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Synthetic Procedure of 2-(1-(4-hydroxy-3-methoxyphenyl)propan-2-yl)-6-methoxy-4-propylphenol

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We use this protocol and it's working

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Abstract

A direct understanding of the degradation reaction pathways of lignin polymers in biomass is difficult due to the complexity of lignin's structure. To overcome the difficulty, simple lignin dimeric and trimeric model compounds which include typical lignin interunit linkages are useful to clarify reaction mechanisms. The following procedure describes the synthetic procedure of a β-5 dimeric lignin model compound: 2-(1-(4-hydroxy-3-methoxyphenyl)propan-2-yl)-6-methoxy-4-propylphenol. Lignin model compounds are useful for screening the effectiveness of catalysts and microoganisms. As well as determining the effect of a treatment on the lignin fraction, in particular the effect on the degree of depolymerization in the lignin polymer.

Materials

Isoeugenol **Sigma Aldrich Catalog #**I7206	Step 1.1
Methanol **Sigma Aldrich Catalog #**M3641	Step 1.1 and Step 1.2
Citric acid **Sigma Aldrich Catalog #**251275	Step 1.1 [see Note 1]
Disodium Hydrogen Phosphate **Sigma Aldrich Catalog #**S9763	Step 1.1 [see Note 1]
Horseradish Peroxidase **Catalog #**P8250-25KU	Step 1.1
Hydrogen Peroxide **Fisher Scientific Catalog #**H325	Step 1.1
Ethyl Acetate **Fisher Scientific Catalog #**E145	Steps 1.1, 2.1, and 2.2
Sodium Chloride **Fisher Scientific Catalog #**S271	Step 1.1 (see Note 2)
Sodium Sulfate **Sigma Aldrich Catalog #**239313	Step 1.1
Palladium on carbon **Sigma Aldrich Catalog #**205680	Step 1.2
Hydrochloric acid **Sigma Aldrich Catalog #**258148	Step 1.2
Hexane mixture of isomers **Sigma Aldrich Catalog #**178918	Steps 2.1 and 2.2
Silica gel **Catalog #**60737	Steps 2.1 and 2.2
Acetone-D6 **Catalog #**DLM-9-25ML	Steps 3.1 and 3.2

Safety warnings

Almost all chemicals used for this procedure are hazardous. Read the Safety Data Sheet (SDS) for all chemicals and follow all applicable chemical handling and waste disposal procedures.

Before start

All glassware is dried in an oven set to 105ºC then cooled in a desiccator prior to use.

Synthetic Procedure

1

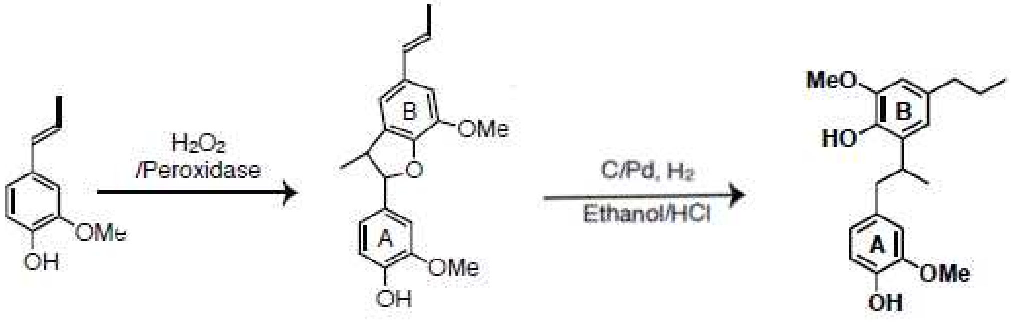

Figure 1. Two-step reaction scheme of 2-(1-(4-hydroxy-3-methoxyphenyl)propan-2-yl)-6-methoxy-4-propylphenol (β-5 dimer).

1.1 A solution of 1480 mL citrate-phosphate buffer (20 mM, pH 3.5) [see Note 1] was heated to 38 °C in a silicone oil bath. A solution of isoeugenol (5.00 mL , 0.0328 mol) in methanol (164 mL) was added in portions with vigorous stirring to the buffer solution. 20 mg horseradish peroxidase (HRP, 2500 U, Type II) was then added to the solution. The mixture was stirred while hydrogen peroxide, H_2O_2, (1.875 mL , 0.0612 mol) was added dropwise over 10 min. The reaction mixture was stirred for an additional 1 h and then filtered using a Büchner funnel. The resulting residue was separated and the funnel was washed with ethyl acetate (EtOAc). The organic solubles and the residue were combined and washed with a saturated solution of brine [see Note 2], and then dried using sodium sulfate (Na_2SO_4).[1,2] The crude product obtained after evaporation of the solvent in vacuo was crystallized from methanol to afford (±)-licarin A (1.3176 g, 24.6%).

Note

Note 1. Preparation of 20 mM citrate-phosphate buffer: 3.84 g Citric acid and 2.84 g disodium hydrogen phosphate are added to 1 L deionized (D.I.) water. Stir until both solids have completely dissolved. Check pH is close to 3.5.

Note

Note 2. Preparation of saturated brine solution: Fill a container partially with D.I. water. Add a spatula full of sodium chloride (NaCl) and stir until dissolved. Repeat until excess NaCl begins to settle onto the bottom of the container.

[1]

CITATION

C. S. Lancefield, N. J. Westwood (2015). The synthesis and analysis of advanced lignin model polymers. Green Chemistry.

LINK

10.1039/c5gc01334h

[2]

CITATION

Ciaran W. Lahive, Paul C. J. Kamer, C. S. Lancefield, Peter J. Deuss (2020). An introduction to model compounds of lignin linking motifs; synthesis and selection considerations for reactivity studies. ChemSusChem.

LINK

10.1002/cssc.202000989

1.2 Licarin a (1.21 g , 3.71 mmol) was charged into a round-bottom flask and dissolved in methanol (45 mL) . 0.45 g 5 wt% Palladium on carbon (Pd-C) was added gently to the reaction mixture followed by 4.66 mL hydrochloric acid.

Safety information

Palladium on carbon can react violently with methanol causing a brief small flame.

The reaction was then stirred at room temperature under a hydrogen filled balloon for 44 hours. After which is was filtered and concentrated *in vacuo*.[3] Crude mixture was purified via flash chromatography to yield the final product as a light yellow oil (0.6785 g, 55.4%).

[3]

CITATION

Fengxia Yue, Fachuang Lu, Matt Regner, Runcang Sun, John Ralph (2017). Lignin-Derived Thioacidolysis Dimers: Reevaluation, New Products, Authentication, and Quantification. ChemSusChem.

LINK

10.1002/cssc.201700101

Purification

2 Flash chromatography was performed using a Teledyne Isco Combiflash® NextGen 300+. Collected fractions were determined using a UV detector with wavelengths set at 254 and 280 nm. Samples were prepared by dissolving the crude material in the smallest amount of compatible solvent. Silica gel (mesh size 70-230) was then added to adsorb the material. Excess solvent was vacuum evaporated and the sample was loaded into a RediSep® R_f 25 g sample cartridge (catalog # 69-3873-240).

2.1 Licarin a can be purified by recrystallization from methanol or by flash chromatography. Column used was a RediSep® Silver 80 g silica gel flash column (catalog # 69-2203-380). Solvent system was hexane (Solvent A) and ethyl acetate (Solvent B). Licarin a was separated from impurities using a ratio of 1:4 ethyl acetate:hexane.

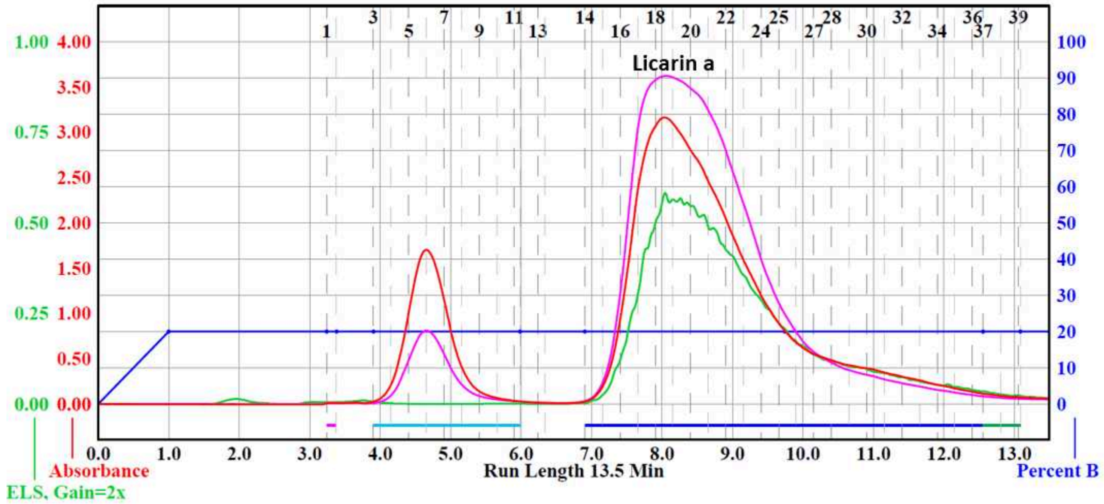

Figure 2. Run program from Combiflash® NextGen 300+ of licarin a separation.

2.2 2-(1-(4-hydroxy-3-methoxyphenyl)propan-2-yl)-6-methoxy-4-propylphenol was purified via flash chromatography. Column used was a RediSep® Silver 40 g silica gel flash column (catalog # 69-2203-340). Solvent system was hexane (Solvent A) and ethyl acetate (Solvent B). Material was separated from impurities using a ratio of 15% ethyl acetate and 75% hexane.

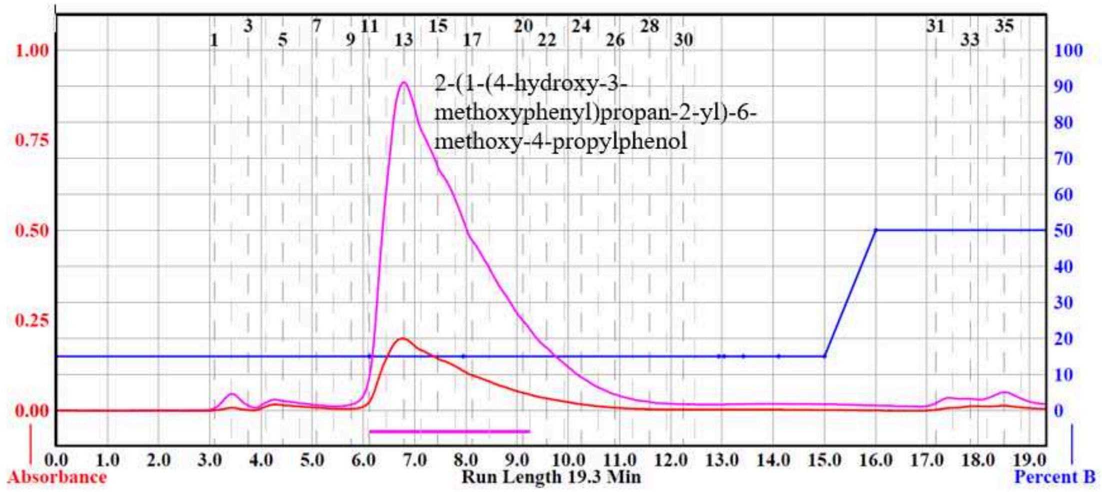

Figure 3. Run program from Combiflash® NextGen 300+ of 2-(1-(4-hydroxy-3-methoxyphenyl)propan-2-yl)-6-methoxy-4-propylphenol separation.

NMR Spectroscopy

3 Nuclear magnetic resonance (NMR) spectra are acquired in a suitable deuterated NMR solvent at 25°C on a Bruker AVANCE 400 MHz spectrometer equipped with a 5 mm BBO probe. Chemical shifts (δ) are reported in ppm. ^{1}H-NMR spectra are recorded with a relaxation delay of 1.0 s and an acquisition time of 4.09 s. The acquisition parameters for ^{13}C-NMR include a 90˚ pulse width, a relaxation delay of 1.0 s, and an acquisition time of 1.36 s. Tetramethylsilane is used as a reference.

3.1

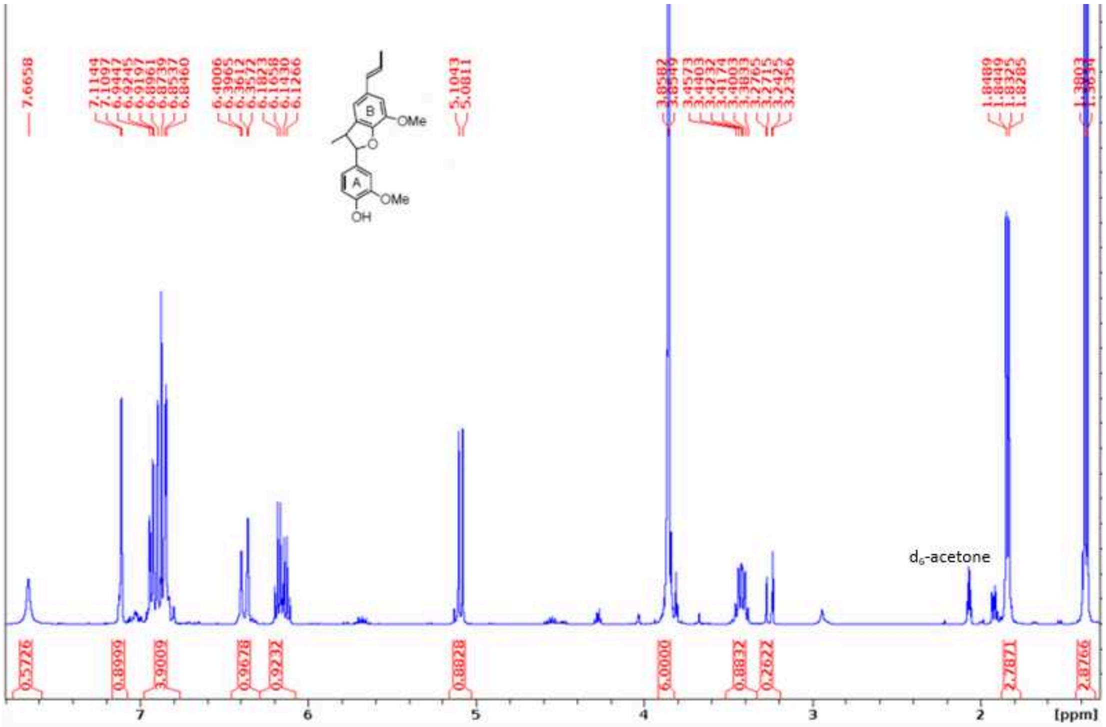

Figure 4. ^{1}H NMR spectrum of licarin a.

^{1}H NMR (400 MHz, d_6-acetone): *δ* 7.67 (s, 1H, ArOH), 7.11-6.84 (m, 5H, aromatic region), 6.40 (dd, *J* =14.2, 1.6 Hz, 1H, Bα), 6.18 (dq, *J* =9.1, 6.6 Hz, 1H, Bβ), 5.10 (d, J=9.3 Hz, 1H, Aα), 3.86 (s, 3H, OMe), 3.85 (s, 3H, OMe), 3.45 (dq, *J* =6.8, 2.3 Hz, 1H, Aβ), 1.84 (dd, *J* =4.9, 1.6 Hz, 3H, Bγ), 1.38 (d, *J*= 6.8 Hz, 3H, Aγ).

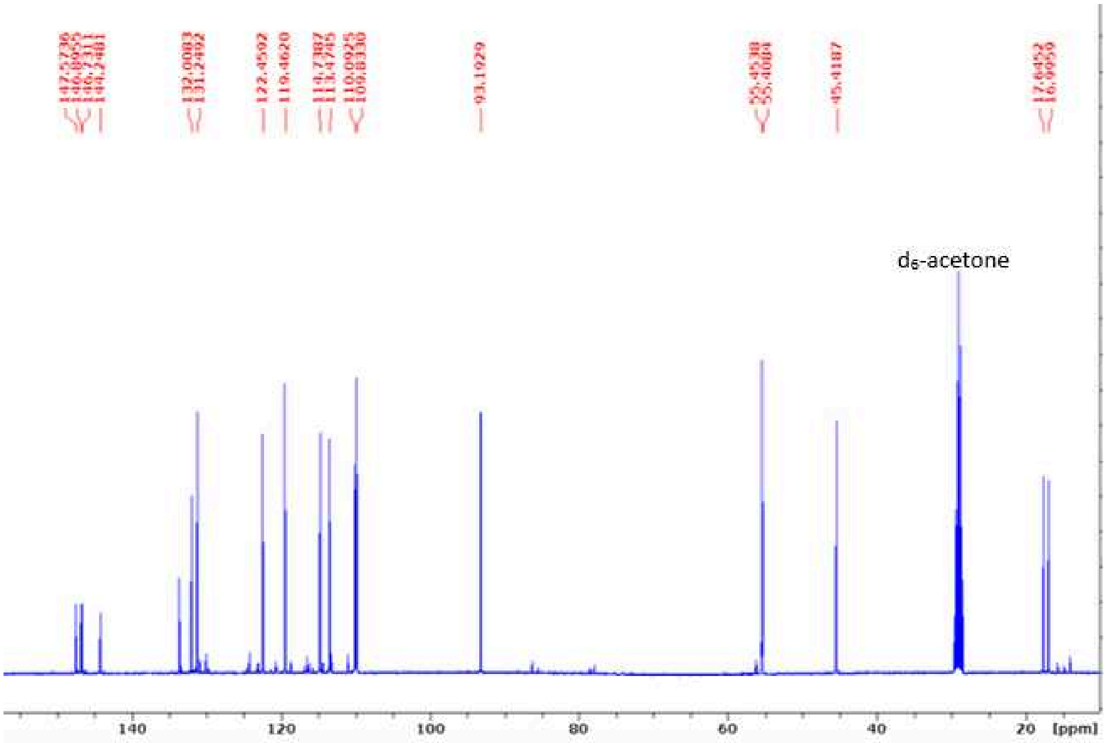

Figure 5. ^{1}H NMR spectrum of licarin a.

^{13}C NMR (100 MHz, d_6-acetone): δ 147.6 (A3), 146.9 (B3), 146.7 (A4), 144.2 (B4), 133.2 (B1), 132.0 (B5), 131.2 (A1), 130.9 (Bα), 122.4 (Bβ), 119.5 (A6), 114.7 (B6), 113.5 (A5), 110.1 (B2), 109.8 (A2), 93.2 (Aα), 55.5 (OMe), 55.4 (OMe), 45.4 (Aβ), 17.6 (Bγ), 16.9 (Aγ).

3.2

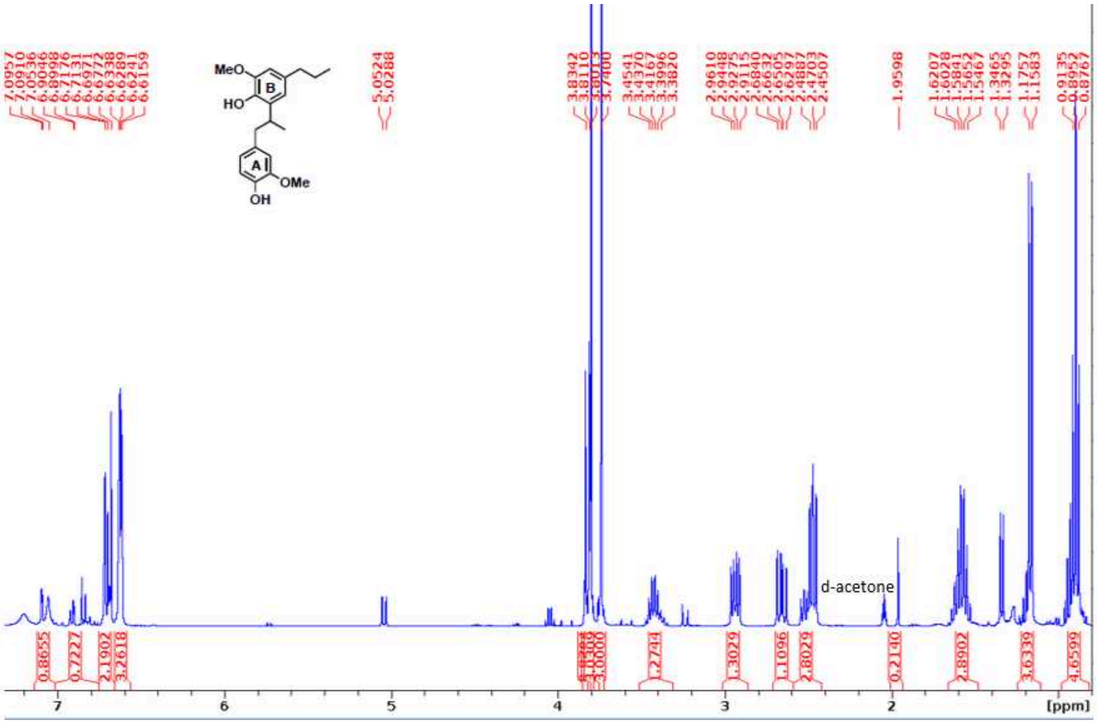

Figure 6. ^{1}H NMR spectrum of 2-(1-(4-hydroxy-3-methoxyphenyl)propan-2-yl)-6-methoxy-4-propylphenol.

^{1}H NMR (400 MHz, d_6-acetone): δ 6.72 (d, J = 1.8 Hz, 1H, A2), 6.69 (d, J = 7.9 Hz, 1H, A5), 6.63 (d, J = 1.9 Hz, 1H, B2), 6.62 (dd, J = 6.8, 1.2 Hz, 1H, A6), 6.61 (d, J = 1.2 Hz, 1H, B6), 3.81 (s, 3H, B3-OMe), 3.74 (s, 3H, A3-OMe), 3.45 (sex, J = 6.8 Hz, 1H, Aβ), 2.96 (dd, J = 6.6 Hz, 1H, Aα1), 2.68 (dd, J = 8.3, 5.1 Hz, 1H, Aα2), 2.48 (t, J = 7.4 Hz, 2H, Bα), 1.62 (sex, J = 7.2 Hz, 2H, Bβ), 1.17 (d, J = 6.9 Hz, 3H, Aγ), 0.91 (t, J = 7.3 Hz, 3H, Bγ).

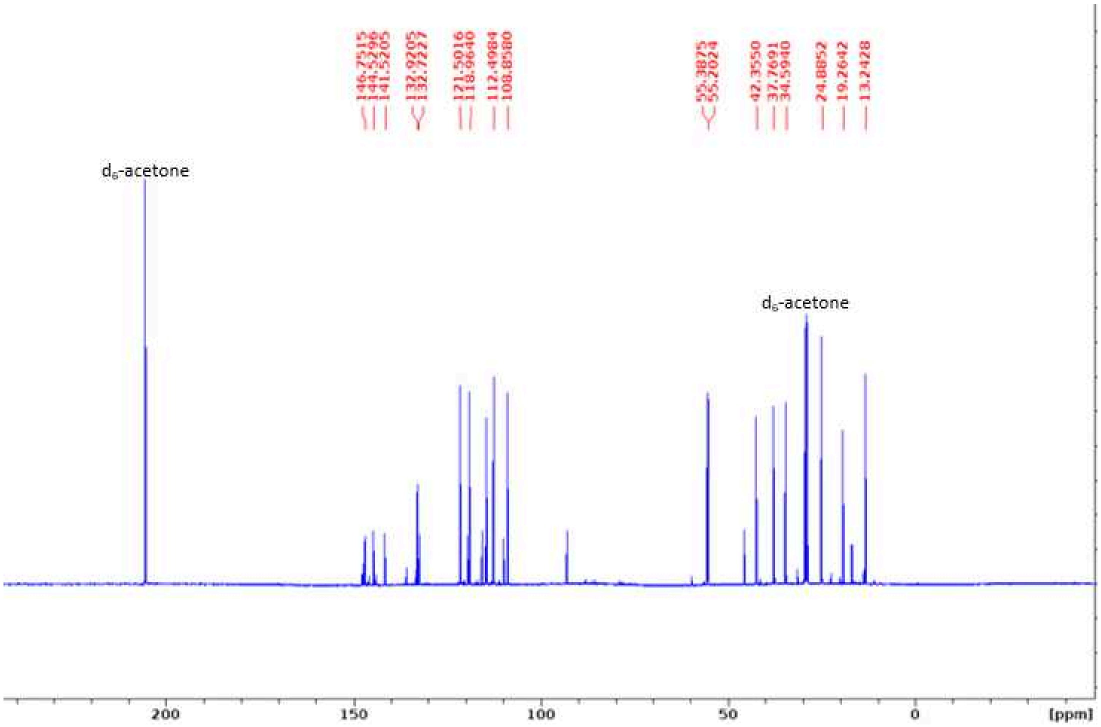

Figure 7. ^{13}C NMR spectrum of 2-(1-(4-hydroxy-3-methoxyphenyl)propan-2-yl)-6-methoxy-4-propylphenol.

^{13}C NMR (100 MHz, d_6-acetone): δ 146.75 (A3), 146.31 (B3), 144.53 (A4), 141.52 (B4), 132.92 (B1), 132.72 (A1), 132.04 (B5), 121.50 (A6), 118.96 (B6), 114.22 (A5), 112.50 (A2), 108.86 (B2), 55.39 (B-OMe), 55.20 (A-OMe), 42.36 (Aα), 37.77 (Bα), 34.59 (Aβ), 24.89 (Bβ), 19.26 (Aγ), 13.24 (Bγ).

[4]

CITATION

S. A. Ralph, L. L. Landucci, J. Ralph (2009). NMR Database of Lignin and Cell Wall Model Compounds.

LINK

https://www.glbrc.org/databases_and_software/nmrdatabase/NMR_DataBase_2009_Complete.pdf

Citations

Step 1.1

Ciaran W. Lahive, Paul C. J. Kamer, C. S. Lancefield, Peter J. Deuss. An introduction to model compounds of lignin linking motifs; synthesis and selection considerations for reactivity studies
10.1002/cssc.202000989

Step 1.1

C. S. Lancefield, N. J. Westwood. The synthesis and analysis of advanced lignin model polymers
10.1039/c5gc01334h

Step 1.2

Fengxia Yue, Fachuang Lu, Matt Regner, Runcang Sun, John Ralph. Lignin-Derived Thioacidolysis Dimers: Reevaluation, New Products, Authentication, and Quantification
10.1002/cssc.201700101

Step 3.2

S. A. Ralph, L. L. Landucci, J. Ralph. NMR Database of Lignin and Cell Wall Model Compounds
https://www.glbrc.org/databases_and_software/nmrdatabase/NMR_DataBase_2009_Complete.pdf