

The Crystal and Molecular Structure of 3-Carboethoxy-4-oxo-6-methylhomopyrimidazole C₁₂H₁₂N₂O₃

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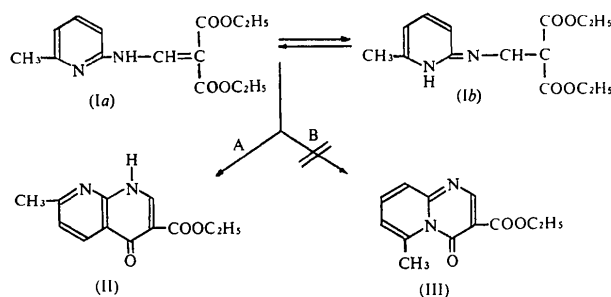
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3-Carboethoxy-4-oxo-6-methylhomopyrimidazole (COMPH) crystallizes in the monoclinic space group $P2_1/a$ and has 8 molecules in the unit cell with the dimensions: $a=8.085$, $b=21.62$, $c=12.91$ Å and $\beta=98.8^\circ$. The phase problem was solved by direct methods and the final atomic parameters were obtained by three-dimensional least-squares refinement. $R=0.102$ for the observed reflexions. In both molecules of the asymmetric unit the same three groups of corresponding atoms form a plane. The conformations of the molecular parts in the three planes were found to be identical for the two independent molecules. The only difference between the two independent molecules is expressed by different inclination angles of the three planes. The COMHP molecule contains a system of conjugated double bonds. Bond lengths compare fairly well with those reported in the literature for similar molecules. The N-C= bond at the carbonyl group is 1.472 Å, which is rather long. The mean length of 24 independent C-H bonds is 1.00 Å with individual deviations averaging 0.06 Å.

Introduction

The first attempt at preparation of 3-carboethoxy-4-oxo-6-methylhomopyrimidazole was made by Lappin (1948) who came to the conclusion that by the condensation reaction of 6-methyl-2-aminopyridine and ethoxide-methylenemalonate the cyclization can be effected only in one of the two possible directions, namely towards naphthiridine.



Closure of the ring at the nitrogen atom was thought to be impossible because of the steric hindrance caused by the substituent in position 6. This opinion held for a long time and was later confirmed by Lappin (1958, 1961) as well as by Adams & Pachter (1952, 1954). In the Research Laboratory of the Chinoin Factory, however, proper conditions were found for optional cyclization resulting in naphthiridine and homopyri-

midazole (Hungarian patent, 1966). From pharmacological investigations it was found that COMHP and its derivatives possess favourable biological activity and an efficacious analgetic action. Further investigation of the conditions concerning the preparation of COMHP would, however, require a detailed knowledge of the conformation of the molecule.

Experimental

The crystals used for X-ray diffraction were crystallized from a solution in petrol saturated at a temperature of 60°C. The colourless transparent crystals are plate-shaped with well-developed planes and edges.

The cell dimensions were determined from Buerger precession photographs taken around the crystallographic axes with Cu $K\alpha$ radiation. The density of the crystal was determined with a pycnometer. The summarized crystallographic data are:

$a = 8.085 \pm 0.02$ Å	M.W. 232.244
$b = 21.62 \pm 0.02$	D_m 1.38 g.cm ⁻³
$c = 12.91 \pm 0.02$	D_x 1.380 g.cm ⁻³
$\beta = 98.8 \pm 0.5^\circ$	$Z = 8$
$F(000) = 976$	$\mu(\text{Cu } K\alpha) = 8.52 \text{ cm}^{-1}$.

The space group $P2_1/a$ has been determined from the systematic absences $h0l$ if h odd and $0k0$ if k odd. Equi-inclination Weissenberg film data, using the multiple-film technique, were taken on 0 to 6, 0 to 3 and 0 to 3 layers around the a , b and c crystal axes respectively. The intensities were eye-estimated using calibrated intensity scales. In total, 2571 reflexions were

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collected and 1215 were unobserved. The reflexions with zero intensity were taken with a value $I_o = \frac{1}{2} I_{\min}$. As the diameter of the crystals used did not exceed 0.3 mm ($\mu R < 0.3$) no absorption correction was made. The intensities were brought to a common scale

by multiple-film and interlayer scaling after applying the Lp corrections. The absolute scale and approximate overall temperature factor ($B = 2.78 \text{ \AA}^2$) were determined by a Wilson plot from all the three-dimensional data.

Table 1. Final fractional coordinates ($\times 10^4$) and anisotropic thermal parameters ($\times 10^4$) for the non-hydrogen atoms

Estimated standard deviations are in parentheses. The b_{ij} are defined by:

$$T = \exp [-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)].$$

Molecule A	x	y	z	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
O(12)	-1640 (6)	-2543 (2)	-1303 (3)	259 (9)	18 (1)	54 (3)	7 (5)	-80 (9)	-10 (3)
O(13)	-1818 (5)	-1621 (2)	-545 (3)	141 (6)	17 (1)	51 (2)	14 (4)	-50 (7)	-1 (2)
O(17)	-488 (5)	-3445 (2)	249 (3)	174 (6)	14 (1)	60 (3)	-20 (4)	-17 (8)	-4 (2)
N(1)	1866 (6)	-2002 (2)	1868 (4)	142 (7)	14 (1)	52 (3)	-19 (4)	-14 (9)	-2 (3)
N(5)	1098 (5)	-3074 (2)	1775 (4)	98 (6)	13 (1)	45 (3)	1 (4)	16 (8)	4 (3)
C(2)	759 (7)	-1904 (2)	998 (5)	127 (8)	15 (1)	57 (4)	-7 (5)	-14 (10)	3 (3)
C(3)	-141 (7)	-2363 (2)	430 (4)	126 (8)	16 (1)	47 (3)	-7 (5)	24 (9)	-4 (3)
C(4)	99 (6)	-2996 (2)	733 (4)	113 (8)	15 (1)	46 (3)	-11 (4)	7 (10)	-4 (3)
C(6)	1191 (7)	-3657 (2)	2281 (5)	134 (8)	15 (1)	63 (4)	3 (5)	7 (11)	4 (4)
C(7)	2283 (8)	-3723 (3)	3187 (5)	185 (10)	20 (1)	63 (4)	12 (6)	-3 (12)	12 (4)
C(8)	3299 (8)	-3241 (3)	3629 (5)	188 (11)	25 (1)	65 (4)	-3 (7)	-30 (13)	15 (4)
C(9)	3156 (8)	-2677 (3)	3172 (5)	167 (10)	22 (1)	59 (4)	-15 (6)	-14 (12)	1 (4)
C(10)	2021 (6)	-2572 (2)	2235 (4)	117 (7)	16 (1)	47 (3)	-6 (5)	19 (10)	-7 (3)
C(11)	-1252 (7)	-2203 (3)	-568 (4)	140 (8)	16 (1)	48 (3)	-10 (5)	-14 (10)	-3 (3)
C(14)	-2935 (7)	-1427 (3)	-1470 (5)	158 (9)	18 (1)	51 (4)	9 (5)	-54 (11)	7 (3)
C(15)	-3331 (8)	-757 (3)	-1314 (5)	166 (10)	20 (1)	77 (5)	6 (6)	-36 (13)	11 (4)
C(16)	47 (8)	-4184 (2)	1882 (6)	184 (10)	15 (1)	94 (5)	-27 (5)	-1 (14)	12 (4)
Molecule B									
O(12)	3322 (7)	-95 (2)	5736 (4)	298 (10)	23 (1)	69 (3)	38 (5)	-128 (9)	-19 (3)
O(13)	3559 (5)	-998 (2)	4957 (3)	182 (7)	21 (1)	60 (3)	29 (4)	-77 (8)	-7 (3)
O(17)	951 (6)	688 (2)	4576 (4)	277 (9)	22 (1)	78 (3)	55 (5)	-118 (10)	-33 (3)
N(1)	616 (6)	-612 (2)	2286 (4)	173 (8)	17 (1)	56 (3)	21 (5)	-57 (9)	-12 (3)
N(5)	-24 (5)	406 (2)	2867 (4)	112 (6)	14 (1)	49 (3)	-5 (4)	0 (8)	-6 (3)
C(2)	1597 (8)	-699 (2)	3197 (5)	169 (9)	16 (1)	57 (4)	9 (5)	-26 (11)	-9 (3)
C(3)	1844 (7)	-275 (2)	4002 (5)	136 (8)	17 (1)	51 (3)	-3 (5)	-1 (10)	-5 (3)
C(4)	970 (7)	298 (2)	3907 (5)	128 (8)	18 (1)	57 (4)	-2 (5)	-20 (10)	-10 (4)
C(6)	-818 (7)	974 (2)	2601 (5)	137 (8)	16 (1)	66 (4)	2 (5)	30 (11)	1 (4)
C(7)	-1810 (8)	1034 (3)	1652 (5)	164 (10)	21 (1)	68 (4)	10 (6)	-39 (12)	14 (4)
C(8)	-2037 (8)	548 (3)	913 (6)	172 (10)	25 (1)	76 (5)	10 (7)	-44 (13)	7 (5)
C(9)	-1237 (7)	5 (3)	1155 (5)	142 (9)	24 (1)	59 (4)	3 (6)	-29 (11)	-6 (4)
C(10)	-200 (7)	-77 (2)	2130 (5)	132 (8)	16 (1)	56 (4)	-5 (5)	5 (10)	-12 (3)
C(11)	2968 (7)	-426 (2)	4986 (5)	146 (9)	18 (1)	53 (4)	-2 (5)	-28 (11)	-5 (4)
C(14)	4772 (9)	-1192 (3)	5861 (5)	208 (11)	22 (1)	76 (4)	24 (6)	-138 (12)	-2 (4)
C(15)	5115 (10)	-1854 (3)	5729 (6)	288 (15)	23 (1)	97 (6)	57 (7)	-119 (16)	-9 (5)
C(16)	-579 (9)	1526 (3)	3330 (6)	251 (13)	14 (1)	89 (5)	32 (6)	-32 (15)	-2 (4)

Table 2. Final fractional coordinates ($\times 10^3$) and isotropic thermal parameters (\AA^2) of the hydrogen atoms

Estimated standard deviations are in parentheses.

	Molecule A				Molecule B			
	x	y	z	B	x	y	z	B
H(1)	55 (7)	-148 (3)	79 (5)	1.69	218 (7)	-110 (2)	323 (4)	0.88
H(2)	228 (9)	-414 (3)	348 (6)	3.66	-230 (7)	144 (3)	150 (5)	1.77
H(3)	417 (11)	-333 (4)	435 (7)	7.16	-276 (10)	61 (4)	25 (6)	4.55
H(4)	373 (9)	-231 (3)	344 (6)	2.80	-120 (10)	-40 (4)	77 (6)	5.07
H(5)	-388 (9)	-169 (3)	-161 (6)	2.94	415 (9)	-112 (3)	657 (6)	3.64
H(6)	-232 (8)	-147 (3)	-208 (6)	2.39	579 (9)	-92 (3)	590 (6)	2.57
H(7)	40 (10)	-436 (4)	122 (6)	4.77	72 (9)	156 (4)	332 (6)	4.22
H(8)	-123 (8)	-404 (3)	174 (5)	1.97	-117 (9)	144 (3)	411 (6)	3.29
H(9)	-6 (11)	-447 (4)	238 (7)	7.29	-105 (9)	186 (3)	307 (6)	3.68
H(10)	-395 (8)	-72 (3)	-68 (5)	2.19	574 (10)	-189 (4)	510 (7)	5.05
H(11)	-227 (8)	-46 (3)	-117 (5)	2.29	420 (10)	-216 (4)	551 (6)	5.14
H(12)	-421 (10)	-61 (4)	-179 (6)	6.09	564 (12)	-203 (4)	634 (7)	7.17

Determination of the structure

The phase problem of the structure was solved in three dimensions from the normalized structure factor mag-

nitudes by the symbolic addition method using the procedure and programs of Main, Woolfson & Germain (1968). From the 495 reflexions with greatest E values (E > 1.43), the signs of 323 E values were deter-

Table 3. Observed and calculated structure factors (x 10)

Unobserved reflexions are marked with an asterisk.

Table with columns for K, Fo, Lc, Fo, Fc, K, Fo, Fc, K, Fo, Fc, K, Fo, Fc, K, Fo, Fc, K, Fo, Fc, K, Fo, Fc, K, Fo, Fc. It contains numerical values for structure factors and some are marked with asterisks.

structure factors of the former 31 atoms, using Domenicano & Vaciago's (1966) program, also revealed the remaining 3 non-hydrogen atoms. After identification of the atomic positions and introduction of the 3 new atoms, the structure factor agreement reduced to R=0.234 for all observed reflexions. From this point on-

wards, the refinement of atomic parameters was carried out by the block-diagonal least-squares method, using Albano, Domenicano & Vaciago's (1966) program which minimizes the function $\Phi = \sum w_h(F_{oh} - \frac{1}{G}|F_{ch}|)^2$, where G is the scaling factor. The weight-

Table 3 (cont.)

Table with multiple columns of numerical data and labels (K, Fo, Fc) for various reflections. The table is organized into groups labeled H=4 L=1, H=4 L=2, H=4 L=3, H=4 L=4, H=5 L=1, H=5 L=2, H=5 L=3, H=5 L=4, H=6 L=1, H=6 L=2, H=6 L=3, H=6 L=4. Each group contains several rows of data points.

ing factor of Cruickshank (1961a), $w_h=1/(a+bF+cF^2)$ was used with $a=4.0$, $b=1$ and $c=0.01$. This refinement, 3 cycles in the isotropic and 3 cycles in the anisotropic mode, gave $R=0.130$. Subsequently, the $F_o - F_c$ difference Fourier function was computed, removing all non-hydrogen atoms. From this the coordinates of all hydrogen atoms could be determined, showing fairly good agreement with the geometrically generated ones. After inclusion of the H atoms, the structure factor agreement reduced to $R=0.110$. Finally 3 cycles of refinement were carried out in the anisotropic mode for the non-hydrogen atoms and 3

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Table 3 (cont.)

Table with 19 columns of data: K Fo Fe K Fo Fe K Fo Fe K Fo Fe K Fo Fe K Fo Fe K Fo Fe K Fo Fe K Fo Fe K Fo Fe. The table contains 19 columns of numerical data representing atomic coordinates or other parameters for different atoms.

Table 4. Atomic least-squares planes of the two molecules in the asymmetric unit and the mean deviations from the plane of atoms forming the planes

The plane constants ($Ax + By + Cz = D$) are referred to the orthogonalized axial system and coordinates are considered in Å.

Atoms forming the planes A and B, respectively	Molecule	A	B	C	D	Mean deviation (Å)
C(2), C(3), C(6), C(7), C(8), C(9), C(10), N(1), N(5), C(11)	A	0.8190	-0.2191	-0.5303	0.6513	0.041
	B	0.8520	0.3483	-0.3910	-1.5923	0.023
C(3), C(11), C(14), C(15), O(12), O(13)	A	0.8633	0.3074	-0.4003	-1.9606	0.017
	B	0.8514	0.3317	-0.4064	-1.6814	0.035
C(3), C(4), N(5), O(17)	A	0.9006	-0.0510	-0.4317	-0.1496	0.009
	B	0.8447	0.4440	-0.2990	-1.1975	0.002

cycles in the isotropic mode for the hydrogen atoms. In the latter refinement all reflexions with $\sin \theta > 0.7$ were omitted. The final atomic parameters together with their estimated standard deviations are listed in Tables 1 and 2.

The structure factors calculated from the final atomic parameters are given in Table 3. The atomic scattering factors for all atoms were taken from *International Tables for X-ray Crystallography* (1962). The final reliability index $R(hkl)$ is 0.102 for the observed and 0.129 for all the reflexions.

The geometry of the molecule

The conformations of the two independent molecules (*A* and *B*) of the asymmetric unit show only slight differences. The atomic numbering and identification of atoms is given for both molecules in one drawing (Fig. 1). In both molecules the same three groups of the corresponding atoms each form a plane. All but the C(4) atom of the bicyclic part of the molecules are in one plane *P1*. A further two planes, *P2* and *P3*, are formed by the carboxy group and the atoms of C(3), N(5), C(4), O(17), respectively. The plane constants of the least-squares planes referred to the orthogonalized axial system along with the mean deviations of the atoms from the planes are given in Table 4. The mean deviations from the best planes are in each case less than or equal to 0.04 Å.

The lines of intersection of the two planes *P2* and *P3* with plane *P1* are defined by the C(3)–C(11) bond and the C(3) and N(5) atoms respectively. The inclination angles of the planes are given in Table 5 from which one can see that these are different for the two molecules *A* and *B*. The greatest difference arises for the planes *P1* and *P2*. While in molecule *A* the inclination angles of the planes *P2* and *P3* with *P1* are 31.6 and 12.1°, in molecule *B* the same angles are 1.0 and 7.6° respectively.

Table 5. *The inclination angles of the atomic planes in the two molecules A and B of the asymmetric unit*

Molecule	(<i>P1</i> , <i>P2</i>)	(<i>P1</i> , <i>P3</i>)	(<i>P2</i> , <i>P3</i>)
<i>A</i>	31.6°	12.1°	20.3°
<i>B</i>	1.0	7.6	8.9

The conformations of atomic groups forming the three planes are the same in molecules *A* and *B*. This fact can be proved by inspecting the bond lengths and bond angles given in Tables 6 and 7.

The thermal motion analysis

The r.m.s. amplitudes and the vectors of the principal axes of thermal vibration ellipsoids of the non-hydrogen atoms were calculated and are listed in Table 8. The last two columns of the Table show, for the two independent molecules *A* and *B*, the inclination angles

of the principal axes to one of the three atomic least-squares planes (*P1*, *P2* and *P3*), *i.e.* to which the corresponding atom belongs. With these angles the rela-

Table 6. *Bond lengths in the two independent molecules A and B with the e.s.d.'s in parentheses*

	Distances (Å)	
	Molecule <i>A</i>	Molecule <i>B</i>
C(2)=C(3)	1.374 (8)	1.377 (8)
C(6)=C(7)	1.361 (8)	1.364 (9)
C(8)=C(9)	1.352 (9)	1.354 (9)
C(3)—C(4)	1.428 (7)	1.422 (8)
C(7)—C(8)	1.394 (9)	1.412 (9)
C(9)—C(10)	1.420 (8)	1.413 (8)
C(3)—C(11)	1.494 (8)	1.481 (8)
C(6)—C(16)	1.508 (9)	1.514 (9)
C(14)—C(15)	1.504 (9)	1.473 (10)
C(4)=O(17)	1.211 (7)	1.209 (7)
C(11)=O(12)	1.203 (7)	1.203 (7)
C(11)—O(13)	1.341 (7)	1.328 (7)
C(14)—O(13)	1.445 (7)	1.467 (8)
N(1)=C(10)	1.319 (7)	1.332 (7)
N(1)—C(2)	1.342 (7)	1.327 (7)
N(5)—C(10)	1.397 (7)	1.405 (7)
N(5)—C(6)	1.416 (7)	1.404 (7)
N(5)—C(4)	1.469 (7)	1.474 (7)
C(2)—H(2)	0.96 (6)	0.98 (5)
C(7)—H(7)	0.98 (7)	0.96 (6)
C(8)—H(8)	1.09 (9)	0.96 (8)
C(9)—H(9)	0.95 (7)	1.00 (8)
C(14)—H(14 <i>a</i>)	0.94 (7)	1.01 (7)
C(14)—H(14 <i>b</i>)	1.00 (7)	1.12 (7)
C(16)—H(16 <i>a</i>)	1.02 (8)	1.06 (8)
C(16)—H(16 <i>b</i>)	1.07 (6)	1.19 (7)
C(16)—H(16 <i>c</i>)	0.90 (9)	0.87 (8)
C(15)—H(15 <i>a</i>)	1.03 (6)	1.00 (8)
C(15)—H(15 <i>b</i>)	1.06 (7)	1.03 (8)
C(15)—H(15 <i>c</i>)	0.92 (8)	0.92 (9)
C—H (mean)	0.99 (7)	1.01 (7)

Table 7. *Bond angles in the two independent molecules A and B with e.s.d.'s in parentheses*

	Molecule <i>A</i>	Molecule <i>B</i>
C(2)—C(3)—C(4)	120.5 (5)°	120.1 (5)°
C(3)—C(4)—C(5)	113.2 (4)	114.3 (5)
C(4)—N(5)—C(10)	118.9 (4)	118.9 (4)
N(5)—C(10)—N(1)	123.9 (5)	123.1 (5)
C(10)—N(1)—C(2)	117.6 (5)	118.2 (5)
N(1)—C(2)—C(3)	124.3 (5)	124.9 (5)
N(5)—C(6)—C(7)	118.1 (5)	119.1 (5)
C(6)—C(7)—C(8)	122.5 (6)	122.3 (6)
C(7)—C(8)—C(9)	119.3 (6)	118.8 (6)
C(8)—C(9)—C(10)	121.1 (6)	120.8 (6)
C(9)—C(10)—N(5)	118.1 (5)	119.7 (5)
C(10)—N(5)—C(6)	120.5 (4)	119.3 (4)
C(7)—C(6)—C(16)	119.9 (5)	119.0 (5)
C(16)—C(6)—N(5)	121.9 (5)	121.8 (5)
C(6)—N(5)—C(4)	120.5 (4)	121.8 (4)
N(5)—C(4)—O(17)	119.8 (5)	118.4 (5)
O(17)—C(4)—C(3)	126.9 (5)	127.3 (5)
O(13)—C(3)—C(11)	119.8 (5)	119.8 (5)
C(3)—C(11)—O(12)	126.0 (5)	126.8 (5)
C(3)—C(11)—O(13)	111.1 (4)	110.9 (5)
O(12)—C(11)—O(13)	122.8 (5)	122.3 (5)
C(11)—O(13)—C(14)	115.2 (4)	116.3 (5)
O(13)—C(14)—C(15)	106.7 (5)	107.5 (5)
C(2)—C(3)—C(11)	119.5 (5)	120.0 (5)

tive positions of the thermal vibration ellipsoids to the planes have been visualized. Some similarity of positioning can be detected in the two molecules.

The thermal motion of both independent molecules *A* and *B* has also been analysed as rigid body molecular vibration on the basis of Cruickshank's (1961*b*) procedure, using the program of Schomaker & Trueblood (1968). The **U** tensors of thermal vibration of the individual atoms calculated from rigid body thermal mo-

tion (U_{calc}) and derived from structure analysis (U_{obs}) show great deviations if the rigid body assumption refers to the whole molecule. This is in compliance with the results obtained by geometrical analysis of the molecule, according to which the three atomic planes of the molecule (*P1*, *P2* and *P3*) may twist relative to each other (Table 5). A satisfactory agreement of the calculated and observed **U** tensors can, however, be obtained if the three atomic groups of the molecules,

Table 8. *The principal axes of thermal vibrational ellipsoids for atoms of the two molecules in the asymmetric unit*

The axes are given by their lengths (Å) and coordinates of their end points referred to crystal axes. The origins of principal axes are considered to be at the site of the corresponding atom, and coordinates are given in fractions multiplied by 10^3 . In the last two columns the angles of principal axes to planes to which they belong are given.

	<i>i</i>	$U_i(\text{Å})$	Molecule <i>A</i>			$U_i(\text{Å})$	Molecule <i>B</i>			Angles to plane in molecule	
			<i>x</i>	<i>y</i>	<i>z</i>		<i>x</i>	<i>y</i>	<i>z</i>	<i>A</i>	<i>B</i>
O(12)	1	0.333	-199	-256	-120	0.374	297	-14	587	77.6	84.4
	2	0.211	-171	-245	-136	0.220	324	0	573	12.3	3.6
	3	0.175	-174	-257	-142	0.182	319	-11	561	2.9	4.1
O(13)	1	0.261	-204	-164	-42	0.304	330	-104	509	77.7	80.8
	2	0.203	-181	-153	-50	0.216	355	-91	502	9.1	3.7
	3	0.161	-196	-160	-64	0.169	341	-98	486	9.7	8.2
O(17)	1	0.263	-74	-343	35	0.378	62	62	473	83.1	75.5
	2	0.213	-62	-340	12	0.206	78	75	450	1.9	5.3
	3	0.171	-58	-351	20	0.184	89	63	447	7.7	12.6
N(1)	1	0.242	165	-198	197	0.287	37	-65	241	90.0	80.4
	2	0.200	176	-195	175	0.190	54	-53	229	0.0	1.5
	3	0.166	175	-206	182	0.175	47	-62	217	0.7	9.9
N(5)	1	0.197	112	-311	164	0.214	-21	39	274	49.1	20.8
	2	0.179	131	-305	179	0.190	-19	46	281	40.0	9.7
	3	0.173	116	-314	183	0.170	-13	35	280	8.6	33.2
C(2)	1	0.239	60	-189	113	0.265	136	-73	331	75.2	78.0
	2	0.189	63	-184	91	0.199	144	-64	311	12.8	2.4
	3	0.182	61	-196	94	0.186	153	-77	311	3.8	11.2
C(3)	1	0.208	5	-242	49	0.226	165	-29	411	30.3	72.1
	2	0.199	-2	-234	31	0.203	172	-20	394	58.1	4.5
	3	0.187	-4	-230	51	0.187	172	-33	390	9.6	18.1
C(4)	1	0.206	-7	-297	83	0.244	82	27	405	74.2	59.9
	2	0.198	1	-293	63	0.207	84	38	389	0.0	0.3
	3	0.171	-4	-305	67	0.177	81	26	381	16.7	29.8
C(6)	1	0.236	130	-367	212	0.234	-85	97	242	61.9	25.0
	2	0.205	142	-363	235	0.211	-56	99	261	22.5	61.9
	3	0.185	125	-374	231	0.197	-77	88	261	15.7	12.3
C(7)	1	0.260	254	-373	308	0.278	-161	101	150	80.1	53.3
	2	0.239	242	-364	329	0.235	-167	113	169	8.9	36.9
	3	0.196	239	-378	329	0.183	-166	99	175	4.7	2.8
C(8)	1	0.284	352	-329	350	0.289	-183	54	75	78.3	59.9
	2	0.241	346	-315	364	0.246	-195	66	95	11.2	27.6
	3	0.199	344	-327	376	0.198	-185	52	102	1.1	11.9
C(9)	1	0.259	339	-272	307	0.258	-141	-5	128	81.1	71.0
	2	0.226	317	-258	309	0.235	-133	10	120	7.9	4.9
	3	0.200	333	-265	329	0.185	-142	0	105	0.9	18.3
C(10)	1	0.208	208	-264	235	0.232	-30	-12	227	8.3	58.1
	2	0.198	223	-259	218	0.208	-42	-3	209	78.5	25.3
	3	0.182	213	-251	232	0.178	-29	-14	205	8.5	18.7
C(11)	1	0.236	-147	-218	-47	0.250	275	-44	510	84.9	70.1
	2	0.201	-130	-212	-65	0.207	290	-33	496	2.3	11.7
	3	0.177	-139	-224	-67	0.180	282	-45	488	2.6	16.1
C(14)	1	0.268	-269	-143	-159	0.347	506	-111	569	68.9	72.0
	2	0.212	-287	-133	-143	0.228	479	-109	590	21.0	13.7
	3	0.160	-281	-145	-137	0.156	492	-121	595	2.5	10.0
C(15)	1	0.286	-314	-78	-148	0.381	545	-181	556	53.9	80.0
	2	0.226	-317	-67	-126	0.241	522	-178	586	35.4	9.3
	3	0.194	-317	-81	-122	0.194	526	-192	580	3.8	2.7
C(16)	1	0.297	-10	-415	207	0.322	-29	155	319	-	-
	2	0.240	-21	-416	177	0.247	-39	155	349	-	-
	3	0.171	-2	-426	189	0.169	-52	145	334	-	-

forming the planes, are each assumed a rigid body separately (Table 9).

By analysing the molecular thermal motion as rigid body in this way, we obtain a negative eigenvalue for the translation tensor ellipsoid in the $P2$ plane of molecule A only and for the rotation tensor ellipsoid in the $P3$ plane of molecule A as well as of molecule B .

In the present molecule atoms with only small mass differences are present. From these facts it can be concluded that negative eigenvalues cannot be traced back only to large mass differences as recently assumed by Neuman (1971) in connection with the thermal analysis of the 3-bromo-2-decalone molecule. For the moment the authors have no explanation of the appear-

Table 9. *The observed and calculated components of U tensors of the individual atoms of both molecules A and B referred to the orthogonalized axial system (in 10^{-2} \AA^2)*

Data are given for both molecules for the atoms of groups each forming a plane ($P1$ and $P2$). The primed atoms are in molecule B .

	U_{11}		U_{22}		U_{33}		U_{12}		U_{13}		U_{23}	
	obs	calc	obs	calc	obs	calc	obs	calc	obs	calc	obs	calc
C(2)	4.43	4.60	3.50	3.35	4.66	4.43	-0.34	-0.64	-1.09	-0.74	0.18	-0.05
C(3)	4.08	3.67	3.84	3.32	3.87	3.76	-0.29	-0.21	0.02	-0.17	-0.28	-0.27
C(6)	4.50	4.66	3.52	3.62	5.18	4.98	0.11	0.14	-0.61	-0.28	0.28	0.33
C(7)	6.28	6.15	4.85	4.76	5.19	5.51	0.39	0.08	-0.89	-1.05	0.83	1.09
C(8)	6.59	6.49	5.91	5.73	5.35	5.11	-0.31	-0.14	-1.62	-1.67	1.04	0.87
C(9)	5.75	5.60	5.20	5.14	4.85	4.62	-0.65	-0.47	-1.11	-1.44	0.04	0.16
C(10)	3.82	4.04	3.82	3.89	3.90	3.95	-0.19	-0.28	-0.11	-0.45	-0.46	-0.16
C(11)	4.86	5.00	3.86	4.05	3.99	4.27	-0.43	-0.33	-0.99	-0.94	-0.18	0.03
N(1)	4.93	4.86	3.35	3.75	4.32	4.53	-0.80	-0.78	-1.03	-0.97	-0.17	-0.20
N(5)	3.22	3.40	3.13	3.36	3.71	3.85	-0.02	0.11	-0.17	0.12	0.30	-0.21
C(3)	4.08	3.81	3.84	3.87	3.87	3.65	-0.29	0.02	0.02	-0.52	-0.28	-0.05
C(11)	4.86	4.94	3.86	3.65	3.99	3.71	-0.43	-0.32	-0.99	-0.96	-0.18	-0.06
C(14)	5.78	5.92	4.27	4.56	4.19	4.56	0.30	-0.16	-2.06	-1.82	0.52	0.46
C(15)	5.95	5.80	4.73	4.73	6.35	6.20	0.12	0.41	-1.93	-2.07	0.80	0.69
O(12)	9.85	9.91	4.31	4.33	4.43	4.60	0.41	0.56	-2.77	-2.68	-0.71	-0.75
O(13)	5.19	5.44	4.13	4.00	4.19	4.30	0.64	0.25	-1.96	-1.65	-0.05	-0.19
C(2')	5.92	6.03	3.82	3.89	4.68	4.81	0.48	0.79	-1.40	-1.64	-0.61	-0.93
C(3')	4.62	4.45	3.92	3.58	4.18	4.08	-0.07	-0.09	-0.66	-0.77	-0.32	-0.39
C(6')	4.42	4.48	3.90	3.79	5.46	5.37	0.09	0.08	-0.06	-0.45	0.07	0.25
C(7')	5.87	5.84	5.08	4.93	5.65	6.20	0.31	0.64	-1.89	-1.46	0.97	0.66
C(8')	6.22	5.99	5.84	5.91	6.28	5.60	0.39	0.36	-2.12	-2.05	0.49	0.42
C(9')	5.05	5.51	5.72	5.34	4.85	4.84	0.20	0.10	-1.50	-1.77	-0.41	-0.36
C(10')	4.45	4.60	3.81	4.11	4.62	4.41	-0.09	0.04	-0.60	-1.14	-0.82	-0.47
C(11')	5.17	5.38	4.21	4.31	4.36	4.27	-0.04	-0.08	-1.39	-1.14	-0.33	-0.17
N(1')	6.31	5.92	4.02	4.20	4.60	4.75	1.04	0.61	-2.21	-1.65	-0.81	-1.10
N(5')	3.82	3.64	3.24	3.50	4.01	4.34	-0.14	-0.27	-0.62	-0.37	-0.41	-0.09
C(3')	4.62	4.49	3.92	4.06	4.18	3.97	-0.07	0.05	-0.66	-0.99	-0.32	-0.08
C(11')	5.17	5.00	4.21	4.24	4.36	4.35	-0.04	0.18	-1.39	-1.56	-0.33	-0.35
C(14')	8.15	8.26	5.23	5.32	6.27	6.61	1.09	1.18	-4.58	-4.03	-0.17	-0.39
C(15')	10.68	10.59	5.42	5.71	7.99	7.82	2.61	2.45	-4.34	-4.70	-0.60	-0.43
O(12')	11.02	11.09	5.43	5.19	5.67	5.64	1.90	1.85	-4.21	-4.19	-1.32	-1.39
O(13')	6.76	6.97	4.99	4.68	4.97	5.05	1.36	1.14	-2.78	-2.50	-0.45	-0.56

Table 10. *Relative positions of the least-squares planes $P1(B)$ and $P2(B)$ of molecule B to $P2(A)$ of molecule A expressed by the distances of all atoms to plane $P2(A)$*

Plane	Atoms forming the plane $P2(A)$	Distances to plane (\AA)				Mean (\AA)
$P2(A)$	C(2), C(10), C(11), C(12), O(2), O(3)	-0.0014, 0.0134,	0.0095, -0.0144	-0.0349,	0.0278,	0.0169
$P2(B)$	Atoms not forming the plane $P2(A)$ C(2), C(10), C(11), C(12), O(2), O(3)	0.3384, 0.3083,	0.3522, 0.4043	0.5061,	0.3954,	0.3841
$P1(B)$	C(1), C(2), C(4), C(5), C(6), C(7), C(8), C(10), N(1), N(2)	0.4326, 0.2811, 0.4264,	0.3384, 0.3137, 0.2605	0.2651, 0.3188,	0.2592, 0.3522,	0.3471

ance of the negative eigenvalues and therefore the data for the libration tensor ellipsoids are not used for the thermal correction of the atomic positional parameters.

Discussion of the structure

In the asymmetric unit of the crystal structure of COMHP, two independent molecules *A* and *B* are present. As far as the conformations of the two molecules are affected by the intermolecular forces in the lattice, the molecules will show differences in their conformations.

The corresponding groups of atoms, each forming a plane in the molecules *A* and *B*, are found to be identical with regard to their conformations, bond lengths and bond angles. Differences in the geometry of the two molecules are detected only in the inclination angles of the three least-squares planes (Table 5). Furthermore, according to the thermal motion analysis of both molecules *A* and *B*, only the three atomic groups forming planes can be treated as rigid bodies, and not the complete molecule. From all these facts it can be concluded with high probability that even when the molecules leave the crystal lattice (*e.g.* in solution or gas phase) the most probable change in the molecular conformation may occur by alterations of the inclination angles of the three least-squares planes. Full knowledge of these facts allows us to make an approximate prediction as to how far the COMHP molecule can adjust itself to a biological molecule of known conformation for a more effective reaction.

In spite of the differences between the two molecules *A* and *B* outlined above, the two molecules can be further treated by consideration of the mean bond lengths and bond angles (Fig. 1).

The COMHP molecule contains a system of conjugated double bonds. The N(5) atom is linked to

three sp^2 C atoms, in spite of the fact that the three bond lengths are significantly different. N(5)–C(4) is the only bond in the bicyclic group which equals the pure N–C single bond, but since according to the literature 1.34 Å has been found for the N–C bond length in the system N–C=O, the present N(5)–C(4) bond has to be considered as lengthened. Actually this is the bond where the difficulty in ring closure has been predicted and where the ring easily opens in aqueous solution. It is also noteworthy that the average of the above-mentioned three bonds belonging to N(5) is 1.421 Å, which is almost the same as has been found in tricycloquinazoline (1.425 Å) (Iball & Motherwell, 1967).

The pairs of bond lengths N(5)–C(6) and C(9)–C(10), C(10)–N(5) and C(7)–C(8), and C(8)–C(9) and C(6)–C(7) are equal within the experimental error and their respective averaged numerical values are 1.413, 1.402 and 1.358 Å. These are in good agreement with the corresponding bonds found in the naphthalene molecule, where lengths in the same sequence are 1.425, 1.416 and 1.36 Å respectively (Cruickshank, 1957).

The bond lengths of N(1)=C(10) and N(1)–C(2) show no significant difference, in agreement with similar bonds found in pyridine derivatives (Restivo & Palenik, 1970).

The C(2)–C(3) bond with the length 1.376 Å is longer than an sp^2 – sp^2 C=C double bond; the C(3)–C(4) bond with length 1.425 Å, is, however, shorter than an sp^2 – sp^2 C–C single bond. A similar phenomenon can be found in uracil (Stewart & Jensen, 1967), with the values of C=C=1.340 Å and C–C=1.43 Å.

The bond lengths and bond angles of the carboxy chain agree with those in a similar chain of the dinitrobenzoate molecule (Barnett & Raymond, 1970).

Among the bond angles, those of C(3)–C(4)–O(1) and C(3)–C(11)–O(12) are noteworthy (Table 7). These angles are significantly enlarged relative to 120° but,

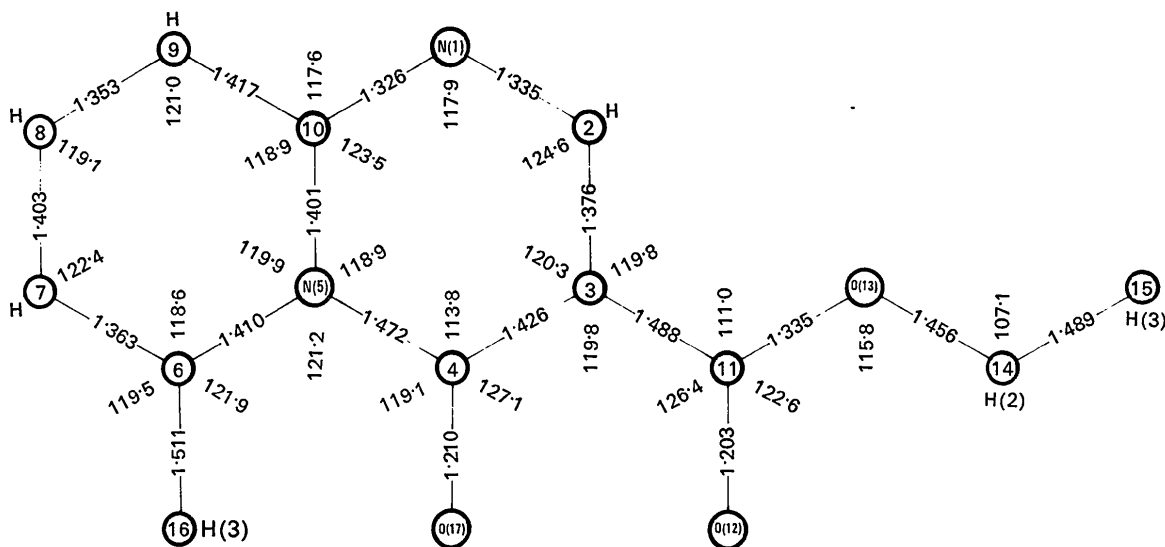


Fig. 1. Atomic numbering and averaged bond lengths and bond angles of the two independent molecules *A* and *B*.

within experimental error, are identical in the two molecules *A* and *B*, though the two planes *P2* and *P3* containing these angles are differently twisted in the two molecules (Table 5). Thus the widening of these two angles cannot be assigned only to the repulsion of the carbonyl oxygens.

The spatial packing of the molecules in the crystal lattice must be discussed from two points of view. First, we shall consider the relative positions of the two independent molecules *A* and *B* (Fig. 2) and then the arrangement of these coupled pairs in the unit cell.

Table 11. *The shortest intermolecular distances between the two independent molecules A and B of the asymmetric unit*

	Distances (Å)		
	From molecule		Average
	<i>A</i> to <i>B</i>	<i>B</i> to <i>A</i>	
N(1)···N(1)	3·212	3·242	3·242
N(1)···H(1)	2·620	2·697	2·659
H(9)···H(15a)	2·648	2·764	2·706
H(9)···H(15b)	2·664	2·519	2·592
H(2)···H(9)	2·742	2·910	2·826
H(8)···H(15b)	2·937	3·014	2·976
N(1)···C(2)	3·323	3·262	3·293

The molecules *A* and *B*, in the most tightly fitted symmetry positions of the two independent molecules, are linked by N···N, N···H and H···H van der Waals contacts, the intermolecular distances of which are given in Table 11. With these distances the two molecules take their relative positions in such a way that on one side the least-squares planes of their carboxy chains *P2(A)* and *P2(B)* (Table 10) are almost parallel with an inclination angle of 1·5° and normal distance of 0·4 Å, and on the other side the atomic arrangement of these two planes has a non-crystallographic centre of symmetry. Taking the midpoints of the corresponding atoms of these two planes, we find the maximum deviation from their average to be less than 0·005 Å.

The spatial packing of the molecule pairs *A-B* compares the molecular close packing with the shortest intermolecular distances listed in Table 12.

Comparing the intermolecular distances at the van der Waals contacts of the *A-B* pairs of molecules with the sum of the van der Waals radii, some differences can be detected depending on whether the contacting atoms are identical or different (Table 11). Thus the shortest N···H distance of 2·659 Å may be composed of the van der Waals radii 1·50 and 1·16 Å. But if we take the minimum values of the N···N and H···H dis-

Table 12. *The shortest intermolecular atomic distances (Å) in the spatial packing of A-B pairs of molecules*

After the distance in parentheses the labels of the two molecules are given to which the corresponding two atoms belong.

From atom in <i>x, y, z</i>	To atom	In position			Distance	Labels of molecules
H(14b)	H(16a)	- <i>x</i> ,	- <i>y</i> ,	- <i>z</i>	2·215	(<i>A-B</i>)
H(16b)	H(2)	-½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	2·492	(<i>A-B</i>)
H(16c)	H(15c)	½- <i>x</i> ,	½+ <i>y</i> ,	1- <i>z</i>	2·522	(<i>B-B</i>)
H(14a)	H(16b)	- <i>x</i> ,	- <i>y</i> ,	1- <i>z</i>	2·535	(<i>B-B</i>)
H(15c)	H(14a)	-1+ <i>x</i> ,	<i>y</i> ,	-1+ <i>z</i>	2·575	(<i>A-B</i>)
H(16a)	H(15a)	½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	2·590	(<i>A-A</i>)
H(16c)	H(15c)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	2·619	(<i>A-A</i>)
H(16a)	H(8)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	2·634	(<i>A-B</i>)
H(16b)	H(8)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	2·689	(<i>A-B</i>)
H(14b)	H(15c)	-1+ <i>x</i> ,	<i>y</i> ,	-1+ <i>z</i>	2·705	(<i>A-B</i>)
H(14a)	H(15c)	-1+ <i>x</i> ,	<i>y</i> ,	-1+ <i>z</i>	2·710	(<i>A-B</i>)
O(12)	H(7)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	2·365	(<i>A-B</i>)
O(12)	H(7)	½- <i>x</i> ,	½+ <i>y</i> ,	1- <i>z</i>	2·386	(<i>B-A</i>)
O(17)	H(8)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	2·522	(<i>A-B</i>)
O(17)	H(8)	½- <i>x</i> ,	½+ <i>y</i> ,	1- <i>z</i>	2·545	(<i>B-A</i>)
O(17)	H(7)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	2·674	(<i>A-B</i>)
O(17)	H(7)	½- <i>x</i> ,	½+ <i>y</i> ,	1- <i>z</i>	2·719	(<i>B-A</i>)
O(17)	H(15a)	½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	2·594	(<i>A-A</i>)
O(17)	H(14b)	1- <i>x</i> ,	- <i>y</i> ,	1- <i>z</i>	2·839	(<i>B-B</i>)
C(2)	H(16b)	½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	2·818	(<i>B-A</i>)
C(4)	H(14b)	1- <i>x</i> ,	- <i>y</i> ,	1- <i>z</i>	2·920	(<i>B-B</i>)
O(17)	C(7)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	3·229	(<i>A-B</i>)
O(17)	C(7)	½+ <i>x</i> ,	½+ <i>y</i> ,	1- <i>z</i>	3·277	(<i>B-A</i>)
O(17)	C(8)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	3·174	(<i>A-B</i>)
O(17)	C(8)	½- <i>x</i> ,	½+ <i>y</i> ,	1- <i>z</i>	3·266	(<i>B-A</i>)
O(17)	C(3)	- <i>x</i> ,	- <i>y</i> ,	1- <i>z</i>	3·247	(<i>B-B</i>)
O(17)	C(14)	½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	3·266	(<i>A-A</i>)
O(12)	C(7)	-½- <i>x</i> ,	-½+ <i>y</i> ,	- <i>z</i>	3·327	(<i>A-B</i>)
O(13)	C(4)	-½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	3·298	(<i>A-A</i>)
O(17)	O(13)	½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	3·287	(<i>A-A</i>)
N(1)	C(4)	½+ <i>x</i> ,	-½- <i>y</i> ,	<i>z</i>	3·186	(<i>A-A</i>)

tances, for van der Waals radii we obtain 1.62 and 1.30 Å, respectively. For H the value 1.16 Å compares with the value 1.17 Å determined by Kitaigorodskii (1961), and the 1.30 Å is nearer to 1.27 Å, the shortest H...H contact found in C₁₂H₂₀ (Sasvári & Löw, 1965).

The same phenomenon can be found in the spatial packing of the molecule-pairs *A*-*B* if instead of the shortest intermolecular distances we take an average, which is 2.571 Å for H...H and 2.581 Å for O...H.

The average intermolecular distances C...H = 2.869 (1.70 + 1.17), C...N = 3.186 (1.70 + 1.486) and C...O = 3.263 Å (1.70 + 1.4) are noteworthy. These can also be regarded as distances of van der Waals contacts to a very good approximation if we take 1.70 Å for the van der Waals radius of C as found in the graphite structure. Only the C...O distance is longer (by 0.16 Å) than can be predicted from the van der Waals radii.

References

- ADAMS, R. & PACHTER, I. J. (1952). *J. Amer. Chem. Soc.* **74**, 5491.
- ADAMS, R. & PACHTER, I. J. (1954). *J. Amer. Chem. Soc.* **76**, 1845.
- ALBANO, V., DOMENICANO, A. & VACIAGO, A. (1966). Full and Block Diagonal Matrix Least-Squares Refinement Program for the IBM 7040 Computer, adapted for the ICT 1905 computer. Centro di Studio per la Strutturistica Chimica del C. N. R., Roma.
- BARNETT, B. L. & RAYMOND, E. D. (1970). *Acta Cryst.* **B26**, 326.
- CRUICKSHANK, D. W. J. (1957). *Acta Cryst.* **10**, 504.
- CRUICKSHANK, D. W. J. (1961*a*). *Computing Methods and the Phase Problem in X-ray Crystal Analysis*. Oxford: Pergamon Press.
- CRUICKSHANK, D. W. J. (1961*b*). *Acta Cryst.* **14**, 896.
- DOMENICANO, A. & VACIAGO, A. (1966). Three-Dimensional Fourier Program for the IBM 7040 Computer, adapted for the ICT 1905 computer. Centro di Studio per la Strutturistica del C.N.R., Roma.
- Hungarian Patent (1966), No. 156119.
- IBALL, J. & MOTHERWELL, W. D. S. (1969). *Acta Cryst.* **B25**, 882.
- International Tables for X-ray Crystallography* (1962). Vol. III. Birmingham: Kynoch Press.
- KITAIGORODSKY, A. I. (1961). *Organic Chemical Crystallography* (English translation). New York: Consultants Bureau.
- LAPPIN, G. R. (1948). *J. Amer. Chem. Soc.* **70**, 3348.
- LAPPIN, G. R. (1958). *J. Org. Chem.* **23**, 1358.
- LAPPIN, G. R. (1961). *J. Org. Chem.* **26**, 2350.
- MAIN, P., WOOLFSON, M. M. & GERMAIN, G. (1968). LSAM System of Computer Programs for the Automatic Solution of Centrosymmetric Crystal Structures by the Logical Symbolic Addition Method, Universities of York, England and Leuven, Belgium.
- NEUMAN, M. A. (1971). Lecture at the ACA Summer Meeting, Ames, Iowa, U.S.A.
- RESTIVO, R. & PALENIK, G. J. (1970). *Acta Cryst.* **B26**, 1397.
- SASVÁRI, K. & LÖW, M. (1965). *Acta Cryst.* **19**, 840.
- SCHOMAKER, V. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* **B24**, 63.
- STEWART, R. F. & JENSEN, L. H. (1967). *Acta Cryst.* **23**, 1102.

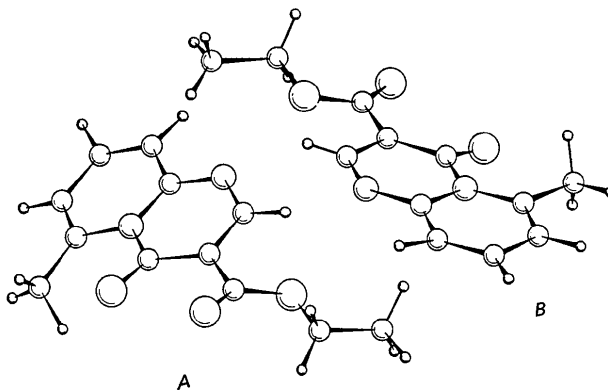


Fig. 2. The perspective view of the two independent molecules *A* and *B* in their relative spatial packing in the unit cell.