic anhydride (40 g, 394.74 mmol, 3 eq.), DMAP (3.2 g, 26.32 mmol, 0.2 eq.) and pyridine (20.8 g, 263 mmol, 2 eq.) were added. The resultant solution was stirred at room temperature for 6 h. Water was added to the reaction mixture, and ethyl acetate was then added. The organic layer was washed with 1N HCl, a saturated sodium hydrogen carbonate aqueous solution, and saturated brine, and was dried with anhydrous sodium sulfate. The organic layer was filtered and concentrated under reduced pressure to give pure compound **35** (24.76 g, 97%). Exp. Mp 74-76 ℃ was matched with the reported mp 77 ℃.

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

Synthesis of 4-formyl-2-methoxy-3-nitrophenyl acetate (36)

Procedure adapted from a literature procedure.

A magnetically stirred suspension of vanillin acetate **35** (5.1 gm, 26.29 mmol, 1 eq.) in dichloromethane (20 ml) was cooled to 0 °C and then treated, dropwise over 0.5 h, with a mixture of HNO_3 (5.5 ml of a 77% aqueous solution) and H_2SO_4 (8.1 ml of a 98% aqueous solution). The ensuing mixture was diluted with dichloromethane (100 ml) and then treated with water (100 ml). The separated aqueous layer was extracted with dichloromethane (2x 50 ml). The combined organic phase were washed with $NaHCO_3$ (2 x 100 ml of a saturated aqueous solution) before being dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give nitrobenzaldehyde **36** (4.021 g, 64%) as a clear yellow oil. NMR results of the synthetic compound **36** align with the data published previously.

Data for 36:

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 7.70 (d, J = 8.5 Hz, 1H), 7.44 (d, J = 11.7 Hz, 1H), 3.95 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.84, 167.65, 149.23, 144.55, 126.25, 126.20, 125.66, 63.09, 20.92.

Synthesis of 3-amino-4-formyl-2-methoxyphenyl acetate (37)

Procedure adapted from a literature procedure.

To a solution of **36** (3.5 g, 14.65 mmol, 1 eq.) in acetic acid (43 ml) at room temperature was added iron powder (4.9 g, 87.87 mmol, 6 eq.). After stirring for 10 h, the residue iron powder was filtered out. Water (30 ml) was added to the mother liquor, and it was extracted with EtOAc (3 x 30 ml). The combined organic phase were washed with brine (20 ml), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography to give the title compound **37** (2.6 g, 85%) as a yellow solid; mp 82-84 °C.

Data for 37:

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.24 (d, *J* = 8.6 Hz, 1H), 6.43 (dd, *J* = 8.6, 0.6 Hz, 3H), 3.76 (s, 1H), 2.33 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 193.05, 168.31, 147.69, 145.20, 138.04, 131.19, 117.69, 110.75, 60.22, 20.87.

Synthesis of 2-bromo-4-hydroxy-3-methoxybenzaldehyde (38)

Procedure adapted from a literature procedure.

To a stirred solution of **37** (0.88 g, 4.24 mmol, 1 eq.) in HBr (2.3 ml, 48%) was added water (3.5 ml), and the mixture was cooled to 0 °C. A cold solution of sodium nitrite (0.44 g, 6.36 mmol, 1.5 eq.) in water (3.5 ml) was added dropwise for 10 min and the mixture was stirred for another 1 h. When diazotisation was complete, commercially available CuBr powder (0.61 g, 4.24 mmol, 1 eq.)) was added and the suspension was heated at 70 °C for 2 h when the solid product separated. The reaction mixture was cooled and extracted with ether (2 x 40 ml). The combined organic phase were washed with brine (5 ml), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography to give the title compound **38** (0.85 g, 86%) as a white solid (mp 149-151 °C, Lit. mp 154-155 °C).

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

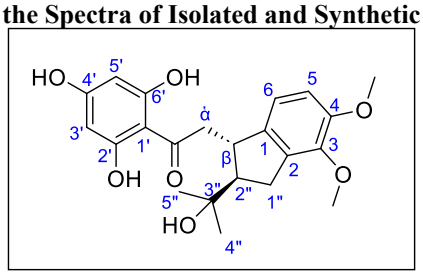
Synthesis of 4-(benzyloxy)-2-bromo-3-methoxybenzaldehyde (23)

Procedure adapted from a literature procedure.

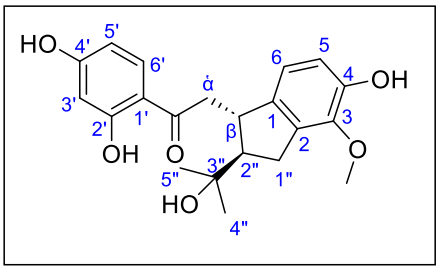
To a solution of **38** (0.79 g, 3.42mmol, 1 eq.) in DMF (7 mL) was added K_2CO_3 (1.4 g, 10.26 mmol, 3 eq.), KI (0.28 g, 1.7 mmol, 0.5 eq.), and the reaction was stirred for 30 min at room temperature; then benzyl bromide (1.2 g, 6.84 mmol, 2 eq.) was added to the solution. After stirring at 60 °C for 11 h, the reaction was quenched with a saturated solution of NH_4Cl, then extracted with ethyl acetate twice (30 mL each). The combined organic phase were washed with brine (5 ml), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography to give the title compound **23** (0.88 g, 80%). as a white solid (mp 98-100 °C, Lit. mp 99-101 °C).

* The melting point has been confirmed to align with the reported value, thus we proceeded to utilize it without any additional characterization.

Comparison of the Spectra of Isolated and Synthetic Compounds



Position	Antiarone K (Isolated)		Antiarone K (1) (synthetic)	
	δ_H (mult. *J*/Hz) 400 MHz	δ_C 100 MHz	δ_H (mult. *J*/Hz) 600 MHz	δ_C 150 MHz
1		142.1		142.1
2		137.0		137.0
3		145.8		145.7
4		152.1		152.1
5	6.76, d (8.2)	112.8	6.76, d (8.2)	112.7
6	6.83, d (8.2)	119.7	6.82, d (8.2)	119.7
1’		105.7		105.6
2’		165.4		165.5
3’	5.94, s	95.9	5.93, s	95.8
4’		165.4		165.5
5’	5.94, s	95.9	5.93, s	95.8
6’		165.4		165.5
1”	3.06, dd (17.2, 4.4)	31.1	3.05, dd (17.1, 9.0)	31.1
	2.95, dd (17.2, 8.8)		2.95, dd (17.1, 4.2)	
2”	2.35, dt (8.8, 4.4)	56.2	2.34, dt (9.0, 4.1)	56.2
3”		72.7		72.6
4”	1.06, s	27.1	1.05, s	27.1
5”	1.08, s	28.0	1.07, s	27.9
α	3.32, dd (16.7, 6.8)	52.6	3.30, dd (16.8, 7.2)	52.6
	3.48, dd (16.7, 6.8)		3.46, dd (16.7, 6.3)	
β	3.82, dt (6.8, 4.4)	43.3	3.80, dt (6.5, 3.5)	43.2
C=O		205.6		205.6
-OMe-3	3.78, s	59.9	3.77, s	59.9
-OMe-4	3.78, s	56.4	3.77, s	56.3
-OH	11.78, br s		11.90, s	
-OH	11.78, br s		11.90, s	
-OH-3”			3.65, s	



Position	Renifolin F (Isolated)		Renifolin F (2) (synthetic)	
	δ_H (mult. *J*/Hz) 400 MHz	δ_C 100 MHz	δ_H (mult. *J*/Hz) 600 MHz	δ_C 150 MHz
1		139.9		140.0
2		135.9		135.9
3		144.1		144.2
4		149.0		149.0
5	6.63, d (8.1)	115.7	6.63, d (8.1)	115.7
6	6.69, d (8.1)	120.1	6.70, d (9.0)	120.1
1’		114.2		114.2
2’		166.3		166.4
3’	6.34, d (2.2)	103.5	6.34, d (2.4)	103.6
4’		165.6		165.6
5’	6.41, dd (8.8, 2.2)	108.8	6.42, dd (8.9, 2.4)	108.8
6’	7.83, d (8.8)	133.9	7.85, d (8.8)	133.9
1”	3.11, dd (16.9, 9.0)	31.5	3.12, dd (16.8, 9.0)	31.5
	2.92, dd (16.9, 4.6)		2.94, dd (16.8, 5.0,)	
2”	2.37, br t (4.4)	56.7	2.38, dt (9.3, 4.9)	56.7
3”		72.7	3.66, s	72.6
4”	1.10, s	26.6	1.11, s	26.7
5”	1.12, s	28.4	1.13, s	28.5
α	3.34, dd (16.3, 6.0)	46.5	3.35, dd (16.3, 6.2)	46.5
	3.20, dd (16.3, 7.2)		3.21, dd (16.4, 7.2)	
β	3.78, overlapped	43.0	3.77, overlapped	43.1
C=O		205.4		205.4
-OMe-3	3.80, s	60.0	3.80, s	60.0
-OH-4	12.66, s			
-OH-2′	12.89, s		12.89, s	
-OH-4′	12.45, s			

NMR Spectra of New Compounds and Selected Known Compounds

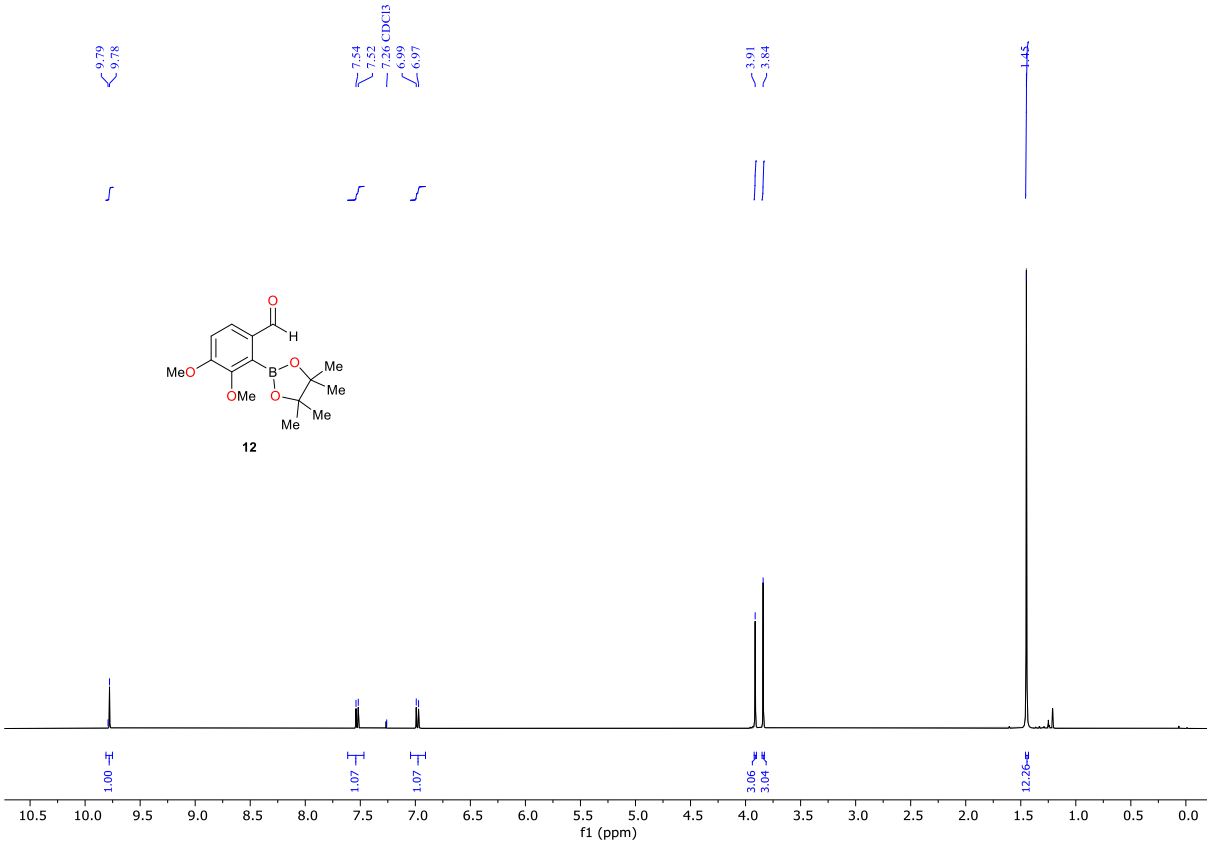


Figure S1. ^{1}H NMR of **12** ($CDCl_3$, 400 MHz)

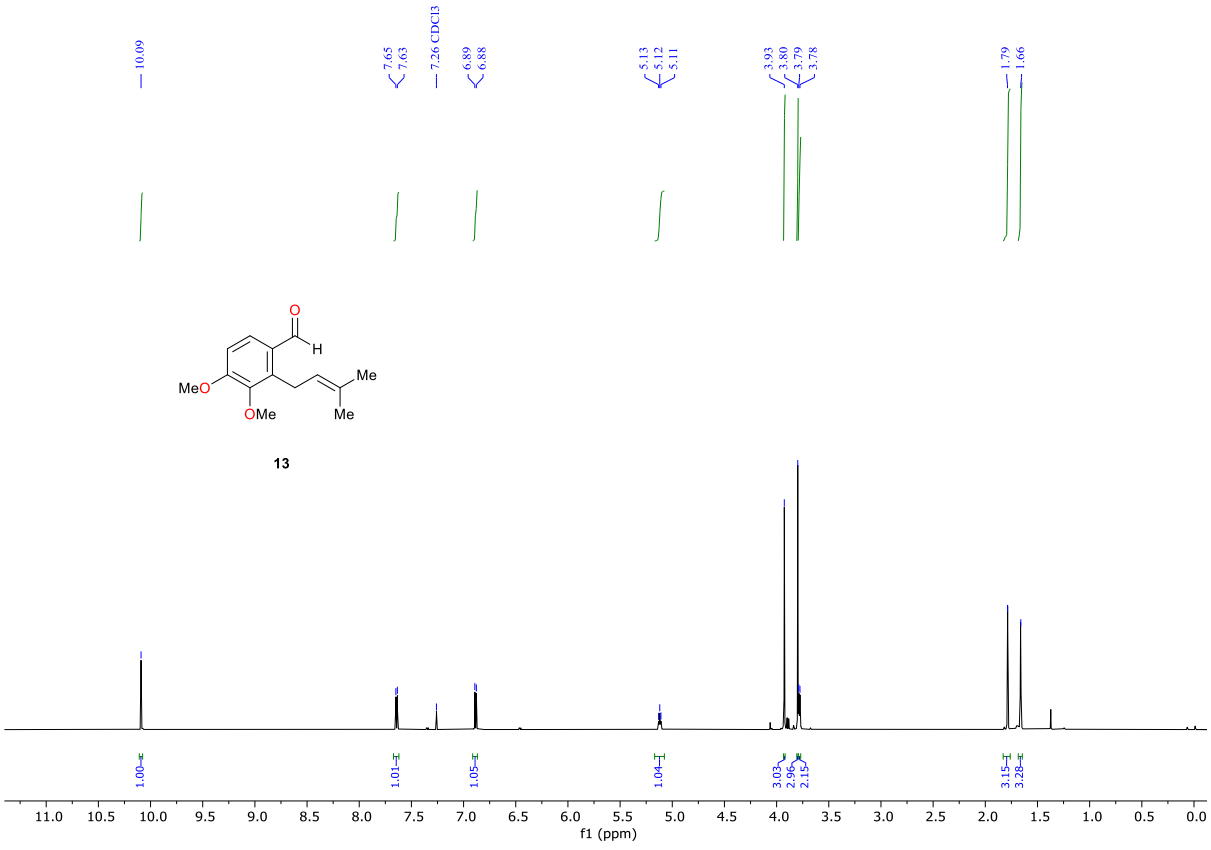


Figure S2. ^{1}H NMR of **13** ($CDCl_3$, 600 MHz)

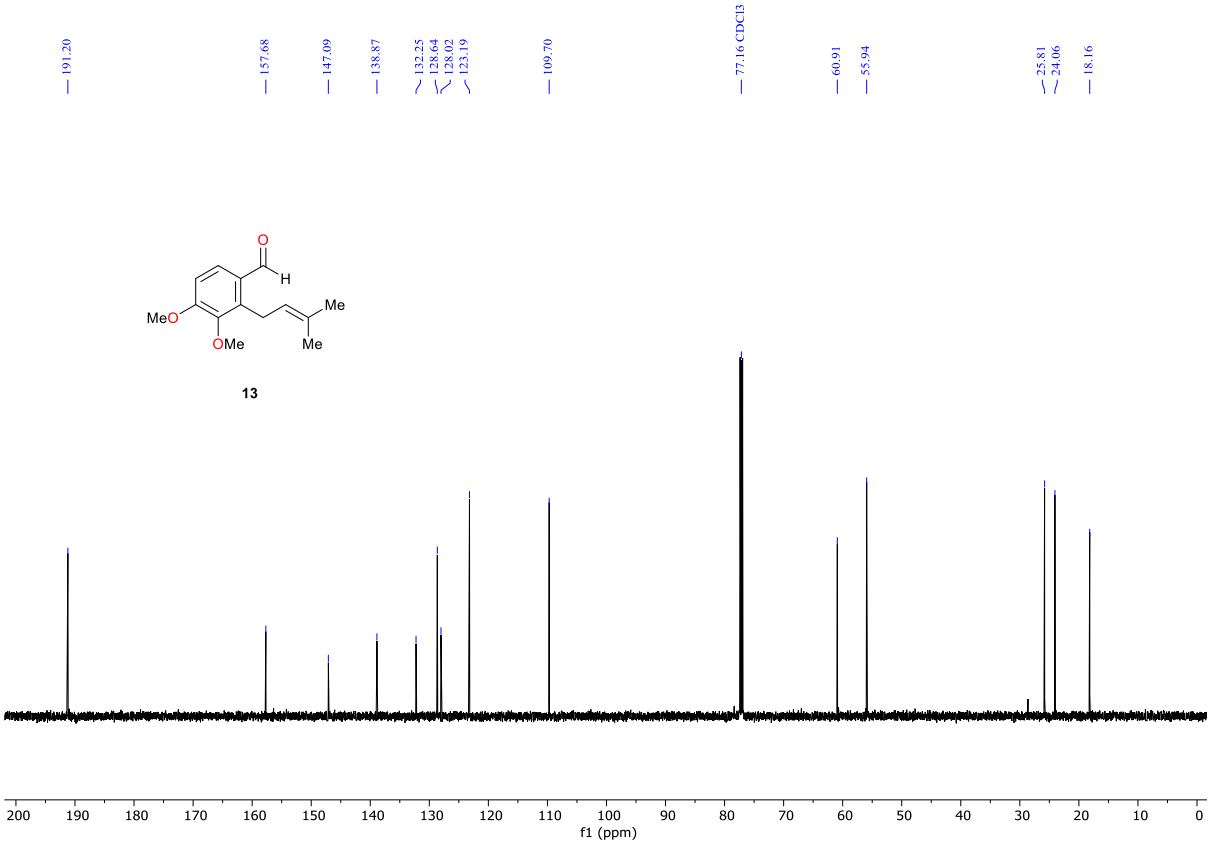


Figure S3. ^{13}C NMR of **13** ($CDCl_3$, 150 MHz)

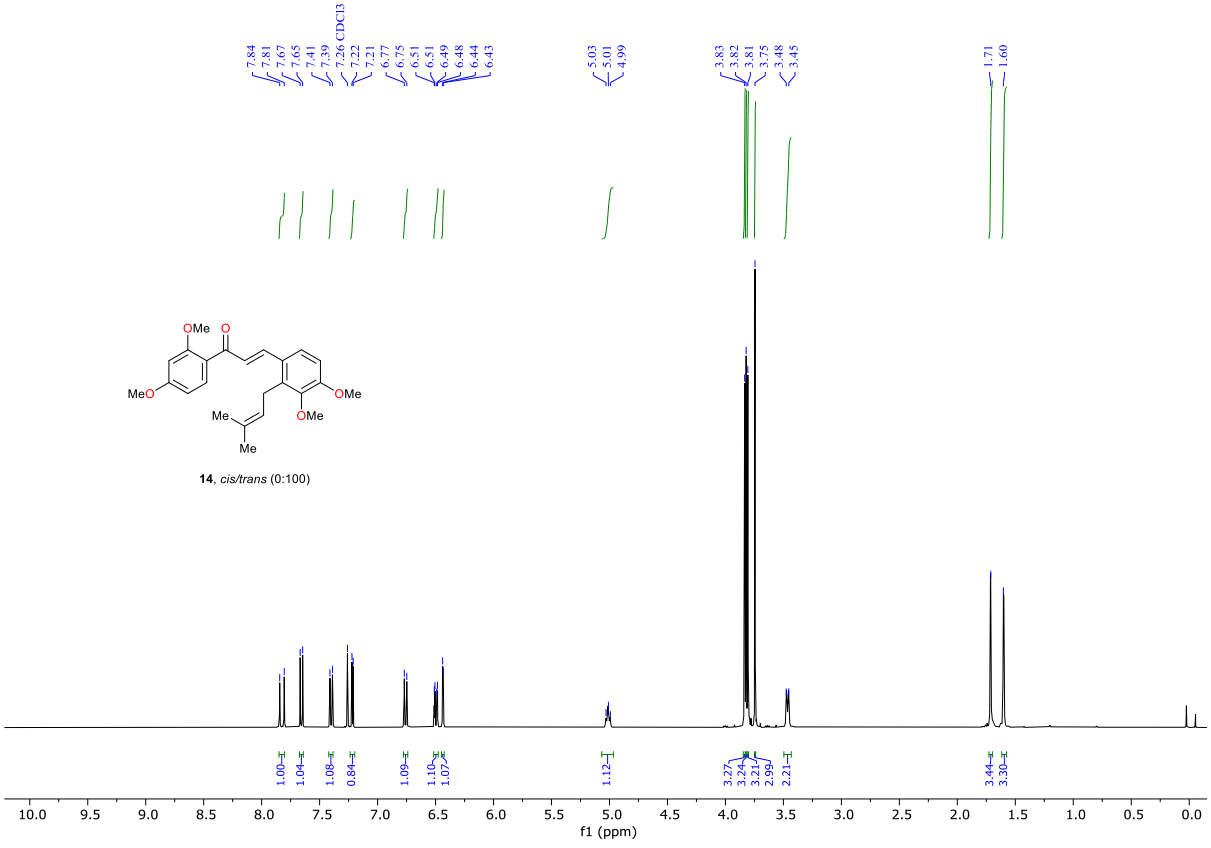


Figure S4. ^{1}H NMR of **14** ($CDCl_3$, 400 MHz)

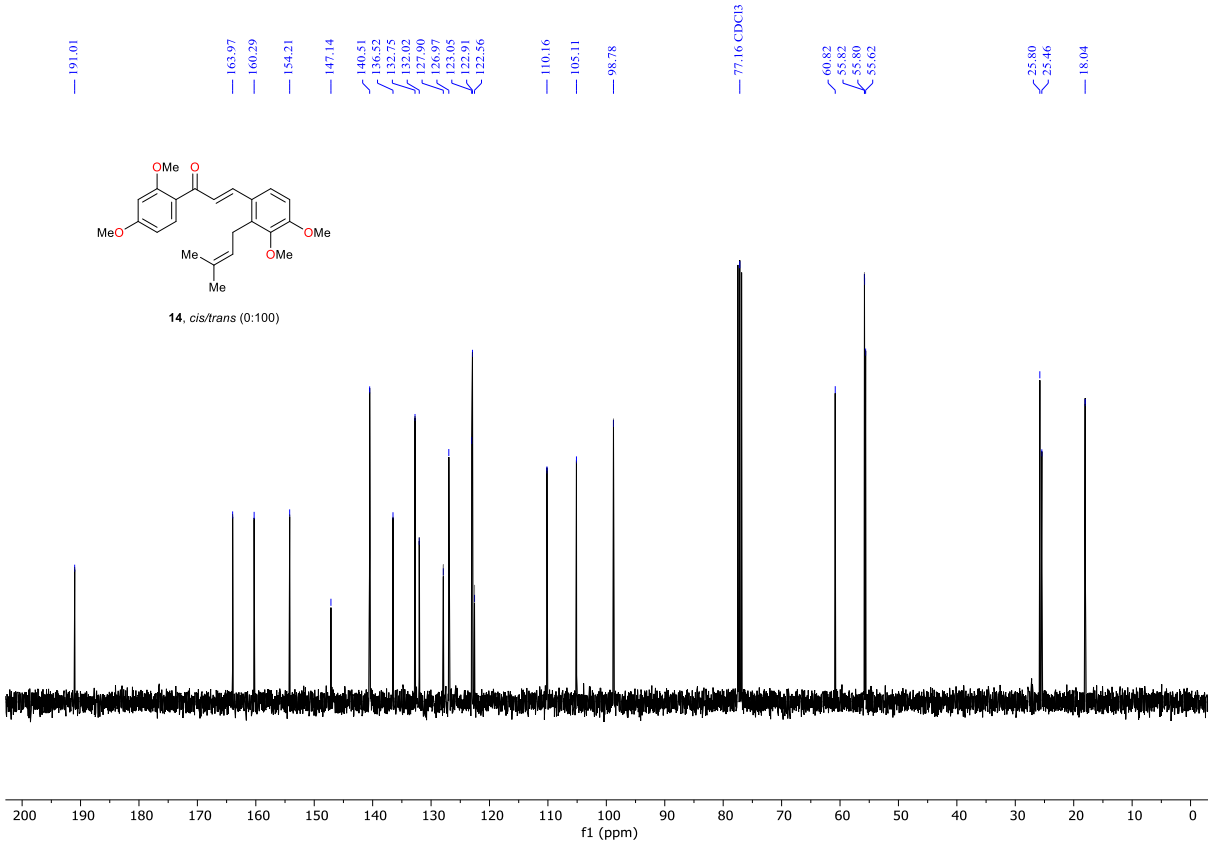


Figure S5. ^{13}C NMR of **14** ($CDCl_3$, 100 MHz)

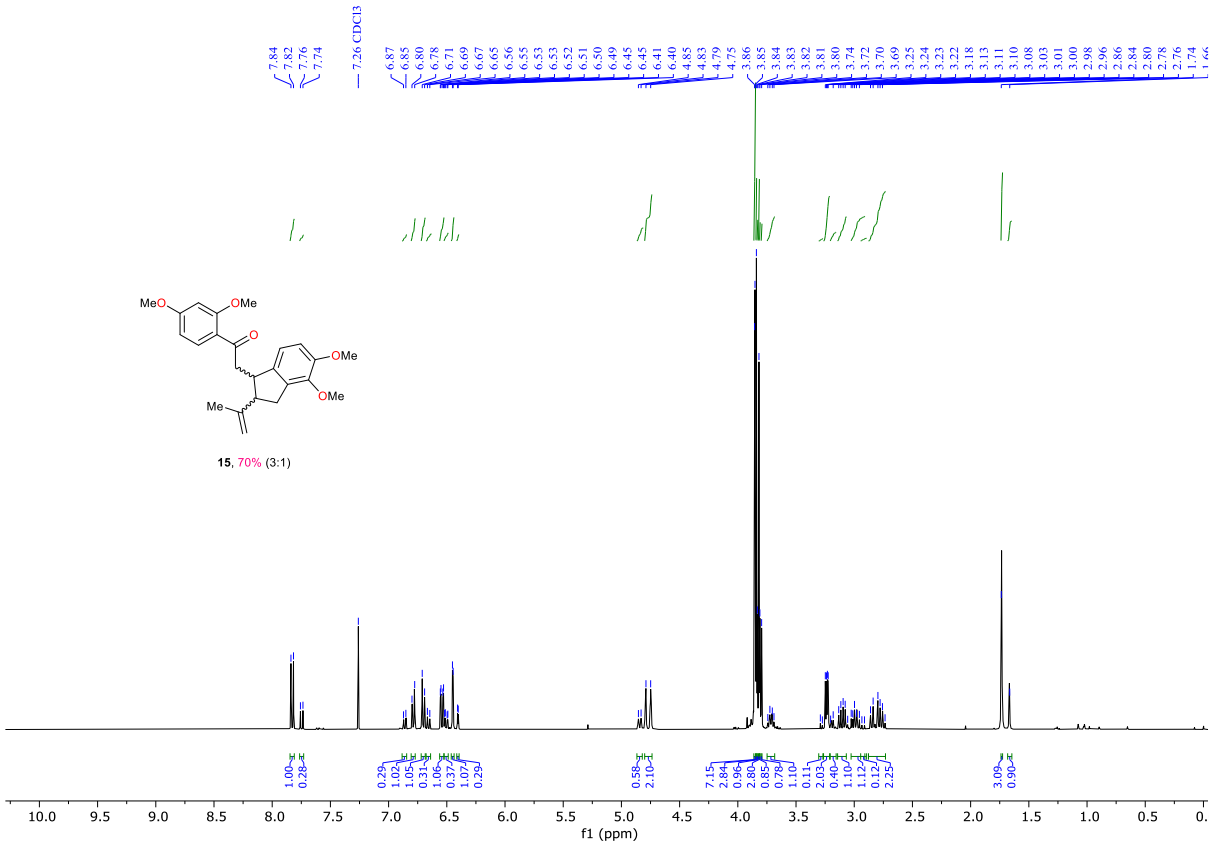


Figure S6. ^{1}H NMR of **15** ($CDCl_3$, 400 MHz)

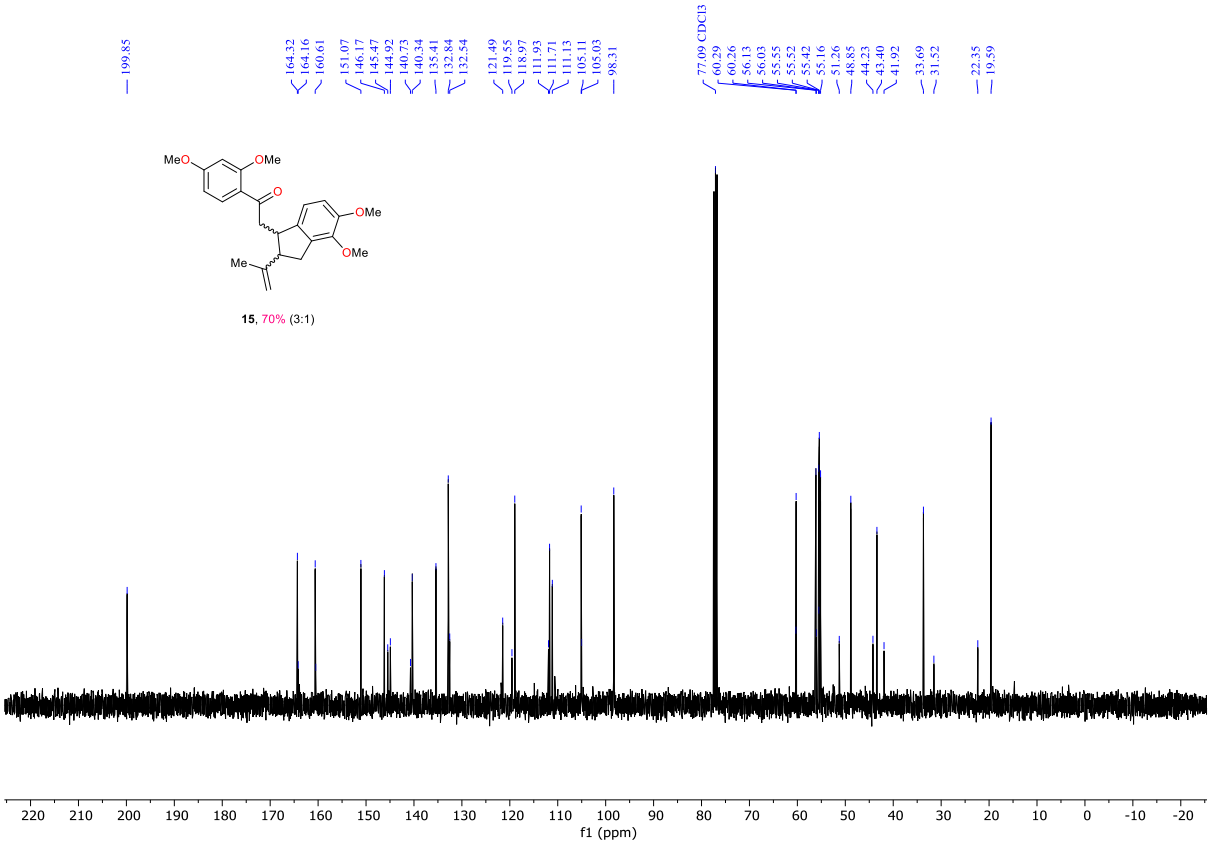


Figure S7. ^{13}C NMR of **15 (**$CDCl_3$, 100 MHz)

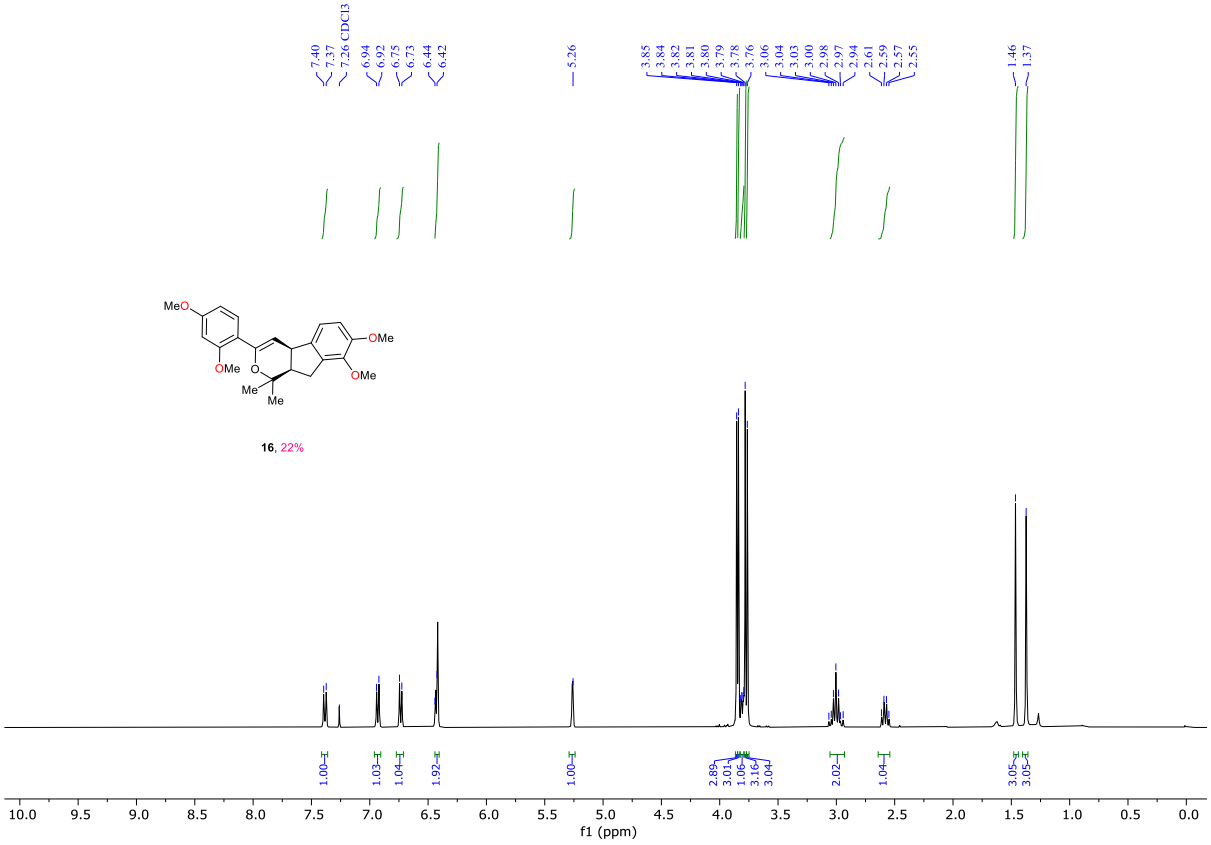


Figure S8. ^{1}H NMR of **16** ($CDCl_3$, 400 MHz)

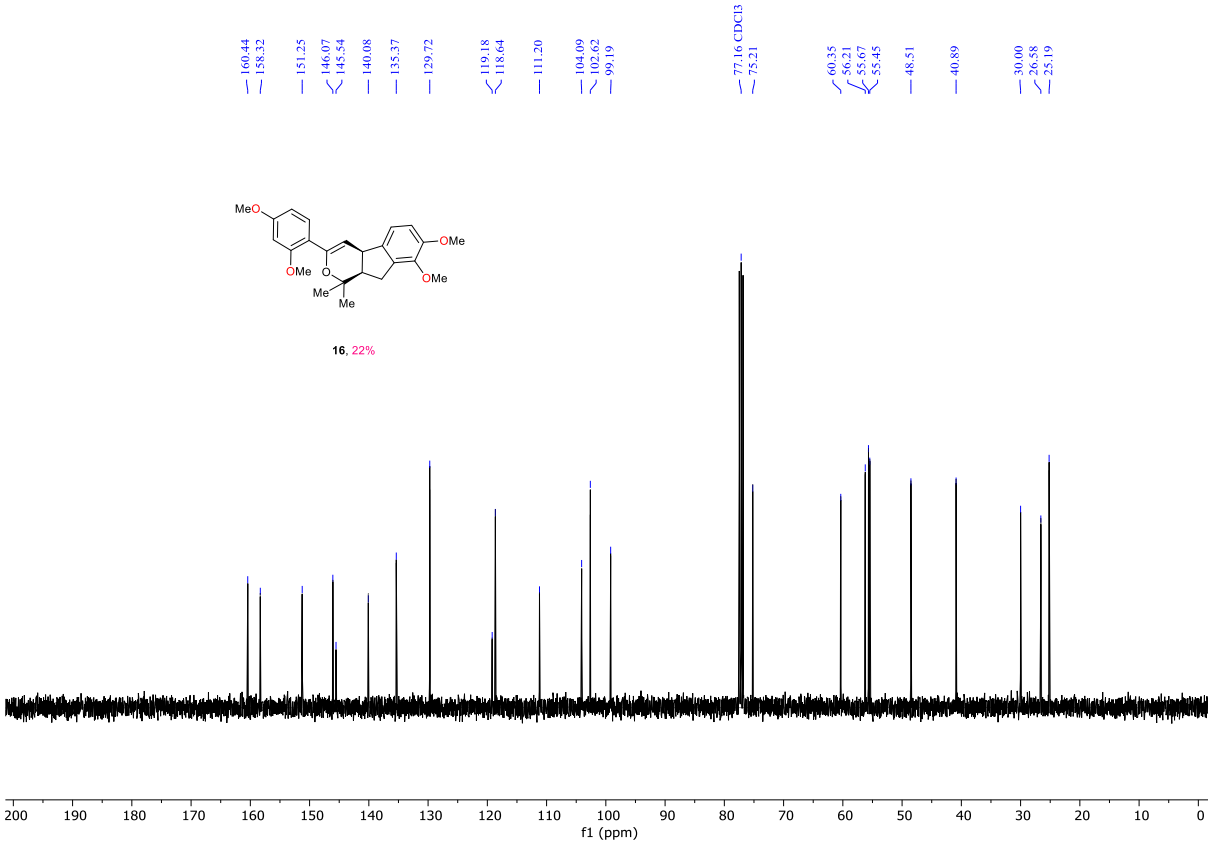


Figure S9. ^{13}C NMR of **16** (CDCl$_3$, 100 MHz)

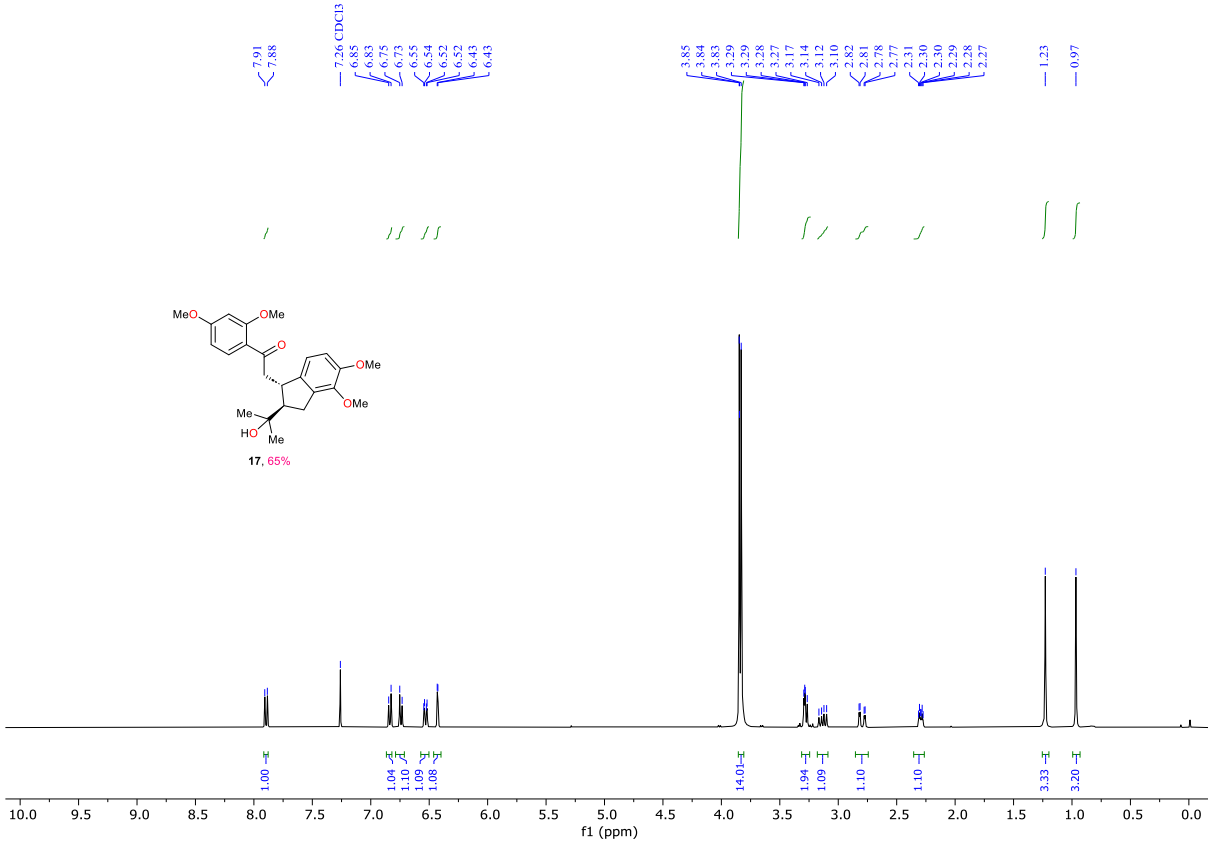


Figure S10. ^{1}H NMR of **17** (CDCl$_3$, 600 MHz)

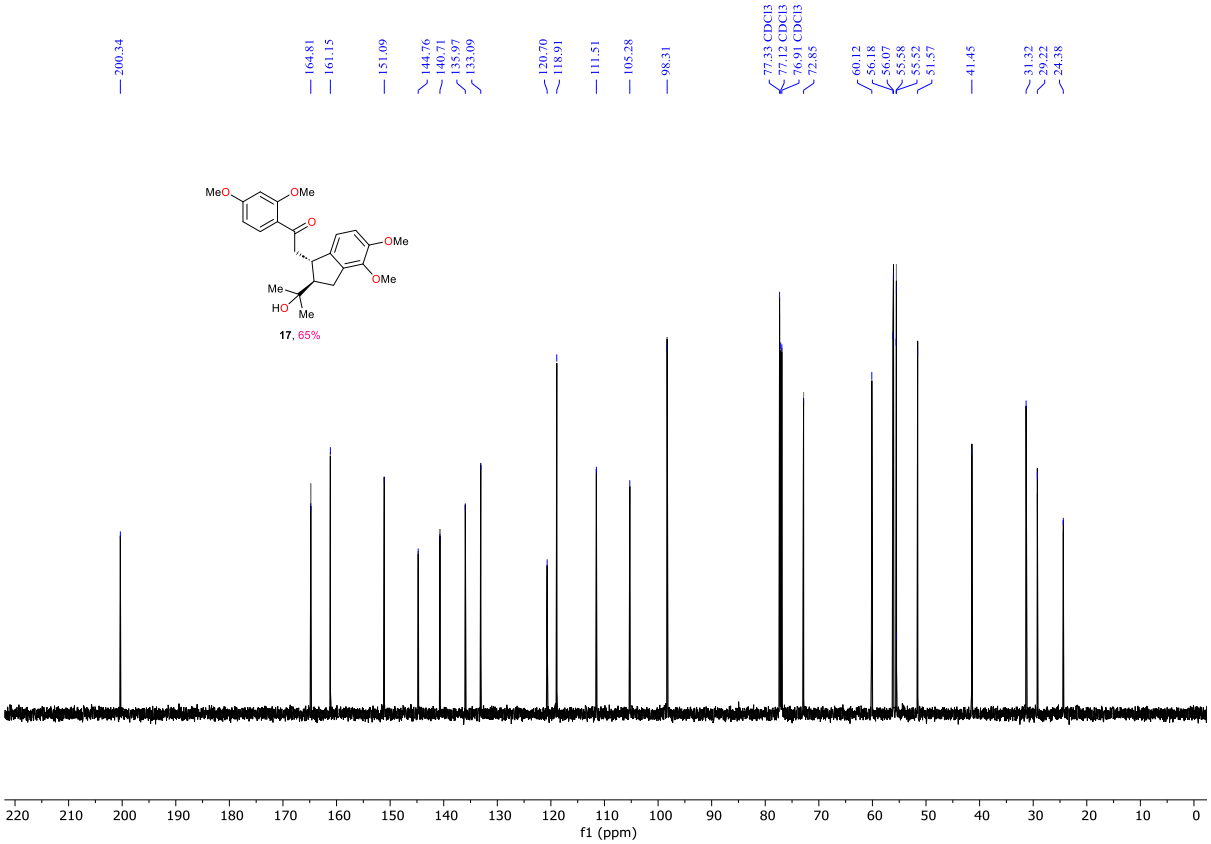


Figure S11. ^{13}C NMR of **17** ($CDCl_3$, 150 MHz)

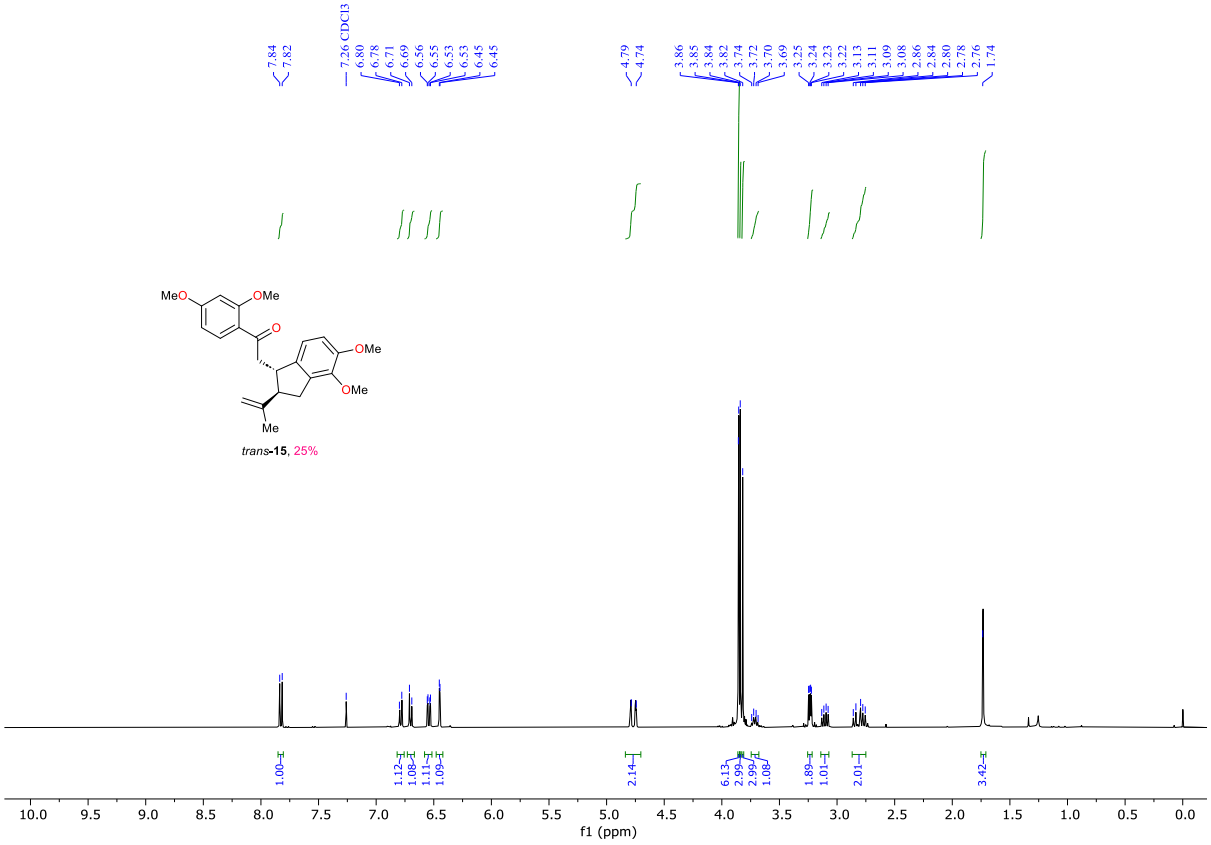


Figure S12. ^{1}H NMR of *trans*-**15** ($CDCl_3$, 400 MHz)

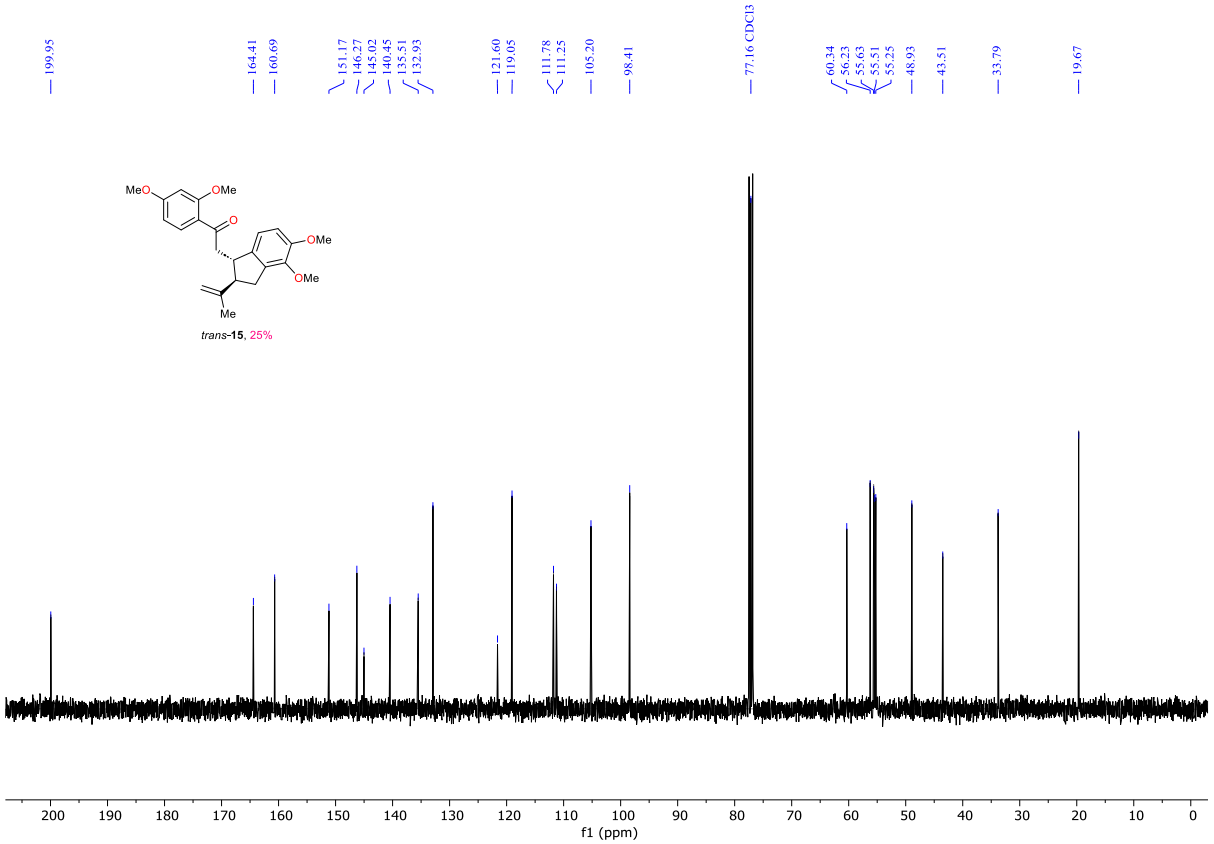


Figure S13. ^{13}C NMR of *trans*-**15** ($CDCl_3$, 100 MHz)

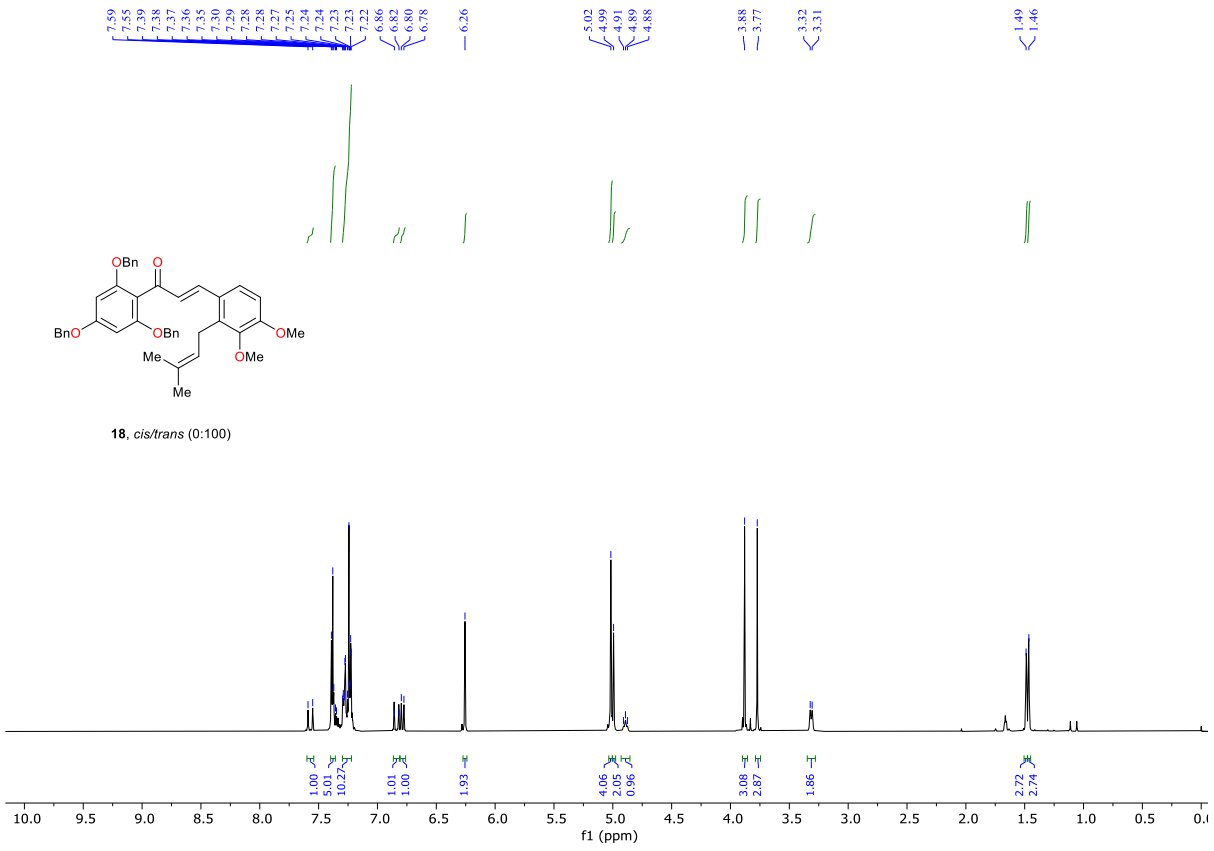


Figure S14. ^{1}H NMR of **18** ($CDCl_3$, 400 MHz)

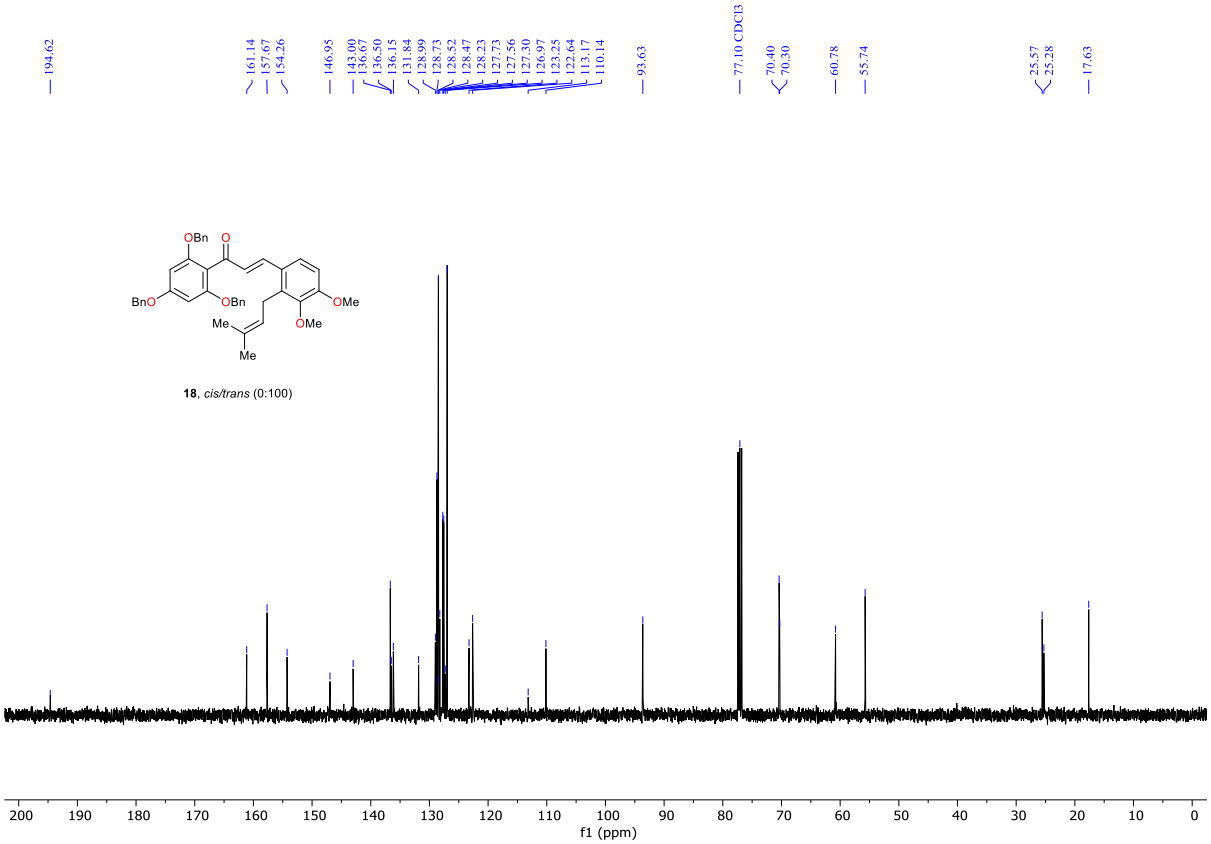


Figure S15. ^{13}C NMR of **18** ($CDCl_3$, 100 MHz)

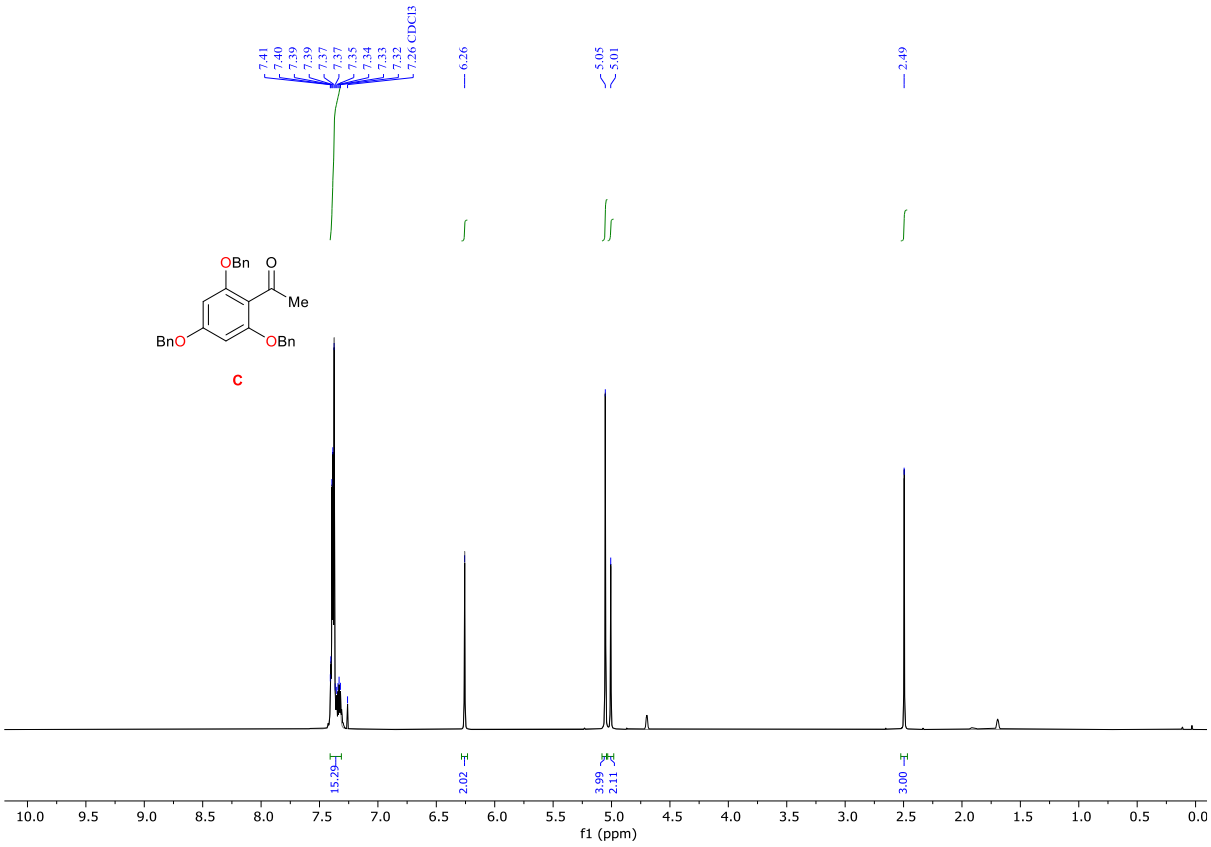


Figure S16. ^{1}H NMR of **C** ($CDCl_3$, 400 MHz)

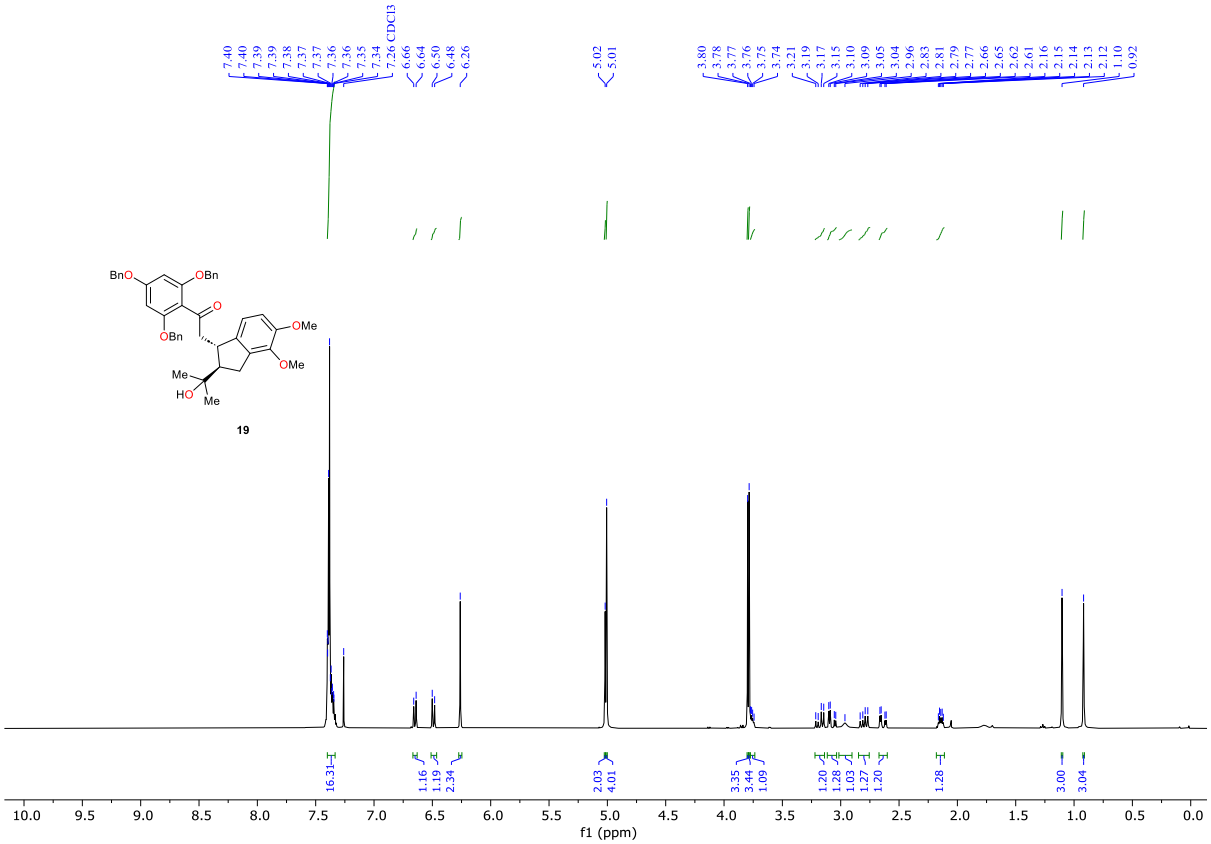


Figure S17. ^{1}H NMR of **19** ($CDCl_3$, 400 MHz)

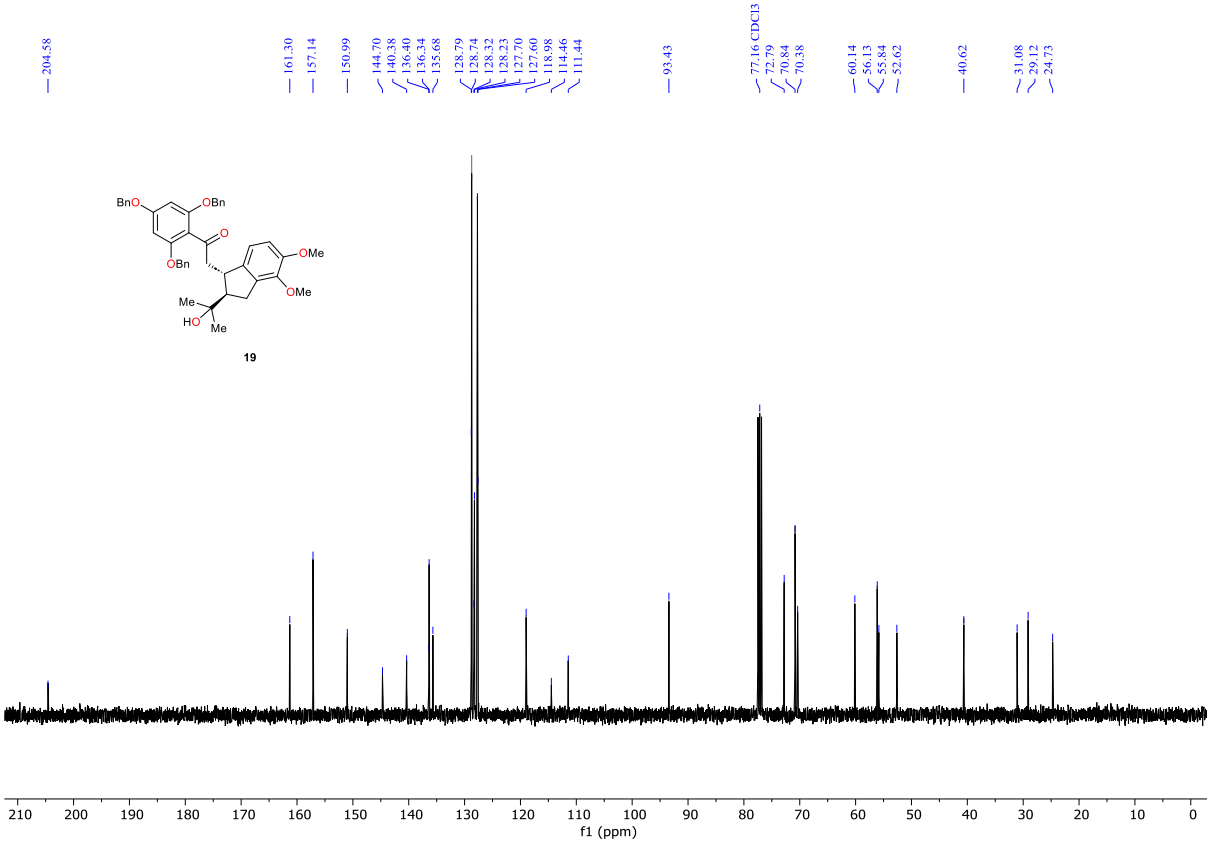


Figure S18. ^{13}C NMR of **19** ($CDCl_3$, 100 MHz)

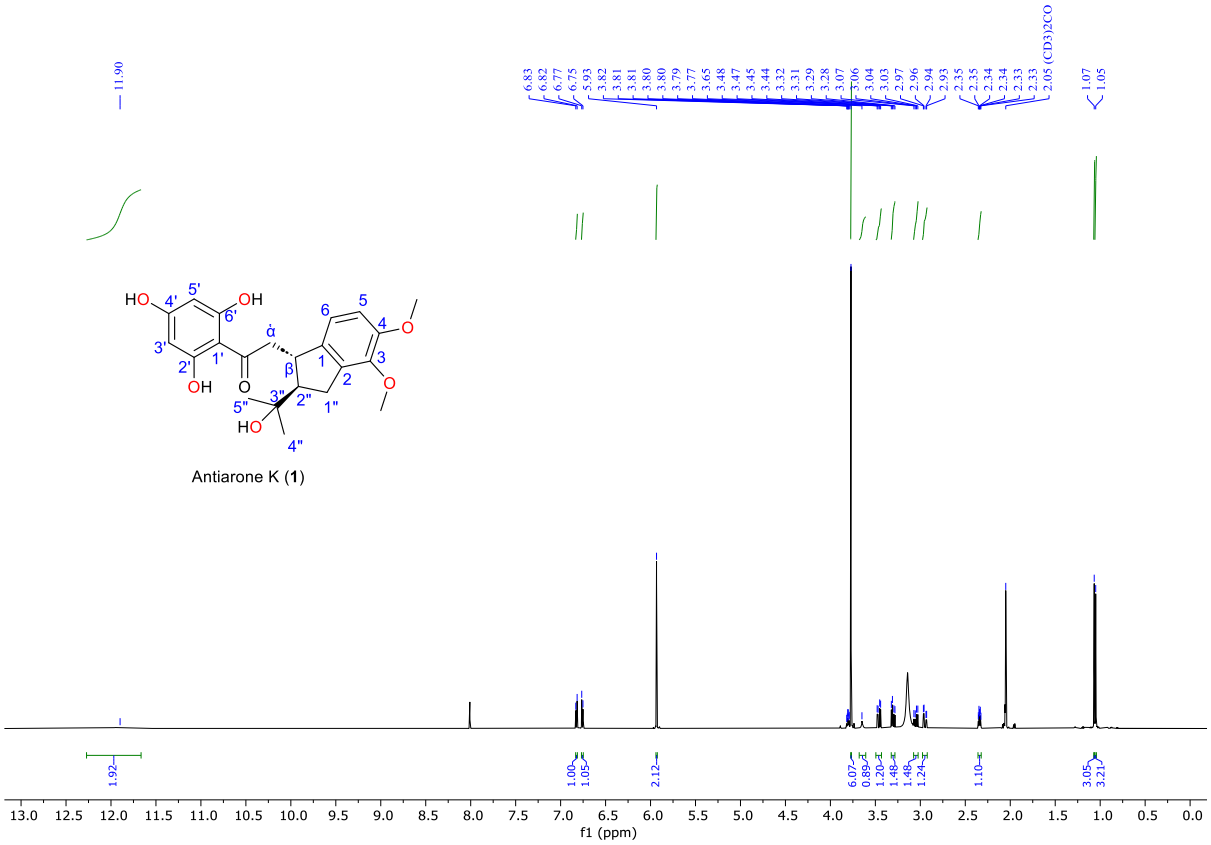


Figure S19. ^{1}H NMR of antiarone K (**1**) (acetone-d$_6$, 600 MHz)

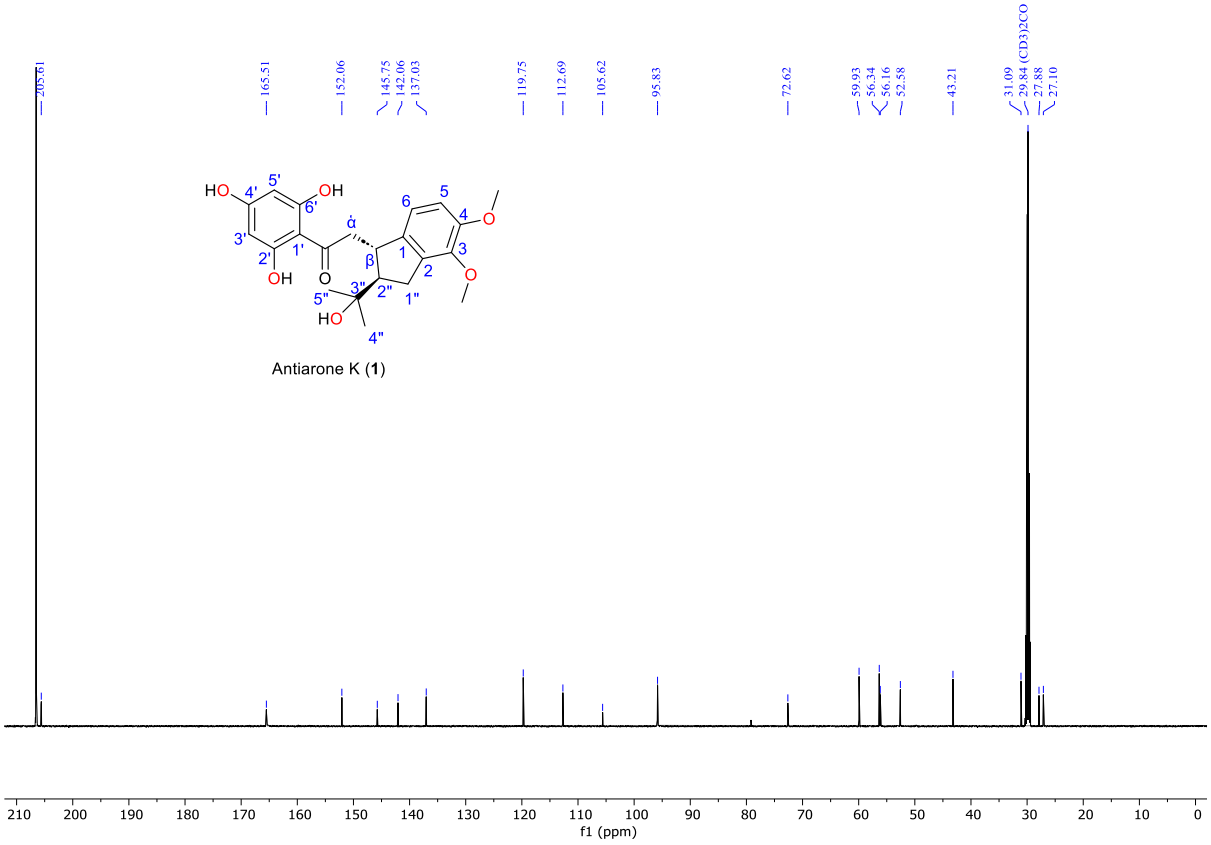


Figure S20. ^{13}C NMR of antiarone K (**1**) (acetone-d$_6$, 150 MHz)

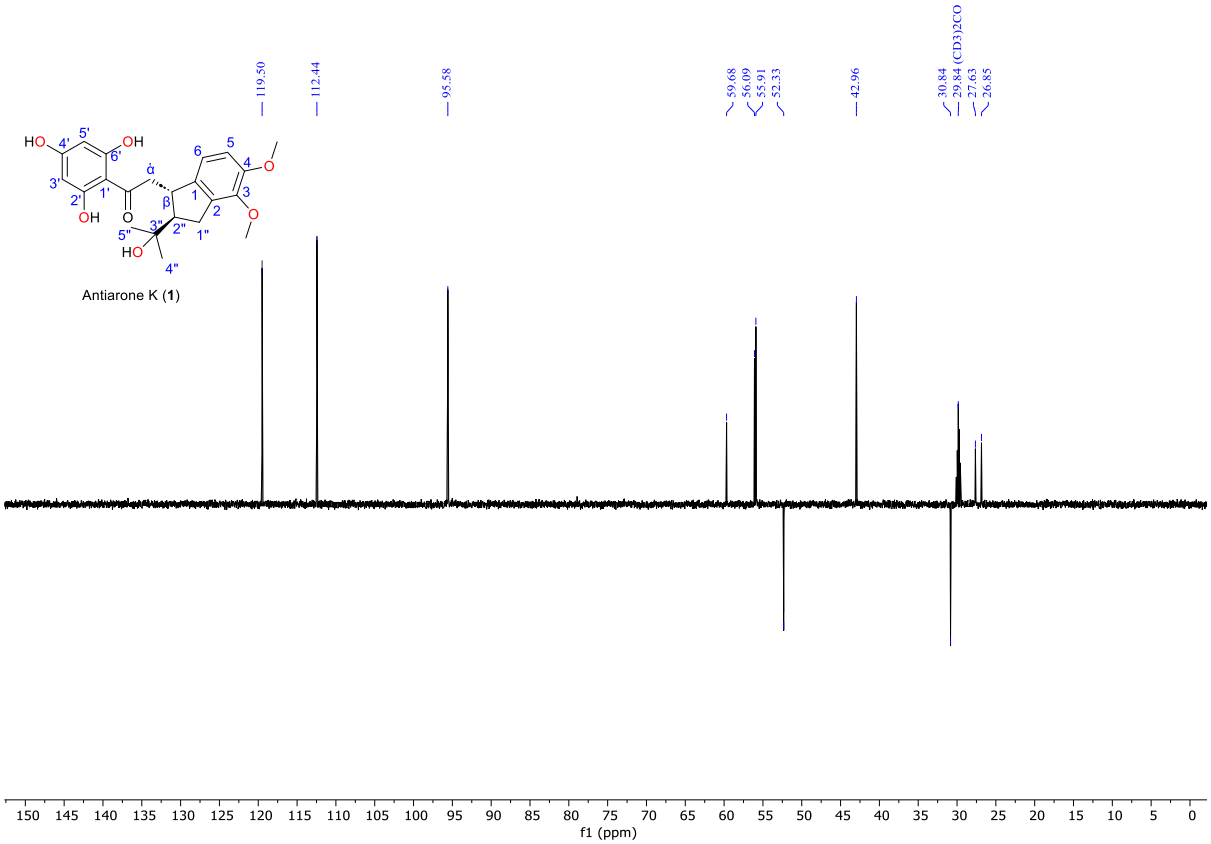


Figure S21. DEPT of antiarone K (**1**) (acetone-d_6, 150 MHz)

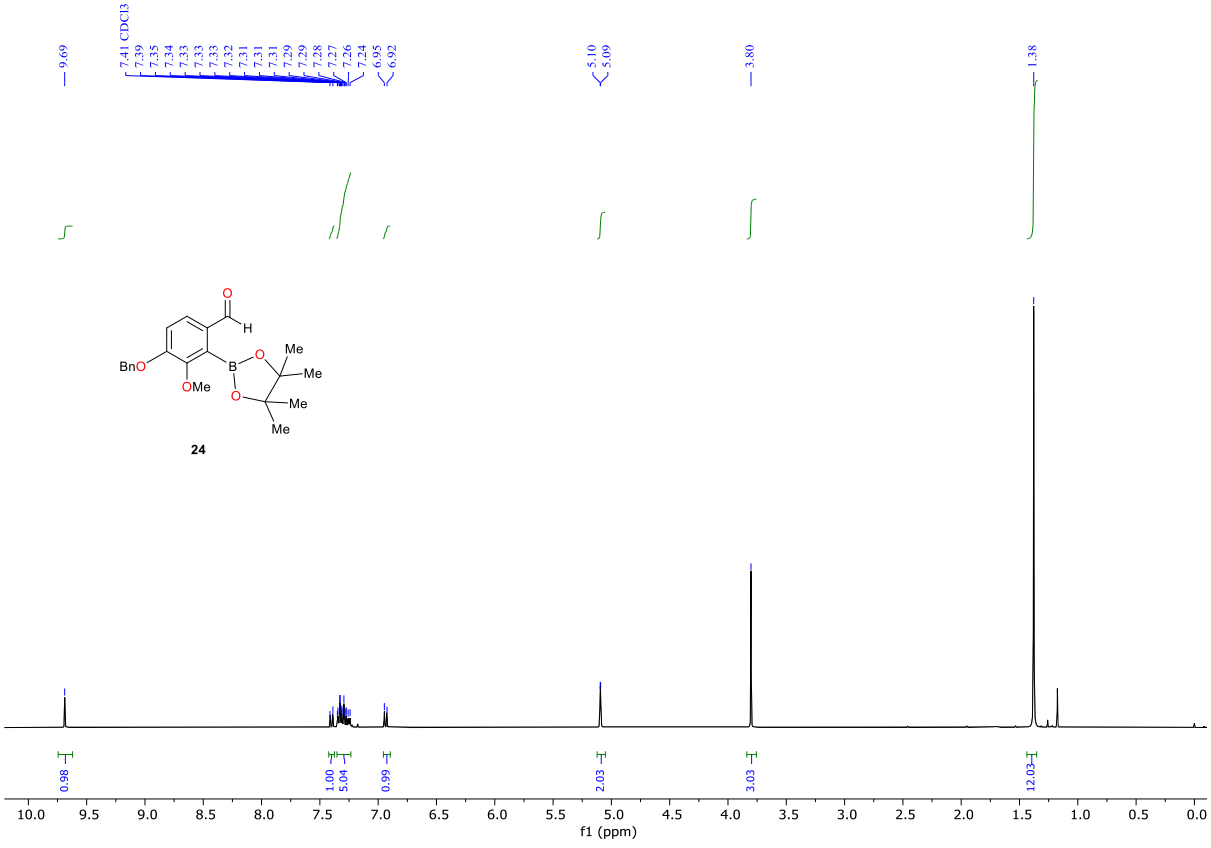


Figure S22. ^{1}H NMR of **24** ($CDCl_3$, 400 MHz)

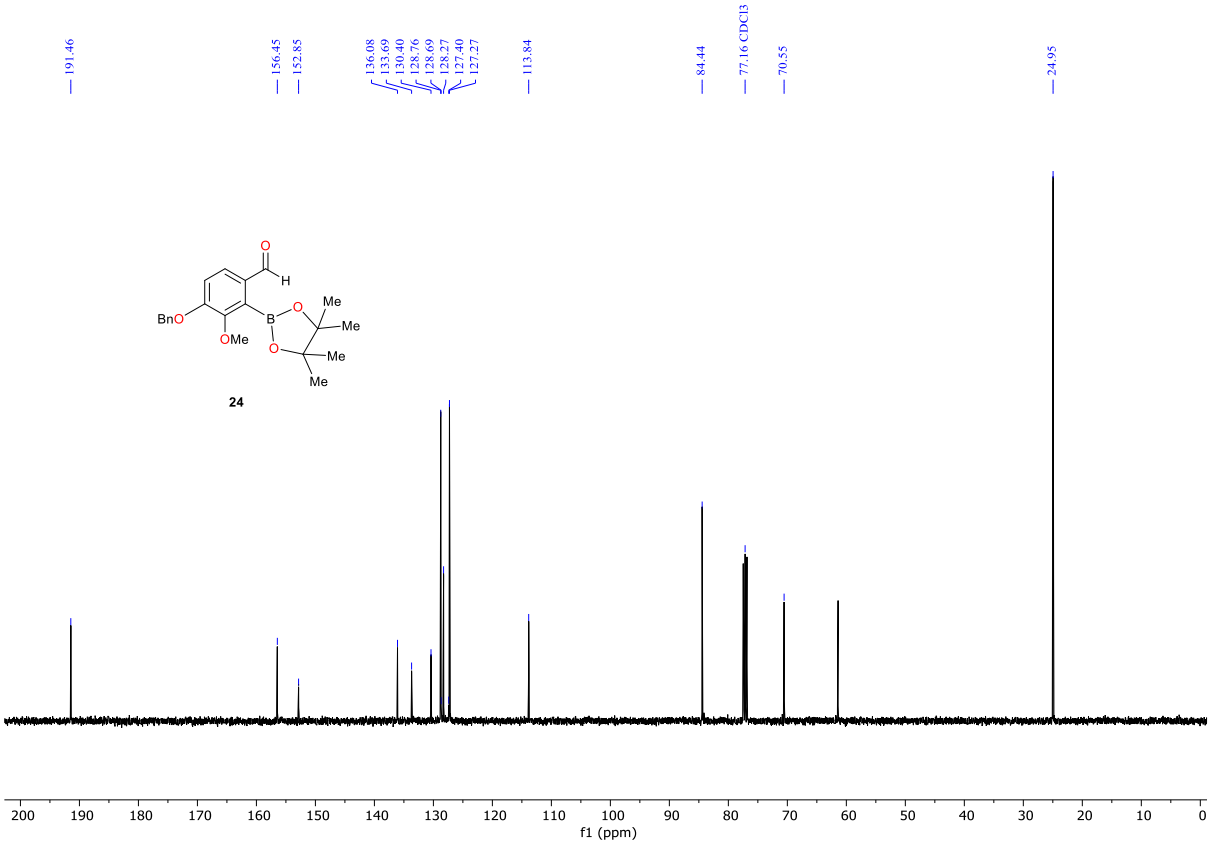


Figure S23. ^{13}C NMR of **24** ($CDCl_3$, 100 MHz)

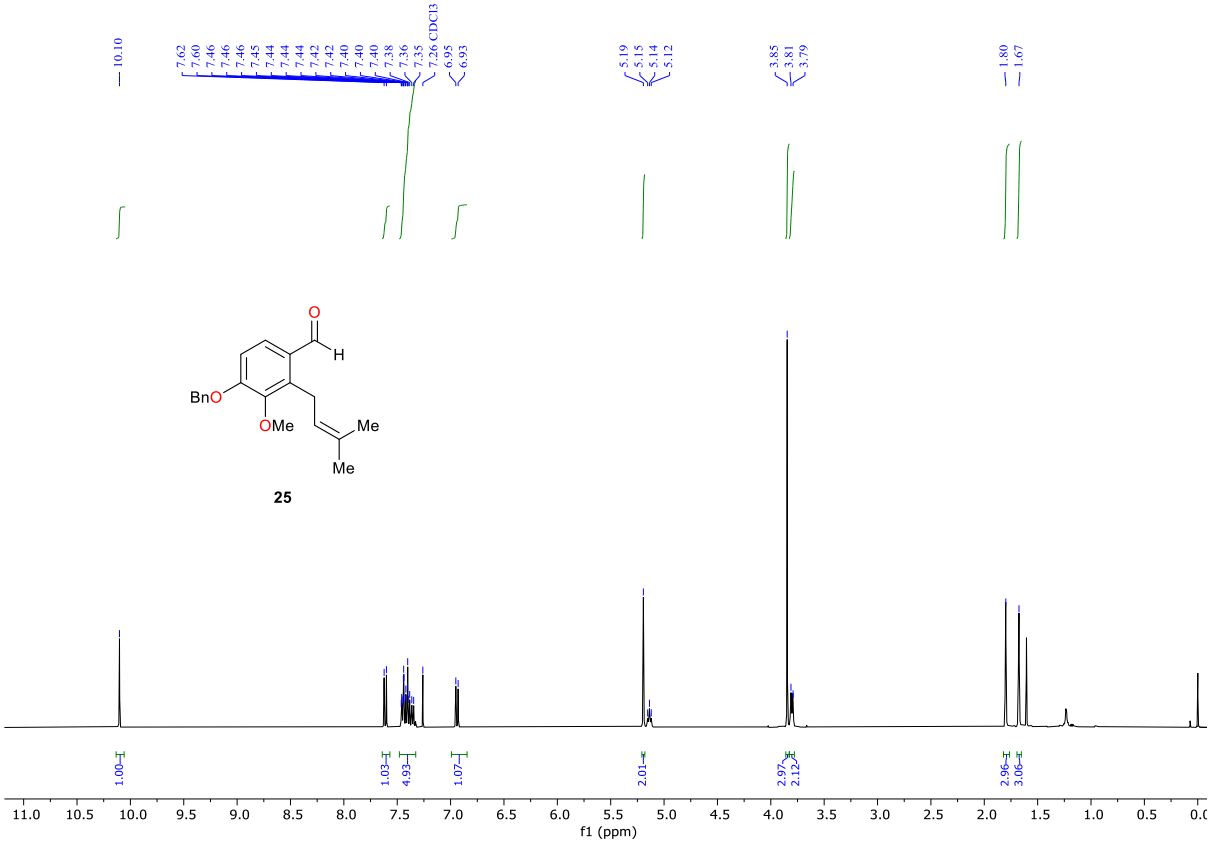


Figure S24. ^{1}H NMR of **25** ($CDCl_3$, 400 MHz)

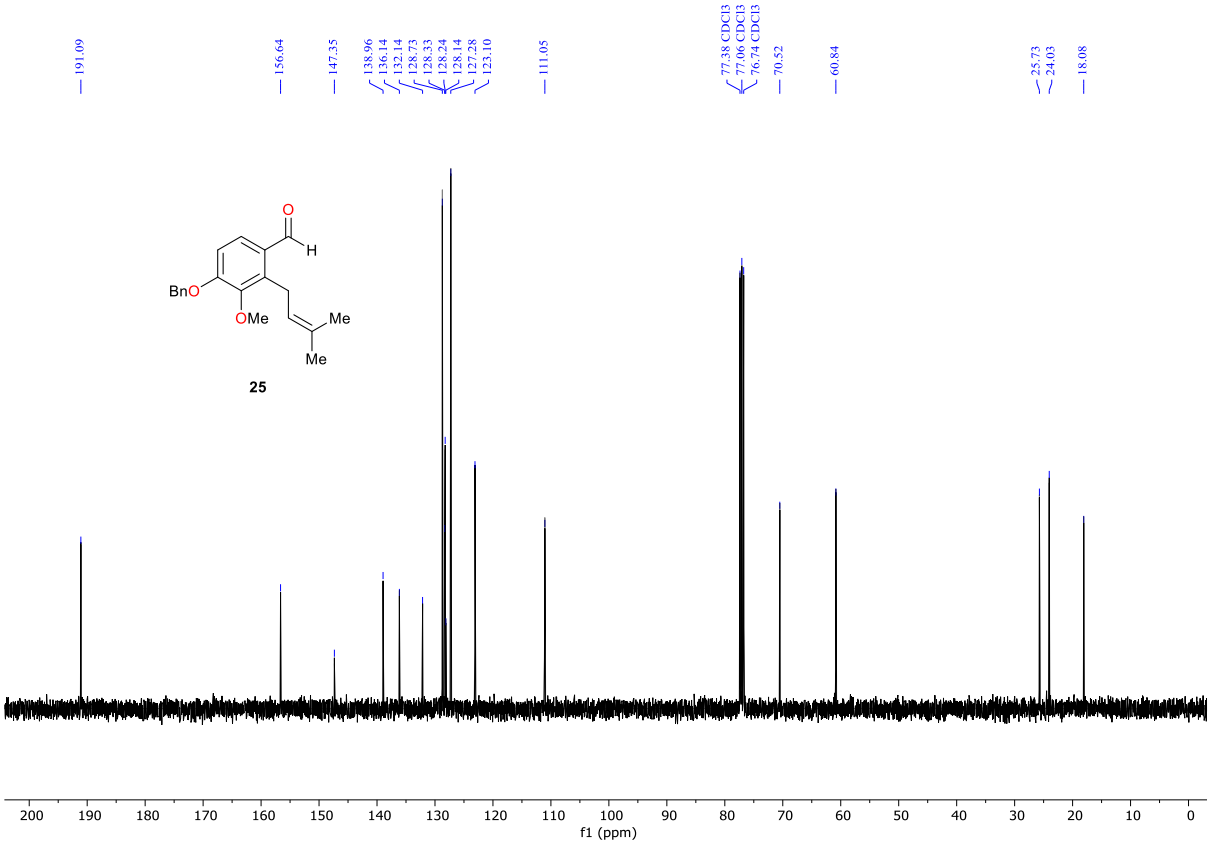


Figure S25. ^{13}C NMR of **25** ($CDCl_3$, 100 MHz)

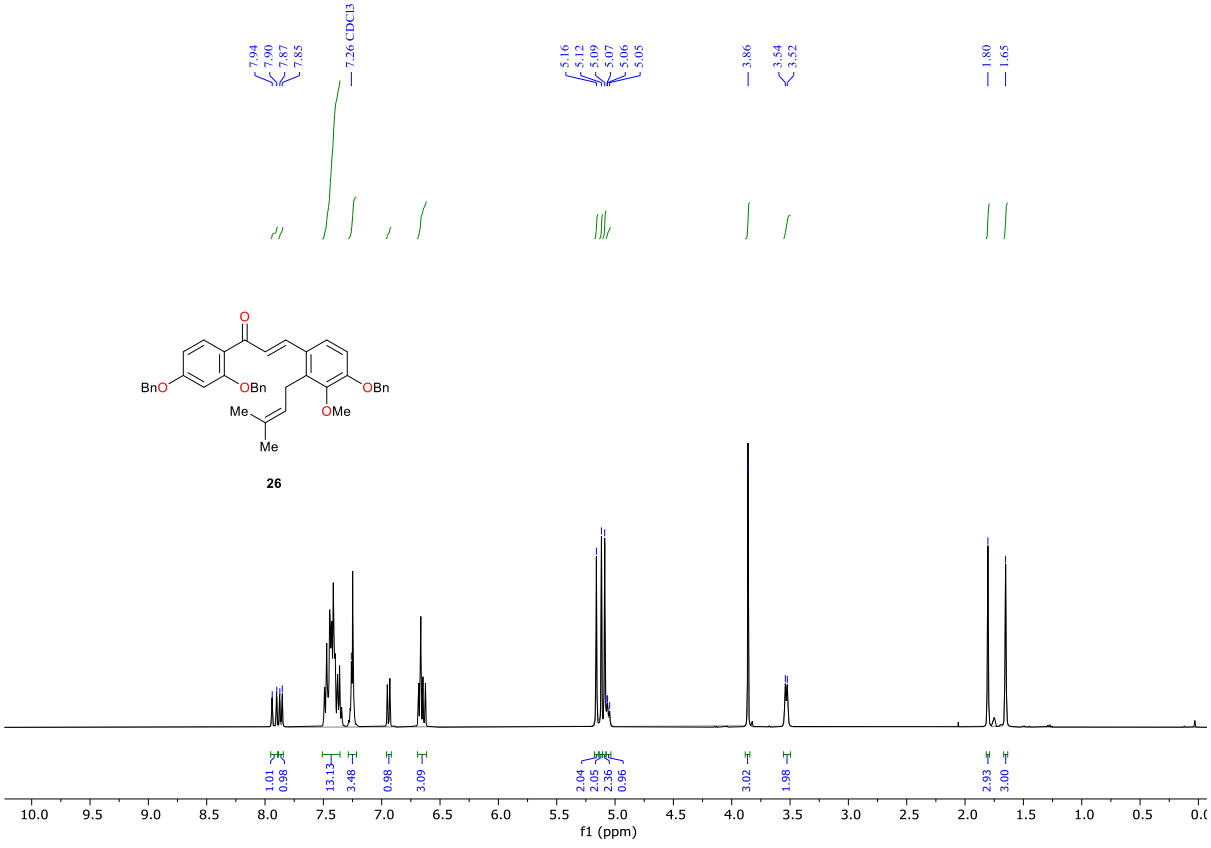


Figure S26. ^{1}H NMR of **26** ($CDCl_3$, 400 MHz)

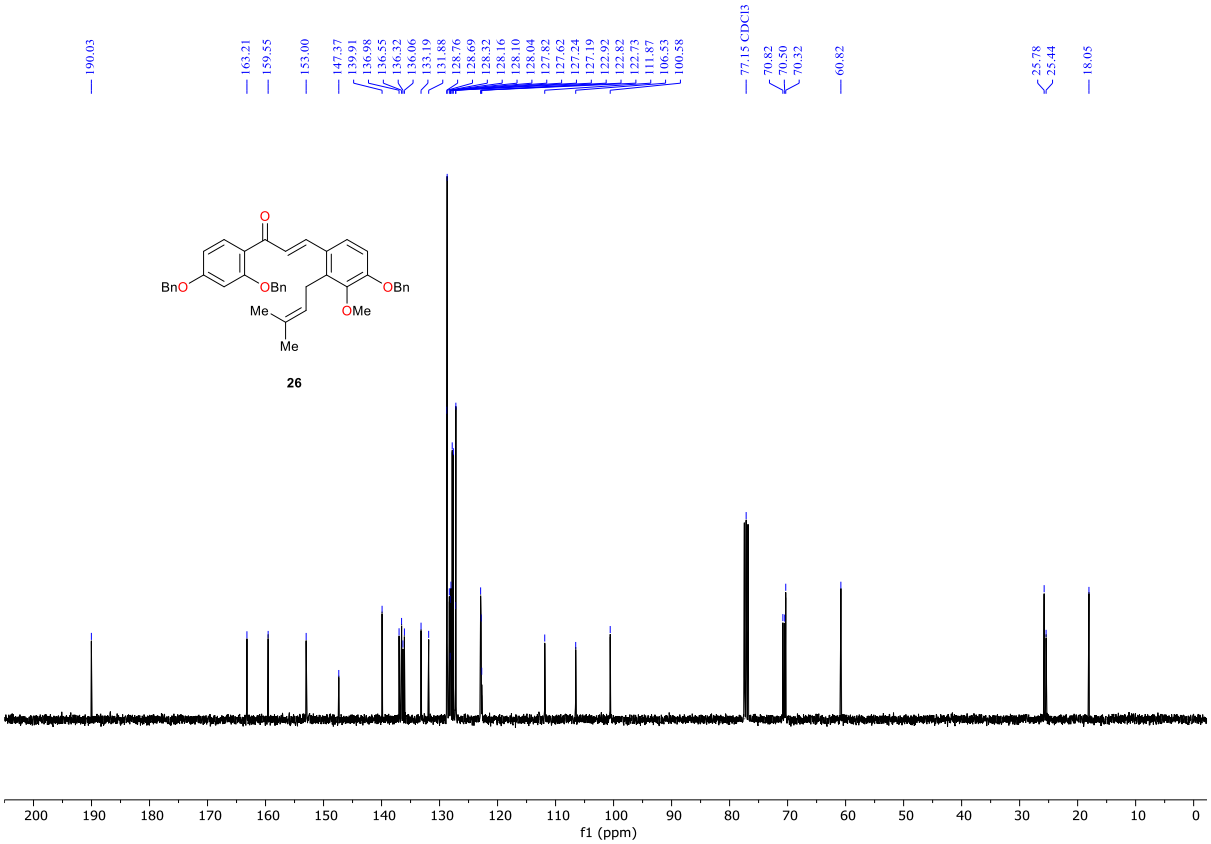


Figure S27. ^{13}C NMR of **26** ($CDCl_3$, 100 MHz)

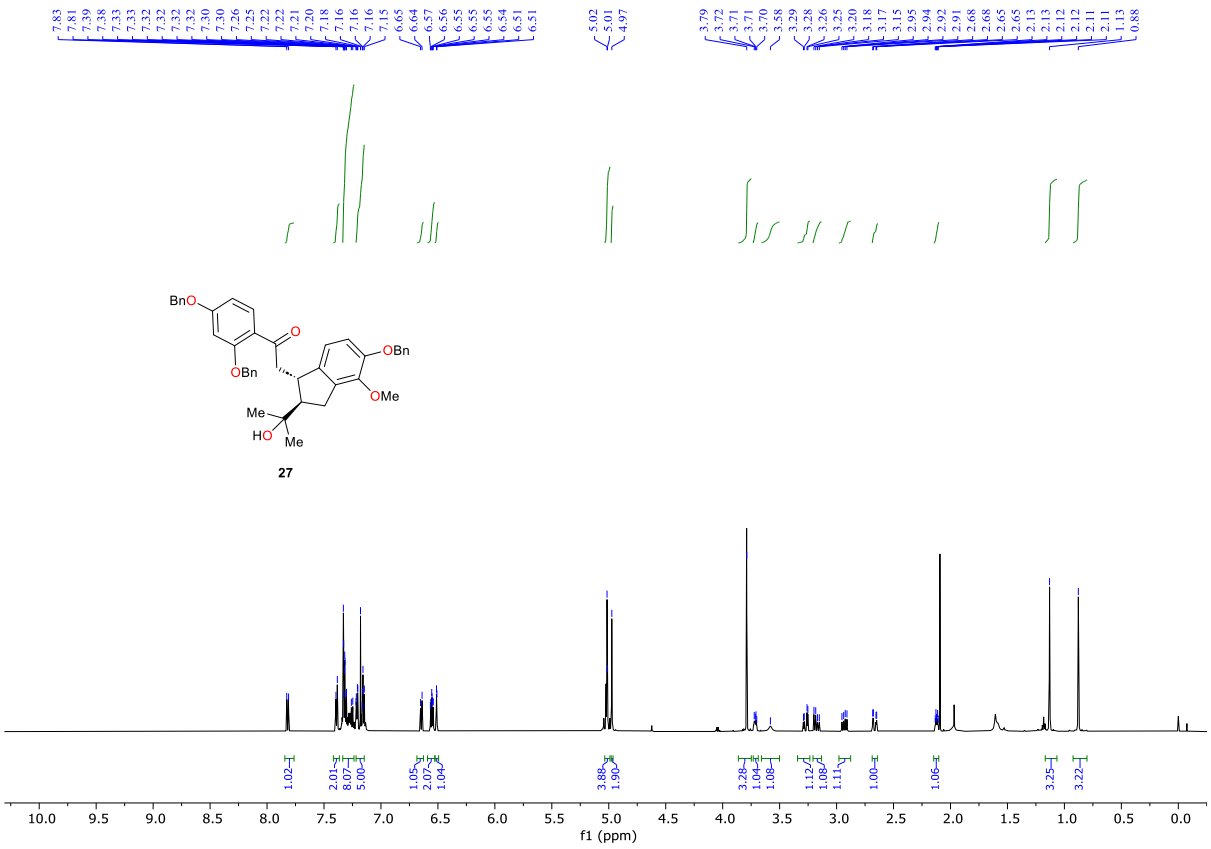


Figure S28. ^{1}H NMR of **27** ($CDCl_3$, 600 MHz)

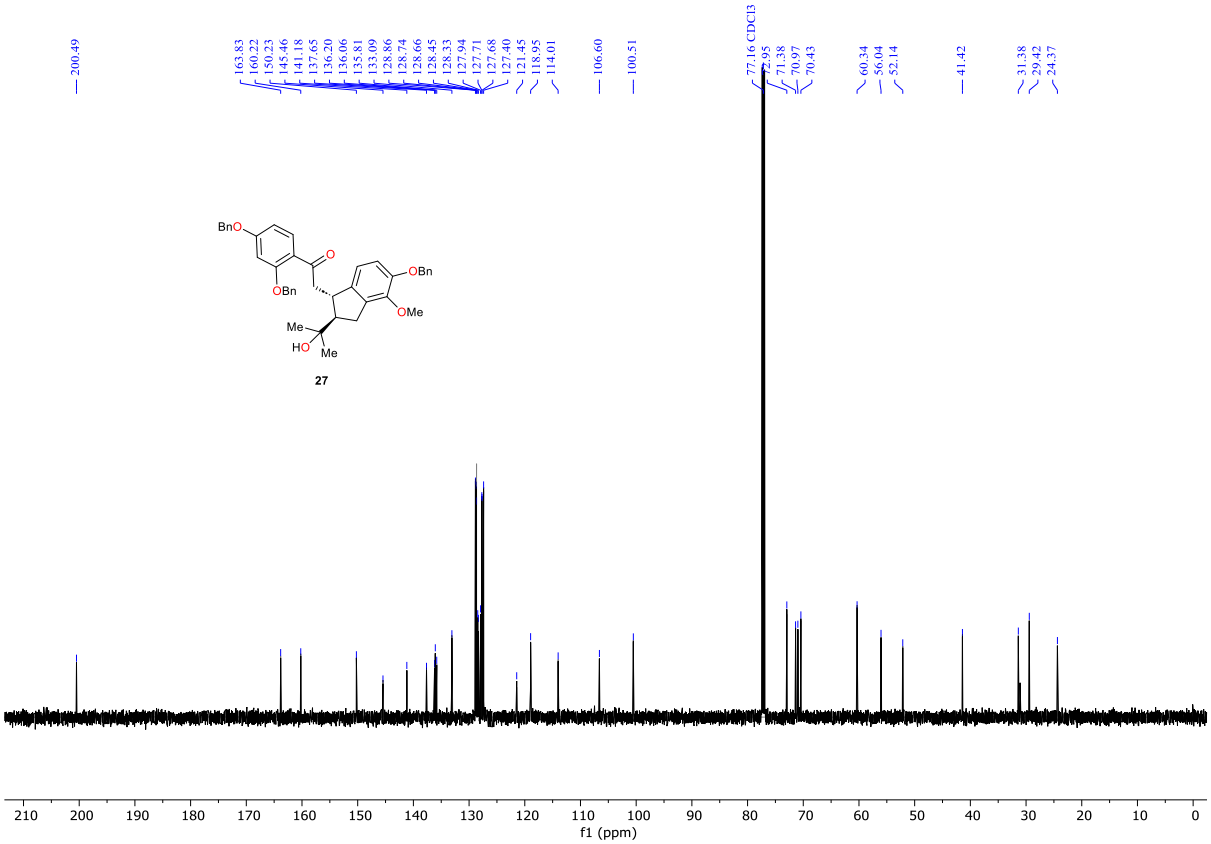


Figure S29. ^{13}C NMR of **27** ($CDCl_3$, 150 MHz)

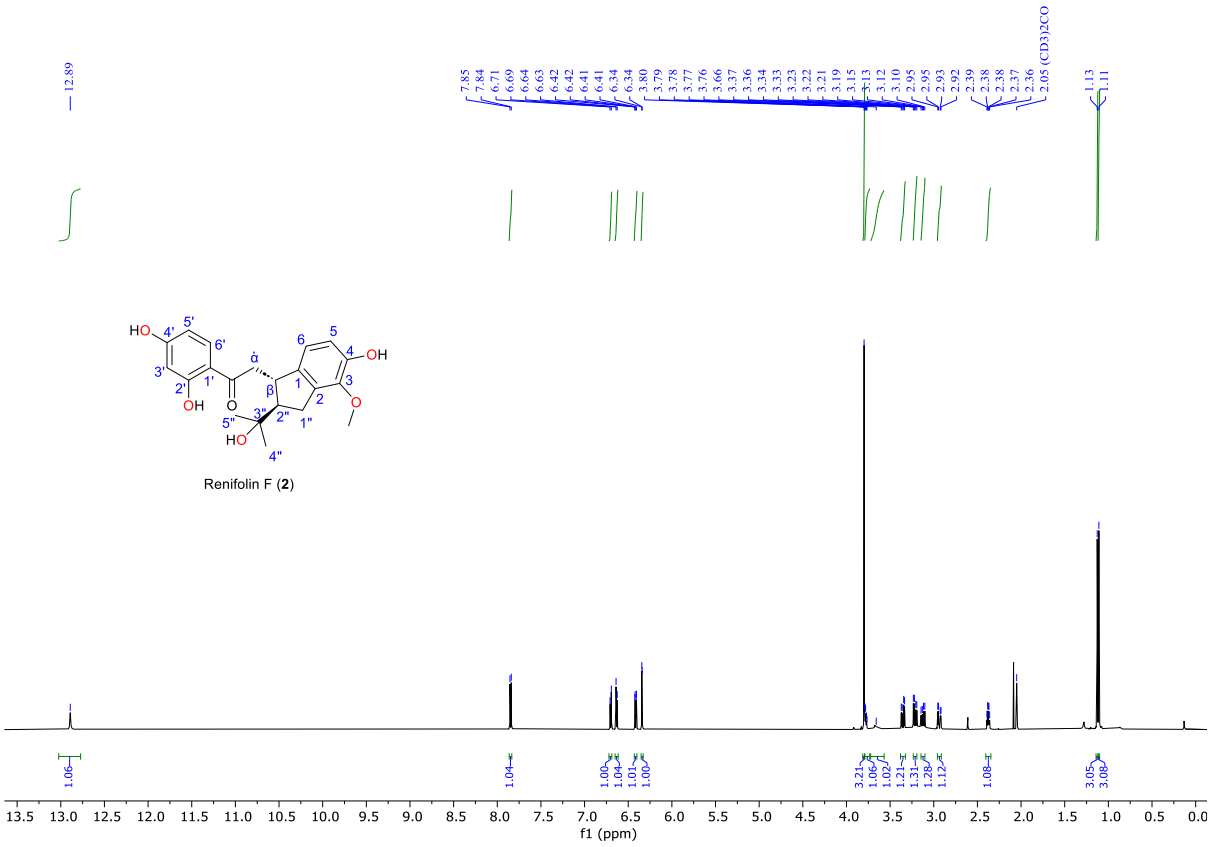


Figure S30. ^{1}H NMR of renifolin F (**2**) (acetone-d_6, 600 MHz)

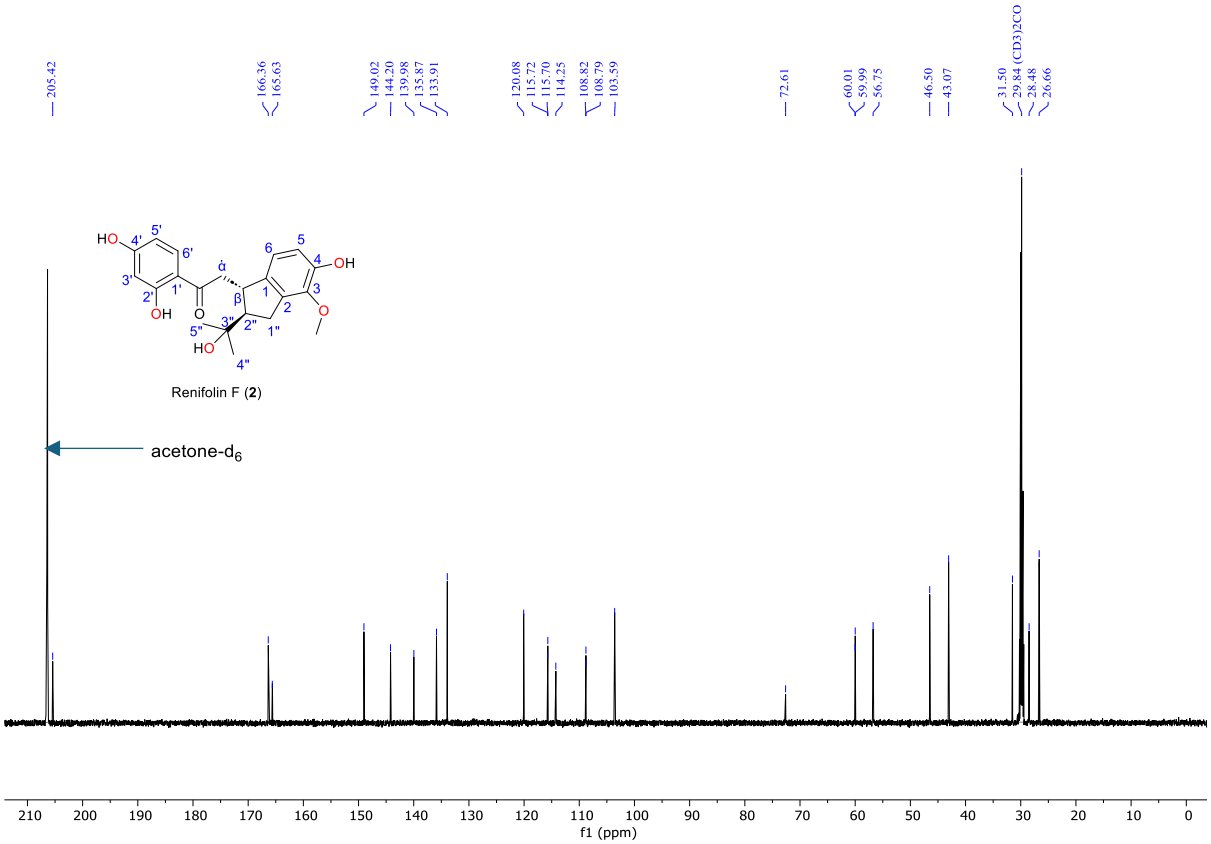


Figure S31. ^{13}C NMR of renifolin F (**2**) (acetone-d_6, 150 MHz)

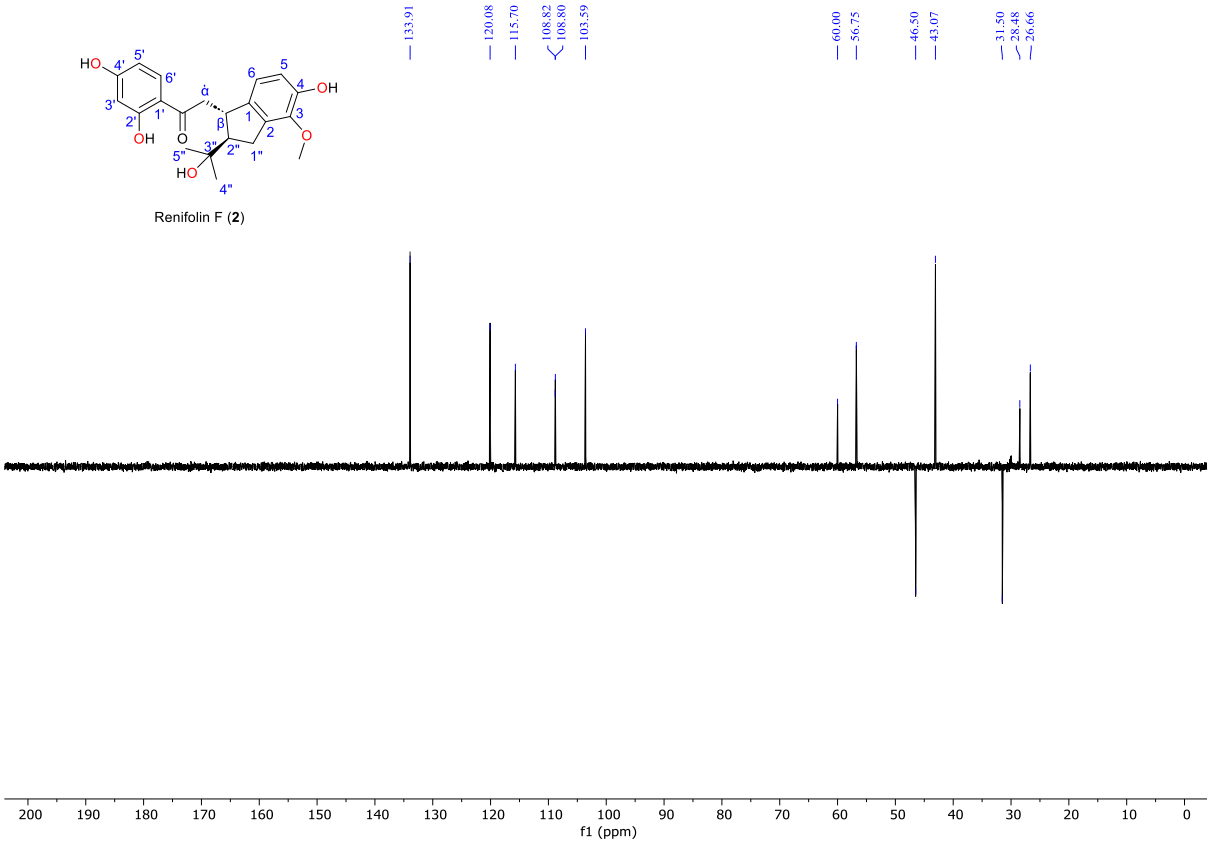


Figure S32. DEPT spectra of renifolin F (**2**) (acetone-d_6, 150 MHz)

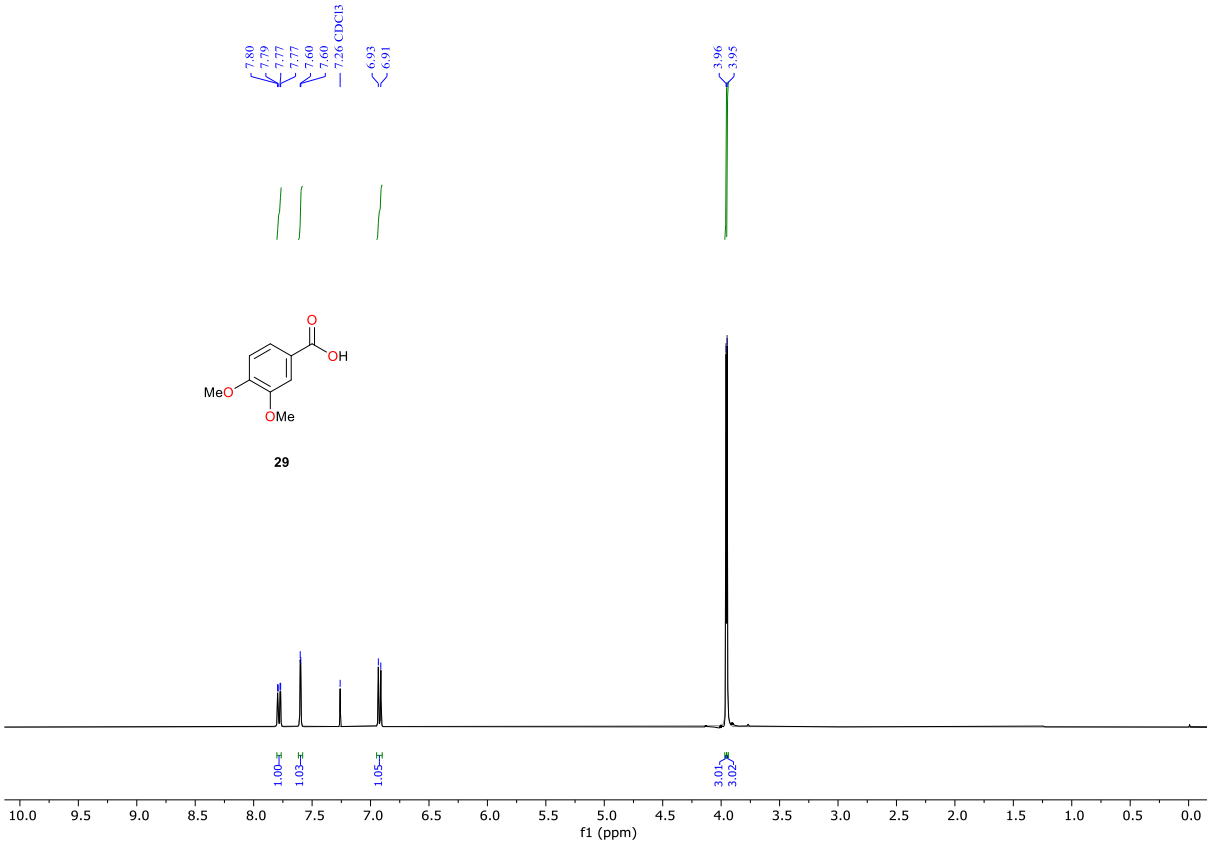


Figure S33. ^{1}H NMR of **29** ($CDCl_3$, 400 MHz)

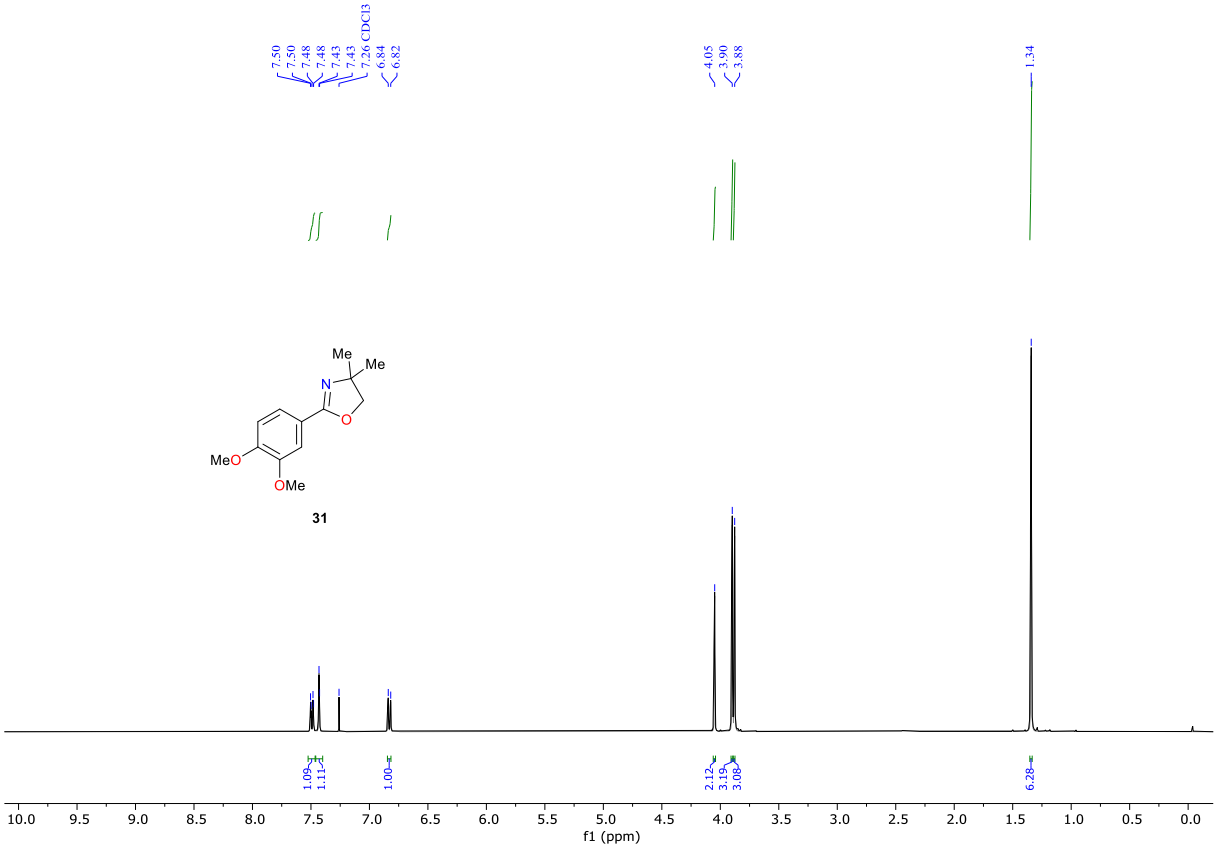


Figure S34. ^{1}H NMR of **31** ($CDCl_3$, 400 MHz)

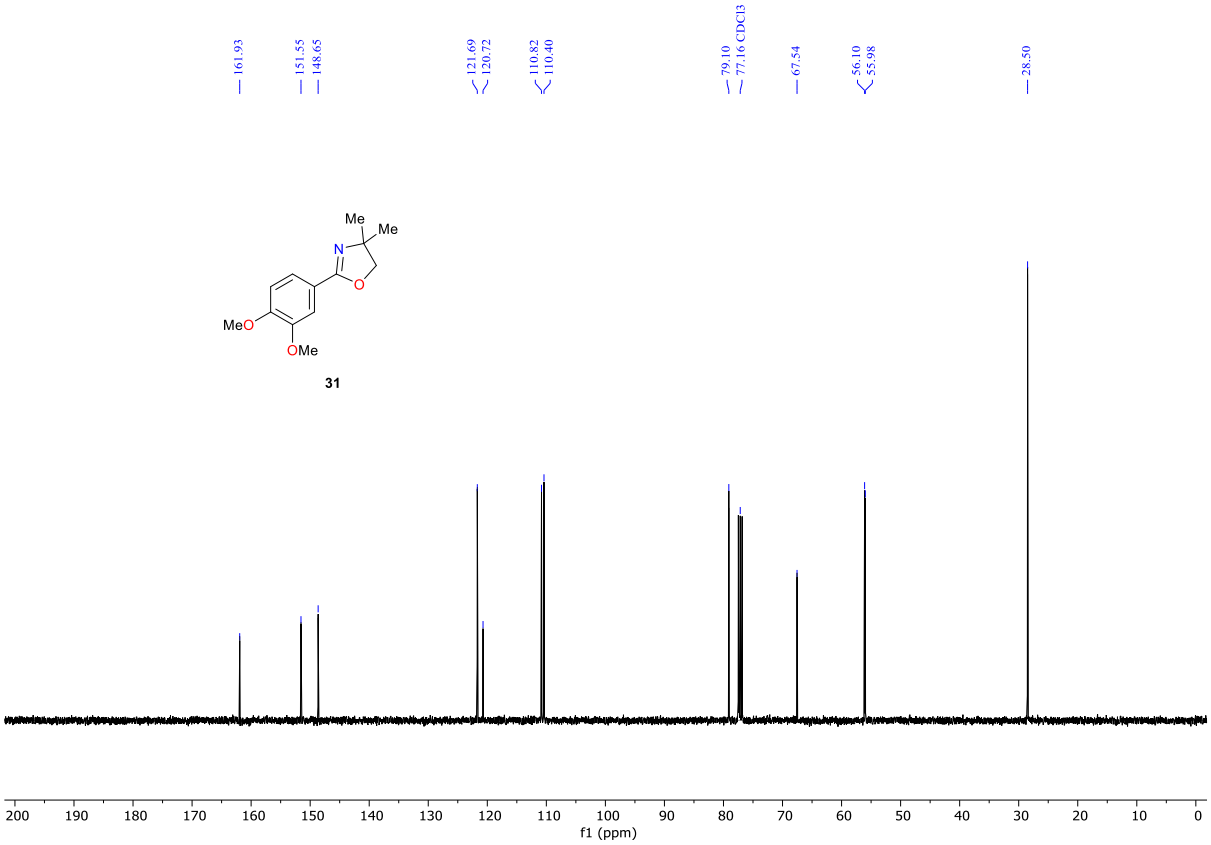


Figure S35. ^{13}C NMR of **31** ($CDCl_3$, 100 MHz)

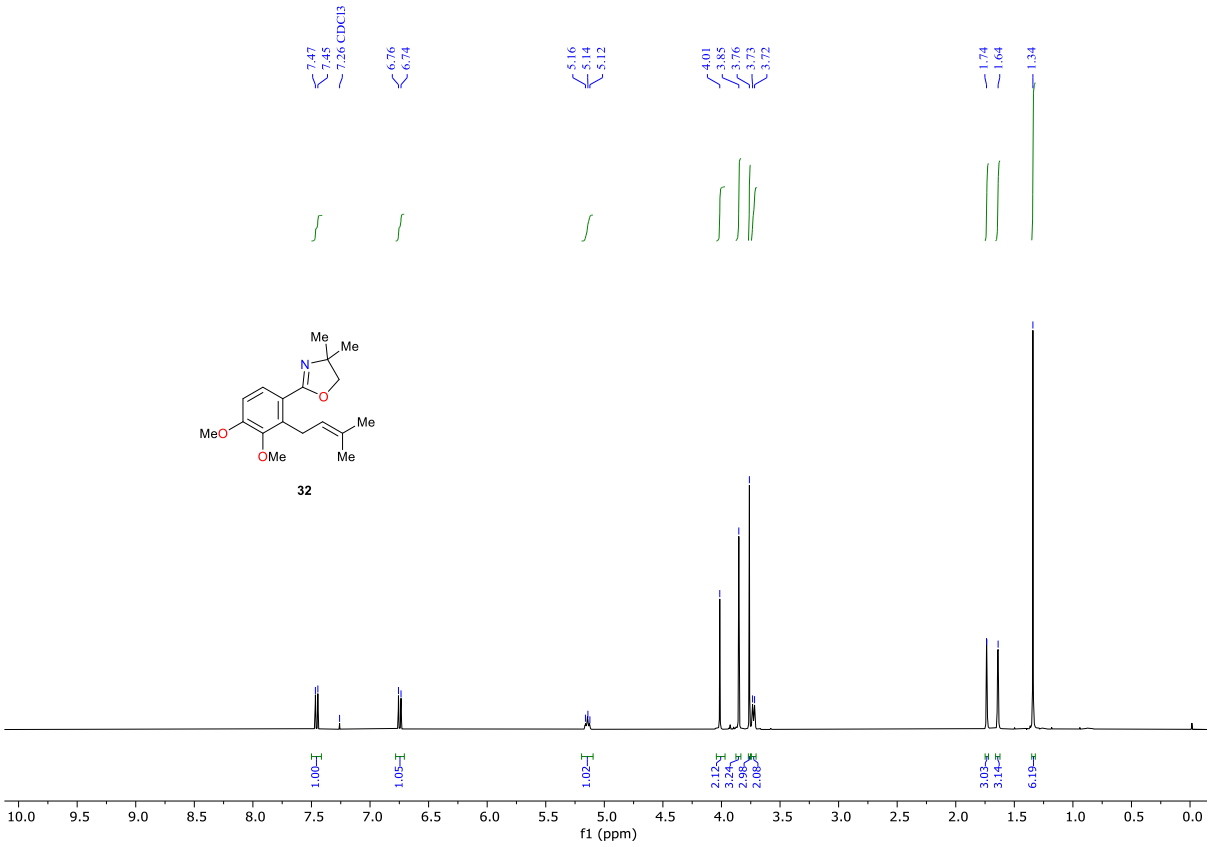


Figure S36. ^{1}H NMR of **32** ($CDCl_3$, 400 MHz)

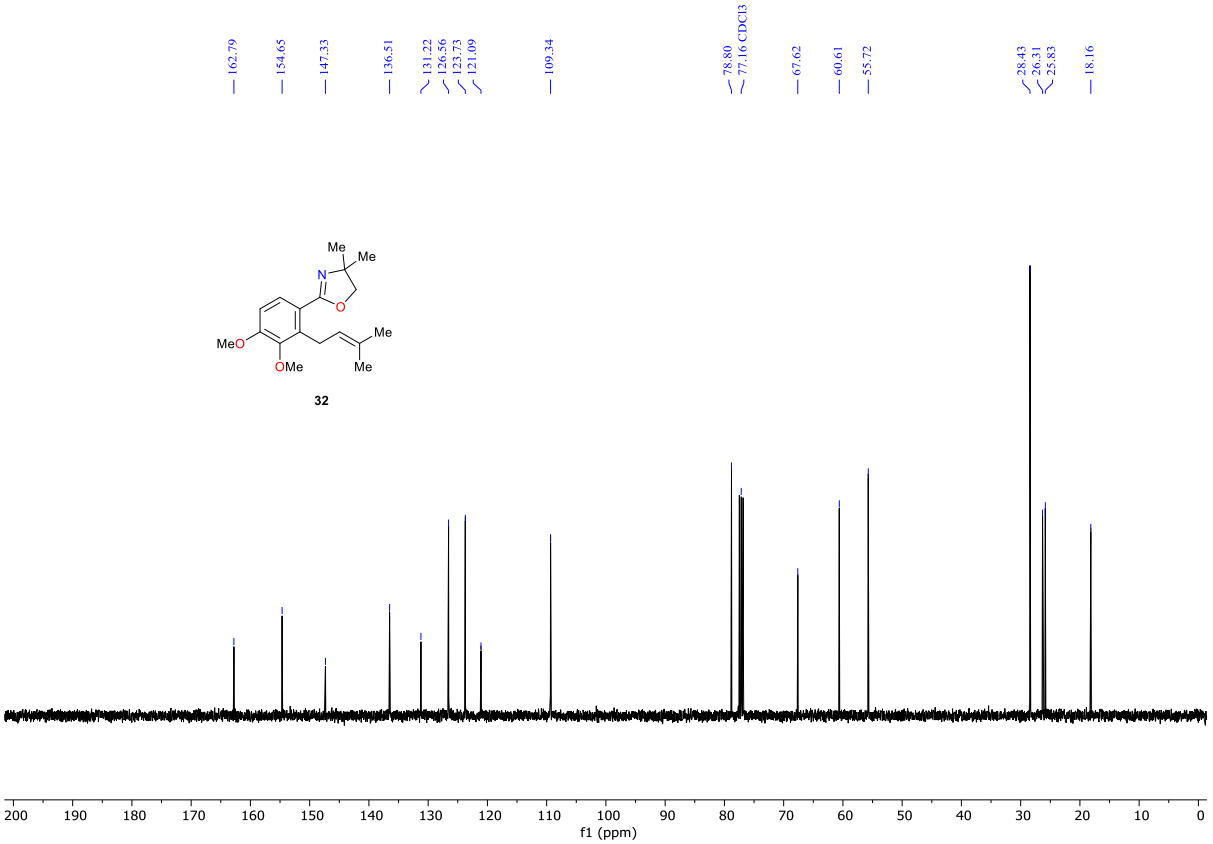


Figure S37. ^{13}C NMR of **32** ($CDCl_3$, 100 MHz)

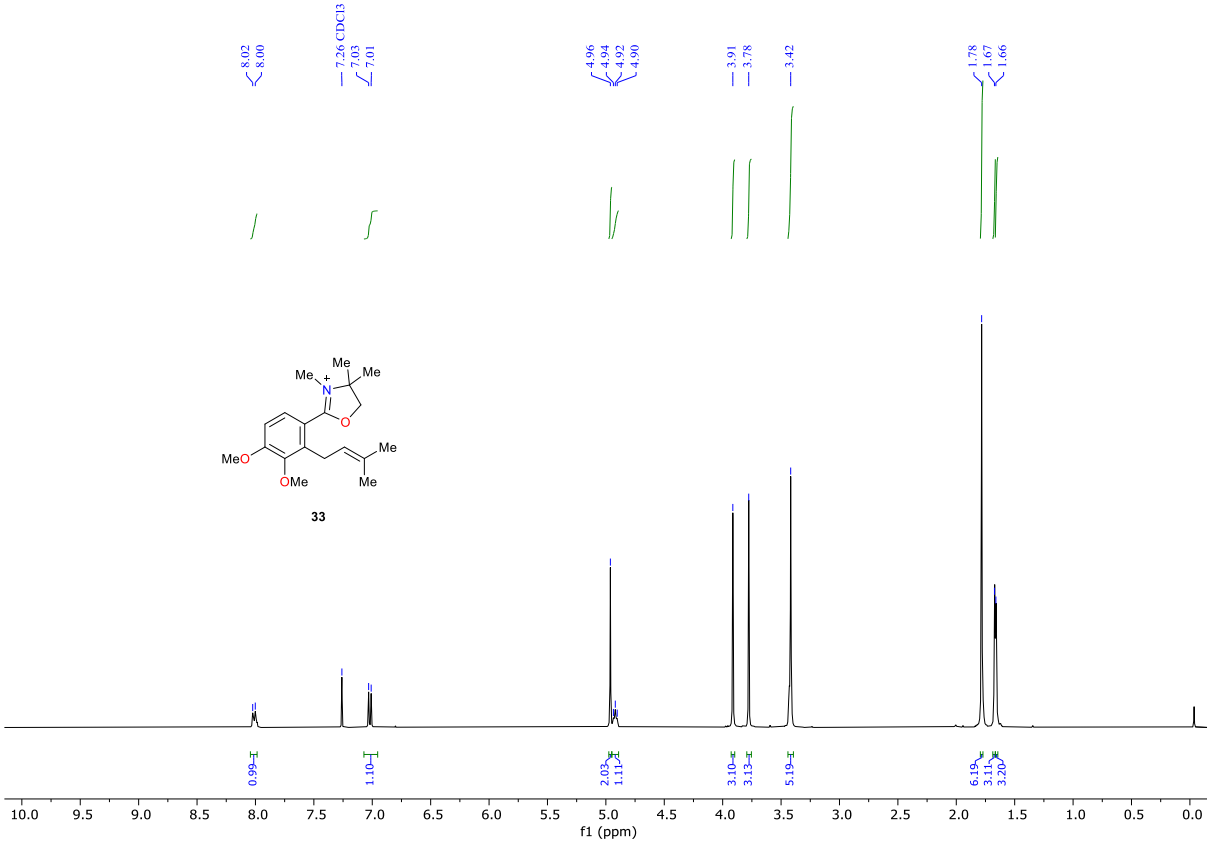


Figure S38. ^{1}H NMR of **33** ($CDCl_3$, 400 MHz)

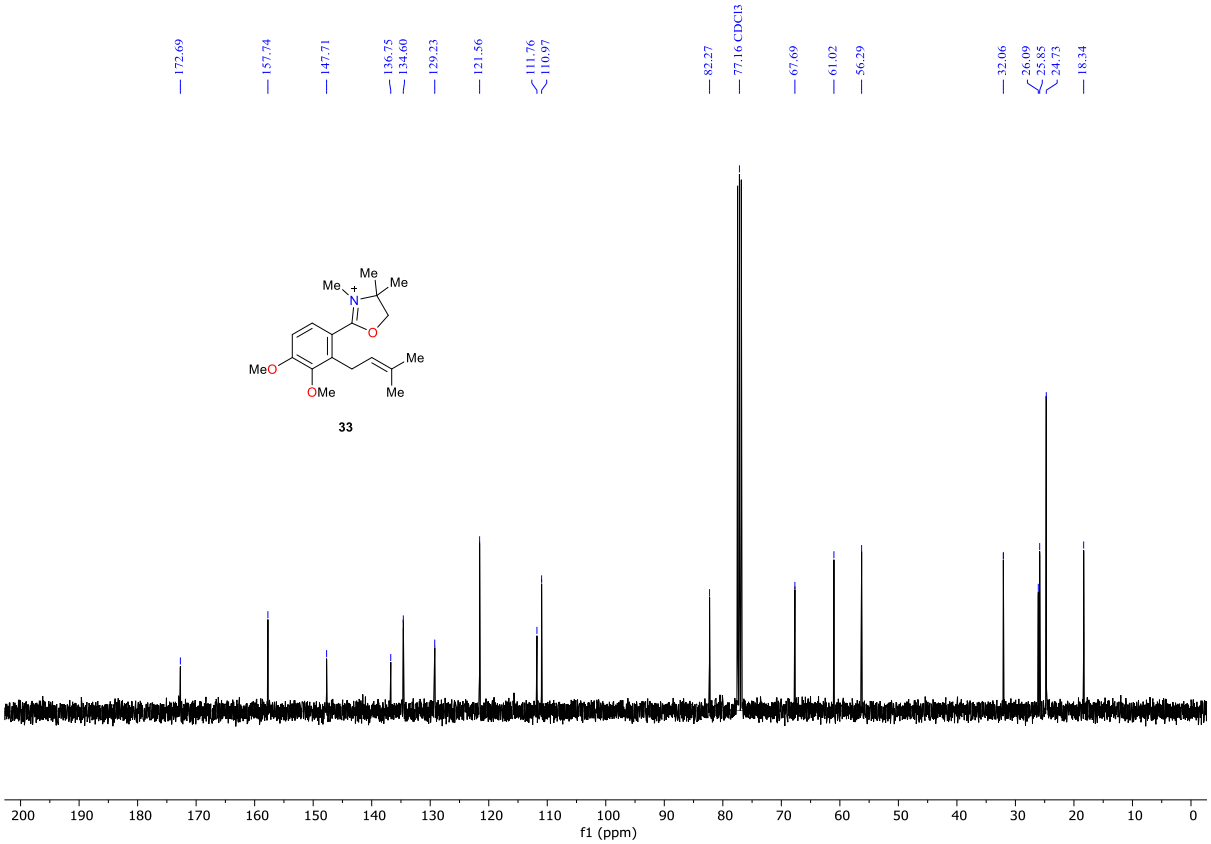


Figure S39. ^{13}C NMR of **33** ($CDCl_3$, 100 MHz)

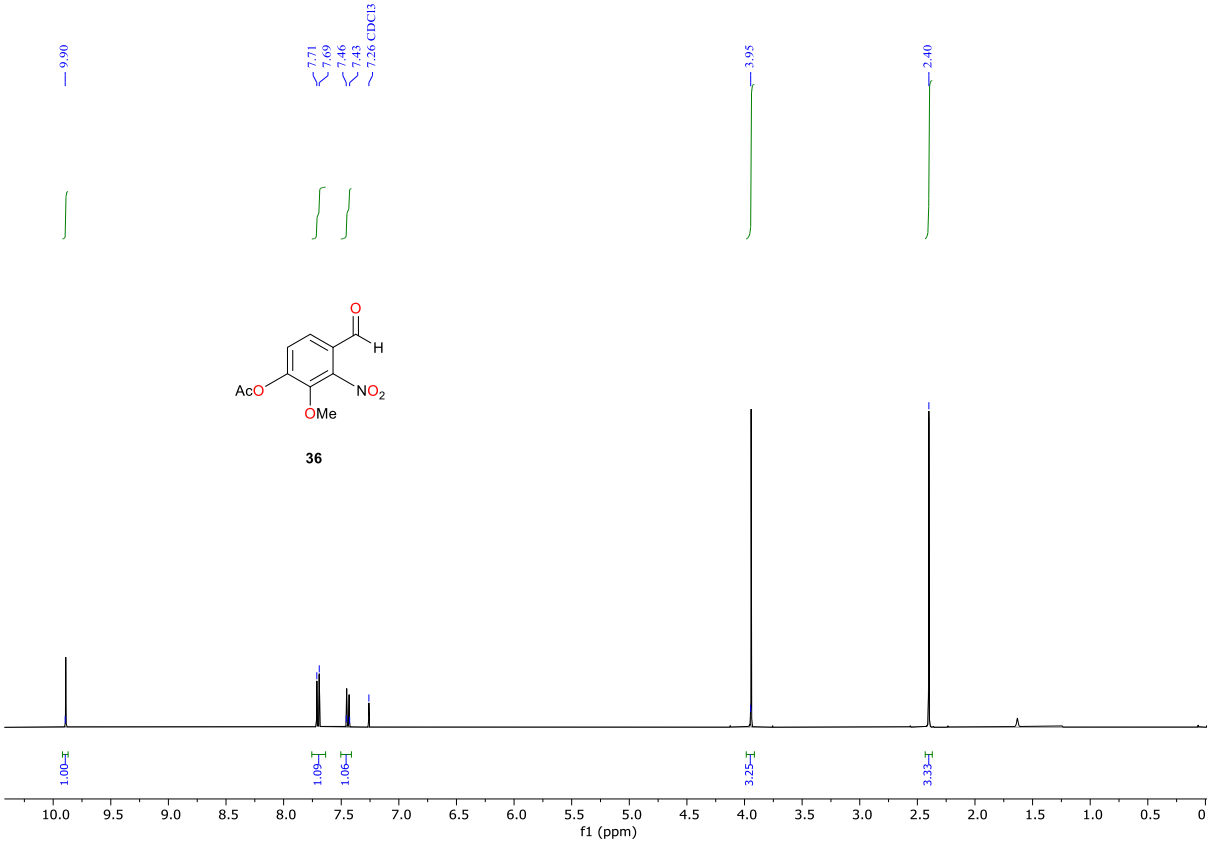


Figure S40. ^{1}H NMR of **36** ($CDCl_3$, 400 MHz)

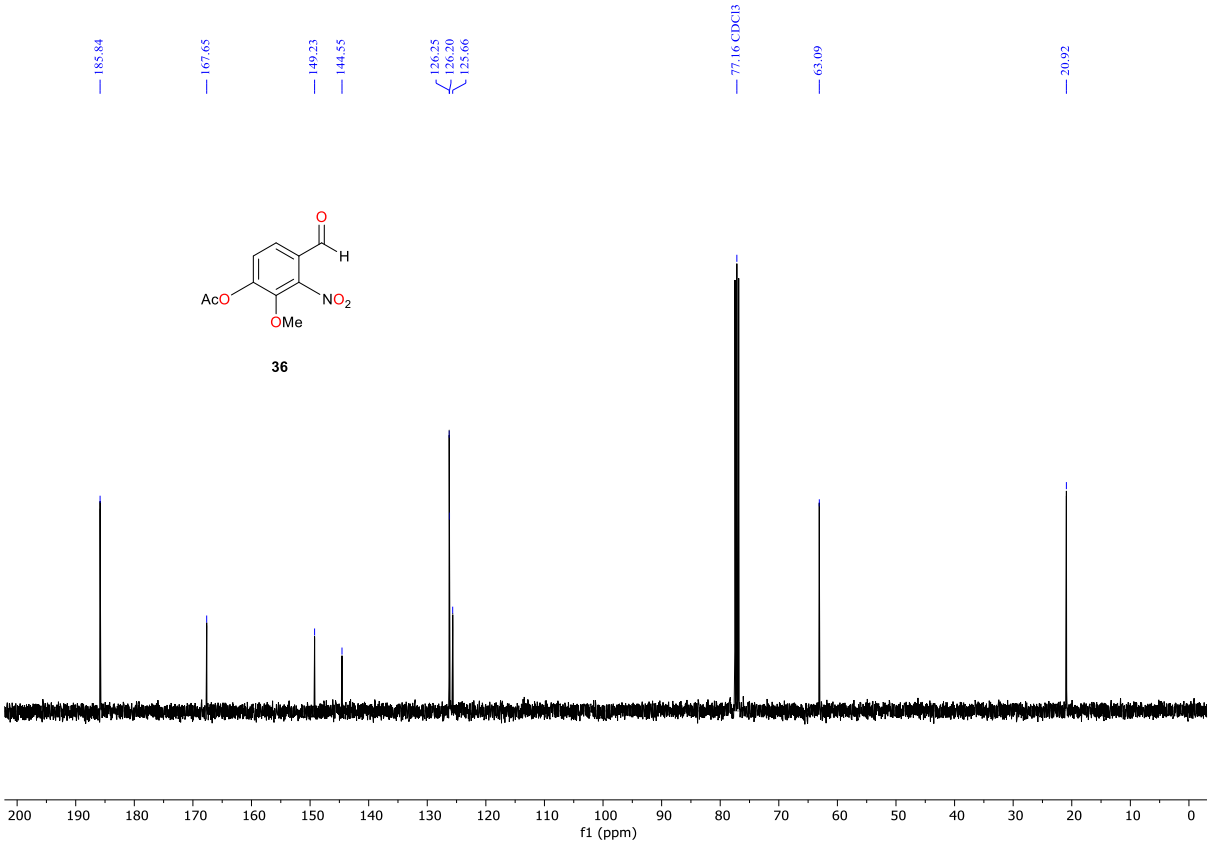


Figure S41. ^{13}C NMR of **36** ($CDCl_3$, 100 MHz)

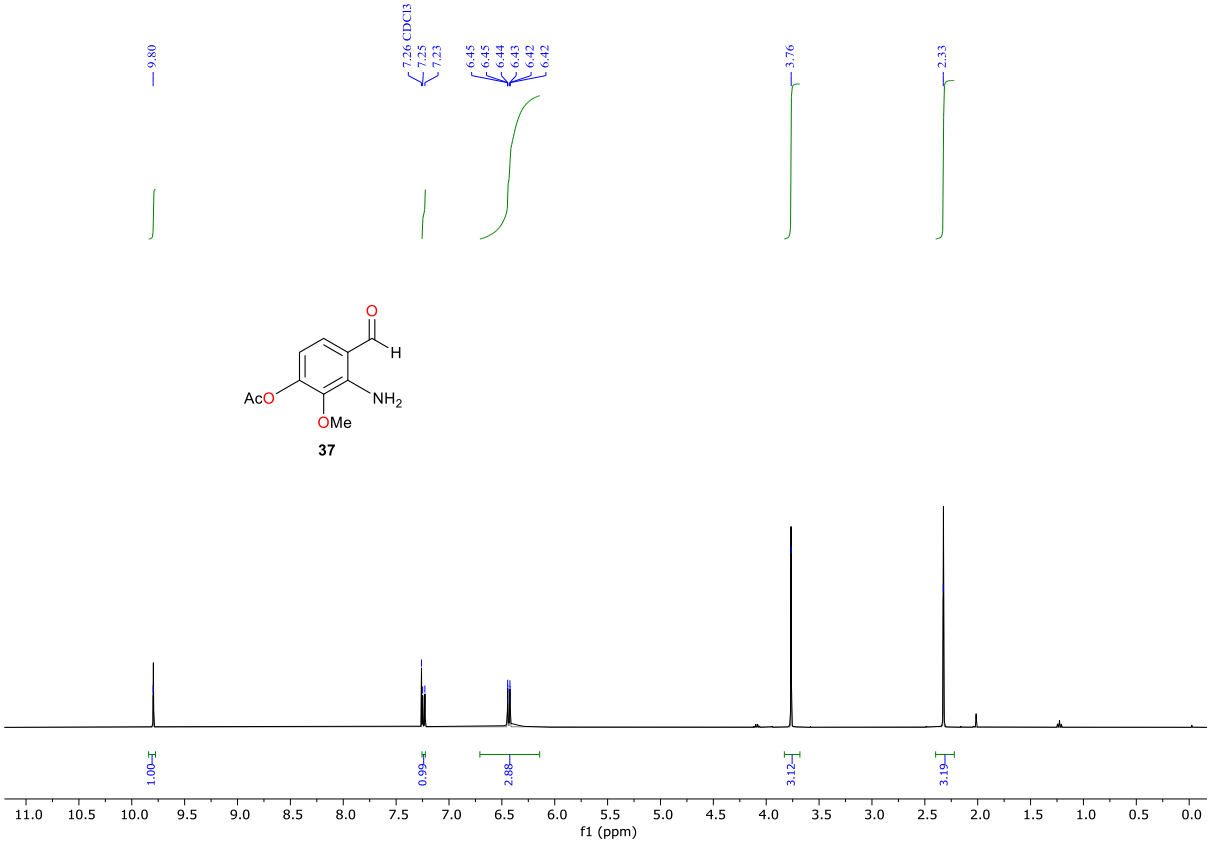


Figure S42. ^{1}H NMR of **37** ($CDCl_3$, 400 MHz)

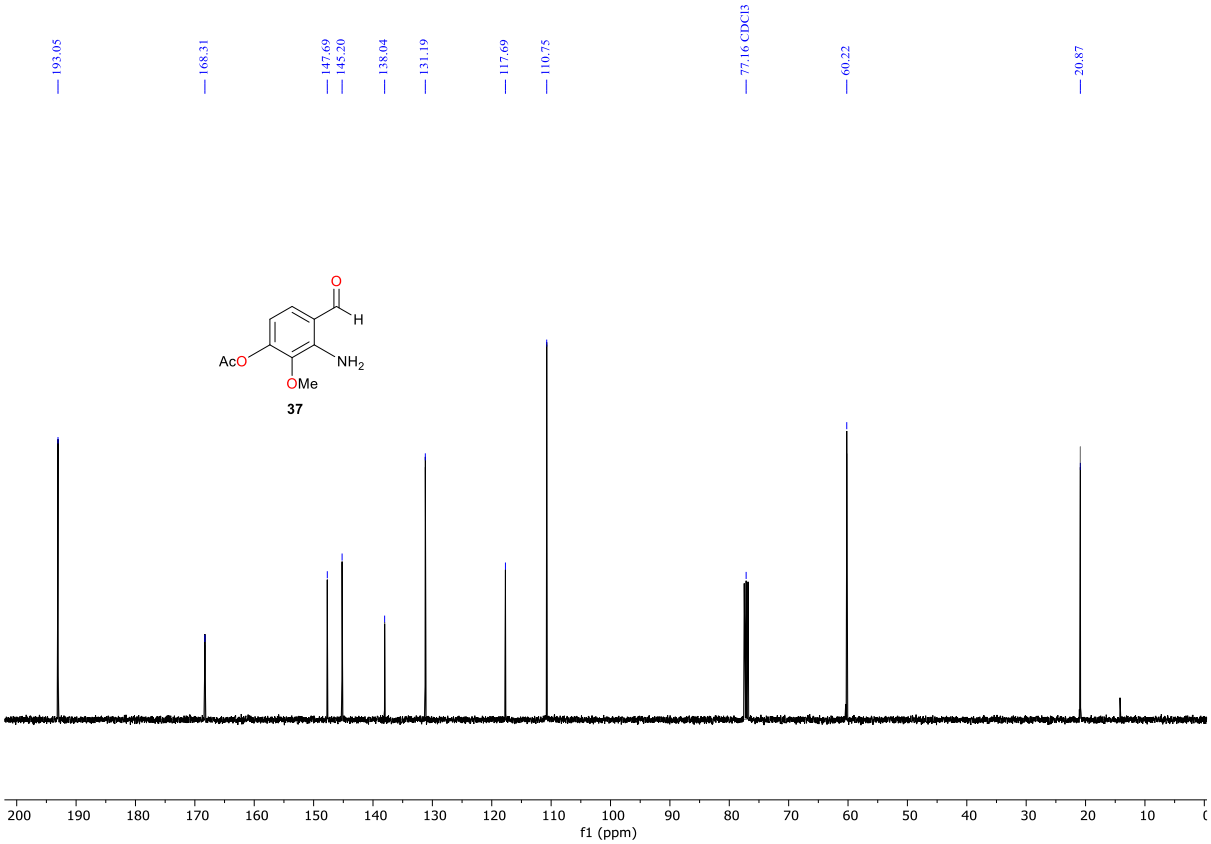


Figure S43. ^{13}C NMR of **37** ($CDCl_3$, 100 MHz)

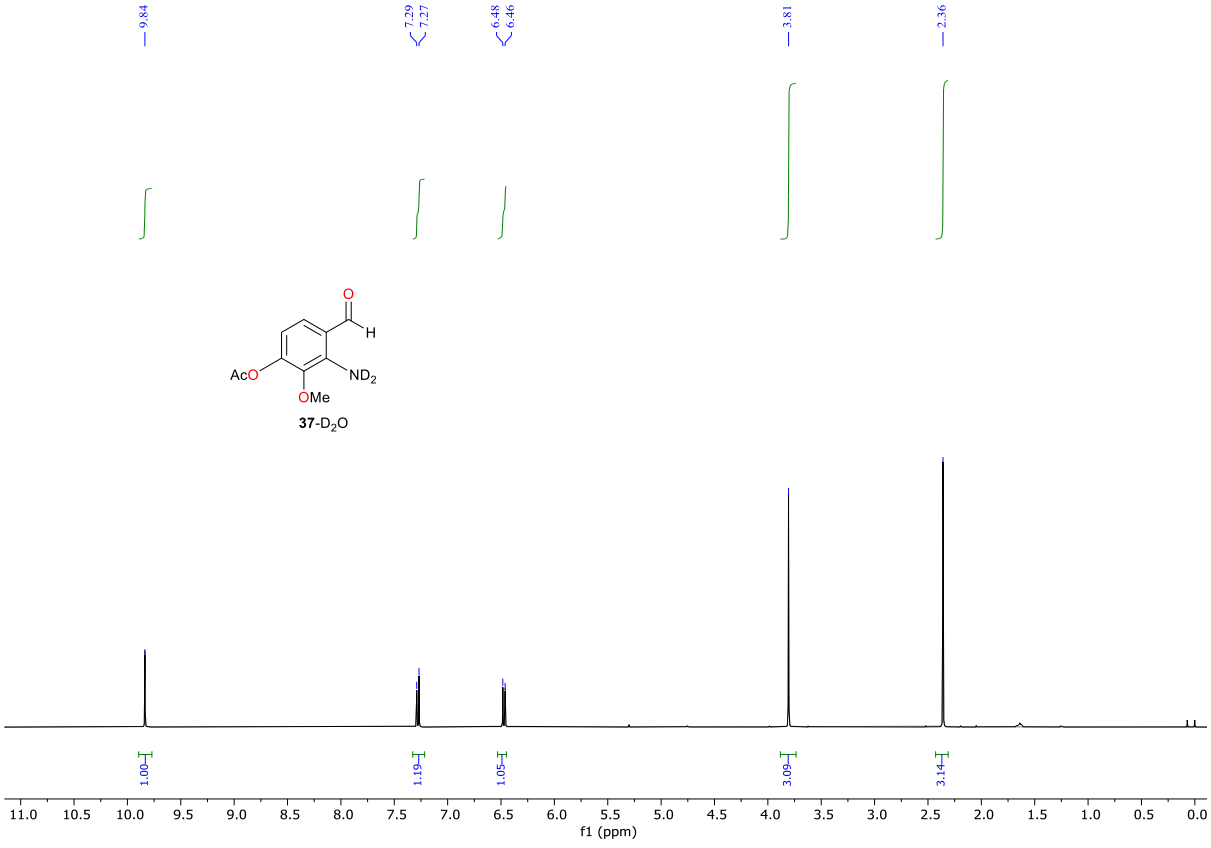


Figure S44. ^{1}H NMR of **37**-D_2O ($CDCl_3$, 400 MHz)

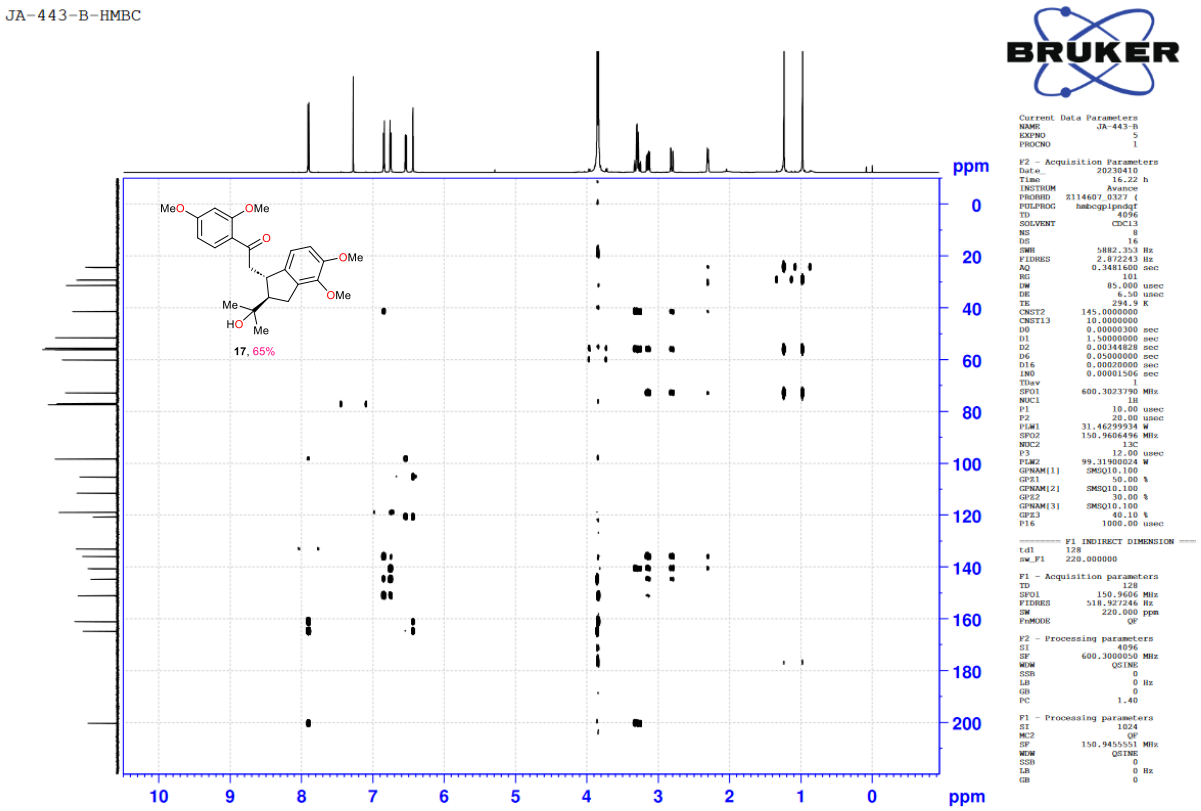


Figure S45. HMBC spectra of **17** ($CDCl_3$, 600 MHz)

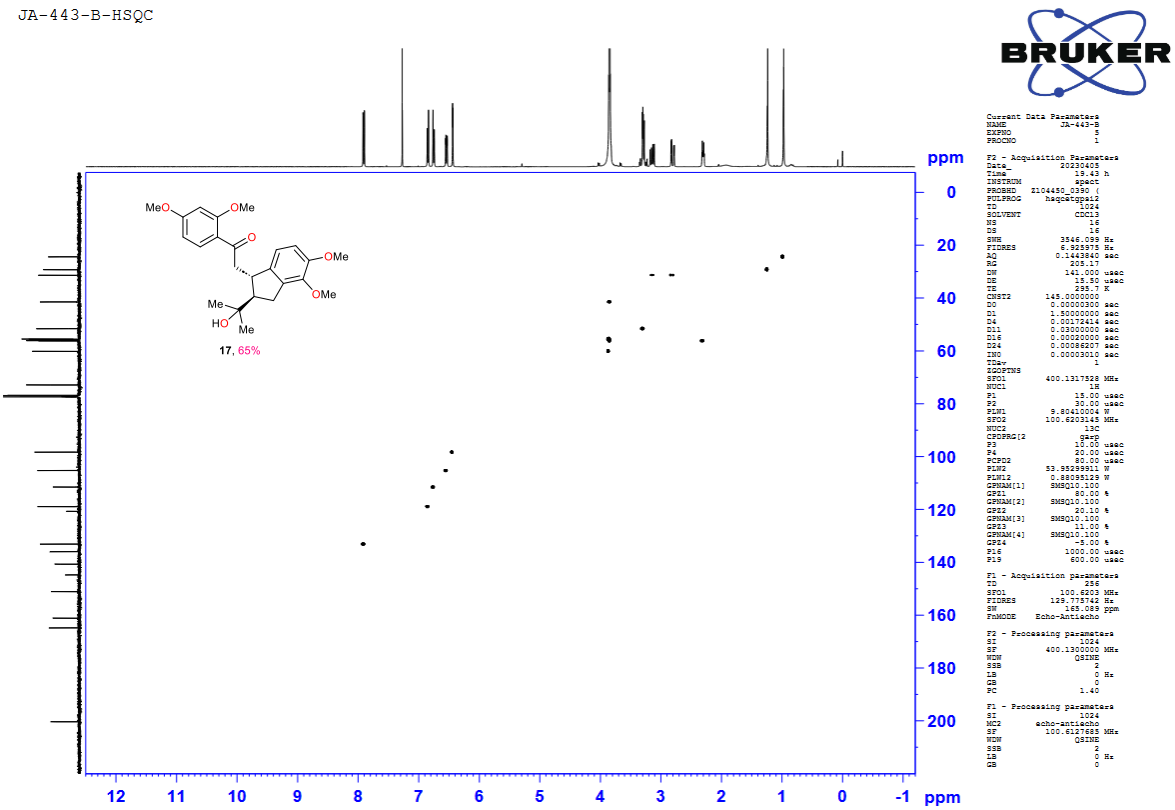


Figure S46. HMQC spectra of **17** ($CDCl_3$, 600 MHz)

Table S1. Several standard demethylation protocols were attempted on 15 but no identifiable product was obtained.

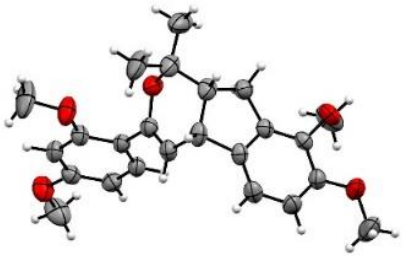
Entry	Reagent (eq.)	Solvent	Temp. (°C)	Time (h)
1	BBr_3 (7)	DCM	0 to rt	15
2	BBr_3 (16)	DCM	0 to rt	34
3	BBr_3 (16)	DCM	-10 to rt	34
4	BBr_3 (30)	DCM	0 to rt	36
5	BBr_3 (40)	DCM	0 to reflux	23
6	BBr_3 (40)	DCM	-78 to rt	16
7	BCl_3 (17)	DCM	0 to rt	18
8	BCl_3 (17)	DCM	0 to rt	18
9	NaSMe (25)	DMF	100	20
10	LiCl (28)	DMF	160	12

X-ray crystallographic data collection for 16

Single crystals of **18** was obtained by dissolving in CH_3Cl:Hex (1:2) and allowed the solvents to slowly evaporate at room temperature. A suitable crystal was selected and mounted on a Bruker APEX-II CCD diffractometer. The crystal was kept at 299.00 K during data collection. Using Olex2 [1], the structure was solved with the olex2.solve [2] structure solution program using Charge Flipping and refined with the olex2.refine [3] refinement package using Gauss-Newton minimization.

References:

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Bourhis, L.J., Dolomanov, O.V., Gildea, R.J., Howard, J.A.K., Puschmann, H. (2015). Acta Cryst. A71, 59-75.
3. Bourhis, L.J., Dolomanov, O.V., Gildea, R.J., Howard, J.A.K., Puschmann, H. (2015). Acta Cryst. A71, 59-75.



CCDC 2349193

Crystal data and structure refinement for 16.

Empirical formula	$C_{24}H_{28}O_5$
Formula weight	396.487
Temperature/K	299.00
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.9416(10)
b/Å	7.4402(10)
c/Å	28.624(4)
α/°	90
β/°	91.123(4)
γ/°	90
Volume/Å^3	2116.9(5)
Z	4
ρ_{calc}g/cm^3	1.244
μ/mm^{-1}	0.086
F(000)	848.6
Crystal size/mm^3	0.329 × 0.116 × 0.072
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.32 to 54.3
Index ranges	-12 ≤ h ≤ 12, -9 ≤ k ≤ 9, -36 ≤ l ≤ 36
Reflections collected	37971
Independent reflections	4687 [R_{int} = 0.0764, R_{sigma} = 0.0438]
Data/restraints/parameters	4687/0/268
Goodness-of-fit on F^2	1.061
Final R indexes [I>=2σ (I)]	R_1 = 0.0505, wR_2 = 0.1158
Final R indexes [all data]	R_1 = 0.0920, wR_2 = 0.1364
Largest diff. peak/hole / e Å^{-3}	0.27/-0.31