Gnidifolin [*trans*-2-(2,4-Dihydroxy-3-methoxybenzyl)-3-(4'-hydroxy-3'-methoxybenzyl)-butyrolactone]

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Abstract. $C_{20}H_{22}O_7$, orthorhombic, $P2_12_12_1$, $a = 21\cdot126$ (5), $b = 10\cdot538$ (3), $c = 8\cdot264$ (3) Å ($\lambda = 1\cdot5418$ Å), $U = 1840$ Å^3, $Z = 4$, $D_x = 1\cdot351$ g cm^{-3}. The structure was solved by the multisolution tangent-formula method. Least-squares refinement, with anisotropic thermal parameters for the C and O atoms, and with fixed contributions for 19 H atoms, gave $R = 0\cdot064$ for 1287 independent significant $[I > 3\sigma(I)]$ reflections whose intensities were measured by automatic single-crystal diffractometry with mono-chromatic Cu $K\alpha$ radiation, scintillation counting, and pulse-height analysis. This new lignan, isolated from *Gnidia latifolia* Gilg., has been identified by the X-ray analysis as the title compound. The lactone ring has an envelope conformation with C(3) displaced by 0·48 Å from the least-squares mean plane of the remaining four ring atoms.

Introduction. In the course of an extensive phyto-chemical study of plants of the *Gnidia* genus, designed to yield antitumor agents (Kupchan, Sweeny, Baxter, Murae, Zimmerly & Sickles, 1975; Kupchan, Sweeny, Murae, Shen & Bryan, 1975; Kupchan *et al.*, 1976; Kupchan, Shizuri, Baxter & Haynes, 1977), Kupchan and his co-workers isolated an inactive lignan from *Gnidia latifolia* Gilg. (Thymelaeaceae) whose physical and chemical properties established it as a previously unknown compound. Its identity and structure have been determined by single-crystal X-ray analysis (Shen, Bryan, Baxter, Sweeny & Kupchan, 1974).
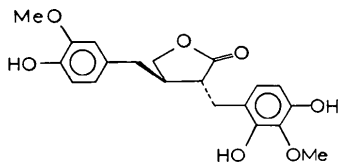
Crystals suitable for X-ray study were provided by Professor S. M. Kupchan. Systematic absences in the axial reflections of odd order, observed on 25° precession photographs taken with Mo $K\alpha$ radiation, uniquely define the space group. Intensity measurements were made with an automatic Picker full-circle diffractometer by use of the $\theta/2\theta$ scan method with a scan

Table 1. *Fractional coordinates* ($\times 10^4$) *and equivalent isotropic B values* (Å^2)

	x	y	z	B
O(1)	364 (3)	3045 (6)	6159 (6)	4·71
O(4)	898 (3)	4766 (5)	5385 (6)	4·25
O(3')	2824 (3)	8039 (6)	1194 (7)	4·63
O(4')	2286 (3)	8686 (5)	−1634 (7)	4·61
O(2'')	278 (3)	2799 (5)	−527 (6)	3·46
O(3'')	−797 (3)	3943 (5)	−1818 (6)	3·72
O(4'')	−1808 (3)	4501 (6)	155 (7)	4·93
C(1)	685 (4)	3585 (8)	5166 (9)	3·80
C(2)	908 (4)	3044 (7)	3562 (9)	3·03
C(3)	1108 (4)	4277 (7)	2640 (9)	3·11
C(4)	1291 (4)	5147 (8)	3999 (9)	3·67
C(5)	1620 (4)	4033 (8)	1376 (9)	3·22
C(6)	405 (4)	2161 (7)	2752 (9)	3·59
C(1')	1812 (3)	5230 (7)	524 (9)	2·98
C(2')	2262 (4)	6038 (8)	1247 (9)	3·46
C(3')	2416 (3)	7206 (8)	543 (9)	3·11
C(4')	2140 (4)	7542 (7)	−926 (9)	3·19
C(5')	1703 (4)	6786 (8)	−1646 (10)	3·84
C(6')	1536 (4)	5596 (8)	−904 (9)	3·37
C(7')	3033 (4)	7840 (9)	2857 (11)	4·85
C(1'')	−174 (3)	2831 (7)	2115 (9)	2·67
C(2'')	−218 (3)	3123 (7)	444 (9)	2·74
C(3'')	−744 (4)	3692 (7)	−170 (9)	3·05
C(4'')	−1267 (4)	3988 (8)	795 (10)	3·64
C(5'')	−1227 (4)	3760 (9)	2475 (11)	4·46
C(6'')	−681 (4)	3162 (8)	3070 (10)	3·82
C(7'')	−535 (4)	5135 (8)	−2284 (11)	4·64
H(2)	1302	2467	3712	4·00*
H(3)	726	4610	2016	
H(4a)	1200	6081	3698	
H(4b)	1745	5080	4281	
H(5a)	1469	3409	562	
H(5b)	2002	3666	1956	
H(6a)	275	1482	3573	
H(6b)	612	1675	1811	
H(2')	2471	5736	2261	
H(5')	1480	7026	−2676	
H(6')	1217	5065	−1418	
H(7'a)	2798	7157	3336	
H(7'b)	2992	8654	3462	
H(7'c)	3504	7626	2746	
H(5'')	−1574	3973	3235	
H(6'')	−674	2936	4262	
H(7''a)	−479	5218	−3460	
H(7''b)	−841	5959	−1876	
H(7''c)	−111	5277	−1725	

* Hydrogen atoms have been labelled to correspond to the carbon of attachment and have been assigned $b = 4\cdot0$ Å^2.

range of 2° in 2θ and a scan speed of 2° min⁻¹. The reflections in an octant of reciprocal space were surveyed with Cu $K\alpha$ radiation using a graphite-crystal monochromator. Intensity significantly above background $[I > 3\sigma(I)]$ was measured at 1287 of the 1362 reciprocal-lattice points with $2\theta < 120°$. Structure amplitudes were derived from these intensities without application of any correction for absorption $[\mu(\text{Cu } K\alpha) = 8.7 \text{ cm}^{-1}]$.

The structure was solved by use of the program *MULTAN* (Germain, Main & Woolfson, 1971) with the 199 $E(hkl) > 1.36$. The atomic parameters were refined by block-diagonal least-squares methods (3 × 3, 6 × 6 blocks) by minimizing the quantity $\Sigma w(|F_o| - k|F_c|)^2$ with a conventional weighting scheme (Hughes, 1941). Anisotropic thermal parameters were used for C and O. From difference electron-density maps the 19 H atoms attached to C were located. These atoms were assigned isotropic B values of 4.0 Å² and contributions for them, in fixed positions, included in the least-squares calculations. At convergence $[\Delta(p) < 0.15\sigma(p)]$ the conventional unweighted and weighted residuals were 0.064 and 0.068.*

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* Lists of structure factors and anisotropic thermal parameters, and details of least-squares mean planes of interest, have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33027 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.
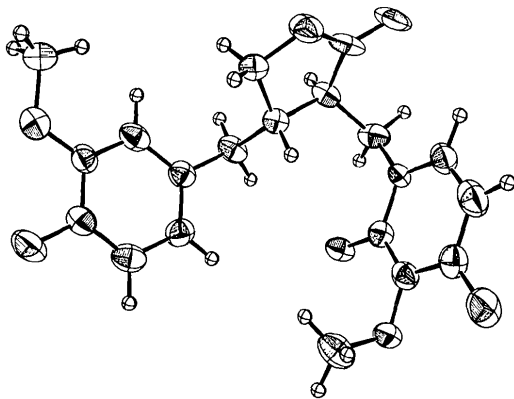
A final $(\rho_o - \rho_c)$ map calculated from structure factors based on all located atoms failed to reveal the positions of the hydroxy H atoms and contained no other structurally significant density. The scattering functions used were taken from Hanson, Herman, Lea & Skillman (1964). No conclusive difference between the two possible enantiomeric structures emerged when account was taken of the anomalous-dispersion terms for O, and the absolute configuration has not been determined. Final atomic coordinates and isotropic thermal parameters are in Table 1. An *ORTEP* plot of the molecule is shown in Fig. 1.

Discussion. The X-ray study has established the chemical identity of the molecule as *trans*-2-(2,4-dihydroxy-3-methoxybenzyl)-3-(4'-hydroxy-3'-meth-oxybenzyl)butyrolactone. Bond distances and angles within the molecule are unexceptional (Fig. 2). The lactone ring has an envelope conformation with C(3) displaced by 0.48 Å from the rigorously coplanar unit formed by the remaining four ring atoms.* The two methylene groups C(5) and C(6) are in a (−)-synclinal relation about the C(2)—C(3) bond, the torsion angle being −84°. The torsion angles C(4)—C(3)—C(5)—C(1') and C(1)—C(2)—C(6)—C(1") are −62 and 70° respectively (see Table 2). As may be seen from consideration of the torsion angles about C(5)—C(1') and C(6)—C(1"), the orientations of the phenyl groups with respect to the bonds C(5)—C(3) and C(6)—C(2) are very similar.
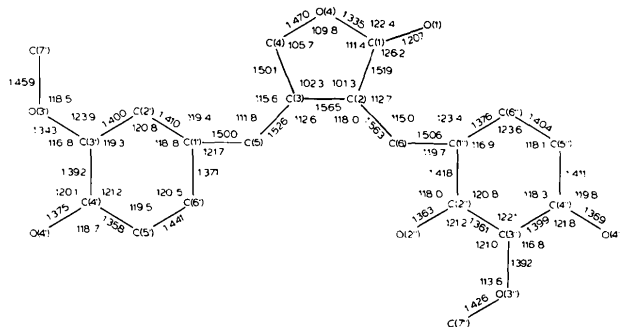
* See deposition footnote.

Fig. 1. *ORTEP* plot with boundary surfaces for C and O drawn at the 50% probability level and arbitrarily for H.

Fig. 2. Bond lengths (Å) and valence angles (°). E.s.d.'s are 0.008–0.011 Å and 0.60–0.75°.

Table 2. *Selected torsion angles* (°)

C(5)—C(3)—C(2)—C(6)	−84	C(1)—C(2)—C(3)—C(4)	28
C(1)—C(2)—C(6)—C(1")	70	C(2)—C(3)—C)4)—O(4)	−30
O(1)—C(1)—C(2)—C(6)	36	C(3)—C(4)—O(4)—C(1)	20
C(2)—C(6)—C(1")—C(6")	−82	C(4)—O(4)—C(1)—C(2)	−1
C(2)—C(6)—C(1")—C(2")	99	O(4)—C(1)—C(2)—C(3)	−18
C(4)—C(3)—C(5)—C(1')	−62	C(3)—C(5)—C(1')—C(2')	83
C(3)—C(5)—C(1')—C(6')	−93	C(2')—C(3')—O(3')—C(7')	−12
C(2")—C(3")—O(3")—C(7")	−87		

The C(3') methoxy group is nearly coplanar with the phenyl ring. By contrast, due to the presence of the C(2'') hydroxy group, the C(3'') methoxy group is aligned with O(3'')–C(7'') nearly perpendicular to the phenyl ring plane. The steric crowding resulting from multiple substitution of the phenyl rings has an effect on the planarity of the rings, with larger than normal deviations from coplanarity being found. Particularly affected are C(3') and C(4'), which are 0·015 and 0·012 Å out of plane, and C(3''), C(4'') and C(5''), which are 0·013, 0·025, and 0·019 Å out of plane.

Although the H atoms of the hydroxy groups could not be found, all three hydroxy groups are presumed to take part in hydrogen bonding, as shown by the intermolecular O···O distances O(1)···O(2''), 2·76 Å; O(4'')···O(3'), 2·93 Å; O(4'')···O(4'), 2·97 Å; and the angles O(1)···O(2'')–C(2''), 128°; C(4'')–O(4'')···O(3'), 136°; and C(4')–O(4')···O(4''), 122°. It is assumed that O(4'') acts as a donor toward O(4') of the same neighbor, but we cannot rule out the possibility that O(4'') may act as a donor

toward O(4') with the proton of the latter not being involved in hydrogen-bond formation.

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5,5'-Diethoxycarbonyl-3,3'-diethyl-4,4'-dimethyl-2,2'-pyrromethene

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Abstract. $C_{21}H_{28}N_2O_4$, monoclinic, $P2_1/c$, $a = 20·372$ (4), $b = 4·572$ (1), $c = 24·404$ (4) Å, $\beta = 113·69$ (2)°, $M_r = 372·5$, $Z = 4$, $D_x = 1·19$ g cm^{-3}. The molecule displays a planar *syn–Z* conformation which is stabilized by intramolecular N–H···N hydrogen bonding. The nitrogen proton is statistically disordered between the two N atoms. As, in addition, the geometries of the two rings are similar, this leads to the pyrromethene system displaying approximate C_{2v} symmetry in the crystal lattice.

Introduction. Cell dimensions were determined by a least-squares fit to settings for 15 reflexions ($\pm hkl$) on a Syntex $P2_1$ four-circle diffractometer (Cu $K\alpha$ radiation, $\lambda = 1·54178$ Å). Intensity measurements were carried

out in the θ–2θ mode ($3·0 \leq 2\theta \leq 135·0°$) with graphite-monochromated Cu $K\alpha$ radiation, at scan speeds varying linearly between 2·93 (150 c.p.s. and below) and 29·30° min^{-1} (4000 c.p.s. and above). Scan and background times were equal. A Lorentz–polarization correction was applied; an absorption [μ(Cu $K\alpha$) = 5·9 cm^{-1}] correction was not applied. After application of the acceptance criterion $F \geq 3·0\sigma(F)$, 3157 unique reflexions were retained for use in the structure analysis. The structure was solved by direct methods (*SHELX* 76, G. M. Sheldrick) and refined by blocked full-matrix least squares with anisotropic temperature factors for all the non-hydrogen atoms. The H atom positional parameters were freely refined with individual isotropic temperature factors. A difference synthesis revealed a corresponding H atom for both of the N atoms. These were