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Acta Cryst. (1980). B**36**, 2465–2467

4,7-Dimethoxy-5-methylphthalide

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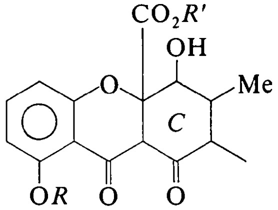
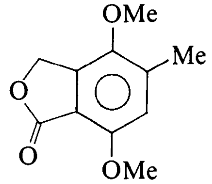
(*Received* 23 *April* 1980; *accepted* 13 *May* 1980)

Abstract. $C_{11}H_{12}O_4$, $M_r = 208{\cdot}2$, m.p. 386 K, monoclinic, $C2/c$, $a = 15{\cdot}475\ (3)$, $b = 10{\cdot}955\ (2)$, $c = 15{\cdot}377\ (5)$ Å, $\beta = 127{\cdot}83\ (2)°$, $V = 2059{\cdot}0$ Å^3, $Z = 8$, $D_c = 1{\cdot}34$ Mg m^{-3}, $F(000) = 440$, Mo $K\alpha$ radiation, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}031$ mm^{-1}. $R = 0{\cdot}065$ for 1145 reflexions with $I > 3\sigma(I)$. The analysis establishes the compound to be the 5-methyl derivative.

Introduction. In the course of experiments directed towards the elaboration of molecules of type (I) characteristic of the ergot pigments (Hooper, Marlow, Whalley, Borthwick & Bowden, 1971), we required 4,7-dimethoxy-5-methylphthalide (II) as a potential synthon for ring *C* of these metabolites. The preparation of (II), together with the isomeric 4,7-dimethoxy-6-methylphthalide, has been reported (Ahad, Banham, Whalley, Ferguson & Siew, 1980), but attempts to differentiate between these isomers by chemical and spectroscopic means were unsuccessful. Hence, as a necessary preliminary to our subsequent work, one of the isomers was examined crystallographically and identified as (II).



(I)



(II)

The space group and preliminary unit-cell information were obtained by photographic measurements. The systematic absences (hkl when $h + k = 2n + 1$, $h0l$ when $h = 2n + 1$ and $l = 2n + 1$) are indicative of space groups $C2/c$ or Cc; space group $C2/c$ was confirmed by successful refinement.

The cell dimensions were refined by least squares from the diffractometer angles of 12 reflexions with θ(Mo $K\alpha$) > 10°. Intensities were measured with an acicular (c) crystal $0{\cdot}24 \times 0{\cdot}24 \times 0{\cdot}72$ mm mounted with c parallel to the axis of a Hilger & Watts Y290 four-circle diffractometer (Ferguson & Roberts, 1978).

Table 1. *Final fractional coordinates* ($\times 10^4$) *with e.s.d.'s in parentheses*

The values in the U_{av} column are the means of the U_{11}, U_{22} and U_{33} values for the atoms ($\times 10^3$).

	x	y	z	U_{av} (Å^2)
C(1)	3929 (3)	4294 (3)	7829 (3)	57
C(2)	4608 (3)	3303 (3)	8401 (3)	56
C(3)	5690 (3)	3550 (4)	9301 (3)	66
C(4)	6077 (3)	4736 (4)	9611 (3)	68
C(5)	5383 (3)	5711 (4)	9009 (4)	76
C(6)	4288 (3)	5483 (3)	8115 (3)	66
C(7)	3344 (3)	6303 (4)	7330 (4)	74
C(8)	2775 (3)	4310 (3)	6873 (3)	58
C(9)	5375 (6)	7851 (6)	9214 (7)	142
C(10)	7255 (3)	4951 (6)	10597 (4)	91
C(11)	4839 (4)	1128 (4)	8598 (4)	82
O(1)	2454 (2)	5483 (3)	6591 (2)	72
O(2)	2135 (2)	3495 (3)	6358 (2)	72
O(3)	5851 (4)	6857 (4)	9328 (6)	145
O(4)	4176 (2)	2174 (3)	8045 (2)	70

Table 2. *Bond distances* (Å) *and angles* (°)

Values in parentheses are the e.s.d.'s in the last decimal place and are calculated from the covariance matrix of the last refinement cycle.

C(1)–C(2)	1·386 (5)	C(5)–C(6)	1·402 (6)
C(1)–C(6)	1·378 (5)	C(5)–O(3)	1·380 (6)
C(1)–C(8)	1·460 (5)	C(6)–C(7)	1·496 (6)
C(2)–C(3)	1·396 (5)	C(7)–O(1)	1·440 (5)
C(2)–O(4)	1·352 (5)	C(8)–O(1)	1·350 (5)
C(3)–C(4)	1·387 (6)	C(8)–O(2)	1·202 (4)
C(4)–C(5)	1·391 (6)	C(9)–O(3)	1·266 (8)
C(4)–C(10)	1·512 (5)	C(11)–O(4)	1·421 (5)
C(2)–C(1)–C(6)	122·5 (3)	C(4)–C(5)–O(3)	116·1 (5)
C(2)–C(1)–C(8)	129·2 (3)	C(6)–C(5)–O(3)	124·5 (5)
C(6)–C(1)–C(8)	108·3 (3)	C(1)–C(6)–C(5)	119·3 (3)
C(1)–C(2)–C(3)	117·3 (3)	C(1)–C(6)–C(7)	107·9 (3)
C(1)–C(2)–O(4)	117·7 (3)	C(5)–C(6)–C(7)	132·8 (4)
C(3)–C(2)–O(4)	125·0 (3)	C(6)–C(7)–O(1)	104·5 (3)
C(2)–C(3)–C(4)	121·7 (3)	C(7)–O(1)–C(8)	110·8 (3)
C(3)–C(4)–C(5)	119·8 (4)	C(1)–C(8)–O(1)	108·5 (3)
C(3)–C(4)–C(10)	119·5 (4)	C(1)–C(8)–O(2)	131·3 (3)
C(5)–C(4)–C(10)	120·8 (5)	O(1)–C(8)–O(2)	120·3 (3)
C(4)–C(5)–C(6)	119·4 (4)	C(2)–O(4)–C(11)	119·9 (3)
		C(5)–O(3)–C(9)	126·8 (5)

Of 1892 reflexions with θ(Mo $K\alpha$) $< 25°$, 697 had $I < 3\sigma(I)$ and were excluded from further calculations. Averaging equivalent reflections and eliminating systematic absences yielded 1145 unique observed reflexions. The structure was solved by weighted multisolution tangent refinement (Germain, Main & Woolfson, 1970) of the phases of 190 reflexions with $|E| > 1{\cdot}2$. The 15 highest peaks in the E map calculated from the phase set of lowest R_α ($=0{\cdot}165$) (Roberts, Pettersen, Sheldrick, Isaacs & Kennard, 1973) corresponded to the 15 non-hydrogen atoms of the molecule.

The structure was refined by full-matrix least squares (Sheldrick, 1976). The H atom positions, obtained from a difference synthesis, were included but not refined. Anisotropic temperature factors were refined for C and O atoms and isotropic for H atoms. The scattering factors of Cromer & Mann (1968) were used for C and O and of Stewart, Davidson & Simpson (1965) for H. The weighting scheme was $w = [\sigma^2(F) + kF^2]^{-1}$ where k is refined by fitting $(F_o - F_c)^2$ to $[\sigma^2(F) + kF^2]$; the final value of k was 0·0129. At convergence, no parameter shift was greater than 0·1 times its e.s.d. Final values of R and $R' = (\sum w\Delta^2/\sum wF_o^2)^{1/2}$ were 0·065 and 0·083 respectively. A final difference synthesis confirmed the completeness of the refinement, there being no chemically significant maxima. Atomic coordinates are in Table 1 and details of the molecular geometry in Table 2.*

Discussion. A view of (II) with the numbering scheme is shown in Fig. 1; the methyl group being in the *para* position to the carbonyl function establishes (II) as the

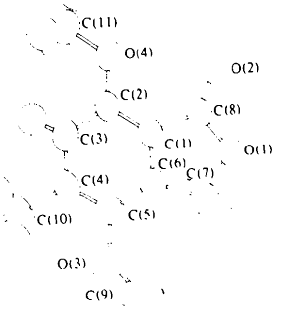


Fig. 1. View of the molecule showing the crystallographic numbering scheme.

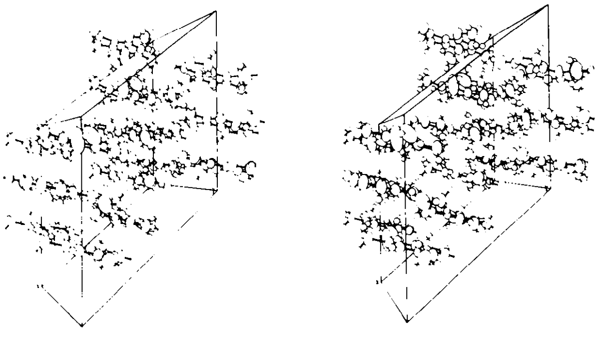


Fig. 2. Stereoview of the crystal structure showing the pattern of stacking along c.

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* Lists of structure factors, hydrogen parameters and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35339 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

5-methyl isomer. The nine atoms of the phthalide ring system are close to coplanar (r.m.s.d. = 0·008 Å) and the six C—C lengths in the aromatic portion of the ring system average 1·390 Å (r.m.s.d. = 0·008 Å) compared with 1·397 ± 0·005 Å in benzene (Sutton, 1965). C(6)—C(7) [1·496 (6) Å] is not significantly different from the expected value (Bartell & Bonham, 1960) (1·505 Å) for a bond between sp^2- and sp^3-hybridized C atoms. Likewise, C(7)—O(1) can be considered normal. On the other side of the five-membered ring, the sp^2-hybridized state of C(8) causes the corresponding lengths, C(8)—C(1) and C(8)—O(1), to be significantly shorter.

The crystal structure (Fig. 2) contains stacks of anti-parallel, planar molecules extending along *c* and formed by centres of symmetry and *c* glides in alternating sequence.

Financial support from the Natural Sciences and Engineering Research Council Canada (in the form of Grants-in-Aid of Research to GF) is gratefully acknowledged.

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Acta Cryst. (1980). B**36**, 2467–2470

Conformation of an O(6)-Substituted Purine Derivative: Structure of 6-Methoxypurine Riboside

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(*Received* 20 *February* 1980; *accepted* 21 *April* 1980)

Abstract. $C_{11}H_{14}N_4O_5.\frac{1}{2}H_2O$, orthorhombic, $P2_12_12_1$, $a = 26.075$ (7), $b = 13.125$ (4), $c = 7.222$ (1) Å, $Z = 8$, $D_c = 1.565$ Mg m^{-3}, μ(Cu $K\alpha$) = 0·99 mm^{-1}. R for the 1743 reflections with $I > \sigma(I)$ is 0·085. The two crystallographically independent molecules assume a conformation in which the methyl group is directed away from the imidazole moiety of the purine base.

Introduction. Various alkylating agents react with nucleic acids *in vivo* and *in vitro*. One of the major reaction sites is the O(6) position of guanine residues. The resulting O(6)-alkyl derivatives would be expected to display one of two favoured conformations about the C(6)—O(6) bond. In order to maintain the partial double-bond character of this bond, the substituent attached to O(6) should lie in or near the purine plane. However, the alkyl group could point either toward or away from the imidazole moiety of the purine. These two alternative conformations might affect the secondary structures of nucleic acids in different ways. For example, if the alkyl group is directed toward the imidazole ring, then the purine derivative might be expected to pair with uracil or thymine bases within double-helical nucleic acids, as postulated by Lawley (1972). On the other hand, if the alternative conformation is assumed, the bulky alkyl group would interfere with any type of Watson–Crick interactions at the reaction site. We determined the crystal structure of 6-methoxypurine riboside to obtain information about

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0567-7408/80/102467-04$01.00