Crystal Structures of the Teonanácatl Hallucinogens. Part II.† Psilocin, $C_{12}H_{15}N_2O$

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The crystal structure of Psilocin, the minor hallucinogenic component of Teonanácatl, the sacred mushroom of Mexico, has been determined. Crystals are monoclinic, space group $P2_1/c$, $a = 1060(3)$, $b = 853(2)$, $c = 1251(3)$ pm, $\beta = 91{\cdot}25(30)°$. Data were collected on a linear diffractometer employing graphite monochromatised Mo-K_α radiation. The structure was solved by direct methods and refined by block diagonal least-squares to R 0·047 over 1132 significant data. There are intermolecular hydrogen bonds between the ethylamino-nitrogen and the indole hydroxy-group, and disorder of the proton in this hydrogen bond suggests that the crystal is composed of a statistical mixture of zwitterions and uncharged species. The molecular conformation is different from that found in psilocybin.

PSILOCIN is the minor hallucinogenic component isolated from the mushroom species *Psilocybe Mexicana* Heim. It is a dephosphorylation product of psilocybin, and is the active species in the central nervous system. Psilocin itself is a rather labile molecule, and it seems that the major function of the phosphate group in psilocybin is to act as a protective group until the molecule reaches its site of action. The crystal structure has been solved in order to determine the conformation of the active species, and to compare this with the conformation of the phosphorylated molecule. It has been suggested [1] that the ethylamino-nitrogen might form an intramolecular bond with the hydroxy-group, simulating the A, B, and C rings of LSD. Such a hydrogen bond is possible, but the hetero-ring thus formed would certainly *not* resemble the C ring of LSD [2,3] either in composition or in conformation. We find no such hydrogen bond: rather we find *inter*molecular hydrogen bonding between the ethylamino-nitrogen and the hydroxy-group.

EXPERIMENTAL

Crystal Data.—Psilocin, $C_{12}H_{15}N_2O$, $M = 203$. Monoclinic, $a = 1060(3)$, $b = 853(2)$, $c = 1251(3)$ pm, $\beta = 91{\cdot}3(3)°$, $U = 1131 \times 10^6$ pm^3, $D_m = 1{\cdot}19$, $D_c = 1{\cdot}19$, $Z = 4$. Space group $P2_1/c$ (C^5_{2h}, No. 14). Mo-K_α radiation, $\lambda = 71{\cdot}07$ pm; μ(Mo-K_α) = 0·55 cm^{-1}.

Structure Analysis.—Data were collected on a linear diffractometer, using graphite monochromatised Mo-K_α radiation. A total of 1751 measurements yielded 1132 significant reflections with $I > 2{\cdot}5\sigma(I)$. Data were corrected for Lorentz and polarisation effects and placed on an absolute scale by means of a Wilson plot:

$$\begin{aligned} B_{\text{overall}} &= 3{\cdot}81 \\ \langle|E|\rangle &= 0{\cdot}773 \\ \langle|E^2 - 1|\rangle &= 0{\cdot}995 \\ \langle|E^2|\rangle &= 0{\cdot}981 \end{aligned}$$

The structure was solved by direct methods using an automated symbolic addition procedure. Acceptance of a single strong indication of positive sign for the 10 0 0 reflection led to initial difficulties (the sign is in fact negative) but the choice of a different starting set of phases gave an E map in which all non-hydrogen atoms were easily located.

Structure factors calculated from the Fourier positions gave R 0·25, which isotropic refinement reduced to 0·15. Inclusion of hydrogen atoms in calculated positions, followed by further refinement employing anisotropic vibrations for C, N, and O, and individual isotropic temperature factors for H reduced R to its final value of 0·047 over 1132 significant reflections and 0·079 over all 1751 data. An isotropic extinction parameter was also refined and reached a value of 37(3), assuming an overall isotropic $\bar{T}$ of 0·02 cm. Structure factors and B_{ij} parameters are deposited as Supplementary Publication No. SUP 20980 (14 pp., 1 microfiche).‡

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† Part I, H. P. Weber and T. J. Petcher, preceding paper.

‡ For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1972, Index issue.

[1] S. H. Snyder and E. Richelson, *Proc. Nat. Acad. Sci. U.S.A.*, 1968, **60**, 206.

[2] R. W. Baker, C. H. Chothia, P. Pauling, and H. P. Weber, *Science*, 1972, **178**, 614.

[3] R. W. Baker, C. H. Chothia, P. Pauling, and H. P. Weber, *Mol. Pharmacol.*, 1973, **9**, 23.

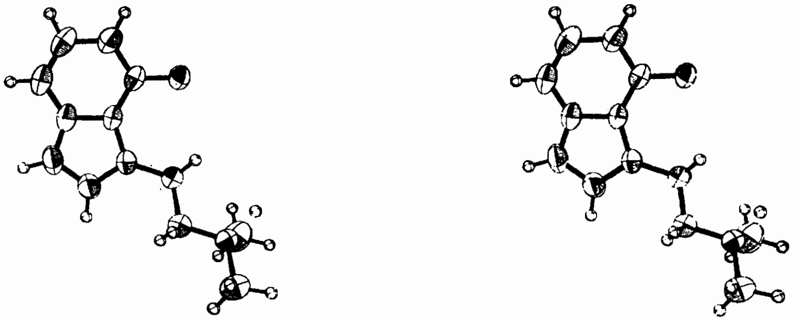

FIGURE 1 A stereo-view of the psilocin molecule, showing 50% probability ellipsoids of thermal motion

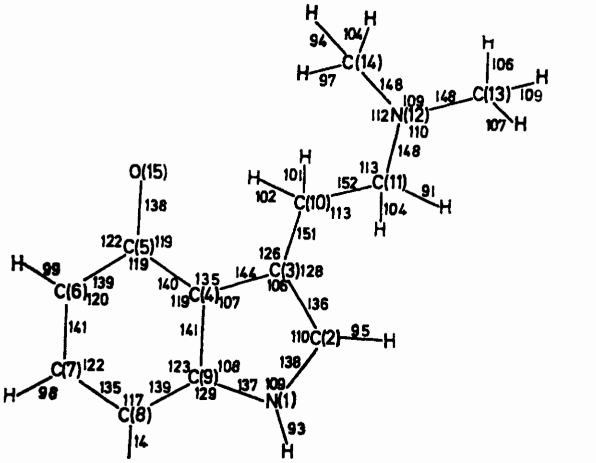

FIGURE 2 Molecular geometry (pm; deg.) and numbering scheme: e.s.d's are C–C ⩽0·5 pm, C–H ⩽5 pm, C–C–C ⩽0·3°

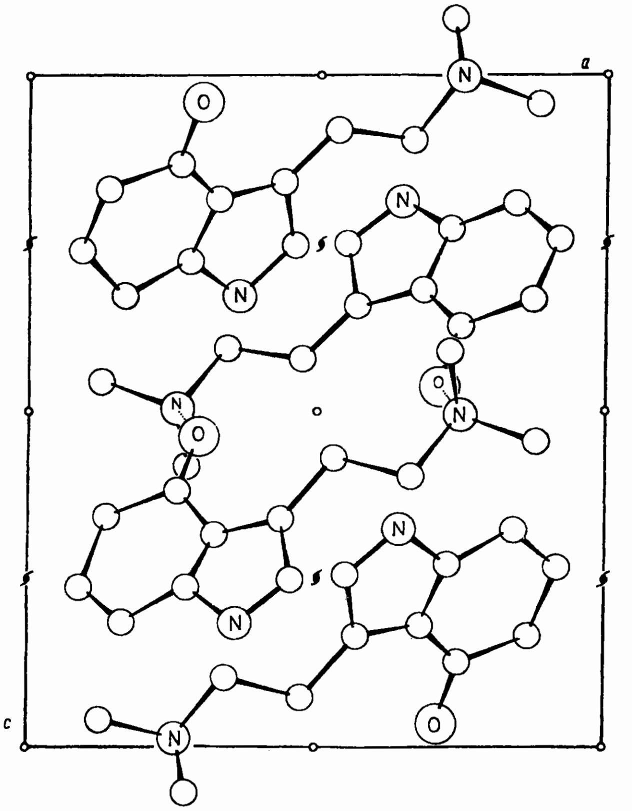

FIGURE 3 The molecular packing viewed down the *b* axis: hydrogen bonding N–H · · · O is indicated thus – – – –

DISCUSSION

The conformation of the molecule is shown as a stereo-pair in Figure 1. The same torsion angles as were given (with the exclusion of those involving P) for psilocybin are presented in Table 1, so that the two compounds may easily be compared. The molecular geometry is presented in Figure 2, which also shows the numbering scheme. Table 2 gives final positions and estimated standard deviations derived from the block-diagonal least-squares refinement, and Figure 3 shows the molecular packing projected down the *b* axis.

TABLE 1

Sufficient torsion angles (deg.) to describe the molecular conformation. Standard deviation ⩽0·4°

C(2)–C(3)–C(10)–C(11)	−20·3
C(4)–C(3)–C(10)–C(11)	+153·3
C(3)–C(10)–C(11)–N(12)	+172·1
C(10)–C(11)–N(12)–C(13)	+169·5
C(10)–C(11)–N(12)–C(14)	−69·2

TABLE 2

Final positions (×10⁴, ×10³ for H) and standard deviations

	x	*y*	*z*	*B*
N(1)	3547(2)	1374(3)	3183(1)	
C(2)	4573(2)	1295(3)	2526(2)	
C(3)	4396(2)	2241(3)	1659(2)	
C(4)	3184(2)	2980(3)	1786(2)	
C(5)	2493(2)	4110(3)	1216(2)	
C(6)	1337(2)	4586(3)	1601(2)	
C(7)	0873(2)	3941(4)	2555(2)	
C(8)	1524(2)	2862(3)	3134(2)	
C(9)	2688(2)	2397(3)	2747(2)	
C(10)	5249(2)	2430(3)	0715(2)	
C(11)	6592(2)	1902(3)	0950(2)	
N(12)	7465(2)	2285(2)	0085(1)	
C(13)	8782(3)	2010(5)	0445(3)	
C(14)	7213(3)	1349(4)	−0888(3)	
O(15)	2993(1)	4760(2)	0312(1)	
H(1)	349(2)	100(3)	387(2)	4·00(76)
H(2)	527(2)	064(3)	271(2)	3·18(68)
H(6)	082(2)	532(3)	117(2)	2·47(61)
H(7)	004(2)	435(3)	372(2)	3·51(70)
H(8)	123(2)	243(3)	377(2)	3·77(72)
H(101)	495(3)	169(3)	011(2)	5·00(85)
H(102)	526(2)	357(3)	050(2)	2·64(63)
H(111)	692(2)	254(2)	161(2)	2·67(62)
H(112)	659(2)	086(3)	113(2)	3·52(69)
H(131)	894(3)	080(5)	063(3)	9·46(127)
H(132)	883(2)	281(2)	104(2)	2·55(60)
H(133)	933(3)	247(4)	−018(3)	7·83(112)
H(141)	635(3)	151(4)	−114(3)	7·44(105)
H(142)	737(3)	026(4)	−067(3)	7·17(101)
H(143)	784(3)	177(3)	−145(2)	5·28(84)
H(12)	730(3)	388(4)	−014(3)	8·43(116)

The bond lengths and angles again correspond rather closely with the mean values found by Falkenberg,[4] and the conformation of the side chain is like that found in serotonine–creatinine sulphate,[5] 5,5-methoxy-*NN*-dimethyltryptamine,[6] and melatonin; [7] *i.e.* it is antiplanar and close to coplanarity with the indole ring system. In contrast to psilocybin, the intermolecular hydrogen bonding scheme is quite simple, there being only one hydrogen bond N(12)–H · · · O(15) [or N(12) · · · H–O(15)]. It is impossible to distinguish unequivocally between the two possibilities as we find N–H = 140, O–H = 122 pm, N–H–O = 173°, σ_{N-H} = 8 pm. These results suggest that the proton is localised on oxygen, but within 3σ limits the bond lengths are equivalent. We think it likely that there is a statistical mixture of neutral molecules and zwitterions in the structure, probably with the uncharged species predominating. Examination of other intermolecular distances shows no abnormal contacts.

[3/2444 *Received*, 28*th November*, 1973]

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