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Short Communications

A New Synthetic Route to Lignin Model Compounds of the 1,2-Diaryl-1,3-propanediol Type

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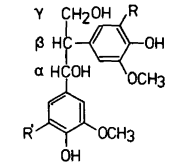
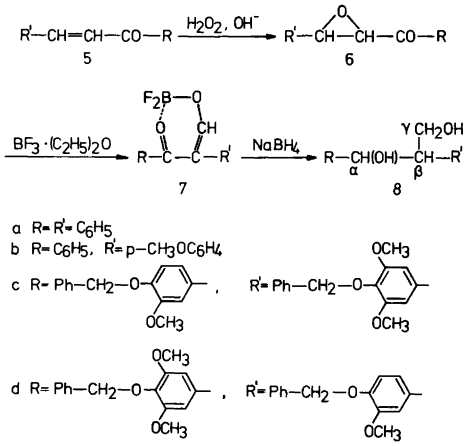
A previous paper[1] described the synthesis of compound *1* and exemplified its use as a model compound for lignin structures of the 1,2-diaryl-1,3-propanediol type. Compound *1* and the related 1,2-diaryl-1,3-propanediols *2* and *4* are formed on "mild hydrolysis" of beech wood.[2] The synthesis of compound *1* described in Ref. 1 involved a



1 R=R'=H
2 R=OCH3, R'=H
3 R=H, R'=OCH3
4 R=R'=OCH3

benzoin condensation. For the preparation of compound *2* by the same method, a benzoin with two differently substituted aryl groups is needed. This is a drawback, since special measures have to be made to obtain asymmetric benzoins. Recently, Nakatsubo and Higuchi[3] reported a synthetic method for the preparation of 1,2-diaryl-1,3-propanediols which does not suffer from this disadvantage. The key step in their synthesis was a reaction of the Claisen type. They prepared both *erythro* and *threo* forms of the previously unknown compound *3*.

This paper describes a new synthetic route to lignin model compounds of the 1,2-diaryl-1,3-propanediol type which is free from limitations as far as dissimilar aryl groups are concerned. This new synthetic route is shown in Scheme 1. Chalcones



Scheme 1.

(*5*) are used as starting materials. Such compounds are easily obtained by base-catalyzed condensation of aromatic aldehydes with acetophenones. The chalcones are converted into chalcone oxides (*6*) by oxidation with alkaline hydrogen peroxide. On treatment with boron trifluoride etherate the chalcone oxides undergo rearrangements resulting in boron fluoride complexes of type *7*. Finally, reduction of these complexes with sodium borohydride gives 1,2-diaryl-1,3-propanediols (*8*).

The preparation of boron fluoride complexes *7a* and *7b* according to the reaction route shown in Scheme 1 has been described previously.[4] Reduction of complex *7a* with sodium borohydride gave compound *8a*. The purified product was identified as the *erythro* form[5] of *8a*. Examination of the acetate of the crude reaction mixture by ^{1}H NMR (solvent, CCl_4) (*cf.* Ref. 5) did not reveal the presence of the *threo* form of diarylpropanediol *8a*. This result suggests that the borohydride reduction of complex *7a* is highly stereoselective. Reduction of complex *7b* gave the *erythro* form of diarylpropanediol *8b*. The configuration was derived from ^{1}H NMR spectral comparisons with the *erythro* form of *8a* and the *erythro* and *threo* forms of compound *3*.[3] Subjecting chalcone *5c* to the reaction sequence in in Scheme 1, followed by catalytic hydrogenation (to remove benzyl groups), gave compound *2*.

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(In a separate experiment the intermediate *8c* was isolated.) Compound *2* has not been synthesized previously. ^{1}H NMR spectral comparisons (see above) suggested that the synthetic product, as well as the lignin hydrolysis product,[2] have the *erythro* configuration. Diarylpropanediol *3* was prepared from chalcone *5d* in a synthesis analogius to the preparation of compound *2* from chalcone *5c*. This synthesis also yielded the *erythro* form exclusively. The ^{1}H NMR spectrum of acetylated product was identical with the spectrum reported[3] for the acetate of the *erythro* form of compound *3*.

Experimental. ^{1}*H NMR spectra* were recorded on a Varian A-60 instrument or a Bruker WH 270 instrument, using chloroform-*d* as solvent, unless otherwise specified.

Standard procedure for $NaBH_4$ reductions of boron fluoride complexes (7). The sample (*x* g) was dissolved in *x*(20–50) ml dioxane and the same volume of $NaBH_4$ reagent (4.0 g $NaBH_4$ in 200 ml 0.25 M NaOH) was added to the solution. The mixture was set aside overnight and was then acidified with dilute hydrochloric acid and extracted with chloroform. The extract was dried over Na_2SO_4 and solvents removed by film evaporation.

*Benzylation of phenols using ion pair technique (*cf. *Ref. 6). Example, preparation of the benzyl ether of 1-(4-hydroxy-3,5-dimethoxyphenyl)-ethanone.* Tetrabutylammonium hydrogen sulfate (8.5 g) was dissolved in 25 ml 2 M NaOH and 1-(4-hydroxy-3,5-dimethoxyphenyl)ethanone (4.9 g) was added to the solution. The mixture was extracted with 2 × 30 ml of chloroform. After addition of benzyl chloride (3.8 g), the extract was refluxed for 30 min, whereupon most of the chloroform was distilled off. A solution of the residue in ether (100 ml) was washed with 2 × 100 ml H_2O, dried over Na_2SO_4, and the solvents removed by film evaporation. Crystallization of the residue from ethanol gave 5.5 g product (m.p. 60–61 °C). ^{1}H NMR spectrum: δ 2.57 (3H, s; CH_3CO), 3.89 (6 H, s; CH_3O), 5.11 (2 H, s; CH_2), ≈7.3 (7 H, m; aromatic protons). The benzyl ethers of 4-hydroxy-3,5-dimethoxybenzaldehyde, 1-(4-hydroxy-3-methoxyphenyl)ethanone and vanillin were prepared analogously.

*3-(4-Benzyloxy-3,5-dimethoxyphenyl)-1-(4-benzyloxy-3-methoxyphenyl)-2-propene-1-one (*5c*).* A solution of 10 g KOH in 10 ml H_2O was added dropwise to a stirred solution of the benzyl ethers of 4-hydroxy-3,5-dimethoxybenzaldehyde (1.36 g) and 1-(4-hydroxy-3-methoxyphenyl)ethanone (1.28 g) in 40 ml ethanol. After 2 h the yellow precipitate formed was filtered off and washed with ethanol and water. Recrystallization from ethanol gave 1.85 g crystals of m.p. 114–116 °C. ^{1}H NMR spectrum: δ 3.89 (6 H, s; CH_3O), 3.99 (3 H, s; CH_3O), 5.08 (2 H, s; CH_2), 5.25 (2 H, s; CH_2), 6.8–7.9 (17 H, m; aromatic and vinyl protons).

*1-(4-Benzyloxy-3,5-dimethoxyphenyl)-3-(4-benzyloxy-3-methoxyphenyl)-2-propene-1-one (*5d*)* was prepared from the benzyl ethers of vanillin and 1-(4-hydroxy-3,5-dimethoxyphenyl)ethanone, using the procedure described for the preparation of chalcone *5c*, m.p. 74–76 °C (from ethanol). ^{1}H NMR spectrum: δ 3.83 (6 H, s; CH_3O), 3.88 (3 H, s; CH_3O), 5.03 (2 H, s; CH_2), 5.12 (2 H, s; CH_2), 6.6–7.9 (17 H, m; aromatic and vinyl protons).

*3-(4-Benzyloxy-3,5-dimethoxyphenyl)-1-(4-benzyloxy-3-methoxyphenyl)-2,3-epoxy-1-propanone (*6c*).* Chalcone *5c* (0.51 g) was dissolved in 7 ml DMSO. 2M NaOH (0.25 ml) and 30 % H_2O_2 (0.6 ml) were added to the solution and the mixture was stirred for 2 h. The reaction mixture was added dropwise with stirring to 180 ml 2 % acetic acid. The precipitate formed was filtered off and washed carefully with water. Recrystallization from acetone gave 0.39 g crystals melting at 136–137 °C. ^{1}H NMR spectrum: δ 3.83 (6 H, s; CH_3O), 3.93 (3 H, s; CH_3O), 4.01 (1 H, d, J = 1.8 Hz; –CH<), 4.19 (1 H, d, J = 1.8 Hz; –CH<), 5.03 (2 H, s; CH_2), 5.22 (2 H, s; CH_2), 6.5–7.8 (15 H, m; aromatic protons).

*1,2-Diphenyl-1,3-propanediol (*8a*).* Boron fluoride complex *7a*[4] (1.1 g) was reduced with sodium borohydride according to the standard procedure. The crude product (0.8 g) melted at 104–107 °C. Purifications by column chromatography [SiO_2; eluent, ethyl acetate–dichloromethane (1:1)] and recrystallization from benzene raised the m.p. to 106–107 °C. Acetylation gave a product of m.p. 83–84 °C. ^{1}H NMR spectrum of acetylated *8a*: δ 1.91 (3 H, s; CH_3), 1.93 (3 H, s; CH_3), 3.43 (1 H, q (approximately), J = 7 Hz; H_β), 4.12 (1 H, dd, J = 6.6 and 11 Hz; H_γ), 4.29 (1 H, dd, J = 6.6 and 11 Hz; H_γ), 6.14 (1 H, d, J = 7.5 Hz; H_α), ≈7.3 (10 H, m, aromatic protons). The *erythro* (m.p. 104 °C; acetate, m.p. 83–84 °C) and *threo* (m.p. 110 °C; acetate, m.p. 69 °C) forms of compound *8a* have been described.[5] On the basis of melting points and ^{1}H NMR data (solvent, CCl_4) (*cf.* Ref. 5) our product could be identified as the *erythro* form of compound *8a*.

*2-(4-Methoxyphenyl)-1-phenyl-1,3-propanediol (*8b*).* Boron fluoride complex *7b*[4] (1.0 g) was reduced by $NaBH_4$ according to the standard procedure. Crystallization from ethanol gave 0.40 g product, m.p. 129–130 °C. ^{1}H NMR spectrum of acetylated *8b*: δ 1.94 (6 H, s; CH_3C), 3.37 (1 H, q (approximately), J = 7 Hz; H_β), 3.79 (3 H, s; CH_3O), 4.09 (1 H, dd, J = 6.7 and 11 Hz; H_γ), 4.29 (1 H, dd, J = 6.7 and 11 Hz; H_γ), 6.09 (1 H, d, J = 7.3 Hz; H_α), 6.7–7.4 (9 H, m, aromatic protons).

2-(4-Hydroxy-3,5-dimethoxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)-1,3-propanediol (2). Chalcone oxide *6c* (1.05 g, ≈2 mmol) was dissolved in 120 ml ether and 8.6 g $BF_3 \cdot (C_2H_5)_2O$ was added to the solution. The reaction mixture was refluxed for 30 min, washed three times with 30 ml water, dried over Na_2SO_4, and the solvent removed by film evaporation. The residue was reduced with sodium borohydride according to the standard procedure. The reduced product was subjected to catalytic hydrogenation in dioxane (40 ml) with 0.2 g 10 % Pd/C as catalyst. After 2 h the hydrogen consumption ceased; the hydrogen uptake was 4 mmol. The catalyst was filtered off and the solvent removed by film evaporation. One half of the reaction product was crystallized from dioxane–ethyl acetate to yield 77 mg of crystals, m.p. 195–197 °C. The second half of the crude product was chromatographed on a silica gel column with ethyl acetate as eluent. A product (122 mg) of m.p. 193–196 °C was thus obtained. Recrystallizations from acetone and dioxane–ethyl acetate gave 99 mg crystals of m.p. 196–199 °C (lit.[2] 192–193 °C). Yield, 28 %. ^{1}H NMR spectrum of acetylated product: δ 1.97 (3 H, s; CH_3CO), 1.99 (3 H, s; CH_3CO), 2.27 (3 H, s; CH_3CO), 2.30 (3 H, s; CH_3CO), 3.37 (1 H, m; H_β), 3.70 (3 H, s; CH_3O), 3.74 (6 H, s; CH_3O), 4.20 (1 H, dd, J=6.8 and 11.1 Hz; H_γ), 4.39 (1 H, dd, J=7.0 and 11.1 Hz; H_γ), 6.10 (1 H, d, J=6.3 Hz; H_α), 6.3–7.0 (5 H, m; aromatic protons).

*2-(4-Benzyloxy-3,5-dimethoxyphenyl)-1-(4-benzyloxy-3-methoxyphenyl)-1,3-propanediol (*8c*).* Chalcone oxide *6c* (0.51 g) was treated with boron trifluoride etherate and reduced with $NaBH_4$ as described above. A fraction (0.25 g) containing diarylpropanediol *8c* was separated from the reaction mixture by column chromatography [60 g SiO_2; eluent, ethyl acetate–dichloromethane (1:1)]. Crystals (0.14 g, m.p. 90–92 °C) were obtained from ethyl acetate. ^{1}H NMR of acetylated product: δ 1.91 (3 H, s; CH_3CO), 1.93 (3 H, s; CH_3CO), 3.32 (1 H, m; H_β), 3.75 (6 H, s; CH_3O), 3.81 (3 H, s; CH_3O), 4.10 (1 H, dd, J=6.8 and 11.4 Hz; H_γ), 4.26 (1 H, dd, J=6.2 and 11.4 Hz; H_γ), 5.00 (2 H, s; CH_2), 5.13 (2 H, s; CH_2), 6.03 (1 H, d, J=7.4 Hz; H_α), 6.36 (2 H, s; ar, syringyl), ≈6.8 (3 H, m; ar, guaiacyl), ≈7.4 (10 H, m; ar, phenyl).

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