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# Molecular Structures of Hallucinogenic Substances: Lysergic Acid Diethylamide, Psilocybin, and 2,4,5-Trimethoxyamphetamine

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### SUMMARY

BAKER, ROY W., CHOTHIA, CYRUS, PAULING, PETER, AND WEBER, HANS PETER-Molecular structures of hallucinogenic substances: lysergic acid diethylamide, psilo: cybin, and 2,4,5-trimethoxyamphetamine. Mol. Pharmacol. 9, 23-32 (1973).

X-ray diffraction structure analyses of the hallucinogenic substances lysergic acid diethylamide o-iodobenzoate monohydrate, N,N-dimethyl-4-phosphoryloxytryptamine monoethanolate (psilocybin), and 2,4,5-trimethoxyamphetamine hydrochloride are reported. They reveal some relationships among the relative structural arrangements of possible pharmacodynamic groups of these substances.

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#### INTRODUCTION

Similarities in effect and cross-tolerances among the most potent hallucinogenic substance known, lysergic acid diethylamide (1), the hallucinogenic substituted tryptamines, and the methoxy-substituted amphetamines (2) indicate that the mechanisms of action of these drugs *in vivo* are similar. Several attempts have been made recently to predict the conformations of these substances and to compare and relate these predicted conformations. The proposals of Snyder and Richelson (3), based on model building, involved a comparison of possible ring system similarities of the

This work was supported by the Medical Research Council of Great Britain and the Science Research Council of Great Britain. molecules. Those of Chothia and Pauling (4), based primarily on known crystal structures of functional groups, led to a somewhat different comparison of the steric relationships of possible functional groups. Kang and Green (5) have considered other conformations as relevant to biological action. We report here the crystal structures of lysergic acid diethylamide, the tryptamine derivative psilocybin, and a trimethoxyamphetamine.

### EXPERIMENTS

Crystals of hysergic acid diethylamide o-iodobenzoate monohydrate are monoclinic, space group P2<sub>1</sub>, a = 1421(2), b = 765(1), e = 1324(2) pm,  $\beta = 115.53(5)$  degrees, Z = 2 formula units per unit cell,  $\rho_{cbs} =$ 

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FIG. 1. Conformation of lysergic acid diethylamide observed in crystals of the o-iodobenzoate, projected on plane of indole ring

1470(10),  $\rho_{calc} = 1510$  kg m<sup>-3</sup>. Threedimensional diffraction data measured on a Hilger and Watts linear diffractometer, using graphite monochromatized MoK<sub>a</sub> radiation, resulted in 1448 symmetry-independent observed  $[I \ge 3\sigma(I)]$  diffraction maxima. The structure was solved by heavy atom and Fourier methods and refined by fullmatrix least-squares analysis to a residual of R = 0.039, using anisotropic thermal parameters for the non-hydrogen atoms and an over-all isotropic thermal parameter for the hydrogen atoms. All hydrogen atom positions of the molecule have been determined from difference syntheses, as has also one of the hydrogen atoms of the water molecule of crystallization, which forms hydrogen bonds to the oxygen atoms of the iodobenzoate anions. The observed conformation in the absolute configuration of the active enantiomer is shown in Fig. 1, pro-

jected on the plane of the indole ring. Certain torsion angles  $(6)^1$  of the observed conformation and distances from the plane are listed in Table 1, and interatomic distances of the major groups, in Table 2. The conformation of lysergic acid diethylamide, accepting values for bonded interatomic distances and angles, lower limits of nonbonded interatomic distances, and other accepted stereochemical principles, has been discussed by Chothia and Pauling (4) as a five-parameter problem. In view of the rigidity of the ring structure, the torsion angles given are sufficient to describe completely the observed  $D_{i}$ 

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<sup>1</sup> The torsion angle of the bonded group  $A \rightarrow X - Y - B$  is the angle between the plane AXY and the plane XYB. It is positive  $0 \rightarrow 180$  degrees if clockwise from the nearer bond AX to the further bond YB. Values of  $0, \pm 60, \pm 120$ , and 180 degrees are termed syn(peri)planar,  $\pm$  synclinal,  $\pm$  anticlinal, and anti(peri)planar, respectively (6).

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### TABLE 1

Distances of all non-hydrogen atoms from leastsquares plane of indole ring of lysergic acid diethylamide, and torsion angles sufficient to describe fully the observed conformation, accepting observed coplanarity of indole ring

Atom	Distance	Group	Torsion angle <sup>a</sup>
	pm		degrees
$N_1$	0	N <sub>1</sub> C <sub>2</sub> C <sub>4</sub>	- 177
C <sub>2</sub>	0	$C_2 - C_3 - C_4 - C_5$	- 150
C:	-4	C <sub>3</sub> -C <sub>4</sub> -C <sub>5</sub> -N <sub>6</sub>	174
C₄	-12	C <sub>5</sub> C <sub>3</sub> N <sub>6</sub> C <sub>17</sub>	-61
Cs	60	C <sub>6</sub> C <sub>5</sub>	177
N.	43	C3-N6-C7-C8	-69
C <sub>7</sub>	107	N <sub>5</sub> -C <sub>7</sub> -C <sub>8</sub> -C <sub>9</sub>	47
Cs	26	$C_7 - C_8 - C_9 - C_{10}$	-12
C,	-4	$C_8 - C_9 - C_{10} - C_{11}$	170
$C_{10}$	15	$C_{8} - C_{9} - C_{10} - C_{5}$	-5
Cn	6	$C_9 - C_{10} - C_{11} - N_{12}$	11
C11	-2	$C_{5}-C_{10}-C_{11}-N_{12}$	164
C11	-4	$C_{10} - C_{11} - C_{12} - C_{13}$	-177
C14	0	$C_{17} - N_{6} - C_{7} - C_{8}$	168
C13	6	$N_{5}-C_{7}-C_{8}-C_{18}$	166
C16	1	$C_7 - C_8 - C_{18} - O$	-24
C17	102	C7-C5-C18-N20	156
C18	114	$C_{10} - C_{9} - C_{8} - C_{18}$	-130
0	233	$C_{9}-C_{8}-C_{18}-O$	96
N20	47	C <sub>9</sub> -C <sub>8</sub> -C <sub>18</sub> -N <sub>20</sub>	-84
Cn	-97	C=-C15-N26-C21	1
C22	168	C18-N26-C21-C22	-108
C31	136	Cs-C15-N20-C31	-178
C32	188	$C_{18} - N_{20} - C_{31} - C_{32}$	

• The torsion angle of the bonded group  $A \rightarrow X \rightarrow Y \rightarrow B$  is the angle between the plane of  $A \rightarrow X \rightarrow Y$  and that of  $X \rightarrow Y \rightarrow B$ . It is positive  $0 \rightarrow +180$  degrees if clockwise from  $A \rightarrow X/Y$  to  $X/Y \rightarrow B$  and negative  $0 \rightarrow -180$  degrees if counterclockwise, viewed from A (6).

conformation, which is identical with that predicted by Chothia and Pauling (4).

The constraints involved in the linked ring system lead to small departures from normal bond and torsion angles. The conformation observed here in protonated lysergic acid diethylamide is similar to that observed in ergotamine, both as a free base and as the brosylate salt.<sup>2</sup> That the observed conformations are similar in three derivatives indicates that the conformation of lysergic acid diethylamide reported here is

<sup>a</sup> H. P. Weber, unpublished observations.

the preferred one. Methyl substitution at position 8, however, leads to a change of conformation<sup>2</sup> and loss of hallucinogenic activity, as observed in 1,8-dimethyl-d-lysergic acid *p*-bromoanilide.<sup>2</sup> Carbon 7 is found below the plane of ring D, and the amide group is axial instead of equatorial as observed in lysergic acid diethylamide and the two ergotamines.

Crystals of psilocybin monoethanolate (N, N - dimethyl - 4 - phosphoryloxytryptamine) are monoclinic, space group  $P2_1/c$ , a = 1216(1), b = 2905(2), c = 883(1) pm, $\beta = 107.37(3)$  degrees, Z = 8 formula units per unit cell, including 8 molecules of ethanol of crystallization. Three-dimensional diffraction data were measured on a fourcircle diffractometer, using  $MoK_{\alpha}$  radiation with balanced filters, and resulted in 4026 symmetry-independent observed diffraction maxima [I  $\geq 3\sigma(I)$ ]. The structure was solved by direct methods, using symbolic addition, and refined by block-diagonal least-squares analysis to a current value of the residual R = 0.041, using anisotropic thermal parameters for the non-hydrogen atoms and isotropic thermal parameters for the hydrogen atoms. The positions of the hydrogen atoms were determined from difference syntheses. The observed conformation of psilocybin is shown in Fig. 2, projected on the plane of the indole ring. Certain torsion angles and distances from the plane are listed in Table 3. Interatomic distances of the major groups are given in Table 4. The two molecules in the asymmetrical unit are nearly, but not quite, identical. The molecule shown in the figure has an angle of 66 degrees between the plane of the indole ring and the ethylamine chain, inclined toward the phosphoryloxy group. In the other molecule this angle is 97 degrees, with the ethylamine chain inclined slightly away from the phosphoryloxy group. The observed conformations are similar to those proposed on stereochemical principles (4). There has been much discussion (3, 4) about the possibility of forming a hydrogen bond between the ammonium nitrogen atom and an oxygen atom of the 4-phosphoryloxy group of the indole ring, to form a ring analogous to ring C of lysergic acid diethylamide. No such hydrogen bond is formed in psilocybin or in any

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				Таві	LE 2				
	Some inter	atomic di	tances of oj	lysergic f the o-iod	acid diethy lobenzoate	ylamide ob	served in	crystals	
C17	147								
A.	553	650							
B	495	558	232						
DB¢	263	401	352	423					
Nı	603	657	291	145	528				
0	410	497	688	740	367	844			
N20	489	607	716	797	383	902	557		
C22	604	719	855	928	525	1035	700	249	
C#2	668	782	772	890	518	983	602	237	426
	N.	C17	A	В	DB	0	N20	N20	C22

A, to the center of ring A, is defined as the arithmetic mean of the distances to C<sub>11</sub>, C<sub>12</sub>, C<sub>13</sub>, C<sub>14</sub>, C<sub>15</sub>, and C<sub>16</sub>.
<sup>b</sup> B, to the center of ring B, is defined as the arithmetic mean of the distances to N<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>15</sub>,

<sup>b</sup> B, to the center of ring B, is defined as the arithmetic mean of the distances to  $N_1$ ,  $U_2$ ,  $U_3$ ,  $U_{15}$ , and  $C_{16}$ .

• DB, to the middle of the  $C_{9}=C_{10}$  double bond, is defined as the arithmetic mean of the distances to  $C_{9}$  and  $C_{10}$ .



FIG. 2. Observed conformation of 1 of the 2 molecules in the asymmetrical unit of psilocybin, projected on plane of indole ring

The conformation of the other molecule in the asymmetrical unit is similar.

## MOLECULAR STRUCTURES OF HALLUCINOGENIC SUBSTANCES

Atom	Atom o	listance	Group	Torsion angle		
-	A	В		A	В	
	p	m		deg	rees	
Nı	-3	-3	$N_1 - C_2 - C_1 - C_{10}$	175	171	
C <sub>2</sub>	2	0	$C_{8} - C_{9} - C_{3} - C_{10}$	-174	175	
C,	2	3	$C_{\bullet} - C_{\bullet} - C_{\bullet} - C_{10}$	8	11	
C₄	-3	-2	$C_{2}-C_{3}-C_{10}-C_{11}$	-107	-72	
C.	0	2	$C_{s}-C_{a}-C_{10}-C_{11}$	65	98	
C	3	2	$C_{2} - C_{10} - C_{11} - N_{12}$	174	- 165	
C	0	2	$C_{10} - C_{11} - N_{12} - C_{13}$	144	84	
C <sub>8</sub>	-2	0	$C_{10} - C_{11} - N_{12} - C_{14}$	91	- 155	
С,	0	1	C <sub>3</sub> C <sub>9</sub> C <sub>4</sub> O <sub>1</sub>	5	3	
<b>C</b> 10	18	26	CCO1	175	176	
<b>C</b> <sub>11</sub>	154	168	$C_s - C_s - C_s - O_1$	-173	-176	
N22	179	213	$C_{1}-C_{1}-P$	-140	148	
C13	260	254	$C_{1} - C_{1} - P_{1}$	44	34	
C14	243	330	$C_{r} - O_{1} - P - O_{2}$	55	50	
P	60	55	$C_{4} - O_{1} - P_{-}O_{2}$	171	166	
01	-16	-11	C	-63	78	
01	211	195		00	-10	
0,	28	46				
0.	22	-34				

TABLE 3 -Distances of all non-hydrogen atoms from plane of indole ring of both molecules of psilocybin in the asymmetrical unit and some observed torsion angles

other known tryptamine derivative. Psilocybin is hydrolyzed in the organism to psilocin (N, N-dimethyl-4-hydroxytryptamine), and psilocin is considered to be the likely active metabolite (1).

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Available crystal structure analyses suggest no definite conclusions about the preferred conformation of biologically active derivatives of tryptamine (Table 5) although there are generally consistent relationships among the hallucinogenic tryptamines. The N, N-dimethyl-5-methoxyhallucinogenic tryptamine HCl (13) is nearly planar, as is the neurotransmitter 5-hydroxytryptamine (serotonin) in crystals of the creatinine sulfate monohydrate (8). In the picrate monohydrate (9), however, 5-hydroxytryptamine has  $\tau_1 = -115$  degrees (Table 5) and  $\tau_3 =$ 67 degrees, similar to the observed conformations of tryptamine HCl (7) and 5-methoxytryptamine (10). Six observed independent conformations of the hallucinogenic substances N, N-dimethyltryptamine (11),

bufotenine (12), and psilocybin are consistent, in that  $\tau_1$  and  $\tau_2$  [ $\tau_1 + (-\tau_2) = 180$ degrees if the indole system is strictly planar] are 90  $\pm$  20 degrees and  $\tau_3$  is approximately 180 degrees. It is only this conformation of tryptamine derivatives which corresponds with the rigid conformation of lysergic acid diethylamide.

Of the seven observations of N, N-dimethyltryptamine, six are consistent: four are bases and two are ethanolates, a large organic anion. The one inconsistent observed conformation is a hydrochloride and forms an N—H  $\cdots$  Cl hydrogen bond (13).

Shulgin, Sargent, and Naranjo (2) have synthesized and tested a large number of substituted amphetamines for hallucinogenic activity. There are no clear-cut conclusions about activity as a function of location of substituents on the benzene ring. We have analyzed the structure of 2,4,5trimethoxyamphetamine, the most potent of the trimethoxyamphetamines. A commonly

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### TABLE 4

# Observed interatomic distances of psilocybin in crystals of the iodide

Molecules A and B are the two molecules in the asymmetrical unit of the crystal.

Molecule A									
C13 C14 A <sup>6</sup> B <sup>b</sup> P O1 N1	148 148 600 501 463 432 589	245 652 594 430 453 688	697 565 606 567 635	256 413 296 290	502 360 144	161 604	461		
	N <sub>12</sub>	C12	C14	A	в	Р	01		
		N	folecul	e B					
C13 C14 A B P O1 N1	151 150 604 495 513 456 577	243 605 548 423 413 642	716 593 643 595 658	256 407 297 293	505 360 145	161 607	462		
	N <sub>12</sub>	Cıa	C14	A	В	Р	01		

• A, to the center of the 6-membered indole ring, is defined as the arithmetic mean of the six distances to  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ , and  $C_9$ .

<sup>b</sup> B, to the center of the 5-membered indole ring, is defined as the arithmetic mean of the five distances to  $N_1$ ,  $C_2$ ,  $C_3$ ,  $C_3$ , and  $C_9$ .

used hallucinogenic amphetamine is a congener having a 4-methyl group instead of a 4-methoxy group.

Crystals of 2,4,5-trimethoxyamphetamine hydrochloride are orthorhombic, space group Pbca, a = 2016.5(5), b = 1707.0(5), c = 829.8(8) pm, Z = 8 formula units per unit cell. Three-dimensional diffraction data collected on a computer-controlled, fourcircle diffractometer, using graphite monochromatized MoK<sub>a</sub> radiation, resulted in 513 symmetry-independent observed [I  $\leq 3\sigma(I)$ ] diffraction maxima. The structure was solved by the heavy atom method, using the chlorine atom, and refined by full-matrix leastsquares analysis to the value of the residual R = 0.040, using anisotropic thermal param-

eters for all atoms except hydrogen and an over-all isotropic thermal parameter for the hydrogen atoms. The hydrogen positions were determined from difference syntheses and refined. The conformation of the molecule as observed in crystals of the hydrochloride is shown in Fig. 3, projected on the plane of the benzene ring. Certain torsion angles and distances from the plane are given in Table 6. Interatomic distances of the major groups are given in Table 7. The observed conformation is unusual; for all other known structures of phenylethylamine derivatives (excepting amino acids) the nitrogen atom is antiplanar with respect to  $C_1$  about the  $C_7$ — $C_8$  bond, and the angle between the planes of the ethylamine chain and the benzene ring is approximately 90 degrees, as seen in Table 8. In the observed structure of 2,4,5-TMA<sup>3</sup> the angle between the planes defined by  $C_8$ — $C_7$ — $C_1$  and the benzene ring is similar to the other compounds, but the  $\alpha$ -methyl group is antiplanar and the nitrogen atom is synclinal with respect to  $C_1$ . This unusual crystallographic conformation (Table 8) may be due to the crystal packing of the compound, which involves an N—H · · · Cl and two N—H · · · O hydrogen bonds.

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This observed unusual conformation of 2,4,5-TMA in crystals of the hydrochloride illustrates one of the dangers of interpreting face-value results of diffraction analyses. For labile molecules such as derivatives of phenylethylamine and tryptamine it is essential to have several observed structures available to determine possible and probable conformations relevant to drug action. We do not consider the unusual conformation observed for 2,4,5-TMA to be responsible for the hallucinogenic effects of this and related compounds. On the basis of the correlation with lysergic acid diethylamide, it is the usually observed conformation of derivatives of phenylethylamine (Table 8) which is relevant to drug and transmitter action. It is the methoxy or other substitution, not changes in conformation, that alters the properties of

<sup>3</sup> The abbreviation used is: 2,4,5-TMA, 2,4,5-trimethoxyamphetamine HCl.

### MOLECULAR STRUCTURES OF HALLUCINOGENIC SUBSTANCES

TABLE	5
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Observed	l conformations in terms of torsion angles of derivatives of	tryptamine
For a review of all	known structures of indole derivatives, see ref. 14.	

Compound	71 <sup>4</sup>	$ au_{2}^{b}$	T3 <sup>C</sup>	Reference
·		degrees		
Tryptamine HCl	-111	69	60	78
5-Hydroxytryptamine creatine				•
sulfate H <sub>2</sub> O	-9	167	173	8
5-Hydroxytryptamine picrate				Ũ
H <sub>2</sub> O	-115	67	67	9
5-Methoxytryptamine	-116	63	55	10
N, N-Dimethyltryptamine				10
a	- 102	79	-176	11
Ь	-90	89	172	
5-Hydroxy-N, N-dimethyl-				
tryptamine (bufotenine)				
a	- 87	89	175	
Ь	-72	102	- 170	12
5-Methoxy-N, N-dimethyl-				
tryptamine HCl	17	161	- 179	13
4-Phosphoryloxy-N, N-dimethyl-				10
tryptamine monoethanolate				
(psilocybin)				
a	- 107	65	174	
Ъ	-72	98	- 165	

•  $\tau_1$  is torsion angle C<sub>2</sub>-C<sub>3</sub>-C<sub>10</sub>-C<sub>11</sub>.

 $\bullet$   $\tau_2$  is torsion angle C<sub>9</sub>-C<sub>7</sub>-C<sub>10</sub>-C<sub>11</sub>.

 $\tau_2$  is torsion angle  $C_3 - C_{10} - C_{11} - C_{12}$ .

Coordinates from Professor K. Tomita.

the compounds, although in the case of the methoxy-substituted amphetamines no clearcut relationship between activity and position of substitution is evident (2).

As in psilocybin, there is no evidence for an intramolecular hydrogen bond between the ammonium nitrogen atom and the oxygen atom in position 2. In the observed conformation the nitrogen atom is on the side of the chain away from oxygen atom  $O_2$  rather than toward it  $(N-O_2 = 392 \text{ pm})$ . The methoxy groups are in the plane of the benzene ring, as is invariably observed (4) except where some neighboring atom interferes, as in mescaline (3,4,5-trimethoxyphenylethylamine), where the methyl of the 4-methoxy group is forced out of the plane by steric hindrance with the two neighboring methoxy groups (4).<sup>4</sup>

<sup>4</sup>C. de Rango, C. Zelwer, G. Tsoucaris, R. Panthasarathy, and F. Cole, manuscript in preparation.

### DISCUSSION

These observed conformational results are not generally consistent with the proposals of Snyder and Richelson (3) and Kang and Green (5), but are in accord with the proposals of Chothia and Pauling (4).

Given the observed conformations of lysergic acid diethylamide and psilocybin and the conformation of hallucinogenic amphetamines as those normally observed in derivatives of phenylethylamine, there are approximate but not exact relationships between what may be pharmacodynamic groups essential for hallucinogenic activity. These approximate relationships are best seen with the aid of Corey-Pauling-Koltun atomic models. The relationships between the aromatic ring system and the charged nitrogen atom (N<sub>6</sub> in lysergic acid diethylamide, N<sub>12</sub> in psilocybin, and N<sub>10</sub> in 2,4,5-TMA) are nearly the same in the three molecules,

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FIG. 3. Conformation of 2,4,5-trimethoxyamphetamine observed in crystals of the hydrochloride, projected on plane of benzene ring

### TABLE 6

Observed distances of all non-hydrogen atoms from plane of benzene ring and certain torsion angles in 2,4,5-trimethoxyamphetamine hydrochloride

Atom	Distance	Group	Torsion angle
	pm		degrees
$C_1$	0	$C_{r} - C_{r} - C_{l} - C_{7}$	179
$C_2$	0	$C_5 - C_6 - C_1 - C_7$	-179
C3	-1	$C_{T} - C_{I} - C_{T} - C_{S}$	68
C.	2	$C_{}C_{1}-C_{}C_{3}$	-114
Cs	-1	$C_1 - C_7 - C_8 - N$	50
C <sub>6</sub>	0	$C_1 - C_7 - C_8 - C_9$	170
01	-2	$C_{1} - C_{2} - O_{2} - C_{21}$	-1
$C_{21}$	-4	$C_{r} - C_{r} - O_{r} - C_{41}$	-12
O4	0	C-C-C-O-Cs	4
$C_{41}$	23		
O۵	-5		
$C_{51}$	1		
$C_7$	-1		
Cs	133		
C,	135		
N10	260		

particularly if one does not try to obtain an exact atom-by-atom fit of the 6-membered aromatic rings. There are also approximate . relationships among the 9,10 double bond of lysergic acid diethylamide, the 4-hydroxyl group of psilocin, and the 2-methoxy group of 2,4,5-TMA and among the ring nitrogen atoms N<sub>1</sub> of lysergic acid diethylamide and psilocybin and the 5-methoxy group of 2,4,5-TMA although these latter relationships are not very convincing. These relationships are shown diagrammatically in Fig. 4.  $\frac{\text{In}}{\frac{\text{the if}}{N}}$ 

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At the level of precision of conformation presented here, it is impossible to find exact relationships among the groups (see tables). However, exact relationships may not be essential for the related activities of the substances.

### ACKNOWLEDGMENTS

We thank Drs. A. Hofmann and A. T. Shulgin for crystalline samples, Dr. Trevor J. Petcher and

# MOLECULAR STRUCTURES OF HALLUCINOGENIC SUBSTANCES

TABLE 7

	(	Observed int	eratomic di	stances of 2,	4,5-trimetho	xyamphetam	ine	
In the the nitrog	conformati zen atom ar	on consider e interchan	ed relevant ged, the dis	to biologic: tances to C <sub>s</sub>	al action, in and N are i	which the r nterchanged	nethyl group 1.	p at C <sub>9</sub> and
N	246							
Å٩	537	407		•				
<b>O</b> 2	444	392	291					
$C_{12}$	570	513	381	145				
04	797	626	292	487	503			
C14	870	698	377	511	493	138		
O <sub>5</sub>	717	553	<b>294</b>	553	634	259	396	
C15	712	<b>5</b> 62	383	637	737	403	540	144
	С,	N	A	O2	$C_{12}$	O,	C14	O <sub>s</sub>

• A, to the center of the 6-membered ring, is defined as the arithmetic mean of the distances to C<sub>1</sub>,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , and  $C_6$ .

TABLE 8	
Observed conformations in terms of torsion angles of derivatives of phenylethylamin. For a review of the known structures of derivatives of phenylethylamine, see ref. 15.	e

Compound	$ au_1{}^a$	$ au_2{}^b$	$ au_3^c$	Reference
Phenylethylamine HCl	73	-113	-171	16
Ephedrine HCl				
Ī	81	-103	-162	17
II	81	-98		18
Dopamine HCl	79	99	174	19
Norepinephrine HCl	82	97	176	20
Amphetamine H <sub>2</sub> SO <sub>4</sub>				
a	71	-109	-175	21
Ъ	77	- 107	-173	
с	69	114	-172	
d	81	-100	-166	
Mescaline HCl	88	-90	175	d
Pseudoephedrine Cu complex				
a	74	-96	-163	22*
Ь	68	-106	-179	
c	74	-103	-172	
6-Hydroxydopamine HCl	83	-94	-175	23
2,4,5-Trimethoxyamphet-				
amine HCl	70	-111	50	

•  $\tau_1$  is torsion angle  $C_2 - C_1 - C_7 - C_8$ . •  $\tau_2$  is torsion angle  $C_6 - C_1 - C_7 - C_8$ . •  $\tau_3$  is torsion angle  $C_1 - C_7 - C_8 - N$ .

\* Coordinates from Dr. George Tsoucaris.

• Coordinates from Dr. Pamela M. Bailey.

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FIG. 4. Diagrammatic representations of conformations of lysergic acid diethylamide, psilocybin, and 2,4,5-trimethoxyamphetamine, showing possible structural correlations

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