

Stereochemical Assignment of the Diastereomers of 1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol from X-Ray Analysis

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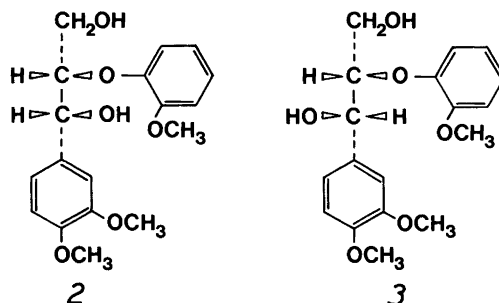
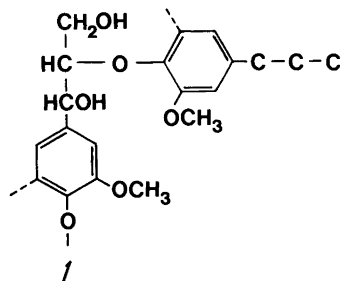
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Arylglycerol- β -aryl ethers (*I*) constitute the most frequent type of intermonomer linkages in lignins.¹ As early as 1952 Adler *et al.*² synthesized an adequate model compound for this important lignin substructure, namely 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol. Later it was shown by Gierer and Norén³ that the product obtained according to Adler *et al.*² was a mixture of the two possible diastereomers, i.e. the *erythro* (*2*) and *threo* (*3*) forms. The stereochemical assignments were made on the basis of electrophoresis experiments in borate buffers: The order of stability of the borate complexes of the diastereomers could be determined and conformational analysis suggests that the *erythro* form can be expected to give the most stable complex with borate. Crystals of the *erythro* form have been obtained (m.p. 97.5-98.5°C).³ The relative stability of the borate complexes of *2* and *3* was alternatively established by chromatography on an anion exchanger, using borate buffer as eluent.⁴

The configuration of lignin model compounds of the arylglycerol- β -aryl ether type has been derived independently by analysis of ¹H NMR spectra of phenyl boronate esters.⁵ ¹H NMR studies were also used to advantage in determination of the stereochemistry of new β -ether models by correlation with NMR data for compounds with known stereochemistry.^{6,7}

In connection with the development of stereoselective syntheses of lignin model compounds it was shown that hydroboration/oxidation of (*Z*)-3-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-2-propenoic acid gave the *erythro* form of 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphen-



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Table 1. Crystal and experimental data for *erythro*-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol, C₁₈H₂₂O₆ (*T* = 290 K).

<i>M_r</i>	334.37
Crystal system	Triclinic
Space group ^a	<i>P</i> $\bar{1}$ (No. 2)
Unit cell dimensions/Å or °	<i>a</i> = 8.085(3), <i>b</i> = 10.149(5), <i>c</i> = 11.318(7) α = 107.57(4) β = 99.37(4) γ = 95.47(8) <i>V</i> = 863.3(8)
<i>Z</i>	2
<i>D_c</i> /g cm ⁻³	1.286
m.p./°C	97–98
μ (MoK α)/mm ⁻¹ (no correction)	0.104
Crystal size/mm	0.29×0.30×0.31
Scan mode	ω -2 θ
2 θ range/°	3.5–50
2 θ scan speed/° min ⁻¹	3.9–29.3
Total no. of reflections measured	3065
No. of observed independent reflections (<i>I</i> > 3 σ (<i>I</i>))	2123
Method used to solve structure	Direct methods (MITHRIL; ^b DIRDIF ^c); successive electron density maps (DRF) ^d
No. of parameters refined	328
Weights calculated according to	$w = [4.0 + 0.015 F_0 ^2 + 0.001 F_0 ^3]^{-1}$ ^e
<i>R</i>	0.059
<i>R_w</i>	0.072
Maximum residual electron density/e Å ⁻³	0.18

^aRef. 10a. ^bRef. 11. ^cRef. 12. ^dRef. 16. ^eRef. 13.

oxy)-1,3-propanediol (2).⁸ Since the net result of hydroboration/oxidation is known to be *syn* addition of water, this provides additional evidence for the *erythro* configuration.

The distribution of *erythro* and *threo* forms of arylglycerol- β -aryl ether structures (*I*) in lignins has recently been studied.⁷ A correct assignment of the isomers of such structures is crucial in work of this kind. The present paper describes a final confirmation of the structure of the crystalline *erythro* isomer, 2, by X-ray analysis. It follows that the second isomer must be the *threo* isomer, 3; this compound has not been obtained in the crystalline state.

The stereochemical assignment of the diastereomers of a model compound for a second type of β -ether structure, 2-(2,6-dimethoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1,3-propanediol, by determination of the crystal structures of the synthetic intermediates (*Z*)-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid

and *threo*-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid will be described in a forthcoming paper.⁹

Experimental

Crystal and experimental data for compound 2 are given in Table 1. Rotation and Weissenberg photographs were taken (CuK radiation) from which the symmetry and approximate cell dimensions were obtained. Diffracted intensities were measured with a Syntex P2₁ diffractometer, using graphite-monochromated MoK α radiation. A 96-step profile was recorded for each reflection and the Lehmann and Larsen profile-analysis method¹⁴ was used to calculate the intensities.¹⁵ Periodic measurements of two test reflections (104 and 04 $\bar{2}$) revealed no loss of intensity during the collection of the data (maximum deviation $\pm 1.4\%$ from the mean values). Correction was made for Lorentz and polarisation effects. Unit

Table 2. Atomic fractional coordinates and B_{eq} (B_{iso} for H) for *erythro*-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol, $\text{C}_{18}\text{H}_{22}\text{O}_6$. All atoms occupy the general two-fold site $2i$ of space group $P\bar{1}$.^a The occupation numbers are 0.5 for C(11A), C(11B), O(5A) and O(5B), and 1 for all other atoms. H(O5A) and H(O5B) could not be located. $B_{\text{eq}} = \frac{4}{3} \sum_i \sum_j \beta_{ij} \mathbf{a}_i \cdot \mathbf{a}_j$.

Atom	x	y	z	$B_{\text{eq}}/\text{\AA}^2$
C(1)	0.1487(4)	0.7324(3)	0.1558(3)	3.94(8)
C(2)	0.2400(4)	0.6817(3)	0.0634(3)	4.54(9)
C(3)	0.4083(4)	0.6608(3)	0.0976(3)	4.39(9)
C(4)	0.4840(4)	0.6908(3)	0.2226(3)	3.76(8)
C(5)	0.3932(4)	0.7466(3)	0.3173(3)	3.67(8)
C(6)	0.2257(4)	0.7663(3)	0.2845(3)	3.64(8)
C(7)	-0.0984(5)	0.7255(4)	0.0051(3)	5.7(1)
C(8)	0.2007(5)	0.8645(4)	0.5009(3)	5.4(1)
C(9)	0.6629(4)	0.6640(3)	0.2580(3)	3.94(8)
C(10)	0.6703(4)	0.5453(3)	0.3146(3)	4.41(9)
C(11A)	0.853(1)	0.5109(7)	0.3400(9)	6.9(3)
C(11B)	0.850(1)	0.5316(8)	0.3688(8)	6.4(2)
C(12)	0.4785(4)	0.3253(3)	0.2463(3)	4.06(8)
C(13)	0.3380(5)	0.3571(3)	0.2954(4)	5.2(1)
C(14)	0.2317(5)	0.2550(4)	0.3170(4)	6.3(1)
C(15)	0.2688(5)	0.1193(4)	0.2883(4)	6.2(1)
C(16)	0.4099(5)	0.0860(3)	0.2394(4)	5.4(1)
C(17)	0.5189(4)	0.1886(3)	0.2201(3)	4.33(9)
C(18)	0.7070(6)	0.0279(4)	0.1405(5)	6.8(1)
O(1)	-0.0161(3)	0.7574(2)	0.1343(2)	5.01(7)
O(2)	0.1269(3)	0.8209(2)	0.3690(2)	4.27(6)
O(3)	0.7630(3)	0.7896(2)	0.3470(3)	5.27(7)
O(4)	0.5807(3)	0.4202(2)	0.2143(2)	4.67(6)
O(5A)	0.8755(7)	0.3961(5)	0.3722(6)	6.7(2)
O(5B)	0.9162(8)	0.4562(8)	0.2777(7)	9.5(2)
O(6)	0.6633(3)	0.1672(2)	0.1744(3)	6.20(8)
H(C2)	0.196(5)	0.669(4)	-0.028(3)	3.6(8)
H(C3)	0.473(4)	0.631(3)	0.031(3)	2.5(7)
H(C5)	0.441(4)	0.769(3)	0.402(3)	2.4(7)
H1(C7)	-0.100(5)	0.637(4)	-0.046(4)	3.8(8)
H2(C7)	-0.037(5)	0.786(4)	-0.035(4)	4.6(9)
H3(C7)	-0.222(5)	0.743(4)	0.013(3)	3.7(8)
H1(C8)	0.235(6)	0.779(5)	0.521(4)	5.9(8)
H2(C8)	0.309(4)	0.946(4)	0.526(3)	3.4(8)
H3(C8)	0.110(5)	0.901(4)	0.545(4)	3.8(8)
H(C9)	0.719(4)	0.634(3)	0.181(3)	2.1(7)
H(C10)	0.609(4)	0.562(3)	0.391(3)	1.3(6)
H1(C11A)	0.891(7)	0.596(5)	0.438(5)	1(1)
H2(C11A)	0.93(1)	0.50(1)	0.26(1)	9(3)
H1(C11B)	0.827(5)	0.449(4)	0.425(4)	-1(1)
H2(C11B)	0.954(9)	0.615(8)	0.406(7)	4(2)
H(C13)	0.311(5)	0.450(4)	0.314(4)	3.7(8)
H(C14)	0.137(5)	0.272(4)	0.342(3)	3.7(8)
H(C15)	0.197(6)	0.050(4)	0.302(4)	6.0(8)
H(C16)	0.436(5)	-0.013(4)	0.217(4)	4.2(9)
H1(C18)	0.812(6)	0.040(5)	0.110(5)	6.3(9)
H2(C18)	0.618(6)	-0.040(5)	0.078(5)	7.2(9)
H3(C18)	0.716(5)	-0.009(4)	0.223(4)	5.0(9)
H(O3)	0.871(5)	0.795(4)	0.324(3)	3.4(8)

^aRef. 10a.

Table 3. Bond distances (Å) and angles (°) in *erythro*-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol, C₁₈H₂₂O₆.

Distance		Distance	
C(1)–O(1)	1.377(4)	C(10)–C(11B)	1.518(9)
C(1)–C(2)	1.379(5)	C(10)–C(11A)	1.549(9)
C(1)–C(6)	1.410(4)	C(11A)–O(5A)	1.342(9)
C(2)–C(3)	1.407(5)	C(11B)–O(5B)	1.312(11)
C(3)–C(4)	1.376(5)	C(12)–C(13)	1.368(5)
C(4)–C(5)	1.406(4)	C(12)–O(4)	1.377(4)
C(4)–C(9)	1.510(4)	C(12)–C(17)	1.410(4)
C(5)–C(6)	1.395(4)	C(13)–C(14)	1.387(5)
C(6)–O(2)	1.369(4)	C(14)–C(15)	1.390(5)
C(7)–O(1)	1.429(4)	C(15)–C(16)	1.374(6)
C(8)–O(2)	1.429(4)	C(16)–C(17)	1.391(5)
C(9)–O(3)	1.435(4)	C(17)–O(6)	1.362(4)
C(9)–C(10)	1.527(4)	C(18)–O(6)	1.443(5)
C(10)–O(4)	1.454(4)		
Angle		Angle	
C(2)–C(1)–C(6)	119.9(3)	C(11A)–C(10)–O(4)	102.8(4)
C(2)–C(1)–O(1)	125.3(3)	C(11B)–C(10)–O(4)	113.4(4)
C(6)–C(1)–O(1)	114.8(3)	C(10)–C(11A)–O(5A)	118.7(6)
C(1)–C(2)–C(3)	120.0(3)	C(10)–C(11B)–O(5B)	109.1(6)
C(2)–C(3)–C(4)	120.8(3)	C(13)–C(12)–C(17)	120.1(3)
C(3)–C(4)–C(5)	119.4(3)	C(13)–C(12)–O(4)	122.7(3)
C(3)–C(4)–C(9)	120.3(3)	C(17)–C(12)–O(4)	117.2(3)
C(5)–C(4)–C(9)	120.2(3)	C(12)–C(13)–C(14)	120.6(3)
C(4)–C(5)–C(6)	120.2(3)	C(13)–C(14)–C(15)	119.6(4)
C(1)–C(6)–C(5)	119.7(3)	C(14)–C(15)–C(16)	120.5(4)
C(1)–C(6)–O(2)	115.5(2)	C(15)–C(16)–C(17)	120.3(3)
C(5)–C(6)–O(2)	124.8(3)	C(12)–C(17)–C(16)	119.0(3)
C(4)–C(9)–C(10)	112.5(2)	C(12)–C(17)–O(6)	116.1(3)
C(4)–C(9)–O(3)	109.2(2)	C(16)–C(17)–O(6)	124.9(3)
C(10)–C(9)–O(3)	109.4(3)	C(1)–O(1)–C(7)	116.6(3)
C(9)–C(10)–C(11A)	111.8(4)	C(6)–O(2)–C(8)	118.2(2)
C(9)–C(10)–C(11B)	113.2(4)	C(10)–O(4)–C(12)	118.1(2)
C(9)–C(10)–O(4)	105.7(2)	C(17)–O(6)–C(18)	118.6(3)

cell dimensions were determined from diffractometer setting angles for 15 reflections.

Intensity statistics strongly indicated a centric structure. Acceptable solutions were obtained, however, only with *P1* using direct methods (Table 1). The subsequent structure analysis was performed in both *P1* and $P\bar{1}$. Final refinement was carried out successfully in $P\bar{1}$. It soon became evident that the CH₂OH group was disordered, but the disorder could be resolved. Block-diagonal least-squares refinement of positional and isotropic thermal parameters for the non-hydrogen atoms gave $R = 0.143$. The introduction of anisotropic thermal parameters reduced

the R -value to 0.096. Twenty-one of the twenty-two hydrogen atoms in the asymmetric unit were located from the subsequent electron density difference map (maximum electron density 0.58 e Å⁻³).¹⁶ Inclusion of atomic coordinates and isotropic thermal parameters for these hydrogen atoms in the refinement gave $R = 0.059$. Due to the disorder, the hydrogen atom attached to the oxygen atom (O5) of the CH₂OH group could not be located.

Further details concerning the refinement of the structure are summarized in Table 1. Atomic scattering factors were taken from Ref. 10b. Calculations were carried out on an IBM 3081 com-

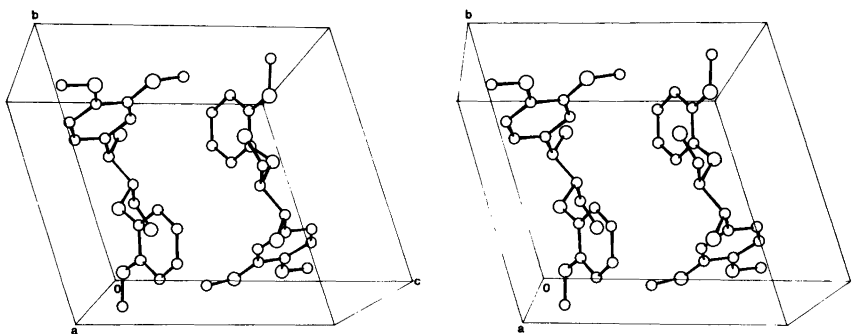


Fig. 1. Stereoscopic view¹⁸ of the unit cell of *erythro*-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol. Hydrogen atoms have been omitted. The disorder is not shown.

puter, using the crystallographic programmes described in Refs. 16 and 17. Lists of structure factors and anisotropic thermal parameters are available from one of the authors (R.S.) on request.

Results

Atomic coordinates and equivalent isotropic thermal parameters are given in Table 2, and bond distances and bond angles involving non-hydrogen atoms in Table 3. Fig. 1 shows a stereoscopic view of the unit cell and Fig. 2 the molecule and the atomic labelling.

The crystals consist of monomeric 1-(3,4-di-

methoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol molecules held together by van der Waals forces and weak hydrogen bonds [$O(2)\cdots O(3)' = 2.891(3) \text{ \AA}$]. The molecules have the *erythro* configuration (see formula 2). The torsion angles $C(4)-C(9)-C(10)-C(11A)$ and $C(4)-C(9)-C(10)-C(11B)$ are $175.3(5)^\circ$ and $-171.3(5)^\circ$, respectively. The aromatic rings are planar (the r.m.s. deviation of the aromatic carbon atoms from their respective least-squares plane is 0.009 \AA).¹⁷ Apart from $C(8)$, the oxygen and carbon atoms of the methoxy groups are coplanar with the corresponding aromatic ring. $C(8)$ and the ether oxygen atom $O(4)$ are both 0.12 \AA out of the respective aromatic ring plane. The aromatic rings form an angle of $87.5(1)^\circ$ with

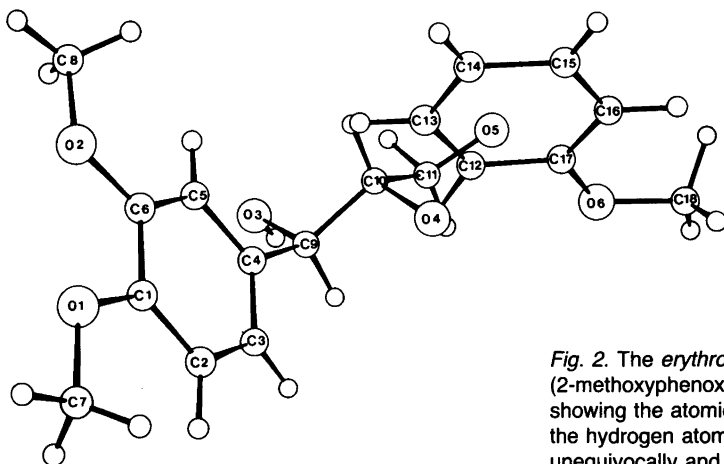


Fig. 2. The *erythro*-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol molecule showing the atomic numbering. Due to the disorder the hydrogen atom $H(5)$ could not be located unequivocally and is therefore omitted.

each other. Further discussion of the structure will be deferred until later.⁹

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References

1. Adler, E. *Wood Sci. Technol.* 11 (1977) 169.
2. Adler, E., Lindgren, B. O. and Saedén, U. *Svensk Papperstidn.* 55 (1952) 245.
3. Gierer, J. and Norén, I. *Acta Chem. Scand.* 16 (1962) 1976.
4. Berndtsson, I. and Lundquist, K. *Acta Chem. Scand., Ser. B 31* (1977) 725.
5. Nakatsubo, F. and Higuchi, T. *Holzforschung* 29 (1975) 193.
6. Johansson, B. and Miksche, G. E. *Acta Chem. Scand.* 26 (1972) 289.
7. Hauteville, M., Lundquist, K. and von Unge, S. *Acta Chem. Scand., Ser. B 40* (1986) 31.
8. Brunow, G. and Lundquist, K. *Acta Chem. Scand., Ser. B 38* (1984) 323.
9. Lundquist, K., Stomberg, R. and von Unge, S. *To be published.*
10. (a). *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1952, Vol. I; (b). *Ibid.* 1974, Vol. IV.
11. Gilmore, C. J. *J. Appl. Crystallogr.* 17 (1984) 42.
12. Beurskens, P. T., Bosman, W. P., Doesburg, H. M., Gould, R. O., van den Hark, T. E. M., Prick, P. A. J., Noordik, J. H., Beurskens, G. and Parthasarathi, V. *DIRDIF: Direct Methods for Difference Structures*. Technical Report 1981/2. Crystallography Laboratory, Toernooiveld, Nijmegen, Netherlands 1981.
13. Cruickshank, D. W. J. *Crystallographic Computing*, Munksgaard, Copenhagen 1970, p. 195.
14. Lehmann, M. S. and Larsen, F. K. *Acta Crystallogr., Sect. A 30* (1974) 580.
15. Lindqvist, O. and Ljungström, E. *J. Appl. Crystallogr.* 12 (1979) 134.
16. Lindgren, O. *An Integrated Set of Crystallographic Programs*. In: *On the Oxygen Coordination of Cerium in Some Sulfates and Chromates*. Thesis, Department of Inorganic Chemistry, Chalmers University of Technology and University of Göteborg, Göteborg 1977.
17. Andersen, L. *An Integrated Set of Crystallographic Programs*. In: *Structure Determination of Some Symmetrical Oxoanions of Sulfur(IV), Selenium(IV) and Tellurium(IV) and Implementation of a General Set of Programs for Crystallographic Computing*. Thesis, Chalmers University of Technology and University of Göteborg, Göteborg 1985.
18. Johnson, C. K. *ORTEP*, Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, TN 1965.

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