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and Allan Zalkin

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The Crystal and Molecular Structure of Melatonin*

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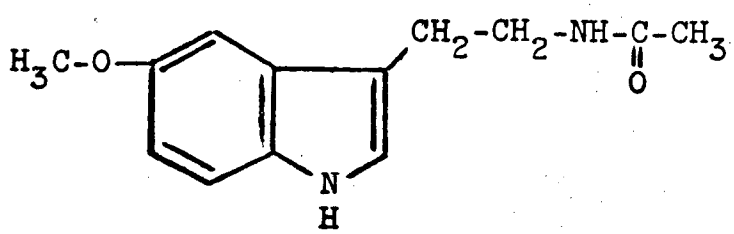
Crystals of melatonin ($C_{13}H_{16}N_2O_2$) are monoclinic, space group $P2_1/c$; $\underline{a}$ = 7.707(2), $\underline{b}$ = 9.252(2), $\underline{c}$ = 17.077(4) Å, β = 96.78(3)°, Z = 4, D_m = 1.272, D_x = 1.276 g cm^{-3}. The structural model was refined to R = 0.036 for 900 independent X-ray reflections measured using an automatic diffractometer. The molecules are nearly flat with the side chain in the fully extended (trans) conformation. Molecules are connected in sheets by weak hydrogen bonds from nitrogen to oxygen, with N—O = 2.90 and 2.96 Å.

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

Introduction

Melatonin, $C_{13}H_{16}N_2O_2$, is formed in the pineal gland of the human brain by N-acetylation of serotonin (Lerner, Case & Takahashi, 1960) followed by methylation (Axelrod & Weissbach, 1960). Its molecular structure is:



We studied its crystal structure as we did that of 5-methoxytryptamine (Quarles, Templeton & Zalkin, 19xx) to gain evidence of the conformations which these and similar molecules might have in biological systems.

Experimental

A crystal of melatonin (Regis Chemical Co., Chicago), 0.35 × 0.27 × 0.10 mm in size, was glued to a glass fiber with General Electric 1202 Clear Industrial Varnish, with the axis of the fiber parallel to the short dimension of the crystal. Cell dimensions were derived by least squares from 2θ values of 13 well-centered, resolved Mo$\underline{K}\alpha_1$ diffraction peaks (λ = 0.70926 Å) measured with a Picker 4-circle automatic diffractometer at room temperature (approx. 23°C). Intensities were measured by the same θ-2θ scan technique described by Quarles, Templeton & Zalkin (19xx) except that Mo$\underline{K}\alpha$ radiation was used and the scan

interval extended from 1.0° below α_1 to 1.0° above α_2. The experiment was monitored by measurement of reflections 006 and 206 after each 50 reflections; the maximum variation was less than 10% with no systematic trend. The measurements included 2275 reflections in the hemisphere with k zero or positive and $(\sin\theta/\lambda) < 0.482$. Equivalent reflections were averaged to yield 1140 independent intensities. Zero weight was assigned to 240 independent reflections for which $I < \sigma(I)$. The factor p in the $(pI)^2$ term of the standard deviation was taken as 0.04 in the final calculations.

The absorption coefficient μ is estimated as 0.94 cm^{-1}, and μt is 0.03 for the largest dimension of the crystal. Under these circumstances the absorption effect is negligible, and no correction was made. An empirical correction for extinction was applied before the final refinement; it increased the structure factor of the strongest reflection by 9%.

Calculations were made with the CDC-6600 and CDC-7600 computers and our unpublished programs. Atomic scattering factors were those of Stewart, Davidson & Simpson (1965) for polar hydrogen atoms, Doyle & Turner (1968) for other atoms, with the almost negligible dispersion corrections of Cromer & Liberman (1970). The polar model for hydrogen atoms (Templeton, Olson, Zalkin & Templeton, 1972) recognizes that the center of gravity of the electron density does not coincide with the proton, and it yields

bond distances for hydrogen which are about 0.1 Å longer than those obtained in the traditional manner. Johnson's (1965) program was used to prepare the figures.

Determination of the Structure

The phases of 151 strong reflections were determined by Sayre's (1952) equation with the program written by Long (1965). The E map for the "best" solution showed the 17 non-hydrogen atoms as the 17 largest peaks. Least-squares refinement reduced $R_1 = \Sigma|\Delta F|/\Sigma|F_o|$ to 0.116 with isotropic thermal parameters and to 0.091 with anisotropic thermal parameters.

The 16 hydrogen atoms were recognized among the 19 highest peaks in a Fourier synthesis of ΔF. They were included in the calculation with isotropic thermal parameters. After correction for extinction and adjustment of the weights, further least-squares refinement reduced $R_2 = (\Sigma w(\Delta F)^2/\Sigma w|F_o|^2)^{1/2}$ to 0.033; R_1 was 0.036 for the 900 reflections included in least squares and 0.054 for 1140 reflections. The standard deviation of an observation of unit weight was 1.01. In the final cycle no parameter shifted more than 0.02σ. The largest peak in a ΔF synthesis, near the end of refinement, was 0.19 $e\text{Å}^{-3}$.

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 atoms designated as shown in Fig. 1.

Observed structure factors, standard deviations, and values of ΔF are listed in Table 6.

Discussion

As seen in Fig. 2, the ethylamine side chain is in the fully extended (trans) conformation, and the entire molecule except for hydrogen atoms is approximately planar. Atoms C(12) and C(13) are respectively 0.31 and 0.62 Å from a mean plane through the indole ring system, but all other non-hydrogen atoms are closer than 0.18 Å to this plane. Each of the nine atoms of the ring system deviates from this plane by 0.019 Å or less. This small but statistically significant deviation from planarity of the ring system consists predominantly of a twist of the pyrrole ring, and the benzene ring is quite flat. Atoms C(3), C(10), and N(2) are 0.038, 0.040, and -0.007 Å from the mean plane of the benzene ring. In 5-methoxytryptamine (Quarles, Templeton & Zalkin, 19xx) we found the pyrrole ring to be flat, but the benzene ring to be non-planar by similar small amounts. In crystals of bufotenin (Falkenberg, 1972b) two kinds of molecules are crystallographically independent and exhibit two other patterns of slight non-planarity of the indole ring system. These facts suggest that the non-planarity in each case is the result of packing forces, and that it has no significance concerning the structure of the isolated molecule.

A comparison of the bond distances in melatonin and in 5-methoxytryptamine, excluding the C(1)—C(2) bond, reveals that those in melatonin are systematically shorter by about 0.007 Å. After a correction of this amount, the differences are quite consistent with the estimated standard deviations according to a probability plot (Hamilton & Abrahams, 1972). Falkenberg (1972a) gave average values for many of these bond distances based on our results and five other accurate structure determinations (two of which included two independent molecules in the same crystal). Compared to these average bond lengths, our results tend to be low by 0.002 Å for melatonin and high by 0.005 Å for 5-methoxytryptamine. Probably at least part of these effects are the result of thermal motion, for which no correction has been made. Perhaps radiation damage to the 5-methoxytryptamine crystal also makes a contribution.

The various C—C bonds in the aromatic ring system differ in length by as much as 0.05 Å, a variation far greater than the small discrepancies discussed above, and this variation is rather consistent in the various crystals. We regard it as a genuine effect of the electronic structure of these molecules.

The C(1)—C(2) bond length is 1.534(4) Å in 5-methoxytryptamine, 1.501(4) Å in melatonin, and various

intermediate values in the other crystals listed by Falkenberg (1972a). We cannot identify the cause of this discrepancy. The conformation difference between gauche and trans does not offer a simple explanation because serotonin picrate monohydrate (Thewalt & Bugg, 1972) is gauche with C—C = 1.513(4) Å in agreement with several cases which are trans.

We attribute no special significance to the conformations of the side chains found in these crystals, but consider them to be the result of crystal packing. Falkenberg (1972a) reports 11 gauche and 9 trans examples among 20 indoleamines, and also a considerable variety of torsion angles where the ethylamine is attached to the ring. We assume that melatonin and similar compounds can exist in either conformation in various environments.

The molecules of melatonin are connected by weak hydrogen bonds between nitrogen and oxygen, N(1)—H(1)···O(2) and N(2)—H(10)···O(2); N—O = 2.96 and 2.90 Å, respectively. These bonds connect the molecules in infinite sheets parallel to <u>b</u> and <u>c</u>. The molecules are arranged in the crystal as shown in Fig. 3.

We thank Professor W. B. Quay for providing the crystals and Mrs. Helena Ruben for assistance with the calculations.

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Table 1. Coordinates of heavy atoms

In this and the following tables the standard deviation of the least significant digit is given in parentheses.

	x	y	z
C(1)	.4374(6)	.1941(3)	.6265(2)
C(2)	.3713(5)	.3244(3)	.5798(2)
C(3)	.3186(4)	.2942(3)	.4945(2)
C(4)	.2389(3)	.3952(3)	.4385(2)
C(5)	.1883(4)	.5403(3)	.4446(2)
C(6)	.1181(4)	.6104(3)	.3777(2)
C(7)	.0954(4)	.5392(4)	.3050(2)
C(8)	.1421(4)	.3977(4)	.2971(2)
C(9)	.2139(4)	.3263(3)	.3650(2)
C(10)	.3373(4)	.1703(4)	.4541(2)
C(11)	.0875(7)	.8303(5)	.4467(3)
C(12)	.5973(4)	.1427(4)	.7551(2)
C(13)	.6738(7)	.2007(4)	.8332(2)
N(1)	.5094(3)	.2346(3)	.7057(1)
N(2)	.2722(4)	.1875(3)	.3765(2)
O(1)	.0660(3)	.7531(2)	.3751(1)
O(2)	.6136(3)	.0145(2)	.7370(1)

Table 2. Anisotropic thermal parameters

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

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(1)	6.3(2)	2.8(2)	3.1(2)	.1(2)	.2(2)	-.1(1)
C(2)	4.3(2)	3.1(2)	3.5(2)	.4(2)	.5(1)	.2(1)
C(3)	4.2(2)	2.6(1)	2.8(2)	.2(1)	.5(1)	-.3(1)
C(4)	3.2(2)	2.8(1)	3.0(2)	-.4(1)	.5(1)	-.0(1)
C(5)	4.0(2)	3.2(2)	3.4(2)	-.3(1)	.6(1)	-.3(2)
C(6)	4.1(2)	3.5(2)	4.2(2)	.1(1)	.2(1)	.3(2)
C(7)	4.7(2)	4.7(2)	3.8(2)	-.1(2)	-.4(1)	1.1(2)
C(8)	4.6(2)	4.8(2)	3.3(2)	-.6(2)	.1(1)	-.2(2)
C(9)	3.8(2)	2.9(2)	3.5(2)	-.1(1)	.3(1)	-.3(1)
C(10)	4.6(2)	3.6(2)	3.4(2)	.1(2)	.4(1)	.3(2)
C(11)	6.6(3)	3.2(2)	7.1(3)	.4(2)	.5(2)	-.1(2)
C(12)	4.2(2)	2.9(2)	3.3(2)	.3(1)	.9(1)	.4(1)
C(13)	6.1(3)	4.2(2)	3.6(2)	.2(2)	.0(2)	-.3(2)
N(1)	5.8(2)	2.1(1)	3.1(1)	.4(1)	.4(1)	-.3(1)
N(2)	5.7(2)	3.5(2)	3.8(2)	-.0(1)	.8(1)	-1.1(1)
O(1)	6.9(1)	3.7(1)	5.8(1)	1.4(1)	.1(1)	.7(1)
O(2)	7.3(1)	2.4(1)	4.2(1)	.61(9)	.89(9)	.06(8)

Table 3. Parameters of hydrogen atoms

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

	x	y	z	B
H(1)	.494(3)	.333(3)	.722(1)	2.5(7)
H(3)	.334(4)	.114(3)	.630(2)	4.6(8)
H(4)	.543(4)	.140(3)	.600(2)	4.9(8)
H(5)	.470(4)	.406(3)	.588(2)	4.9(8)
H(6)	.265(4)	.368(3)	.605(1)	3.2(7)
H(7)	.203(3)	.595(3)	.499(2)	3.3(6)
H(8)	.037(3)	.597(3)	.256(2)	4.0(7)
H(9)	.121(4)	.344(3)	.241(2)	5.9(9)
H(10)	.282(3)	.123(3)	.338(2)	2.5(7)
H(11)	.382(4)	.067(3)	.474(2)	4.4(8)
H(12)	.017(5)	.782(4)	.494(2)	7.3(11)
H(13)	.045(4)	.933(4)	.430(2)	5.7(9)
H(14)	.222(5)	.823(4)	.478(2)	6.9(10)
H(15)	.673(4)	.318(4)	.836(2)	6.4(9)
H(16)	.597(5)	.163(4)	.877(2)	7.5(11)
H(17)	.806(6)	.173(4)	.846(2)	8.2(12)

Table 4. Bond distances (Å)

C(1)-C(2)	1.501(4)	N(1)-H(1)	0.97(3)
C(2)-C(3)	1.491(4)	C(1)-H(3)	1.09(3)
C(3)-C(4)	1.425(4)	C(1)-H(4)	1.09(3)
C(4)-C(5)	1.406(4)	C(2)-H(5)	1.07(3)
C(4)-C(9)	1.400(4)	C(2)-H(6)	1.05(3)
C(5)-C(6)	1.368(4)	C(5)-H(7)	1.06(3)
C(6)-C(7)	1.398(4)	C(7)-H(8)	1.05(3)
C(7)-C(8)	1.369(4)	C(8)-H(9)	1.08(3)
C(8)-C(9)	1.391(4)	N(2)-H(10)	0.90(3)
C(9)-N(2)	1.368(4)	C(10)-H(11)	1.06(3)
N(2)-C(10)	1.370(4)	C(11)-H(12)	1.11(4)
C(10)-C(3)	1.354(4)	C(11)-H(13)	1.04(4)
C(6)- O(1)	1.379(3)	C(11)-H(14)	1.12(4)
O(1)-C(11)	1.409(4)	C(13)-H(15)	1.09(4)
C(1)-N(1)	1.449(4)	C(13)-H(16)	1.07(4)
N(1)-C(12)	1.326(3)	C(13)-H(17)	1.05(4)
C(12)-O(2)	1.236(3)		
C(12)-C(13)	1.494(4)		

Table 5. Bond angles (deg)

N(1)-C(1)-C(2)	110.9(3)
C(1)-C(2)-C(3)	113.9(3)
C(2)-C(3)-C(4)	125.4(3)
C(2)-C(3)-C(10)	128.6(3)
C(4)-C(3)-C(10)	106.0(3)
C(3)-C(4)-C(5)	132.7(3)
C(3)-C(4)-C(9)	107.8(3)
C(5)-C(4)-C(9)	119.4(3)
C(4)-C(5)-C(6)	118.4(3)
C(5)-C(6)-C(7)	121.0(3)
C(5)-C(6)-O(1)	124.4(3)
C(7)-C(6)-O(1)	114.7(3)
C(6)-C(7)-C(8)	122.1(3)
C(7)-C(8)-C(9)	117.1(3)
C(4)-C(9)-C(8)	122.0(3)
C(4)-C(9)-N(2)	106.9(3)
C(8)-C(9)-N(2)	131.1(4)
C(3)-C(10)-N(2)	110.3(3)
C(13)-C(12)-N(1)	117.2(3)
C(13)-C(12)-O(2)	121.8(3)
N(1)-C(12)-O(2)	121.1(2)
C(1)-N(1)-C(12)	122.5(3)
C(9)-N(2)-C(10)	108.9(3)
C(6)-O(1)-C(11)	117.0(3)

Table 6. Observed structure factors, standard deviations, and values of $|F_o| - |F_c|$

(Table to be reproduced photographically)

OBSERVED STRUCTURE FACTORS, STANDARD DEVIATIONS, AND DIFFERENCES (X 6.0) FOR
TABLE OF OBSERVED AND CALCULATED STRUCTURE FACTORS FOR REL F(0,0,0) = 2977
SG = ESTIMATED STANDARD DEVIATION OF FOB. DEL = /FOB/-/FCA/. * INDICATES ZERO WEIGHTED DATA.

L	FCB	SG	DEL
H,K=		0,	0
2	94	8	2
4	136	3	C
6	167	6	4
8	156	4	3
10	84	2	-6
12	158	6	-0
14	45	8	-3
16	155	3	-4
H,K=		0,	1
1	269	6	-6
2	145	4	-2
3	137	3	-6
4	119	3	-0
5	45	10	-7
6	38	5	3
7	93	3	2
8	230	5	11
9	64	3	1
10	47	3	-0
11	71	2	1
12	18	14	-6
13	14	11	-7
14	40	5	-8
15	93	3	1
16	19	25	-19*
H,K=		0,	2
0	532	11	-31
1	230	5	-5
2	174	4	0
3	211	5	-6
4	378	8	2
5	65	5	-1
6	201	6	4
7	18	5	-1
8	177	4	6
9	65	2	4
10	55	2	-1
11	59	2	8
12	71	2	-C
13	13	17	1*
14	48	4	2
15	11	22	1*
H,K=		0,	3
1	81	3	-1
2	51	6	8
3	81	2	-1
4	46	2	C
5	63	2	2
6	70	2	0
7	22	3	-C
8	92	2	4
9	89	2	4
10	29	4	-6
11	69	2	0
12	13	15	-1*
13	167	4	-3
14	46	6	-3
15	41	5	6
H,K=		0,	4
0	0	12	-13*
1	145	3	2
2	149	3	4
3	13	15	1C*
4	64	2	1
5	106	2	2
6	90	3	5
7	71	3	C
8	44	3	-5
9	67	2	2
10	62	2	3
11	26	6	3
12	21	6	5
13	6	22	-1*
14	17	19	-0*
H,K=		0,	5
1	113	2	4
2	198	4	10
3	95	3	6
4	104	2	0
5	57	2	2
6	52	2	-1
7	90	2	-1
8	0	12	-5*
9	74	2	-1
10	81	3	0
11	127	3	-5
12	19	17	-8
13	75	4	-5
H,K=		0,	6
0	138	3	1
1	8	12	-1C*
2	20	7	1

L	FOB	SG	DEL
3	27	7	7
4	37	3	5
5	103	4	0
6	84	3	2
7	36	7	-9
8	53	4	-4
9	53	2	1
10	106	4	1
11	39	3	-4
12	43	5	5
H,K=		0,	7
1	29	8	0
2	48	3	1
3	57	4	-4
4	73	2	0
5	62	3	-0
6	155	3	2
7	0	18	-4*
8	42	7	-2
9	35	6	-1
10	93	2	-5
H,K=		0,	8
0	32	38	3*
1	32	3	9
2	107	3	-1
3	55	4	2
4	55	3	-6
5	12	24	-8*
6	52	4	-8
7	89	2	1
H,K=		1,	0
-16	11	19	-9*
-14	170	4	5
-12	42	2	-1
-10	171	3	2
-8	124	3	3
-6	33	5	2
-4	439	8	-5
-2	316	6	-2
0	182	4	-11
2	730	15	4
4	36	16	3
6	283	6	3
8	54	2	8
10	205	5	-2
12	159	4	1
14	147	4	-2
H,K=		1,	1
-16	105	6	-6
-15	23	100	-10*
-14	72	4	1
-13	52	5	-1
-12	55	2	1
-11	117	3	-1
-10	0	16	-17*
-9	166	4	5
-8	117	3	2
-7	177	4	2
-6	53	6	1
-5	171	4	-2
-4	226	5	-6
-3	355	7	-4
-2	170	4	-9
-1	94	2	-0
0	269	5	-8
1	142	4	-5
2	335	9	-1
3	75	5	1
4	95	5	-0
5	58	4	5
6	105	3	2
7	78	2	2
8	220	5	9
9	13	20	4*
10	71	4	3
11	6	12	-2*
12	67	3	2
13	142	3	-3
14	69	9	-5
15	12	21	-6*
H,K=		1,	2
-16	27	5	-9
-15	91	4	-2
-14	0	23	-5*
-13	35	3	-2
-12	5	13	5*
-11	41	2	3
-10	222	5	4
-9	106	3	4
-8	106	2	2
-7	8	10	-1*
-6	97	3	2
-5	166	4	1

L	FOB	SG	DEL
-4	101	4	0
-3	279	6	-6
-2	94	4	-5
-1	102	3	-3
0	220	5	-6
1	147	4	-3
2	7	26	-11*
3	26	26	-2*
4	46	4	-2
5	82	2	2
6	280	6	8
7	250	7	15
8	220	5	5
9	79	2	-2
10	9	12	9*
11	60	2	2
12	73	3	-1
13	91	3	-1
14	65	6	1
15	11	23	-5*
H,K=		1,	3
-15	11	15	5*
-14	41	9	2
-13	74	3	0
-12	17	7	8
-11	63	3	0
-10	0	12	-1*
-9	31	6	1
-8	85	3	6
-7	238	5	4
-6	93	2	1
-5	20	5	-3
-4	12	16	5*
-3	118	3	2
-2	73	4	0
-1	0	22	-4*
0	46	5	-1
1	138	3	-4
2	47	3	3
3	274	6	4
4	99	2	1
5	179	6	6
6	108	2	-0
7	31	4	-1
8	166	3	9
9	82	2	7
10	13	16	3*
11	17	13	15
12	17	20	14*
13	75	4	-7
14	24	9	-3
H,K=		1,	4
-14	71	2	-3
-13	24	8	-2
-12	32	5	4
-11	17	7	-1
-10	76	2	2
-9	8	15	2*
-8	81	2	1
-7	36	3	2
-6	4	16	3*
-5	136	3	1
-4	81	2	-1
-3	215	4	2
-2	176	4	7
-1	92	2	3
0	70	2	1
1	45	4	3
2	53	2	-1
3	44	2	0
4	142	3	-0
5	93	2	3
6	22	4	-0
7	19	4	-4
8	15	18	1*
9	29	5	-1
10	10	12	5*
11	79	2	0
12	13	16	-0*
13	44	4	-0
14	12	20	-1*
H,K=		1,	5
-13	31	6	-4
-12	29	12	-5
-11	90	3	1
-10	44	5	4
-9	8	17	-9*
-8	19	9	8
-7	26	3	-3
-6	138	3	-2
-5	65	2	1
-4	56	2	-8
-3	6	14	-2*

L	FOB	SG	DEL
-2	90	2	2
-1	128	3	4
0	210	4	7
1	213	5	3
2	42	4	-0
3	113	3	7
4	98	2	2
5	52	2	3
6	82	3	1
7	9	13	-4*
8	42	3	1
9	43	2	-1
10	13	15	7*
11	35	9	4
12	46	4	-3
13	5	19	-3*
H,K=		1,	6
-12	15	11	8
-11	0	15	-1*
-10	25	8	3
-9	124	3	2
-8	129	3	-6
-7	9	14	7*
-6	69	2	4
-5	24	6	1
-4	32	4	-1
-3	99	3	-1
-2	43	4	5
-1	115	2	-1
0	148	3	2
1	36	3	6
2	25	8	-2
3	0	13	-14*
4	53	3	1
5	12	16	7*
6	57	2	-1
7	113	3	2
8	57	5	-0
9	50	4	2
10	85	2	-3
11	49	5	-4
H,K=		1,	7
-10	69	4	-0
-9	26	8	11
-8	108	3	-4
-7	0	25	-5*
-6	127	3	0
-5	85	2	-1
-4	86	3	2
-3	15	20	14*
-2	64	2	1
-1	28	6	2
0	21	5	1
1	38	3	3
2	19	11	12
3	60	2	3
4	135	3	1
5	84	3	1
6	158	4	-7
7	35	5	-5
8	125	3	-3
9	20	24	7*
H,K=		1,	8
-7	65	2	0
-6	23	6	2
-5	62	3	3
-4	76	4	0
-3	17	21	14*
-2	46	6	-6
-1	37	5	-5
0	21	23	3*
1	28	13	-4
2	62	2	-4
3	110	3	0
4	119	3	0
5	8	19	-4*
6	27	8	-4
H,K=		2,	0
-16	84	4	5
-14	61	3	2
-12	41	5	5
-10	145	3	0
-8	64	3	5
-6	8	12	-4*
-4	131	4	-2
-2	964	20	8
0	145	4	2
2	260	6	-6
4	49	5	-1
6	184	4	0
8	5	11	4*
10	66	3	1
12	25	11	-6

L	FOB	SG	DEL
14	113	4	-2
H,K=		2,	1
-16	67	7	-5
-15	7	40	-3*
-14	69	3	4
-13	12	50	-4*
-12	98	7	-6
-11	35	42	-15*
-10	150	3	1
-9	38	3	-1
-8	73	2	2
-7	108	2	-3
-6	92	2	-2
-5	162	4	-3
-4	240	5	-11
-3	50	11	4
-2	1007	21	0
-1	673	19	1
0	338	8	-14
1	291	6	-12
2	118	4	0
3	175	4	-0
4	78	3	-3
5	103	4	3
6	12	13	-5*
7	0	16	-3*
8	41	4	2
9	61	3	-0
10	85	2	-2
11	11	13	-10*
12	49	10	1
13	28	6	-9
14	103	2	-3
15	55	7	-12
H,K=		2,	2
-15	46	4	2
-14	44	7	0
-13	33	11	-3
-12	0	19	-14*
-11	48	3	-3
-10	33	9	-2
-9	26	5	4
-8	52	5	2
-7	73	3	1
-6	57	2	-0
-5	90	3	-1
-4	34	5	2
-3	6	20	-0*
-2	152	4	-8
-1	70	5	-4
0	59	6	-2
1	43	7	-0
2	103	3	-5
3	90	3	8
4	9	11	8*
5	41	6	1
6	225	5	5
7	49	2	2
8	81	2	1
9	84	2	1
10	54	2	1
11	109	2	1
12	121	3	1
13	39	10	0
14	67	2	-3
H,K=		2,	3
-15	46	3	-2
-14	7	24	-0*
-13	39	4	-1
-12	14	17	-7*
-11	8	16	2*
-10	110	4	1
-9	0	19	-11*
-8	93	2	-1
-7	17	10	8
-6	99	2	-4
-5	20	3	3
-4	35	3	0
-3	42	6	-0
-2	183	3	-5
-1	99	2	0
0	69	2	-3
1	39	6	-1
2	174	5	-2
3	148	3	0
4	151	3	6
5	101	3	0
6	11	14	-2*
7	59	2	2
8	83	3	-1
9	11	16	-6*
10	66	2	-3
11	91	2	-3

L	FOB	SG	DEL
12	22	16	7
13	0	24	-8*
14	40	5	-2
H,K=		2,	4
-14	58	6	-3
-13	100	4	-1
-12	103	4	1
-11	66	2	0
-10	76	5	2
-9	56	3	-1
-8	104	2	-3
-7	21	8	-8
-6	44	3	-0
-5	9	11	8*
-4	88	2	3
-3	46	2	5
-2	28	2	2
-1	209	4	1
0	180	5	8
1	45	2	-1
2	75	2	1
3	152	3	3
4	24	6	-1
5	44	4	2
6	44	3	-2
7	60	4	1
8	53	2	2
9	23	4	-7
10	6	14	-5*
11	140	3	-4
12	35	17	-7
13	22	16	-4
H,K=		2,	5
-13	46	4	-2
-12	38	10	-1
-11	67	5	2
-10	22	5	6
-9	29	5	-3
-8	16	7	1
-7	34	2	1
-6	51	2	-3
-5	113	3	2
-4	113	3	-3
-3	79	3	-5
-2	90	2	2
-1	51	2	-1
0	36	4	8
1	18	7	8
2	52	2	-0
3	8	11	-9*
4	90	2	-0
5	0	16	-3*
6	27	4	3
7	42	4	-2
8	93	2	-1
9	36	3	1
10	8	18	-2*
11	81	4	-2
12	32	4	-5
H,K=		2,	6
-11	0	14	-0*
-10	35	5	4
-9	16	19	6*
-8	55	6	3
-7	81	3	1
-6	38	4	-0
-5	67	2	1
-4	43	5	2
-3	24	8	8
-2	38	5	-7
-1	32	3	1
0	94	3	2
1	54	2	0
2	18	20	5*
3	116	3	1
4	108	3	1
5	126	3	-3
6	36	5	-3
7	86	4	-3
8	32	12	-2
9	0	19	-3*
10	76	4	1
H,K=		2,	7
-9	39	5	-2
-8	79	2	-2
-7	72	3	3
-6	91	4	1
-5	19	11	0
-4	32	5	3
-3	45	4	0
-2	87	3	2
-1	19	14	-4
0	62	2	1

L	FOB	SG	DEL
1	92	3	-1
2	61	3	4
3	38	3	5
4	65	4	1
5	87	4	-1
6	52	2	-0
7	74	4	-4
8	140	3	-1
H,K=		2,	8
-6	44	3	1
-5	48	3	2
-4	21	26	1*
-3	87	2	-4
-2	5	22	-1*
-1	11	27	8*
0	81	4	-0
1	17	20	5*
2	34	6	-4
3	6	15	1*
4	7	22	-5*
5	67	2	-0
H,K=		3,	0
-14	60	5	2
-12	95	3	1
-10	99	3	-2
-8	163	3	0
-6	106	2	1
-4	227	5	1
-2	151	4	-0
0	42	6	-3
2	107	3	-3
4	109	3	1
6	121	3	2
8	40	4	3
10	38	4	0
12	104	4	-2
14	47	2	2
H,K=		3,	1
-15	28	26	-3*
-14	11	23	2*
-13	52	3	3
-12	78	3	1
-11	55	5	1
-10	96	3	0
-9	72	3	0
-8	74	3	4
-7	39	3	4
-6	134	3	-5
-5	229	5	-4
-4	38	2	0
-3	56	2	-2
-2	114	3	-4
-1	100	4	-4
0	320	8	-9
1	163	6	-6
2	90	2	-4
3	12	14	-5*
4	135	4	1
5	238	5	-2
6	53	3	-0
7	89	3	-1
8	157	4	7
9	42	2	-4
10	8	21	-13*
11	182	4	0
12	23	34	-8*
13	10	18	-15*
14	20	8	4
H,K=		3,	2
-15	32	15	-0
-14	16	12	8
-13	62	6	2
-12	38	3	-0
-11	8	14	-1*
-10	44	6	4
-9	15	17	5*
-8	93	2	-0
-7	78	2	-0
-6	52	2	-1
-5	22	7	5
-4	148	3	-5
-3	14	8	1
-2	265	6	-9
-1	99	3	-8
0	138	5	8
1	39	3	-2
2	142	3	-1
3	99	2	-3
4	56	2	1
5	48	2	2
6	61	3	1
7	33	7	1
8	21	7	2

L	FOB	SG	DEL
9	44	5	-8
10	63	2	0
11	64	3	2
12	24	26	-4*
13	29	7	-9
H,K=		3,	3
-14	11	14	-3*
-13	72	5	-2
-12	54	2	2
-11	11	17	3*
-10	36	3	2
-9	54	3	2
-8	83	2	2
-7	31	6	-2
-6	33	7	-8
-5	145	3	3
-4	94	3	-3
-3	57	2	-1
-2	14	9	4
-1	34	4	1
0	29	6	-5
1	54	2	0
2	56	2	-1
3	4	16	-6*
4	168	4	5
5	28	4	-2
6	143	3	1
7	111	4	2
8	21	4	14
9	66	3	5
10	39	2	4
11	88	2	-3
12	9	24	-2*
13	45	9	-10
H,K=		3,	4
-13	47	3	1
-12	66	3	1
-11	38	6	11
-10	18	8	9
-9	61	2	-1
-8	125	3	3
-7	31	5	5
-6	10	12	6*
-5	82	2	1
-4	5	11	1*
-3	131	3	-2
-2	86	2	-2
-1	26	4	-3
0	40	2	2
1	138	3	3
2	62	2	-8
3	118	3	-2
4	48	2	-1
5	22	9	2
6	42	4	1
7	86	2	8
8	40	4	-2
9	9	22	-6*
10	23	8	3
11	32	9	-3
12	8	16	-7*
H,K=		3,	5
-12	11	19	7*
-11	62	4	-1
-10	93	3	-2
-9	29	6	-5
-8	13	16	4*
-7	7	17	2*
-6	16	8	2
-5	89	2	2
-4	20	6	19
-3	84	2	2
-2	64	3	2
-1	105	2	-1
0	12	13	12*
1	38	5	-2
2	15	7	3
3	16	19	7*
4	66	2	4
5	13	15	0*
6	48	2	-1
7	29	10	4
8	33	4	-1
9	18	24	-1*
10	26	5	-1
11	54	4	-1
H,K=		3,	6
-10	64	2	-3
-9	2	29	-20*
-8	35	3	-1
-7	35	8	4
-6	147	3	-2
-5	17	20	8*

L	FOB	SG	DEL
-4	15	17	-2*
-3	14	19	7*
-2	74	3	-2
-1	45	2	0
0	109	3	1
1	34	5	4
2	112	2	-2
3	40	6	8
4	83	3	-0
5	86	3	-2
6	72	3	-3
7	81	3	2
8	42	8	4
9	9	20	7*
H,K=		3,	7
-8	33	4	-3
-7	55	6	-2
-6	5	24	-C*
-5	10	19	-9*
-4	18	18	-C*
-3	12	22	-6*
-2	67	3	-2
-1	33	3	1
0	15	23	-5*
1	108	3	1
2	28	7	1
3	56	5	5
4	69	4	-5
5	61	6	-4
6	95	3	-5
H,K=		3,	8
-3	15	20	5*
-2	85	3	-6
-1	71	2	-2
0	44	4	2
1	0	22	-8*
2	63	3	3
H,K=		4,	0
-14	87	3	4
-12	97	3	C
-10	67	6	-1
-8	24	4	3
-6	155	3	1
-4	159	3	-5
-2	9	11	2*
0	153	3	-2
2	157	3	4
4	54	4	3
6	13	7	8
8	10	21	2*
10	64	3	-1
12	6	24	3*
H,K=		4,	1
-14	23	14	-2
-13	13	22	-5*
-12	17	21	4*
-11	71	2	-0
-10	18	6	-4
-9	41	2	0
-8	17	10	-2
-7	39	3	2
-6	162	5	-3
-5	14	14	8*
-4	310	8	-5
-3	246	5	-9
-2	170	5	-4
-1	11	14	4*
0	70	2	-1
1	15	17	5*
2	33	3	1
3	40	2	1
4	99	2	-2
5	32	7	2
6	103	3	4
7	57	7	-3
8	23	11	2
9	51	2	1
10	22	9	-4
11	27	7	-2
12	64	3	-2
H,K=		4,	2
-14	49	4	1
-13	9	18	-4*
-12	35	11	4
-11	10	18	5*
-10	27	4	-7
-9	20	3	3
-8	39	2	2
-7	39	2	-2
-6	33	3	-8
-5	7	11	4*
-4	88	3	-2
-3	249	5	-8

L	FOB	SG	DEL
-2	250	6	-6
-1	29	11	-7
0	114	3	-2
1	18	8	-2
2	70	2	-8
3	92	2	2
4	141	4	-2
5	9	15	2*
6	15	7	2
7	26	8	-1
8	48	2	-2
9	38	3	-3
10	103	4	-2
11	14	19	-8*
12	74	3	-2
H,K=		4,	3
-13	81	4	0
-12	17	19	-9*
-11	20	25	9*
-10	72	3	3
-9	63	3	2
-8	22	7	-6
-7	29	6	2
-6	16	8	-6
-5	51	2	1
-4	93	2	-1
-3	127	3	1
-2	55	3	-0
-1	86	2	1
0	43	3	1
1	116	2	2
2	55	3	1
3	16	17	1*
4	72	2	-1
5	78	2	0
6	51	4	8
7	17	15	13
8	38	4	-3
9	79	2	-1
10	54	6	2
11	26	11	-8
H,K=		4,	4
-12	62	4	-1
-11	28	4	-8
-10	14	18	-1*
-9	39	4	7
-8	9	13	3*
-7	19	9	8
-6	82	3	-1
-5	70	2	0
-4	20	23	5*
-3	13	16	13*
-2	61	3	2
-1	15	20	3*
0	29	14	-8
1	0	13	-3*
2	13	21	5*
3	41	2	1
4	31	5	-3
5	10	19	5*
6	47	2	0
7	15	21	11*
8	15	20	9*
9	76	4	-2
10	54	3	-3
H,K=		4,	5
-11	44	6	-0
-10	15	18	10*
-9	80	2	1
-8	17	22	-8*
-7	15	10	11
-6	28	8	-1
-5	21	22	-3*
-4	0	16	-5*
-3	49	3	2
-2	12	13	1*
-1	20	17	-5
0	29	6	7
1	73	3	-1
2	84	2	-2
3	100	3	-1
4	38	4	3
5	55	2	-3
6	18	10	6*
7	29	17	-5
8	39	6	1
9	5	20	-4*
H,K=		4,	6
-9	29	8	2
-8	52	9	1
-7	26	12	-3
-6	0	18	-9*
-5	7	22	2*

L	FOB	SG	DEL
-4	114	3	-1
-3	18	16	17
-2	17	21	5*
-1	58	5	-3
0	74	4	1
1	48	2	2
2	16	21	11*
3	108	3	1
4	43	3	-0
5	23	27	-4*
6	117	3	-4
7	24	10	3
H,K=		4,	7
-6	0	15	-8*
-5	34	5	1
-4	30	6	-5
-3	4	26	-4*
-2	77	2	1
-1	17	28	-4*
0	27	4	1
1	50	4	-2
2	17	19	6*
3	24	10	-1
H,K=		5,	0
-12	93	3	2
-10	73	2	-0
-8	32	6	0
-6	69	2	0
-4	16	12	-16
-2	82	2	8
0	59	2	1
2	75	4	-2
4	60	5	1
6	157	4	4
8	35	6	4
10	134	5	2
H,K=		5,	1
-13	9	15	5*
-12	29	8	2
-11	0	18	-17*
-10	4	27	3*
-9	75	2	-2
-8	0	13	-1*
-7	5	13	-16*
-6	22	18	3
-5	98	3	-4
-4	127	3	8
-3	40	6	-4
-2	6	15	-1*
-1	40	2	-2
0	29	7	-1
1	64	2	3
2	68	3	5
3	69	2	1
4	47	3	4
5	22	4	-2
6	7	14	-4*
7	18	21	16*
8	57	6	2
9	46	4	5
10	63	3	-1
H,K=		5,	2
-12	16	8	1
-11	30	10	-2
-10	16	27	8*
-9	11	18	9*
-8	18	14	3
-7	87	3	-1
-6	36	3	-1
-5	71	3	-0
-4	39	4	2
-3	33	5	1
-2	94	3	-0
-1	118	3	-3
0	114	4	-1
1	37	4	7
2	39	5	1
3	92	2	2
4	77	3	-0
5	11	13	3*
6	23	13	9
7	50	2	2
8	24	13	4
9	116	3	5
10	21	13	-4
H,K=		5,	3
-12	10	20	0*
-11	0	19	-7*
-10	23	18	1
-9	23	19	-8
-8	21	18	-2
-7	89	4	4
-6	71	4	-1

L	FOB	SG	DEL
-5	25	10	-3
-4	15	17	13*
-3	126	3	-2
-2	75	2	-1
-1	37	6	-3
0	47	4	-1
1	41	2	1
2	43	3	-2
3	11	19	3*
4	11	17	-4*
5	8	22	4*
6	11	18	10*
7	19	21	6*
8	12	19	1*
9	7	21	-3*
H,K=		5,	4
-10	41	3	3
-9	27	20	-1
-8	22	10	14
-7	54	3	5
-6	19	23	11*
-5	43	2	-0
-4	37	11	3
-3	11	14	2*
-2	9	14	8*
-1	45	3	-1
0	30	8	-1
1	28	9	-2
2	58	2	2
3	40	5	9
4	62	4	1
5	68	3	2
6	40	5	2
7	19	7	7
8	14	17	10*
H,K=		5,	5
-9	15	25	10*
-8	46	4	1
-7	0	18	-7*
-6	21	24	-1*
-5	31	16	-2
-4	0	20	-9*
-3	28	10	2
-2	24	17	-2
-1	27	4	1
0	8	18	-3*
1	78	2	1
2	19	22	-1*
3	36	5	-4
4	81	3	2
5	80	6	-0
6	30	7	-2
H,K=		5,	6
-6	10	16	9*
-5	6	19	4*
-4	17	17	8*
-3	31	7	5
-2	68	5	5
-1	55	5	-2
0	57	3	-2
1	12	26	-4*
2	61	2	1
3	14	20	-3*
H,K=		6,	0
-10	35	6	4
-8	104	3	-2
-6	77	4	3
-4	36	5	4
-2	32	4	-2
0	31	8	-2
2	26	4	2
4	88	4	5
6	45	4	2
8	12	15	7*
H,K=		6,	1
-11	12	22	-4*
-10	0	15	-5*
-9	7	25	-3*
-8	0	28	-2*
-7	18	21	2*
-6	27	7	6
-5	4	18	-11*
-4	23	13	0
-3	40	5	1
-2	43	2	3
-1	49	2	2
0	16	19	8*
1	43	5	1
2	21	11	4
3	52	3	8
4	34	6	2
5	12	21	6*
6	9	19	5*

L	FOB	SG	DEL
7	37	5	2
H,K=		6,	2
-10	25	27	3*
-9	18	9	-6
-8	57	3	8
-7	33	5	4
-6	83	3	2
-5	158	5	-1
-4	104	4	0
-3	92	4	4
-2	29	4	-3
-1	39	4	7
0	34	10	3
1	52	6	3
2	18	21	1*
3	13	16	13*
4	19	14	-4
5	9	18	-6*
6	10	19	0*
7	24	5	-0
H,K=		6,	3
-9	19	20	19*
-8	19	21	15*
-7	42	9	-7
-6	31	9	8
-5	41	8	-7
-4	104	4	-5
-3	17	21	13*
-2	16	21	3*
-1	24	4	21
0	13	15	3*
1	34	9	6
2	48	5	-2
3	54	4	1
4	12	24	-1*
5	13	15	-8*
6	11	20	6*
H,K=		6,	4
-7	6	19	-5*
-6	0	19	-5*
-5	59	5	8
-4	28	9	4
-3	31	6	5
-2	6	14	-14*
-1	26	8	5
0	30	12	-1
1	49	2	1
2	49	3	1
3	25	5	-5
4	26	9	4
H,K=		6,	5
-4	8	15	-2*
-3	8	16	6*
-2	20	7	-3
-1	34	6	-6
0	30	6	-7
1	64	3	-1
H,K=		7,	0
-6	16	19	3*
-4	29	10	-5
-2	10	22	16*
0	62	4	5
2	59	4	-1
H,K=		7,	1
-7	23	6	4
-6	42	5	7
-5	6	23	-6*
-4	29	7	4
-3	18	9	-3
-2	27	7	4
-1	17	19	-4*
0	7	14	-2*
1	15	22	2*
2	8	15	4*
3	1	14	-11*
H,K=		7,	2
-5	47	2	2
-4	11	23	-11*
-3	51	6	-3
-2	13	23	12*
-1	15	18	-6*
0	20	6	-2
1	29	6	4
2	0	14	-9*

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Figure Captions

Fig. 1. Atomic numbering in melatonin.

Fig. 2. Molecular conformation.

Fig. 3. Molecular packing; a toward back, b down, c to the left.

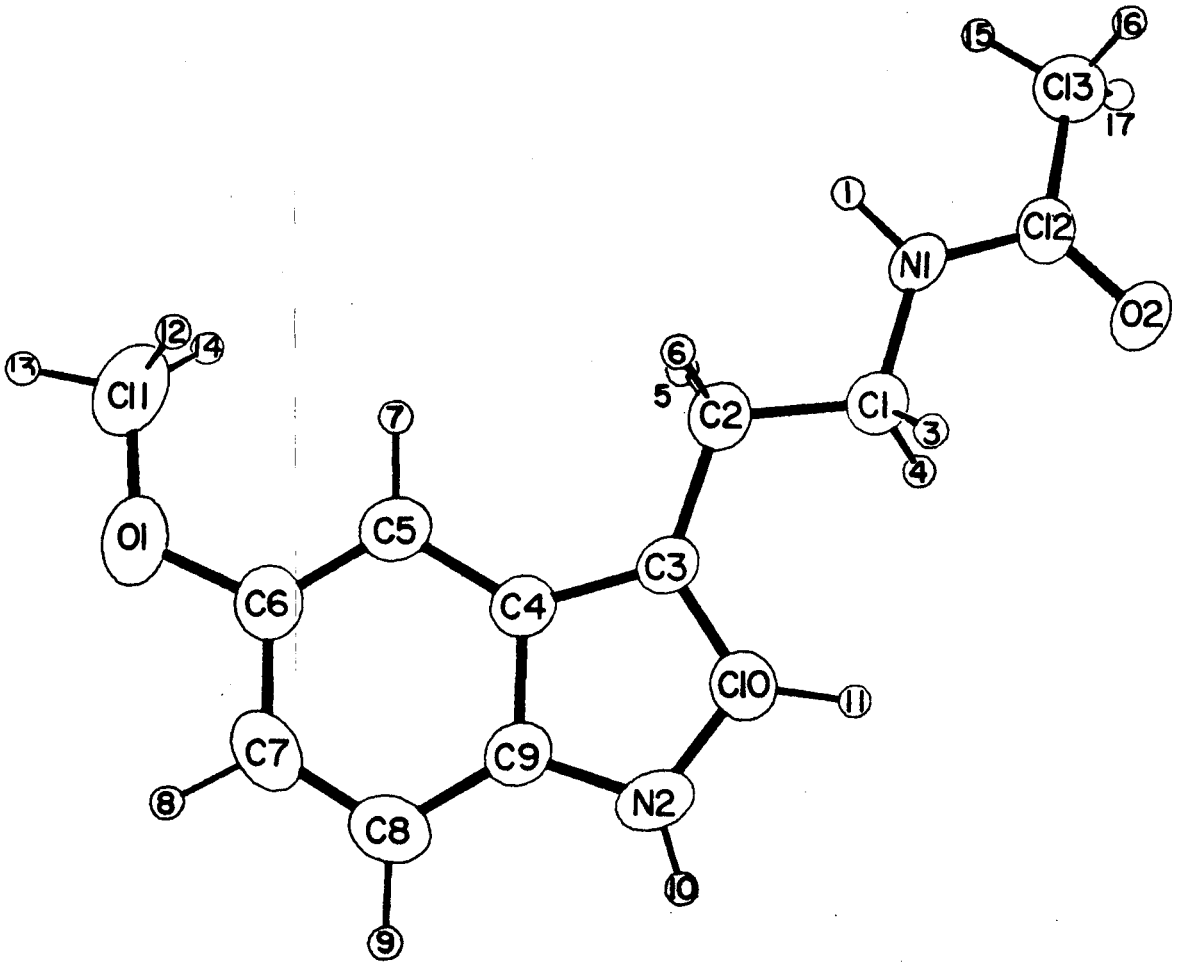

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Fig. 1.

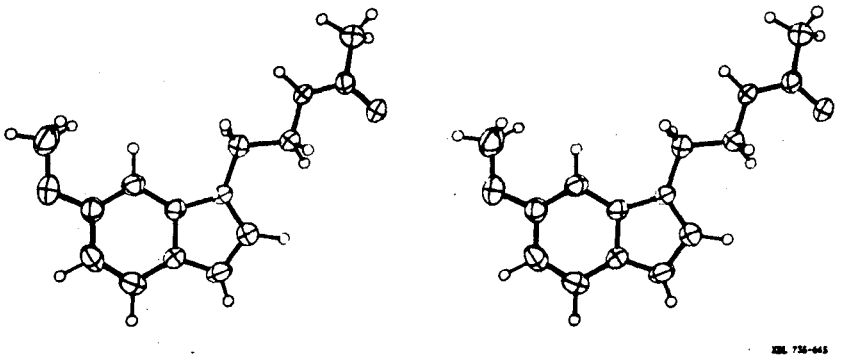

Fig. 2.

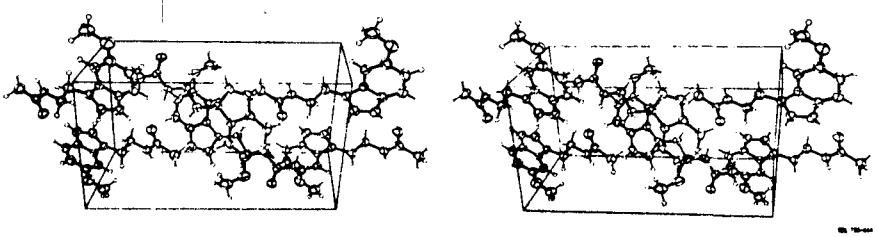

Fig. 3.

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