Stereochemical Assignment of the *threo* and *erythro* Forms of 2-(2,6-Dimethoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1,3-propanediol from X-Ray Analyses 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

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The crystal structures of (*Z*)-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid (**7**) and *threo*-2-(2,6-dimethoxyphenoxy)-3-(dimethoxyphenyl)-3-hydroxypropanoic acid (**10**) were determined from single-crystal X-ray diffractometer data. Starting from these compounds one could obtain the *erythro* (**8**) and *threo* (**11**) forms of 2-(2,6-dimethoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1,3-propanediol, a model compound for arylglycerol-β-syringyl ether structures in lignins. These syntheses provide independent proof of the stereochemical assignments of **8** and **11**. ^{1}H NMR spectral comparisons with these compounds permitted the stereochemical assignment of other arylglycerol-β-syringyl ethers. Acid **7** crystallizes in the monoclinic space group $P2_1/c$ (No. 14) with $a = 8.797(4)$, $b = 13.000(7)$, $c = 15.731(6)$ Å, $\beta = 98.66(3)°$ and $Z = 4$. Least-squares refinement of 319 structural parameters gave $R = 0.039$ for 2035 observed $[I>3\sigma(I)]$ reflections. Acid **10** crystallizes in the monoclinic space group $C2/c$ (No. 15) with $a = 31.795(11)$, $b = 5.468(2)$, $c = 25.748(8)$ Å, $\beta = 122.18(2)°$ and $Z = 8$. Least-squares refinement of 332 structural parameters gave $R = 0.041$ for 2211 observed $[I>3\sigma(I)]$ reflections. The molecules in both **7** and **10** are held together by van der Waals forces and, in pairs, by strong hydrogen bonds (2.639 Å in **7** and 2.673 Å in **10**) between the carboxy groups.

A preceding paper[1] described the crystal structure of the *erythro* form of 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol, which constitutes a lignin model compound representative of arylglycerol-β-aryl ether structures in lignins (formulas 1–4 are examples of such structures). On the basis of ^{1}H NMR spectral comparisons (primarily involving signals from side chain protons) with this model compound it is possible to make stereochemical as-
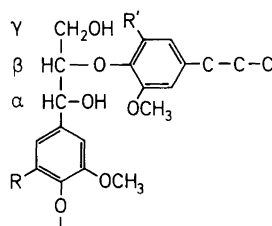
1: R = R' = H
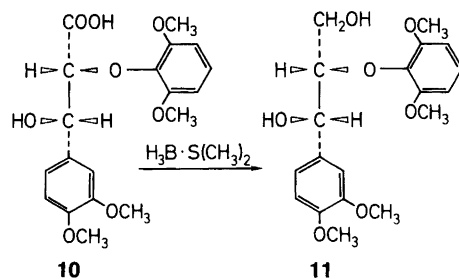2: R = OCH₃, R' = H
3: R = R' = OCH₃
4: R = H, R' = OCH₃
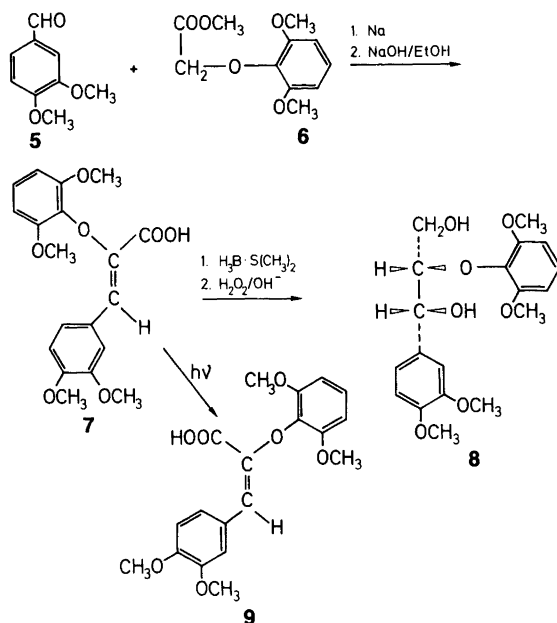
Scheme 1.

signments of the diastereomers of other lignin model compounds of the β-ether type.[2]

Hardwood lignins (birch lignin is an example) consist of similar amounts of syringyl units and guaiacyl units. In this case one has to consider four main types of β-ether structures (1–4) (cf. Refs. 2 and 3). These structural types can be divided into two classes, namely arylglycerol-β-guaiacyl ethers (1,2) and arylglycerol-β-syringyl ethers (3,4); the model compound mentioned in the preceding paragraph is representative for the former class of structures. Replacement of a guaiacyl group by a syringyl group in the side chain influences the ^{1}H NMR signals of the side chain protons and jeopardizes to some extent the stereochemical assignments made by NMR correlations. It was therefore desirable to make an independent assignment of the *erythro* and *threo* forms of a model compound of the arylglycerol-β-syringyl ether type. This paper describes the stereochemical assignment of the *erythro* (8) and *threo* (11) forms of such a compound, namely 2-(2,6-dimethoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1,3-propanediol.

The *erythro* form 8 (liquid) was prepared according to Scheme 1. The intermediate unsaturated acid 7 was obtained in a pure crystalline state, although in very low yield. The stereochemical

assignment of the *erythro* isomer is based on a determination of the crystal structure of acid 7 (see below), together with the assumption that the addition of water via hydroboration/oxidation proceeds in the expected *syn* mode. ^{13}C and ^{1}H NMR spectral data for acid 7 and its stereoisomer (9), obtained by photochemical isomerization, exhibit the expected similarity to those for the corresponding isomers[4] of 3-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-2-propenoic acid.

The *threo* isomer 11 was obtained by reduction of acid 10 (the synthesis of which will be reported in a subsequent paper[5]) with borane/dimethyl sulfide complex (Scheme 2). The stereochemical as-

Scheme 2.

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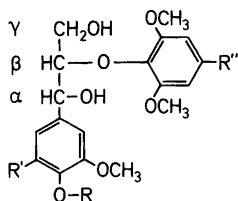
12: R = R' = R" = H
13: R = CH₃, R' = OCH₃, R" = CH₂OH
14: R = H, R' = OCH₃, R" = CH₂OH
15: R = H, R' = OCH₃, R" = CH₃

signment of the reduction product is based on a determination of the crystal structure of the acid used as starting material, i.e. *threo*-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid (**10**) (see below).

The synthesis of the *erythro* (**8**) and *threo* (**11**) forms of the current model compound on a preparative scale will be treated in a forthcoming paper.[5] The *threo* isomer has been obtained in crystalline form (m.p. 110–112 °C); crystals suitable for X-ray analysis have not been obtained hitherto.

¹H NMR spectral comparisons with **8** and **11** provide a good basis for the stereochemical assignment of arylglycerol-β-syringyl ethers; this is exemplified in Table 1. The ¹H NMR data given in Table 1 complement those reported in Ref. 2.

*The crystal structures of compounds **7** and **10**.* Atomic coordinates and equivalent isotropic

thermal parameters are given in Tables 2 and 3, and bond distances, bond angles and selected torsion angles involving non-hydrogen atoms in Tables 4 and 5. Figs. 1 and 2 show stereoscopic views of the unit cells, and Figs. 3 and 4 the molecules and the atomic labelling.

The crystals of both **7** and **10** consist of monomeric molecules held together by van der Waals forces and strong hydrogen bonds between the carboxyl groups [in **7** O(3)···O(4)' is 2.639(3) Å, H(O3)···O(4)' 1.78(4) Å and H(O4)···O(3)' 1.82 (7) Å; in **10** O(4)···O(5)' is 2.673(3) Å and H(O5)···O(4)' 1.73(4) Å; in neither **7** nor **10** do the O—H···O angles deviate significantly from 180°]. Acid **10** is further stabilized by a hydrogen bond between O(3) and O(7)' [2.907(3) Å, H(O3)···O(7)' is 2.08(4) Å and O(3)—H(O3) ···O(7)' 162(2)°]. The crystal structure determinations show that **7** has the Z-configuration and **10** the *threo*-configuration.

The aromatic C—C bond distances are normal, with mean values of 1.396(11) (the r.m.s. deviation is given for a mean value) and 1.385(10) Å in **7** and **10**, respectively.

The C(sp²)—O$_{methoxy}$ bond lengths in **7** and **10**, with mean values of 1.371(2) and 1.364(2) Å, respectively, agree well with each other and with the value of 1.370(3) Å observed for 4-amino-5-chloro-2-methoxy-*N*-{2-[*N*-(*p*-methoxybenzyl)-methylamino]-1,1-dimethylethyl}benzamide.[7] The C(sp³)-O$_{methoxy}$ bond distances (mean values 1.431(4) and 1.425(6) Å in **7** and **10**) are also similar to that observed in the latter compound [1.433(4) Å].

Table 1. ¹H NMR data for acetate derivatives of some lignin model compounds of the arylglycerol-β-syringyl ether type. Solvent, CDCl₃.

Compound	δ/ppm vs. TMS (J/Hz)						
	Hα	Hβ[a]	H(γ₁)	H(γ₂)	Hα'	OCH₃	COCH₃
8 (*erythro*)	6.04 (4.6)	4.68	4.23 (3.7, 11.9)	4.46 (6.0, 11.9)		3.76,[b] 3.85, 3.86	1.96, 2.12
11 (*threo*)	6.13 (7.2)	4.60	3.88 (4.7, 11.9)	4.32 (3.8, 11.9)		3.79,[b] 3.86, 3.87	1.93, 2.01
12 (*erythro*)	6.10 (5.0)	4.63	4.26 (3.6, 11.9)	4.49 (5.5, 11.9)		3.74,[b] 3.80	1.97, 2.14, 2.29
12 (*threo*)	6.16 (6.4)	4.55	3.96 (4.6, 11.8)	4.36 (4.7, 11.8)		3.76,[b] 3.82	1.99,[b] 2.30
13 (*erythro*)	6.03 (4.8)	4.65	4.25 (3.5, 11.9)	4.48 (5.8, 11.9)	5.01	3.77,[b] 3.82, 3.84[b]	1.98, 2.11, 2.15
13 (*threo*)	6.10 (6.8)	4.55	3.91 (4.5, 11.9)	4.35 (4.0, 11.9)	5.03	3.80,[b] 3.83, 3.85[b]	1.98, 2.02, 2.11
14 (*erythro*)	6.07 (5.2)	4.63	4.27 (3.6, 11.9)	4.48 (5.2, 11.9)	5.01	3.75, 3.79	1.98, 2.11, 2.14, 2.31
14 (*threo*)	6.12 (6.2)	4.53	3.98 (4.6, 11.8)	4.36 (4.8, 11.8)	5.02	3.77, 3.80	2.00, 2.01, 2.10, 2.32
15 (*erythro*)	6.07 (5.0)	4.58	4.27 (3.7, 11.8)	4.47 (5.2, 11.8)	2.29	3.72, 3.79	1.98, 2.13, 2.31

[a]Multiplet. [b]6H.

Table 2. Atomic fractional coordinates and B_{eq} (B_{iso} for H) for (Z)-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid (**7**), $C_{19}H_{20}O_7$. All atoms occupy the general four-fold site 4e of space group $P2_1/c$.[6a] The occupation numbers are 0.64(7) for H(O3), 0.36(8) for H(O4) and 1 for all other atoms. O(3) and O(4) probably suffer from slight unresolved disorder.

$$B_{eq} = \frac{4}{3} \sum_i \sum_j \beta_{ij} \mathbf{a}_i \cdot \mathbf{a}_j.$$

Atom	x	y	z	$B_{eq}/\text{Å}^2$
C(1)	0.3483(3)	0.3934(2)	0.5158(1)	3.89(6)
C(2)	0.4506(3)	0.3309(2)	0.4814(2)	4.11(6)
C(3)	0.4794(3)	0.3463(2)	0.3972(2)	4.06(6)
C(4)	0.4050(2)	0.4252(2)	0.3463(1)	3.63(5)
C(5)	0.3002(3)	0.4884(2)	0.3818(1)	3.80(6)
C(6)	0.2724(3)	0.4732(2)	0.4650(1)	3.76(6)
C(7)	0.3905(3)	0.3101(2)	0.6532(2)	5.35(7)
C(8)	0.1023(3)	0.6168(2)	0.4570(2)	6.17(8)
C(9)	0.4391(2)	0.4378(2)	0.2586(1)	3.65(5)
C(10)	0.3858(2)	0.5066(2)	0.1975(1)	3.54(5)
C(11)	0.4349(2)	0.5045(2)	0.1115(1)	3.73(6)
C(12)	0.1436(2)	0.6029(2)	0.1730(1)	3.53(5)
C(13)	0.0854(3)	0.7029(2)	0.1758(2)	4.20(6)
C(14)	−0.0686(3)	0.7219(2)	0.1433(2)	5.36(8)
C(15)	−0.1611(3)	0.6422(2)	0.1077(2)	6.33(9)
C(16)	−0.1048(3)	0.5437(2)	0.1027(2)	5.59(8)
C(17)	0.0488(3)	0.5236(2)	0.1360(2)	4.19(6)
C(18)	0.0213(4)	0.3445(2)	0.0971(2)	6.19(9)
C(19)	0.1397(4)	0.8819(2)	0.2051(2)	6.06(9)
O(1)	0.3115(2)	0.3856(1)	0.5971(1)	4.91(5)
O(2)	0.1743(2)	0.5319(1)	0.5045(1)	5.40(5)
O(3)	0.3899(2)	0.5785(1)	0.0594(1)	4.68(4)
O(4)	0.5182(2)	0.4305(1)	0.0925(1)	4.93(5)
O(5)	0.2945(2)	0.5898(1)	0.2135(1)	3.86(4)
O(6)	0.1143(2)	0.4276(1)	0.1357(1)	5.54(5)
O(7)	0.1860(2)	0.7760(1)	0.2135(1)	5.33(5)
H(C2)	0.507(3)	0.275(2)	0.517(2)	2.9(6)
H(C3)	0.548(3)	0.302(2)	0.371(1)	2.2(5)
H(C5)	0.250(2)	0.540(2)	0.351(1)	1.5(5)
H1(C7)	0.348(3)	0.318(2)	0.709(2)	4.4(7)
H2(C7)	0.373(3)	0.239(2)	0.631(2)	3.2(6)
H3(C7)	0.505(4)	0.326(2)	0.665(2)	5.5(8)
H1(C8)	0.184(4)	0.666(2)	0.445(2)	4.8(7)
H2(C8)	0.048(4)	0.648(2)	0.494(2)	5.0(8)
H3(C8)	0.038(3)	0.596(2)	0.403(2)	4.0(7)
H(C9)	0.510(2)	0.388(2)	0.241(1)	1.3(4)
H(C14)	−0.109(3)	0.788(2)	0.148(2)	4.3(7)
H(C15)	−0.267(4)	0.653(2)	0.083(2)	5.3(8)
H(C16)	−0.174(4)	0.487(2)	0.077(2)	4.8(7)
H1(C18)	0.086(4)	0.284(3)	0.099(2)	6.9(9)
H2(C18)	−0.071(3)	0.328(2)	0.130(2)	4.7(7)
H3(C18)	−0.017(4)	0.358(2)	0.036(2)	4.8(7)
H1(C19)	0.222(4)	0.923(3)	0.238(2)	7(1)
H2(C19)	0.128(4)	0.905(3)	0.145(2)	7(1)
H3(C19)	0.043(3)	0.894(2)	0.225(2)	4.2(7)
H(O3)	0.418(5)	0.573(3)	0.010(3)	3.4(9)
H(O4)	0.553(9)	0.429(6)	0.047(5)	3(2)

Table 3. Atomic fractional coordinates and B_{eq} (B_{iso} for H) for *threo*-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid (**10**), $C_{19}H_{22}O_8$. All atoms occupy the general eight-fold site 8*f* of space group *C2/c*.[6a]

$$B_{eq} = \frac{4}{3} \sum_i \sum_j \beta_{ij} \mathbf{a}_i \cdot \mathbf{a}_j.$$

Atom	x	y	z	$B_{eq}/\text{Å}^2$
C(1)	0.31845(8)	0.1917(5)	0.2703(1)	3.38(8)
C(2)	0.30229(9)	0.3432(5)	0.2988(1)	3.77(9)
C(3)	0.32024(9)	0.3168(5)	0.3611(1)	3.94(9)
C(4)	0.35414(8)	0.1352(5)	0.3947(1)	3.43(8)
C(5)	0.37111(9)	−0.0144(5)	0.3661(1)	3.49(8)
C(6)	0.35411(8)	0.0121(4)	0.3048(1)	3.43(8)
C(7)	0.2634(1)	0.3703(7)	0.1728(1)	4.6(1)
C(8)	0.4054(1)	−0.3094(6)	0.3064(1)	4.6(1)
C(9)	0.37128(9)	0.0922(5)	0.4612(1)	3.69(9)
C(10)	0.39813(8)	0.3100(4)	0.5025(1)	3.19(8)
C(11)	0.44271(8)	0.3856(4)	0.4994(1)	3.19(8)
C(12)	0.40793(9)	0.3989(5)	0.5995(1)	3.68(9)
C(13)	0.4416(1)	0.5863(5)	0.6277(1)	4.2(1)
C(14)	0.4369(1)	0.7479(6)	0.6659(1)	5.3(1)
C(15)	0.3984(1)	0.7164(7)	0.6753(1)	5.7(1)
C(16)	0.3649(1)	0.5297(7)	0.6480(1)	5.4(1)
C(17)	0.3689(1)	0.3688(5)	0.6091(1)	4.3(1)
C(18)	0.2973(2)	0.139(1)	0.5872(2)	7.0(2)
C(19)	0.5103(1)	0.7986(7)	0.6356(2)	5.6(1)
O(1)	0.30182(6)	0.1977(4)	0.20925(7)	4.36(7)
O(2)	0.36876(7)	−0.1266(4)	0.27306(8)	4.83(7)
O(3)	0.32876(7)	0.0378(4)	0.46399(9)	5.49(8)
O(4)	0.44321(6)	0.5756(3)	0.47527(8)	4.21(7)
O(5)	0.47898(6)	0.2273(3)	0.52265(8)	4.19(7)
O(6)	0.41316(6)	0.2301(3)	0.56316(7)	3.57(6)
O(7)	0.33736(7)	0.1803(4)	0.57806(9)	5.31(8)
O(8)	0.47801(7)	0.5942(4)	0.61487(9)	5.25(8)
H(C2)	0.2791(9)	0.461(5)	0.276(1)	0.8(4)
H(C3)	0.308(1)	0.426(5)	0.379(1)	2.0(5)
H(C5)	0.394(1)	−0.132(5)	0.389(1)	1.5(5)
H1(C7)	0.277(1)	0.537(6)	0.188(1)	2.7(6)
H2(C7)	0.233(1)	0.343(5)	0.176(1)	2.3(6)
H3(C7)	0.257(1)	0.346(6)	0.133(1)	3.3(7)
H1(C8)	0.393(1)	−0.432(6)	0.324(1)	3.3(7)
H2(C8)	0.412(1)	−0.384(7)	0.279(2)	3.8(8)
H3(C8)	0.436(1)	−0.234(6)	0.339(1)	3.2(7)
H(C9)	0.3958(9)	−0.049(5)	0.478(1)	1.4(5)
H(C10)	0.3732(9)	0.451(5)	0.491(1)	1.3(5)
H(C14)	0.459(1)	0.871(7)	0.686(2)	3.8(8)
H(C15)	0.396(1)	0.830(6)	0.705(1)	3.7(7)
H(C16)	0.339(1)	0.509(6)	0.653(1)	3.6(7)
H1(C18)	0.280(1)	−0.011(7)	0.560(2)	3.8(8)
H2(C18)	0.310(1)	0.096(7)	0.631(2)	4.6(8)
H3(C18)	0.275(2)	0.268(8)	0.572(2)	5.4(8)
H1(C19)	0.492(1)	0.957(7)	0.622(2)	4.5(8)
H2(C19)	0.532(1)	0.766(6)	0.622(1)	4.0(8)
H3(C19)	0.532(1)	0.793(6)	0.683(1)	3.2(7)
H(O3)	0.336(1)	0.054(7)	0.501(2)	4.5(9)
H(O5)	0.506(1)	0.300(7)	0.522(2)	4.7(8)

Table 4. Bond distances (Å) and angles (°) in (Z)-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid (7), $C_{19}H_{20}O_7$. The average C–H bond length is 0.98(3) Å.

Distance		Distance		Distance	
C(1)–O(1)	1.369(3)	C(7)–O(1)	1.428(3)	C(12)–C(17)	1.397(3)
C(1)–C(2)	1.382(3)	C(8)–O(2)	1.426(4)	C(13)–O(7)	1.370(3)
C(1)–C(6)	1.414(3)	C(9)–C(10)	1.344(3)	C(13)–C(14)	1.396(4)
C(2)–C(3)	1.400(3)	C(10)–O(5)	1.393(3)	C(14)–C(15)	1.383(4)
C(3)–C(4)	1.402(3)	C(10)–C(11)	1.482(3)	C(15)–C(16)	1.380(4)
C(4)–C(5)	1.412(3)	C(11)–O(3)	1.286(3)	C(16)–C(17)	1.398(4)
C(4)–C(9)	1.464(3)	C(11)–O(4)	1.272(3)	C(17)–O(6)	1.375(3)
C(5)–C(6)	1.381(3)	C(12)–O(5)	1.393(3)	C(18)–O(6)	1.434(4)
C(6)–O(2)	1.369(3)	C(12)–C(13)	1.401(3)	C(19)–O(7)	1.437(3)

Angle		Angle	
C(2)–C(1)–C(6)	119.4(2)	O(3)–C(11)–O(4)	123.3(2)
C(2)–C(1)–O(1)	125.5(2)	C(13)–C(12)–C(17)	120.0(2)
C(6)–C(1)–O(1)	115.1(2)	C(13)–C(12)–O(5)	115.3(2)
C(1)–C(2)–C(3)	120.5(2)	C(17)–C(12)–O(5)	124.6(2)
C(2)–C(3)–C(4)	120.6(2)	C(12)–C(13)–C(14)	119.5(2)
C(3)–C(4)–C(5)	118.4(2)	C(12)–C(13)–O(7)	116.2(2)
C(3)–C(4)–C(9)	118.4(2)	C(14)–C(13)–O(7)	124.3(2)
C(5)–C(4)–C(9)	123.1(2)	C(13)–C(14)–C(15)	119.7(3)
C(4)–C(5)–C(6)	120.8(2)	C(14)–C(15)–C(16)	121.6(3)
C(1)–C(6)–C(5)	120.3(2)	C(15)–C(16)–C(17)	119.1(3)
C(1)–C(6)–O(2)	115.4(2)	C(12)–C(17)–C(16)	120.0(2)
C(5)–C(6)–O(2)	124.3(2)	C(12)–C(17)–O(6)	116.5(2)
C(4)–C(9)–C(10)	130.5(2)	C(16)–C(17)–O(6)	123.4(2)
C(9)–C(10)–C(11)	121.5(2)	C(1)–O(1)–C(7)	117.8(2)
C(9)–C(10)–O(5)	122.4(2)	C(6)–O(2)–C(8)	117.0(2)
C(11)–C(10)–O(5)	115.7(2)	C(10)–O(5)–C(12)	123.2(2)
C(10)–C(11)–O(3)	117.6(2)	C(17)–O(6)–C(18)	118.2(2)
C(10)–C(11)–O(4)	119.0(2)	C(13)–O(7)–C(19)	118.0(2)

Selected torsion angles

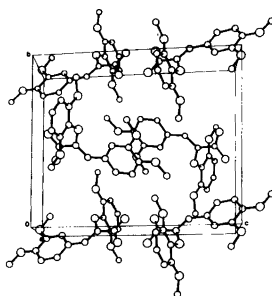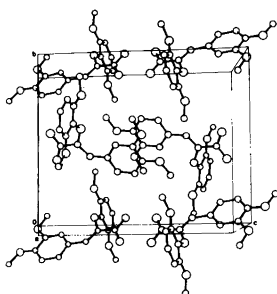|			
C(2)–C(1)–O(1)–C(7)	3.4(3)	O(5)–C(10)–C(11)–O(3)	0.0(3)
C(1)–C(6)–O(2)–C(8)	176.5(3)	O(5)–C(10)–C(11)–O(4)	−179.9(3)
C(3)–C(4)–C(9)–C(10)	−179.4(3)	C(10)–O(5)–C(12)–C(13)	−161.3(3)
C(9)–C(10)–C(11)–O(3)	−173.6(3)	C(12)–C(17)–O(6)–C(18)	−179.0(3)
C(9)–C(10)–C(11)–O(4)	6.5(3)	C(12)–C(13)–O(7)–C(19)	169.8(3)

Fig. 1. Stereoscopic view[18] of the unit cell of (Z)-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid (7), $C_{19}H_{20}O_7$. Hydrogen atoms have been omitted.

Table 5. Bond distances (Å) and angles (°) in *threo*-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid (**10**), $C_{19}H_{22}O_8$. The average C−H bond length is 0.97(3) Å.

Distance		Distance		Distance	
C(1)−O(1)	1.366(3)	C(8)−O(2)	1.424(4)	C(12)−C(17)	1.400(4)
C(1)−C(2)	1.376(3)	C(9)−C(10)	1.520(4)	C(13)−O(8)	1.365(3)
C(1)−C(6)	1.402(3)	C(9)−O(3)	1.423(3)	C(13)−C(14)	1.388(4)
C(2)−C(3)	1.393(4)	C(10)−C(11)	1.518(3)	C(14)−C(15)	1.381(5)
C(3)−C(4)	1.380(4)	C(10)−O(6)	1.436(3)	C(15)−C(16)	1.367(5)
C(4)−C(5)	1.388(3)	C(11)−O(4)	1.216(3)	C(16)−C(17)	1.388(4)
C(4)−C(9)	1.514(3)	C(11)−O(5)	1.305(3)	C(17)−O(7)	1.361(3)
C(5)−C(6)	1.378(3)	C(12)−O(6)	1.386(3)	C(18)−O(7)	1.431(5)
C(6)−O(2)	1.365(3)	C(12)−C(13)	1.376(4)	C(19)−O(8)	1.415(4)
C(7)−O(1)	1.430(4)				

Angle		Angle	
C(2)−C(1)−C(6)	119.3(2)	C(10)−C(11)−O(5)	114.7(2)
C(2)−C(1)−O(1)	125.1(2)	O(4)−C(11)−O(5)	123.5(2)
C(6)−C(1)−O(1)	115.6(2)	C(13)−C(12)−C(17)	120.5(2)
C(1)−C(2)−C(3)	120.8(2)	C(13)−C(12)−O(6)	120.9(2)
C(2)−C(3)−C(4)	120.1(2)	C(17)−C(12)−O(6)	118.6(2)
C(3)−C(4)−C(5)	119.1(2)	C(12)−C(13)−C(14)	120.1(3)
C(3)−C(4)−C(9)	120.8(2)	C(12)−C(13)−O(8)	114.7(2)
C(5)−C(4)−C(9)	120.1(2)	C(14)−C(13)−O(8)	125.2(3)
C(4)−C(5)−C(6)	121.4(2)	C(13)−C(14)−C(15)	119.0(3)
C(1)−C(6)−C(5)	119.4(2)	C(14)−C(15)−C(16)	121.5(3)
C(1)−C(6)−O(2)	115.4(2)	C(15)−C(16)−C(17)	120.0(3)
C(5)−C(6)−O(2)	125.2(2)	C(12)−C(17)−C(16)	118.8(3)
C(4)−C(9)−C(10)	113.5(2)	C(12)−C(17)−O(7)	115.4(2)
C(4)−C(9)−O(3)	108.1(2)	C(16)−C(17)−O(7)	125.7(3)
C(10)−C(9)−O(3)	108.9(2)	C(1)−O(1)−C(7)	116.3(2)
C(9)−C(10)−C(11)	111.7(2)	C(6)−O(2)−C(8)	117.3(2)
C(9)−C(10)−O(6)	105.0(2)	C(10)−O(6)−C(12)	116.2(2)
C(11)−C(10)−O(6)	111.1(2)	C(17)−O(7)−C(18)	117.6(3)
C(10)−C(11)−O(4)	121.8(2)	C(13)−O(8)−C(19)	118.2(2)

Selected torsion angles

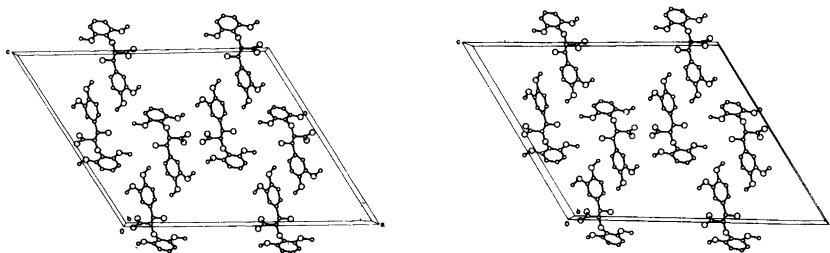|			
C(2)−C(1)−O(1)−C(7)	−2.4(3)	C(9)−C(10)−C(11)−O(4)	110.2(3)
C(1)−C(6)−O(2)−C(8)	179.2(3)	C(9)−C(10)−C(11)−O(5)	−67.5(3)
C(3)−C(4)−C(9)−O(3)	58.8(3)	C(9)−C(10)−O(6)−C(12)	−139.1(3)
C(3)−C(4)−C(9)−C(10)	−62.0(3)	C(10)−O(6)−C(12)−C(13)	−77.7(3)
O(3)−C(9)−C(10)−O(6)	62.1(3)	C(12)−C(13)−O(8)−C(19)	172.1(4)
O(3)−C(9)−C(10)−C(11)	−177.4(3)	C(12)−C(17)−O(7)−C(18)	178.9(4)

Fig. 2. Stereoscopic view[18] of the unit cell of *threo*-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid (**10**), $C_{19}H_{22}O_8$. Hydrogen atoms have been omitted.
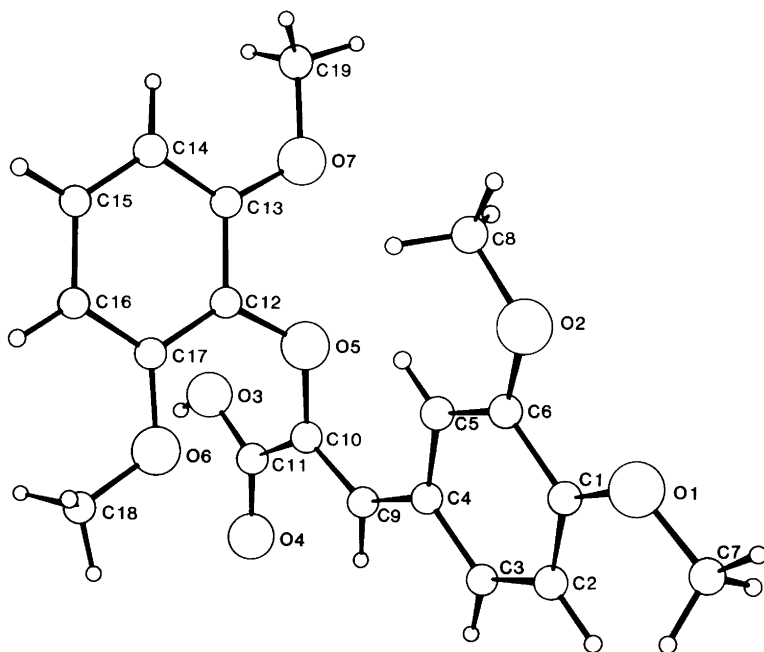
Fig. 3. The (Z)-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid molecule showing the atomic numbering.
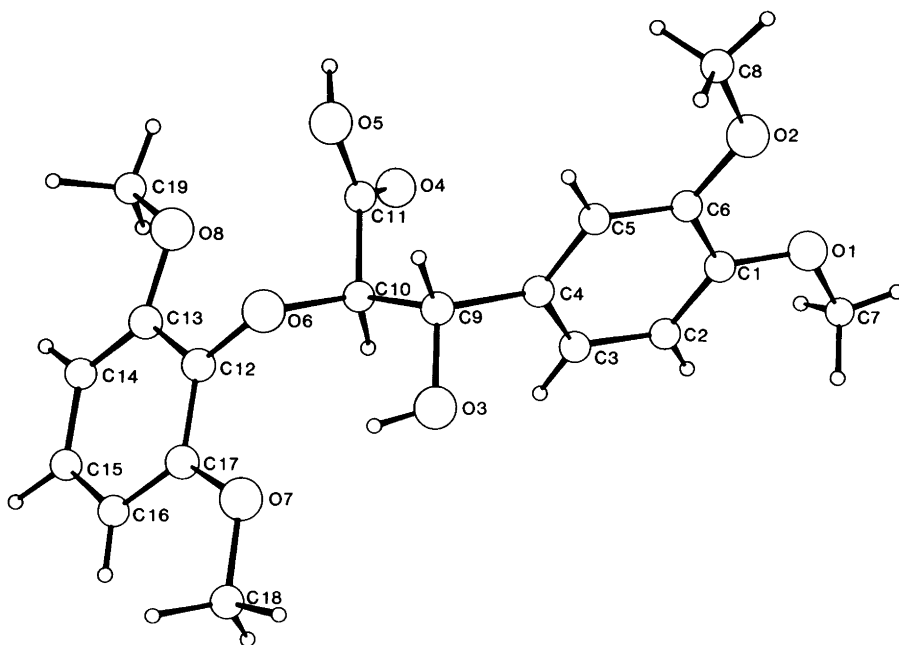
Fig. 4. The *threo*-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid molecule showing the atomic numbering.

The C−O and C=O bond lengths in the carboxyl group have typical values in **7**, while only average values were observed for **10** as a result of statistical disorder; the positions of the =O and −OH fragments are mutually interchangeable in the crystal.

The C(9)−C(10) bond distance in **7** is normal for a double bond. The angles C(5)−C(4)−C(9) (123.1°), C(9)−C(10)−O(5) (122.4°) and C(4)−C(9)−C(10) (130.5°) are all larger than 120°, and the O(5)···H(C5) distance is 2.34(2) Å; normal bond angles (i.e. 120°) would give a distance of 1.7 Å, which is sterically unfavorable.

The maximum deviations of the benzene ring carbon atoms and the methoxy oxygen atoms from the ring planes are 0.009(3) and 0.016(3) Å, respectively, in **7** and 0.012(2) and 0.067(4) Å, respectively, in **10**. The methoxy carbon atoms are also situated near these planes, deviations in the range 0.015–0.094 Å in **7** and 0.011–0.169 Å in **10** being observed.

A striking feature is that the C−C−O$_{methoxy}$ bond angle involving the ring carbon atom *cis* to the methyl is always larger (≈125°) than that involving the *trans* counterpart (≈116°). In **7**, the average C−C−O$_{methoxy}$ angles are 124.4(7)° and 115.8(6)°, and in **10**, 125.3(2)° and 115.3(7)°, respectively. In the above-mentioned benzamide the corresponding angles are 124.5(2)° and 116.1(2)°, respectively [in this compound C(21) is *cis* to C(19), not to C(17) as shown in Fig. 1 in Ref. 7]. Furthermore, the methoxy hydrogen atoms closest to the benzene ring tend to be as remote as possible from the ring planes [on an average 0.8(2) Å in **7** and 0.8(1) Å in **10**; as a consequence the third hydrogen atom in each methoxy group lies near the ring plane, on an average 0.1(1) Å in both **7** and **10**]. Both these effects tend to minimize the repulsion between the hydrogen atoms of C$_{ring}$ and O$_{methoxy}$ [average distances 2.35(12) Å in **7** and 2.36(6) Å in **10**].

The two benzene ring planes form an angle of 96.1(1)° with each other in **7** and 93.7(1)° in **10**. Furthermore, the maximum deviation of C(4), C(9), C(10), C(11) and O(5) from the plane which they define, is 0.033(2) Å in **7**. O(3) and O(4) are 0.031(4) and 0.068(3) Å, respectively, out of this plane, which forms an angle of 5.5(1)° with the benzene ring defined by C(1) to C(6).

The observations regarding bond distances and bond angles reported above are in accordance with those made for a series of related com-

pounds.[1,5] Mean values in 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol[1] are C−C(aromatic) 1.391(14) Å, C(sp^2)−O$_{methoxy}$ 1.369(6) Å, C(sp^3)−O$_{methoxy}$ 1.434(7) Å, and C−C−O$_{methoxy}$ 125.0(2)° and 115.5(5)°, respectively.

Experimental

NMR spectra. ^{1}H NMR spectra were recorded at 270 MHz with a Bruker WH270 instrument (temperature ≈300 K). ^{13}C NMR spectra were recorded at 100.6 MHz with a Varian XL-400 instrument. Deuteriochloroform was used as solvent (internal reference: TMS).

Thin layer chromatography (TLC) was performed on silica gel plates (Merck, Kieselgel 60 F$_{254}$) with toluene–dioxane–acetic acid (90:25:4) as eluent. Spots were made visible by UV light, and by spraying with formalin-H$_2$SO$_4$ (1:9) and subsequent heating. R$_f$ values: **10**, 0.09; 2,6-dimethoxyphenoxyacetic acid, 0.16; **9**, 0.20; **11**, 0.27; veratryl alcohol, 0.28; **7**, 0.31; veratric acid, 0.34; **6**, 0.43; **5**, 0.47.

(2,6-Dimethoxyphenoxy)acetic acid was prepared from 2,6-dimethoxyphenol and monochloroacetic acid.[5] M.p. 79–80 °C.

Methyl (2,6-dimethoxyphenoxy)acetate (**6**) (for related syntheses see Ref. 8). Tetrabutylammonium hydrogen sulfate (19.2 g, 56.5 mmol), NaOH (4.52 g, 113 mmol) and 2,6-dimethoxyphenoxyacetic acid (12.0 g, 56.5 mmol) were dissolved in 50 ml of H$_2$O. Methyl iodide (8 ml) in trichloromethane (50 ml) was added and the mixture was stirred for 30 min. The organic layer was separated and heated under reflux for 30 min. The solvent was removed by film evaporation and 300 ml ether was added to the residue. The ether solution, freed from precipitated tetrabutylammonium iodide, was dried over Na$_2$SO$_4$ and the solvent evaporated. The residual oil was distilled (120 °C, 5 Pa). The product (yield 10.8 g, 85 %) crystallized on standing (m.p. 58 °C). ^{1}H NMR: δ 3.80 (3H, s; OCH$_3$), 3.84 (6H, s; OCH$_3$), 4.62 (2H, s; CH$_2$), 6.57 (2H, d, *J* = 8.3 Hz; aromatic protons), 6.99 (1H, t, *J* = 8.3 Hz; aromatic proton).

(Z)-2-(2,6-Dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid (**7**) (for related syn-

theses see Ref. 9). Ester **6** (3.50 g, 15.5 mmol) and veratraldehyde (2.70 g, 16.3 mmol) were dissolved in 10 ml of THF. Sodium (0.91 g, 18 mmol) dispersed in mineral oil (45 % Na) was added (nitrogen atmosphere). When the initial vigorous reaction (controlled by means of an ice-bath) had ceased, the reaction mixture was kept at 50 °C for 5 h (oil-bath). After cooling and addition of ethanol (25 ml), the major part of the solvents was removed under reduced pressure. A solution of NaOH (0.9 g) in ethanol (95 %, 25 ml) was added and the mixture set aside overnight. The reaction mixture was transferred to a separatory funnel with the help of 0.1 M NaOH, washed with a small amount of ether, acidified with hydrochloric acid and extracted exhaustively with ether. The ether extract was dried (Na_2SO_4) and solvents removed by film evaporation. The oily residue (5.0 g) was chromatographed on a silica gel column (150 g SiO_2), using mixtures of dichloromethane and ethyl acetate as eluent. The eluate containing acid **7** (TLC) was collected and solvents removed by film evaporation. A product (0.76 g) consisting mainly of **7** and veratric acid was obtained. Extraction with boiling water (4×20 ml) left a residue consisting of chromatographically pure **7** (0.23 g), melting at 150–154 °C. Recrystallization from ethyl acetate gave orange crystals (yield 0.13 g, 2.3 %) melting at 155–157 °C. ^{1}H NMR: δ 3.75 (6H, s; OCH_3), 3.80 (3H, s; OCH_3), 3.88 (3H, s; OCH_3), 7.03 (1H, s; vinyl proton), 6.5–7.6 (6H, m; aromatic protons). ^{13}C NMR: δ 55.7 (OCH_3), 55.8 (OCH_3), 56.5 (OCH_3, two groups), 106–152 (aromatic and vinyl C), 167.8 (CO, $^3J_{CH}$ = 3.7 Hz).

(E)-2-(2,6-Dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid (**9**) was obtained by photochemical isomerization of **7**. A solution of **7** (25 mg) in 0.5 ml of $CDCl_3$ was irradiated for 4 h in a Rayonet photochemical reactor (RPR 100) fitted with 3500 Å lamps. NMR data for **9** were obtained by examination of the total reaction mixture. From an ^{1}H NMR analysis the yield of acid **9** could be estimated as 20 %. ^{1}H NMR: δ 3.85 (3H, s; OCH_3), 3.86 (3H, s; OCH_3), 3.88 (6H, s; OCH_3), 6.30 (1H, s; vinyl proton), 6.6–7.3 (6H, m; aromatic protons). ^{13}C NMR: δ 55.8 (OCH_3), 55.9 (OCH_3), 56.3 (OCH_3, two groups), 105–155 (aromatic and vinyl C), 164.0 (CO, $^3J_{CH}$ = 9.9 Hz).

erythro-2-(2,6-Dimethoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1,3-propanediol (**8**). Acid **7** (0.1 g, 0.28 mmol) was subjected to hydroboration [$BH_3 \cdot S(CH_3)_2$]/oxidation (See Ref. 4 and references therein). The crude product was acetylated and examined by ^{1}H NMR spectroscopy, which revealed the presence of the acetate derivative of *erythro* form **8** as a major constituent (the *threo* isomer **11** was not present in detectable amounts). ^{1}H NMR data for the acetate derivative of **8** are given in Table 1.

threo-2-(2,6-Dimethoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1,3-propanediol (**11**) was prepared by reduction of acid **10** (synthesis described in Ref. 5) with borane/dimethyl sulfide complex in THF solution according to a procedure used for the reduction of related compounds.[10] ^{1}H NMR data for the acetate derivative of **11** are given in Table 1.

Determinations of crystal structures. Crystal and experimental data for **7** and **10** are given in Table 6. Rotation and Weissenberg photographs were taken of several crystals of both **7** and **10** (CuKα radiation) from which the symmetry, conditions for reflections, approximate cell dimensions and information about the suitability for single-crystal work, were obtained. Diffracted intensities were measured with a Syntex $P2_1$ diffractometer, using graphite-monochromated MoKα radiation. A 96-step profile was recorded for each reflection and the Lehmann and Larsen profile-analysis method[15] was used to calculate the intensities.[16] Periodic measurements of test reflections showed no significant loss of intensity during the collection of the data. Correction was made for Lorentz and polarization effects. Unit cell dimensions were determined from diffractometer setting angles for about 15 reflections.

Structure determination and refinement. (a) *(Z)-2-(2,6-Dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid* (**7**). The atomic coordinates of all non-hydrogen atoms except C(18) were determined by direct methods (MITH-RIL[12]), and those for C(18) from geometrical considerations. Least-squares refinement[13,17] of positional and isotropic thermal parameters for the non-hydrogen atoms gave R = 0.119. Inclusion of anisotropic thermal parameters gave R =

Table 6. Crystal and experimental data for (Z)-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-2-propenoic acid (**7**), $C_{19}H_{20}O_7$, and *threo*-2-(2,6-dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid (**10**), $C_{19}H_{22}O_8$ (T = 290 K).

	7 ($C_{19}H_{20}O_7$)	**10** ($C_{19}H_{22}O_8$)
M_r	360.36	378.38
Crystal system	Monoclinic	Monoclinic
Space group[a]	$P2_1/c$ (No. 14)	$C2/c$ (No. 15)
Unit cell dimensions/Å or °	a = 8.797(4)	a = 31.795(11)
	b = 13.000(7)	b = 5.468(2)
	c = 15.731(6)	c = 25.748(8)
	β = 98.66(3)	β = 122.18(2)
	V = 1779(1)	V = 3788(2)
Z	4	8
D_c/g cm^{-3}	1.345	1.327
M.p./°C	155–157	141–143
μ(MoKα)/mm^{-1}	0.111	0.112
Crystal size/mm	0.15×0.20×0.40	0.09×0.40×0.46
Reflections for cell determination (No, θ range/°)	14	15
	5.6 < θ < 13.2	3.0 < θ < 9.7
Scan mode	ω-2θ	ω-2θ
2θ range/°	3.5–50	3.5–50
2θ scan speed/° min^{-1}	1.5–5.9	1.5–5.9
Total No. of reflections measured	3528	3807
No. of observed independent reflections [$I > 3\sigma(I)$]	2035	2211
Correction for absorption	–	Empirical[b]
Method used to solve structure	Direct methods (MITHRIL)[c]; electron density difference maps (DRF)[d]	
No. of parameters refined	319	332
Weights calculated according to $w = (a+\|F_o\|+c\|F_o\|^2+d\|F_o\|^3)^{-1}$ [e]	a = 6.0	a = 8.0
	c = 0.020	c = 0.007
	d = 0.0	d = 0.0
R	0.039	0.041
Maximum residual electron density/e Å^{-3}	0.13	0.27

[a]Ref. 6a. [b]Ref. 11. [c]Ref. 12. [d]Ref. 13. [e]Ref. 14.

0.077. From the subsequent electron density difference map all hydrogen atoms were located (maximum electron density 0.51 e Å^{-3}).[13] Inclusion of atomic coordinates and isotropic thermal parameters for the hydrogen atoms in the refinement gave R = 0.040. The structure analysis shows that one molecule is hydrogen-bonded to its centrosymmetric counterpart through the car-boxylic acid groups in the same way as in acetic acid. During the refinement the hydrogen atom originally designated H(O4) moved towards O(3)' ($\bar{x}, \bar{y}, \bar{z}$) and assumed an unreasonably high B-value (8 Å^2). Moreover, the observed C–O distances in the carboxy group became very much the same (1.287 and 1.273 Å, respectively). This was taken to be due to disorder of the carboxy

group. Judging from the electron density difference map, which showed an elongated maximum between O(3) and O(4)' [O(3)' and O(4)], the hydrogen atom of the carboxy group can be attached to either O(3) or O(4). The occupation numbers of H(O3) and H(O4) were varied, keeping their sum equal to one, and the most probable values were taken to be those for which the *B*-values became equal. This gave a final *R*-value of 0.039.

(b) threo-2-(2,6-Dimethoxyphenoxy)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoic acid **(10)**. The atomic coordinates of all non-hydrogen atoms were determined by direct methods (MITHRIL[12]). Intensity statistics strongly indicated a centric structure, but an acceptable solution was obtained only with *Cc*. The 54 positions obtained were, however, centrosymmetrically related in pairs. After origin displacement the structure analysis was performed in space group *C2/c*. Full-matrix least-squares refinement[13,17] of positional and isotropic thermal parameters for the non-hydrogen atoms gave *R* = 0.125. The introduction of anisotropic thermal parameters for these atoms reduced the *R*-value to 0.083. The hydrogen atoms were located from the subsequent electron density difference map (maximum electron density 0.61 e Å^{-3}).[13] Inclusion of atomic coordinates and isotropic thermal parameters for the hydrogen atoms in the refinement gave *R* = 0.042; an empirical correction[11] for the effects of absorption then gave *R* = 0.041.

Further details concerning the refinement of both structures are summarized in Table 6. Atomic scattering factors were taken from Ref. 6b. Calculations were carried out on an IBM 3081 computer, using the crystallographic programmes in Refs. 13 and 17. Lists of structure factors and anisotropic thermal parameters are available from one of the authors (R.S.) on request.

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