Catalyst-free decarboxylation of 4-hydroxycinnamic acids: efficient synthesis of 4-vinylphenols

Qian Yang3,†, Youjuan Li1,2,†, Huanhuan Liu1,2, Enhua Wang3, Mei Peng1,2, Tingfei Deng1,2, Xiong Pan1,2, Zhongsheng Luo1,2, Yanfang Yan1,2, Lishou Yang1,2 and Xiaosheng Yang1,2

1State Key Laboratory of Functions and Applications of Medicinal Plants, Guizhou Medical University, Guiyang 550014, People’s Republic of China
2The Key Laboratory of Chemistry for Natural Products of Guizhou Province and Chinese Academy of Sciences, Guiyang 550014, People’s Republic of China
3Department of Medicine and Food, Guizhou Vocational College of Agriculture, Guiyang 550041, People’s Republic of China

We report herein an efficient protocol for the synthesis of 4-vinylphenols by a catalyst-free decarboxylation of trans-4-hydroxycinnamic acids. A variety of 4-vinylphenols has been synthesized in moderate to excellent yields. This protocol also features no polymerization.

1. Introduction

4-Vinylphenols are of both natural and biological interest. They are part of a large number of significant natural products such as 4-vinylphenol, 4-vinylcatechol, 2,6-dimethoxy-4-vinylphenol and many others [1–5]. Most of these compounds display varied bioactivities such as anti-oxidant [6–10], anti-mutagenic [9], anti-fungal [11] and anti-cancer [12–14] properties (figure 1). They are also building blocks in the synthesis of bioactive compounds [15–17]. In addition, they are widely used in industry [18]. Therefore, the synthesis of 4-vinylphenols has gained widespread attention.

However, the susceptibility of the hydroxy function toward polymerization often results in the formation of polymers [19]. To overcome this barrier chemical [20–27] and biological [28–32] protocols have been developed, but most of them suffer from narrow substrate scope. To the best of our knowledge, the most
efficient synthetic routes reported for the preparation of 4-vinylphenols involve (i) piperidine-catalysed Knoevenagel–Doebner [20] and Knoevenagel reaction [21] from 4-hydroxybenzaldehydes and malonic acid (scheme 1a); (ii) decarboxylation of 4-hydroxycinnamic acids using DBU [22], [C2C1Im][OAc] [23] or Bacillus subtilis [28] (scheme 1b). But these methods only test 4-hydroxycinnamic acids bearing electron-donating groups (EDG) [20–23,28] and suffer some disadvantages such as the use of a base catalyst (Stamford/Joshi/Setti/Singh’s work), the addition of polymerization inhibitor (Setti’s work), need of microwave-assisted (Joshi/Setti’s work) and long reaction times (Stamford/Kourist’s work). Several catalyst-free decarboxylation methods of cinnamic acids have been reported, however, they need using some sort of biocatalysts [29,33,34].

Herein, we report an efficient procedure for the preparation of 4-vinylphenols from trans-4-hydroxycinnamic acids by a catalyst-free decarboxylative reaction without any additive (scheme 1c). This approach tolerates 4-hydroxycinnamic acids bearing electron-donating/withdrawing groups and containing substituents on the double bond. Additionally, it can effectively inhibit the polymerization in the absence of inhibitor.

2. Results and discussion

Our initial studies were carried out with readily available 4-hydroxycinnamic acid 1a as a test substrate. 1a in DMF was stirred at 200°C for 60 min under an air atmosphere to give the desired product 2a in 15% yield.

anti-oxidant/cancer/mutagenic  anti-fungal  phenylalanine hydrolase inhibitor

Figure 1. Selected bioactive 4-vinylphenols.

(a) Knoevenagel-Doebner and Knoevenagel reaction from 4-hydroxybenzaldehydes and malonic acid

Stamford’s work

\[
\text{cat. Piperidine}
\]

\[
\text{malonic acid, pyridine}
\]

Reflex, 4 h

Joshi’s work

\[
\text{cat. Piperidine}
\]

\[
\text{malonic acid/\text{AcOH}}
\]

microwave, 5–20 min

(b) decarboxylation of 4-hydroxycinnamic acids

Setti’s work

\[
\text{cat. DBU}
\]

hydroquinone (a polymerization inhibitor)

solid support

microwave, 15–30 min

Singh’s work

\[
\text{[C2C1Im][OAc]}
\]

100–140°C 1 h

Kourist’s work

\[
\text{Bacillus subtilis}
\]

IChCl: 2Gly-water

30°C, 250 r.p.m., 8–72 h

(c) \textit{This work}: catalyst-free decarboxylation of 4-hydroxycinnamic acids

DMF, heating, 30 min

14 examples

63–96% yield

\( R^1, R^2 = \text{H, OH, -OCH}_3, -\text{OC}_2\text{H}_5, \text{-Cl, Br, -NO}_2, \text{-CH}_3 \)

\( R^1 = \text{H or -CH}_3 \)

\[ \text{catalyst-free}
\]

\[ \text{no polymerization}
\]

\[ \text{good functional group tolerance}
\]

Scheme 1. The most efficient approaches for the synthesis of 4-vinylphenols.
To further improve the reaction yield, control experiment was performed. To our delight, we found that decreasing the reaction time to 30 or 40 min had obvious effect on the reaction (table 1, entries 2–3). However, a decrease in the yield was observed upon further decreasing the reaction time (table 1, entry 4). Subsequently, we investigated the effect of solvents on the efficiency of the decarboxylation. Unfortunately, the reaction performed in DMA, ethylene glycol, DMSO, 1,4-dioxane or DCE exerted detrimental effect on the yield (table 1, entries 5–9). We tried to lower the temperature but failed. The reaction was conducted under microwave irradiation at 100°C, yielding 2a only in 45% yield (table 1, entry 10). Therefore, the optimized reaction conditions were determined as 1a (0.2 mmol) in DMF (1 ml) at 200°C for 30 min under an air atmosphere (table 1, entry 3). With the optimized reaction conditions in hand, a gram scale reaction was carried out and provided the product 2a in 87% yield (table 1, entry 11).

Under the optimized conditions, the scope of this decarboxylation was then examined by varying 4-hydroxycinnamic acids 1 (table 2). It is apparent from table 2 that 4-vinylphenols bearing electron-donating/withdrawing groups were prepared in excellent yields (86–96%) and no polymers were detected under the given conditions. Specifically, we investigated the decarboxylation of some natural products such as p-coumaric acid (1a), caffeic acid (1b), ferulic acid (1c) and sinapinic acid (1d), achieving corresponding 4-vinylphenols in excellent yields (2a–2d). Meanwhile, employing methyl- or ethoxy-substituted 4-hydroxycinnamic acids (1e–1g) also afforded the products in high yields (2e–2g). However, electron-withdrawing group (NO2, F, Cl or Br) gave lower yields (2h–2l). Moreover, 4-hydroxycinnamic acids containing methyl on the double bond (1p and 1q) were also compatible with the current conditions, providing the corresponding products 2p and 2q in moderate yields (68% and 63%). The products 2p and 2q exist in the E forms, based on their NMR spectra and in accordance with literature report [35]. Next, we tested several cinnamic acids without 4-hydroxyl substituent under the optimized reaction conditions. Unfortunately, no corresponding vinylbenzenes were detected (scheme 2).

In addition, we found that the polymerization product 2aa was isolated in 48% yield when the reaction time and temperature were increased (table 3, 2aa). Subsequently, we tested another two substrates bearing electron-donating/withdrawing group (table 3, 1f and 1l). Moderate yields were obtained. Obviously, for electron-withdrawing group (Br) substituted substrate, related polymer was got in higher yield (table 3, 2ff versus 2ll).

Plausible mechanisms for the decarboxylation and polymerization of 4-hydroxycinnamic acids are depicted in scheme 3. Species 3 is formed under elevated reaction temperature. Finally, hydrogen
Table 2. Evaluation of substrate scope.\textsuperscript{a}

| entry | substrates 1 | temp. (°C) | products 2 | yield (%)\textsuperscript{b} |
|-------|--------------|------------|------------|-----------------------------|
| 1     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{1a} \\
|       | &\text{HO} &\text{1b} \\
|       | &\text{HO} &\text{1c} \\
|       | &\text{HO} &\text{1d} \\
|       | &\text{HO} &\text{1e} \\
|       | &\text{HO} &\text{1f} \\
|       | &\text{HO} &\text{1g} \\
|       | &\text{HO} &\text{1h} \\
| 2     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 3     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 4     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 5     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 6     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 7     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 8     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 9     | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\
| 10    | \begin{align*} &R^1 &\text{COOH} \\
|       | &\text{HO} &\text{2a} \\
|       | &\text{HO} &\text{2b} \\
|       | &\text{HO} &\text{2c} \\
|       | &\text{HO} &\text{2d} \\
|       | &\text{HO} &\text{2e} \\
|       | &\text{HO} &\text{2f} \\
|       | &\text{HO} &\text{2g} \\
|       | &\text{HO} &\text{2h} \\

(Continued.)
Table 2. (Continued.)

| entry | substrates 1 | temp. (°C) | products 2 | yield (%)\(^b\) |
|-------|--------------|------------|------------|-----------------|
| 11    | ![substrate 11](image1) | 140        | ![substrate 2k](image2) | 89              |
| 12    | ![substrate 12](image3) | 140        | ![substrate 2l](image4) | 87              |
| 13    | ![substrate 13](image5) | 200        | ![substrate 2l](image6) | 68              |
| 14    | ![substrate 14](image7) | 200        | ![substrate 2q](image8) | 63              |

\(^a\)Reaction conditions: 1 (0.2 mmol), DMF (1 ml).
\(^b\)Isolated yield.

Scheme 2. Decarboxylation of cinnamic acids without 4-hydroxyl substituent.

Table 3. Synthesis of 4-vinylphenol dimers.\(^a\)

| entry | substrates | temp. (°C) | dimers | yield (%)\(^b\) |
|-------|------------|------------|--------|-----------------|
| 1     | ![substrate 1a/1f/1l](image9) | 220        | ![dimers 2aa/2ff/2ll](image10) | 48              |
| 2     | ![substrate 1a](image11) | 200        | ![dimers 2aa/2ff/2ll](image12) | 50              |
| 3     | ![substrate 1l](image13) | 170        | ![dimers 2aa/2ff/2ll](image14) | 67              |

\(^a\)Reaction conditions: 1a/1f/1l (0.2 mmol), DMF (1 ml).
\(^b\)Isolated yield.
transfer followed by release of a molecule of carbon dioxide ensures the formation of 4-vinylphenol 2a. Radical polymerization of styrene initiated at higher reaction temperature, yielding intermediate 6 followed by expelling hydrogen radical leads to the polymerization product 2aa.

3. Conclusion

In summary, we have developed an efficient method for the preparation of 4-vinylphenols via a catalyst-free decarboxylation of 4-hydroxycinnamic acids. This method features good functional group tolerance and no polymerization. However, corresponding polymers were obtained in moderate yields when under harsher reaction conditions.

4. Experimental section

4.1. General information

Unless otherwise noted, all reagents, catalysts and solvents were purchased from commercial suppliers and used without further purification. Column chromatography was performed with silica gel (200–300 mesh). Melting points were determined using a X-4 melting point apparatus with microscope. The IR spectra were recorded with Mattson FTIR spectrometer 5000. Absorption maxima were measured in cm⁻¹. ¹H and ¹³C NMR spectra were achieved on a Bruker Avance 600 MHz spectrometer (¹H 600 MHz; ¹³C 151 MHz; ¹⁹F 565 MHz) in CDCl₃, CD₃OD, DMF-d₇, DMSO-d₆. High-resolution mass spectra were measured on a ThermoFish QE Focus facility. Thin-layer chromatographies were done on pre-coated silica gel 60F254 plates (Merck).

4.2. General procedure for the synthesis of 4-vinylphenols (2a–2l and 2p–2q)

4.2.1. Procedure for 4-vinylphenols bearing electron-donating groups (2a–2g and 2p)

To a stirred solution of DMF (1 ml) was added 4-hydroxycinnamic acids (1a–1g and 1p) (0.2 mmol) in 5 ml pressure-resistant reaction bottle. The reaction mixture was stirred at 130–200°C until the completion of the starting materials as monitored by TLC (30 min). The reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was dried over Na₂SO₄ and evaporated under reduced pressure. The resulting crude compound was purified by silica gel column chromatography to yield the pure product (2a–2g and 2p), which was dissolved immediately in methanol for storage.

4.2.1.1. 4-Vinylphenol 2a

Light yellow solid, yield 89%, mp 72–74°C. IR (KBr plate): νmax 3328, 3019, 2924, 2850, 1609, 1228, 834 cm⁻¹. ¹H NMR (600 MHz, DMSO-d₆) δ 7.29–7.23 (m, 2H), 6.72 (d, J = 8.5 Hz, 2H), 6.60 (dd, J = 17.6, 10.9 Hz, 1H), 5.57 (dd, J = 17.6, 0.9 Hz, 1H), 5.03 (dd, J = 10.9, 0.8 Hz, 1H). ¹³C NMR (151 MHz, DMSO-d₆) δ 157.78, 136.86, 128.77, 127.89, 115.79, 111.12. HRMS-ESI (m/z): [M + H]+ calcd. for C₈H₉O: 121.06479; found, 121.06487.

4.2.1.2. 2-Hydroxy-4-vinylphenol 2b

Light yellow oil, yield 87%. IR (KBr plate): νmax 3346, 2929, 1604, 1524, 1281, 1111, 815 cm⁻¹. ¹H NMR (600 MHz, CD₃OD) δ 6.94 (d, J = 1.8 Hz, 1H), 6.78 (dd, J = 8.1, 1.8 Hz, 1H), 6.75 (d, J = 8.1 Hz, 1H), 6.61...
J = 17.6, 10.9 Hz, 1H), 5.56 (dd, J = 17.6, 0.9 Hz, 1H), 5.06 (dd, J = 10.9, 0.8 Hz, 1H). 13C NMR (151 MHz, CD3OD) δ 145.16, 144.98, 136.75, 130.03, 118.31, 114.82, 112.21, 109.34. HRMS-ESI (m/z): [M + H]+ calcd. for C8H9O2: 137.05971; found, 137.05946.

4.2.1.3. 2-Methoxy-4-vinylphenol 2c
Colourless oil, yield 94%. IR (KBr plate): νmax 3411, 2924, 2852, 1603, 1514, 1463, 1269, 817. 1H NMR (600 MHz, CDCl3) δ 6.95–6.91 (m, 2H), 6.87 (d, J = 8.1 Hz, 1H), 6.64 (dd, J = 17.5, 10.8 Hz, 1H), 5.65 (s, 1H), 5.59 (d, J = 17.5 Hz, 1H), 5.13 (d, J = 10.9 Hz, 1H), 3.91 (s, 3H). 13C NMR (151 MHz, CDCl3) δ 146.59, 145.64, 136.63, 130.28, 120.08, 114.35, 111.47, 108.01, 55.89. HRMS-ESI (m/z): [M + H]+ calcd. for C9H11O2: 151.07536; found, 151.07515.

4.2.1.4. 2,6-Dimethoxy-4-vinylphenol 2d
Yellow oil, yield 94%. IR (KBr plate): νmax 3144, 2938, 2844, 1605, 1462, 1213, 1115, 837. 1H NMR (600 MHz, CDCl3) δ 6.65 (s, 2H), 6.61 (dd, J = 17.5, 10.9 Hz, 1H), 5.60 (d, J = 17.5 Hz, 1H), 5.56 (s, 1H), 5.15 (d, J = 10.8 Hz, 1H), 3.90 (s, 6H). 13C NMR (151 MHz, CDCl3) δ 147.06, 136.83, 134.76, 129.18, 111.87, 102.9, 56.26. HRMS-ESI (m/z): [M + H]+ calcd. for C10H13O3: 181.08592; found, 181.08562.

4.2.1.5. 2-Ethoxy-4-vinylphenol 2e
White solid, yield 90%, mp 125–127°C. IR (KBr plate): νmax 3436, 2979, 2850, 1606, 1513, 1237, 1122, 823. 1H NMR (600 MHz, CD3OD) δ 6.99 (d, J = 1.7 Hz, 1H), 6.85 (dd, J = 8.1, 1.7 Hz, 1H), 6.74 (d, J = 8.1 Hz, 1H), 6.61 (dd, J = 17.6, 10.9 Hz, 1H), 5.56 (d, J = 17.6 Hz, 1H), 5.04 (d, J = 10.9 Hz, 1H), 4.10 (q, J = 7.0 Hz, 2H), 1.42 (t, J = 7.0 Hz, 3H). 13C NMR (151 MHz, CD3OD) δ 146.77, 146.59, 136.73, 129.95, 119.41, 114.84, 110.25, 109.67, 64.19, 13.76. HRMS-ESI (m/z): [M + H]+ calcd. for C10H13O2: 165.09101; found, 165.09073.

4.2.1.6. 2-Methyl-4-vinylphenol 2f
Yellow oil, yield 93%. IR (KBr plate): νmax 3375, 2922, 2850, 1599, 1461, 1267, 822. 1H NMR (600 MHz, DMF-d7) δ 7.24 (d, J = 1.5 Hz, 1H), 7.14 (dd, J = 8.2, 2.1 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 6.63 (dd, J = 17.6, 10.9 Hz, 1H), 5.60 (d, J = 17.6 Hz, 1H), 5.01 (dd, J = 10.9, 1.0 Hz, 1H), 2.18 (s, 3H). 13C NMR (151 MHz, DMF-d7) δ 158.04, 141.10, 133.70, 130.49, 129.88, 121.53, 116.99, 34.39. HRMS-ESI (m/z): [M-H]− calcd. for C9H9O: 133.06479; found, 133.06454.

4.2.1.7. 2,6-Dimethyl-4-vinylphenol 2g
Yellow oil, yield 96%. IR (KBr plate): νmax 3436, 2924, 2853, 1600, 1513, 1237, 1122, 823. 1H NMR (600 MHz, CDCl3) δ 7.05 (s, 2H), 6.59 (dd, J = 17.6, 10.9 Hz, 1H), 5.58 (d, J = 17.6 Hz, 1H), 5.08 (d, J = 10.9 Hz, 1H), 4.65 (s, 1H), 2.25 (s, 6H). 13C NMR (151 MHz, CDCl3) δ 152.09, 136.46, 129.90, 126.59, 122.97, 111.16, 15.91. HRMS-ESI (m/z): [M + H]+ calcd. for C10H13O: 149.09609; found, 149.09592.

4.2.1.8. (E)-1-(4-hydroxyphenyl)propene 2p
Colourless oil, yield 68%. IR (KBr plate): νmax 3388, 2964, 2927, 1615, 1558, 1507, 1457, 1239, 853.03, 688. 1H NMR (600 MHz, CDCl3) δ 7.24 (d, J = 15.7 Hz, 1H), 7.14 (dd, J = 8.2, 2.1 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 6.63 (dd, J = 17.6, 10.9 Hz, 1H), 5.58 (d, J = 17.6 Hz, 1H), 5.08 (d, J = 10.9 Hz, 1H), 4.65 (s, 1H), 2.25 (s, 6H). 13C NMR (151 MHz, CDCl3) δ 154.77, 130.75, 130.32, 127.04, 123.36, 115.39, 18.39. HRMS-ESI (m/z): [M+H]+ calcd. for C10H13O: 149.09609; found, 149.09592.

4.2.2. Procedure for 4-vinylphenols bearing electron-withdrawing groups (2h–2l and 2q)
To a stirred solution of DMF (1 ml) was added 4-hydroxycinnamic acids (1h–1l and 1q) (0.2 mmol) in 5 ml pressure-resistant reaction bottle. The reaction mixture was stirred at 140–200°C until the completion of the starting materials as monitored by TLC (30 min). The reaction mixture was quenched with water and extracted with dichloromethane. The dichloromethane layer was washed with pure water 2–3 times. The combined extract was dried over Na2SO4. The filtrate was evaporated under reduced pressure to yield the pure product (2h–2l and 2q), which was dissolved immediately in methanol for storage.
4.2.2.1. 2-Nitro-4-vinylphenol 2h
Yellow oil, yield 86%. IR (KBr plate): ν_max 3418, 2925, 2853, 1536, 1322, 1260, 802. 1H NMR (600 MHz, CDCl_3) δ 10.57 (s, 1H), 8.09 (d, J = 2.0 Hz, 1H), 7.67 (dd, J = 8.7, 2.1 Hz, 1H), 7.13 (d, J = 8.7 Hz, 1H), 6.65 (dd, J = 17.6, 10.9 Hz, 1H), 5.73 (d, J = 17.5 Hz, 1H), 5.32 (d, J = 10.9 Hz, 1H). 13C NMR (151 MHz, CDCl_3) δ 154.59, 134.85, 134.11, 130.53, 122.42, 120.16, 114.96. HRMS-ESI (m/z): [M + H]^+ calcd. for C_8H_8O_3N: 166.04987; found, 166.04968.

4.2.2.2. 2-Fluoro-4-vinylphenol 2i
Colourless oil, yield 87%. IR (KBr plate): ν_max 3436, 2924, 2852, 1612, 1094. 1H NMR (600 MHz, CDCl_3) δ 7.15 (dd, J = 11.8, 2.0 Hz, 1H), 7.06 (d, J = 8.3 Hz, 1H), 6.96–6.93 (m, 1H), 6.59 (dd, J = 17.5, 10.9 Hz, 1H), 5.61–5.58 (m, 1H), 5.56 (s, 1H), 5.17 (d, J = 10.8 Hz, 1H). 13C NMR (151 MHz, CDCl_3) δ 151.15(237.72), 143.30(14.33), 135.46(2.19), 131.14(6.21), 123.03(2.74), 117.18, 112.80(18.79). HRMS-ESI (m/z): [M-H]^- calcd. for C_8H_6OF: 137.03972; found, 137.03989.

4.2.2.3. 2-Chloro-4-vinylphenol 2j
Yellow oil, yield 86%. IR (KBr plate): ν_max 3498, 2923, 2850, 1619, 1261, 1099, 804. 1H NMR (600 MHz, CDCl_3) δ 7.38 (d, J = 2.0 Hz, 1H), 7.23 (dd, J = 8.4, 2.0 Hz, 1H), 6.98–6.96 (m, 1H), 6.59 (dd, J = 17.5, 10.9 Hz, 1H), 5.61 (d, J = 17.5 Hz, 1H), 5.58 (s, 1H), 5.18 (d, J = 10.9 Hz, 1H). 13C NMR (151 MHz, CDCl_3) δ 150.92, 135.10, 131.60, 126.61, 126.36, 120.08, 116.21, 113.03. HRMS-ESI (m/z): [M-H]^- calcd. for C_8H_6OCl: 153.01017; found, 153.01038.

4.2.2.4. 2-Bromo-4-vinylphenol 2k
Colourless oil, yield 89%. IR (KBr plate): ν_max 3425, 2919, 2850, 1602, 1126, 1041, 963, 903, 854, 824, 691. 1H NMR (600 MHz, CDCl_3) δ 7.52 (s, 1H), 7.28 (s, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.58 (dd, J = 17.5, 10.9 Hz, 1H), 5.61 (d, J = 17.5 Hz, 1H), 5.53 (s, 1H), 5.17 (d, J = 10.9 Hz, 1H). 13C NMR (151 MHz, CDCl_3) δ 151.85, 134.94, 132.01, 129.65, 127.08, 116.03, 113.06, 110.44. HRMS-ESI (m/z): [M + H]^+ calcd. for C_8H_8OBr: 198.97530; found, 198.97460.

4.2.2.5. 3-Bromo-4-vinylphenol 2l
Colourless oil, yield 87%. IR (KBr plate): ν_max 3405, 2925, 2850, 1619, 1261, 1099, 804. 1H NMR (600 MHz, CDCl_3) δ 7.44 (d, J = 8.5 Hz, 1H), 7.06 (d, J = 2.5 Hz, 1H), 6.97–6.93 (m, 1H), 6.59 (dd, J = 17.5, 10.9 Hz, 1H), 5.61 (d, J = 17.5 Hz, 1H), 5.58 (s, 1H), 5.18 (d, J = 10.9 Hz, 1H). 13C NMR (151 MHz, CDCl_3) δ 155.74, 135.03, 130.23, 127.48, 123.87, 119.45, 115.08, 114.62. HRMS-ESI (m/z): [M + H]^+ calcd. for C_8H_8OBr: 198.97530; found, 198.97508.

4.2.2.6. (E)-1-(2-chloro-4-hydroxyphenyl)propene 2q
Colourless oil, yield 63%. IR (KBr plate): ν_max 3390, 2962, 2931, 2848, 1615, 1493, 1435, 1252, 1222, 1041, 963, 903, 854, 824, 691. 1H NMR (600 MHz, CDCl_3) δ 7.38 (d, J = 8.5 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 6.59 (dd, J = 17.5, 10.9 Hz, 1H), 6.58 (dd, J = 17.5, 10.9 Hz, 1H), 6.53 (s, 1H), 5.24 (d, J = 10.9 Hz, 1H). 13C NMR (151 MHz, CDCl_3) δ 154.89, 132.80, 128.83, 127.44, 126.66, 126.60, 114.48. HRMS-ESI (m/z): [M + H]^+ calcd. for C_9H_8OCl: 168.02541.

4.3. General procedure for the synthesis of 4-vinylphenol dimers (2aa/2ff/2ll)
To a stirred solution of DMF (1 ml) were added 4-hydroxycinnamic acids 1a/1f/1l (0.2 mmol) in 5 ml pressure-resistant reaction bottle. The reaction mixture was stirred at 170–220°C until the completion of the starting materials as monitored by TLC (2 h). The reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution, dried over Na_2SO_4 and evaporated under reduced pressure. The resulting crude compound was purified by silica gel column chromatography and dried by vacuum freeze-drying, affording the pure dimer (2aa/2ff/2ll). The pure product was dissolved immediately in methanol for storage.

4.3.1. Dimer 2aa
Light yellow oil, yield 48%. IR (KBr plate): ν_max 3328, 3021, 2962, 1610, 15121233,1171, 834. 1H NMR (600 MHz, CDCl_3) δ 7.23 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 8.5 Hz, 2H), 6.81–6.74 (m, 4H), 6.31 (d, J =
15.9 Hz, 1H), 6.20 (dd, J = 15.9, 6.8 Hz, 1H), 4.82 (s, 1H), 4.74 (s, 1H), 3.55 (p, J = 6.7 Hz, 1H), 1.41 (d, J = 7.0 Hz, 3H). $^{13}$C NMR (151 MHz, CDCl$_3$) δ 154.69, 153.82, 138.13, 133.54, 130.63, 128.42, 127.56, 127.43, 115.37, 115.23, 41.64, 21.40. HRMS-ESI (m/z): [M + H]$^+$ calcd. for C$_{16}$H$_{17}$O$_2$: 241.1223; found, 241.12279.

4.3.2. Dimer 2ff

Light yellow oil, yield 50%. IR (KBr plate): $\nu_{\text{max}}$ 3416, 2960, 2921, 1611, 15 021 263,1114, 814. $^1$H NMR (600 MHz, CD$_3$OD) δ 7.09 (s, 1H), 7.01 (dd, J = 8.2, 2.1 Hz, 1H), 6.97 (s, 1H), 6.90 (dd, J = 8.2, 2.1 Hz, 1H), 6.69 (dd, J = 15.1, 8.2 Hz, 2H), 6.25 (d, J = 15.9 Hz, 1H), 6.16 (dd, J = 15.8, 6.8 Hz, 1H), 4.62 (s, 2H), 3.46 (p, J = 7.2 Hz, 1H), 2.19 (s, 3H), 2.18 (s, 3H), 1.39 (d, J = 7.0 Hz, 3H). $^{13}$C NMR (151 MHz, CD$_3$OD) δ 142.81, 141.78, 127.48, 123.49, 120.83, 120.65, 119.76, 119.27, 116.87, 116.30, 116.17, 116.06, 107.50, 107.46, 43.85, 25.47, 20.29, 20.21. HRMS-ESI (m/z): [M + H]$^+$ calcd. for C$_{16}$H$_{17}$O$_2$: 267.13796; found, 267.13870.

4.3.3. Dimer 2fl

Light yellow oil, yield 67%. IR (KBr plate): $\nu_{\text{max}}$ 3405, 2965, 2923, 1603, 1485, 1228, 1209, 875. $^1$H NMR (600 MHz, CD$_3$OD) δ 7.40 (d, J = 8.6 Hz, 1H), 7.16 (d, J = 8.5 Hz, 1H), 7.04 (d, J = 2.5 Hz, 1H), 7.00 (d, J = 2.5 Hz, 1H), 6.80 (dd, J = 8.5, 2.5 Hz, 1H), 6.75 (dd, J = 8.6, 2.4 Hz, 1H), 6.69–6.64 (m, 1H), 6.17 (dd, J = 15.8, 6.3 Hz, 1H), 4.62 (s, 2H), 4.10–4.00 (m, 2H), 1.41 (d, J = 7.0 Hz, 3H). $^{13}$C NMR (151 MHz, CD$_3$OD) δ 157.24, 156.27, 134.86, 134.08, 128.48, 128.34, 127.15, 127.09, 123.58, 123.02, 118.98, 118.68, 114.85, 114.80, 40.22, 19.49. HRMS-ESI (m/z): [M + H]$^+$ calcd. for C$_{16}$H$_{13}$Br$_2$O$_2$: 394.92768; found, 394.92844.

Data accessibility. The datasets supporting this article have been uploaded as part of the electronic supplementary material [36].

Authors’ contributions. Q.Y.: investigation, methodology; Y.L.: investigation, methodology; H.L.: methodology; E.W.: data curation; M.P.: data curation, formal analysis; T.D.: data curation; X.P.: data curation; Z.L.: writing—original draft; Y.Y.: writing—review and editing; X.Y.: funding acquisition, project administration, writing—original draft, writing—review and editing; E.W.: data curation. All authors gave final approval for publication and agreed to be held accountable for the work performed therein.

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