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Reactions of Lignin-related Cinnamaldehydes and Cinnamyl Alcohols with Borane and Sodium Tetrahydridoborate

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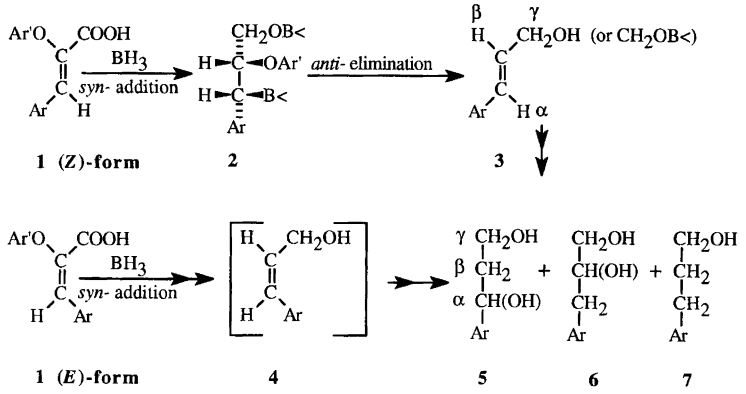
Hydroboration/oxidation of 3-(3,4-dimethoxyphenyl)-2-propen-1-ol [and also 3-(3,4-dimethoxyphenyl)propenal] gives a mixture of 1-(3,4-dimethoxyphenyl)-1,3-propanediol, 3-(3,4-dimethoxyphenyl)-1,2-propanediol and 3-(3,4-dimethoxyphenyl)-1-propanol; the same compounds are obtained as by-products when the lignin model 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol is synthesized by hydroboration/oxidation of α-(2-methoxyphenoxy)-3,4-dimethoxycinnamic acid. (*Z*)-3-(3,4-dimethoxyphenyl)-2-propen-1-ol and (*E*)-α-(2-methoxyphenoxy)-3,4-dimethoxycinnamic acid give comparatively large amounts of 3-(3,4-dimethoxyphenyl)-1,3-propanediol. The results support the view that the by-products are formed via 3-(3,4-dimethoxyphenyl)-2-propen-1-ol. Small amounts of the same by-products are obtained on tetrahydridoborate reduction of (*E*)-3-(3,4-dimethoxyphenyl)propenal [in addition to the main product, (*E*)-3-(3,4-dimethoxyphenyl)-2-propen-1-ol]. Analogous results were obtained with (*E*)-3-phenylpropenal. Models representative of lignin units of the cinnamaldehyde and cinnamyl alcohol types have been prepared and precise ^{1}H NMR spectral data (400 MHz, 300 K) for the compounds are reported.

Arylglycerol β-aryl ethers constitute the most important type of structural element in lignins. Previous papers[1–5] report a stereoselective synthetic route to lignin models representative of such a structural element that involves a treatment of an α-aryloxycinnamic acid with borane (or borane–dimethyl sulfide complex) and subsequent oxidation with alkaline hydrogen peroxide. In connection with the preparation of the diastereomers of a lignin model of the β-ether type, 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol, starting from acid **1**, the by-products **5–7** were detected in the final reaction mixtures obtained from both the *Z*-form and the *E*-form of the starting material (Refs. 1, 2, 5 and unpublished data). The formation of **5–7** from **1** is expected to proceed via intermediates of type **2** as shown in Scheme 1. The intermediates undergo elimination reactions leading to cinnamyl alcohols (**3** was detected in the reaction mixture from the *Z*-form of acid **1**[1]) and these compounds (**3** and **4**) are in turn converted into mixtures of **5–7** (Scheme 1, cf. Refs. 1, 2 and 5). Comparatively large amounts of **5**



Ar= 3,4-dimethoxyphenyl, Ar'= 2-methoxyphenoxy

Scheme 1.

were present in the reaction mixture from the *E*-form of acid **1**.[5] This could be due to differences in the reaction patterns of **3** and **4** (**4** is presumed to be an intermediate in the reaction of the *E*-form of acid **1**, Scheme 1). To elucidate this point **3** and **4** were subjected to hydroboration/oxidation. It appears from the proportions of **5–7**, in the reaction mixtures obtained from **3** (**5**, 26%; **6**, 61%; **7**, 13%) and **4** (**5**, 35%; **6**, 48%; **7**, 16%), that **5** is formed in comparatively high yield from **4** (the compounds in the reaction mixtures were analysed as acetate derivatives by ^{1}H NMR spectroscopy). The results from the experiments with **3** and **4** support the reaction routes suggested for the formation of the by-products **5–7** from **1** (Scheme 1) and provide a basis for improvements of the synthesis of lignin models of the arylglycerol β-aryl ether type starting from α-aryloxycinnamic acids.

The *E*-form of 3-(3,4-dimethoxyphenyl)-2-propen-1-ol (**3**) was prepared by reduction of **8** with sodium tetrahydridoborate. The *Z*-form (**4**) was obtained by photochemical conversion of **8** into (*Z*)-3-(3,4-dimethoxyphenyl)propenal (**9**) and subsequent reduction of this compound with sodium tetrahydridoborate (Scheme 2). Sodium tetrahydridoborate reduction of **8** gave **3** in high yield, but small amounts of compounds **5–7** were formed as by-products. Reduction in dioxane–water (1:1) [or dioxane–0.25 M NaOH (1:1)] gave about 0.5% yield of each one of these compounds. Somewhat larger amounts of the by-products were obtained when ethanol was used as the reaction medium (the amount of each one of the compounds corresponded to about 1% yield).

As judged from the hydroboration/oxidation experiments, an explanation for the formation of **5–7** on tetrahydridoborate reduction of **8** would be that hydroboration/autoxidation occurs to some extent. It is noteworthy in this context that trace amounts of **5–7** were also formed when **3** was treated with tetrahydridoborate in dioxane–water solution. The formation of saturated alcohols on tetrahydridoborate reduction of conjugated carbonyl compounds has been interpreted to be a result of 'conjugate reduction'.[6] We think the possibility that typical hydroboration reactions play a role in this context should be considered in some instances.

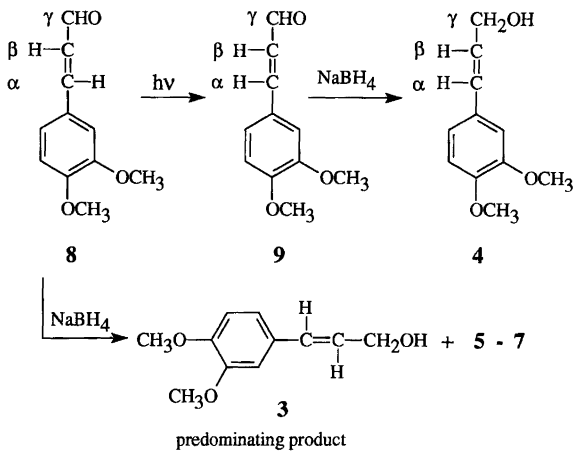
It has been reported that tetrahydridoborate reduction of 3-phenylpropenal (**10**) gives solely 3-phenyl-2-propen-1-ol (**14**).[6] We have studied the tetrahydridoborate reduction of (*E*)-3-phenylpropenal in dioxane–water (1:1) solution. It was found that in addition to the main product, (*E*)-3-phenyl-2-propen-1-ol, small amounts of **11–13** (≈0.5% yield of each one of the compounds) were present in the reaction mixtures (Scheme 3). Hydroboration/oxidation of (*E*)-3-phenylpropenal gave a mixture of **11–13** (**11**, 38%; **12**, 38%; **13**, 24%). Compounds **11–13** in the reaction products were analysed as acetate derivatives by ^{1}H NMR spectroscopy. Separation of the compounds was carried out by ion-exchange chromatography with an anion exchanger using a procedure previously applied for the separation of diastereomers of arylglycerol β-aryl ethers.[7]

The amount of identified by-products formed when cinnamyl alcohols are prepared by tetrahydridoborate reduction of cinnamaldehydes is small (2–3%) and does not lower the yield dramatically. However, the formation of by-products is of importance since purification procedures are required to obtain the cinnamyl alcohols in a pure state.

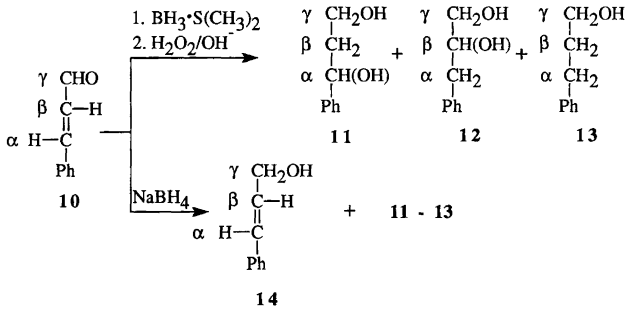
Experimental

Dioxane was freshly distilled over Na. Merck Kieselgel 60 (230–400 mesh) was used for flash chromatography. ^{1}H NMR spectra were recorded at 400 MHz with a Varian XL-400 (VXR-5000) instrument (temperature, 300 K). Deuteriochloroform was used as the solvent [internal reference, $(CH3)_4Si$].

Thin layer chromatography (TLC) was performed on silica gel plates (Merck, Kieselgel 60 F_{254}) with toluene–dioxane–acetic acid (90:25:4) as the eluent (R_f values: **5** and **6**, 0.10; **7**, 0.29; **3**, 0.30; **4**, 0.32; **8**, 0.44; **9**, 0.48) or on reversed-phase plates (Merck, RP-18 F_{254}s) using methanol–water (1:2) as the eluent (R_f values: **7**, 0.08; **6**, 0.21; **5**, 0.28). Spots were made visible by UV light as well as by spraying with formalin–H_2SO_4 (1:9) and heating.



Scheme 2.



Scheme 3.

Acetylations were performed as described in Ref. 8. *1-(3,4-Dimethoxyphenyl)ethanol* was prepared according to Ref. 9, m.p. 33°C.

*(E)-3-(3,4-Dimethoxyphenyl)propenal (**8**)* was prepared by the Vilsmeier reaction starting from 1-(3,4-dimethoxyphenyl)ethanol (7.29 g). The procedure described in Ref. 10 for the synthesis of 3-(4-methoxyphenyl)propenal was followed. The crude product (obtained by extraction of the reaction mixture with ether and, finally, with chloroform) was purified by flash chromatography [180 g SiO_2; eluent, toluene–ethyl acetate (15:1)]. Recrystallization from benzene–hexane gave 4.3 g product of m.p. 83–84°C (Lit.[11] 83–84°C). Yield: 56%. ^{1}H NMR: δ 3.93 (3 H, s, OCH_3), 3.94 (3 H, s, OCH_3), 6.62 (1 H, dd, J = 7.6 and 15.7 Hz, Hβ), 6.91 (1 H, d, J = 8.2 Hz, H-Ar), 7.08 (1 H, d, J = 2.1 Hz, H-Ar), 7.17 (1 H, dd, J = 2.1 and 8.2 Hz, H-Ar), 7.42 (1 H, d, J = 15.7 Hz, Hα), 9.67 (1 H, d, J = 7.6 Hz, CHO).

*(E)-3-(3,4-Dimethoxyphenyl)-2-propen-1-ol (**3**).* Aldehyde **8** (0.77 g) was dissolved in 95% ethanol (15 ml) and $NaBH_4$ (150 mg) was added to the solution. After 3.5 h, water (20 ml) was added to the reaction mixture. Extraction was performed with chloroform (3 × 30 ml). The extract was dried (Na_2SO_4) and solvents were removed by film evaporation. Crystallization from benzene–hexane gave 0.67 g product of m.p. 78.0–78.5°C (Lit.[12] 79–80°C). Subsequent recrystallization from methanol–water[13] raised the m.p. to 79°C. ^{1}H NMR of the acetate derivative: δ 2.10 (3 H, s, CH_3CO), 3.88 (3 H, s, OCH_3), 3.90 (3 H, s, OCH_3), 4.71 (2 H, dd, J = 0.9 and 6.7 Hz, CH_2), 6.16 (1 H, dt, J = 6.7 and 15.9 Hz, Hβ), 6.60 (1 H, ≈d, J = 15.9 Hz, Hα), 6.80–6.96 (3 H, m, H-Ar).

*(Z)-3-(3,4-Dimethoxyphenyl)propenal (**9**)* was prepared by photochemical isomerization of the *E*-isomer. A solution of **8** (0.42 g) in methylene chloride (80 ml) was irradiated for 3 h in a Rayonet Photochemical reactor (RPR 100) fitted with 3500 Å lamps. The crude product consisted of a mixture of the isomers; the *Z*-form/*E*-form ratio was 1:3. Purification was accomplished by flash chromatography [60 g SiO_2; eluents, toluene–ethyl acetate (1:15) and (1:10)]; the *Z*-form was eluted before the *E*-form. An essentially pure fraction of the *Z*-form was obtained (^{1}H NMR, cf. Ref. 14). M.p. 56–58°C (from benzene–hexane). ^{1}H NMR: δ 3.91 (3 H, s, OCH_3), 3.93 (3 H, s, OCH_3), 6.12 (1 H, dd, J = 8.0 and 11.6 Hz, Hβ), 6.90 (1 H, d, J = 8.0 Hz, H-Ar), 6.93 (1 H, d, J = 2.0 Hz, H-Ar), 7.02 (1 H, dd, J = 2.0 and 8.0 Hz, H-Ar), 7.52 (1 H, d, J = 11.6 Hz, Hα), 10.02 (1 H, d, J = 8.0 Hz, CHO).

*(Z)-3-(3,4-Dimethoxyphenyl)-2-propen-1-ol (**4**).* Aldehyde **9** (87 mg) was reduced ($NaBH_4$–ethanol, cf. the procedure given for the preparation of **3**) and the crude product was purified by flash chromatography [40 g SiO_2; eluents were mixtures of ethyl acetate and methylene chloride (1:12, 1:10)]. The *Z*-form was eluted before the *E*-form. A product (83 mg) of m.p. 50–51°C was obtained. ^{1}H NMR data agreed with those given for **4** in Ref. 15. ^{1}H NMR of the acetate derivative: δ 2.09 (3 H, s, CH_3CO), 3.886 (3 H, s, OCH_3), 3.892 (3 H, s, OCH_3), 4.85 (2 H, dd, J = 1.5 and 6.7 Hz, CH_2), 5.74 (1 H, dt, J = 6.7 and 11.6 Hz, Hβ), 6.61 (1 H, ≈d, J = 11.6 Hz, Hα), 6.76–6.85 (3 H, m, H-Ar).

Hydroboration/oxidation experiments. Procedure A. A solution of 2 M $BH_3 \cdot S(CH_3)_2$ in THF (2*a* ml) was slowly injected into a solution of the substrate (*a* mmol) in THF (10*a* ml) (magnetic stirring, argon atmosphere). After 1.5 h, water (4*a* ml), 35% H_2O_2 (0.8*a* ml) and 2 M NaOH (4*a* ml) were added dropwise to the reaction mixture. After vigorous stirring for 1 h, the reaction mixture was transferred to a separatory funnel, by the use of water (20*a* ml) and chloroform (40*a* ml) and was neutralized with 2 M hydrochloric acid. The layers were separated and the aqueous layer was extracted with chloroform (2 × 20*a* ml). The combined organic layers were dried (Na_2SO_4) and the solvents removed by film evaporation.

Procedure B. Procedure A was followed except for the introduction of an additional extraction of the aqueous layer with ethyl acetate (2 × 10*a* ml). The products were dissolved in methanol and the solution was evaporated to dryness in order to remove residual boric acid.

*Hydroboration/oxidation of (E)-3-(3,4-dimethoxyphenyl)propenal (**8**).* Procedure A was followed. The extracted material and the aqueous layers were examined by TLC. The extracted material was acetylated and analysed for **5–7** by ^{1}H NMR spectroscopy. ^{1}H NMR of the diacetate of 1-(3,4-dimethoxyphenyl)-1,3-propanediol (**5**): δ 2.04 (3 H, s, CH_3CO), 2.06 (3 H, s, CH_3CO), 2.09 (1 H, m, Hβ), 2.25 (1 H, m, Hβ), 3.87 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 4.02 (1 H, ddd, J = 6.1, 6.1 and 11.3 Hz, Hγ), 4.14 (1 H, ddd, J = 6.1, 7.3, and 11.3 Hz, Hγ), 5.81 (1 H, dd, J = 6.1 and 8.2 Hz, Hα), 6.81–6.93 (3 H, m, H-Ar). ^{1}H NMR of the diacetate of 3-(3,4-dimethoxyphenyl)-1,2-propanediol (**6**): δ 2.04 (3 H, s, CH_3CO), 2.08 (3 H, s, CH_3CO), 2.81 (1 H, dd, J = 7.0 and 14.0 Hz, Hα), 2.88 (1 H, dd, J = 7.0 and 14.0 Hz, Hα), 3.86 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 4.03 (1 H, dd, J = 6.1 and 11.9 Hz, Hγ), 4.23 (1 H, dd, J = 3.4 and 11.9 Hz, Hγ), 5.25 (1 H, ddt, J = 3.4, 6.1 and 7.0 Hz, Hβ), 6.71–6.82 (3 H, m, H-Ar). ^{1}H NMR of the acetate of 3-(3,4-dimethoxyphenyl)-1-propanol (**7**): δ 1.94 (2 H, m, Hβ), 2.06 (3 H, s, CH_3CO), 2.64 (2 H, ≈t, J = 7.6 Hz, Hα), 3.86 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 4.09 (2 H, t, J = 6.7 Hz, Hγ), 6.69–6.82 (3 H, m, H-Ar).

*Hydroboration/oxidation of (E)-3-(3,4-dimethoxyphenyl)-2-propen-1-ol (**3**) and (Z)-3-(3,4-dimethoxyphenyl)-2-propen-1-ol (**4**).* Procedure B was followed. The amount of reaction products left in the aqueous layers was negligible (TLC). The extracted materials were acetylated and the acetate examined by ^{1}H NMR spectroscopy. The pres-

ence of **5–7** could be demonstrated (cf. the hydroboration/oxidation experiment with **8**); the yields of the compounds were estimated by integrations.

*Reduction experiments with (E)-3-(3,4-dimethoxyphenyl)propenal (**8**) using $NaBH_4$ as the reagent.* Aldehyde **8** (5 mmol) was dissolved in 95% ethanol (20 ml) [alternatively dioxane–water (1:1) or dioxane–0.25 M NaOH (1:1) was used as the solvent] and $NaBH_4$ (0.20 g) was added (magnetic stirring). After 8 h ice–water (20 ml) was added and the mixture was extracted with chloroform ($40 + 3 \times 20$ ml). The organic layer was dried (Na_2SO_4) and solvents were removed by film evaporation. The major part of the **3** formed was removed by crystallization from methanol–water. The materials in the mother liquor were acetylated and examined by ^{1}H NMR spectroscopy, which revealed the presence of **5–7** (cf. the hydroboration/oxidation experiment with **8**). The aqueous layer was examined by TLC. Traces of **5** and **6** were detected (comparatively small amounts of these compounds were present in the aqueous layers from reduction experiments in dioxane-containing media). (In the experiments with dioxane–0.25 M NaOH (1:1) as the solvent, the reaction mixture was neutralised with 1 M HCl prior to extraction.)

*Hydroboration/oxidation of (E)-3-phenylpropenal (**10**).* Procedure A was followed. The reaction product obtained was acetylated and analysed by ^{1}H NMR spectroscopy.

*Reduction of (E)-3-phenylpropenal (**10**) with $NaBH_4$.* The procedure used in the experiments with **8** was followed [solvent, dioxane–water (1:1)]. The major part of the (*E*)-3-phenyl-2-propen-1-ol (**14**) formed was removed by crystallization from methanol–water. The materials present in the mother liquor were acetylated and analysed by ^{1}H NMR spectroscopy. The spectrum revealed the presence of **11–13** and acetylated (*E*)-3-phenyl-2-propen-1-ol.

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