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

BY ROBERT B. BATES, MICHAEL A. BRUCK AND FERNANDO A. CAMOU

Department of Chemistry, University of Arizona, Tucson, Arizona 85721, *USA*

ARNOLD R. MARTIN* AND SHAM S. NIKAM

Department of Pharmaceutical Sciences, University of Arizona, Tucson, Arizona 85721, *USA*

AND DAVID L. NELSON

Department of Pharmacology and Toxicology, University of Arizona, Tucson, Arizona 85721, *USA*

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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-

* To whom correspondence should be addressed.

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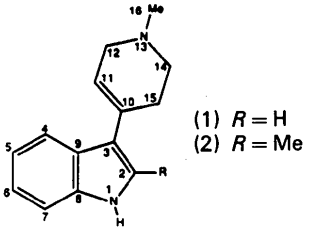
methyl derivative of (1) has near-planar forms of much higher energy in accordance with expectation.

Introduction. The title compound (1) is a crystalline member of a series of (tetrahydropyridyl)indoles that mimic the receptor-binding (Euvrard & Boissier, 1980; Hunt, Nedelec, Euvrard & Boissier, 1981), biochemical (Euvrard & Boissier, 1980; Hunt, Nedelec, Euvrard & Boissier, 1981; Hunt & Oberlander, 1981), physiological (Taylor, Duckles & Nelson, 1986) and behavioral (Hunt & Oberlander, 1981) properties attributed to the neurotransmitter serotonin. A more potent member of the series, the 5-methoxy demethyl derivative RU24969, has been the subject of numerous recent investigations (Sills, Wolfe & Frazer, 1984; Green, Guy & Gardner, 1984; Middlemiss, 1985; Hoyer, Engel & Kalkman, 1985; Raiteri, Maura, Bonanno & Pittaluga, 1986). These and recent studies in our laboratories involving an expanded series of analogs of (1) suggest that an approximately coplanar arrangement of the indole and tetrahydropyridyl rings is optimal for serotonin agonist activity, since: (*a*) saturation of the double bond in the tetrahydropyridyl ring (thus increasing the energy of near-coplanar forms through lack of resonance stabilization) causes a 3·5-fold reduction in activity at 5-hydroxytryptamine 1a binding sites, and (*b*) introduction of a 2-methyl group [*e.g.* to give (2), with greatly destabilized near-planar forms owing to steric repulsions] produces a 12-fold decrease in affinity at both 5-hydroxytryptamine 1a and 2 binding sites. We decided to seek support for these ideas by studying the conformational properties of (1) and (2) with the aid of X-ray diffraction and molecular-mechanics calculations.



(1) R = H
(2) R = Me

Experimental. (1) was prepared by adding 1-methyl-4-piperidone (11·3 ml, 50 mmol) in 4 equal portions over 6 h to a stirred solution of indole (5·85 g, 25 mmol) and ammonium acetate (2·31 g, 50 mmol) in 100 ml of refluxing acetic acid and heating for a further 30 h. The dark-brown solution was concentrated under vacuum, poured into saturated Na_2CO_3 solution, and warmed on a water bath until no further precipitation occurred (6–7 h). The filtered product was chromatographed (silica; $CHCl_3$, MeOH, NH_3) and recrystallized by slow evaporation from 95% EtOH to give 4·58 g (65%) of (1) as pale-yellow needles, m.p. 491–493 K (reported 483–493 K; Freter, 1975). Crystal dimensions 1·1 × 0·7 × 0·65 mm. Syntex $P2_1$ diffractometer. Cell constants from 25 reflections with $25 \le 2\theta \le 35°$. Systematic absences: $0kl$, $l = 2n + 1$, $h0l$, $h = 2n + 1$. $2\theta_{max} = 60°$. Range of hkl: 0→27, 0→9, 0→−12. θ–2θ scans at 2–8° min^{-1}. Three check reflections ($11\bar{1}$, $13\bar{2}$, $22\bar{2}$) every 46 data points; correction (linear between check points) applied for observed 9·1% decay. Nine reflections too strong to measure accurately (omitted from calculations): $00\bar{2}$, 110, 200, $20\bar{2}$, $21\bar{1}$, $21\bar{2}$, $31\bar{1}$, $31\bar{2}$, $40\bar{1}$. No absorption correction. 1162 of 1457 reflections with $I > 3\sigma(I)$ used in F^2 full-matrix refinement. Structure solved using *MULTAN* (Main, Woolfson & Germain, 1971). 13 atoms found in first E map, remaining 3 non-H atoms in F maps. H atoms added in calculated positions (N–H, C–H = 0·95 Å) and restrained to ride on the atom to which they are bonded, with fixed isotropic temperature factors of 5·0 Å^2. Final refinement (144 parameters) of non-H atoms with anisotropic temperature factors gave $R = 0·043$, $wR = 0·057$ with $w = 4F^2/\sigma^2(F^2)$ and $p = 0·04$, $S = 2·0$. $(\Delta/\sigma)_{max} = 0·03$. $\Delta\rho = \pm 0·2$ e Å^{-3}. No anomalous-dispersion or extinction corrections. Program: *SDP* (Frenz, 1978) run on MicroVAX. Scattering factors from Cromer & Waber (1974).

Discussion. Fig. 1 shows a molecule of (1) in the crystal and Table 1 gives the final positional and equivalent isotropic temperature factors.*

The molecule in the crystal has the indole and alkene systems sufficiently close to the planar *transoid* arrangement [torsion angle C2–C3–C10–C11 = −159·2 (2)°, *i.e.*, 20·8 (2)° from *transoid*] to permit π overlap between these systems. To understand better what conformations might be preferred in solution, we calculated the energies of conformations upon clockwise rotation about the C2–C3–C10–C11 angle using the molecular-mechanics program *MMPMI*

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, bond distances and angles, and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51318 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

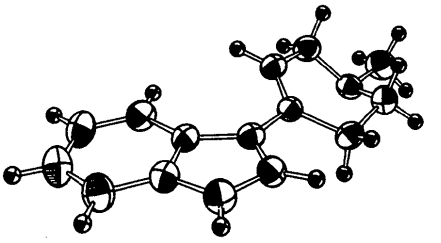


Fig. 1. *ORTEP* (Johnson, 1965) view of a molecule of (1), with 50% probability thermal ellipsoids for non-H atoms and arbitrary spheres for H atoms.

Table 1. *Positional parameters and their e.s.d.'s*

$B_{eq} = 8\pi^2(U_{11} + U_{22} + U_{33})/3.$

	x	y	z	B_{eq}(Å^2)
C3	0·9514 (1)	0·5865 (3)	0·929	2·44 (4)
N1	0·9091 (1)	0·3129 (3)	1·0405 (3)	3·30 (5)
C2	0·9616 (2)	0·4491 (3)	1·0414 (3)	2·92 (5)
C4	0·8502 (2)	0·6014 (4)	0·7298 (3)	3·22 (5)
C5	0·7941 (2)	0·5008 (5)	0·6816 (4)	4·00 (6)
C6	0·7717 (2)	0·3282 (4)	0·7545 (4)	4·38 (7)
C7	0·8077 (2)	0·2534 (4)	0·8752 (4)	3·76 (6)
C8	0·8642 (1)	0·3553 (4)	0·9242 (3)	2·72 (4)
C9	0·8883 (2)	0·5299 (3)	0·8529 (3)	2·62 (4)
C10	0·9985 (1)	0·7498 (3)	0·8947 (3)	2·27 (4)
C11	0·9808 (2)	0·9129 (3)	0·8201 (3)	2·80 (4)
C12	1·0301 (2)	1·0689 (3)	0·7718 (3)	3·15 (5)
N13	1·1014 (1)	0·9992 (3)	0·7787 (3)	2·85 (4)
C14	1·1150 (2)	0·9129 (4)	0·9268 (3)	3·28 (5)
C15	1·0713 (2)	0·7237 (3)	0·9442 (3)	3·12 (5)
C16	1·1500 (2)	1·1601 (4)	0·7480 (5)	4·43 (7)

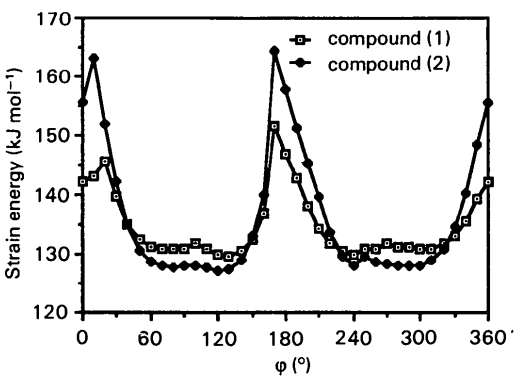


Fig. 2. *MMPMI* results for (1) and (2).

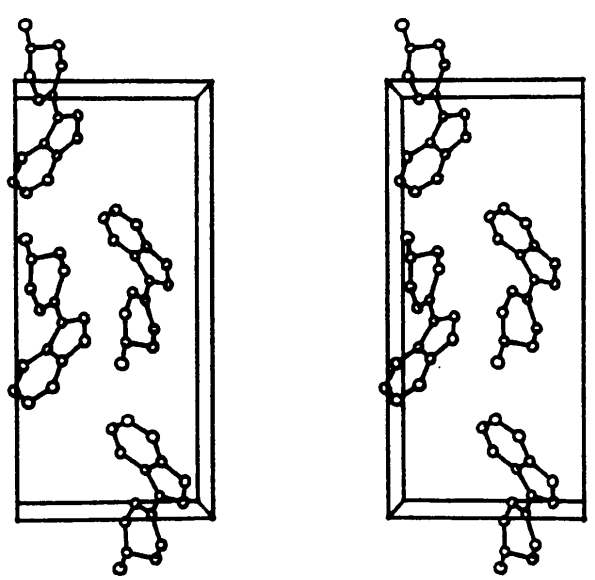


Fig. 3. *ORTEP* view of a unit cell with *a* axis vertical and *c* horizontal.

(Serena Software, Bloomington, IN 47402-3076, USA; this program takes π overlap into account) and minimizing the energy each 10° from 0 to 360°. The results are depicted in Fig. 2 along with the results calculated for the 2-methyl derivative (2). The calculations indicate that the unfavorable steric repulsions in the planar forms outweigh the favorable resonance interactions in these forms, resulting in the forms twisted $90 \pm 40°$ from coplanarity sharing near-minimum energy status. The maximum energy forms, which occur at about 10 and 170° in both compounds, are about 20 kJ mol^{-1} higher than minimum energy for (1) and 40 kJ mol^{-1} higher than minimum for (2), in qualitative accordance with expectation. The X-ray conformation of (1) is calculated to be 7 kJ mol^{-1} higher than the minimum energy conformation; this energy is presumably provided in the crystal by intermolecular hydrogen bonds from N1 to N13 [3·000 (2) Å apart]. These hydrogen bonds connect molecules in adjacent unit cells in the *y* direction (see Fig. 3), creating chains of molecules in the *z* direction.

These findings support the view that the active conformation of (1) is a near-planar form which as a result of its higher energy in the case of (2) is not present in sufficient concentration for significant activity.

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