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Structure of the Alkaloid Wisanine (2-Methoxypiperine)

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Abstract. (*E*,*E*)-1-[5-(6-Methoxy-1,3-benzodioxol-5-yl)-1-oxo-2,4-pentadienyl]piperidine, $C_{18}H_{21}NO_4$, $M_r =$ 315·148, monoclinic, $C2/c$, $a =$ 15·646 (2), $b =$ 10·297 (2), $c =$ 20·480 (3) Å, $\beta =$ 93·0 (1)°, $V =$ 3294·9 (4) Å^3, $Z = 8$, $d_m =$ 1·28 Mg m^{-3}, $F(000) =$ 1344, λ(Mo $K\alpha$) = 0·7107 Å, μ(Mo $K\alpha$) = 0·076 mm^{-1}. Final $R_F =$ 0·075 for 2722 reflections. The molecular dimensions and conformation are similar to those of 1-piperoylpiperidine (piperine).

Introduction. Wisanine is the major constituent of the amide alkaloids in the root of *Piper guineense* (West African black or Ashanti pepper). Isolation of the pale-yellow compound was carried out by Addae-Mensah, Torto, Dimonyeka, Baxter & Sanders (1977); Addae-Mensah, Torto & Baxter (1976) showed that wisanine was the 2-methoxy derivative of 1-piperoylpiperidine (piperine), whose crystal structure has been reported (Bordner & Mullins, 1974; Grynpas & Lindley, 1975). The present analysis was carried out to compare structural details for the unsubstituted and substituted molecules.

Intensities of 2722 independent reflections within the limits 2·5 ≤ θ ≤ 25° were measured from an approximate cube (crystallized from ethyl acetate, edge ~0·5 mm) on a Philips PW 1100 four-circle diffractometer (graphite-monochromated Mo $K\alpha$ radiation, $\omega/2\theta$ scan, scan width 1·4° in ω, scan speed 0·05° ω s^{-1}, background counted for half the scan time at each scan extremity); the crystal showed no signs of instability over the period of the measurements. Absorption corrections were not applied. The structure was solved with *MULTAN* (Main, Woolfson, Lessinger, Germain & Declercq, 1977) and refined to $R_F =$ 0·075 with *SHELX* (Sheldrick, 1976) {$R_w =$ 0·077; the weighting scheme was $w(F) = 0{\cdot}4541/[\sigma^2(F) + 0{\cdot}0021F^2]$}. Atomic coordinates are in Table 1.*

Table 1. *Atomic coordinates and equivalent isotropic temperature factors* (*all* × 10^4)

E.s.d.'s are in parentheses; H atom positions were calculated and refined in a separate block.

	x	y	z	U_{eq} (Å^2)*
C(1)	2095 (1)	2640 (3)	5986 (1)	548
C(2)	1815 (1)	1847 (2)	6471 (1)	504
C(3)	2124 (1)	1935 (2)	7101 (1)	518
C(4)	2762 (1)	2872 (2)	7257 (1)	507
C(5)	3038 (2)	3659 (2)	6753 (1)	548
C(6)	2705 (2)	3562 (3)	6111 (1)	607
C(7)	3131 (2)	3031 (2)	7919 (1)	510
C(8)	3007 (2)	2294 (2)	8440 (1)	587
C(9)	3405 (2)	2575 (2)	9074 (1)	571
C(10)	3336 (2)	1879 (3)	9610 (1)	619
C(11)	3766 (2)	2279 (3)	10236 (1)	576
C(12)	3566 (2)	65 (3)	10714 (1)	760
C(13)	4295 (2)	−845 (3)	10875 (1)	887
C(14)	4741 (2)	−511 (3)	11526 (1)	827
C(15)	5023 (2)	890 (3)	11518 (1)	791
C(16)	4273 (2)	1780 (3)	11354 (1)	797
C(17)	1136 (2)	1274 (3)	5526 (1)	733
C(18)	4428 (2)	4481 (3)	6621 (2)	1067
O(1)	1185 (1)	1027 (2)	6213 (1)	694
O(2)	1663 (1)	2358 (2)	5404 (1)	755
O(3)	3647 (1)	4587 (2)	6914 (1)	818
O(4)	4040 (1)	3392 (2)	10301 (1)	809
N(1)	3855 (1)	1406 (2)	10729 (1)	650
H(3)	1919 (14)	1359 (23)	7420 (10)	621
H(6)	2916 (13)	4147 (21)	5776 (10)	710
H(7)	3491 (14)	3717 (24)	7988 (11)	727
H(8)	2668 (14)	1563 (23)	8383 (11)	708
H(9)	3757 (13)	3361 (21)	9102 (10)	701
H(10)	3009 (14)	1120 (25)	9588 (11)	733
H(121)	3134 (18)	43 (30)	11083 (14)	1151
H(122)	3311 (16)	−151 (26)	10322 (12)	816
H(131)	4114 (17)	−1707 (27)	10857 (14)	1080
H(132)	4735 (21)	−688 (29)	10542 (17)	1222
H(141)	4314 (17)	−530 (24)	11880 (13)	892
H(142)	5268 (17)	−1085 (28)	11618 (13)	1043
H(151)	5433 (17)	1006 (28)	1164 (13)	1044
H(152)	5305 (15)	1126 (24)	11942 (12)	924
H(161)	4459 (16)	2709 (26)	11326 (13)	980
H(162)	3818 (17)	1621 (25)	11701 (13)	1120
H(171)	547 (15)	1415 (23)	5402 (11)	769
H(172)	1378 (17)	554 (25)	5306 (14)	977
H(181)	4863 (16)	5144 (29)	6832 (14)	1202
H(182)	4318 (24)	4499 (40)	6109 (19)	2053
H(183)	4635 (26)	3510 (44)	6713 (21)	2259

* $U_{eq} = \frac{1}{3}$ trace $\tilde{\mathrm{U}}$.

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* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35704 (20 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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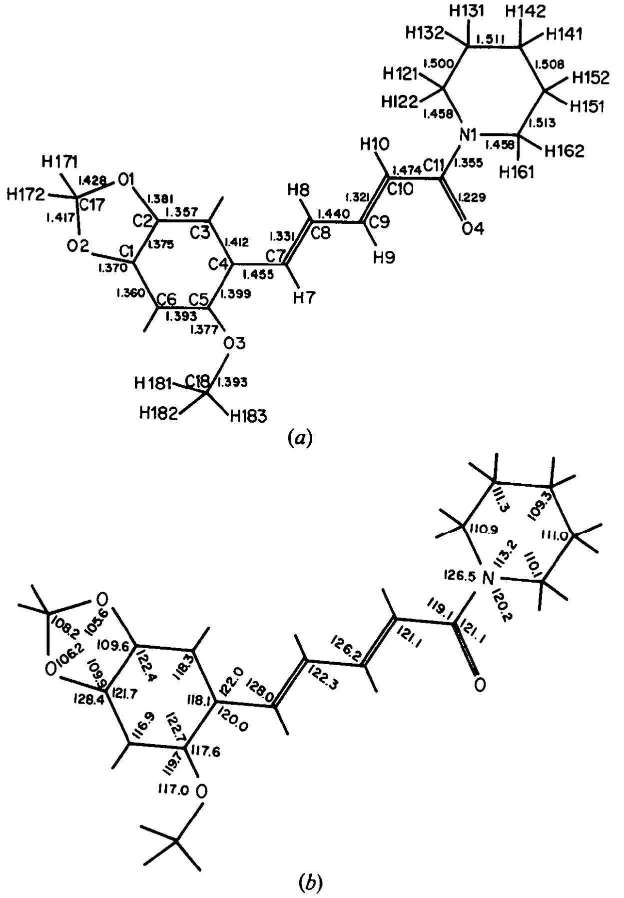

Fig. 1. (*a*) Bond lengths (Å) and atomic numbering in wisanine. The e.s.d.'s of the bond lengths are in the range 0·003–0·004 Å. The C—H distances lie in the range 0·90—1·07 Å, with mean e.s.d. ~0·03 Å. C(18) is 1·05 (1) Å from the mean plane of C(1)–C(6) and O(4) is 0·32 (1) Å from the mean plane of C(7)–C(11). [In piperine O(4) is 0·03 Å from the mean plane of the pentadiene chain.] (*b*) Bond angles (°); the e.s.d.'s of the bond angles lie in the range 0·1–0·3°.

Table 2. *Best planes for various groups of atoms in wisanine*

Least-squares planes are defined with respect to orthogonal axes **XO, YO, ZO** where **XO**||**a***, **YO**||**c** × **a***, **ZO**||**c**. Distances of atoms from these planes are in square brackets (e.s.d.'s ~0·004 Å).

Plane (1): C(6), C(5), C(4), C(3), C(2), O(1), O(2), C(1)

$$-0{\cdot}7056X + 0{\cdot}6699Y + 0{\cdot}2310Z = 2{\cdot}3129$$

[C(6) 0·0025, C(5) –0·0003, C(4) 0·0055, C(3) 0·0008, C(2) –0·0121, O(1) 0·0064, O(2) 0·006, C(1) –0·0089, C(17) –0·0932, C(18) –1·0541]

Plane (2): C(7), C(8), C(9), C(10), C(11)

$$0{\cdot}7960X - 0{\cdot}5462Y - 0{\cdot}2610Z = -1{\cdot}9850$$

[C(7) 0·0084, C(8) –0·0114, C(9) –0·0055, C(10) 0·0119, C(11) –0·0034, O(4) –0·3175, N(1) 0·3365]

Plane (3): C(12), C(13), C(15), C(16)

$$-0{\cdot}4471X - 0{\cdot}3108Y + 0{\cdot}8387Z = 15{\cdot}6503$$

[C(12) –0·0040, C(13) 0·0040, C(15) –0·0040, C(16) 0·0040, N(1) –0·6285, C(14) 0·6728]

Plane (4): C(11), C(12), C(16)

$$0{\cdot}8818X - 0{\cdot}2850Y - 0{\cdot}3758Z = -3{\cdot}2426$$

[N(1) 0·0016]

Dihedral angles (°) (e.s.d.'s ~ 0·5°)

Plane (1) – Plane (2)	171·1
Plane (2) – Plane (3)	113·9

The atom numbering, and bond distances and angles are shown in Fig. 1 and the results of planarity calculations in Table 2. The intermolecular distances (not given in detail) correspond to van der Waals interactions and the packing shows no noteworthy features.

Discussion. The two sets of dimensions reported for the piperine molecule agree well,* and the mean bond lengths also agree well with our results. There appears to be a small but systematic difference in C—C—C bond angles along the pentadiene chains of the two molecules; as one proceeds from the benzodioxolyl rings to the piperidine ring the values for piperine are (mean values given): 126·4, 125·2, 124·0, 122·1, 119·0° (e.s.d.'s ~ 0·4°). In contrast to this steady diminution, our values alternate: 128·0, 122·3, 126·2 121·1, 119·1° (e.s.d.'s ~ 0·2°). The overall conformations of the two molecules are the same, and the same inclination is found between the planes of the aromatic ring and the pentadiene chain (8·9° here and 8·5° in piperine). However, the substituted amide portion of the molecule is twisted about C(10)–C(11) more in wisanine than in piperine [torsion angles C(9)–C(10)–C(11)–O(4) are 15·5 (4) and 1·8° respectively].

We have used the Cambridge Data File (Allen *et al.*, 1979) to compare dimensions found here for the piperidyl ring with those in the literature. 59 compounds were found by fragment search and 13 were retained in calculating average dimensions. These compounds are noted here by their Data File acronyms, with the number of crystallographically independent piperidyl rings in parentheses: CPRPCY(2), DPIPDS(2), HPCANO(1), PIBZCH(2), PIPACP(1), PIPAMP(1), PIPCMP(1), PIPINE10(1), PIPTHS(2), THEXPL(1), XEPACP(1), PIPOSD(2), TPIPPH(6). The criteria for retention were: (i) no disorder, (ii) no atoms heavier than Cl, (iii) $R \leq 0{\cdot}08$, (iv) $\sigma[d(\mathrm{C{-}C})] < {\sim}0{\cdot}01$ Å. Statistical results for the

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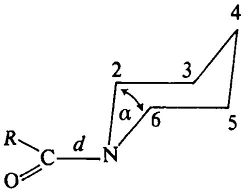
* The unit cell given by Bordner & Mullins (1974) (BM) can be converted into that of Grynpas & Lindley (1975) (GL) by multiplication by the matrix 101/010/100. There appears to be a transcription error in $b_{\mathrm{GL}}(=13{\cdot}364$ Å) because $b_{\mathrm{BM}}(=13{\cdot}663$ Å) gives better agreement with the experimental density; the two sets of y coordinates agree well.

fragment dimensions are given in Table 3. The values found for wisanine agree well with the mean values in regard to bond lengths and somewhat less well in regard to bond angles. The discrepancies for the torsion angles are still larger; one notes (Table 3) that in some piperidyl moieties the torsion angles are all rather similar (small sample standard deviation, as in wisanine) while in others there is a fairly large spread (as in piperine). Packing effects will influence torsion angles more than bond angles or bond lengths.

Table 3. *Mean dimensions* (Å *and* deg) *for the piperidyl fragment* (*see text for description of sample used; corrections for thermal vibrations have not been applied*)



Bond	Mean	Sample standard deviation	Maximum	Minimum	Values for wisanine
N—2	1·465	0·011	1·479	1·432	1·452
N—6	1·469	0·010	1·489	1·450	1·458
2—3	1·515	0·011	1·537	1·490	1·500
3—4	1·520	0·013	1·547	1·493	1·511
4—5	1·517	0·015	1·546	1·484	1·508
5—6	1·517	0·013	1·537	1·485	1·513
2—N—6	111·2	1·8	113·7	108·2	113·2
N—2—3	110·5	0·8	111·9	109·1	110·9
2—3—4	111·2	0·7	113·6	110·4	111·3
3—4—5	110·2	1·1	112·2	107·2	109·3
4—5—6	110·9	0·6	112·2	109·9	111·0
5—6—N	110·3	0·8	112·2	108·4	110·1
Endocyclic torsion angles*					
6—N—2—3	59·7	2·2	63·3	55·4	57·1
2—N—6—5	−60·1	1·9	−63·3	−56·2	−56·8
N—2—3—4	−56·2	2·0	−59·8	−52·1	−56·5
2—2—4—5	53·2	1·3	55·3	50·8	55·9
3—4—5—6	−53·6	1·4	−55·8	−50·8	−55·4
4—5—6—N	57·0	1·7	59·9	54·0	55·5

* Arbitrary signs.

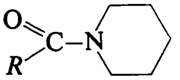
A comprehensive discussion of the C(sp^2)—N(piperidyl) bond has recently been given by Gilli & Bertolasi (1979). We consider only five molecules with  groupings (Table 4). In all these molecules the C—N bond has appreciable double-bond character [d(C=N) = 1·26 and d[C(sp^2)—N(sp^3)] = 1·43 Å (Gilli & Bertolasi, 1979)]. Concomitantly the spatial distribution of bonds about the piperidyl N atom is much closer to planar than pyramidal. In addition, the endocyclic angle at N in the molecules of Table 4 is significantly larger than the mean value for piperidyl rings obtained from the Data File (Table 3). (We have no explanation for the discrepant value reported for *N*-benzoyl-2,6-dimethylpiperidine.) These features together confirm appreciable interaction between piperidyl N and the carbonyl group, and participation of the N atom lone pair in this interaction.

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Table 4. *Comparison of dimensions in five molecules with piperidylcarbonyl groupings* (*see Table* 3 *for labelling of molecule*)

	d (Å)	α (°)	τ(6—N—C=O) (°)	Deviation of N from plane 2, 6, C (Å)	Mean* torsion angles in piperidine ring (°)	Reference
Piperidine	1·350 (4)	112·9 (4)	−2·8	0·095	54·9 (3·5)	(*a*), (*b*)
Wisanine	1·355 (3)	113·2 (2)	0·6	0·002	56·2 (6)	Present work
1-[(*p*-1-Hydroxyiminoethyl)phenoxyacetyl]-piperidine	1·342 (4)	113·5 (3)	3·3	0·04	55·1 (8)	(*c*)
N-Benzoyl-2,6-dimethylpiperidine	1·349 (6)	119·3 (7)†	7·2	0·068	52 (4·8)	(*d*)
p-Nitrobenzoylpiperidine	1·350 (4)	114·2 (3)	8·1	0·045	56 (1)	(*e*)

References: (*a*) Bordner & Mullins (1974). (*b*) Grynpas & Lindley (1975). (*c*) Tranqui, Cromer & Boucherle (1974). (*d*) Arte, Feneau-Dupont, Declercq, Germain & Van Meerssche (1977*b*). (*e*) Arte, Feneau-Dupont, Declercq, Germain & Van Meerssche (1977*a*).

* Experimental e.s.d.'s of individual endocyclic torsion angles are ~1°. The values in parentheses are the sample e.s.d.'s.

† Recalculation *via* the Data File coordinates confirms the value cited.

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The Structure of Pentachlorobenzene

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Abstract. C_6HCl_5, orthorhombic, $Pca2_1$, $Z = 4$, $a = 16{\cdot}802\,(5)$, $b = 3{\cdot}856\,(1)$, $c = 13{\cdot}279\,(2)$ Å, $D_c = 1{\cdot}893$ Mg m^{-3}. The structure was solved from an $h0l$ projection and refined to $R = 0{\cdot}023$ for 665 independent reflections. Intramolecular Cl···Cl repulsions produce shortenings in the C(1)–C(6) and C(5)–C(6) bonds.

Introduction. The crystal structure of the title compound was determined to provide a large data base in connection with a study of Cl···Cl nonbonded interactions in crystals (Hsu & Williams, 1980). In the cited work, no evidence for nonbonded anisotropy above a threshold level was found in a study of five perchlorohydrocarbons: hexachlorobenzene, octachloronaphthalene, octachlorofulvalene, decachlorophenanthrene, and decachloropyrene. However, Wheeler & Colson (1976) and Munowitz, Wheeler & Colson (1977) claim that significantly anisotropic Cl···Cl interactions are present in one or more of the three crystal forms of *p*-dichlorobenzene.

Translucent crystals with good face development were grown with material obtained from the Aldrich Chemical Company; an approximately cubic-shaped crystal with an edge length of 0·2 mm was selected. X-ray diffraction data showed the crystals to be orthorhombic, with systematic absences $h0l{:}h = 2n$ and $0kl{:}l = 2n$, space group $Pca2_1$. 863 independent reflections were collected with an Enraf–Nonius CAD-4 diffractometer (Mo $K\alpha$ radiation), using the $\theta,2\theta$ scan method. 464 of the lowest-angle reflections were collected as Friedel pairs. Three reference reflections remained essentially constant throughout the data collection. Lorentz and polarization corrections were made in the usual manner.

The structure was solved from an $h0l$ projection with *SHELX* 76 (Sheldrick, 1976). A rigid-body projection was refined for the x direction to $R = 24\%$. A difference Fourier map was sufficient to determine the rotational orientation. The geometric constraints were removed and the structural parameters were refined to $R = 5\%$.

The structure was then refined for the entire data set with a constrained benzene ring to $R = 27\%$. The thermal parameters of the Cl atoms were converted to anisotropic ones and the refinement continued to $R = 4\%$. The H atom was found on a difference Fourier map and refined with an isotropic temperature factor. The H scattering factors were those of Stewart, Davidson & Simpson (1965). The C and Cl scattering factors were those of Cromer & Mann (1968). The benzene ring was unconstrained and the thermal parameters were anisotropic. This final refinement adjusted 102 structural parameters, plus a scale factor, to minimize the R factor $\{R = [\sum w(F_o - F_c)^2/\sum wF_o^2]^{1/2}\}$. The weights were defined as the squares of the reciprocals of the estimated standard deviations of the structure factors. The final R was 0·023 for reflections significantly above background [665 reflections with $F > 3\sigma(F)$]. The final electron density

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