# Supplementary Information

# The first diastereoselective synthesis of cinerins A–C, PAF-antagonistic macrophyllin-type bicyclo[3.2.1]octane neolignans, using a novel Pd-catalysed oxyarylation †

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**Table of contents**

**MATERIALS AND INSTRUMENTS.**

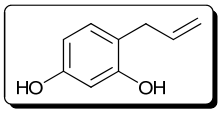
IR spectra were recorded on a Thermo Nicolet 6700 spectrometer. Spectra from liquid substances were recorded as film between NaCl plates; solids were recorded in a form of KBr pill. NMR spectra were recorded at 300 MHz ($^1$H NMR) and at 75.4 MHz ($^{13}$C NMR) on a Bruker Avance 300 Spectrometer using TMS as internal standard and $CDCl_3$ as solvent. Chemical shifts (δ) are presented in ppm. Coupling constants are given in Hz. Optical rotation values were measured on a Jasco DIP-1000 digital polarimeter. Electron impact mass spectra (EIMS) were recorded on trace DSQ II GC/MS system (Axel Semrau GmbH & Co. KG). High resolution mass spectra (HRMS) were recorded on $QToF_{micro}$ Micromass Manchester Waters Inc. spectrometer with ESI in positive mode.

Column chromatography (CC) purifications were carried out using silica gel (Acros, particle size 35–70 μm). Solvents used in CC were commercially available and distilled before use. Reactions were monitored by thin layer chromatography (TLC), which was performed on commercial silica gel on aluminium sheets (Merck, Silica gel 60 $F_{254}$). TLC plates were afterwards dipped into the Pancaldi solution (molybdatophosphorus acid and Ce(IV)sulphate in 4% sulphuric acid); upon heating, organic substances were oxidised giving blue spots on a white to light blue background. The solvents used in reactions were distilled prior to use; dry solvents were prepared according to published procedures.[1] If not stated otherwise, reactions were performed in dry solvents under nitrogen atmosphere and organic extracts (layers) were dried over $MgSO_4$. All reagents and solvents were of commercial quality from freshly opened containers. All substances that are not described in the following synthetic procedures were obtained from commercial suppliers (Acros, Aldrich, Fluka, Merck-Schuchardt, Riedel de Haen or Roth).

[1] Armarego, W. L. F.; Chai C. Purification of Laboratory Chemicals, 6th ed., Butterworth Heinemann, **2009**.

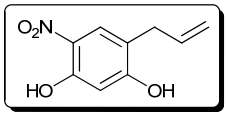
## EXPERIMENTAL PROCEDURES AND SPECTRAL DATA OF COMPOUNDS

### 4-allyl-resorcinol 9
### Pd-catalysed, triethylborane promoted *C*-allylation of resorcinol 6



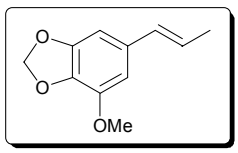

Into a $N_2$-purged flask, containing $Pd(PPh_3)_4$ (580 mg, 0.5 mmol) and resorcinol **6** (1.10 g, 10 mmol), were successively added anhydrous THF (25 mL), allyl alcohol (820 μL, 12 mmol), and triethylborane (50 mL, 50 mmol, 1 M hexane solution) via a syringe. The resulting homogeneous solution was stirred at room temperature for 24 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with 2 M aq. HCl, sat. $NaHCO_3$, and brine. The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel (cyclohexane:EtOAc, 8:1) to give 1.16 g of **9** (77% yield) as white solid (m.p. 68–69°C). $^1$H NMR: $\delta_H$ 6.94 (d, $J$ = 7.6 Hz, 1H. Ar-H), 6.37 (dd, $J$ = 7.6 Hz, 2.4, 1H, A-H), 6.36 (s, 1H, Ar-H), 6.00 (ddt, $J$ = 17.4, 9.9, 6.4 Hz, 1H, Ar-$CH_2$-*CH*=$CH_2$), 5.15 (dd, $J$ = 17.4, 1.5 Hz, 1H, Ar-$CH_2$-CH=*$CH_2$*), 5.14 (dd, $J$ = 9.9, 1.5 Hz, 1H, Ar-$CH_2$-CH=*$CH_2$*), 5.12 (s, 2H, 2 x OH), 3.34 (d, $J$ = 6.4 Hz, 2H, Ar-*$CH_2$*-CH=$CH_2$).

### 2-allyl-5-nitrobenzene-1,3-diol (4-allyl-6-nitroresorcinol) 10.




To a solution of allylresorcinol **9** (676 mg, 4.5 mmol) in acetone (50 mL) was added zirconyl nitrate (1.03 g, 4.5 mmol) and the resulting mixture stirred at room temperature for 3 h. After completion of the reaction, as monitored by TLC, the solvent was removed under reduced pressure. Water was added and the product extracted into ethyl acetate (3 x 20 mL). The combined organic layer were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude product, which was purified by flash chromatography (silica gel, cyclohexane:$Et_2O$ 2:1), affording 553 mg of **10** (63% yield) as pale orange solid (mp 85–86°C). $^1$H NMR: $\delta_H$ 10.84 (s, 1H, Ar-OH), 7.90 (s, 1H, Ar-H), 6.51 (s, 1H, Ar-H), 6.22 (s, 1H, Ar-OH), 5.98 (tdd, $J$ = 16.7, 10.2, 6.4 Hz, 1H, Ar-$CH_2$-*CH*=$CH_2$), 5.26–5.21 (m, 1H, Ar-$CH_2$-CH=*$CH_2$*), 5.18 (ddd, $J$ = 12.2, 3.1, 1.6 Hz, 1H, Ar-$CH_2$-CH=*$CH_2$*), 3.37 (d, $J$ = 6.3 Hz, 2H, Ar-*$CH_2$*-CH=$CH_2$); $^{13}$C NMR: $\delta_C$ 162.8, 156.9, 135.4, 156.0, 128.1, 127.4, 120.4, 118.2, 104.9, 34.3; HRMS-ESI: 196.0405 $[M+H]^+$ (calcd. for $C_9H_{10}NO_4$, 196.0610).

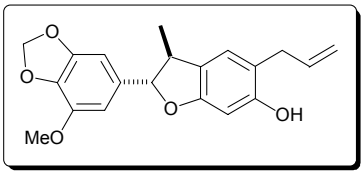
### (*E*)-4-methoxy-6-(prop-1-enyl)benzo[d][1,3]dioxole (*E*-isomyristicin 4)




A solution of EtMgBr in THF (3 M, 50 mmol) was added dropwise to a solution of 5-methoxy-piperonal (1.80 g, 10 mmol) in dry THF (20 mL) at 0°C, the mixture was stirred for 3 hours at room temperature, and the excess of EtMgBr was destroyed with MeOH (2 mL). The reaction mixture was diluted with water and extracted with ether (3 x 20 mL). The combined organic extracts were washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude alcohol was used without purification for the subsequent dehydratisation. A solution of crude

alcohol (10 mmol) in 25 mL of dry toluene was treated with 2.5 g (15 mmol) of anhydrous $CuSO_4$. The reaction mixture was heated under reflux for 2 hours. All inorganic insolubles were filtered and washed with toluene. After the evaporation of the solvent, the residue was purified by silica gel column chromatography (elution with hexane: ethyl acetate = 2:1) to afford 1.16 g of **4** (61 % yield) as a pale yellow oil that spontaneously crystallized (mp 41–42°C). $^1$H NMR: $\delta_H$ 6.58 (d, $J$ = 1.4 Hz, 1H), 6.48 (d, $J$ = 1.4 Hz, 1H), 6.30 (dd, $J$ = 15.7, 1.6 Hz, 1H), 6.09 (qd, $J$ = 15.6, 6.6 Hz, 1H), 5.95 (s, 2H), 3.91 (s, 3H), 1.86 (dd, $J$ = 6.54, 1.57 Hz, 3H); HRMS-ESI: 193.0858 $[M+H]^+$ (calcd. for $C_9H_{10}NO_4$, 193.0865).

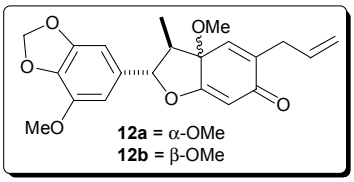
***rac*-2,3-*trans*-3',4'-methylene-5'-methoxy-3-methyl-5-allyl-2,3-dihydrobenzofuran-6-ol 11**.




Zinc dust (100 mg) and acetic acid (4 mL) were added successively to a stirred solution of **10** (527 mg, 2.7 mmol) in $CH_2Cl_2$ (80 mL) at room temperature. After 1 h, the reaction mixture was filtered and the solvent was removed under reduced pressure. A portion of toluene (5 mL) was placed into the flask and it was removed under reduced pressure. This procedure was repeated three times to remove the excess of the acid. The crude aminophenol **5** was used in the next step without further purification.

The crude aminophenol **5** and MeCN (25 mL) were placed into a one-necked round-bottomed Pyrex flask. The solution was cooled to 0 ºC for 10 min and $NOPF_6$ (486 mg, 2.7 mmol) was added. The reaction was stirred for 2 h and $ZnCO_3$ (340 mg, 5.4 mmol), $Pd_2(dba)_3$ (124 mg, 5 mol %) and isomyristicin **4** (635 mg, 3.3 mmol) were added successively. The reaction mixture was stirred for 20 h and 10% $NaHCO_3$ solution (10 mL) was added. The aqueous phase was extracted with ethyl acetate (3 x 10 mL) and the combined organic layers were washed with water. The organic extracts were dried ($MgSO_4$), filtered and the solvents were evaporated *in vacuo*. The crude product was purified by flash chromatography (silica gel, toluene) to give 579 mg of 2,3-dihydrobenzofuran neolignan **11** (63% yield) as colourless viscous oil. $^1$H NMR: $\delta_H$ 6.87 (s, 1H, H-4), 6.60 (d, $J$ = 1.2 Hz, 1H, H-2'), 6.57 (d, $J$ = 1.2 Hz, 1H, H-6'), 6.41 (s, 1H, H-7), 6.14 (s, 2H, $OCH_2O$), 5.98 (tdd, $J$ = 16.5, 10.1, 6.5 Hz, 1H, Ar-$CH_2$-*CH*=$CH_2$), 5.32–5.26 (m, 1H, Ar-$CH_2$-CH=*$CH_2$*), 5.18 (m, 1H, Ar-$CH_2$-CH=*$CH_2$*), 5.10 (d, $J$ = 9.0 Hz, 1H, H-2), 4.97 (s, 1H, OH), 3.88 (s, 3H, Ar-$OCH_3$), 3.40 (m, 1H, H-3), 3.37 (br. d, $J$ = 6.3 Hz, 2H, Ar-*$CH_2$*-CH=$CH_2$), 1.42 (d, $J$ = 6.6 Hz, 3-*$CH_3$*). $^{13}$C NMR: $\delta_C$ 158.7 (C-7a), 154.2 (C-6), 149.4 (C-3'), 143.8 (C-5'), 136.8 (C-9), 134.1 (C-4'), 133.5 (C-1'), 125.9 (C-4), 121.9 (C-3a), 115.9 (C-10), 111.8 (C-5), 103.9 (C-5'), 103.5 (C-2'), 101.5 ($OCH_2O$), 100.8 (C-7), 94.0 (C-2), 56.3 (5'-$OCH_3$), 45.2 (C-3), 32.0 (C-8), 17.6 (3-$CH_3$). IR (film): $\tilde{\nu}$ 3600–3250, 1640, 1510, 1475 $cm^{-1}$. EIMS: *m/z* (%) 340 (100), 325 (28), 284 (33), 189 (41), 175 (50). HRMS-ESI: 341.1372 $[M+H]^+$ (calcd. for $C_{20}H_{21}O_5$, 341.1389).

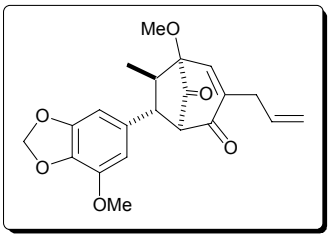
***rac*-2,3-*trans*-3a*α*-methoxy- and *rac*-2,3-*trans*-3a*β*-methoxy-5-allyl-3',4'-methylene-5'-methoxy-3-methyl-3,3a-dihydrobenzofuran-6(2*H*)-one 12a and 12b**.




To a mixture of **11** (550 mg, 1.6 mmol) and HMDS (90 mg, 1.12 mmol) in anhydrous $CH_3CN$ (10 mL), $CuSO_4 \cdot 5H_2O$ (39 mg, 0.016 mmol) was added and the resulting suspension was stirred at

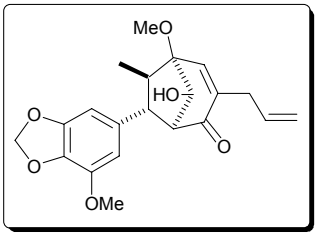
room temperature for 1h. The solids were filtered off and the solution was concentrated. The silylether **3** was used in the next step without further purification. To a solution of silylether **3** (728 mg) in dry MeOH (10 mL) was added dropwise a solution of PIDA (1.10 g, 3.2 mmol) in dry MeOH (15 mL) at room temperature. After addition, the reaction mixture was stirred for 2 h at the same temperature and the solvent was removed under reduced pressure. The residue was fractionated by flash chromatography (silica gel, cyclohexane:AcOEt:$Me_2CO$ 10:1:0.5) to obtain 217 mg of **12b** (36% yield) as colorless oil and 293 mg of **12a** (50%) as slightly yellowish oil. **12b**: $^1$H NMR: $\delta_H$ 6.60 (d, *J* = 1.0 Hz, 1H, H-6'), 6.56 (d, *J* = 1.0 Hz, 1H, H-2'), 6.28 (s, 1H, H-4), 6.02 (s, 2H, $OCH_2O$), 5.80 (s, 1H, H-7), 5.80–5.85 (m, 1H, Ar-$CH_2$-*CH*=$CH_2$), 5.39 (1H, s, H-2), 5.08–5.16 (m, 2H, Ar-$CH_2$-CH=*$CH_2$*), 3.84 (s, 3H, Ar-$OCH_3$), 3.05–3.18 (m, 2H, Ar-*$CH_2$*-CH=$CH_2$), 3.15 (s, 3H, 3a-$OCH_3$), 2.15–2.21 (m, 1H, H-3), 1.13 (d, *J* = 6.8, 3H, 3-$CH_3$). **12a**: $^1$H NMR: $\delta_H$ 6.65 (d, *J* = 1.0 Hz, 1H, H-6'), 6.72 (d, *J* = 1.0 Hz, 1H, H-2'), 6.21 (s, 1H, H-4), 6.59 (s, 2H, $OCH_2O$), 5.87 (s, 1H, H-7), 5.82–5.86 (m, 1H, Ar-$CH_2$-*CH*=$CH_2$), 5.26 (1H, s, H-2), 5.05–5.13 (m, 2H, Ar-$CH_2$-CH=*$CH_2$*), 3.84 (s, 3H, Ar-$OCH_3$), 3.12 (d, *J* = 6.9 Hz, 2H, Ar-*$CH_2$*-CH=$CH_2$), 3.05 (s, 3H, 3a-$OCH_3$), 2.76–2.71 (m, 1H, H-3), 1.14 (d, *J* = 7.5 Hz, 3H, 3-$CH_3$). $^{13}$C NMR: $\delta_C$ 186.8 (C-6), 172.4 (C-7a), 151.8 (C-5'), 148.5 (C-3'), 142.5 (C-5), 137.0 (C-4'), 134.9 (C-1'), 134.8 (C-9), 131.5 (C-4), 117.0 (C-10), 106.8 (C-2'), 104.6 (C-7), 103.9 (C-6'), 101.4 ($OCH_2O$), 94.1 (C-2), 80.2 (C-3a), 56.4 (Ar-$OCH_3$), 50.5 (3a-$OCH_3$), 46.8 (C-3), 33.1 (C-8), 16.3 (3-$CH_3$). IR (film): $\tilde{\nu}$ 1650, 1620, 1512, 1478, 1420, 1356, 1255 cm$^{-1}$. EI-MS: m/z (%) 370 (90), 345 (30), 301 (20), 221 (51), 192 (100), 177 (46). HRMS-ESI: 371.1455 $[M+H]^+$ (calcd. for $C_{21}H_{23}O_6$, 371.1495).

***rac-exo*-aryl-2,3-*trans*-$\Delta^{8'}$-5,5'-dimethoxy-3,4-methylenedioxy-2',3',4',5'-tetrahydro-2',4'-dioxo-7.3',8.5'-neolignan 13**.



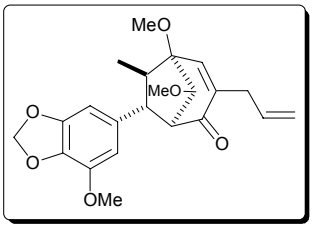

A solution of **12a** (270 mg, 0.73 mmol) in dry MeOH (10 mL) containing a catalytic amount of *p*-toluenesulfonic acid (10 mg, 0.05 mmol) was vigorously heated under reflux for 2 h. The residue obtained after removal of MeOH was purified by flash chromatography (silica gel, cyclohexane:AcOEt 6:1) to afford 208 mg of **13** as a colorless oil (77% yield). $^1$H NMR: $\delta_H$ 7.05 (s, 1H, H-6'), 6.67 (d, *J* = 0.7 Hz, 1H, H-6), 6.55 (d, *J* = 0.7 Hz, 1H, H-2), 5.94 (s, 2H, $OCH_2O$), 5.87-5.83 (m, 1H, H-8'), 5.08–5.20 (m, 1H, H-9'), 3.83 (s, 3H, 5-$OCH_3$), 3.62 (s, 3H, 5'-$OCH_3$), 3.52 (s, 1H, H-3'), 3.12–3.08 (m, 2H, H-7'), 2.49-2.43 (m, 2H, H-7, H-8), 1.07 (d, *J* = 6.6 Hz, 3H, H-9). $^{13}$C NMR: $\delta_C$ 202.2 (C-2'), 194.4 (C-4'), 147.9 (C-6'), 145.7 (C-3), 144.0 (C-5), 140.5 (C-1'), 137.5 (C-4), 137.0 (C-1), 133.9 (C-8'), 118.1 (C-9'), 109.8 (C-6), 103.5 (C-2), 101.3 ($OCH_2O$), 89.4 (C-5'), 69.9 (C-3'), 56.2 (5-$OCH_3$), 53.9 (5'-$OCH_3$), 49.3 (C-8), 45.4 (C-7), 32.8 (C-7'), 13.9 (C-9). IR (film): $\tilde{\nu}$ 1750, 1680 cm$^{-1}$. HRMS-ESI: 371.1502 $[M+H]^+$ (calcd. for $C_{21}H_{23}O_6$, 371.1495).

***rac-exo*-aryl-2,3-*trans*-$\Delta^{8'}$-5,5'-dimethoxy-3,4-methylenedioxy-*endo*-4'-hydroxy-2',3',4',5'-tetrahydro-2'-oxo-7.3',8.5'-neolignan 1 (cinerin B).**



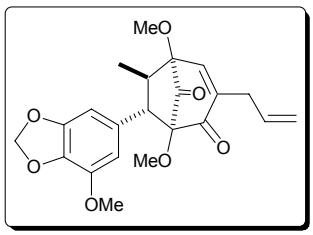

To a solution of **13** (80 mg, 0.22 mmol) in dry EtOH (20 mL) was added dropwise a solution of $NaBH_4$ (10 mg, 0.39 mmol) in dry EtOH (5 mL) at –15 °C. The resulting reaction mixture was stirred for 15 min at –15 °C. Water was added and the aqueous phase extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with water, sat. $NaHCO_3$ and dried over $Mg_2SO_4$. The crude oily product obtained upon filtration and removal of the solvent was purified by flash chromatography (silica gel, cyclohexane:AcOEt 4:1) to give 65 mg of **1** (80% yield) as a slightly yellow oil. $^1$H NMR: $\delta_H$ 6.86 (s, 1H, H-6'), 6.68 (br. s, 1H, H-6), 6.48 (br. s, 1H, H-2), 5.93 (d, $J$ = 0.7 Hz, 1H, $OCH_2O$), 5.81–5.85 (m, 1H, H-8'), 5.14–5.17 (m, 1H, H-9'), 4.21 (s, 1H, H-4'), 3.86 (s, 3H, 5-$OCH_3$), 3.46 (s, 3H, 5'-$OCH_3$), 3.15 (s, 1H, H-3'), 3.02–3.06 (m, 2H, H-7'), 2.64–2.68 (m, 1H, H-8), 2.51 (s, 1H, 4-OH), 2.40 (d, $J$ = 7.5 Hz, 2H, H-7), 0.99 (d, $J$ = 6.8Hz, 3H, H-9). $^{13}$C NMR: $\delta_C$ 198.5 (C-2'), 149.1 (C-6'), 148.2 (C-3), 143.5 (C-5), 139.9 (C-1'), 135.8 (C-4), 134.3 (C-8'), 132.9 (C-1), 118.0 (C-9'), 109.8 (C-6), 103.9 (C-2), 101.3 ($OCH_2O$), 89.8 (C-5'), 75.4 (C-4'), 56.2 (5-$OCH_3$), 53.8 (C-3'), 53.7 (5'-$OCH_3$), 52.2 (C-7), 47.2 (C-8), 32.5 (C-7'), 13.2 (C-9). IR (film): $\tilde{\nu}$ 3465 (br), 1690, 1580, 1535 cm$^{-1}$. HRMS-ESI: 373.1625 $[M+H]^+$ (calcd. for $C_{21}H_{25}O_6$: 373.1651).

***rac-exo*-aryl-2,3-*trans*-$\Delta^{8'}$-5,5',4'-trimethoxy-3,4-methylenedioxy-2',3',4',5'-tetrahydro-2'-oxo-7.3',8.5'-neolignan 14 (cinerin B methylether).**



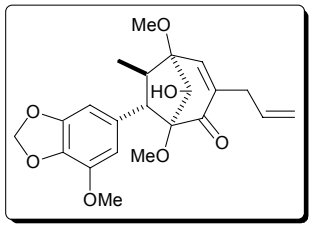

Powdered KOH (660 mg, 1.28 mmol) was added to a solution of cinerin B (**1**) (112 mg, 0.30 mmol), methyl iodide (41 µL, 0.66 mmol) and 18-crown-6 (84 mg, 0.32 mmol) in 10 mL of $CCl_4$. The mixture was refluxed for 9 h to achieve the completition of reaction monitored by TLC. The resulting mixture was filtered over celite, the excess of MeI and $CCl_4$ were removed at reduced pressure and the residue was purified by flash chromatography (silica gel, cyclohexane:AcOEt 10:1) to give 33 mg of cinerin B methylether **14** (27% yield) as colorless oil. $\delta_H$ $^1$H NMR: $\delta_H$ 6.87 (s, 1H, H-6'), 6.61 (d, $J$ = 1.0 Hz, 1H, H-6), 6.49 (d, $J$ = 1.0 Hz, 1H, H-2), 5.94 (s, 2H, $OCH_2O$), 5.88–5.84 (m, 1H, H-8'), 5.15–5.17 (m, 2H, H-9'), 4.20 (s, 1H, H-4'), 3.87 (s, 3H, 5-$OCH_3$), 3.48 (s, 3H, 5'-$OCH_3$), 3.40 (s, 3H, 4'-$OCH_3$), 3.08–3.04 (m, 2H, H-7'), 2.94 (s, 1H, H-3'), 2.87-2.84 (m, 1H, H-8), 2.42 (d, $J$ = 7.5 Hz, 1H, H-7), 0.88 (d, $J$ = 7.0 Hz, 3H, H-9). $^{13}$C NMR: $\delta_C$ 198.8 (C-2'), 148.8 (C-6'), 148.6 (C-3), 143.7 (C-5), 139.7 (C-1'), 135.5 (C-4), 134.2 (C-8'), 132.2 (C-1), 117.9 (C-9'), 110.0 (C-6), 104.2 (C-2), 101.0 ($OCH_2O$), 90.4 (C-5'), 95.7 (C-4'), 56.5 (5-$OCH_3$), 53.2 (C-3'), 54.3 (5'-$OCH_3$), 55.5 (4'-$OCH_3$), 52.5 (C-7), 46.7 (C-8), 32.0 (C-7'), 13.5 (C-9). HRMS-ESI: 387.1801 $[M+H]^+$ (calcd. for $C_{22}H_{27}O_6$: 387.1808).

***rac-exo*-aryl-2,3-*trans*-$\Delta^{8'}$-5,5',3'-trimethoxy-3,4-methylenedioxy-2',3',4',5'-tetrahydro-2',4'-dioxo-7.3',8.5'-neolignan 15 (cinerin A)**.




Prepared according to the previous procedure using **13** (120 mg, 0.32 mmol) instead of cinerin B (**1**). The resulting mixture was filtered over celite, the excess of MeI and $CCl_4$ were removed at reduced pressure and the residue was purified by flash chromatography (silica gel, cyclohexane:AcOEt 10:1) to give 27 mg of **15** (21% yield) as colorless oil. $^1$H NMR: $\delta_H$ 7.09 (s, 1H, H-6'), 6.72 (d, *J* = 1.3 Hz, 1H, H-6), 6.53 (d, *J* = 1.3 Hz, 1H, H-2), 5.94 (s, 2H, $OCH_2O$), 5.88–5.82 (m, 1H, H-8'), 5.15–5.19 (m, 1H, H-9'), 3.84 (s, 3H, 5-$OCH_3$), 3.48 (s, 3H, 5'-$OCH_3$), 3.34 (s, 3H, 3'-$OCH_3$), 3.09–3.07 (m, 2H, H-7'), 2.44–2.42 (m, 2H, H-7, H-8), 1.09 (d, *J* = 7.0 Hz, 3H, H-9). $^{13}$C NMR: $\delta_C$ 203.8 (C-4'), 199.1 (C-2'), 149.5 (C-3), 147.7 (C-6'), 143.8 (C-5), 140.7 (C-1'), 135.1 (C-4), 134.4 (C-8'), 131.8 (C-1), 118.4 (C-9'), 110.4 (C-6), 104.8 (C-2), 101.6 ($OCH_2O$-3,4), 90.2 (C-5'), 89.0 (C-3'), 56.7 (5-$OCH_3$), 54.9 (5'-$OCH_3$), 54.6 (3'-$OCH_3$), 49.9 (C-7), 48.7 (C-8), 33.0 (C-7'), 14.1 (C-9); IR (film): $\tilde{\nu}$ 1775, 1695 cm$^{-1}$. HRMS-ESI: 401.1618 $[M+H]^+$ (calcd. for $C_{22}H_{25}O_7$: 401.1600).

***rac-exo*-aryl-2,3-*trans*-$\Delta^{8'}$-5,5',3'-trimethoxy-3,4-methylenedioxy-*endo*-4'-hydroxy-2',3',4',5'-tetrahydro-2'-oxo-7.3',8.5'-neolignan 2 (cinerin C)**.




Prepared from cinerin A (**15**) (25.5 mg, 63 μmol) according to the same procedure used to reduce **13** to cinerin B (**1**). The crude product after work up was purified by flash chromatography (silica gel, cyclohexane:AcOEt:$Me_2CO$ 14:1:1) affording 21 mg of **2** (82 % yield) as colorless needles (m.p. 182–184°C). $^1$H NMR: $\delta_H$ 6.87 (s, 1H, H-6'), 6.70 (d, *J* = 1.2 Hz, 1H, H-6), 6.51 (d, *J* = 1.2 Hz, H-2), 5.93 (s, 2H, $OCH_2O$), 5.87–5.83 (m, 1H, H-8'), 5.14–5.19 (m, 2H, H-9'), 4.24 (s, 1H, H-4'), 3.87 (s, 3H, 5-$OCH_3$), 3.47 (s, 3H, 3'-$OCH_3$), 3.34 (s, 3H, 5'-$OCH_3$), 3.14–3.04 (m, 2H, H-7'), 2.89–2.86 (m, 1H, H-8), 2.64 (s, 1H, 4-OH), 2.43 (d, J = 8.0 Hz, 1H, H-7), 0.93 (d, *J* = 7.0 Hz, 3H, H-9). $^{13}$C NMR: $\delta_C$ 198.1 (C-2'), 149.2 (C-6'), 148.6 (C-3), 142.9 (C-5), 139.4 (C-1'), 134.3 (C-8'), 134.2 (C-1), 132.0 (C-4), 117.7 (C-9'), 110.2 (C-2), 104.6 (C-6), 101.2 ($OCH_2O$), 89.7 (C-3'), 87.0 (C-3'), 75.0 (C-4'), 56.5 (5-$OCH_3$), 56.2 (C-7), 54.4 (5'-$OCH_3$), 53.6 (3'-$OCH_3$), 47.7 (C-8), 32.4 (C-7'), 13.2 (C-9). IR (KBr): $\tilde{\nu}$ 3430, 1695, 1630 cm$^{-1}$. EI-MS: m/z (%) 402 (72), 384 (2), 370 (3), 210 (17), 194 (100), 192 (37), 169 (66), 165 (26), 150 (11), 135 (9). HRMS-ESI: 403.1729 $[M+H]^+$ (calcd. for $C_{22}H_{27}O_7$: 403.1757).

## $^{1}$H and $^{13}$C NMR SPECTRA

Figure S1. $^{1}$H NMR spectrum (300 MHz in $CDCl_3$) of compound **10**

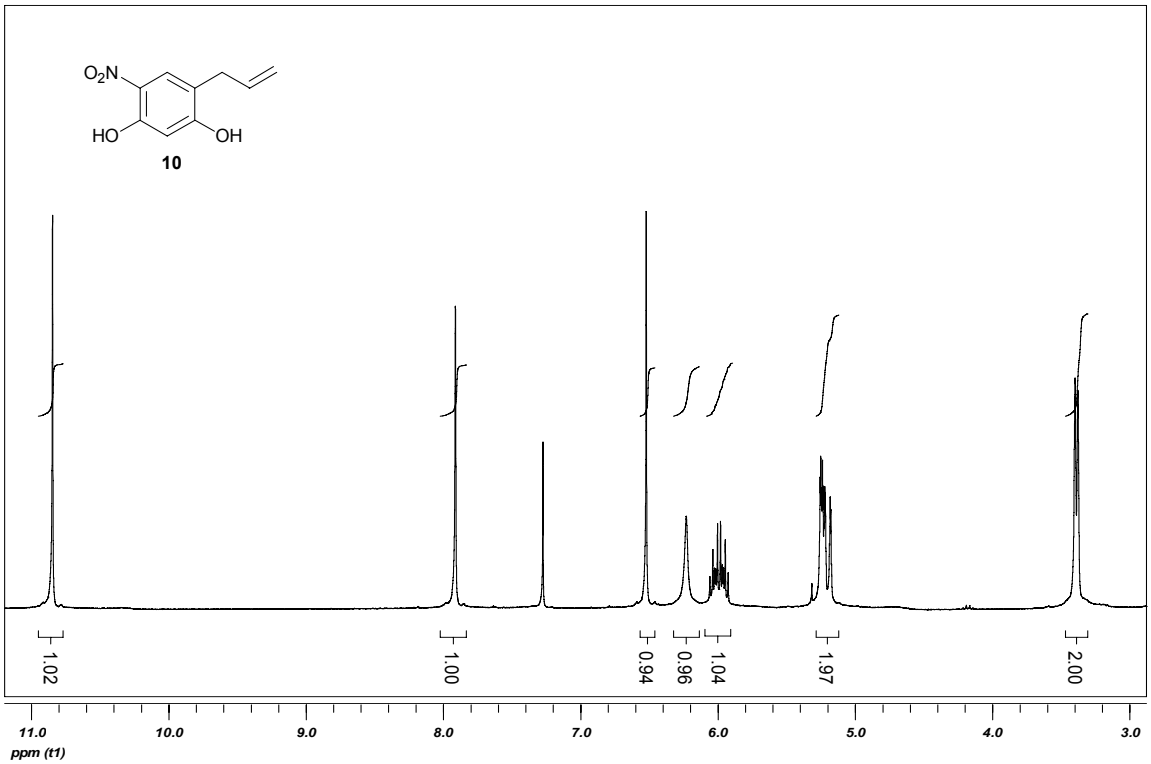



Figure S2. $^{13}$C NMR spectrum (75.4 MHz in $CDCl_3$) of compound **10**

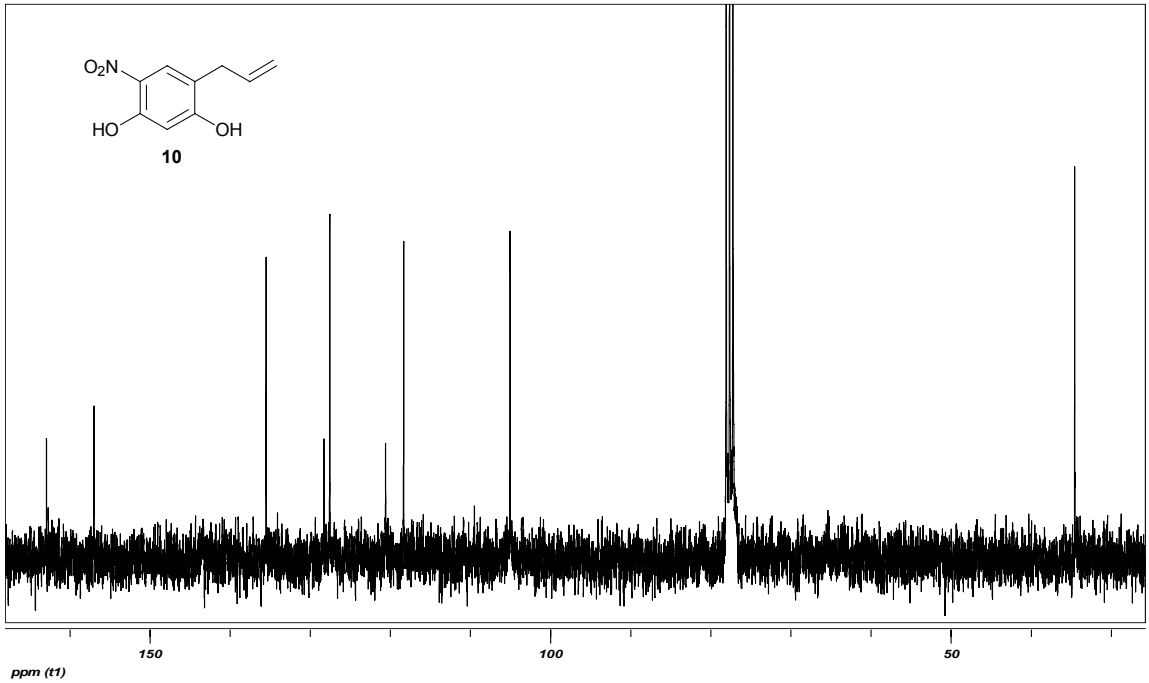


Figure S3. $^{1}H$ NMR spectrum (300 MHz in $CDCl_3$) of compound **11**

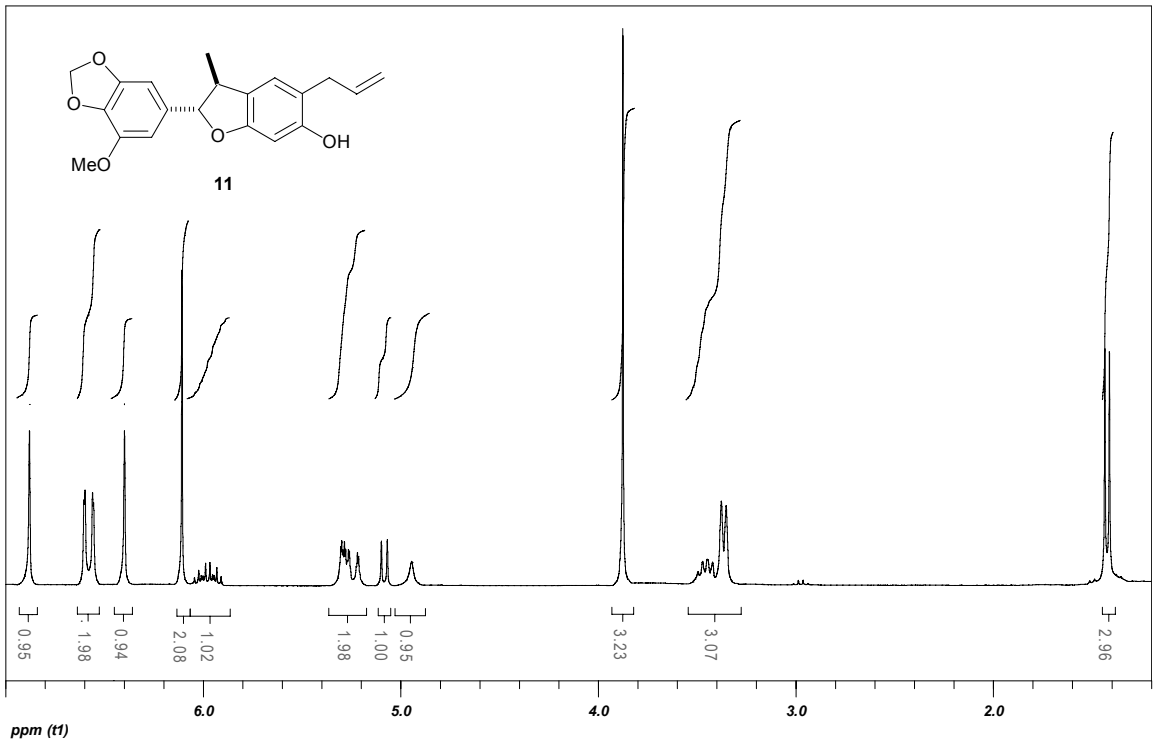



Figure S4. $^{13}C$ NMR spectrum (75.4 MHz in $CDCl_3$) of compound **11**

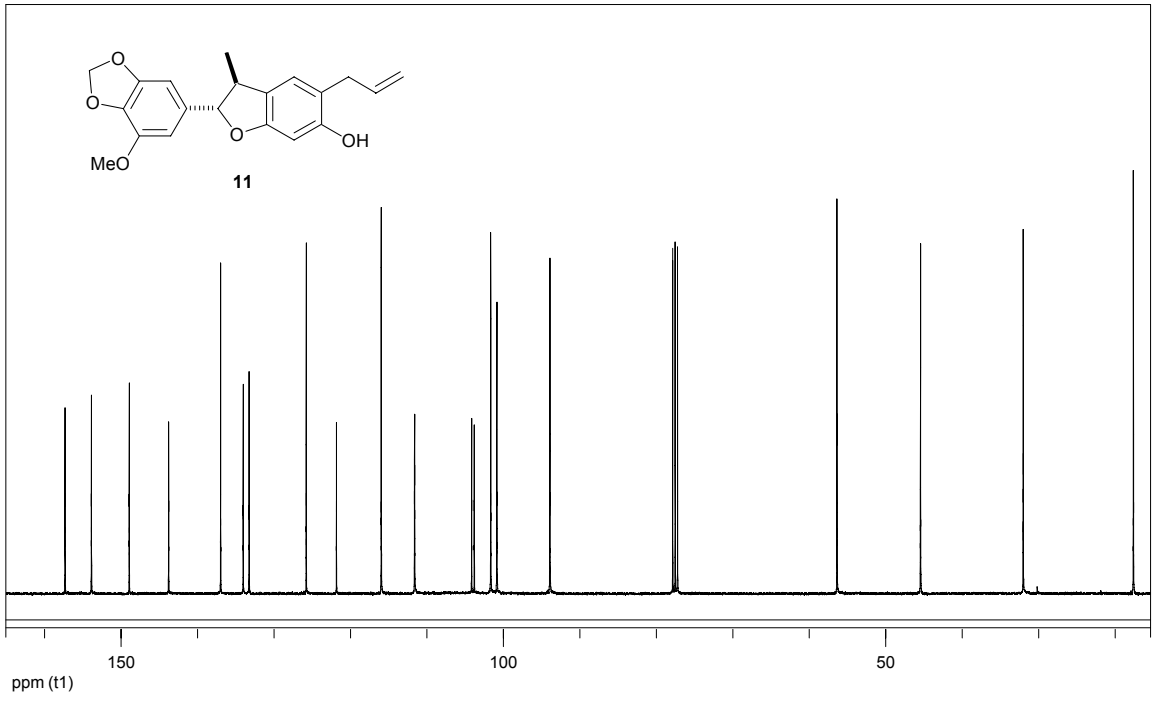


Figure S5. $^{1}H$ NMR spectrum (300 MHz in $CDCl_3$) of compound **12a**

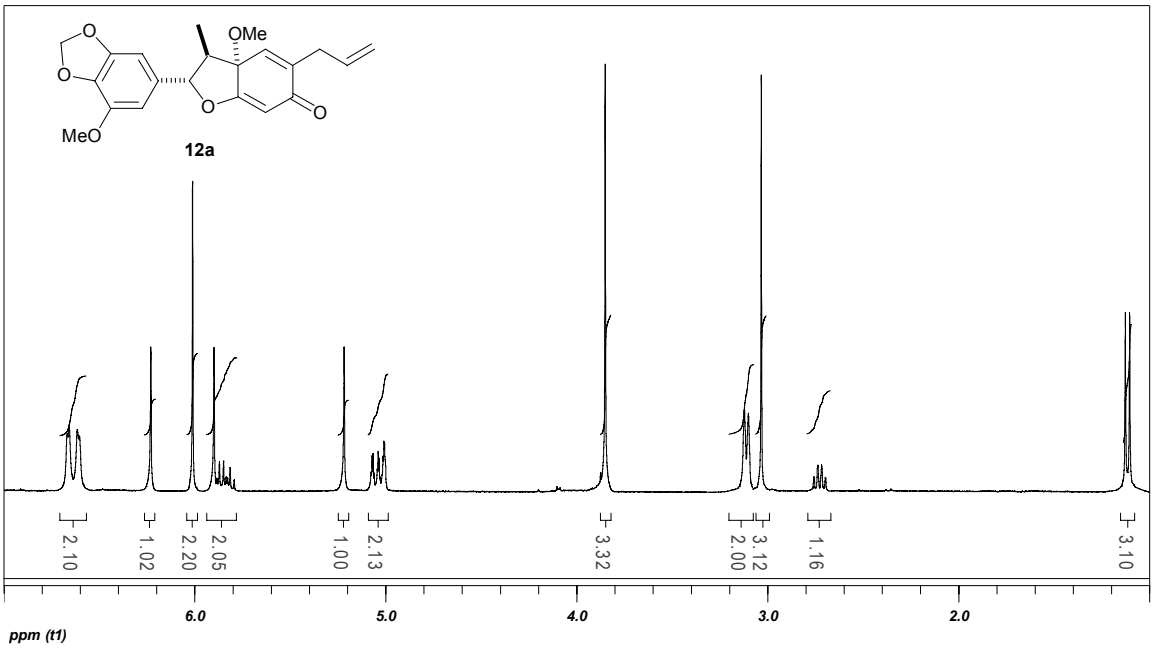



Figure S6. $^{13}C$ NMR spectrum (75.4 MHz in $CDCl_3$) of compound **12a**

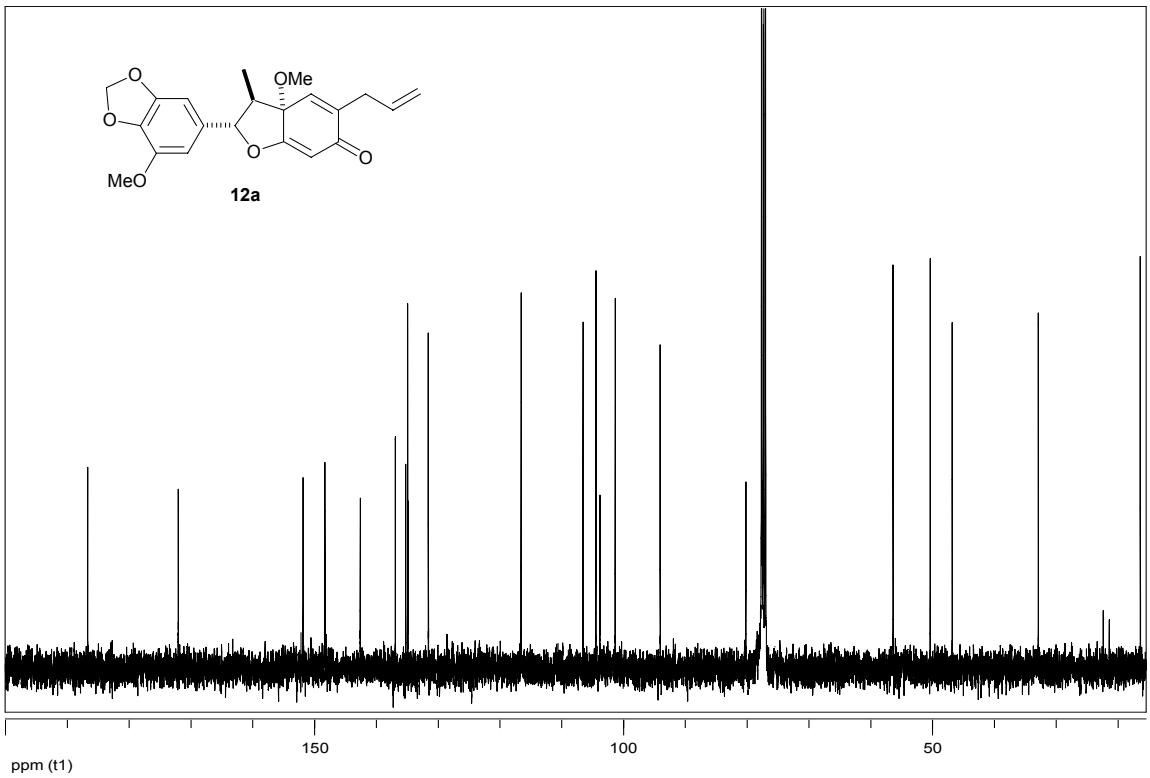


Figure S7. $^{1}H$ NMR spectrum (300 MHz in $CDCl_3$) of compound **13**

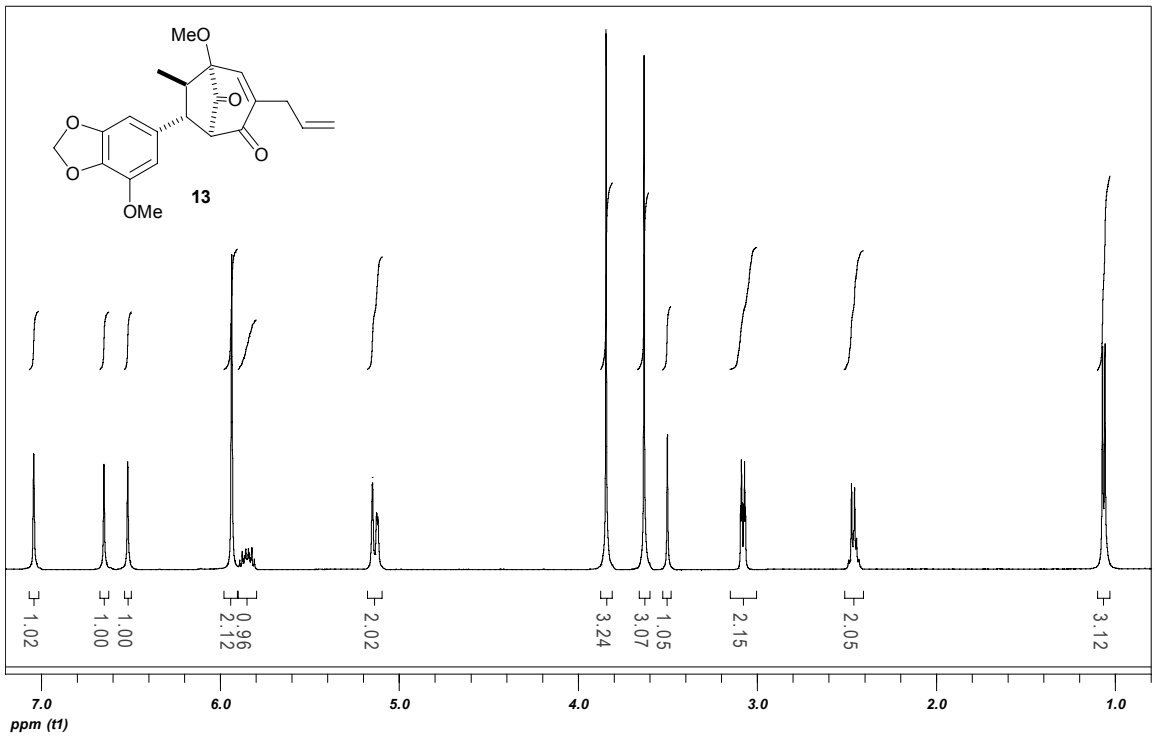



Figure S8. $^{13}C$ NMR spectrum (75.4 MHz in $CDCl_3$) of compound **13**

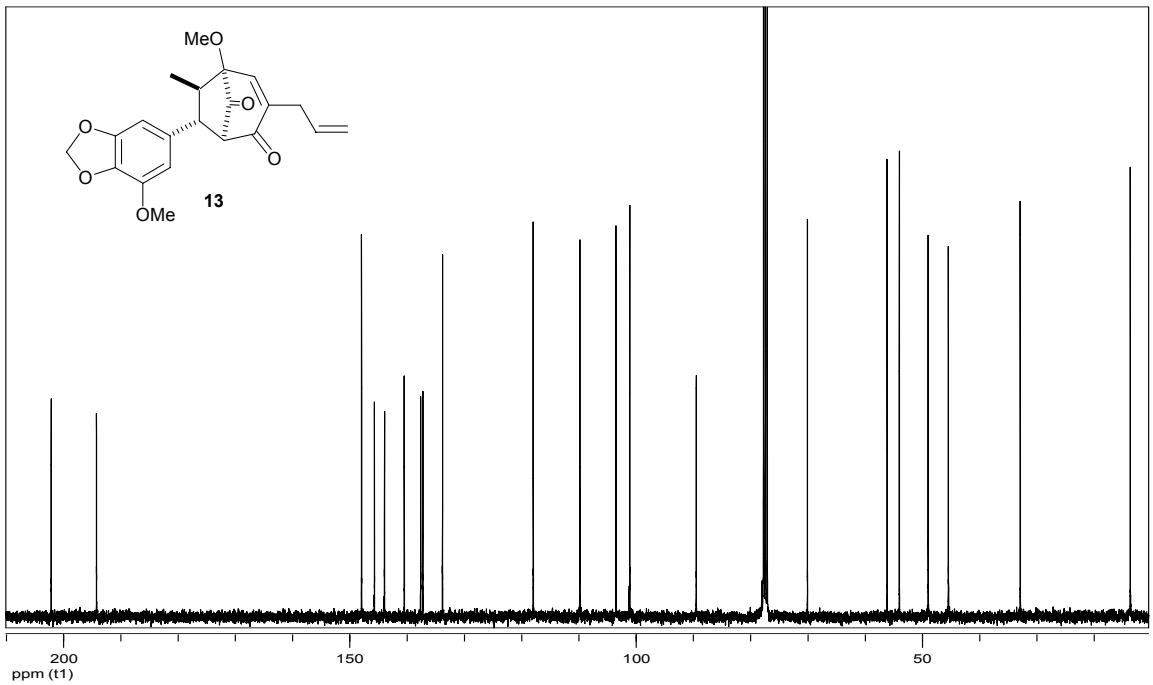


Figure S9. $^{1}H$ NMR spectrum (300 MHz in $CDCl_3$) of cinerin B (**1**)

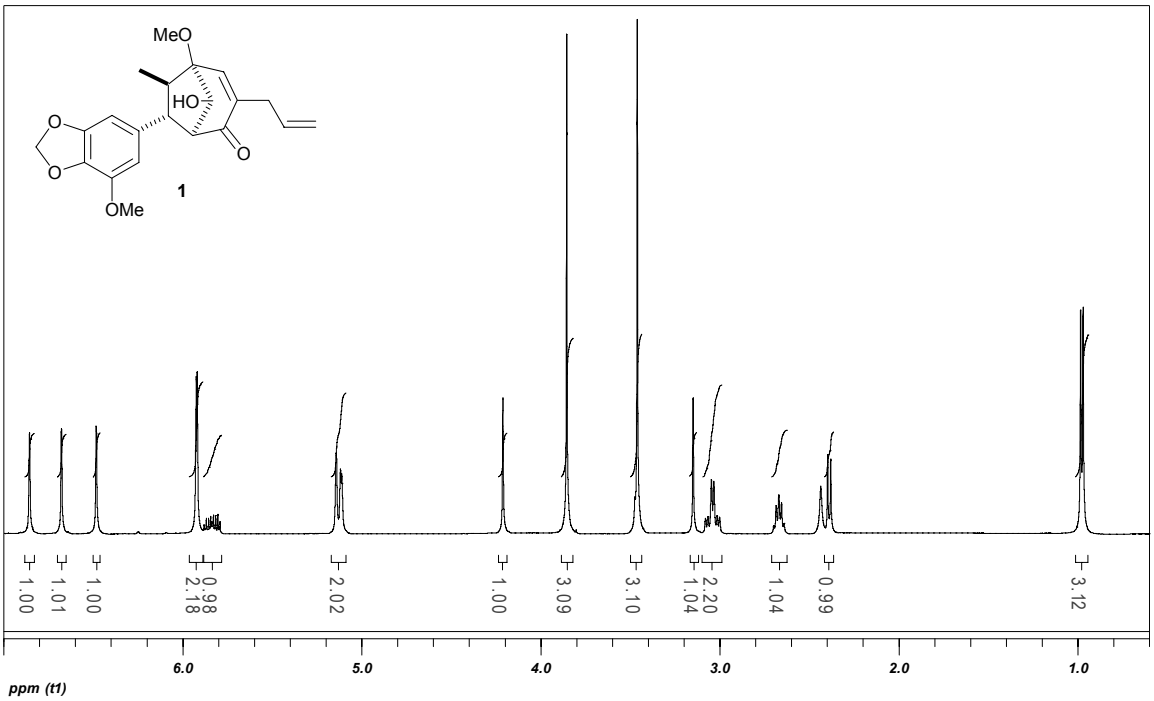



Figure S10. $^{13}C$ NMR spectrum (75.4 MHz in $CDCl_3$) of cinerin B (**1**)

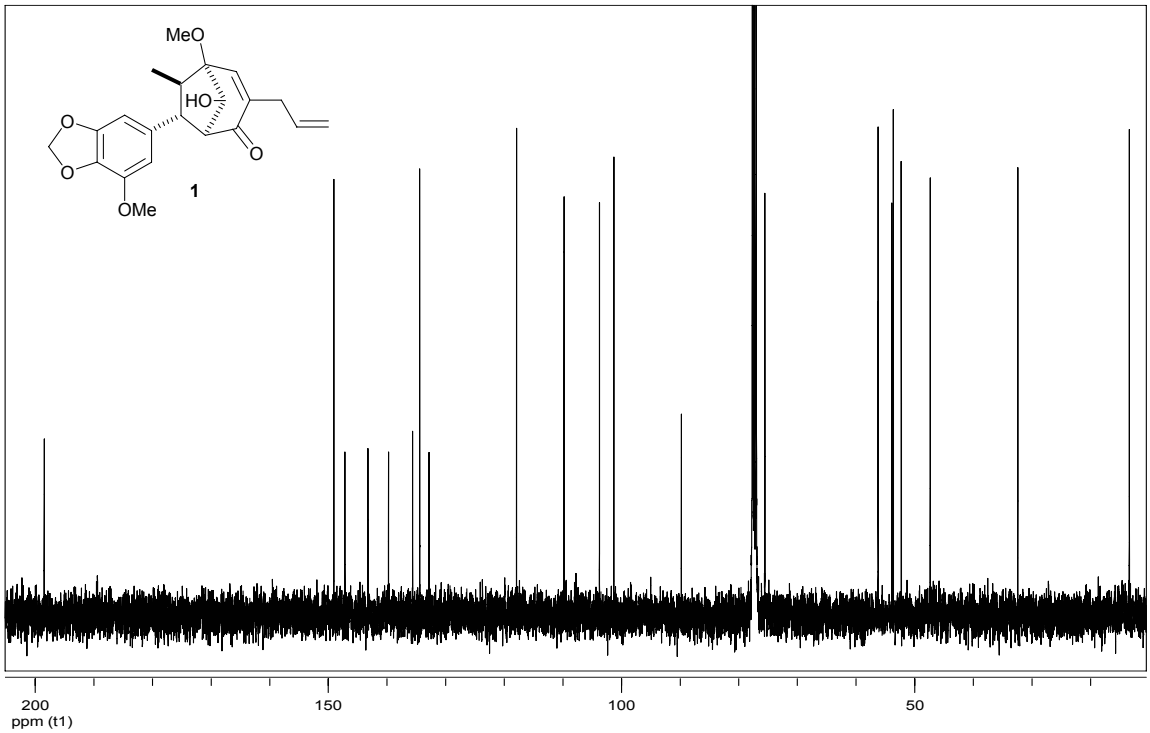


Figure S11. $^{1}H$ NMR spectrum (300 MHz in $CDCl_3$) of compound **14**

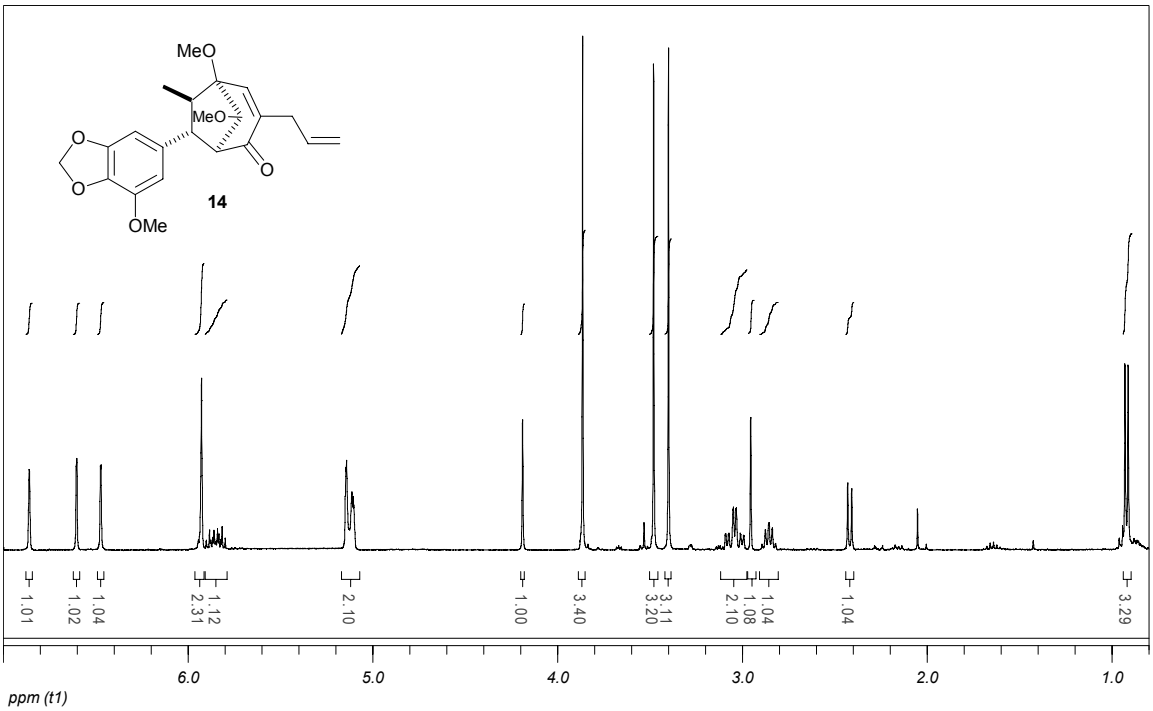



Figure S12. $^{13}C$ NMR spectrum (75.4 MHz in $CDCl_3$) of compound **14**

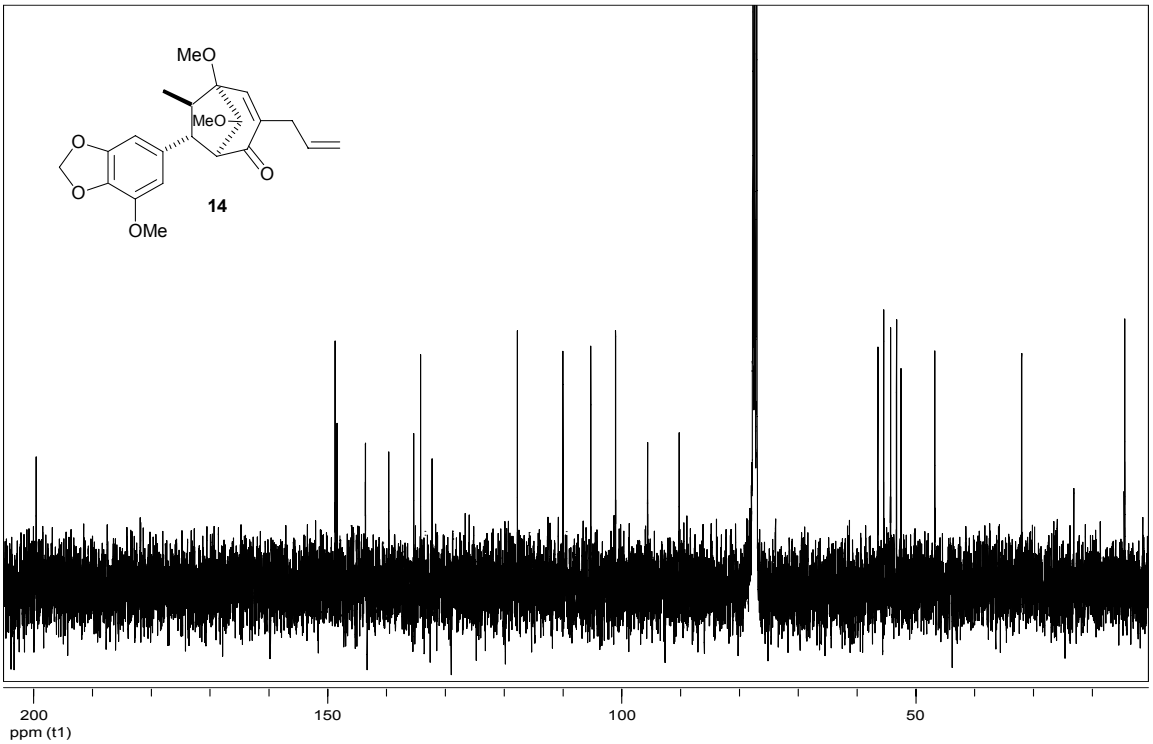


Figure S13. $^{1}H$ NMR spectrum (300 MHz in $CDCl_3$) of cinerin A (**15**)

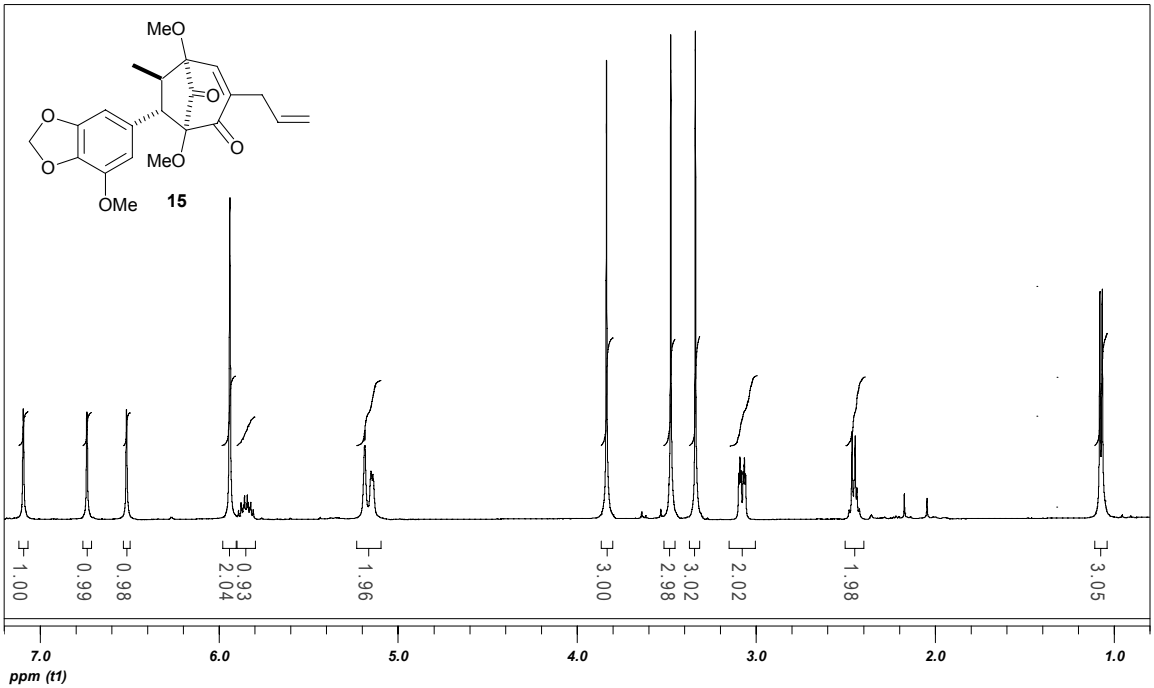



Figure S14. $^{13}C$ NMR spectrum (75.4 MHz in $CDCl_3$) of cinerin A (**15**)

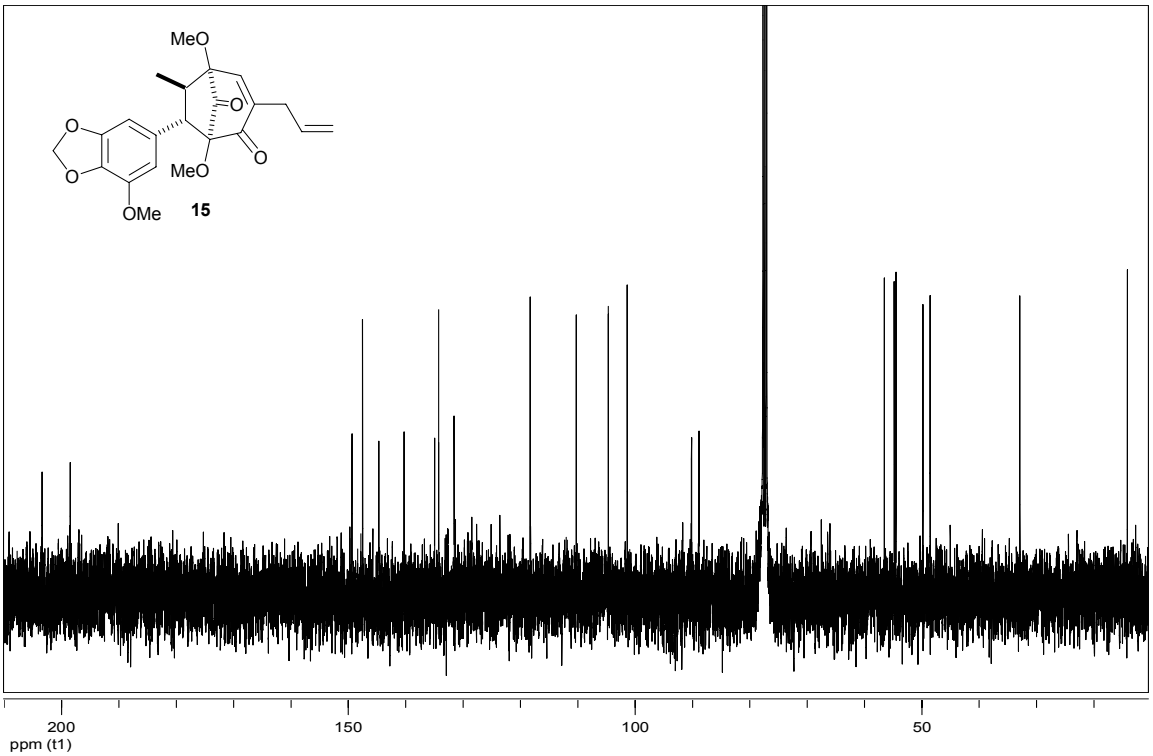


Figure S15. $^{1}$H NMR spectrum (300 MHz in $CDCl_3$) of cinerin C (**2**)

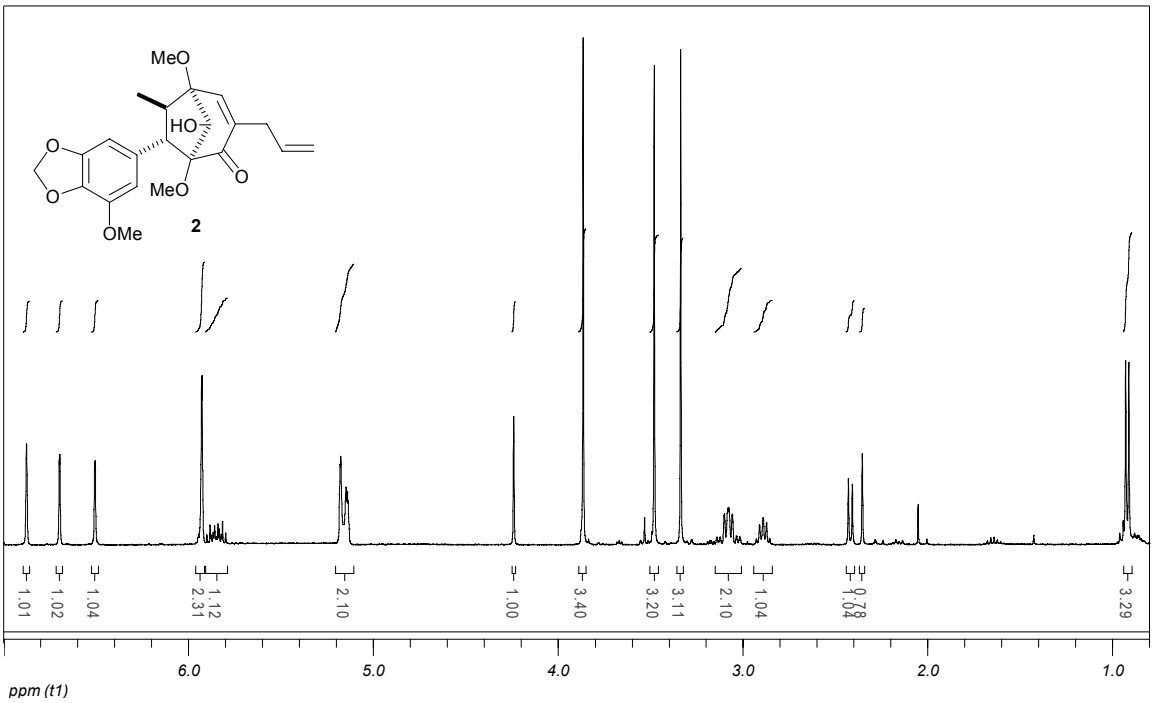



Figure S16. $^{13}$C NMR spectrum (75.4 MHz in $CDCl_3$) of cinerin C (**2**)