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# Supporting Information



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# First Total Synthesis of (±)-Symbioimine

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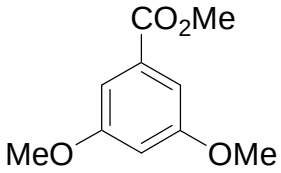
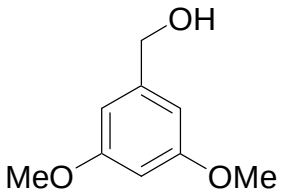
## *Experimental Section*

**General**. Unless otherwise noted, all reactions were performed in oven-dried glassware. All solvents used in the reactions were purified before use. Dry diethyl ether, tetrahydrofuran, and toluene were distilled from sodium and benzophenone, whereas dry dichloromethane, dimethylformamide, pyridine, and triethylamine were distilled from $CaH_2$. Petroleum ether with a boiling range of 40-60 °C was used. Reactions were generally run under nitrogen atmosphere. All commercially available compounds (Acros, Aldrich, Fluka, Merck) were used without purification. $^1H$ and $^{13}C$ NMR: Bruker Avance 400, spectra were recorded at 295 K either in $CDCl_3$ or DMSO-$d_6$; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (δH 7.25, δC 77.0 ppm), DMSO-$d_6$ (δH 2.49, δC 39.5 ppm). Melting points: Büchi Melting Point B-540, uncorrected. EI-MS: Finnigan Triple-Stage-Quadrupol (TSQ-70). HRMS (FT-ICR): Bruker Daltonic APEX 2 with electron spray ionization (ESI). Flash chromatography: J. T. Baker silica gel 43-60 μm. Thin-layer chromatography Machery-Nagel Polygram Sil G/UV254. The compounds having the same number of skeletal carbon atoms as symbioimine were numbered according to the natural product.

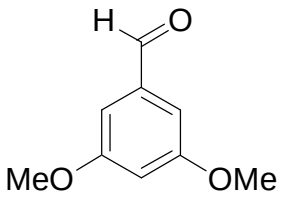



**Methyl 3,5-dimethoxybenzoate**: To a mechanically stirred suspension of 3,5-dihydroxy-benzoic acid (100 g, 0.65 mol) and $K_2CO_3$ (360 g, 2.6 mol, 4 equiv) in acetone (1 L) was added dimethyl sulphate (217 mL, 2.3 mol, 3.5 equiv) at room temperature. The reaction mixture was vigorously stirred at reflux for 4 h, then cooled to room temperature and filtered. The filter solid was rinsed with acetone (2 × 100 mL) and most of the acetone was removed with a rotary evaporator. The residue was diluted with 5% $NH_4OH$ solution (500 mL), stirred 5 min, and extracted with $Et_2O$ (500 + 2 ×100 mL). The $Et_2O$ solution was washed with 5% HCl, then with saturated $NaHCO_3$ solution, dried with $Na_2SO_4$, filtered and evaporated to dryness (10 mbar) at the rotary evaporator. The crude product was dissolved in hot MeOH (200 mL), and the solution allowed to cool to 23 °C, followed by slow dropwise addition of deionized water (100 mL) inducing crystallization. The crystals were filtered through a sintered frit, rinsed on the filter with a cooled (4 °C) mixture of deionized water/methanol (1/2), (2 × 100 mL), then dried under vacuum to remove all water; yield 122 g (0.624 mol, 96%) as a white powder, m.p. 42 °C.

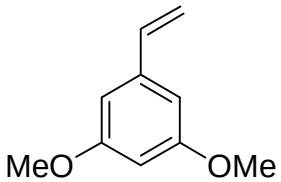



**(3,5-Dimethoxyphenyl)methanol**: $NaBH_4$ (26.5 g, 0.70 mol, 5 equiv) was added to a solution of methyl 3,5-dimethoxybenzoate (27.46 g, 0.140 mol) in DME (250 mL). The mixture was heated to reflux and MeOH (125 mL) was slowly added within 2 h while keeping the inner temperature above 70 °C. The mixture was refluxed for an additional 1 h, then most of solvent was evaporated. The residue was diluted with $Et_2O$ and quenched with water. The layers were separated and the aqueous layer extracted with $Et_2O$. The combined organic layers were washed with water and brine, dried with $Na_2SO_4$, filtered, and concentrated in

vacuo to give pure (by NMR) (3,5-dimethoxyphenyl)methanol as a colorless oil, which is crystallized when stored, yield 23.28 g (138.5 mmol, 99%), m.p. 47-47.5 °C.

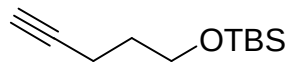



**3,5-Dimethoxybenzaldehyde**: To a stirred suspension of pyridinium dichromate (45.1 g, 1.2 equiv) in $CH_2Cl_2$ (100 mL) was added a solution of (3,5-dimethoxyphenyl)methanol (16.8 g, 0.1 mol) in $CH_2Cl_2$ (50 mL) dropwise at room temperature. The mixture was stirred at room temperature for 24 h, then filtered through a pad of celite. The filter pad was washed with $CH_2Cl_2$ (2 × 30 mL). Most of the $CH_2Cl_2$ was removed under reduced pressure, and the residue was diluted with $Et_2O$ (100 mL). The ether solution was washed two times with 5% NaOH, then with 5% HCl, saturated $NaHCO_3$ solution, and finally with brine, followed by drying with $Na_2SO_4$ and concentration in vacuo. The crude product was dissolved in a minimum amount of hot MeOH, and recrystallized by slow addition of deionized water. The crystals were filtered, rinsed with a cold MeOH/$H_2O$ mixture, and then dried under vacuum to remove all water; yield 13.5 g (81 mmol, 81%) as colorless crystals, m.p. 46-47 °C.



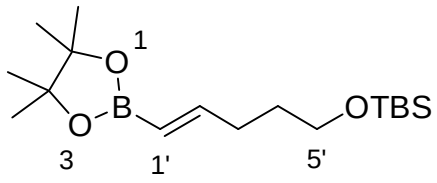

**4**

**1,3-Dimethoxy-5-vinylbenzene (4)**: This reaction was performed under an inert atmosphere. To a suspension of methyl triphenylphosphonium bromide (23.2 g, 65 mmol, 1.2 equiv) in dry THF (100 mL), KO*t*Bu (8.5 g, 76 mmol, 1.4 equiv) was added in one portion. The mixture was stirred for 2 h at room temperature, then cooled to -70 to -80 °C followed by the dropwise addition of a solution of 3,5-dimethoxybenzaldehyde (9.0 g, 54.2 mmol) in dry THF (50 mL) at -70 to -65 °C. Then the cooling bath was removed, and the mixture allowed to warm to room temperature. Now, the reaction was quenched with dry MeOH (10 mL). The solvents were evaporated under reduced pressure and the residue passed through a short pad (4 cm) of silica gel using petroleum ether/ethyl acetate, 15:1 as eluent, to give 8.54 g (52.0 mmol, 96%) of 3,5-dimethoxystyrene as a colorless oil. $R_f$ = 0.45 (petroleum ether/ethyl acetate, 10:1).



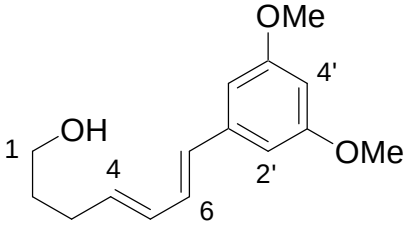

***tert*-Butyl(dimethyl)(pent-4-ynyloxy)silane**: A solution of TBSCl (59.0 g, 0.394 mol, 1.1 equiv) in dry DMF (200 mL) was added dropwise to a mixture of pentyn-5-ol (30.0 g, 0.357 mol) and imidazole (60.4 g, 0.89 mol, 2.5 equiv) at 0 °C. The mixture was stirred at room temperature for 12 h, then quenched with water (1 L) and extracted with petroleum ether (3 × 200 mL). The extracts were washed with water and brine, dried $Na_2SO_4$, filtered, and evaporated in vacuo. The crude silyl ether was distilled at around 65 °C (10 mbar) to provide 64 g (90%) of product. Alternatively, it can be passed through a short pad of silica gel to yield 70 g (99%) of *tert*-butyl(dimethyl)(pent-4-ynyloxy)silane as a colorless oil. $R_f$ = 0.85 (petroleum ether/ethyl acetate, 10:1); $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.04 (s, 6H, $CH_3Si$), 0.88 (s, 9H, $(CH_3)_3CSi$), 1.71 (tt, *J* = 7.1, 6.1 Hz, 2H, C*H*$_2$$CH_2O$), 1.91 (t, *J* = 2.8 Hz,

1H, HC=C), 2.26 (td, *J* = 7.1, 2.8 Hz, 2H, $CH_2C$=), 3.68 (t, *J* = 6.1 Hz, 2H, $CH_2O$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.4 ($CH_3Si$), 14.8 (*C*$H_2C$=), 18.3 (($CH_3)_3$*C*Si), 25.9 ((*C*$H_3)_3$CSi), 31.5 ($CH_2CH_2O$), 61.4 ($CH_2O$), 68.2 (H*C*=C-), 84.2 (HC=*C*-).




**6**

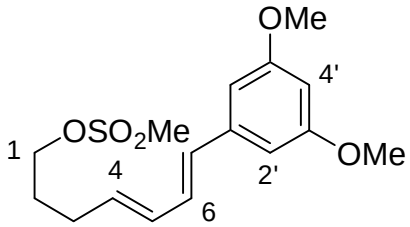
***tert*-Butyl(dimethyl){[(4E)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-enyl]oxy}silane (6)**: To a stirred solution of *tert*-butyl(dimethyl)(pent-4-ynyloxy)silane (30 g, 0.152 mol) was added dropwise at room temperature catecholborane (19.4 mL, 0.182 mol, 1.2 equiv) within 1 h under an inert atmosphere. After complete addition, the mixture was stirred at 70 °C for 12 h, then cooled to 23 °C, followed by the addition of pinacol (25.0 g, 0.212 mol, 1.4 equiv). The mixture was stirred for 3 h at room temperature before it was diluted with petroleum ether (400 mL) and stirred for 10 min. The precipitate was filtered off and the filtrate washed with 5% NaOH (5 × 100 mL) and once with brine. The organic layer was dried with $Na_2SO_4$, filtered, and evaporated in vacuo. The residue was distilled at 108-110 °C (0.4 mbar) to give 42 g (85%) of the vinyl boronate as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.02 (s, 6H, $CH_3Si$), 0.87 (s, 9H, $(CH_3)_3CSi$), 1.24 (s, 12H, $((CH_3)_2CO)_2B$-), 1.62 (tt, *J* = 7.1, 6.3 Hz, 2H, -C*H*$_2CH_2O$-), 2.19 (td, *J* = 7.1, 6.3 Hz, 2H, -C*H*$_2$CH=), 3.59 (t, *J* = 6.3 Hz, 2H, -$CH_2O$-), 5.43 (d, *J* = 17.9 Hz, 1H, -C*H*=CBH), 6.63 (dt, *J* = 17.9, 6.3 Hz, 1H, -CH=C*H*B$pin_2$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.3 ($CH_3Si$), 18.3 (($CH_3)_3$*C*Si), 24.8 (((*C*$H_3)_2CO)_2$B-), 25.9 ((*C*$H_3)_3$CSi), 31.3 ($CH_2$), 32.1 ($CH_2$), 62.6 (-$CH_2O$-), 83.0 (((CH$_3)_2$*C*O)$_2$B-), 118.9 (-HC=*C*HB-), 154.2 (-H*C*=CHB-); HRMS (ESI): calcd for $C_{17}H_{35}BO_3Si$ $[M+H]^+$ 326.25576, found 326.25579.



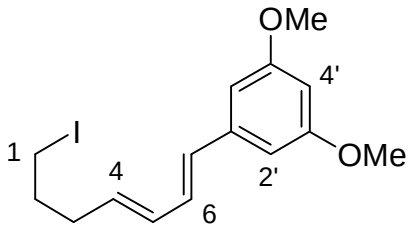

**7**

**(4*E*,6*E*)-7-(3,5-Dimethoxyphenyl)hepta-4,6-dien-1-ol (7)**: Solid $Na_2CO_3$ (21.2 g, 0.2 mol) was added in one portion to a stirred solution of 3,5-dimethoxystyrene (**4**) (32.0 g, 0.195 mol) and $Pd(OAc)_2$ (2.24 g, 10 mmol) in dry DMF (300 mL). Then oxygen was bubbled through the mixture for 10 min, then the flask was connected to an oxygen filled rubber balloon and the mixture heated to 60 °C. Then, a solution of boronate **6** (32.6 g, 0.1 mol) in DMF (50 mL) was added via siringe pump over 12 h while keeping the temperature of the flask at 60 °C and the mixture under a positive oxygen pressure. After complete addition, the was mixture stirred for an additional 2 h at 60 °C before it was cooled to room temperature. The mixture was diluted with EtOAc (500 mL) and poured into ice-cold water (1.5 L). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 200 mL). The combined organic extracts were washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and evaporated in vacuo. The crude diene was filtered through a short pad of silica gel (5% of EtOAc in hexane, $R_f$ = 0.4), giving a mixture of unreacted styrene **4** together with the TBS-protected dienol. The solvents were evaporated, and the residue dissolved in MeOH (300

mL). A solution of concentrated HCl (10 mL), dissolved in MeOH (50 mL) was added dropwise to this solution at room temperature. The mixture was stirred for 30 min, then MeOH was evaporated in vacuo at room temperature, and EtOAc (100 mL) and water (500 mL) were added to the residue. The layers were separated and the aqueous phase extracted with EtOAc (2 × 100 mL). The combined EtOAc extracts were washed with 5% $NaHCO_3$ and with brine, dried over anhydrous $Na_2SO_4$, filtered, and evaporated. Flash chromatography of the residue (hexane/EtOAc, 2:1) afforded to 17.75 g of styrene **4** ($R_f$ = 0.7-0.8) and 14.6 g (68% based on the recovered styrene **6**, or 59% based on the reacted boronate **6**) of alcohol **7**. $R_f$ = 0.2 (hexane/ethyl acetate, 2:1); $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.69 (tt, *J* = 7.1, 6.5 Hz, 2H, 2-H), 2.23 (td, *J* = 7.3, 7.1 Hz, 2H, -C*H*$_2$CH=), 3.66 (t, *J* = 6.5 Hz, 2H, -$CH_2$O-), 3.78 (s, 6H, $OCH_3$), 5.82 (dt, *J* = 15.2, 7.3 Hz, 1H, 4-H), 6.20 (dd, *J* = 15.2, 10.6 Hz, 1H, 5-H), 6.33 (t, *J* = 2.3 Hz, 1H, 4'-H), 6.37 (d, *J* = 15.7 Hz, 1H, 7-H), 6.52 (d, *J* = 2.3 Hz, 2H, 2'-H), 6.72 (dd, *J* = 15.7, 10.6 Hz, 1H, 6-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 29.1 ($CH_2$), 32.1 ($CH_2$), 55.2 ($OCH_3$), 62.2 ($OCH_2$), 99.5 (C-4'), 104.1 (C-2'), 129.6, 130.3, 130.8, 135.1, 139.5 (C-1'), 160.8 (C-3').



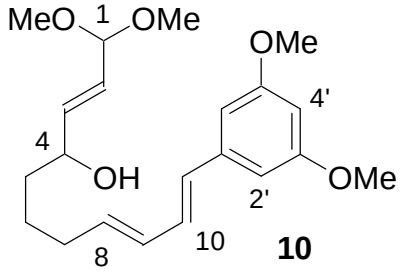

**(4*E*,6*E*)-7-(3,5-Dimethoxyphenyl)hepta-4,6-dienyl methanesulfonate**: MsCl (5.86 mL, 75 mmol, 1.3 equiv) was added dropwise at -30 °C to a stirred solution of alcohol **7** (14.4 g, 58 mmol) and $NEt_3$ (16.2 mL, 116 mmol, 2 equiv) in dry $CH_2Cl_2$ (300 mL) under inert atmosphere. The reaction was stirred 1 h at -30 °C, then allowed to warm to room temperature and quenched with water (300 mL). After separation of the layers, the aqueous phase was extracted with $CH_2Cl_2$ (2 × 100 mL). The combined $CH_2Cl_2$ extracts were washed with brine (2 × 50 mL), dried over anhydrous $Na_2SO_4$, filtered, and evaporated. The residue was chromatographed through short pad of silica gel (hexane/EtOAc, 2:1, $R_f$ = 0.25), to provide 18.6 g (57 mmol, 98%) of mesylate. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.86 (tt, *J* = 7.3, 6.8 Hz, 2H, 2-H), 2.25 (td, *J* = 7.3, 7.1 Hz, 2H, -C*H*$_2$CH=), 2.98 (s, 3H, $OSO_2CH_3$), 3.78 (s, 6H, $OCH_3$), 4.22 (t, *J* = 6.5 Hz, 2H, 1-H), 5.76 (dt, *J* = 15.2, 7.3 Hz, 1H, 4-H), 6.22 (dd, *J* = 15.2, 10.3 Hz, 1H, 5-H), 6.33 (t, *J* = 2.3 Hz, 1H, 4'-H), 6.38 (d, *J* = 15.4 Hz, 1H, 7-H), 6.52 (d, *J* = 2.3 Hz, 2H, 2'-H), 6.70 (dd, *J* = 15.4, 10.3 Hz, 1H, 6-H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 28.5 ($CH_2$), 28.5 ($CH_2$), 37.2 ($OSO_2CH_3$), 55.2 ($OCH_3$), 69.2 ($OCH_2$), 99.6 (C-4'), 104.1 (C-2'), 129.2, 130.9, 131.7, 133.1, 139.3 (C-1'), 160.8 (C-3'); HRMS (ESI): calcd for $C_{16}H_{22}O_5S$ $[M+H]^+$ 327.12606, found 327.12610.




**8**

**1-[(1*E*,3*E*)-7-Iodohepta-1,3-dienyl]-3,5-dimethoxybenzene (8)**: NaI (45 g, 0.3 mol, 5.2 equiv) was added in one portion to a stirred solution of the foregoing mesylate (18.6 g, 57 mmol) in dry acetone (200 mL) under inert atmosphere. The mixture was stirred in the dark

for 24 h, then diluted with petroleum ether (100 mL) and water (200 mL). The layers were separated and the aqueous phase extracted with petroleum ether (100 mL). The combined organic layers were washed with brine (2 × 50 mL), dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was chromatographed through a short pad of silica gel (hexane/EtOAc, 10:1, $R_f$ = 0.4), to yield 19.1 g (53.3 mmol, 93%) of the iodide **8** as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.94 (tt, *J* = 7.1, 6.8 Hz, 2H, 6'-H), 2.26 (td, *J* = 7.1, 6.8 Hz, 2H, 5'-H), 3.20 (t, *J* = 6.8 Hz, 2H, 7'-H), 3.79 (s, 6H, $OCH_3$), 5.75 (dt, *J* = 15.2, 7.1 Hz, 1H, 4'-H), 6.25 (dd, *J* = 15.2, 10.4 Hz, 1H, 3'-H), 6.34 (t, *J* = 2.3 Hz, 1H, 4-H), 6.40 (d, *J* = 15.7, 1H, 1'-H), 6.53 (d, *J* = 2.3 Hz, 2H, 2,6-H), 6.71 (dd, *J* = 15.7, 10.4 Hz, 1H, 2'-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 6.3 (C-7'), 32.7 ($CH_2$), 33.3 ($CH_2$), 55.3 ($OCH_3$), 99.6 (C-4), 104.2 (C-2,6), 129.4 (=CH-), 130.8 (=CH-), 131.7 (=CH-), 133.2 (=CH-), 139.4 (C-1), 160.8 (C-3); HRMS (ESI): calcd for $C_{15}H_{19}IO_2$ $[M+H]^+$ 359.05025, found 359.05007.

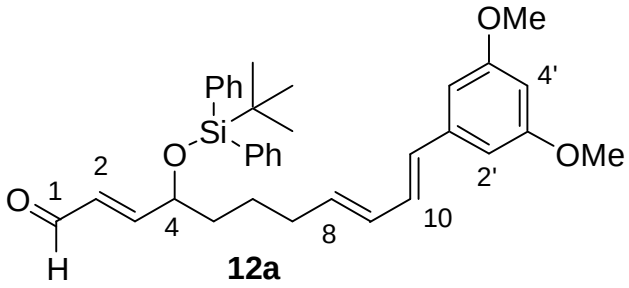



**10**

**(2*E*,8*E*,10*E*)-11-(3,5-Dimethoxyphenyl)-1,1-dimethoxyundeca-2,8,10-trien-4-ol (10)**: To a solution of iodide **8** (1.5 g, 4.19 mmol) in dry $Et_2O$ (20 mL), prepared under inert atmosphere, was added *t*-BuLi (1.5 M in hexane, 7 mL, 10.5 mmol, 2.5 equiv) in a dropwise fashion at -80 °C over 15 min. The mixture was stirred at -80 °C for 0.5 h, then fumaraldehyde monodimethyl acetal (0.65 g, 5.0 mmol, 1.2 equiv) in $Et_2O$ (5 mL) was added dropwise. The mixture was stirred for 15 min at -80 °C, then quenched with half-saturated $NH_4Cl$ solution, and allowed to warm to room temperature. After separation of the layers, the water phase was extracted with $Et_2O$ (2 × 20 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was chromatographed quickly through silica gel (hexane/EtOAc/$NEt_3$, 100:100:1, $R_f$ = 0.35) to yield the acetal **10** (0.91 g, 3.3 mmol, 60 %) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.44-1.68 (m, 2H, H-5,6), 2.15 (q, *J* = 6.7 Hz, 1H, 7-H), 3.31 (s, 6H, acetal $OCH_3$), 3.78 (s, 6H, $OCH_3$), 4.16 (br s, 1H, 4-H), 4.78 (d, *J* = 4.8 Hz, 1H, 1-H), 5.65 (ddd, *J* = 15.9, 4.8, 1.0 Hz, 1H, 2-H), 5.79 (dt, *J* = 15.2, 7.1 Hz, 1H, 8-H), 5.88 (dd, *J* = 15.2, 6.1 Hz, 1H, 3-H), 6.18 (dd, *J* = 15.2, 10.4 Hz, 1H, 9-H), 6.33 (t, *J* = 2.3 Hz, 1H, 4'-H), 6.36 (d, *J* = 15.7, 1H, 1'-H), 6.52 (d, *J* = 2.3 Hz, 2H, 2',6'-H), 6.70 (dd, *J* = 15.7, 10.4 Hz, 1H, 10-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 25.7 (C-6), 32.6 (C-7), 36.5 (C-5), 52.7 (acetal $OCH_3$), 52.7 (acetal $OCH_3$), 55.3 ($OCH_3$), 71.8 (C-4), 99.6 (C-4'), 102.4 (C-1), 104.2 (C-2',6'), 126.7 (C-2), 129.8 (C-10), 130.2 (C-11), 130.8 (C-9), 135.5 (C-8), 137.5 (C-3), 139.6 (C-1'), 160.8 (C-3',5').

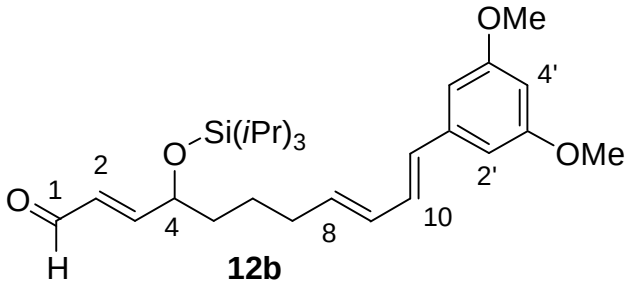
**General procedure for silylation and acetal cleavage of 10**: A solution of TBSCl (4.05 g, 27 mmol, 2 equiv) in anhydrous $CH_2Cl_2$ (10 mL) was added to a stirred solution of alcohol **10** (4.89 g, 13.5 mmol) and imidazole (4.66 g, 67.5 mmol, 5 equiv) in $CH_2Cl_2$ (40 mL) under an inert atmosphere within 15 min at 0 °C. The mixture was allowed to reach room temperature overnight, then diluted with petroleum ether (150 mL) and washed with 5% $NaHCO_3$ and with brine. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was dissolved in acetone (300 mL) and Amberlyst-15 (1.5 g) was added in one portion. The mixture was stirred at 23 °C for 40 min, then filtered through a pad of $Na_2CO_3$, and the filtrate was evaporated. The residue was purified by flash chromatography

(hexane/EtOAc, 10:1, $R_f$ = 0.25) to give 4.8 g (11.16 mmol, 83%) of **12c** as a colorless oil. The corresponding TBDPS and TIPS protected aldehydes **12a** and **12b** were prepared by the same procedure giving 80% of **12a** and 75% of **12b**.



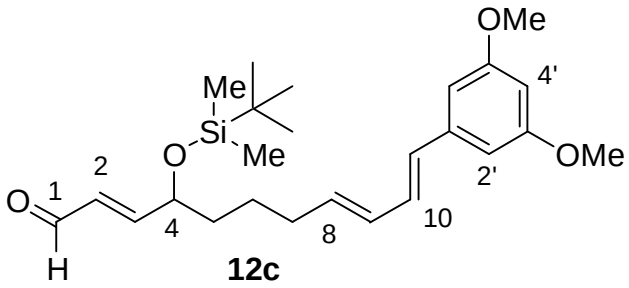

**12a**

**(2*E*,8*E*,10*E*)-4-{[*tert*-Butyl(diphenyl)silyl]oxy}-11-(3,5-dimethoxyphenyl)undeca-2,8,10-trienal (12a)**: 0.45 mmol scale, yield 203 mg (80%). $R_f$ = 0.2 (hexane/EtOAc, 10:1). $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.08 (s, 9H, $(CH_3)_3CSi$), 1.24-1.60 (m, 6H, $CH_2$), 3.80 (s, 6H, $OCH_3$), 4.48 (q, *J* = 5.1 Hz, 1H, 4-H), 5.67 (dt, *J* = 15.2, 7.1 Hz, 1H, 8-H), 6.10 (dd, *J* = 15.2, 10.6 Hz, 1H, 9-H), 6.25 (ddd, 1H, *J* = 15.7, 8.1 Hz, *J* = 1.3 Hz, 1H, 2-H), 6.34 (t, 1H, *J* = 2.3 Hz, 1H, 4'-H), 6.35 (d, 1H, *J* = 15.7, 1H, 11-H), 6.53 (d, 2H, *J* = 2.3 Hz, 2H, 2',6'-H), 6.64-6.70 (m, 2H, 3,10-H), 7.32-7.47 (m, 6H, *m*,*p*-PhSi), 7.60 (br d, *J* = 6.8 Hz, 2H, *o*-PhSi), 7.60 (br d, 2H, *J* = 6.8 Hz, *o*-PhSi), 9.45 (d, 1H, *J* = 8.1 Hz, 1-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 19.3 ($(CH_3)_3CSi$), 23.6 ($CH_2$), 27.0 ($(CH_3)_3CSi$), 32.5 ($CH_2$), 36.1 ($CH_2$), 55.3 ($OCH_3$), 72.3 (C-4), 99.6 (C-4'), 104.2 (C-2'), 127.7, 127.7, 129.7, 129.9, 130.3, 130.8, 131.0, 133.2, 133.5, 135.1, 135.8, 139.6 (C-1'), 159.0 (C-3), 160.9 (C-3'), 193.5 (C-1).



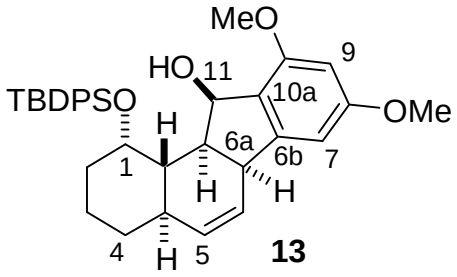

**12b**

**(2*E*,8*E*,10*E*)-11-(3,5-Dimethoxyphenyl)-4-[(triisopropylsilyl)oxy]undeca-2,8,10-trienal (12b)**: 0.105 mmol scale, yield 40 mg (75%). $R_f$ = 0.25 (hexane/EtOAc, 20:1). $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.05 (br s, 21H, *i*PrSi), 1.34-1.58 (m, 2H, $CH_2$), 1.65-1.72 (m, 2H, $CH_2$), 2.15 (q, *J* = 7.1 Hz, 2H, 7-H), 3.78 (s, 6H, $OCH_3$), 4.59 (q, *J* = 5.1 Hz, 1H, 4-H), 5.77 (dt, *J* = 14.9, 7.1 Hz, 1H, 8-H), 6.17 (dd, *J* = 14.9, 10.6 Hz, 1H, 9-H), 6.28 (dd, *J* = 15.6, 7.8 Hz, 1H, 2-H), 6.33 (t, *J* = 2.3 Hz, 1H, H-4'), 6.37 (d, *J* = 15.4 Hz, 1H, 11-H), 6.52 (d, *J* = 2.3 Hz, 2H, 2',6'-H), 6.70 (dd, *J* = 15.4, 10.6 Hz, 1H, 10-H), 6.79 (dd, *J* = 15.6, 5.1 Hz, 1H, 3-H), 9.58 (d, *J* = 7.8 Hz, 1H, 1-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 12.3 ($(CH_3)_2CHSi$), 18.0 ($(CH_3)_2CHSi$), 23.6 ($CH_2$), 32.7 ($CH_2$), 36.8 ($CH_2$), 55.3 ($OCH_3$), 71.6 (C-4), 99.6 (C-4'), 104.2 (C-2'), 129.6, 130.3, 130.9, 131.0, 135.1, 139.5 (C-1'), 160.0 (C-3), 160.8 (C-3',5'), 193.6 (C-1); HRMS (ESI) calcd for $C_{28}H_{44}O_4Si$ $[M+H]^+$ 473.30816, found 473.30817.




**12c**

**(2*E*,8*E*,10*E*)-4-{[*tert*-Butyl(dimethyl)silyl]oxy}-11-(3,5-dimethoxyphenyl)undeca-2,8,10-trienal (12c)**: $^{1}$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.02 (s, 3H, $(CH_3)_2Si$), 0.06 (s, 3H, $(CH_3)_2Si$), 0.91 (s, 9H, $(CH_3)_3CSi$), 1.43-1.53 (m, 1H, 6-H), 1.56-1.66 (m, 1H, 5-H), 2.15 (q, 1H, *J* = 7.1 Hz, 1H, 7-H), 3.78 (s, 6H, $OCH_3$), 4.42 (ddd, *J* = 5.8, 4.6, 1.5 Hz, 1H, 4-H), 5.78 (dt, *J* = 15.2, 7.1 Hz, 1H, 8-H), 6.17 (dd, *J* = 15.2, 10.6 Hz, 1H, 9-H), 6.25 (ddd, *J* = 15.6, 8.1, 1.5 Hz, 1H, 2-H), 6.33 (t, *J* = 2.3 Hz, 1H, 4'-H), 6.37 (d, *J* = 15.6, 1H, 11-H), 6.52 (d, *J* = 2.3 Hz, 2H, 2',6'-H), 6.71 (dd, *J* = 15.6, 10.6 Hz, 1H, 10-H), 6.78 (dd, *J* = 15.6, 4.6 Hz, 1H, 3-H), 9.56 (d, *J* = 8.1 Hz, 1H, 1-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -4.9 ($(CH_3)_2Si$), -4.7 ($(CH_3)_2Si$), 18.1 ($(CH_3)_3CSi$), 24.4 (C-6), 25.7 ($(CH_3)_3CSi$), 32.6 (C-7), 36.5 (C-5), 55.3 ($OCH_3$). 71.4 (C-4), 99.6 (C-4'), 104.2 (C-2',6'), 129.6 (C-10), 130.3 (C-11), 130.7 (C-2), 130.9 (C-9), 135.2 (C-8), 139.5 (C-1'), 160.0 (C-3), 160.8 (C-3',5'), 193.6 (C-1).

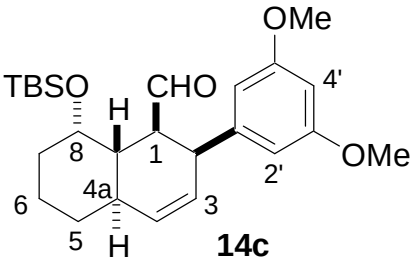



**13**

**1-(2,2-Dimethyl-1,1-diphenylpropoxy)-8,10-dimethoxy-2,3,4,4a,6a,11,11a,11b-octahydro-1*H*-benzo[a]fluoren-11-ol (13)**: To a solution of trienal **12a** (50 mg, 0.09 mmol) in dry $CH_2Cl_2$ (5 mL) was added $MeAlCl_2$ (1 M in $CH_2Cl_2$, 0.1 mL, 1.1 equiv) dropwise at -80 °C under inert atmosphere. The mixture was stirred at -80 °C for 3 h, quenched with water (20 mL) and allowed to warm to room temperature. The resulting mixture was extracted with $CH_2Cl_2$ (2 × 20 mL), extracts were washed with saturated $NaHCO_3$ solution, dried over over $Na_2SO_4$, filtered, and evaporated. The residue was purified by flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.35) to provide tetracycle **13** (25 mg, 50%) as a colorless oil. $^{1}$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.66 (t, *J* = 11.2 Hz, 1H, CH), 0.88 (m, 1H, $CH_2$), 1.14 (s, 9H, $(CH_3)_3CSi$), 1.24-1.40 (m, 3H), 1.66-1.93 (m, 3H), 2.55 (br t, *J* = 11.2 Hz, 1H, 4a-H), 2.63 (dd, *J* = 12.1, 6.8 Hz, 1H, 11a-H), 3.75 (s, 1H, $OCH_3$), 3.77 (s, 1H, $OCH_3$), 3.96 (br s, 1H, 6a-H), 4.35 (s, 1H, 1-H), 4.78 (s, 1H, 11-H), 5.61 (br d, *J* = 9.9 Hz, 1H, 5-H), 6.02 (ddd, *J* = 9.9, 3.8, 3.0 Hz, 1H, 6-H), 6.21 (s, 1H, 9-H), 6.30 (s, 1H, 7-H), 7.35-7.50 (m, 6H, *m*-,*p*-PhSi), 7.75 (br d, *J* = 6.8 Hz, 2H, *o*-PhSi), 7.82 (br d, *J* = 6.8 Hz, 2H, *o*-PhSi); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 19.6 ($(CH_3)_3CSi$), 20.3 ($CH_2$), 27.3 ($(CH_3)_3CSi$), 33.0 (CH), 33.3 ($CH_2$), 33.5 ($CH_2$), 43.2 (CH), 44.0 (CH), 48.1 (CH), 55.2 ($OCH_3$), 55.4 ($OCH_3$), 68.4 (C-11), 73.6 (C-1), 96.7 (C-9), 99.6 (C-7), 124.7 (C-6), 127.5, 127.7, 129.7, 129.9, 133.8 (C-5), 136.2, 136.3, 150.0 (C-6b), 157.5 (C-10), 162.3 (C-8).

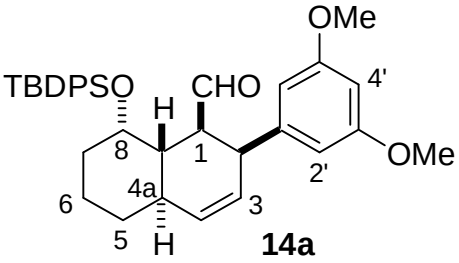
**General procedure for the $Me_2AlCl$ mediated IMDA reaction**: To a stirred solution of trienal **12c** (650 mg, 1.5 mmol) in dry $CH_2Cl_2$ (30 mL) at -80 °C was added via syringe $Me_2AlCl$ (1 M in $CH_2Cl_2$, 2.4 mL, 2.4 mmol, 1.6 equiv) within 0.5 h under an inert atmosphere. The mixture was stirred for 2.5 h at -80 °C, then treated with MeOH (5 mL) and

5% $NaHCO_3$ solution (10 mL) at this temperature, followed by warming to room temperature. The mixture was diluted with 5% $NaHCO_3$ solution (100 mL) and extracted with $Et_2O$ (3 × 50 mL). The organic extracts were washed with brine, dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 10:1, $R_f$ = 0.25) to yield 0.553 g (1.275 mmol, 85%) of cycloadduct **14c** as colorless crystals. The TIPS- and TBDPS-protected IMDA adducts were prepared in a similar fashion.



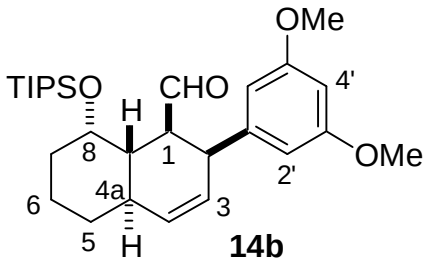

**14c**

**8-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-(3,5-dimethoxyphenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalene-1-carbaldehyde (14c)**: m.p. 65 °C; $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = -0.08 (s, 3H, $(CH_3)_2Si$), -0.02 (s, 3H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3CSi$), 1.20 (qd, *J* = 12.6, 3.8 Hz, 1H, $CH_2$), 1.43 (br t, *J* = 13.6 Hz, 1H, $CH_2$), 1.54 (br d, *J* = 13.6 Hz, 1H, $CH_2$), 1.70-1.90 (m, 3H, $CH_2$), 1.85 (dd, *J* = 11.6, 10.4 Hz, 1H, 8a-H), 2.43 (br t, *J* = 10.4 Hz, 1H, 4a-H), 2.79 (ddd, *J* = 11.6, 6.8, 4.3 Hz, 1H, 1-H), 3.74 (s, 6H, $OCH_3$), 3.75 (br s, 1H, 2-H), 3.95 (br s, 1H, 8-H), 5.54 (ddd, *J* = 9.9, 4.3, 2.8 Hz, 1H, 3-H), 5.74 (br d, *J* = 9.9 Hz, 1H, 4-H), 6.29 (d, *J* = 2.3 Hz, 2H, 2',6'-H), 6.31 (t, *J* = 2.3 Hz, 1H, 4'-H), 9.16 (d, *J* = 4.3 Hz, 1H, CHO); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.2 $(CH_3)_2Si$), -4.2 $(CH_3)_2Si$), 18.1 ($(CH_3)_3CSi$), 20.5 (C-6), 25.9 ($(CH_3)_3CSi$), 33.1 (C-5), 33.2 (C-4a), 33.9 (C-7), 40.1 (C-8a), 43.2 (C-2), 51.4 (C-1), 55.2 ($OCH_3$), 67.1 (C-8), 98.7 (C-4'), 108.1 (C-2',6'), 125.9 (C-4), 133.9 (C-3), 141.7 (C-1'), 160.6 (C-3',5'), 205.9 (CHO); HRMS (ESI): calcd for $C_{25}H_{38}O_4Si$ $[M+Na]^+$ 453.24316, found 453.24298.



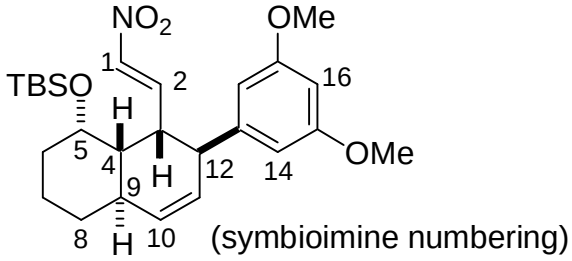

**14a**

**8-{[*tert*-Butyl(diphenyl)silyl]oxy}-2-(3,5-dimethoxyphenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalene-1-carbaldehyde (14a)**: m.p. 109 °C; $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.06 (s, 9H, $(CH_3)_3CSi$), 1.14-1.30 (m, 2H, $CH_2$), 1.47 (br d, *J* = 13.1 Hz, 1H, $CH_2$), 1.64 (br d, *J* = 13.9 Hz, 1H, $CH_2$), 1.80 (t, *J* = 10.9 Hz, 1H, 8a-H), 1.83-1.94 (m, 2H, $CH_2$), 2.61 (br dd, *J* = 12.4, 10.9 Hz, 1H, 4a-H), 2.95 (ddd, *J* = 11.4, 6.6, 3.6 Hz, 1H, 1-H), 3.70 (s, 6H, $OCH_3$), 3.77 (br s, 1H, 2-H), 4.07 (br s, 1H, 8-H), 5.57 (ddd, *J* = 9.9, 4.3, 2.8 Hz, 1H, 3-H), 5.77 (br d, *J* = 9.9 Hz, 1H, 4-H), 6.22 (d, *J* = 2.3 Hz, 2H, 2',6'-H), 6.26 (t, *J* = 2.3 Hz, 1H, 4'-H), 7.30-7.42 (m, 6H, *m*-,*p*-PhSi), 7.57-7.64 (m, 4H, *o*-PhSi), 8.88 (d, *J* = 3.6 Hz, 1H, CHO); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 19.5 ($(CH_3)_3CSi$), 20.8 ($CH_2$), 27.2 ($(CH_3)_3CSi$), 33.2 ($CH_2$), 33.3 ($CH_2$), 33.4 (C-4a), 40.3 (C-8a), 43.2 (C-2), 51.1 (C-1), 55.2 ($OCH_3$), 68.6 (C-8), 98.6 (C-4'), 108.2 (C-2',6'), 126.1 (C-3), 127.3, 127.4, 129.5, 129.7, 133.3, 133.7 (C-4), 134.6, 136.0, 136.13, 141.6 (C-1'), 160.5 (C-3',5'), 204.7 (CHO).



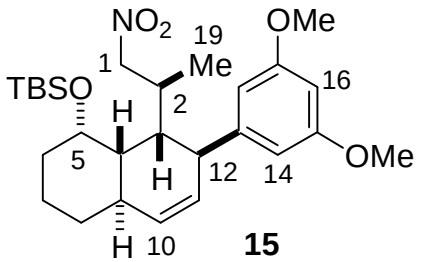

**14b**

**2-(3,5-Dimethoxyphenyl)-8-[(triisopropylsilyl)oxy]-1,2,4a,5,6,7,8,8a-octahydro-naphthalene-1-carbaldehyde (14b)**: colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.02 (br s, 21H, *i*$Pr_3Si$), 1.22 (qd, *J* = 12.6, 3.8 Hz, 1H, $CH_2$), 1.43-1.59 (m, 2H, $CH_2$), 1.78-1.92 (m, 4H), 2.47 (br dd, *J* = 12.4, 10.6 Hz, 1H, 4a-H), 2.89 (ddd, *J* = 11.4, 6.6, 4.1 Hz, 1H, 1-H), 3.74 (s, 6H, $OCH_3$), 3.77 (m, 2-H), 4.16 (s, 1H, 8-H), 5.56 (ddd, *J* = 9.9, 4.6, 2.8 Hz, 1H, 3-H), 5.75 (br d, *J* = 9.9 Hz, 1H, 4-H), 6.29 (d, *J* = 2.3 Hz, 2H, 2',6'-H), 6.31 (t, *J* = 2.3 Hz, 1H, 4'-H), 9.25 (d, *J* = 4.1 Hz, 1H, CHO); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 12.9 ($(CH_3)_2$*C*HSi), 18.3 ((*C*$H_3)_2$CHSi), 20.9 ($CH_2$), 32.9 (C-4a), 33.2 ($CH_2$), 34.2 ($CH_2$), 40.6 (C-8a), 43.3 (C-2), 51.3 (C-1), 55.2 ($OCH_3$), 67.6 (C-8), 98.8 (C-4'), 108.2 (C-2',6'), 125.8 (C-3), 133.9 (C-4), 141.6 (C-1'), 160.6 (C-3',5'), 206.0 (CHO).



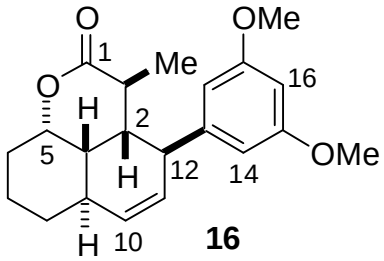

(symbioimine numbering)

**rel-(4*S*,4a*S*,5*R*,6*S*,8a*R*)-4-{[*tert*-Butyl(dimethyl)silyl]oxy}-6-(3,5-dimethoxyphenyl)-5-[(*E*)-2-nitrovinyl]-1,2,3,4,4a,5,6,8a-octahydronaphthalene**: A mixture of aldehyde **14c** (20 mg, 0.046 mmol) and $NH_4OAc$ (20 mg) in $MeNO_2$ was stirred at 60 °C for 24 h under an inert atmosphere. Thereafter, excess $MeNO_2$ (1 mL) was evaporated under reduced pressure and the residue purified by flash chromatography (hexane/EtOAc, 10:1, $R_f$ = 0.3) to provide 19 mg (0.04 mmol, 88%) of nitroalkene as a colorless oil. $^{1}$H NMR (400 MHz, $CDCl_3$): δ[ppm] = -0.03 (d, *J* = 4.0 Hz, 6H, $(CH_3)_2$Si), 0.84 (s, 9H, $(CH_3)_3$CSi), 1.05-1.15 (m, 1H, $CH_2$), 1.24-1.61 (m, 3H, $CH_2$), 1.70 (br d, *J* = 12.9 Hz, 1H, $CH_2$), 1.77 (ddd, *J* = 13.1, 3.8, 3.5 Hz, 1H, 4-H), 1.93 (br d, *J* = 12.9 Hz, 1H, $CH_2$), 2.49 (dd, *J* = 13.1, 11.4 Hz, 1H, 9-H), 2.55 (br d, *J* = 9.9 Hz, 1H, 3-H), 3.28 (d, *J* = 3.8 Hz, 1H, 5-H), 3.79 (br s, 7H, H-12, $OCH_3$), 5.58 (ddd, *J* = 9.9, 4.6, 2.8 Hz, 1H, 11-H), 5.84 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.36 (s, 3H, 16,14-H), 7.11 (d, *J* = 13.6 Hz, 1H, 1-H), 7.67 (dd, *J* = 13.6, 9.9 Hz, 1H, 2-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] =-4.2 ($(CH_3)_2$Si), -4.1 ($(CH_3)_2$Si), 18.1 ($(CH_3)_3$*C*Si), 20.5 ($CH_2$), 25.9 ((*C*$H_3)_3$CSi), 31.0 (CH), 32.9 ($CH_2$), 34.1 ($CH_2$), 43.1 (CH), 45.6 (CH), 49.3 (CH), 55.4 ($OCH_3$), 71.1 (C-5), 98.4 (C-16), 107.1 (C-14), 124.1 (C-11), 135.0 (C-10), 139.0 (C-2), 145.3 (C-13), 146.9 (C-1), 160.8 (C-15).




**15**

**4-{[*tert*-Butyl(dimethyl)silyl]oxy}-6-(3,5-dimethoxyphenyl)-5-[(1*S*)-1-methyl-2-nitroethyl]-1,2,3,4,4a,5,6,8a-octahydronaphthalene (15)**: A solution of the foregoing nitroalkene (180 mg, 0.38 mmol) in dry $Et_2O$ (5 mL) was slowly added to a stirred solution of MeMgBr (3 M in $Et_2O$, 2 mL, 6 mmol) in $Et_2O$ (12 mL) at -80 °C under inert atmosphere. The reaction was stirred at -80 °C for 3 h, then quenched with a 10% solution of glacial acetic acid in dry $Et_2O$ (10 mL) and allowed to warm to 0 °C. Saturated $NaHCO_3$ solution (20 mL) was then added, the mixture stirred for 30 min at room temperature, and then extracted with $Et_2O$ (3 × 20 mL). The combined organic extracts were washed with brine, dried over $Na_2SO_4$, filtered, and evaporated. The residue was purified by flash chromatography (hexane/EtOAc, 10:1, $R_f$ = 0.35) to give 0.148 g (0.30 mmol, 80%) of the nitro compound **15** as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.08 (s, 3H, $(CH_3)_2Si$), 0.12 (s, 3H, $(CH_3)_2Si$), 0.92 (s, 9H, $(CH_3)_3CSi$), 1.00 (d, *J* = 7.1 Hz, 3H, $CH_3$), 1.01-1.07 (m, 1H, $CH_2$), 1.30 (br t, *J* = 11.4 Hz, 1H, $CH_2$), 1.48-1.57 (m, 2H, 3-H, $CH_2$), 1.65 (br d, *J* = 3.5 Hz, 1H, $CH_2$), 1.75 (br d, *J* = 15.6 Hz, 1H, $CH_2$), 1.83 (ddd, *J* = 13.1, 4.6, 3.5 Hz, 1H, 4-H), 1.90 (br d, *J* = 13.9 Hz, 1H, $CH_2$), 2.56 (br t, *J* = 11.4 Hz, 1H, 9-H), 3.17 (d, *J* = 4.6 Hz, 1H, 12-H), 3.52 (q, *J* = 7.1 Hz, 1H, 2-H), 3.78 (s, 6H, $OCH_3$), 3.90 (br s, 1H, 5-H), 4.36 (dd, *J* = 11.6, 7.1 Hz, 1H, 1-H), 4.55 (dd, *J* = 11.6, 8.9 Hz, 1H, 1-H), 5.60 (ddd, *J* = 9.9, 4.6, 2.1 Hz, 1H, 11-H), 5.78 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.30 (t, *J* = 2.3 Hz, 1H, 16-H), 6.35 (d, *J* = 2.3 Hz, 2H, 14-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.0 (C-18), -3.2 (C-18), 14.6 (C-21), 18.3 (C-19), 20.3 ($CH_2$), 26.1 (C-20), 31.5 (CH), 32.9 (CH), 34.4 ($CH_2$), 35.0 ($CH_2$), 41.4 (CH), 43.0 (CH), 46.2 (CH), 55.3 ($OCH_3$), 72.0 (C-5), 81.8 (C-1), 98.1 (C-16), 106.6 (C-14), 126.2 (C-11), 134.8 (C-10), 147.4 (C-13), 160.6 (C-15).




**16**

**4-(3,5-Dimethoxyphenyl)-3-methyl-3a,4,6a,7,8,9,9a,9b-octahydrobenzo[de]chromen-2(3*H*)-one (16)**: To a solution of nitro compound **15** (48 mg, 0.098 mmol) in THF (1 mL) was added TBAF (1M in THF, 1 mL) the mixture was stirred for 24 h at room temperature. It was diluted with water (25 mL) and extracted with $Et_2O$ (3 × 15 mL). The combined organic extracts were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude product was dissolved in dichloromethane (2 mL), PDC (200 mg) was added and the mixture stirred at room temperature for 24 h. Then, the mixture was diluted with $Et_2O$ (30 mL), washed with water and brine. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.3) to provide 21 mg (0.062 mmol, 65%) of lactone **16** as colorless crystals, m.p. 153-155 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.14 (qd, *J* = 12.1, 4.6 Hz, 1H, $CH_2$), 1.52 (d, *J* = 7.1 Hz, 3H, $CH_3$), 1.46-1.72 (m, 4H), 1.79 (dd, *J* = 11.4, 3.0 Hz, 1H, CH), 1.89 (dd, *J* = 12.6, 2.0 Hz, 1H, $CH_2$), 2.03 (br d, *J* = 14.7 Hz, 1H, $CH_2$), 2.13 (br t, *J* = 11.9 Hz, 1H, 9-H), 2.43 (qd, *J* = 7.1, 4.5 Hz, 1H, 2-H), 3.26 (br s, 1H, 12-H), 3.79 (s, 6H, $OCH_3$), 4.30-4.34 (br s, 1H, 5-H), 5.59 (dt, *J* = 9.9, 3.0 Hz, 1H, 11-H), 5.80 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.34 (t, *J* = 2.3 Hz, 1H, 16-H), 6.37 (d, *J* = 2.3 Hz, 2H, 14-H); $^{13}$C NMR (100 MHz, CDCl3): δ[ppm] = 16.2 (C-19), 21.0 ($CH_2$), 30.0 (CH), 30.7 ($CH_2$), 31.3 ($CH_2$), 36.0 (CH), 37.1 (CH), 44.2 (CH), 46.3 (CH), 55.3 ($OCH_3$), 78.4 (C-5), 97.7 (C-16), 106.5 (C-14), 125.9 (C-10), 132.3 (C-11), 146.8 (C-16), 160.9 (C-15,17), 174.9 (C-1).

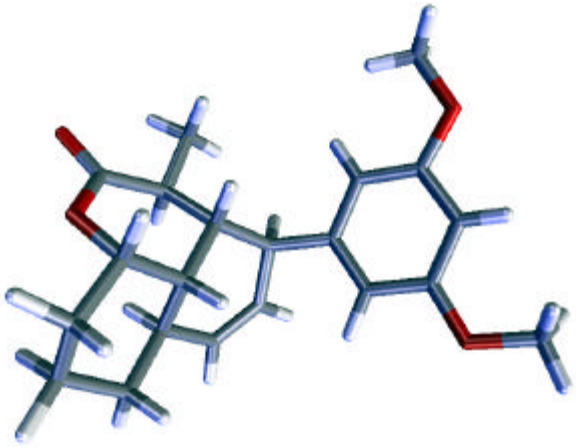
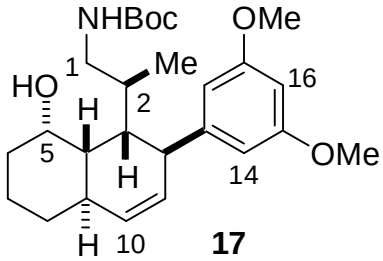
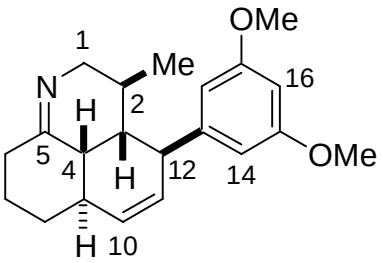


**Figure** 1. X-ray structure of lactone **16**




**17**

***tert*-Butyl-2-[2-(3,5-dimethoxyphenyl)-8-hydroxy-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]propylcarbamate (17)**: A solution of nitro compound **15** (100 mg, 0.204 mmol) in dry THF (5 mL) was added dropwise at -30 °C to a stirred mixture of $LiAlH_4$ (200 mg) in THF (2 mL) under an inert atmosphere within 20 min. Subsequently, the mixture was stirred at room temperature for 12 h and, finally refluxed for 1 h. Then the mixture was cooled to 0 °C and treated with *i*-PrOH (3 mL). The resulting mixture was diluted with $Et_2O$ and filtered through celite. The filtrate was concentrated and the crude amine dissolved in MeOH (10 mL). Then, $NEt_3$ (1 mL) and $Boc_2O$ (0.7 g) were added sequentially at 0 °C and the mixture stirred at room temperature for 0.5 h. The MeOH was evaporated under reduced pressure and the residue diluted with $Et_2O$, washed with $KHSO_4$ (1 M) and with brine. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 10:1, $R_f$ = 0.35). The obtained carbamate was dissolved in THF (5mL) and TBAF (1 M in THF, 5 mL) was added dropwise. The mixture was heated to 60 °C for 48 h under an inert atmosphere, then diluted with water (50 mL), and extracted with $Et_2O$ (3 × 30 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.15) to give 50 mg (0.112 mmol, 55% from **15**) of carbamate **17** as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.95 (d, *J* = 7.1 Hz, 3H, $CH_3$), 1.04 (qd, *J* = 12.4, 3.5 Hz, 1H, $CH_2$), 1.41 (s, 9H, *t*-Bu), 1.46-1.91 (m, 6H), 2.44 (br dd, *J* = 11.6, 11.1 Hz, 1H, 9-H), 2.65 (qd, *J* = 7.1, 2.0 Hz, 1H, 2-H), 2.97-3.06 (m, 1H, 1-H), 3.20-3.30 (m, 2H, 1,3-H), 3.79 (s, 6H, $OCH_3$), 3.85 (br s, 1H, 12-H), 4.77 (s, 1H, 5-H), 5.60 (dt, *J* = 9.9, 3.0 Hz, 1H, 11-H), 5.75 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.29 (t, *J* = 2.3 Hz, 1H, 16-H), 6.37 (d, *J* = 2.3 Hz, 2H, 14-H); $^{13}$C NMR (100 MHz, CDCl3): δ[ppm] = 15.6 (C-19), 20.2 ($CH_2$), 28.4 ($CH_3$)$_3$C), 30.9 (CH), 32.7 (CH), 33.9 ($CH_2$), 35.6 ($CH_2$), 42.0 (CH), 46.6 (CH), 47.7 (C-1), 55.3 ($OCH_3$), 71.1 (C-5), 79.2 ($CH_3$)$_3$*C*), 97.7 (C-16), 106.9 (C-14), 127.0 (C-11), 134.7 (C-10), 148.4 (C-13), 156.4 (C=O), 160.5 (C-15).

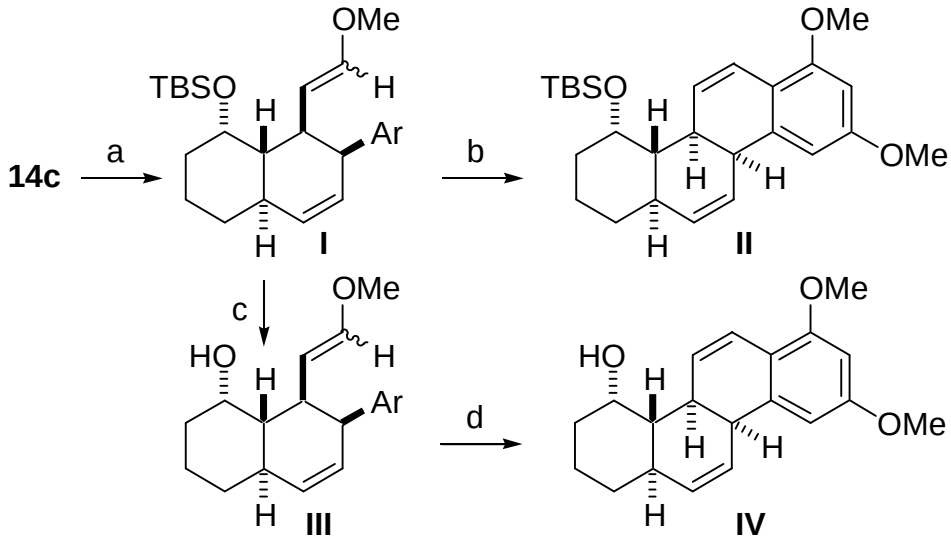



**18** (***epi***-symbioimine analog)

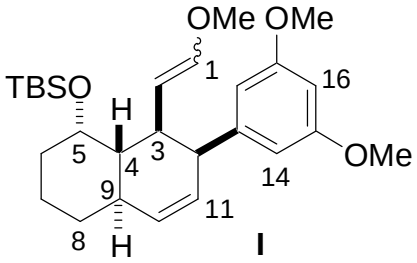
***epi*-symbioimine analog, 4-(3,5-dimethoxyphenyl)-3-methyl-2,3a,4,6a,7,8,9,9b-octahydro-3H-benzo[de]quinoline (18)**: PDC (200 mg) was added to a solution of alcohol **17** (50 mg, 0.112 mmol) in $CH_2Cl_2$ (5 mL) and the mixture stirred for 24 h at room temperature. It was diluted with $Et_2O$ and filtered through silica gel. The resulting solution was concentrated under reduced pressure and subjected to flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.25). The obtained ketone seems not to be all too stable, for example it quickly decomposes in $CDCl_3$. For the hydrolysis of the carbamate, AcCl (3 drops) was added to dry MeOH (5 mL) to generate an anhydrous solution of HCl. This solution was added to the previously obtained ketone, and the mixture refluxed for 0.5 h. Then, $NEt_3$ (0.2 mL) was added and the solution concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/$NEt_3$, 100:1, $R_f$ = 0.5 in MeOH, 0.05 in EtOAc) to give 27 mg (0.086 mmol, 80%) of imine **18** as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.08 (d, *J* = 6.3 Hz, 3H, $CH_3$), 1.38-1.52 (m, 1H, 8a-H), 1.59-1.69 (m, 1H, 7a-H), 1.65 (br d, *J* = 13.4 Hz, 1H, 3-H), 1.68-1.82 (m, 1H, 2-H), 1.95-2.13 (m, 4H, 4,7b,8b,9-H), 2.22 (tdd, *J* = 12.6, 5.3, 3.1 Hz, 1H, 6a-H), 2.35 (dd, *J* = 12.1, 3.8 Hz, 1H, 6b-H), 3.00 (ddd, *J* = 16.9, 10.6, 2.8 Hz, 1H, 1a-H), 3.47 (br s, 1H, 12-H), 3.72 (dd, *J* = 16.9, 4.5 Hz, 1H, 1b-H), 3.78 (s, 6H, $OCH_3$), 5.61 (br d, *J* = 10.2 Hz, 1H, 11-H), 5.73 (d, *J* = 10.2 Hz, 1H, 10-H), 6.31 (t, *J* = 2.3 Hz, 1H, 16-H), 6.36 (d, *J* = 2.3 Hz, 2H, 14,18-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 16.90 ($CH_3$), 27.6 (C-2), 28.1 (C-7), 33.2 (C-8), 39.0 (C-6), 39.6 (C-4), 40.5 (C-12), 41.7 (C-9), 44.0 (C-3), 55.3 ($OCH_3$), 58.3 (C-1), 97.4 (C-16), 106.3 (C-14), 127.4 (C-10), 130.6 (C-11), 148.9 (C-13), 160.8 (C-15), 175.3 (C-5).

## *Attempts to homologate aldehyde 14c with methoxymethyl-phosphorane*

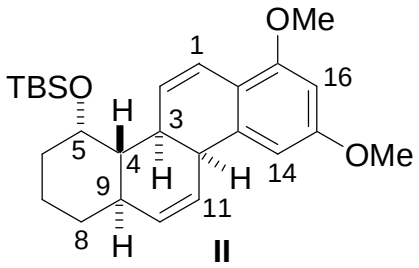
This plan called for a C1 extension with methoxymethylphosphorane followed by alkylation of the enamine of the homologated aldehyde. As expected, the mixture of *cis*/*trans* enol ethers **19** was obtained in good yield (Scheme 1). However, the acid-induced cleavage of **19** afforded the tetracyclic compound **20**. Again, the Friedel-Crafts cyclization was so fast, that the desired homologated aldehyde could never be detected in the LC-MS of the reaction mixture. Even hydrolysis of the hydroxyl derivative **21**, which should have given a more stable cyclic hemiacetal led to the tetracyclic compound **22**.




***Scheme 1***. Attempts to homologate aldehyde **14c** with methoxymethylphosphorane. a) $MeOCH_2PPh_3^+Cl^-$, NaHMDS, THF, 0 °C, 0.5 h (70%); b) Amberlyst 15, acetone, $H_2O$, rt, 24 h, **II** (52%) + **IV** (31%); c) TBAF, THF, 50 °C, 24 h, (85%); d) Amberlyst 15, acetone, $H_2O$, rt, 24 h (80%).

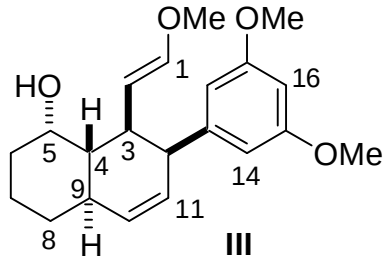



**4-{[*tert*-Butyl(dimethyl)silyl]oxy}-6-(3,5-dimethoxyphenyl)-5-[(*E*)-2-methoxyvinyl]-1,2,3,4,4a,5,6,8a-octahydronaphthalene (I)**: To a stirred slurry of methoxymethyl triphenylphosphonium chloride (600 mg, 1.75 mmol) in dry THF (5 mL), a solution of $NaN(SiMe_3)_2$ (275 mg, 1.5 mmol) in THF (3 mL) was added dropwise at 0 °C under an inert atmosphere. The deep red solution was stirred at 0 °C for 10 min then cooled to -50 °C. At this point, aldehyde **14c** (215 mg, 0.5 mmol) in THF (2 mL) was added -50 °C. Then the mixture was heated to 0 °C for 30 min, cooled and treated with saturated $NH_4Cl$ solution (20 mL) and extracted with petroleum ether (3 × 25 mL). The combined organic extracts were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 10:1, $R_f$ = 0.3) to give 159 mg (0.35 mmol, 70%) of enol ether **I** as a 30:70 mixture of *cis*/*trans* isomers as a colorless oil. $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.2, -4.0, -3.5, 18.2, 18.3, 20.6, 20.7, 25.9, 26.1, 33.5, 33.5, 34.2, 34.3, 34.4, 34.9, 38.9, 43.7, 43.9, 45.8, 49.2, 55.2, 55.2, 55.3, 59.2, 67.3, 67.4, 97.6, 98.1, 103.9, 107.5, 109.1, 109.2, 127.3, 127.4, 133.5, 133.8, 143.8, 144.6, 146.0, 159.6, 159.8; HRMS (ESI) calcd $C_{27}H_{42}O_4Si$ $[M+H]^+$ 459.29251, found 459.29309.




II

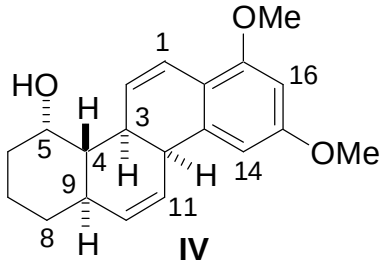
**4-{[*tert*-Butyl(dimethyl)silyl]oxy}-7,9-dimethoxy-1,2,3,4,4a,4b,10b,12a-octahydrochrysene (II)**: To the enol ether **I** (142 mg, 0.31 mmol) in acetone (10 mL) was added Amberlyst-15 (400 mg), and the mixture stirred at room temperature for 24 h. The resulting solution was filtered through a pad of dry $Na_2CO_3$, and the filtrate concentrated under reduced pressure. The residue was subjected to flash chromatography (hexane/EtOAc, 10:1, $R_f$ = 0.45) to furnish tetracycle **II** (69 mg, 0.16 mmol, 52%) as colorless crystals, m.p. 138-140 °C. Further elution with hexane/EtOAc, 4:1, $R_f$ = 0.3 gave the corresponding alcohol **IV** (30 mg, 0.096 mmol, 31%) as colorless crystals, m.p. 153-155 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.07 (s, 3H, $(CH_3)_2Si$), 0.12 (s, 3H, $(CH_3)_2Si$), 0.93 (s, 9H, $(CH_3)_3CSi$), 0.83-0.98 (m, 1H, $CH_2$), 1.17-1.28 (m, 2H, CH, $CH_2$), 1.35-1.45 (m, 1H, $CH_2$), 1.64-1.72 (m, 2H, $CH_2$), 2.36-2.47 (m, 2H, CH), 3.53 (br t, *J* = 5.6 Hz, 1H, 12-H), 3.80 (s, 3H, $OCH_3$), 3.81 (s, 3H, $OCH_3$), 4.08 (br s, 1H, 5-H), 5.68 (d, *J* = 9.9 Hz, 1H, 10-H), 5.96 (dd, *J* = 10.1, 6.1 Hz, 1H, 2-H), 6.13 (ddd, *J* = 9.9, 5.6, 2.5 Hz, 1H, 11-H), 6.28 (d, *J* = 2.0 Hz, 1H, 16-H), 6.45 (br s, 1H, 14-H), 6.78 (d, *J* = 10.1 Hz, 1H, 1-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.1 $(CH_3)_2Si$), -3.6 $(CH_3)_2Si$), 18.2 $(CH_3)_3CSi$), 20.5 ($CH_2$), 25.9 ($CH_3)_3CSi$), 32.4 ($CH_2$), 33.7 ($CH_2$), 34.4 (CH), 35.3 (CH), 37.8 (C-12), 43.6 (CH), 55.2 ($OCH_3$), 55.5 ($OCH_3$), 67.1 (C-5), 95.4 (C-16), 104.5 (C-14), 115.0 (C-18), 120.6 (C-1), 125.1 (C-11), 127.1 (C-2), 134.5 (C-10), 141.2 (C-13), 155.4 (C-17), 159.7 (C-15); HRMS (ESI) calcd for $C_{26}H_{38}O_3Si$ $[M+H]^+$ 427.26630, found 427.26643.




III

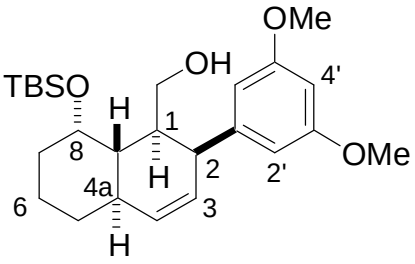
**7-(3,5-Dimethoxyphenyl)-8-[(*E*)-2-methoxyvinyl]-1,2,3,4,4a,7,8,8a-octahydronaphthalen-1-ol (III)**: To a stirred solution of silyl ether **I** (70 mg, 0.15 mmol) in THF (1 mL), TBAF (1 M in THF, 2 mL) was added dropwise, and the mixture heated to 50 °C for 24 h under inert atmosphere. Then the mixture was diluted with water and extracted with $Et_2O$. The ether extracts were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.2) to yield 44 mg (0.127 mmol, 85%) of alcohol **III** as a single *E*-isomer (enol ether double bond). $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.06-1.17 (m, 1H, $CH_2$), 1.24-1.43 (m, 2H, 4-H, $CH_2$), 1.53-1.85 (m, 4H, $CH_2$), 2.35 (br dd, *J* = 12.4, 10.9 Hz, 1H, 9-H), 2.49 (ddd, *J* = 10.9, 6.4, 5.6 Hz, 1H, 3-H), 3.33 (br dd, *J* = 5.6, 4.6 Hz, 1H, 12-H), 3.38 (s, 3H, $OCH_3$), 3.76 (s, 6H, $OCH_3$), 3.85 (br s, 1H, 5-H), 4.02 (dd, *J* = 12.9, 10.9 Hz, 1H, 2-H), 5.58 (ddd, *J* = 9.9, 4.6, 2.8 Hz, 1H, 11-H), 5.73 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.33 (s, 3H, 14,16-H), 6.43 (d, *J* = 12.9 Hz, 1H, 1-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 20.6 ($CH_2$), 33.0 ($CH_2$), 33.2 ($CH_2$), 34.8 (C-9), 39.6 (C-3), 42.3 (C-4), 48.8 (C-12), 55.2 ($OCH_3$), 55.6 ($OCH_3$), 66.3 (C-5), 98.2 (C-16),

103.8 (C-2), 109.0 (C-14), 127.5 (C-11), 133.6 (C-10), 143.3 (C-13), 146.4 (C-1), 159.9 (C-15).



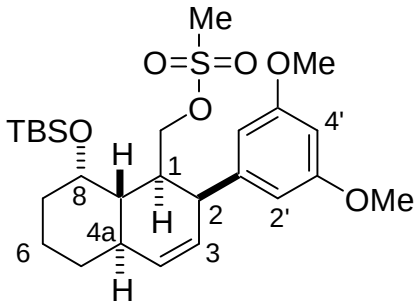

**IV**

**7,9-Dimethoxy-1,2,3,4,4a,4b,10b,12a-octahydrochrysen-4-ol (IV)**: A mixture of the enol ether **I** (25 mg, 0.072 mmol) and Amberlyst-15 (100 mg) in acetone (2 mL) and water (0.07 mL) was stirred for 24 h at room temperature. The resulting mixture was worked up as described previously to give (18 mg, 0.058 mmol, 80%) of the tetracycle **IV**. $R_f$ = 0.3 (petroleum ether/ethyl acetate, 4:1). $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.84-0.94 (m, 1H, $CH_2$), 1.23-1.31 (m, 2H, 4-H, $CH_2$), 1.38-1.47 (br d, 1H, $CH_2$), 1.53-1.68 (m, 3H, $CH_2$), 2.21 (br dd, *J* = 11.9, 11.6 Hz, 1H, 9-H), 2.40 (ddd, *J* = 10.9, 6.8, 5.8 Hz, 1H, 3-H), 3.50 (br dd, *J* = 5.8, 5.6 Hz, 1H, 12-H), 3.74 (s, 6H, $OCH_3$), 4.03 (d, *J* = 2.3 Hz, 1H, 5-H), 5.65 (d, *J* = 9.9 Hz, 1H, 10-H), 5.94 (dd, *J* = 10.1, 6.3 Hz, 1H, 2-H), 6.08 (ddd, *J* = 9.9, 5.6, 2.5 Hz, 1H, 11-H), 6.21 (d, *J* = 2.0 Hz, 1H, 16-H), 6.38 (br s, 1H, 14-H), 6.73 (d, *J* = 10.1 Hz, 1H, 1-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 20.4 ($CH_2$), 32.2 ($CH_2$), 33.5 ($CH_2$), 34.6 (C-3), 35.4 (C-9), 37.8 (C-12), 42.5 (C-4), 55.3 ($OCH_3$), 55.5 (C-19), 66.3 (C-5), 95.5 (C-16), 104.5 (C-14), 114.8 (C-18), 120.8 (C-1), 125.5 (C-11), 126.4 (C-2), 133.9 (C-10), 140.7 (C-13), 155.5 (C-17), 159.8 (C-15); HRMS (ESI) calcd for $C_{20}H_{24}O_3$ $[M+H]^+$ 313.17982, found 313.17978.

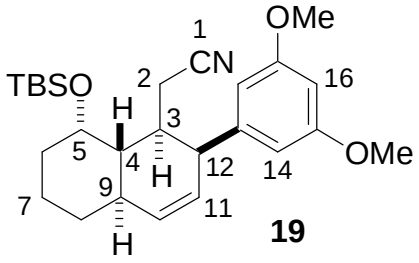



**[8-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-(3,5-dimethoxyphenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]methanol**: $NaBH_4$ (74 mg, 2.0 mmol, 4 equiv) was added to a stirred solution of aldehyde **14c** (215 mg, 0.5 mmol) in EtOH (2 mL) at 0 °C. The mixture was stirred at room temperature until the starting material had disappeared (24 h). Thereafter, the mixture was diluted with water (10 mL) and petroleum ether (50 mL). Then saturated $NH_4Cl$ (10 mL) was added dropwise to destroy the excess borohydride. The mixture was extracted with $Et_2O$ (3 × 25 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 10:1, $R_f$ = 0.2) to provide 214 mg (0.495 mmol, 99%) of the primary alcohol as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.04 (s, 3H, $(CH_3)_2Si$), 0.06 (s, 3H, $(CH_3)_2Si$), 0.90 (s, 9H, $(CH_3)_3CSi$), 1.09-1.19 (m, 1H, $CH_2$), 1.37-1.53 (m, 3H, $CH_2$), 1.70-1.84 (m, 3H, 8a-H, $CH_2$), 2.06-2.15 (m, 1H, 1-H), 2.46 (br dd, *J* = 12.4, 10.4 Hz, 1H, 4a-H), 3.35-3.44 (m, 1H, C*H*$_2$OH), 3.77 (s, 6H, $OCH_3$), 3.79 (m, 1H, C*H*$_2$OH), 4.03 (br s, 1H, 8-H), 5.55 (ddd, *J* = 9.9, 4.8, 2.8 Hz, 1H, 3-H), 5.67 (br d, *J* = 9.9 Hz, 1H, 4-H), 6.35 (t, *J* = 2.3 Hz, 1H, 4'-H), 6.50 (d, *J* = 2.3 Hz, 2H, 2',6'-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.3 ($(CH_3)_2Si$), -3.5 ($(CH_3)_2Si$), 18.2 ($(CH_3)_3CSi$), 20.5 ($CH_2$), 25.9 ($(CH_3)_3CSi$), 33.4 ($CH_2$), 34.0 ($CH_2$), 34.8 (C-4a), 41.1 (C-8a), 41.3 (C-1), 44.5 (C-2), 55.2

($OCH_3$), 61.7 ($CH_2OH$), 67.0 (C-8), 98.4 (C-4'), 108.2 (C-2',6'), 127.3 (C-3), 133.8 (C-4), 144.3 (C-1'), 160.6 (C-3',5'); HRMS (ESI) calcd for $C_{25}H_{40}O_4Si$ $[M+H]^+$ 433.27686, found 427.27694.



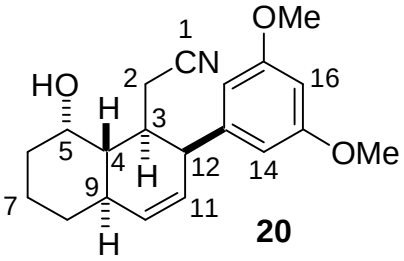

**[8-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-(3,5-dimethoxyphenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]methyl methanesulfonate**: MsCl (0.115 mL, 1.5 mmol, 1.7 equiv) was added dropwise to a stirred solution of the foregoing primary alcohol (380 mg, 0.88 mmol) and $NEt_3$ (0.56 mL, 4 mmol, 4.5 equiv) in dry $CH_2Cl_2$ (10 mL) at -50 °C. The mixture was stirred for 1 h at -30 °C, then allowed to warm to room temperature within 1 h and treated with a saturated $NaHCO_3$ solution (30 mL). The resulting mixture was extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic extracts were washed with saturated $NaHCO_3$ solution, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Flash chromatography of the residue (hexane/EtOAc, 10:1, $R_f$ = 0.15-0.2) afforded 430 mg (0.84 mmol, 96%) of the mesylate as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.07 (s, 6H, $(CH_3)_2Si$), 0.91 (s, 9H, $(CH_3)_3CSi$), 1.20 (qd, *J* = 12.9, 3.6 Hz, 1H, $CH_2$), 1.30-1.43 (m, 2H), 1.52 (br d, 1H, *J* = 13.6 Hz, $CH_2$), 1.65-1.86 (m, 3H), 2.40 (dddd, *J* = 11.1, 10.8, 5.6, 3.6 Hz, 1H, 1-H), 2.49 (br dd, *J* = 12.4, 10.6 Hz, 1H, 4a-H), 2.83 (s, 3H, $SO_2CH_3$), 3.62 (dd, *J* = 10.8, 8.6 Hz, 2H, $CH_2$Oms, 2-H), 3.62 (br s, 1H, 2-H), 3.77 (s, 6H, $OCH_3$), 3.86 (br s, 1H, 8a-H), 4.32 (dd, *J* = 8.6, 3.6 Hz, 1H, $CH_2$OMs), 5.57 (ddd, *J* = 9.9, 4.8, 2.8 Hz, 1H, 3-H), 5.68 (br d, *J* = 9.9 Hz, 1H, 4-H), 6.34 (d, *J* = 2.3 Hz, 2H, 2',6'-H), 6.44 (t, *J* = 2.3 Hz, 1H, 4'-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.5 ($(CH_3)_2Si$), -3.5 ($(CH_3)_2Si$), 18.2 ($(CH_3)_3CSi$), 20.3 ($CH_2$), 25.8 ($(CH_3)_3CSi$), 33.1 ($CH_2$), 33.8 ($CH_2$), 34.8 (CH), 36.9 (CH), 38.3 (CH), 40.9 (CH), 43.1 (CH), 55.2 ($OCH_3$), 66.6 (C-8), 69.2 ($CH_2$OMs), 98.5 (C-4'), 108.8 (C-2',6'), 126.9 (C-3), 133.2 (C-4), 142.3 (C-1'), 160.3 (C-3',5'); HRMS (ESI) calcd for $C_{26}H_{42}NO_6SSi$ $[M+H]^+$ 511.25441, found 511.25345.




**19**

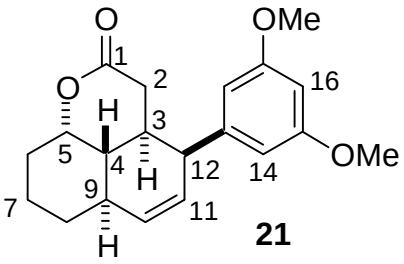
**[8-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-(3,5-dimethoxyphenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]acetonitrile (19)**: A mixture of the foregoing mesylate (430 mg, 0.84 mmol) and NaCN (490 mg, 10 mmol) in DMSO (6 mL) was stirred at 50 °C for 48 h under an inert atmosphere. Afterwards, the mixture was poured into water (100 mL) and extracted with hexane (3 × 30 mL). The combined organic extracts were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 20:1, $R_f$ = 0.25) to furnish 355 mg (0.805 mmol, 95%) of nitrile **19** as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.04 (s, 3H, $(CH_3)_2Si$),

0.07 (s, 3H, $(CH_3)_2Si$), 0.91 (s, 9H, $(CH_3)_3CSi$), 1.14 (qd, *J* = 12.9, 3.8 Hz, 1H, $CH_2$), 1.25-1.40 (m, 2H, CH, $CH_2$), 1.52 (br d, *J* = 13.2 Hz, 1H, $CH_2$), 1.62 (dd, *J* = 16.2, 11.9 Hz, 1H, 2-H), 1.64-1.75 (m, 1H, $CH_2$), 1.82 (m, 2H, $CH_2$), 2.33 (dddd, *J* = 11.9, 9.1, 5.6, 2.8 Hz, 1H, 3-H), 2.43 (br dd, *J* = 12.4, 10.6 Hz, 1H, 9-H), 2.47 (dd, *J* = 16.2, 2.8 Hz, 1H, 2-H), 3.69 (br t, *J* = 5.6 Hz, 1H, 12-H), 3.78 (s, 6H, $OCH_3$), 3.82 (br s, 1H, 5-H), 5.60 (ddd, 1H, *J* = 9.9, 4.6, 2.8 Hz, 11-H), 5.69 (br d, *J* = 9.9 Hz, 1H, H-10), 6.37 (t, *J* = 2.3 Hz, 1H, 16-H), 6.50 (d, *J* = 2.3 Hz, 2H, H-14,18); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.4 $(CH_3)_2Si$), -3.5 $(CH_3)_2Si$), 17.6 ($CH_2$), 18.1 (($CH_3)_3CSi$), 20.2 ($CH_2$), 25.8 (($CH_3)_3CSi$), 32.9 ($CH_2$), 33.7 ($CH_2$), 35.0 (CH), 36.9 (CH), 42.3 (CH), 44.7 (CH), 55.3 ($OCH_3$), 66.5 (C-5), 99.0 (C-16), 108.5 (C-14), 119.6 (C-1), 126.7 (C-11), 133.3 (C-10), 141.8 (C-13), 160.5 (C-15); HRMS (ESI) calcd for $C_{26}H_{39}NO_3Si$ $[M+H]^+$ 442.27720, found 442.27717.




**20**

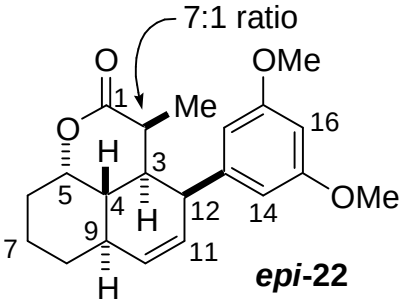
**[2-(3,5-Dimethoxyphenyl)-8-hydroxy-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]acetonitrile (20)**: To a stirred solution of nitrile **19** (345 mg, 0.78 mmol) in THF (2 mL) was added dropwise TBAF (1 M in THF, 5 mL) at room temperature. The mixture was stirred at room temperature for 2 h then diluted with EtOAc (40 mL), washed with water and brine. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Flash chromatography of the residue (hexane/EtOAc, 2:1, $R_f$ = 0.25) afforded hydroxynitrile **20** (250 mg, 0.76 mmol, 98%) as colorless crystals, m.p. 142-143 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.14 (qd, *J* = 12.9, 3.8 Hz, 1H, $CH_2$), 1.34-1.88 (m, 7H), 1.78 (dd, *J* = 16.2, 11.1 Hz, 1H, 2-H), 2.30-2.44 (m, 2H, 3,9-H), 2.54 (dd, *J* = 16.2, 4.1 Hz, 1H, 2-H), 3.67 (br s, 1H, 12-H), 3.78 (s, 6H, $OCH_3$), 3.85 (br s, 1H, 5-H), 5.60 (ddd, *J* = 9.9, 4.6, 2.8 Hz, 1H, 11-H), 5.69 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.37 (t, *J* = 2.3 Hz, 1H, 16-H), 6.48 (d, *J* = 2.3 Hz, 2H, 14,18-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 17.9 ($CH_2$), 20.1 ($CH_2$), 32.8 ($CH_2$), 34.0 ($CH_2$), 35.1 (CH), 36.9 (CH), 41.3 (CH), 45.0 (CH), 55.3 ($OCH_3$), 65.4 (C-5), 98.9 (C-16), 108.6 (C-14), 120.0 (C-1), 127.1 (C-11), 132.9 (C-10), 141.6 (C-13), 160.5 (C-15); HRMS (ESI) calcd for $C_{20}H_{25}NO_3$ $[M+H]^+$ 328.19072, found 328.19057.




**21**

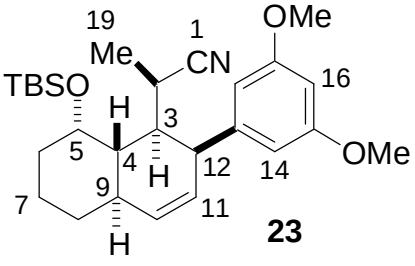
**4-(3,5-Dimethoxyphenyl)-3a,4,6a,7,8,9,9a,9b-octahydrobenzo[de]chromen-2(3*H*)-one (21)**: The hydroxynitrile **20** (40 mg, 0.12 mmol) was dissolved in EtOH (4 mL). KOH (50% in water 0.4 mL) was added and the mixture stirred at 80 °C for 24 h under inert atmosphere. Then, the mixture was cooled to room temperature, diluted with water (30 mL) and acidified with 5% HCl to pH 1. The mixture was extracted with EtOAc (3 × 25 mL). The extracts were washed with water and dried over $Na_2SO_4$, filtered and concentrated in vacuo. The crude hydroxy acid, obtained as a white solid was refluxed in toluene (10 mL) together with

*p*TsOH*$H_2O$ (50 mg, 0.26 mmol) for 1 h. After cooling, the toluene was evaporated under reduced pressure, and the residue subjected to flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.25) to give lactone **21** (36 mg, 0.110 mmol, 90%) as colorless crystals, m.p. 125-126 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.11-1.22 (m, 1H, $CH_2$), 1.42-1.52 (m, 1H, $CH_2$), 1.62-1.93 (m, 7H), 2.10-2.20 (m, 1H, 3-H), 2.29 (br dd, *J* = 14.9, 11.6 Hz, 1H, 9-H), 2.55 (dd, *J* = 15.2, 2.5 Hz, 1H, 2-H), 3.56 (br dd, *J* = 5.1, 4.6 Hz, 1H, 12-H), 3.77 (s, 6H, $OCH_3$), 4.24 (q, *J* = 7.5 Hz, 1H, 5-H), 5.65 (ddd, *J* = 9.6, 4.6, 2.8 Hz, 1H, 11-H), 5.83 (br d, *J* = 9.6 Hz, 1H, 10-H), 6.29 (d, *J* = 2.3 Hz, 2H, 14-H), 6.36 (t, *J* = 2.3 Hz, 1H, 16-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 18.2 ($CH_2$), 26.4 ($CH_2$), 26.8 ($CH_2$), 35.0 (C-2), 35.6 (C-4), 36.1 (C-9), 38.3 (C-3), 45.8 (C-12), 55.3 ($OCH_3$), 74.6 (C-5), 98.3 (C-16), 108.2 (C-14), 127.9 (C-11), 134.1 (C-10), 141.3 (C-13), 160.5 (C-15), 174.5 (C-1). HRMS (ESI) calcd for $C_{20}H_{24}O_4$ $[M+H]^+$ 329.17474, found 329.17480.



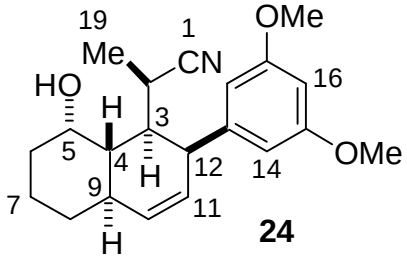

***epi*-22**

***epi*-4-(3,5-Dimethoxyphenyl)-3-methyl-3a,4,6a,7,8,9,9a,9b-octahydrobenzo[de]chromen-2(3*H*)-one, epi-22**: *n*BuLi (2.5 M in hexanes, 80 µL, 0.2 mmol, 2 equiv) was added dropwise to a stirred solution of *i*$Pr_2$NEt (28 µL, 0.2 mmol, 2 equiv) in anhydrous THF (1 mL) at 0 °C under inert atmosphere. The solution was stirred for 15 min at 0 °C then cooled to -80 °C. A solution of lactone **21** (33 mg, 0.10 mmol) in THF (0.5 mL) was added dropwise to the LDA solution. The mixture was stirred for 3 h at -80 °C followed by the addition of MeI (25 µL, 0.4 mmol, 4 equiv). Stirring was continued at -80 °C for 0.5 h then the mixture was allowed to reach room temperature. The reaction was quenched by excessive addition of water and the mixture extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.3) to give *epi*-**22** and **22** as a 7:1 mixture of diastereomers. It was not possible to separate the two diastereomers by flash chromatography. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.44 (d, *J* = 7.3 Hz, 3H, $CH_3$), 1.20-1.99 (m, 7H, 4-H, $CH_2$), 2.22 (ddd, *J* = 12.1, 6.3, 2.5 Hz, 1H, 3-H), 2.36 (br dd, *J* = 15.2, 11.9 Hz, 1H, 9-H), 2.83 (qd, *J* = 7.3, 2.5 Hz, 1H, 2-H), 3.54 (m, 1H, 12-H), 3.78 (s, 6H, $OCH_3$), 4.53 (dt, *J* = 8.9, 7.1 Hz, 1H, 5-H), 5.65 (ddd, *J* = 9.6, 3.6, 3.0 Hz, 1H, 11-H), 5.73 (br d, *J* = 9.6 Hz, 1H, 10-H), 6.38 (s, 3H, 14,16-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 9.5 ($CH_3$), 17.1 ($CH_2$), 26.1 ($CH_2$), 26.3 ($CH_2$), 32.0 (C-4), 34.3 (C-9), 39.6 (C-2), 40.5 (C-3), 45.9 (C-12), 55.3 ($OCH_3$), 75.4 (C-5), 98.4 (C-14), 108.9 (C-16), 128.3 (C-11), 133.2 (C-10), 143.3 (C-13), 160.8 (C-15), 176.1 (C-1).



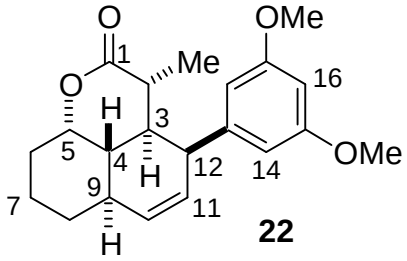

**23**

**2-[8-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-(3,5-dimethoxyphenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]propanenitrile (23)**: *n*BuLi (2.5 M in hexanes, 0.8 mL, 2 mmol, 2 equiv) was added dropwise to a stirred solution of *i*$Pr_2$NEt (281 µL, 2 mmol, 2 equiv) in anhydrous THF (5 mL) at 0 °C under inert atmosphere. The solution was stirred for 15 min at 0 °C and cooled to -80 °C. A solution of nitrile **19** (420 mg, 0.95 mmol) in THF (5 mL) was added dropwise to this LDA solution. The mixture was stirred for 1 h at -80 °C followed by the addition of MeI (124 µL, 2 mmol, 2 equiv). Stirring was continued at -80 °C for 0.5 h then the mixture was allowed to reach room temperature. The reaction was quenched by the addition an excess of half-saturated $NH_4Cl$ solution. The product was extracted with petroleum ether (3 × 30 mL). The combined organic extracts were washed with brine, dried over $Na_2SO_4$, filtered, and evaporated. The residue was purified by flash chromatography (hexane/EtOAc, 20:1, $R_f$ = 0.25) to provide 398 mg (0.874 mmol, 92%) of alkylated nitrile **23** as a colorless viscous oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.05 (s, 3H, $(CH_3)_2Si$), 0.08 (s, 3H, $(CH_3)_2Si$), 0.56 (d, 3H, *J* = 7.3 Hz, $CH_3$), 0.91 (s, 9H, $(CH_3)_3CSi$), 1.17-1.28 (m, 1H, $CH_2$), 1.37-1.60 (m, 3H, 4-H, $CH_2$), 1.67-1.90 (m, 3H, $CH_2$), 2.34 (ddd, *J* = 10.6, 6.0, 4.5 Hz, 1H, 3-H), 2.49 (br dd, *J* = 11.6, 10.8 Hz, 1H, 9-H), 2.96 (qd, *J* = 7.3, 4.5 Hz, 1H, 2-H), 3.75 (br s, 1H, 12-H), 3.79 (s, 6H, $OCH_3$), 3.89 (br s, 1H, 5-H), 5.58 (br d, *J* = 9.9 Hz, 1H, 11-H), 5.64 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.36 (s, 1H, H-16), 6.57 (s, 2H, H-14); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = -5.5 $(CH_3)_2Si$), -3.4 $(CH_3)_2Si$), 12.7 ($CH_3$), 18.2 (($CH_3)_3$*C*Si), 20.4 ($CH_2$), 25.1 (C-2), 25.8 (($CH_3)_3$CSi), 33.1 ($CH_2$), 33.9 ($CH_2$), 34.8 (C-9), 41.01 (C-3), 41.6 (C-4), 44.5 (C-12), 55.3 ($OCH_3$), 67.5 (C-5), 99.0 (C-16), 108.8 (C-14), 122.9 (C-1), 127.6 (C-11), 132.4 (C-10), 143.8 (C-13), 160.6 (C-15); HRMS (ESI) calcd for $C_{27}H_{41}NO_3Si$ $[M+H]^+$ 456.29285, found 456.29278.



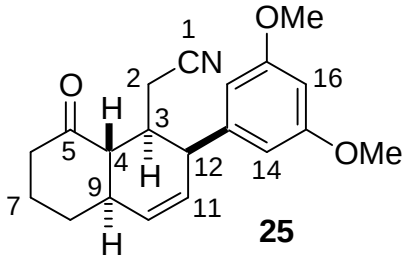

**24**

**2-[2-(3,5-Dimethoxyphenyl)-8-hydroxy-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]propanenitrile (24)**: To a solution of silyl ether **23** (348 mg ,0.76 mmol) in THF (1.5 mL) was added TBAF (1 M in THF, 5 mL) dropwise at 0 °C under inert atmosphere followed by stirring of the mixture at room temperature for 24 h. After complete deprotection (checked by TLC), the mixture was diluted with EtOAc. The layers were separated, and the organic layer washed with water and brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 2:1, $R_f$ = 0.25) to give 240 mg (0.704 mmol, 92%) of hydroxynitrile **24** as colorless crystals, m.p. 159-160 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.86 (d, *J* = 7.3 Hz, 3H, $CH_3$), 1.17-1.30 (m, 1H, $CH_2$), 1.54-1.90 (m, 6H, 4-H, $CH_2$), 2.29-2.36 (m, 1H, 3-H), 2.40 (br dd, *J* = 11.6, 10.4 Hz, 1H, 9-H), 3.06 (qd, *J* = 7.3, 3.0 Hz, 1H, 2-H), 3.63 (br s, 1H, 12-H), 3.78 (s, 6H, $OCH_3$), 4.04 (br s, 1H, 5-H), 5.56 (br d, *J* = 9.9 Hz, 1H, 11-H), 5.63 (br d, *J* = 9.9 Hz, 1H, 10-H), 6.37 (br s, 1H, 16-H), 6.53 (br s, 2H, 14-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 14.9 ($CH_3$), 20.2 ($CH_2$), 26.0 (C-2), 33.2 ($CH_2$), 34.1 ($CH_2$), 34.9 (C-9), 40.7 (C-4), 40.8 (C-3), 45.6 (C-12), 55.3 ($OCH_3$), 66.0 (C-5), 98.9 (C-16), 109.1 (C-14), 122.5 (C-1), 127.7 (C-11), 131.9 (C-10), 142.9 (C-13), 160.6 (C-15); HRMS (ESI) calcd for $C_{21}H_{27}NO_3$ $[M+H]^+$ 342.20637, found 343.20625.



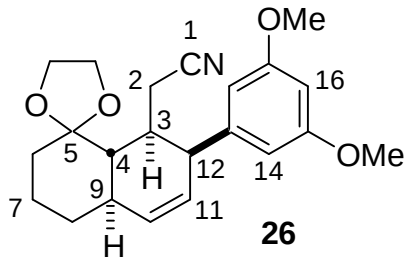

**22**

**4-(3,5-Dimethoxyphenyl)-3-methyl-3a,4,6a,7,8,9,9a,9b-octahydrobenzo[de]chromen-2(3H)-one (22)**: TBAF (1 M in THF, 2 mL) was added to a solution of silyl ether **23** (20 mg, 44 μmol) at room temperature under inert atmosphere. The solution was stirred for 12 h, then diluted with EtOAc (40 mL) and washed with water (20 mL), and brine (20 mL). The organic layer was dried over $Na_2SO_4$, filtered, and evaporated. The crude alcohol **24** ($R_f$ = 0.6, hexane/EtOAc, 1:1) was dissolved in toluene (2 mL). To this solution TMSCl (0.5 mL) and concentrated HCl (0.05 mL) were added and the mixture was stirred at 110 °C for 24 h under inert atmosphere. After cooling, the toluene was removed in vacuo and the residue purified by flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.25) to furnish lactone **22** (11.2 mg, 33 μmol, 75%), m.p. 117-118 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.13 (m, 1H), 1.39 (d, *J* = 6.3 Hz, 3H, $CH_3$), 1.54-1.78 (m, 2H), 1.73-2.03 (m, 5H), 2.22 (br t, *J* = 11.6 Hz, 1H, 9-H), 2.26 (dq, *J* = 13.4, 6.8 Hz, 1H, 2-H), 3.65 (br s, 1H, 12-H), 3.79 (s, 6H, $OCH_3$), 4.27 (dd, *J* = 5.8, 5.6 Hz, 1H, 5-H), 5.65 (ddd, *J* = 9.6, 4.6, 2.8 Hz, 1H, 11-H), 5.78 (br d, *J* = 9.6 Hz, 1H, 10-H), 6.37 (t, *J* = 2.3 Hz, 1H, 16-H), 6.47 (d, *J* = 2.3 Hz, 2H, 14-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 13.0 ($CH_3$), 19.8 ($CH_2$), 27.7 ($CH_2$), 28.3 ($CH_2$), 36.5 (CH), 36.6 (CH), 39.2 (CH), 44.7 (CH), 45.7 (CH), 55.3 ($OCH_3$), 72.3 (C-5), 98.1 (C-16), 108.9 (C-14), 129.7 (C-11), 133.6 (C-10), 141.6 (C-13), 160.5 (C-15), 177.6 (C-1); HRMS (ESI) calcd for $C_{21}H_{26}O_4$ $[M+H]^+$ 343.19039, found 343.19018.



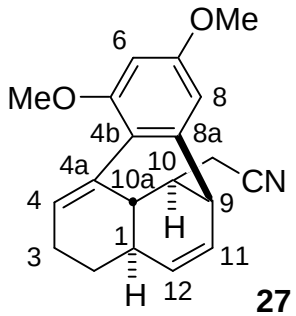

**25**

**[2-(3,5-Dimethoxyphenyl)-8-oxo-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]acetonitrile (25)**: To a stirred solution of hydroxynitrile **20** (105 mg, 0.35 mmol) in dry $CH_2Cl_2$ (4 mL) was added dropwise a solution of Dess-Martin periodinane (15% in $CH_2Cl_2$, 1.5 mL) at 0 °C. The mixture was stirred at room temperature for 3 h, before it was diluted with $CH_2Cl_2$ (20 mL) and washed with saturated $Na_2CO_3$ solution of (2 × 10 mL). The organic layer was dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.25) to give 103 mg (0.347 mmol, 99%) of ketone **25** as colorless crystals, m.p. 105 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.58-1.85 (m, 3H, $CH_2$), 2.02-2.49 (m, 7H), 3.11 (d, *J* = 16.2 Hz, 1H, $CH_2$), 3.68 (br s, 1H, 12-H), 3.79 (s, 6H, $OCH_3$), 5.72 (ddd, *J* = 10.1, 4.0, 2.0 Hz, 1H, 11-H), 5.76 (br d, *J* = 10.1 Hz, 1H, 10-H), 6.38 (t, *J* = 2.3 Hz, 1H, 16-H), 6.48 (d, *J* = 2.3 Hz, 2H, 14-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 18.0 ($CH_2$), 27.5 ($CH_2$), 35.3 ($CH_2$), 34.4 (CH), 42.8 ($CH_2$), 43.8 (C-12), 45.0 (CH), 50.4 (CH), 55.3 ($OCH_3$), 99.1 (C-16), 108.6 (C-14), 119.4 (C-1), 128.3 (C-11), 123.0 (C-10), 140.9 (C-13), 160.7 (C-15), 211.6 (C-5); HRMS (ESI) calcd for $C_{20}H_{23}NO_3$ $[M+Na]^+$ 348.15707, found 348.15690.



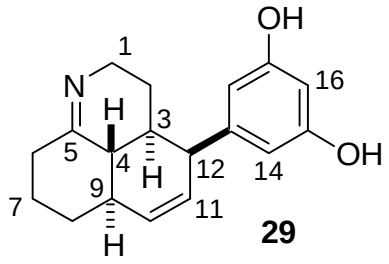

**26**

**[7'-(3,5-dimethoxyphenyl)-3',4',4a',7',8',8a'-hexahydro-2'H-spiro[1,3-dioxolane-2,1'-naphthalen]-8'-yl]acetonitrile (26)**: A solution of ethylene glycol (0.28 mL, 5 mmol), ketone **25** (145 mg, 0.48 mmol), and CSA (60 mg, 0.25 mmol) in toluene (20 mL) was refluxed for 12 h with azeotropic removal of water using a Dean-Stark apparatus. After cooling, the toluene was evaporated under reduced pressure and the residue subjected to flash chromatography (hexane/EtOAc, 4:1) yielding acetal **26** (111 mg, 0.326 mmol, 68%, $R_f$ = 0.3) as colorless crystals, m.p. 146-147 °C, and polycycle **27** (29 mg, 0.096 mmol, 20%, $R_f$ = 0.2) as colorless crystals, m.p. 128-130 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 1.15-1.30 (m, 2H, $CH_2$), 1.45-2.03 (m, 6H), 2.32 (br dd, *J* = 12.4, 10.4 Hz, 1H, 9-H), 2.38-2.47 (m, 1H, 3-H), 2.62 (dd, *J* = 16.9, 4.0 Hz, 1H, $CH_2$), 3.67 (br s, 1H, 12-H), 3.78 (s, 6H, $OCH_3$), 3.82-4.08 (m, 4H, acetal $CH_2$), 5.68 (s, 2H, 10,11-H), 6.36 (br s, 1H, 16-H), 6.50 (br s, 2H, 14-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 20.1 ($CH_2$), 22.9 ($CH_2$), 32.6 ($CH_2$), 34.0 ($CH_2$), 37.1 (C-3), 40.9 (C-9), 43.3 (C-4), 45.7 (C-12), 55.3 ($OCH_3$), 62.3 (acetal $CH_2$), 63.4 (acetal $CH_2$), 98.9 (C-16), 108.5 (C-14), 110.7 (C-5), 120.7 (C-1), 127.5 (C-11), 132.4 (C-10), 141.6 (C-13), 160.5 (C-15); HRMS (ESI) calcd for $C_{22}H_{27}NO_4$ $[M+Na]^+$ 392.18323, found 392.18339.



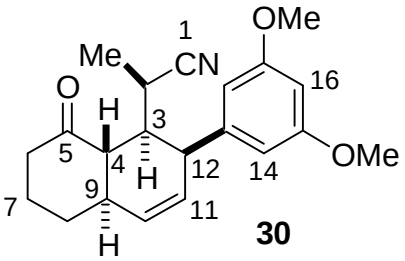

**27**

**(5,7-Dimethoxy-1,2,3,9,10,10a-hexahydro-1,9-ethenophenanthren-10-yl)acetonitrile (27)**: $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.96-1.05 (m, 1H, $CH_2$), 1.96-2.42 (m, 8H), 2.78 (br s, 1H, $CH_2$), 3.31 (br s, 1H, 9-H), 3.81 (s, 3H, $OCH_3$), 3.82 (s, 3H, $OCH_3$), 5.38 (br d, *J* = 9.6 Hz, 1H, 12-H), 5.55 (ddd, *J* = 9.6, 5.8, 2.5 Hz, 1H, 11-H), 6.36 (d, *J* = 2.3 Hz, 1H, 6-H), 6.41 (d, *J* = 2.3 Hz, 1H, 8-H), 6.80-6.85 (m, 1H, 4-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 21.2 ($CH_2$), 23.5 ($CH_2$), 28.7 ($CH_2$), 36.5 (CH), 36.9 (CH), 37.9 (CH), 42.3 (CH), 55.3 ($OCH_3$), 55.3 ($OCH_3$), 97.7 (C-6), 104.8 (C-8), 115.9 (CN), 118.9 (C-4b), 125.1 (C-4), 129.9 (C-11), 132.0 (C-4a), 134.1 (C-12), 137.5 (C-8a), 157.7 (C-5), 159.1 (C-7).



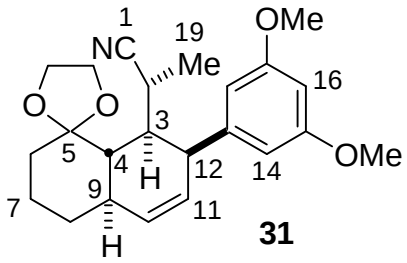

**29**

***Nor*-methyl-*de*-sulfo-symbioimine (freebase, 29)**: To a stirred solution of nitrile **26** (70 mg, 205 μmol) in dry $Et_2O$ (2 mL) was added dropwise a solution of $LiAlH_4$ (1 M in $Et_2O$, 1 mL, 1 mmol) at 0 °C under inert atmosphere. The reaction was stirred at room temperature for 12 h then quenched by dropwise addition of *i*-PrOH (1 mL). The mixture was diluted with $Et_2O$ and filtered through celite. Concentration of the filtrate under reduced pressure afforded 62 mg (179 μmol, 87%, colorless oil) of amine **28** which was used in the next step without further purification. To a stirred solution of the amine (50 mg, 144 μmol) in $CH_2Cl_2$ (2 mL) was added a solution of $BBr_3$ (1 M in $CH_2Cl_2$, 1 mL, 1 mmol) dropwise at -80 °C under inert atmosphere. The mixture was slowly warmed to room temperature and stirred for 10 h, then poured into a half-saturated solution of $NaHCO_3$ (20 mL), and extracted with EtOAc (4 × 20 mL). The combined organic extracts were washed with brine (2 × 10 mL), dried over $Na_2SO_4$, filtered, and evaporated. The residue was purified by flash chromatography ($CHCl_3$/MeOH/$NEt_3$, 100:25:1, $R_f$ = 0.3) to yield (22.5 mg , 80 μmol, 55%) of imine **29** as a white powder, m.p. 248-250 °C, decomp. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.52 (qd, 1H, *J* = 12.4, 4.6 Hz, $CH_2$), 1.22-1.37 (m, 1H, $CH_2$), 1.43-1.57 (m, 1H, $CH_2$), 1.73-2.11 (m, 5H), 2.08 (br dd, *J* = 12.9, 12.4 Hz, 1H, $CH_2$), 2.24 (br d, *J* = 12.9 Hz, 1H, $CH_2$), 2.85 (dd, *J* = 7.1, 6.6 Hz, 2H, 1-H), 3.24-3.31 (m, 1H, 12-H), 3.47 (br dd, *J* = 17.4, 15.9 Hz, 1H, 6-H), 5.57 (br d, *J* = 9.9 Hz, 1H, 11-H), 5.76 (d, *J* = 9.9 Hz, 1H, 10-H), 6.01 (s, 2H, 14-H), 6.07 (br s, 1H, 16-H), 9.13 (br s, 2H, OH); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 25.4 ($CH_2$), 25.8 ($CH_2$), 31.1 ($CH_2$), 36.7 (CH), 40.7 (CH), 41. 9 (CH), 45.0 (C-12), 45.5 (C-1), 48.3 (C-6), 100.8 (C-16), 107.9 (C-14), 129.0 (C-11), 132.2 (C-10), 142.0 (C-13), 157.7 (C-15), 170.8 (C-5); HRMS (ESI) calcd for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.16451, found 284.16463.



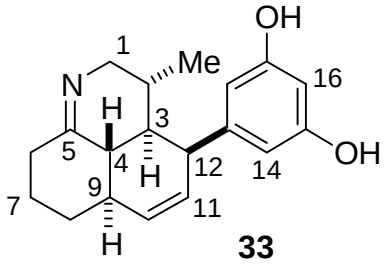

**30**

**2-[2-(3,5-Dimethoxyphenyl)-8-oxo-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]propane-nitrile (30)**: To a stirred solution of hydroxynitrile **24** (235 mg, 0.69 mmol) in dry $CH_2Cl_2$ (8 mL) was added a solution of Dess-Martin periodinane (15% in $CH_2Cl_2$, 4mL) dropwise at 0 °C. The mixture was then stirred at room temperature for 8 h. The resulting mixture was diluted with $CH_2Cl_2$ (30 mL) and washed with saturated $Na_2CO_3$ solution (2 × 20 mL). The organic layer was dried over $Na_2SO_4$, filtered, and evaporated. The residue was subjected to flash chromatography (hexane/EtOAc, 4:1, $R_f$ = 0.25) providing 233 mg (0.69 mmol, 99%) of ketone **30** as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.51 (d, *J* = 7.6 Hz, 3H, $CH_3$), 1.64-1.88 (m, 2H, $CH_2$), 2.08 (br d, 1H, $CH_2$), 2.16-2.31 (m, 2H, 3-H, $CH_2$), 2.37 (br d, *J* = 12.6 Hz, 1H, 6-H), 2.48 (td, *J* = 12.6, 6.6 Hz, 1H, 6-H), 2.60-2.67 (m, 2H, 4,9-H), 3.58-3.65 (m, 1H, 2-H), 3.72 (br s, 1H, 12-H), 3.79 (s, 1H, $OCH_3$), 5.73 (br d, *J* = 10.1 Hz, 1H, 10-H), 5.78 (br d, *J* = 10.1 Hz, 1H, 11-H), 6.37 (s, 1H, 16-H), 6.59 (s, 2H, 14-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 13.0 (C-20), 24.8 (C-2), 27.6 ($CH_2$), 32.6 ($CH_2$), 38.9 (C-9), 42.6 (C-6), 43.8 (C-12), 45.1 (C-3), 50.1 (C-4), 55.4 ($OCH_3$), 99.1 (C-16), 108.7 (C-14), 122.9 (C-1), 129.4 (C-11), 129.9 (C-10), 142.4 (C-13), 160.7 (C-15), 211.7 (C-5).




**31**

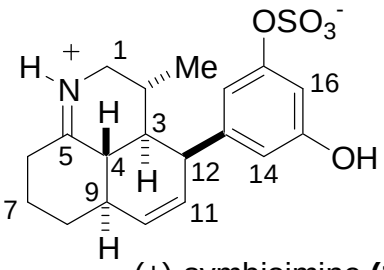
**2-[7'-(3,5-Dimethoxyphenyl)-3',4',4a',7',8',8a'-hexahydro-2'H-spiro[1,3-dioxolane-2,1'-naphthalen]-8'-yl]propanenitrile (31)**: A solution of ethylene glycol (0.76 mL, 13.7 mmol), ketone **30** (233 mg, 0.69 mmol), and CSA (79 mg, 0.34 mmol) in benzene (20 mL) was refluxed for 6 h with azeotropic removal of using a Dean-Stark apparatus. After cooling, the toluene was evaporated under reduced pressure and the residue purified by flash chromatography (hexane/EtOAc, 4:1) to give the acetal **31** (260 mg, 0.68 mmol, 99%) as a colorless oil. $R_f$ = 0.3 (hexane/EtOAc, 4:1); $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.93 (d, *J* = 7.1 Hz, 3H, $CH_3$), 1.33-1.43 (m, 2H, $CH_2$), 1.52-1.65 (m, 1H, $CH_2$), 1.71 (dd, *J* = 11.1, 5.8 Hz, 1H, 4-H), 1.70-1.79 (m, H, $CH_2$), 1.87-1.99 (m, 2H, $CH_2$), 2.21 (dd, *J* = 5.8, 2.8 Hz, 1H, 3-H), 2.36 (br dd, *J* = 11.6, 11.1 Hz, 1H, 9-H), 2.69 (qd, *J* = 7.1, 2.8 Hz, 1H, 2-H), 3.59 (br s, 1H, 12-H), 3.80 (s, 6H, $OCH_3$), 3.83-4.05 (m, 4H, acetal $CH_2$), 5.80 (br d, *J* = 9.1 Hz, 1H, 10-H), 6.06 (br d, *J* = 9.1 Hz, 1H, 11-H), 6.36 (s, 1H, 16-H), 6.53 (s, 2H, 14-H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 16.4 ($CH_3$), 23.3 ($CH_2$), 27.0 (C-2), 31.7 ($CH_2$), 34.6 ($CH_2$), 39.2 (C-9), 43.1 (C-3), 45.2 (C-12), 46.9 (C-4), 55.3 ($OCH_3$), 63.8 (acetal $CH_2$), 64.0 (acetal $CH_2$), 98.3 (C-16), 107.4 (C-14), 110.7 (C-1), 123.6 (C-5), 128.7 (C-11), 133.5 (C-10), 144.0 (C-13), 160.9 (C-15); HRMS (ESI) calcd for $C_{23}H_{29}NO_4$ $[M+H]^+$ 384.21693, found 384.21699.




**33**

***De*-sulfo-symbioimine (33)**: To a stirred solution of nitrile **31** (170 mg, 0.44 mmol) in anhydrous $Et_2O$ (5 mL) was added a solution of $LiAlH_4$ (1 M in $Et_2O$, 4 mL, 4 mmol) dropwise at 0 °C under inert atmosphere. The reaction was stirred at room temperature for 12 h then quenched by the dropwise addition of *iso*-propanol (10 mL). The mixture was diluted with $Et_2O$ and filtered through celite. The filtrate was concentrated under reduced pressure to afford 151 mg (0.39 mmol, 89%, colorless oil) of amine **32** which was used in the next step without further purification. To a stirred solution of crude amine (151 mg, 0.39 mmol) in $CH_2Cl_2$ (10 mL) was added a solution of $BBr_3$ (1 M in $CH_2Cl_2$, 5 mL, 5 mmol) dropwise at -80 °C under inert atmosphere. The mixture was slowly warmed to room temperature while being stirred for 12 h, and finally poured into half-saturated $NaHCO_3$ solution (50 mL). The mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine (2 × 20 mL), dried over $Na_2SO_4$, filtered, and evaporated. The residue was purified by flash chromatography ($CHCl_3$/MeOH/$NEt_3$, 240:30:5, $R_f$ = 0.3) to give (71 mg, 242 μmol, 55%) of imine **33** as a white powder (m.p. > 250 °C, decomp.). $^1$H NMR (400 MHz, $CDCl_3$): δ[ppm] = 0.92 (br s, 4H, H-2,19), 1.25-1.39 (m, 1H, $CH_2$), 1.42-1.57 (m, 2H), 1.84-2.14 (m, 5H), 2.23 (br d, *J* = 13.4 Hz, 1H, $CH_2$), 2.80-2.92 (m, 1H, 1-H), 3.38-3.50 (m, 2H, 1,12-H), 5.57 (br dd, *J* = 9.6, 4.3 Hz, 1H, 11-H), 5.70 (br d, *J* = 9.6 Hz, 1H, 10-H), 6.05 (s, 1H, 16-H), 6.15 (s, 2H, 14-H), 9.12 (br s, 2H, OH); $^{13}$C NMR (100 MHz, $CDCl_3$): δ[ppm] = 16.6 ($CH_3$),

25.4 (C-7), 27.5 (C-2), 31.3 (C-8), 36.8 (C-6), 34.0 (C-9), 42.5 (C-12), 42.6 (C-4), 43.9 (C-3), 56.2 (C-1), 100.8 (C-16), 108.5 (C-14), 129.9 (C-11), 131.4 (C-10), 141.9 (C-13), 157.8 (C-15), 170.0 (C-5); HRMS (ESI) calcd for $C_{19}H_{23}NO_2$ $[M+H]^+$ 298.18016, found 298.18019.

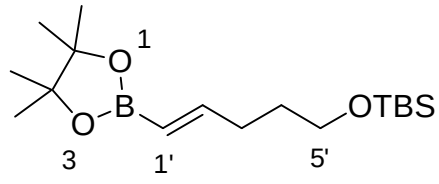



(±)-symbioimine **(1)**

**(±)-Symbioimine (1)**: To a solution of the free base **33** (15 mg, 50 μmol) of in dry pyridine (2 mL) was added $SO_3$/Py complex (80 mg, 0.5 mmol) at room temperature. The mixture was stirred at 60-70 °C under inert atmosphere for 6 h, until the starting product had disappeared by TLC ($R_f$ = 0.3-0.4 in $CHCl_3$/MeOH, 4:1). Then the pyridine was evaporated under reduced pressure and the residue purified by flash chromatography ($CHCl_3$/MeOH, 4:1, $R_f$ = 0.25) afforded the alkaloid **1** (3.8 mg, 10 μmol, 20%). Further with $CHCl_3$/MeOH/*i*PrOH/$H_2O$ 2:2:1:0.5, $R_f$ = 0.2) afforded 20 mg of the bisulfate derivative of symbioimine. To this bisulfate in dioxane (1 mL) and water (0.5 mL) was added *p*TsOH*$H_2O$ (5 mg, 26 μmol) and the mixture stirred for 6 h at room temperature, before it was neutralized with 1 drop of pyridine. The solvents were evaporated under reduced pressure and the residue subjected to flash chromatography ($CHCl_3$/MeOH, 4:1, $R_f$ = 0.25) to give further symbioimine (**1**) (10.3 mg, 27 μmol, 54%) as a white powder, m.p. 228-229 °C (decomp.). The combined yield of **1** from imine **33** was 74%. In addition, some **33** (10%) was recovered from the hydrolysis experiment. HRMS (ESI) calcd for $C_{19}H_{23}NO_5S$ $[M+H]^+$ 378.13697, found 378.13664.

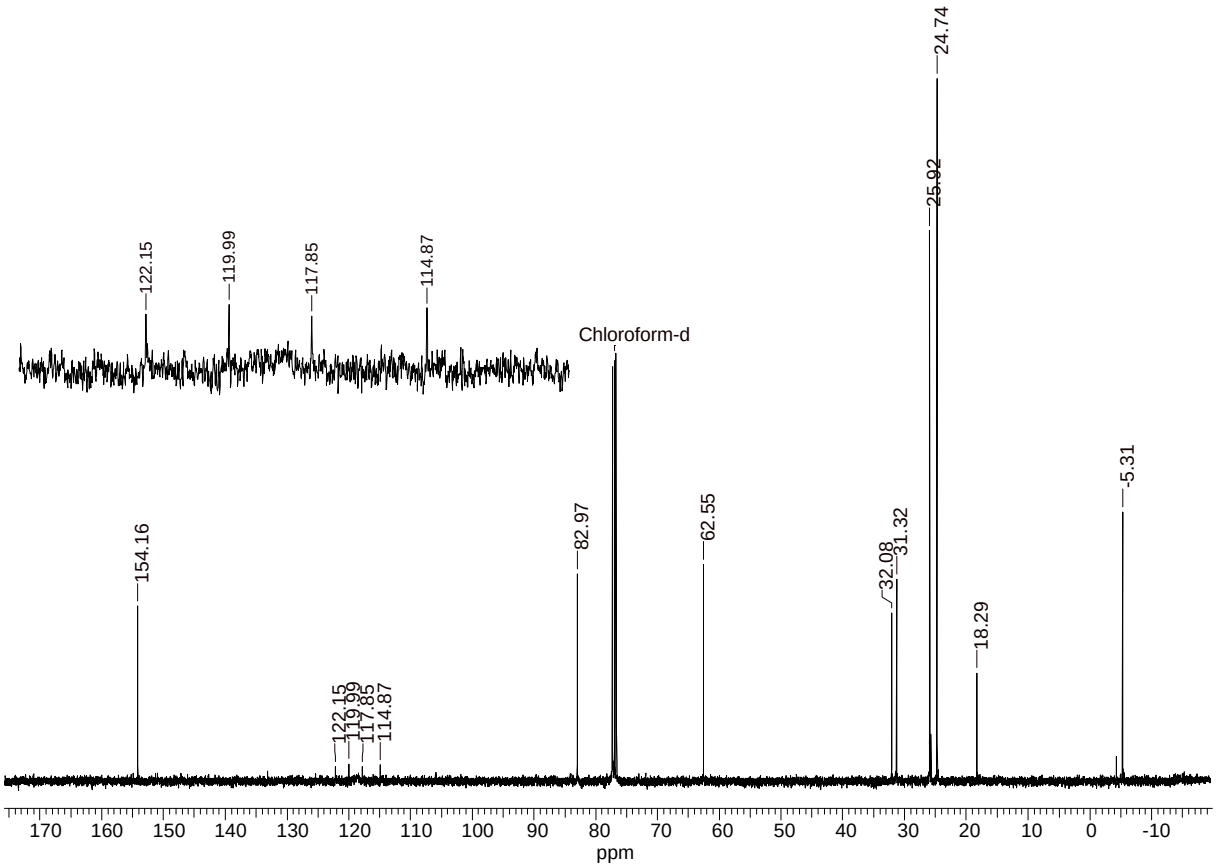
**Table 1**. Comparison of $^{13}C$ chemical shifts of synthetic symbioimine and with that of the natural compound.

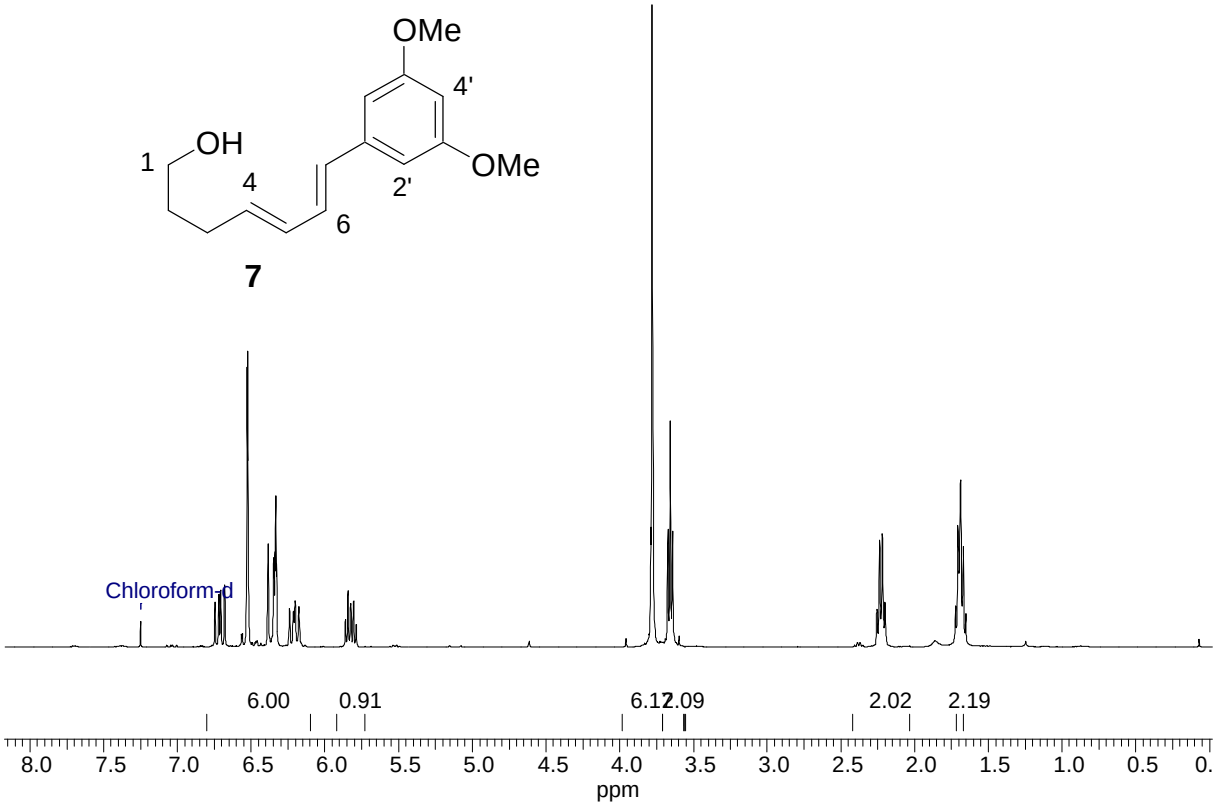
| Atom No. | Synthetic, ppm | Natural, ppm | D**, ppm.** |
|---|---|---|---|
| 1 | 50.0 | 50.0 | **0.0** |
| 2 | 26.2 | 26.2 | **0.0** |
| 3 | 40.8 | 41.1 | **0.3** |
| 4 | 40.3 | 40.1 | **0.2** |
| 5 | 187.4 | 188.0 | **-0.6** |
| 6 | 33.6 | 33.8 | **-0.2** |
| 7 | 24.4 | 24.4 | **0.0** |
| 8 | 29.8 | 29.8 | **0.0** |
| 9 | 41.5 | 41.4 | **0.1** |
| 10 | 130.5 | 130.4 | **0.1** |
| 11 | 129.6 | 129.5 | **0.1** |
| 12 | 41.7 | 41.7 | **0.0** |
| 13 | 139.9 | 139.8 | **0.1** |
| 14 | 112.8 | 112.8 | **0.0** |
| 15 | 154.1 | 154.1 | **0.0** |
| 16 | 106.0 | 105.8 | **0.2** |
| 17 | 157.3 | 157.2 | **0.1** |
| 18 | 111.8 | 111.7 | **0.2** |
| 19 | 15.6 | 15.6 | **0.0** |

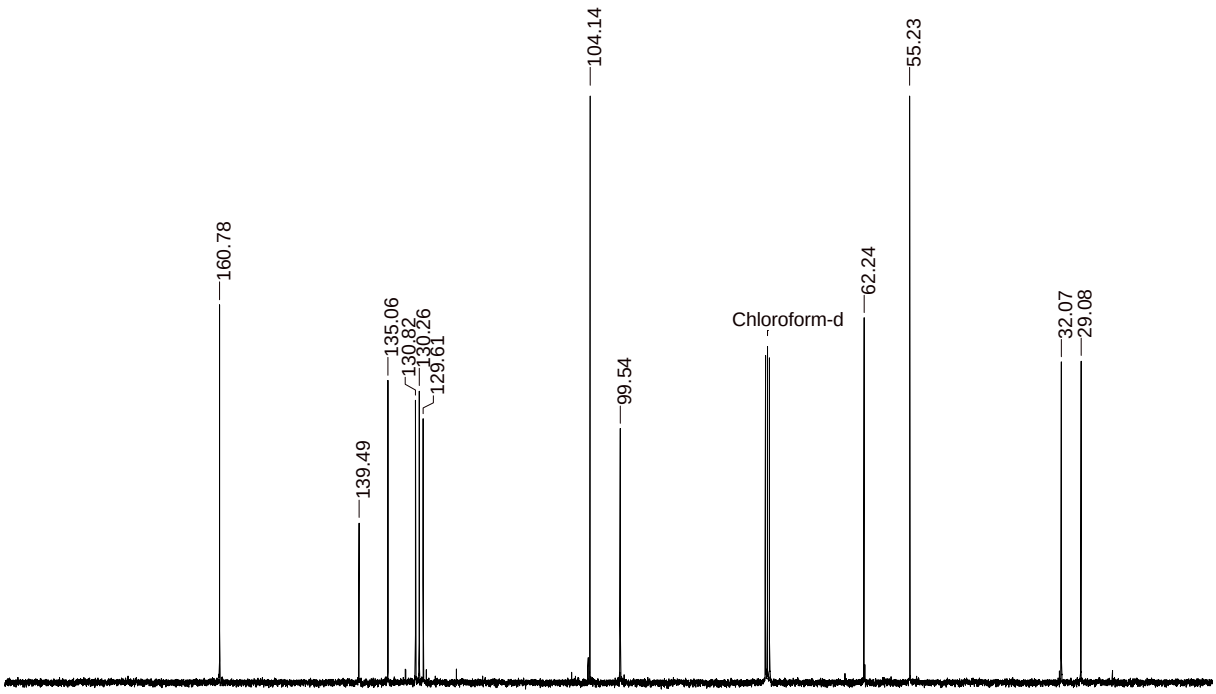

1
O
B
O
OTBS
3
1'
5'

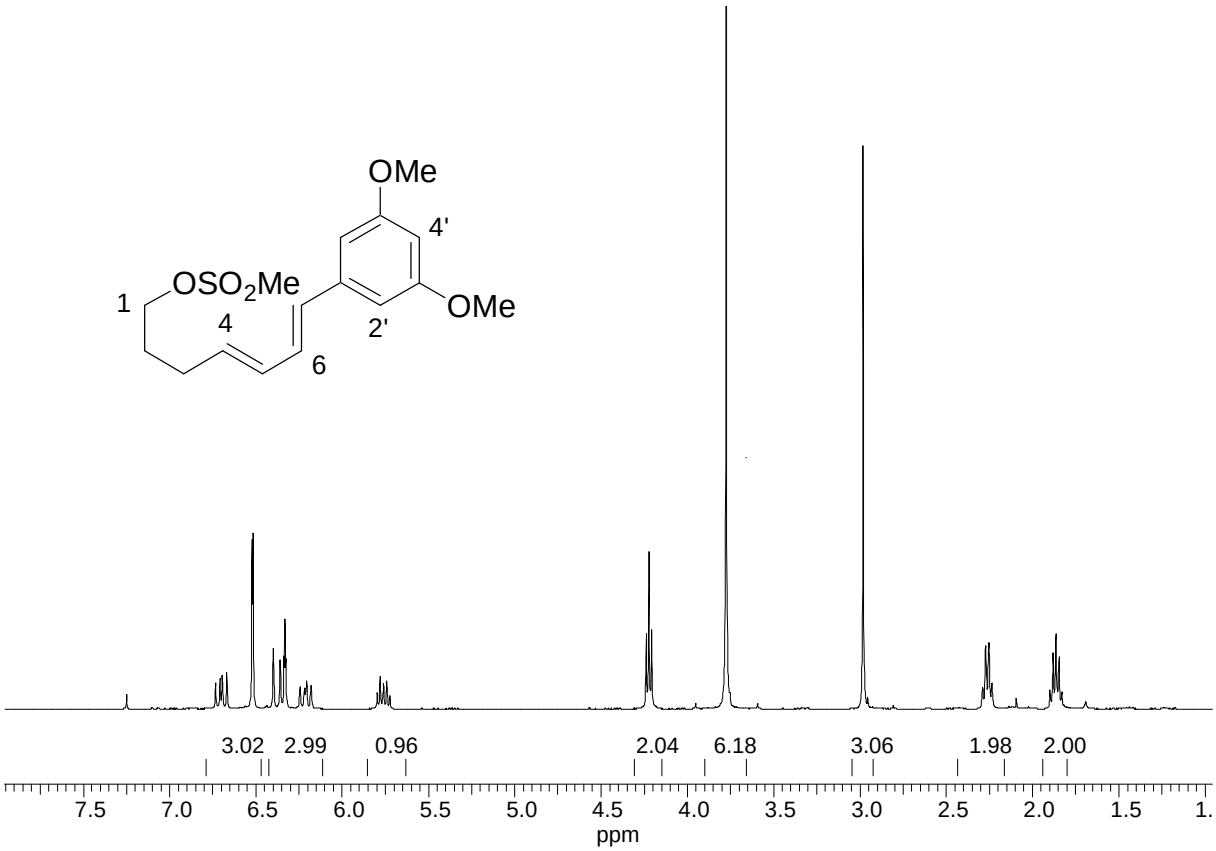
**6**

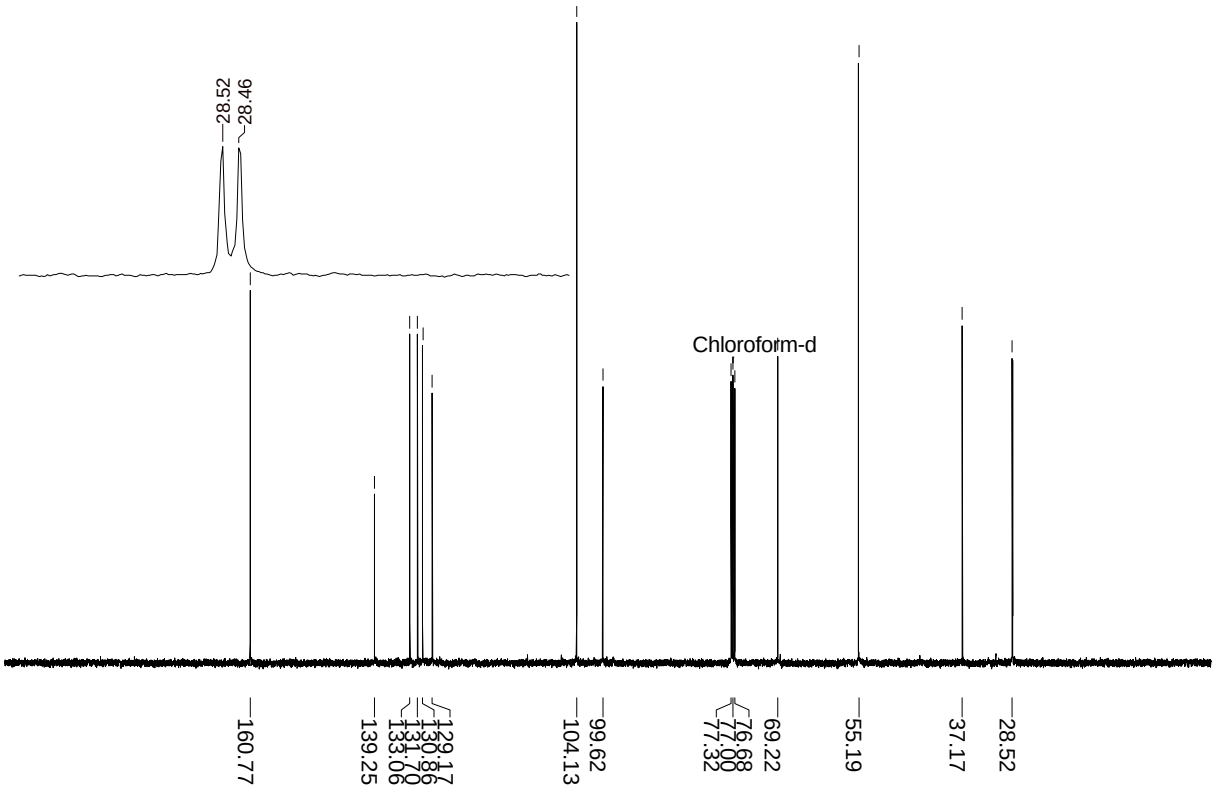

1.20
1.02
2.05
2.09
2.02
12.00
9.07
6.02
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

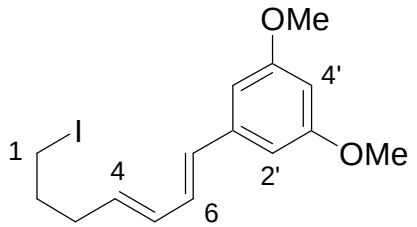

24.74
25.92
122.15
119.99
117.85
114.87
Chloroform-d
154.16
82.97
62.55
32.08
31.32
18.29
-5.31
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm


OMe
4'
OH
1
4
2'
OMe
6
7
Chloroform-d
6.00
0.91
6.12
2.09
2.02
2.19
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.
ppm


160.78
139.49
135.06
130.82
130.26
129.61
104.14
99.54
Chloroform-d
62.24
55.23
32.07
29.08

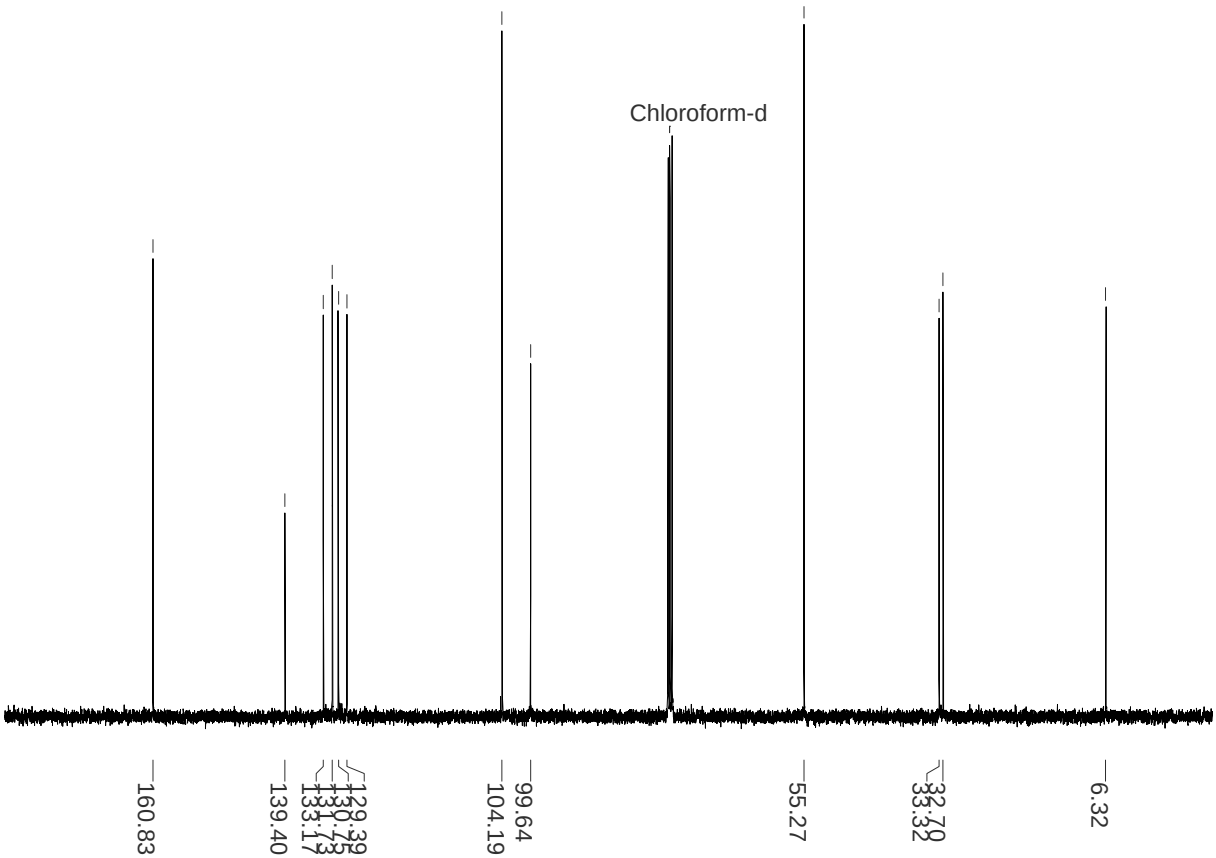

OMe
4'
1
OSO2Me
4
2'
OMe
6
3.02
2.99
0.96
2.04
6.18
3.06
1.98
2.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.
ppm

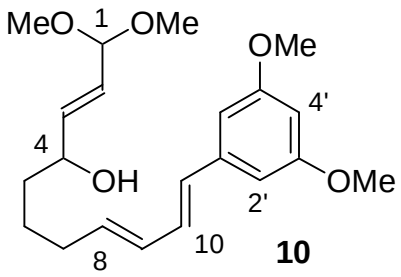

28.52
28.46
Chloroform-d
160.77
139.25
133.06
104.13
99.62
77.32
69.22
55.19
37.17
28.52


OMe
4'
1
I
4
2'
OMe
6

**8**

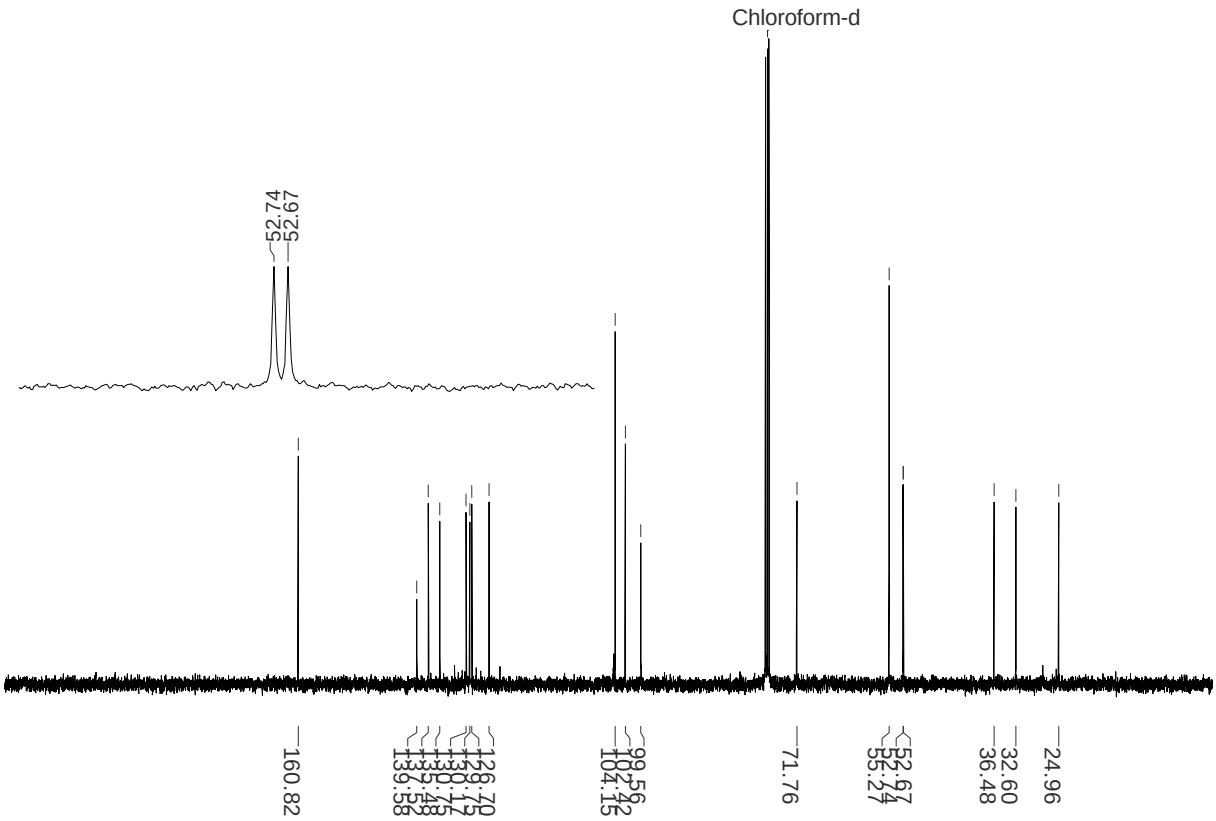

3.14
3.06
1.00
6.36
2.09
2.03
2.07
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

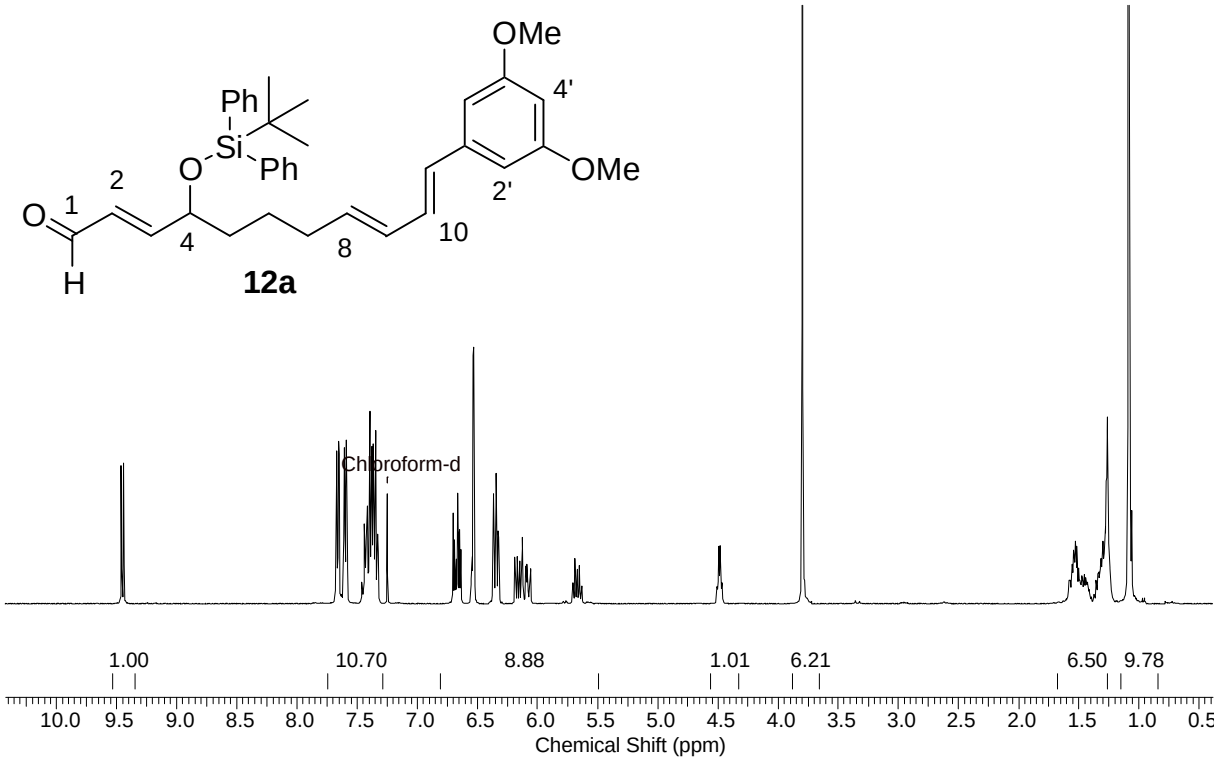

Chloroform-d
160.83
139.40
133.17
131.73
130.45
129.39
104.19
99.64
55.27
33.32
32.70
6.32

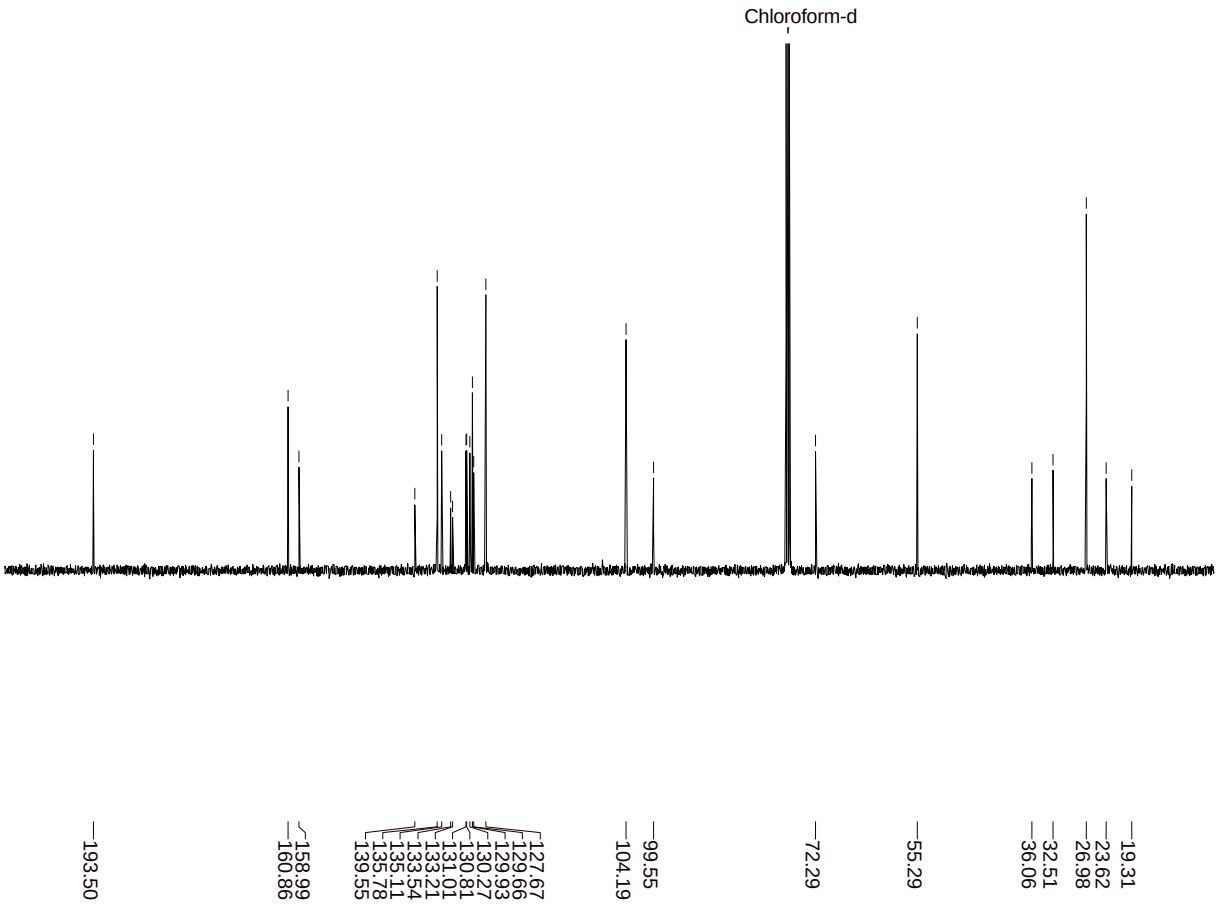

MeO
1
OMe
OMe
4'
4
OH
OMe
2'
10
8

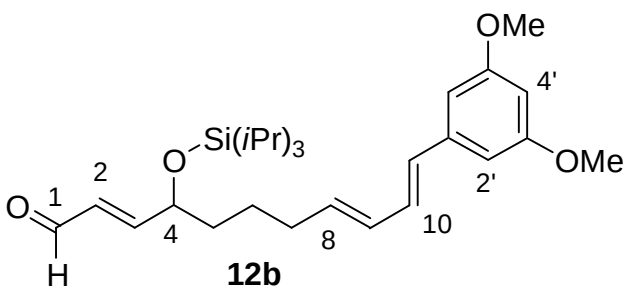
**10**


Chloroform-d
0.05
1.02
2.04
3.15
2.93
0.98
1.00
6.58
6.10
1.91
4.11
10.0 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
ppm


Chloroform-d
52.74
52.67
160.82
136.56
135.48
130.12
128.70
104.15
71.76
55.27
36.48
32.60
24.96

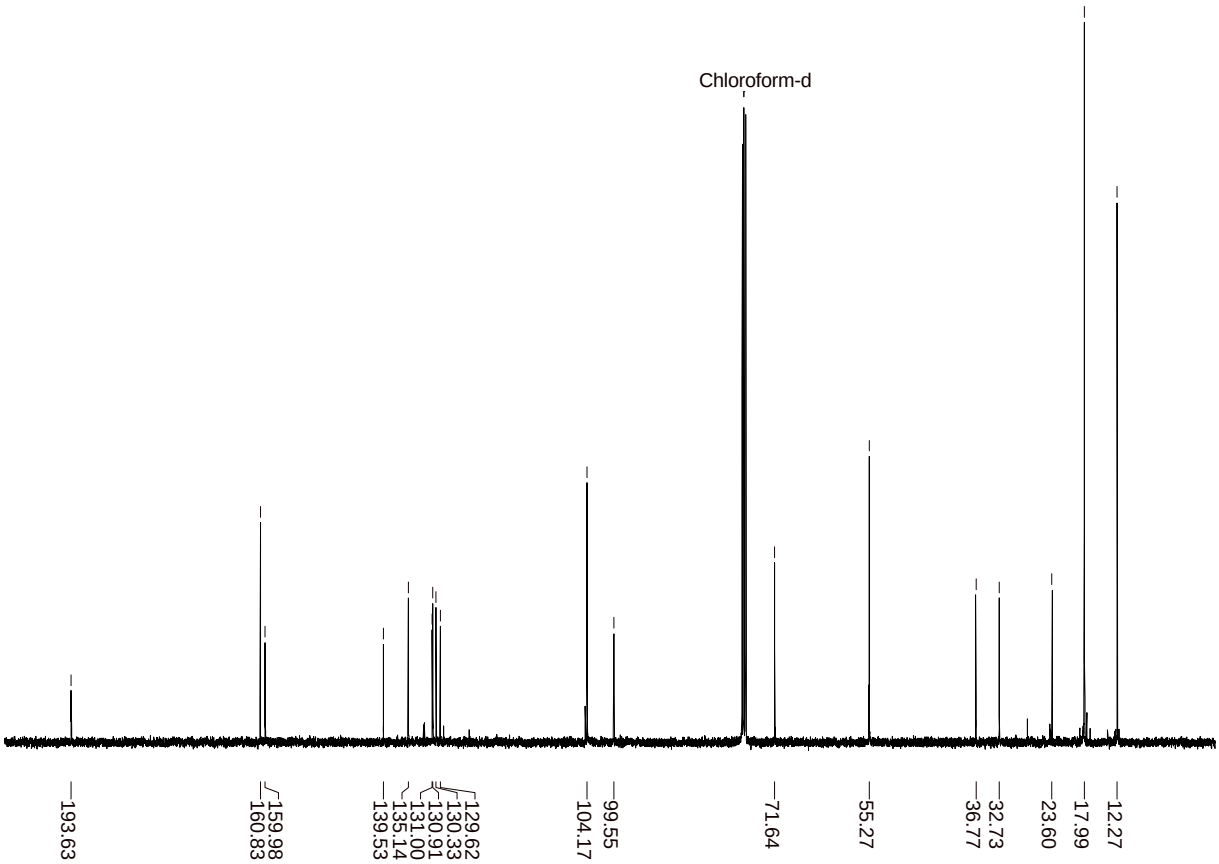

OMe
4'
Ph
Si
Ph
O
2
2'
OMe
O
1
4
8
10
H
12a
Chloroform-d
1.00
10.70
8.88
1.01
6.21
6.50
9.78
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)

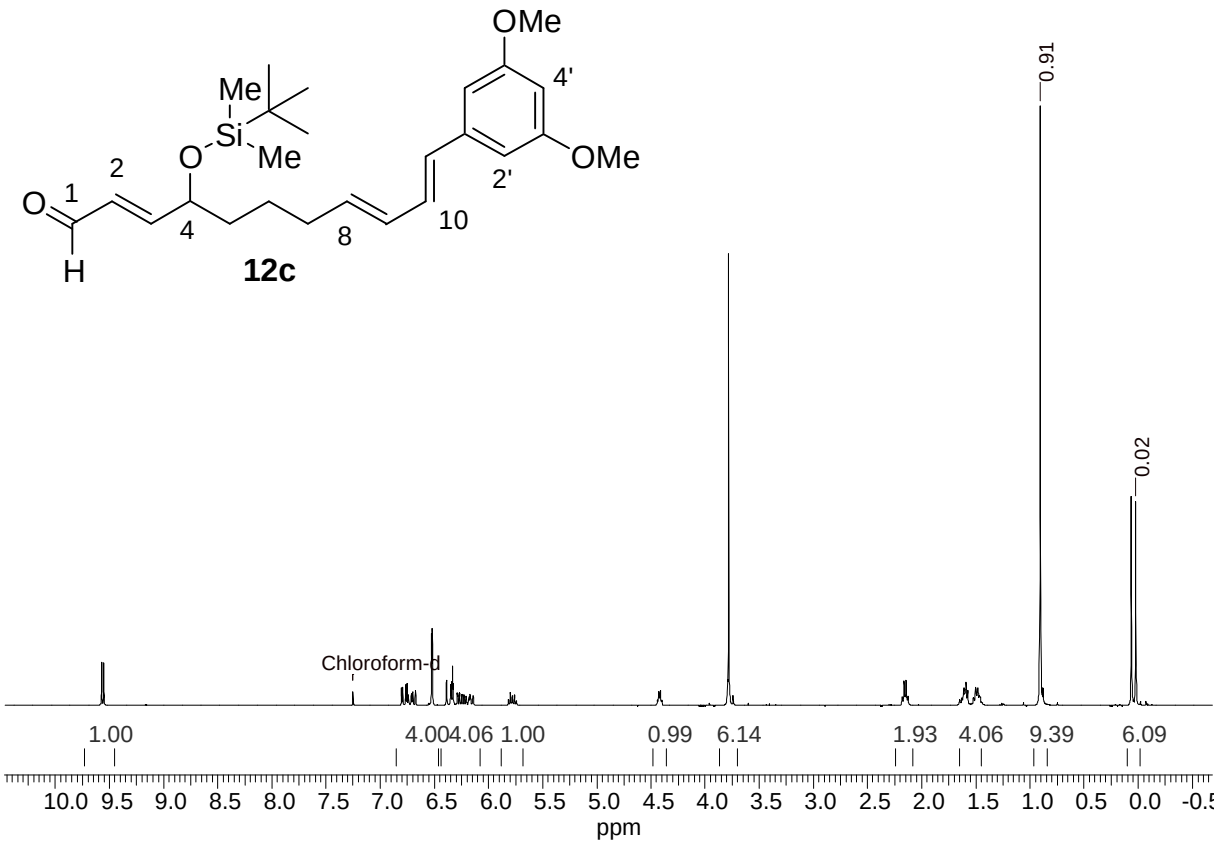

Chloroform-d
193.50
160.86
158.99
139.55
135.78
135.11
133.54
133.21
131.01
130.81
130.27
129.93
129.66
127.67
104.19
99.55
72.29
55.29
36.06
32.51
26.98
23.62
19.31

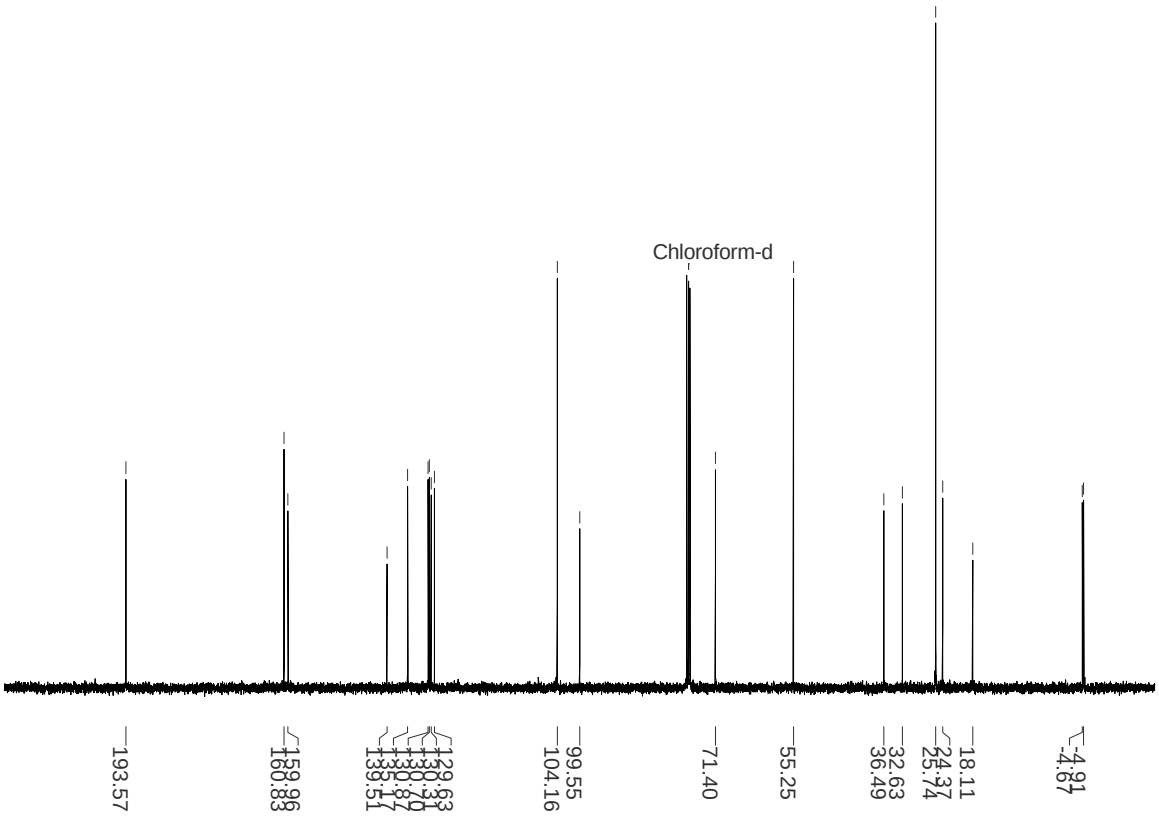

OMe
4'
Si(iPr)3
O
2
OMe
2'
O
1
10
4
8
H

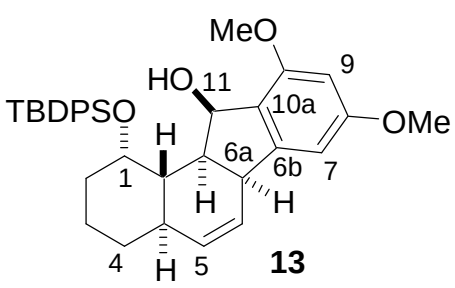
**12b**


1.00
8.00
0.88
0.98
6.18
1.76
4.80
22.12
10.0 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
ppm


Chloroform-d
193.63
160.83
159.98
139.53
135.14
131.00
130.91
130.33
129.62
104.17
99.55
71.64
55.27
36.77
32.73
23.60
17.99
12.27

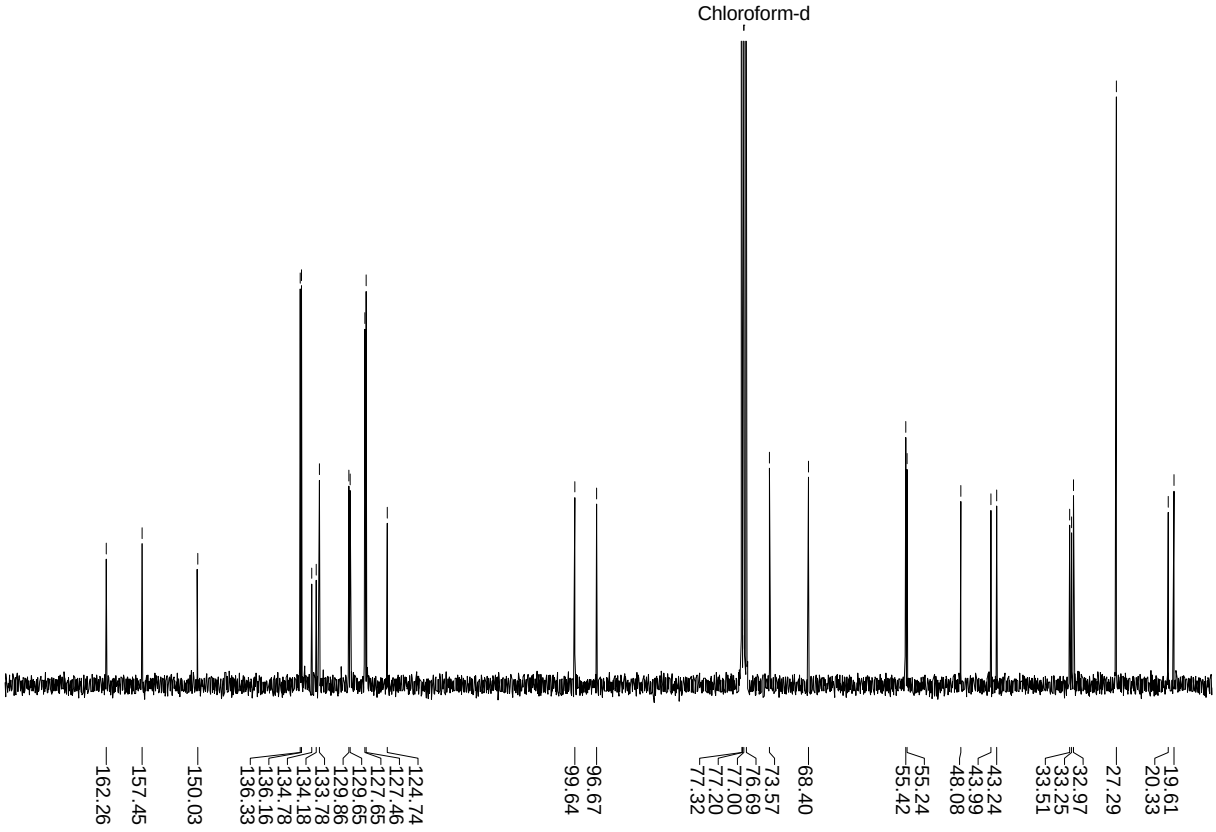

OMe
4'
Me
Si
Me
O
2'
OMe
2
1
O
4
8
10
H
12c
0.91
0.02
Chloroform-d
1.00
4.00
4.06
1.00
0.99
6.14
1.93
4.06
9.39
6.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

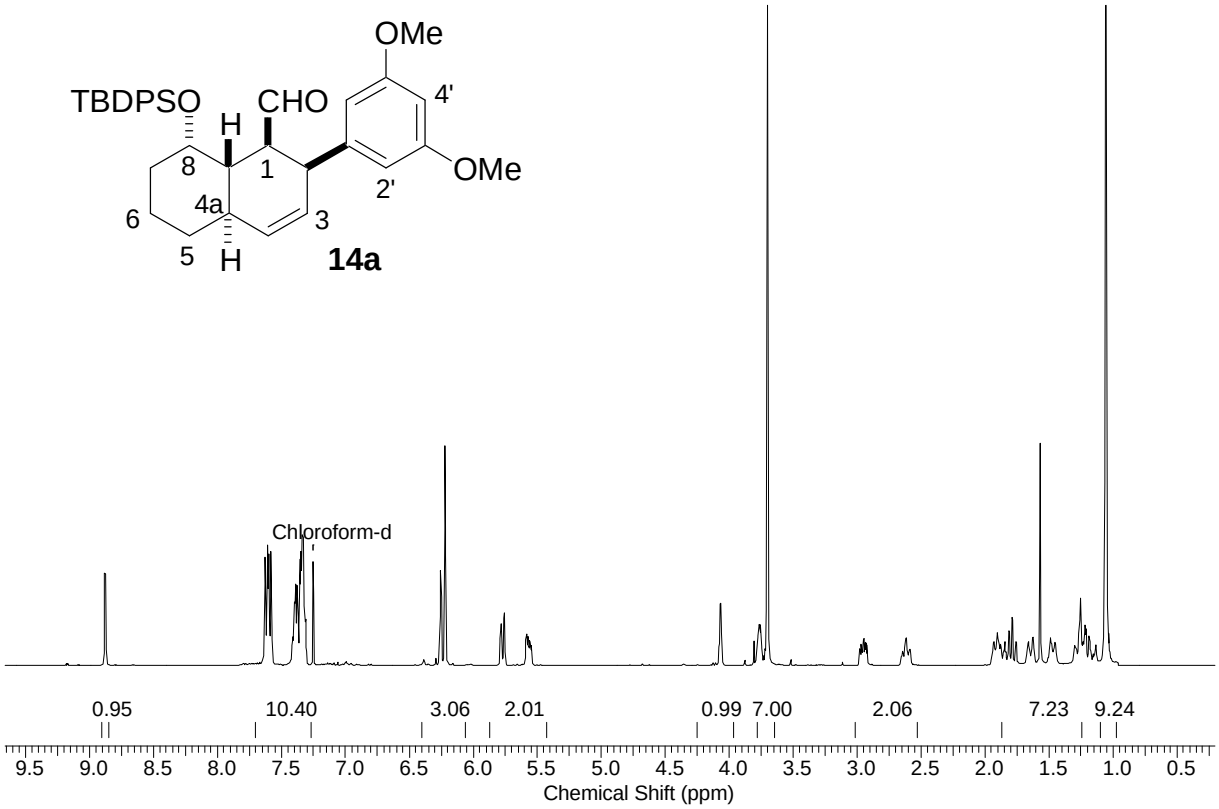

Chloroform-d
193.57
159.96
160.83
139.51
129.63
104.16
99.55
71.40
55.25
36.49
32.63
25.74
24.37
18.11
-4.91
-4.67

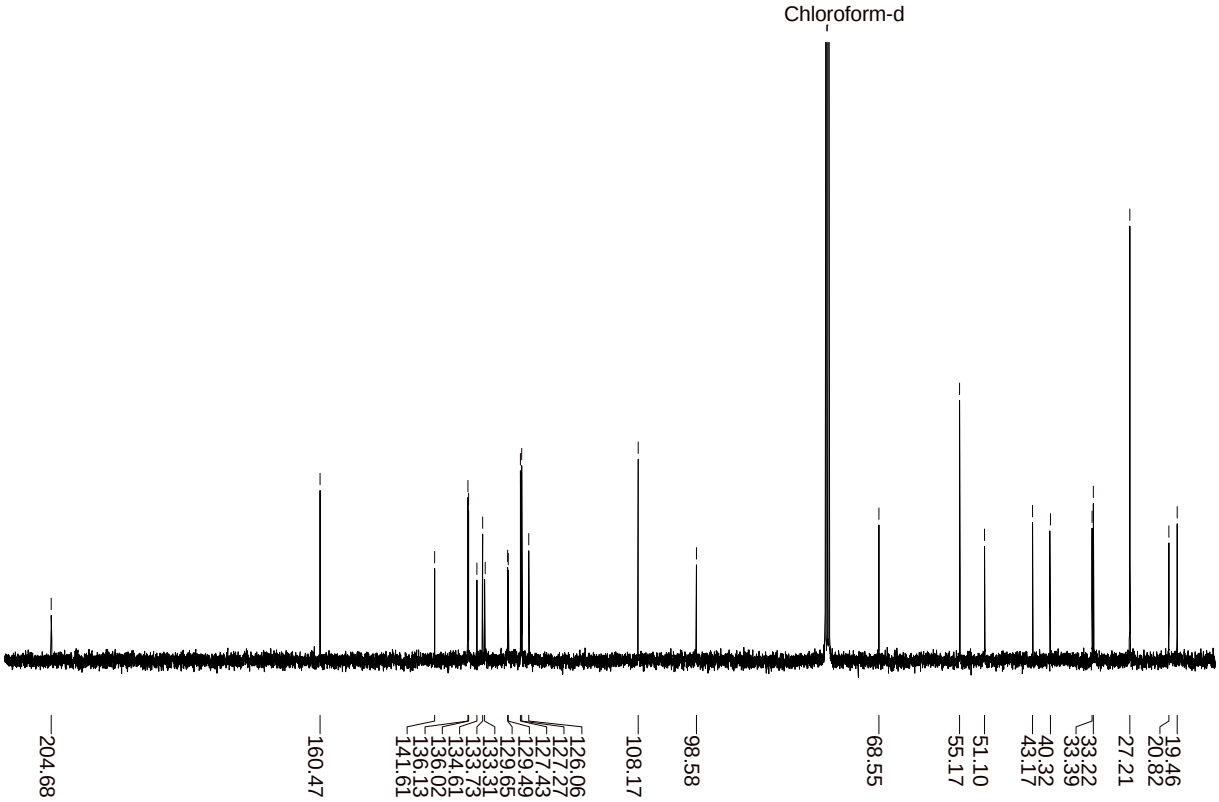

MeO
9
HO
11
10a
TBDPSO
OMe
H
6a
6b
7
1
H
H
4
H
5

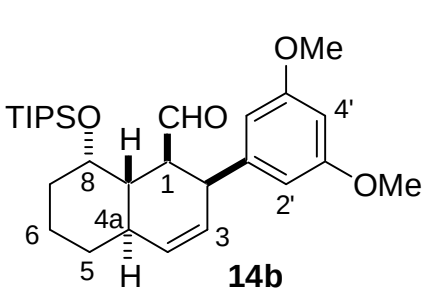
**13**


Chloroform-d
10.68
2.08
1.00
1.01
0.97
1.01
1.00
6.05
1.99
3.16
1.05
1.08
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
ppm


Chloroform-d
162.26
157.45
150.03
136.33
136.16
134.78
134.18
133.78
129.86
129.65
127.46
124.74
99.64
96.67
77.32
77.00
76.69
73.57
68.40
55.42
55.24
48.08
43.99
43.24
33.51
33.25
32.97
27.29
20.33
19.61

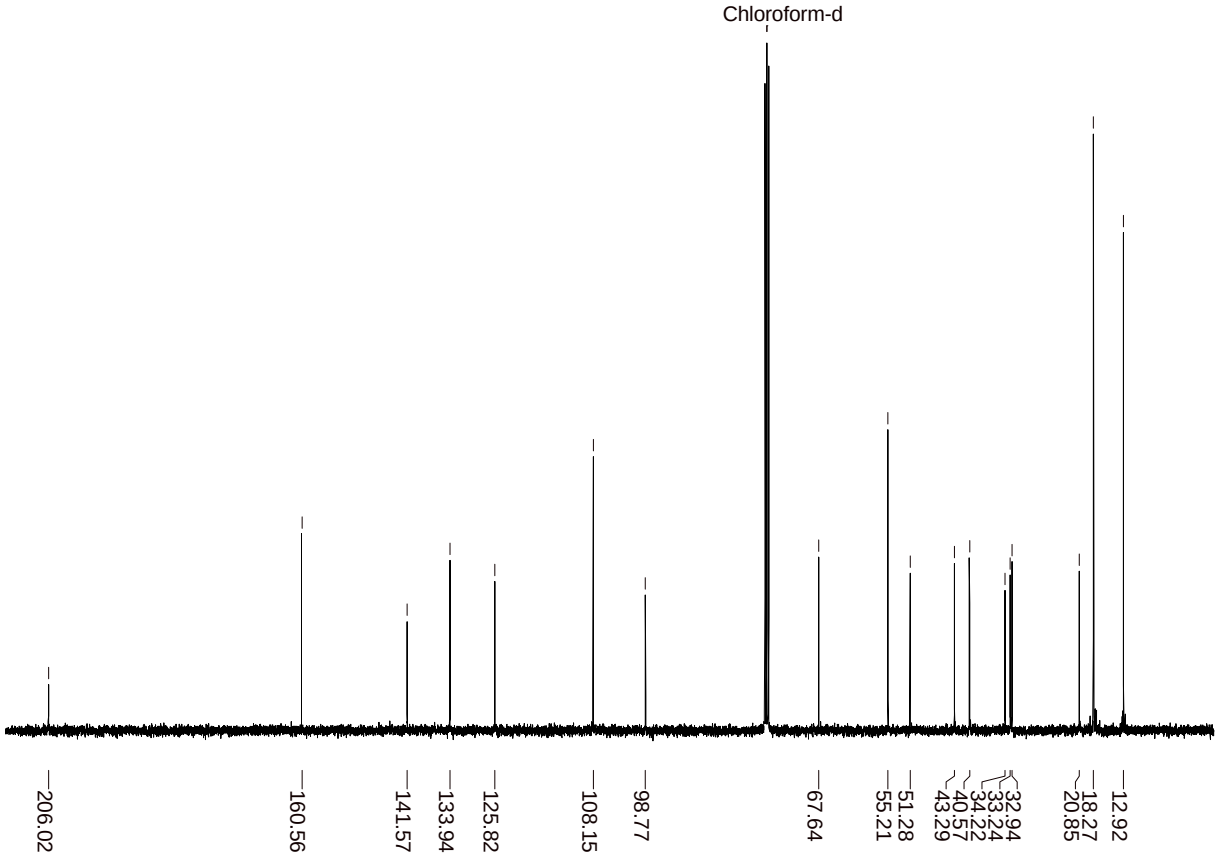

OMe
TBDPSO
CHO
4'
H
8
1
OMe
2'
4a
6
3
5
H
14a
Chloroform-d
0.95
10.40
3.06
2.01
0.99
7.00
2.06
7.23
9.24
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)

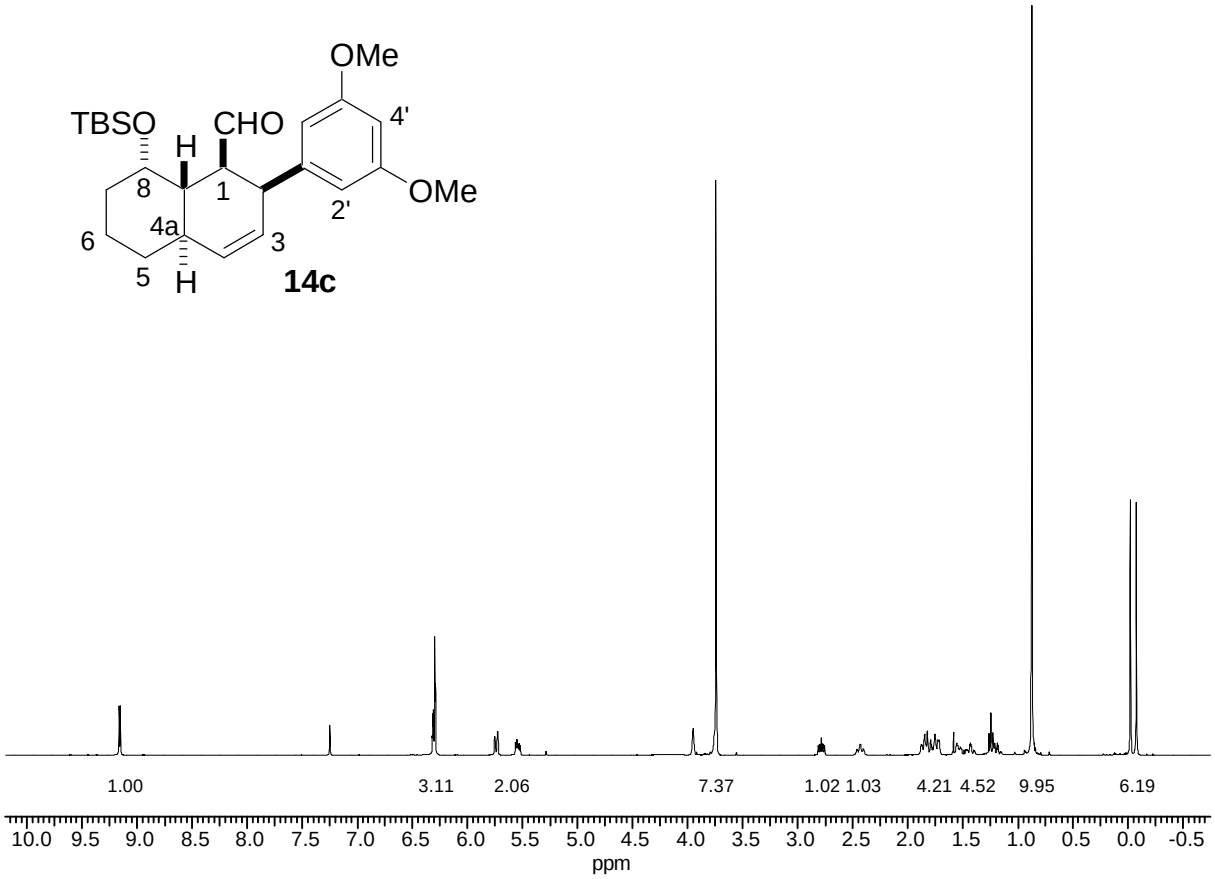

Chloroform-d
204.68
160.47
141.61
136.13
136.02
134.61
133.73
133.31
129.65
129.49
127.43
127.27
126.06
108.17
98.58
68.55
55.17
51.10
43.17
40.32
33.39
33.22
27.21
20.82
19.46

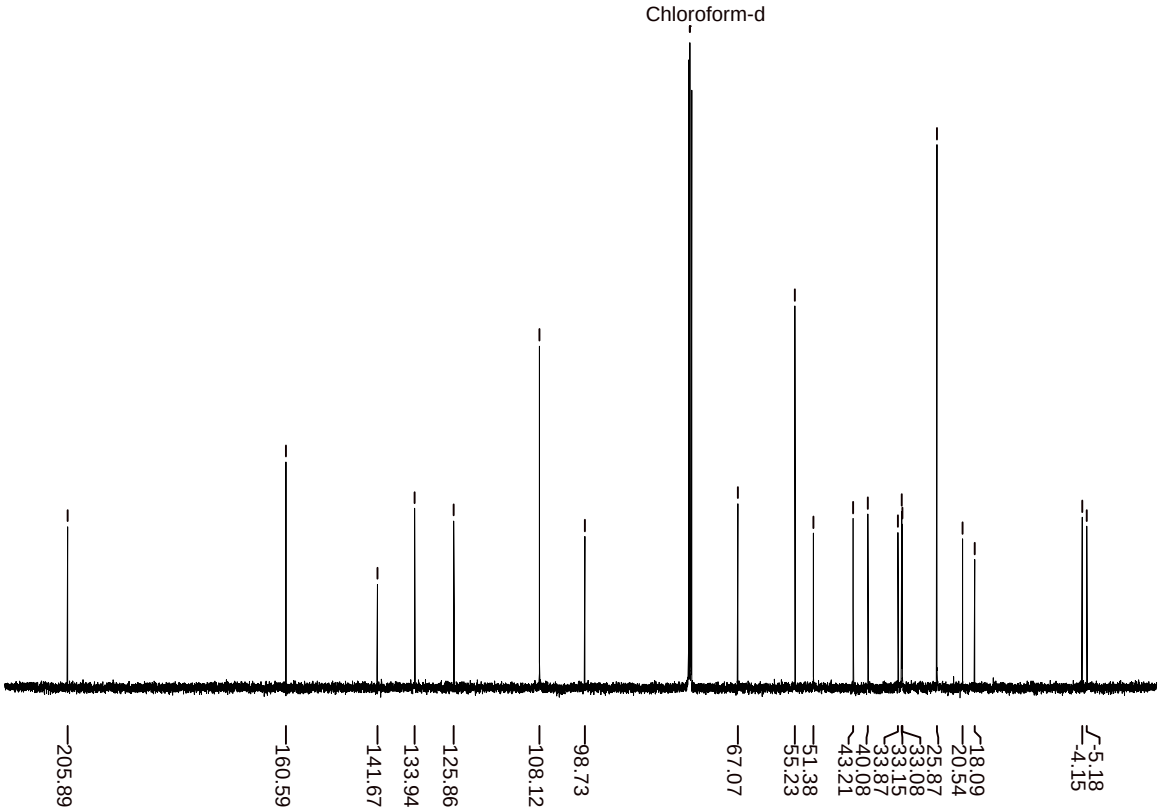

OMe
TIPSO
CHO
4'
H
8
1
2'
OMe
4a
6
3
5
H

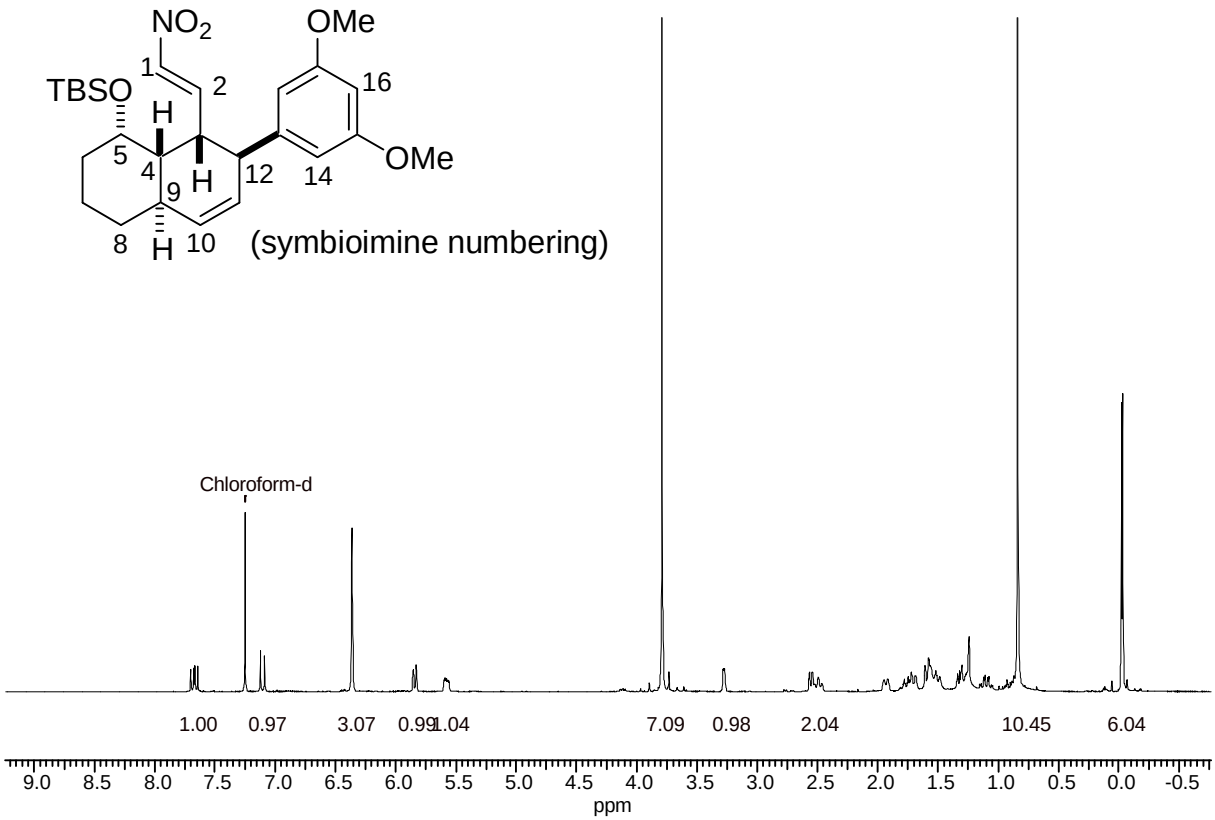
**14b**

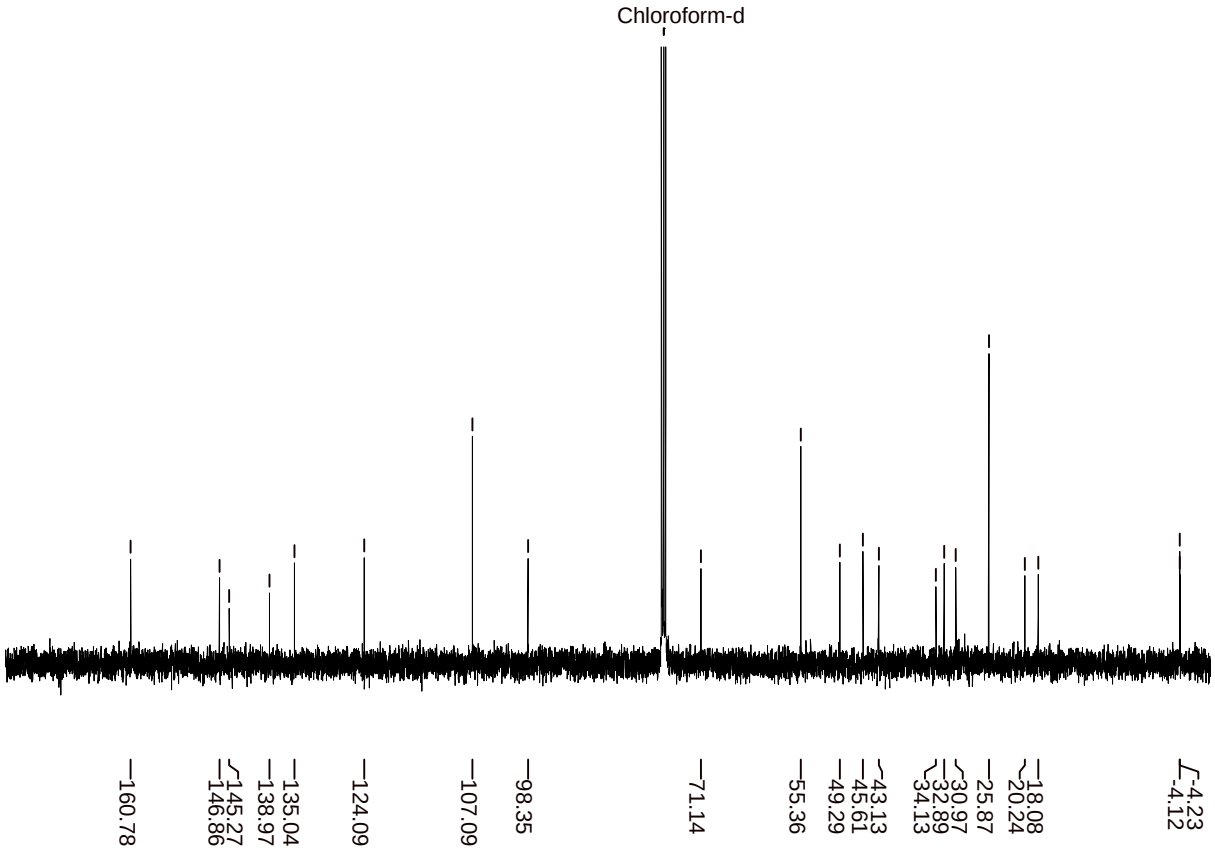

1.00
3.01
2.02
1.00
7.08
0.99
1.00
4.07
4.40
21.36
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

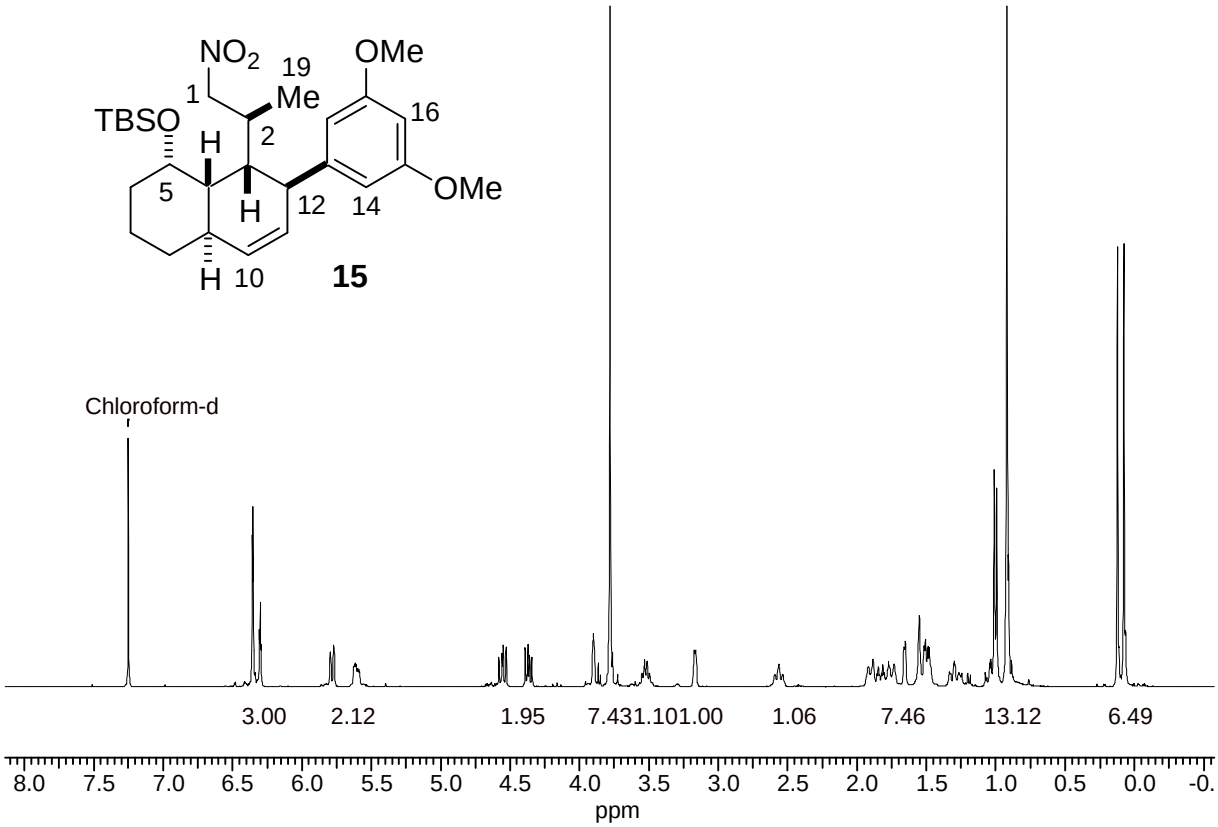

Chloroform-d
206.02
160.56
141.57
133.94
125.82
108.15
98.77
67.64
55.21
51.28
43.29
40.57
34.22
33.24
32.94
20.85
18.27
12.92

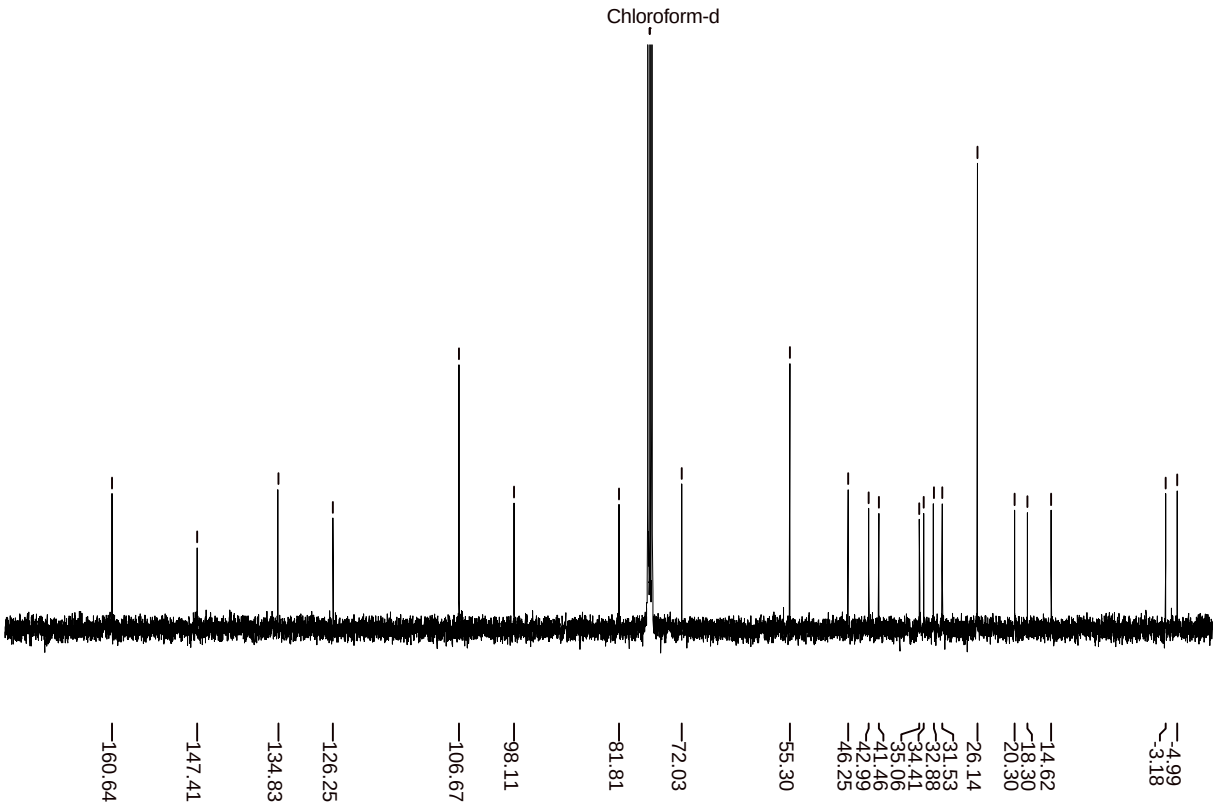

OMe
TBSO
CHO
4'
H
8
1
2'
OMe
4a
6
3
5
H
14c
1.00
3.11
2.06
7.37
1.02 1.03
4.21 4.52
9.95
6.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

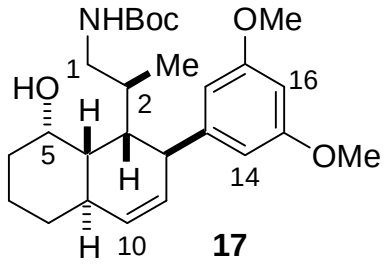

Chloroform-d
205.89
160.59
141.67
133.94
125.86
108.12
98.73
67.07
55.23
51.38
43.21
40.08
33.87
33.15
33.08
25.87
20.54
18.09
-4.15
-5.18


NO2
OMe
TBSO
H
H
H
OMe
1
2
4
5
8
9
10
12
14
16
(symbioimine numbering)
Chloroform-d
1.00
0.97
3.07
0.99
1.04
7.09
0.98
2.04
10.45
6.04
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
ppm


Chloroform-d
160.78
146.86
145.27
138.97
135.04
124.09
107.09
98.35
71.14
55.36
49.29
45.61
43.13
34.13
32.89
30.97
25.87
20.24
18.08
-4.12
-4.23

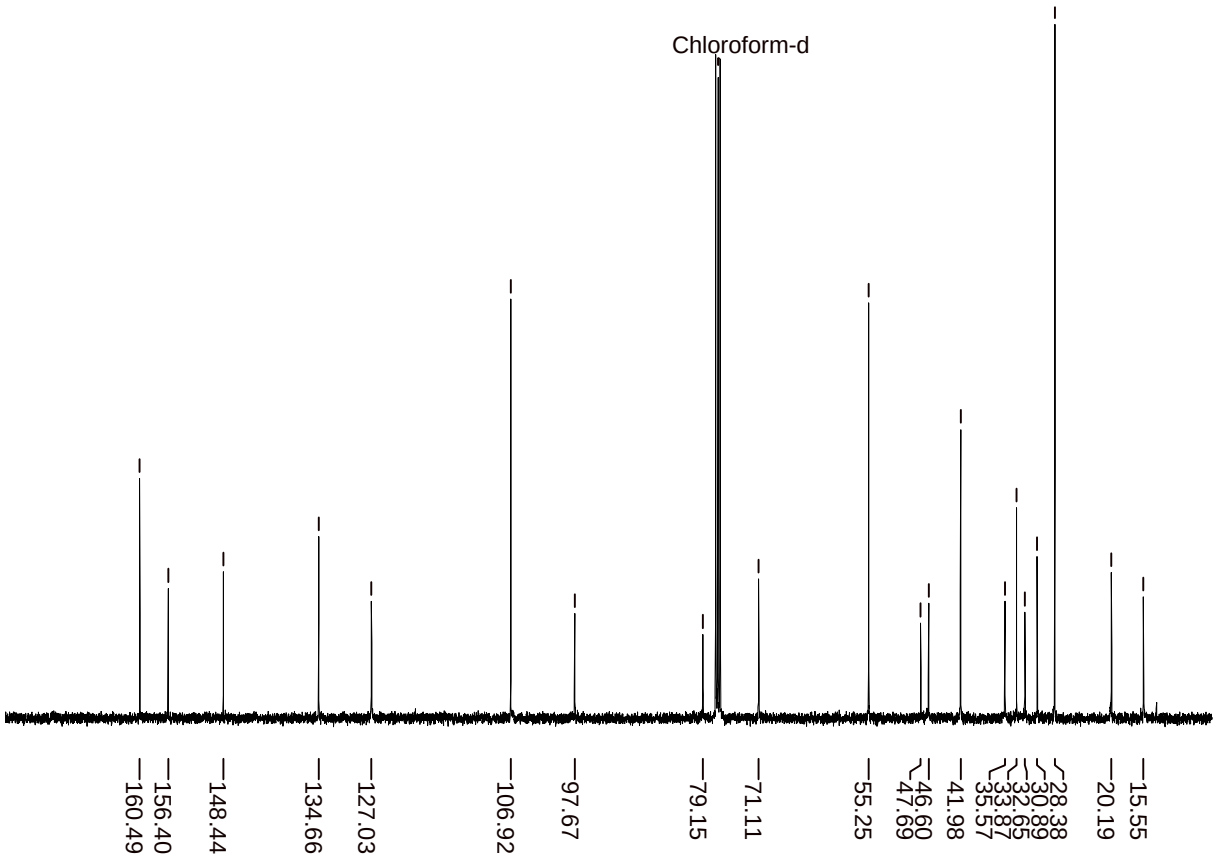

NO2
19
OMe
1
Me
16
TBSO
2
H
5
H
12
14
OMe
H
10
15
Chloroform-d
3.00
2.12
1.95
7.43
1.10
1.00
1.06
7.46
13.12
6.49
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
ppm

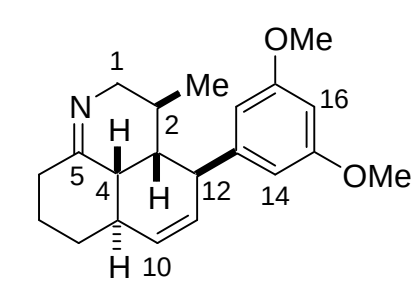

Chloroform-d
160.64
147.41
134.83
126.25
106.67
98.11
81.81
72.03
55.30
46.25
42.99
41.46
35.06
34.41
32.88
31.53
26.14
20.30
18.30
14.62
-3.18
-4.99


NHBoc
OMe
1
Me
16
HO
H
2
5
H
14
OMe
H
10

**17**

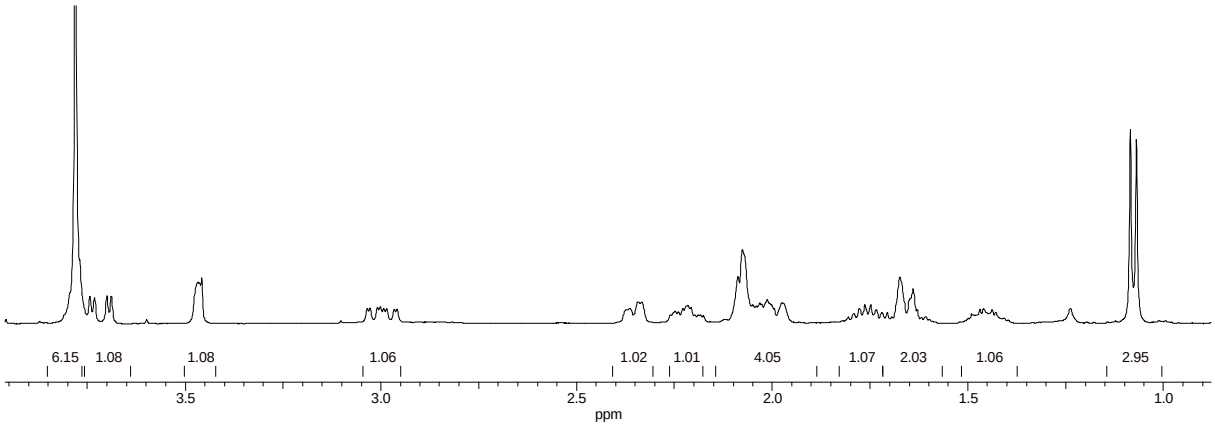

Chloroform-d
2.95
2.00
1.06
6.95
3.05
2.24
0.96
5.90
4.09
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

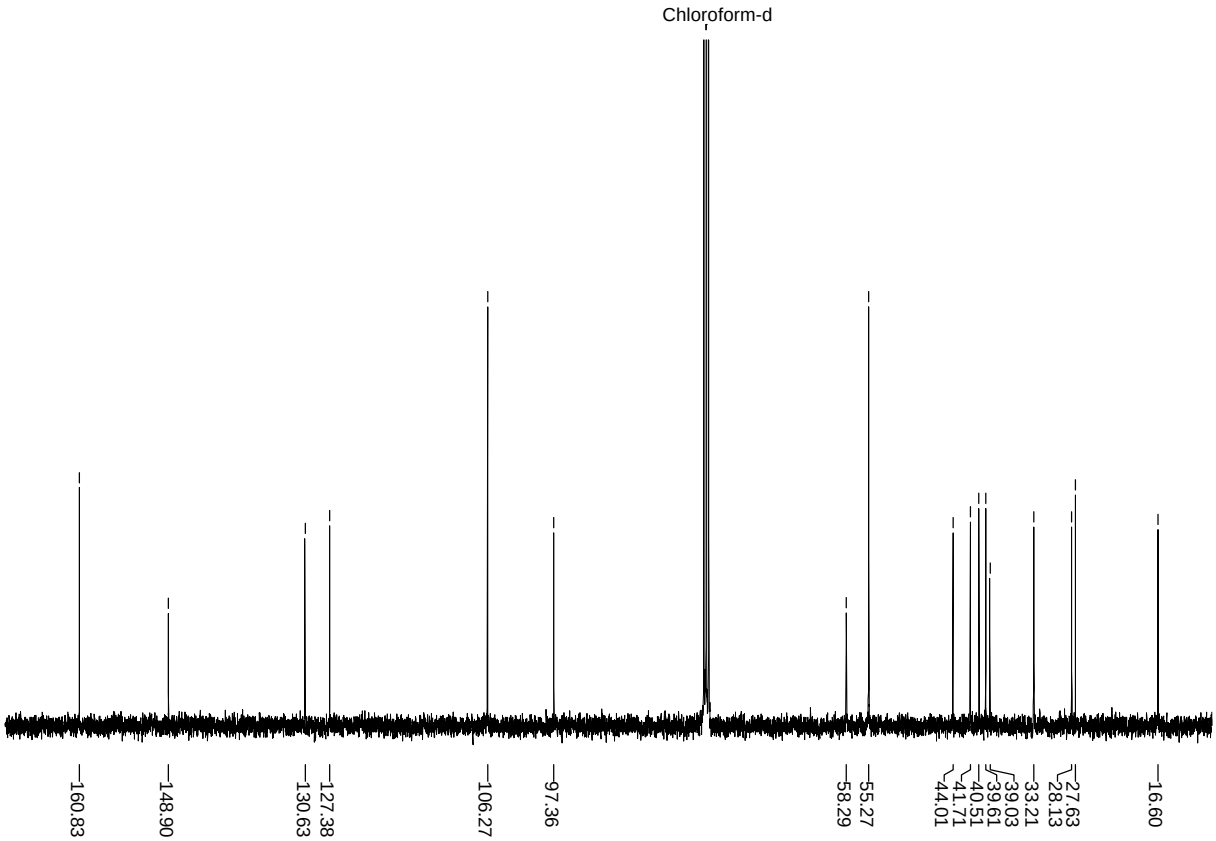

Chloroform-d
160.49
156.40
148.44
134.66
127.03
106.92
97.67
79.15
71.11
55.25
47.69
46.60
41.98
35.57
33.87
32.65
30.89
28.38
20.19
15.55

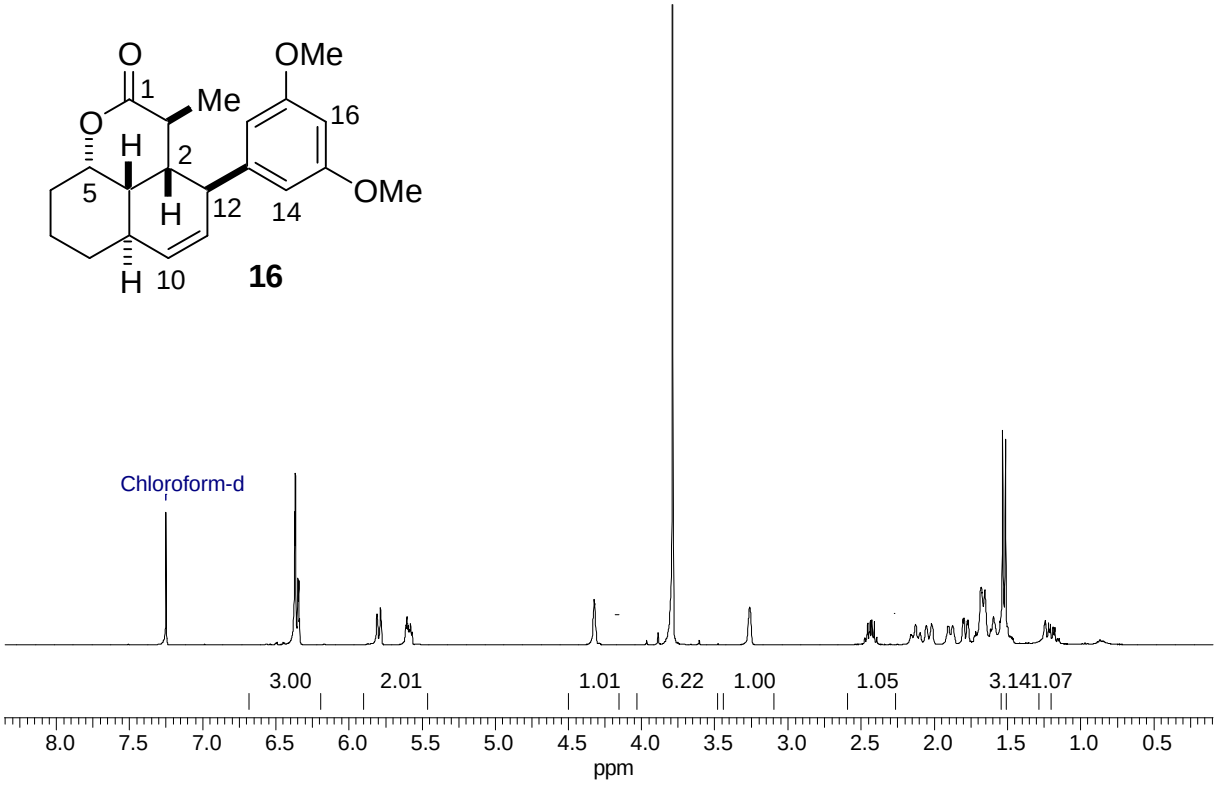


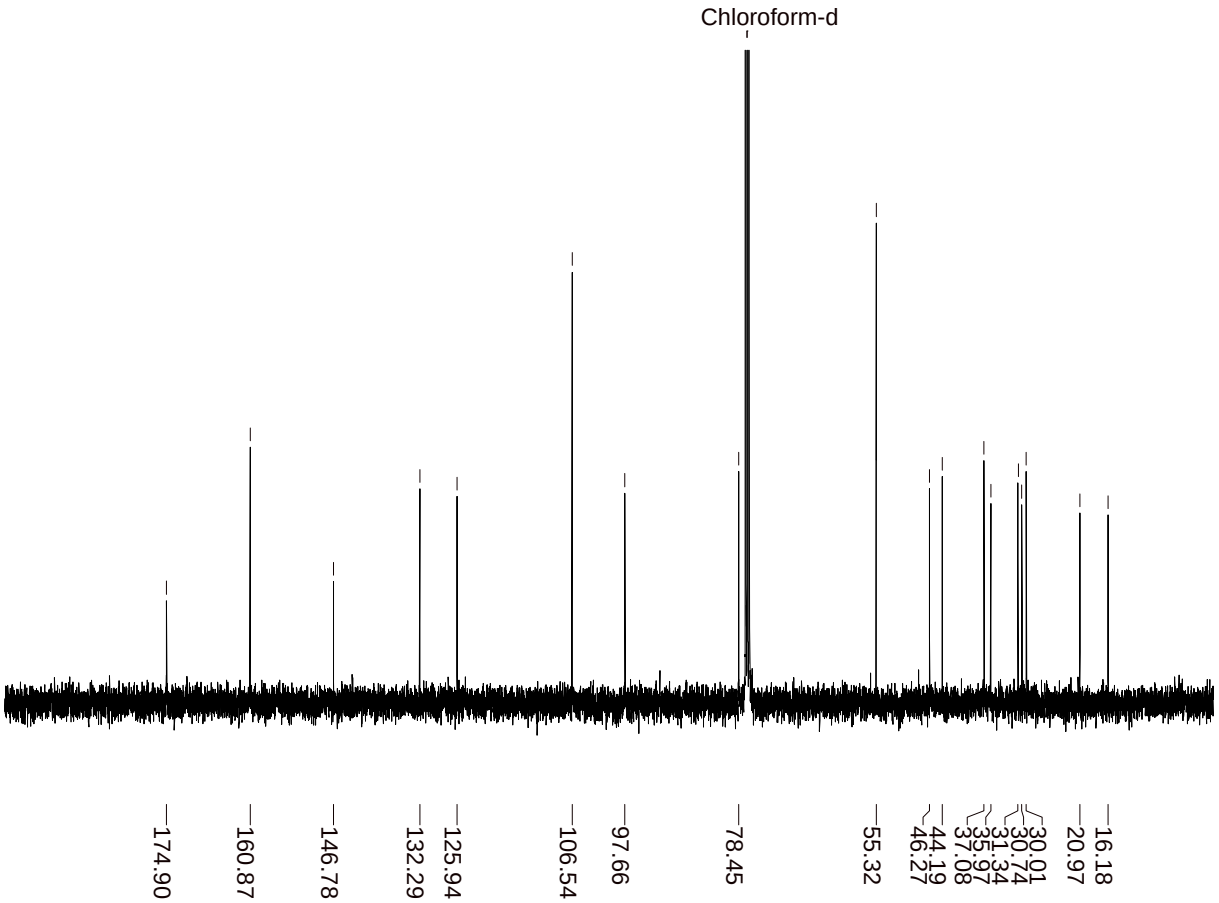

**18** (***epi***-symbioimine analog)

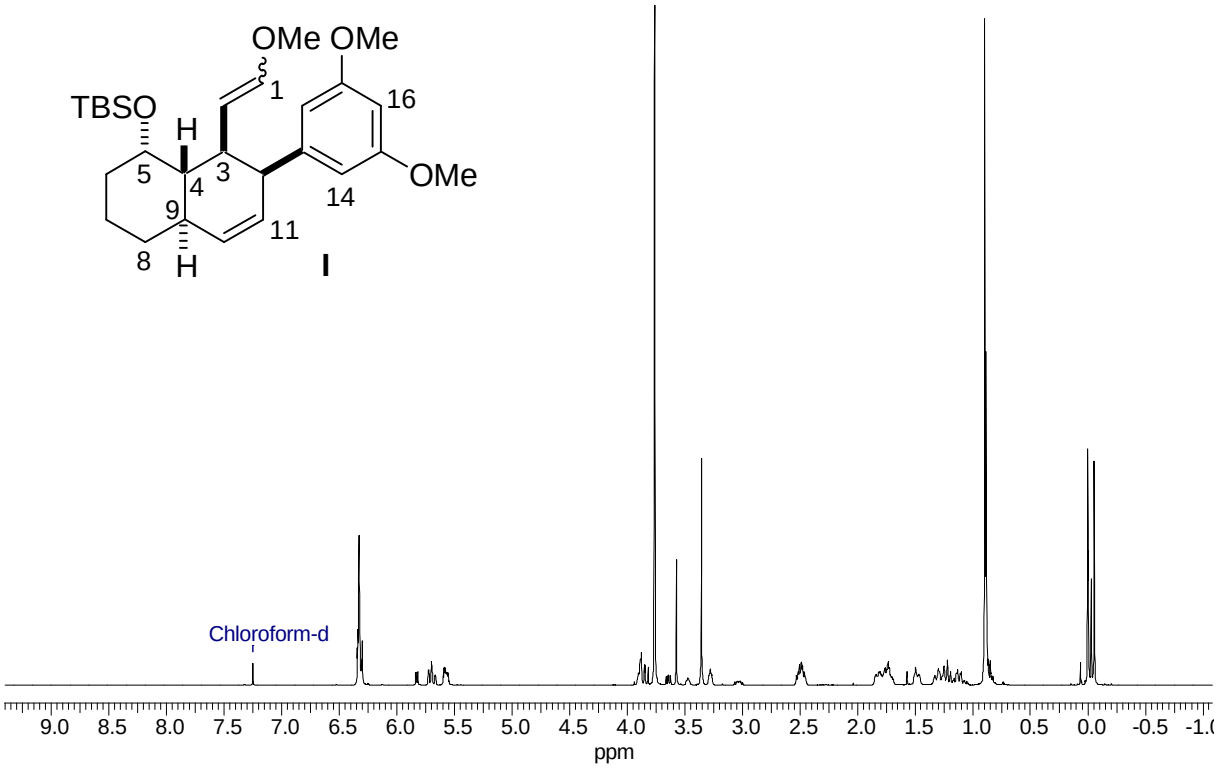


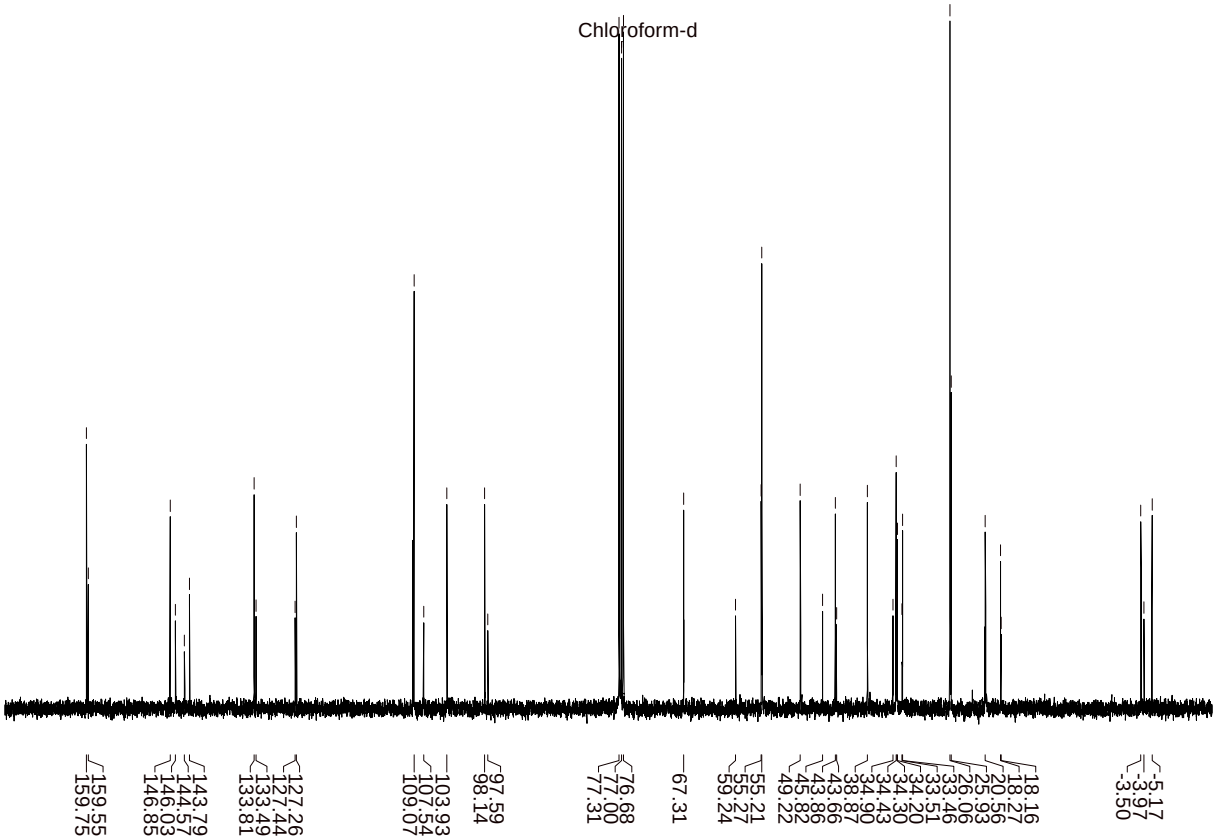



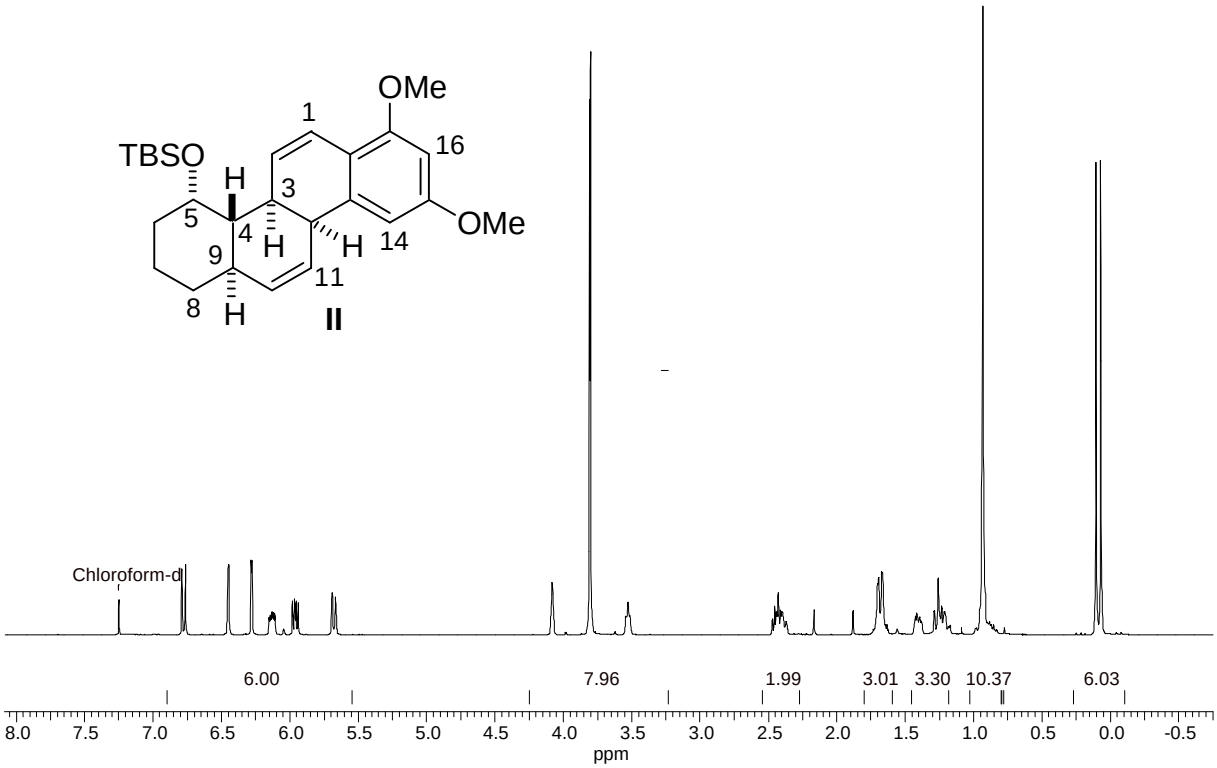



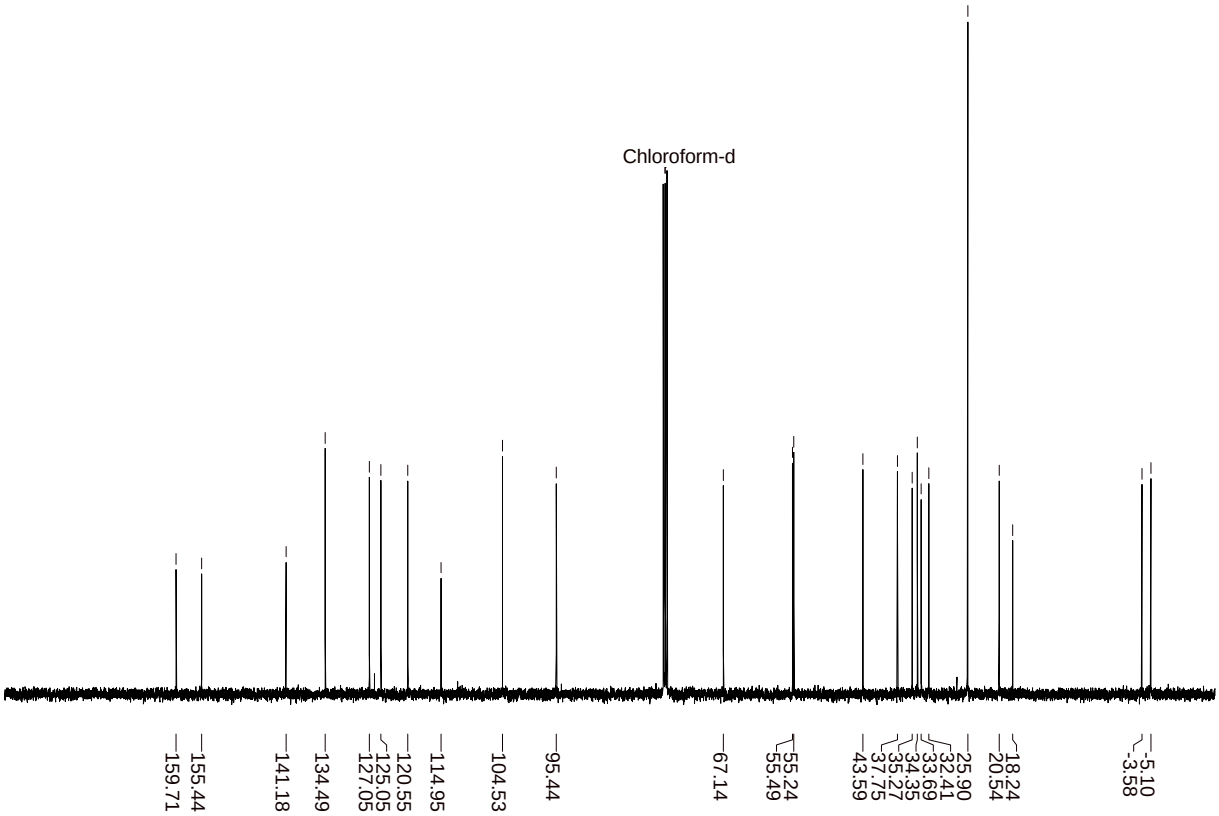

O
1
Me
OMe
16
O
H
2
5
H
12
14
OMe
H
10
16
Chloroform-d
3.00
2.01
1.01
6.22
1.00
1.05
3.14
1.07
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

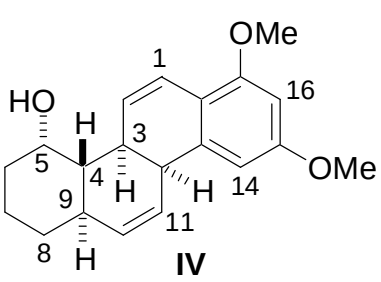

Chloroform-d
174.90
160.87
146.78
132.29
125.94
106.54
97.66
78.45
55.32
46.27
44.19
37.08
35.97
31.34
30.74
30.01
20.97
16.18


OMe OMe
TBSO
H
1
16
5
4
3
OMe
14
9
11
8
H
I
Chloroform-d
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
ppm


Chloroform-d
159.75
159.55
146.85
146.03
144.57
143.79
133.81
133.49
127.44
127.26
109.07
107.54
103.93
98.14
97.59
77.31
77.00
76.68
67.31
59.24
55.27
55.21
49.22
45.82
43.86
43.66
38.87
34.90
34.43
34.30
34.20
33.51
33.46
26.06
25.93
20.56
18.27
18.16
-3.50
-3.97
-5.17

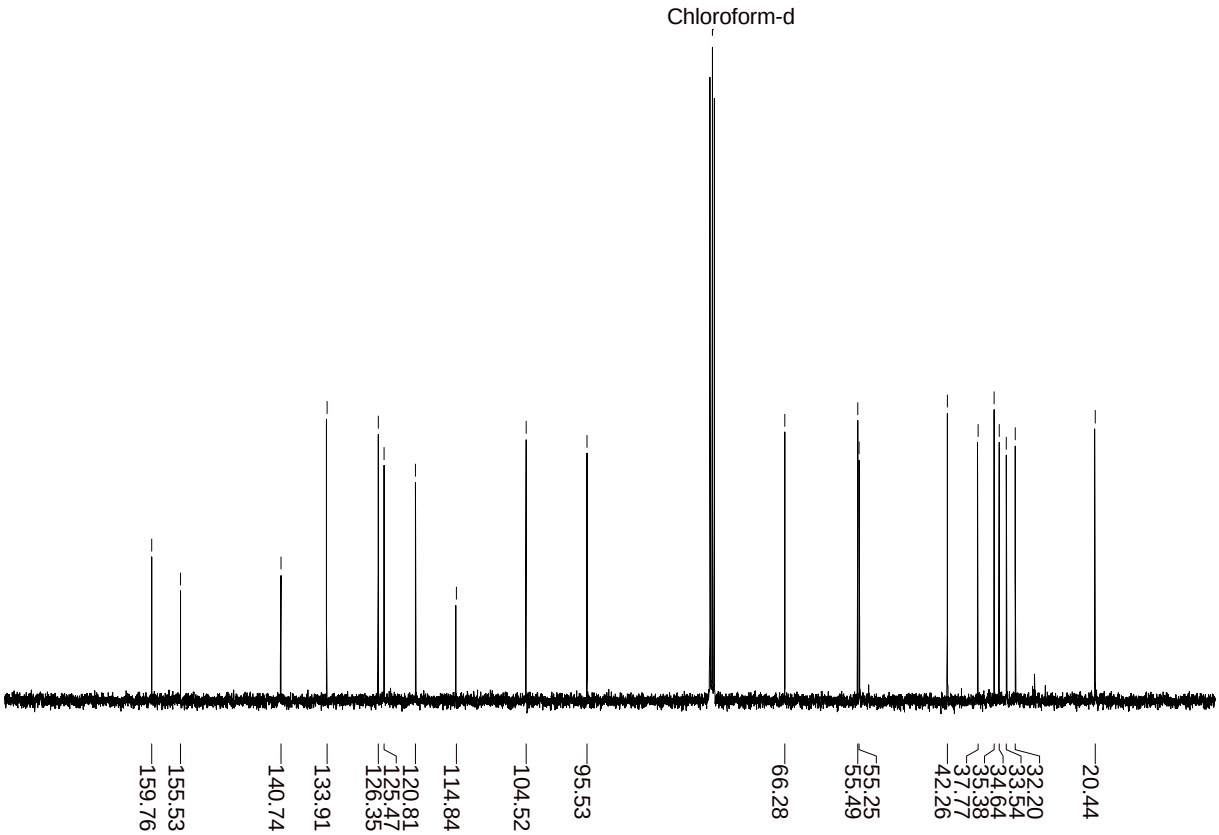

OMe
1
16
TBSO
H
3
5
4
H
H
14
OMe
9
11
8
H
II
Chloroform-d
6.00
7.96
1.99
3.01
3.30
10.37
6.03
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

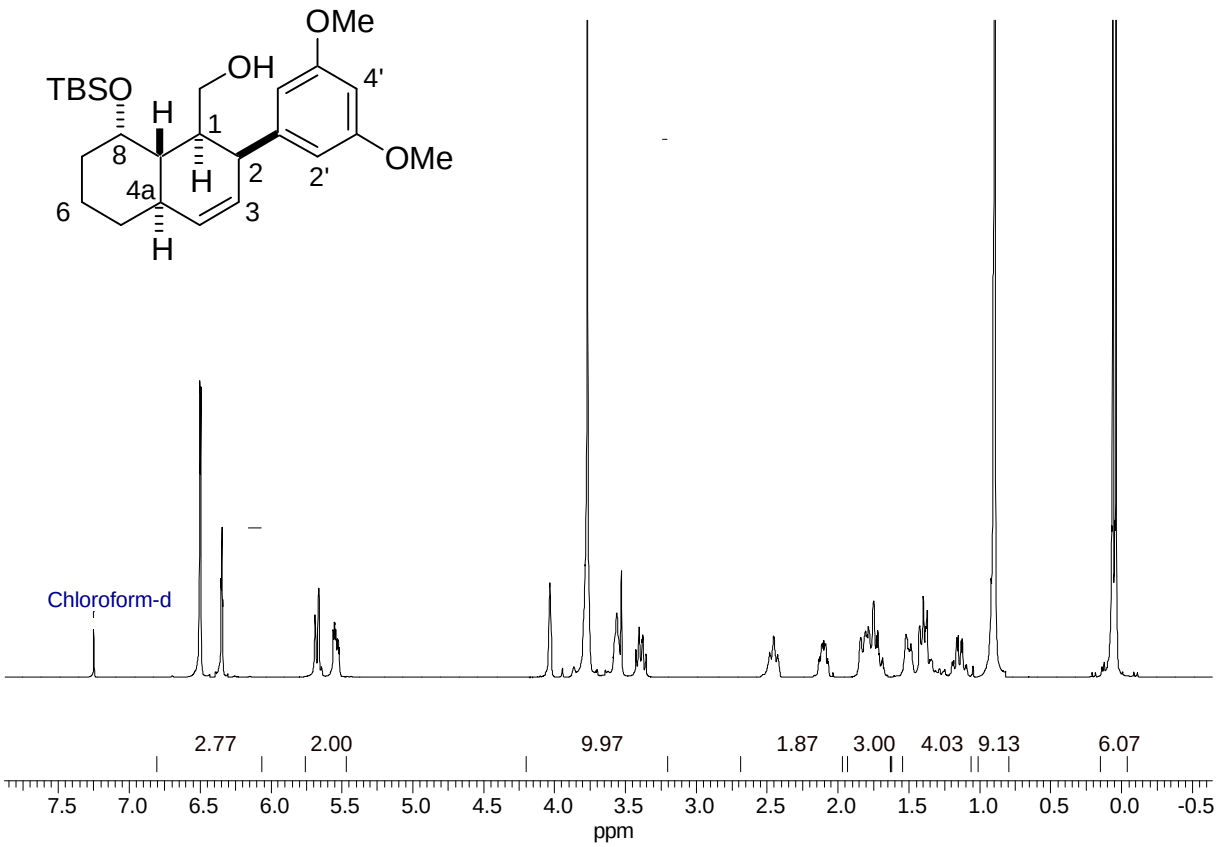

Chloroform-d
159.71
155.44
141.18
134.49
127.05
125.05
120.55
114.95
104.53
95.44
67.14
55.49
55.24
43.59
37.75
35.27
34.35
33.69
32.41
25.90
20.54
18.24
-3.58
-5.10

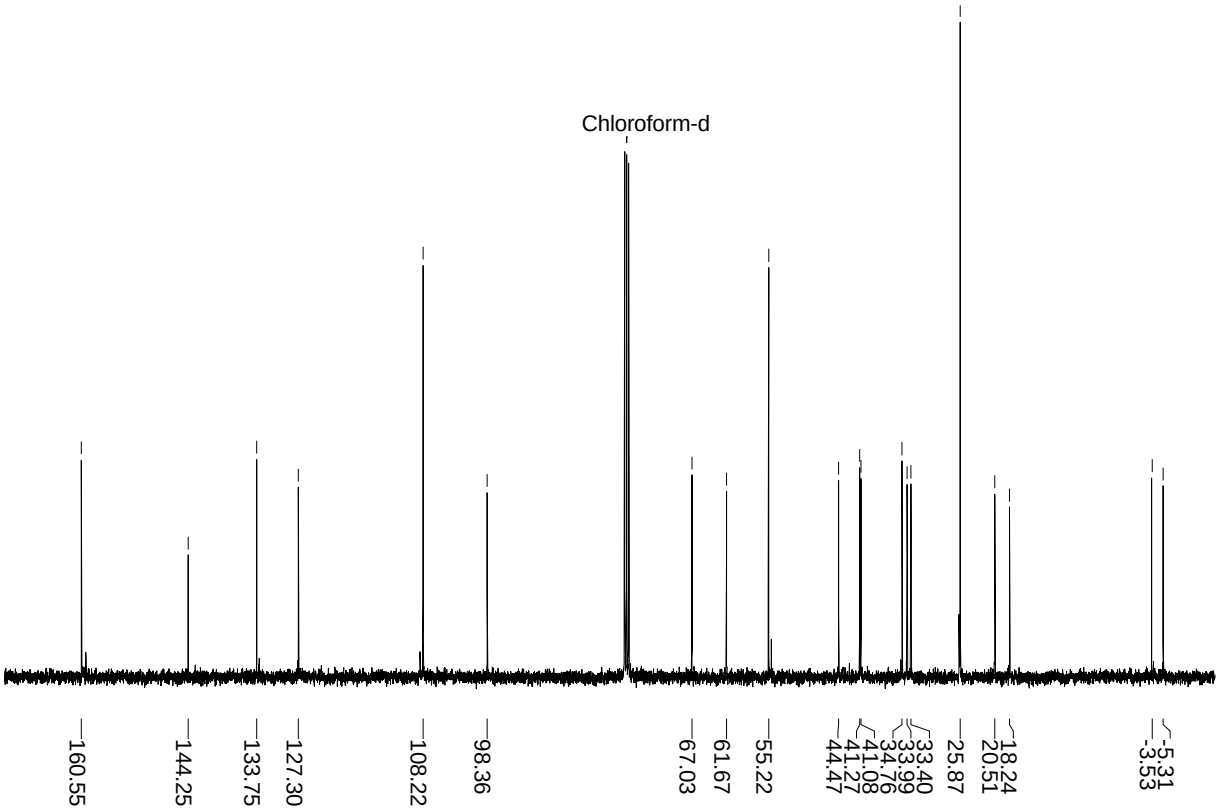

OMe
1
16
HO
H
3
5
4
H
H
14
OMe
9
11
8
H

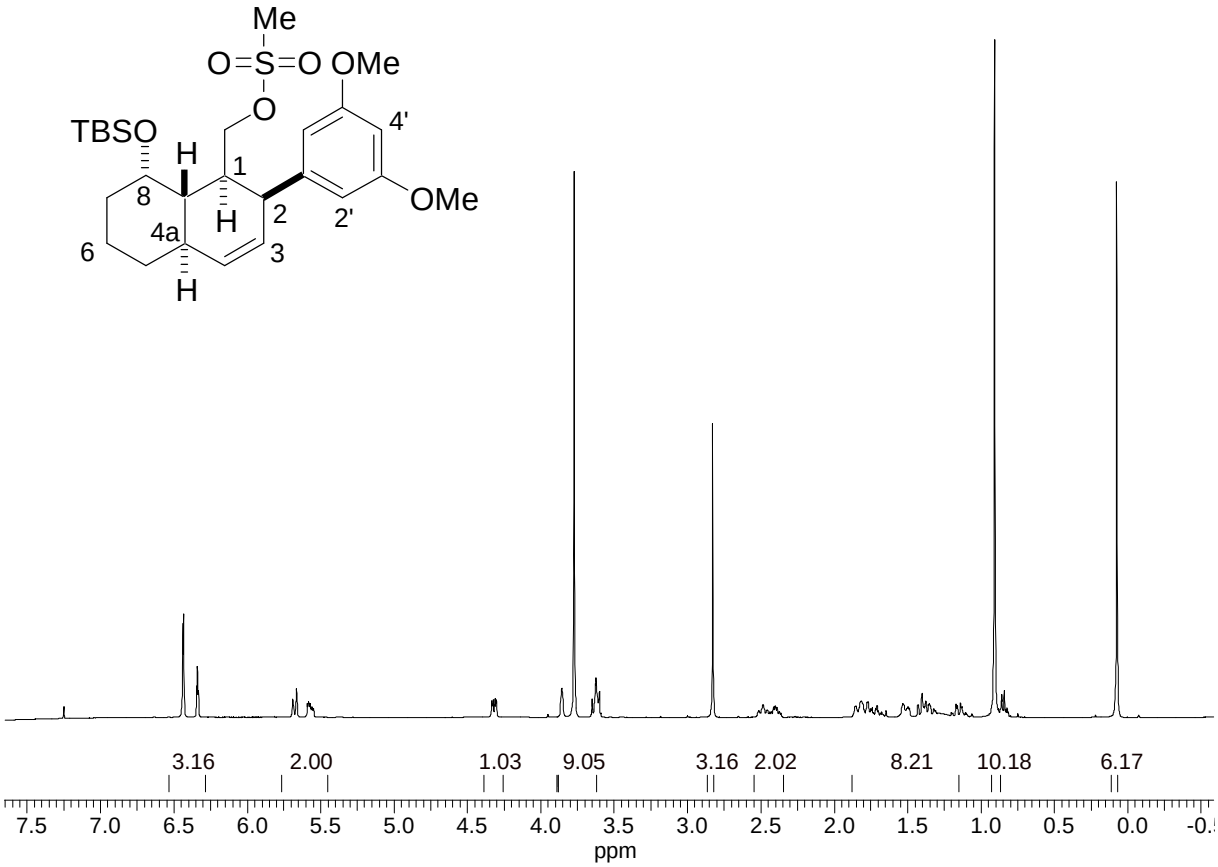
**IV**

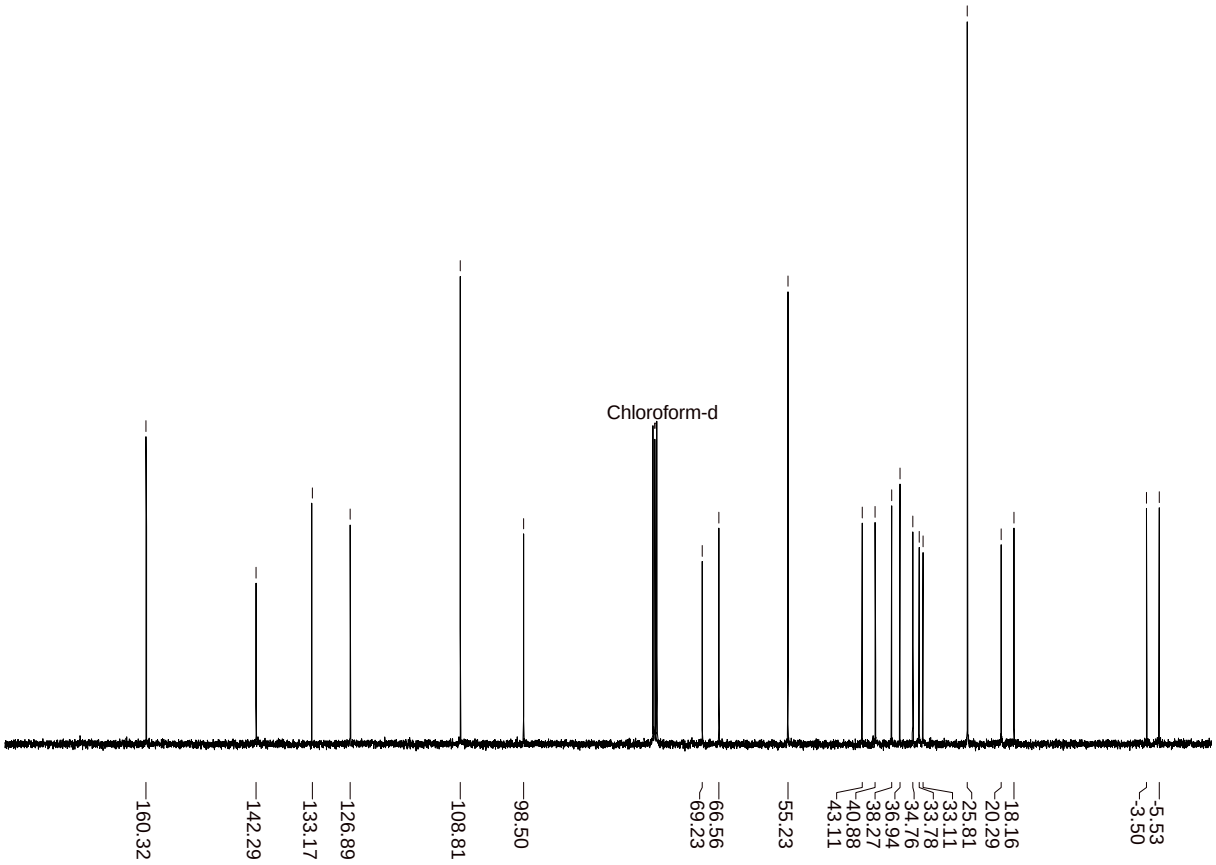

Chloroform-d
6.00
8.13
2.14
3.17
4.05
1.12
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

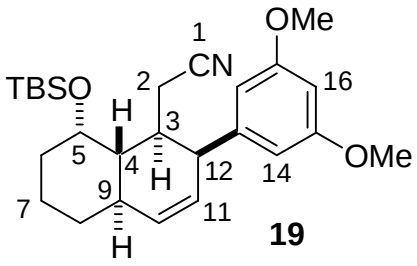

Chloroform-d
159.76
155.53
140.74
133.91
126.35
125.47
120.81
114.84
104.52
95.53
66.28
55.49
55.25
42.26
37.77
35.38
34.64
33.54
32.20
20.44


OMe
OH
TBSO
H
1
4'
8
2
2'
OMe
4a
H
6
3
H
Chloroform-d
2.77
2.00
9.97
1.87
3.00
4.03
9.13
6.07
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
ppm


Chloroform-d
160.55
144.25
133.75
127.30
108.22
98.36
67.03
61.67
55.22
44.47
41.27
41.08
34.76
33.99
33.40
25.87
20.51
18.24
-3.53
-5.31

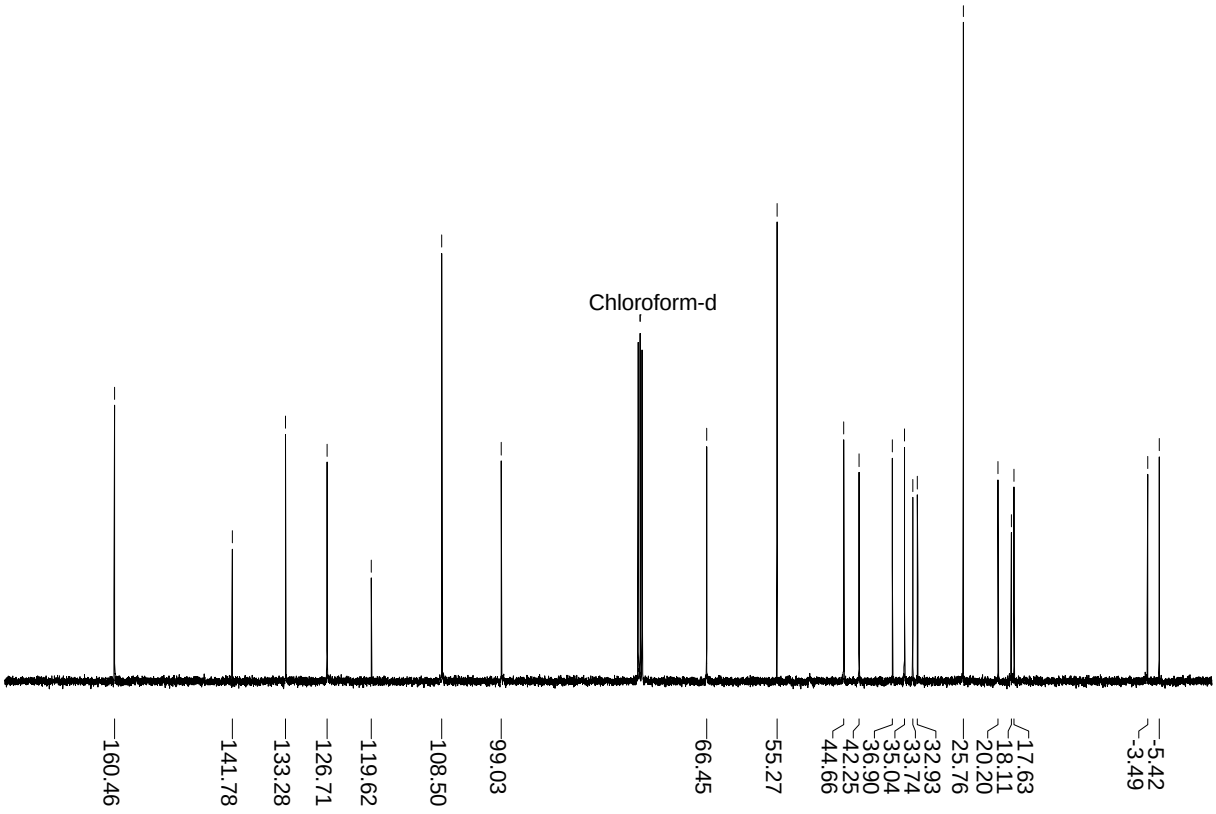

Me
O=S=O OMe
O
TBSO
H
1
8
4'
OMe
2
2'
H
4a
6
3
H
3.16
2.00
1.03
9.05
3.16
2.02
8.21
10.18
6.17
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

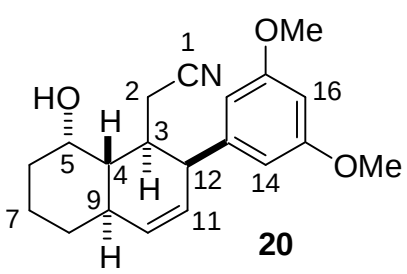

Chloroform-d
160.32
142.29
133.17
126.89
108.81
98.50
69.23
66.56
55.23
43.11
40.88
38.27
36.94
34.76
33.78
33.11
25.81
20.29
18.16
-3.50
-5.53


OMe
1
CN
2
16
TBSO
H
3
5
4
H
12
14
OMe
9
7
11
H

**19**

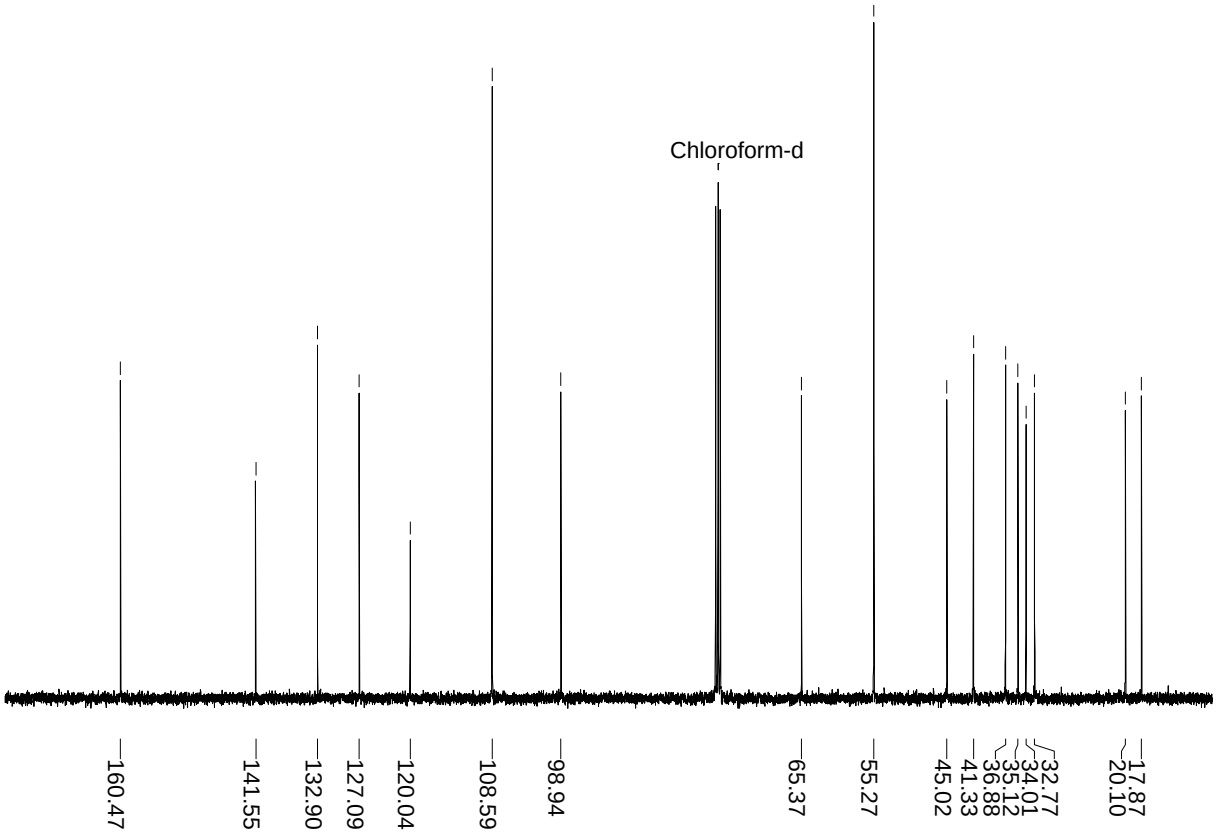

Chloroform-d
3.00
2.00
8.06
3.05
8.73
9.33
6.15
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

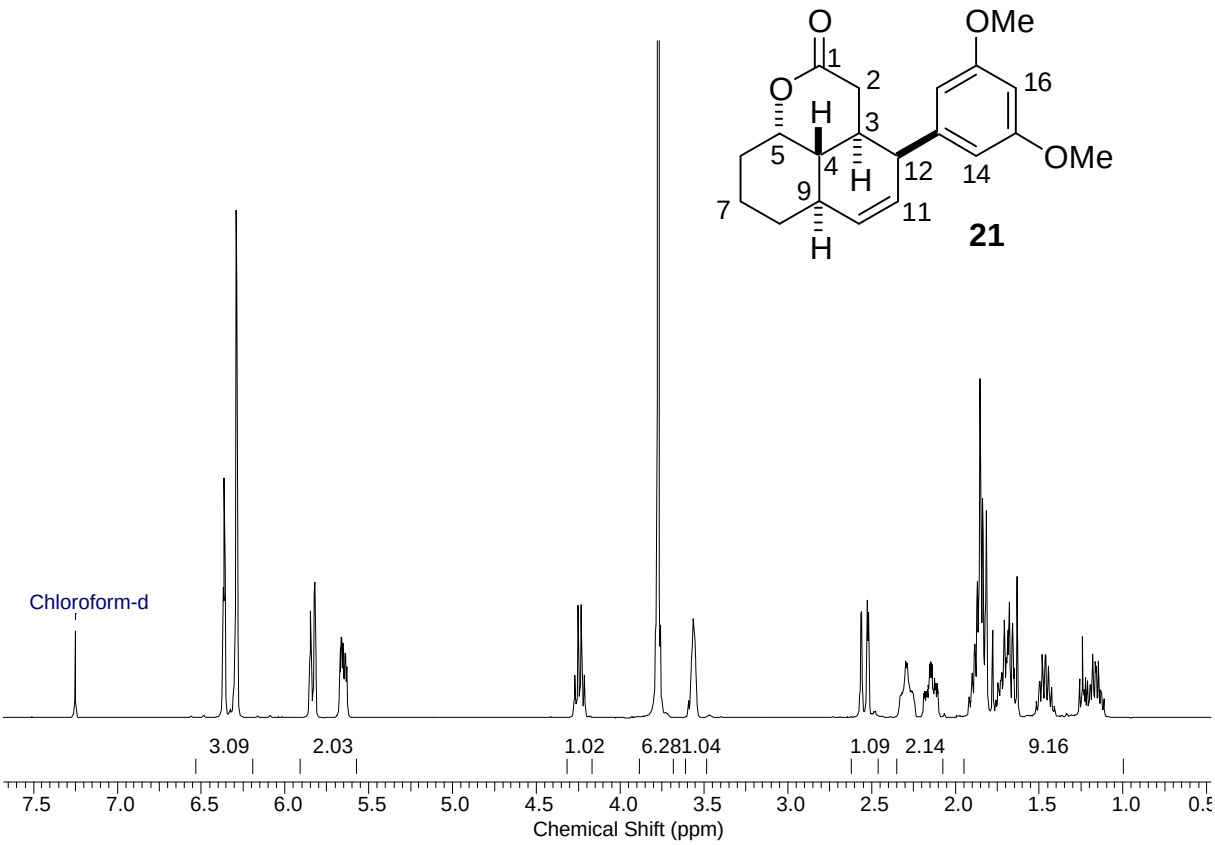

Chloroform-d
160.46
141.78
133.28
126.71
119.62
108.50
99.03
66.45
55.27
44.66
42.25
36.90
35.04
33.74
32.93
25.76
20.20
18.11
17.63
-3.49
-5.42

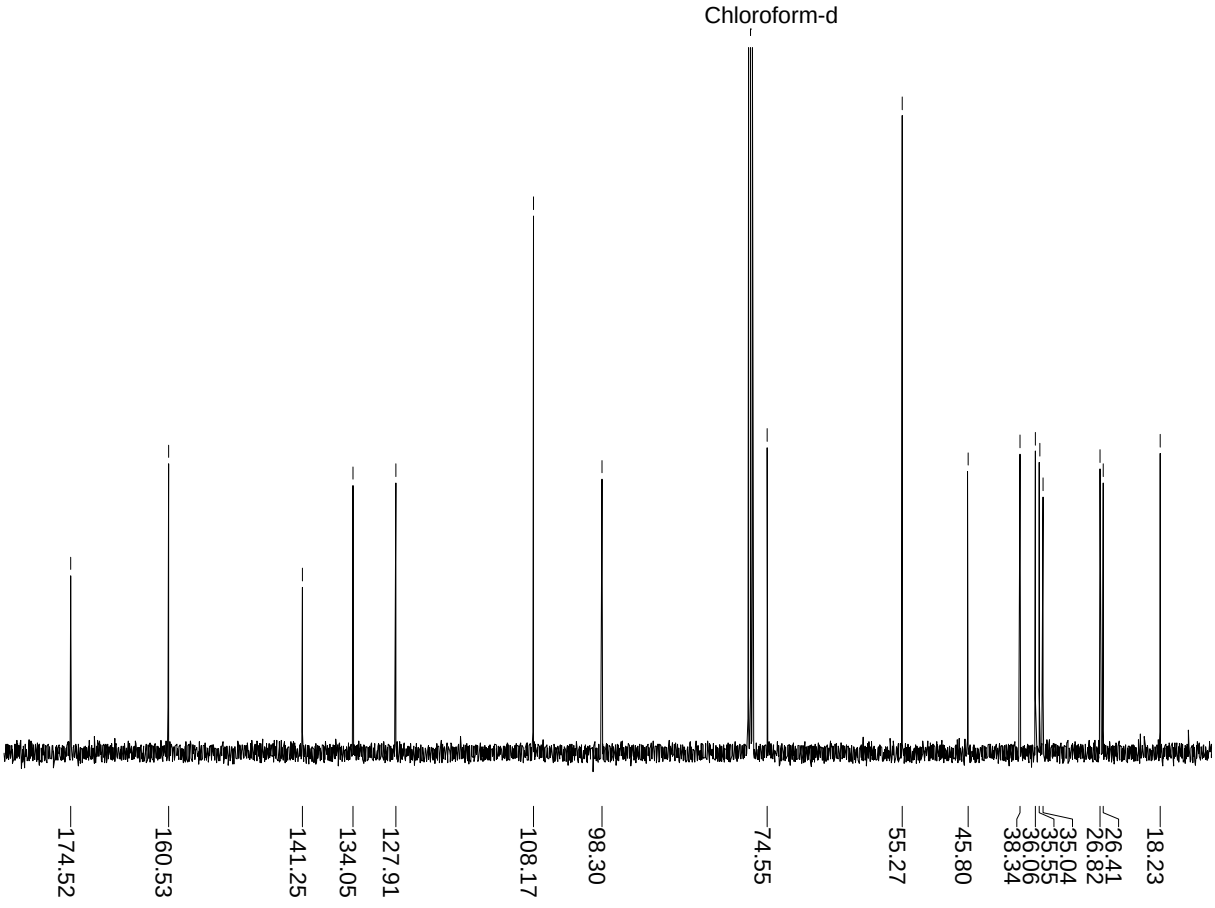

1
OMe
CN
2
16
HO
H
3
5
4
H
12
14
OMe
9
7
11
H

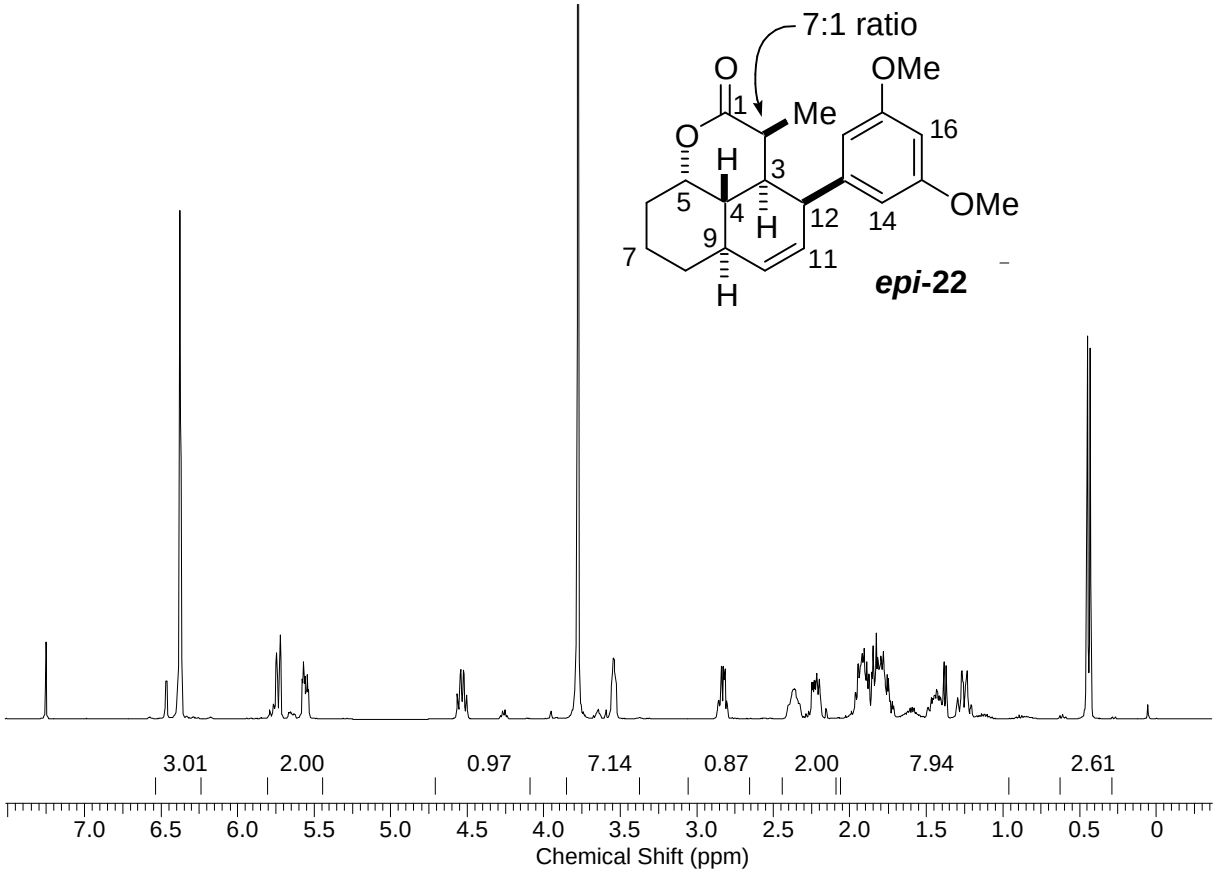
**20**

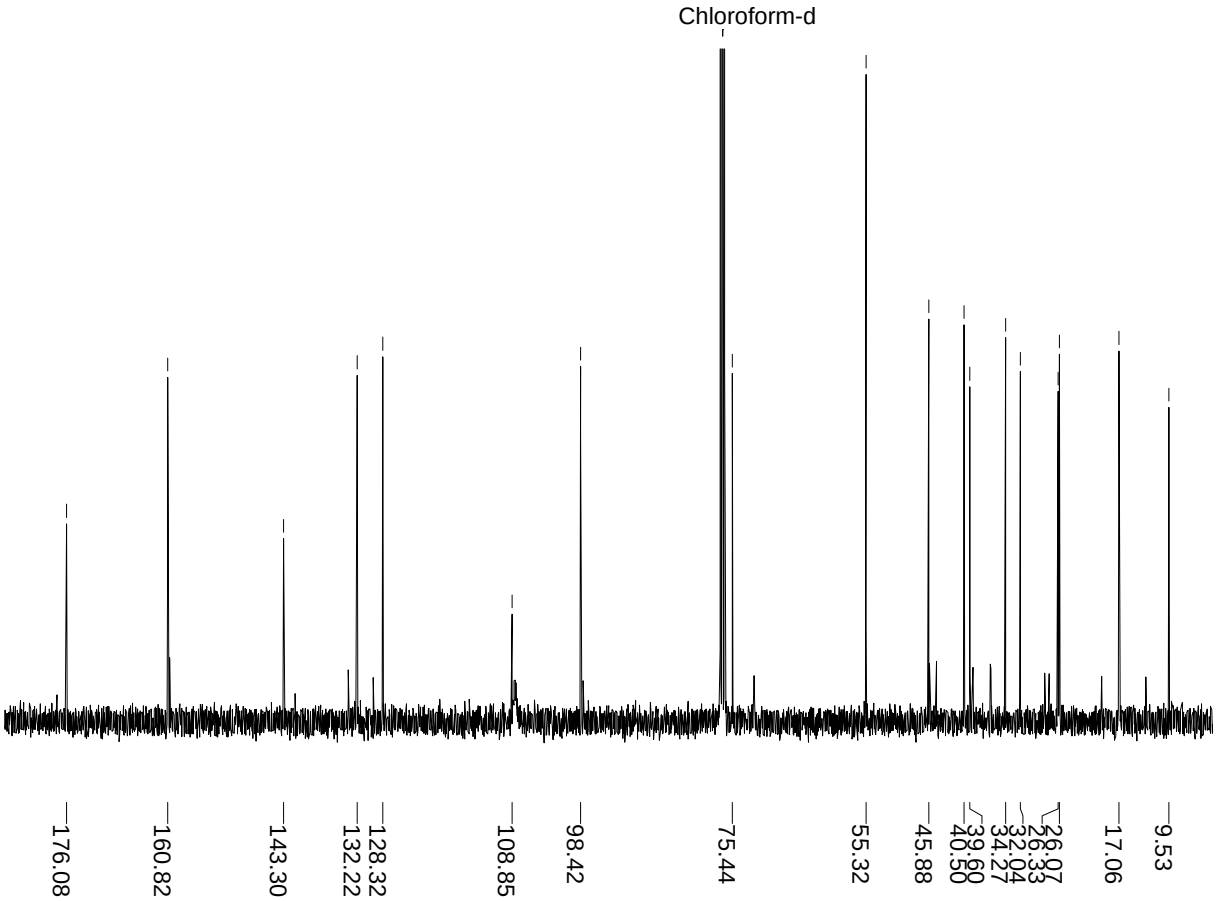

Chloroform-d
3.00
2.00
8.07
3.10
9.48
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

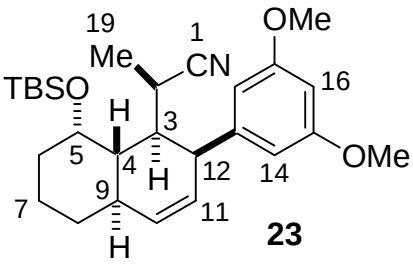

Chloroform-d
160.47
141.55
132.90
127.09
120.04
108.59
98.94
65.37
55.27
45.02
41.33
36.88
35.12
34.01
32.77
20.10
17.87


O
OMe
1
2
16
O
H
3
5
4
H
12
14
OMe
9
7
11
H
21
Chloroform-d
3.09
2.03
1.02
6.28
1.04
1.09
2.14
9.16
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
Chemical Shift (ppm)


Chloroform-d
174.52
160.53
141.25
134.05
127.91
108.17
98.30
74.55
55.27
45.80
38.34
36.06
35.55
35.04
26.82
26.41
18.23

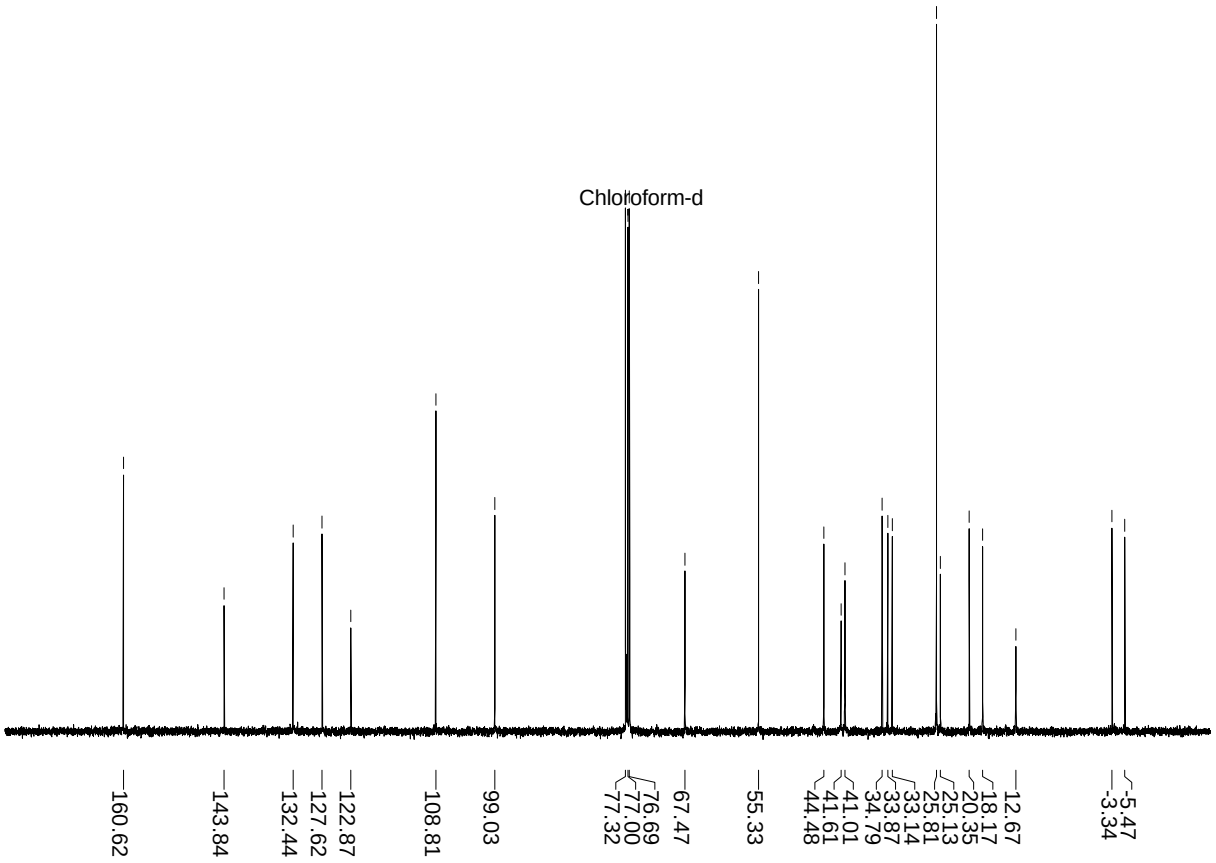

7:1 ratio
O
OMe
1
Me
O
16
H
3
5
4
H
12
14
OMe
9
7
11
H
epi-22
3.01
2.00
0.97
7.14
0.87
2.00
7.94
2.61
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

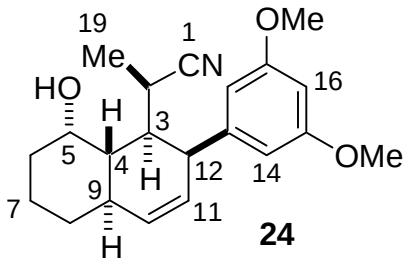

Chloroform-d
176.08
160.82
143.30
132.22
128.32
108.85
98.42
75.44
55.32
45.88
40.50
39.60
34.27
32.04
26.33
26.07
17.06
9.53


19
Me
1
CN
OMe
16
TBSO
H
3
5
4
H
12
14
OMe
9
7
11
H

**23**

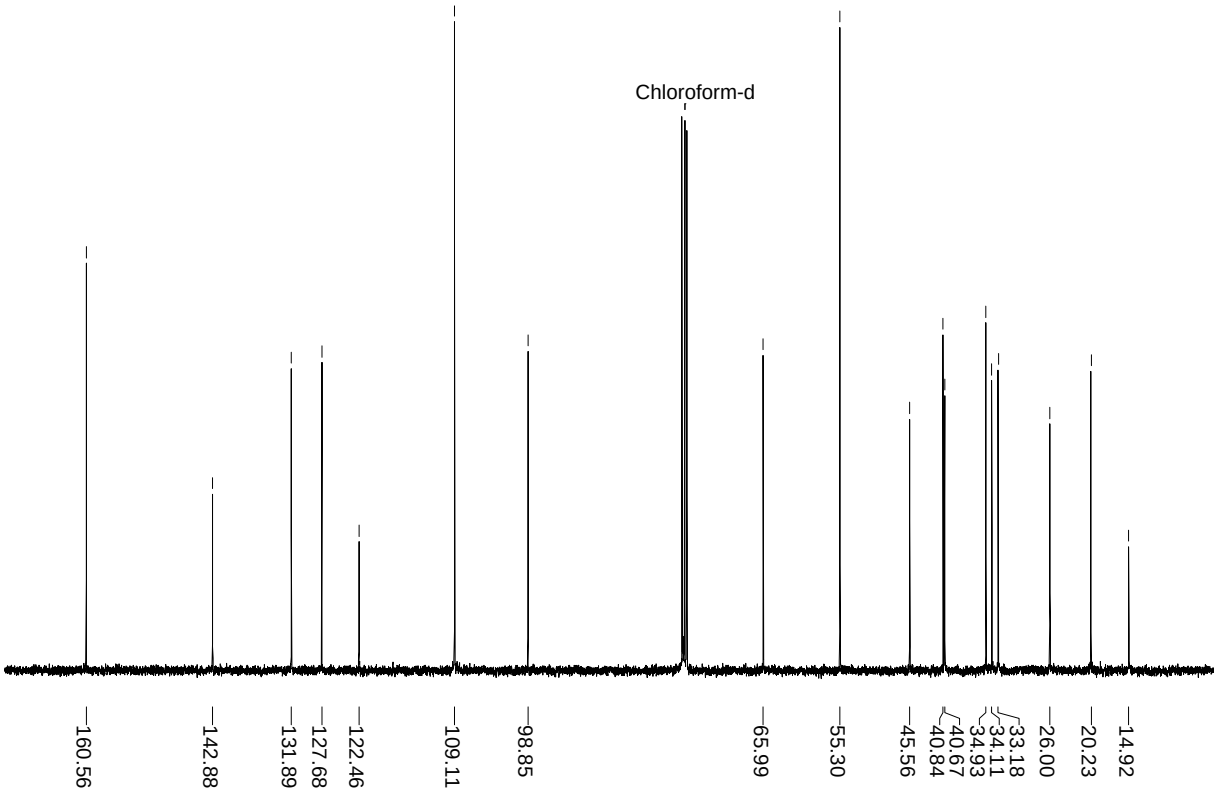

Chloroform-d
3.07
2.00
8.33
0.98
2.04
7.50
9.42
3.00
6.20
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

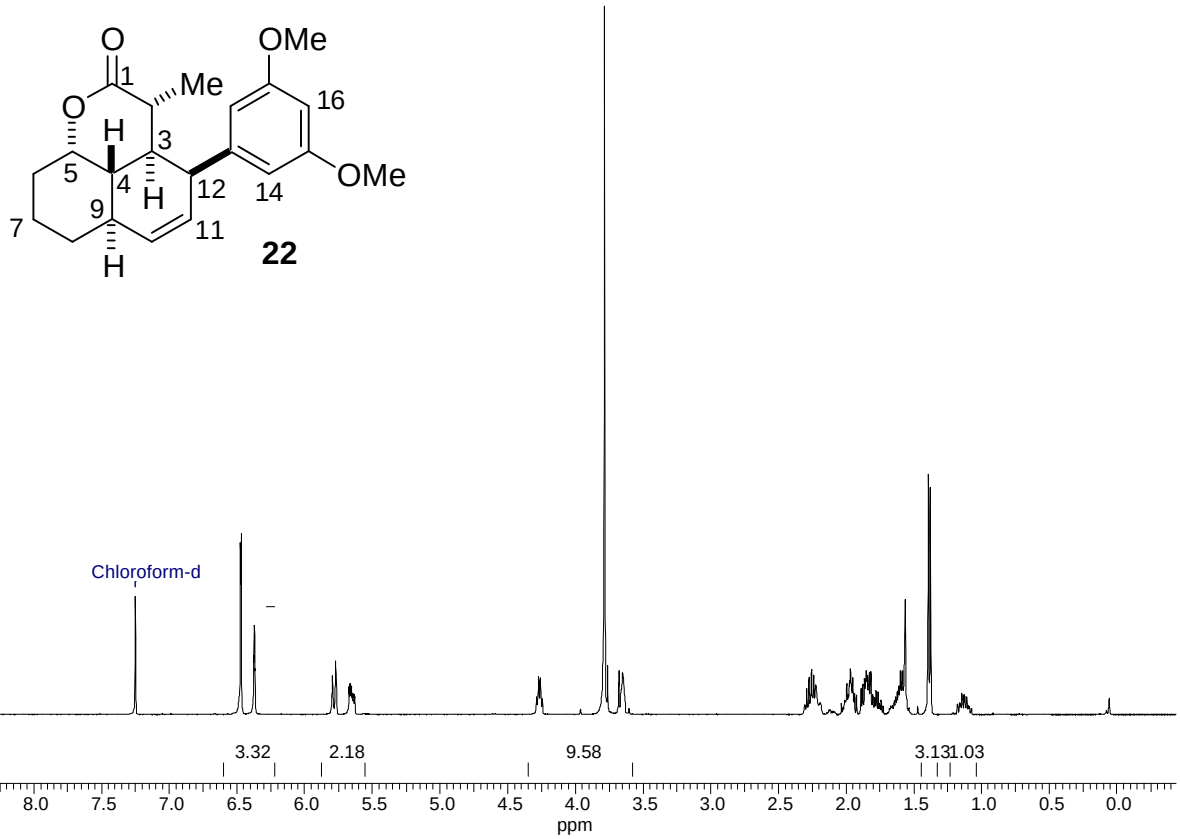

Chloroform-d
160.62
143.84
132.44
127.62
122.87
108.81
99.03
76.69
77.00
77.32
67.47
55.33
41.61
44.48
41.01
34.79
33.87
33.14
25.81
25.13
20.35
18.17
12.67
-5.47
-3.34

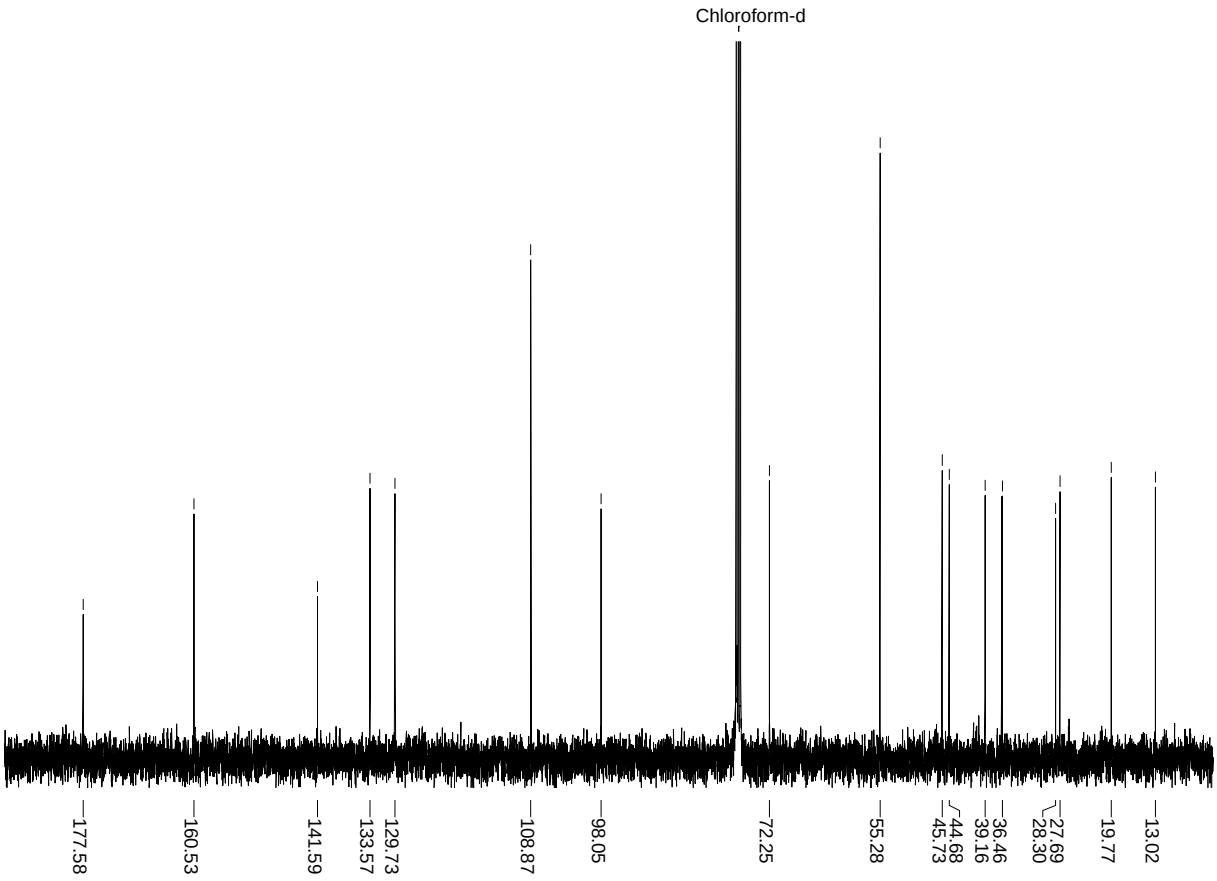

19
Me
1
CN
OMe
16
HO
H
3
5
4
H
12
14
OMe
9
7
11
H

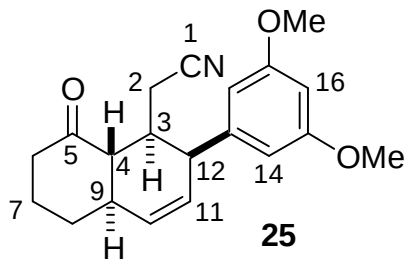
**24**


Chloroform-d
3.07
2.00
8.28
0.99
2.23
6.20
1.26
3.15
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
ppm


Chloroform-d
160.56
142.88
131.89
127.68
122.46
109.11
98.85
65.99
55.30
45.56
40.84
40.67
34.93
34.11
33.18
26.00
20.23
14.92

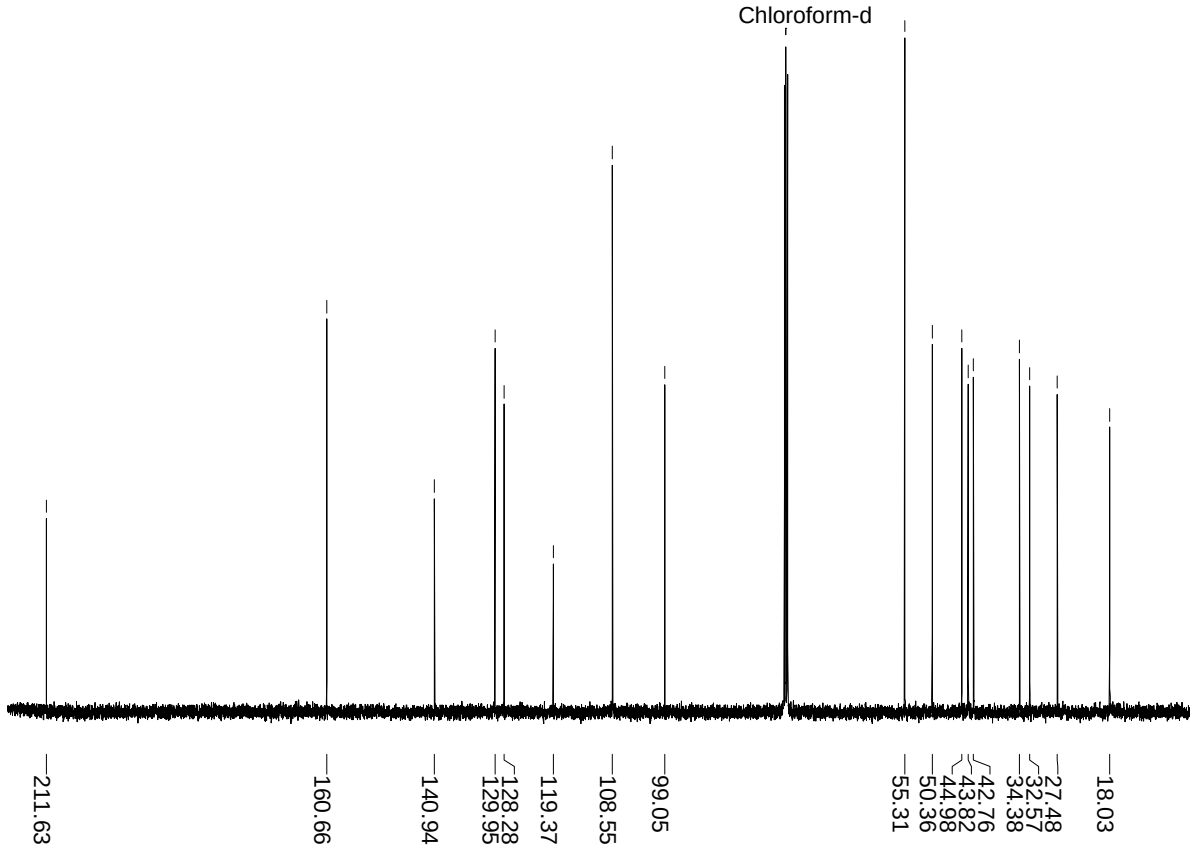

O
1
Me
OMe
16
O
H
3
5
4
H
12
14
OMe
9
7
11
H
22
Chloroform-d
3.32
2.18
9.58
3.13
1.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

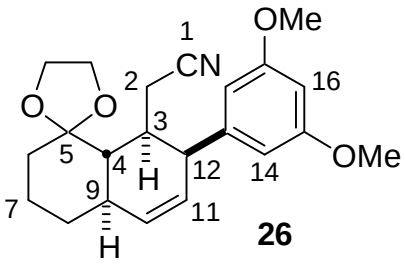

Chloroform-d
177.58
160.53
141.59
133.57
129.73
108.87
98.05
72.25
55.28
45.73
44.68
39.16
36.46
28.30
27.69
19.77
13.02


1
CN
OMe
2
16
O
H
3
5
4
H
12
14
OMe
9
7
H
11

**25**

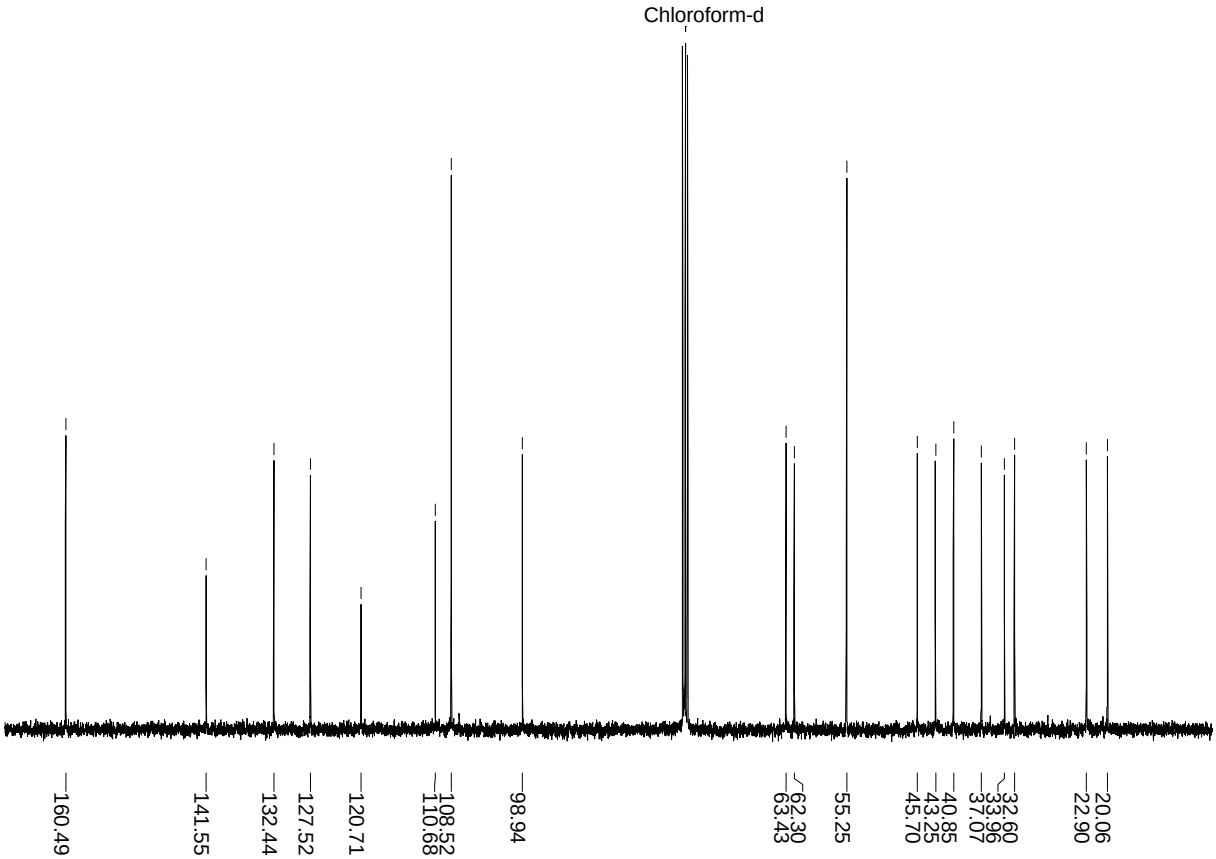

Chloroform-d
3.00
2.00
7.07
1.00
7.12
3.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

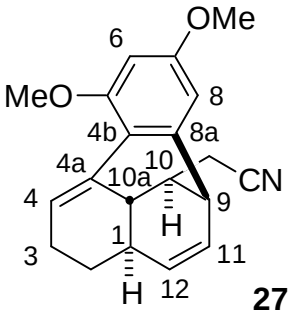

Chloroform-d
211.63
160.66
140.94
128.28
129.95
119.37
108.55
99.05
55.31
50.36
44.98
43.82
42.76
34.38
32.57
27.48
18.03


1
CN
2
OMe
16
O
O
3
5
4
H
12
14
OMe
9
7
11
H

**26**

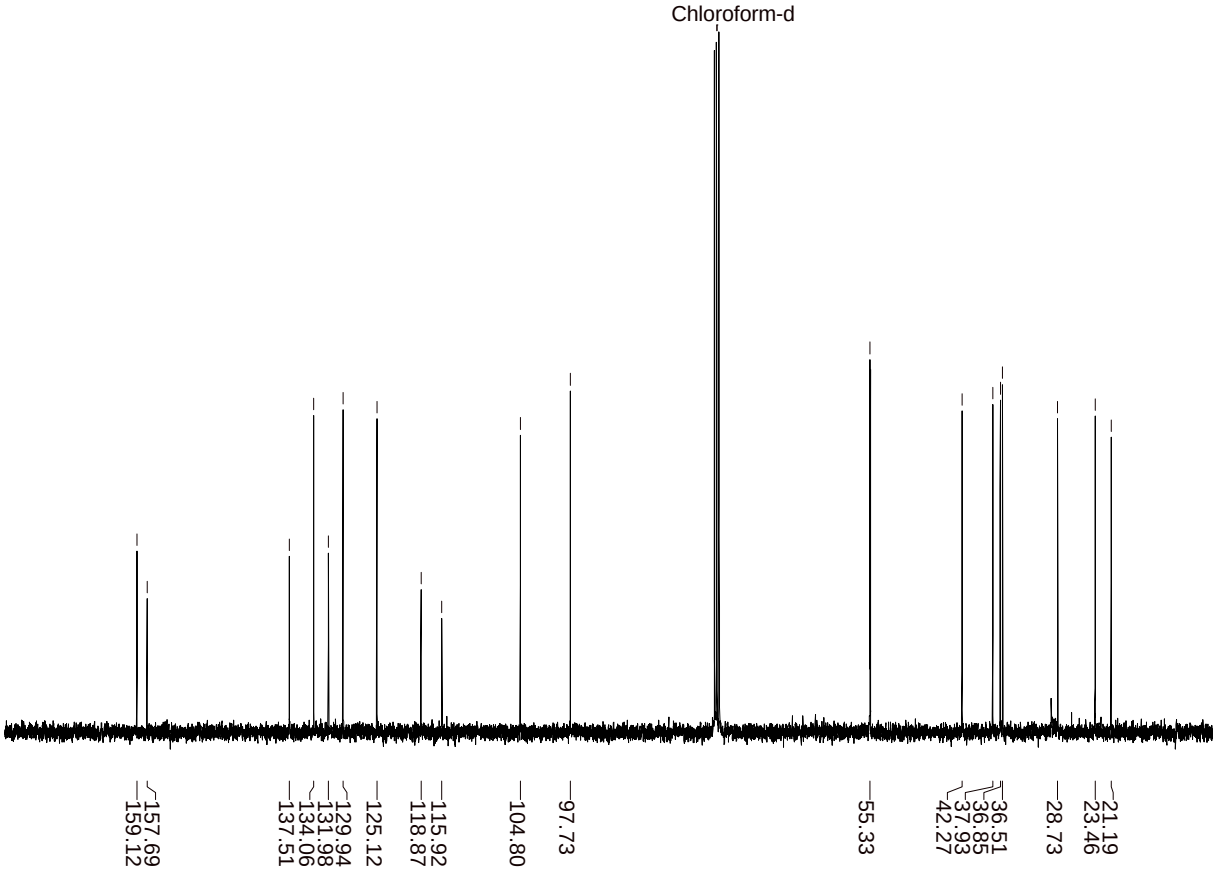

Chloroform-d
3.09
2.00
11.23
3.10
9.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

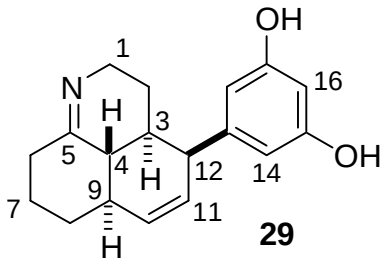

Chloroform-d
160.49
141.55
132.44
127.52
120.71
110.68
108.52
98.94
63.43
62.30
55.25
45.70
43.25
40.85
37.07
33.96
32.60
22.90
20.06


OMe
6
MeO
8
4b
8a
4a
10
10a
CN
4
9
H
1
3
11
H
12

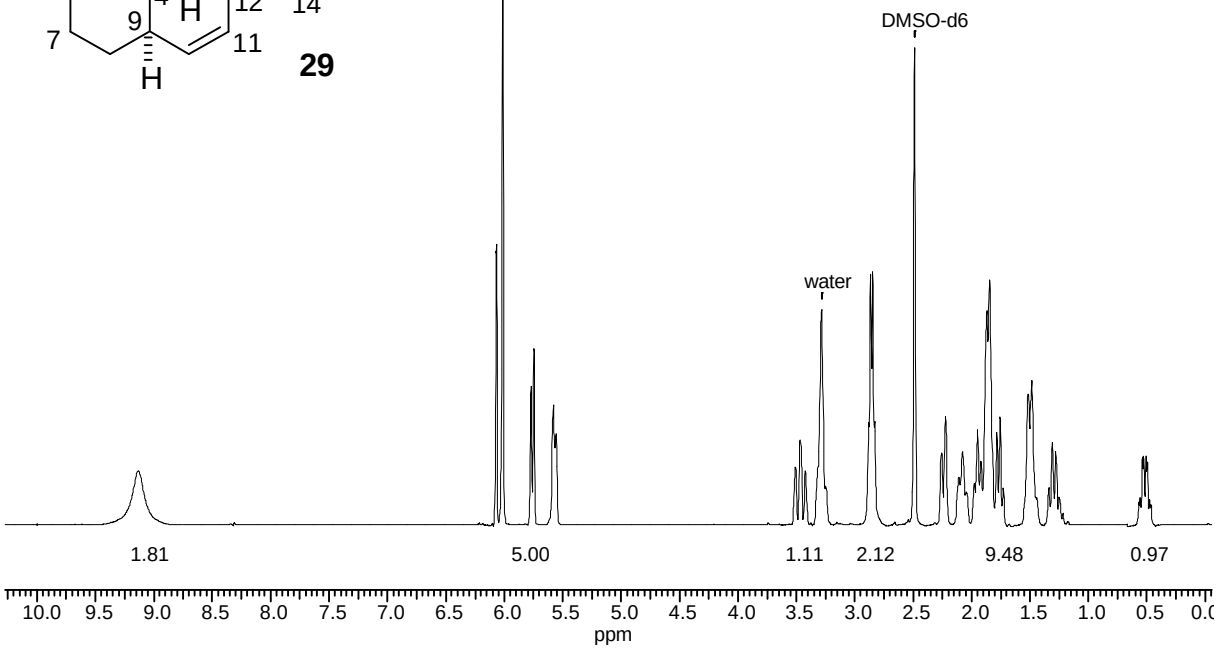
**27**

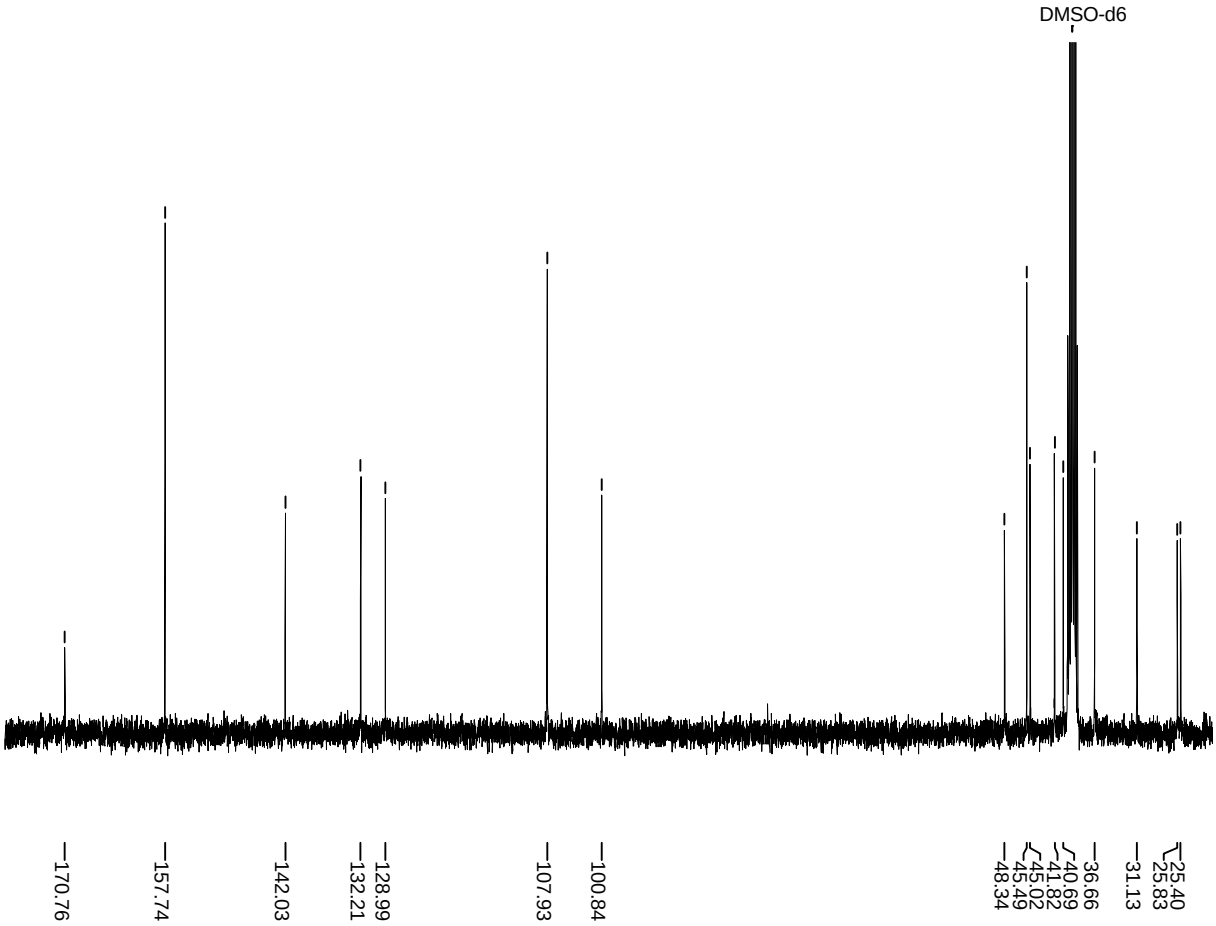

Chloroform-d
1.04
2.11
2.16
6.37
1.06
1.08
8.00
1.17
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

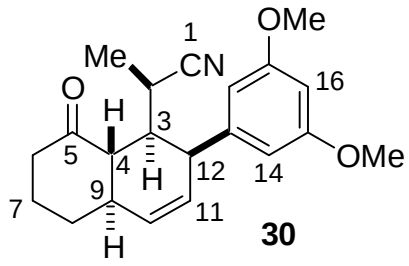

Chloroform-d
157.69
159.12
137.51
134.06
131.98
129.94
125.12
118.87
115.92
104.80
97.73
55.33
42.27
37.93
36.85
36.51
28.73
23.46
21.19


OH
1
N
H
3
16
5
4
H
12
14
OH
9
7
11
H

**29**

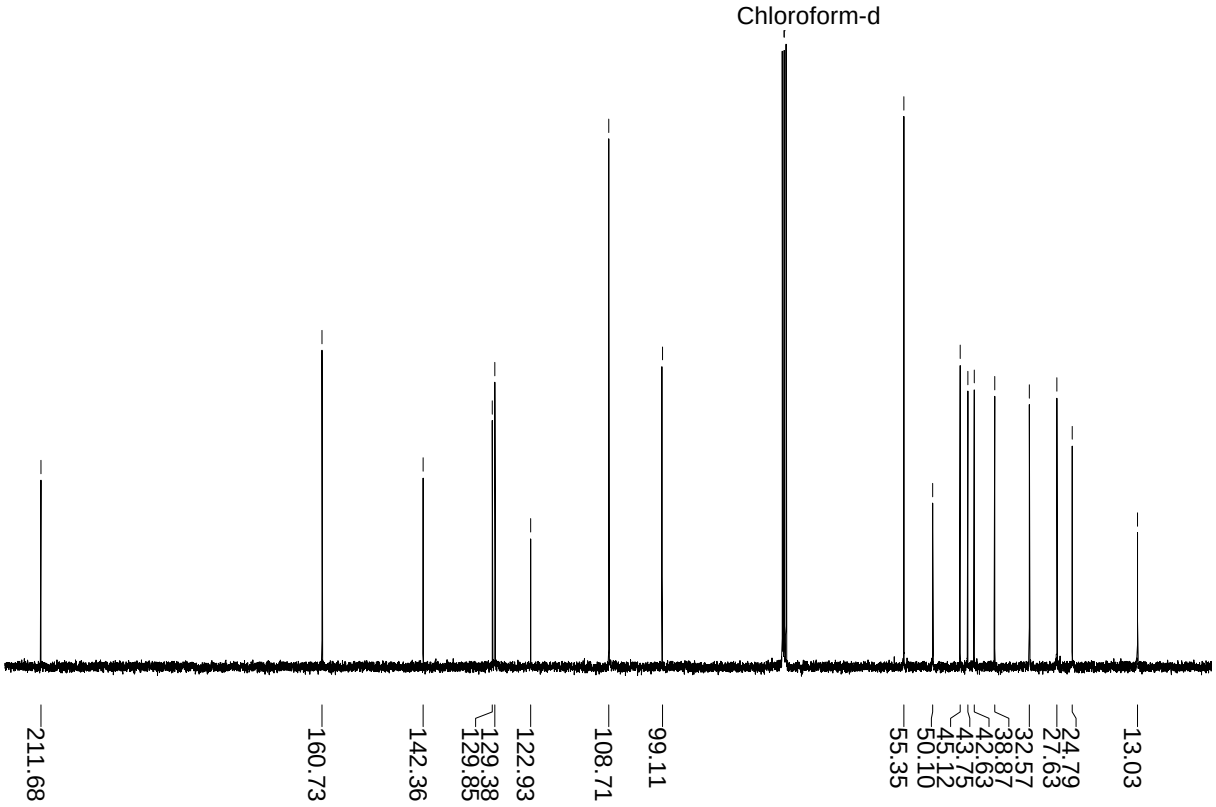

DMSO-d6
water
1.81
5.00
1.11
2.12
9.48
0.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

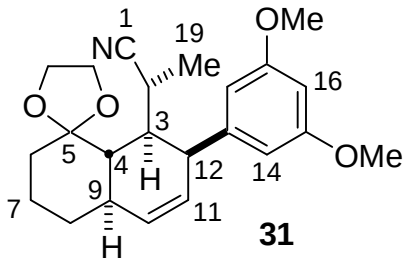

DMSO-d6
170.76
157.74
142.03
132.21
128.99
107.93
100.84
48.34
45.49
45.02
41.82
40.69
36.66
31.13
25.83
25.40


OMe
1
Me
CN
16
O
H
3
5
4
H
12
14
OMe
9
7
11
H

**30**

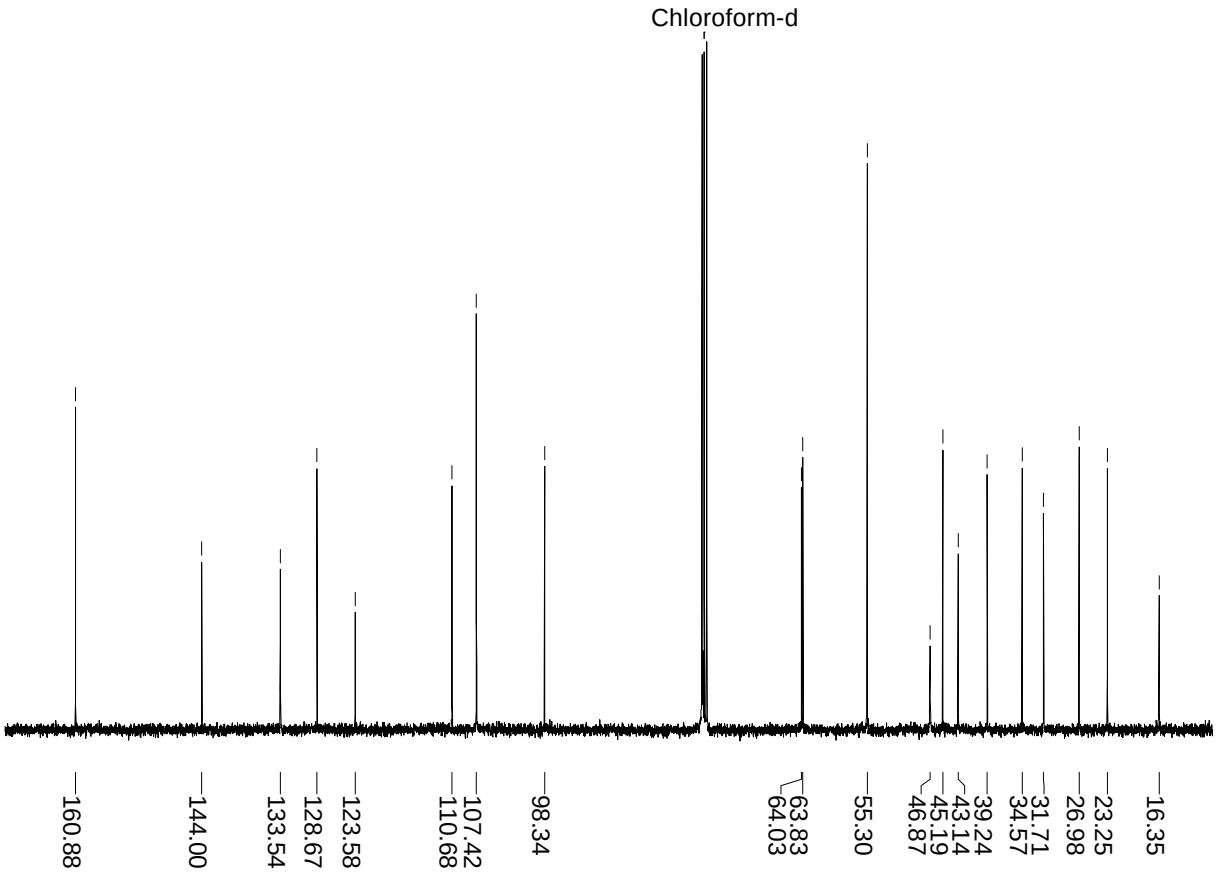

Chloroform-d
3.05
2.00
8.35
9.58
3.01
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

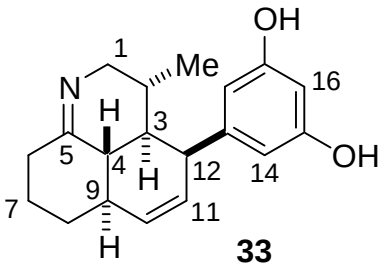

Chloroform-d
211.68
160.73
142.36
129.38
129.85
122.93
108.71
99.11
55.35
50.10
45.12
43.75
42.63
38.87
32.57
27.63
24.79
13.03


1
NC
19
Me
OMe
16
O
O
3
5
4
H
12
14
OMe
9
7
11
H

**31**

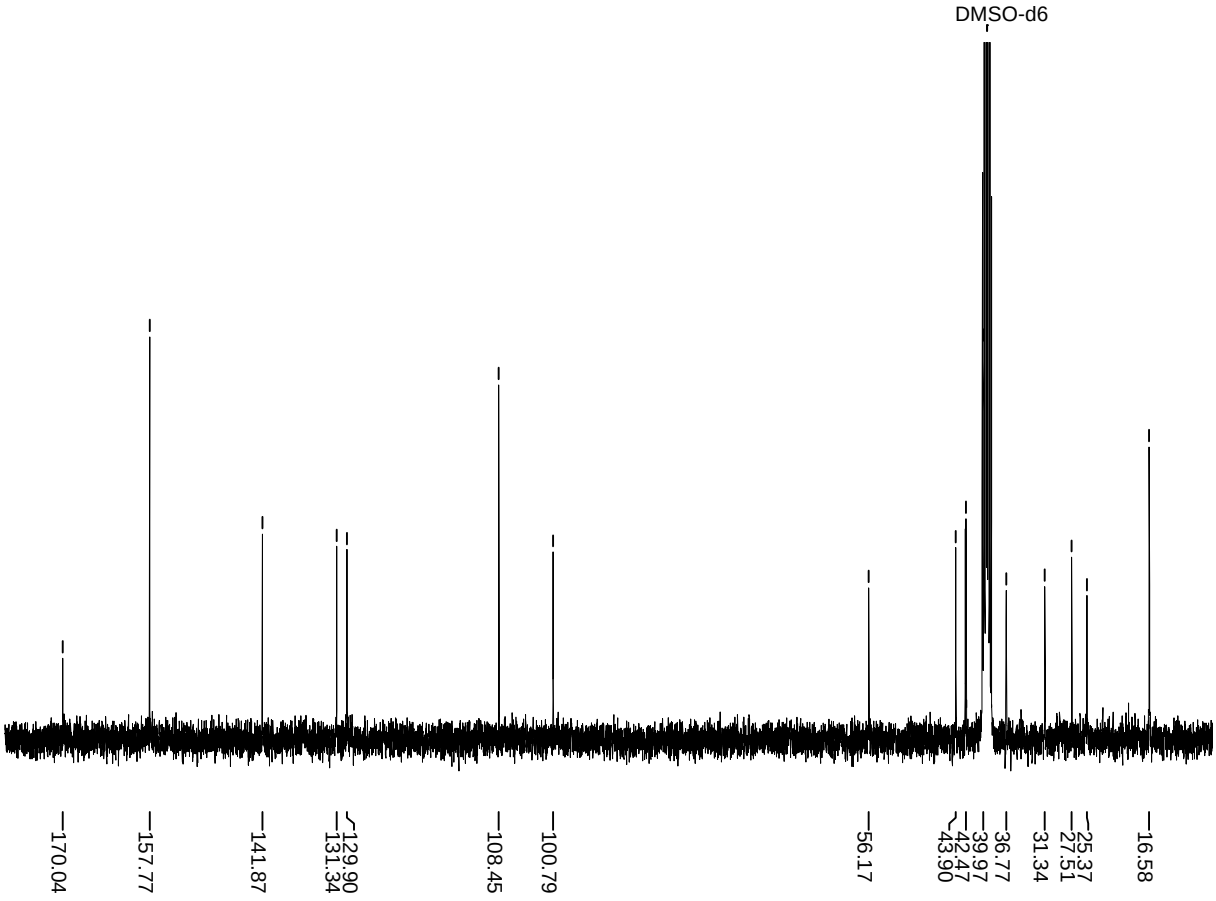

Chloroform-d
3.07
2.00
11.37
3.22
7.50
3.11
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

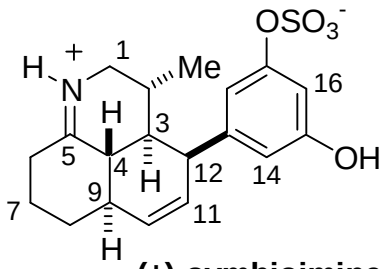

Chloroform-d
160.88
144.00
133.54
128.67
123.58
110.68
107.42
98.34
64.03
63.83
55.30
46.87
45.19
43.14
39.24
34.57
31.71
26.98
23.25
16.35


OH
1
Me
16
N
H
3
5
4
H
12
14
OH
9
7
11
H

**33**


DMSO-d6
water
2.12
5.09
1.04
6.11
3.06
3.78
10.0 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
ppm


DMSO-d6
170.04
157.77
141.87
129.90
131.34
108.45
100.79
56.17
43.90
42.47
39.97
36.77
31.34
27.51
25.37
16.58




**(±)-symbioimine (1)**