

# Supporting Information

## Acid-Catalysed Iterative Generation of *o*-Quinone Methides for the Synthesis of Dioxabicyclo[3.3.1]nonanes: Total Synthesis of Myristicyclins A-B

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## General experimental

Melting points are recorded using Tempo melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on Nicolet 6700 spectrophotometer and JASCO, FT/IR-4100 spectrophotometer.  $^1\text{H}$  (400 and 500 MHz) and  $^{13}\text{C}$  (100 and 125MHz) spectra were recorded on Bruker Avance 400 and 500 spectrophotometers. The chemical shifts ( $\delta$  ppm) and coupling constants (Hz) are reported in the standard fashion with reference to internal chloroform (at 7.26 ppm for  $^1\text{H}$  and the central line 77.16 ppm for  $^{13}\text{C}$  of  $\text{CDCl}_3$ ). In the  $^{13}\text{C}$  NMR spectra, the nature of the carbons (C, CH,  $\text{CH}_2$  or  $\text{CH}_3$ ) was determined by recording the DEPT-135 experiment and is given in parentheses. NOE spectrum was recorded in Bruker Avance 400 spectrophotometer.  $^1\text{H}$ - $^1\text{H}$  NOESY spectrum was recorded in Bruker Avance 500 spectrometer. High resolution mass measurements were carried out using Micro mass Q-ToF instrument using direct inlet mode. Analytical thin-layer chromatography (TLC) was performed on glass plates (7.5 x 2.5 and 7.5 x 5.0 cm) coated with Merck silica gel G containing 13% calcium sulphate as binder or on pr 0.2 mm thick Merck 60 F245 silica plates and various combinations of ethyl acetate and hexanes were used as eluent. Visualization of spots was accomplished by exposure to iodine vapour and  $\text{KMnO}_4$  stains. All compounds were purified using silica gel [Acme's silica gel (100-200 mesh)] chromatography (approximately 15-20 g per 1 g of the crude product) and gave spectroscopic data consistent with being  $\geq 95\%$  the assigned structure. All small-scale dry reactions were carried out using standard syringe septum technique. Dry THF was obtained by distillation over sodium-benzophenone ketyl. dichloromethane, benzene, acetonitrile and chloroform were distilled from calcium hydride prior to use.

## EXPERIMENTAL PROCEDURES AND SPECTRAL DATA

**Note:** In the cases wherein diastereomeric mixtures of products were obtained, the data for the major isomer have been mentioned and the diastereomeric ratio measured on the crude reaction mixture by  $^1\text{H}$  NMR.

### Experimental procedure for the synthesis of bicyclic acetals

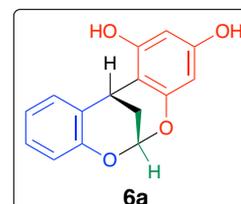
#### (6*S*\*,12*R*\*)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (**6a**):

To a cold (0 °C) magnetically stirred solution of salicylaldehyde (**2a**) (87  $\mu\text{L}$ , 0.82 mmol), ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol), in dry  $\text{CH}_3\text{CN}$  (8 mL), was added trimethyl orthoformate (136  $\mu\text{L}$ , 1.23 mmol) and stirred for 10 min. Then the ethyl vinyl ether (EVE) (**3a**) (124  $\mu\text{L}$ , 1.23 mmol) was added slowly at 0 °C the resulting mixture was stirred at room temperature and then the phenol **5a** (155 mg, 1.23 mmol) in dry  $\text{CH}_3\text{CN}$  (2 mL), was slowly added at 0 °C the resulting mixture was stirred for 1h at 0 °C then slowly warmed to room temperature. After completion of the reaction (TLC control), the reaction mixture was carefully quenched with saturated sodium hydrogen carbonate solution (10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL), the combined organic layer was washed with brine and dried over anhydrous sodium sulphate. Evaporation of the solvent and purification of the residue on silica gel column, using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as an eluent afforded the required bicyclic product **6a** (124 mg, 59%).

**Physical appearance:** Pale red foamy solid.

**R<sub>f</sub>:** 0.4 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3341, 2854, 1626, 1599, 1427, 1221, 1135, 1107, 1121, 902, 753  $\text{cm}^{-1}$ .



**$^1\text{H}$  NMR (500 MHz, DMSO-*d*<sub>6</sub>):**  $\delta$  9.54 (s, 1H), 9.11 (s, 1H), 7.30-7.25 (m, 1H), 7.06 (td,  $J = 7.7, 1.6$  Hz, 1H), 6.87-6.79 (m, 2H), 6.14-6.10 (m, 1H), 5.91 (d,  $J = 2.2$  Hz, 1H), 5.76 (d,  $J = 2.2$  Hz, 1H), 4.17 (q,  $J = 2.9$  Hz, 1H), 2.10-2.00 (m, 2H).

**$^{13}\text{C}$  NMR (125 MHz, DMSO-*d*<sub>6</sub>, DEPT):**  $\delta$  156.7 (C), 154.7 (C), 151.8 (C), 151.0 (C), 128.1 (C), 127.8 (CH), 127.2 (CH), 120.6 (CH), 115.6 (CH), 105.4 (C), 95.7 (CH), 94.1 (CH), 91.6 (CH), 25.3 ( $\text{CH}_2$ ), 23.2 (CH).

**HRMS (ESI,  $\text{M}+\text{Na}^+$ ):**  $m/z$  calcd. for  $\text{C}_{15}\text{H}_{12}\text{NaO}_4$  256.2585, found 256.2583.

#### (6*S*\*,12*R*\*)-9-(benzyloxy)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (**6b**):

The reaction of salicylaldehyde (**2b**) (185 mg, 0.81 mmol), ethyl vinyl ether (EVE) (**3a**) (122  $\mu\text{L}$ , 1.22 mmol) and phenol **5a** (153 mg, 1.22 mmol) in the presence of ( $\pm$ )-camphor sulphonic

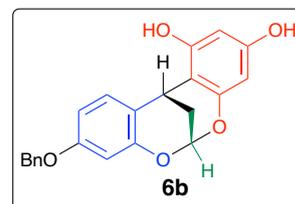
acid (CSA) (9.5 mg, 0.04 mmol), trimethyl orthoformate (135  $\mu\text{L}$ , 1.22 mmol) in dry  $\text{CH}_3\text{CN}:\text{MeOH}$  [3/2v/v] (8 mL) at 0  $^\circ\text{C}$  to room temperature as described for the bicyclic product **6a** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6b** (211 mg, 72%).

**Physical appearance:** White solid.

**m.p.:** 88-90  $^\circ\text{C}$

**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3485, 3064, 2939, 2863, 2245, 1954, 1636, 1457, 1265, 1192, 1055, 831, 762  $\text{cm}^{-1}$ .



**$^1\text{H}$  NMR (500 MHz, Methanol- $d_4$ ):**  $\delta$  7.37-7.17 (m, 6H), 6.49 – 6.43 (m, 2H), 5.97 (q,  $J = 2.0$  Hz, 1H), 5.91 (d,  $J = 2.2$  Hz, 1H), 5.85 (d,  $J = 2.3$  Hz, 1H), 4.91 (s, 2H), 4.18 (q,  $J = 2.6$  Hz, 1H), 2.00 (q,  $J = 3.2$  Hz, 2H).

**$^{13}\text{C}$  NMR (125 MHz, Methanol- $d_4$ , DEPT):**  $\delta$  159.7 (C), 157.8 (C), 156.0 (C), 153.5 (C), 153.4 (C), 138.8 (C), 129.5 (CH), 129.5 (2 x CH), 128.9 (2 x CH), 128.6 (CH), 122.3 (C), 109.0 (CH), 108.2 (C), 103.6 (CH), 96.8 (CH), 95.7 (CH), 93.7 (CH), 71.1 ( $\text{CH}_2$ ), 27.2 ( $\text{CH}_2$ ), 24.7 (CH).

**HRMS (ESI,  $\text{M}+\text{Na}^+$ ):**  $m/z$  calcd. for  $\text{C}_{22}\text{H}_{18}\text{NaO}_5$  385.1046, found 385.1046.

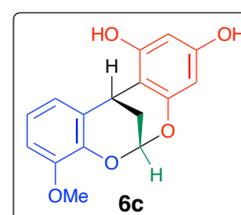
**(6*R*\*,12*R*\*)-8-methoxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (6c):**

The reaction of salicylaldehyde (**2c**) (125 mg, 0.82 mmol), EVE (**3a**) (124  $\mu\text{L}$ , 1.23 mmol) and phenol **5a** (136 mg, 1.23 mmol) in presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (137  $\mu\text{L}$ , 1.23 mol) in dry  $\text{CH}_3\text{CN}$  (8 mL) at 0  $^\circ\text{C}$  to room temperature as described for the bicyclic product **6a** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6c** (175 mg, 74%).

**Physical appearance:** Pale red foamy solid.

**R<sub>f</sub>:** 0.4 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3351, 2976, 2873, 1646, 1609, 1447, 1231, 1125, 1101, 906, 754  $\text{cm}^{-1}$ .



**$^1\text{H}$  NMR (400 MHz, Acetonitrile- $d_3$ ):**  $\delta$  7.36 (s, 1H), 6.92 (dd,  $J = 7.6, 1.7$  Hz, 1H), 6.85-6.71 (m, 1H), 6.12 (q,  $J = 2.0$  Hz, 1H), 5.93 (s, 1H), 5.89 (s, 1H), 4.24 (q,  $J = 2.6$  Hz, 1H), 3.77 (s, 3H), 2.11 (q,  $J = 2.7$  Hz, 2H).

**<sup>13</sup>C NMR (100 MHz, Acetonitrile-*d*<sub>3</sub>, DEPT):**  $\delta$  157.5 (C), 155.2 (C), 153.4 (C), 148.9 (C), 141.4 (C), 129.7 (C), 121.7 (CH), 120.8 (CH), 111.2 (C), 107.5 (C), 96.6 (CH), 95.9 (CH), 93.1 (CH), 56.4 (CH<sub>3</sub>), 26.1 (CH<sub>2</sub>), 24.6 (CH).

**HRMS (ESI, M+H<sup>+</sup>):** m/z calcd. for C<sub>16</sub>H<sub>15</sub>O<sub>5</sub> 287.0914, found 287.0912.

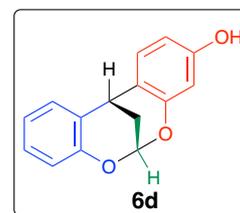
**(6*S*, \*12*R*\*)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-3-ol (6*d*):**

The reaction of salicylaldehyde (**2a**) (87  $\mu$ L, 0.82 mmol), EVE (**3a**) (124  $\mu$ L, 1.23 mmol) and phenol **5b** (1.23 mmol, 136 mg) in presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (136  $\mu$ L, 1.23 mmol) in dry CH<sub>3</sub>CN (8 mL) at 0 °C to room temperature as described for the bicyclic product **6a** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6d** (150 mg, 76%).

**Physical appearance:** Pale red foamy solid.

**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3364, 2925, 1616, 1579, 1437, 1234, 1105, 1112, 911, 756 cm<sup>-1</sup>.



**<sup>1</sup>H NMR (500 MHz, Methanol-*d*<sub>4</sub>):**  $\delta$  7.03 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.97-6.83 (m, 2H), 6.69 (t, *J* = 7.7 Hz, 2H), 6.22 (h, *J* = 6.1, 4.2 Hz, 2H), 5.89 (q, *J* = 2.1 Hz, 1H), 3.69 (q, *J* = 2.6 Hz, 1H), 1.93 (q, *J* = 2.4 Hz, 2H).

**<sup>13</sup>C NMR (125 MHz, Methanol-*d*<sub>4</sub>, DEPT):**  $\delta$  158.2 (C), 153.0 (C), 152.3 (C), 129.4 (C), 129.2 (CH), 128.7 (CH), 128.6 (CH), 122.3 (CH), 119.9 (C), 117.2 (CH), 109.8 (CH), 104.1 (CH), 93.6 (CH), 32.1 (CH), 26.9 (CH<sub>2</sub>).

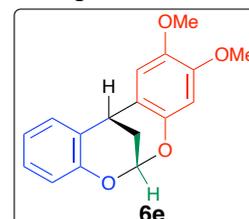
**HRMS (ESI, M+K<sup>+</sup>):** m/z calcd. for C<sub>15</sub>H<sub>12</sub>KO<sub>3</sub> 279.0418, found 279.0411.

**(6*S*\*,12*R*\*)-2,3-dimethoxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine (6*e*):**

The reaction of salicylaldehyde (**2a**) (87  $\mu$ L, 0.82 mmol), EVE (**3a**) (124  $\mu$ L, 1.23 mmol) and phenol **5c** (189 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (136  $\mu$ L, 1.23 mmol) in dry CH<sub>3</sub>CN (8 mL) at 0 °C to room temperature followed by at 0 °C to room temperature as described for the bicyclic product **6a** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6e** (198 mg, 85%).

**Physical appearance:** White Solid

**R<sub>f</sub>:** 0.4 (1: 3, EtOAc:petroleum ether).



**IR (neat):** 2936, 2878, 1636, 1599, 1427, 1221, 1135, 1107, 1121, 907, 765 $\text{cm}^{-1}$ .

**$^1\text{H}$  NMR (500 MHz, Acetonitrile- $d_3$ ):**  $\delta$  7.33 (dt,  $J = 7.4, 1.4$  Hz, 1H), 7.11 (tt,  $J = 8.0, 1.4$  Hz, 1H), 6.91 (tt,  $J = 7.5, 1.2$  Hz, 1H), 6.87 (t,  $J = 4.0$  Hz, 2H), 6.52 (d,  $J = 1.0$  Hz, 1H), 6.12 (p,  $J = 2.1$  Hz, 1H), 3.97 (d,  $J = 3.4$  Hz, 1H), 3.77 (d,  $J = 1.1$  Hz, 3H), 3.74 (d,  $J = 1.1$  Hz, 3H), 2.23 (d,  $J = 1.1$  Hz, 2H).

**$^{13}\text{C}$  NMR (125 MHz, Acetonitrile- $d_3$ , DEPT):**  $\delta$  152.2 (C), 150.0 (C), 145.6 (C), 144.9 (C), 128.9 (C), 128.8 (CH), 128.6 (CH), 122.2 (CH), 118.9 (C), 116.9 (CH), 112.2 (CH), 102.0 (CH), 93.3 (CH), 57.1 ( $\text{CH}_3$ ), 56.5 ( $\text{CH}_3$ ), 31.5 (CH), 26.4 ( $\text{CH}_2$ ).

**HRMS (ESI,  $\text{M}+\text{Na}^+$ ):**  $m/z$  calcd. for  $\text{C}_{17}\text{H}_{16}\text{NaO}_4$  309.0941, found 309.0940.

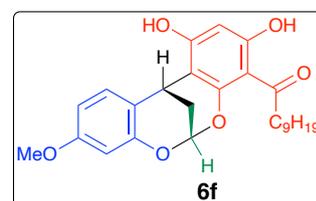
***1-((6S\*,12R\*)-1,3-dihydroxy-9-methoxy-12H-6,12-methanodibenzo[d,g][1,3]dioxocin-4-yl)decan-1-one (6f):***

To a cold (0 °C) magnetically stirred solution of salicylaldehyde **2d** (99 mg, 0.66 mmol), ( $\pm$ )-camphor sulphonic acid (CSA) (7.6 mg 0.04 mmol), in dry  $\text{CH}_3\text{CN}:\text{MeOH}$  [3:1v/v] (8 mL), was added trimethyl orthoformate (110  $\mu\text{L}$ , 0.99 mmol) and stirred for 10 min. Then the EVE (**3a**) (99  $\mu\text{L}$ , 0.99 mmol,) was added slowly at 0 °C the resulting mixture was stirred at room temperature and then the phenol **5d** (277 mg, 0.99 mmol,) in dry  $\text{CH}_3\text{CN}$  (2 mL), was slowly added at 0 °C the resulting mixture was stirred for 1h at 0 °C then slowly warmed to room temperature. After completion of the reaction (TLC control), the reaction mixture was carefully quenched with saturated sodium hydrogen carbonate solution (10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL), the combined organic layer was washed with brine and dried over anhydrous sodium sulphate. Evaporation of the solvent and purification of the residue on silica gel column, using diethyl ether:petroleum ether (from 1% to 25% diethyl ether) as an eluent afforded the required bicyclic product **6f** and **6f'**. The major regio isomer, **6f** (133 mg, 46%) and the minor **6f'** (64 mg, 22%).

**Physical appearance:** Pale brown sticky liquid.

**R<sub>f</sub>:** 0.3 (1: 2.7:0.3,  $\text{Et}_2\text{O}:\text{pet ether}:\text{MeOH}$ ).

**IR (neat):** 3341, 2925, 2854, 1699, 1656, 1599, 1427, 1261, 1135, 1107, 1121, 1045, 902, 753 $\text{cm}^{-1}$ .



**$^1\text{H}$  NMR (400 MHz, Benzene- $d_6$ ):**  $\delta$  14.58 (s, 1H), 6.67 (d,  $J = 2.5$  Hz, 1H), 6.53 (dd,  $J = 8.4, 2.5$  Hz, 1H), 6.23 (s, 1H), 5.91 (s, 1H), 5.73 (q,  $J = 2.1$  Hz, 1H), 4.18 (q,  $J = 2.9$  Hz, 1H), 3.24 (s, 3H), 3.01 (qt,  $J = 16.4, 7.4$  Hz, 2H), 1.73 (p,  $J = 7.4$  Hz, 2H), 1.63-1.53 (m, 2H), 1.34-1.28 (m, 12H), 0.92 (t,  $J = 6.8$  Hz, 3H).

**<sup>13</sup>C NMR (100 MHz, Benzene-*d*<sub>6</sub>, DEPT):**  $\delta$  206.6 (C), 165.9 (C), 160.4 (C), 159.3 (C), 154.7 (C), 152.5 (C), 128.4 (CH), 120.2 (C), 108.6 (C), 107.2 (CH), 106.2 (C), 102.4 (CH), 97.5 (CH), 92.6 (CH), 55.3 (OCH<sub>3</sub>), 45.0 (CH<sub>2</sub>), 32.7 (CH<sub>2</sub>), 30.5 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 25.5 (CH<sub>2</sub>), 25.4 (2 x CH<sub>2</sub>), 23.7 (CH), 23.5 (CH<sub>2</sub>), 14.8 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. for C<sub>26</sub>H<sub>32</sub>NaO<sub>6</sub> 463.0291, found 463.0293.

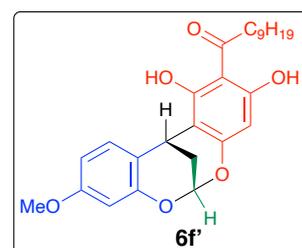
**Minor diastereomer: 1-((6*S*\*,12*R*\*)-1,3-dihydroxy-9-methoxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)decan-1-one (6*f*’):**

**Physical appearance:** Pale yellow sticky liquid.

**R<sub>f</sub>:** 0.4 (1: 2.7:0.3, Et<sub>2</sub>O: pet ether: MeOH).

**IR (neat):** 3361, 2945, 2875, 1708, 1676, 1599, 1427, 1243, 1135, 1107, 1121, 1065, 902, 753 cm<sup>-1</sup>.

**<sup>1</sup>H NMR (500 MHz, Benzene-*d*<sub>6</sub>):**  $\delta$  14.94 (s, 1H), 7.51 (d, *J* = 8.4



Hz, 1H), 6.65 (d, *J* = 2.5 Hz, 1H), 6.47 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.24 (s, 1H), 5.64 (s, 1H), 4.34 (d, *J* = 3.7 Hz, 1H), 3.21 (s, 3H), 3.04 (qt, *J* = 16.2, 7.3 Hz, 2H), 1.62 (dt, *J* = 13.2, 2.7 Hz, 2H), 1.54 (dt, *J* = 13.2, 2.8 Hz, 2H), 1.43-1.37 (m, 2H), 1.30 (m, 10H), 0.90 (t, *J* = 6.9 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, Benzene-*d*<sub>6</sub>, DEPT):**  $\delta$  206.8 (C), 163.5 (C), 160.4 (C), 158.9 (C), 157.6 (C), 152.6 (C), 120.4 (CH), 108.8 (C), 108.4 (CH), 106.0 (C), 102.5 (CH), 95.4 (CH), 93.2 (CH), 55.2 (OCH<sub>3</sub>), 44.7 (CH<sub>2</sub>), 32.6 (CH<sub>2</sub>), 30.5 (CH<sub>2</sub>), 30.4 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 26.2 (CH<sub>2</sub>), 25.4 (CH<sub>2</sub>), 23.5 (CH), 23.4 (CH<sub>2</sub>), 14.7 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. for C<sub>26</sub>H<sub>32</sub>NaO<sub>6</sub> 463.0291, found 463.0293.

**1-((6*S*\*,12*R*\*)-1,3-dihydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-4-yl)decan-1-one (6*g*):**

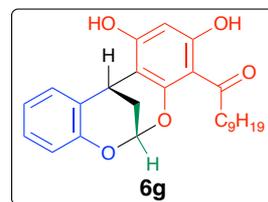
To a cold (0 °C) magnetically stirred solution of salicylaldehyde (**2a**) (87  $\mu$ L, 0.82 mmol), ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol), in dry CH<sub>3</sub>CN (8 mL), was added trimethyl orthoformate (136  $\mu$ L, 1.23 mmol) and stirred for 10 min. Then the EVE (**3a**) (124  $\mu$ L, 1.23 mmol) was added slowly at 0 °C the resulting mixture was stirred at room temperature and then the phenol **5d** (345 mg, 1.23 mmol) in dry CH<sub>3</sub>CN (2 mL), was slowly added at 0 °C the resulting mixture was stirred for 1h at 0 °C then slowly warmed to room temperature. After completion of the reaction (TLC control), the reaction mixture was carefully quenched with saturated sodium hydrogen carbonate solution (10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL), the combined organic layer was washed with brine and dried over

anhydrous sodium sulphate. Evaporation of the solvent and purification of the residue on silica gel column, using EtOAc:petroleum ether (from 1% to 20% ethyl acetate) as an eluent afforded the required bicyclic product **6g** and **6g'**. The major regioisomer, **6g** (185 mg, 55%) and the minor **6g'** (81 mg, 24%).

**Physical appearance:** Pale yellow semi solid.

**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3341, 2925, 2854, 1698, 1626, 1599, 1427, 1231, 1135, 1107, 1121, 1055, 902, 753cm<sup>-1</sup>.



**<sup>1</sup>H NMR (500 MHz, Benzene-*d*<sub>6</sub>):**  $\delta$  14.57 (s, 1H), 7.52-7.46 (m, 1H), 7.02-6.90 (m, 1H), 6.88 (s, 1H), 6.85-6.79 (m, 1H), 6.04 (d, *J* = 7.1 Hz, 1H), 5.72 (s, 1H), 4.25 (d, *J* = 7.7 Hz, 1H), 3.10 (t, *J* = 5.7 Hz, 2H), 1.50 (d, *J* = 13.5 Hz, 2H), 1.31-1.26 (m, 2H), 0.93 (p, *J* = 6.7 Hz, 12H), 0.83 (s, 3H).

**<sup>13</sup>C NMR (125 MHz, Benzene-*d*<sub>6</sub>, DEPT):**  $\delta$  206.7 (C), 165.8 (C), 160.1 (C), 154.8 (C), 151.7 (C), 122.0 (CH), 116.8 (CH), 106.9 (C), 105.9 (C), 97.5 (CH), 92.6 (CH), 44.9 (CH<sub>2</sub>), 32.6 (CH<sub>2</sub>), 30.4 (2 x CH<sub>2</sub>), 30.3 (2 x CH<sub>2</sub>), 30.1 (2 x CH<sub>2</sub>), 25.6 (2 x CH<sub>2</sub>), 25.0 (CH<sub>2</sub>), 24.3 (CH), 23.4 (CH<sub>2</sub>), 14.7 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. for C<sub>25</sub>H<sub>30</sub>NaO<sub>5</sub> 433.1985, found 433.1985

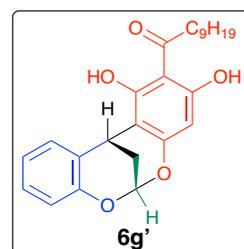
**Minor diastereomer 1-((6*S*\*,12*R*\*)-1,3-dihydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)decan-1-one (6g'):**

**Physical appearance:** Pale yellow sticky solid.

**R<sub>f</sub>:** 0.4 (1: 3, EtOAc: pet ether).

**IR (neat):** 3356, 2945, 2874, 1703, 1626, 1599, 1428, 1251, 1135, 1107, 1121, 1045, 902, 753cm<sup>-1</sup>.

**<sup>1</sup>H NMR (500 MHz, Benzene-*d*<sub>6</sub>):**  $\delta$  14.83 (s, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 6.93-6.87 (m, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 5.77 (d, *J* = 2.6 Hz, 1H), 5.57 (s, 1H), 4.31 (d, *J* = 3.7 Hz, 1H), 3.09-2.90 (m, 2H), 1.73 (p, *J* = 7.3 Hz, 2H), 1.56 (dt, *J* = 13.1, 2.7 Hz, 1H), 1.51 (dt, *J* = 13.0, 2.7 Hz, 1H), 1.27 (m, 12H), 0.91 (t, *J* = 6.9 Hz, 3H).



**<sup>13</sup>C NMR (125 MHz, Benzene-*d*<sub>6</sub>, DEPT):**  $\delta$  206.3 (C), 162.9 (C), 158.2 (C), 157.0 (C), 151.0 (C), 128.4 (CH), 127.7 (CH), 121.4 (CH), 116.0 (CH), 107.5 (C), 105.2 (C), 94.8 (CH), 92.5 (CH), 44.0 (CH<sub>2</sub>), 31.9 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.4 (CH<sub>2</sub>), 25.0 (CH<sub>2</sub>), 24.7 (2 x CH<sub>2</sub>), 23.4 (CH), 22.7 (CH<sub>2</sub>), 14.0 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. for C<sub>25</sub>H<sub>30</sub>NaO<sub>5</sub> 433.1985, found 433.1985.

**(6*S*\*,12*R*\*)-methyl 1,3-dihydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-13-carboxylate (6*h*):**

The reaction of salicylaldehyde (**2a**) (87  $\mu$ L, 0.82 mmol), ethyl aceto-acetate (**3b**) (133  $\mu$ L, 1.23 mmol) and phenol **5a** (155 mg, 1.23 mmol) in presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (136  $\mu$ L, 1.23 mmol) in dry CH<sub>3</sub>CN (8 mL) at 0 °C to room temperature as described for the bicyclic product **6a** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6h** (180 mg, 68%).

**Physical appearance:** Pale brown sticky liquid.

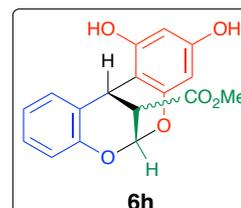
**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3341, 2925, 2854, 1754, 1626, 1599, 1427, 1251, 1135, 1107, 1041, 902, 753cm<sup>-1</sup>.

**<sup>1</sup>H NMR (500 MHz, Methanol-*d*<sub>4</sub>):**  $\delta$  7.32 (dd,  $J$  = 15.5, 7.2 Hz, 2H), 7.01 (dd,  $J$  = 12.0, 4.9 Hz, 1H), 6.99-6.92 (m, 1H), 6.73 (s, 1H), 6.22 (s, 1H), 5.91 (d,  $J$  = 2.3 Hz, 1H), 4.66 (d,  $J$  = 2.4 Hz, 1H), 3.50 (s, 3H), 3.14 (t,  $J$  = 2.6 Hz, 1H).

**<sup>13</sup>C NMR (125 MHz, Methanol-*d*<sub>4</sub>, DEPT):**  $\delta$  170.9 (C), 158.4 (C), 156.5 (C), 153.3 (C), 152.3 (C), 129.6 (CH), 129.1 (C), 128.6 (CH), 122.3 (CH), 116.8 (CH), 105.6 (C), 97.2 (CH), 95.6 (CH), 93.1 (CH), 52.7 (OCH<sub>3</sub>), 41.7 (CH), 28.2 (CH).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. for C<sub>17</sub>H<sub>14</sub>NaO<sub>6</sub> 337.0683, found 337.0679.



**(2*S*\*,4*R*\*)-2-ethoxy-4-(2,4,6-trimethoxyphenyl)chroman (7):**

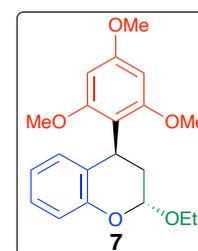
The reaction of salicylaldehyde (**2a**) (87  $\mu$ L, 0.82 mmol), EVE (**3a**) (124  $\mu$ L, 1.23 mmol) and trimethoxy benzene (**5e**) (207 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (136  $\mu$ L, 1.23 mmol) in dry CH<sub>3</sub>CN (8 mL) at 0 °C to room temperature as described for the bicyclic product **6a** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **7** (187 mg, 66%).

**Physical appearance:** White solid.

**R<sub>f</sub>:** 0.5 (1: 2, EtOAc:petroleum ether).

**IR (neat):** 2925, 2854, 1626, 1599, 1427, 1221, 1135, 1107, 1121, 902, 753 cm<sup>-1</sup>.

**<sup>1</sup>H NMR (400 MHz, Chloroform-*d*):**  $\delta$  7.08-6.99 (m, 1H), 6.91-6.79 (m, 1H), 6.78-6.61 (m, 2H), 6.16 (s, 2H), 5.33 (t,  $J$  = 2.5 Hz, 1H), 5.22 (dp,  $J$  = 8.2, 2.7 Hz, 1H),



4.97-4.78 (m, 2H), 3.82 (s, 3H), 3.63 (s, 3H), 3.52 (s, 3H), 2.59 (dddd,  $J = 12.6, 9.8, 4.4, 2.0$  Hz, 1H), 2.12-1.91 (m, 1H), 1.22 (t,  $J = 7.1$  Hz, 3H).

**$^{13}\text{C}$  NMR (100 MHz, Chloroform- $d$ , DEPT):**  $\delta$  160.2 (C), 160.1 (C), 159.8 (C), 153.5 (C), 127.3 (C), 127.3 (CH), 127.0 (CH), 126.3 (CH), 120.5 (CH), 102.3 (C), 98.7 (CH), 97.2 (CH), 91.5 (CH), 63.6 (CH<sub>2</sub>), 56.2 (CH<sub>3</sub>), 55.9 (CH<sub>3</sub>), 55.4 (CH<sub>3</sub>), 31.1 (CH<sub>2</sub>), 25.7 (CH), 15.2 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):**  $m/z$  calcd. for C<sub>20</sub>H<sub>24</sub>NaO<sub>5</sub> 433.1985, found 433.1985.

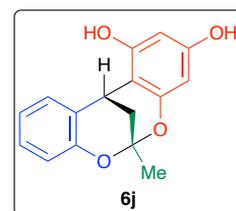
**(6*S*\*,12*R*\*)-6-methyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (6j):**

To a cold (0 °C) magnetically stirred solution of salicylaldehyde (**2a**) (87  $\mu\text{L}$ , 0.82 mmol), ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol), in dry CH<sub>3</sub>CN (8 mL), was added trimethyl orthoformate (280  $\mu\text{L}$ , 2.46 mmol) and stirred for 10 min. Then the ketone **8a** (92  $\mu\text{L}$ , 1.23 mmol) was added slowly at 0 °C the resulting mixture was stirred at room temperature. and then the phenol **5a** (155 mg, 1.23 mmol) in dry CH<sub>3</sub>CN (2 mL), was slowly added at 0 °C the resulting mixture was stirred for 1h at 0 °C then slowly warmed to room temperature. After completion of the reaction (TLC control), the reaction mixture was carefully quenched with saturated sodium hydrogen carbonate solution (10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL), the combined organic layer was washed with brine and dried over anhydrous sodium sulphate. Evaporation of the solvent and purification of the residue on silica gel column, using EtOAc:petroleum ether (from 1% to 15% ethyl acetate) as an eluent afforded the required bicyclic product **6j** (168 mg, 76%)

**Physical appearance:** white solid.

**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3341, 2925, 2854, 1626, 1599, 1427, 1221, 1135, 1107, 1121, 902, 753cm<sup>-1</sup>.



**$^1\text{H}$  NMR (500 MHz, Acetonitrile- $d_3$ ):**  $\delta$  7.30 (dd,  $J = 7.5, 1.7$  Hz, 1H), 7.05 (td,  $J = 7.7, 1.7$  Hz, 1H), 6.86-6.80 (m, 1H), 6.77 (dd,  $J = 8.1, 1.3$  Hz, 1H), 5.90 (d,  $J = 2.2$  Hz, 1H), 5.83 (d,  $J = 2.2$  Hz, 1H), 4.27 (t,  $J = 3.1$  Hz, 1H), 2.13 (d,  $J = 3.1$  Hz, 2H), 1.76 (s, 3H).

**$^{13}\text{C}$  NMR (125 MHz, Acetonitrile- $d_3$ , DEPT):**  $\delta$  157.5 (C), 155.2 (C), 154.2 (C), 153.1 (C), 128.6 (CH), 128.4 (CH), 121.7 (CH), 116.6 (CH), 107.1 (2 x C), 99.1 (C), 96.4 (CH), 95.8 (CH), 31.6 (CH<sub>2</sub>), 27.6 (CH<sub>3</sub>), 27.0 (CH).

**HRMS (ESI, M+Na<sup>+</sup>):**  $m/z$  calcd. for C<sub>16</sub>H<sub>14</sub>NaO<sub>4</sub> 283.0784, found 283.0795.

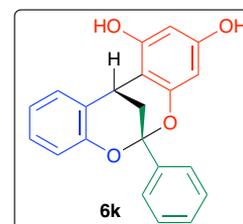
**(6*R*\*,12*R*\*)-6-phenyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (6k):**

The reaction of salicylaldehyde (**2a**) (87  $\mu\text{L}$ , 0.82 mmol), ketone **8b** (144  $\mu\text{L}$ , 1.23 mmol) and phenol **5a** (155 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (280  $\mu\text{L}$ , 2.46 mmol) dry  $\text{CH}_3\text{CN}$  (8 mL) at 0  $^\circ\text{C}$  to room temperature as described for the bicyclic product **6j** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6k** (215 mg, 79%).

**Physical appearance:** White solid.

**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3412, 2895, 2814, 1634, 1609, 1432, 1239, 1147, 1137, 1129, 904, 756 $\text{cm}^{-1}$ .



**$^1\text{H}$  NMR (500 MHz, Acetonitrile- $d_3$ ):**  $\delta$  7.77-7.67 (m, 2H), 7.43 (dt,  $J = 12.8, 6.9$  Hz, 3H), 7.41-7.34 (m, 1H), 7.10 (td,  $J = 7.7, 1.7$  Hz, 1H), 6.93 (d,  $J = 8.1$  Hz, 1H), 6.89 (t,  $J = 7.4$  Hz, 1H), 6.01-5.95 (m, 2H), 4.35 (d,  $J = 3.2$  Hz, 1H), 2.26 (t,  $J = 3.4$  Hz, 2H).

**$^{13}\text{C}$  NMR (125 MHz, Acetonitrile- $d_3$ , DEPT):**  $\delta$  157.7 (C), 155.4 (C), 154.3 (C), 153.2 (C), 142.8 (C), 129.8 (2 x CH), 129.4 (2 x CH), 128.7 (CH), 128.6 (CH), 126.7 (CH), 122.2 (CH), 116.9 (CH), 107.1 (2 x C), 99.8 (C), 96.9 (CH), 96.1 (CH), 33.8 ( $\text{CH}_2$ ), 27.4 (CH).

**HRMS (ESI,  $\text{M}+\text{Na}^+$ ):**  $m/z$  calcd. For  $\text{C}_{21}\text{H}_{16}\text{NaO}_4$  355.0941, found 355.0944.

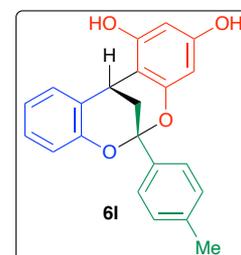
**(6*R*\*,12*R*\*)-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (**6l**):**

The reaction of salicylaldehyde (**2a**) (87  $\mu\text{L}$ , 0.82 mmol), ketone **8c** (165  $\mu\text{L}$ , 1.23 mmol) and phenol **8a** (155 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (280  $\mu\text{L}$ , 2.46 mmol) in dry  $\text{CH}_3\text{CN}$  (8 mL) at 0  $^\circ\text{C}$  to room temperature as described for the bicyclic product **6j** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6l** (213 mg, 75%).

**Physical appearance:** brown foamy solid.

**R<sub>f</sub>:** 0.4 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3338, 2945, 2866, 1621, 1591, 1447, 1224, 1136, 1127, 1101, 902, 751 $\text{cm}^{-1}$ .



**$^1\text{H}$  NMR (500 MHz, Acetonitrile- $d_3$ ):**  $\delta$  7.57 (d,  $J = 7.8$  Hz, 2H), 7.37 (d,  $J = 7.5$  Hz, 1H), 7.24 (d,  $J = 7.8$  Hz, 2H), 7.09 (t,  $J = 7.7$  Hz, 1H), 7.01-6.68 (m, 2H), 5.99 (s, 2H), 4.35 (s, 1H), 2.35 (s, 3H), 2.25-2.15 (m, 2H).

**<sup>13</sup>C NMR (125 MHz, Acetonitrile-*d*<sub>3</sub>, DEPT):**  $\delta$  157.8 (C), 155.5 (C), 154.4 (C), 153.3 (C), 140.0 (C), 139.7 (C), 129.9 (CH), 128.8 (CH), 128.8 (C), 128.6 (2 x CH), 126.7 (CH), 122.1 (2 x CH), 116.9 (CH), 107.1 (C), 99.8 (C), 96.9 (CH), 96.1 (CH), 33.9 (CH<sub>2</sub>), 27.5 (CH), 21.3 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. For C<sub>22</sub>H<sub>18</sub>NaO<sub>4</sub> 369.1097, found 369.1092.

**(6*R*\*,12*R*\*)-6-(4-methoxyphenyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (6*m*):**

The reaction of salicylaldehyde (**2a**) (87  $\mu$ L, 0.82 mmol), ketone **8d** (185 mg, 1.23 mmol) and phenol **5a** (155 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol) and trimethyl orthoformate (280  $\mu$ L, 2.46 mmol) in dry CH<sub>3</sub>CN (8 mL) at 0 °C to room temperature as described for the bicyclic product **6j** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6m** (206 mg, 69%).

**Physical appearance:** Pale brown foamy solid.

**R<sub>f</sub>:** 0.4 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 3365, 2874, 1646, 1595, 1432, 1241, 1165, 1189, 909, 753 cm<sup>-1</sup>.

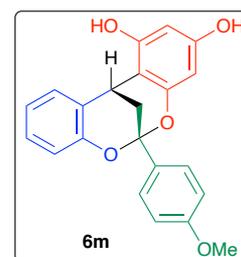
**<sup>1</sup>H NMR (500 MHz, Acetonitrile-*d*<sub>3</sub>):**  $\delta$  7.61 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 7.7 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 2H), 6.89 (t, *J* = 10.6 Hz, 2H), 5.96 (s, 2H), 4.33 (s, 1H), 3.79 (s, 3H), 2.24 (s, 2H).

**<sup>13</sup>C NMR (125 MHz, Acetonitrile-*d*<sub>3</sub>, DEPT):**  $\delta$  161.0 (C) 157.6 (C), 155.3 (C), 154.4 (C), 153.2 (C), 135.0 (C), 128.7 (C), 128.7 (CH), 128.5 (CH), 128.1 (2 x CH), 122.1 (CH), 116.9 (CH), 114.5 (2 x CH), 107.1 (C), 99.7 (C), 96.8 (CH), 96.1 (CH), 56.1 (CH<sub>3</sub>), 33.8 (CH<sub>2</sub>), 27.5 (CH).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. For C<sub>22</sub>H<sub>18</sub>NaO<sub>5</sub> 385.1046, found 385.1047.

**(6*R*\*,12*R*\*)-6-(4-nitrophenyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-1,3-diol (6*n*):**

The reaction of salicylaldehyde (**2a**) (87  $\mu$ L, 0.82 mmol), ketone **8f** (135 mg, 1.23 mmol) and phenol **5a** (155 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol), trimethyl orthoformate (280  $\mu$ L, 2.46 mmol) in dry CH<sub>3</sub>CN (8 mL) at 0 °C to room temperature as described for the bicyclic product **6j** followed by purification on a silica gel



column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6n** (252 mg, 81%).

**Physical appearance:** Pale yellow solid.

**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

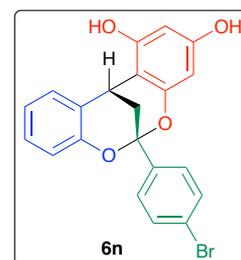
**IR (neat):** 3355, 2945, 2857, 1624, 1609, 1537, 1427, 1358, 1221, 1135, 1107, 1121, 908, 754 cm<sup>-1</sup>.

**<sup>1</sup>H NMR (400 MHz, Acetonitrile-d<sub>3</sub>):** δ 8.25 (dq, *J* = 9.5, 2.6 Hz, 2H),

7.94-7.86 (m, 2H), 7.42-7.35 (m, 2H), 7.00-6.87 (m, 2H), 5.98 (s, 2H), 4.39 (t, *J* = 3.1 Hz, 1H), 2.27 (dd, *J* = 3.2, 1.9 Hz, 2H).

**<sup>13</sup>C NMR (100 MHz, Acetonitrile-d<sub>3</sub>, DEPT):** δ 157.7 (C), 155.3 (C), 153.8 (C), 152.7 (C), 149.2 (C), 128.8 (C), 128.7 (CH), 128.5 (CH), 128.2 (2 x CH), 124.8 (C), 124.5 (2 x CH), 122.5 (CH), 117.0 (CH), 106.9 (C), 99.3 (C), 97.1 (CH), 96.1 (CH), 33.3 (CH), 27.2 (CH<sub>2</sub>).

**HRMS (ESI, M+H<sup>+</sup>):** m/z calcd. For C<sub>21</sub>H<sub>16</sub>O<sub>6</sub> 378.0972, found 378.1002.



**(6R\*,12R\*)-6-(4-bromophenyl)-12H-6,12-methanodibenzo[d,g][1,3]dioxocine-1,3-diol (6o):**

The reaction of salicylaldehyde (**2a**) (87 μL, 0.82 mmol), ketone **8e** (163 mg, 1.23 mmol) and phenol **5a** (155 mg, 1.23 mmol) in the presence of (±)-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol), trimethyl orthoformate (280 μL, 2.46 mmol) in dry CH<sub>3</sub>CN (8 mL) at 0 °C to room temperature as described for the bicyclic product **6j** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6o** (246 mg, 73%).

**Physical appearance:** white solid.

**R<sub>f</sub>:** 0.3 (1: 3, EtOAc:petroleum ether).

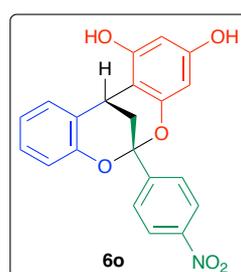
**IR (neat):** 3449, 2935, 2866, 1626, 1599, 1417, 1242, 1137, 1105, 1122, 905, 756 cm<sup>-1</sup>.

**<sup>1</sup>H NMR (500 MHz, Methanol-d<sub>4</sub>):** δ 7.60-7.52 (m, 4H), 7.42-7.37 (m,

1H), 7.10-7.03 (m, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 5.97 (s, 2H), 4.36 (d, *J* = 3.1 Hz, 1H), 2.17 (d, *J* = 3.1 Hz, 2H).

**<sup>13</sup>C NMR (125 MHz, Methanol-d<sub>4</sub>, DEPT):** δ 158.2 (C), 156.2 (C), 154.3 (C), 153.4 (C), 142.8 (C), 132.5 (CH), 129.4 (2 x CH), 129.1 (CH), 129.0 (2 x CH), 128.5 (CH), 123.7 (C), 122.3 (CH), 117.0 (CH), 107.2 (C), 99.7 (C), 97.1 (CH), 95.8 (CH), 34.5 (CH<sub>2</sub>), 28.0 (CH).

**HRMS (ESI, M+K<sup>+</sup>):** m/z calcd. For C<sub>21</sub>H<sub>15</sub>BrKO<sub>4</sub> 433.0093, found 433.0092.



**(6*S*\*,12*R*\*)-ethyl 1,3-dihydroxy-6-methyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-13-carboxylate (6*p*):**

The reaction of salicylaldehyde (**2a**) (87  $\mu\text{L}$ , 0.82 mmol), ketone **8g** (155.3  $\mu\text{L}$ , 1.23 mmol) and phenol **5a** (155 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol), trimethyl orthoformate (280  $\mu\text{L}$ , 2.45 mmol) in dry  $\text{CH}_3\text{CN}$  (8 mL) at 0  $^\circ\text{C}$  to room temperature as described for the bicyclic product **6j** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **6p** (214 mg, 76%).

**Physical appearance:** Pale red sticky liquid.

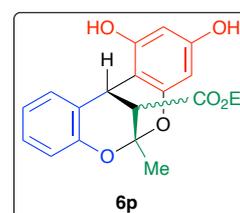
**R<sub>f</sub>:** 0.4 (1:3, EtOAc:petroleum ether).

**IR (neat):** 3358, 2954, 2854, 1754, 1646, 1587, 1427, 1233, 1137, 1107, 1121, 906, 757 $\text{cm}^{-1}$ .

**<sup>1</sup>H NMR (400 MHz, Benzene-*d*<sub>6</sub>):**  $\delta$  7.55 (td,  $J = 7.4, 1.6$  Hz, 2H), 6.15 (d,  $J = 2.1$  Hz, 1H), 6.10 (d,  $J = 2.1$  Hz, 1H), 6.03 (s, 2H), 4.80 (d,  $J = 2.6$  Hz, 1H), 3.69 (q,  $J = 7.3$  Hz, 2H), 2.76 (d,  $J = 2.6$  Hz, 1H), 2.05 (s, 3H), 0.78 (t,  $J = 7.1$  Hz, 3H).

**<sup>13</sup>C NMR (100 MHz, Benzene-*d*<sub>6</sub>, DEPT):**  $\delta$  169.9 (C), 156.3 (C), 154.7 (C), 153.7 (C), 152.9 (C), 128.9 (CH), 125.2 (CH), 121.9 (CH), 116.8 (CH), 107.9 (C), 104.9 (C), 98.7 (C), 97.3 (CH), 96.9 (CH), 61.8 (CH<sub>2</sub>), 45.1 (CH), 31.4 (CH), 26.4 (CH<sub>3</sub>), 14.1 (CH<sub>3</sub>).

**HRMS (ESI, M+H<sup>+</sup>):**  $m/z$  calcd. For  $\text{C}_{19}\text{H}_{19}\text{O}_6$  343.1176, found 343.1177.



**2-methoxy-2-methyl-4-(2,4,6-trimethoxyphenyl)chroman (9):**

The reaction of salicylaldehyde (**2a**) (87  $\mu\text{L}$ , 0.82 mmol), ketone **8a** (92  $\mu\text{L}$ , 1.23 mmol) and trimethoxy benzene (**5e**) (207 mg, 1.23 mmol) in the presence of ( $\pm$ )-camphor sulphonic acid (CSA) (9.5 mg, 0.04 mmol), trimethyl orthoformate (272  $\mu\text{L}$ , 2.46 mmol) in dry  $\text{CH}_3\text{CN}$  (8 mL) at 0  $^\circ\text{C}$  to room temperature as described for the bicyclic product **6j** followed by purification on a silica gel column using EtOAc:petroleum ether (from 1% to 25% ethyl acetate) as eluent furnished the bicyclic product **9** (216 mg, 76%).

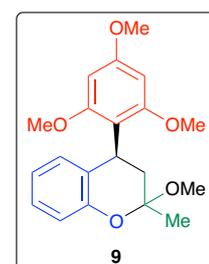
**Physical appearance:** White foamy solid.

**m.p.:** 88-90  $^\circ\text{C}$

**R<sub>f</sub>:** 0.6 (1: 3, EtOAc:petroleum ether).

**IR (neat):** 2936, 1581, 1368, 1221, 1185, 1132, 1042, 731 $\text{cm}^{-1}$ .

**<sup>1</sup>H NMR (500 MHz, Benzene-*d*<sub>6</sub>):**  $\delta$  7.14 (d,  $J = 17.1$  Hz, 1H), 7.08-7.01 (m, 2H), 6.78 (td,  $J = 7.5, 1.5$  Hz, 1H), 6.20 (d,  $J = 2.3$  Hz, 1H), 6.09 (d,  $J = 2.3$  Hz, 1H), 5.55



(dd,  $J = 12.7, 6.1$  Hz, 1H), 3.40 (d,  $J = 1.7$  Hz, 3H), 3.34 (s, 3H), 3.23-3.16 (m, 3H), 3.02 (s, 3H), 2.76 (t,  $J = 12.8$  Hz, 1H), 2.20 (dd,  $J = 12.9, 6.1$  Hz, 1H), 1.45 (d,  $J = 1.7$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz, Benzene- $d_6$ , DEPT):  $\delta$  161.0 (C), 160.8 (C), 160.4, (C) 153.1 (C), 128.6 (C), 127.9 (CH), 126.9 (CH), 121.2 (CH), 117.3 (CH), 113.2 (C), 99.5 (C), 92.9 (CH), 91.4 (CH), 55.8 (CH<sub>3</sub>), 55.5 (CH<sub>3</sub>), 55.1 (CH<sub>3</sub>), 49.0 (CH<sub>3</sub>), 37.6 (CH<sub>2</sub>), 28.2 (CH), 23.7 (CH<sub>3</sub>).

HRMS (ESI,  $\text{M}+\text{Na}^+$ ):  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{24}\text{NaO}_5$  367.1516, found 367.1517.

### A Gram Scale Total Synthesis of Myristicyclins A and B

#### *1-((6S\*,12R\*)-9-(benzyloxy)-1,3-dihydroxy-12H-6,12-methanodibenzo[d,g][1,3]dioxocin-4-yl)decan-1-one (6r)*:

To a cold (0 °C) magnetically stirred solution of salicylaldehyde **2b** (1.03 g, 5.69 mmol), ( $\pm$ )-camphor sulphonic acid (CSA) (66 mg, 0.28 mmol), in dry  $\text{CH}_3\text{CN}:\text{MeOH}$  [3:1v/v] (40 mL), was added trimethyl orthoformate (945  $\mu\text{L}$ , 8.54 mmol) and stirred for 10 min. Then the ethyl vinyl ether (**3a**) (811  $\mu\text{L}$ , 8.54 mmol) was added slowly at 0 °C the resulting mixture was stirred at room temperature and then the phenol **5d** (2.393 g, 8.54 mmol) in dry  $\text{CH}_3\text{CN}$  (10 mL), was slowly added at 0 °C the resulting mixture was stirred for 1h at 0 °C then slowly warmed to room temperature. After completion of the reaction (TLC control), the reaction mixture was carefully quenched with saturated sodium hydrogen carbonate solution (10 mL). The aqueous layer was extracted with diethyl ether (3 x 40 mL), the combined organic layer was washed with brine and dried over anhydrous sodium sulphate. Evaporation of the solvent and purification of the residue on silica gel column, using diethyl ether: pet ether (from 1% to 25% diethyl ether) as an eluent afforded the required bicyclic product **6r** and **6r'** the major regioisomer **6r** (1.294 g, 44%) and the minor **6r'** (509 mg, 17%).

**Physical appearance:** white foamy solid.

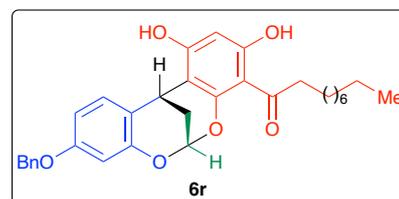
**R<sub>f</sub>:** 0.3 (1: 2.7:0.3, Et<sub>2</sub>O: pet ether: MeOH).

**IR (neat):** 3341, 2925, 2854, 1696, 1626, 1599, 1427, 1249, 1135, 1107, 1121, 1055, 903, 755  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR (500 MHz, Benzene- $d_6$ ):  $\delta$  14.75 (s, 1H), 14.69

(s, 1H), 7.45 (d,  $J = 8.4$  Hz, 2H), 7.31-7.22 (m, 2H), 7.10 (d,  $J = 7.4$  Hz, 1H), 6.90-6.86 (m, 2H), 6.84 (d,  $J = 2.5$  Hz, 1H), 6.03 (s, 1H), 5.81 (t,  $J = 2.1$  Hz, 1H), 4.74 (s, 2H), 4.26 (q,  $J = 2.7$  Hz, 1H), 3.17-3.00 (m, 2H), 1.47 (s, 2H), 1.44-1.37 (m, 2H), 1.07-1.02 (m, 12H), 0.99 (t,  $J = 6.8$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz, Benzene- $d_6$ , DEPT):  $\delta$  206.7 (C), 165.8 (C), 159.6 (C), 159.6 (C), 154.7 (C), 152.5 (C), 137.7 (C), 129.0 (2x CH), 128.6 (2 x CH), 128.0 (CH), 120.5 (C), 109.4 (CH),



107.3 (C), 106.1 (C), 103.5 (CH), 97.6 (CH), 92.7 (CH), 70.5 (CH<sub>2</sub>), 45.0 (CH<sub>2</sub>), 32.7 (CH<sub>2</sub>), 30.5 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 30.1 (2 x CH<sub>2</sub>), 25.6 (CH<sub>2</sub>), 25.3 (2 x CH<sub>2</sub>), 23.7 (CH), 23.5 (CH<sub>2</sub>), 14.8 (CH<sub>3</sub>).

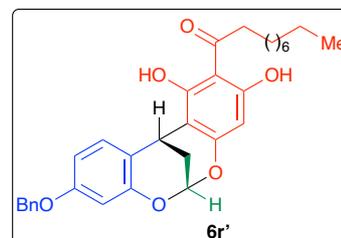
**HRMS (ESI, M+H<sup>+</sup>):** m/z calcd. for C<sub>32</sub>H<sub>37</sub>O<sub>6</sub> 517.2585 found 517.2579.

**Minor diastereomer 1-((6S\*,12R\*)-9-(benzyloxy)-1,3-dihydroxy-12H-6,12-methanodibenzo[d,g][1,3]dioxocin-2-yl)decan-1-one (6r<sup>2</sup>):**

**Physical appearance:** white solid.

**R<sub>f</sub>:** 0.3 (1: 2.7:0.3, Et<sub>2</sub>O: pet ether: MeOH).

**IR (neat):** 3401, 2965, 2834, 1705, 1636, 1589, 1447, 1231, 1135, 1107, 1121, 1049, 902, 753cm<sup>-1</sup>.



**<sup>1</sup>H NMR (500 MHz, Benzene-*d*<sub>6</sub>):** δ 14.84 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 2H), 7.04 (d, *J* = 7.3 Hz, 3H), 6.74 (s, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 5.76 (s, 1H), 5.44 (s, 1H), 4.62 (s, 2H), 4.30 (s, 1H), 2.98 (qt, *J* = 16.3, 7.5 Hz, 2H), 1.73 (p, *J* = 7.2 Hz, 2H), 1.58 (d, *J* = 13.2 Hz, 1H), 1.51 (d, *J* = 13.2 Hz, 1H), 1.33 (t, *J* = 8.2 Hz, 2H), 1.28 (d, *J* = 23.4 Hz, 10H), 0.91 (t, *J* = 7.0 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, Benzene-*d*<sub>6</sub>, DEPT):** δ 206.9 (C), 163.5 (C), 159.5 (C), 158.4 (C), 157.6 (C), 152.5 (C), 137.9 (C), 129.5 (2 x CH), 129.0 (CH), 128.6 (2 x CH), 128.0 (C), 120.6 (C), 109.3 (CH), 108.9 (C), 105.8 (C), 103.5 (CH), 95.4 (CH), 93.2 (CH), 70.4 (CH<sub>2</sub>), 44.7 (CH<sub>2</sub>), 32.6 (CH<sub>2</sub>), 30.4 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 26.0 (CH<sub>2</sub>), 25.4 (CH<sub>2</sub>), 23.5 (CH), 23.4 (CH<sub>2</sub>), 14.7 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):** m/z calcd. for C<sub>32</sub>H<sub>36</sub>NaO<sub>6</sub> 539.2404, found 539.2407.

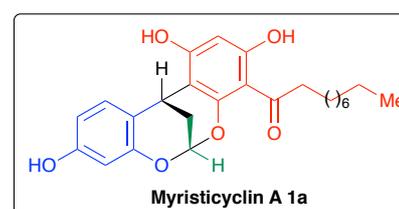
**1-((6S\*,12R\*)-1,3,9-trihydroxy-12H-6,12-methanodibenzo[d,g][1,3]dioxocin-4-yl)decan-1-one (1a):<sup>1</sup>**

To a magnetically stirred solution of Benzyl ether **6r** (1.29 g) in dry THF:MeOH [1:1v/v] (18 mL), was added Pd(OH)<sub>2</sub>/C (10%) and stirred for 1.5h, at rt in an atmosphere of hydrogen created by evacuative displacement of air by hydrogen (balloon) and then the catalyst was filtered off through a celite pad. Evaporation of the solvent and purification of the residue on silica gel column, using ethyl acetate: pet ether as an eluent afforded the required bicyclic product myristicyclins A (**1a**) (1.006g, 96%).

**Physical appearance:** Pale red solid.

**R<sub>f</sub>:** 0.3 (1: 2.7:0.3, EtOAc: petroleum ether:MeOH).

**IR (neat):** 3341, 2935, 2844, 1699, 1629, 1597, 1457, 1261, 1135, 1107, 1121, 1048, 902, 756cm<sup>-1</sup>.



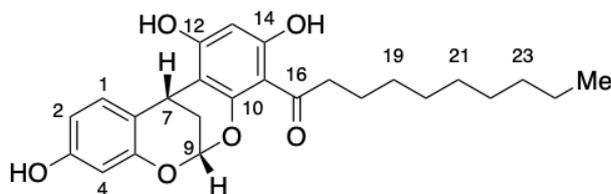
**<sup>1</sup>H NMR (500 MHz, Methanol-*d*<sub>4</sub>):**  $\delta$  6.96 (d, *J* = 8.4 Hz, 1H), 6.14 (d, *J* = 6.8 Hz, 2H), 6.00 (s, 1H), 5.74 (s, 1H), 4.05 (d, *J* = 3.8 Hz, 1H), 3.06-2.56 (m, 2H), 1.87 (qt, *J* = 13.2, 2.8 Hz, 2H), 1.45 (hept, *J* = 6.7 Hz, 2H), 1.30-0.99 (m, 12H), 0.71 (t, *J* = 6.8 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, Methanol-*d*<sub>4</sub>, DEPT):**  $\delta$  207.1 (C), 165.9 (C), 162.8 (C), 158.1 (C), 155.3 (C), 152.9 (C), 129.6 (CH), 120.2 (C), 109.6 (CH), 108.7 (C), 105.3 (C), 103.9 (CH), 97.2 (CH), 93.6 (CH), 45.4 (CH<sub>2</sub>), 33.2 (CH<sub>2</sub>), 30.8 (2 x CH<sub>2</sub>), 30.8 (CH<sub>2</sub>), 30.6 (CH<sub>2</sub>), 26.5 (2 x CH<sub>2</sub>), 24.3 (CH), 23.9 (CH<sub>2</sub>), 14.6 (CH<sub>3</sub>).

**HRMS (ESI, M+Na<sup>+</sup>):** *m/z* calcd. for C<sub>25</sub>H<sub>30</sub>NaO<sub>6</sub> 449.1936, found 449.1934

#### Comparison of <sup>1</sup>H NMR spectral data of myristicyclins A (1a) in CD<sub>3</sub>OD

Reported <sup>a</sup>	Synthesized
7.19 (d, <i>J</i> = 9.0 Hz, 1H)	6.96 (d, <i>J</i> = 8.4 Hz, 1H),
6.30 (m, 2H)	6.14 (d, <i>J</i> = 6.8 Hz, 2H),
6.19 (s, 1H)	6.00 (s, 1H), .)
5.81 (s, 1H)	5.74 (s, 1H),
4.28 (s, 1H)	4.05 (d, <i>J</i> = 3.8 Hz, 1H),
3.04- 2.95 (m, 2H)	3.06 – 2.56 (m, 2H)
2.10 (d, <i>J</i> = 13.0 Hz, 1H)	1.87 (d, <i>J</i> = 13.2 Hz, 1H)
2.05 (d, <i>J</i> = 13.0 Hz 1H)	1.83 (d, <i>J</i> = 13.3 Hz, 1H)
1.66 (m, 2H)	1.45 (m, 2H),
1.40-1.31 (m, 12H)	1.30 – 0.99 (m, 12H),
0.91 (t, <i>J</i> = 7.0Hz, 3H)	0.71 (t, <i>J</i> = 6.8 Hz, 3H)



### Comparison of $^{13}\text{C}$ NMR spectral data of myristicyclins A (1a) in $\text{CD}_3\text{OD}$

Positions	Reported <sup>a</sup>	Synthesized	Positions	Reported <sup>a</sup>	Synthesized
16	206.9	207.1	13	97.1	97.2
12	165.8	165.9	9	93.5	93.6
14	162.8	162.8	17	45.2	45.4
3	158	158.1	23	33.1	33.2
10	155.1	155.3	19	30.7	30.8
5	152.8	152.9	20-22	30.6	30.8
1	129.4	129.6	8	26.4	30.6
6	120.1	120.2	18	26.4	26.5
11	109.5	109.6	7	23.8	24.3
2	108.7	108.7	24	23.7	23.9
15	105.2	105.3	25	14.4	14.6
4	103.8	103.9			

<sup>a</sup> Ireland, C. M. and coworkers, *Org. Lett.* **2014**, *16*, 346.

### *1-((6S\*,12R\*)-1,3,9-trihydroxy-12H-6,12-methanodibenzo[d,g][1,3]dioxocin-2-yl)decan-1-one (1b):<sup>1</sup>*

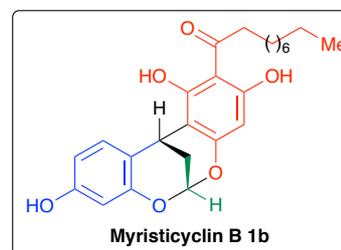
To a magnetically stirred solution of benzyl ether **6r'** (509 mg) in dry THF:MeOH [1:1v/v] (18 mL), was added Pd(OH)<sub>2</sub>/C (10%) and stirred for 1.5h at rt in an atmosphere of hydrogen created by evacuative displacement of air by hydrogen (balloon) and then the catalyst was filtered off through a celite pad. Evaporation of the solvent and purification of the residue on silica gel column, using ethyl acetate: pet ether as an eluent afforded the required bicyclic product myristicyclins B (**1b**) (0.376g, 91%).

**Physical appearance:** Pale red solid.

**R<sub>f</sub>:** 0.4 (1: 2.7:0.3, EtOAc: petroleum ether: MeOH).

**IR (neat):** 3361, 2936, 2825, 1705, 1636, 1595, 1427, 1221, 1129, 1108, 1121, 1066, 906, 759cm<sup>-1</sup>.

**<sup>1</sup>H NMR (500 MHz, Methanol-*d*<sub>4</sub>):**  $\delta$  6.99 (d, *J* = 8.2 Hz, 1H), 6.17-6.10 (m, 2H), 5.87 (s, 1H), 5.69 (s, 1H), 4.04 (s, 1H), 2.87 (p, *J* = 8.8, 7.7 Hz, 2H), 1.92 (d, *J* = 13.4 Hz, 1H), 1.87 (d, *J* = 13.2 Hz, 1H), 1.46 (q, *J* = 7.6 Hz, 2H), 1.11 (s, 12H), 0.72 (t, *J* = 6.9 Hz, 3H).

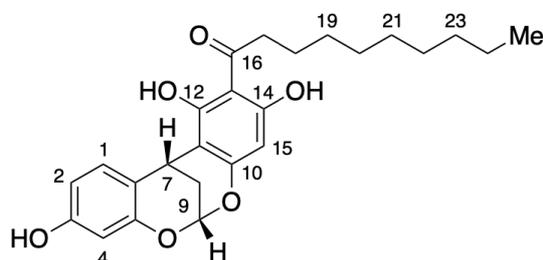


<sup>13</sup>C NMR (125 MHz, Methanol-*d*<sub>4</sub>, DEPT): δ 208.3 (C), 163.7 (C), 162.3 (C), 158.7 (C), 158.6 (C), 153.0 (C), 129.7 (CH), 120.2 (C), 109.6 (CH), 108.2 (C), 106.6 (C), 103.9 (CH), 95.5 (CH), 94.0 (CH), 45.1 (CH<sub>2</sub>), 33.2 (CH<sub>2</sub>), 30.8 (2 x CH<sub>2</sub>), 30.6 (CH<sub>2</sub>), 27.2 (CH<sub>2</sub>), 26.3 (2 x CH<sub>2</sub>), 24.0 (CH), 23.9 (CH<sub>2</sub>), 14.6 (CH<sub>3</sub>).

HRMS (ESI, M+H<sup>+</sup>): m/z calcd. for C<sub>25</sub>H<sub>31</sub>O<sub>6</sub> 427.2115, found 427.2112.

#### Comparison of <sup>1</sup>H NMR spectral data of myristicyclins B (1b) in CD<sub>3</sub>OD

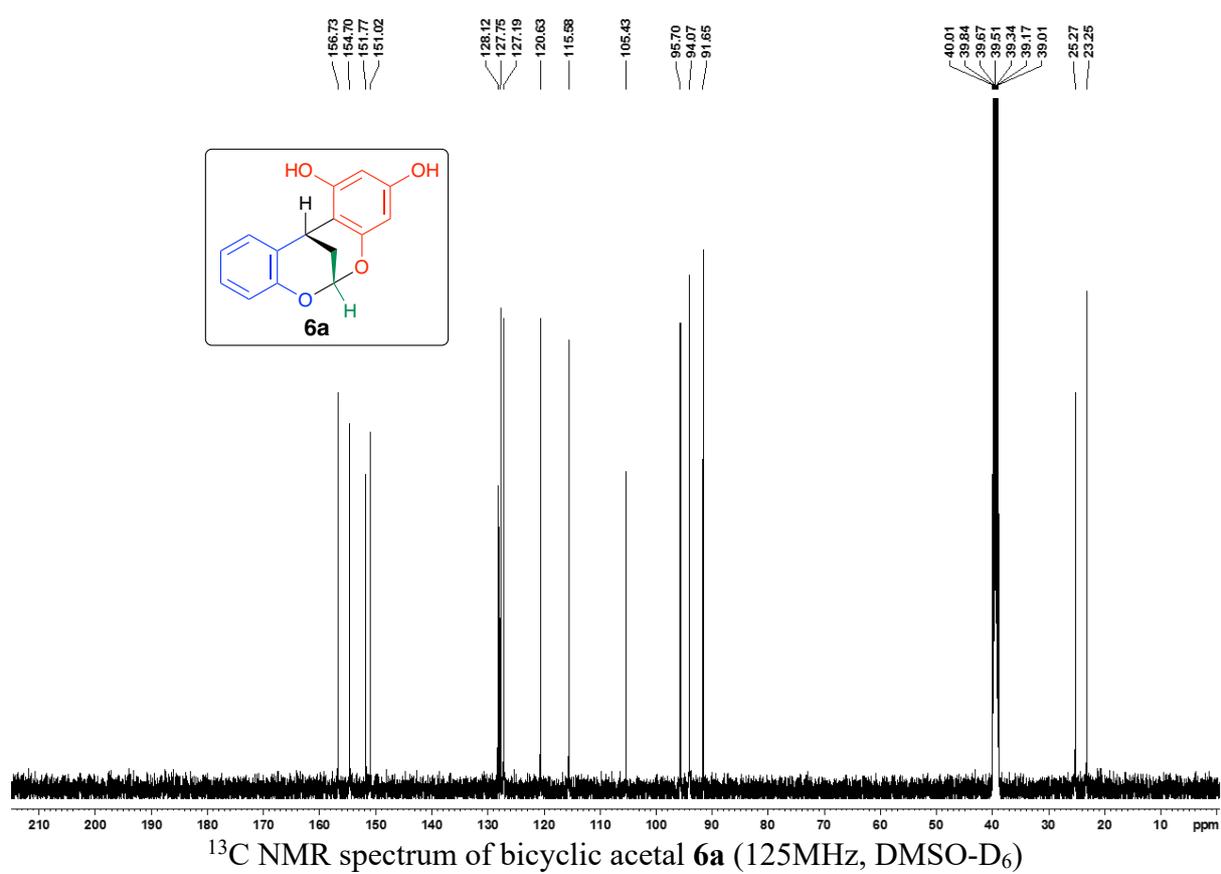
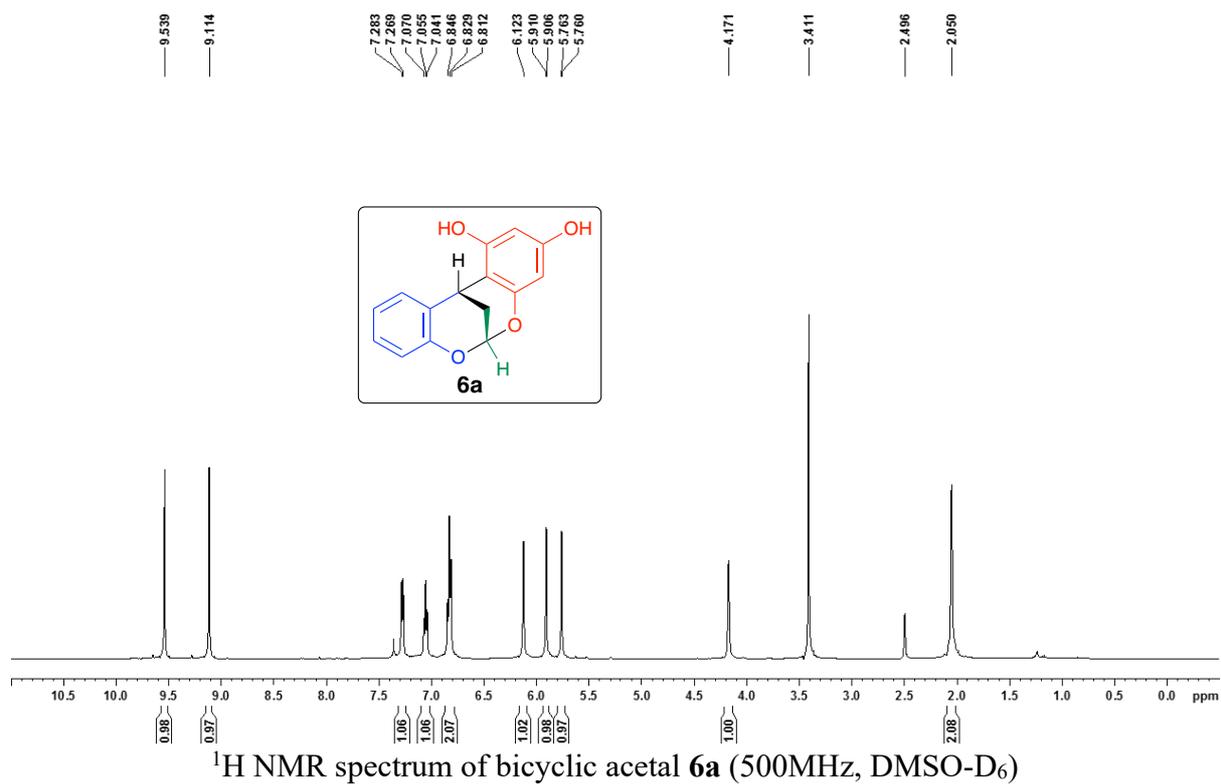
Reported <sup>a</sup>	Synthesized
7.16 (d, <i>J</i> = 8.2 Hz, 1H)	6.99 (d, <i>J</i> = 8.2 Hz, 1H)
6.27 (m, 2H)	6.17 (m, 2H)
6.04 (brs, 1H)	5.87 (s, 1H)
5.77 (s, 1H)	5.69 (s, 1H),
4.22 (brs, 1H)	4.04 (s, 1H)
3.09, (t, <i>J</i> = 7.5 Hz, 2H)	2.87 (t, <i>J</i> = 7.7 Hz, 2H)
2.09 (dd, <i>J</i> = 12.0, 2.5 Hz, 1H)	1.92 (d, <i>J</i> = 13.4 Hz, 1H),
2.07 (dd, <i>J</i> = 12.0, 2.5 Hz, 1H)	1.87 (d, <i>J</i> = 13.2 Hz, 1H),
1.61 (m, 2H)	1.46 (m, 2H),
1.32-1.25 (m, 12H)	1.11 (m, 12H),
0.90 (t, <i>J</i> = 9.8 Hz, 3H)	0.72 (t, <i>J</i> = 9.6 Hz, 3H)

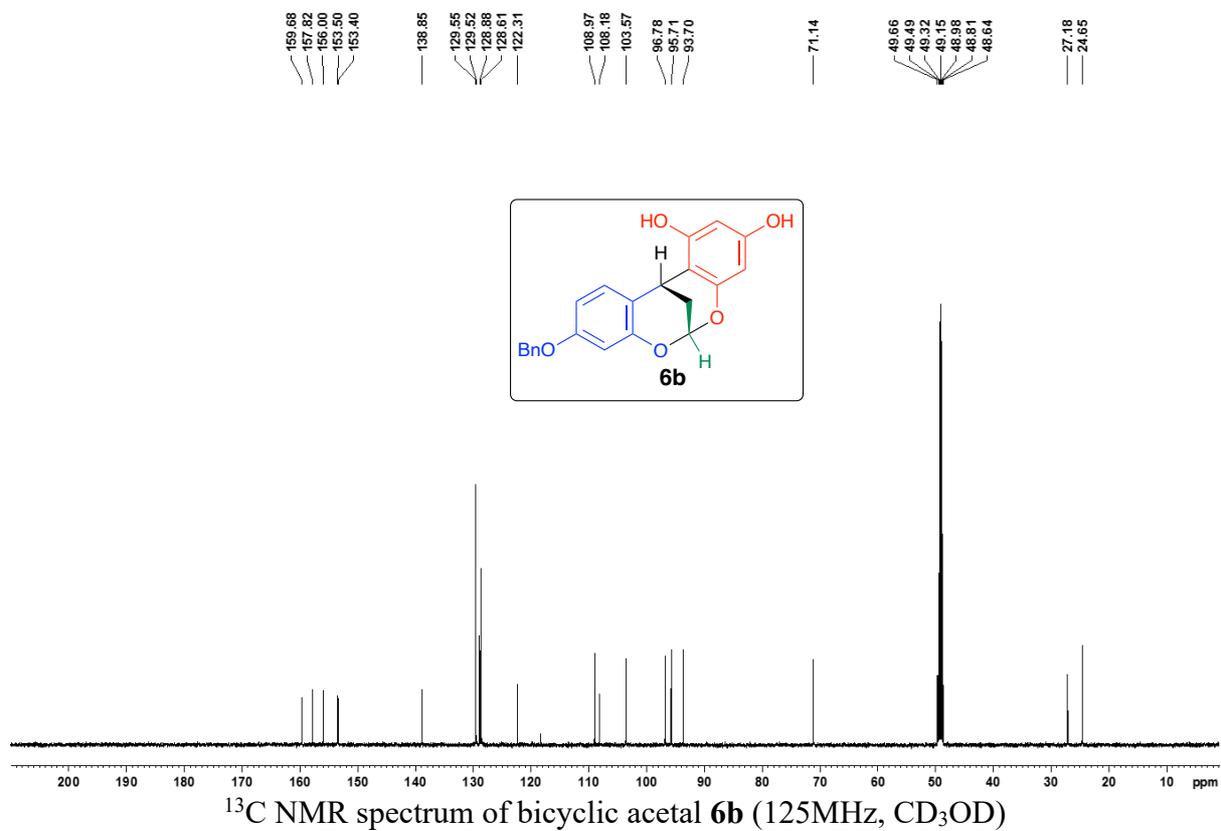
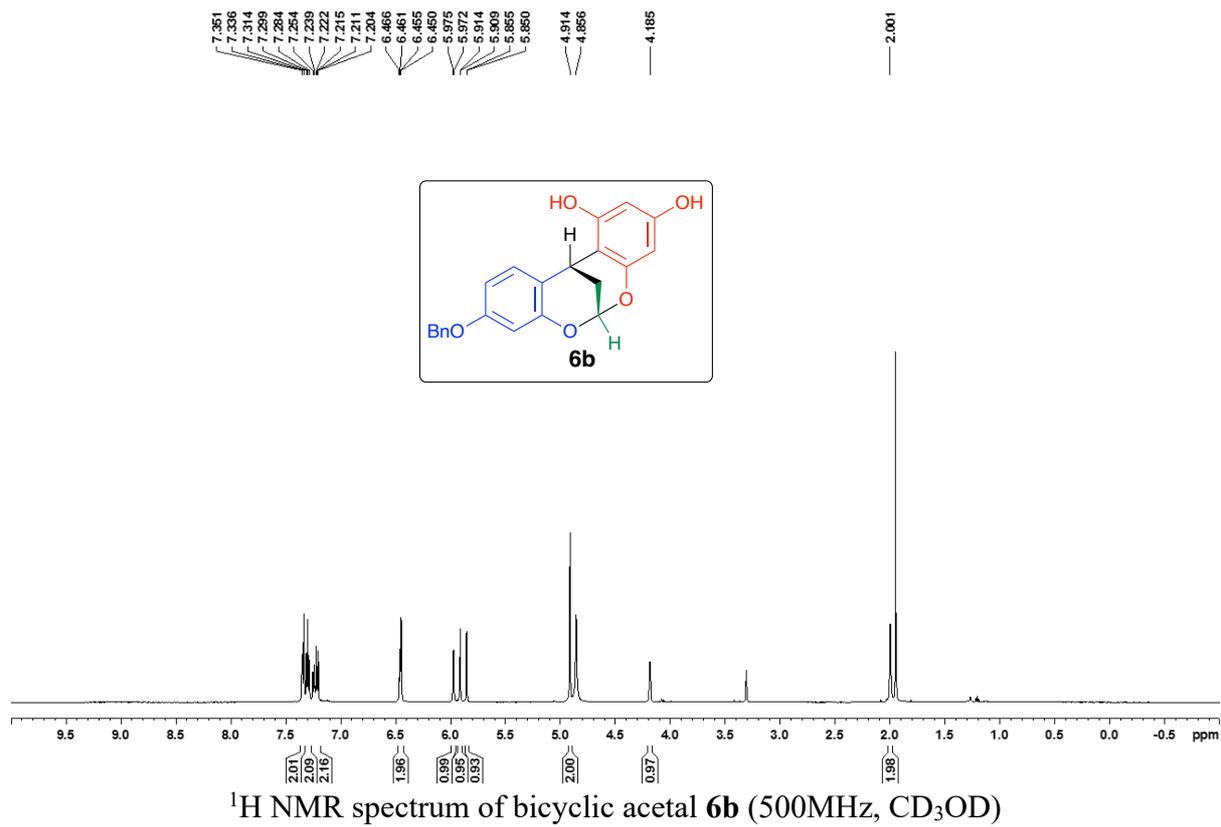


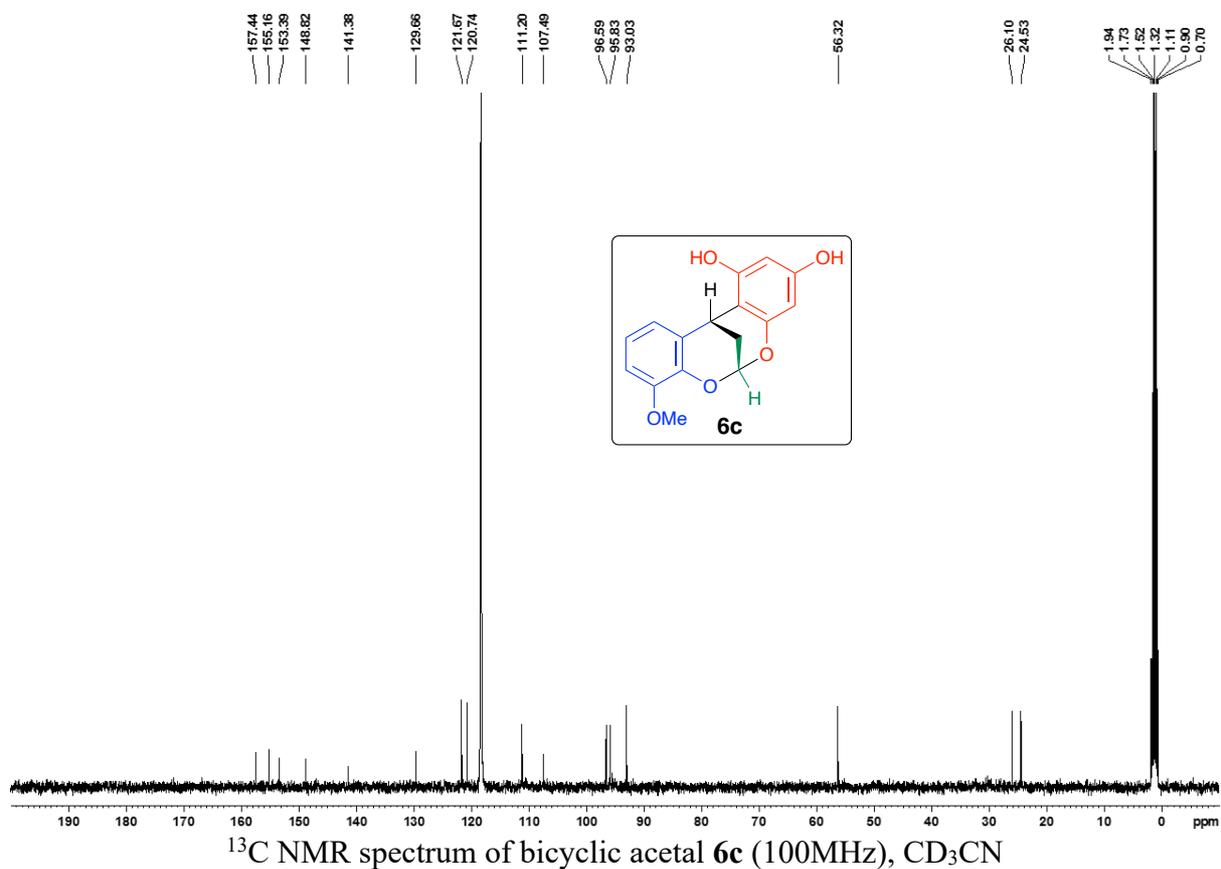
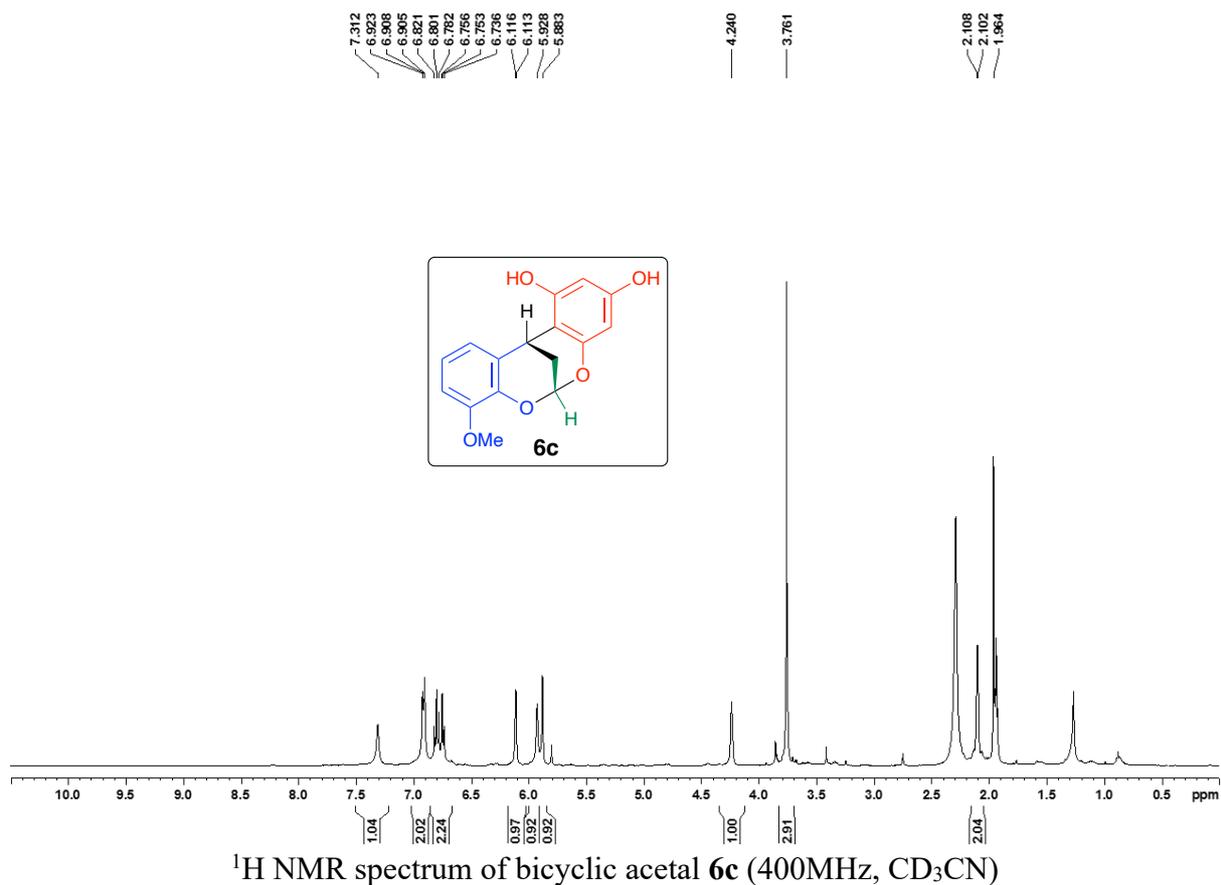
#### Comparison of <sup>13</sup>C NMR spectral data of myristicyclins B (1b) in CD<sub>3</sub>OD

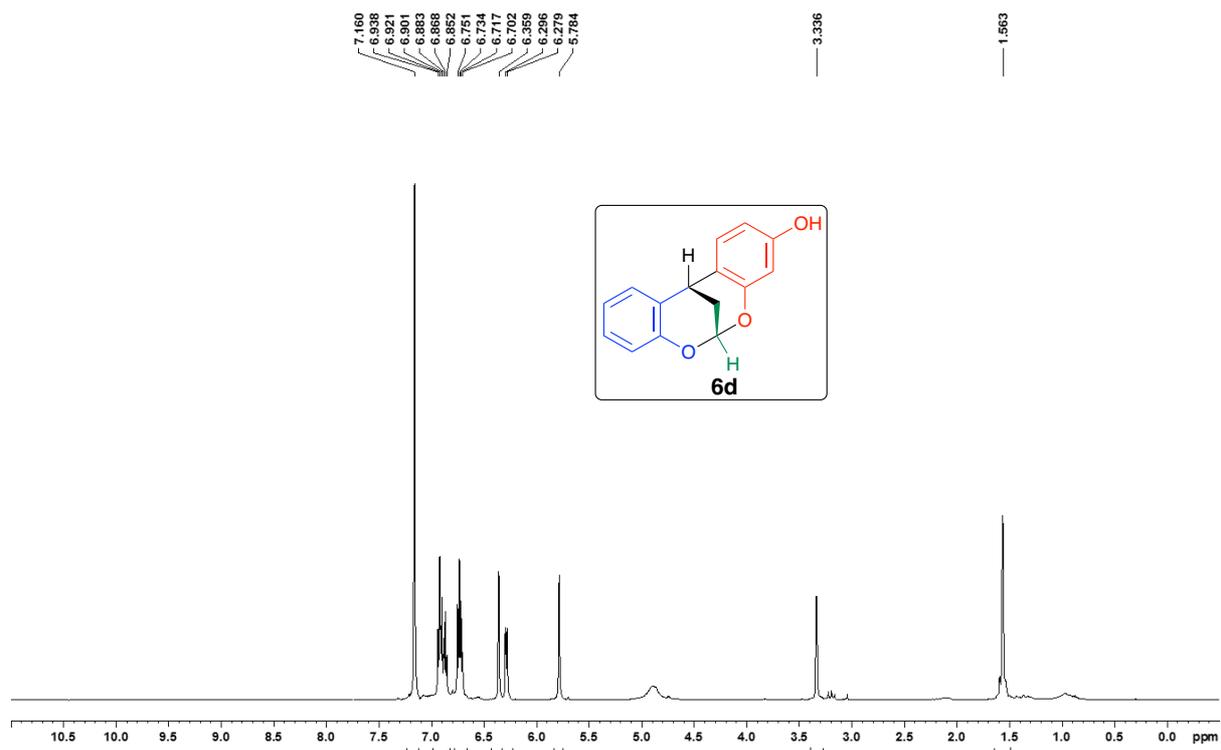
Positions	Reported <sup>a</sup>	Synthesized	Positions	Reported <sup>a</sup>	Synthesized
16	208.2	208.3	15	98*	95.5
14	164*	163.7	9	93.8	94.0
12	161.2	162.3	17	45	45.1
10	158.5	158.7	23	33	33.2
3	157.9	158.6	19	30.6	30.8
5	152.8	153.0	20-22	30.4	30.6
1	129.5	129.7	8	27	27.2
6	120	120.2	18	26.1	26.3
2	109.5	109.6	7	23.8	24.0
11	108.2	108.2	24	23.7	23.9
4	103.8^	106.6	25	14.4	14.6
13	103.4	103.9			

<sup>a</sup> Ireland and co-workers *Org. Lett.* **2014**, *16*, 346

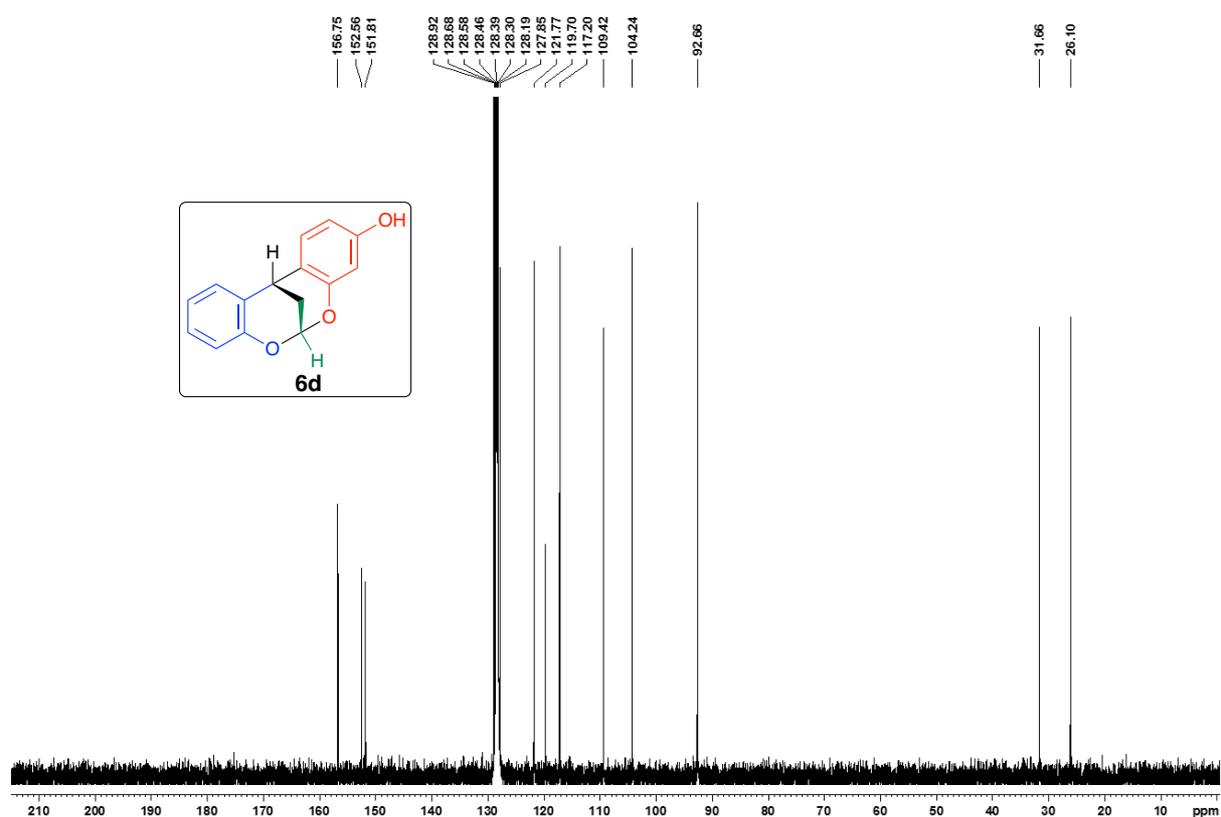




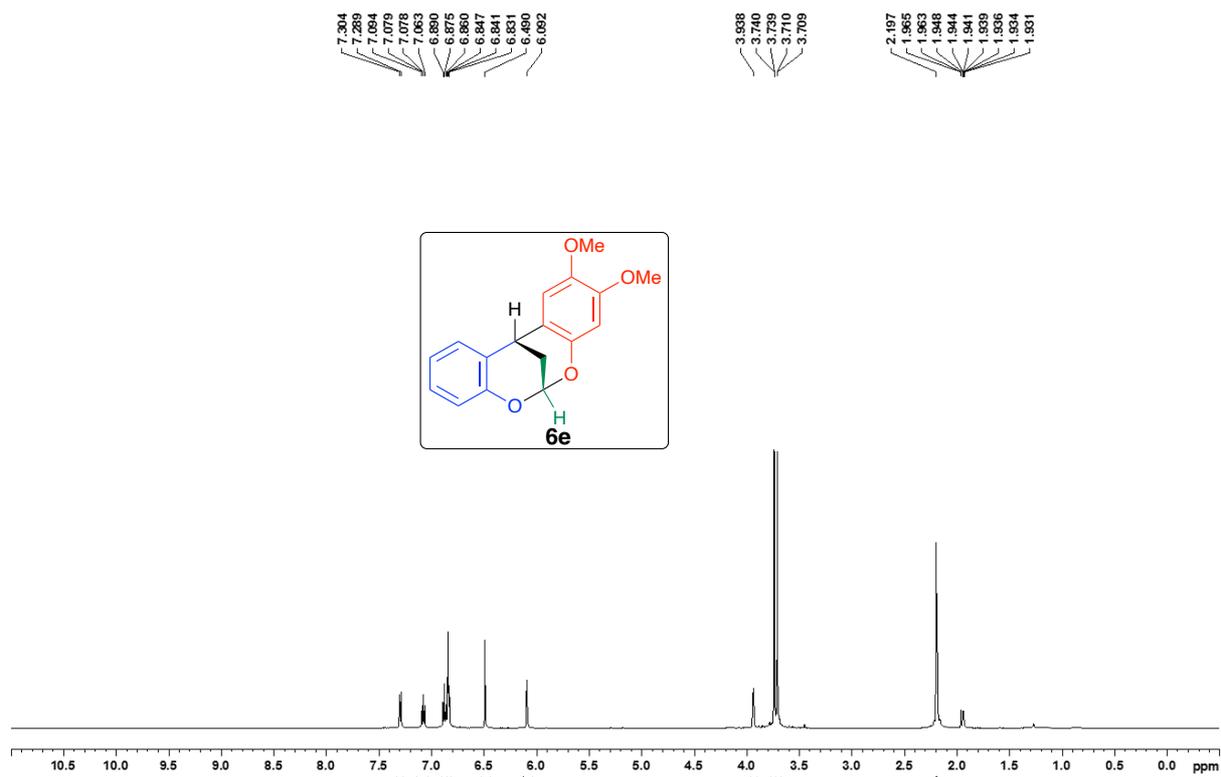




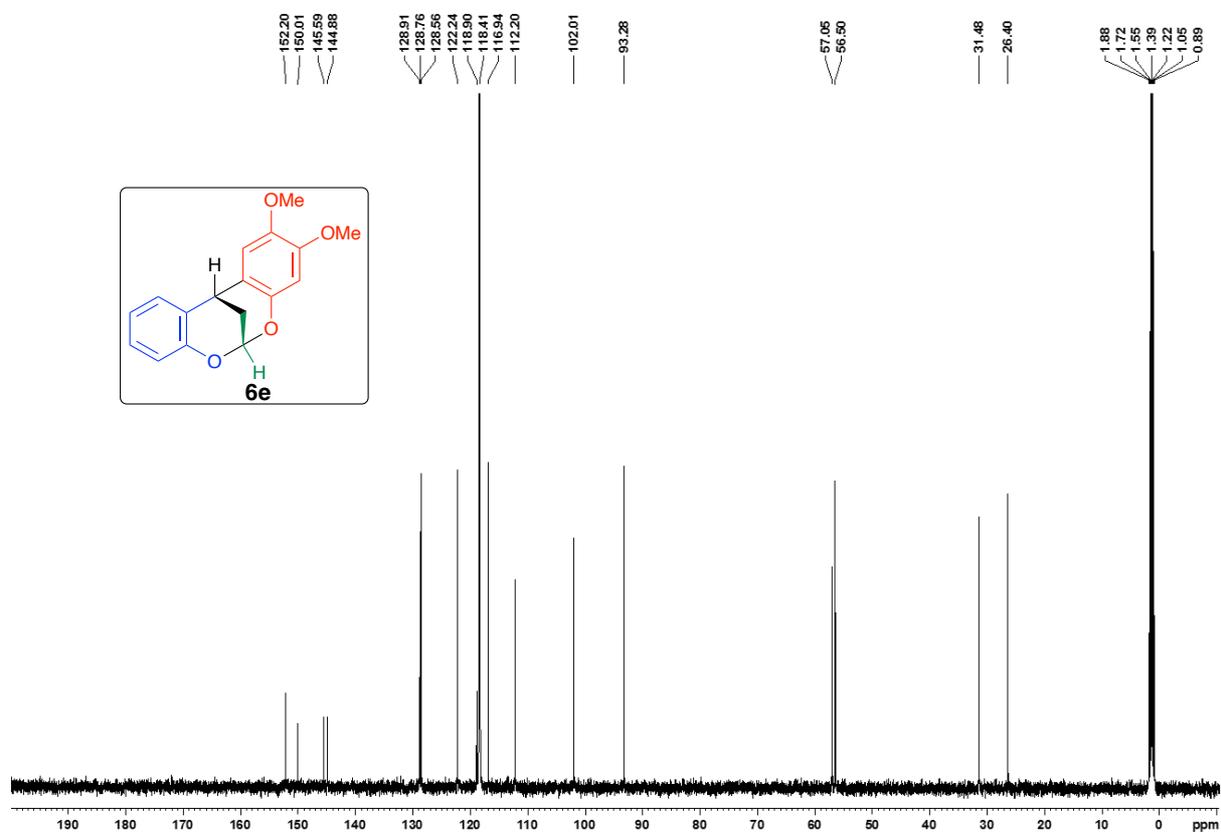
$^1\text{H}$  NMR spectrum of bicyclic acetal **6d** (500MHz,  $\text{CD}_3\text{OD}$ )



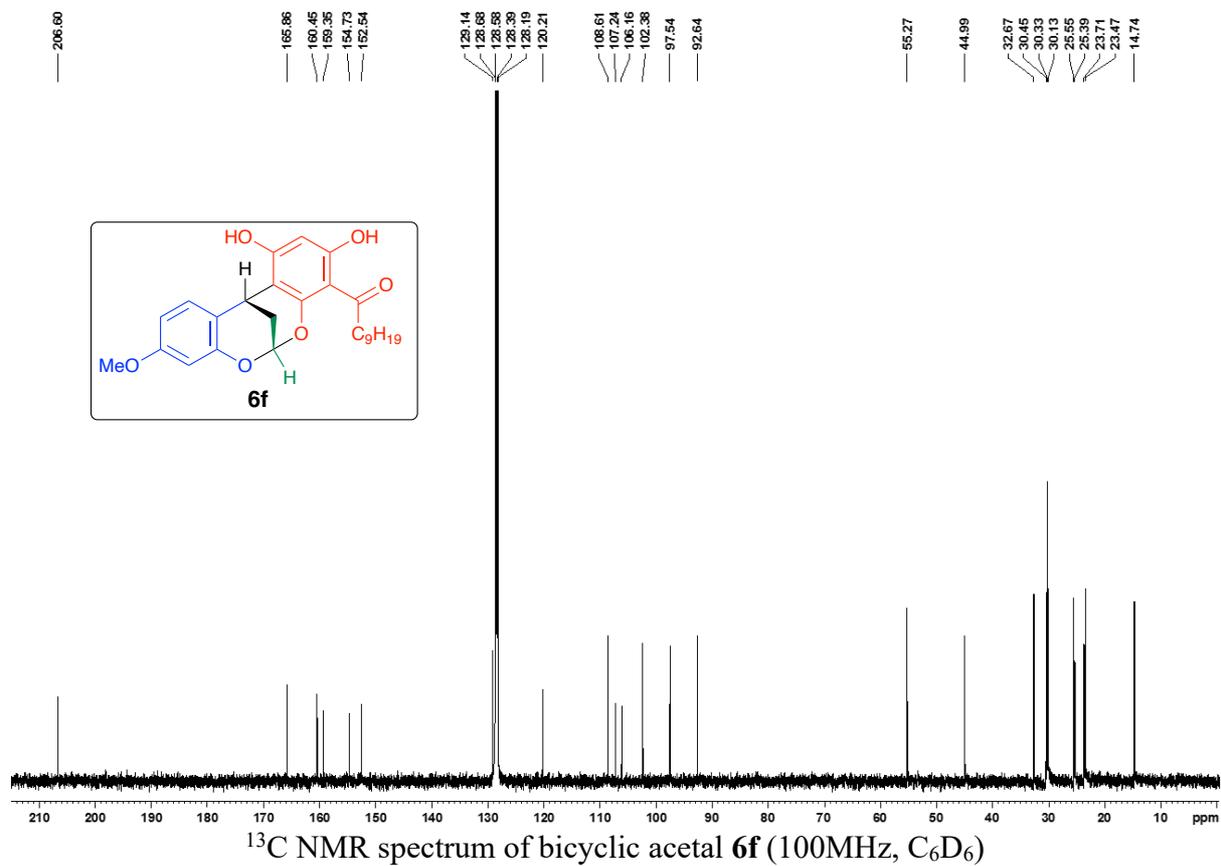
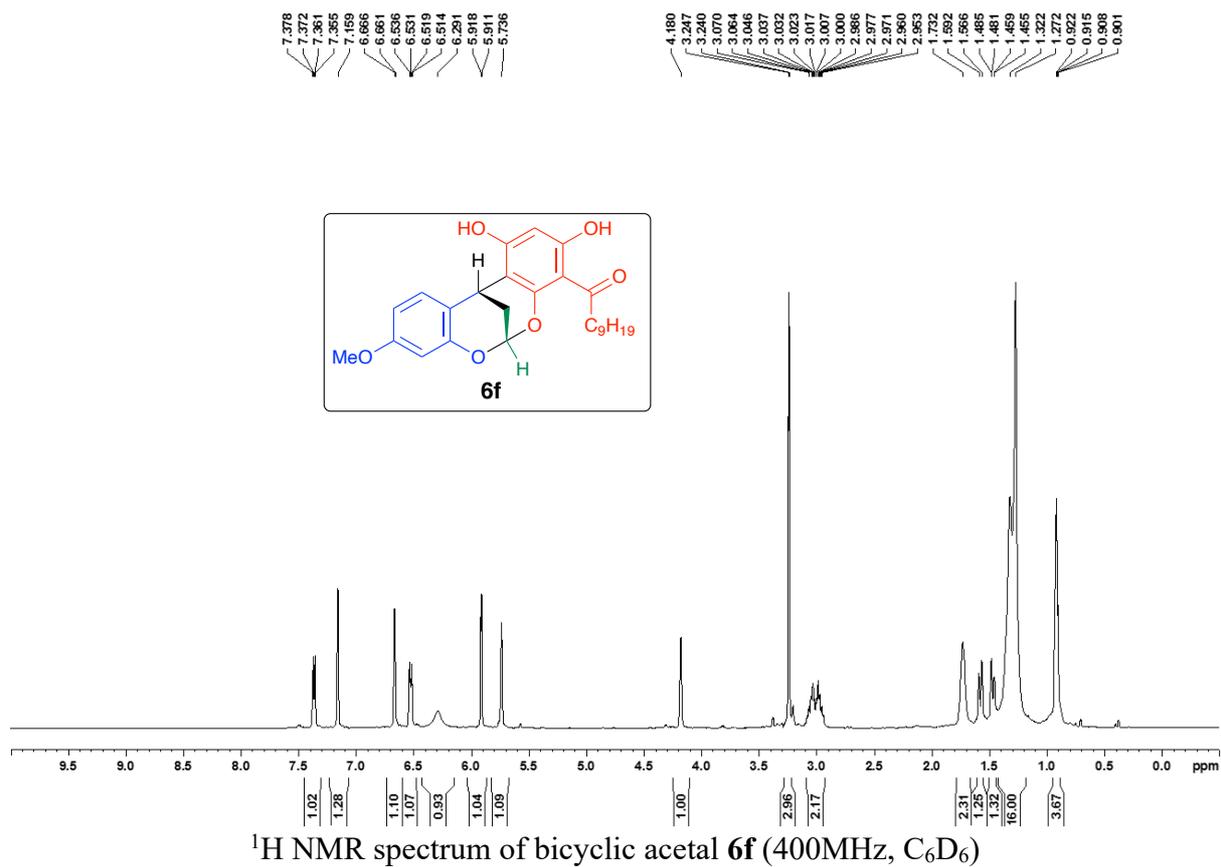
$^{13}\text{C}$  NMR spectrum of bicyclic acetal **6d** (125MHz,  $\text{CD}_3\text{OD}$ )

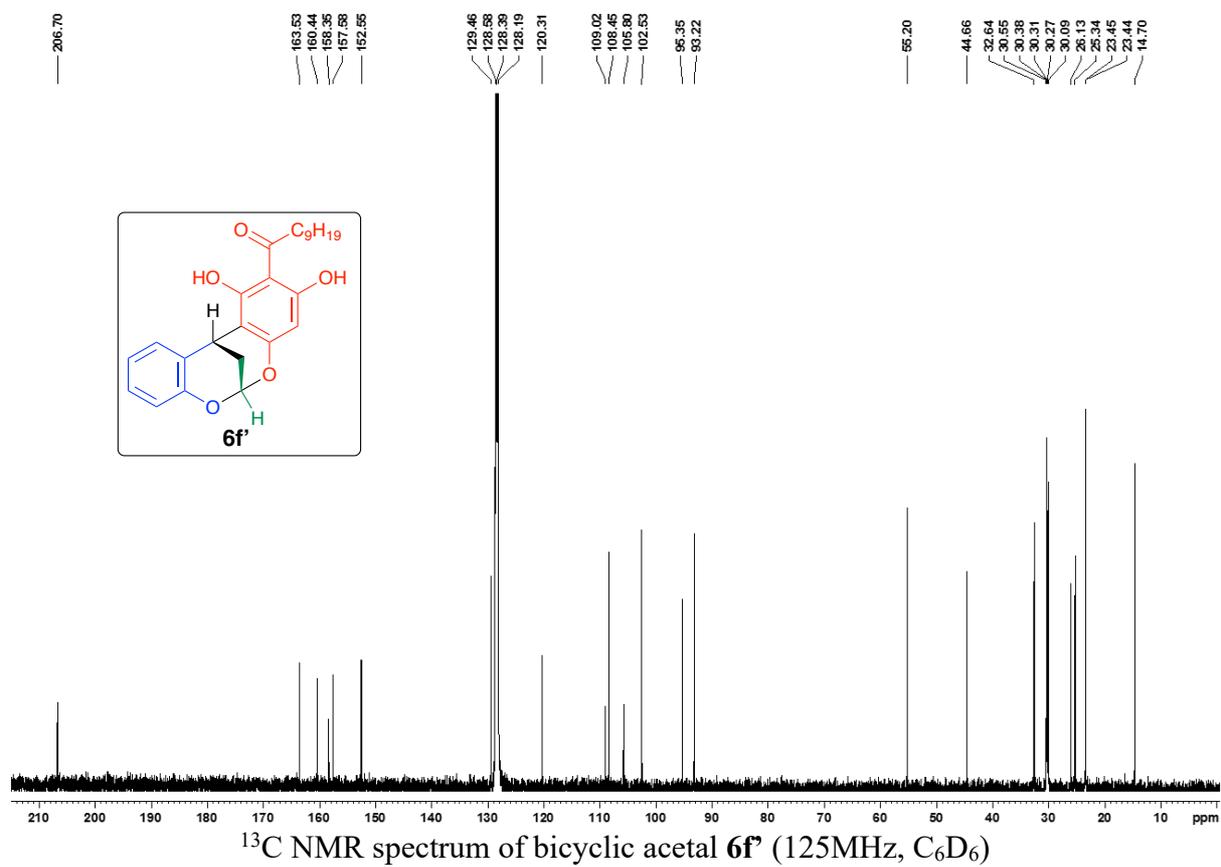
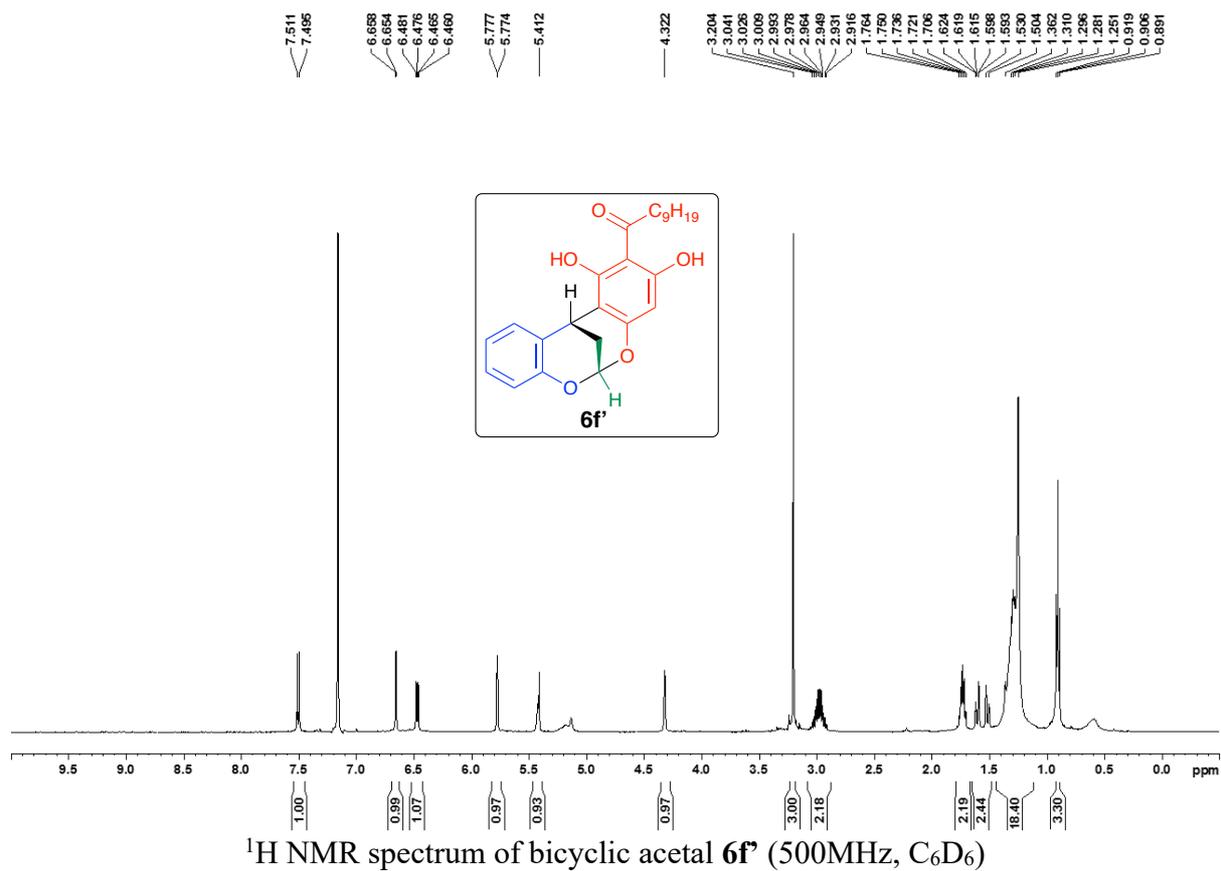


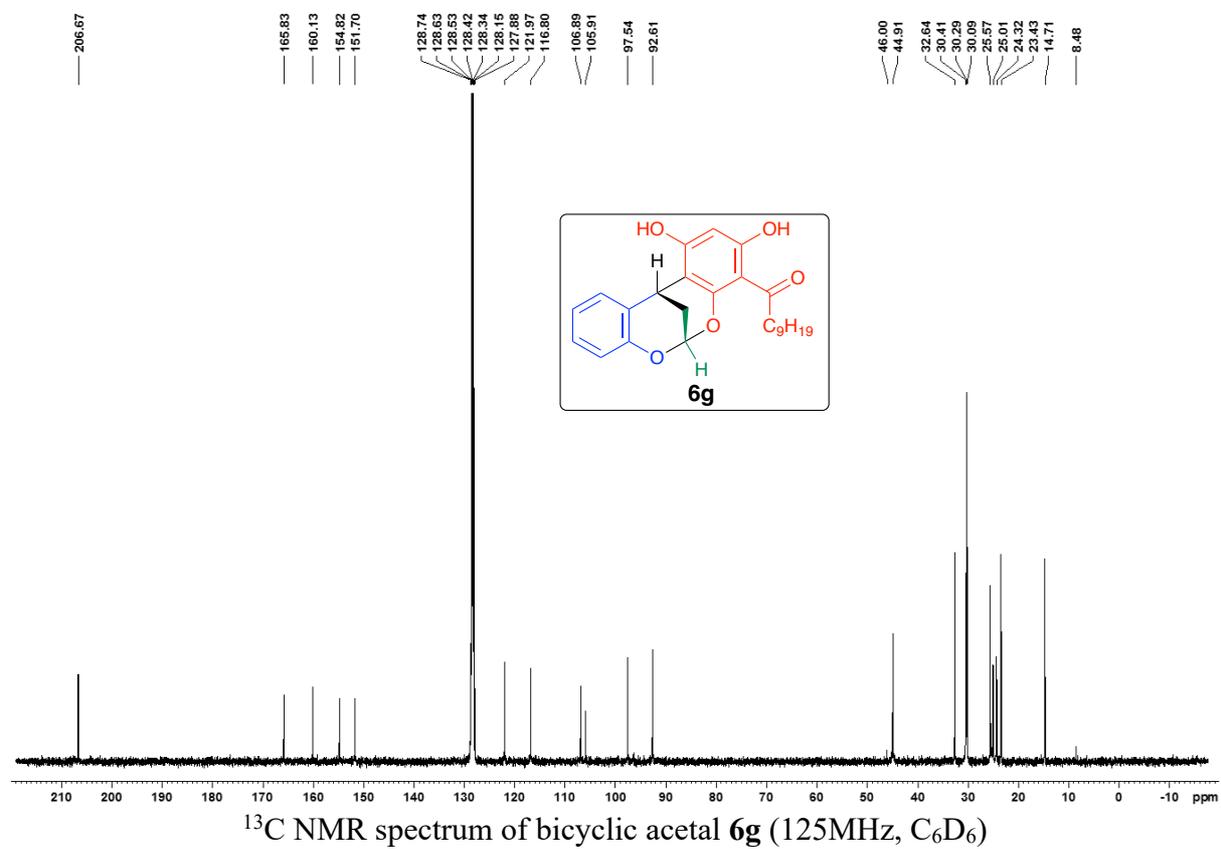
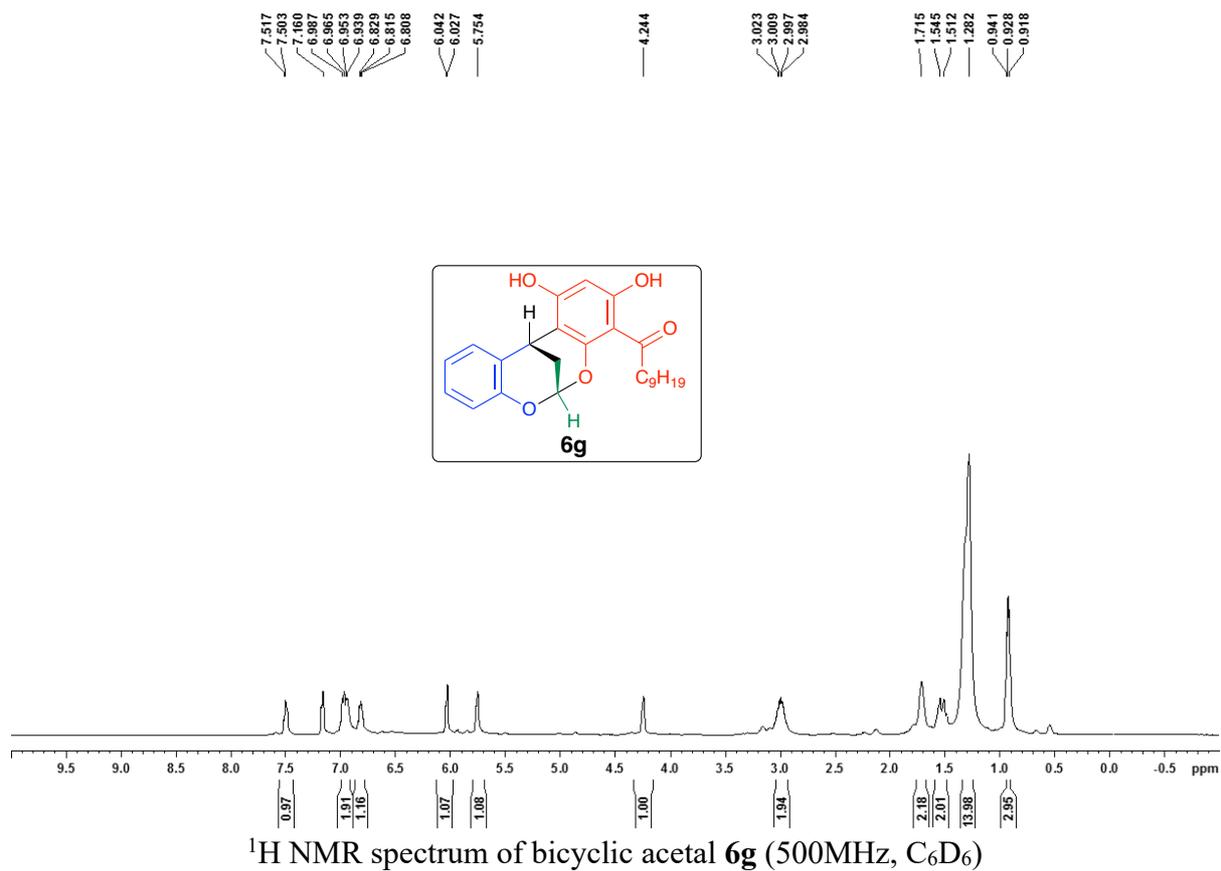
<sup>1</sup>H NMR spectrum of bicyclic acetal **6e** (500MHz, CD<sub>3</sub>CN)

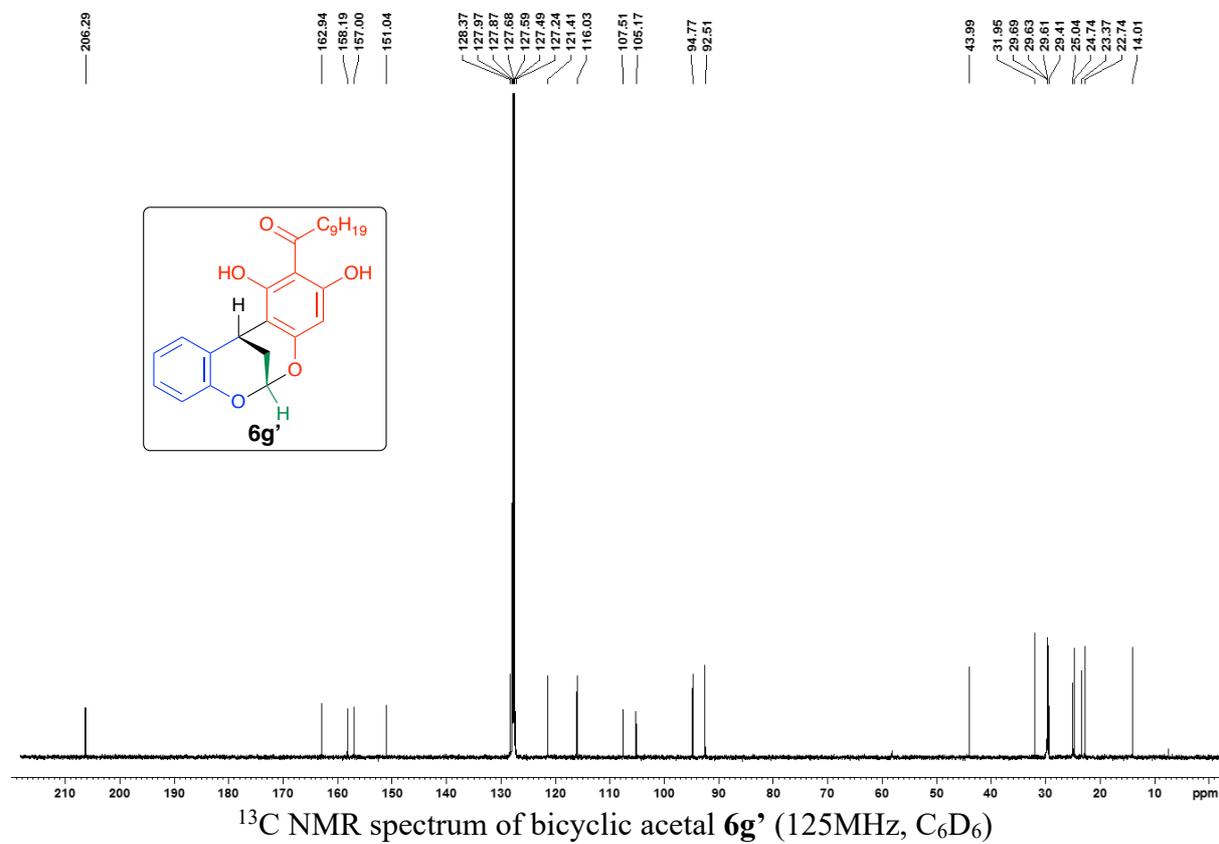
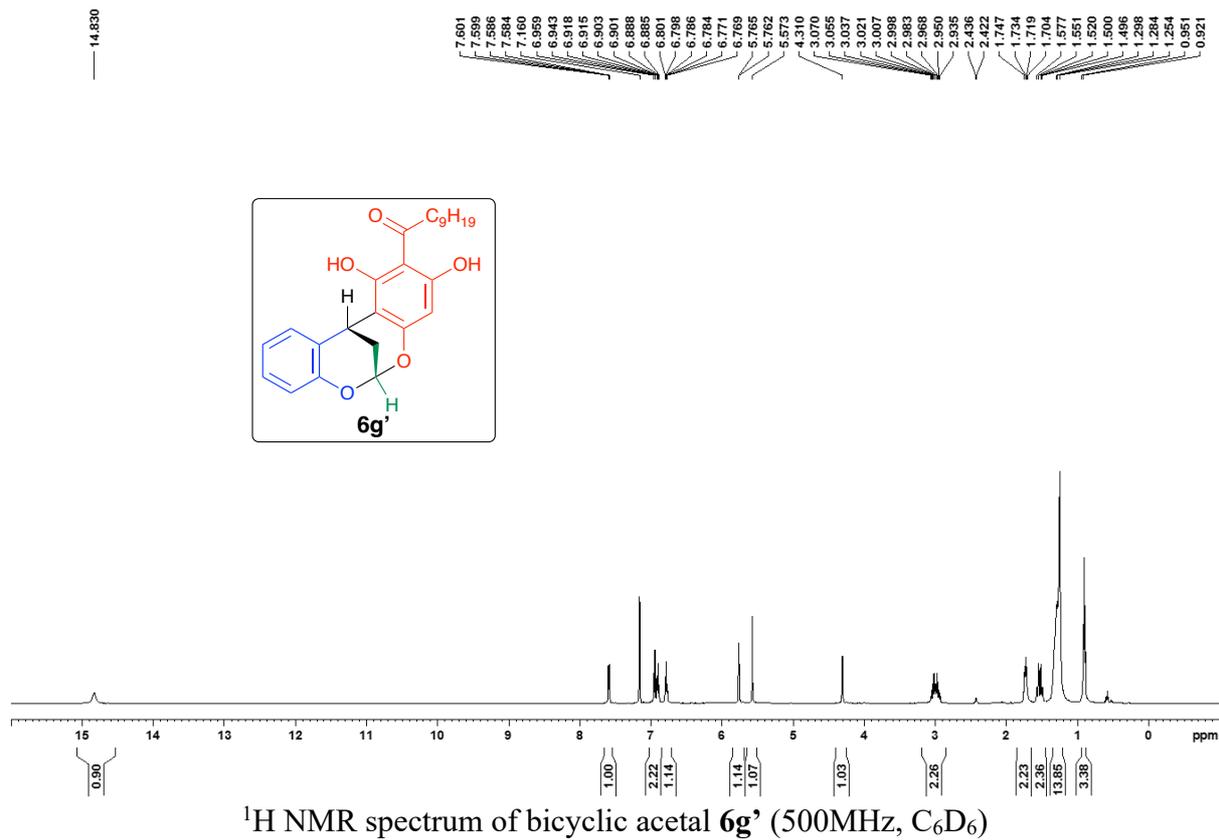


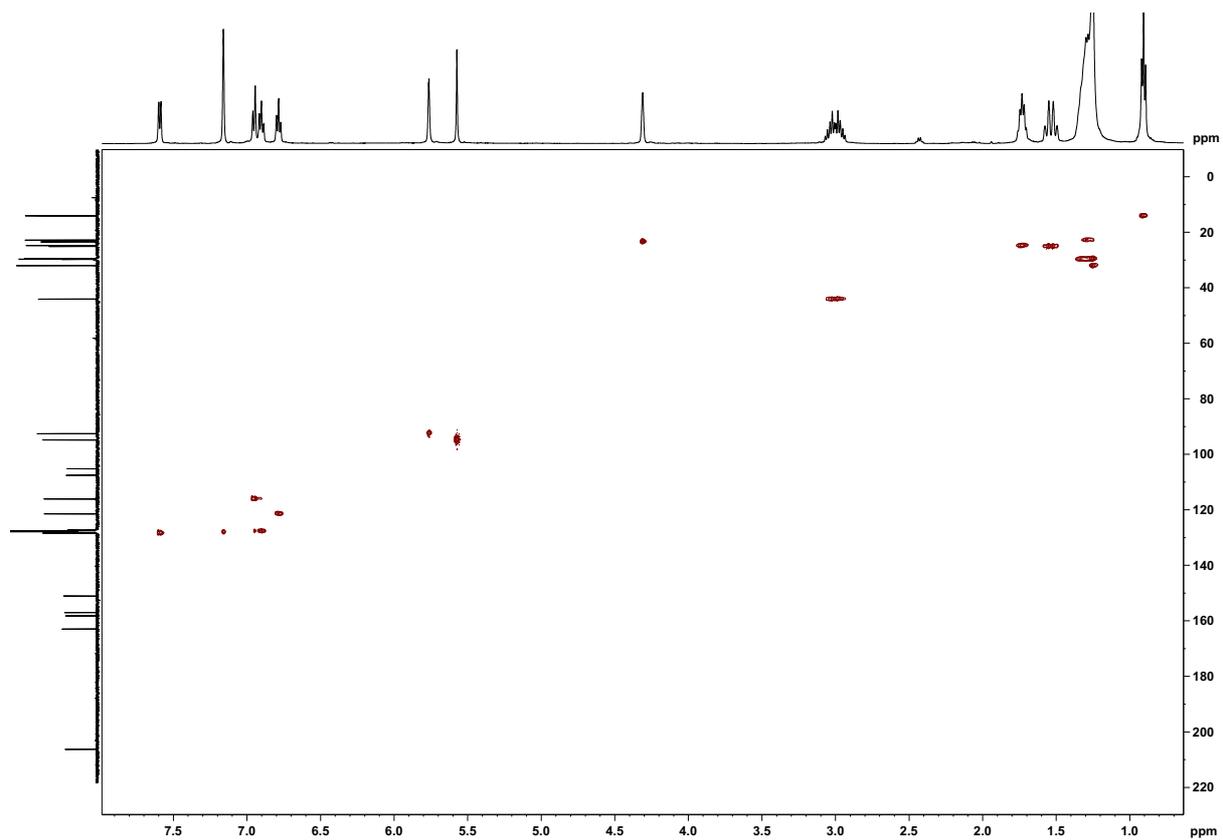
<sup>13</sup>C NMR spectrum of bicyclic acetal **6e** (125MHz, CD<sub>3</sub>CN)



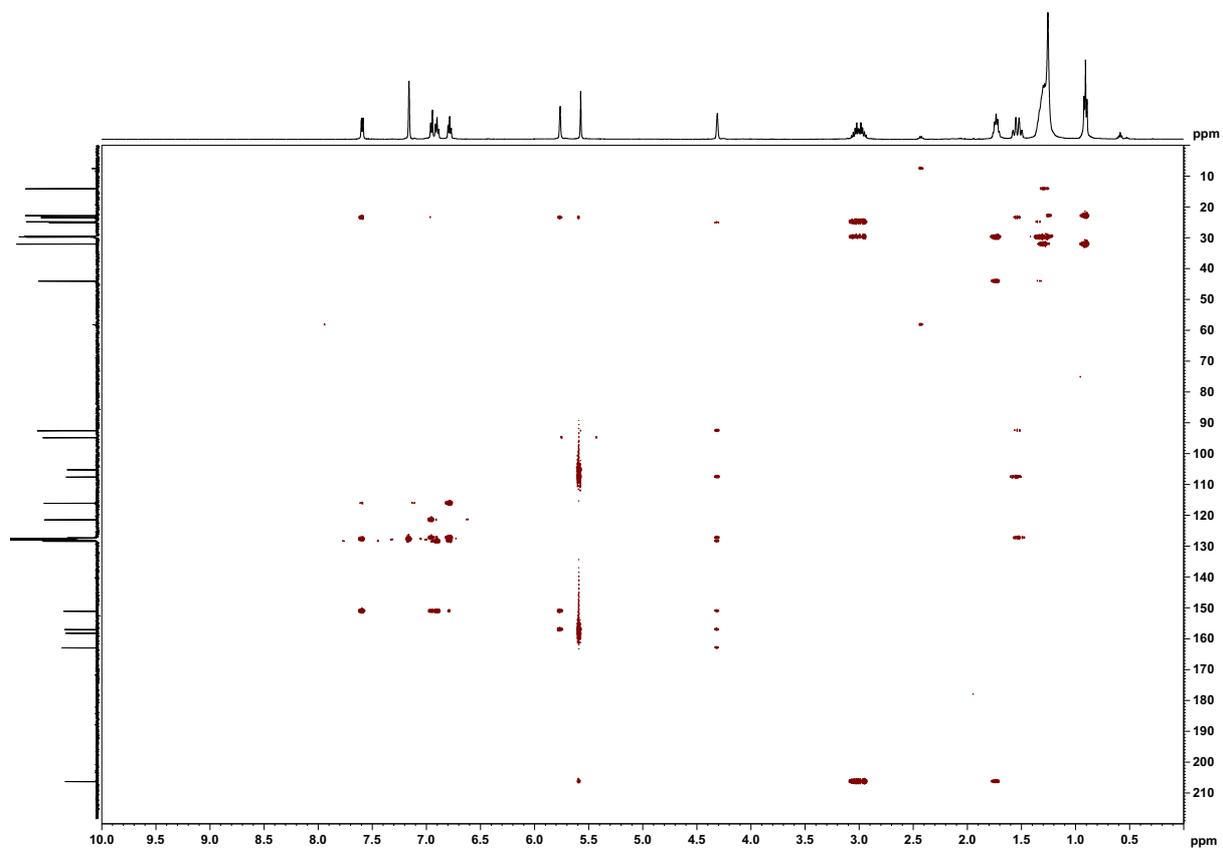




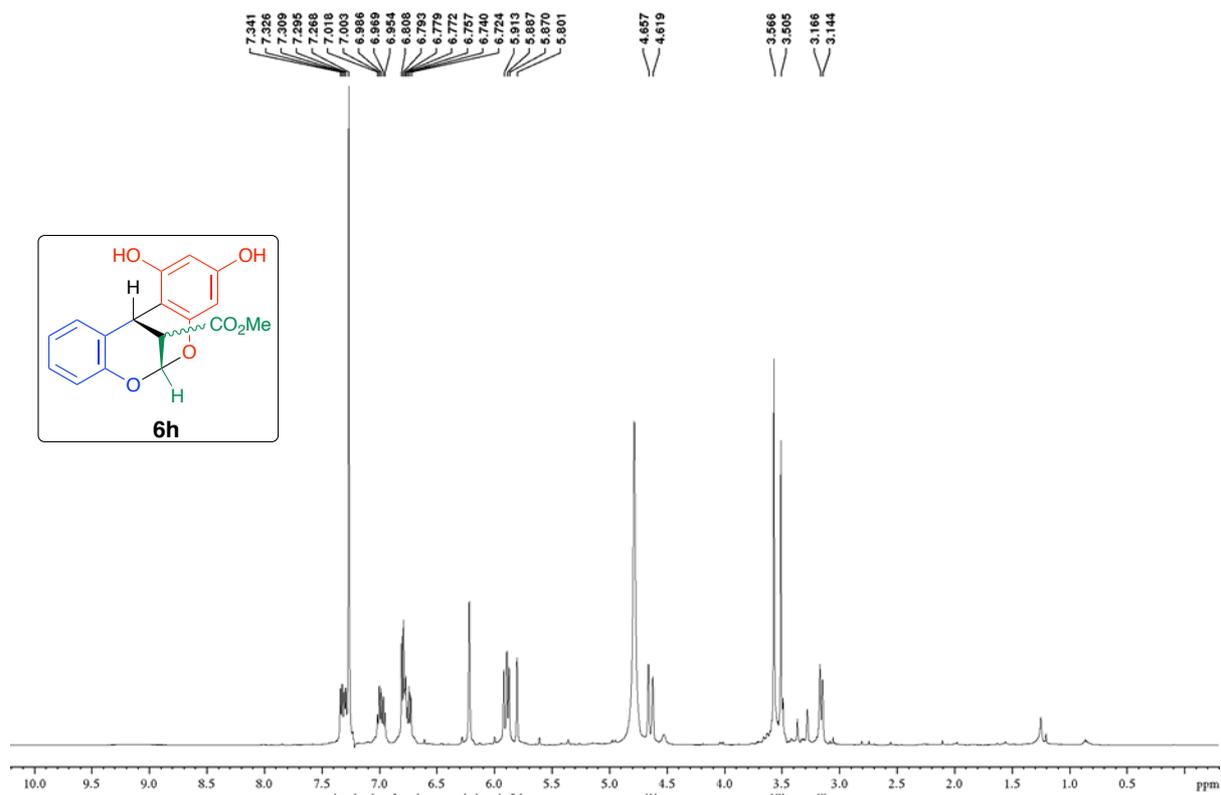




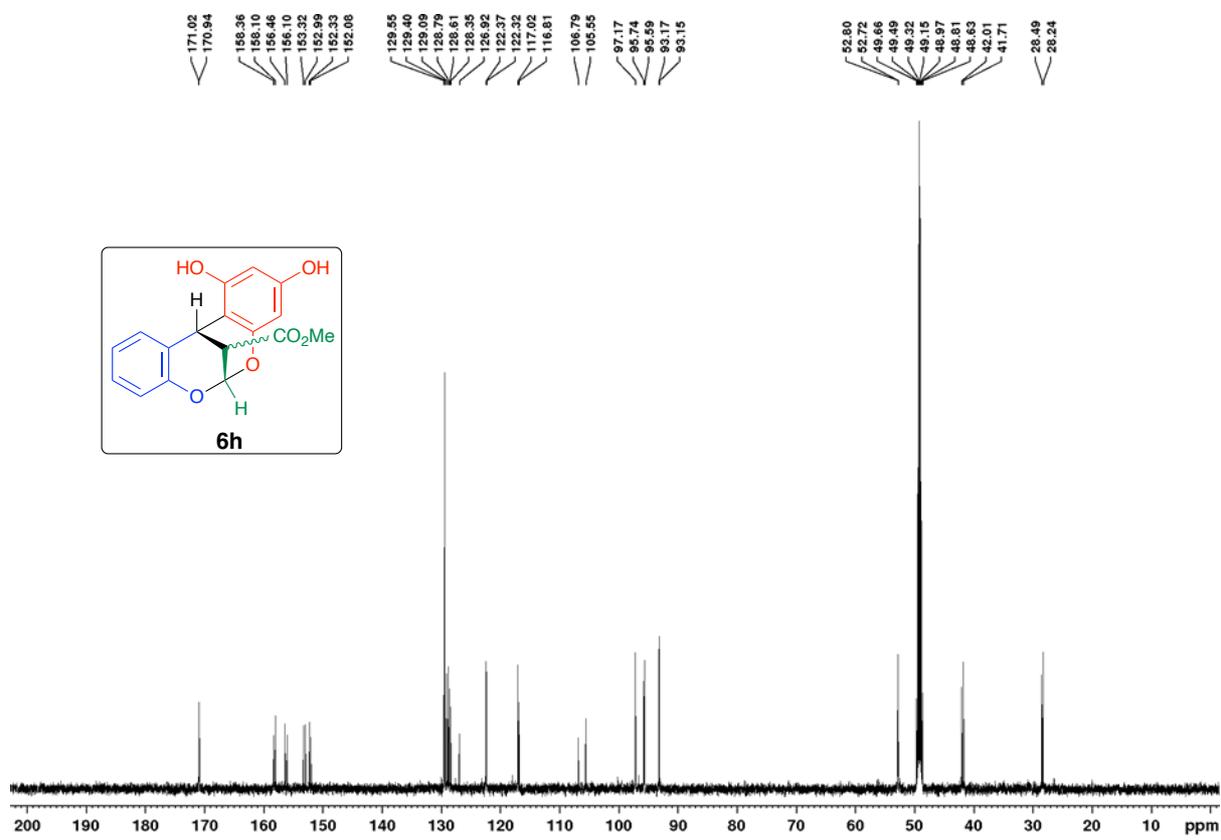
HSQC spectrum of bicyclic acetal **6g'** (500MHz)



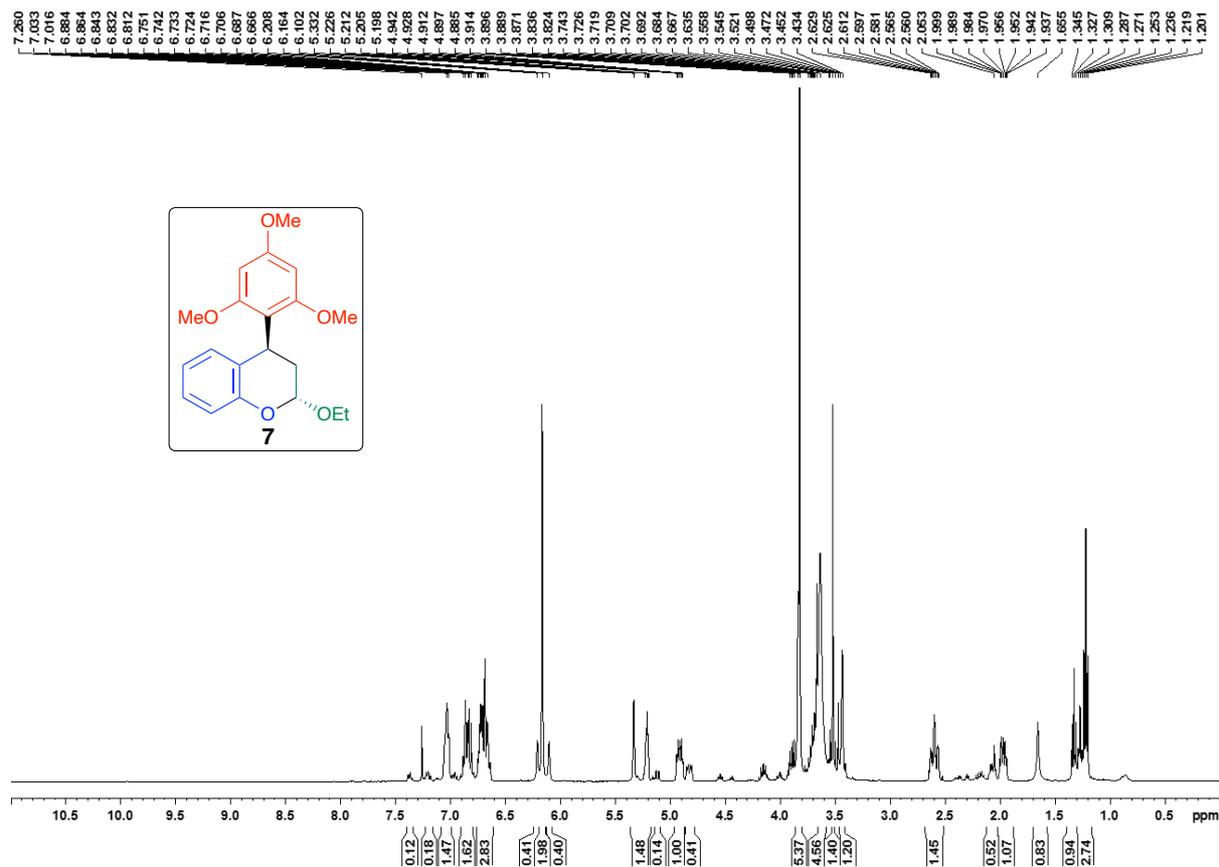
HMBC spectrum of bicyclic acetal **6g'** (500MHz)



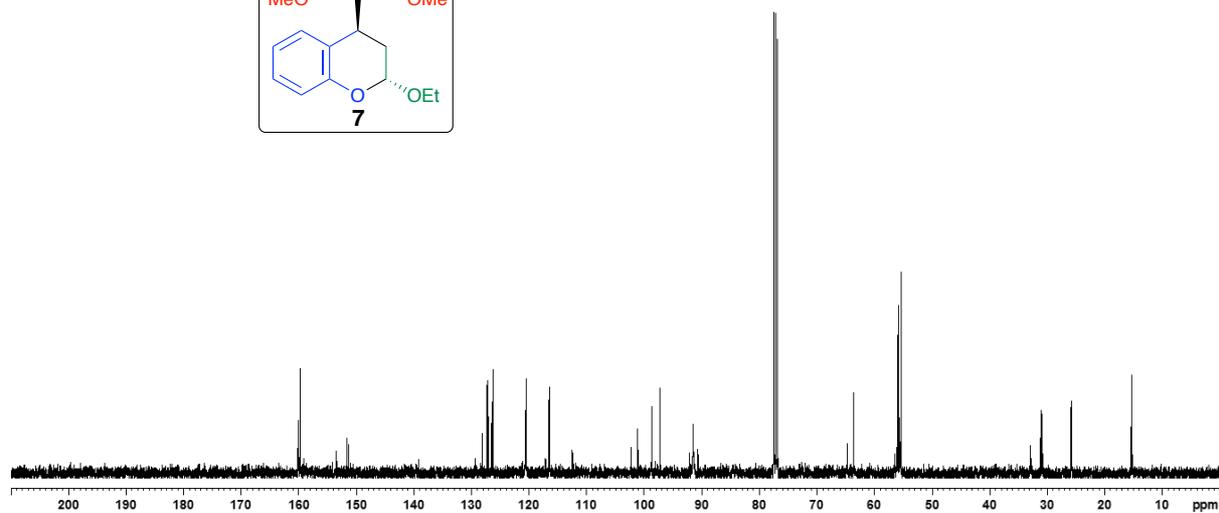
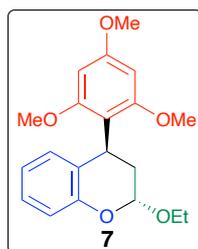
<sup>1</sup>H NMR spectrum of bicyclic acetal **6h** (500MHz, Benzene-D<sub>6</sub> and CD<sub>3</sub>OD)



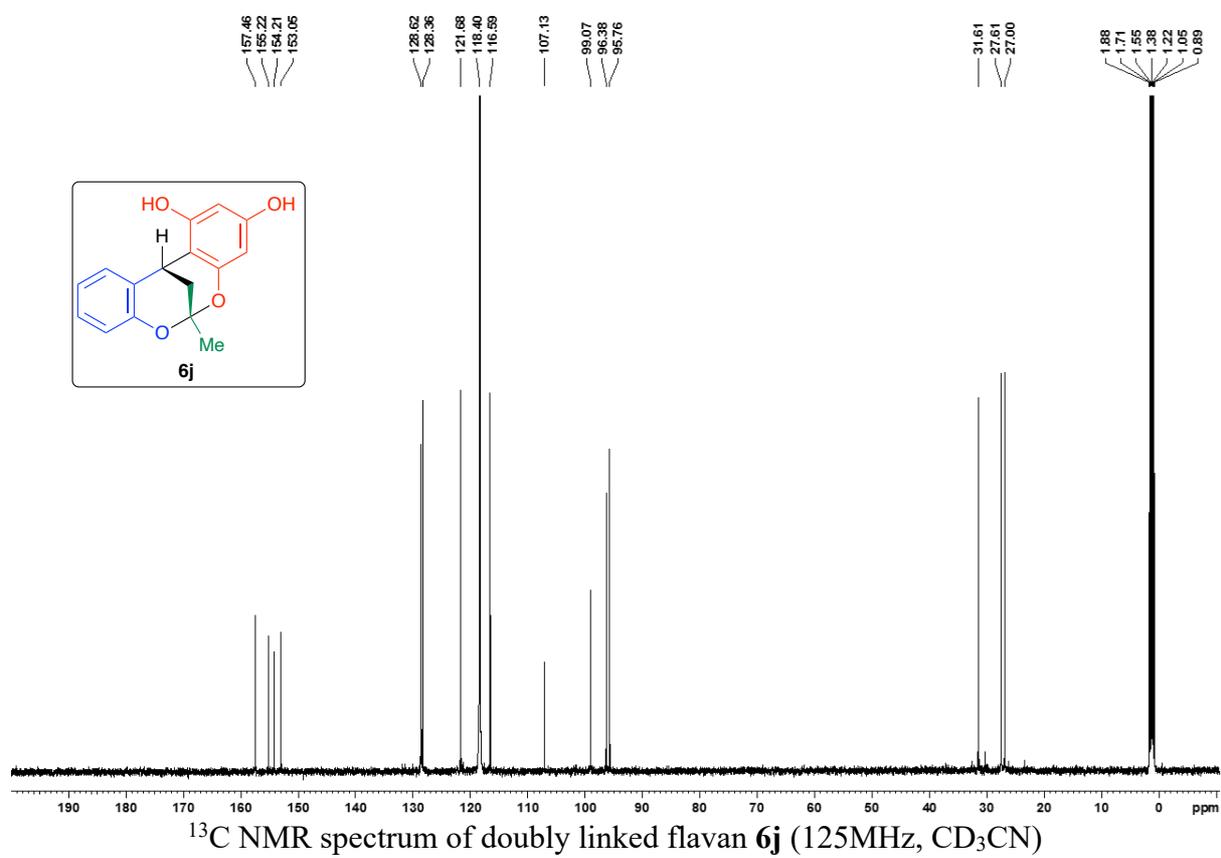
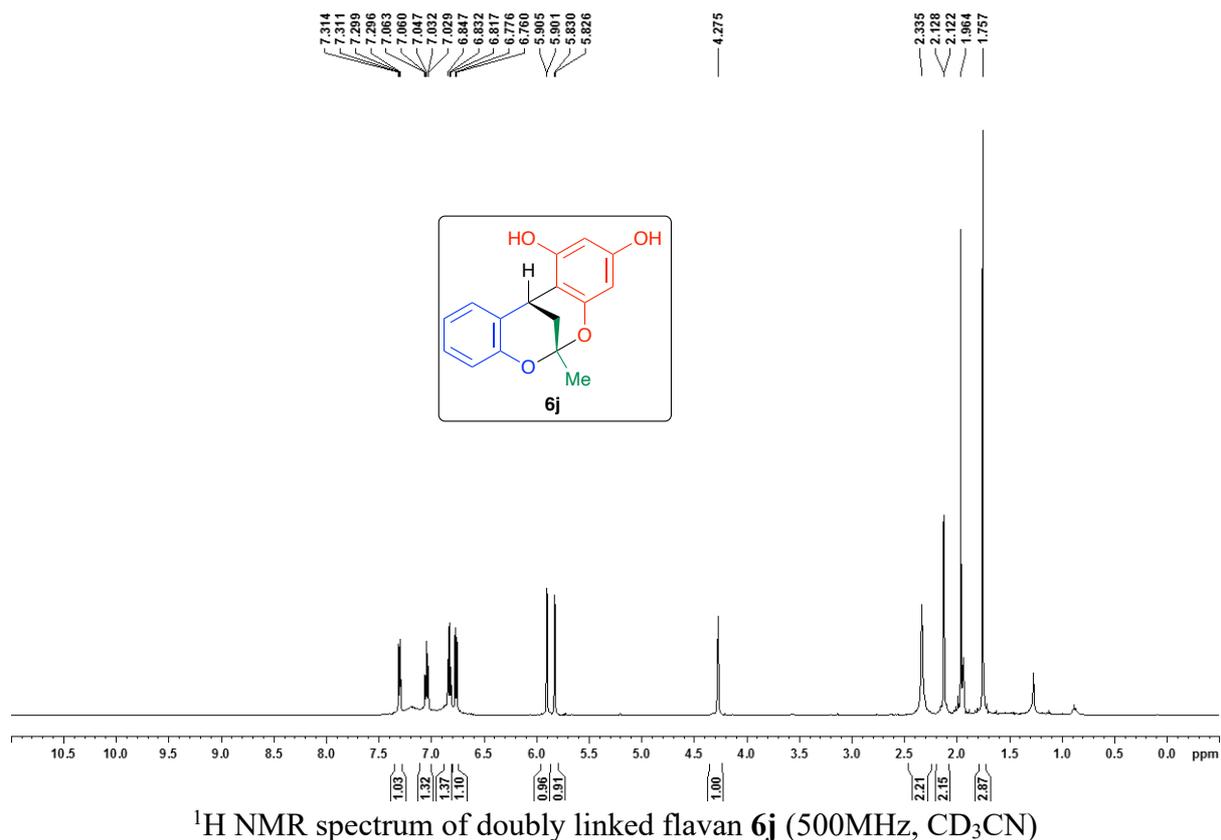
<sup>13</sup>C NMR spectrum of bicyclic acetal **6h** (500MHz, Benzene-D<sub>6</sub> and CD<sub>3</sub>OD)

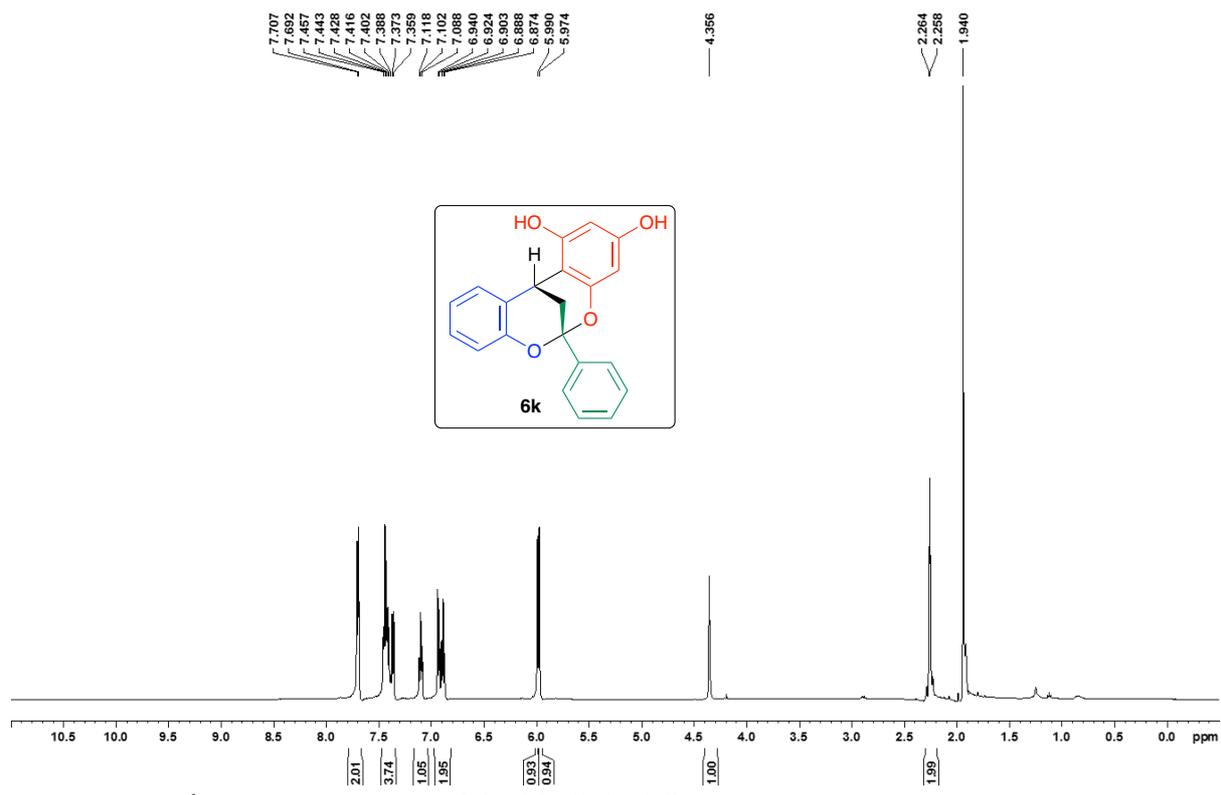


**<sup>1</sup>H NMR spectrum of cassiaflavan 7 (400MHz, CDCl<sub>3</sub>)**

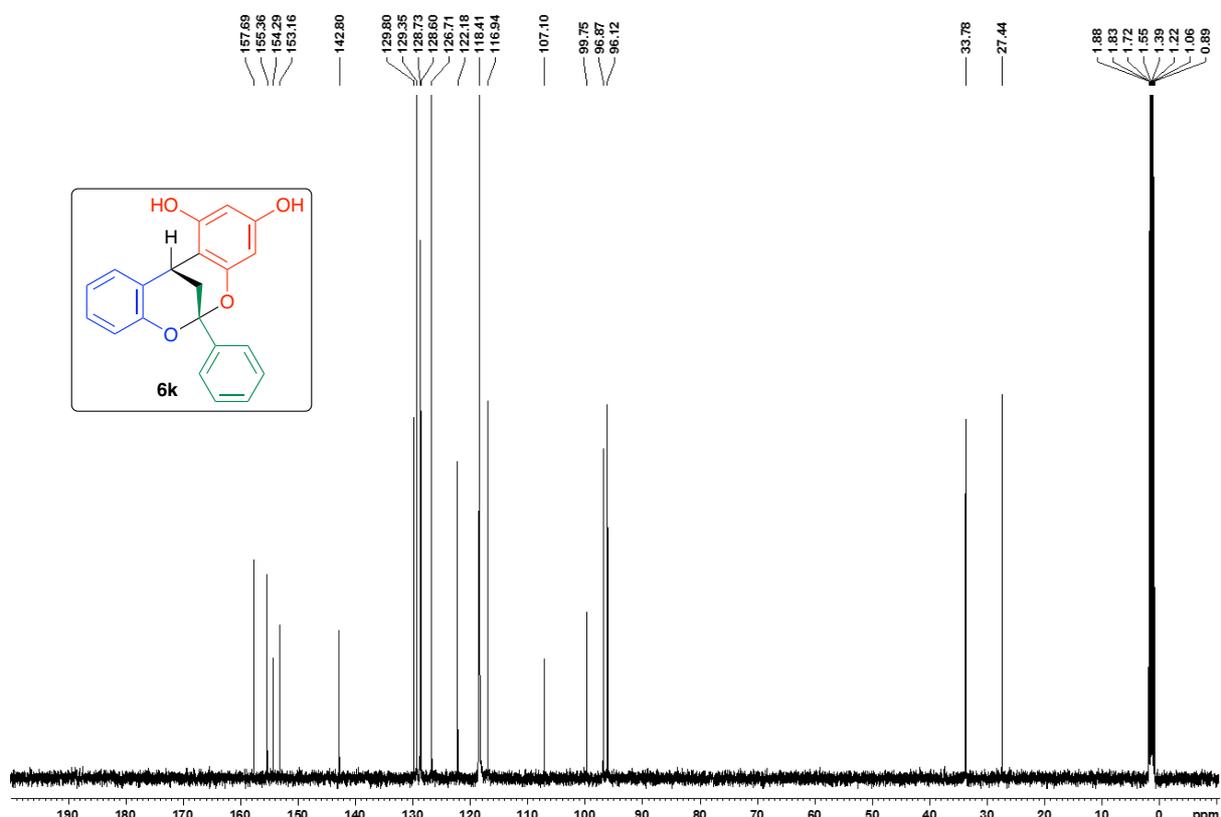


**<sup>13</sup>C NMR spectrum of cassiaflavan 7 (125MHz, CDCl<sub>3</sub>)**

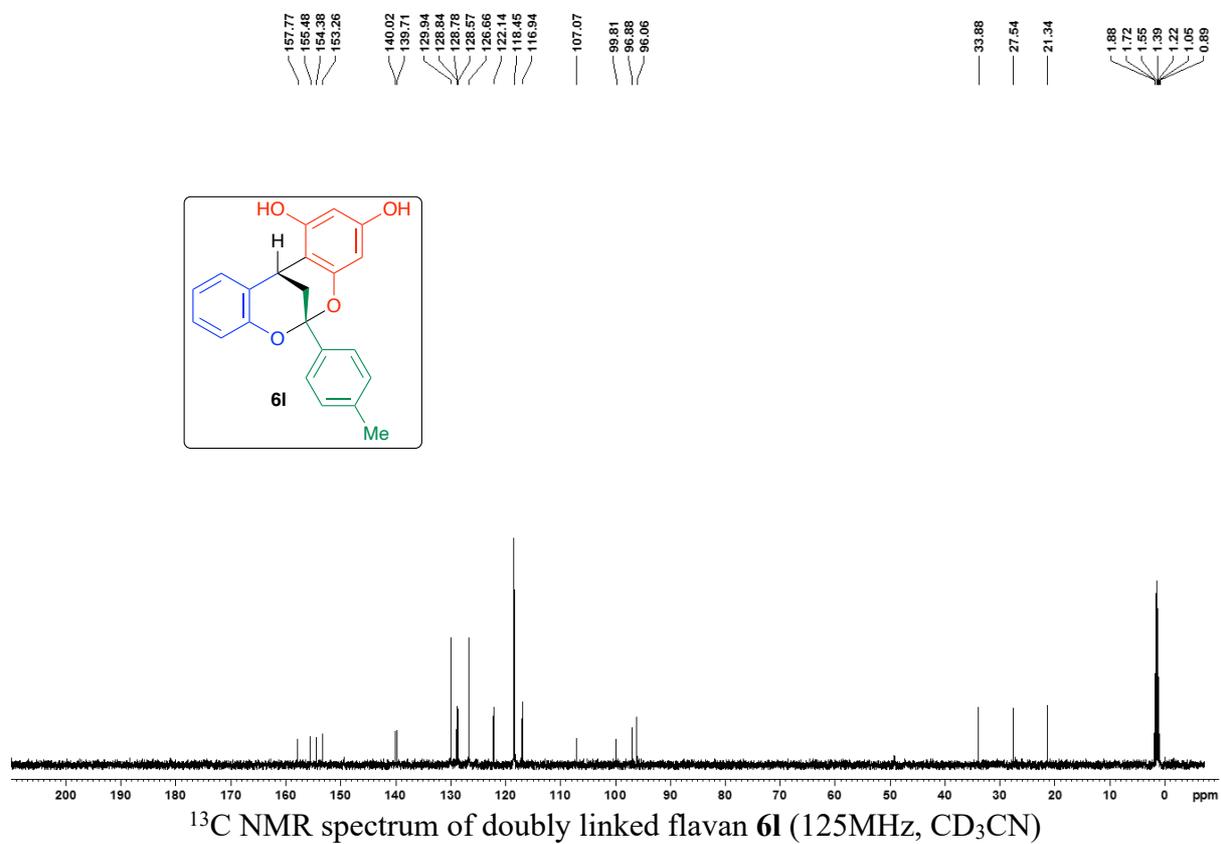
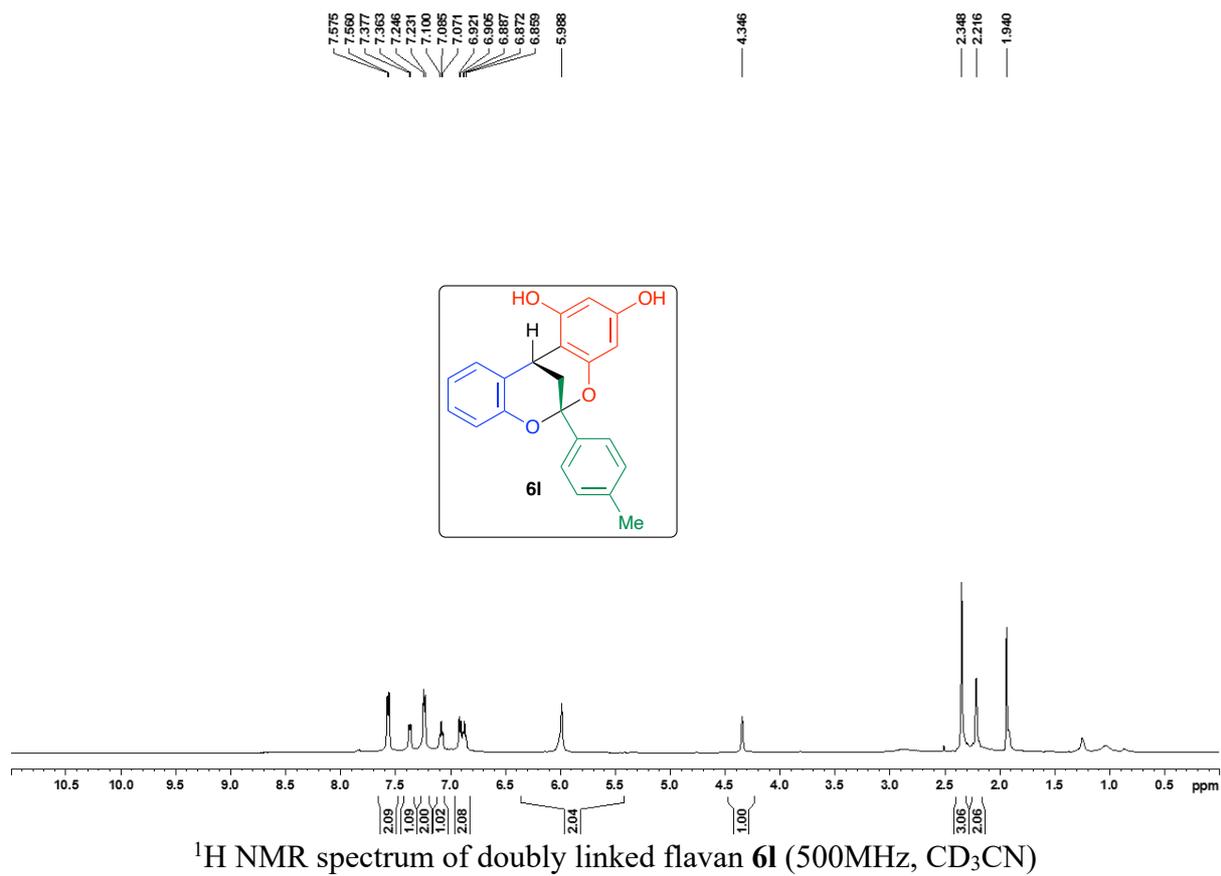


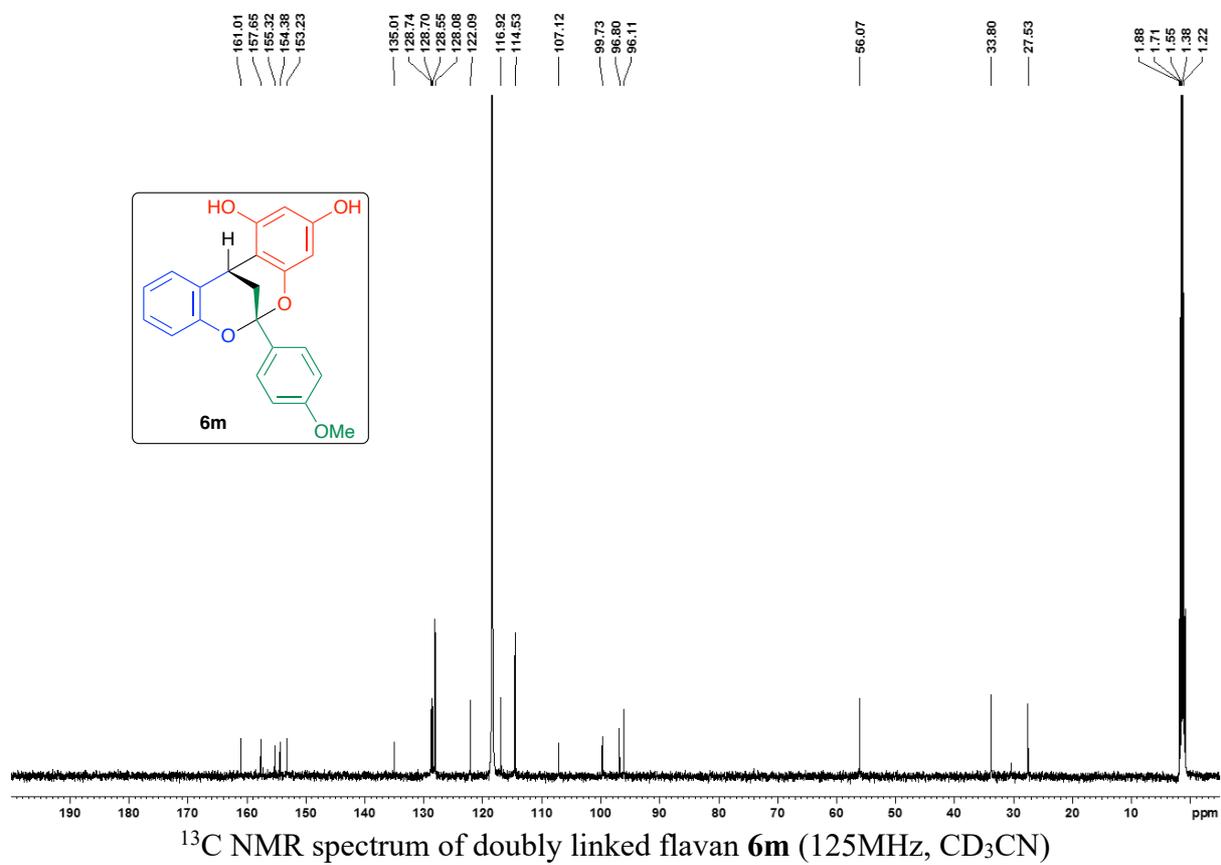
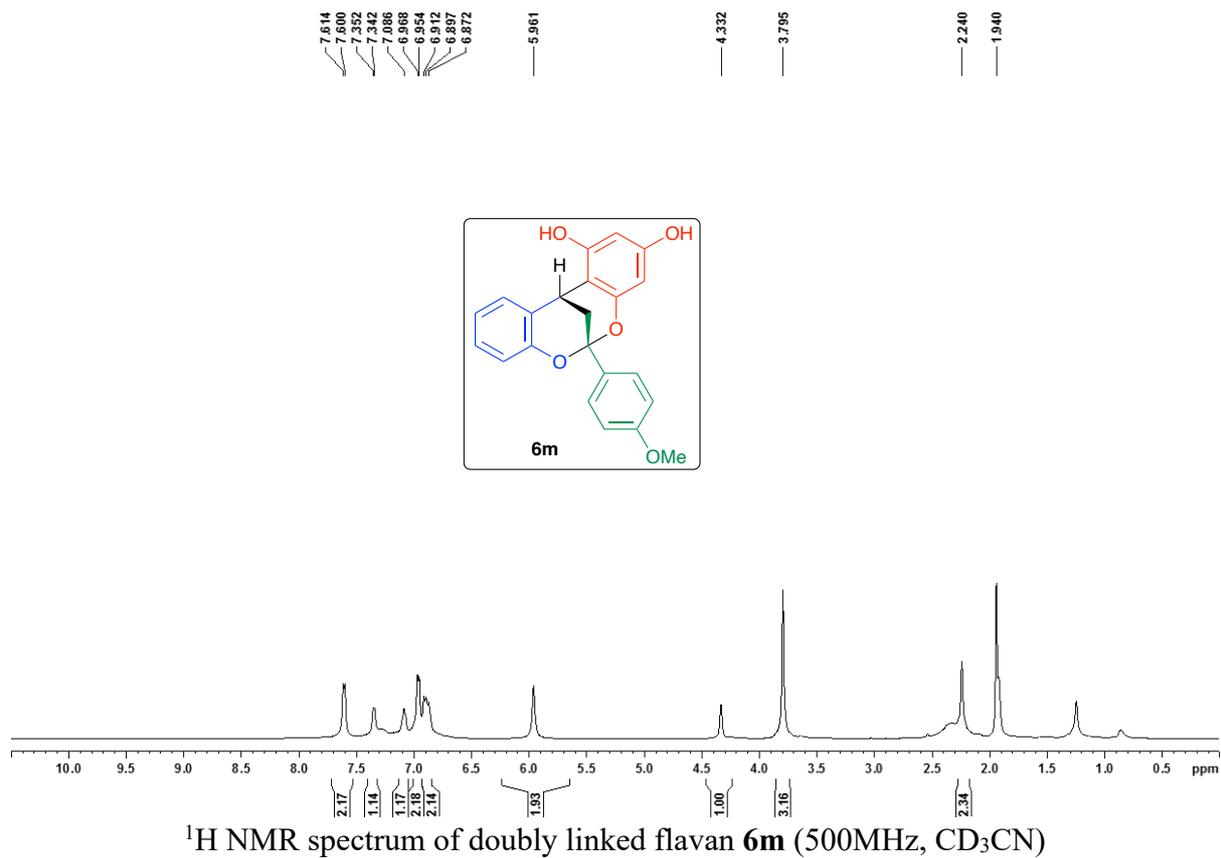


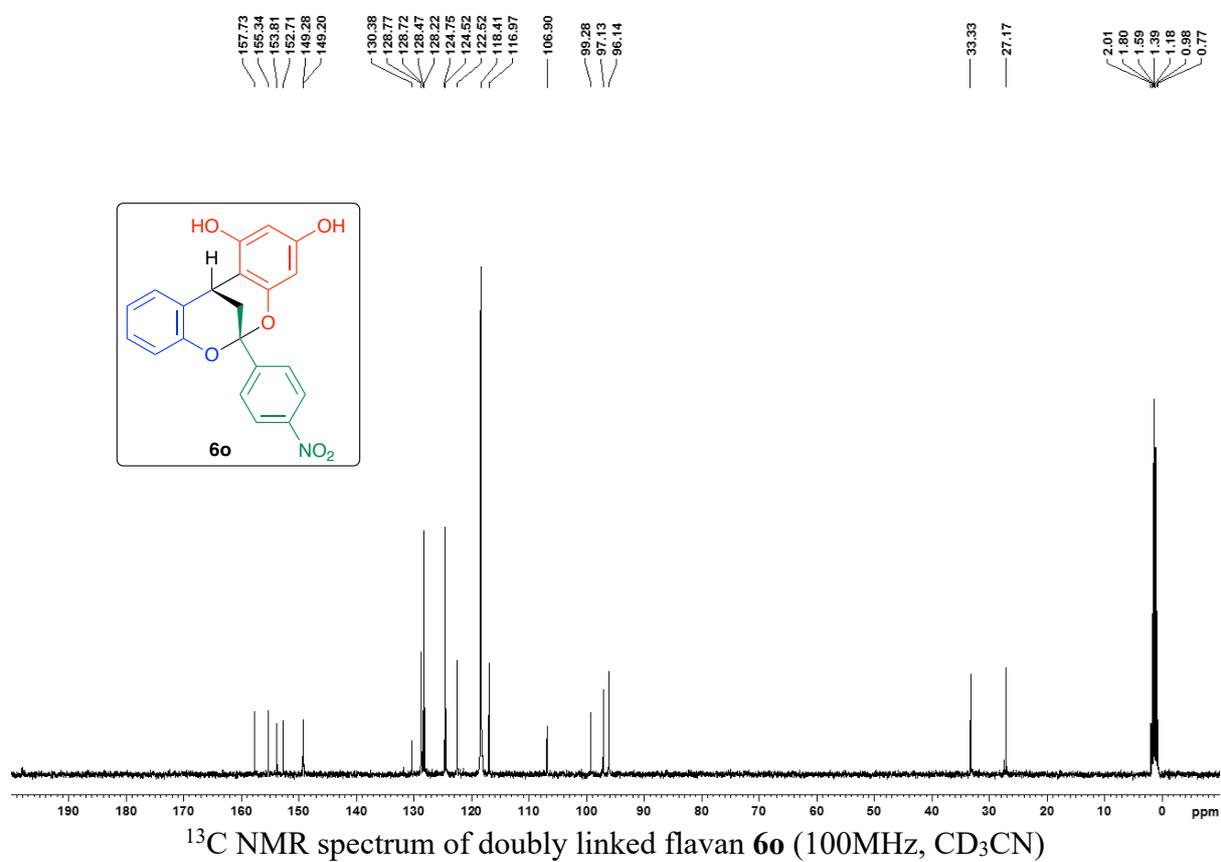
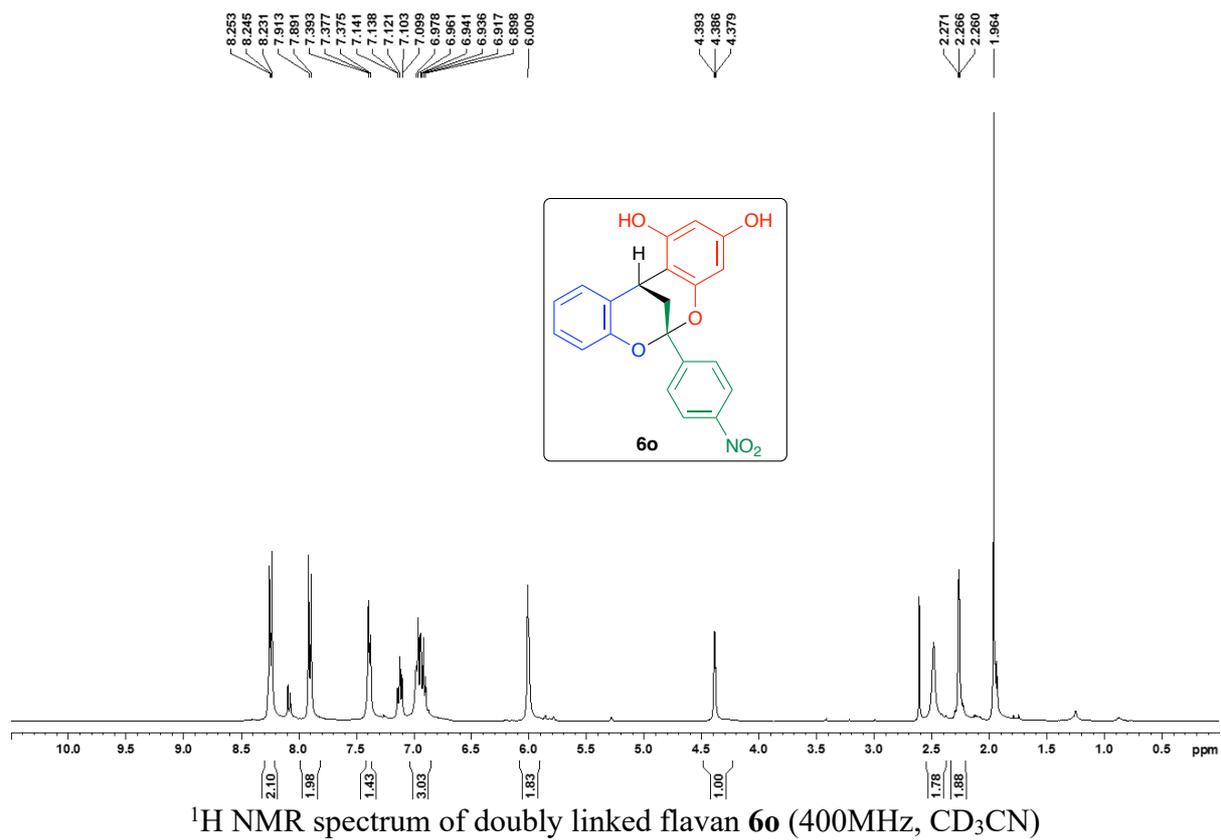
<sup>1</sup>H NMR spectrum of doubly linked flavan **6k** (500MHz, CD<sub>3</sub>CN)

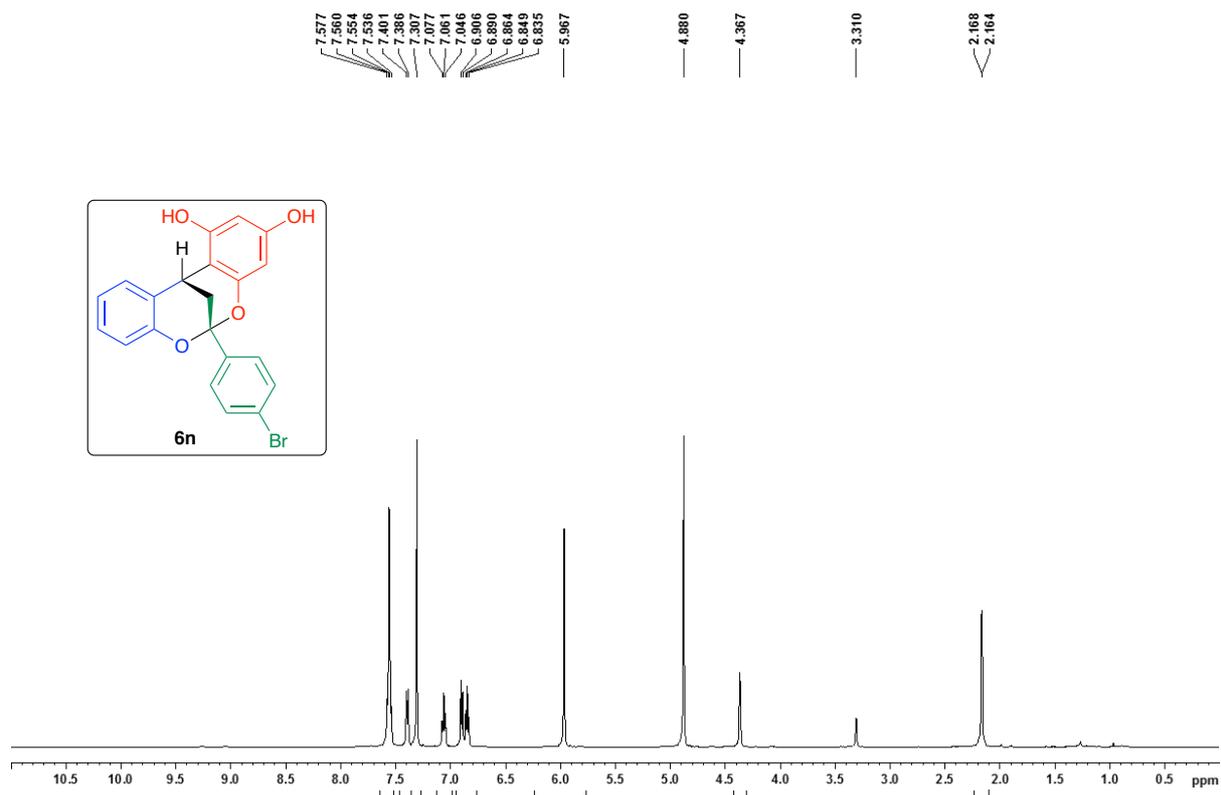


<sup>13</sup>C NMR spectrum of doubly linked flavan **6k** (125MHz, CD<sub>3</sub>CN)

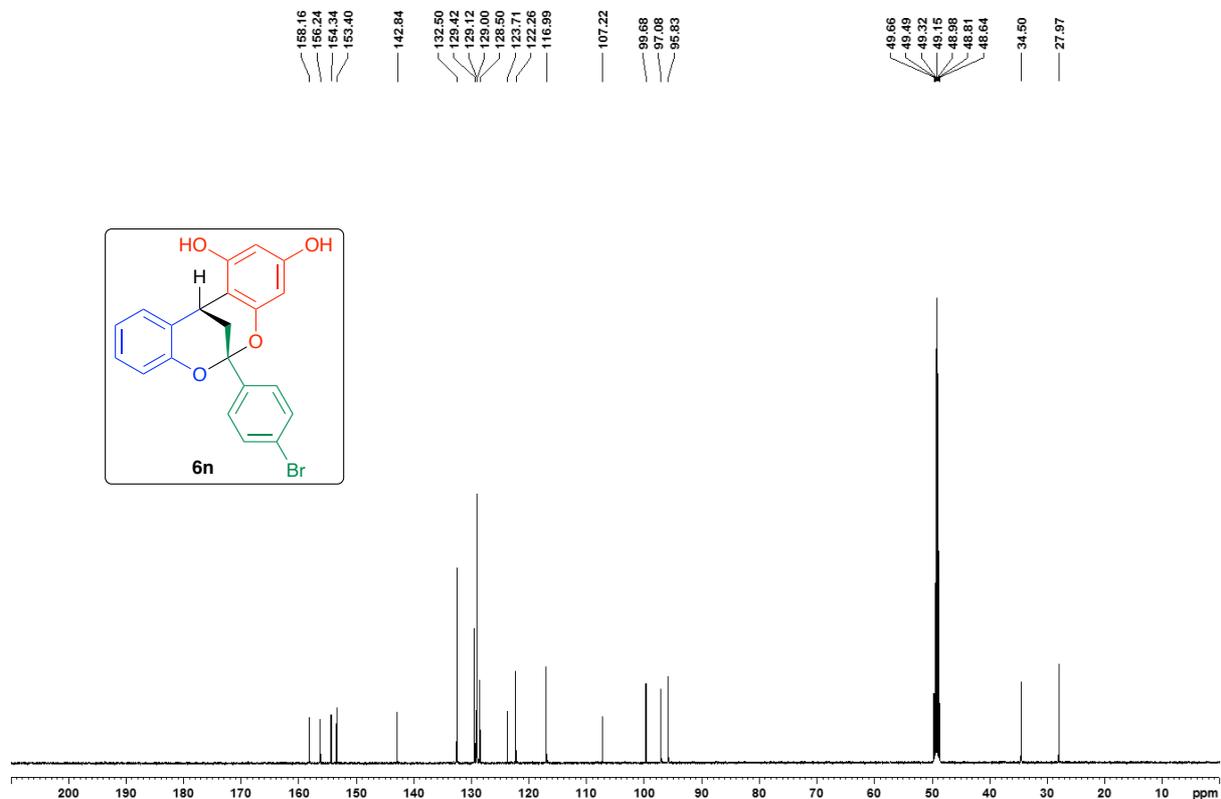




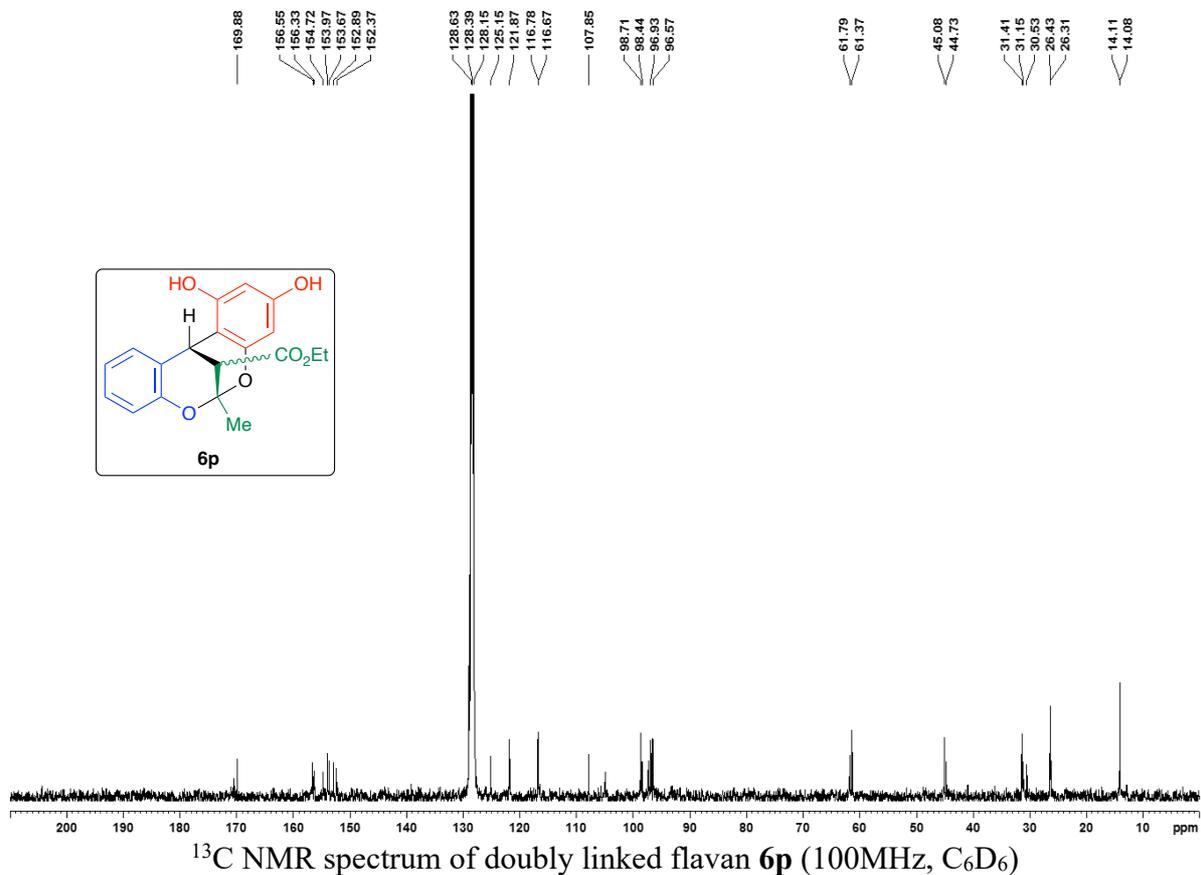
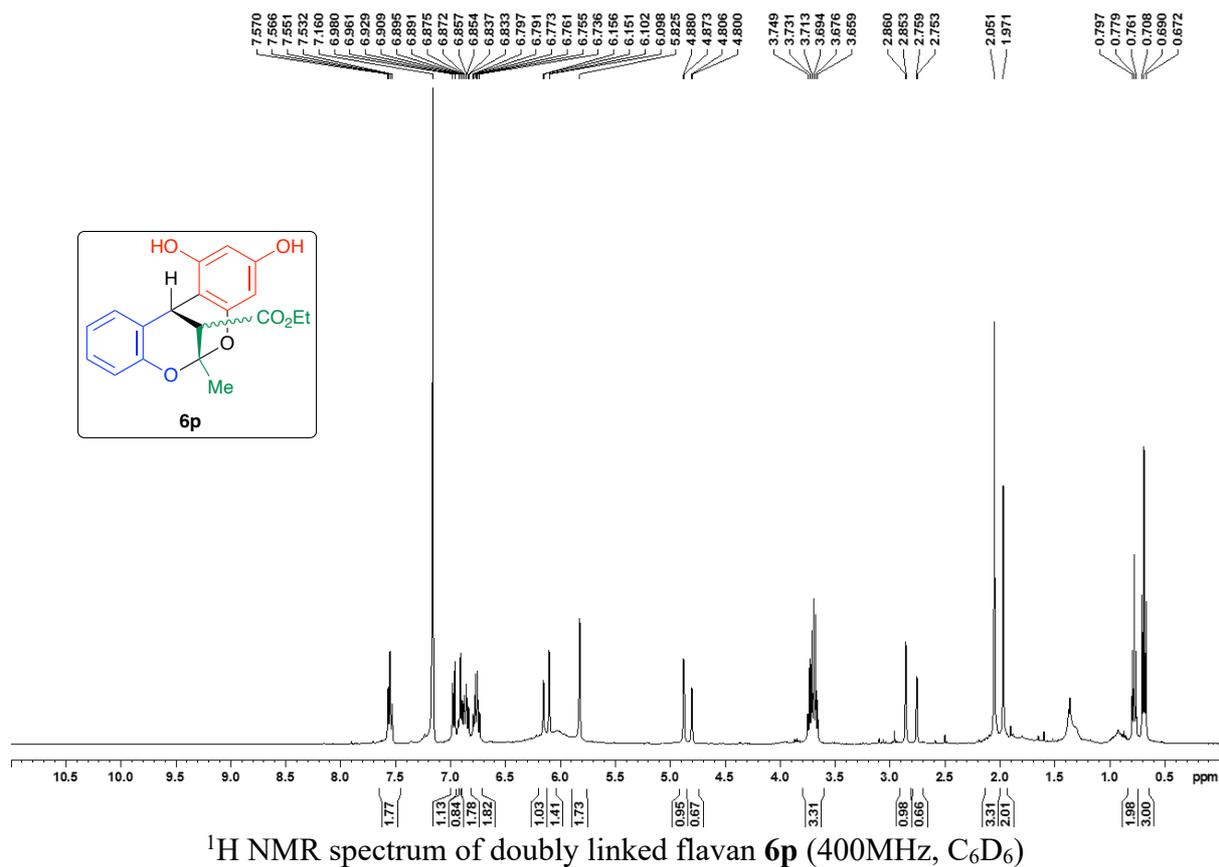


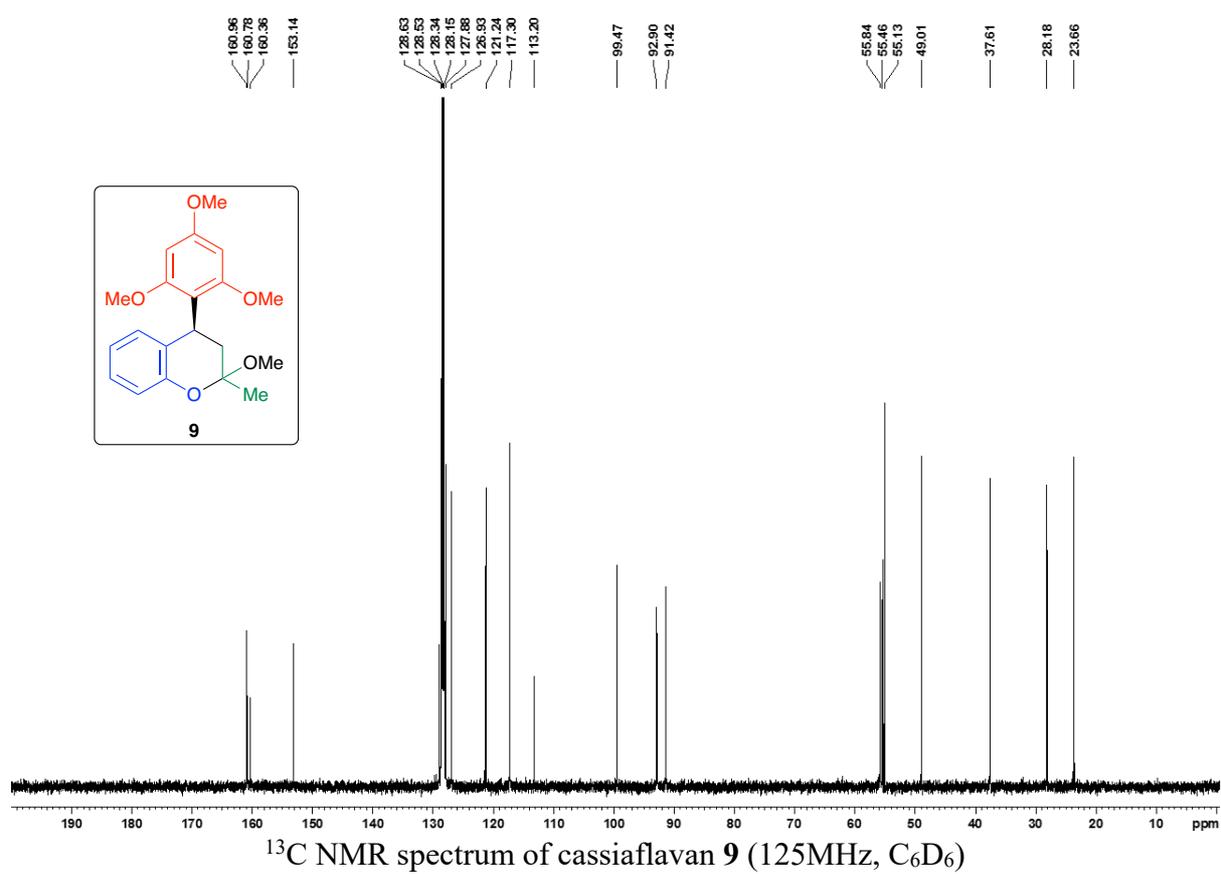
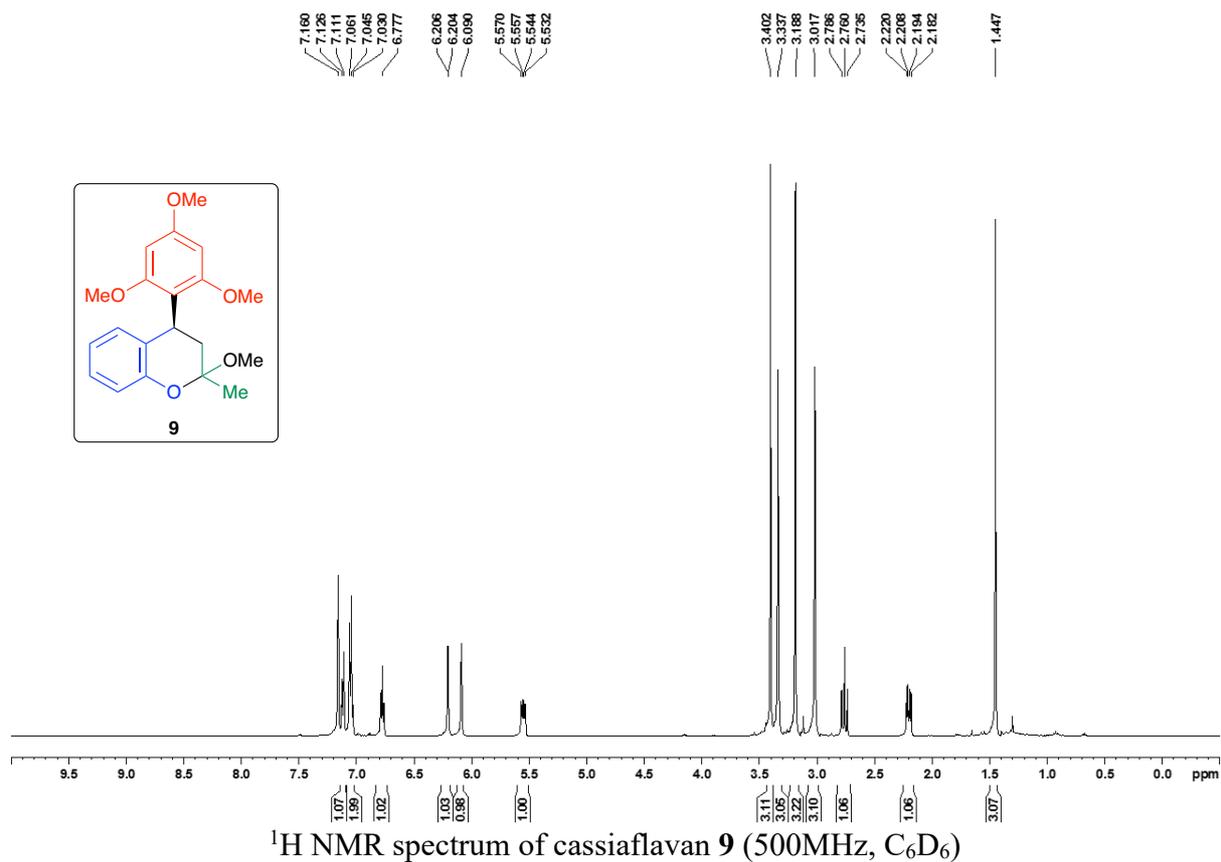


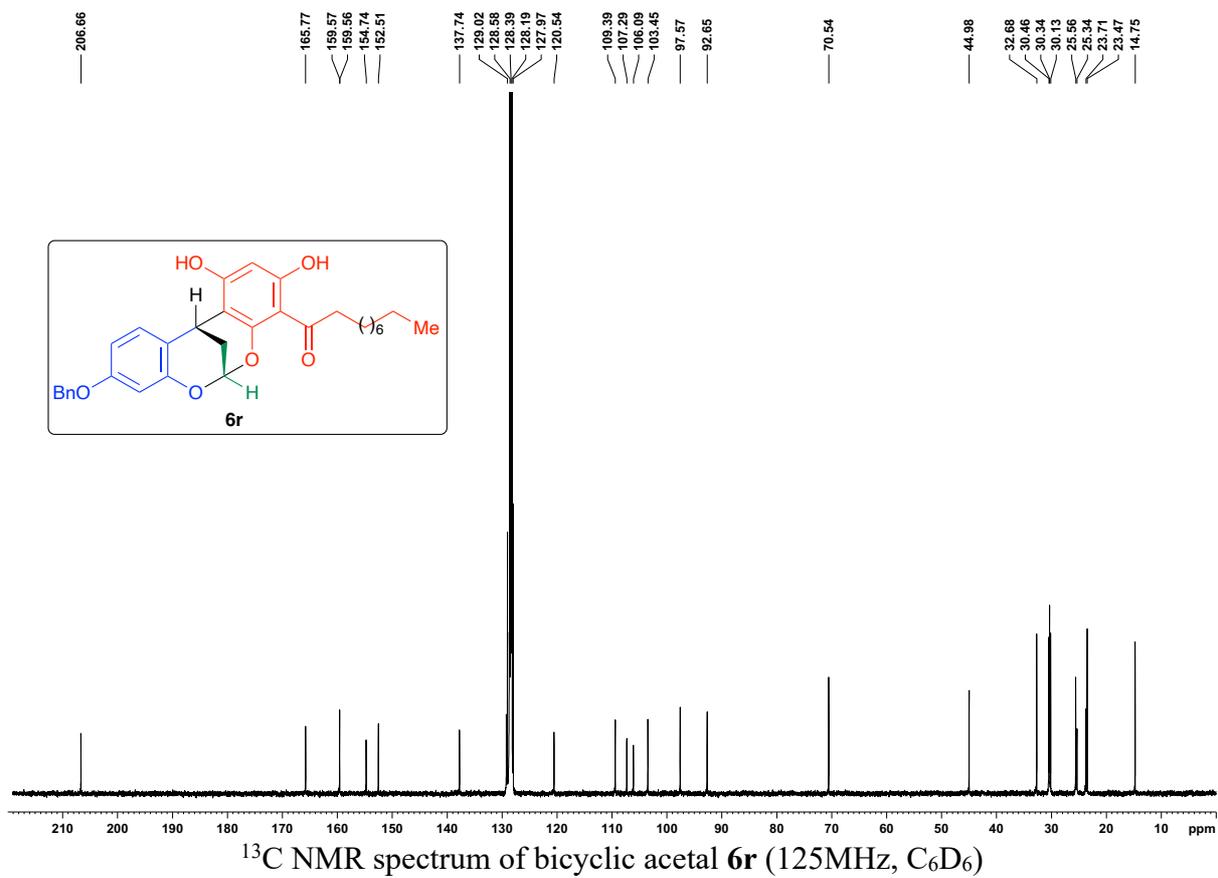
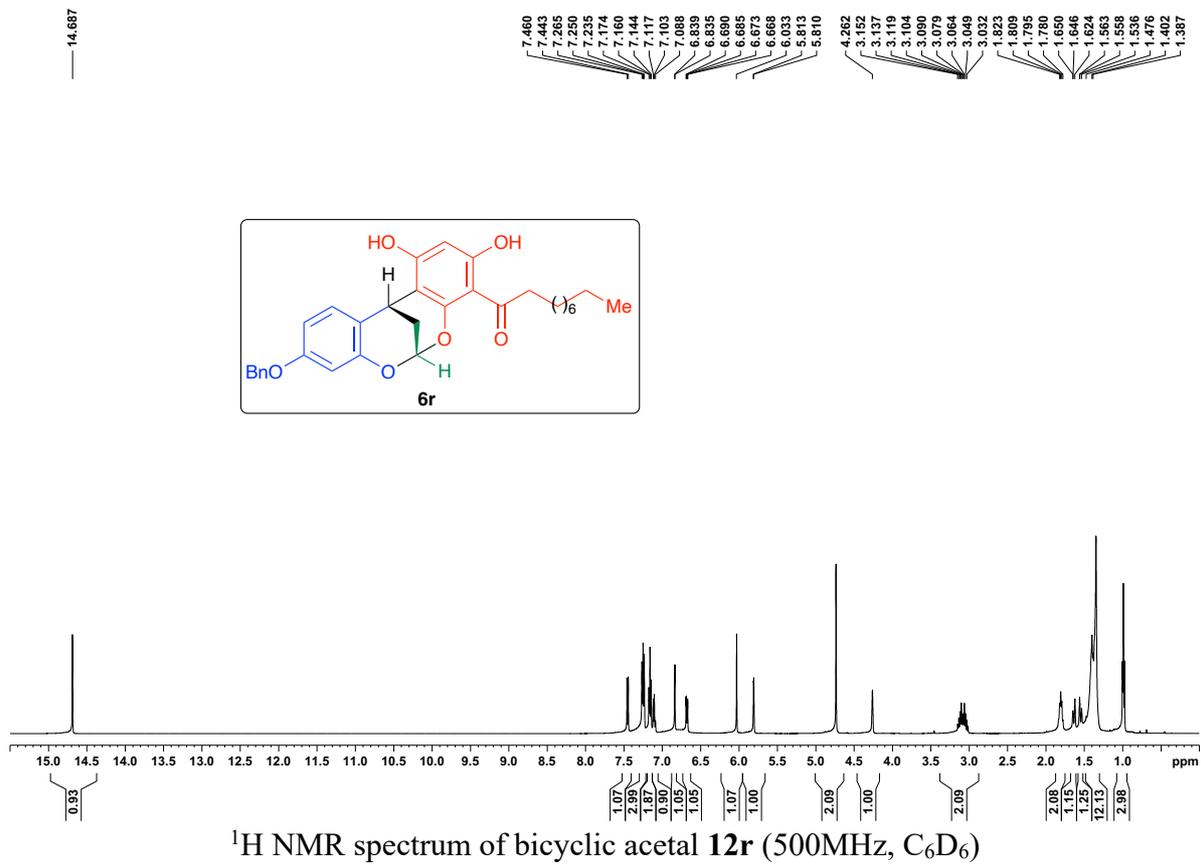
<sup>1</sup>H NMR spectrum of doubly linked flavan **6n** (500MHz, CD<sub>3</sub>OD)

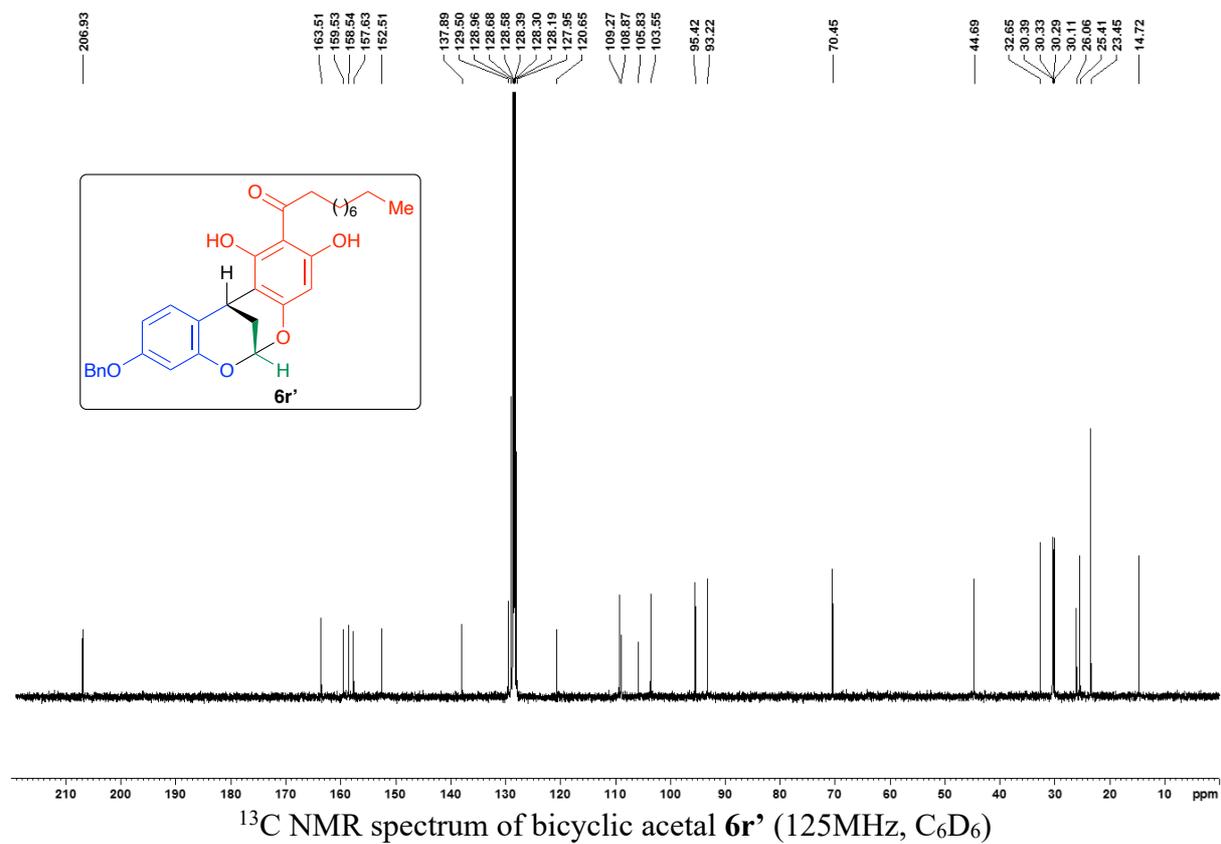
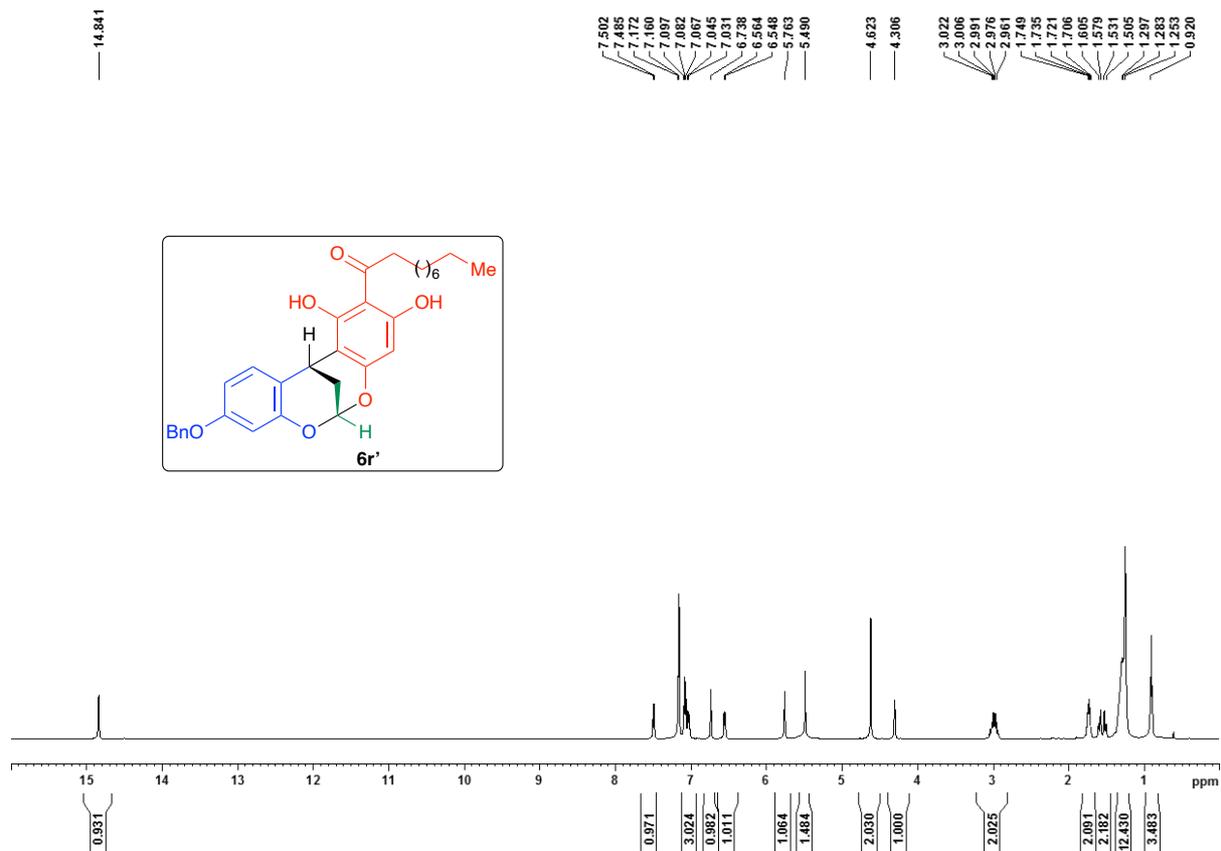


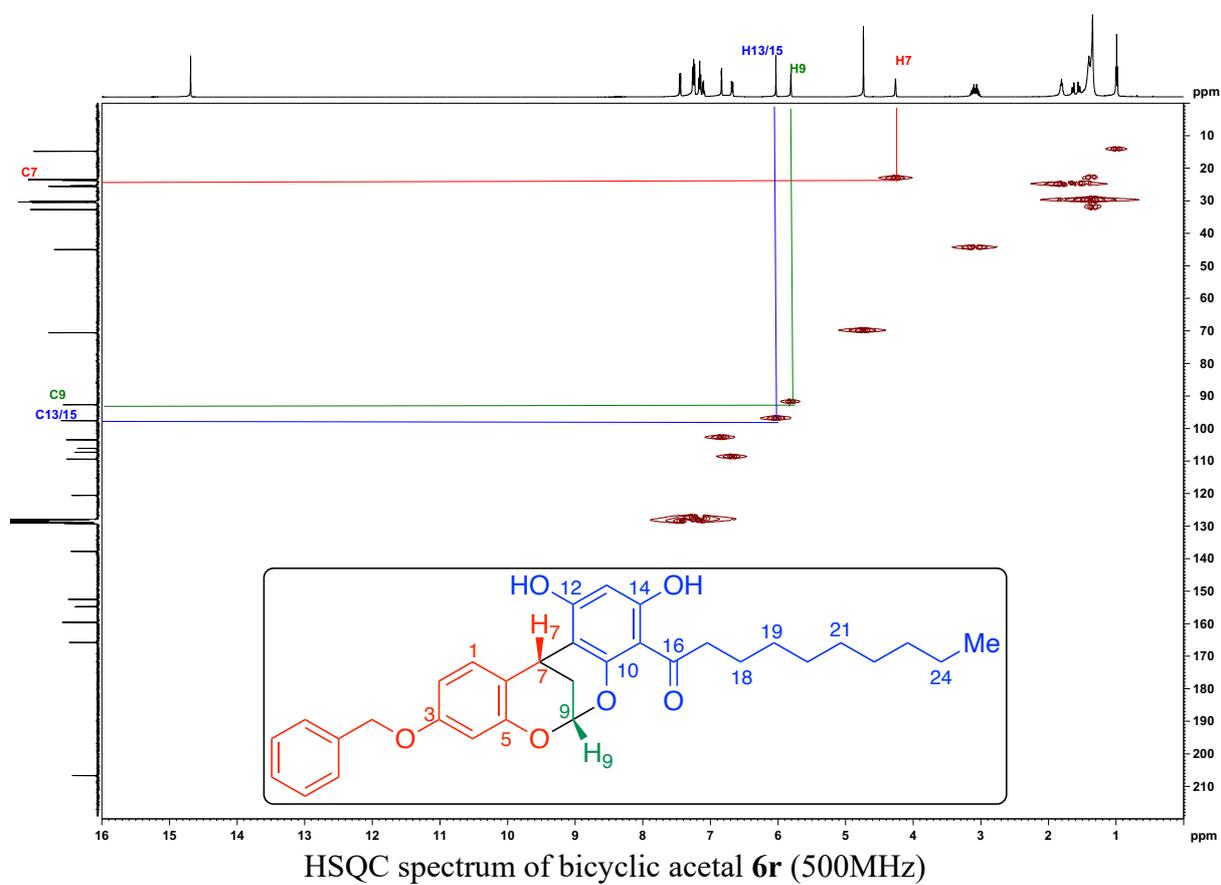
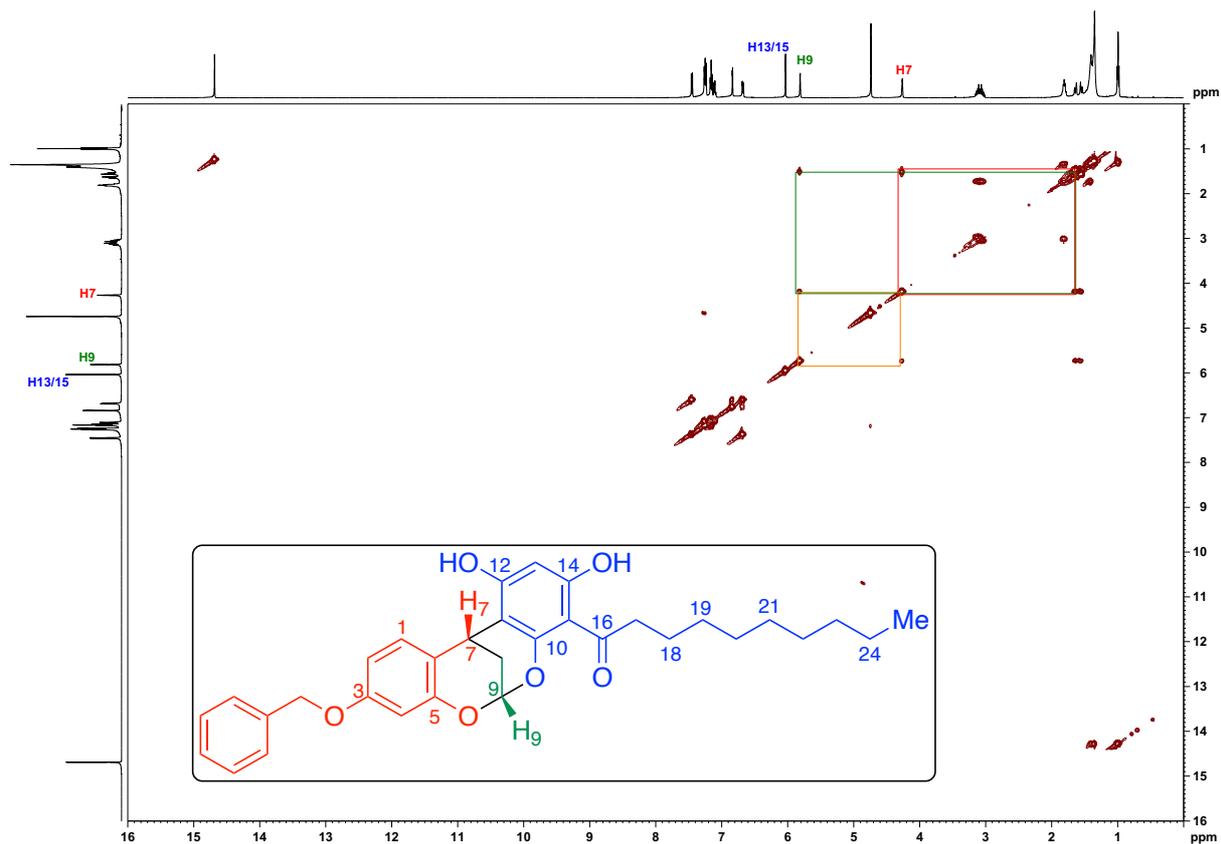
<sup>13</sup>C NMR spectrum of doubly linked flavan **6n** (125MHz, CD<sub>3</sub>OD)

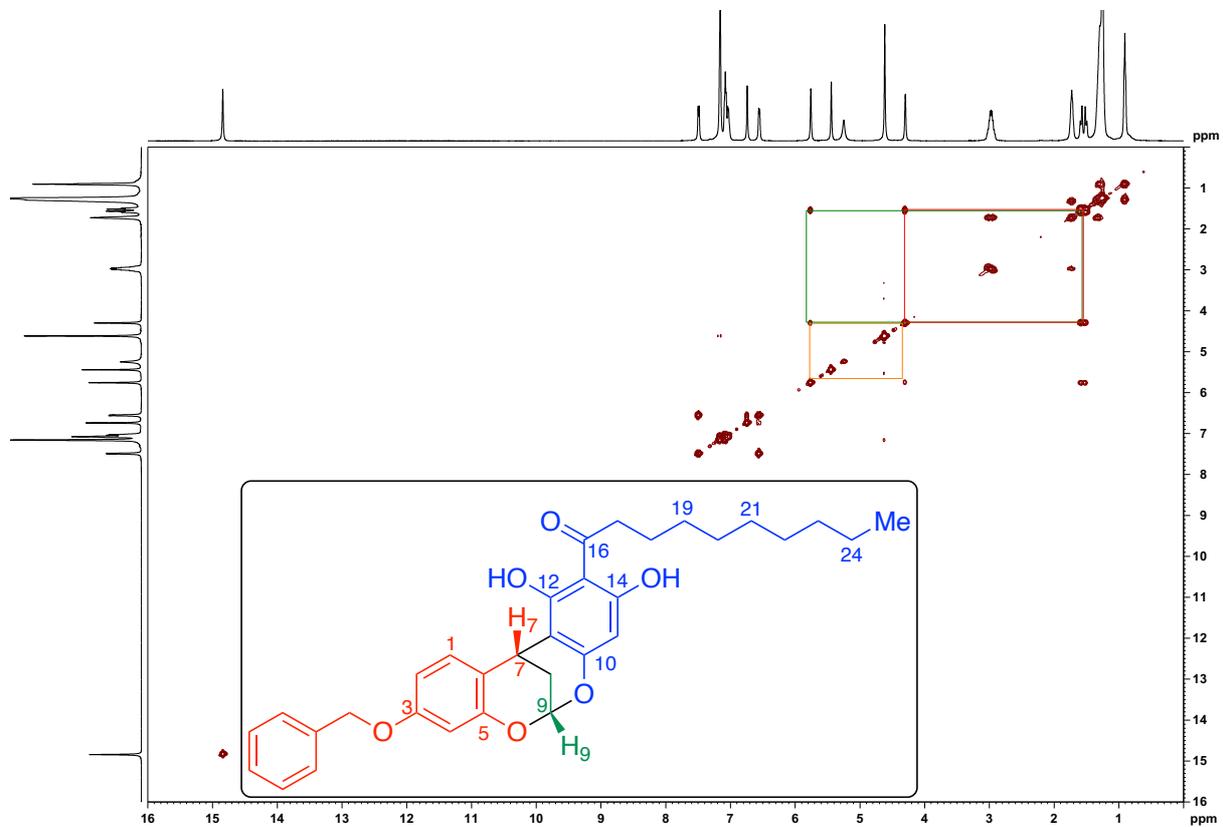
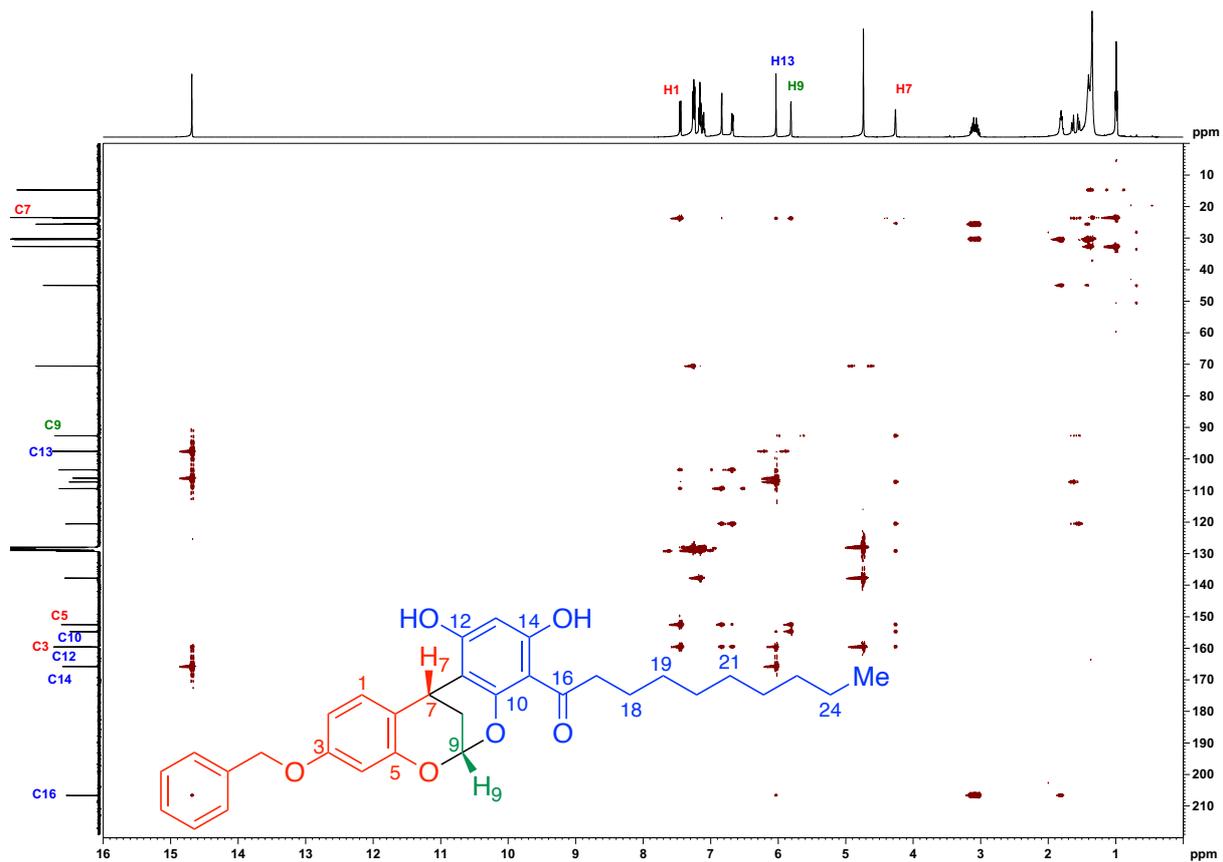


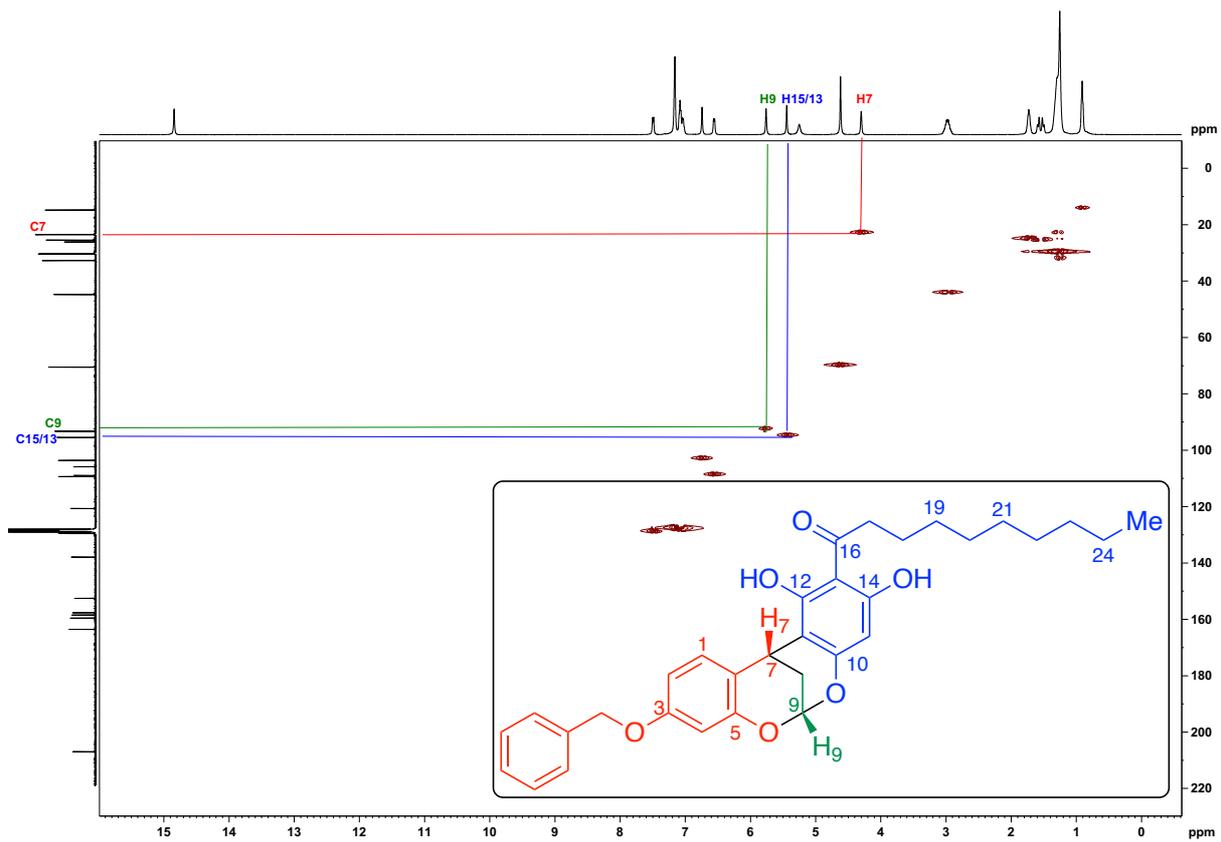




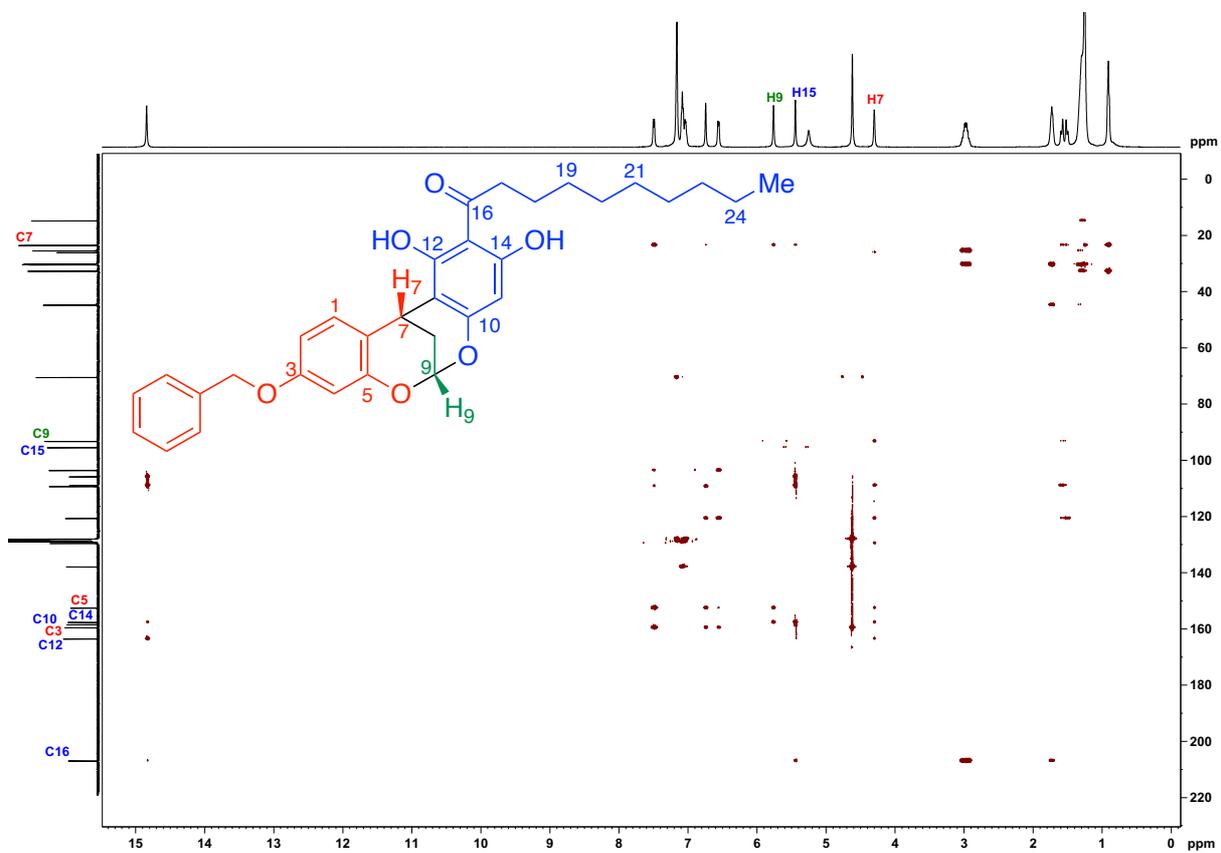




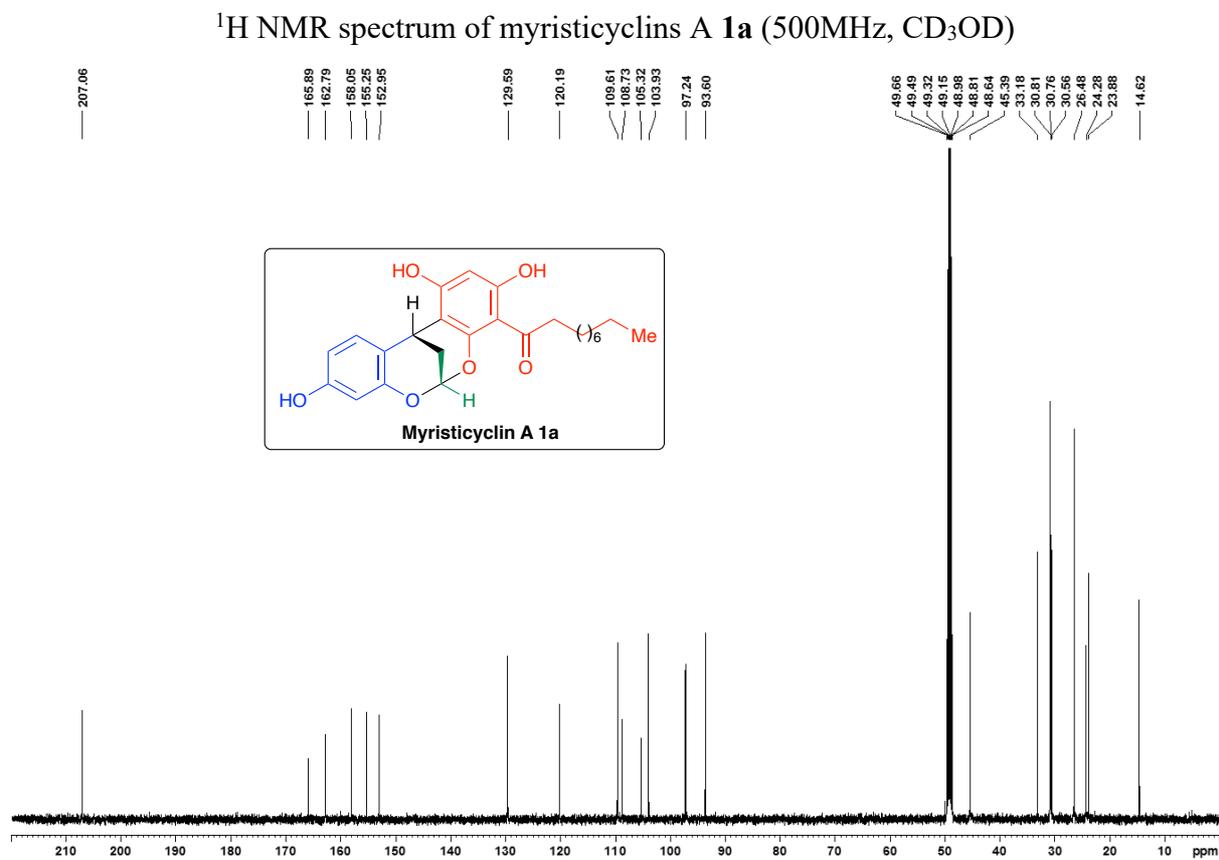
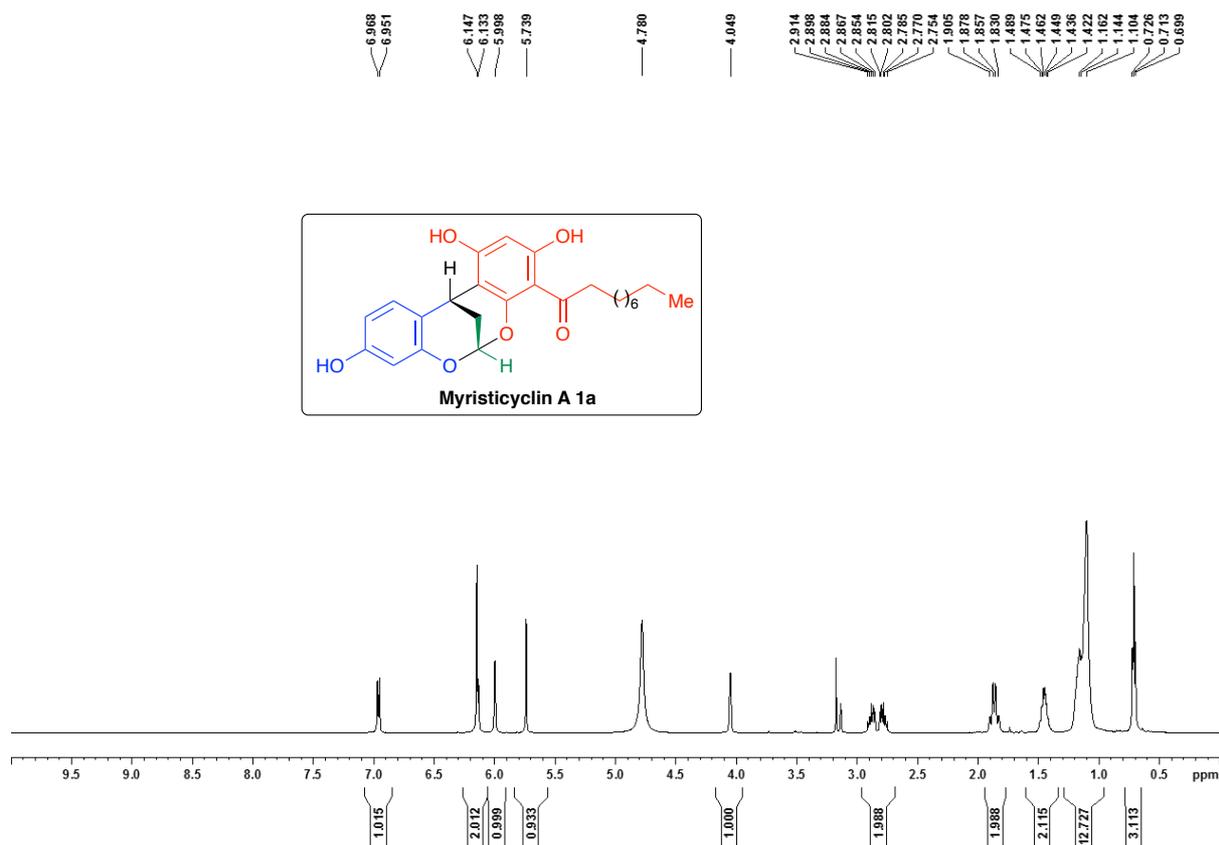


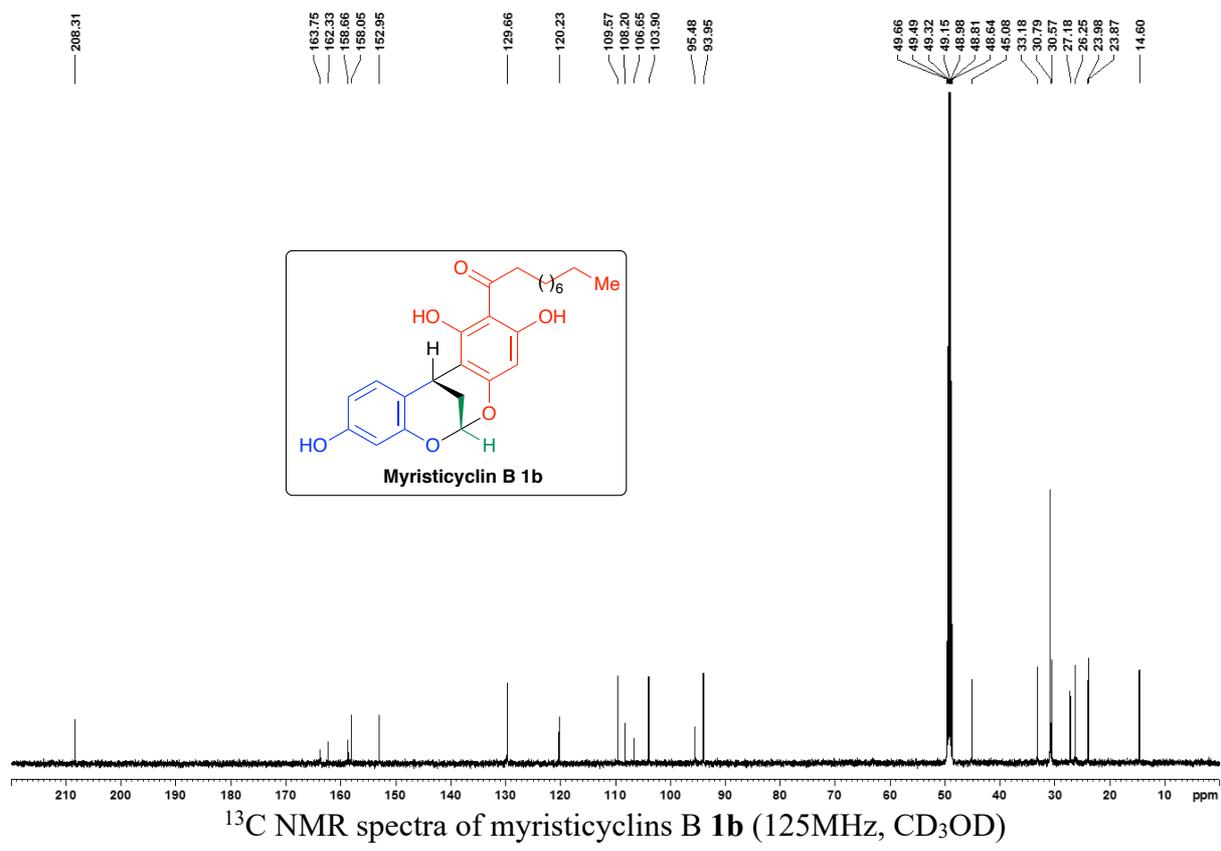
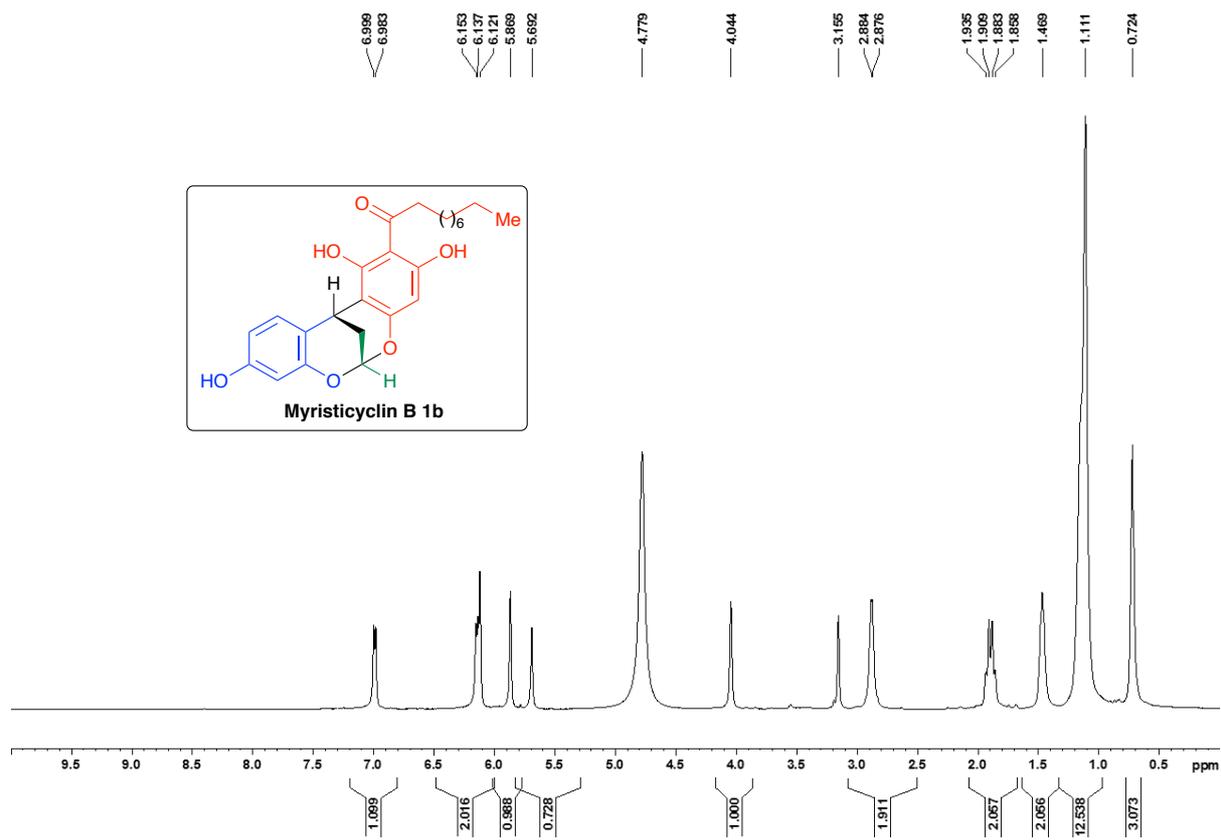


HSQC spectrum of bicyclic acetal **6r'** (500MHz)



HMBC spectrum of bicyclic acetal **6r'** (500MHz)





## X-Ray crystallographic analysis and data

### Crystal data and structure refinement for bicyclic acetal 6j

Identification code	6j		
Solvent	Pet. Ether:PrOH		
CCDC	2097413		
Bond precision:	C-C = 0.0061 Å	Wavelength= 1.54184	
Cell:	a=5.3663(2) alpha= 90	b=7.4309(3) beta= 90	c=32.7640(14) gamma= 90
Temperature:	150 K		
	Calculated	Reported	
Volume	1306.51(9)	1306.52(10)	
Space group	P 21 21 21	P 21 21 21	
Hall group	P 2ac 2ab	-P P 2ac 2ab	
Moiety formula	C16 H14 O4, H2 O	C16 H14 O4, H2 O	
Sum formula	C16 H16 O5	C16 H16 O5	
Mr	288.29	288.29	
Dx, g cm <sup>-3</sup>	1.466	1.466	
Z	4	4	
Mu (mm <sup>-1</sup> )	0.909	0.909	
F000	608.0	608.0	
F000'	610.08		
h,k,l max	6,8,38	6,8,38	
Nref	2231[ 1352]	2231[ 1352]	
Tmin,Tmax	0.840,0.968	0.528,1.000	
Tmin'	0.835		
Correction method=	NUMERICAL		
Data completeness =	1.64/0.99	Theta(max)= 64.994	
R(reflections) =	0.0534( 1825)	wR2(reflections)= 0.1347( 2219)	
S = 1.023	Npar = 196		

*Crystal data and structure refinement for doubly linked flavan 6o*

Identification code	<b>6o</b>		
Solvent	Pet. Ether:MeOH		
CCDC	2097414		
Bond precision:	C-C = 0.0093 Å	Wavelength= 0.71073	
Cell:	a= 20.6534(16) alpha= 90	b= 5.5621(6) beta= 92.131(7)	c= 17.0891(15) gamma= 90
Temperature:	150 K		
	Calculated	Reported	
Volume	1961.8(3)	1961.8(3)	
Space group	P 21/c	P 1 21/c 1	
Hall group	-P 2ybc	-P 2ybc	
Moiety formula	C21 H15 Br O4, 0.5(C6 H6)	C21 H15 Br O4, C3 H3	
Sum formula	C24 H18 Br O4	C24 H18 Br O4	
Mr	450.28	450.29	
Dx, g cm <sup>-3</sup>	1.525	1.525	
Z	4	4	
Mu (mm <sup>-1</sup> )	2.124	2.124	
F000	916.0	916.0	
F000'	915.26		
h,k,l max	24,6,20	24,6,20	
Nref	3463	3460	
Tmin,Tmax	0.792,0.936	0.694,1.000	
Tmin'	0.792		
Correction method=	NUMERICAL		
Data completeness =	0.999	Theta(max)= 24.999	
R(reflections) =	0.0663( 2036)	wR2(reflections)= 0.2376( 3460)	
S = 1.061	Npar = 264		

*Crystal data and structure refinement for cassiaflavan 9*

Identification code	9		
Solvent	Pet. Ether:Ethylacetate		
CCDC	2097415		
Bond precision:	C-C = 0.0041 Å	Wavelength= 0.71073	
Cell:	a= 7.4157(3) alpha=) 90	b= 9.0593(5) beta= 90	c= 26.5028(14) gamma= 90
Temperature:	100 K		
	Calculated	Reported	
Volume	1780.49(15)	1780.49(15)	
Space group	P 21 21 21	P 21 21 21	
Hall group	P 2ac 2ab	P 2ac 2ab	
Moiety formula	C20 H24 O5	0.5(C20 H24 O5)	
Sum formula	C20 H24 O5	C10 H12 O2.50	
Mr	344.39	172.20	
Dx, g cm <sup>-3</sup>	1.285	1.285	
Z	4	8	
Mu (mm <sup>-1</sup> )	0.092	0.092	
F000	736.0	736.0	
F000'	736.40		
h,k,l max	8,10,31	8,10,31	
Nref	3125[ 1828]	3114	
Tmin,Tmax	0.979,0.990	0.851,1.000	
Tmin'	0.975		
Correction method=	NUMERICAL		
Data completeness =	1.70/1.00	Theta(max)= 24.993	
R(reflections) =	0.0414( 2880)	wR2(reflections)= 0.1007( 3114)	
S = 1.036	Npar = 230		

***Crystal data and structure refinement for doubly linked flavan 6r'***

Identification code	<b>6r'</b>		
Solvent	Pet. Ether:Ethylacetate		
CCDC	2097423		
Bond precision:	C-C = 0.0087 Å	Wavelength= 1.54184	
Cell:	a= 14.4688(7) alpha= 90	b= 8.0297(5) beta= 90	c= 46.845(3) gamma= 90
Temperature:	150 K		
	Calculated	Reported	
Volume	5442.5(6)	5442.4(6)	
Space group	P b c a	P b c a	
Hall group	-P 2ac 2ab	-P 2ac 2ab	
Moiety formula	C <sub>32</sub> H <sub>36</sub> O <sub>6</sub>	C <sub>32</sub> H <sub>36</sub> O <sub>6</sub>	
Sum formula	C <sub>32</sub> H <sub>36</sub> O <sub>6</sub>	C <sub>32</sub> H <sub>36</sub> O <sub>6</sub>	
Mr	516.61	516.61	
Dx, g cm <sup>-3</sup>	1.261	1.261	
Z	8	8	
Mu (mm <sup>-1</sup> )	0.694	0.694	
F000	2208.0	2208.0	
F000'	2214.75		
h,k,l max	17,9,55	17,9,55	
Nref	4634	4618	
Tmin,Tmax	0.905,0.986	0.031,1.000	
Tmin'	0.870		
Correction method=	NUMERICAL		
Data completeness =	0.997	Theta(max)= 64.998	
R(reflections) =	0.0917( 2095)	wR2(reflections)= 0.3225( 4618)	
S = 1.000	Npar = 346		

## Reference:

1. Lu, Z.; Van Wagoner, R. M.; Pond, C. D.; Pole, A. R.; Jensen, J. B.; Blankenship, D. A.; Grimberg, B. T.; Kiapranis, R.; Matainaho, T. K.; Barrows, L. R.; Ireland, C. M., Myristicyclins A and B: Antimalarial Procyanidins from *Horsfieldia spicata* from Papua New Guinea. *Org. Lett.* **2014**, *16* (2), 346.