

On the Synthesis and Stereochemistry of Certain Lignin-Related α -Aryloxycinnamic Acids and Enol Ethers

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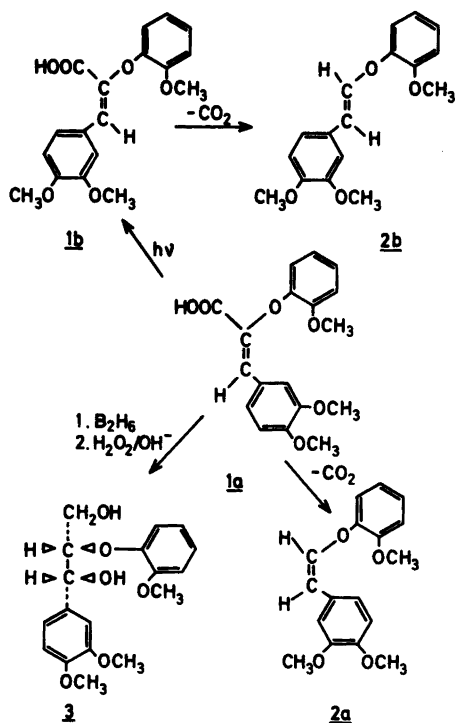
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The preparation of lignin model compound **3** from α -(2-methoxyphenoxy)-3,4-dimethoxycinnamic acid by treatment with diborane/alkaline hydrogen peroxide has been described previously.¹⁻³ Since **3** has the *erythro* configuration and hydration of double bonds *via* borane treatment is known to be a *syn* addition, it was concluded that the starting material had the *trans* configuration [(*Z*)-configuration]; *i.e.* the structure of the starting material is represented by formula **1a**. The stereochemical assignment of **3** is based on studies of the stability of borate complexes⁴ and ¹H NMR examinations.⁵

We have now performed a series of experiments which confirms the (*Z*) configuration of **1a**. From ¹³C NMR spectral studies,³ J_{CH} for the coupling between the carboxyl carbon and the vinyl proton was determined to be 3.4 Hz, while $^3J_{CH}$ for the corresponding coupling in **1b** was 9.2 Hz. ¹³C NMR data are in accordance with the (*Z*) configuration of **1a** and the (*E*) configuration of **1b**.⁶ Copper-catalyzed decarboxylation of **1a** gave **2a** (¹H NMR), while **1b** underwent this reaction with formation of **2b** (¹H NMR). Since copper-catalyzed decarboxylations of α -substituted cinnamic acids have been found to proceed with retention of configuration,⁷ the decarboxylation experiments provide additional evidence for the stereochemical assignments of **1a** and **1b**.

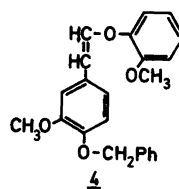
The studies with **1a** described above demonstrate conclusively that this compound has the (*Z*) configuration. It follows that the product formed on borane/alkaline hydrogen peroxide treatment (*syn* addition) must be the *erythro* isomer **3**. Thus our studies on **1a** provide additional evidence for the stereochemical assignment of **3**.

Acid-catalyzed hydrolysis of **3** has recently been studied by Hoo and Sarkanen.⁸ They found that depending on the reaction conditions varying amounts of enol ethers **2a** and **2b** are formed.



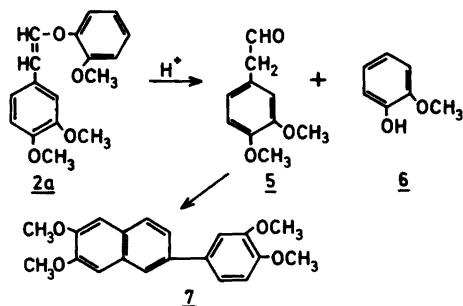
These two isomeric enol ethers were not, however, obtained pure on a preparative scale. The decarboxylation experiments described above offered a possibility of preparing **2a** and **2b**. The (*Z*) isomer (**2a**) was obtained crystalline (m.p. 76 °C). The (*E*) isomer of the enol ether (**2b**) from decarboxylation of **1b** was contaminated with about 10 % of the (*Z*) form. This could be explained by a partial conversion of **1b** into **1a** during the decarboxylation treatment. It was, however, possible to obtain the (*E*) isomer in an essentially pure state by column chromatography of the product.

The applicability of decarboxylation of α -aryloxy substituted cinnamic acids as a synthetic route to styryl aryl ethers was further illustrated by the preparation of the (*Z*) isomer of enol ether **4** (m.p. 89 °C) from α -(2-methoxyphenoxy)-4-benzyloxy-3-methoxycinnamic acid.³ Compound



4, presumably contaminated with the (*E*) isomer, has previously been described in connection with studies of the alkaline degradation of lignin model compounds.⁹

Hoo and Sarkanen⁸ noted that the enol ethers **2a** and **2b** were unexpectedly stable to acid hydrolysis (related enol ethers with a three-carbon side chain were found to be instantaneously hydrolyzed by such treatment). We have confirmed this observation in studies of the acid degradation of **2a**. Thus, detectable amounts of the starting material (together with traces of the (*E*) isomer) were present in the reaction mixture even after 2 h reflux with 0.2 M hydrochloric acid in dioxane–water (9:1). The predominant hydrolysis products were guaiacol



(**6**) and homoveratraldehyde (**5**). In addition, 6,7-dimethoxy-2-(3,4-dimethoxyphenyl)naphthalene (**7**) was found in the reaction mixture. Obviously the latter compound is produced from initially formed homoveratraldehyde in an acid-catalyzed autocondensation reaction; acid-catalyzed conversion of homoveratraldehyde into **7** has been reported previously.¹⁰

Interestingly, Reznikov and co-workers¹¹ have reported spectral evidence for the formation of the same reaction product (presumably **7**) in acidolysis experiments with homoveratraldehyde as well as 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1-ethanol.

Experimental. *NMR spectra* were recorded with a Bruker WH 270 instrument. Chloroform-*d* was used as solvent, unless otherwise specified. $^3J_{CH}$ values were determined in runs with a sweep width of 2000 Hz (number of scans, 6000). *UV spectra* were recorded with a Cary 210 instrument.

Thin layer chromatography (TLC) was performed on silica gel with toluene-dioxane-acetic acid (180:25:4) (R_F values: **1b**, 0.20; **1a**, 0.33), dichloromethane–hexane (1:1) (R_F values: **2b**, 0.40; **2a**, 0.50), ethyl acetate–hexane (1:1) (R_F values: **7**, 0.48; **5**, 0.50; **2a** and **2b**, 0.63; **6**, 0.67)

as eluents. Spots were made visible by spraying with formalin – H_2SO_4 (1:9) and subsequent heating (140 °C).

(*Z*)- α -(2-Methoxyphenoxy)-3,4-dimethoxycinnamic acid (**1a**) was prepared according to previously^{1–3} described procedures. ^{13}C NMR spectrum (67.9 MHz, $DMSO-d_6$): δ 55.3 (OCH₃), 55.7 (OCH₃), 56.0 (OCH₃), 112–115 (aromatic and vinyl C), 164.2 (CO, $^3J_{CH}=3.4$ Hz). 1H NMR spectrum (270 MHz): δ 3.73 (3H, s; OCH₃), 3.87 (3 H, s; OCH₃), 3.94 (3H, s; OCH₃), 7.45 (1 H, s; vinyl proton ?), 6.7–7.5 (7H, m; aromatic protons). The UV spectrum (solvent, 0.1 M HCl in 95 % ethanol) exhibited a maximum at 320 nm ($\epsilon=19\ 700$).

(*E*)- α -(2-Methoxyphenoxy)-3,4-dimethoxycinnamic acid (**1b**) was prepared by photochemical isomerization of **1a**. A solution of **1a** (480 mg) in ethanol (200 ml) was irradiated for 3 h in a Rayonet Photochemical reactor (RPR 100) fitted with 3500 Å lamps. The residue obtained on evaporation of the ethanol was triturated with boiling ether (25 ml). Crystals (140 mg) precipitated from the ether solution on standing at room temperature. Recrystallization from ethanol gave 84 mg of **1b** of m.p. 184–185 °C. ^{13}C NMR spectrum (67.9 MHz, $DMSO-d_6$): δ 55.8 (OCH₃), 56.1 (OCH₃), 111–150 (aromatic and vinyl C), 164.4 (CO, $^3J_{CH}=9.2$ Hz). 1H NMR spectrum (270 MHz): δ 3.86 (3H, s; OCH₃), 3.88 (3H, s; OCH₃), 3.90 (3H, s; OCH₃), 6.58 (1H, s; vinyl proton ?), 6.5–7.40 (7 H, m; aromatic protons). The UV spectrum (solvent, 0.1 M HCl in 95 % ethanol) exhibited a maximum at 315 nm ($\epsilon=10\ 700$).

(*Z*)-1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)ethene (**2a**). Acid **1a** (780 mg) was dissolved in quinoline (4 ml) and copper chromite¹² (50 mg) was added to the solution. The mixture was heated for 30 min at 215–220 °C. After addition of 2 M hydrochloric acid (35 ml), the reaction mixture was extracted with ether (2×50 ml). The ether extract was subjected to a series of washings (2 M hydrochloric acid, $NaHCO_3$ solution, water) and dried over Na_2SO_4 . Removal of the solvent by film evaporation gave a brown oily residue (0.50 g). Purification by column chromatography [60 g SiO_2 ; eluent, dichloromethane–ethyl acetate (4:1)] gave a product which crystallized spontaneously. Recrystallization from ethanol gave white needles of m.p. 76 °C (0.32 g, yield 47 %). 1H NMR spectrum (270 MHz): δ 3.87 (3H, s; OCH₃), 3.88 (3H, s; OCH₃), 3.90 (3H, s; OCH₃), 5.55 (1H, d, $J=6.8$ Hz; vinyl proton), 6.53 (1H, d, $J=6.8$ Hz; vinyl proton), 6.8–7.6 (7H, m; aromatic protons). Exact mass measurements of the molecular ion gave *m/e* 286.1185. Calc. for $C_{17}H_{18}O_4$: *m/e* 286.120500.

The UV spectrum (ethanol) exhibited a maximum at 267 nm ($\epsilon=24\ 100$).

(E)-1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)ethene (2b). Acid 1b (150 mg) was added to refluxing quinoline (2 ml) and 150 mg copper chromite.¹² Work-up (cf. the preparation of 2a) gave a crude product weighing 130 mg. Column chromatography [50 g SiO₂; eluent, dichloromethane-hexane (1:1)] gave fractions consisting of 2a and 2b (20 mg), 2b and traces of 2a (46 mg), and 2b (12 mg). ¹H NMR spectrum (270 MHz): δ 3.86 (3H, s; OCH₃), 3.87 (3H, s; OCH₃), 3.89 (3H, s; OCH₃), 6.26 (1H, d, $J=12.4$ Hz; vinyl proton), 7.01 (1H, d, $J=12.4$ Hz; vinyl proton), 6.7-7.2 (7 H, m; aromatic protons). The UV spectrum (ethanol) exhibited a maximum at 269 nm ($\epsilon=22\ 000$).

(Z)-1-(4-Benzyloxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)ethene (4) was prepared from α -(2-methoxyphenoxy)-4-benzyloxy-3-methoxycinnamic acid³ in analogy with the preparation of 2a. M.p. 89 °C (from ethanol). ¹H NMR spectrum: δ 3.87 (3H, s; OCH₃), 3.91 (3H, s; OCH₃), 5.15 (2H, s; CH₂), 5.53 (1H, d, $J=6.8$ Hz; vinyl proton), 6.52 (1H, d, $J=6.8$ Hz; vinyl proton), 6.8-7.6 (12 H, m; aromatic protons).

Acidolysis of enol ether 2a. Enol ether 2a (94 mg) was refluxed with 10 ml 0.2 M hydrochloric acid in dioxane-water (9:1) for 2 h. 0.4 M NaHCO₃ solution was added (4.5 ml) and the mixture extracted with 2×20 ml of chloroform. The extract was dried over Na₂SO₄ and solvents removed by film evaporation. The residue was dissolved in 10 ml of ether and the solution extracted with 2×5 ml 15 % NaHSO₃ solution.

Acidification of the extract and storage under reduced pressure to remove liberated SO₂ resulted in a slow¹³ liberation of homoveratraldehyde (5). After several days 16 mg of essentially pure (¹H NMR) homoveratraldehyde could be isolated by extraction with dichloromethane. ¹H NMR spectrum (270 MHz): δ 3.61 (2H, d, $J=2.3$ Hz; CH₂), 3.87 (3H, s; OCH₃), 6.7-6.9 (4H, m; aromatic protons), 9.73 (1H, t, $J=2.4$ Hz; CHO). The IR spectrum showed a strong band at 1720 cm⁻¹ (C=O).

Evaporation of the ether gave a residue weighing 80 mg. Preparation TLC [SiO₂; eluent, hexane-ethyl acetate (3:1)] gave fractions of guaiacol (28 mg), and starting material containing traces of guaiacol and 2b (6 mg), and a crystalline compound (5 mg). The crystals melted at 179-180 °C. The product was identified as 6,7-dimethoxy-2-(3,4-dimethoxyphenyl) naphthalene (7) (a compound which is known to form on acid treatment of homoveratraldehyde¹⁰) on the basis of its m.p. (lit.¹⁰ 179-180 °C) and its ¹H NMR properties. ¹H NMR spectrum: δ 3.94 (3H,

s; OCH₃), 3.98 (3H, s; OCH₃), 4.01 (3H, s; OCH₃), 4.02 (3H, s; OCH₃), 6.9-7.9 (8H, m; aromatic protons).

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