Electronic Supplementary Material (ESI) for Green Chemistry.

Selective modification of the β-β linkage in DDQ-treated Kraft lignin analysed by 2D NMR spectroscopy

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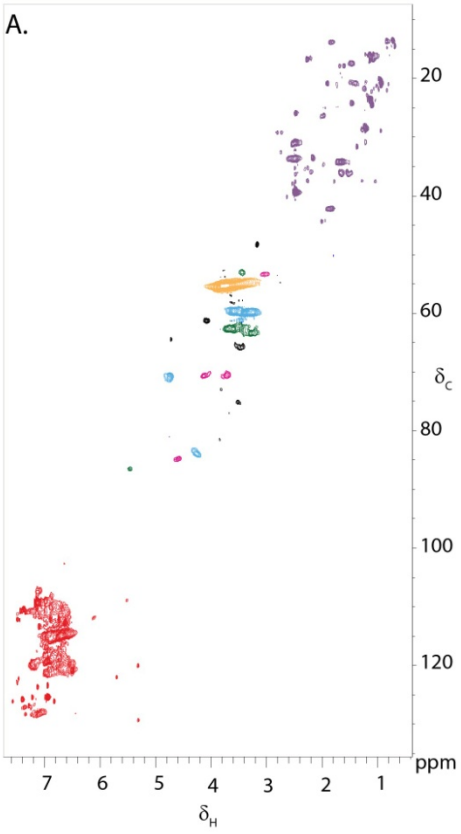
Supplementary Information

A.



B.

Width of the Carbon dimension	Signals integration relative to the aromatic region			Experiment Time
	β-O-4	β-5	β–β	
Full	1.91	0.54	0.86	20 min
47 to 133 ppm	1.89	0.51	0.86	12 min
50 to 90 ppm	1.93	0.59	0.90	6 min

C.

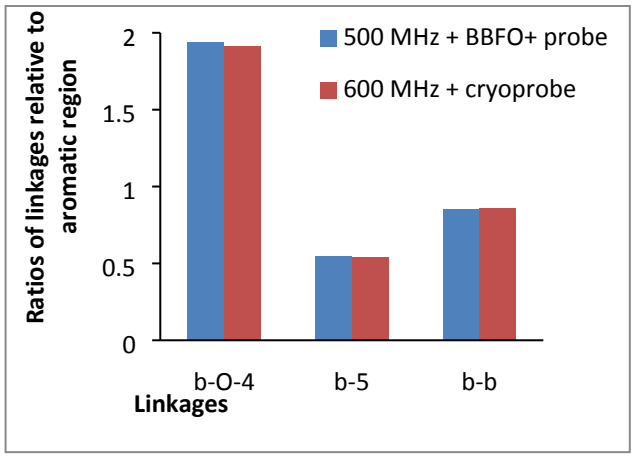


Fig. S1 Summary of the **r**atios obtained using a 600 MHz spectrometer fitted with a cryoprobe at a concentration of 100 mg of substrate in 0.6 mL of DMSO-*d*6.A. Full width 2D HSQC NMR spectrum (δ_c/δ_H 50-95/2.5-6.0) of isolated Kraft lignin. Contours are colour coded according to the linkage they are assigned to (see Figure 2 legend). Black cross peaks currently correspond to unassigned signals; B. Table comparing the ratios of integral intensities obtained for specific linkages relative to the aromatic region using the 600 MHz spectrometer fitted with a cryoprobe (coloured in red); C. Representative comparison of the different ratios of linkages obtained for Kraft lignin using a 600 MHz (with cryoprobe) and a 500 MHz spectrometer (with BBFO+ probe).

NMR methods

NMR spectra were acquired on a Bruker Avance III 600 MHz spectrometer fitted with a 5 mm CPTCI cryoprobe. The central DMSO solvent peak was used as internal reference (δ_C 39.5, δ_H 2.49 ppm). The $^{1}H,^{13}C$-HSQC experiment was acquired using standard Bruker pulse sequence 'hsqcetgpsp.3' (phase-sensitive gradient-edited-2D HSQC using adiabatic pulses for inversion and refocusing). Composite pulse sequence 'adiabatic' was used for broadband decoupling during acquisition. 2048 data points was acquired over 12 ppm spectral width (acquisition time 142 ms) in F2 dimension using 4 scans with 1 s interscan delay and the d4 delay was set to 1.8 ms (1/4J, J = 140 Hz). The spectrum was processed using squared cosinebell in both dimesnions and LPfc linear prediction (32 coefficients) in F1. Volume integration of cross peaks in the HSQC spectra was carried out using MestReNova software.

Standard HSQC experiments For spectral width of 150 ppm 256 increments were acquired in F1 dimension (acquisition time 5.6 ms) that resulted in the total experimental time of 20 min.

Short HSQC experiments For spectral width of 40 ppm 76 increments were acquired in F1 dimension (acquisition time 6.3 ms) that resulted in the total experimental time of 6 min.

HSQC experiments including the aromatic region For spectral width of 86 ppm 156 increments were acquired in F1 dimension (acquisition time 5.9 ms) that resulted in the total experimental time of 12 min.

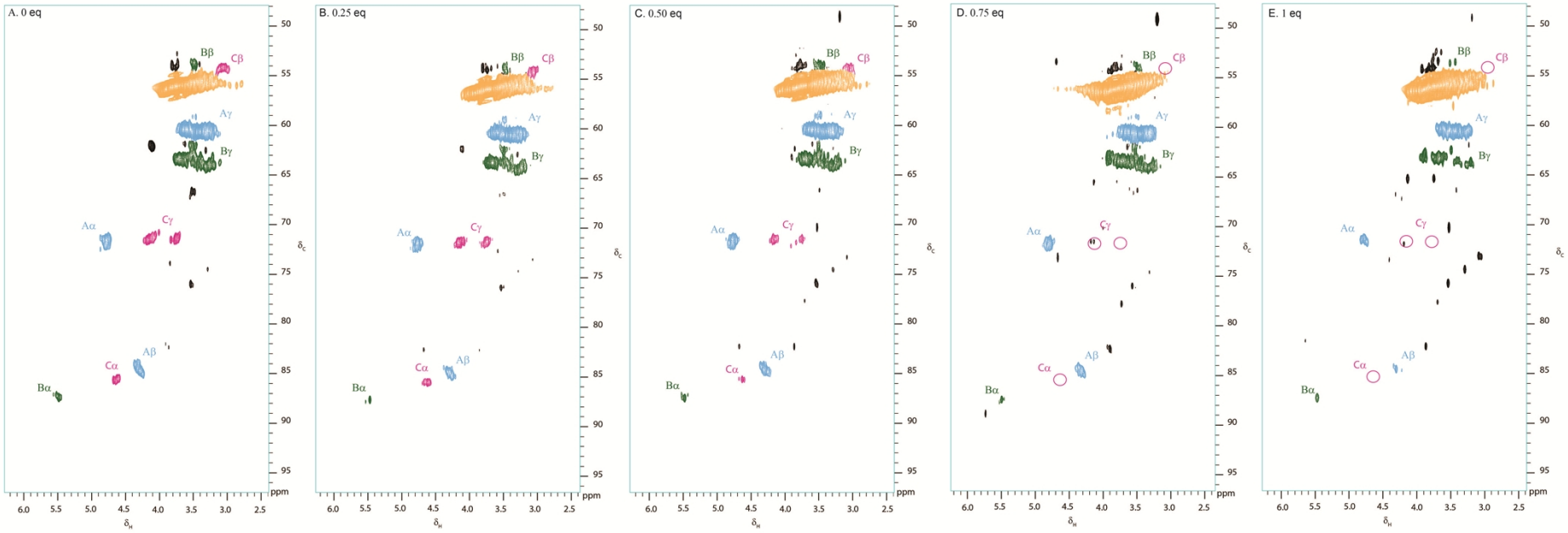


Fig. S2 Partial 2D HSQC NMR spectra (δ_c/δ_H 50-95/2.5-6.0) of A. isolated Kraft lignin after stirring in DMF overnight; B. Kraft lignin after treatment with 0.25 weight equivalents of DDQ; C. Kraft lignin after treatments with 0.5 weight equivalents of DDQ; D. Kraft lignin after treatment with 0.75 weight equivalents of DDQ; E. Kraft lignin after treatment with 1 weight equivalent of DDQ. Contours are colour coded according to the linkage they are assigned to (see Figure 2 legend). Black cross peaks currently correspond to unassigned signals. NMR samples were run on a 500 MHz spectrometer at a concentration of 100 mg of substrate in 0.6 mL of DMSO-*d*6.

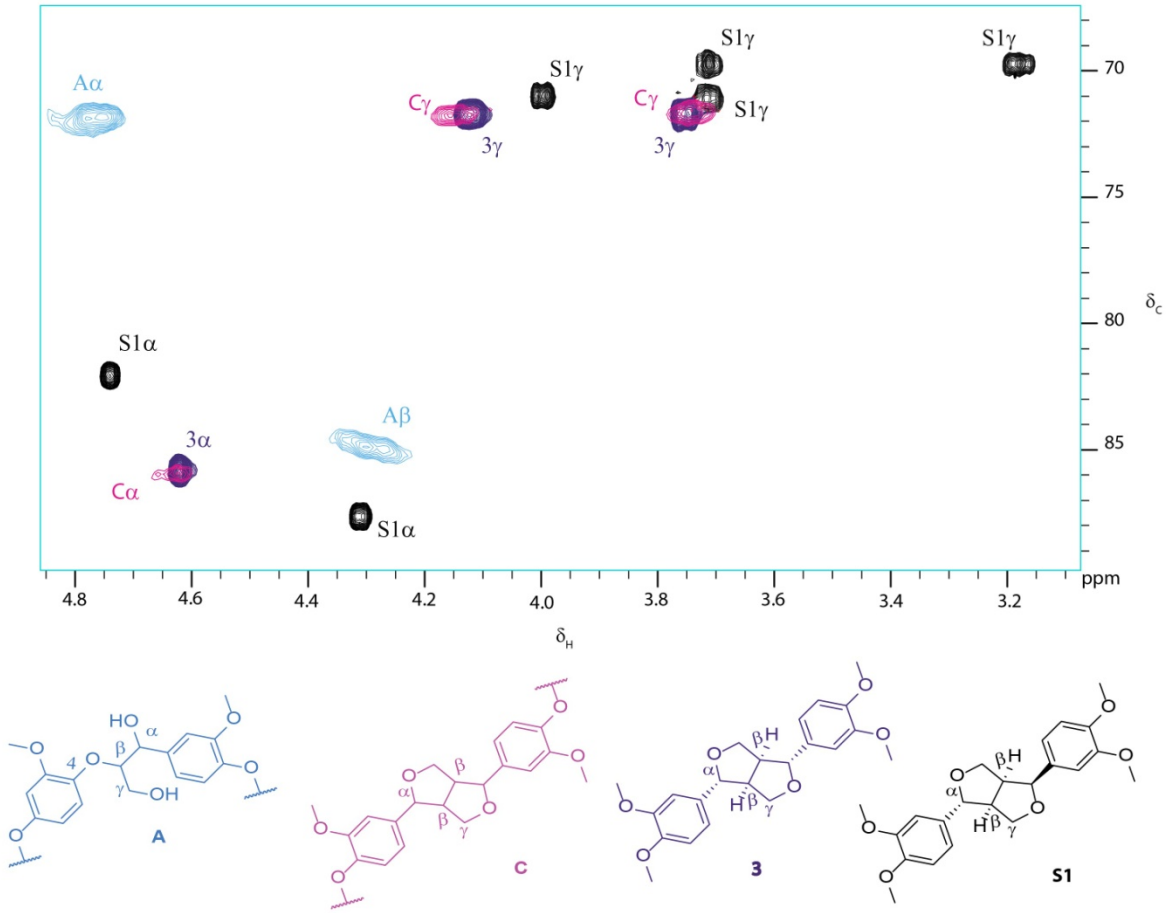


Fig. S3 Overlay of partial 2D HSQC (δ_c/δ_H 68-90/3.2-4.8) spectra of Kraft lignin (shown in blue and pink) and a mixture of epimers **3**/**S1** (shown in purple/black). Contours are colour coded according to the linkage/structure they are assigned to. For clarity the signals assigned to the **C**β, **3**β and **S1**β protons are shown.

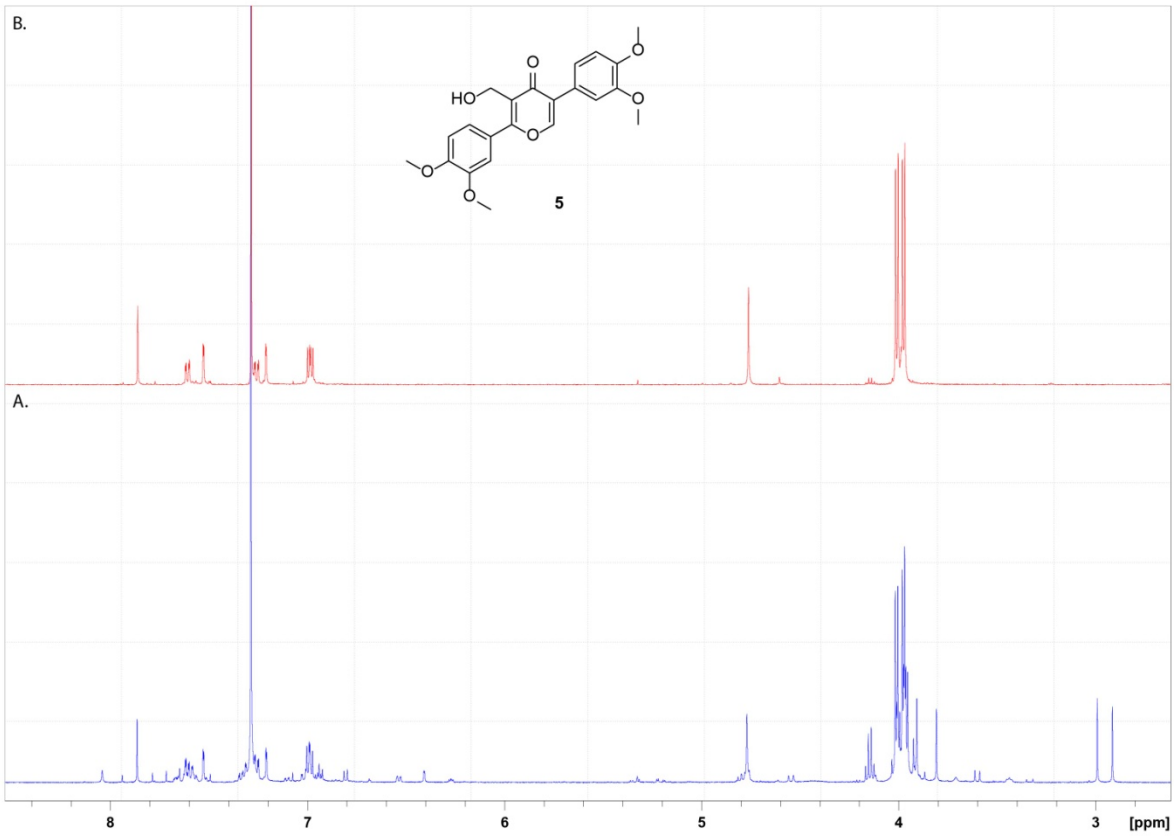


Fig. S4 NMR spectra of A. crude reaction mixture of the reaction of eudesmin (**3**) with 3 equivalents of DDQ; B. isolated pyran-4-one **5** following column chromatography.

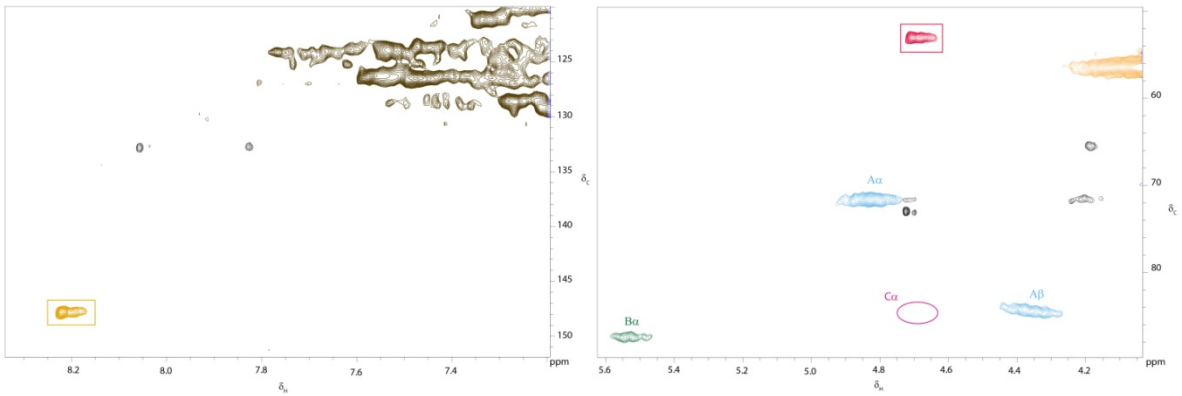


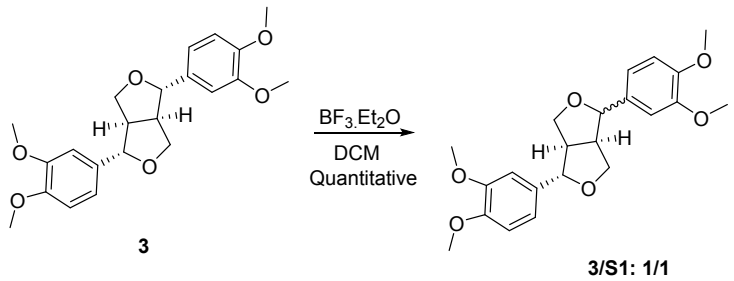
Fig. S5 Partial 2D HSQC NMR spectra of a mixture of Kraft lignin after treatment with 0.75 weight equivalents of DDQ (100 mg) and an authentic sample of pyran-4-one **5** (10 mg): **A.** aromatic region (δ_c/δ_H 120-150/7.4-8.4) and **B.** aliphatic region (δ_c/δ_H 50-90/4.0-5.6). Overlap of the cross peaks both at δ_c/δ_H 147.3/8.21 ppm and δ_c/δ_H 52.9/4.65 ppm corresponding to the aromatic pyran-4-one **5** CH group and methylene group in **5** are shown in orange and red boxes respectively. Contours are colour coded according to the linkage they are assigned to (see Figures 2 and 5 legends).

Table S1 Mean ratios of the β-O-4, β-β and β-5 linkages, relative to the aromatic region, in Kraft lignin following treatment with different amounts of DDQ

Number of weight equivalent of DDQ	Mean ratios ± standard deviations		
	β-O-4	β-β	β-5
0	2.65 ± 0.10	1.17 ± 0.08	0.82 ± 0.06
0.25	2.72 ± 0.06	1.13 ± 0.03	0.76 ± 0.03
0.5	2.60 ± 0.18	0.68 ± 0.09	0.75 ± 0.04
0.75	1.91 ± 0.21	0.15 ± 0.04	0.63 ± 0.06
1	1.90 ± 0.17	0.13 ± 0.11	0.60 ± 0.02

Each sample analysed was stirred overnight in DMF in the absence or presence of DDQ and the lignin precipitated from Et_2O. Each NMR analysis was run 3 times and quantification was performed by integration of the cross peaks and normalised relative to the aromatic region. Mean values ± SD are shown ($n \geq 3$).

To confirm the relative configuration of the β–β linkage in Kraft lignin, eudesmin (**3**) was treated with $BF_3.Et_2O$ to give a 1:1 mixture of eudesmin (**3**) and *epi*eudesmin (**S1**) (Scheme S1).[1]



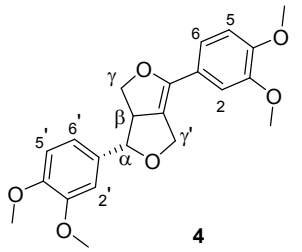
Scheme S1 Synthesis of *epi*eudesmin (**S1**)[1]

As expected, overlay of the respective 2D HSQC spectrum of eudesmin (**3**) and *epi*eudesmin (**S1**) with the spectrum of Kraft lignin suggested that the epimer naturally occurring in lignin had the same relative configuration as eudesmin (**3**) (Figure S2).[2]

General

Kraft lignin was supplied by MeadWestvaco Corporation, Richmond, VA. All chemicals and anhydrous DMF were purchase from Sigma Aldrich (UK) and Alpha Aesar and were used without further purification unless stated otherwise. DDQ was recrystallised from chloroform. Thin layer chromatography (TLC) analysis was performed using glass plates coated with silica gel (with fluorescent indicator UV_{254}). Developed plates were air dried and analysed under a UV lamp (254/365 nm). Flash chromatography was performed using silica gel (40-63μm, Fluorochem).

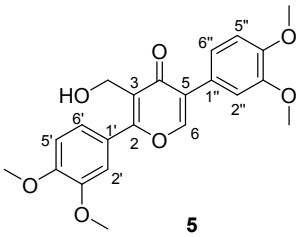
Synthesis of (3*S*)-3,6-*bis*(3,4-dimethoxyphenyl)-3a,4-dihydro-1*H*,3*H*-furofuran, 4



4

DDQ (9 mg, 0.039 mmol) was added to a solution of eudesmin (**3**) (15 mg, 0.039 mmol) in anhydrous DMF (1.5 mL). The reaction mixture was stirred at room temperature overnight before being concentrated *in vacuuo* to give an amber solid. **4** proved unstable to column chromatography, the spectral assignment is therefore based on 1:1 mixture with eudesmin (**3**): ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 3.28 - 3.33 (m, 1H, Hβ), 3.51 (d, *J* = 12.0 Hz, 1H, Hγ'$_1$), 3.86 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.06 (dd, *J* = 9.3, 1.8 Hz, 1H, Hγ$_1$), 4.58 (d, *J* = 12.0 Hz, 1H, Hγ'$_1$), 4.62 (d, *J* = 5.8 Hz, 1H, Hα), 4.71 (dd, *J* = 9.3, 7.3 Hz, 1H, Hγ$_2$), 6.34 (d, *J* = 2.0 Hz, 1H, H2'), 6.48 (dd, *J* = 8.2, 2.0 Hz, 1H, H6'), 6.80 - 6.95 (m, 2H, H2 and H5'), 7.26 - 7.30 (m, 2H, H5 and H6); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 54.0 (Cβ), 55.9 (OCH_3), 56.0 (OCH_3), 68.9 (Cγ), 75.5 (Cγ'), 88.0 (Cα), 107.8 (C2'), 109.2 (C5), 110.6 (C2), 117.7 (C6'), 118.3 (C5'), 118.5 (C5), 103.1 (Cβ'), 131.1 (Cα'), 131.6 (C1'), 148.1 (C4'), 148.5 (C4), 148.7 (C3'), 149.3 (C3).

Synthesis of 2,5-*bis*(3,4-dimethoxyphenyl)-3-(hydroxymethyl)-*4H*-pyran-4-one, 5



5

DDQ (27 mg, 0.117 mmol, 3 mole eq.) was added to a solution of eudesmin (**3**) (15 mg, 0.039 mmol) in anhydrous DMF (1.5 mL). The reaction mixture was stirred at room temperature overnight before being concentrated *in vacuuo* to give a yellow solid. The crude product was purified by column chromatography (hexanes/EtOAc: 2/8) to give a beige solid (8 mg, 0.019 mmol, 50%). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 3.96 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.76 (s, 2H, CH_2-OH), 6.98 (m, 2H, H2' and H2''), 7.20 (d, *J* = 2.0 Hz, 1H, H5''), 7.23 – 7.27 (m, 1H, H6''), 7.52 (d, *J* = 2.0 Hz, 1H, H5'), 7.60 (dd, *J* = 8.3, 2.0 Hz, 1H, H6'), 7.86 (s, 1H,

H6). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 55.5 (CH_2-OH); 56.5 (OCH_3), 56.6 (OCH_3), 110.1 (H2' or H2''), 110.2 (H5'), 111.1 (H2' or H2''), 111.2 (H5''), 119.4, 120.2 (H6'), 124.0 (H6''), 127.5, 131.2, 147.5 (H6), 149.0, 149.3 (C3' or C4'), 149.5, 153.2 (C3' or C4'), 153.5 (C3" or C4"), 153.6 (C3" or C4"), 190.3 (C=O). Spectral data are in accordance with the literature.[4,5]

References

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