Electronic Supplementary Material (ESI) for ChemComm.


# Ni Catalyzed Domino Transformation of Enopyranoses and 2-Iodo Phenols/Anilines to Pyrano cis fused dihydro-Benzofurans/Indoles

Monika Bhardwaj,[ab] Bisma Rasool,[ab] and Debaraj Mukherjee*[ab]

[a] Natural Products and Medicinal Chemistry Division, Indian Institute of Integrative Medicine (CSIR-IIIM), Canal Road, Jammu-180001, India

[b] Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 20002, India

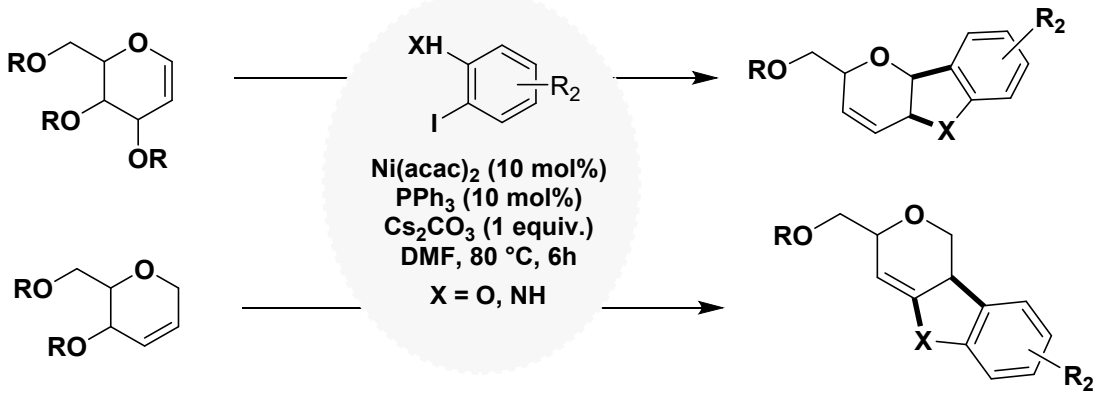
## Supporting Information

**Table of Contents** **Page No.**

1. **General Information:** All reagents were purchased from commercial sources and used without treatment. Silica gel coated aluminum plates were used for TLC. The products were purified by column chromatography on silica gel (100-200 mesh) using hexane–ethyl acetate as the eluent. $^{1}H$ NMR (400 MHz) spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$, using $CDCl_3$ (for 1 H, δ = 7.26) as the internal standard. $^{13}C$ NMR (101 MHz) spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$ using $CDCl_3$ (for $^{13}C$, δ = 77.0) as internal standard. Chemical shifts are expressed in parts per million (δ ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet, m = multiplet, s br = singlet broad. Exact mass of all products were analysed by using HRMS having QTOF analyser.

## 2. General Experimental Procedures

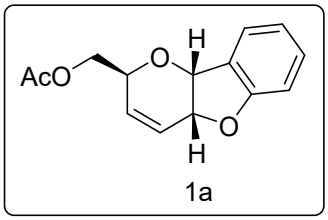
### 3.1 General experimental procedure for the synthesis of pyrano C2-C1 and C3-C2 fused heterocycles (A)




To a solution of glycal (1 equiv) in DMF (3 mL) taken in an oven dried sealed tube charged with magnetic bead, 2-iodophenol/2-iodoanniline (1.2 equiv), $Ni(acac)_2$ (0.10 equiv) and $PPh_3$ (0.10 equiv) were added. In the same solution $Cs_2CO_3$ (1 equiv) was added and the reaction mixture was allowed to stir at 80 °C for 6 hrs. After the completion of the reaction, the reaction mixture was diluted with 20 mL of ethyl acetate and washed with 20 mL brine. The organic layer was dried over magnesium sulphate and

evaporated to dryness. The residue was purified by column chromatography over silica gel (60-120 mesh) with pet ether/ ethyl acetate as eluent to afford the desired compound.

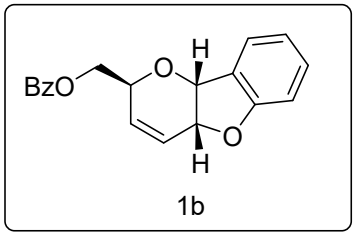
## 3. Characterization Data of Products:



1a

Prepared by general procedure A using tri-*O*-acetyl-D-glucal (50 mg, 0.18 mmol), $Ni(acac)_2$ (4.6 mg, 0.018 mmol), $PPh_3$ (4.7 mg, 0.018 mmol), 2-iodophenol (47 mg, 0.22 mmol) and $Cs_2CO_3$ (58 mg, 0.18 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **1a** as yellow oil in 75 % yield, 33 mg.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.33 (d, J = 7.3 Hz, 1H), 7.19 (t, J = 3.7 Hz, 1H), 6.88 (t, J = 7.4 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 6.13 (dd, J = 10.4, 3.9 Hz, 1H), 6.05 – 5.99 (m, 1H), 5.47 (d, J = 6.1 Hz, 1H), 4.76 – 4.69 (m, 1H), 4.39 – 4.30 (m, 2H), 4.03 (d, J = 8.6 Hz, 1H), 2.05 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.8, 160.2, 131.1, 130.6, 125.9, 125.7, 123.8, 121.1, 110.8, 74.5, 72.9, 68.9, 63.9, 20.9. HRMS (ESI+): m/z calcd. For $C_{14}H_{14}NaO_4$ $(M+Na)^+$: 269.0790; found 269.0796

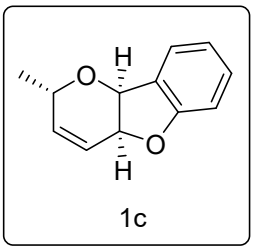


1b

Prepared by general procedure A using tri-*O*-benzoyl-D-glucal (50 mg, 0.11 mmol), $Ni(acac)_2$ (2.8 mg, 0.011 mmol), $PPh_3$ (4.7 mg, 0.011 mmol), 2-iodophenol (29 mg, 0.13 mmol) and $Cs_2CO_3$ (36 mg, 0.11 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. The

resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 98:2) to afford **1b** as yellow oil in 53 % yield, 18 mg.

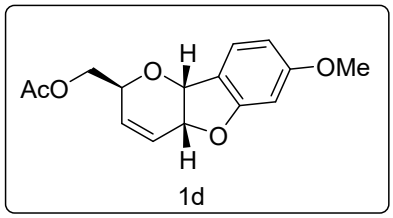
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 8.00 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.55 – 7.49 (m, 1H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.36 – 7.30 (m, 1H), 7.17 (d, *J* = 1.4 Hz, 1H), 6.88 (td, *J* = 7.4, 0.9 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.18 (ddd, *J* = 10.5, 4.0, 1.9 Hz, 1H), 6.15 – 6.08 (m, 1H), 5.54 (d, *J* = 6.0 Hz, 1H), 4.77 – 4.71 (m, 1H), 4.61 (dd, *J* = 11.8, 6.8 Hz, 1H), 4.51 – 4.45 (m, 1H), 4.31 (dd, *J* = 11.8, 3.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 166.3, 160.1, 133.2, 131.2, 130.7, 129.7, 128.5, 126.0, 123.7, 121.1, 110.8, 74.5, 72.9, 69.1, 64.6. HRMS (ESI+): m/z calcd. For $C_{19}H_{16}NaO_4$ $(M+Na)^+$: 331.0946; found 331.0949.



1c

Prepared by general procedure A using di-*O*-acetyl-L-rhamnal (50 mg, 0.23 mmol), $Ni(acac)_2$ (6 mg, 0.023 mmol ), $PPh_3$ (6 mg, 0.023 mmol), 2-iodophenol (61 mg, 0.27 mmol) and $Cs_2CO_3$ (75 mg, 0.23 mmol ). The reaction mixture was stirred at 80 °C for 6 hrs. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **1c** as yellow oil in 79 % yield, 34 mg.

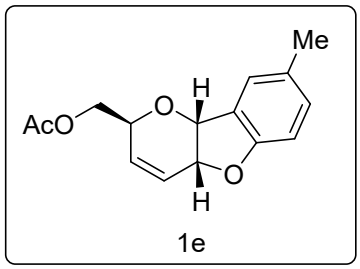
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.41 (d, J = 7.3 Hz, 1H), 7.25 (t, J = 7.8 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 8.1 Hz, 1H), 6.12 (dd, J = 10.4, 2.4 Hz, 1H), 6.06 – 5.98 (m, 1H), 5.50 (d, J = 6.2 Hz, 1H), 4.86 – 4.76 (m, 1H), 4.31 (d, J = 6.5 Hz, 1H), 1.34 (d, J = 6.8 Hz, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 160.2, 137.3, 130.3, 126.1, 125.8, 120.9, 120.9, 110.8, 74.7, 72.6, 66.1, 19.5. HRMS (ESI+): m/z calcd. For $C_{12}H_{13}O_2$ $(M+H)^+$: 189.0916; found 189.0912.



1d

Prepared by general procedure A using tri-*O*-acetyl-D-glucal (50 mg, 0.18 mmol), $Ni(acac)_2$ (4.6 mg, 0.018 mmol), $PPh_3$ (4.7 mg, 0.018 mmol), 2-iodo-5-methoxyphenol (52 mg, 0.21 mmol) and $Cs_2CO_3$ (59 mg, 0.18 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. After the completion of the reaction, the resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **1d** as brown oil in 57% yield, 28 mg.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.19 (d, J = 3.7 Hz, 1H), 6.45 – 6.39 (m, 1H), 6.34 (s, 1H), 6.15 – 6.09 (m, 1H), 6.02 (d, J = 10.3 Hz, 1H), 5.38 (d, J = 5.8 Hz, 1H), 4.76 – 4.69 (m, 1H), 4.32 (d, J = 8.5 Hz, 2H), 4.07 – 4.01 (m, 2H), 3.70 (s, 3H), 2.04 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.8, 162.3, 161.7, 131.3, 126.2, 123.8, 107.4, 96.8, 75.4, 72.4, 68.8, 63.94, 55.5, 20.8. HRMS (ESI+): m/z calcd. For $C_{15}H_{17}O_5$ $(M+H)^+$: 277.1076; found 277.1080.

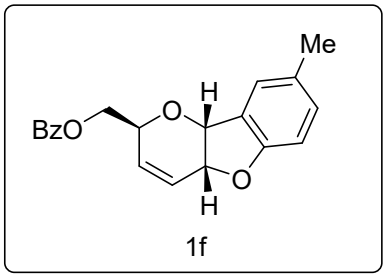


1e

Prepared by general procedure A using tri-*O*-acetyl-D-glucal (50 mg, 0.18 mmol), $Ni(acac)_2$ (4.6 mg, 0.018 mmol), $PPh_3$ (4.7 mg, 0.018 mmol), 2-iodo-4-methylphenol (50 mg, 0.22 mmol) and $Cs_2CO_3$ (58 mg, 0.18 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **1e** as yellow oil in 53 % yield, 25 mg.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.16 – 7.12 (m, 1H), 6.98 (dd, *J* = 7.9, 1.0 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 6.18 – 6.11 (m, 1H), 6.02 (ddd, *J* = 10.4, 3.0, 0.9 Hz, 1H), 5.41 (d, *J* = 6.0 Hz, 1H), 4.74 – 4.66 (m, 1H), 4.35 (d, *J* = 8.1 Hz, 2H), 4.02 (d, *J* = 8.4 Hz, 1H), 2.24 (s, 3H),

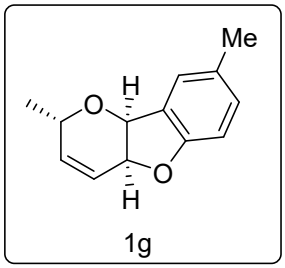
2.06 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.9, 158.0, 131.2, 130.9, 130.6, 126.2, 125.6, 123.9, 110.4, 74.5, 72.7, 69.1, 63.7, 20.9, 20.8. HRMS (ESI+): m/z calcd. For $C_{15}H_{16}NaO_4$ $(M+Na)^+$: 283.0946; found 283.0950.



1f

Prepared by general procedure A using tri-*O*-benzoyl-D-glucal (50 mg, 0.11 mmol), $Ni(acac)_2$ (2.8 mg, 0.011 mmol), $PPh_3$ (4.7 mg, 0.011 mmol), 2-iodo-4-methylphenol (31 mg, 0.13 mmol) and $Cs_2CO_3$ (36 mg, 0.11 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 98:2) to afford **1f** as yellow oil in 54 % yield, 19 mg.

**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 8.00 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.52 (ddd, *J* = 6.9, 4.1, 1.3 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.15 – 7.12 (m, 1H), 6.98 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 6.18 (ddd, *J* = 10.5, 4.0, 1.9 Hz, 1H), 6.14 – 6.09 (m, 1H), 5.48 (d, *J* = 5.9 Hz, 1H), 4.73 – 4.68 (m, 1H), 4.61 (dd, *J* = 11.8, 6.8 Hz, 1H), 4.52 – 4.46 (m, 1H), 4.30 (dd, *J* = 11.8, 3.6 Hz, 1H), 2.23 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 166.3, 158.1, 133.2, 131.2, 131.1, 130.6, 129.8, 129.7, 128.5, 126.3, 125.7, 123.8, 110.4, 74.6, 72.9, 69.2, 64.6. HRMS (ESI+): m/z calcd. For $C_{20}H_{18}NaO_4$ $(M+Na)^+$: 345.1103; found 345.1107.

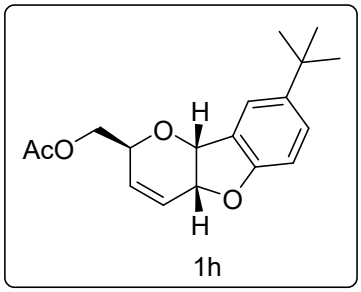


1g

Prepared by general procedure A using di-*O*-acetyl-L-rhamnal (50 mg, 0.23 mmol), $Ni(acac)_2$ (6 mg, 0.023 mmol ), $PPh_3$ (6 mg, 0.023 mmol), 2-iodo-4-methylphenol (65 mg, 0.27 mmol)

and $Cs_2CO_3$ (75 mg, 0.23 mmol ). The reaction mixture was stirred at 80 °C for 6 hrs. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 99:1) to afford **1g** as yellow oil in 47 % yield, 22 mg.

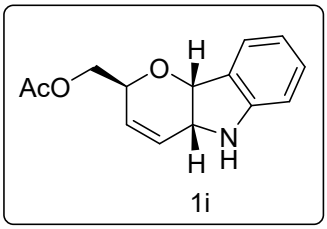
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.15 – 7.12 (m, 1H), 7.00 – 6.94 (m, 1H), 6.67 (d, J = 8.2 Hz, 1H), 6.04 (ddd, J = 10.4, 3.0, 0.7 Hz, 1H), 5.94 (ddd, J = 10.4, 4.0, 2.0 Hz, 1H), 5.37 (d, J = 6.2 Hz, 1H), 4.74 – 4.67 (m, 1H), 4.25 (d, J = 6.8 Hz, 1H), 2.24 (s, 3H), 1.26 (d, J = 6.8 Hz, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 137.1, 130.9, 130.4, 126.1, 120.8, 110.4, 74.8, 72.5, 66.2, 20.8, 19.4. HRMS (ESI+): m/z calcd. For $C_{13}H_{14}NaO_2$ $(M+Na)^+$: 225.0891; found 225.0894.



1h

Prepared by general procedure A using tri-*O*-acetyl-D-glucal (50 mg, 0.18 mmol), $Ni(acac)_2$ (4.6 mg, 0.018 mmol), $PPh_3$ (4.7 mg, 0.018 mmol), 4-(tert-butyl)-2-iodophenol (60 mg, 0.22 mmol) and $Cs_2CO_3$ (58 mg, 0.18 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **1h** as yellow oil in 61 % yield, 33 mg.

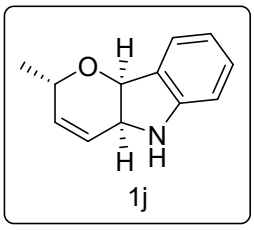
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.36 (s, 1H), 7.22 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 6.15 (dd, *J* = 10.4, 4.1 Hz, 1H), 6.06 – 5.99 (m, 1H), 5.41 (d, *J* = 5.9 Hz, 1H), 4.69 (t, *J* = 5.0 Hz, 1H), 4.39 – 4.30 (m, 2H), 4.07 (q, *J* = 6.8 Hz, 1H), 2.07 (d, *J* = 0.9 Hz, 3H), 1.24 (d, *J* = 1.0 Hz, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.9, 157.9, 144.3, 130.9, 127.8, 125.2, 123.8, 122.6, 110.1, 74.7, 72.9, 69.1, 63.9, 34.4, 31.6, 31.6, 31.6, 20.9. HRMS (ESI+): m/z calcd. For $C_{18}H_{22}NaO_4$ $(M+Na)^+$: 325.1416; found 325.1398.



1i

Prepared by general procedure A using tri-*O*-acetyl-D-glucal (50 mg, 0.18 mmol), $Ni(acac)_2$ (4.6 mg, 0.018 mmol), $PPh_3$ (4.7 mg, 0.018 mmol), 2-iodoanniline (47 mg ,0.21 mmol ) and $Cs_2CO_3$ (59 mg, 0.18 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. After the completion of the reaction, the resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **1i** as brown oil in 64 % yield, 28 mg.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.32 (d, J = 7.3 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 6.84 (t, J = 7.3 Hz, 1H), 6.72 (d, J = 7.7 Hz, 1H), 5.90 (q, J = 10.7 Hz, 2H), 5.58 (d, J = 6.8 Hz, 1H), 4.34 (dd, J = 18.8, 7.5 Hz, 2H), 4.22 – 4.04 (m, 2H), 2.14 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.9, 150.4, 129.6, 128.3, 126.8, 125.4, 119.7, 111.5, 74.9, 67.9, 64.9, 53.8, 20.9. HRMS (ESI+): m/z calcd. For $C_{14}H_{16}NO_3$ $(M+H)^+$: 246.1130; found 246.1133.

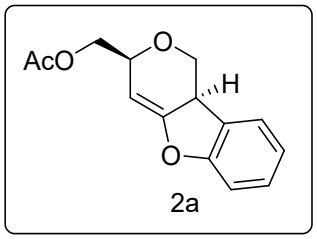


1j

Prepared by general procedure A using di-*O*-acetyl-L-rhamnal (50 mg, 0.23 mol), $Ni(acac)_2$ (6 mg, 0.023 mol), $PPh_3$ (6 mg, 0.023 mmol), 2-iodoanniline (59 mg, 0.27 mmol) and $Cs_2CO_3$ (75 mg, 0.23 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. After the completion of the reaction, the resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **1j** as brown oil in 70 % yield, 30 mg.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.30 (d, J = 7.5 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.82 (t, J = 7.4 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.86 (d, J = 10.4 Hz, 1H), 5.72 (d, J = 10.3 Hz, 1H),

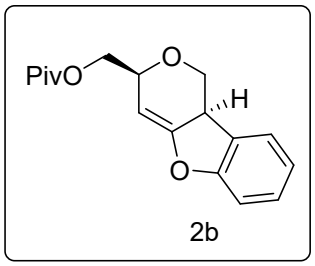
5.55 (d, J = 7.0 Hz, 1H), 4.27 (d, J = 6.7 Hz, 1H), 4.11 (d, J = 3.9 Hz, 1H), 1.30 (d, J = 6.8 Hz, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 134.2, 129.3, 125.3, 124.1, 119.5, 111.5, 75.2, 65.0, 53.8, 20.4. HRMS (ESI+): m/z calcd. For $C_{12}H_{14}NO$ $(M+H)^+$: 188.1075; found 188.1083.



2a

Prepared by general procedure A using di-*O*-acetyl-D-glucal (50 mg, 0.23 mmol), $Ni(acac)_2$ (6 mg, 0.023 mmol), $PPh_3$ (6 mg, 0.023 mmol), 2-iodophenol (59 mg, 0.27 mmol) and $Cs_2CO_3$ (75 mg, 0.23 mmol ). The reaction mixture was stirred at 80 °C for 6 hrs. After the completion of the reaction, the resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **2a** as yellow oil in 67 % yield, 38 mg.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.15 (dd, J = 16.4, 7.7 Hz, 2H), 6.85 (t, J = 7.4 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 5.38 (d, J = 4.5 Hz, 1H), 4.98 – 4.92 (m, 1H), 4.53 (s, 2H), 4.22 (dd, J = 10.6, 5.1 Hz, 1H), 3.48 (t, J = 11.1 Hz, 1H), 3.40 – 3.30 (m, 1H), 2.08 (s, 3H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 170.5, 159.1, 154.7, 129.2, 126.7, 124.8, 120.8, 110.2, 98.4, 75.4, 66.5, 63.2, 39.4, 20.9. HRMS (ESI+): m/z calcd. For $C_{14}H_{15}O_4$ $(M+H)^+$: 247.0970; found 247.0977.

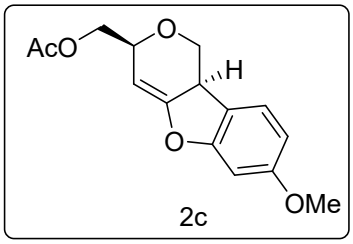


2b

Prepared by general procedure A using di-*O*-pivolyl-D-glucal (50 mg, 0.16 mmol), $Ni(acac)_2$ (4 mg, 0.016 mmol), $PPh_3$ (4 mg, 0.016 mmol), 2-iodophenol (42 mg ,0.19 mmol) and $Cs_2CO_3$ (52 mg, 0.16 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. After the

completion of the reaction, the resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **2b** as colorless oil in 73 % yield, 34 mg.

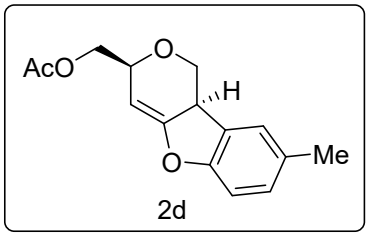
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.23 – 7.14 (m, 2H), 6.88 (td, J = 7.5, 0.9 Hz, 1H), 6.85 – 6.80 (m, 1H), 5.38 (d, J = 4.6 Hz, 1H), 5.03 – 4.95 (m, 1H), 4.63 – 4.48 (m, 2H), 4.23 (ddd, J = 10.7, 5.1, 0.6 Hz, 1H), 3.49 (dd, J = 11.5, 10.7 Hz, 1H), 3.37 (ddd, J = 11.7, 6.5, 5.4 Hz, 1H), 1.23 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 177.8, 159.1, 155.2, 129.2, 126.8, 124.8, 120.7, 110.2, 96.9, 75.5, 66.5, 62.5, 39.5, 38.8, 27.2. HRMS (ESI+): m/z calcd. For $C_{17}H_{21}O_4$ $(M+H)^+$: 289.1440; found 289.1449.



2c

Prepared by general procedure A using di-*O*-acetyl-D-glucal (50 mg, 0.23 mmol), $Ni(acac)_2$ (6 mg, 0.023 mmol), $PPh_3$ (6 mg, 0.023 mmol), 2-iodophenol (67 mg, 0.27 mmol) and $Cs_2CO_3$ (75 mg, 0.23 mmol). The reaction mixture was stirred at 80 °C for 6 hrs. After the completion of the reaction, the resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **2c** as brown oil in 62 % yield, 39 mg.

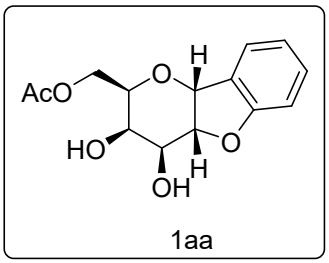
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.09 – 6.97 (m, 1H), 6.34 (d, *J* = 7.0 Hz, 2H), 5.31 (d, *J* = 4.3 Hz, 1H), 4.96 – 4.84 (m, 1H), 4.48 (s, 2H), 4.13 (dd, *J* = 10.7, 5.1 Hz, 1H), 3.69 (d, *J* = 4.3 Hz, 3H), 3.38 (t, *J* = 11.1 Hz, 1H), 3.23 (dt, *J* = 11.7, 6.0 Hz, 1H), 2.03 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.5, 161.1, 160.5, 154.7, 130.1, 124.8, 118.7, 107.9, 106.3, 106.2, 101.5, 98.4, 96.9, 76.3, 66.8, 63.2, 55.5, 50.1, 38.9, 20.8. HRMS (ESI+): m/z calcd. For $C_{15}H_{17}O_5$ $(M+H)^+$: 277.1076; found 277.1084.



2d

Prepared by general procedure A using di-*O*-acetyl-D-glucal (50 mg, 0.23 mmol), $Ni(acac)_2$ (6 mg, 0.023 mmol), $PPh_3$ (6 mg, 0.023 mmol), 2-iodo-4-methylphenol (64 mg, 0.27 mmol) and $Cs_2CO_3$ (75 mg, 0.23 mmol ). The reaction mixture was stirred at 80 °C for 6 hrs. After the completion of the reaction, the resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 97:3) to afford **2d** as yellow oil in 70 % yield, 42 mg.

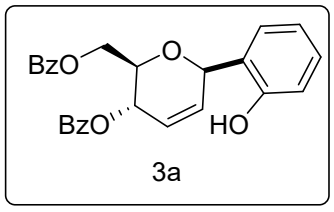
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 6.96 – 6.93 (m, 1H), 6.89 (ddd, J = 8.1, 1.3, 0.5 Hz, 1H), 6.64 (d, J = 8.1 Hz, 1H), 5.33 (d, J = 4.6 Hz, 1H), 4.88 (ddd, J = 6.7, 4.6, 0.7 Hz, 1H), 4.49 (d, J = 0.8 Hz, 2H), 4.16 (ddd, J = 10.8, 5.2, 0.7 Hz, 1H), 3.49 – 3.38 (m, 1H), 3.33 – 3.21 (m, 1H), 2.22 (s, 3H), 2.04 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.5, 156.9, 154.6, 130.1, 129.5, 126.67, 125.3, 109.7, 98.5, 75.4, 66.6, 63.3, 39.5, 20.9, 20.8. HRMS (ESI+): m/z calcd. For $C_{15}H_{16}NaO_4$ $(M+Na)^+$: 283.0946; found 283.0942.



1aa

Prepared by using compound **1a** (50 mg, 0.20 mmol), in *t*-butanol: acetone: $H_2O$ (2:1:1), followed by the addition of OsO4 (10 mg, 0.04 mmol) and NMO (28 mg, 0.24 mmol) at rt. The reaction was stirred at rt untill complete consumption of starting material was observed by TLC. The solvent was evaporated in vacuo and the resulting reaction mixture was diluted with ethyl acetate washed with brine, dried over $NaSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 75:25) to afford **1aa** as colourless oil in 60% yield, 33 mg.

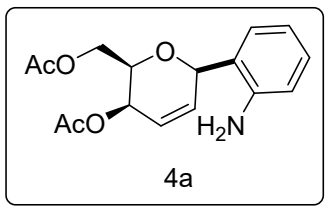
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.27 (d, *J* = 7.4 Hz, 1H), 7.19 – 7.16 (m, 1H), 6.90 (td, *J* = 7.4, 0.9 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 5.57 (d, *J* = 7.0 Hz, 1H), 4.61 (dd, *J* = 7.0, 6.4 Hz, 1H), 4.33 (qd, *J* = 11.8, 6.3 Hz, 2H), 3.98 (t, *J* = 3.1 Hz, 1H), 3.86 (dd, *J* = 6.4, 3.2 Hz, 1H), 3.82 (ddd, *J* = 7.1, 5.6, 3.1 Hz, 1H), 2.03 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 171.3, 159.5, 130.7, 125.4, 125.2, 121.6, 111.1, 84.1, 75.5, 72.0, 71.3, 68.0, 62.4, 20.9. HRMS (ESI+): m/z calcd. For $C_{14}H_{16}NaO_6$ $(M+Na)^+$: 303.0845; found 303.0849.



3a

Prepared by general procedure A using tri-*O*-benzoyl-D-glucal (50 mg, 0.11 mmol), $Ni(acac)_2$ (2.8 mg, 0.011 mmol), $PPh_3$ (3 mg, 0.011 mmol), 2-iodophenol (29 mg, 0.13 mmol) and $Cs_2CO_3$ (36 mg, 0.11 mmol). The reaction mixture was stirred at 80 °C then quenched after 30 min. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 85:15) to afforded **3a** as yellow oil in 74% yield, 35 mg.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 8.04 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 7.21 (d, J = 7.5 Hz, 2H), 7.10 – 7.01 (m, 1H), 6.99 – 6.92 (m, 2H), 6.80 – 6.69 (m, 1H), 5.93 (dd, J = 10.2, 4.5 Hz, 1H), 5.82 (d, J = 10.3 Hz, 1H), 4.54 – 4.46 (m, 1H), 4.42 (t, J = 7.0 Hz, 1H), 4.17 (d, J = 11.8 Hz, 1H), 4.07 (dd, J = 11.8, 4.7 Hz, 1H), 3.42 (s, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 166.8, 154.7, 153.0, 133.2, 131.4, 130.4, 130.0, 129.7, 129.7, 128.6, 128.4, 126.9, 125.5, 121.5, 120.1, 116.9, 116.8, 73.3, 68.8, 65.9, 38.6. HRMS (ESI+): m/z calcd. For $C_{26}H_{23}O_6$ $(M+H)^+$: 431.1495; found 431.1498.



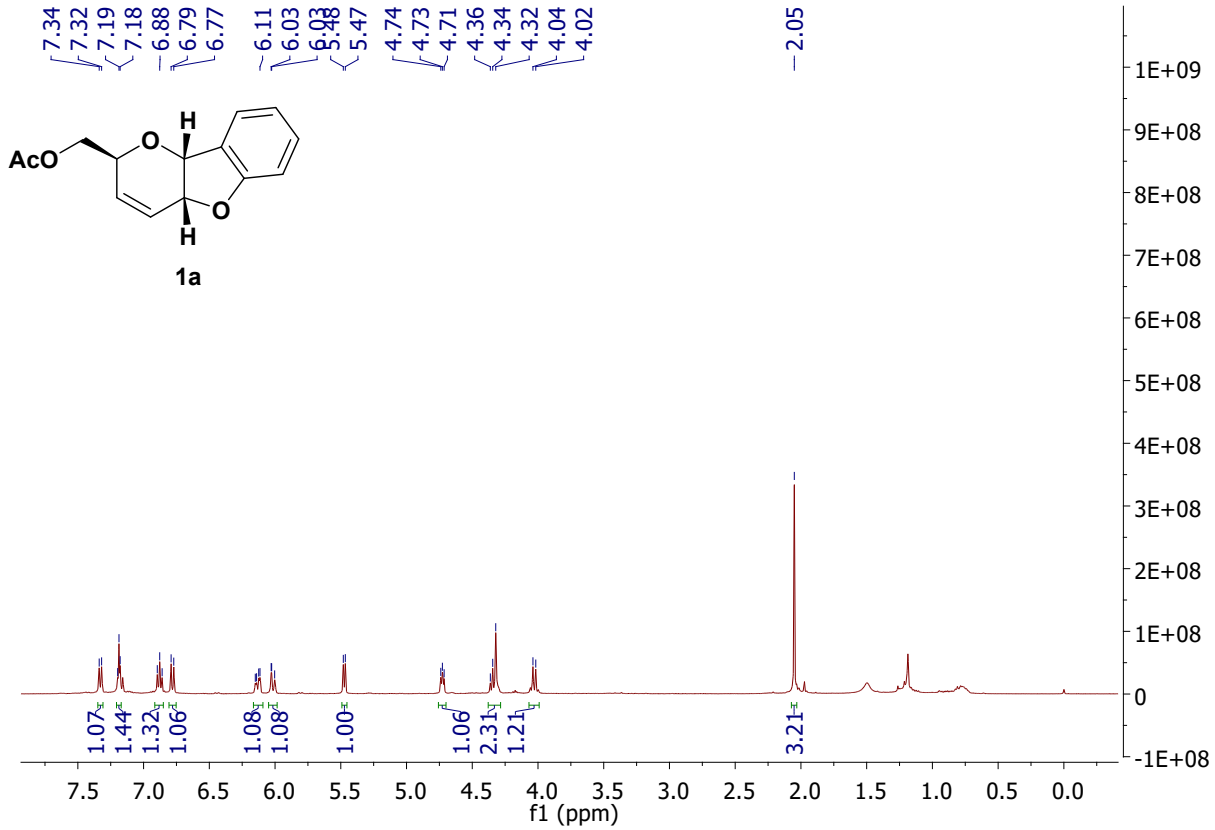
4a

Prepared by general procedure A using tri-*O*-acetyl-D-galactal (50 mg, 0.18 mmol), $Ni(acac)_2$ (4.6 mg, 0.018 mmol), $PPh_3$ (4.7 mg, 0.018 mmol), 2-iodoanniline (46 mg ,0.21 mmol ) and $Cs_2CO_3$ (59 mg, 0.18 mmol). The reaction mixture was stirred at 80 °C then quenched after 30 min. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (Hexane: EtOAc; 90:10) to afford **4a** as brown oil in 65 % yield, 36 mg

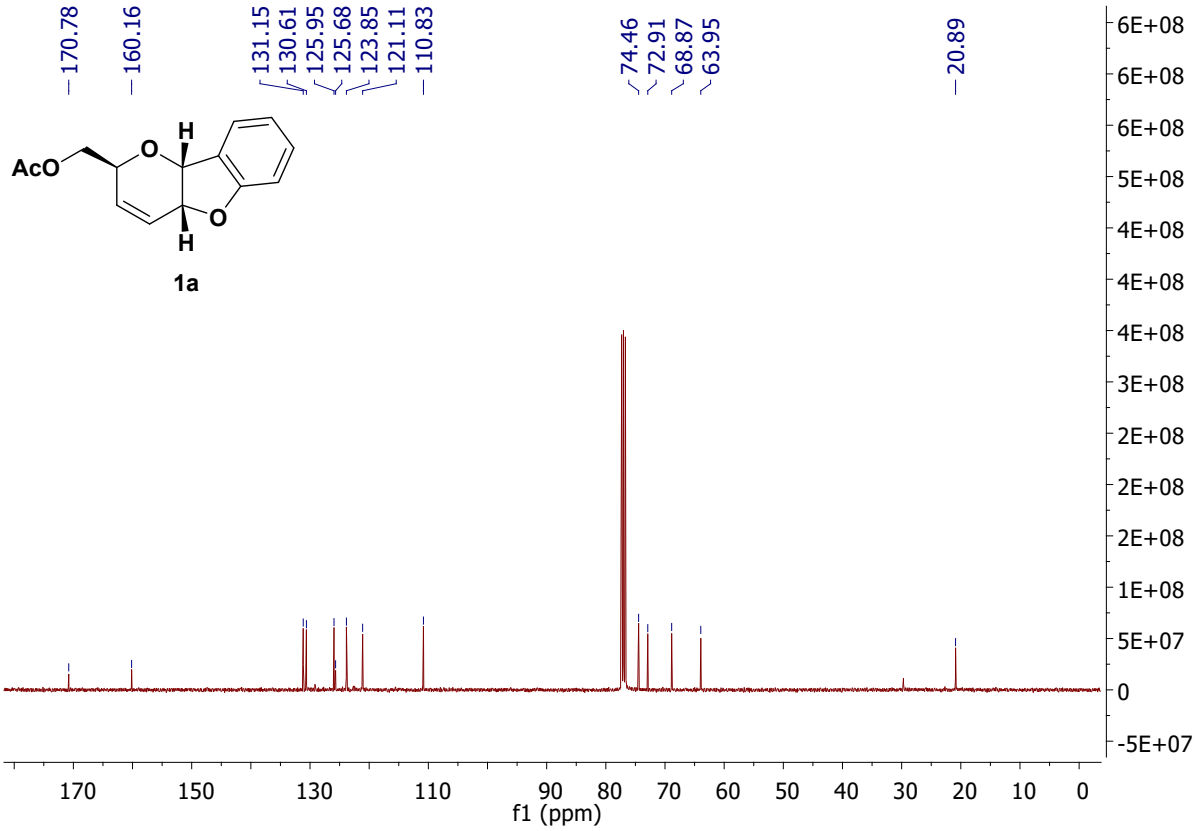
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.09 (td, *J* = 7.6, 1.4 Hz, 1H), 6.93 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.69 – 6.60 (m, 2H), 6.34 (ddd, *J* = 10.3, 3.8, 0.7 Hz, 1H), 6.18 (ddd, *J* = 10.2, 5.1, 1.9 Hz, 1H), 5.42 (dd, *J* = 3.6, 1.9 Hz, 1H), 5.05 (dd, *J* = 5.1, 2.4 Hz, 1H), 4.08 (qd, *J* = 11.4, 6.4 Hz, 2H), 3.87 – 3.77 (m, 1H), 2.05 (s, 3H), 1.89 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 170.5, 170.5, 146.6, 133.3, 129.8, 129.2, 124.1, 121.9, 117.6, 116.2, 72.1, 68.6, 64.0, 62.6, 20.9, 20.7. HRMS (ESI+): m/z calcd. For $C_{16}H_{20}NO_5$ $(M+H)^+$: 306.1341; found 306.1350.

## 4. Spectral Data

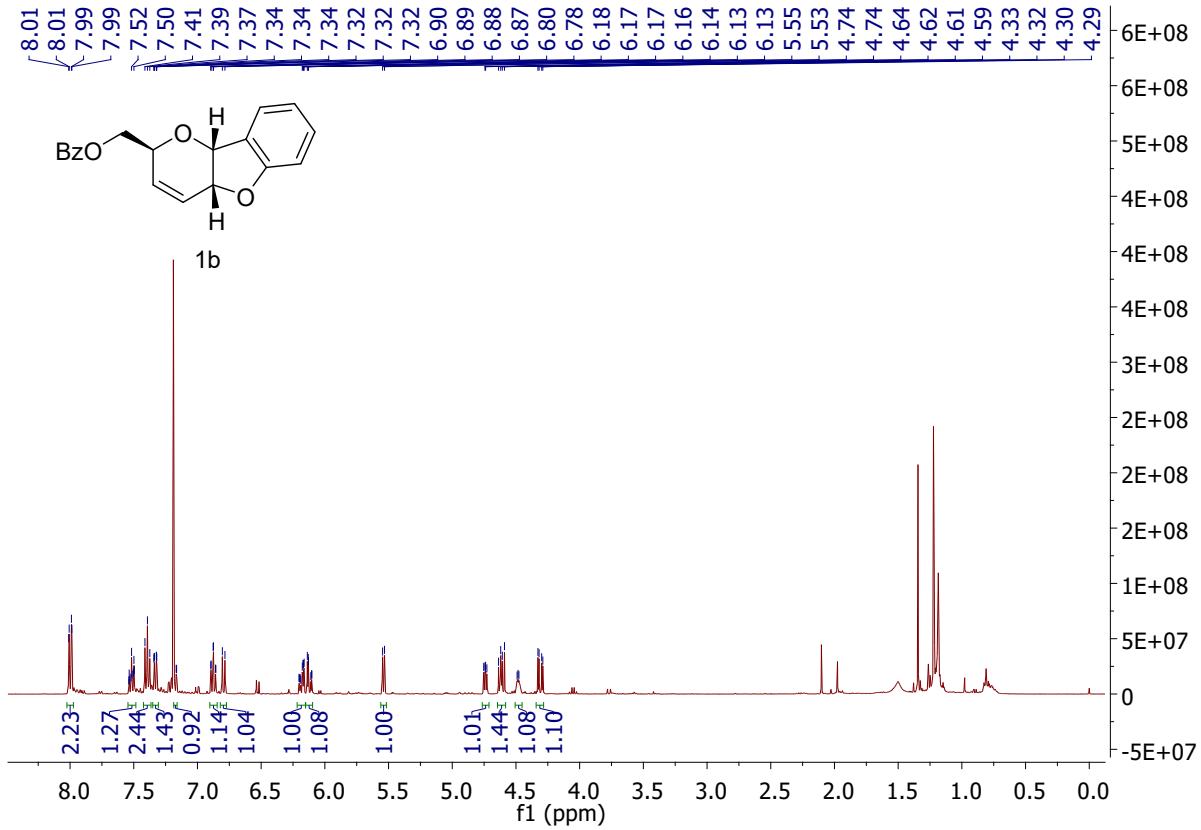
**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1a**



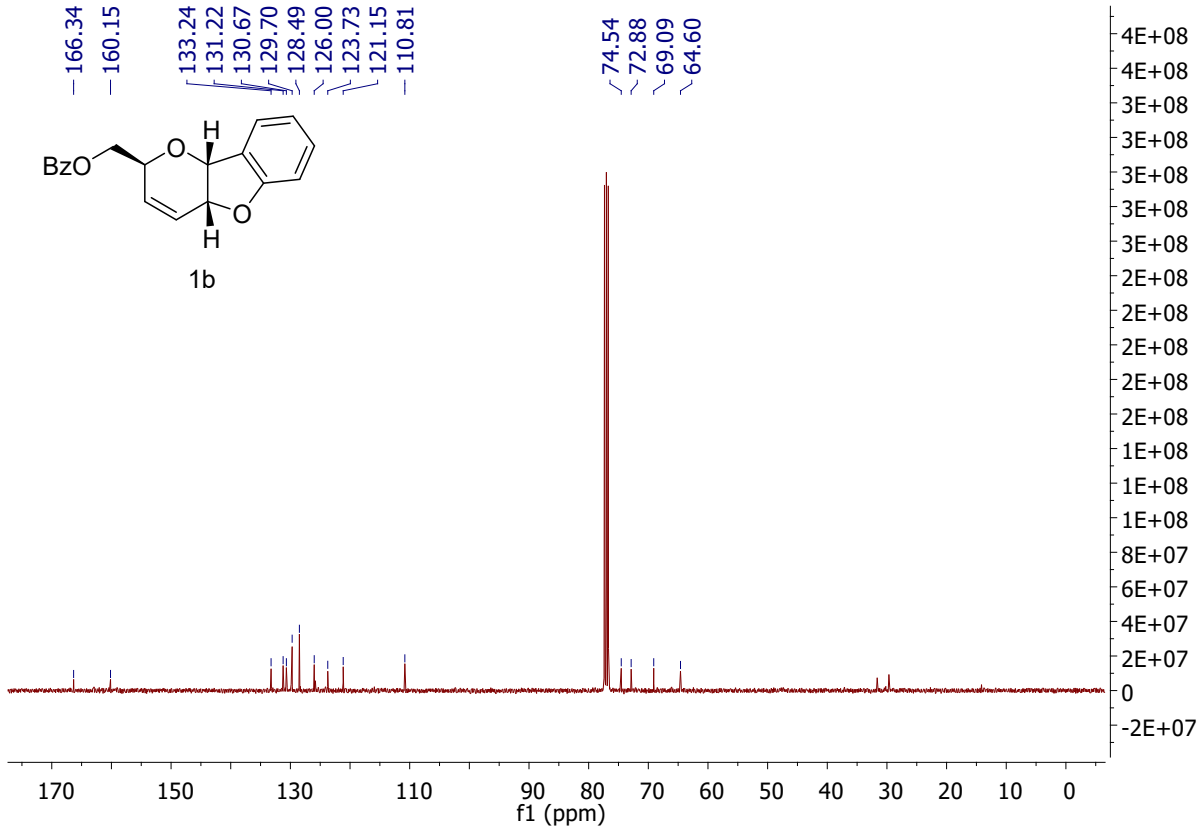

**$^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1a**



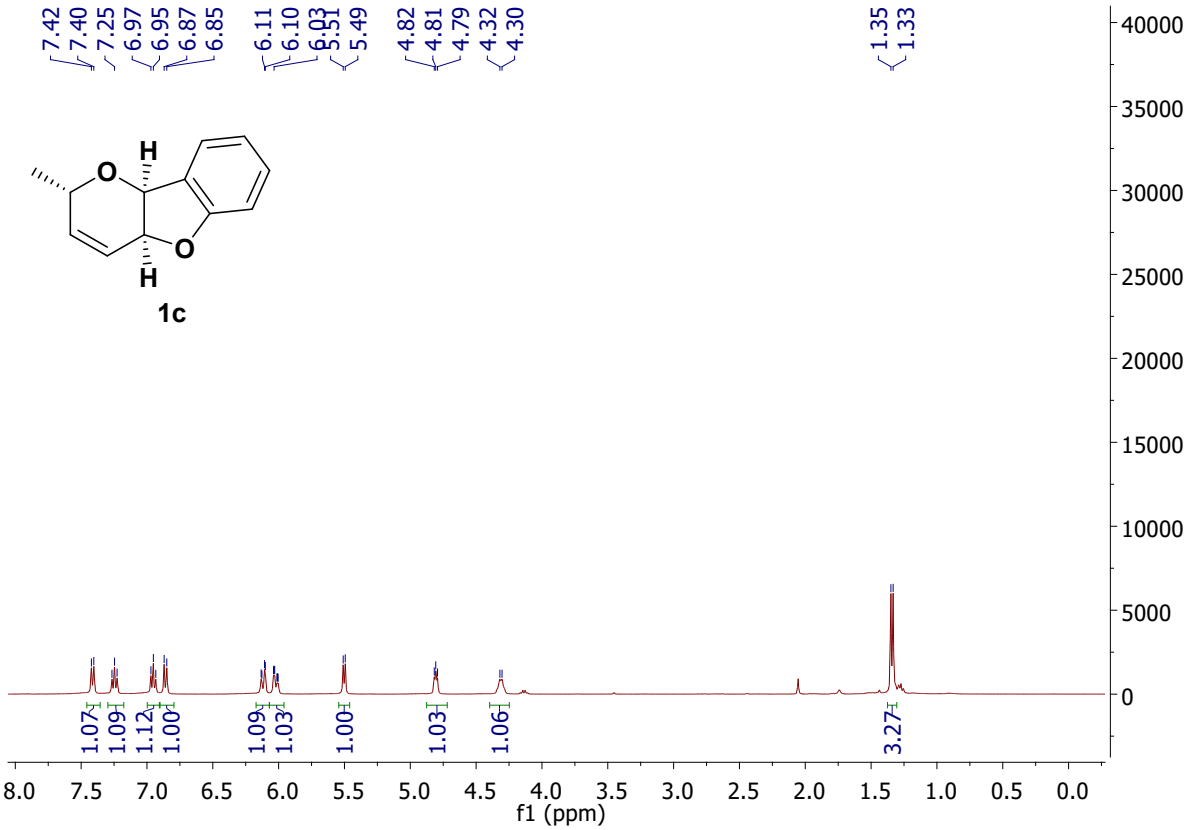
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1b



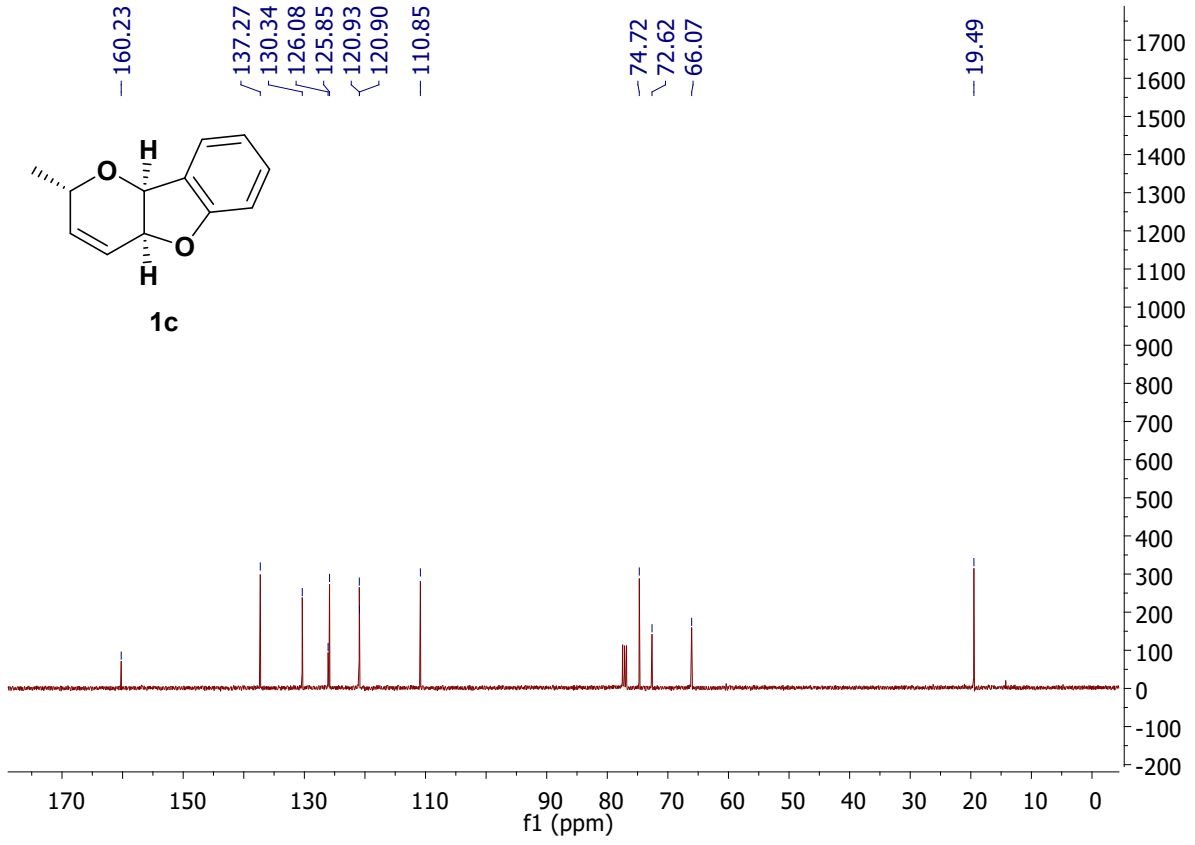

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1b



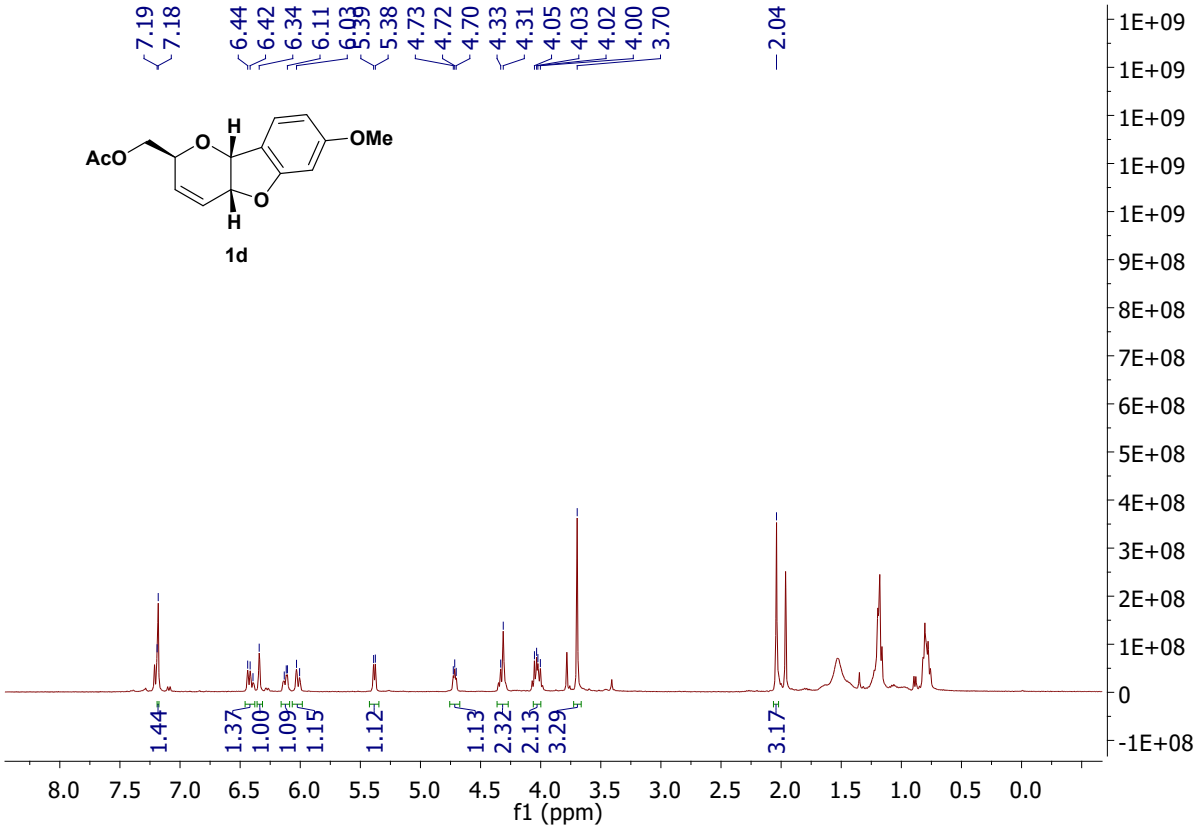
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1c



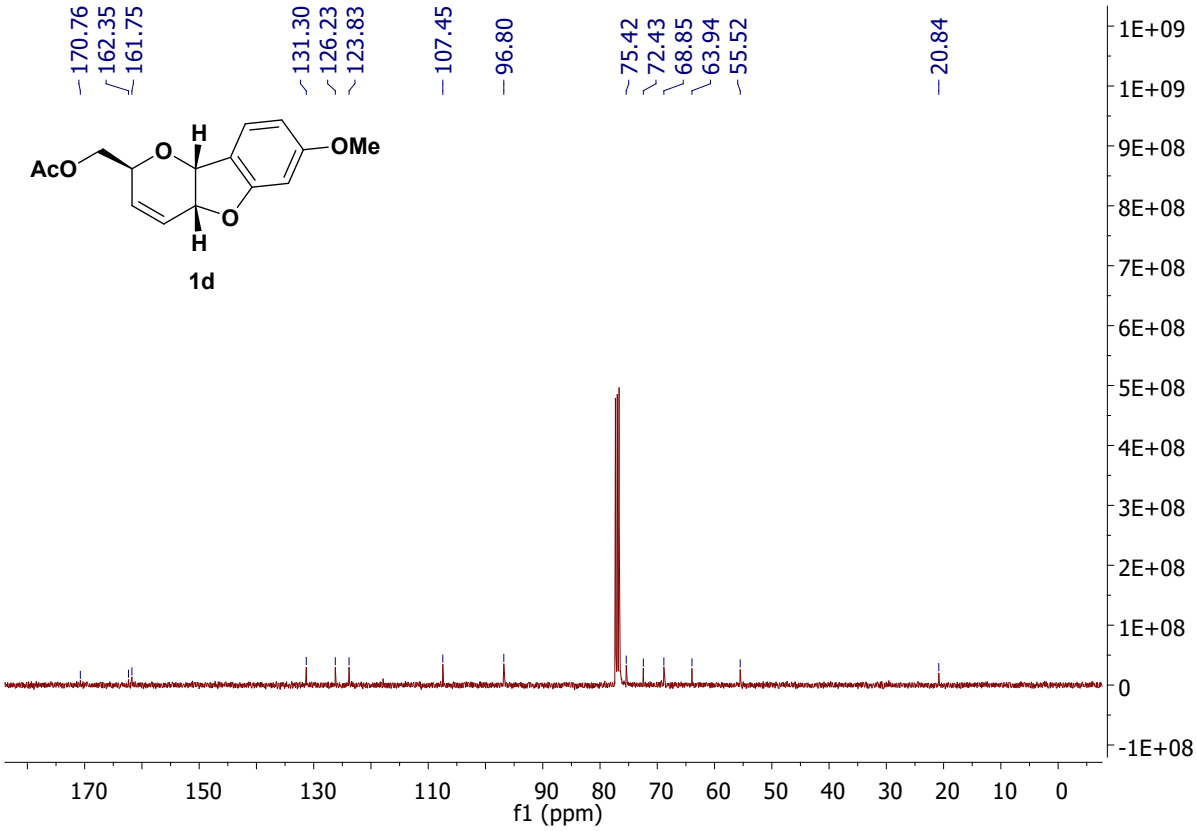

## $^{13}$C NMR (101 MHz, CDCl3) of compound 1c



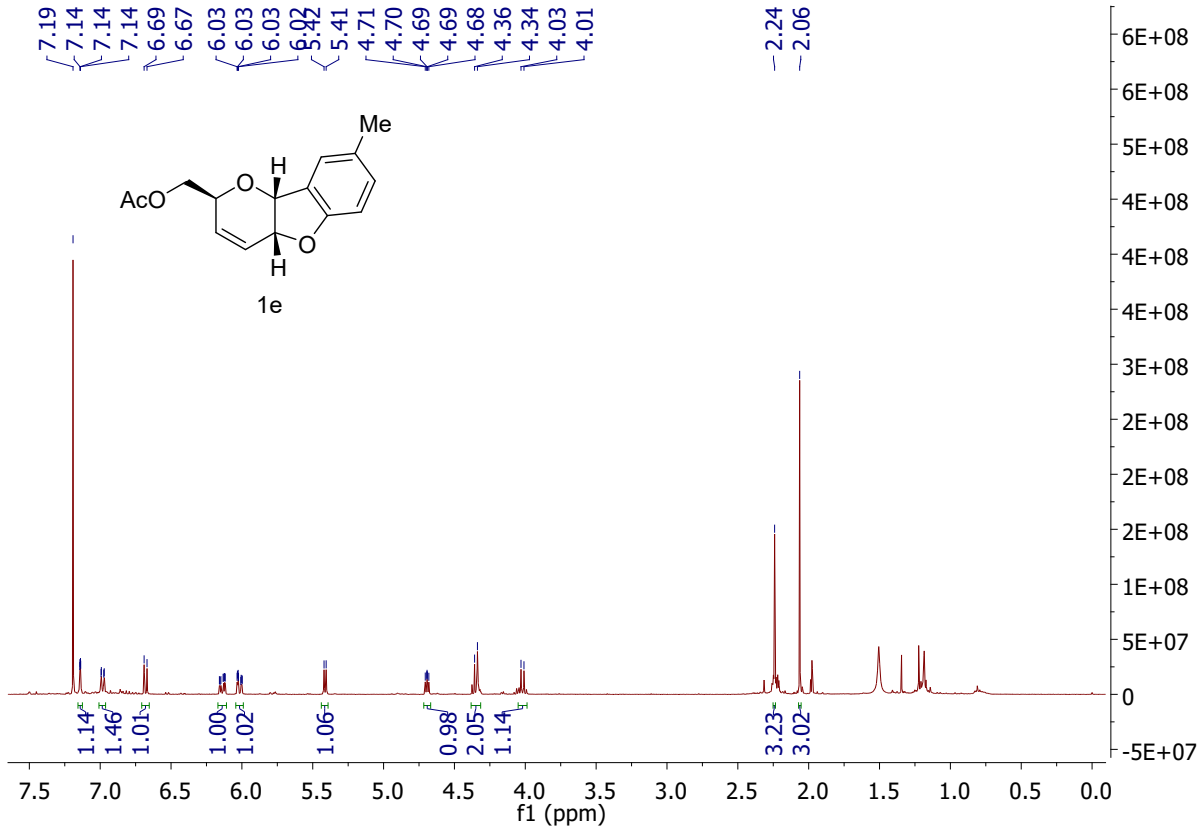
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1d



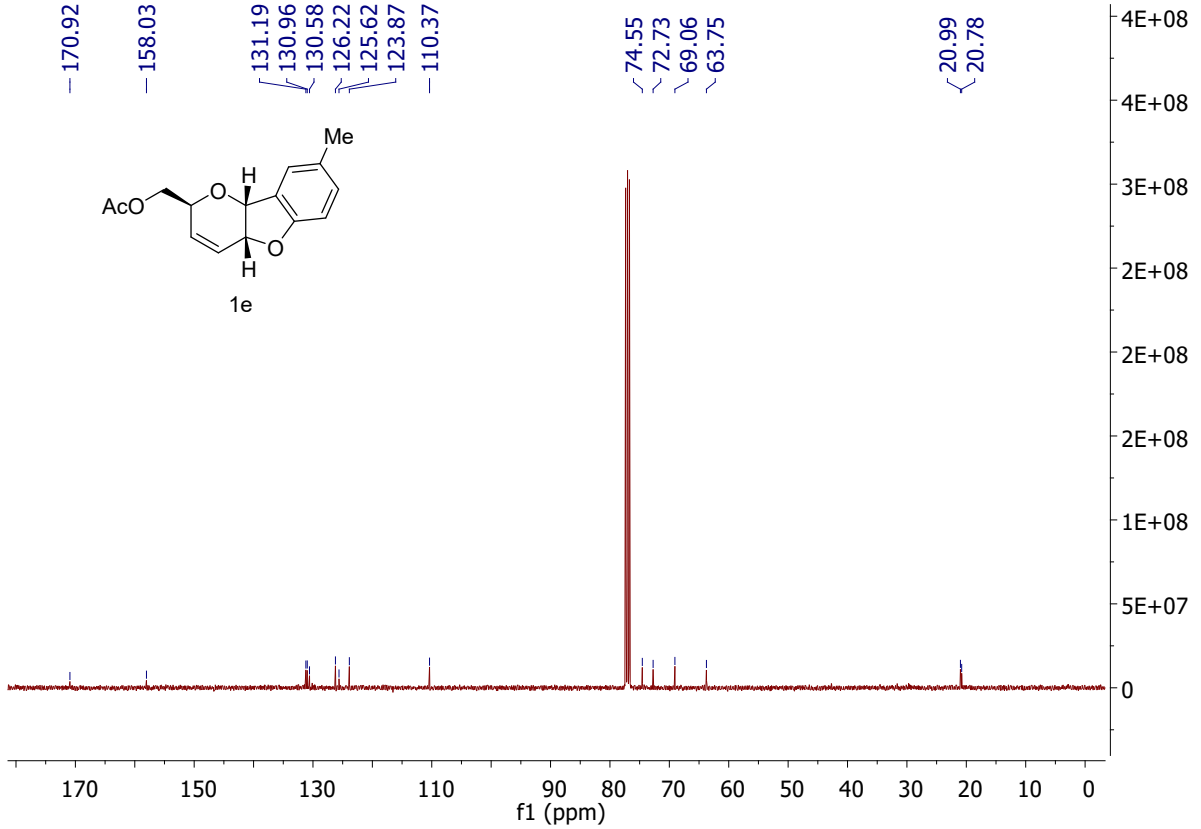

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1d



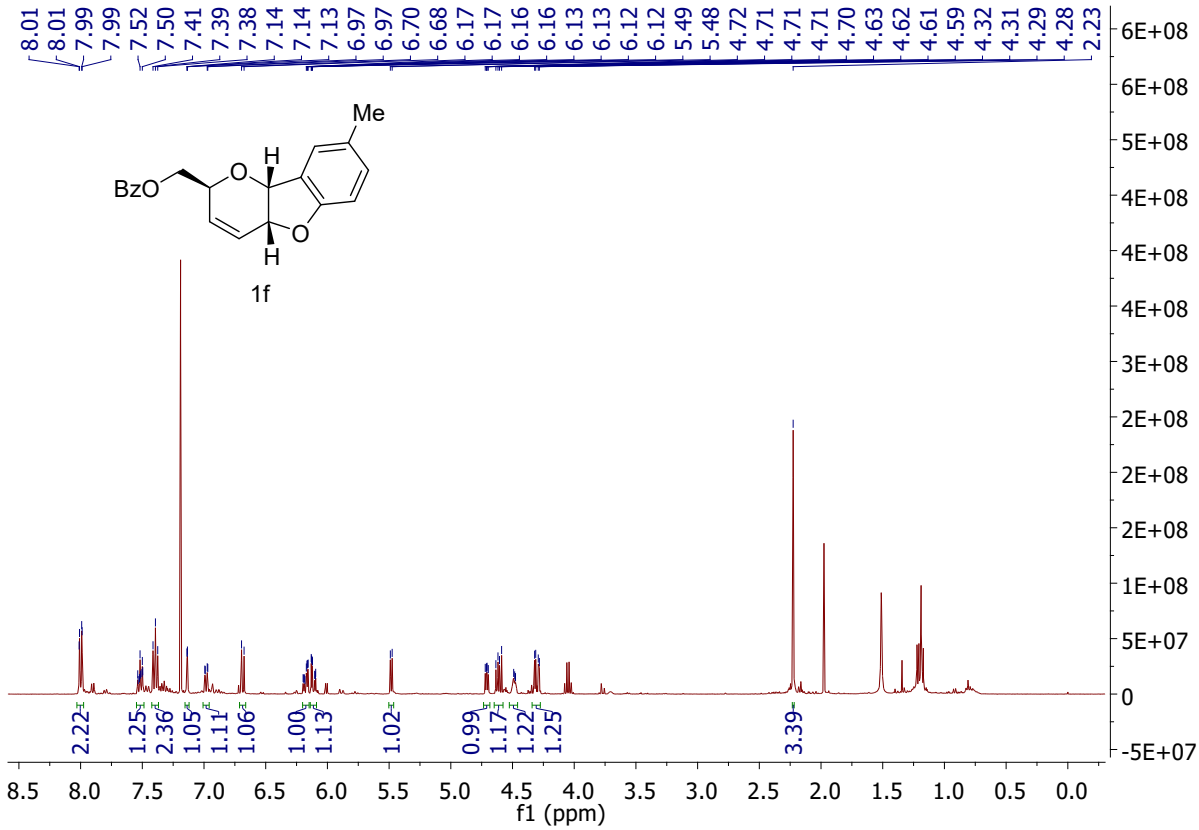
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1e



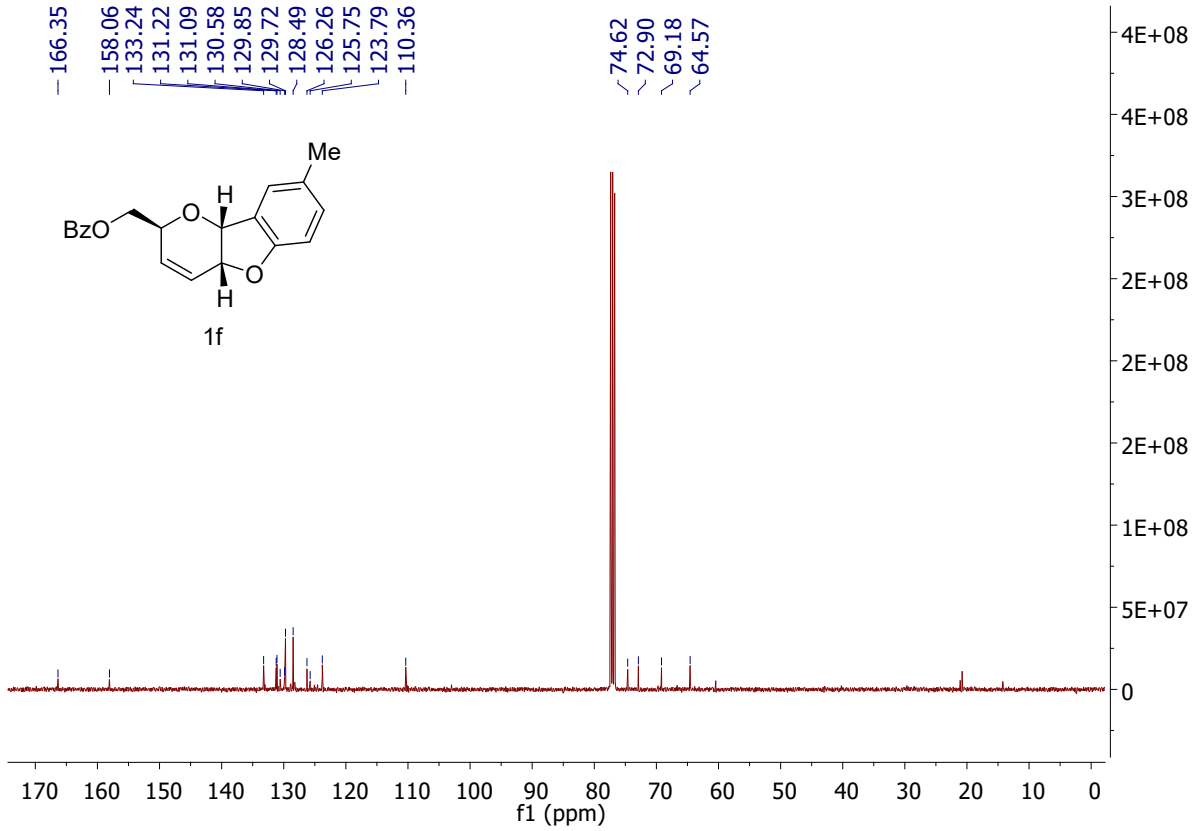

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1e



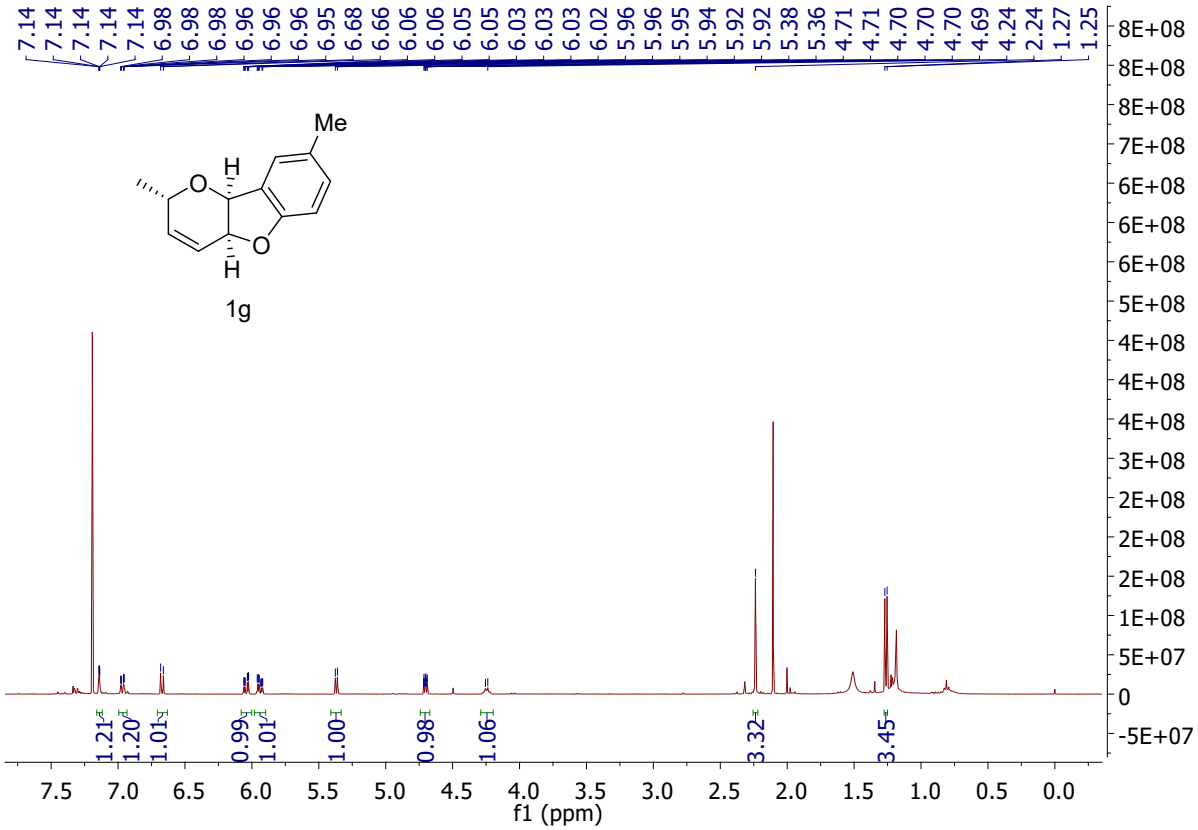
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1f



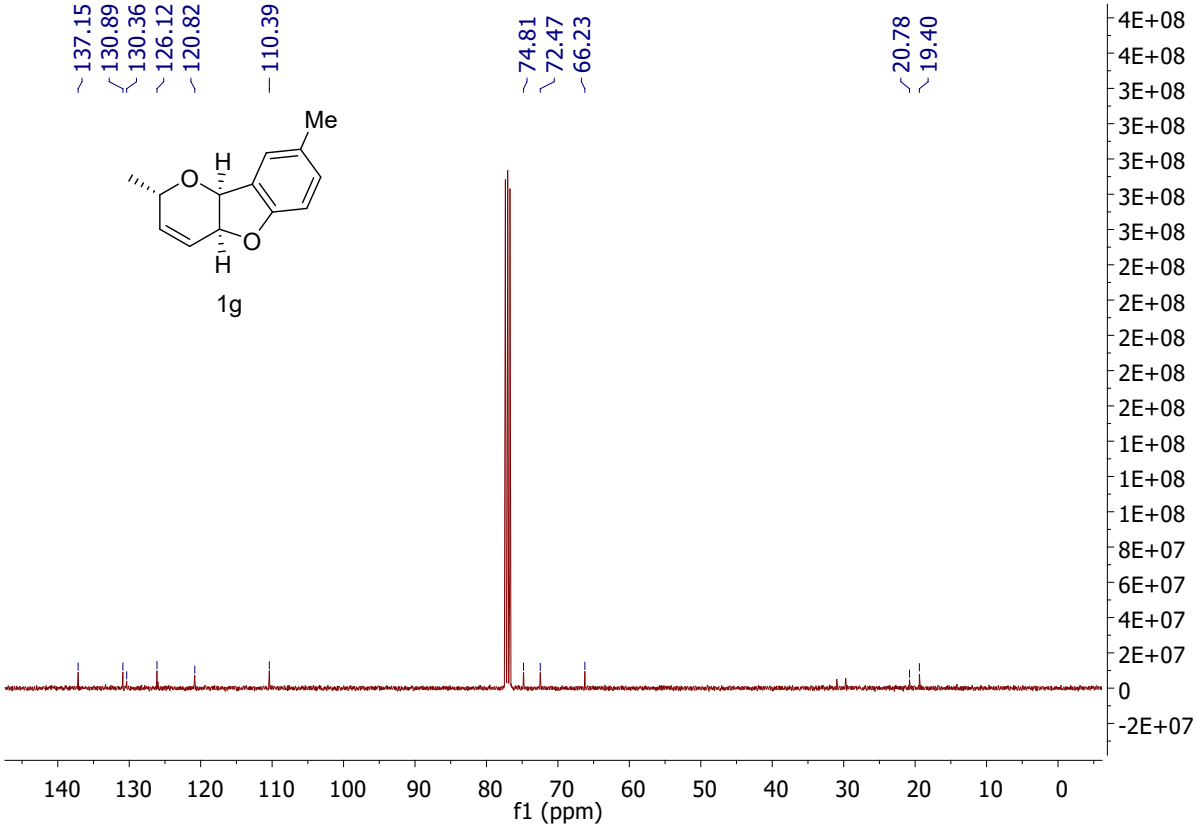

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1f



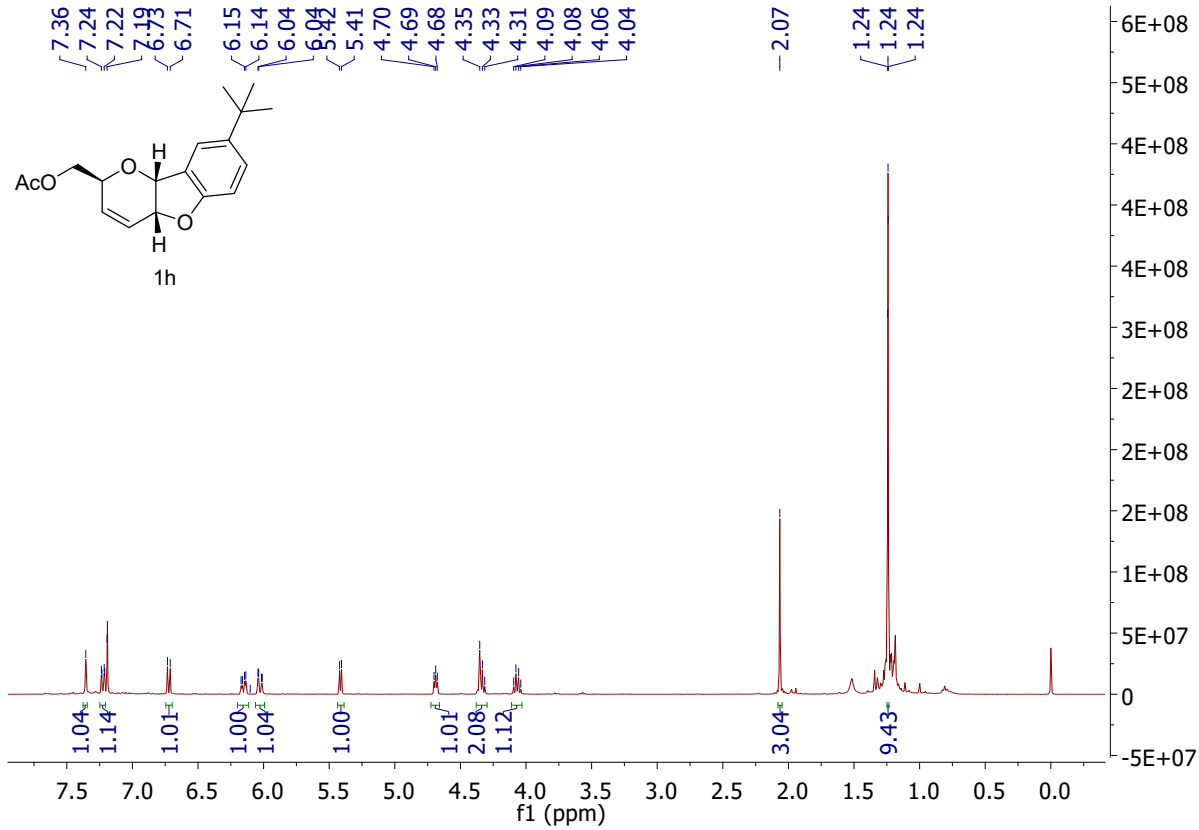
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1g



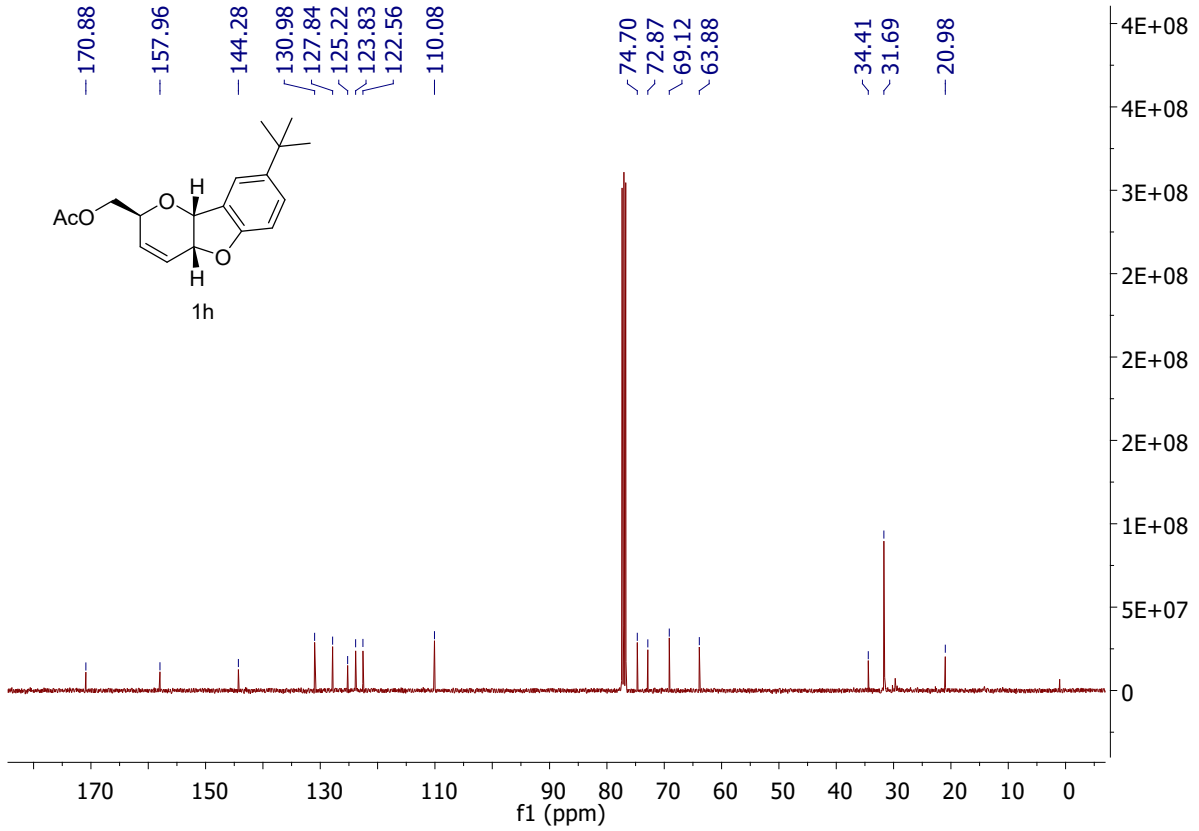

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1g



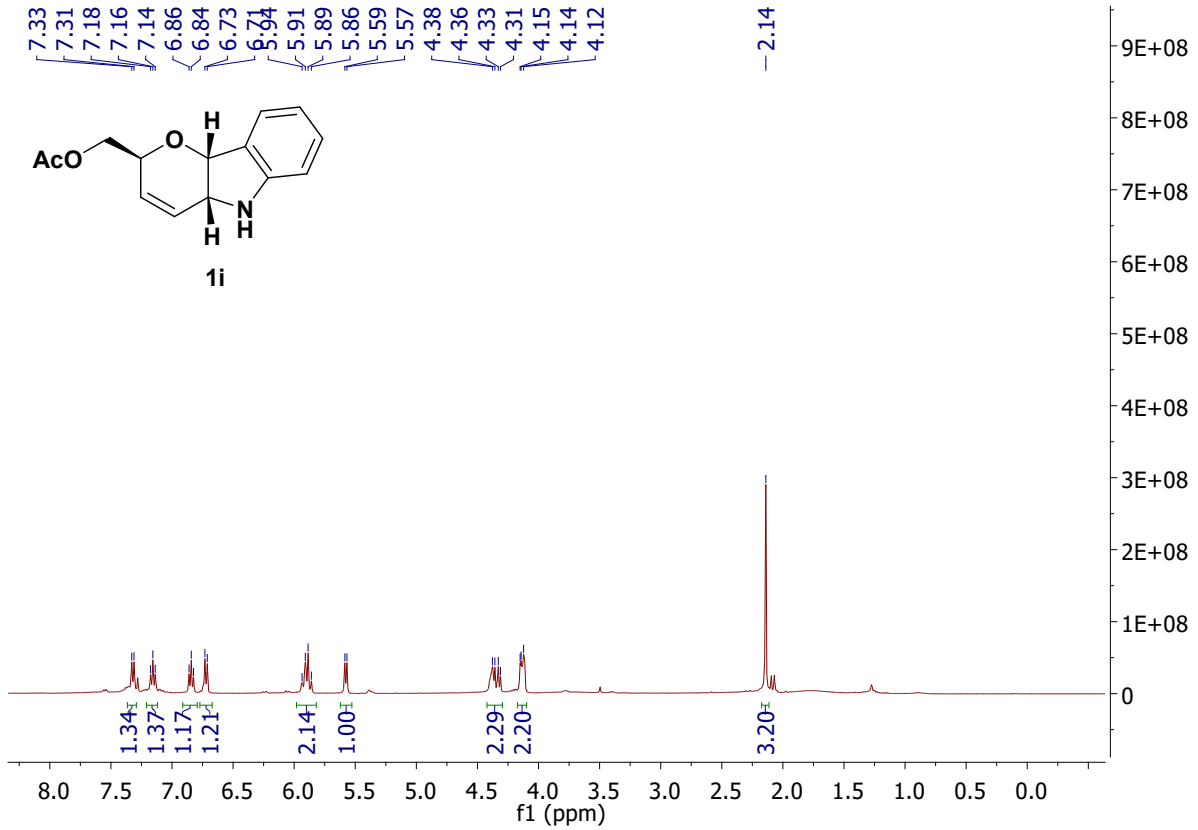
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1h



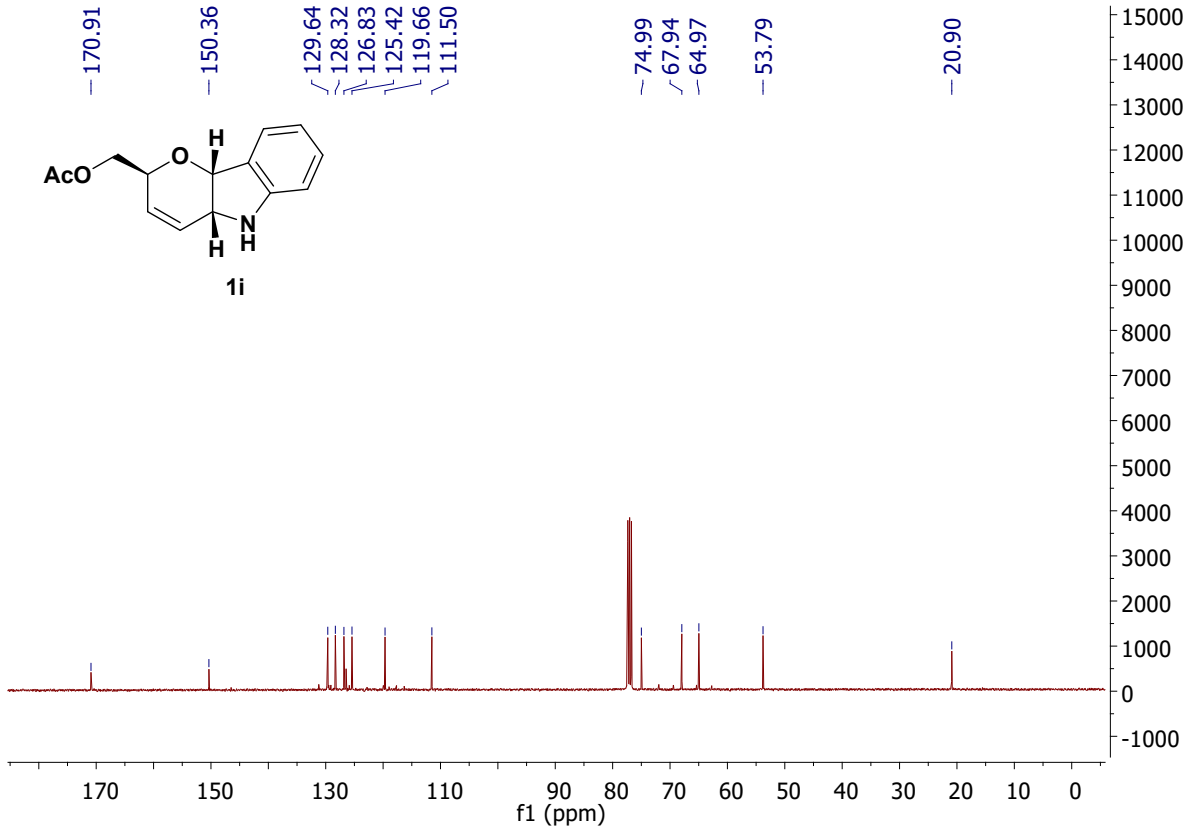

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1h



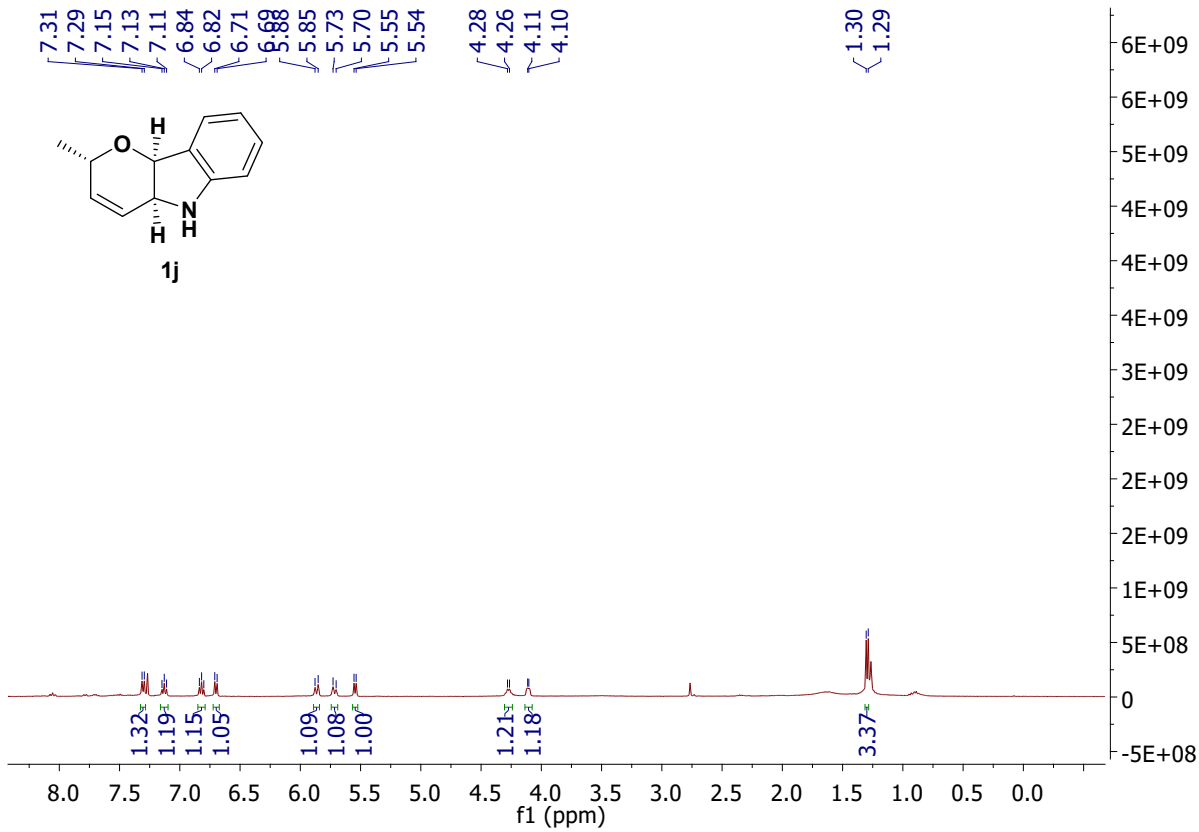
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1i



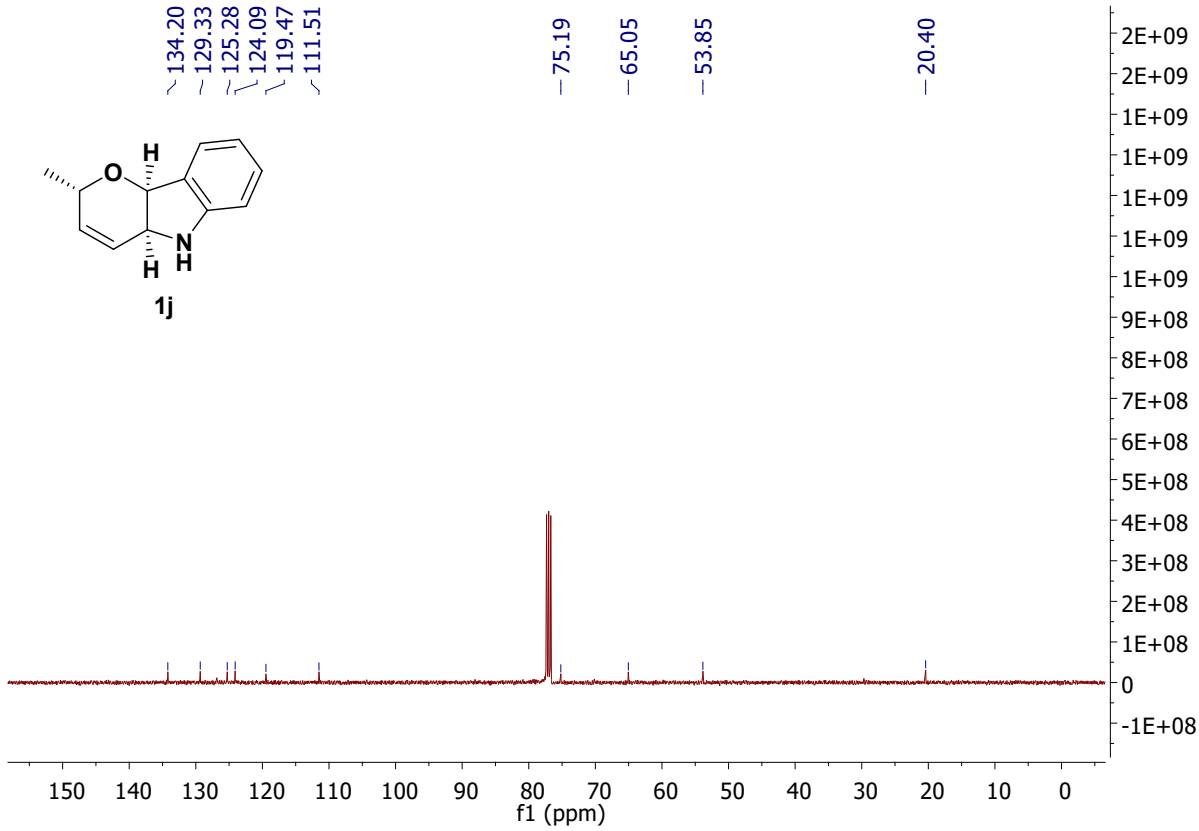

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1i



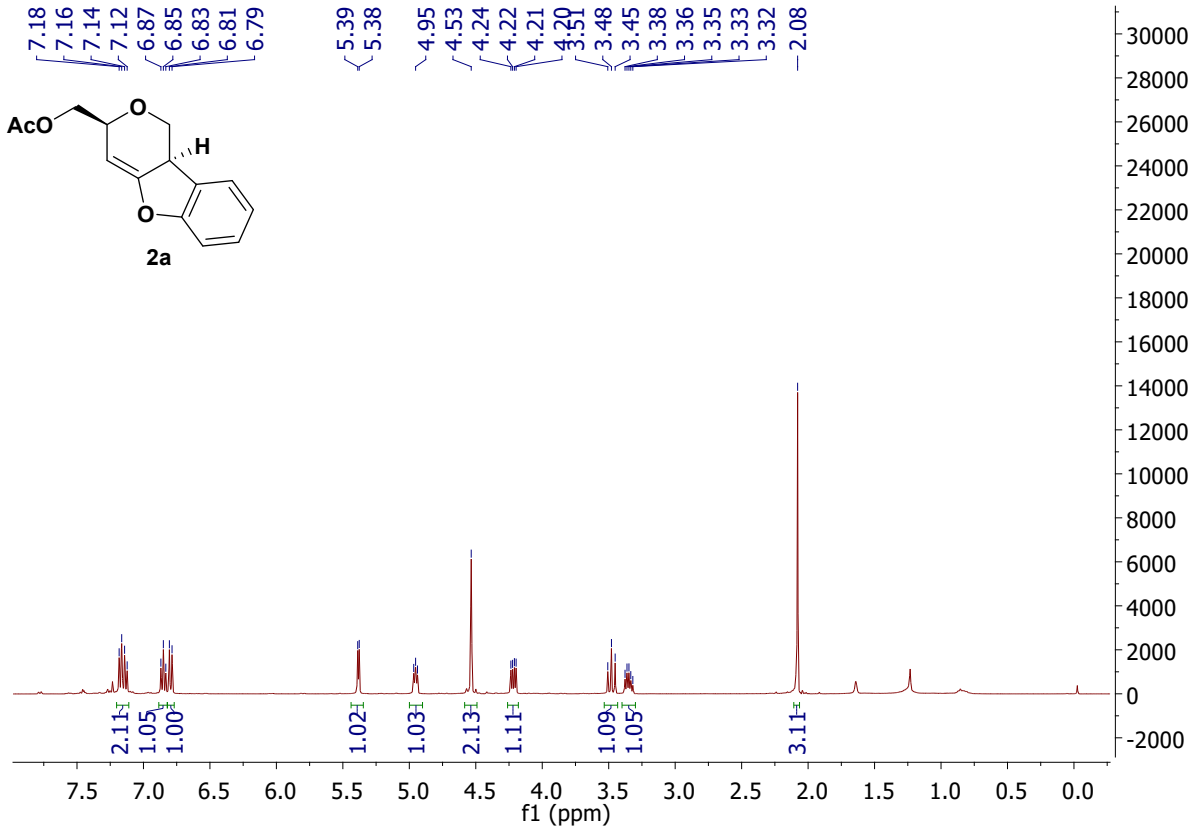
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1j



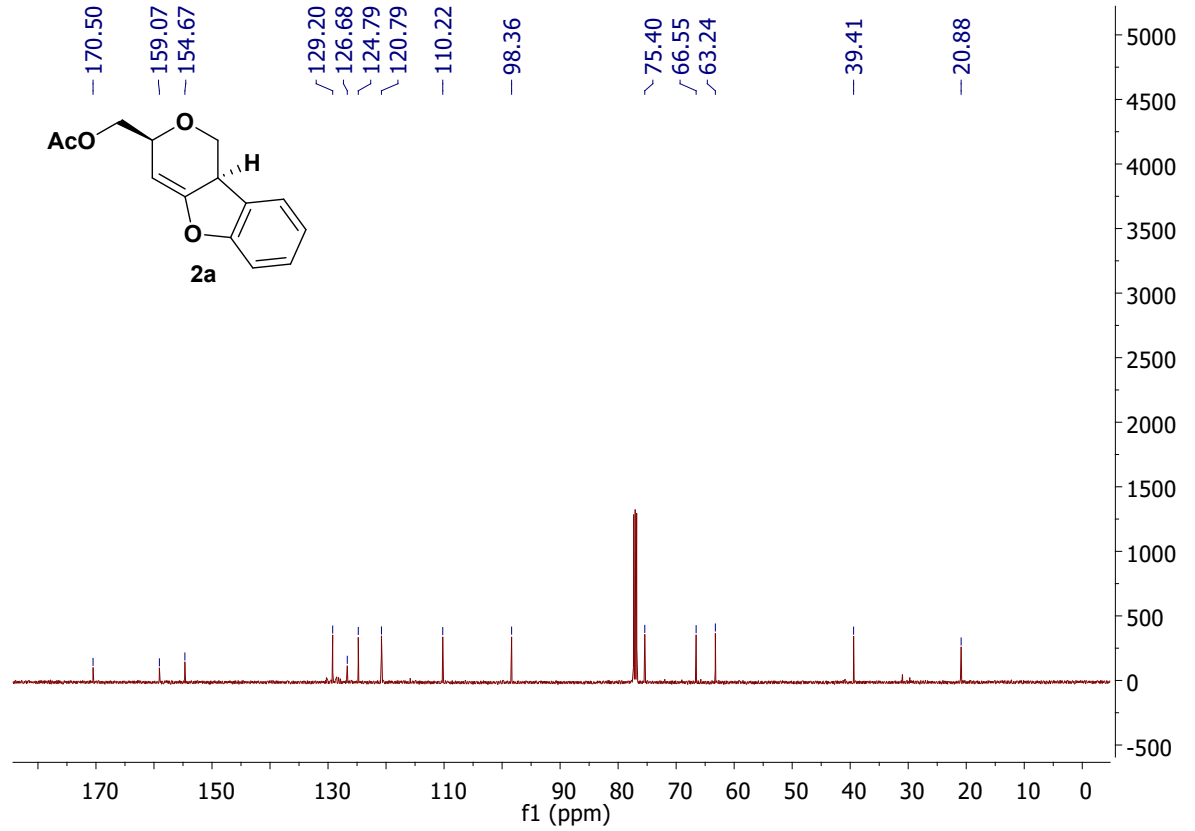

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1j



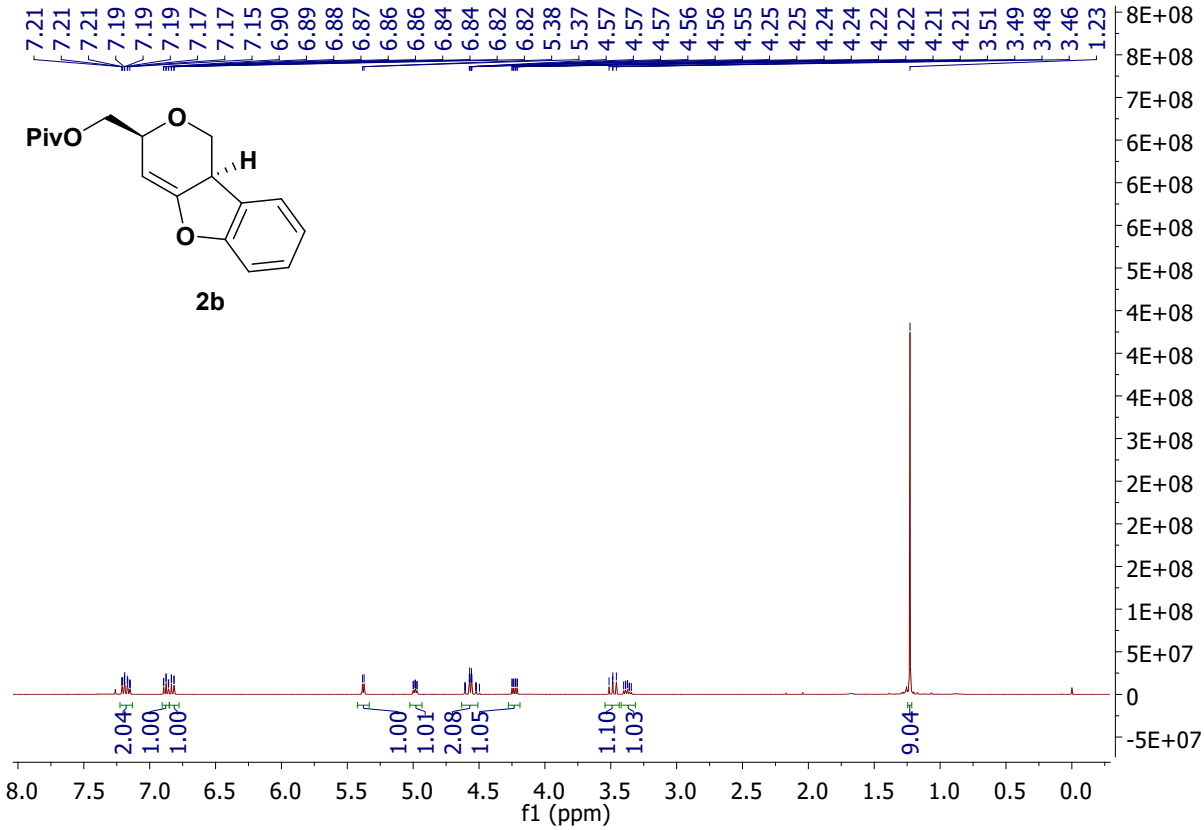
## $^{1}$H NMR (400 MHz, CDCl3) of compound 2a



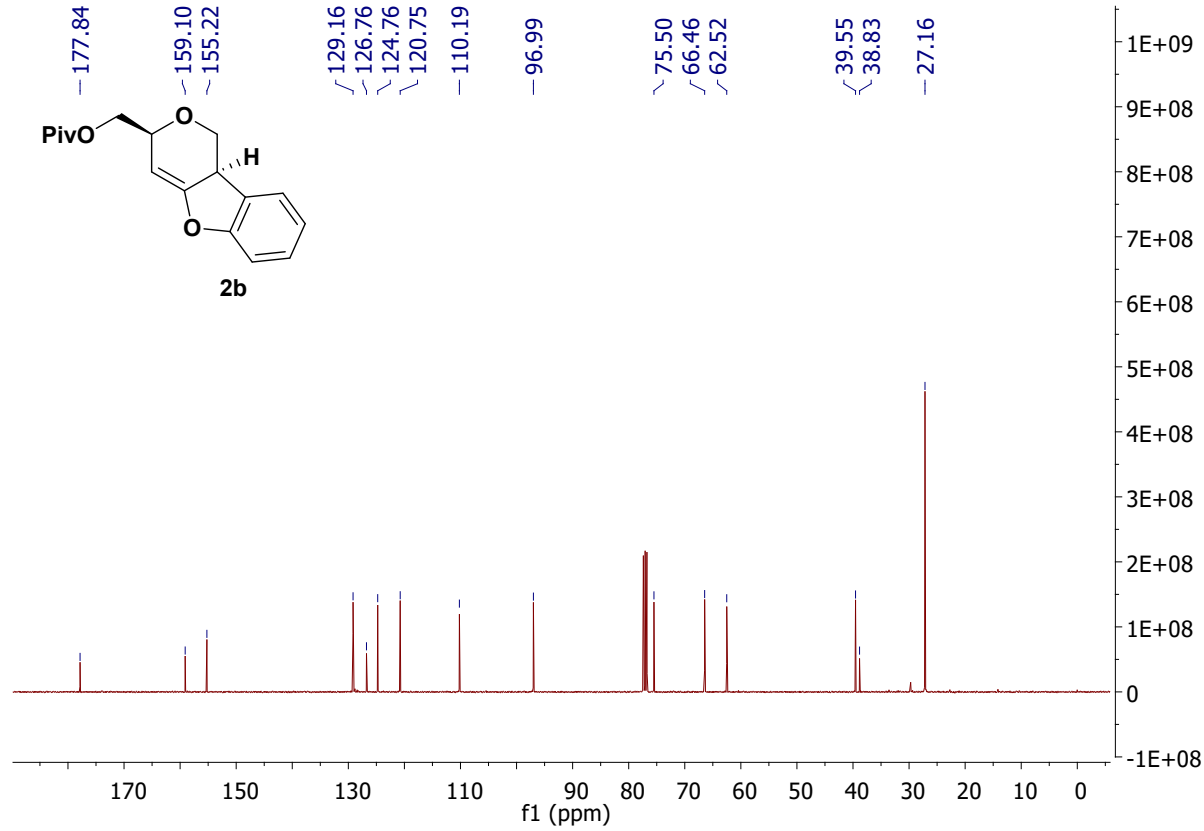

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 2a



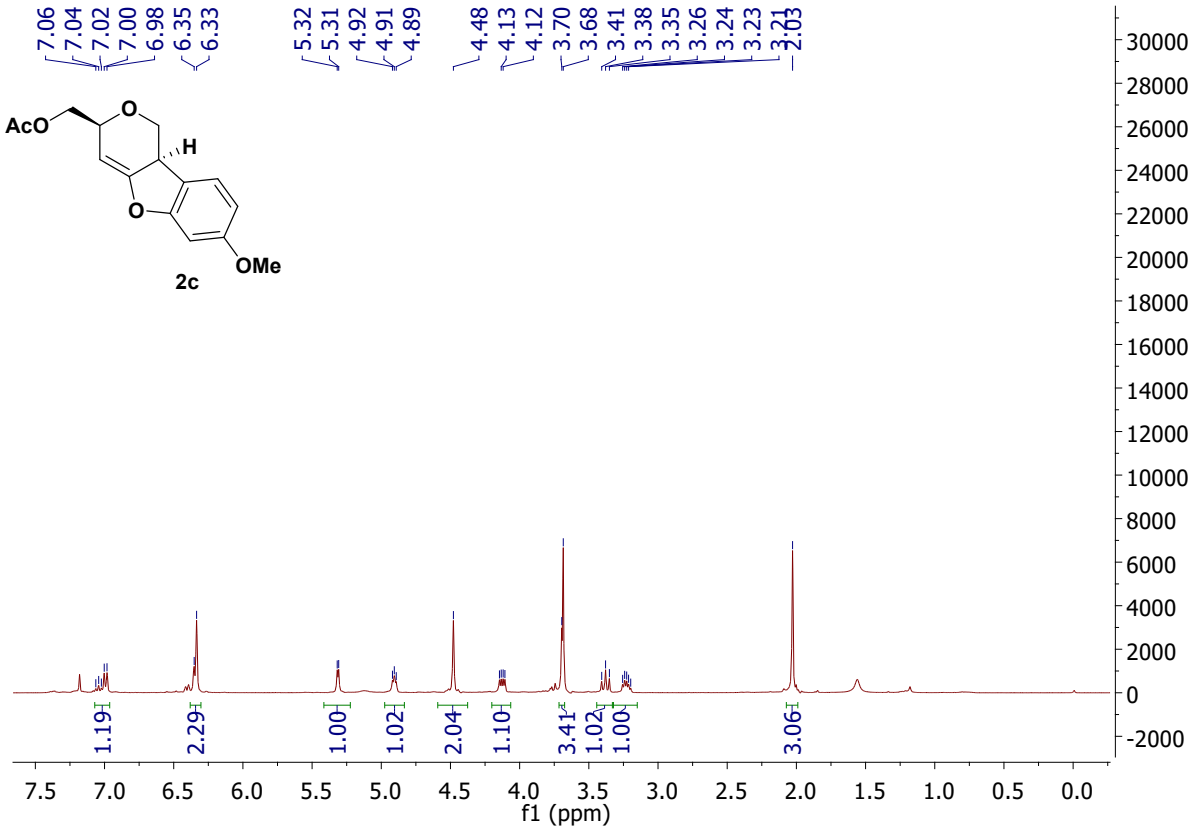
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 2b



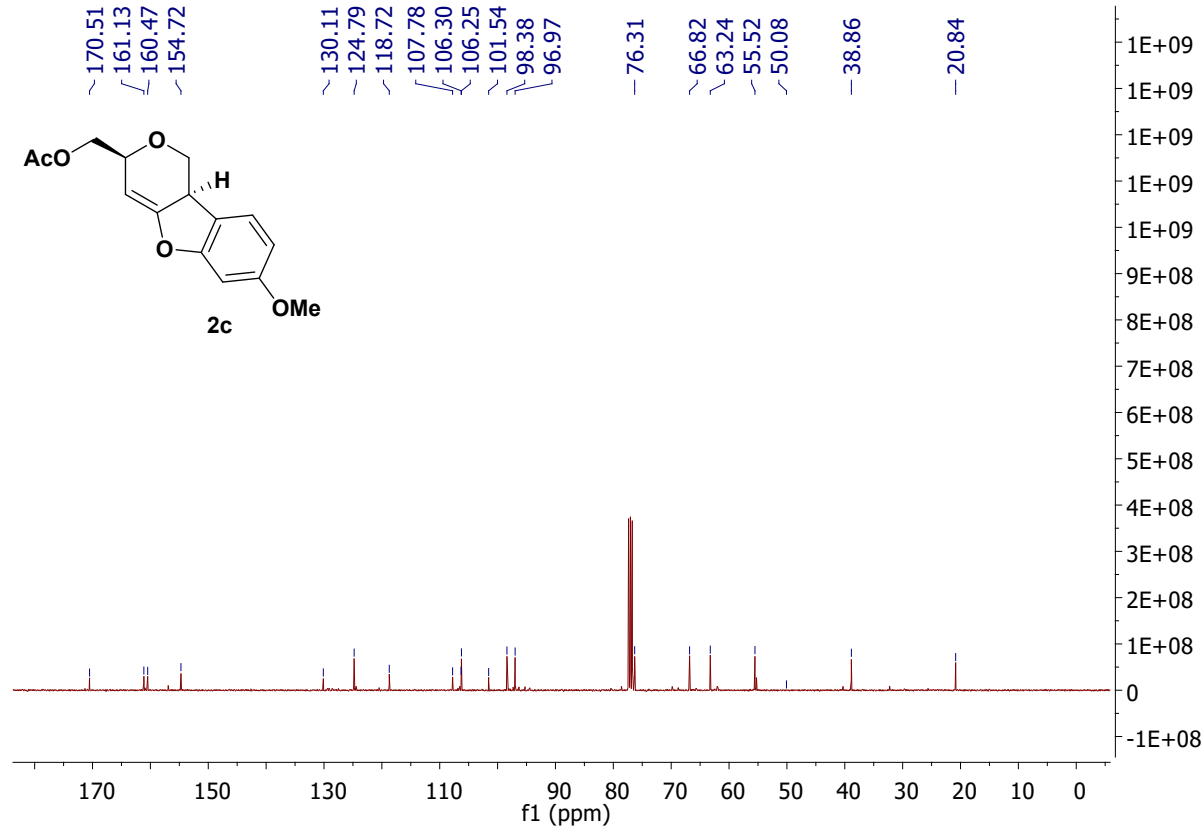

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 2b



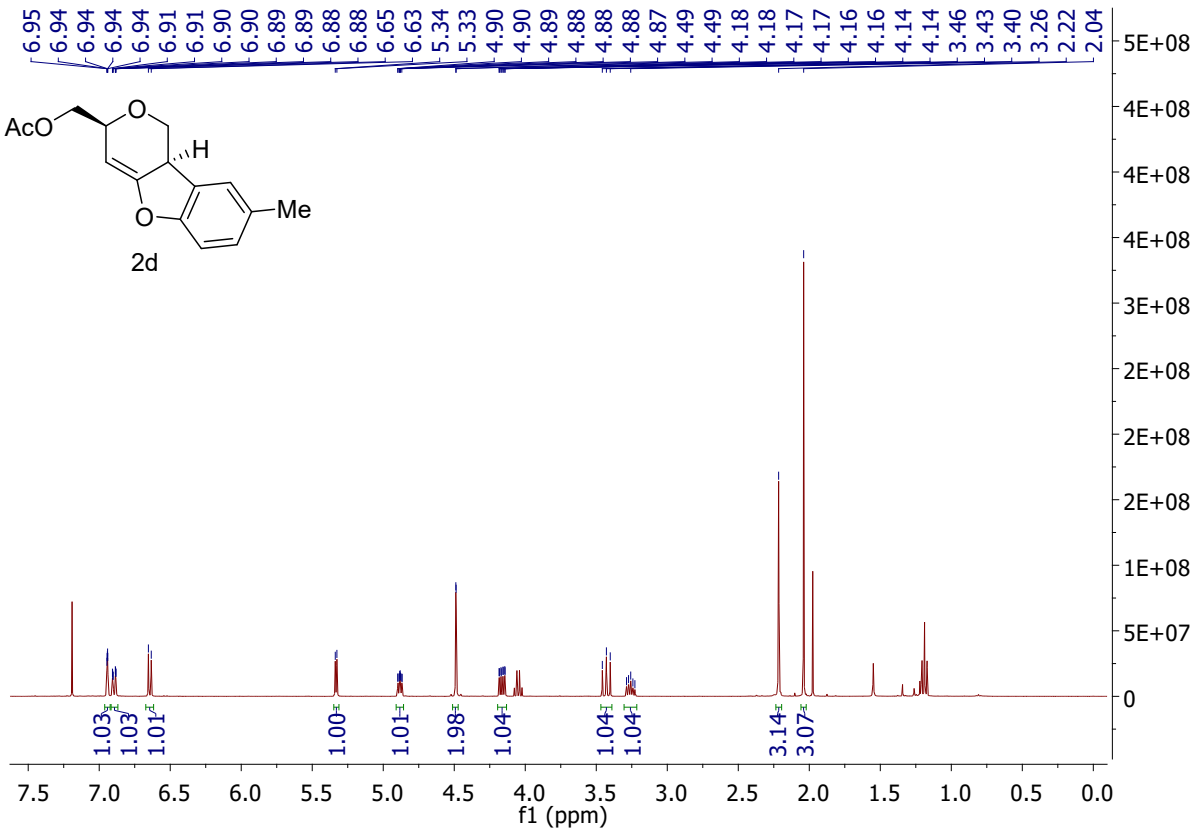
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 2c



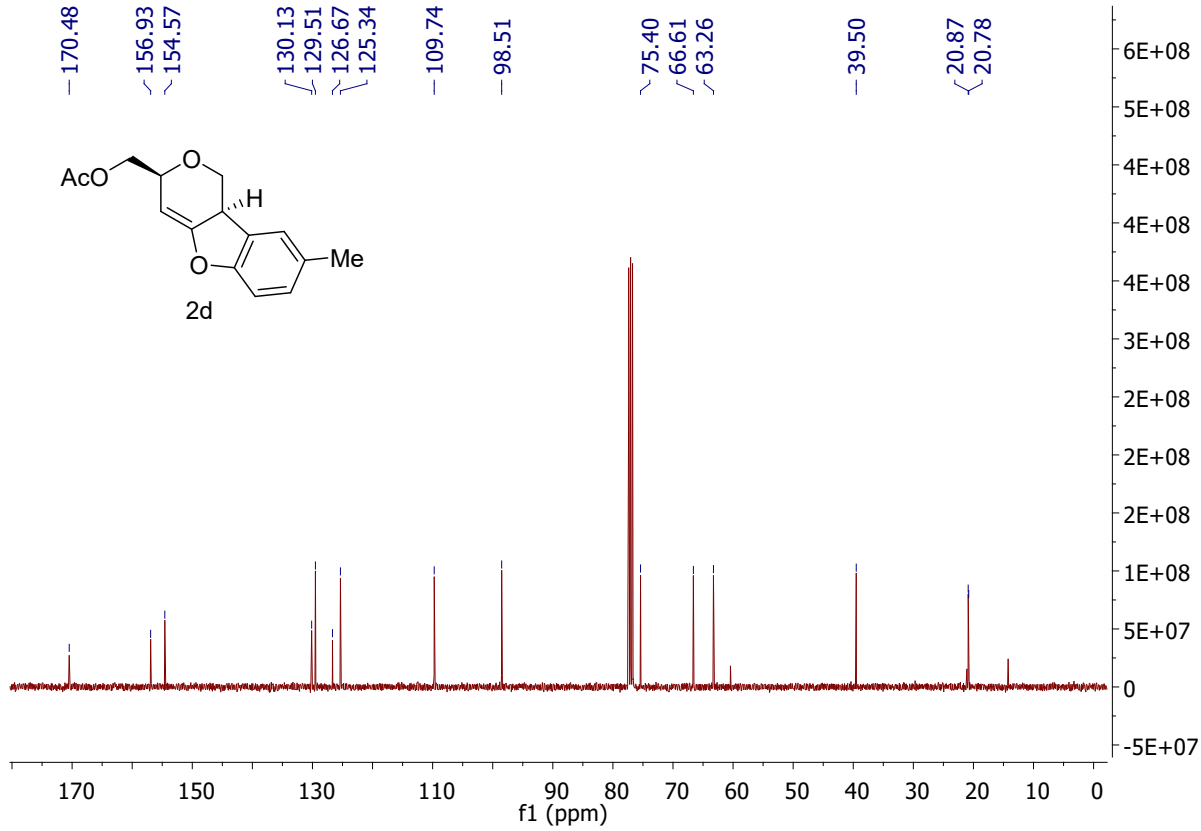

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 2c



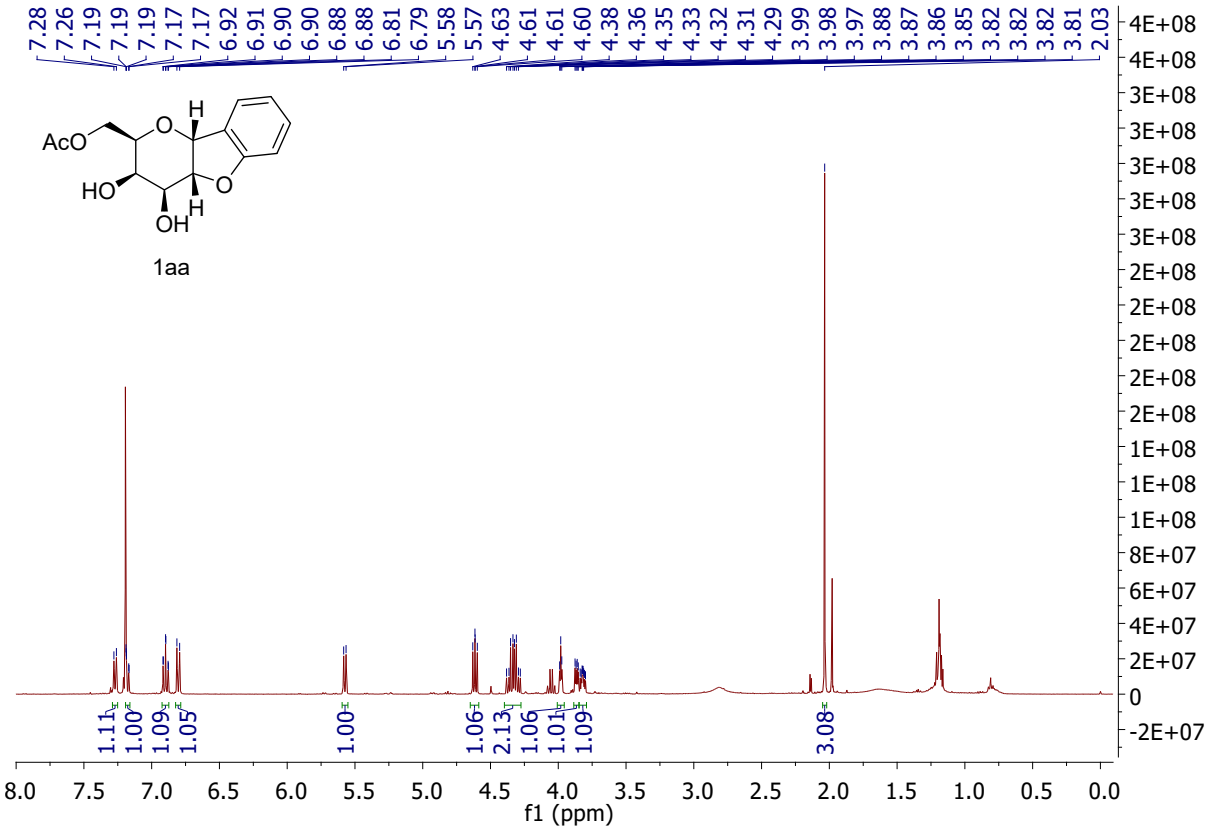
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 2d



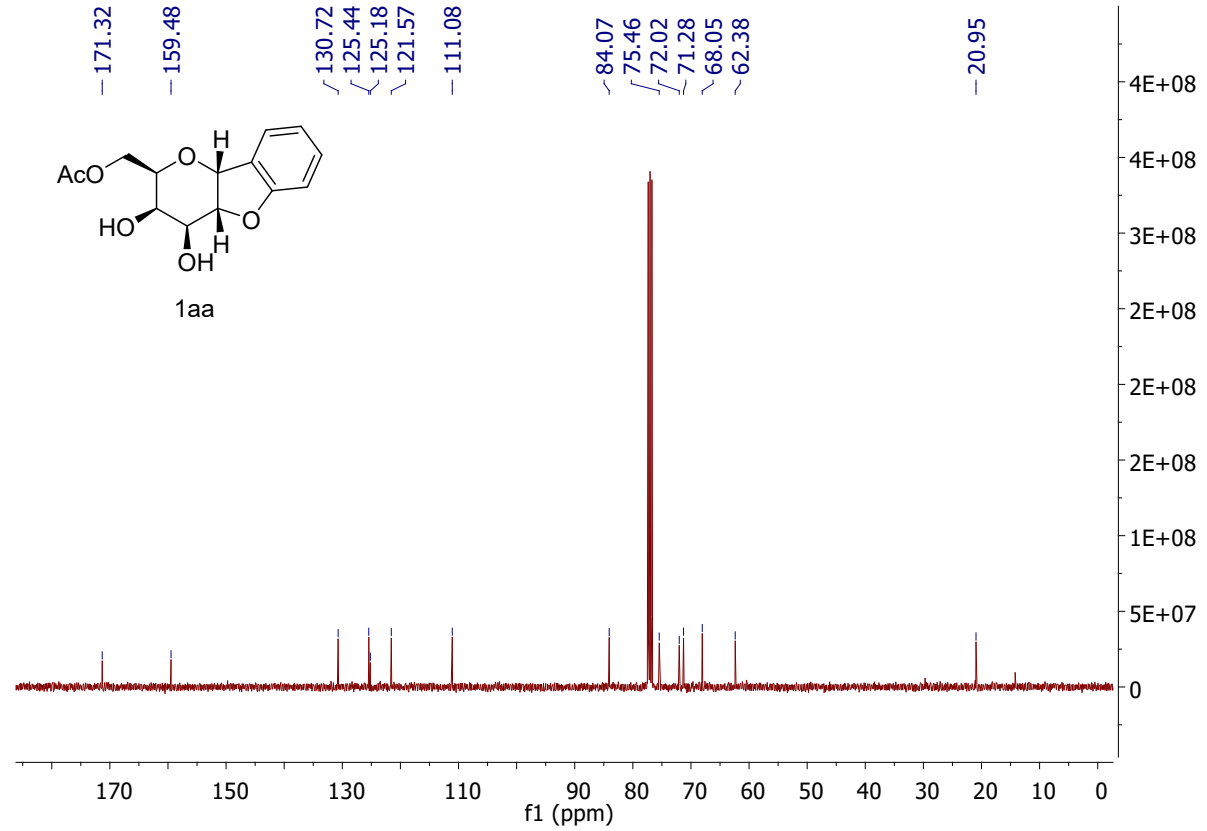

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 2d



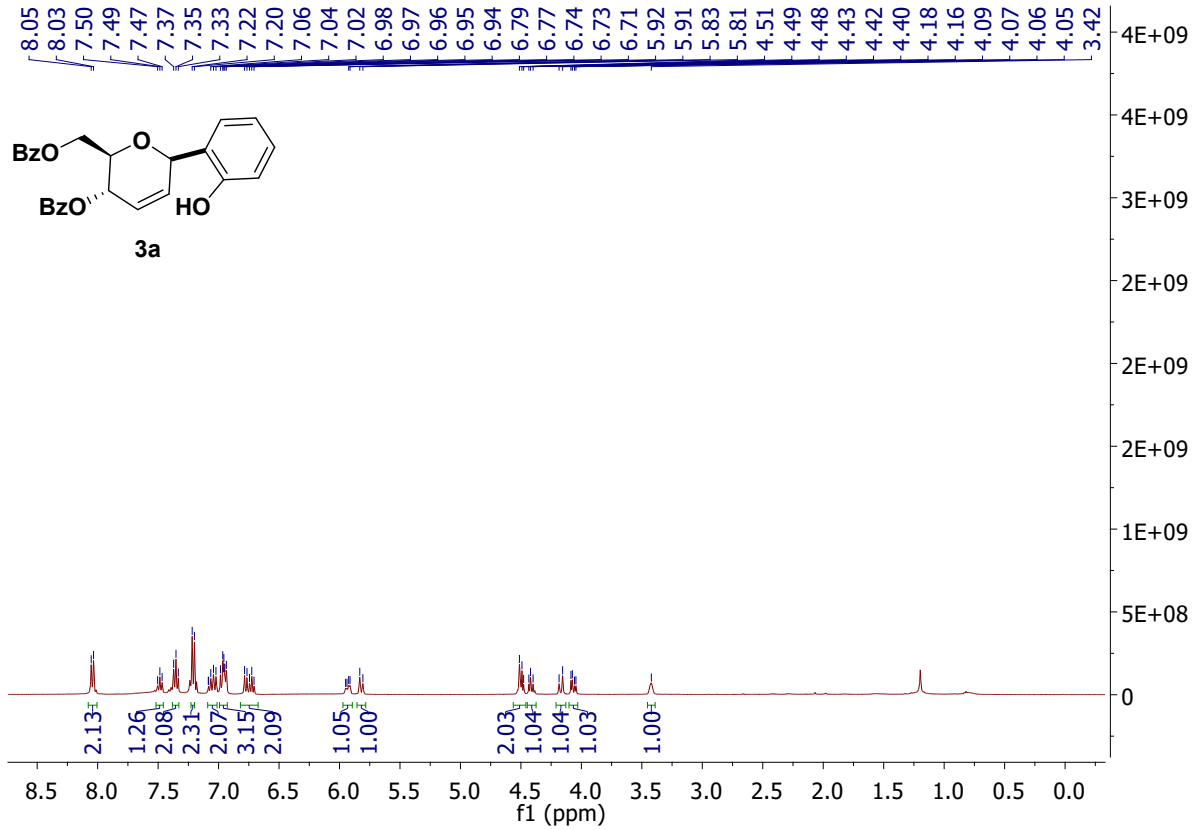
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1aa



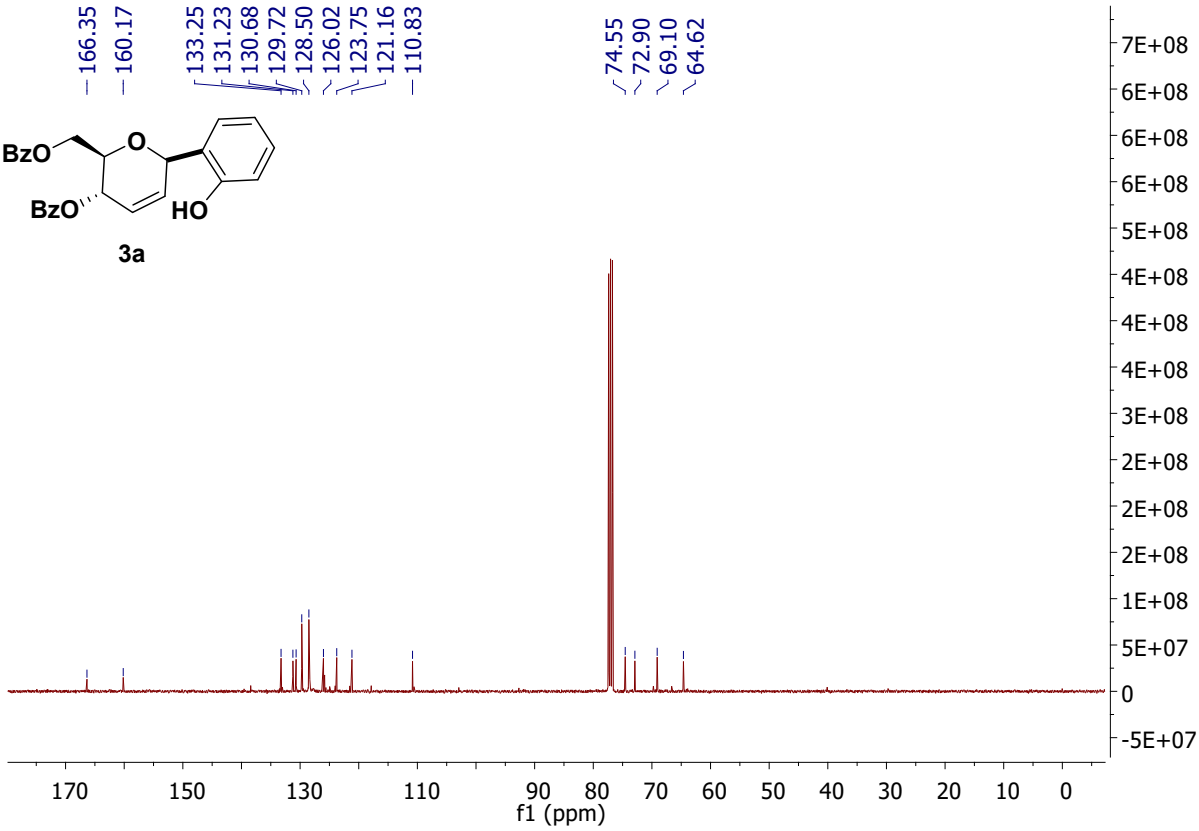

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1aa



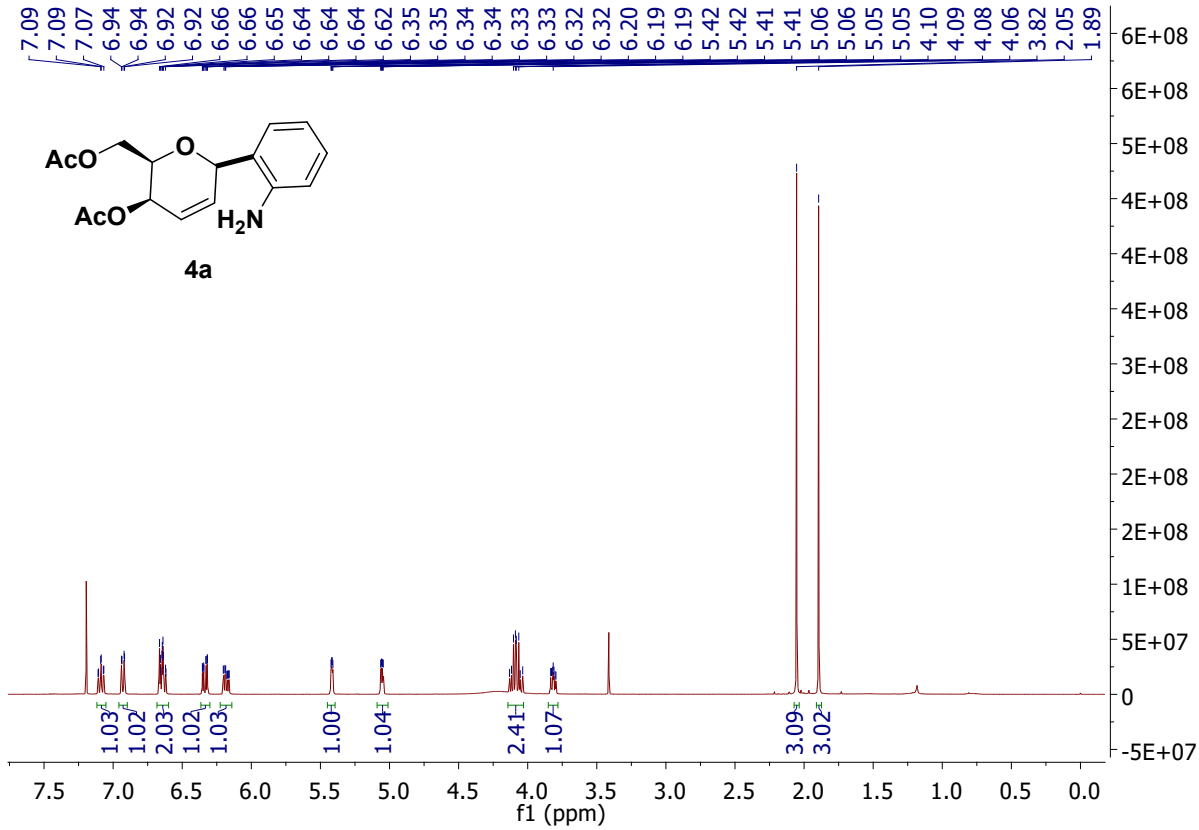
## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 3a



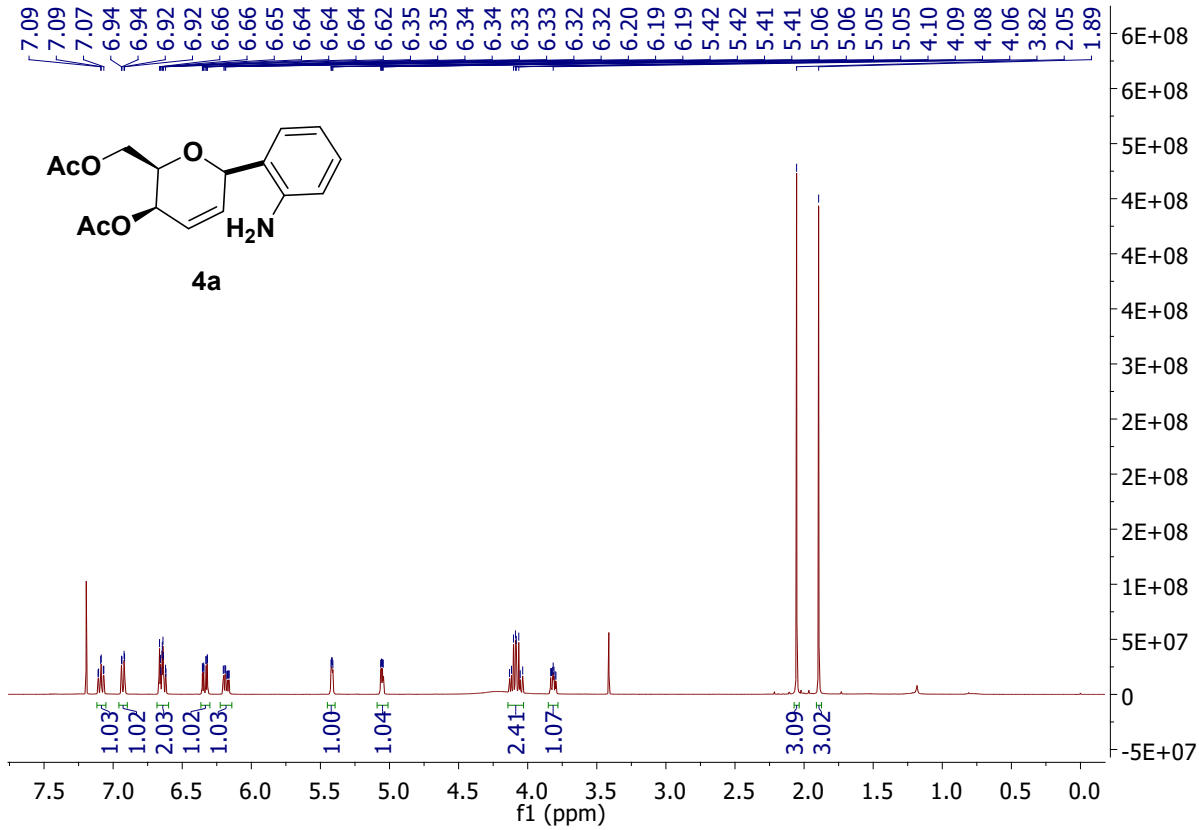

## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 3a



## $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 4a

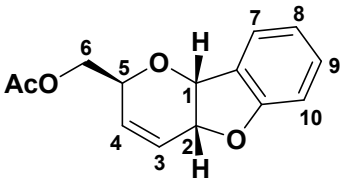



## $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 4a

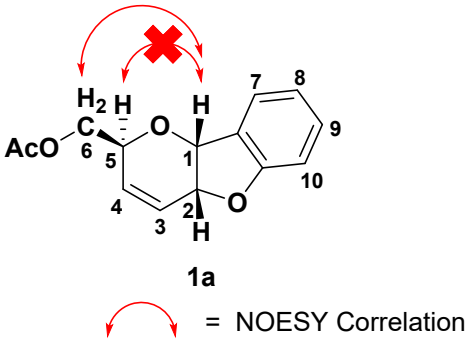


## 5. 2D Data of Compounds 1a, 1aa and 2a

### Structure determination of compound 1a:



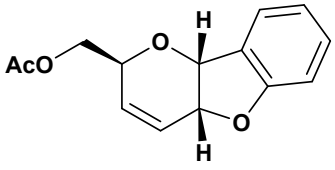

1a



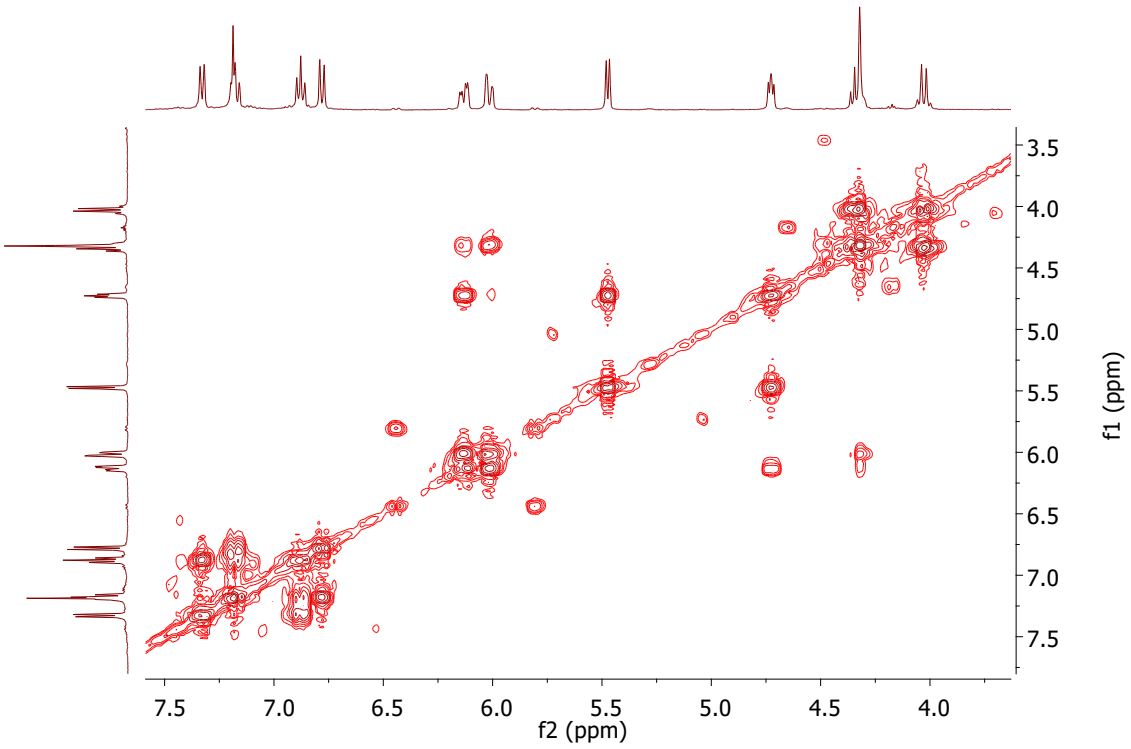

| Atom Position | Type of Atom | $^{1}$H(ppm) | $^{13}$C (ppm) |
|---|---|---|---|
| 1 | CH | 5.47 | 72.9 |
| 2 | CH | 4.72 | 74.5 |
| 3 | CH | 6.13 | 123.8 |
| 4 | CH | 6.01 | 131.1 |
| 5 | CH | 4.34 | 68.9 |
| 6 | CH2 | 4.34, 4.02 | 63.9 |
| 7 | CH | 7.17 | 130.6 |
| 8 | CH | 6.87 | 121.1 |
| 9 | CH | 7.32 | 125.9 |
| 10 | CH | 6.78 | 110.8 |
| | OAc | 2.05 | 20.9, 170.8 |

The structure of product **1a** was confirmed by 2D NMR analysis. Presence of two peaks at δ values 6.01 and 6.13 ppm in 1H NMR suggested the presence of double bond at C3-C4 position. COSY data showed the correlation of H1-H2, H2-H3, H4-H5 confirming their adjacent nature. In NOESY experiment we observed the correlation between H1 and H6, but no correlation was seen between H1 and H5 and finally from 2D NMR of dihydroxylated product **1aa** we confirmed the formation of pyrano *cis*- fused *dihydro*-benzofurans.

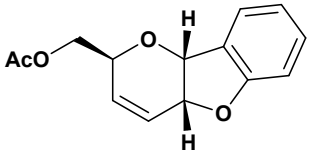
### COSY of 1a



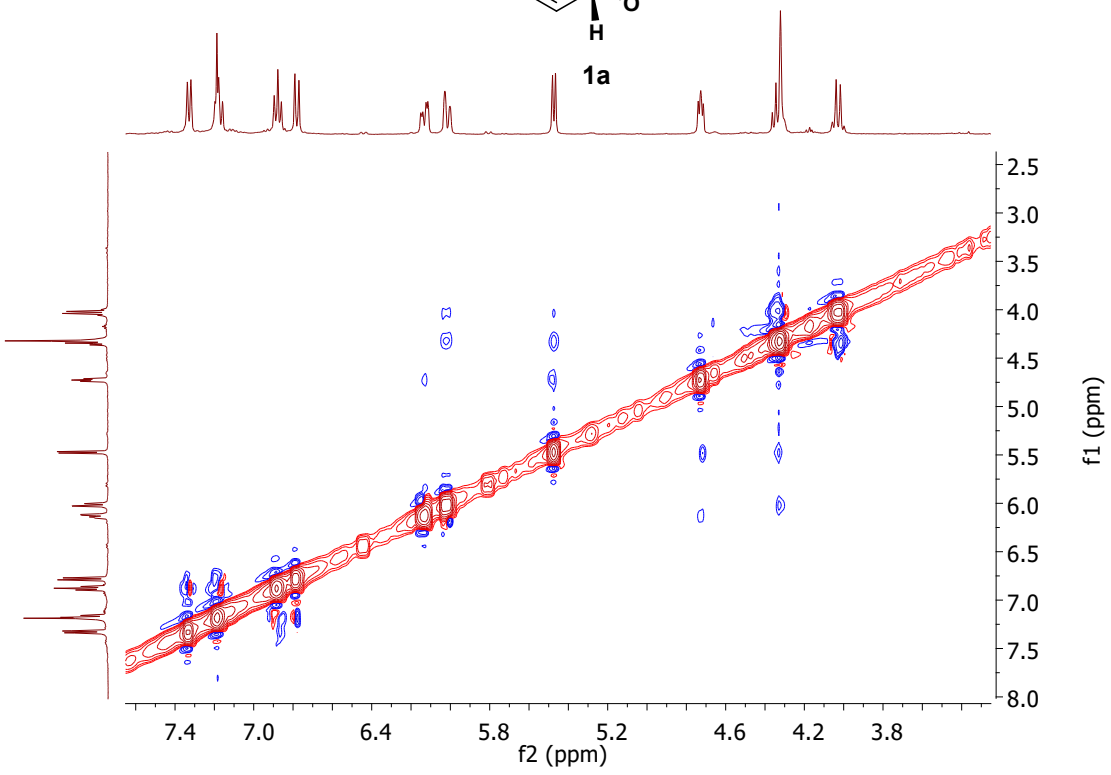

1a



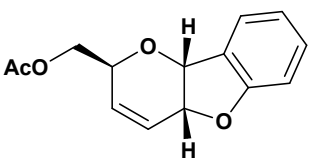

**NOESY of 1a**

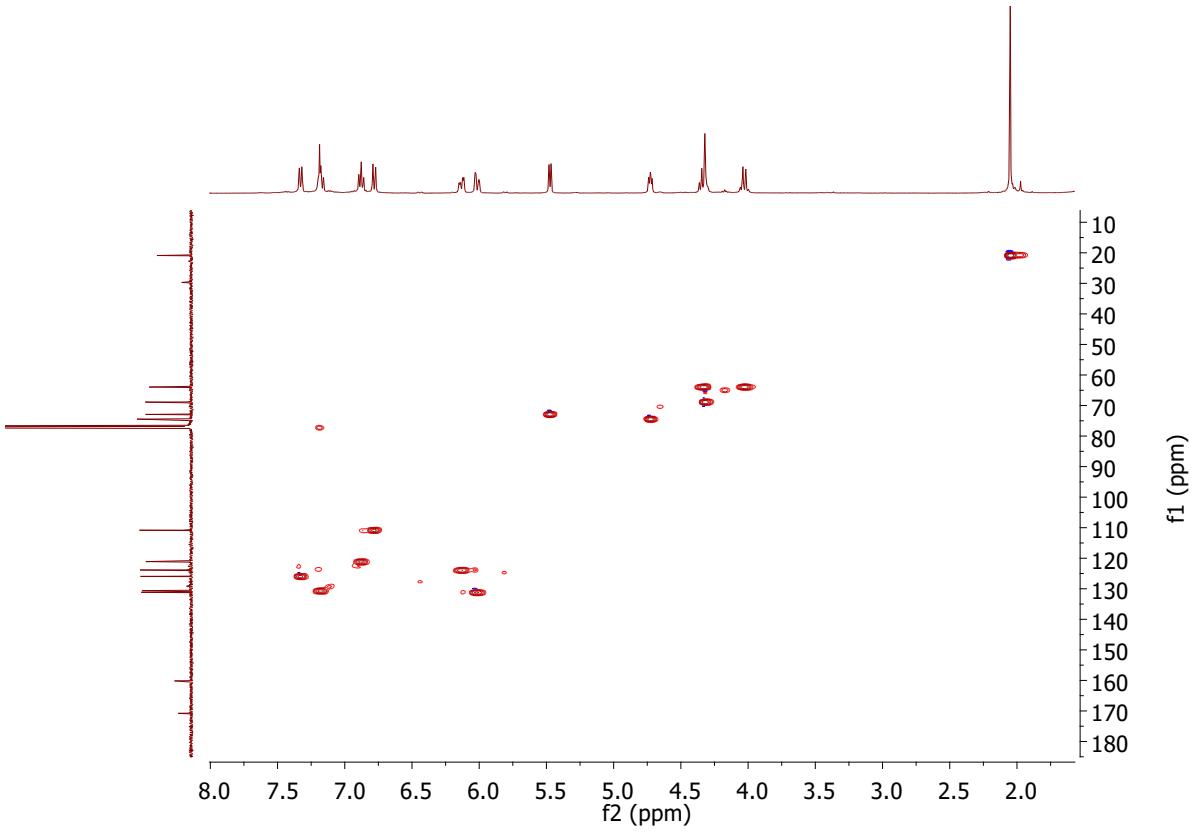


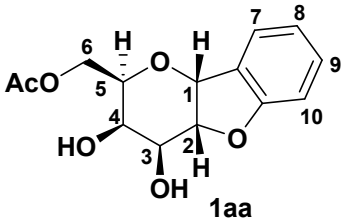

**1a**




**HSQC of 1a**

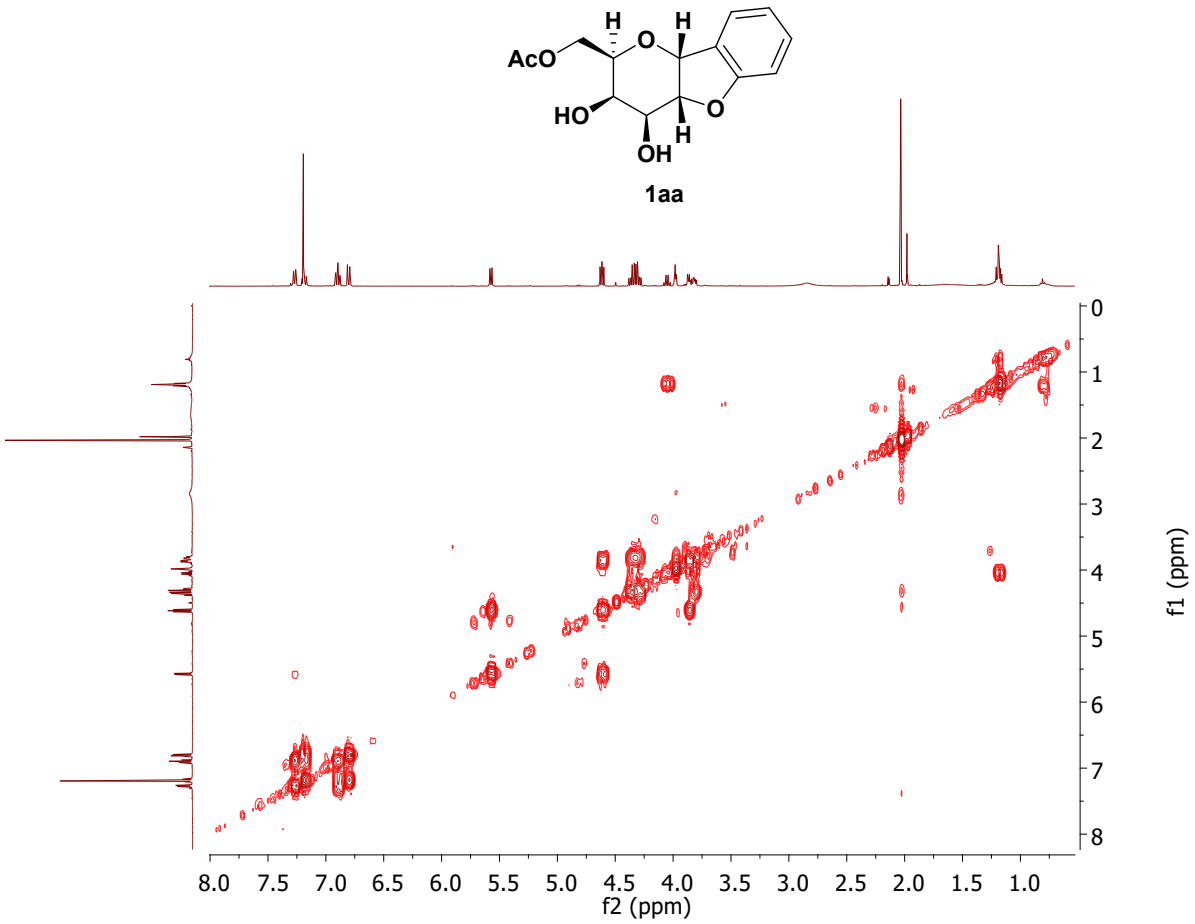




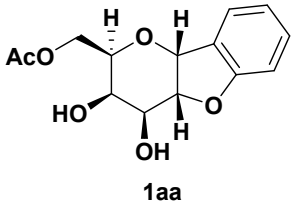



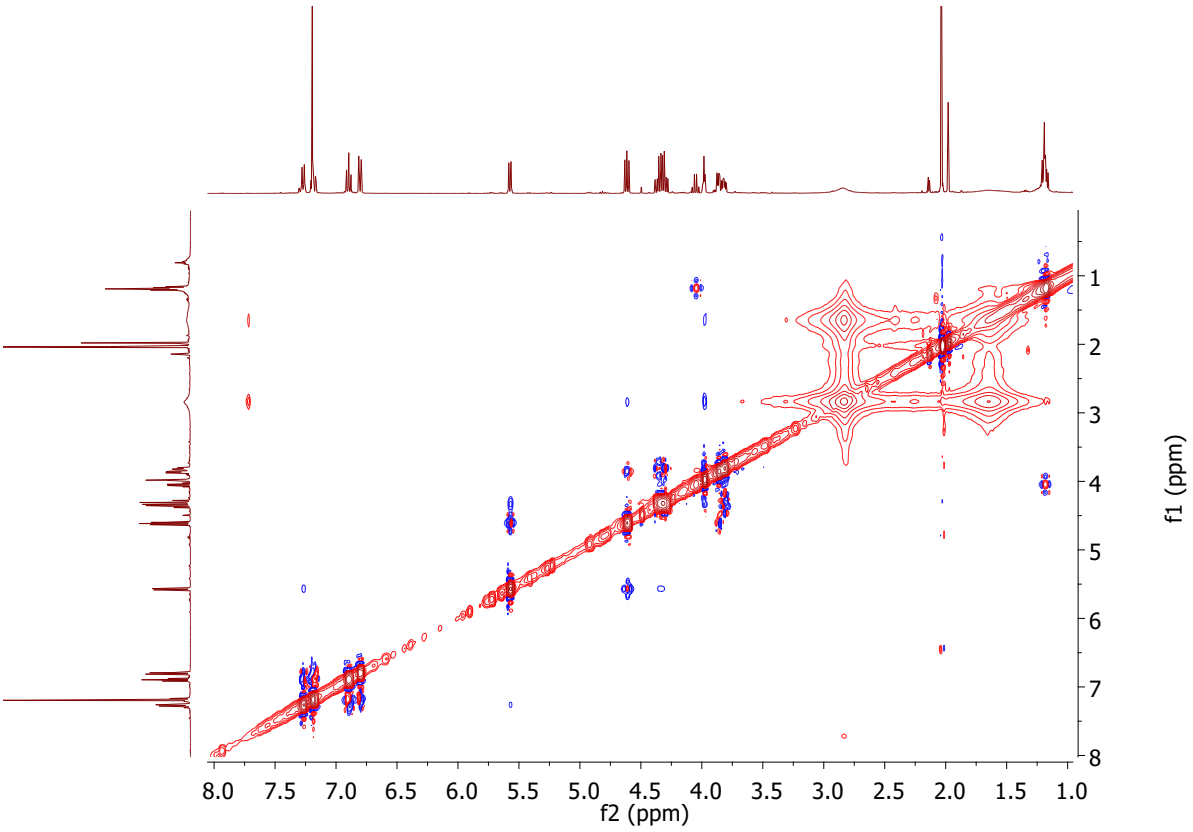

| Atom Position | Type of Atom | $^{1}$H(ppm) | $^{13}$C (ppm) |
|---|---|---|---|
| 1 | CH | 5.57 | 75.5 |
| 2 | CH | 4.61 | 84.1 |
| 3 | CH | 3.86 | 71.3 |
| 4 | CH | 3.98 | 68.0 |
| 5 | CH | 3.82 | 72.0 |
| 6 | CH2 | 4.33 | 62.3 |
| 7 | CH | 7.18 | 130.7 |
| 8 | CH | 6.90 | 121.6 |
| 9 | CH | 7.27 | 125.4 |
| 10 | CH | 6.80 | 111.0 |
| | OAc | 2.03 | 20.9, 171.3 |

**COSY of 1aa**

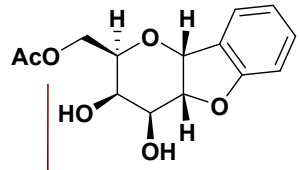

AcO
H
O
H
HO
O
H
OH
1aa
f1 (ppm)
f2 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
0 1 2 3 4 5 6 7 8

**NOESY of 1aa**

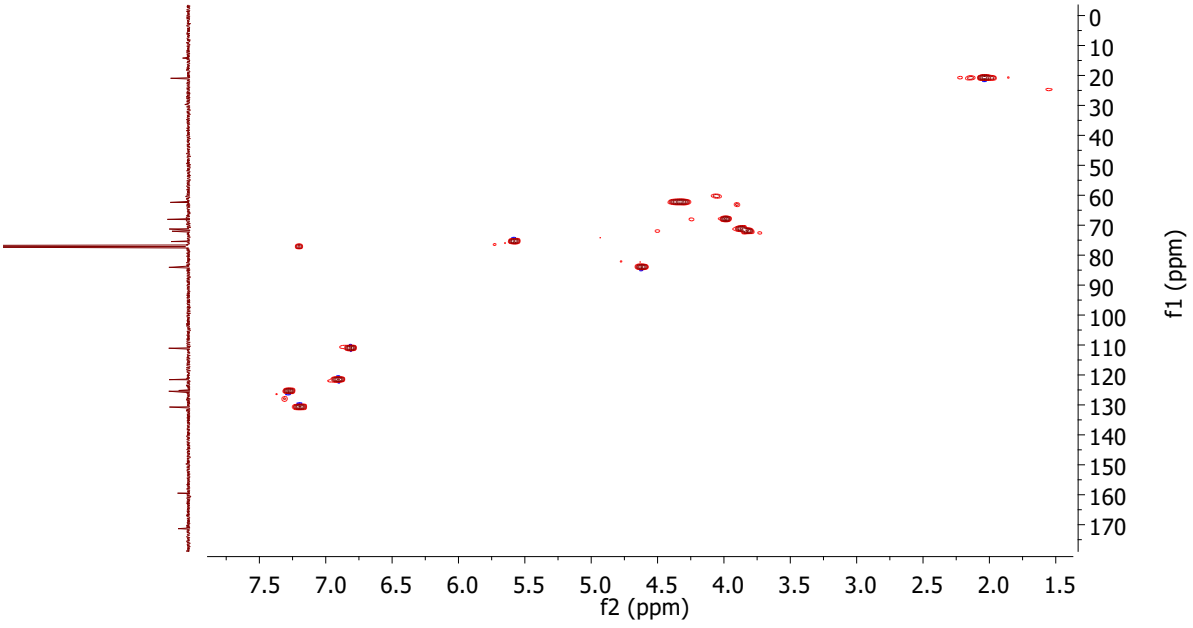

AcO
H
O
H
HO
O
H
OH
1aa



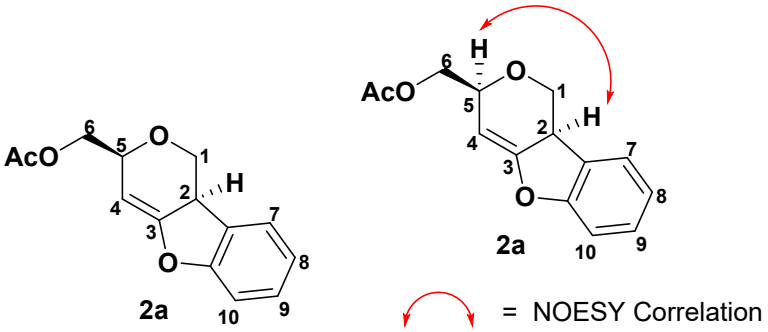

## HSQC of 1aa




1aa



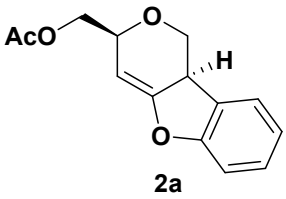
**5c. Structure determination of compound 2a:**

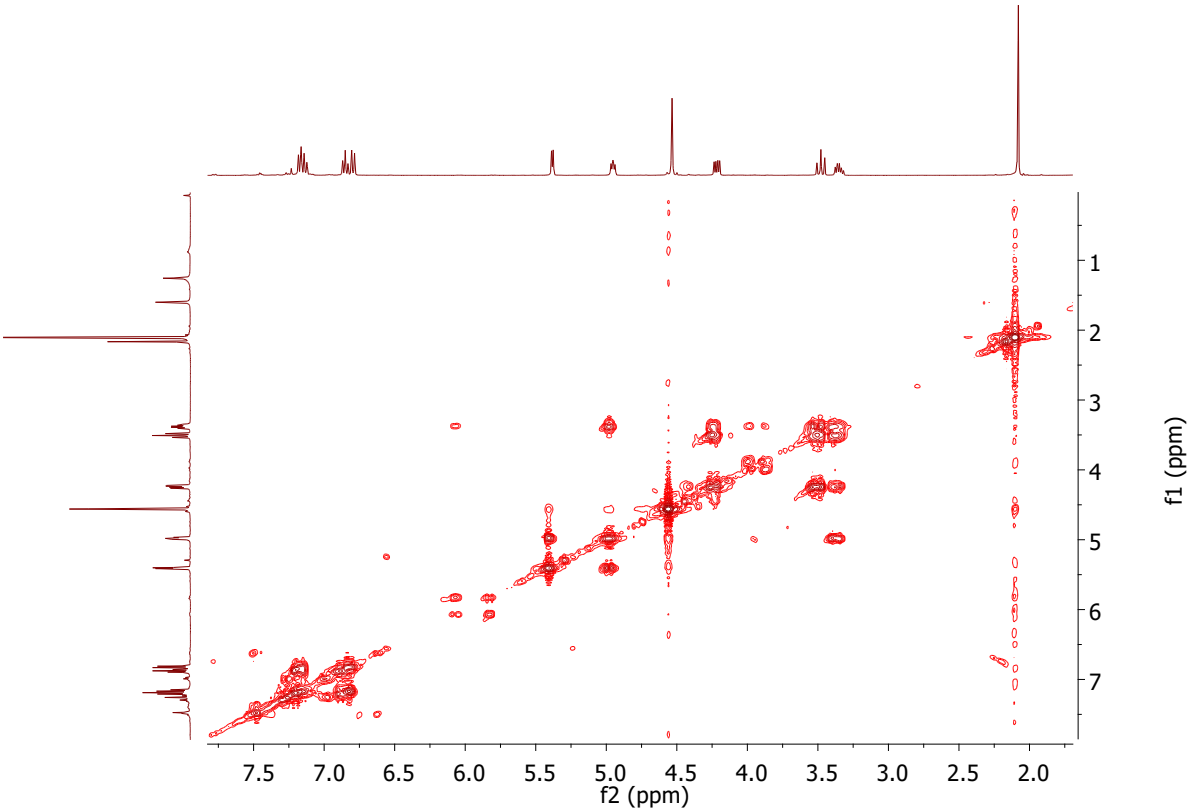



| Atom Position | Type of Atom | $^{1}$H(ppm) | $^{13}$C (ppm) |
|---|---|---|---|
| 1 | CH2 | 3.51, 4.24 | 66.5 |
| 2 | CH | 3.38 | 39.4 |
| 3 | C | - | 159.1 |
| 4 | CH | 5.41 | 98.4 |
| 5 | CH | 4.98 | 75.4 |
| 6 | CH2 | 4.56 | 63.2 |
| 7 | CH | 7.19 | 124.7 |
| 8 | CH | 6.88 | 120.7 |
| 9 | CH | 7.19 | 129.2 |
| 10 | CH | 6.82 | 110.2 |
| | OAc | 2.11 | 20.87, 170.5 |

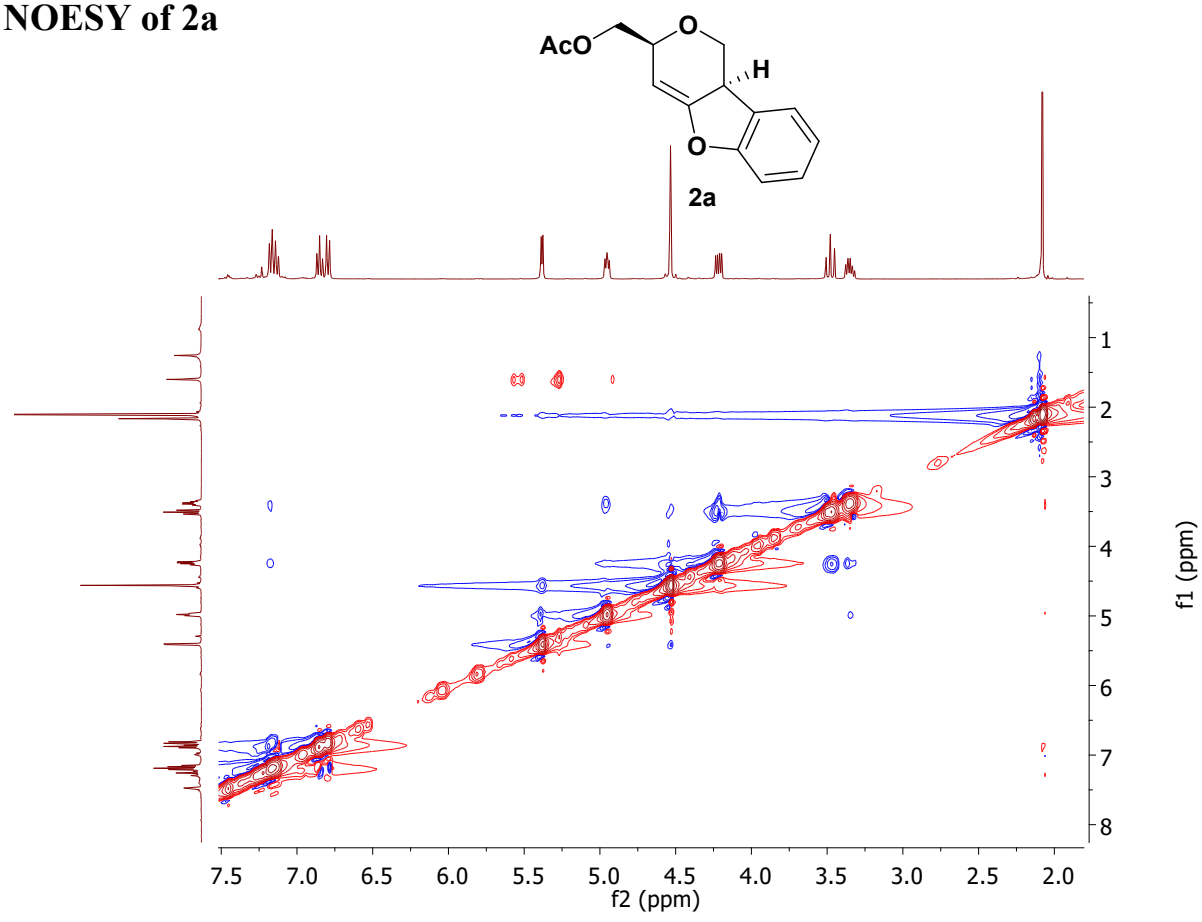
The structure of product **2a** was confirmed by extensive NMR analysis. The furan oxygen is attached at quaternary C-3 at δ value 159.1. In COSY data we observed the correlation between H4-H5 and H1-H2 which confirmed their adjacent nature. In NOESY experiment we observed correlation between H2 and H5 which indicated α stereochemistry of H2. H4 also showed the correlation with H6, this confirmed the structure of 2a.

## COSY of 2a

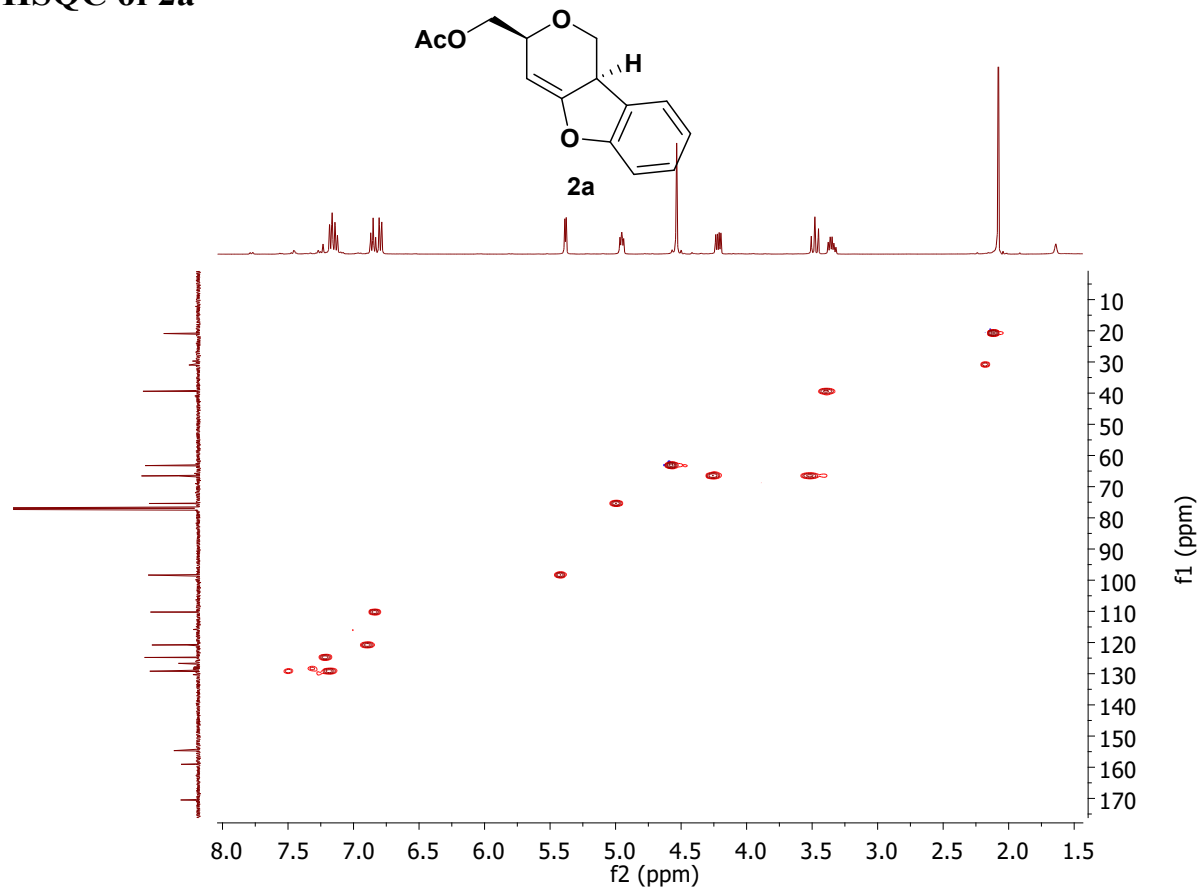



7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f2 (ppm)
1
2
3
4
5
6
7
f1 (ppm)

**NOESY of 2a**


AcO
O
H
O
2a
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f2 (ppm)
1
2
3
4
5
6
7
8
f1 (ppm)

**HSQC of 2a**


AcO
O
H
O
2a
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
f1 (ppm)
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
f2 (ppm)