

Revealing the fate of the phenylcoumaran linkage during lignin oxidation reactions

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S1.0 General remarks

Commercially available compounds were purchased and used as received unless otherwise stated. DDQ was recrystallised from chloroform prior to use.

NMR: ^1H and ^{13}C NMR analysis was performed on a Bruker Avance II 400 MHz, Bruker Avance 500 MHz or a Bruker Avance III 500 MHz spectrometer with the residual solvent peak used as the chemical shift (δ) reference. Multiplicities are provided using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet and the J couplings are reported in Hz. NMR spectra were processed using TopSpin 3.5 or MestReNova 11.0.

Lignin NMR analysis was performed on Bruker Avance III 500 MHz or 700 MHz spectrometers equipped with nitrogen cooled cryoprobes (Prodigy) using previously described methods as follows:¹ The ^1H - ^{13}C -HSQC experiment was acquired using standard Bruker pulse sequence 'hsqcetgpsp.2' (phase-sensitive gradient-edited-2D HSQC using adiabatic pulses for inversion and refocusing). Composite pulse sequence 'garp4' was used for broadband decoupling during acquisition. In general 2048 data points was acquired over 12 ppm spectral width (acquisition time 170 ms) in F2 dimension using 24 scans with 1 s interscan delay and the d4 delay was set to 1.8 ms ($1/4J$, $J = 140$ Hz). A spectral width of 86 ppm (47-133 ppm) and 128 increments were acquired in F1 dimension (acquisition time 5.9 ms). The spectrum was processed using squared cosinebell in both dimensions and LPfc linear prediction (32 coefficients) in F1. d_6 -DMSO was used as the solvent for unacetylated lignins and CDCl_3 for acetylated lignin.

Column chromatography was performed using Fluorochem Silicagel (60Å 40-63 micron).

Thin layer chromatography was performed on pre-coated aluminium plates (60/kieselguhr F₂₅₄ Merk) and visualized under UV light (254 nm) or by staining with KMnO_4 , 1% iron (III) chloride (for phenolics) or 2,4-dinitrophenylhydrazine (for aldehydes and ketones) where appropriate.

Mass spectrometry data were acquired through the University of St Andrews School of Chemistry mass spectrometry service or through the EPSRC national mass spectrometry service center (Swansea, UK).

IR spectra were obtained on a Shimadzu IRAffinity-1S FourierTransform IR spectrophotometer as thin films. Analysis was carried out using Shimadzu IRsolution v1.50 and only characteristic peaks are reported.

Melting points were recorded on a Gallenkamp melting point apparatus.

S2.0 General procedure for screening model compounds reactivity with DDQ

Substrate (e.g. Compound **1**, 10 mg, 0.028 mmol) was placed in a 3 mL screw cap vial equipped with a magnetic stirring bar. DDQ (e.g. 6.3 mg, 0.028 mmol) was added to the vial followed by 1,4-dioxane (0.84 mL). The reaction was allowed to stir at either room temperature or at 60 °C (in an oil bath) for 24 hours. The reaction was then filtered through a cotton wool plug, aq. NaHCO₃ was added and the product extracted in to DCM (x3). The combined organic extracts were washed several times with H₂O, brine, dried with MgSO₄ and concentrated *in vacuo*. The concentrated product was then placed in a desiccator under vacuum overnight prior to being analysed by ¹H NMR. See **Figure S1-Figure S7** for crude NMR analyses.

S2.1 DDQ oxidation of model compound **1** at room temperature.

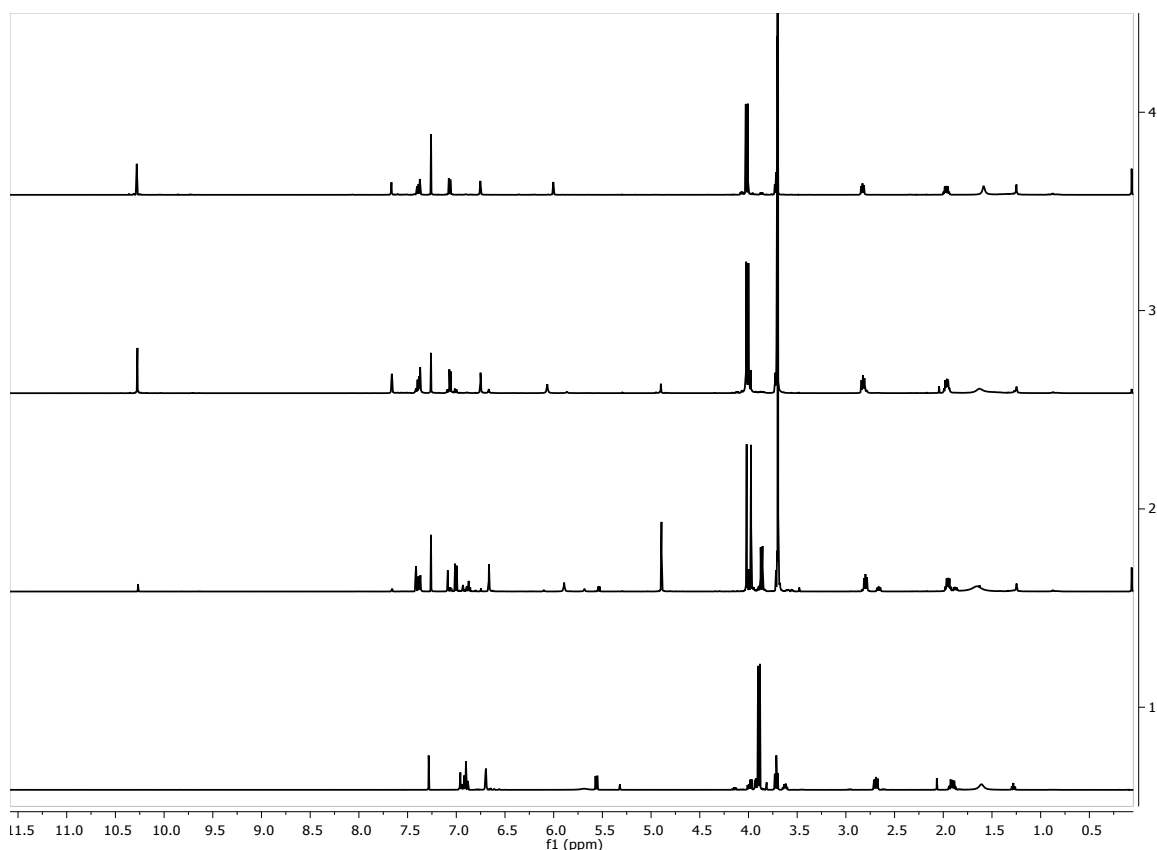
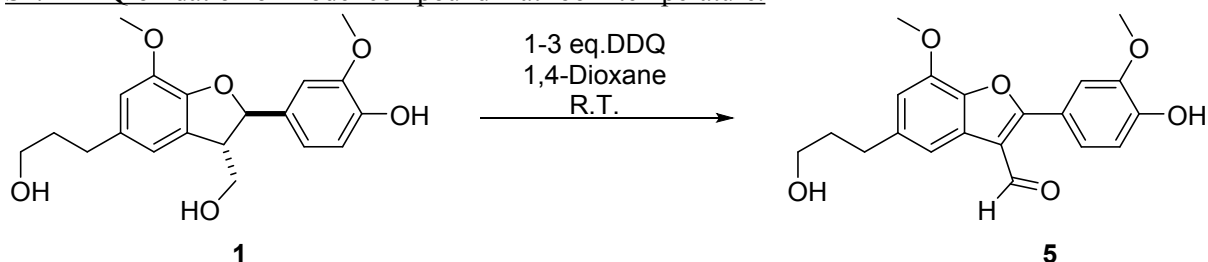


Figure S1: Crude ¹H NMR spectra obtained following the reaction of phenolic β-5 model compound (**1**) with X equivalents of DDQ at room temperature in 1,4-dioxane. 1) Starting material. 2) 1 eq. 3) 2 eq. and 4) 3 eq.

S2.2 DDQ oxidation of model compound **1** at 60 °C.

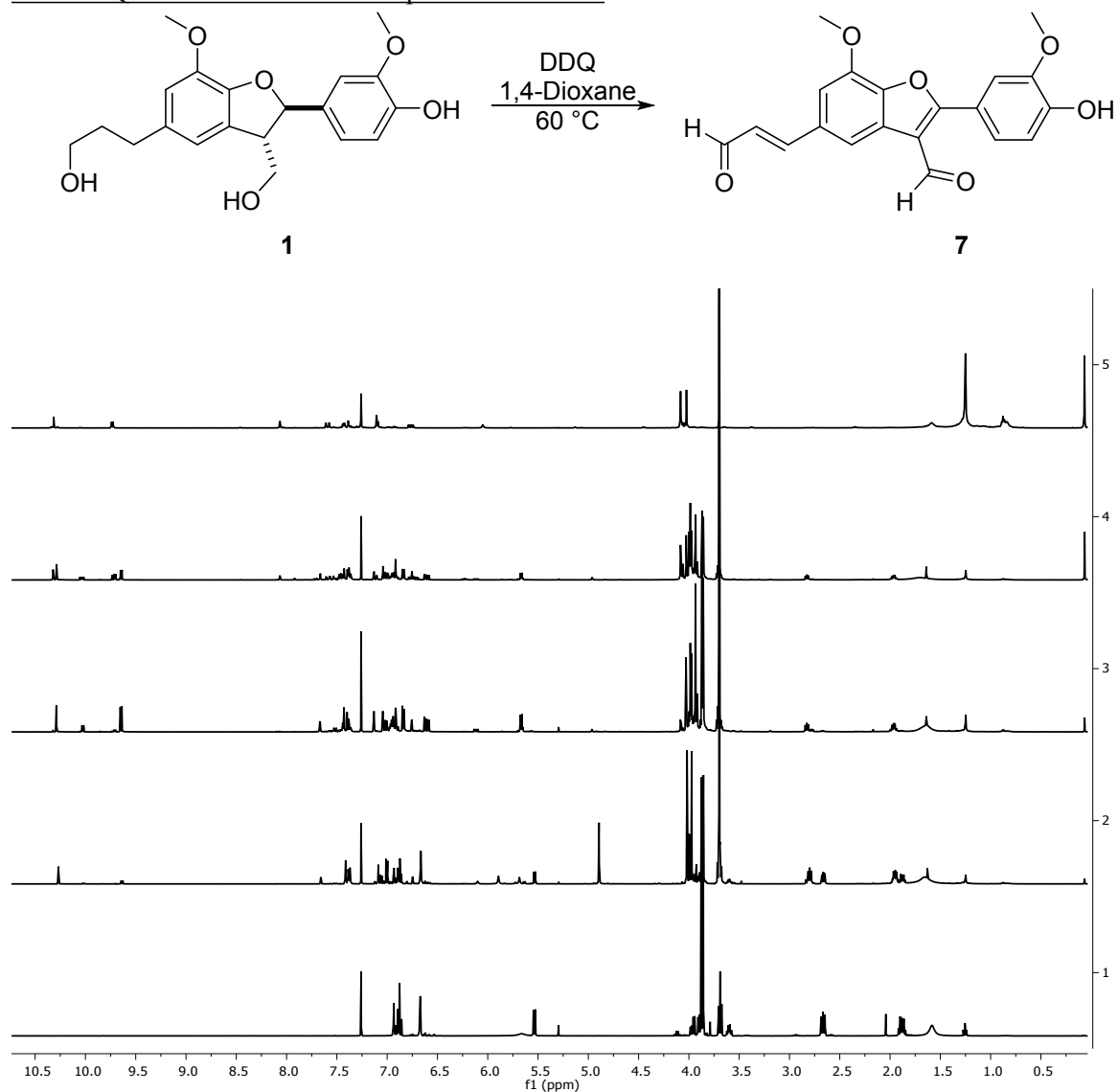


Figure S2: Crude ¹H NMR spectra obtained following the reaction of phenolic β-5 model compound (**1**) with X equivalents of DDQ at 60 °C in 1,4-dioxane. 1) Starting Material. 2) 1 eq. 3) 2 eq. 4) 3 eq. and 5) 10eq.

S2.3 DDQ oxidation of model compound **2** at room temperature.

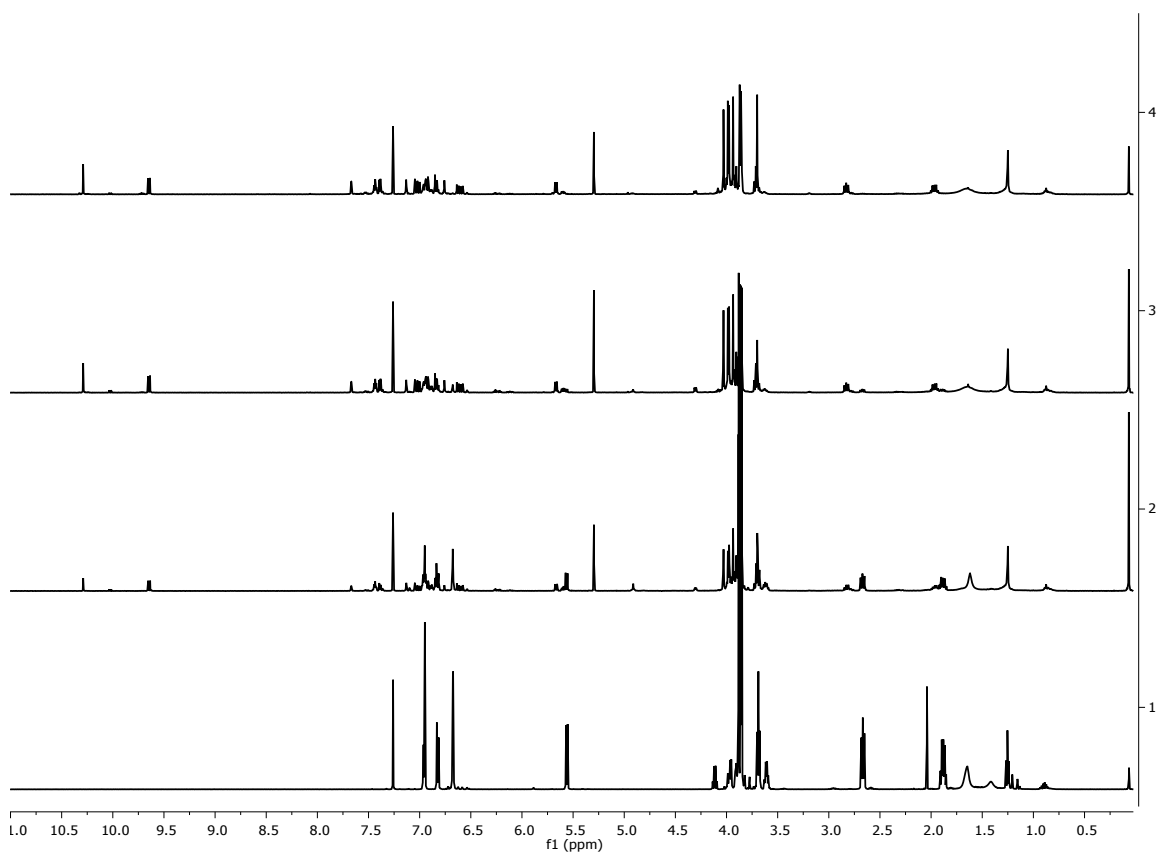
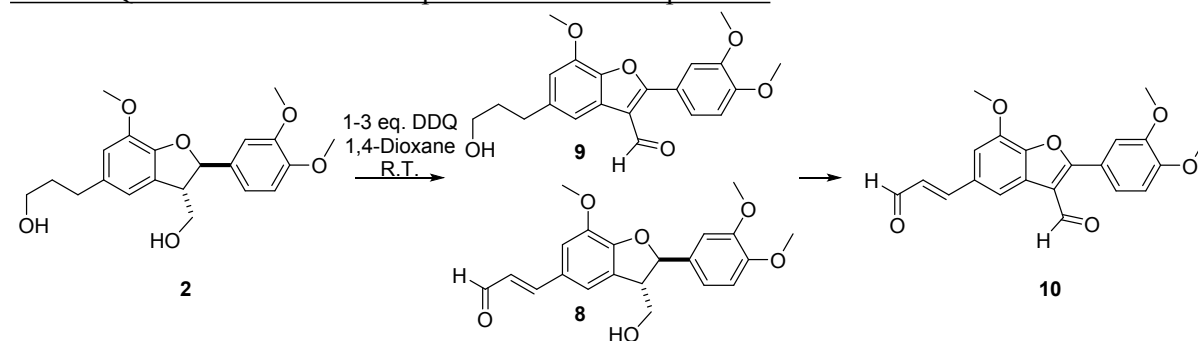


Figure S3: Crude ¹H NMR spectra obtained following the reaction of non-phenolic β-5 model compound (**2**) with X equivalents of DDQ at room temperature in 1,4-dioxane. 1) Starting Material. 2) 1 eq. 3) 2 eq. and 4) 3 eq.

S2.4 DDQ oxidation of model compound **2** at 60 °C

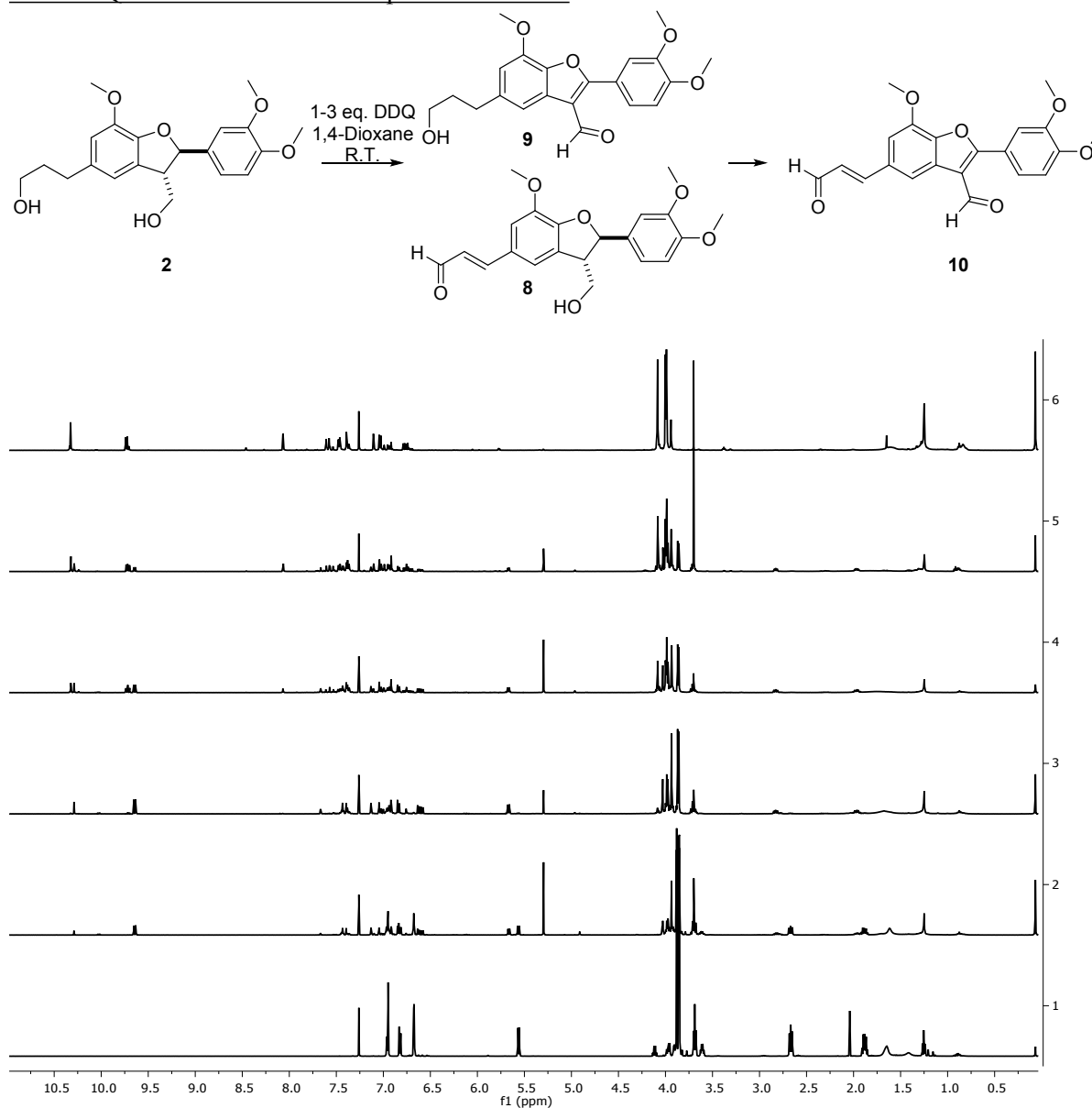


Figure S4: Crude ¹H NMR spectra obtained following the reaction of non-phenolic β-5 model compound (**2**) with X equivalents of DDQ at 60 °C in 1,4-dioxane. 1) Starting Material. 2) 1 eq. 3) 2 eq. and 4) 3 eq. 5) 4 eq. and 6) 10 eq.

S2.5 DDQ oxidation of model compound **3** at room temperature.

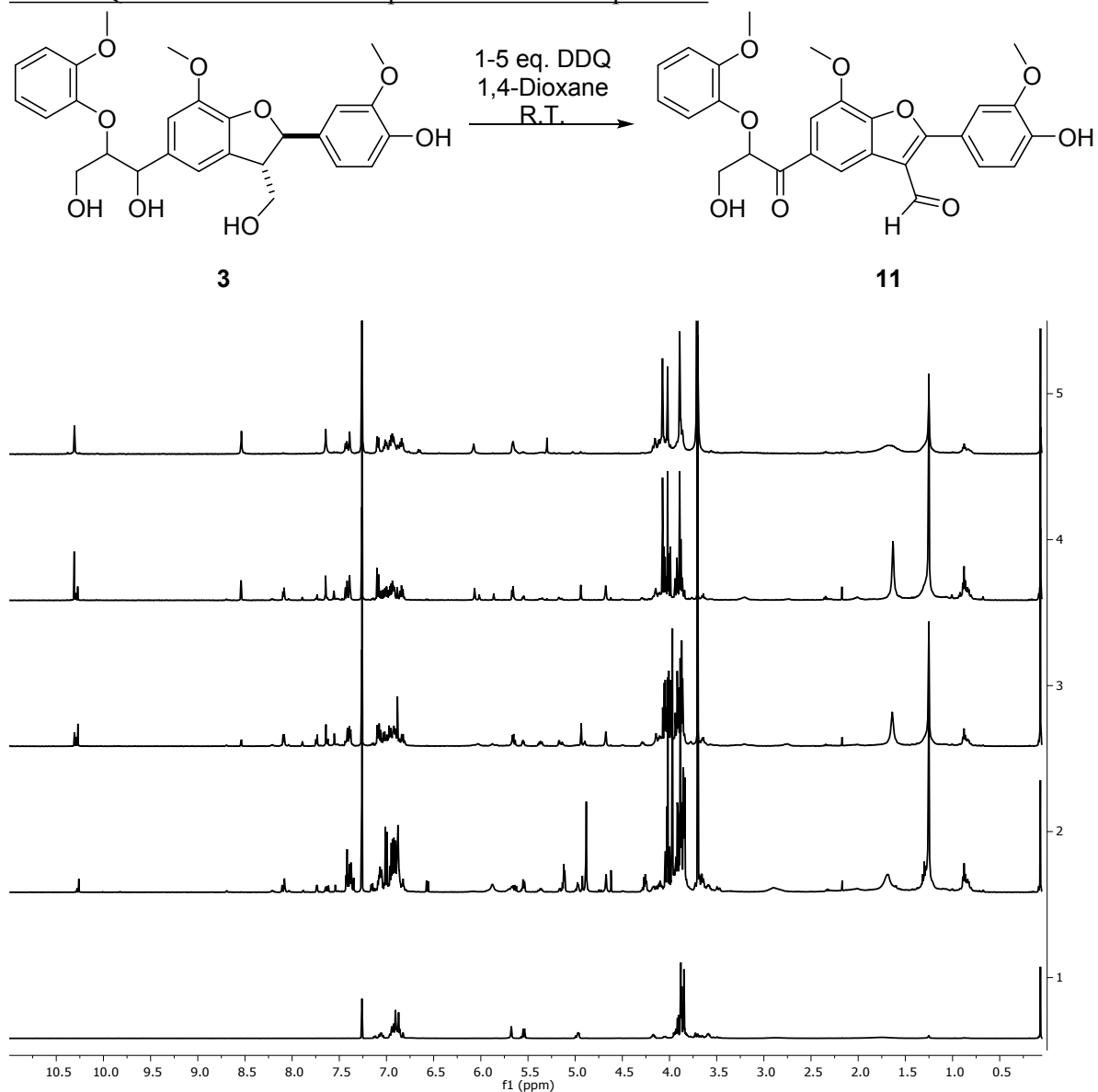


Figure S5: Crude ^1H NMR spectra obtained following the reaction of phenolic β -O-4 β -5 model compound (**3**) with X equivalents of DDQ at 60 $^\circ\text{C}$ in 1,4-dioxane. 1) Starting Material. 2) 1 eq. 3) 2 eq. 4) 3 eq. and 5) 5 eq.

S2.6 DDQ oxidation of model compound **4** at room temperature.

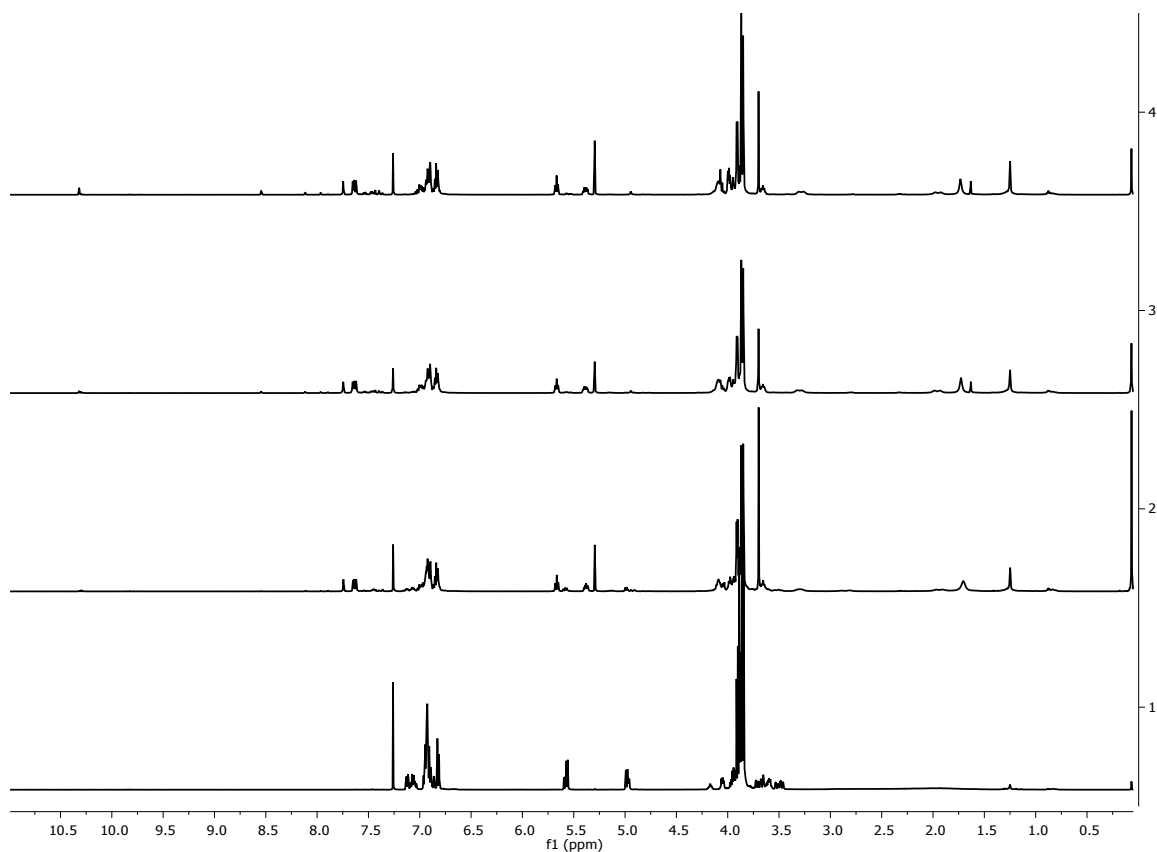
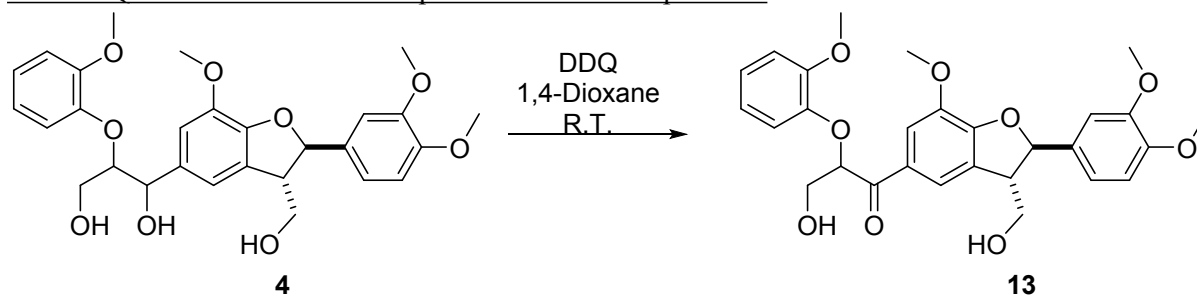


Figure S6: Crude ¹H NMR spectra obtained following the reaction of non-phenolic β-O-4 β-5 model compound (**4**) with X equivalents DDQ at room temperature in 1,4-dioxane. 1) Starting Material. 2) 1 eq. 3) 2 eq. and 4) 3 eq.

S2.7 DDQ oxidation of model compound **4** at 60 °C.

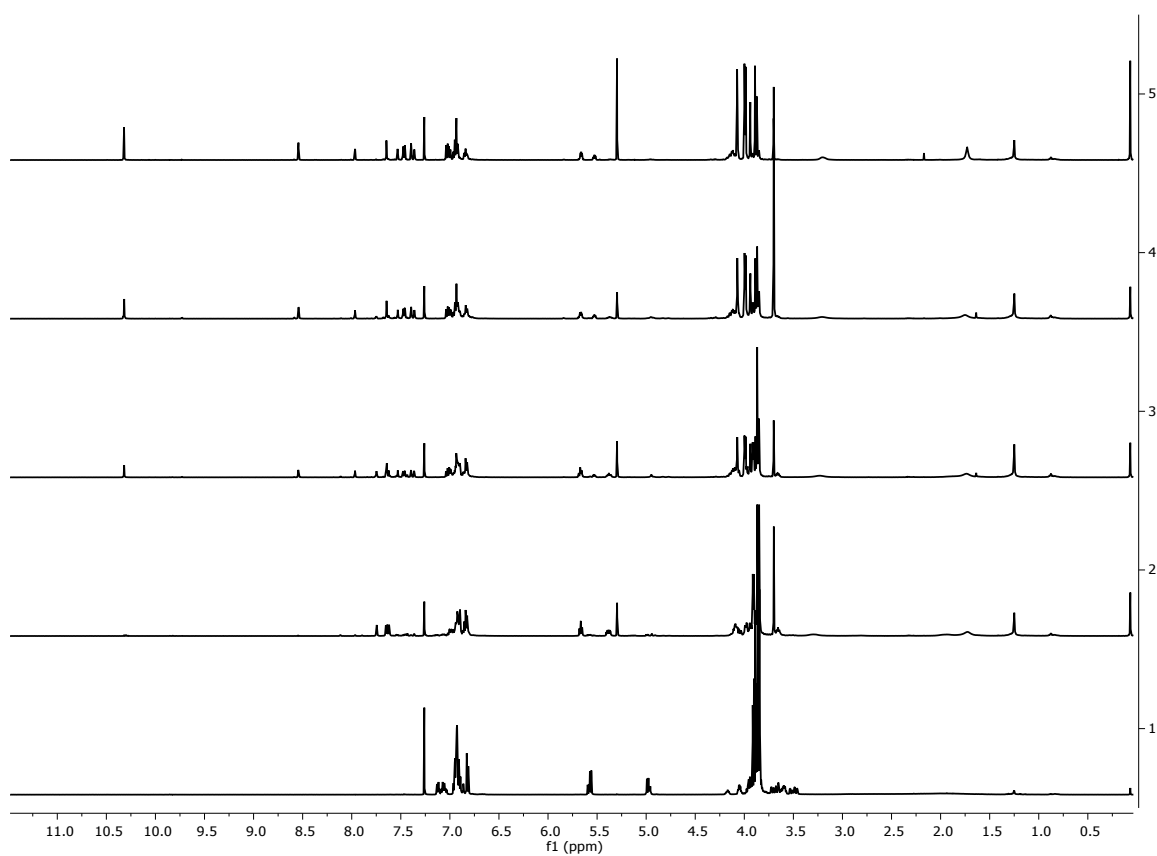
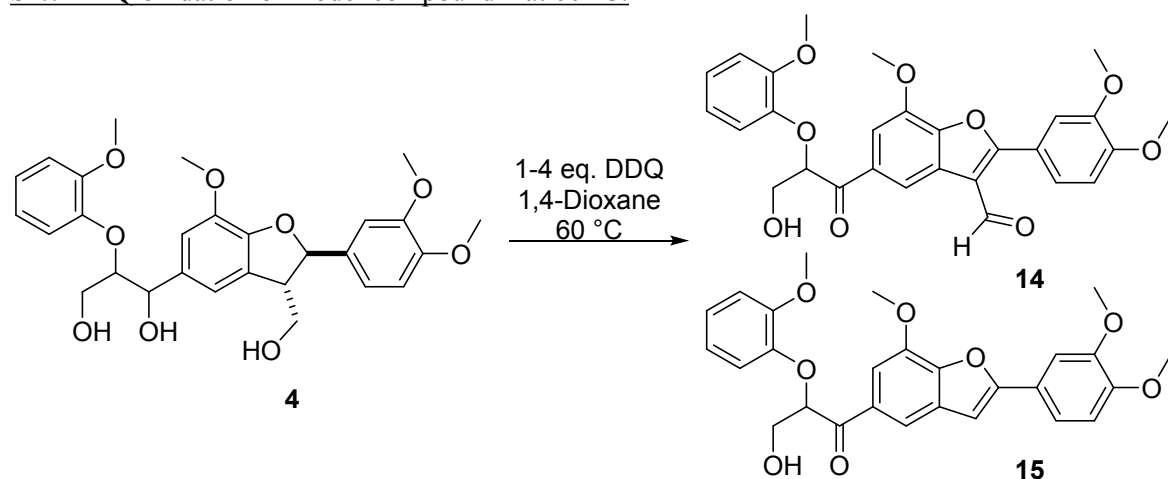


Figure S7: Crude ^1H NMR spectra obtained following the reaction of non-phenolic β -O-4 β -5 model compound (**4**) with X equivalents of DDQ at 60 °C in 1,4-dioxane. 1) Starting Material. 2) 1 eq. 3) 2 eq. 4) 3 eq. and 5) 4 eq.

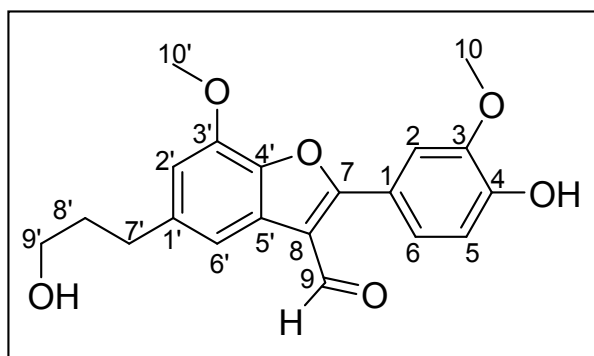
S3.0 Model Compound Synthesis

Compounds **1** and **2** were synthesised following literature procedures.²

Compounds **3** and **4** were synthesised following literature procedures.³

Compounds **19** and **20** were synthesised from compounds **1** and **2** by acetylation with pyridine/acetic anhydride following usual procedures.^{4,5}

S4.0 Upscaled DDQ oxidations for product isolation and characterisation



2-(4-hydroxy-3-methoxyphenyl)-5-(3-hydroxypropyl)-7-methoxybenzofuran-3-carbaldehyde (**5**)

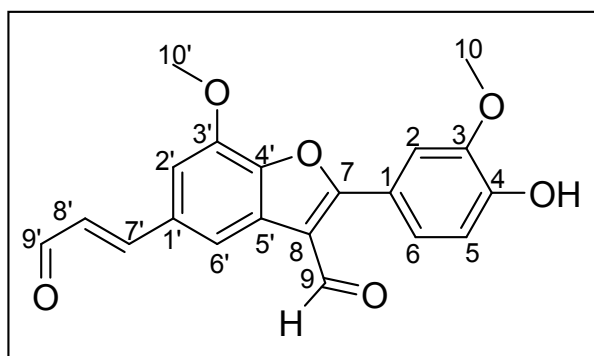
Synthesised following the general procedure at room temperature using compound **1** (50 mg, 0.14 mmol, 1.0 eq.) and DDQ (95 mg, 0.42 mmol, 3.0 eq.). Purification via column chromatography (0-60 % EtOAc:PET Ether) allowed for the isolation of compound **5** as an off white solid (28 mg 0.078 mmol, 57%).

¹H NMR (500 MHz, CDCl₃): δ 10.28 (s, 1H, H₉), 7.67 (d, J = 1.4 Hz, 1H, H_{6'}), 7.43 – 7.36 (m, 2H, H₂/H₅/H₆), 7.07 (d, J = 8.2 Hz, 1H, H₂/H₅/H₆), 6.75 (d, J = 1.4 Hz, 1H, H_{2'}), 6.02 (s, 1H C₄-OH), 4.03 (s, 3H, H_{10'}), 4.01 (s, 3H, H₁₀), 3.72 (t, J = 6.4 Hz, 2H, H_{9'}), 2.83 (t, J = 7.7 Hz, 2H, H_{7'}), 2.03 – 1.92 (m, 2H, H_{8'}).

¹³C NMR (126 MHz, CDCl₃): δ 187.0(C₉), 166.2, 148.8, 147.1(C₃), 144.7(C_{3'}), 141.8, 140.1, 127.4, 123.8 (C₂/C₅/C₆), 120.8, 116.9, 115.1 (C₂/C₅/C₆), 113.7 (C_{6'}), 111.2 (C₂/C₅/C₆), 108.9 (C_{2'}), 62.4(C_{9'}), 56.4(C₁₀), 56.2 (C_{10'}), 34.9 (C_{8'}), 32.7(C_{7'}).

HR MS: [M - H]⁻ m/z calc: 355.1187 [M - H]⁻ m/z found: 355.1185

(Data is consistent with that reported in the literature)⁶



2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-5-(3-oxoprop-1-en-1-yl)benzofuran-3-carbaldehyde (**7**)

Synthesised following the general procedure at 60 °C using compound **1** (100 mg, 0.14 mmol, 1.00 eq.) and DDQ (630 mg, 2.78 mmol, 10.0 eq.). Purification via column chromatography (0-80 % EtOAc:PET Ether) allowed for the isolation of compound **7** as a white solid (16.6 mg 0.047 mmol, 17%). Crude NMR analysis (Figure S2) suggested quite a clean reaction and so the low yield is attributed to losses during work-up and

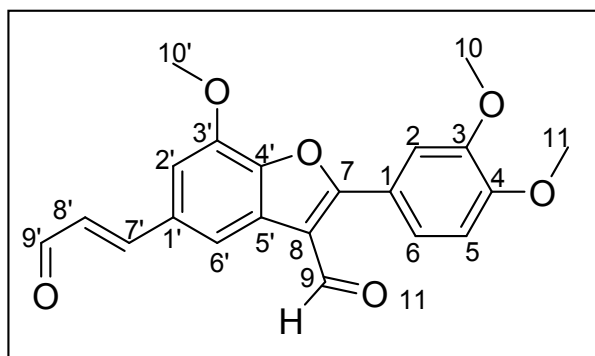
purification.

¹H NMR (400 MHz, CDCl₃): δ 10.32 (s, 1H), 9.74 (d, J = 7.6 Hz, 1H), 8.07 (d, J = 1.5 Hz, 1H), 7.60 (d, J = 15.9 Hz, 1H), 7.44 (dd, J = 8.2, 2.0 Hz, 1H), 7.39 (d, J = 2.0 Hz, 1H), 7.13 – 7.08 (m, 2H), 6.77 (dd, J = 15.9, 7.6 Hz, 1H), 6.02 (s, 1H), 4.08 (s, 3H), 4.03 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 193.8, 186.6, 166.7, 153.2, 149.2, 147.2, 145.5, 144.8, 132.3, 128.6, 128.1, 124.0, 120.2, 116.9, 116.7, 115.3, 111.1, 106.7, 56.5, 56.3.

HR MS: [M - H]⁻ m/z calc: 351.0874 [M - H]⁻ m/z found: 351.0873

(Data is consistent with that reported in the literature)⁷



2-(3,4-dimethoxyphenyl)-7-methoxy-5-(3-oxoprop-1-en-1-yl)benzofuran-3-carbaldehyde (**10**)

Synthesised following the general procedure at 60 °C using compound **2** (100 mg, 0.27 mmol, 1.0 eq.) and DDQ (606 mg, 2.67 mmol, 10.0 eq.). Purification via column chromatography (0-60 % EtOAc:PET Ether) allowed for the isolation of compound **10** as a white solid (39 mg, 0.11 mmol, 44%).

¹H NMR (500 MHz, CDCl₃): δ 10.33 (s, 1H, H₉), 9.74 (d, *J* = 7.7 Hz, 1H, H_{9'}), 8.07 (d, *J* = 1.4 Hz, 1H, H₂/H_{6'}), 7.60 (d, *J* = 15.9 Hz, 1H, H_{7'}), 7.47 (dd, *J* = 8.4, 2.1 Hz, 1H, H₆), 7.39 (d, *J* = 2.1 Hz, 1H, H₂/H₅), 7.11 (d, *J* = 1.4 Hz, 1H, H₂/H_{6'}), 7.04 (d, *J* = 8.4 Hz, 1H, H₂/H₅), 6.77 (dd, *J* = 15.9, 7.7 Hz, 1H, H_{8'}), 4.09 (s, 3H, -OCH₃), 4.00 (s, 3H, -OCH₃), 3.99 (s, 3H, -OCH₃).

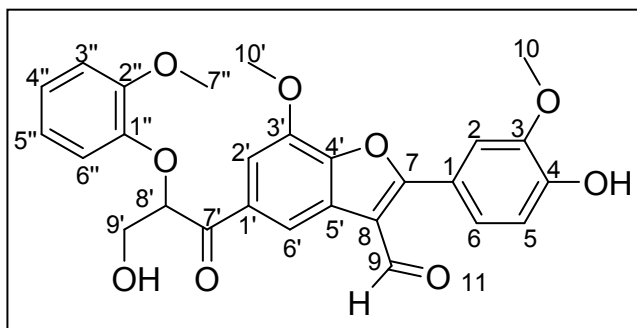
¹³C NMR (126 MHz, CDCl₃): δ 193.8 (C₉), 186.6 (C_{9'}), 166.6 (C₇), 153.2 (H_{7'}), 152.2 (C₃/C₄), 149.7 (C₃/C₄), 145.5 (C_{3'}), 144.8, 132.3 (C_{1'}), 128.6 (C_{8'}), 128.1, 123.3 (C₆), 120.7, 116.9 (C₂/C_{6'}), 116.8, 111.5 (C₂/C₅), 111.4 (C₂/C₅), 106.7 (C₂/C_{6'}), 56.4 (-OCH₃), 56.33 (-OCH₃), 56.29 (-OCH₃).

HR MS: [M + H]⁺ *m/z* calc: 367.1176 [M + H]⁺ *m/z* found: 367.1179

IR: (thin film) 1684, 1670, 1653, 1559, 1541, 1506, 1474, 1456, 1026.

(Data is consistent with that reported in the literature)⁸

5-(3-hydroxy-2-(2-methoxyphenoxy)propanoyl)-2-(4-hydroxy-3-methoxyphenyl)-7-methoxybenzofuran-3-carbaldehyde (**11**)



Compound **3** (100 mg 0.201 mmol 1.00 eq) was dissolved in dioxane (2.95 ml) and DDQ (227 mg, 1.00 mmol 5.00 eq) was added and the reaction allowed to proceed at room temperature for 24 hours. The reaction was then filtered through a cotton plug. Due to the products solubility in H₂O aqueous extraction of residual DDQ/DDQH₂ was not possible. The organic layer was concentrated *in vacuo* prior to being dissolved in DCM and transferred directly to a silica

chromatography column. The column was eluted with 1-5% MeOH/DCM which allowed isolation of compound **11** as a yellow solid (29.1 mg 0.598 mmol, 30%).

¹H NMR (500 MHz, CDCl₃): δ 10.31 (s, 1H, H₉), 8.53 (d, *J* = 1.5 Hz, 1H, H_{6'}), 7.64 (d, *J* = 1.5 Hz, 1H, H_{2'}), 7.42 (dd, *J* = 8.2, 1.9 Hz, 1H, H₆), 7.38 (d, *J* = 2.0 Hz, 1H, H₂/H₅), 7.09 (d, *J* = 8.2 Hz, 1H, H₂/H₅), 7.02 (ddd, *J* = 8.1, 7.4, 1.6 Hz, 1H, Ar-H), 6.95 (ddd, *J* = 15.1, 8.1, 1.6 Hz, 2H, Ar-H), 6.84 (ddd, *J* = 8.0, 7.4, 1.6 Hz, 1H, Ar-H), 6.08 (s, 1H, C₄-OH), 5.67 (dd, *J* = 5.8, 3.5 Hz, 1H, H_{8'}), 4.19 – 4.09 (m, 2H, H_{9'}), 4.07 (s, 3H, -OCH₃), 4.02 (s, 3H, -OCH₃), 3.89 (s, 3H, -OCH₃).

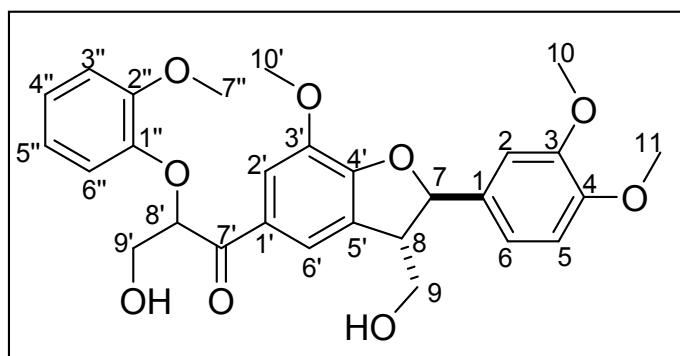
¹³C NMR (101 MHz, CDCl₃): δ 196.1 (C₉), 186.4 (C_{7'}), 166.9 (C₄), 150.8, 149.3, 147.2, 146.8, 146.1, 145.6, 133.3, 127.4, 123.97 (C₆), 123.92, 121.3, 120.1, 118.9, 116.8 (C₈), 116.5 (C_{6'}), 115.3 (C₂/C₅), 112.4, 111.1 (C₂/C₅), 108.0 (C_{2'}), 84.0 (C_{8'}), 63.8 (C_{9'}), 56.5 (-OCH₃), 56.4 (-OCH₃), 56.0 (-OCH₃).

HR MS: [M - H]⁻ *m/z* calc: 491.1348 [M - H]⁻ *m/z* found: 491.1348

IR: (thin film) 1684, 1653, 1593, 1506, 1254, 1161, 1126, 1020.

MP: 88-90 °C

1-(2-(3,4-Dimethoxyphenyl)-3-(hydroxymethyl)-7-methoxy-2,3-dihydrobenzofuran-5-yl)-3-hydroxy-2-(2-methoxyphenoxy)propan-1-one (**13**)



Synthesised following the general procedure at room temperature using compound **4** (200 mg, 0.390 mmol 1.00 eq.) and DDQ (106 mg 0.780 mmol, 2.00 eq.). Purification via column chromatography (10-70 % Acetone:PET Ether) allowed for the isolation of compound **13** as a pale yellow solid (137 mg 0.269 mmol, 69%, mixture of racemic diastereomers).

¹H NMR (500 MHz, CDCl₃): δ 7.80 – 7.57 (m, 2H, Ar-H), 7.01 – 6.80 (m, 7H, Ar-H), 5.71 – 5.62 (m, 1H, H7), 5.46 – 5.34 (m, 1H, H8'), 4.08 (q, J = 14.7, 11.1 Hz, 2H, H9'), 4.01 – 3.93 (m, 2H, H9), 3.91 (s, 1.5H, -OCH₃), 3.90 (s, 1.5H, -OCH₃), 3.88 – 3.82 (m, 9H, -OCH₃), 3.69 – 3.61 (m, 1H, H8).

¹³C NMR (126 MHz, CDCl₃): δ 195.2 (C7'), 194.9 (C7'), 153.7, 150.3, 150.1, 149.42, 149.36, 146.93, 146.85, 144.69, 132.7, 132.6, 129.3, 129.2, 128.53, 128.47, 123.6, 123.4, 121.4, 119.14, 119.09, 119.0, 118.9, 117.9, 117.3, 113.18, 113.16, 112.5, 111.2, 110.1, 109.4, 107.6, 89.4 (C7), 84.3 (C8'), 84.2 (C8'), 63.9 (C9'), 63.83 (C9'), 63.75 (C9), 56.2 (-OCH₃), 56.10 (-OCH₃), 56.07 (-OCH₃), 56.0 (-OCH₃), 53.0 (C8).

¹H NMR (700 MHz, DMSO-*d*₆): δ 7.74 (s, 1H, H2'/H6'), 7.60 (s, 1H, H2'/H6'), 6.99 – 6.94 (m, 3H, Ar-H), 6.89 (m, 2H, Ar-H), 6.80 – 6.74 (m, 2H, Ar-H), 5.67 – 5.59 (m, 2H, H7 + H8'), 5.20 (m, 1H, C9'-OH), 5.12 (m, 1H, C9-OH), 3.95 – 3.89 (m, 2H, H9'), 3.85 (s, 3H, -OCH₃), 3.77 – 3.68 (m, 11H, 3 x -OCH₃ + H9), 3.59 – 3.54 (m, 1H, H8).

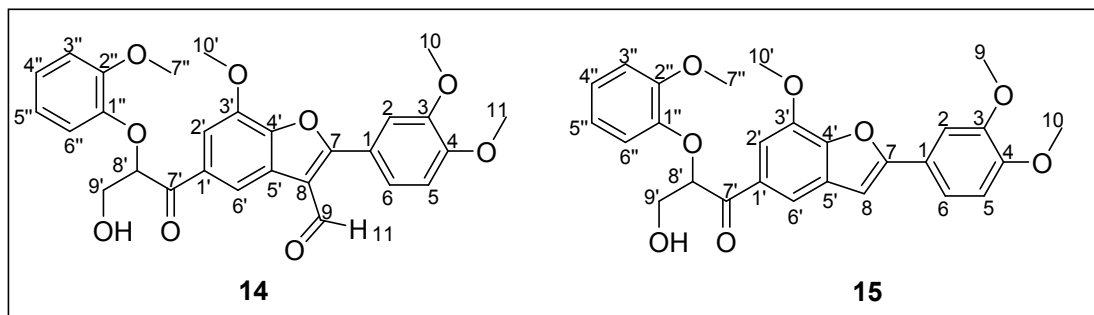
¹³C NMR (176 MHz, DMSO-*d*₆): δ 194.8 (C7'), 194.7 (C7'), 152.5, 149.2, 149.1, 148.8, 146.9, 146.9, 143.6, 133.0, 129.7, 129.7, 128.9, 121.6, 121.5, 120.5, 118.9, 118.4, 114.5, 114.3, 112.8, 112.7, 112.6, 111.7, 109.9, 88.4 (C7), 81.5 (C8'), 81.4 (C8'), 62.6 (C9/C9'), 62.5 (C9/C9'), 55.8 (-OCH₃), 55.6 (-OCH₃), 55.5 (-OCH₃), 52.4 (-OCH₃).

HR MS: [M + H]⁺ m/z calc: 511.1963 [M + H]⁺ m/z found: 511.1958

IR: (thin film) 1684, 1591, 1506, 1456, 1254, 1157, 1126, 1020.

MP: 74-76 °C

1-(2-(3,4-Dimethoxyphenyl)-3-(hydroxymethyl)-7-methoxy-2,3-dihydrobenzofuran-5-yl)-3-hydroxy-2-(2-methoxyphenoxy)propan-1-one (**14**) and 1-(2-(3,4-dimethoxyphenyl)-7-methoxybenzofuran-5-yl)-3-hydroxy-2-(2-methoxyphenoxy)propan-1-one (**15**)



yl)-3-hydroxy-2-(2-methoxyphenoxy)propan-1-one (**15**)

Synthesised following the general procedure at 60 °C using compound **4** (200 mg, 0.390 mmol, 1.00 eq.) and DDQ (443 mg, 1.95 mmol, 5.0 eq.). Purification via preparative TLC allowed for the isolation

of compound **14** as an off white solid (76 mg 0.15 mmol, 38%) and compound **15** as an off white solid (43 mg 0.090 mmol, 23%)

Compound 14

¹H NMR (500 MHz, CDCl₃): δ 10.32 (s, 1H, H₉), 8.55 (d, J = 1.5 Hz, 1H, H₂'/H₆'), 7.65 (d, J = 1.6 Hz, 1H, H₂'/H₆'), 7.47 (dd, J = 8.3, 2.1 Hz, 1H, Ar-H), 7.40 (d, J = 2.1 Hz, 1H, Ar-H), 7.05 – 7.02 (m, 1H, Ar-H), 7.02 – 6.99 (m, 1H, Ar-H), 6.97 – 6.95 (m, 1H, Ar-H), 6.94 – 6.92 (m, 1H, Ar-H), 6.86 – 6.82 (m, 1H, Ar-H), 5.66 (dd, J = 6.0, 3.5 Hz, 1H, H₈'), 4.18 – 4.09 (m, 2H, H₉'), 4.08 (s, 3H, C10'), 4.00 (s, 3H, -OCH₃), 3.99 (s, 3H, -OCH₃), 3.90 (s, 3H, -OCH₃).

¹³C NMR (126 MHz, CDCl₃): δ 196.1 (C7'), 186.4 (C9), 166.8, 152.3, 150.8, 149.7, 146.9, 146.1, 145.6 (C3'), 133.3, 129.2, 128.4, 127.4, 125.4, 123.9, 123.3, 121.3, 120.6, 118.9, 118.6, 117.0, 116.5, 112.4, 111.5, 111.4, 108.0, 106.3, 84.1 (C8'), 63.8 (C9'), 56.4 (C10'), 56.3 (-OCH₃), 56.1 (-OCH₃), 56.0 (-OCH₃).

¹H NMR (700 MHz, DMSO-*d*₆): δ 10.28 (s, 1H), 8.48 (d, J = 1.4 Hz, 1H), 7.70 (d, J = 1.4 Hz, 1H), 7.62 (dd, J = 8.4, 2.1 Hz, 1H), 7.55 (d, J = 2.1 Hz, 1H), 7.21 (d, J = 8.5 Hz, 1H), 6.98 (dd, J = 8.1, 1.4 Hz, 1H), 6.90 (td, J = 7.7, 1.6 Hz, 1H), 6.84 (dd, J = 8.1, 1.6 Hz, 1H), 6.79 (td, J = 7.7, 1.5 Hz, 1H), 5.72 (t, J = 5.0 Hz, 1H), 5.31 (t, J = 5.7 Hz, 1H), 4.05 (s, 3H), 3.97 (t, J = 5.3 Hz, 2H), 3.90 (s, 3H), 3.89 (s, 3H), 3.74 (s, 3H).

¹³C NMR (176 MHz, DMSO-*d*₆): δ 196.6, 186.72, 165.69, 151.9, 149.4, 149.1, 146.8, 144.9, 144.7, 133.4, 127.0, 122.9, 122.0, 120.6, 119.7, 116.0, 115.3, 115.2, 112.7, 112.1, 111.7, 108.1, 81.9, 62.5, 56.1, 55.9, 55.8, 55.5.

HR MS: [M + H⁺] *m/z* calc: 507.1650 [M + H⁺] *m/z* found: 507.1640

IR: (thin film) 1659, 1595, 1503, 1260, 1126, 1017.

MP: 82-84 °C

Compound 15

¹H NMR (700 MHz, CDCl₃): δ 7.97 (d, J = 1.3 Hz, 1H, H₂'/H₆'), 7.53 (d, J = 1.3 Hz, 1H, H₂'/H₆'), 7.47 (dd, J = 8.4, 1.9 Hz, 1H), 7.36 (d, J = 2.0 Hz, 1H), 7.01 (td, J = 7.8, 1.5 Hz, 1H), 6.97 – 6.89 (m, 4H), 6.83 (td, J = 7.7, 1.4 Hz, 1H), 5.52 (dd, J = 6.6, 4.0 Hz, 1H, H₈'), 4.15 – 4.09 (m, 2H, H₉'), 4.07 (s, 3H, -OCH₃), 3.99 (s, 3H, -OCH₃), 3.94 (s, 3H, -OCH₃), 3.87 (s, 3H, -OCH₃).

¹³C NMR (176 MHz, CDCl₃): δ 196.0 (C7'), 158.0, 150.7, 150.2, 149.4, 147.2, 147.1, 145.6, 131.4, 131.0, 123.9, 122.7, 121.3, 118.9, 118.5, 115.8, 112.4, 111.4, 108.3, 106.3, 100.8, 84.9 (C8'), 64.0 (C9'), 56.30 (-OCH₃), 56.25 (-OCH₃), 56.1 (-OCH₃), 56.0 (-OCH₃).

¹H NMR (700 MHz, DMSO-*d*₆): δ 8.11 (d, J = 1.4 Hz, 1H, H₂'/H₆'), 7.54 – 7.42 (m, 4H, Ar-H), 7.10 (d, J = 8.4 Hz, 1H, Ar-H), 6.97 (dd, J = 8.1, 1.4 Hz, 1H, Ar-H), 6.88 (td, J = 7.7, 1.7 Hz, 1H, Ar-H), 6.83 – 6.75 (m, 2H, Ar-H), 5.78 (t, J = 4.9 Hz, 1H, H₈'), 5.24 (t, J = 5.8 Hz, 1H, C9'-OH), 4.02 (s, 3H, -OCH₃), 3.97 – 3.93 (m, 2H, H₉'), 3.88 (s, 3H, -OCH₃), 3.82 (s, 3H, -OCH₃), 3.75 (s, 3H, -OCH₃).

¹³C NMR (176 MHz, DMSO-*d*₆): δ 196.2 (C7'), 157.1, 149.9, 149.22, 149.1, 146.9, 145.9, 144.7, 131.8, 130.6, 121.9, 121.7, 120.6, 117.9, 115.4, 114.7, 112.7, 112.1, 108.3, 106.1, 101.5, 81.6 (C8'), 62.6 (C9'), 55.9 (-OCH₃), 55.7 (-OCH₃), 55.6 (-OCH₃), 55.5 (-OCH₃).

HR MS: [M + H⁺] *m/z* calc: 479.1700 [M + H⁺] *m/z* found: 479.1692

IR: (thin film) 1684, 1506, 1456, 1252, 1217, 1165, 1018.

MP: 78-81 °C

S5.0 Oxidation of model softwood lignin polymer.

To a lignin model polymer **S1** containing β -O-4, β - β and β -5 units (unit ratio 74:9:17, 26 mg)⁹ in 1,4-dioxane/methanol (9:1, 0.50 mL) was added DDQ (26 mg). The reaction mixture was stirred for 16 hours, filtered through a plug of cotton wool and precipitated in Et₂O (10 mL). The polymer was then collected by filtration and dried *in vacuo* to give the oxidised model polymer **S2** as a brown powder (~26 mg). See Figure S10 for HSQC NMR analysis.

S6.0 Lignin Experimental

S6.1 Lignin Extraction Procedure

Douglas fir sawdust (300 g) was added to 1,4-dioxane:0.5 M HCl_{aq} (8:2, ~10 mL/g, overall 0.1 M HCl). This was heated at gentle reflux for 1.5 hr and then filtered after cooling. The filter cake was washed with a mixture of 1,4-dioxane:water (8:2). The filtrate was concentrated *in vacuo* giving a brown/red gum. The gum-like material was then dissolved in a minimum amount of acetone:H₂O (ca. 9:1) and added dropwise to vigorously stirred H₂O (at least 10x volume). The precipitate was collected (filtration), washed well with water, and dried in a desiccator over CaCl₂. The dried precipitate was then dissolved in acetone:MeOH (9:1, 1 volume) and added dropwise to diethyl ether (10x volume). Precipitated dioxasolv lignin was further reprecipitated from acetone:MeOH (9:1, 1 volume) into ethyl acetate (10x volume) and dried in a vacuum oven overnight prior to analysis.

S6.2 Lignin Oxidation Procedure

DDQ (1-2 weight equivalent) was added to a solution of Douglas fir dioxosolv lignin (100 mg) in dioxane (6 mL). The mixture was then stirred at room temperature/60 °C for 24 hours. The reaction mixture was centrifuged to remove DDQH₂ after which the supernatant was removed and then added to diethyl ether (100 mL) to induce precipitation of lignin. The mixture was then centrifuged and the precipitated lignin was collected before being dried in the desiccator under vacuum.

S6.3 Lignin Acetylation Procedure

To Douglas fir dioxasolv lignin (100 mg) was added pyridine (1.5 mL) and acetic anhydride (1.5 mL). The mixture was then stirred at room temperature for 16 hours. The reaction mixture was then quenched with ethanol and concentrated *in vacuo*. The product was dissolved in ethanol and concentrated *in vacuo* a further 4 times. The product was then dissolved in chloroform and washed sequentially with 1 M HCl, a saturated solution of NaHCO₃ and an EDTA solution. The organic layer was then dried over MgSO₄, filtered and dried *in vacuo* prior to analysis.

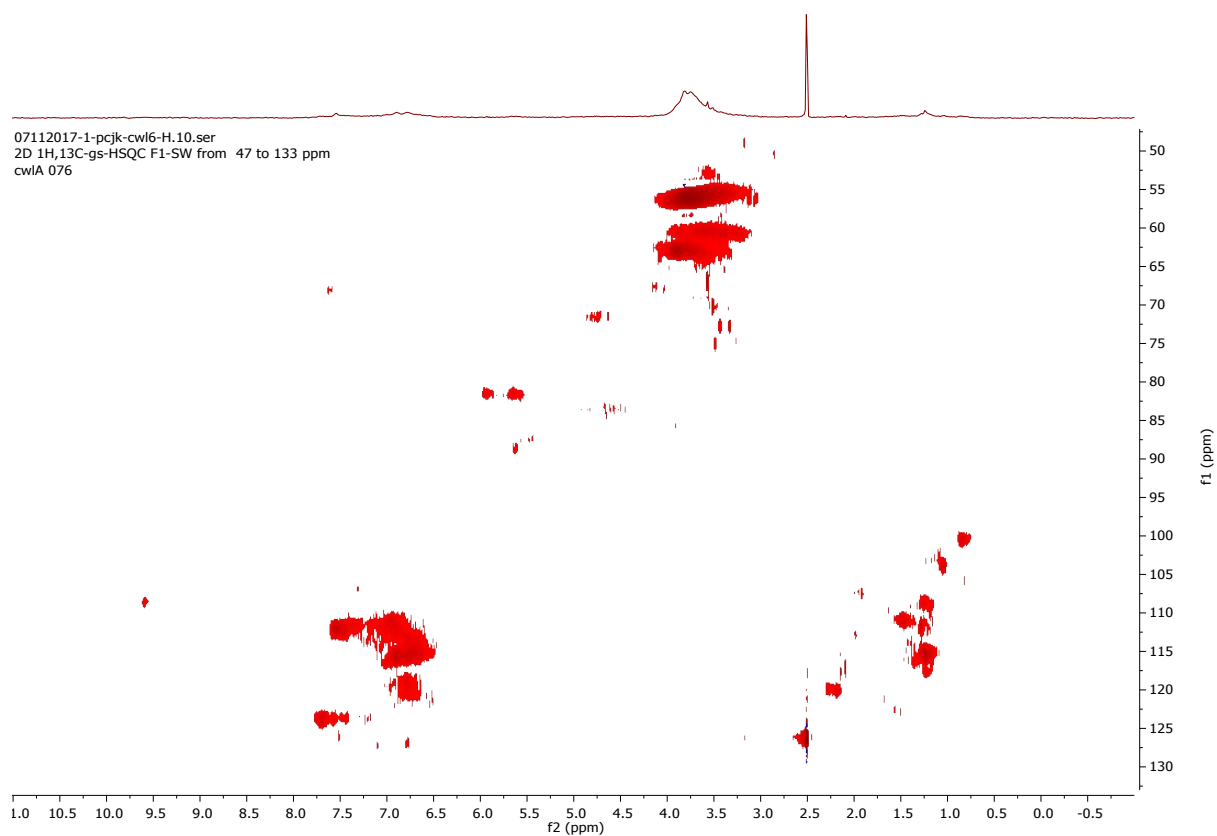
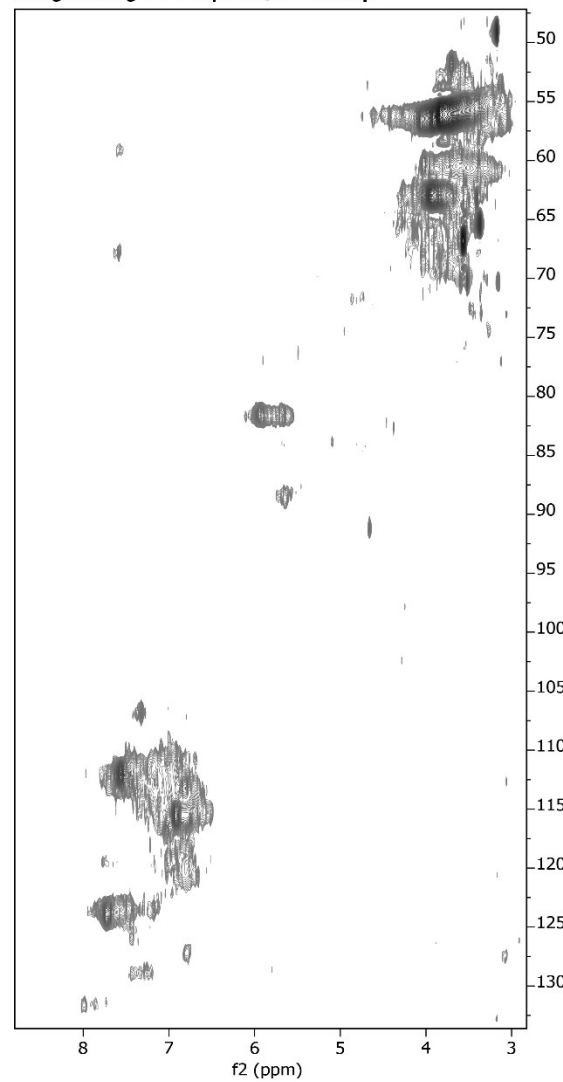
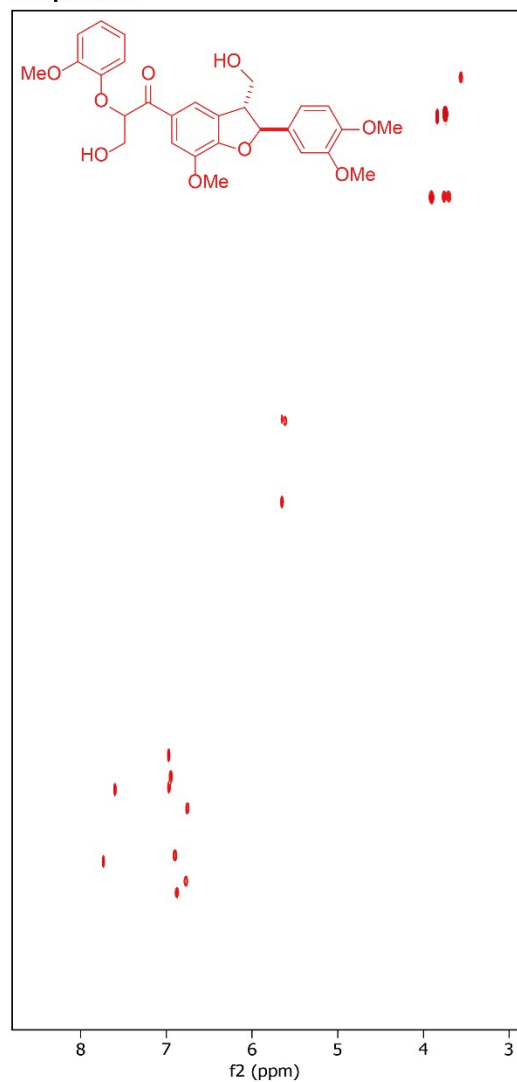


Figure S8 2D HSQC NMR spectrum of oxidised Douglas fir dioxosolv lignin in $\text{DMSO}-d_6$ obtained using 1 wt. eq. DDQ at room temperature for 24 hrs

Douglas fir lignin - 2 eq. DDQ, room temp



Compound 13



Overlay

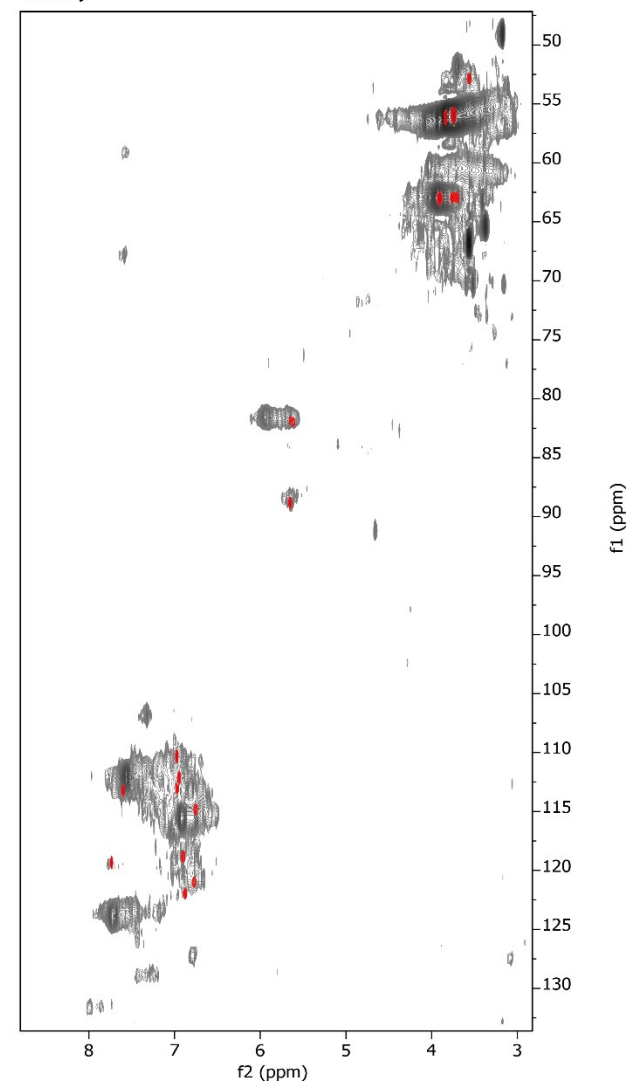


Figure S9 Comparison of model compound **13** to room temperature oxidised Douglas fir lignin. Characteristic cross peaks for the assignment of the β -5 unit next to an oxidised β -O-4 unit are seen at *ca.* 5.6/88.4 ppm and 7.7/119 ppm in the model and lignin spectra.

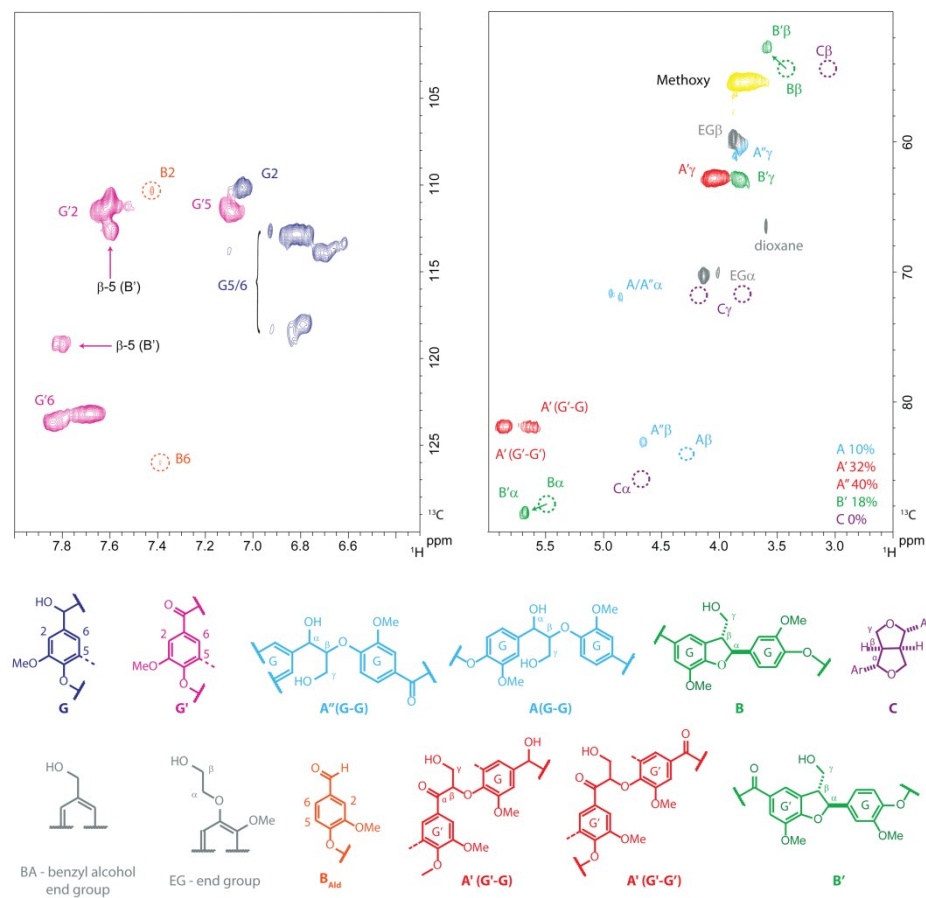


Figure S10: 2D HSQC NMR analysis of a DDQ oxidised model softwood lignin polymer (starting ratios A:B:C = 74:17:9). *Reagents and conditions:* 1 wt eq. DDQ, 1,4-dioxane/MeOH (9:1), r.t, 16 h. NMR – 500 MHz, d_6 -acetone/ D_2O (9:1).

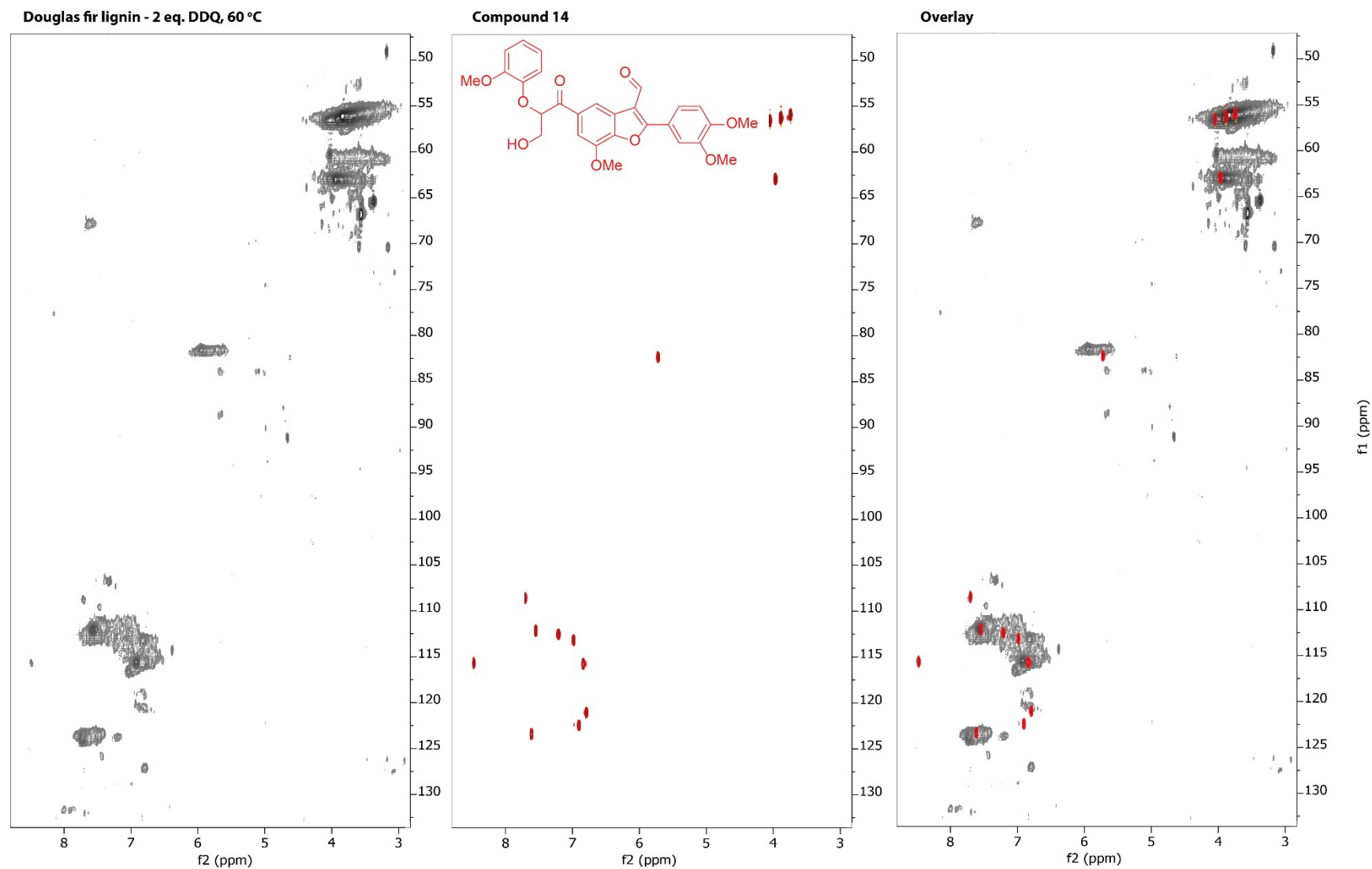


Figure S11 Comparison of model compound **14** to 60 °C oxidised Douglas fir lignin. Characteristic cross peaks for the assignment of the oxidised β -5 unit are seen at *ca.* 7.7/108 ppm and 8.5/116 ppm in the model and lignin spectra.

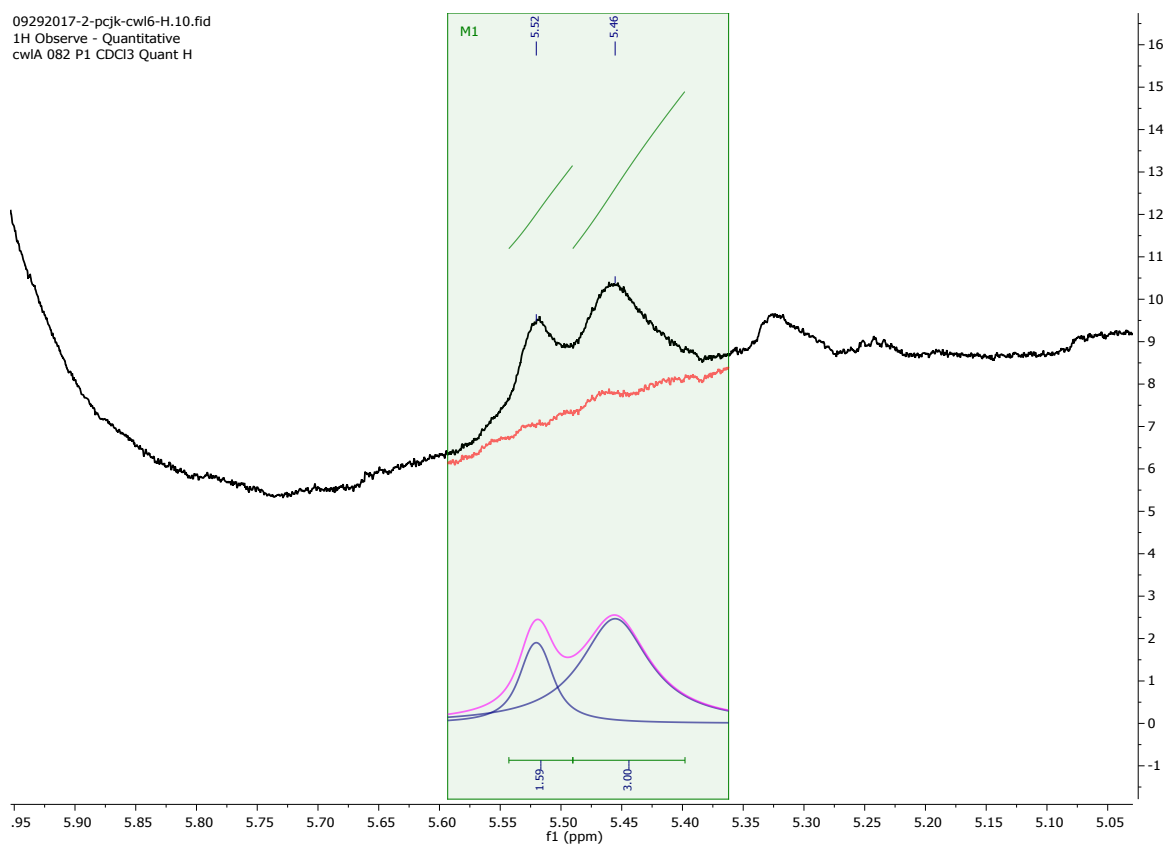


Figure S12: Quantitative ^1H NMR of acetylated Douglas fir dioxasolv lignin in CDCl_3 ($D_1 = 30$ s) showing the integrations of the peaks corresponding to the phenolic (5.52 ppm) and etherified (5.46 ppm) β -5 linkages. Deconvolution of these peaks in MestReNova (above) gave peak areas of 1:3 for the phenolic and non-phenolic peaks respectively.

S7.0 References

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S8.0 Trilignol analysis and references

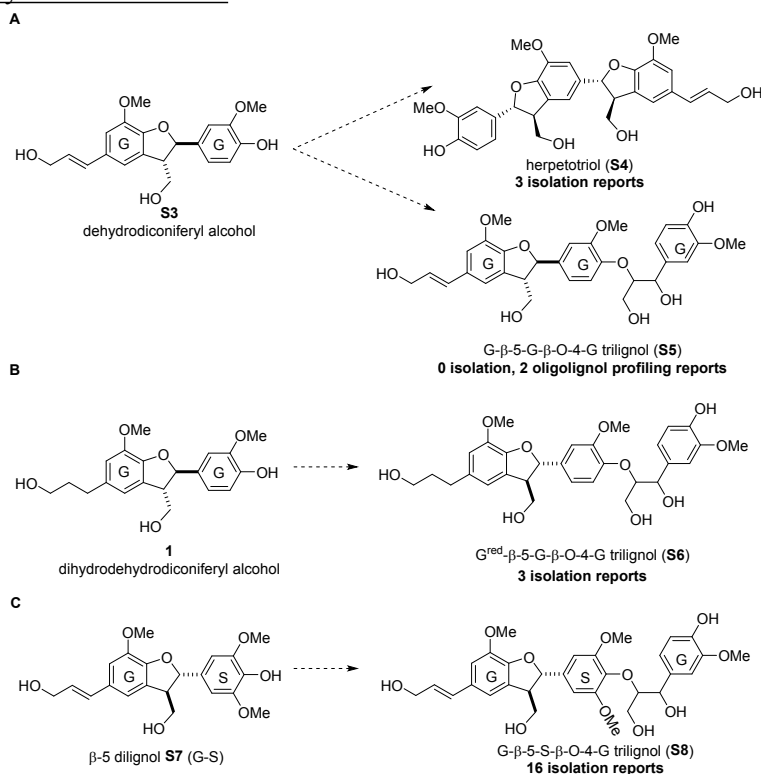


Figure S14 Natural β-5 trilignols or lignans coupled through the phenolic position. The relative lack of trilignols such as **S5** and **S6** indicates that the natural oxidative coupling of the β-5 dilignols **S3** and/or **1** may be difficult. Data from the SciFinder database – November 2017. Different diastereomers of **S5**, **S6** and **S8** were grouped for counting purposes. **S5** was identified in mass spectrometry based profiling of oligolignol from poplar xylem extracts.

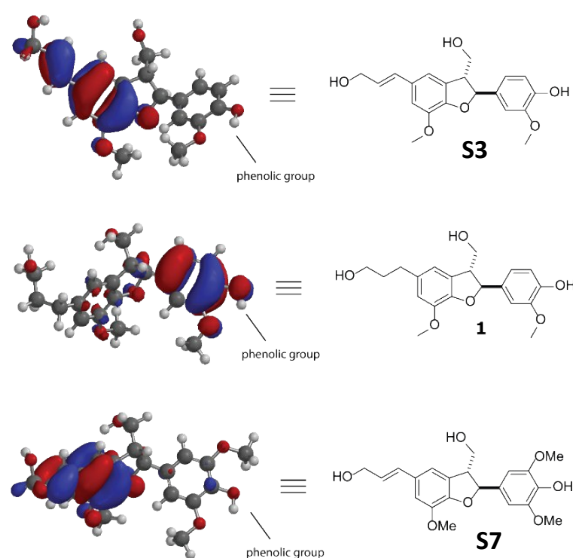


Figure S13: HOMO electron density maps of dilignol **S3**, the saturated derivative **1** and dilignol **S7**. Images are plotted at IsoValue = 0.032. No orbital density is seen on the phenolic oxygen in **S1**, however a small amount can be seen in **S7** and much more in **1**. For each compound the lowest energy conformer identified from a conformer search, using the Merck Molecular Force Field (MMFF), was optimised at the AM1 level of theory and the HOMO density maps calculated at the HF/STO-3G level of theory. Calculations were carried out in the Spartan software package.

We found from surveying lignan type natural products and available data from profiling of oligolignols *in planta*^{31,32} that oxidative coupling of dihydrodehydrodiconiferyl alcohol **1** and dehydrodiconiferyl alcohol **S3** appears to be possible but perhaps quite challenging, whilst closely related β -5 dilignols such as **S7**, in which the terminal phenolic unit is a syringyl rather than guaiacyl unit, appear to cross couple quite readily. This was qualitatively judged by the relative numbers of natural products identified which have likely arisen from oxidative coupling of each substrate with coniferyl alcohol (Figure S13). Additionally, preliminary electron density calculations (See Figure S14) suggest that the allyl group in **S3** dominates the HOMO in this dilignol, consistent with previous reports.²⁹ However this effect is less apparent in **S7** and does not exist in **1**, with more electron orbital density being present on the phenolic groups in **S7** and **1** compared to **S3**, as needed for oxidation by peroxidases and laccases.

S4: Isolations^{1–3} MS Identifications or other⁴

S5: MS Identifications or other^{4,5}

S6: Isolations^{6–8}

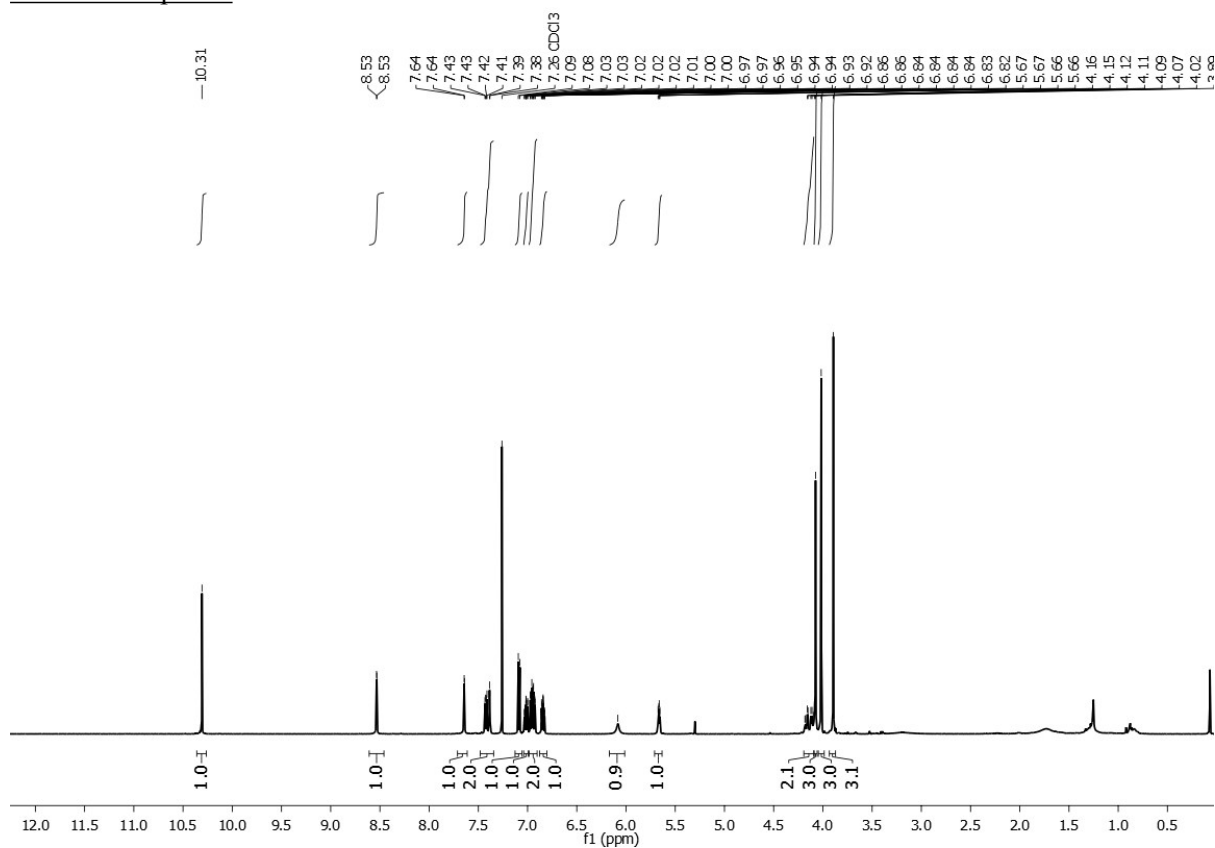
S8: Isolations^{9–24}

References for trilignol identifications:

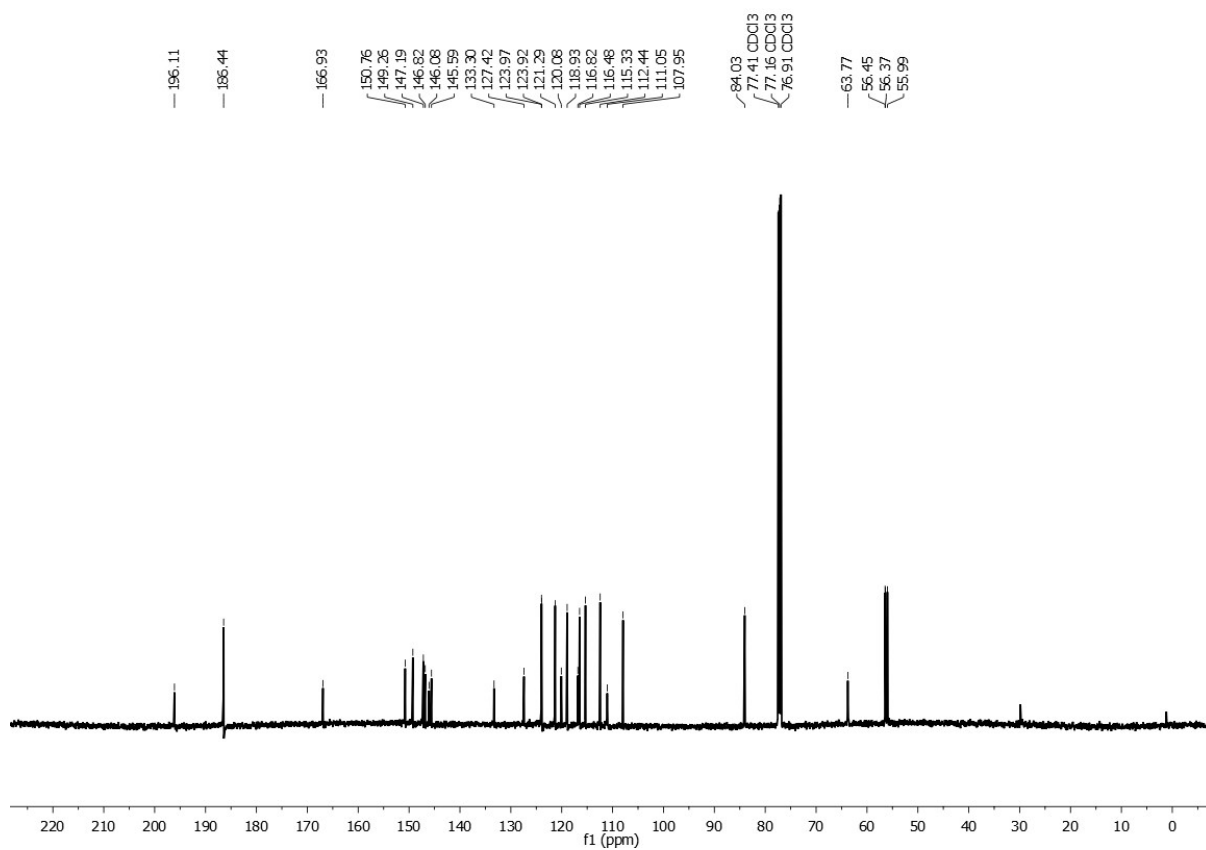
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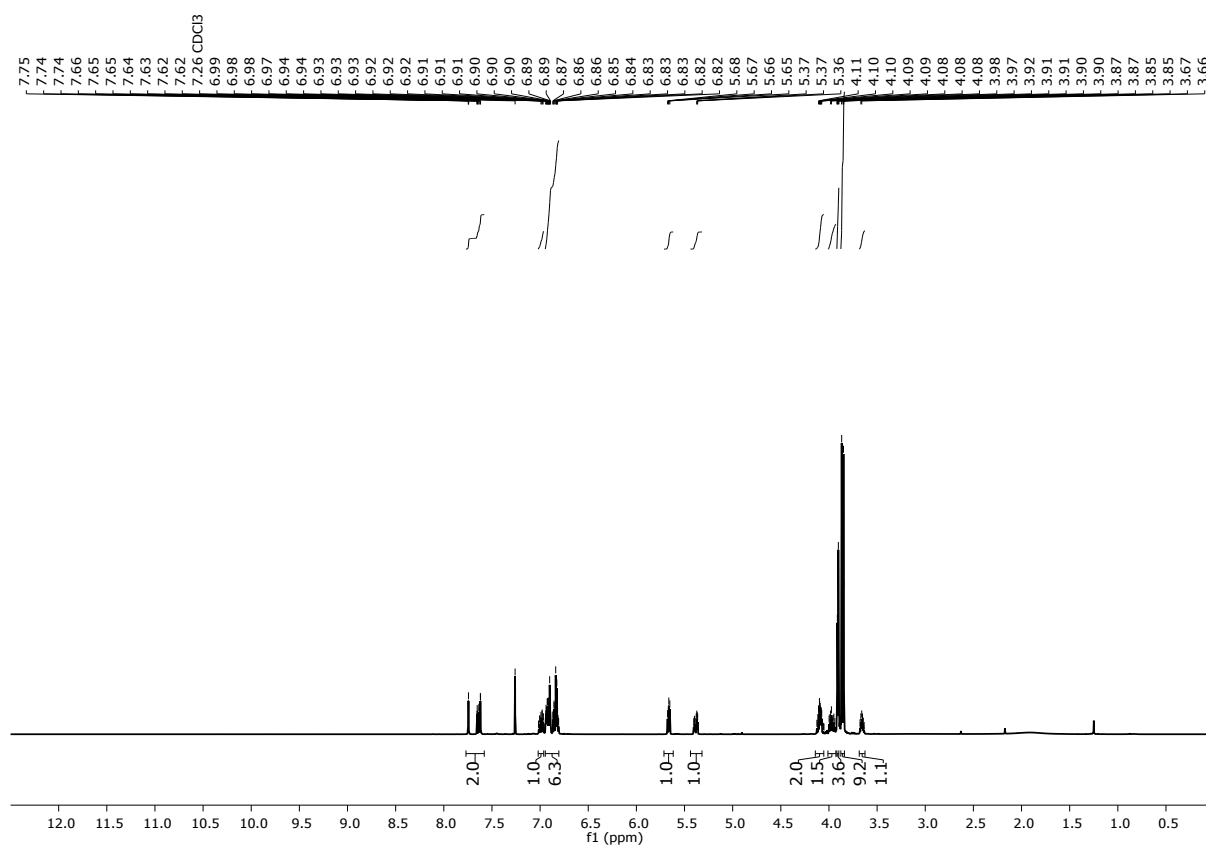
S9.0 NMR Spectra



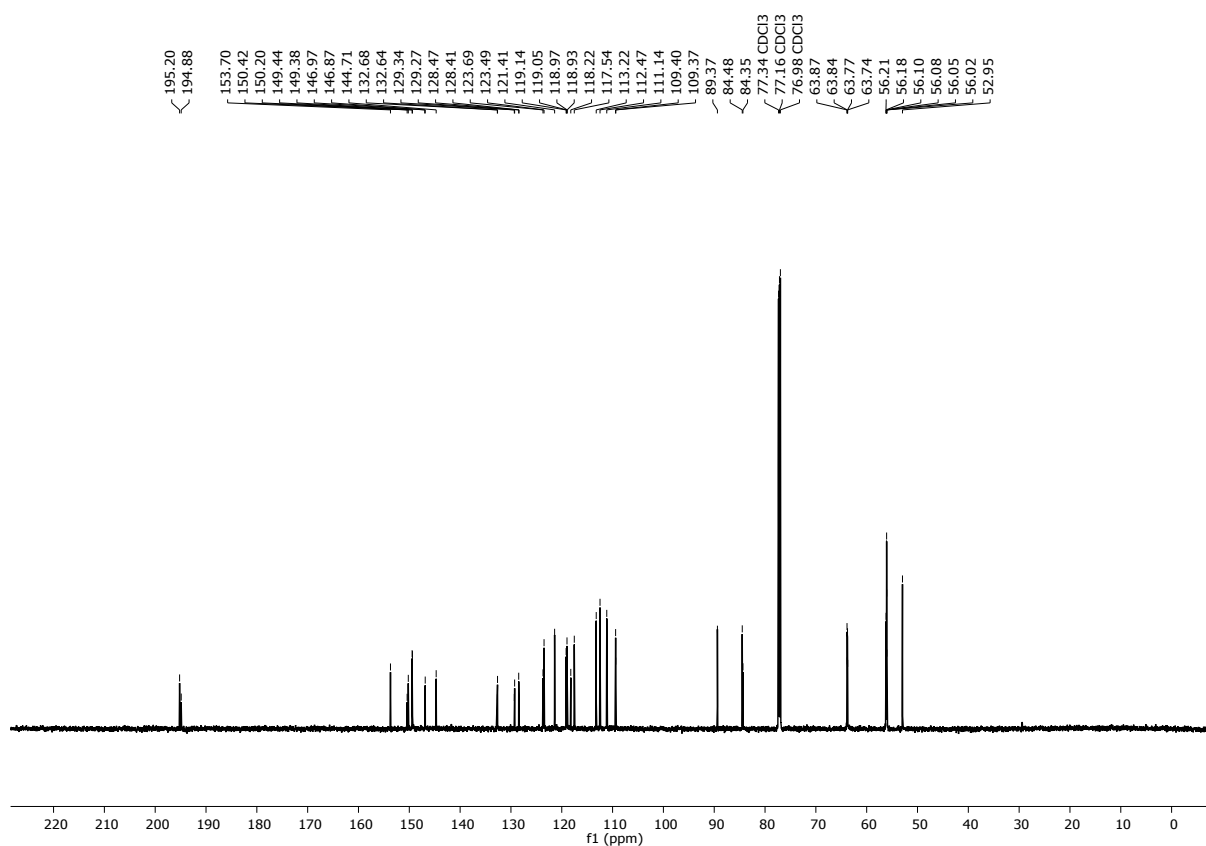
Compound **11**: ¹H NMR, 500 MHz, CDCl₃



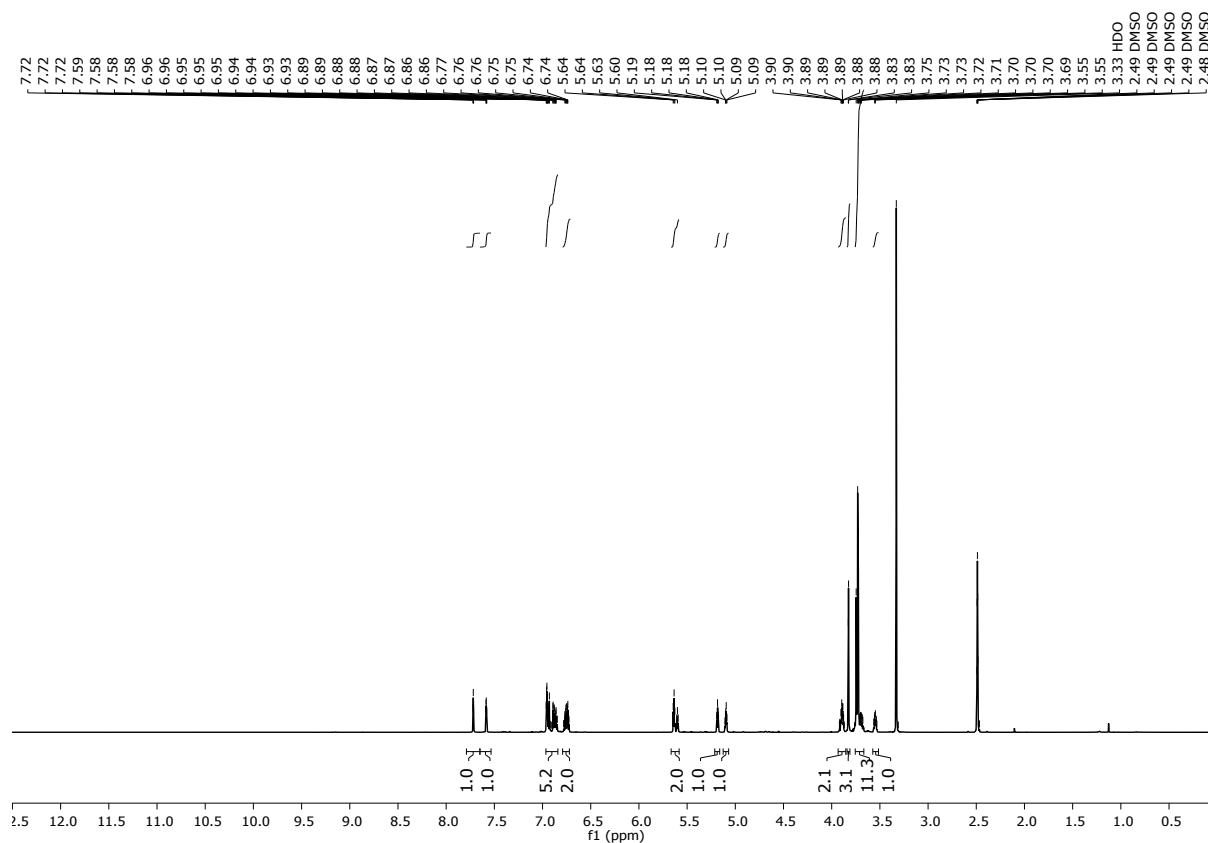
Compound **11**: ¹³C NMR, 126 MHz, CDCl₃



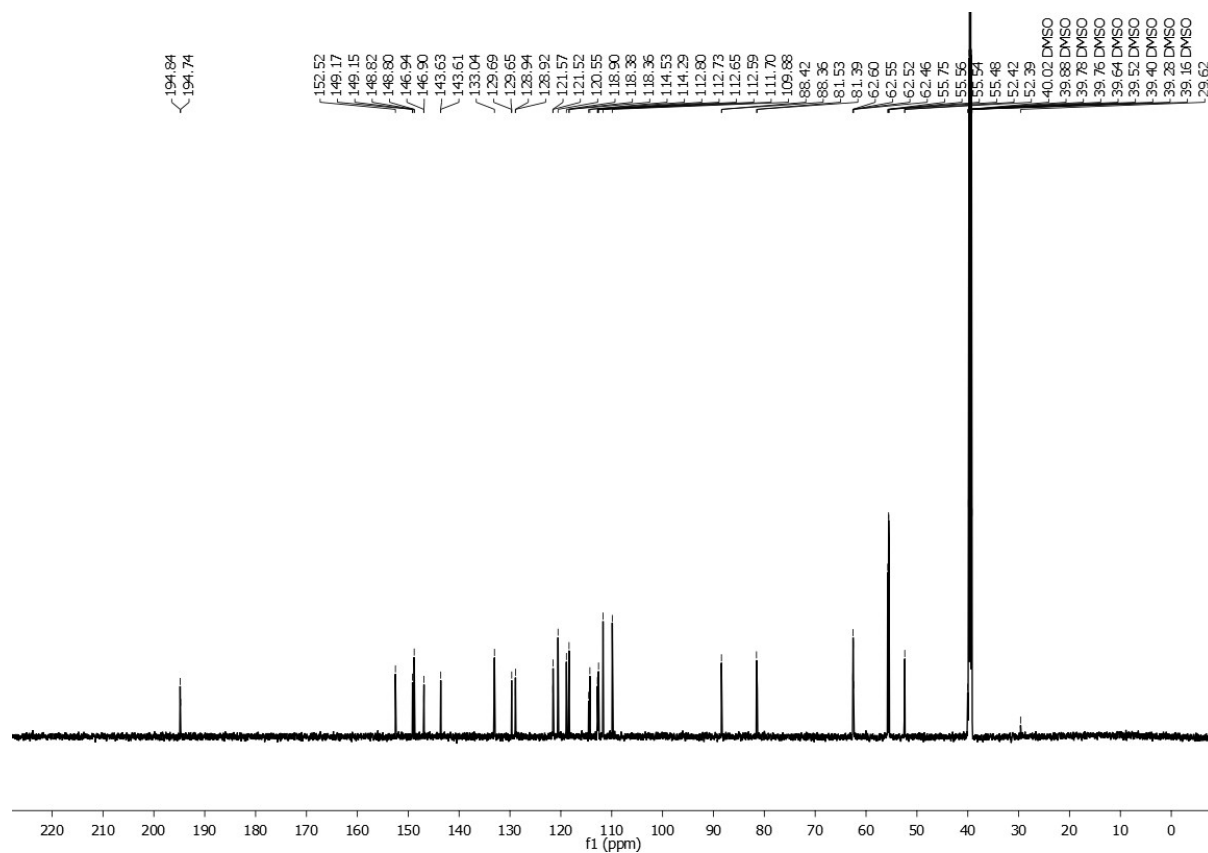
Compound **13**: ¹H NMR, 700 MHz, CDCl₃



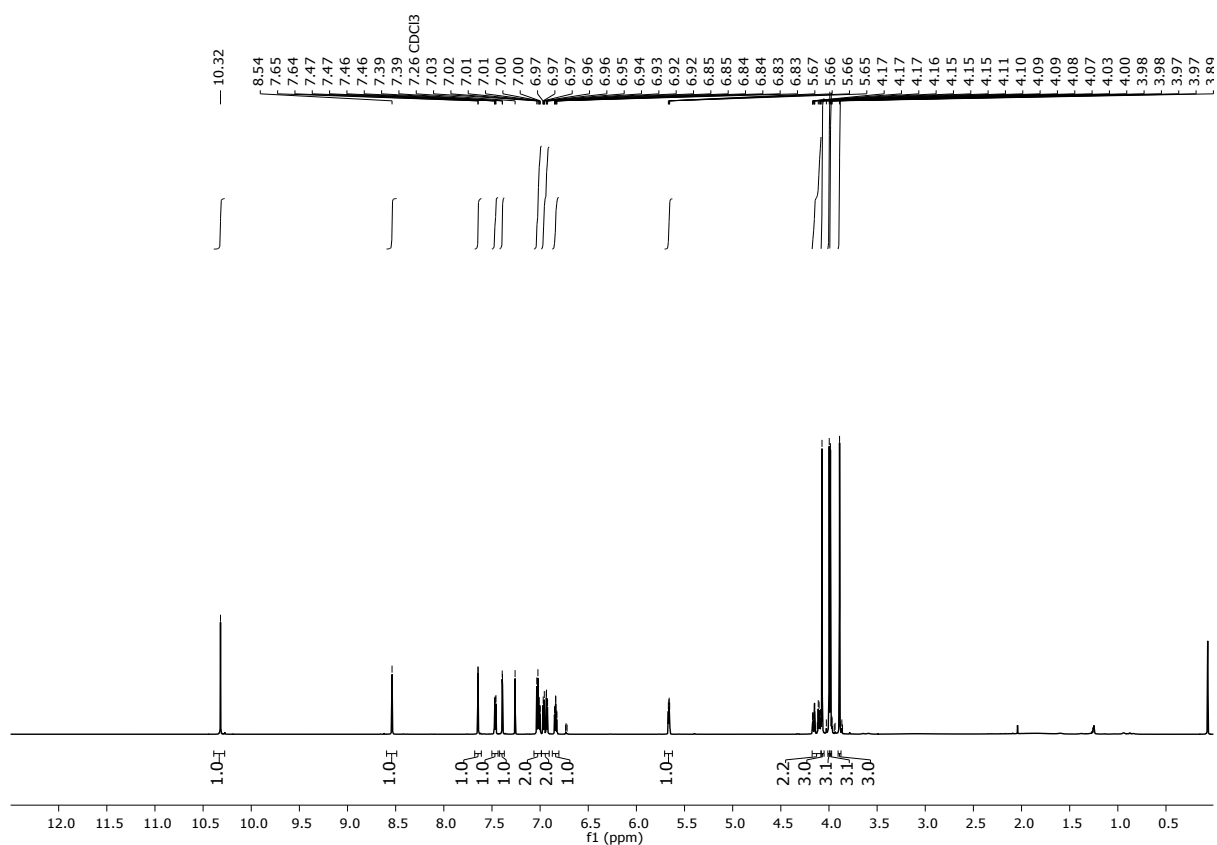
Compound **13**: ¹³C NMR, 176 MHz, CDCl₃



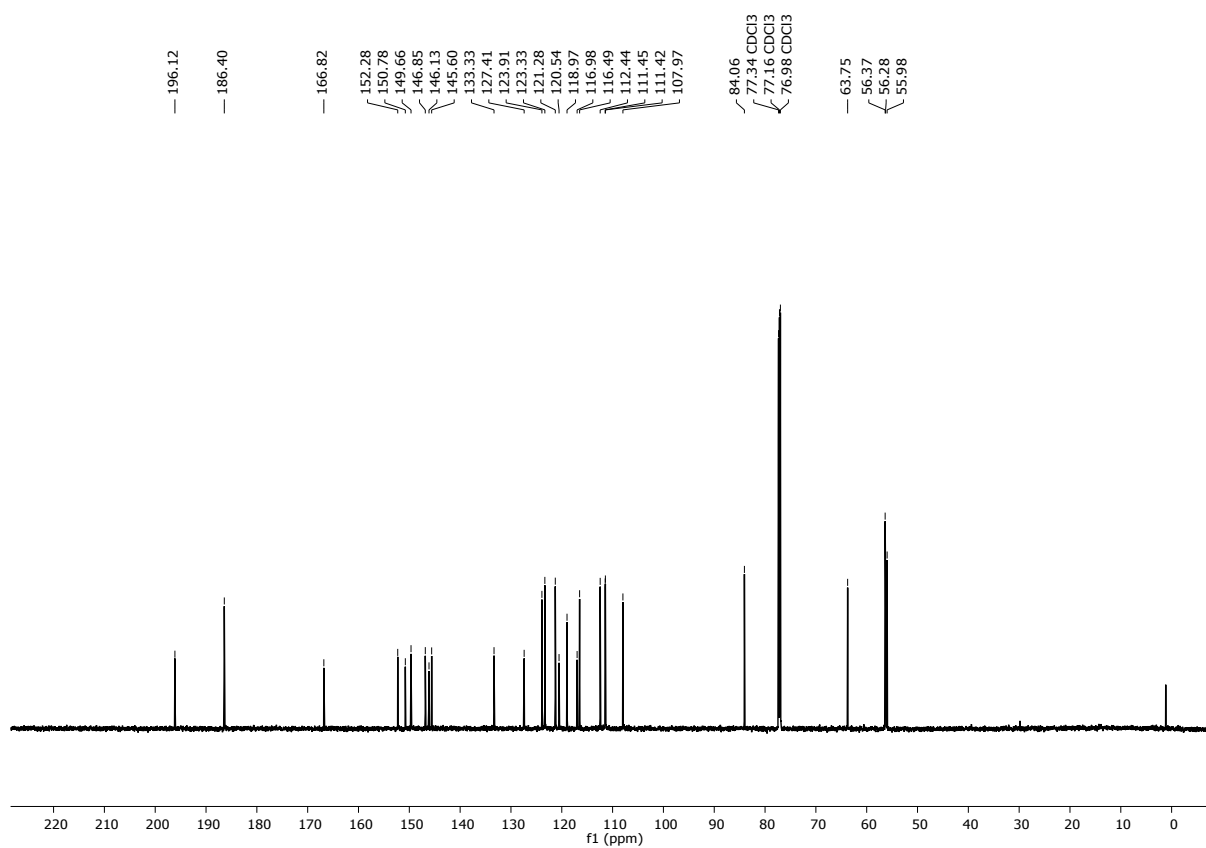
Compound **13**: ^1H NMR, 700 MHz, $\text{DMSO}-d_6$



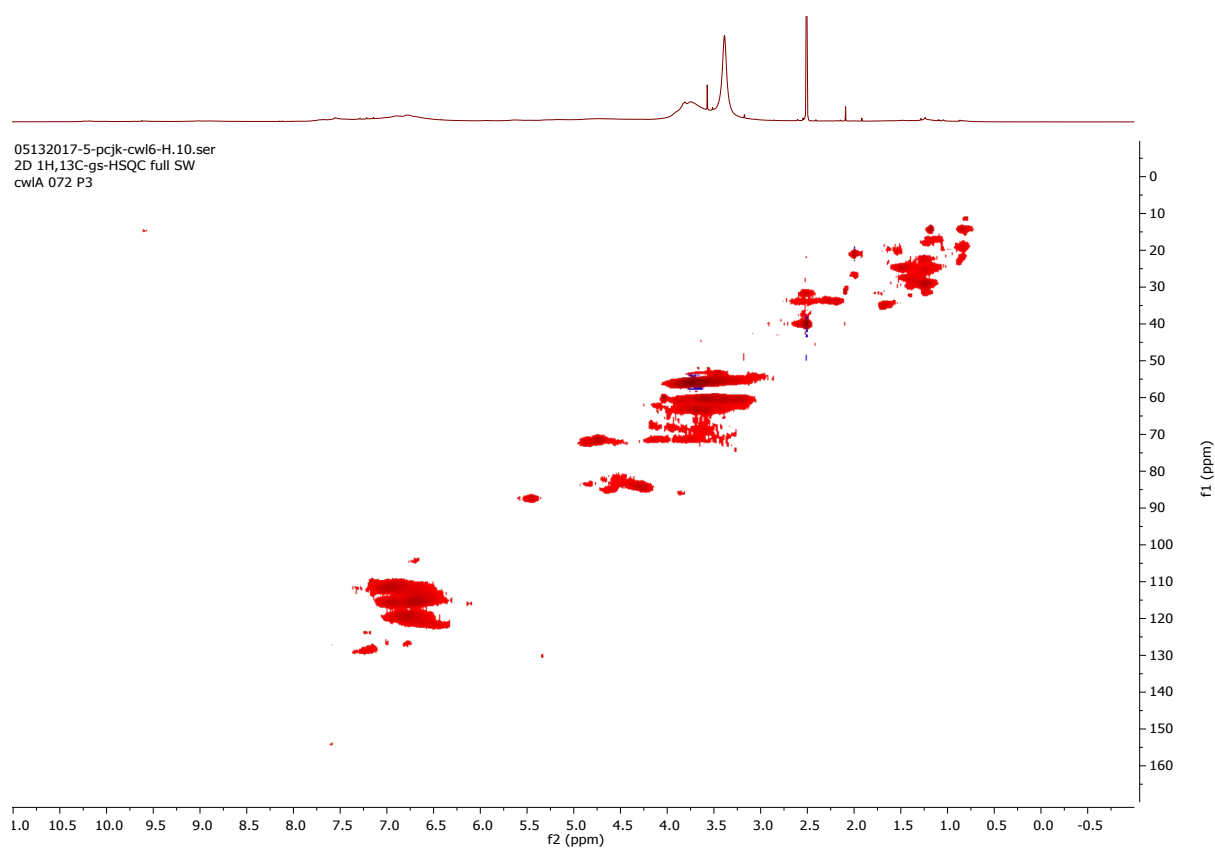
Compound **13**: ^{13}C NMR, 176 MHz, $\text{DMSO}-d_6$



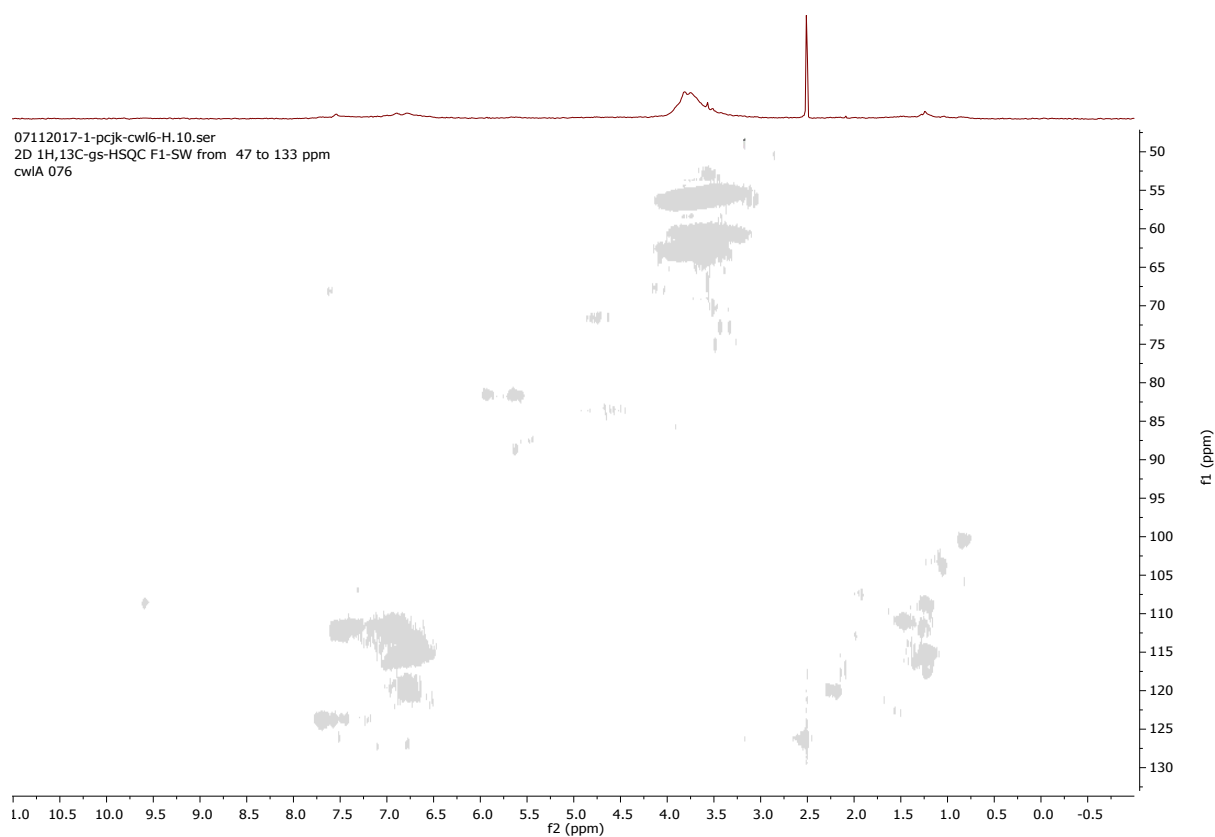
Compound **14**: ^1H NMR, 700 MHz, CDCl_3



Compound **14**: ^{13}C NMR, 176 MHz, CDCl_3



2D HSQC NMR of Douglas fir dioxosolv lignin in $\text{DMSO}-d_6$



2D HSQC NMR of oxidised Douglas fir dioxosolv lignin in $\text{DMSO}-d_6$. Oxidised with 1 eq. DDQ at room temperature for 24 hrs

