

Short Note

2,2'-((5,5',6,6'-Tetramethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(methanylylidene))dimalononitrile

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Abstract: This report discusses the synthesis of a biosourced divanillin derivative obtained by Knoevenagel condensation. The compound was fully characterized by proton (¹H), carbon (¹³C), heteronuclear single quantum coherence (HSQC), homonuclear correlation spectroscopy (COSY), and heteronuclear multiple bond correlation (HMBC) NMR, as well as high-resolution mass spectroscopy (HRMS). We also investigated the optical properties through UV-visible spectroscopy and Fourier-transform infrared (FTIR) spectroscopy. At last, the thermal properties of this divanillin derivative were evaluated by thermogravimetric analysis (TGA) as well as differential scanning calorimetry (DSC).

Keywords: vanillin; biosourced; Knoevenagel condensation; dyes; organic pigments

1. Introduction

Several organic pigments can be obtained from natural sources. For instance, indigo can be extracted from *Isatis tinctoria*, β-carotene from vegetables (i.e., carrots, orange peel), chlorophyll from plants and algae, and guaiazulene from the Australian cypress-pine *Callitris intratropica* [1–4]. Similarly, Tyrian purple and phenazine pigments can also be obtained from microbial and bacterial sources [5,6]. However, due to their sourcing, most of these pigments cannot be produced in large quantities. Indeed, most of the organic pigments used today are sourced from petrochemicals. For instance, synthetic pigments such as azo, phthalocyanine, quinacridone, and anthraquinone, as well as VAT dyes, are produced industrially [7–9].

By contrast, lignocellulosic materials are promising alternatives as they are the most abundant materials on the planet and can be broken down into several aromatic platform chemicals [10,11]. One compound of interest obtained from lignin is vanillin [12]. Vanillin possesses three functional groups (hydroxy, aldehyde, methoxy) and can be transformed into a plethora of compounds for pigments purposes [13]. Moreover, vanillin can also be dimerized into divanillin, opening the way to expand its chemistry for pigments, materials and bioactive compounds applications (Figure 1).

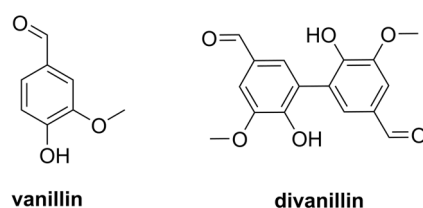


Figure 1. Chemical structures of vanillin and divanillin.



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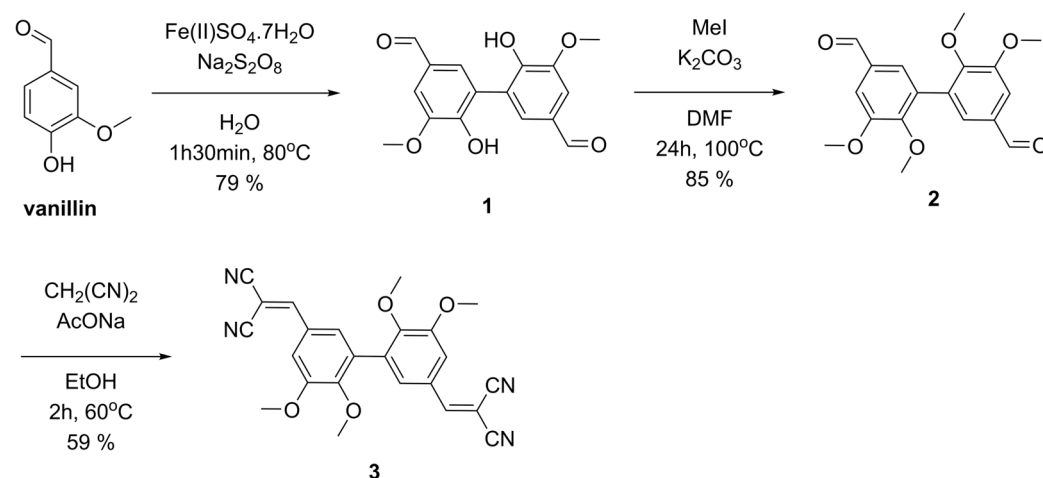
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In this work, we report on the preparation of a novel biosourced divanillin-based pigment prepared from vanillin (compound **3**, Scheme 1). This research showcases how renewable lignocellulosic material can be transformed successfully into biosourced pigment.



Scheme 1. Synthesis of 2,2'-((5,5',6,6'-tetramethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(methanylylidene))dimalononitrile **3**.

2. Results

Herein, we present the synthesis of 2,2'-((5,5',6,6'-tetramethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(methanylylidene))dimalononitrile **3** as shown in Scheme 1. First, vanillin was dimerized in the presence of iron(II)sulfate heptahydrate and iron persulfate in water. The resulting mixture was stirred for 1 h 30 min at 80 °C. After filtration and drying under vacuum (48 h, 80 °C), compound **1** (divanillin) was obtained in a yield of 79% [14]. Then, compound **1** was methylated using methyl iodide with potassium carbonate in *N,N*-dimethylformamide (DMF). The reaction was carried out at 100 °C for 24 h. After cooling and filtration, compound **2** was obtained in 85% yield [15]. At last, compound **3** was prepared by a Knoevenagel condensation reaction using malononitrile and sodium acetate in ethanol. After reacting for 2 h at 60 °C, the mixture was acidified and purified by redispersion in a 1:1 mixture of EtOH/acetone to afford newly prepared 2,2'-((5,5',6,6'-tetramethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(methanylylidene))dimalononitrile **3** in a 59% yield [16]. The procedure is further explained in detail in the experimental section.

The structure of compound **3** was clearly confirmed using an array of spectroscopic techniques. First, compound **3** was characterized by Fourier-transform infrared spectroscopy (FTIR), identifying the presence of nitrile groups (-CN) at 2227 cm⁻¹ and the absence of carbonyl groups (aldehydes at 1690 cm⁻¹ from compound **2**, see Supplementary Information).

Then, NMR spectroscopy provided important information about the arrangement and connection of hydrogen and carbon atoms. ¹H NMR analysis of compound **3** shows signals for the hydrogen atoms of the vinylene group (CN₂-C=C-H) at 8.46 ppm as a singlet. The protons from the methoxy groups are observed at 3.90 and 3.72 ppm. At last, C-H protons from the benzene rings are observed as a multiplet at 7.78 and 7.43 ppm. Concerning the ¹³C NMR spectrum, all carbon atoms are present. The signals of the carbon atom corresponding to the vinylene group are observed at 160.38 ppm (CH=C-CN₂) and 79.86 ppm (CH=C-CN₂) ppm, while carbon atoms from the nitrile groups are observed at 113.93 ppm and 113.57 ppm, respectively (CH=C-CN₂). Carbon atoms from the methoxy are clearly identified at 60.76 and 55.97 ppm (O-CH₃). Finally, carbon atoms from the benzene rings are observed between 152.33 to 114.42 ppm.

Two-dimensional NMR experiments were also carried out, namely COSY, HMBC, and HSQC (see Supplementary Information). The COSY spectrum showed the limited ^1H - ^1H direct bond coupling, thus confirming that protons from the methoxy groups and aromatic protons are independent of each other. Secondly, the HSQC spectrum showed the direct ^{13}C - ^1H bond, confirming that the protons of the methoxy groups are attached to the carbon atoms at 60.76 and 55.97 ppm ($\text{O}-\text{CH}_3$). Likewise, aromatic protons at 7.78 and 7.43 ppm are attached to the carbons between 126.7 to 114.3 ppm. At last, the HMBC spectrum highlighted the long-range ^1H - ^{13}C coupling present in compound **3**. The 1-D and 2-D NMR spectra are all in accordance with the proposed chemical structure for compound **3**.

Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) provide meaningful information about the thermal behavior of compound **3** (see Supporting Information). TGA and DSC were carried out to evaluate the thermal stability of compound **3** and the presence of thermal transitions (such as fusion (T_f) and crystallization (T_c)), respectively. TGA thermograms showed that compound **3** is stable up to 298 °C (T_d) under air. On the other hand, DSC analysis of compound **3** showed fusion (T_f) at 250 °C upon heating (10 °C/min) and crystallization (T_c) at 167 °C when cooling (10 °C/min).

The high-resolution mass spectroscopy (HR-MS) accurately determined the molecular weight of the compound. Likewise, Fourier-transform infrared spectroscopy (FTIR) successfully identified key functional groups through their specific vibrational patterns.

Moreover, UV-visible spectroscopy (in solution) has been carried out on compounds **2** and **3** (Figure 2). We observe an absorption peak at 275 nm for compound **2**, whereas compound **3** showed a peak at 364 nm, highlighting the fact they are two different compounds. As expected, increasing the conjugation length with the presence of nitrile groups attached to the ethylene redshifted the absorption maximum of compound **2** from 275 nm to 364 nm (compound **3**).

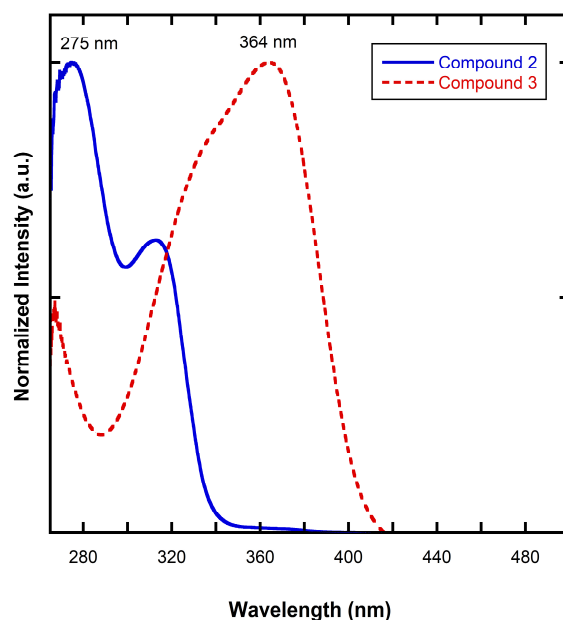


Figure 2. UV-visible spectra of compounds **2** (blue) and **3** (red) in DMF.

3. Materials and Methods

All reagents and chemicals were obtained from sources (Sigma-Aldrich (Oakville, QC, Canada), Oakwood Chemical (Estill, SC, USA), and Ambeed (Arlington Hts, IL, USA)) except biosourced vanillin, which was graciously provided by Borregaard. All chemicals were used as received without further purification. The ^1H and ^{13}C NMR spectra of the compounds were recorded using a Bruker Fourier 300 spectrometer in the appropriate

deuterated solvents at 293 K. Chemical shifts were reported as δ values (ppm) relative to the residual solvent signals: DMSO- d_6 (^1H NMR = 2.50 ppm, ^{13}C NMR = 39.52 ppm). Coupling constants are reported to the nearest 0.5 Hz. FT-IR spectroscopy was performed on solid samples (ATR) using Agilent Technologies Cary 630 FTIR. Electrospray ionization (ESI) high-resolution mass spectrometry (HRMS) was carried out using an Agilent 6210 LC time-of-flight mass spectrometer. Thermogravimetric analysis (TGA) was performed on a TA TGA Q500 under air at a heating rate of 20 °C/min. The degradation temperature (T_d) was determined after a 5% weight loss of the initial sample. Differential scanning calorimetry (DSC) was carried out using a TA DSC Q2000 under a constant nitrogen flow, with calibration performed using an indium standard. The DSC scans included initial heating from 0 °C to 250 °C, followed by cooling from 250 °C to 0 °C, and a final heating step temperature (T_d) and 5 °C/min to obtain the temperature of fusion (T_f). UV-visible spectra were recorded on an Agilent Technologies Cary 60 Spectrophotometer in *N,N*-dimethylformamide (DMF). Preparation of compounds **1** and **2** has been previously reported in the literature [14,15]. However, for the benefit of the reader, their experimental protocols are reported below.

3.1. Synthetic Procedures

3.1.1. Synthesis of 6,6'-Dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-dicarbaldehyde **1**

In a three neck-flask, was added vanillin (50 g, 329 mmol, 1 Eq.) in water (2.50 L). Then, iron(II) sulfate heptahydrate (1.83 g, 6.57 mmol, 0.02 Eq.) was added, followed by the addition of sodium persulfate (41.5 g, 174 mmol, 0.53 Eq.) in small portions. The mixture was heated at 80 °C for 1 h 30 min. The mixture was cooled to 45–50 °C, and the precipitate was filtered. The resulting solid was washed with hot water (70–80 °C, 3 $\times$ 500 mL). The solid was then dried under vacuum at 80 °C for 24 h to give the title compound **1** in a yield of 79%. ^1H NMR and ^{13}C NMR data are consistent with the same data reported in the literature [14].

3.1.2. Synthesis of 5,5',6,6'-Tetramethoxy-[1,1'-biphenyl]-3,3'-dicarbaldehyde **2**

In a three-neck flask equipped with a condenser and a thermometer, were added compound **1** (25 g, 82.7 mmol, 1 Eq.), potassium carbonate (48.0 g, 347 mmol, 4.2 Eq.), and DMF (383 mL). Then, iodomethane (70.4 g, 496 mmol, 6 Eq.) was added. The mixture was heated to 100 °C for 24 h. The mixture was cooled down to room temperature. The precipitate was filtered and washed with acetone (100 mL) to remove insoluble salts. The filtrate was poured into 3 L of cold water (0–5 °C), and the resulting precipitate was filtered and washed with cold water (1 L). The solid was then dried under vacuum at 80 °C for 24 h to give the title compound **2** in a yield of 85%. ^1H NMR and ^{13}C NMR data are consistent with the same data reported in the literature [15].

3.1.3. Synthesis of 2,2'-((5,5',6,6'-Tetramethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(methanylylidene))dimalononitrile **3**

Into a three-neck flask equipped with a condenser and a thermometer, we added compound **2** (0.5 g, 1.51 mmol, 1 Eq.), malononitrile (0.53 g, 8.00 mmol 5.3 Eq), and sodium acetate (0.369 g, 4.53 mmol, 3 Eq.) in ethanol (20 mL). The resulting mixture was stirred at 60 °C for 2 h. The mixture was cooled to room temperature, poured into water (100 mL), and acidified at pH 1–2 with concentrated HCl. The precipitate was filtered, redispersed in a 1:1 EtOH/acetone solution (50 mL), and heated at reflux while applying vigorous stirring for 15 min. Then, the dispersion was cooled to room temperature. The solid was filtered and dried to give the targeted compound in 59% yield (382 mg). Yellow solid (m.p. 250 °C) ^1H NMR (300 MHz, DMSO- d_6) δ 8.46 (s, 2H, $\text{CN}_2\text{-C}=\text{C-H}$), 7.78 (m, 2H, Ar), 7.43 (m, 2H, Ar), 3.90 (s, 6H, O- CH_3), 3.72 (s, 6H, O- CH_3); ^{13}C NMR (75 MHz, DMSO- d_6) δ 160.38 ($\text{CH}=\text{C}$ -

CN₂), 152.33 (Ar), 151.32(Ar), 131.27(Ar), 126.63(Ar), 126.51(Ar), 114.42(Ar), 113.93 (CH=C-CN₂), 113.57 (CH=C-CN₂), 79.86 (CH=C-CN₂), 60.76 (O-CH₃), 55.97 (O-CH₃). HRMS Electrospray ionization (ESI) m/z calculated for [M + Na]⁺ C₂₄H₁₈N₄O₄Na⁺ = 449.1226, found: 449.1228; IR (ATR) $\nu_{\max}$, cm⁻¹: 2947 (C-H), 2227 (C≡N), 1278 (C-O-C).

Supplementary Materials: Figure S1. ¹H NMR spectra of compound 3; Figure S2. ¹³C NMR spectra of compound 3; Figure S3. HSQC NMR spectra of compound 3; Figure S4. HMBC NMR spectra of compound 3; Figure S5. COSY NMR spectra of compound 3; Figure S6. HRMS (ESI) spectra of compound 3; Figure S7. FTIR spectra of compound 2; Figure S8. FTIR spectra of compound 3; Figure S9. TGA thermogram of compound 3 under air (20°C/min); Figure S10. DSC thermogram of compound 3 (10°C/min).

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References

- Gökhan, K.; Seferoğlu, Z.; Berdnikova, D.V. Photochromic derivatives of indigo: Historical overview of development, challenges and applications. *Beilstein J. Org. Chem.* **2024**, *20*, 228–242.
- Kyriakopoulou, K.; Papadaki, S.; Krokida, M. Life cycle analysis of β -carotene extraction techniques. *J. Food. Eng.* **2015**, *167*, 51–58. [\[CrossRef\]](#)
- Zhao, W.; Sasaki, S.; Tamiaki, H.; Sanehira, Y.; Wei, Y.; Chen, G.; Wang, X.-F. Enhancement of performance in chlorophyll-based bulk-heterojunction organic-inorganic solar cells upon aggregate management via solvent engineering. *Org. Electron.* **2018**, *59*, 419–426. [\[CrossRef\]](#)
- Rangel-Yagui, C.O.; Danesi, E.D.G.; Monteiro de Carvalho, J.C.; Sato, S. Chlorophyll production from *Spirulina platensis*: Cultivation with urea addition by fed-batch process. *Bioresour. Technol.* **2004**, *92*, 133–141. [\[CrossRef\]](#) [\[PubMed\]](#)
- Lee, J.; Kim, J.; Song, J.E.; Song, W.-S.; Kim, E.-J.; Kim, Y.-G.; Jeong, H.-J.; Kim, H.R.; Choi, K.-Y.; Kim, B.-G. Production of Tyrian purple indigoid dye from tryptophan in *Escherichia coli*. *Nat. Chem. Biol.* **2021**, *17*, 104–112. [\[CrossRef\]](#) [\[PubMed\]](#)
- Schmitz, S.; Rosembaum, M.A. Controlling the production of *Pseudomonas* phenazines by modulating the genetic repertoire. *ACS Chem. Biol.* **2020**, *15*, 3244–3252. [\[CrossRef\]](#) [\[PubMed\]](#)
- Morin, J.-F. Recent advances in the chemistry of vat dyes for organic electronics. *J. Mater. Chem. C* **2017**, *5*, 12298–12307. [\[CrossRef\]](#)
- Hunger, K.; Schmidt, M.U. *Industrial Organic Pigments: Production, Crystal Structures, Properties, Applications*, 4th ed.; Wiley-VCH Verlag GmbH & Co KGaA: Weinheim, Germany, 2018; pp. 1–673.
- Christie, R.; Abel, A. Organic pigments: General principles. *Phys. Sci. Rev.* **2021**, *6*, 807–834. [\[CrossRef\]](#)
- Isikgor, F.H.; Becer, C.R. Lignocellulosic biomass: A sustainable platform for the production of bio-based chemicals and polymers. *Polym. Chem.* **2015**, *6*, 4497–4559. [\[CrossRef\]](#)
- Becker, J.; Wittmann, C. A field of dreams: Lignin valorization into chemicals, materials, fuels, and health-care products. *Biotech. Adv.* **2019**, *37*, 107360. [\[CrossRef\]](#) [\[PubMed\]](#)
- Gendron, D. Vanillin: A promising biosourced building block for the preparation of various heterocycles. *Front. Chem.* **2022**, *10*, 949355. [\[CrossRef\]](#) [\[PubMed\]](#)

13. Pandian, B.; Ramalingam, S.; Sreeram, K.J.; Rao, J.R. Natural pigment: Preparation of brown pigment from lignin biomass for coloring application. *Dye. Pigment.* **2021**, *195*, 109704. [[CrossRef](#)]
14. Fang, Z.; Nikafshar, S.; Hegg, E.L.; Nejad, M. Biobased divanillin as a precursor for formulating biobased epoxy resin. *ACS Sustain. Chem. Eng.* **2020**, *8*, 9095–9103. [[CrossRef](#)]
15. Savonnet, E.; Le Coz, C.; Grau, E.; Grelier, S.; Deffort, B.; Cramail, H. Divanillin-based aromatic amines: Synthesis and use as curing agents for fully vanillin-based epoxy thermosets. *Front. Chem.* **2019**, *7*, 606. [[CrossRef](#)] [[PubMed](#)]
16. Pigot, C.; Peralta, S.; Bui, T.-T.; Nechab, M.; Dumur, F. Push-pull dyes based on Michler's aldehyde: Design and characterization of the optical and electrochemical properties. *Dye. Pigment.* **2022**, *202*, 110278. [[CrossRef](#)]

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