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and Allan Zalkin

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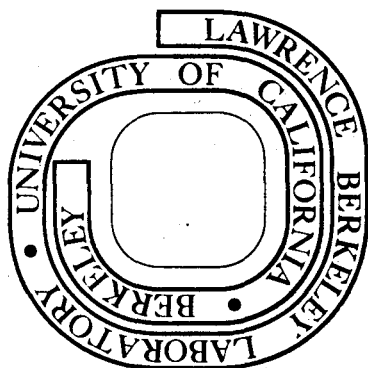
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# The Crystal and Molecular Structure of 5-Methoxytryptamine\*

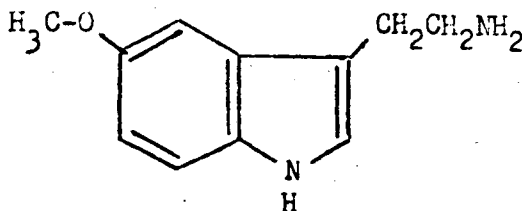
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Crystals of 5-methoxytryptamine ( $C_{11}H_{14}N_2O$ ) are monoclinic, space group Pc;  $a = 6.110(2)$ ,  $b = 9.532(3)$ ,  $c = 8.831(3)$  Å,  $\beta = 98.72(1)^\circ$ ,  $Z = 2$ ,  $D_m = 1.242$  g cm<sup>-3</sup>,  $D_x = 1.245$  g cm<sup>-3</sup>. The structural model was refined to  $R = 0.025$  for 746 independent X-ray reflections measured with an automatic diffractometer. The indole ring system deviates from planarity by small but significant amounts which correspond to a bending in the benzene ring. The ethylamine side chain is in the bent (gauche) conformation rather than fully extended. Each indole nitrogen atom donates its hydrogen atom to form a hydrogen bond to the amine nitrogen of the next molecule, with  $N-N = 2.916(3)$  Å.

\*Work performed under the auspices of the  
U. S. Atomic Energy Commission.

## Introduction

Serotonin and related molecules have attracted widespread attention because of their involvement in the function of the central nervous system (Garattini & Valzelli, 1965). We have studied the crystal structures of two of these substances because molecular dimensions and conformations are relevant to studies of biological function. In this paper we describe the structure of 5-methoxytryptamine:



In another paper we will describe the structure of melatonin and compare the dimensions of these closely related molecules.

## Experimental

Crystals of 5-methoxytryptamine from the Regis Chemical Company, Chicago, were well-formed, thin, colorless, transparent plates. They were stable when stored at 5°C over Drierite, but turned brown when exposed to the atmosphere for a month. Exposure to X-rays hastened the color change and caused diffraction intensities to decrease, but the decrease was only one or two percent during the three-day period in which the intensity data were collected.

Oscillation and Weissenberg photographs showed monoclinic symmetry and systematic absences for  $h0l$  if  $l$  is odd, corresponding to space groups  $P2/c$  and  $Pc$ . The cell volume and the density permit only two molecules per cell. Space group  $P2/c$  is eliminated because it would require four molecules per unit cell (or a multiple of four) unless the molecules lie on the 2-fold axis, and the molecule of 5-methoxytryptamine lacks that symmetry.

Cell dimensions at room temperature (approx.  $23^{\circ}C$ ) were determined from measurements of resolved  $CuK\alpha$  doublets ( $\lambda = 1.54051 \text{ \AA}$  for  $K\alpha_1$ ) with a General Electric Co. manual diffractometer for  $h00$ ,  $0k0$ , and  $00l$  reflections. The density was measured by flotation in ethylene chloride and ethyl acetate.

A crystal with dimensions  $0.34 \times 0.10 \times 0.032 \text{ mm}$  was mounted on a glass fiber with epoxy resin. Intensity data were measured with a scintillation counter,  $CuK\alpha$  radiation, a graphite monochromator, and a Picker automatic diffractometer. Attenuators were used when the counting rate would have exceeded 10,000 c/sec. A  $\theta-2\theta$  scan technique was used, starting  $0.9^{\circ}$  below the position for  $K\alpha_1$  and scanning at  $1^{\circ}/\text{min}$  to  $0.9^{\circ}$  above the  $K\alpha$  position. Backgrounds were counted for 10 sec at positions  $0.7^{\circ}$  from the ends of the scan (all angles in  $2\theta$ ). Measurements

were made of 1604 reflections in the hemisphere with  $k$  positive and  $2\theta < 124.5^\circ$  ( $\sin\theta/\lambda < 0.574$ ). Averaging of Bijvoet pairs ( $hkl$  and  $\bar{h}\bar{k}\bar{l}$ ) yielded 807 independent reflections of which 61 had intensities less than  $\sigma(I)$  and were assigned zero weight.

Formulas are given elsewhere for the calculation of standard deviations of the average intensities and for the conversion to structure factors, their standard deviations, and the corresponding weights in least-squares refinement (St. Clair, Zalkin & Templeton, 1971, 1972). The additional term in  $\sigma^2(I)$  was  $(0.05 I)^2$  initially and  $(0.03 I)^2$  in the last calculations. No correction for absorption was made; with  $\mu = 6.6 \text{ cm}^{-1}$  the attenuation would be about 12% in the most extreme case.

Calculations were made with the CDC-6600 computer and our unpublished programs. Atomic scattering factors were those of Stewart, Davidson & Simpson (1965) for spherical hydrogen atoms and Cromer & Mann (1968) for other atoms. Dispersion corrections for these light atoms were ignored. Johnson's (1965) program was used to prepare the figures.

#### Determination of the Structure

The Patterson function suggested approximately the correct orientation for the plane of the flat indole ring system. A trial-and-error method described by

Quarles (1970) determined the structure of the eleven heavy atoms comprising these rings and their immediate substituents. Fourier methods revealed the rest of the atoms. With 14 heavy atoms and anisotropic thermal parameters  $R_1 = \Sigma |\Delta F| / \Sigma |F_o|$  was reduced to 0.064 and  $R_2 = (\Sigma w(\Delta F)^2 / \Sigma w(F_o)^2)^{1/2}$  to 0.080. Inclusion of the 14 hydrogen atoms (with isotropic thermal parameters) reduced  $R_1$  to 0.033 and  $R_2$  to 0.035. An empirical extinction correction factor, which was 1.18 for the structure factor of the strongest reflection, and adjustment of the intensity parameter in the standard deviation formula together reduced  $R_1$  to 0.025 and  $R_2$  to 0.026, in each case for the 746 reflections included in least squares. Including 61 reflections of zero weight,  $R_1$  was 0.028. In the last cycle, no parameter shifted as much as 3% of its standard deviation. The standard deviation of an observation of unit weight was 1.11. Inspection revealed no systematic trend of either  $|F_o|/|F_c|$  or  $w(\Delta F)^2$  as a function of intensity or Bragg angle. No peaks in the final  $\Delta F$  synthesis were higher than  $0.15 \text{ e}/\text{\AA}^3$ .

The final coordinates and thermal parameters are listed in Tables 1, 2, and 3, and bond distances and angles in Tables 4 and 5 with the atoms designated as shown in Fig. 1. Observed and calculated structure factors are listed in Table 6.



Discussion

The molecular conformation is shown in Fig. 2. The ethylamine side chain is bent into the gauche or synclinal conformation. The bond distances and angles are in good agreement with corresponding values for melatonin, with which they will be compared elsewhere, and with the results for several other similar molecules which have been reviewed by Falkenberg (1972a). The nine atoms of the indole ring system are very nearly planar, but deviations from planarity are significant in comparison to the estimated standard deviations, about 0.004 Å. The largest deviation from a mean plane is 0.015 Å. Seven of the atoms, however, are within 0.004 Å of a plane fitted to the pyrrole ring; the other two atoms, C(7) and C(8), are respectively 0.040 and 0.036 Å to one side of this plane. Atoms O(1) and C(2), the first atoms of the side chains, are 0.006 and 0.007 Å, respectively, from this same plane. Deviations from planarity of similar magnitude have been observed in melatonin and in other indole derivatives for which the structures have been determined with high precision (Falkenberg, 1972b, Falkenberg & Carlström, 1971, and Bergman, Abrahamsson & Dahlén, 1971), but no consistent pattern of the deviations is evident.

The molecules are connected by hydrogen bonds of the type N(2)-H(10)···N(1), with the N-N distance 2.916(3) Å

and the N-H-N angle  $170(3)^\circ$ . The molecules connected by these bonds form strings running in the [101] direction. Otherwise there are no close intermolecular interactions. The packing of the molecules is shown in Fig. 3.

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Table 1. Coordinates of heavy atoms<sup>a</sup>

Atom	x	y	z
C(1)	.3467(0)	.3571(3)	.9726(0)
C(2)	.5789(7)	.2923(3)	.0040(5)
C(3)	.6839(6)	.3048(2)	.1689(4)
C(4)	.6088(6)	.2435(2)	.3008(4)
C(5)	.4265(6)	.1572(2)	.3189(4)
C(6)	.4050(6)	.1152(3)	.4647(4)
C(7)	.5609(6)	.1535(3)	.5922(4)
C(8)	.7384(7)	.2375(3)	.5765(5)
C(9)	.7606(6)	.2834(2)	.4291(4)
C(10)	.8715(6)	.3782(3)	.2241(4)
C(11)	.0721(7)	.0109(3)	.8763(5)
N(1)	.3332(6)	.4970(3)	.5195(5)
N(2)	.9196(6)	.3666(3)	.3801(4)
O(1)	.2350(6)	.0321(2)	.4990(4)

<sup>a</sup>In this and the following tables the standard deviation of the least significant digit is given in parentheses.

Table 2. Anisotropic thermal parameters<sup>a</sup>

Atom	B <sub>11</sub>	B <sub>22</sub>	B <sub>33</sub>	B <sub>12</sub>	B <sub>13</sub>	B <sub>23</sub>
C(1)	3.5(1)	4.0(1)	2.8(1)	-.3(1)	-.06(9)	.6(1)
C(2)	3.9(1)	4.1(1)	2.9(1)	.1(1)	.79(9)	.1(1)
C(3)	2.9(1)	3.2(1)	2.9(1)	.43(9)	.60(9)	.15(9)
C(4)	2.4(1)	2.51(9)	2.7(1)	.31(8)	.21(8)	.02(8)
C(5)	2.7(1)	2.7(1)	2.5(1)	.18(8)	-.07(9)	-.17(8)
C(6)	3.3(1)	3.0(1)	3.0(1)	.00(9)	.40(9)	.16(9)
C(7)	4.2(1)	4.0(1)	2.5(1)	.1(1)	.1(1)	.35(9)
C(8)	3.7(1)	3.7(1)	2.7(1)	.0(1)	-.51(9)	-.2(1)
C(9)	2.5(1)	2.7(1)	3.2(1)	.25(9)	.17(9)	-.24(9)
C(10)	2.9(1)	3.8(1)	4.0(1)	.2(1)	.87(9)	.4(1)
C(11)	3.8(1)	4.0(1)	4.2(1)	.7(1)	.6(1)	-.2(1)
N(1)	2.9(1)	3.7(1)	6.0(2)	-.12(9)	-.2(1)	-1.0(1)
N(2)	2.67(9)	4.0(1)	4.0(1)	-.27(9)	.13(8)	-.11(9)
O(1)	4.14(9)	4.88(9)	3.09(8)	-1.19(8)	.31(6)	.89(7)

<sup>a</sup>The temperature factor is  $\exp((-B_{11}a^2h^2 - 2B_{12}a^*b^*hk - \dots)/4)$ .

Table 3. Parameters of hydrogen atoms<sup>a</sup>

Atom	x	y	z	B
H(1)	.344(7)	.501(4)	.630(6)	9.0(12)
H(2)	.411(7)	.449(4)	.455(5)	7.7(12)
H(3)	.248(4)	.300(2)	.027(3)	3.1(5)
H(4)	.292(5)	.354(3)	.862(4)	4.0(6)
H(5)	.563(4)	.189(3)	.977(3)	3.6(6)
H(6)	.673(6)	.339(3)	.938(4)	5.6(8)
H(7)	.318(4)	.126(3)	.229(3)	2.6(5)
H(8)	.532(5)	.119(3)	.692(3)	4.3(6)
H(9)	.845(5)	.262(4)	.663(4)	5.4(7)
H(10)	.046(6)	.415(4)	.434(4)	5.9(8)
H(11)	.972(6)	.433(3)	.160(4)	5.2(7)
H(12)	.969(5)	.072(3)	.929(3)	4.3(6)
H(13)	.006(5)	.067(4)	.320(4)	5.4(8)
H(14)	.131(5)	.068(3)	.792(4)	4.8(6)

<sup>a</sup>The isotropic temperature factor is  $\exp(-B\lambda^{-2}\sin^2\theta)$ .

Table 4. Bond distances, Å

Atoms	Distance	Atoms	Distance
N(1)-H(1)	.99(5)	C(7)-C(8)	1.372(4)
N(1)-H(2)	.92(5)	C(8)-H(9)	.96(3)
N(1)-C(1)	1.457(4)	C(8)-C(9)	1.398(3)
C(1)-H(3)	.99(3)	C(9)-C(4)	1.404(3)
C(1)-H(4)	.99(3)	C(9)-N(2)	1.374(3)
C(1)-C(2)	1.534(4)	N(2)-H(10)	.96(4)
C(2)-H(5)	1.02(3)	N(2)-C(10)	1.368(4)
C(2)-H(6)	.98(4)	C(10)-C(3)	1.368(4)
C(2)-C(3)	1.504(3)	C(10)-H(11)	1.04(3)
C(3)-C(4)	1.439(3)	O(1)-C(6)	1.376(3)
C(4)-C(5)	1.413(3)	O(1)-C(11)	1.416(3)
C(5)-H(7)	1.00(2)	C(11)-H(12)	1.02(3)
C(5)-C(6)	1.374(3)	C(11)-H(13)	.95(3)
C(6)-C(7)	1.408(4)	C(11)-H(14)	1.03(3)
C(7)-H(8)	.98(3)		



Table 5. Bond angles, deg

Atoms	Angles
N(1)-C(1)-C(2)	115.04(25)
C(1)-C(2)-C(3)	112.98(23)
C(2)-C(3)-C(4)	127.57(25)
C(2)-C(3)-C(10)	126.63(27)
C(4)-C(3)-C(10)	105.80(21)
C(3)-C(4)-C(5)	132.98(21)
C(3)-C(4)-C(9)	106.89(20)
C(9)-C(4)-C(5)	120.13(21)
C(4)-C(5)-C(6)	117.70(21)
C(5)-C(6)-C(7)	121.65(23)
C(5)-C(6)-O(1)	123.84(20)
C(7)-C(6)-O(1)	114.51(25)
C(6)-C(7)-C(8)	121.31(25)
C(7)-C(8)-C(9)	117.79(24)
C(8)-C(9)-C(4)	121.40(22)
C(8)-C(9)-N(2)	130.29(24)
C(4)-C(9)-N(2)	108.30(20)
C(9)-N(2)-C(10)	108.04(22)
N(2)-C(10)-C(3)	110.97(22)
C(6)-O(1)-C(11)	117.70(21)

Table 6. Observed (FOB) and calculated (FCA) structure factors for 5-methoxytryptamine

(Table to be reproduced photographically)

TABLE OF OBSERVED AND CALCULATED STRUCTURE FACTORS FOR 5-ETHYLADIPIC ACID

Table with multiple columns containing numerical data for structure factors, including observed and calculated values for various reflections. The table is organized into several sections based on h, k, l indices.

## Figure Captions

- Fig. 1. Bond distances ( $\text{\AA}$ ) and designation of atoms.
- Fig. 2. Molecular conformation.
- Fig. 3. Molecular packing, viewed down a, with b horizontal and c vertical.

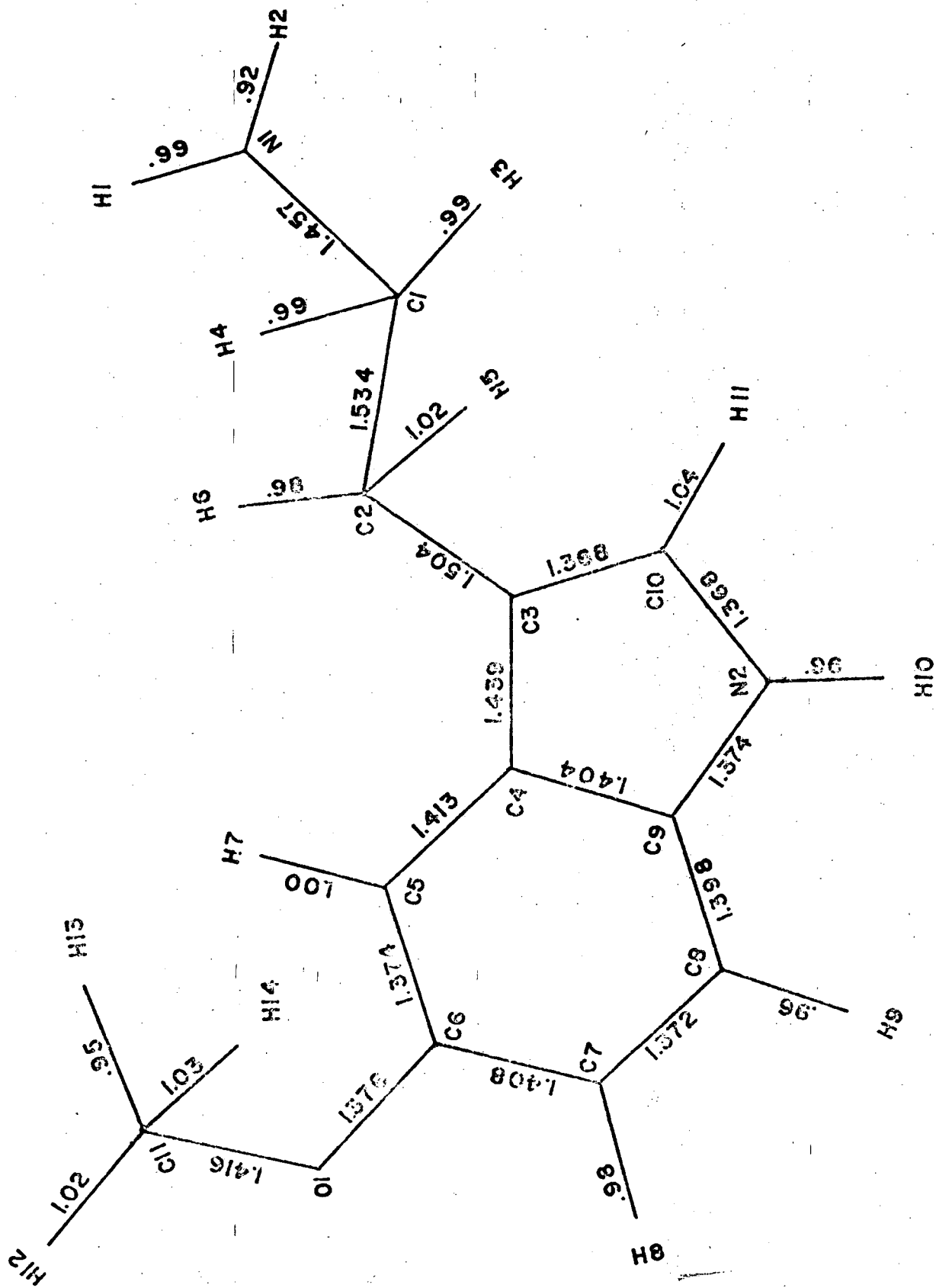
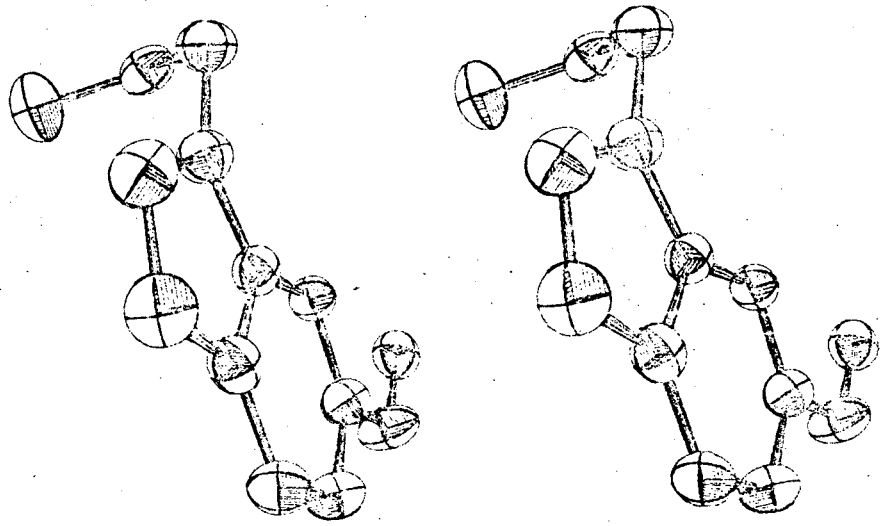


Figure 1.



XBL 704-836

Figure 2.

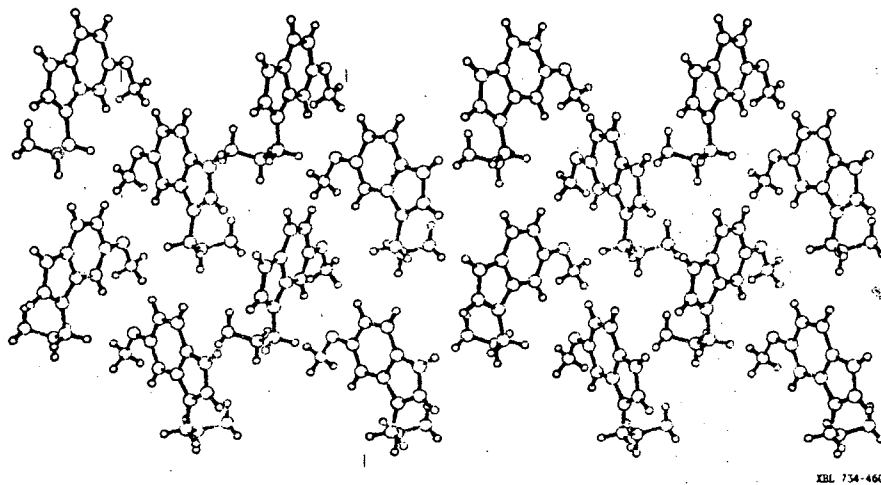


Figure 3.

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