Studies on Hydrobenzoins: Preparation, Crystal Structure and Stability of Borate Complexes

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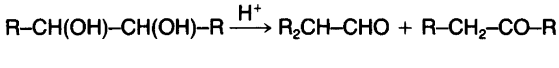
The *meso* and *racemic* forms of hydrobenzoin [1,2-diphenyl-1,2-ethanediol], hydroanisoin [1,2-bis(4-methoxyphenyl)-1,2-ethanediol] and hydroveratroin [1,2-bis(3,4-dimethoxyphenyl)-1,2-ethanediol] have been prepared by reduction of the corresponding benzoins by sodium tetrahydridoborate and by the borane–dimethyl sulfide complex. The *meso* and *racemic* forms could be separated by ion exchange chromatography on an anion exchanger, using a borate solution as the eluent. Borate complexes of the *racemic* forms were more stable than those of the corresponding *meso* forms. Hydrobenzoins are useful as model compounds in connection with studies of acid-catalysed reactions and microbial degradation of lignins.

The crystal structures of the *meso* forms of hydroanisoin and hydroveratroin have been determined from single-crystal X-ray diffraction data. *meso*-Hydroanisoin crystallizes in the space group $P2_1/c$ with $a = 15.269(6)$, $b = 5.035(2)$, $c = 9.198(4)$ Å, $\beta = 98.75(3)°$ and $Z = 2$. Full-matrix least-squares refinement of 127 structural parameters gave $R = 0.039$ for 1047 observed $[I>3\sigma(I)]$ reflections. *meso*-Hydroveratroin crystallizes in the space group $P2_1/n$ with $a = 8.185(2)$, $b = 12.605(3)$, $c = 8.414(2)$ Å, $\beta = 109.74(2)°$ and $Z = 2$. Full-matrix least-squares refinement of 153 structural parameters gave $R = 0.036$ for 1086 $[I>3\sigma(I)]$ reflections.

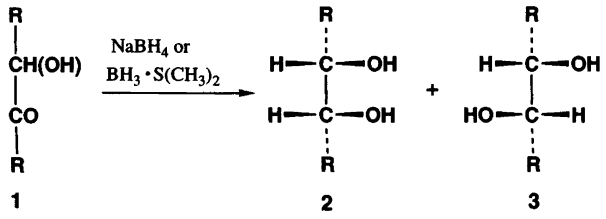
Methoxylated hydrobenzoins (1,2-diaryl-1,2-ethanediols) are of interest as substrates in connection with studies on the properties of oxidizing enzymes of the ligninase type and the biodegradation of lignin.[1] Recently such hydrobenzoins also have been used as lignin model compounds in studies of acid-catalysed reactions of lignin in dioxane–water solution. Thus the yields of aldehyde and ketone on acid treatment (Scheme 1) are dependent on the catalyst and the medium; a high dioxane content and certain catalysts (HBr and – to a smaller extent – HCl) increase the yield of the ketone.[2] The reactions that lead to formation of aldehydes and ketones have analogies in the acid-catalysed degradation reactions of structural elements in lignin of the β-O-4 and β-1 types. The use of hydrobenzoins in the aforementioned research areas prompted the development of convenient methods for their preparation and also examination of their structures and properties.

Methods for the preparation of the *meso* (**2**) and *racemic* (**3**) forms of a series of hydrobenzoins [1,2-diphenyl-1,2-ethanediol (**2a**, **3a**), 1,2-bis(4-methoxyphenyl)-1,2-ethanediol (**2b**, **3b**), 1,2-bis(3,4-dimethoxyphenyl)-1,2-ethanediol



R = 4-methoxyphenyl or 3,4-dimethoxyphenyl

Scheme 1.



a; R = Phenyl
b; R = 4-Methoxyphenyl
c; R = 3,4-Dimethoxyphenyl

Scheme 2.

(**2c**, **3c**)] (Scheme 2) are reported. All of the compounds have been described in the literature (hydrobenzoin,[3] hydroanisoin,[4] hydroveratroin[5]); it is notable that (±)-hydrobenzoin (**3a**)[3] and (±)-hydroveratroin (**3c**)[5] crystallize as conglomerates making it possible to pick out the individual enantiomers. The compounds were examined by ^{1}H NMR spectroscopy. The stability of their borate complexes was studied by ion exchange chromatography on an anion exchanger using a borate solution as the eluent. Furthermore, determination of the crystal structures of **2b** and **2c** provided detailed structural information about these compounds.

The hydrobenzoins were prepared by reduction of the corresponding benzoins (**1**) by sodium tetrahydridoborate or the borane–dimethyl sulfide complex (Scheme 2). The

Table 1. Ion exchange chromatography of borate complexes of hydrobenzoins.[a]

Compound	Elution volume[b]/ml
meso-Hydroanisoin (**3b**)	204
meso-Hydroveratroin (**3c**)[c]	209
meso-Hydrobenzoin (**3a**)	226
(±)-Hydroveratroin (**2c**)	231
(±)-Hydroanisoin (**2b**)	308
(±)-Hydrobenzoin (**2a**)	385

[a]For comparison the elution volumes of the previously examined[7] lignin models *erythro*-veratrylglycerol β-guaiacyl ether (193 ml) and *threo*-veratrylglycerol β-guaiacyl ether (143 ml) were determined. [b]The width of the elution peaks was 60–100 ml. [c]This compound is only slightly soluble in the eluent.

meso forms (**2**) invariably dominated in the reaction products and could be isolated by fractional crystallization. The yields of the racemic forms (**3**) were about 15% when tetrahydridoborate was used as the reducing agent. The borane reagent gave varying yields of racemic forms in the range 5–25%; (±)-hydroanisoin and (±)-hydroveratroin were at most obtained in 10% yield. The influence of the reaction parameters on the yield of the racemic forms in experiments with the borane reagent will be further investigated. The racemic forms (**3**) were isolated from the mother liquors from fractional crystallization of the *meso* forms by ion exchange chromatography on an anion exchanger using borate solution as the eluent. In all cases the racemic form gave the stronger borate complex and was eluted after the *meso* form (Table 1). This is expected from a conformational analysis of the borate complexes: in the borate complex of the *meso* forms the bulky aryl substituents are *cis* orientated and energetically unfavourable interactions between these groups cannot be avoided (cf. Ref. 6). It is evident from Table 2 that ^{1}H NMR spectroscopy can be used for the steric classification of hydrobenzoins. Comparisons of the ^{1}H NMR spectra of the acetates of the *meso* and racemic forms show that the acetate signal appears at higher field in the *meso* forms while the methine proton signals are found at slightly lower field in these isomers. The methine proton signal in underivatized *meso* forms (δ 4.7–4.8) appeared at somewhat lower field than the corresponding signal from racemic forms (δ 4.6–4.7); the position of the signal varied noticeably with the concentration in the solution examined.

The crystal structures of meso-*hydroanisoin* (**2b**) *and* meso-*hydroveratroin* (**2c**). Fractional atomic coordinates and equivalent isotropic thermal parameters are given in Tables 3 and 4, and bond distances, bond angles and selected torsion angles in Tables 5 and 6. Figs. 1 and 2 show stereoscopic views of the unit cells and Figs. 3 and 4 the molecules and the atomic labelling. Crystal data and experimental data for *meso*-hydroanisoin (**2b**) and *meso*-hydroveratroin (**2c**) are given in Table 7.

The crystals of both compounds consist of monomeric centrosymmetric molecules held together by van der Waals forces and hydrogen bonds. The hydrogen bonds are moderately strong in **2b** while they are weak in **2c**. Twin formation was observed for **2b**.

Table 3. Atomic fractional coordinates and B_{eq} (B_{iso} for H) for *meso*-hydroanisoin (**2b**), $C_{16}H_{18}O_4$.

Atom	*x*	*y*	*z*	B_{eq}
C(1)	0.37330(9)	0.5541(3)	0.4873(1)	2.75(3)
C(2)	0.3251(1)	0.7025(3)	0.3762(2)	3.56(4)
C(3)	0.2361(1)	0.6548(4)	0.3315(2)	4.11(4)
C(4)	0.1935(1)	0.4599(4)	0.3991(2)	3.93(4)
C(5)	0.2395(1)	0.3104(4)	0.5107(2)	3.95(4)
C(6)	0.3294(1)	0.3585(3)	0.5533(2)	3.54(4)
C(7)	0.0591(1)	0.2242(6)	0.4114(4)	6.83(8)
C(8)	0.47141(9)	0.6026(3)	0.5321(1)	2.57(3)
O(1)	0.10492(8)	0.4282(3)	0.3465(2)	6.14(5)
O(2)	0.49657(7)	0.5923(2)	0.6878(1)	2.89(3)
H(C2)	0.353(1)	0.841(4)	0.332(2)	2.8(4)
H(C3)	0.203(1)	0.757(4)	0.253(2)	2.8(4)
H(C5)	0.211(1)	0.171(4)	0.559(2)	2.7(4)
H(C6)	0.362(1)	0.250(4)	0.632(2)	2.3(4)
H1(C7)	0.087(2)	0.037(6)	0.400(3)	6.7(8)
H2(C7)	0.061(2)	0.269(6)	0.521(4)	6.5(8)
H3(C7)	0.002(2)	0.229(5)	0.359(3)	5.3(6)
H(C8)	0.4870(9)	0.782(3)	0.495(2)	0.3(3)
H(O2)	0.494(1)	0.742(4)	0.722(2)	2.0(4)

[a]T = 290 K. $B_{eq} = \frac{4}{3}\sum_i \sum_j \beta_{ij}\, a_i\, a_j$.

Table 2. ^{1}H NMR data for acetates of a series of hydrobenzoins (**2**, **3**).

Compound	δ values (ppm) vs. Me_4Si			
	CH_3CO	OCH_3	CHAr	Aromatic protons
meso-Hydrobenzoin (**3a**)	2.00		6.09	7.0–7.4
(±)-Hydrobenzoin (**2a**)	2.07		6.05	7.0–7.4
meso-Hydroanisoin (**3b**)	1.98	3.79	6.01	6.8–7.2
(±)-Hydroanisoin (**2b**)	2.06	3.74	5.99	6.7–7.1
meso-Hydroveratroin (**3c**)	2.01	3.80, 3.86	6.02	6.6–6.9
(±)-Hydroveratroin (**2c**)	2.10	3.76, 3.81	5.97	6.5–6.8

Table 4. Atomic fractional coordinates and B_{eq} (B_{iso} for H) for *meso*-hydroveratroin (**2c**), $C_{18}H_{22}O_6$.

Atom	*x*	*y*	*z*	B_{eq}
C(1)	0.6550(2)	0.0940(1)	0.4388(2)	3.48(5)
C(2)	0.7314(2)	0.0394(1)	0.3369(2)	3.30(5)
C(3)	0.8840(2)	0.0749(1)	0.3209(2)	2.97(4)
C(4)	0.9644(2)	0.1664(1)	0.4067(2)	3.22(4)
C(5)	0.8903(2)	0.2199(1)	0.5077(2)	3.74(5)
C(6)	0.7356(3)	0.1831(1)	0.5230(2)	3.80(5)
C(7)	0.8867(3)	−0.0621(2)	0.1280(3)	3.94(6)
C(8)	1.2012(3)	0.2863(2)	0.4618(3)	5.47(8)
C(9)	0.4873(2)	0.0534(2)	0.4537(2)	3.72(5)
O(1)	0.9671(2)	0.0286(1)	0.2228(1)	3.73(4)
O(2)	1.1135(2)	0.1946(1)	0.3785(2)	4.22(4)
O(3)	0.3630(2)	0.0422(1)	0.2887(2)	4.72(4)
H(C2)	0.674(3)	−0.019(2)	0.276(2)	1.7(4)
H(C5)	0.944(2)	0.285(2)	0.568(2)	1.9(4)
H(C6)	0.682(2)	0.219(2)	0.590(2)	1.8(4)
H1(C7)	0.872(2)	−0.117(2)	0.201(3)	1.8(4)
H2(C7)	0.776(3)	−0.044(2)	0.050(3)	2.2(4)
H3(C7)	0.967(3)	−0.085(2)	0.068(3)	2.5(4)
H1(C8)	1.231(3)	0.276(2)	0.581(3)	4.0(6)
H2(C8)	1.127(3)	0.348(2)	0.423(3)	3.7(6)
H3(C8)	1.315(4)	0.284(2)	0.434(3)	5.0(6)
H(C9)	0.437(2)	0.111(1)	0.515(2)	1.0(3)
H(O3)	0.254(5)	0.055(2)	0.295(4)	5.7(7)

[a] $T = 290$ K. $B_{eq} = \frac{4}{3} \sum_i \sum_j \beta_{ij}\, a_i\, a_j$.

All bond distances and bond angles are normal, as is evident from Tables 5 and 6, as are the orientations of the methoxy groups. The maximum deviation of the benzene ring carbon atoms from the respective aromatic ring plane is 0.005(1) Å in **2b** and 0.003(1) Å in **2c**. As expected, the methoxy oxygen atoms as well as the benzylic carbon atoms are situated almost in the respective ring planes. The methoxy carbon atoms are also situated near the ring planes; the largest deviations are 0.038(4) Å in **2b** and 0.069(4) Å in **2c**. The two aromatic ring planes are parallel to each other in both **2b** and **2c**; this follows from the molecular symmetry.

Experimental

Tetrahydrofuran (THF) was freshly distilled over Na. Silica gel for flash chromatography was Merck Kieselgel 60 (230–400 mesh). Melting points were determined using an Olympus BHA polarizing microscope in conjunction with a Mettler FP52 hot stage and FP5 control unit.

^{1}H NMR spectra were recorded at 270 MHz with a Bruker WH270 instrument (temperature ≈ 300 K). Deuteriochloroform was used as a solvent (internal reference, Me_4Si).

Thin layer chromatography (TLC) was performed on silica gel plates (Merck, Kieselgel 60 F_{254}) with toluene–dioxane–acetic acid (90:25:4) (R_F values: **3c**, 0.14; **2c**, 0.15; **3b**, 0.27; **2b**, 0.30; **3a**, 0.34; **2a**, 0.36) and ethyl acetate (R_F values: **3c**, 0.32; **2c**, 0.33; **3b**, 0.49; **2b**, 0.52; **3a**, 0.56; **2a**, 0.57) as eluents. Spots were made visible by UV light and by spraying with formalin–H_2SO_4 (1:9) and subsequent heating.

Table 5. Bond distances (Å) and angles (°) in *meso*-hydroanisoin (**2b**), $C_{16}H_{18}O_4$.

Bond distances

C(1)–C(2)	1.384(2)	C(3)–C(4)	1.377(2)	C(4)–O(1)	1.375(2)
C(1)–C(6)	1.383(2)	C(4)–C(5)	1.376(2)	C(7)–O(1)	1.425(3)
C(1)–C(8)	1.512(2)	C(5)–C(6)	1.390(2)	C(8)–O(2)	1.427(2)
C(2)–C(3)	1.380(2)	C(8)–C(8)′	1.528(3)		

Bond angles

C(2)–C(1)–C(6)	118.1(1)	C(1)–C(6)–C(5)	121.6(2)
C(2)–C(1)–C(8)	120.5(1)	C(1)–C(8)–C(8)′	112.8(1)
C(6)–C(1)–C(8)	121.4(1)	C(3)–C(4)–O(1)	115.5(2)
C(1)–C(2)–C(3)	121.0(2)	C(5)–C(4)–O(1)	124.2(2)
C(2)–C(3)–C(4)	120.1(2)	C(1)–C(8)–O(2)	111.8(1)
C(3)–C(4)–C(5)	120.3(2)	C(8)′–C(8)–O(2)	106.3(1)
C(4)–C(5)–C(6)	119.0(2)	C(4)–O(1)–C(7)	117.1(2)

Hydrogen bonds

O–H···O	O···O	H···O	∠O···O
O(2)–H(O2)···O(2) (1−*x*, 1/2+*y*, 3/2−*z*)	2.761(1)	1.95(2)	173(2)

Torsion angles

C(2)–C(1)–C(8)–C(8)′	−101.2(2)	C(1)–C(8)–C(8)′–O(2)′	57.1(1)
C(2)–C(1)–C(8)–O(2)	139.1(2)	O(2)–C(8)–C(8)′–O(2)′	−180.0(2)
C(1)–C(8)–C(8)′–C(1)′	−180.0(2)	C(5)–C(4)–O(1)–C(7)	−0.9(3)

Table 6. Bond distances (Å) and angles (°) in *meso*-hydroveratroin (**2c**), $C_{18}H_{22}O_6$.

Bond distances

C(1)–C(2)	1.401(2)	C(3)–C(4)	1.401(2)	C(3)–O(1)	1.366(2)
C(1)–C(6)	1.372(3)	C(4)–C(5)	1.376(2)	C(4)–O(2)	1.367(2)
C(1)–C(9)	1.510(2)	C(5)–C(6)	1.394(3)	C(7)–O(1)	1.422(2)
C(2)–C(3)	1.375(2)	C(9)–C(9)′	1.533(4)	C(8)–O(2)	1.415(3)
				C(9)–O(3)	1.424(2)

Bond angles

C(2)–C(1)–C(6)	118.8(2)	C(2)–C(3)–O(1)	125.1(2)
C(2)–C(1)–C(9)	119.4(2)	C(4)–C(3)–O(1)	114.8(1)
C(6)–C(1)–C(9)	121.8(2)	C(3)–C(4)–O(2)	114.6(1)
C(1)–C(2)–C(3)	120.5(2)	C(5)–C(4)–O(2)	125.8(2)
C(2)–C(3)–C(4)	120.1(2)	C(1)–C(9)–O(3)	108.8(1)
C(3)–C(4)–C(5)	119.6(2)	C(9)′–C(9)–O(3)	109.8(2)
C(4)–C(5)–C(6)	119.8(2)	C(3)–O(1)–C(7)	116.8(1)
C(1)–C(6)–C(5)	121.2(2)	C(4)–O(2)–C(8)	117.4(2)
C(1)–C(9)–C(9)′	111.6(2)		

Hydrogen bonds

O–H···O	O···O	H···O	∠O–H···O
O(3)–H(O3)···O(1) ($x-1$, y, z)	3.102(2)	2.24(4)	154(2)
O(3)–H(O3)···O(2) ($x-1$, y, z)	3.078(2)	2.34(3)	137(2)

Torsion angles

C(2)–C(1)–C(9)–C(9)′	67.2(2)	O(3)–C(9)–C(9)′–O(3)′	180.0(2)
C(2)–C(1)–C(9)–O(3)	−54.0(2)	C(2)–C(3)–O(1)–C(7)	1.2(2)
C(1)–C(9)–C(9)′–C(1)′	180.0(2)	C(5)–C(4)–O(2)–C(8)	0.8(2)
C(1)–C(9)–C(9)′–O(3)′	59.3(2)		

Ion exchange chromatography. Separation of the *racemic* and *meso* forms of the hydrobenzoins was accomplished by ion exchange chromatography; this was carried out on an anion exchange column (25 g QAE-Sephadex A-25, Pharmacia; column dimensions: 2×36 cm) using 0.06 M $K_2B_4O_7$ in acetone–water (1:4) as the eluent. Bed volume: 125 ml. Fractions of 11 ml were collected. Flow rate: ca. 60 ml h^{-1}. The samples were dissolved in 10–20 ml of the eluent and applied to the column. Results from analytical experiments are summarized in Table 1.

^1H NMR spectrometric determination of the meso *form/ racemic form ratio of hydrobenzoins in crude synthetic products*. A sample of the crude product (ca. 15 mg) was

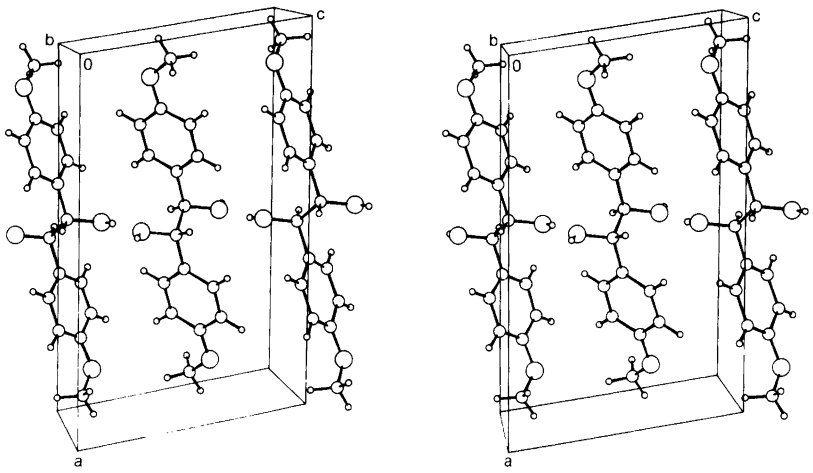


Fig. 1. Stereoscopic view[14] of the unit cell of *meso*-hydroanisoin (**2b**).

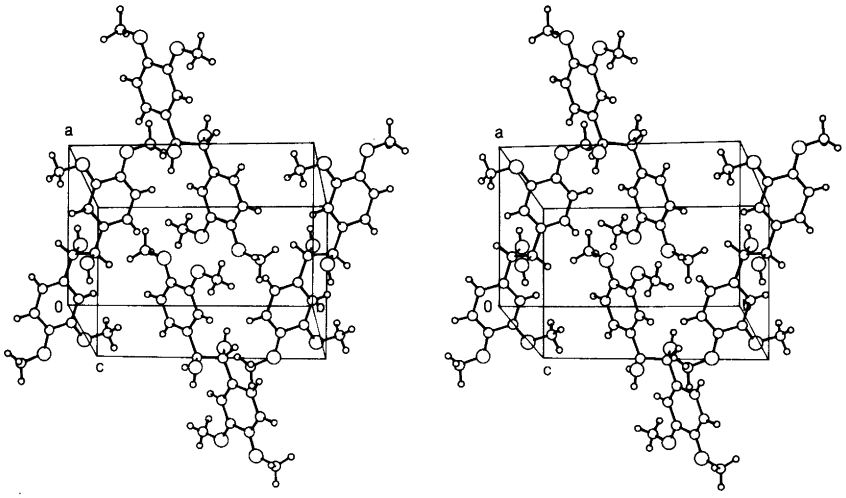


Fig. 2. Stereoscopic view[14] of the unit cell of *meso*-hydroveratroin (**2c**).

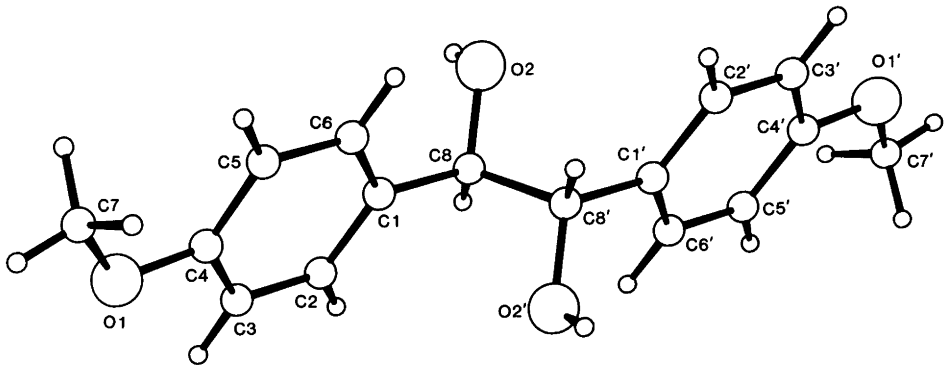


Fig. 3. The *meso*-hydroanisoin molecule showing the atomic numbering.

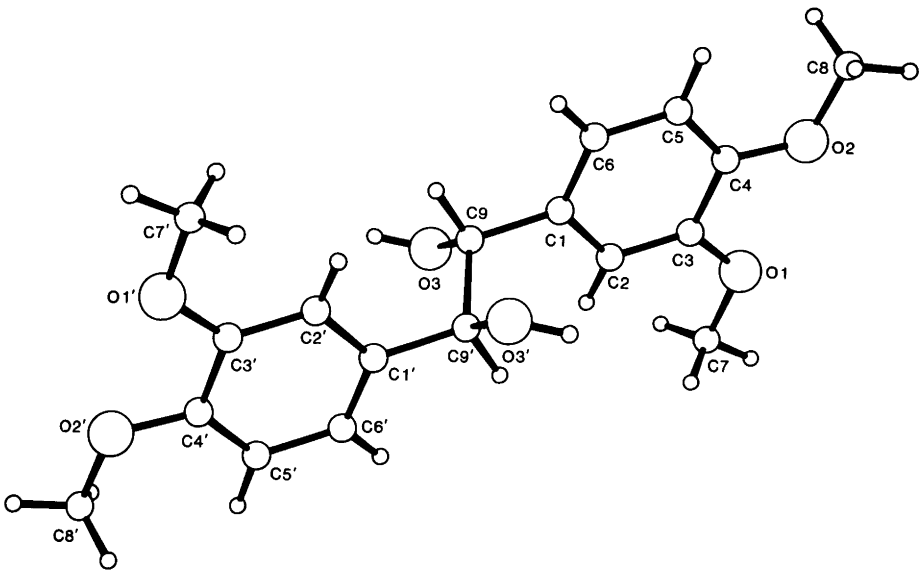


Fig. 4. The *meso*-hydroveratroin molecule showing the atomic numbering.

Table 7. Crystal and experimental data for *meso*-hydroanisoin (**2b**), $C_{16}H_{18}O_4$, and *meso*-hydroveratroin (**2c**), $C_{18}H_{22}O_6$.

	meso-Hydroanisoin	*meso*-Hydroveratroin
M_r	274.32	334.37
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$ (No. 14)	$P2_1/n$ (No. 14)
Unit cell dimensions/Å or °	a = 15.269(6)	a = 8.185(2)
	b = 5.035(2)	b = 12.605(3)
	c = 9.198(4)	c = 8.414(2)
	β = 98.75(3)	β = 109.74(2)
	V = 698.9(5)	V = 817.1(3)
Z	2	2
D_c/g cm^{-3}	1.304	1.359
μ(Mo K_α)/mm^{-1}	0.100	0.109
Crystal size/mm	0.10×0.54×0.88	0.25×0.27×0.27
No. of reflections for cell determination (θ range/°)	15	15
	(4.6<θ<14.6)	(3.0<θ<14.4)
Scan mode	ω–2θ	ω–2θ
2θ range/°	3.5<2θ<50.0	3.5<2θ<50.0
2θ scan speed/° min^{-1}	2.9–9.8	1.5–3.9
Total No. of reflections measured	1383	1517
No. of observed independent reflections [I>3σ(I)]	1047	1086
Test reflections (% standard deviation)	2 2 $\bar{1}$ (1.6)	0 2 2 (1.1)
	7 1 1 (1.7)	2 1 $\bar{1}$ (1.0)
No. of parameters refined	127	153
Weights calculated according to	a = 4.0	a = 4.0
$w = (a + \lvert F_o\rvert + c\lvert F_o\rvert^2)^{-1}$	c = 0.04	c = 0.04
R (R_w)	0.039 (0.045)	0.036 (0.042)
Maximum residual electron density/e Å^{-3}	0.26	0.14

treated with a mixture of acetic anhydride (1.5 ml) and pyridine (1.5 ml) overnight (25 ml flask). The reaction was quenched by addition of ethanol. Acetic acid and pyridine were released by the sequential addition and removal (film evaporation) of ethanol (10–15 ml) 6–7 times. The products were analysed by ^{1}H NMR spectrometry and the relative yield of the diastereoisomers was determined from integrations of the signals from acetate groups, benzylic protons and methoxy groups. Qualitative ^{1}H NMR spectral data for the hydrobenzoins examined (**2**, **3**) are summarized in Table 2.

Syntheses

Anisoin (**1b**) was prepared according to Sumrell *et al.*[8a] using ethanol–water as the reaction medium. M.p. 109–111 °C (lit.[8b] 113 °C).

Veratroin (**1c**) was prepared by refluxing a mixture of veratraldehyde (15.0 g, distilled *in vacuo*) and KCN (3.0 g) in 60 ml of ethanol–water (3:1) (cf. Kubiczek[9]). Water (150 ml) was added to the reaction product and the mixture was extracted with chloroform (200 + 100 ml). The extract was dried over Na_2SO_4 and solvents removed by film evaporation. Veratroin was isolated from the residue (14.5 g) by flash chromatography. A 2.9 g portion of the crude product gave 1.2 g essentially pure veratroin on flash chromatography on 65 g silica gel using ethyl acetate–dichloromethane (9:1) as the eluent. Veratroin was found in the eluate 200–550 ml.

Preparation of meso-*hydroanisoin* (**2b**) *by reduction of anisoin with* $NaBH_4$. A mixture of anisoin (3.00 g), $NaBH_4$ (0.63 g), ethanol (75 ml) and 0.1 M NaOH (75 ml) was stirred magnetically for 3.5 h at room temperature. Water (100 ml) and 2 M HCl (13.5 ml) was added to the reaction mixture (final pH < 3) which, subsequently, was transferred to a separatory funnel and extracted with chloroform (200 ml, 100 ml and 50 ml). The extract was dried over Na_2SO_4 and the solvent was removed by film evaporation. The residue weighed 2.9 g. Recrystallization of the product from ethanol gave 2.05 g *meso*-hydroanisoin of m.p. 171–172 °C (lit.[4] 167–168 °C). Yield: 68 %.

Preparation of meso-*hydroveration* (**2c**) *by reduction of veratroin with* $NaBH_4$. This was performed according to the analogous synthesis of hydroanisoin described above. Recrystallization of the product from ethanol gave *meso*-hydroveratroin of m.p. 205–206 °C (lit.[5] 210–211 °C) in 58 % yield.

Preparation of meso-hydroveratroin (**2c**) *by reduction of veratroin with borane–dimethyl sulfide complex.* Borane–dimethyl sulfide complex (3.0 ml of a 2 M solution in THF) was injected into a solution of 2.0 g veratroin in 25 ml THF (argon atmosphere). The mixture was kept for 2 h at room temperature (magnetic stirring). Methanol (5 ml) was

slowly added to decompose excess borane reagent. Solvents were removed by film evaporation. To ensure complete removal of boric acid a second portion of methanol was added and subsequently removed by film evaporation. Recrystallization of the product from ethanol gave 1.57 g of *meso*-hydroveratroin of m.p. 203–205 °C. Yield: 78 %.

(±)-Hydroanisoin (**3b**). Anisoin (6.00 g) was reduced with $NaBH_4$ using the procedure described above. Recrystallization of the crude product (5.83 g) from ethanol gave *meso*-hydroanisoin (4.34 g). The residue (1.38 g) obtained on evaporation of the solvent from the mother liquor was divided into two portions and subjected to ion exchange chromatography on QAE-Sephadex A-25 (38 g). The conditions were those used in the analytical experiments described above. The eluate containing (±)-hydroanisoin (TLC) was extracted with chloroform. Drying (Na_2SO_4) and removal of solvents gave crude (±)-hydroanisoin (0.96 g). Crystallization from ethanol–water (2:1) gave (±)-hydroanisoin (0.76 g) of m.p. 118–120 °C. Recrystallization raised the m.p. to 121–122 °C (lit.[4] 120–123 °C).

(±)-Hydroveratroin (**3c**). Mother liquors from the reduction experiments with veratroin were collected and the major part of residual *meso*-hydroveratroin was released by crystallization from ethanol. Repeated ion exchange chromatography [cf. the preparation of (±)-hydroanisoin] and subsequent chromatography on a silica gel column [eluent: acetone–dichloromethane (1:5)] gave a product which, according to ^1H NMR spectroscopy and analytical ion exchange chromatography, was (±)-hydroveratroin. Crystallization from ethanol gave a product which melted over the range 140–160 °C. Dissolution in chloroform and subsequent removal of the chloroform gave, however, a product with the m.p. reported for (±)-hydroveratroin in the literature (169–170 °C[5]).

*Hydrobenzoin [*meso (**2a**) *and racemic* (**3a**) *forms]* was prepared from commercial benzoin according to the procedures used for the preparation of the corresponding isomers of hydroanisoin described above.

X-Ray work. Crystal and experimental data for **2b** and **2c** are given in Table 7. Rotation and Weissenberg photographs were taken of both compounds (Cu K_α radiation) from which crystal symmetry, conditions for reflections and approximate cell dimensions were obtained. Diffracted intensities were measured with a Syntex $P2_1$ diffractometer, using graphite-monochromated Mo K_α radiation. Periodic measurements of test reflections showed no loss in 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 15 reflections for each crystal used.

Structure determination. (a) meso-*Hydroanisoin* (**2b**). Two different crystals were examined. Crystal **I** has the cell dimensions given in Table 7. Crystal **II** showed a diffraction pattern which could be indexed according to a unit cell with $a = 30.558(12)$, $b = 5.029(2)$, $c = 9.221$ Å, $\beta = 98.61(3)°$, $V = 1401.0(9)$ Å^3, $Z = 4$. Within the limits of experimental error, crystal **II** has a unit cell twice as large as crystal **I**. In both cases the space group is $P2_1/c$. Crystal **II** showed, however, further, unusual reflection conditions; this might indicate twin formation.

The atomic coordinates of all non-hydrogen atoms were determined by direct methods (MITHRIL[10]). Least-squares refinement of positional and thermal parameters for the non-hydrogen atoms gave $R = 0.142$ (isotropic thermal parameters) and 0.084 (anisotropic thermal parameters), respectively, for crystal **I**. The corresponding *R*-values for crystal **II** became 0.226 and 0.199, respectively. In the latter case there were large differences between the observed and calculated structure factors for certain reflections. Comparison between the two structure models revealed that crystal **II** is, in fact, a twin crystal, consisting of two fragments P and Q. Incidentally, within the limits of experimental error $\mathbf{b}_Q = -\mathbf{b}_P$, $\mathbf{c}_Q = -\mathbf{c}_P$ and $\mathbf{a}_Q = 1/2(2\mathbf{a}_P + \mathbf{c}_P)$, leading to a diffraction pattern for the twin crystal **II** consistent with a 'unique' unit cell with $\mathbf{A} = 2\mathbf{a}_P$, $\mathbf{B} = \mathbf{b}_P$ and $\mathbf{C} = \mathbf{c}_P$. Thus, no splitting of the reflections was observed.

The subsequent structure analysis was performed on data from crystal **I**. An electron density difference map based on the parameters obtained according to the refinement of positional and anisotropic thermal parameters for the non-hydrogen atoms revealed all hydrogen atoms (maximum electron density 0.72 e Å^{-3}. Inclusion of atomic coordinates and isotropic thermal parameters for the hydrogen atoms in the refinement gave $R = 0.039$. The twin model was further tested by calculating the R = value for *hkl*-reflections from crystal **II** with *h* odd (these are due to only one of the twin fragments); R 0.053 was obtained using the atomic parameters arrived at for crystal **I**.

(b) meso-*Hydroveratroin* (**2c**). All non-hydrogen atoms could be located by direct methods (MITHRIL[10]). Least-squares refinement of positional and thermal parameters for these atoms led to the R values 0.125 (isotropic thermal parameters) and 0.087 (anisotropic thermal parameters), respectively. An electron density difference map based on these last two parameters revealed all hydrogen atomic positions. The introduction of these and isotropic thermal parameters for the hydrogen atoms in the refinement gave a final R value of 0.036.

Further details concerning the refinement of the structures are summarized in Table 7. Atomic scattering factors were taken from Ref. 11. Calculations were carried out on an IBM 3081 computer, using the crystallographic programs described in Refs. 12 and 13. Lists of structure factors and anisotropic thermal parameters are available from one of the authors (R.S.) on request.

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