SYNTHESIS OF 1,2-BIS(4-HYDROXY-3-METHOXYPHENYL)- AND 1,2-BIS(3,4-DIMETHOXYPHENYL)-1,3-PROPANEDIOL

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New application of Prins reaction is described, consisting in addition of formaldehyde to alkoxy stilbenes. Thus, (*E*)-4,4′-dibenzyloxy-3,3′-dimethoxystilbene and (*E*)-3,3′,4,4′-tetramethoxystilbene were transformed to the corresponding substituted *trans*-4,5-diaryl-1,3-dioxanes which after acetolysis and deacetylation (and also debenzylation in the former case) afforded a mixture of stereoisomers of the title compounds, representing a β-1 dilignol grouping. Pure *erythro*-isomers were separated by crystallisation and, together with the *threo*-isomers, were identified by physico-chemical methods.

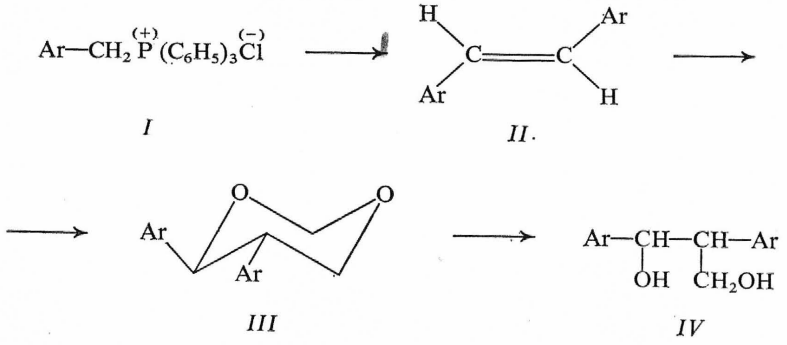
It has been proved[1] that the β−1 bonding of monomeric units is a significant structural feature of the lignin macromolecule. Characteristic for this grouping is its transformation to stilbene derivatives in acid as well as in alkaline medium; this was confirmed by study of model compounds of the 1,2-diaryl-1,3-propanediol type[1,2]. The formal reversal of this degradation, represents a synthetic route to above mentioned models which is the subject of this paper.

The starting stilbenes were prepared in high yields by Wittig synthesis[3]. We did not study the stereochemical outcome of the reaction and separated directly the pure (*E*)-stilbenes by crystallisation. Gierer and coworkers have shown[4] that ^{1}H-NMR spectra of similar geometric isomers, *e.g.* of 4,4′-diacetoxy-3,3′-dimethoxystilbene, differ *inter alia* in the shift of the six-proton singlet of methoxy groups. Since the signals of olefinic protons were overlapped by the complex multiplet of aromatic protons, the isomeric purity of the prepared stilbenes was proved by the presence of one six-proton singlet due to the 3- and 3′-OCH_3 groups and by the overall shape of the spectra, including integration.

The obtained (*E*)-stilbenes were subjected to the Prins reaction under conditions described in our previous paper[5]. The crystalline products proved to be pure *trans*-isomers as shown by their large coupling constant $J_{\alpha\beta}$ (10 Hz, diaxial coupling). The good yield (60−70%) of the crystalline *trans*-isomers proves that, similarly to (*E*)-β-bromostyrenes[5], the reaction with formaldehyde is predominantly a *syn*-addition.

Acetolysis of *trans*-4,5-diaryl-1,3-dioxanes afforded pairs of acetates of stereo-

isomeric 1,2-diaryl-1,3-propanediols which were directly deacetylated and the *erythro*-isomers of the resulting diols were separated by crystallisation. Pure *threo*-isomers were obtained by column chromatography of the mother liquors. The diols *IVa* were debenzylated almost quantitatively by catalytic hydrogenation over 5% palladium on charcoal.



a, Ar = C_6H_3-3-OCH_3,4-$OCH_2C_6H_5$
b, Ar = C_6H_3-3,4-$(OCH_3)_2$
c, Ar = C_6H_3-3-OCH_3,4-OH

SCHEME 1

Configuration of the isomeric 1,2-diaryl-1,3-propanediols was determined by comparison of ^{1}H-NMR coupling constants of the protons H_α and H_β in the corresponding acetates. Isomers with larger value of $J_{\alpha\beta}$ (7·6–8·4 Hz) were assigned *threo*-configuration whereas those with smaller $J_{\alpha\beta}$ (6·0–7·4 Hz) were regarded as *erythro*-isomers[6]. Our results agree with the data of Nakatsubo and Higuchi[7] who on the basis of a ^{1}H-NMR study of phenylboronates of 1-syringyl-2-guaiacyl-1,3-propanediol assigned *erythro*-configuration to 1,2-diguaiacyl-1,3-propanediol, prepared by hydrolysis of lignin by Nimz[8] and which is identical with our *erythro-IVc*.

EXPERIMENTAL

Melting points were determined on a Kofler block. ^{1}H-NMR spectra were measured at 25°C on a Tesla BS 487B (80 MHz) instrument in deuteriochloroform and hexadeuterio-2-propanone, using tetramethylsilane as internal standard. The signals were assigned to the corresponding protons by INDOR method. Mass spectra were taken on a JMS-D100 (JEOL) spectrometer (74 eV, emission 300 μA). The reactions were followed by thin-layer chromatography (silica gel G, Merck); spots were visualized by spraying a 5% (vol) solution of sulfuric acid in ethanol, followed by heating. Preparative chromatography was carried out on columns filled with dry silica gel 60 (Merck). Chloroform solutions were dried over anhydrous sodium sulfate, partly decolorised with silica gel, filtered and concentrated under diminished pressure (water pump) at 40°C.

(*E*)-4,4′-Dibenzyloxy-3,3′-dimethoxystilbene (*IIa*) and (*E*)-3,3′,4,4′-Tetramethoxystilbene (*IIb*)

Phosphonium salts *Ia* and *Ib* were prepared by heating the corresponding substituted benzyl chloride with an equivalent amount of triphenylphosphine in dimethylformamide at 80°C for 2 h. After cooling ether was added to incipient turbidity and the separated precipitate filtered. Crystallisation from chloroform–benzene mixture afforded the product in 73—80% yield. The salt *Ia* melted at 242—245°C (reported[9] m.p. 244—245°C). Compound *Ib* formed hygroscopic rhomboidal crystals, m.p. 233—236·5°C. For $C_{27}H_{26}ClO_2P$ (448·9) calculated: 72·23% C, 5·84% H, 7·90% Cl; found: 72·06% C, 5·50% H, 8·26% Cl.

Dry phosphonium salt *Ia* or *Ib* (0·01 mol) was dissolved in lithium methoxide solution, prepared from 70 mg (0·01 mol) of lithium and 30 ml of methanol. To the stirred solution the corresponding substituted benzaldehyde (0·01 mol) was added and stirring was continued for 48 h at room temperature. The precipitate was filtered and crystallised from acetic acid, affording the *trans*-isomer in 76—82% yield.

IIa: M.p. 183—184·5°C. ^{1}H-NMR ($CDCl_3$), ppm: 6·88—7·50, m, 16 H (aromatic and olefinic protons); 5·14, s, 4 H (—CH_2—); 3·88, s, 6 H (—OCH_3). Mass spectrum: *m/e* (rel. intensity, %): 453 (1·6), 452 (7·1), 362 (3·8), 361 (11·4), 242 (1·4), 207 (1·4), 106 (35·7), 91 (100). For $C_{30}H_{28}O_4$ (452·5) calculated: 79·62% C, 6·24% H; found: 79·37% C, 6·21% H.

IIb: M.p. 154—155°C (reported[10] m.p. 156—157°C). ^{1}H-NMR ($CDCl_3$), ppm: 6·74—7·18, m, 8 H (aromatic and olefinic protons); 3·85 and 3·90, s, 6 H (3- and 4-OCH_3).

trans-4,5-Bis(4-benzyloxy-3-methoxyphenyl)-1,3-dioxane (*IIIa*) and *trans*-4,5-Bis(3,4-dimethoxyphenyl)-1,3-dioxane (*IIIb*)

Boron trifluoride etherate (0·3 ml) was added to a stirred mixture of the stilbene *IIa* or *IIb* (0·01 mol), paraformaldehyde (1 g) and dichloromethane (40 ml) and stirring was continued for 90 min (*IIa*) or 60 min (*IIb*). After completion of the reaction (thin-layer chromatography) the mixture was diluted with chloroform, washed with saturated aqueous solution of sodium hydrogen carbonate and worked up. Part of the product was obtained by crystallisation and mother liquors were purified by column chromatography.

IIIa: Obtained in 70% yield, m.p. 136—138°C (butanone–heptane). ^{1}H-NMR ($CDCl_3$), ppm: 4·54, d, 1 H (H_α), 5·28 and 4·94 dd, 2 H(O—CH_2—O) $J_{\alpha\beta}$ = 10 Hz. Mass spectrometry: *m/e* (rel. intensity, %): 513 (0·8), 512 (2·1), 422 (1·1), 232 (1·3), 231 (9·3), 230 (44), 150 (20), 149 (20), 92 (6·7), 91 (100). For $C_{32}H_{32}O_6$ (512·6) calculated: 74·98% C, 6·29% H; found: 75·28% C, 6·50% H.

IIIb: Obtained in 63% yield, m.p. 100—102°C (benzene–diisopropyl ether). ^{1}H-NMR spectrum (hexadeuterio-2-propanone), ppm: 4·60, d, 1 H (H_α), 4·94 and 5·14, dd, 2 H (O—CH_2—O), $J_{\alpha\beta}$ = 10 Hz. Mass spectrum: *m/e* (rel. intensity, %): 360 (0·2), 263 (1·6), 189 (4·6), 175 (5·6), 164 (12·7), 143 (11·2), 144 (8·6), 109 (26·8), 107 (13·2), 89 (90·2), 88 (41·5), 87 (65·9), 59 (100), 58 (100). For $C_{20}H_{24}O_6$ (360·4) calculated: 66·65% C, 6·71% H; found: 66·51% C, 6·68% H.

erythro- and *threo*-1,2-Bis(4-benzyloxy-3-methoxyphenyl)-1,3-propanediol (*IVa*) and *erythro*- and *threo*-1,2-Bis(3,4-dimethoxyphenyl)-1,3-propanediol (*IVb*)

Boron trifluoride etherate (60 µl) was added at room temperature to a stirred solution of *IIIa* or *IIIb* (1 mmol) in a mixture of acetic acid and acetic anhydride (1 : 1; 12 ml). After 1 hour's standing the acetolysis was complete and the mixture was poured into saturated solution of sodium

hydrogen carbonate. The product was taken up in chloroform and the extract worked up. The resulting viscous oil was deacetylated by treatment with sodium methoxide in methanol (about 20 mg of sodium in 30 ml of methanol). Yield of mixtures of *erythro-* and *threo-IVa* or *erythro-* and *threo-IVb* 83–87%. The *erythro*-isomers were obtained by crystallisation from butanone–heptane, *threo*-isomers were isolated by column chromatography of the mother liquors using chloroform–acetone mixtures as eluants (15 : 1 and 12 : 1 for *IVa* and *IVb*, respectively). Their physical constants, elemental analyses and ^{1}H-NMR data are listed in Table I. The mass spectra of the stereoisomeric compounds were almost identical, containing the following peaks: *IVa*: 498 (0·8), 482 (1·2), 468 (1·6), 452 (9·6), 391 (2·5), 377 (5), 361 (11·3), 360 (16·7), 271 (14·2), 240 (100), 149 (75), 92 (>100), 91 (>100); *IVb*: 348 (1), 346 (0·5), 330 (5), 312 (4·7), 300 (83·3), 285 (30·8), 164 (>100), 167 (100), 165 (100), 139 (100).

erythro- and *threo*-1,2-Bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol (*IVc*)

A solution of *erythro-IVa* or *threo-IVa* (100 mg) in dioxane (5 ml) was hydrogenated over palladium on charcoal (5%, 20 mg) under normal pressure at room temperature. After 2·5 h the catalyst was filtered off and the filtrate concentrated, leaving almost quantitative yield of chromatographically homogeneous product. This was identified in the form of its tetraacetate, prepared by acetylation with acetic anhydride in pyridine. The acetylated stereoisomeric compounds exhibited almost identical mass spectra: *m/e* (rel. intensity, %): 489 (1·7), 488 (7·2), 445 (1·7), 444 (7·2), 385 (1·7), 368 (0·7), 343 (0·9), 326 (0·9), 271 (2·3), 250 (4·4), 236 (17·8), 208 (19·4), 194 (50), 191 (27·8), 152 (56), 150 (94), 43 (100).

TABLE I

1,2-Diaryl-1,3-propanediols

Compound	M.p., °C (acetate, m.p.)	Composition (mol.wt.)	Calculated/Found		^{1}H-NMR of acetate H_α, ppm ($J_{\alpha\beta}$, Hz)
			% C	% H	
erythro-IVa	106–108[a]	$C_{31}H_{32}O_6$	74·38	6·44	6·01
	(118–120)[b]	(500·6)	74·10	6·51	(7·4)
treo-IVa	—		74·38	6·44	5·99
	—		74·21	6·46	(8·4)
erythro-IVb	133–134·5[a]	$C_{19}H_{24}O_6$	65·50	6·94	6·06
	87–89[b]	(348·4)	65·54	7·02	(6·9)
treo-IVb	—		65·50	6·94	5·99
	—		65·55	6·90	(8·4)
erythro-IVc	146·5–149[c]	$C_{17}H_{20}O_6$	63·74	6·29	6·06
	132–134[b]	(320·3)	63·69	6·41	(6·0)
treo-IVc	—		63·74	6·29	6·01
	—		63·67	6·32	(7·6)

[a] From butanone–heptane, [b] from methanol, [c] from chloroform–heptane.

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