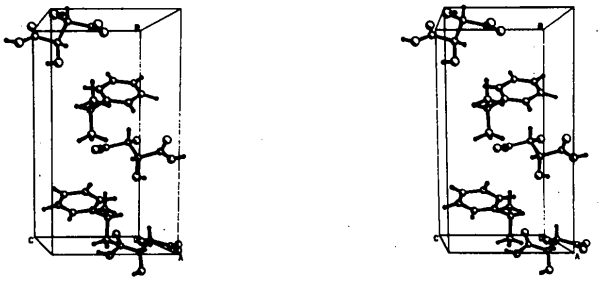

Fig. 2. Stereoscopic view of the unit cell.

Table 3. *Hydrogen-bond distances* (Å) *and angles* (°)

	O–H	H···O	O···O	O–H···O
O3–HO3···O1^{i}	0·89	1·62	2·498	168
N1–HN1···O1^{ii}	0·87	2·07	2·930	173
N1–HN3···O2^{iii}	1·01	1·84	2·844	178
N1–HN2···O5^{iv}	0·95	1·98	2·879	157
O5–HO5···O2	0·79	2·08	2·622	126
O5–HO5···O4^{v}	0·79	2·32	2·834	124
O6–HO6···O3	0·77	2·22	2·655	116

Symmetry code: (i) $x, y, 1+z$; (ii) $-1-x, -0{\cdot}5-y, -1-z$; (iii) $-x, -0{\cdot}5+y, -1-z$; (iv) $-x, -0{\cdot}5+y, -z$; (v) $-1+x, y, z$.

C(3), C(4) atoms depart from an analogous plane (r.m.s.d. = 16·2%); this effect is mainly due to the repulsion between the β-hydroxyl groups and the neighbouring carboxyl O atoms.

The existence of dissymmetry in these two regions is similar to that in other reported X-ray structures (Kroon *et al.*, 1984; Moerman, Ouwerkerk & Kroon, 1985; Kroon, 1982). In particular, the title structure bears a striking resemblance to the *meso*-tartrate analogue, due to the approximate correspondence between their fractional coordinates (applying the adequate translation and symmetry operations), obviously except for atoms O(6) and H(3), which are interchanged as a consequence of the different configuration at C(3). The similarity between the (+)-tartrate and *meso*-tartrate structures lies in the fact that O(6) is antiperiplanar to the carboxyl group, which is very unusual, since it corresponds to an energetically unfavourable conformation. In this case the carboxyl groups are rotated from the C–C(α)–O(H) planes by 1·1 and 30·8°, which is more dissymmetric than in other reported tartrate moieties.

Crystal packing is drawn in Fig. 2 and Table 3 shows that the HO5 atom is involved in a bifurcated inter- and intramolecular hydrogen bond and is, as usual, coplanar with the donor and acceptor atoms (sum of the coordination angles is 360·0°).

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References

International Tables for X-ray Crystallography (1974). Vol. IV, pp. 99, 149. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

KROON, J. (1982). *Molecular Structure and Biological Activity*, edited by J. F. GRIFFIN & W. L. DUAX, pp. 151–163. New York: Elsevier Biomedical.

KROON, J., DUISENBERG, J. M. & PEERDEMAN, A. F. (1984). *Acta Cryst.* C**40**, 645–647.

MAIN, P., GERMAIN, G. & WOOLFSON, M. M. (1984). *MULTAN*11/84. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univ. of York, England.

MOERMAN, W., OUWERKERK, M. & KROON, J. (1985). *Acta Cryst.* C**41**, 1205–1208.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Acta Cryst. (1989). C**45**, 106–109

Structure of L-Phenylalanyl-L-proline Monohydrate

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Abstract. $C_{14}H_{18}N_2O_3.H_2O$, $M_r = 280{\cdot}3$, tetragonal, $P4_12_12$, $a = 8{\cdot}162\ (4)$, $c = 41{\cdot}41\ (3)$ Å, $V = 2758{\cdot}7$ Å^3, $Z = 8$, $D_m = 1{\cdot}32$, $D_x = 1{\cdot}35$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 7{\cdot}30$ cm^{-1}, $F(000) = 1200$, $R = 0{\cdot}037$, $wR = 0{\cdot}039$ for 840 unique reflections [$F > 2\sigma(F)$]. The peptide linkage is in *cis* conformation. The pyrrolidine ring exists as twist, $^{\beta}T_{\alpha}$. The crystal structure is stabilized by a three-dimensional network of N–H···O, O–H···O and C–H···O hydrogen bonds.

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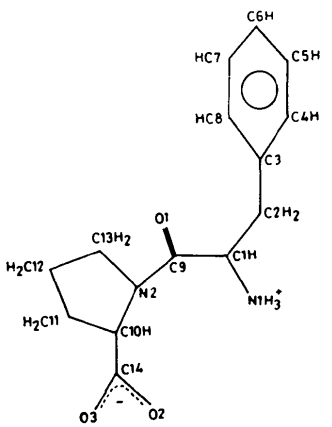
Introduction. Proline is a unique amino acid which imposes restrictions on the conformation of proteins due to its pyrrolidine ring system (Balasubramanian, Lakshminarayanan, Sabesan, Tegoni, Venkatesan & Ramachandran, 1971; Ashida & Kakudo, 1974). The conformational aspects of the pyrrolidine ring system are of particular interest as they reveal different modes of puckering in the five-membered ring system (Chacko, Swaminathan & Veena Ravichandran, 1984). In this context several structural studies of dipeptides involving proline have been reported. Here we present the crystal structure of L-phenylalanyl-L-proline monohydrate (LFLP) (1).



(1)

Experimental. The dipeptide (LFLP) was crystallized from ethanol at room temperature (300 K). Colourless plate-like crystal, dimensions 0·5 × 0·3 × 0·3 mm. D_m measured by flotation method in bromoform and benzene. Three-dimensional intensity data were collected by Nonius CAD-4 diffractometer [λ(Cu $K\alpha$) = 1·5418 Å]. Cell constants by least-squares fit of 20 reflections with θ range 10–60°, max. $2\theta = 140°$, ω–2θ scan, data collected for the range $0 \le h \le 9$, $0 \le k \le 9$ and $0 \le l \le 50$. Three standard reflections, measured every 100 reflections, showed no significant variations in intensity. A total of 1624 observations was reduced (Lp^{-1}) to a set of 840 unique reflections with $F > 2\sigma(F)$ used in the structure determination. The structure was solved by *SHELX*86 (Sheldrick, 1986). Refinement carried out by full-matrix least-squares method *SHELX*76 (Sheldrick, 1976). In the final stage the non-hydrogen atoms were refined with anisotropic thermal parameters and hydrogens with isotropic thermal parameters. Convergence reached, the final $R = 0.037$, $wR = 0.039$, $w = 1/[\sigma(F)^2 + 0.01142(F_o)^2]$, and $S = 0.46$. Ratio of max. least squares shift to e.s.d. in final cycle is 0·065. Max. and min. heights in final difference Fourier synthesis are 0·33 and −0·20 e Å^{-3} respectively. The atomic scattering factors for C, N, O and H from *International Tables for X-ray Crystallography* (1974).

Table 1. *Atomic coordinates* (× 10^4) *for non-hydrogen atoms and equivalent isotropic thermal vibrational parameters* (× 10^3) *with e.s.d.'s in parentheses*

$U_{eq} = (U_{11} + U_{22} + U_{33})/3.$

	x	y	z	U_{eq}(Å^2)
C(1)	5653 (8)	1245 (8)	992 (1)	28 (3)
C(2)	6461 (8)	2277 (9)	729 (1)	37 (4)
C(3)	5531 (9)	2237 (8)	412 (1)	32 (3)
C(4)	4173 (9)	3260 (9)	371 (1)	42 (4)
C(5)	3344 (10)	3214 (9)	75 (2)	48 (5)
C(6)	3841 (12)	2199 (10)	−173 (2)	54 (5)
C(7)	5179 (11)	1183 (10)	−131 (2)	52 (5)
C(8)	6019 (9)	1197 (9)	165 (2)	43 (4)
C(9)	5350 (8)	−518 (8)	879 (1)	26 (3)
C(10)	2354 (8)	38 (9)	768 (1)	31 (4)
C(11)	1529 (9)	−670 (10)	475 (1)	48 (5)
C(12)	1880 (10)	−2504 (11)	507 (2)	53 (5)
C(13)	3631 (9)	−2570 (9)	630 (1)	40 (4)
C(14)	1304 (8)	−110 (9)	1075 (2)	35 (4)
N(1)	6785 (6)	1135 (7)	1272 (1)	30 (3)
N(2)	3868 (6)	−932 (6)	780 (1)	25 (3)
O(1)	6549 (6)	−1164 (6)	867 (1)	35 (3)
O(2)	−68 (6)	584 (7)	1053 (1)	53 (3)
O(3)	1830 (6)	−892 (6)	1313 (1)	43 (3)
OW	237 (6)	−6081 (6)	892 (1)	42 (3)

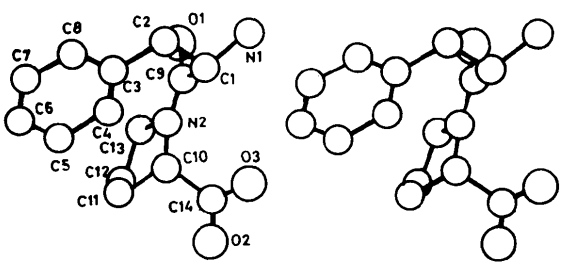


Fig. 1. Stereoview of the molecule.

Discussion. Final parameters of the atoms are listed in Table 1.* A stereoscopic diagram of the molecule is shown in Fig. 1. The bond lengths, bond angles, torsion angles and hydrogen-bond lengths are given in Table 2. The dimensions of the peptide group are in good agreement with the average values of peptide dimensions (Marsh & Donohue, 1967; Ramanadham & Chidambaram, 1978). The bond angles around the N(pro) [N(2)] atom are significantly affected by the internal rotation of the peptide bond between the phenylalanyl and prolyl residues. It is observed (Yamane, Ashida, Shimonishi, Kakudo & Sasada, 1976) that, when the prolyl residue exists in the *cis* form, the angle C′–N–C$^\alpha$ [C(9)–N(2)–C(10) = 130·0 (4)°] is larger than the corresponding angle in peptides existing in the *trans* form. Also, the angle C′–N–C$^\delta$ [C(9)–N(2)–C(13) = 118·6 (4)°] in the

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51268 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond lengths* (Å), *bond angles* (°), *torsion angles* (°) *and hydrogen-bond lengths* (Å) *and angles* (°)

C(1)–C(2)	1·527 (8)	C(9)–O(1)	1·248 (8)
C(2)–C(3)	1·517 (7)	C(9)–N(2)	1·321 (8)
C(3)–C(4)	1·398 (10)	C(10)–N(2)	1·468 (8)
C(4)–C(5)	1·401 (10)	C(10)–C(11)	1·503 (8)
C(5)–C(6)	1·380 (12)	C(11)–C(12)	1·530 (12)
C(6)–C(7)	1·382 (13)	C(12)–C(13)	1·518 (11)
C(7)–C(8)	1·405 (12)	C(13)–N(2)	1·487 (8)
C(3)–C(8)	1·388 (10)	C(10)–C(14)	1·538 (9)
C(1)–C(9)	1·533 (9)	C(14)–O(2)	1·258 (8)
C(1)–N(1)	1·485 (6)	C(14)–O(3)	1·250 (9)

C(1)–C(2)–C(3)	112·9 (5)	N(2)–C(9)–O(1)	123·2 (4)
C(2)–C(3)–C(4)	119·3 (5)	C(9)–N(2)–C(10)	130·0 (4)
C(3)–C(4)–C(5)	118·3 (5)	C(9)–N(2)–C(13)	118·6 (4)
C(4)–C(5)–C(6)	121·7 (6)	C(10)–N(2)–C(13)	111·2 (4)
C(5)–C(6)–C(7)	119·9 (6)	N(2)–C(10)–C(14)	113·5 (5)
C(6)–C(7)–C(8)	119·4 (6)	N(2)–C(10)–C(11)	101·4 (4)
C(3)–C(8)–C(7)	120·5 (6)	C(11)–C(10)–C(14)	112·8 (5)
C(4)–C(3)–C(8)	120·2 (5)	C(10)–C(11)–C(12)	102·9 (5)
C(2)–C(3)–C(8)	120·5 (5)	C(11)–C(12)–C(13)	103·9 (5)
C(2)–C(1)–C(9)	111·7 (5)	C(12)–C(13)–N(2)	103·3 (5)
C(2)–C(1)–N(1)	108·8 (4)	C(10)–C(14)–O(2)	113·6 (5)
C(9)–C(1)–N(1)	106·4 (4)	C(10)–C(14)–O(3)	120·0 (5)
C(1)–C(9)–O(1)	117·8 (4)	O(2)–C(14)–O(3)	126·3 (5)
C(1)–C(9)–N(2)	118·8 (4)		

N(1)–C(1)–C(2)–C(3)	χ_1	170·6 (5)
C(1)–C(2)–C(3)–C(4)	χ_2	81·6 (7)
C(1)–C(2)–C(3)–C(8)	χ_3	−91·3 (7)
C(2)–C(3)–C(4)–C(5)		179·3 (6)
C(2)–C(3)–C(8)–C(7)		−178·7 (7)
C(1)–C(9)–N(2)–C(10)	ω	−2·4 (9)
N(1)–C(1)–C(9)–O(1)	ψ	−42·5 (7)
N(1)–C(1)–C(9)–N(2)		141·8 (5)
C(9)–N(2)–C(10)–C(14)	φ	−91·4 (7)
N(2)–C(10)–C(14)–O(2)	ψ_1	−173·2 (6)
N(2)–C(10)–C(14)–O(3)	ψ_2	5·5 (9)
C(13)–N(2)–C(10)–C(11)	θ	−27·3 (6)
N(2)–C(10)–C(11)–C(12)	χ_1	40·0 (6)
C(10)–C(11)–C(12)–C(13)	χ_2	−39·3 (7)
C(11)–C(12)–C(13)–N(2)	χ_3	22·2 (7)
C(12)–C(13)–N(2)–C(10)	χ_4	3·1 (7)

D–H···*A*	Symmetry code	*D*–*A*	H···*A*	*D*–H···*A*
N(1)–H1N1···O(1)	(i)	2·815 (7)	1·97 (5)	145 (3)
N(1)–H2N1···O*W*	(ii)	2·816 (7)	2·08 (5)	152 (4)
N(1)–H3N1···O(2)	(iii)	2·761 (7)	1·82 (6)	156 (4)
O*W*–H1O*W*···O(2)	(iv)	2·814 (8)	1·93 (6)	172 (4)
O*W*–H2O*W*···O(3)	(ii)	2·692 (7)	1·76 (5)	172 (3)
C(1)–H1C1···O(3)	(ii)	3·197 (8)	2·39 (4)	146 (3)

Symmetry code (i) $\frac{1}{2}-x+1, \frac{1}{2}+y, \frac{1}{4}-z$; (ii) $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{4}-z$; (iii) $x+1, y, z$; (iv) $x, y-1, z$.

present structure is smaller than the corresponding angle in peptides existing in the *trans* conformation.

The dipeptide (LFLP) exists as a zwitterion with nitrogen N(1) of phenylalanine protonated as NH_3^+ and the carboxyl group of the proline residue as ionized COO^-. The peptide linkage is nearly planar. The conformation of the pyrrolidine ring corresponds to the twist form, ${}^{\beta}T_{\alpha}$ [pseudorotational phase angle $P = 157{\cdot}9\ (3)°$, max. amplitude of pucker $\tau_m = 41{\cdot}9\ (3)°$] according to the pseudorotational concept of the five-membered ring system (Chacko, Swaminathan & Veena, 1983) with C^{α}[C(10)] and C^{β}[C(11)] oriented *endo* and *exo* respectively with respect to the C′[C(14)] atom. Interestingly, the peptide linkage exists in the *cis* conformation [$\omega = -2{\cdot}4\ (9)°$] [C(1)–C(9)–N(2)–C(10)], as in the structure of L-prolyl-L-hydroxyproline monohydrate (Arnoux, Prange & Pascard, 1977). The peptide linkage existing in the *cis* conformation is rare in the linear peptides. However, in proline-containing linear as well as cyclic peptides their occurrence as *cis* is more predominant (Nair & Vijayan, 1981).

The rotation about the N–C^{α} and C^{α}–C′ bonds of the peptide linkage is denoted by φ and ψ (Edsall, Flory, Kendrew, Liquori, Nemethy, Ramachandran & Scheraga, 1966). In the present case we have one ψ angle for the N-terminal phenylalanyl residue and one φ angle and two angles ψ_1 and ψ_2 for the C-terminal prolyl residue. The ψ angle for the N-terminal residue is −42·5 (7)° [N(1)–C(1)–C(9)–O(1)]. The φ angle for the C-terminal residue is −91·4 (7)° [C(9)–N(2)–C(10)–C(14)] and ψ_1 and ψ_2 have values −173·2 (6) [N(2)–C(10)–C(14)–O(2)] and 5·5 (9)° [N(2)–C(10)–C(14)–O(3)] respectively. The conformational angles of the peptide linkage are of interest as they represent the minimum-energy states of the peptide conformation.

The molecular packing viewed down the *b* axis is shown in Fig. 2. The NH_3^+ group of the phenylalanyl residue is hydrogen bonded to symmetry-related O(1), water oxygen (O*W*) and translated O(2) atom (along *a* axis). The N–H···O hydrogen bonds are of lengths 2·815 (7), 2·816 (7) and 2·761 (7) Å respectively. The water molecule (O*W*) enters into O–H···O hydrogen bonds with respect to O(2) and O(3) atoms of the carboxyl group at a distance of 2·814 (8) and

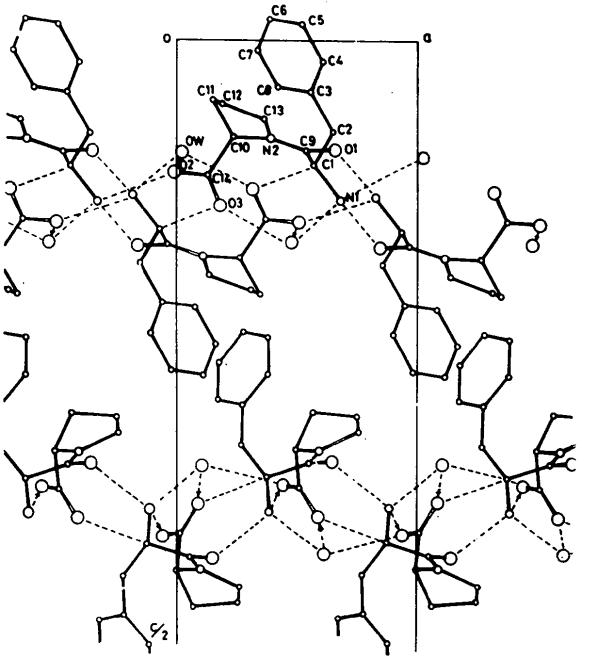


Fig. 2. Packing diagram along the *b* axis.

2·692 (7) Å respectively. There exists a C^{α}—H···O hydrogen bond [3·197(8)Å] in this structure. However, the hydrogen-bond angle [C(1)—H1C1···O(3) = 146 (3)°] suggests that it is a weak C—H···O interaction. It is interesting to observe that C^{α}—H···O hydrogen bonds exists in other dipeptides involving prolyl residues carried out in this laboratory: L-Pro-L-Val.H_2O and L-Pro-Gly.H_2O (Narasimhan & Chacko, 1982), L-Pro-L-Tyr (Veena Ravichandran & Chacko, 1987) and L-Pro-L-Ile.H_2O (Panneerselvam, Chacko & Veena Ravichandran, 1988). Our calculations show that a C^{α}—H···O hydrogen bond also exists in the structures of L-Pro-L-Met.H_2O (Yadava & Padmanabhan, 1981) and L-Pro-L-Ala.H_2O (Yadava & Padmanabhan, 1978). Our analysis regarding the observation of C—H···O hydrogen bonds corroborates the existence of C—H···O hydrogen bonds deduced from neutron diffraction data (Taylor & Kennard, 1982).

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References

ARNOUX, B., PRANGE, T. & PASCARD, C. (1977). *Cryst. Struct. Commun.* **6**, 29–32.

ASHIDA, T. & KAKUDO, M. (1974). *Bull. Chem. Soc. Jpn.* **47**, 1129–1133.

BALASUBRAMANIAN, R., LAKSHMINARAYANAN, A. V., SABESAN, M. N., TEGONI, G., VENKATESAN, K. & RAMACHANDRAN, G. N. (1971). *Int. J. Protein Res.* **3**, 25–33.

CHACKO, K. K., SWAMINATHAN, S. & VEENA, K. R. (1983). *Curr. Sci.* **52**, 660–663.

CHACKO, K. K., SWAMINATHAN, S. & VEENA RAVICHANDRAN, (1984). *Acta Cryst.* A**40**, C101.

EDSALL, J. T., FLORY, P. J., KENDREW, J. C., LIQUORI, A. M., NEMETHY, G. RAMACHANDRAN, G. N. & SCHERAGA, H. A. (1966). *J. Mol. Biol.* **15**, 399–407.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

MARSH, R. E. & DONOHUE, J. (1967). *Adv. Protein. Chem.* **22**, 235–256.

NAIR, C. M. K. & VIJAYAN, M. (1981). *J. Indian Inst. Sci.* **63**, 81–103.

NARASIMHAN, P. & CHACKO, K. K. (1982). *Cryst. Struct. Commun.* **11**, 2051–2056.

PANNEERSELVAM, K., CHACKO, K. K. & VEENA RAVICHANDRAN (1988). Unpublished results.

RAMANADHAM, M. & CHIDAMBARAM, R. (1978). *Advances in Crystallography. Amino Acids: Systematics of Molecular Structure, Conformation and Hydrogen Bonding*, pp. 81–103. New Delhi: Oxford & IBH Publishing Co.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

SHELDRICK, G. M. (1986). *SHELX*86. Program for crystal structure determination. Univ. of Cambridge, England.

TAYLOR, R. & KENNARD, O. (1982). *J. Am. Chem. Soc.* **104**, 5063–5070.

VEENA RAVICHANDRAN & CHACKO, K. K. (1987). Unpublished results.

YADAVA, V. S. & PADMANABHAN, V. M. (1978). *Acta Cryst.* A**34**, S72.

YADAVA, V. S. & PADMANABHAN, V. M. (1981). *Acta Cryst.* A**37**, C66.

YAMANE, T., ASHIDA, T., SHIMONISHI, K., KAKUDO, M. & SASADA, Y. (1976). *Acta Cryst.* B**32**, 2071–2076.

Acta Cryst. (1989). C**45**, 109–111

3-(1-Methyl-1,2,3,6-tetrahydropyrid-4-yl)indole

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Abstract. $C_{14}H_{16}N_2$, $M_r = 212·3$, orthorhombic, $Pca2_1$, $a = 19·424$ (3), $b = 6·770$ (1), $c = 8·899$ (1) Å, $V = 1170·2$ (3) Å^3, $Z = 4$, $D_x = 1·20$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0·71073$ Å, $\mu = 0·7$ cm^{-1}, $F(000) = 456$, $T = 296$ K, final $R = 0·043$ for 1162 observed reflections. The π systems in the title compound (1), a serotonin mimic, are in a 'near-planar' conformation (actually twisted 21° from the *transoid* conformation) as has been postulated to be essential for activity. Molecular-mechanics calculations indicate that the inactive 2-

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