Tetrahedron Vol. 34, pp. 1849–1852

0040-4020/78/0615-1849/$02.00/0

THE CRYSTAL AND MOLECULAR STRUCTURE OF (−)-PHASEOLLIN

C. DEMARTINIS and M. F. MACKAY*

Department of Physical Chemistry, La Trobe University, Bundoora, Victoria, Australia 3083

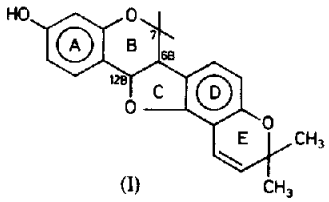
and

B. J. POPPLETON

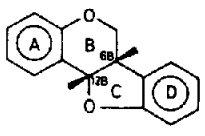
Division of Applied Organic Chemistry, C.S.I.R.O., P.O. Box 4331, G.P.O. Melbourne, Victoria, Australia 3001 and Division of Chemical Physics, C.S.I.R.O., P.O. Box 160, Clayton, Victoria, Australia 3168

(*Received in the UK 8 November 1977; Accepted for publication 9 December 1977*)

Abstract—X-ray analysis has defined the molecular structure of (−)-phaseollin $C_{20}H_{18}O_4$, a pterocarpan with lipophilic antifungal activity, isolated from *Phaseolus vulgaris* L. The orthohombic crystals belong to the space group $P2_12_12_1$ with $a = 6.540(3)$, $b = 12.975(6)$, $c = 19.388(4)$ Å and $Z = 4$. The structure was solved by direct methods from diffractometer data measured with CuKα radiation, and refined to a final R index of 0.083 for the 992 observed terms. The molecular skeleton (I) has a *cis* B/C ring junction. Viewed down C(6B)–C(7) the conformation is staggered; ring C is envelope whereas ring B is skewed with C(6B) and C(7) lying respectively above and below the plane of the other ring atoms.



(I)



(II)

INTRODUCTION

(−)-Phaseollin, $C_{20}H_{18}O_4$, a pterocarpan with lipophilic antifungal activity, has been isolated from *Phaseolus vulgaris* L. (family Leguminosae) following fungal innoculation.[1] Together with a number of structurally-related compounds also isolated from natural sources,[2,3] phaseollin forms a series of pterocarpans which have the basic ring structure (II). Most of these compounds have been found to exhibit antifungal activity[2,4] and, apart from phaseollin and pisatin, $C_{17}H_{14}O_6$,[5] have been extracted from apparently healthy plant tissue. Some earlier studies of pterocarpans and derivatives led to the proposal that their characteristic antifungal activity may depend upon the molecular shape.[2] For the benzofurobenzopyran ring system, which has asymmetric centres C(6B), C(12B), a *cis* B/C ring junction was concluded from consideration of Dreiding models.[6] Of the two possible conformations resulting from the *cis* fusion, proton magnetic resonance data indicated assignment of the staggered.[7]

Apart from the configuration at 6B, 12B, the molecular formula (I) assigned to phaseollin was based on UV,[1] IR and NMR spectra.[8] An X-ray analysis of crystals of phaseollin was undertaken to define the structure and so establish unequivocally the conformation of the basic structure (II). A report of this work which included the essential features of the molecular structure has been presented earlier.[9]

EXPERIMENTAL

Colourless orthorhombic needles of phaseollin, $C_{20}H_{18}O_4$, were found from Weissenberg photographs to belong to the space group $P2_12_12_1$. Accurate unit cell parameters were determined by a least-squares fit of 2θ values, measured for fifteen strong reflections on a four-circle diffractometer with CuKα radiation. The crystal density was determined by flotation in a xylene-bromoform mixture and indicated four molecules in the unit cell.

Crystal data. (−)-Phaseollin, $C_{20}H_{18}O_4$. F.W. = 322.36, Orthorhombic space group $P2_12_12_1$. $a = 6.540(3)$, $b = 12.975(6)$, $c = 19.388(4)$ Å, $U = 1645.2(1.1)$ Å^3; F(000) = 680, $D_m = 1.30$, $D_c = 1.30$ g cm^{-3}, $Z = 4$; μ(CuKα) = 6.50 cm^{-1}. Three-dimensional intensity data were measured with CuKα radiation (graphite crystal monochromator) on a Rigaku-AFC four-circle diffractometer. The crystal was aligned with its a axis, the longest crystal axis, approximately parallel to the ϕ axis of the diffractometer. The intensities were recorded by the ω-2θ scan technique with a scan rate of 4° min^{-1} and 10 s stationary background counts. Three reference reflections were monitored every 50 reflections and showed no significant variation in intensity over the data collection period. Of the 1621 non-equivalent terms measured to a 2θ maximum of 130°, 992 had values for which $|F_o| > 3\sigma|F_o|$ and thus were considered observed. The intensities were corrected for Lorentz and polarization factors but not for absorption or extinction. Scattering factors used in the analysis were those given by Cromer and Mann[10] for C and O and by Stewart *et al.*[11] for H.

The structure was solved by direct methods with the X-ray system.[12] Phases of 208 |E| terms with values greater than 1.50 were derived by application of the

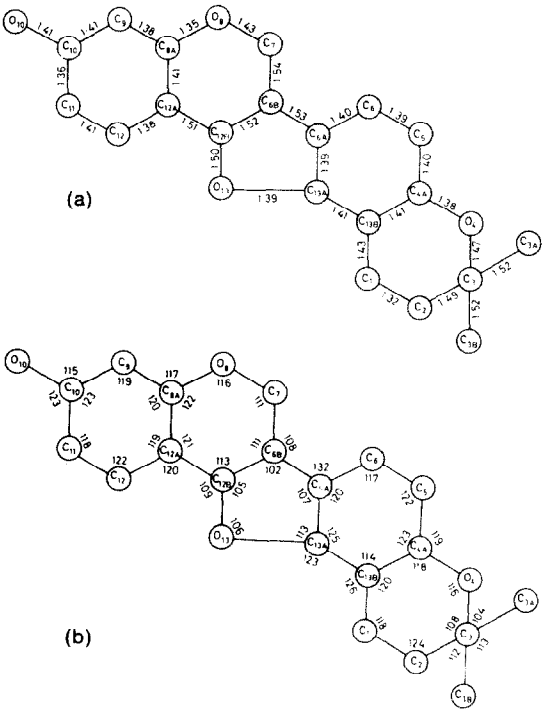


Fig. 1. (a) Bond lengths. The estimated standard deviations range from 0.01 to 0.02 Å. (b) Bond angles. The estimated standard deviations are 1°.

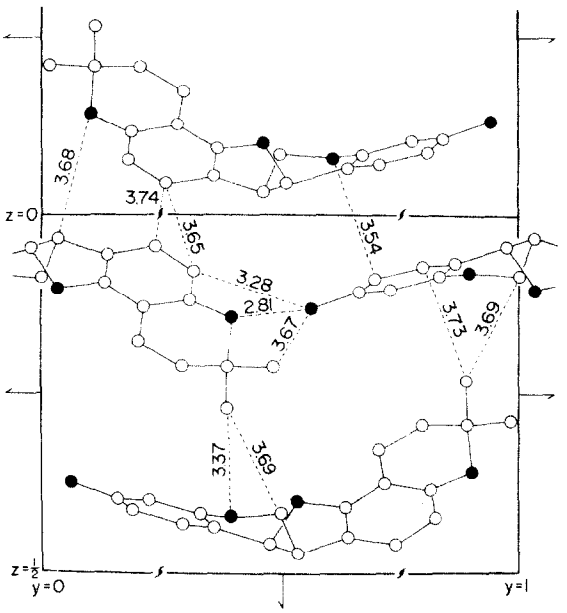


Fig. 3. The projection of the structure down the *a* axis.

tangent formula.[13] The final phased set of reflections had an R(Karle)[13] of 0.29 and scale factor, $\langle|E_o|\rangle/\langle|E_c|\rangle = 1.07$. From the subsequent E-map the sites of eleven non-hydrogen atoms were located. A further two E-maps, calculated with phases derived from a starting set based on the partial structures, revealed the sites of all the remaining non-hydrogen atoms. Structure amplitudes calculated with an overall temperature factor determined by a Wilson plot, and with all atoms included as C, yielded a reliability index, $R = \Sigma\,||F_o| - |F_c||/\Sigma\,|F_o|$ of 0.22.

From the molecular formula, differentiation of the C and O atoms were made. Least-squares refinement in which the atoms were given individual isotropic temperature factors reduced R to 0.14. Apart from the hydrogen of the hydroxyl group, H atoms were included in the refinement at calculated positions assuming a C–H bond length of 1.08 Å and with an isotropic thermal parameter, $U = 0.05$ Å^2 for the methyl H atoms and one of 0.04 Å^2 for the remainder. The hydrogen parameters were not refined. In the final refinements, the C and O atoms were given anisotropic temperature factors and their parameters were refined in three blocks corresponding to positional and thermal parameters for 10, 9 and 9 atoms respectively. The least-squares refinements were made with SHELX76 program,[14] the function minimized being $w[|F_o| - |F_c|]^2$ with $w = 1.0$. A final R of 0.083 was attained for the 992 observed terms.

Final atomic coordinates with their estimated standard deviations are given in Table 1. Bond lengths and angles are given in Fig. 2, while some short intermolecular distances are given in Table 2—see also Fig. 3. Figure 2 has been prepared from the output of the ORTEP program.[15] Tables of calculated and observed structure amplitudes and anisotropic thermal parameters for the non-hydrogen atoms are available on request from the authors.

Description of the structure. A perspective view of the phaseollin molecule is given in Fig. 2, while a conventional representation of the molecular structure is shown as (I). The molecular skeleton consists of five ring systems fused together to form a rigid framework which is approximately propeller in shape. As predicted by previous workers, the B/C ring junction is *cis*.[6,7] The staggered conformation of the benzofurobenzopyran ring

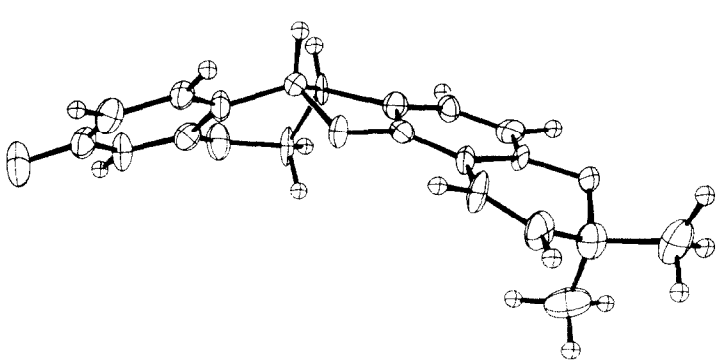


Fig. 2. A perspective view of the molecule with thermal ellipsoids scaled to 50% probability.

Table 1. (a) Final atomic coordinates of the non-hydrogen atoms with their estimated standard deviations in parentheses. All values have been multiplied by 10^4. (b) Calculated H atom coordinates ($\times 10^3$). The methyl H atoms were given an isotropic thermal parameter, U = 0.05 Å^2 and all others were given a value, U = 0.04 Å^2. The atoms were given the same numbering as the C to which they were bonded.

		x/a	y/b	z/c		x/a	y/b	z/c
(a)	C(1)	−932(19)	7115(8)	−3281(6)	O(8)	6232(12)	3907(5)	−4205(4)
	C(2)	−1410(22)	7938(10)	−2914(7)	C(8A)	4570(16)	3303(8)	−4131(6)
	C(3)	−168(21)	8901(10)	−2906(7)	C(9)	4897(18)	2287(8)	−3950(6)
	C(3A)	−1501(24)	9858(10)	−2858(8)	C(10)	3209(18)	1619(8)	−3907(6)
	C(3B)	1485(24)	8877(13)	−2355(7)	O(10)	3688(14)	615(5)	−3686(5)
	O(4)	842(13)	9005(5)	−3580(4)	C(11)	1269(18)	1928(8)	−4057(6)
	C(4A)	1774(19)	8129(7)	−3836(6)	C(12)	988(17)	2960(7)	−4266(5)
	C(5)	3545(21)	8229(9)	−4235(6)	C(12A)	2584(17)	3650(8)	−4299(6)
	C(6)	4499(18)	7387(8)	−4537(6)	C(12B)	2221(19)	4739(7)	−4540(5)
	C(6A)	3539(18)	6432(9)	−4453(6)	O(13)	1124(11)	5328(5)	−3986(4)
	C(6B)	4187(17)	5341(7)	−4658(6)	C(13A)	1805(18)	6342(8)	−4042(6)
	C(7)	5869(18)	4994(8)	−4153(7)	C(13B)	833(18)	7173(8)	−3711(6)
(b)	H(1)	−186	643	−326	H(6)	593	746	−481
	H(2)	−276	791	−259	H(6B)	478	526	−518
	H(3A)	−220	990	−235	H(7)	726	541	−427
	H(3A′)	−51	1051	−293	H(7′)	539	517	−363
	H(3A″)	−268	986	−325	H(9)	643	201	−385
	H(3B)	77	884	−185	H(11)	−1	141	−401
	H(3B′)	249	822	−242	H(12)	−52	322	−441
	H(3B″)	236	958	−240	H(12B)	140	468	−502
	H(5)	417	899	−432				

Table 2. Contact distances less than 3.75 Å. Estimated standard deviations range from 0.01 to 0.02 Å.

O(4) ..... O(10)^{I}	2.81 Å	O(10) ..... C(5)^{VI}	3.28 Å
O(4) ..... C(6B)^{II}	3.68	O(13) ..... C(7)^{VIII}	3.48
O(8) ..... C(3B)^{III}	3.37	C(3B) ..... C(7)^{IX}	3.69
O(8) ..... C(11)^{IV}	3.54	C(3B) ..... C(12)^{X}	3.73
O(8) ..... C(12)^{V}	3.35	C(4A) ..... C(6)^{II}	3.55
O(10) ..... C(3)^{VI}	3.69	C(5) ..... C(6)^{II}	3.65
O(10) ..... C(3A)^{VII}	3.67	C(6) ..... C(6)^{II}	3.74
O(10) ..... C(3B)^{VI}	3.72	C(6) ..... C(6A)^{XI}	3.63
O(10) ..... C(4A)^{VI}	3.47	C(6) ..... C(13A)^{XI}	3.55

Symmetry code

I:	x	1+y	z	VII:	1+x	−1+y	z
II:	$-\frac{1}{2}+x$	$1\frac{1}{2}-y$	−1−z	VIII:	−1+x	y	z
III:	1−x	$-\frac{1}{2}+y$	$-\frac{1}{2}-z$	IX:	1−x	$\frac{1}{2}+y$	$-\frac{1}{2}-z$
IV:	$\frac{1}{2}+x$	$\frac{1}{2}-y$	−1−z	X:	−x	$\frac{1}{2}+y$	$-\frac{1}{2}-z$
V:	1+x	y	z	XI:	$\frac{1}{2}+x$	$1\frac{1}{2}+y$	−1−z
VI:	x	−1+y	z				

system, with the torsion angle, O(8)[C(7), C(6B)]C(12B) = 56.3°, agrees with the assignment based on proton magnetic resonance data.[7] Conformational detail in the benzofuran and benzopyran ring systems, however, differs from the deductions of Pachler and Underwood.[7] Ring C is envelope with four atoms planar within ±0.02 Å and C(12B) lying +0.44 Å out-of-plane, while ring B is skewed with atoms O(8), C(8A), C(12A) and C(12B) planar within ±0.01 Å and C(6B) and C(7) lying +0.12 and −0.55 Å respectively from the plane. Consequently the two aromatic rings are mutually inclined at 48.6° and are not approximately perpendicular to each other as previously implied.[4] By virtue of the double bond between C(1) and C(2) and its fusion to ring D, ring E is a distorted half-chair, C(2) and C(3) deviating from the coplanarity of the other four atoms (±0.03 Å) by −0.32 and −0.69 Å respectively.

The aromatic C–C bonds have an average value 1.39 Å (mean deviation 0.02 Å), the double bond C(1)–C(2) is 1.32 Å in length, the C(sp^3)–O bonds have a mean value 1.47 Å while the C(sp^2)–O bonds have a mean value 1.38 Å. The angles subtended at the O atoms range in value from 106 to 116°. These dimensions agree with expected values for comparable lengths and angles.[16]

The molecular packing in the crystal is illustrated in Fig. 3. The molecules are aligned with their long axes approximately parallel to the *b* crystal axis. There is an intermolecular hydrogen bond between O(4) of ring E and the hydroxyl oxygen O(10) of 2.81 Å. These interactions link the molecules related by the translation along *b* into chains parallel to *b*. Most of the other short intermolecular contacts involve one of the oxygen atoms—see Table 2 and Fig. 3. As there are no unusually short intermolecular approaches, it would appear that the molecules are held together in the crystal along *a* and *c* by van der Waals interactions.

Acknowledgements—We are grateful to Dr. D. R. Perrin of the Division of Plant Industry, C.S.I.R.O., Canberra. A.C.T., who suggested this interesting problem and who kindly supplied the crystals.

REFERENCES

[1]I. A. M. Cruickshank and D. R. Perrin, *Life Sci.* **9**, 680 (1963).
[2]D. R. Perrin and I. A. M. Cruickshank, *Phytochemistry* **8**, 971 (1969).
[3]C. M. Brink, J. P. Engelbrecht and D. E. Graham, *J. S. African Chem. Inst.* **23**, 24 (1970).
[4]H. D. Van Etten, *Phytochemistry* **15**, 655 (1976).
[5]I. A. M. Cruickshank and D. R. Perrin, *Nature* **187**, 799 (1960); *Idem., J. Am. Chem. Soc.* **84**, 1919 (1962).
[6]H. Suginome, *Experientia* **28**, 161 (1962); H. Suginome and T. Iwadare, *Ibid.* **28**, 163 (1962).
[7]K. G. R. Pachler and W. G. E. Underwood, *Tetrahedron* **23**, 1817 (1967).
[8]D. R. Perrin, *Tetrahedron Letters* 29 (1964).
[9]C. DeMartinis, M. F. Mackay, D. R. Perrin and B. J. Poppleton, *Ibid.* 2981 (1977).
[10]D. T. Cromer and J. B. Mann, *Acta Cryst.* **A24**, 321 (1968).
[11]R. F. Stewart, E. R. Davidson and W. T. Simpson, *J. Chem. Phys.* **42**, 3175 (1965).
[12]J. M. Stewart, C. J. Kruger, H. L. Ammon, C. Dickerson and S. R. Hall, X-RAY-72. *A System of Computer Codes for Crystallography*, Technical Report TR-192, University of Maryland (1972).
[13]I. L. Karle and J. Karle, *Acta Cryst.* **21**, 849 (1966).
[14]G. M. Sheldrick, SHELX76. *Program for Crystal Structure Determination* (1976).
[15]C. K. Johnson, *Fortran Thermal-ellipsoid Plot Program (ORTEP)*. Oak Ridge National Laboratory, Oak Ridge, Tennessee (1965).
[16]*Tables of Interatomic Distances and Configurations in Molecules and Ions*. (1965). (Suppl. 1956–59). Special Publication No. 18. The Chemical Society, London.

Anisotropic thermal parameters of the non-hydrogen atoms with their estimated standard deviations in parentheses. All values have been multiplied by 10^3.

	$T = \exp[-2\pi^2(U_{11}h^2 + U_{22}k^2 + U_{33}l^2 + 2U_{23}kl + 2U_{13}hl + 2U_{12}hk)]$					
	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	23(7)	13(5)	60(8)	−7(6)	14(6)	−5(6)
C(2)	32(8)	37(8)	52(8)	0(7)	14(8)	16(8)
C(3)	38(9)	29(7)	47(8)	2(7)	2(7)	0(7)
C(3A)	48(10)	39(8)	66(10)	−13(8)	18(9)	6(8)
C(3B)	48(9)	73(10)	41(9)	−8(8)	−3(8)	−14(9)
O(4)	36(5)	14(4)	27(4)	2(3)	1(4)	1(4)
C(4A)	37(7)	4(5)	24(7)	0(5)	4(6)	−8(5)
C(5)	42(8)	26(6)	28(6)	1(5)	−9(6)	−14(6)
C(6)	37(7)	19(6)	31(6)	6(5)	6(6)	−2(5)
C(6A)	30(7)	32(7)	34(7)	−2(6)	1(6)	9(6)
C(6B)	13(7)	11(6)	38(6)	3(5)	11(6)	8(6)
C(7)	12(6)	6(5)	80(8)	1(5)	10(7)	0(5)
O(8)	28(4)	27(4)	73(5)	1(4)	−4(4)	2(4)
C(8A)	27(6)	31(6)	36(6)	−6(5)	0(5)	−5(5)
C(9)	38(7)	18(5)	63(8)	1(6)	7(6)	4(6)
C(10)	37(7)	28(6)	46(7)	−7(6)	−4(6)	6(5)
O(10)	51(5)	26(4)	97(6)	5(4)	−11(6)	4(4)
C(11)	31(6)	32(6)	49(7)	−7(6)	8(6)	−1(5)
C(12)	22(5)	22(5)	34(6)	−4(4)	−9(5)	0(5)
C(12A)	36(7)	15(5)	46(7)	0(5)	−14(6)	2(6)
C(12B)	53(8)	22(5)	22(6)	−4(5)	−5(6)	10(6)
O(13)	17(4)	14(4)	41(5)	−1(3)	5(4)	1(4)
C(13A)	34(7)	19(6)	29(6)	5(5)	−14(6)	−9(6)
C(13B)	26(6)	15(5)	32(6)	−3(5)	−3(6)	6(5)