

# The Crystal and Molecular Structure of 6-Deoxy-6-azidodihydroisomorphine, C<sub>17</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>

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6-Deoxy-6-azidodihydroisomorphine (azidomorphine) crystallizes in the orthorhombic space group  $P2_12_12_1$  with 4 molecules in a unit cell of dimensions  $a=8.230$ ,  $b=13.605$  and  $c=14.142$  Å. The phase problem was solved by direct methods and the final atomic parameters were obtained by three-dimensional least-squares refinement. The final conventional  $R$  is 0.044 for the observed reflexions. The molecule is T-shaped like the codeine and morphine molecules with the difference that in the title molecule the carbocyclic  $C$  ring has become saturated and has changed from a boat to a chair form, considerably flattened and distorted relative to the piperidine  $D$  ring. In the spatial packing the molecules, linked by  $O-H \cdots N$  hydrogen bonds, form endless linear chains parallel to the  $b$  crystal axis.

## Introduction

6-Deoxy-6-azidodihydroisomorphine ( $6\beta$ -azido-4,5 $\alpha$ -epoxy-3-hydroxy-17-methyl-morphinan) (azidomorphine) was prepared from dihydromorphine through 3- $O$ -acetyl-6- $O$ -tosyldihydromorphine with  $NaN_3$  in DMF under conditions suitable for  $S_N2$  reactions (Bognár, Makleit & Mile, 1969). Considering the advantageous pharmacological activity (Knoll, Fürst & Kelemen, 1971) of this new morphine derivative, it was of interest to determine the crystal structure which gives the conformation of the whole molecule, from which the steric position of the azido group as well as the conformation of the  $C$  ring could be determined.

## Experimental

The crystals used for X-ray diffraction had been crystallized from a solution in ether. The colourless transparent crystals had a hexagonal prismatic shape with well developed planes and edges, elongated in the direction of the  $b$  axis. The samples used had an average thickness of 0.3 mm and a length of about 0.8 mm.

The cell dimensions were determined from Buerger precession photographs taken about the crystallographic axes with  $Cu K\alpha(Ni)$  radiation. The crystallographic data are as follows:

$a = 8.230$ (2) Å	$D_m = 1.297$ g cm <sup>-3</sup>
$b = 13.605$ (6)	$D_x = 1.311$ g cm <sup>-3</sup>
$c = 14.142$ (4)	M.W. 312.379
$V = 1583.47$ Å <sup>3</sup>	$Z = 4$
$F(000) = 640$	$\mu(Cu K\alpha) = 7.21$ cm <sup>-1</sup> .

The space group  $P2_12_12_1$  was determined from the systematic absences  $h00$ ,  $0k0$  and  $00l$  when  $h$ ,  $k$  and  $l$  respectively are odd. The intensities of 1377 independent reflexions were measured by the equi-inclination procedure on the semi-automatic two circle Stoe-Güttinger single-crystal diffractometer. After setting the crystal and counter at the equi-inclination position of a reciprocal layer, all intensities of the corresponding two-dimensional reciprocal layer were measured automatically in the region of  $2\theta$  rotation between  $5^\circ$  and  $136^\circ$ . The positioning of the counter and crystal as well as the counting intensity of the reflexion peak and background were controlled by the Güttinger electronics according to a data set previously computed and stored on punched paper tape. Intensities of all reflexions were measured in the fixed counter position  $2\theta'$  referred to the corresponding reciprocal lattice point. The counts for the reflexion peaks were recorded in an interval of  $2.5^\circ$  with a scanning speed of  $1^\circ \text{ min}^{-1}$ . 60 s background counting was carried out at each end of the peak scan. After finishing the recording of a layer several reflexions of medium intensity were re-measured to control the stability of the intensity measurement. The deviations were always less than 5%, despite the fact that after a few days a slight decomposition of the crystal could be observed.

The integrated intensity was calculated according to the expression

$$I = I_2 - \frac{T_2}{T_1 + T_3} (I_1 + I_3) \quad (1)$$

where  $I_2$  and  $T_2$  are the total counts and counting time, respectively, for the reflexion peak. The other symbols

in the expression refer to the two background measurements. The standard deviation of the intensity is expressed by

$$\sigma(I) = \left[ I_2 + \left( \frac{T_2}{T_1 + T_3} \right)^2 (I_1 + I_3) \right]^{1/2}. \quad (2)$$

Reflexions with  $I < 2\sigma(I)$  were taken as unobserved. With this restriction 159 reflexions out of the total of 1377 were designated unobserved. The size of the crystal satisfied the condition  $\mu R < 0.3$  and no absorption correction was made.

After the Lorentz-polarization correction was applied, the absolute scale and approximate isotropic temperature factor  $B = 3.65 \text{ \AA}^2$  were determined by a Wilson plot.

### Determination of the structure

The phase problem was solved by direct methods using  $E$  values computed from the observed structure factor values in the conventional way. The *MULTAN* program of Main, Woolfson & Germain was used, with local modifications, on the ICL-1903A computer for the phase determination. In addition to the three origin-determining reflexions, two starting and one enantiomorph-defining reflexions were used. Starting with  $E$  values of 196 reflexions ( $E \geq 1.40$ ), taking 1200 as the maximum number of phase relationships, and using as a criterion of sign acceptance a probability greater than 0.80, the program produced 8 sets of phases as possible solutions, of which two had high ABSFOM values. For these two sets of phases the relevant figures of merit are as follows:

Set	ABSFOM	RESID
1	1.2148	35.54
2	1.1842	29.68

From our experience the correct solution can be expected from the first set with the higher ABSFOM. From the  $E$ -map calculation, however, it turned out that the correct solution was the second set with the smaller RESID.

The  $E$  map, calculated with the second set of phases, revealed all non-hydrogen atoms of the molecule, giving a structure-factor agreement of  $R = 19.7\%$  for the observed reflexions. Starting with the  $E$ -map coordinates the structure was refined in the isotropic mode by full matrix least-squares calculations and then in the anisotropic mode by block-diagonal least-squares with the program of Albano, Domenicano & Vaciago (1966). The program minimizes the function  $\Phi = \sum w_h [F_{oh} - (1/G)|F_{ch}|]^2$  where  $G$  is the scaling factor. The weighting factor of Cruickshank (1961a) [ $w_h = 1/(a + bF + cF^2)$ ] was used with  $a = 5.0$ ,  $b = 1.0$  and  $c = 0.02$ . For refinement, only the observed reflexions were used. After 3 cycles of isotropic and 3 cycles of anisotropic refinement the reliability index for the observed reflexions decreased to 7.8%. Introducing all the H atoms, obtained from the difference Fourier function, and calculating a further two cycles of refinement in the anisotropic mode for non-hydrogen and the isotropic mode for the hydrogen atoms reduced the final structure-factor agreement values to  $R = 0.044$  and  $R = 0.051$  for the observed reflexions and for all the reflexions, respectively. The final atomic parameters and their standard deviations are listed in Tables 1 and 2. The

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

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

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

	$x$	$y$	$z$	$b_{11}$	$b_{22}$	$b_{33}$	$b_{12}$	$b_{13}$	$b_{23}$
C(1)	4253 (5)	1957 (3)	2038 (3)	107 (5)	44 (3)	54 (2)	-9 (7)	-13 (6)	21 (4)
C(2)	4215 (5)	1066 (3)	2504 (3)	101 (5)	54 (3)	65 (2)	23 (7)	-4 (6)	-32 (4)
C(3)	2892 (5)	777 (3)	3055 (3)	130 (6)	35 (3)	49 (2)	3 (7)	-33 (6)	-8 (4)
C(4)	1598 (5)	1414 (3)	3081 (3)	101 (5)	43 (3)	43 (2)	-9 (6)	-4 (5)	0 (4)
C(5)	-404 (4)	2352 (3)	3709 (3)	101 (5)	46 (3)	51 (2)	-20 (6)	9 (6)	3 (4)
C(6)	432 (5)	2833 (4)	4555 (3)	118 (5)	70 (3)	38 (2)	26 (8)	27 (5)	4 (4)
C(7)	403 (6)	3948 (4)	4521 (3)	172 (7)	59 (3)	42 (2)	20 (9)	-6 (7)	-24 (4)
C(8)	1294 (5)	4505 (3)	3625 (3)	159 (6)	54 (3)	42 (2)	-8 (8)	-34 (7)	-5 (4)
C(9)	1232 (5)	4171 (3)	1803 (3)	126 (6)	44 (3)	42 (2)	2 (7)	-12 (6)	-3 (4)
C(10)	2882 (5)	3634 (3)	1667 (3)	127 (6)	45 (3)	53 (2)	-23 (7)	8 (6)	10 (4)
C(11)	2944 (4)	2610 (3)	2078 (3)	111 (5)	39 (3)	41 (2)	-4 (6)	7 (5)	-10 (3)
C(12)	1629 (4)	2291 (3)	2588 (2)	92 (5)	33 (2)	42 (2)	6 (6)	-13 (5)	-16 (3)
C(13)	62 (4)	2840 (3)	2762 (2)	79 (4)	36 (2)	41 (2)	4 (5)	1 (5)	-6 (3)
C(14)	377 (4)	3946 (3)	2750 (2)	112 (5)	32 (3)	42 (2)	8 (6)	-25 (5)	-7 (3)
C(15)	-1179 (5)	2597 (3)	1971 (3)	120 (5)	39 (3)	54 (2)	-9 (7)	-36 (6)	0 (4)
C(16)	-526 (6)	2948 (3)	1017 (3)	183 (7)	39 (3)	48 (2)	3 (8)	-56 (7)	-10 (4)
N(17)	-5 (4)	3981 (3)	1049 (2)	158 (5)	54 (3)	36 (1)	0 (7)	-17 (5)	2 (3)
O(18)	209 (3)	1341 (2)	3648 (2)	115 (4)	39 (2)	55 (1)	2 (4)	27 (4)	8 (3)
O(30)	2938 (4)	-86 (2)	3551 (2)	147 (4)	40 (2)	65 (2)	24 (5)	-37 (5)	4 (3)
N(60)	-342 (5)	2483 (3)	5440 (2)	174 (6)	99 (4)	50 (2)	60 (8)	68 (6)	17 (4)
N(61)	373 (4)	1837 (3)	5856 (2)	137 (5)	69 (3)	43 (2)	-52 (7)	20 (5)	-3 (3)
N(62)	926 (6)	1230 (4)	6318 (3)	225 (7)	97 (4)	65 (2)	-45 (9)	-21 (8)	54 (5)
C(170)	551 (7)	4322 (4)	118 (3)	251 (10)	72 (4)	45 (2)	5 (11)	2 (9)	-1 (5)



Table 4. *Least-squares planes of the molecule with normal distances to planes for atoms forming the planes and for some other atoms not forming the planes*

The plane constants ( $Ax + By + Cz = D$ ) are referred to crystal axes and coordinates are considered in Å. In parentheses are given the deviations from planes for the same atoms in the codeine molecule.

Plane		A	B	C	D
P1		0.40724	0.43583	0.80263	4.91323
P2		0.93669	-0.34439	-0.06328	-1.62823
P3		0.82311	-0.54594	-0.15635	-2.95831
P4		0.57591	0.68117	0.45203	5.63849

Plane	Atoms	Distances to plane (Å)			
P1	C(1), C(2), C(3), C(4)	-0.0141	-0.0262	-0.0156	-0.0421
		(-0.0440)	(-0.0208)	(0.0200)	(-0.0454)
	C(9), C(10), C(11), C(12)	0.0194	0.0996	-0.0203	-0.0712
—	C(13), O(18), O(30)	(0.1831)	(0.0873)	(-0.0905)	(-0.1586)
		-0.0734	-0.0927	0.0511	
	C(5), C(14)	(-0.1533)	(0.1014)	(0.1208)	
P2	C(5), C(6), C(7), C(8)	0.5560	0.6744		
		(0.3593)	(0.7740)		
	C(13), C(14)	-0.1172	0.2262	-0.3155	0.2843
—	N(60), N(61), N(62)	(-0.0882)	(0.3046)	(-0.1960)	(-0.1393)
		0.0982	-0.1761		
		(-0.2291)	(0.3480)		
P3	C(9), C(13), C(14), C(15)	-0.2857	0.5310	1.2004	
	C(16), N(17)	0.2963	0.2803	-0.3252	-0.2050
—	C(170)	(-0.3006)	(-0.2584)	(0.3088)	(0.1954)
		0.1875	-0.2339		
		(-0.1927)	(0.2474)		
P4	C(14), C(6), N(60), N(61)	0.0953			
		(-0.0225)			
	N(62)	0.1035	-0.0219	-0.0158	-0.0209
—	C(5), C(7), C(8), C(13)	-0.0449	1.1014	1.2818	-1.2115
		-1.2793			

Table 5. *Bond lengths with their estimated standard deviations in parentheses*

For comparison the bond lengths of the non-hydrogen atoms in the codeine molecule are also given.

	Azidomor- phine	Codeine		Azidomor- phine	Codeine
C(1)—C(2)	1.380 (6) Å	1.401 Å	C(7)—C(8)	1.542 (6) Å	1.324 Å
C(1)—C(11)	1.398 (6)	1.387	C(8)—C(14)	1.529 (5)	1.497
C(2)—C(3)	1.395 (6)	1.372	C(9)—C(14)	1.544 (5)	1.561
C(3)—C(4)	1.374 (6)	1.388	C(9)—N(17)	1.497 (5)	1.521
C(3)—O(30)	1.368 (5)	1.399	C(9)—C(10)	1.554 (6)	1.539
C(4)—C(12)	1.382 (5)	1.369	C(10)—C(11)	1.510 (6)	1.496
C(4)—O(18)	1.400 (5)	1.370	C(11)—C(12)	1.371 (5)	1.399
C(5)—C(6)	1.527 (6)	1.516	C(12)—C(13)	1.511 (5)	1.504
C(5)—C(13)	1.543 (5)	1.532	C(13)—C(14)	1.527 (5)	1.564
C(5)—O(18)	1.468 (5)	1.472	C(13)—C(15)	1.550 (5)	1.535
C(6)—N(60)	1.483 (6)	—	C(15)—C(16)	1.529 (6)	1.530
N(60)—N(61)	1.210 (5)	—	C(16)—N(17)	1.470 (6)	1.468
N(61)—N(62)	1.147 (6)	—	N(17)—C(170)	1.469 (6)	1.506
C(6)—C(7)	1.518 (7)	1.531			
C(1)—H(1)	0.94 (6)		C(10)—H(101)	0.97 (5)	
C(2)—H(2)	0.95 (5)		C(10)—H(102)	1.02 (5)	
O(30)—H(30)	0.97 (6)		C(14)—H(14)	1.10 (5)	
C(5)—H(5)	0.98 (5)		C(15)—H(151)	1.00 (6)	
C(6)—H(6)	0.98 (4)		C(15)—H(152)	1.08 (5)	
C(7)—H(71)	1.08 (6)		C(16)—H(161)	0.96 (6)	
C(7)—H(72)	1.01 (6)		C(16)—H(162)	0.94 (6)	
C(8)—H(81)	1.12 (6)		C(170)—H(171)	1.12 (6)	
C(8)—H(82)	1.12 (5)		C(170)—H(172)	1.12 (6)	
C(9)—H(9)	1.11 (5)		C(170)—H(173)	1.11 (6)	

The three N atoms of the azido group are coplanar with the C(6) and C(14) atoms with a maximum deviation of 0.1 Å. This plane (*P*4 in Table 4) is tilted to the best plane of the C ring (*P*2 in Table 4) at an angle of 74.0°.

The atoms C(5) and C(14) deviate from the plane

*P*1 so that the inclination angles of planes [C(13), C(5), O(18)] and [C(9), C(14), C(13)] with plane *P*1 are 36.9° and 49.8°, respectively.

The plane constants and normal atomic distances to the planes are given in Table 4. The bond lengths and bond angles are in Tables 5 and 6.

Table 6. Bond angles with their estimated standard deviations in parentheses

For comparison the corresponding angles of the codeine molecule are also given.

	Azidomor- phine	Codeine		Azidomor- phine	Codeine
C(1)—C(2)—C(3)	122.1 (4)°	120.2°	C(8)—C(14)—C(13)	112.9 (3)°	108.1°
C(2)—C(3)—C(4)	116.2 (4)	118.1	C(9)—C(14)—C(13)	106.4 (3)	107.8
C(2)—C(3)—C(30)	120.4 (4)	127.3	C(9)—N(17)—C(170)	111.8 (3)	113.1
C(3)—C(4)—C(12)	121.1 (4)	120.8	C(9)—N(17)—C(16)	112.7 (3)	113.5
C(3)—C(4)—O(18)	127.1 (4)	127.0	C(9)—C(10)—C(11)	114.6 (3)	115.4
C(4)—C(3)—O(30)	123.3 (4)	114.5	C(10)—C(9)—C(14)	114.4 (3)	114.0
C(4)—C(12)—C(11)	123.6 (3)	122.7	C(10)—C(9)—N(17)	115.2 (3)	113.0
C(4)—C(12)—C(13)	109.2 (3)	109.4	C(10)—C(11)—C(12)	117.9 (3)	118.6
C(4)—O(18)—C(5)	104.4 (3)	107.7	C(10)—C(11)—C(1)	126.6 (4)	125.8
C(5)—C(6)—N(60)	109.3 (4)	112.5*	C(11)—C(1)—C(2)	121.4 (4)	122.5
C(5)—C(6)—C(7)	113.3 (4)	113.8	C(11)—C(12)—C(13)	127.1 (3)	127.3
C(5)—C(13)—C(12)	98.1 (3)	101.3	C(12)—C(4)—O(18)	111.4 (3)	111.9
C(5)—C(13)—C(15)	111.8 (3)	112.4	C(12)—C(11)—C(1)	115.4 (3)	115.2
C(5)—C(13)—C(14)	118.4 (3)	116.8	C(12)—C(13)—C(15)	109.8 (3)	112.2
C(6)—C(5)—O(18)	107.0 (3)	111.0	C(12)—C(13)—C(14)	109.9 (3)	105.5
C(6)—C(7)—C(8)	109.5 (4)	119.8	C(13)—C(5)—O(18)	105.5 (3)	105.1
C(6)—N(60)—N(61)	115.8 (4)	—	C(13)—C(15)—C(16)	109.8 (3)	112.6
N(60)—N(61)—N(62)	173.0 (4)	—	C(14)—C(9)—N(17)	105.8 (3)	105.2
C(7)—C(6)—N(60)	109.9 (4)	111.1*	C(14)—C(13)—C(15)	108.3 (3)	108.4
C(7)—C(8)—C(14)	109.2 (3)	120.6	C(15)—C(16)—N(17)	112.0 (3)	110.7
C(8)—C(14)—C(9)	114.4 (3)	112.5	C(16)—N(17)—C(170)	111.4 (3)	110.4
C(6)—C(5)—C(13)	112.6 (4)	112.9			

\* In codeine N(60) is replaced by O(60).

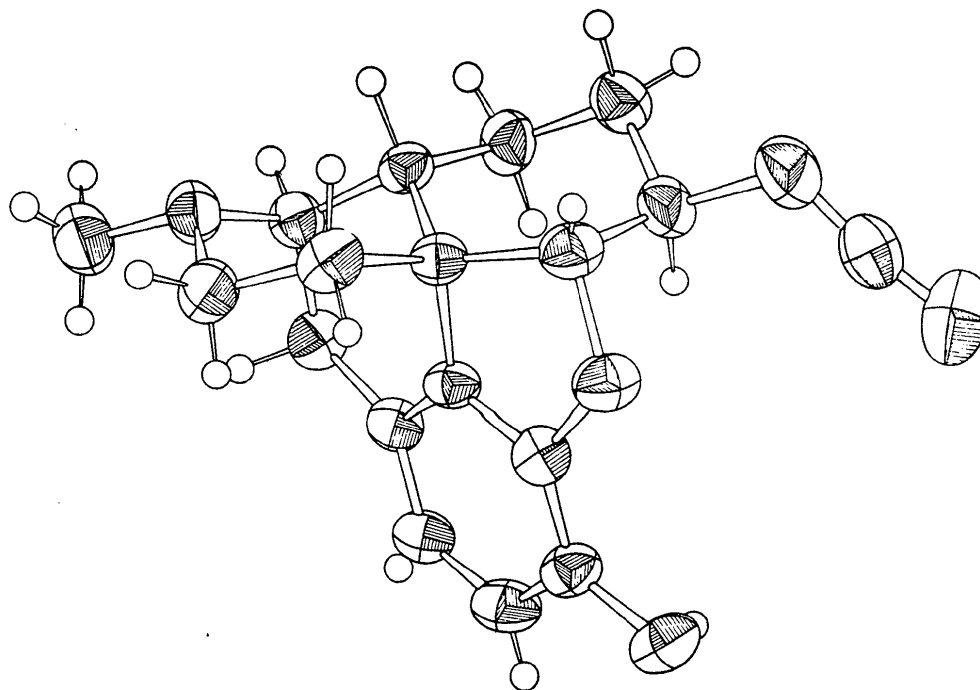


Fig. 2. Perspective view of the azidomorphine molecule, where the non-hydrogen atoms are represented by their thermal motion ellipsoids.

## Thermal motion analysis

The r.m.s. amplitudes and the vectors of principal axes of the thermal vibration ellipsoids of the non-hydrogen atoms have been calculated and are listed in Table 7. The molecule with the atoms represented by their thermal motion ellipsoids can be seen in Fig. 2 [ORTEP plot (Johnson, 1965)].

Table 7. *The principal axes of thermal vibration ellipsoids for atoms in the asymmetric unit*

The axes are given by their lengths (Å) and their vector components expressed as fractional coordinates ( $\times 10^3$ ) referred to crystal axes with the origin at the site of the corresponding atom.

	<i>i</i>	$U_i$ (Å)	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	1	0.247	431	187	219
	2	0.190	444	190	198
	3	0.188	438	206	208
C(2)	1	0.275	425	118	234
	2	0.209	433	118	258
	3	0.179	441	101	248
C(3)	1	0.240	272	75	319
	2	0.194	271	82	298
	3	0.178	286	65	302
C(4)	1	0.210	156	144	323
	2	0.204	152	155	305
	3	0.183	139	137	307
C(5)	1	0.229	-46	231	356
	2	0.212	-50	222	376
	3	0.178	-60	241	372
C(6)	1	0.261	52	301	458
	2	0.212	60	278	466
	3	0.177	58	282	447
C(7)	1	0.258	60	408	445
	2	0.234	63	386	458
	3	0.188	42	388	441
C(8)	1	0.246	103	432	371
	2	0.227	128	447	359
	3	0.191	118	427	351
C(9)	1	0.217	106	413	191
	2	0.204	112	430	179
	3	0.198	109	412	170
C(10)	1	0.236	288	369	182
	2	0.222	267	373	163
	3	0.187	274	353	170
C(11)	1	0.214	287	269	195
	2	0.193	272	259	211
	3	0.183	294	273	215
C(12)	1	0.217	156	222	272
	2	0.174	143	231	256
	3	0.165	162	218	253
C(13)	1	0.205	6	289	262
	2	0.181	10	296	280
	3	0.165	26	282	276
C(14)	1	0.221	54	398	263
	2	0.181	55	393	282
	3	0.171	38	382	272
C(15)	1	0.246	-132	261	212
	2	0.197	-130	271	193
	3	0.183	-134	252	192
C(16)	1	0.272	-80	293	113
	2	0.202	-64	304	93
	3	0.183	-59	284	94
N(17)	1	0.236	27	398	100
	2	0.224	1	415	106
	3	0.188	6	397	118

Table 7 (cont.)

	<i>i</i>	$U_i$ (Å)	<i>x</i>	<i>y</i>	<i>z</i>
O(18)	1	0.244	32	137	381
	2	0.192	39	126	362
	3	0.187	32	145	360
O(30)	1	0.267	309	-7	339
	2	0.221	314	0	362
	3	0.182	304	-20	358
N(60)	1	0.324	-16	268	551
	2	0.253	-15	238	554
	3	0.185	-20	247	534
N(61)	1	0.271	21	201	583
	2	0.214	27	178	573
	3	0.189	20	179	592
N(62)	1	0.336	78	143	643
	2	0.268	62	118	627
	3	0.222	91	114	645
C(170)	1	0.294	91	434	12
	2	0.260	57	413	12
	3	0.213	55	432	-3

The thermal motion of the molecule has also been analysed as rigid-body vibration on the basis of Cruickshank's (1961*b*) procedure, using the program of Schomaker & Trueblood (1968). By comparing  $U$  tensors of the individual atoms calculated from the rigid-body thermal motion ( $U_{\text{calc}}$ ) with those derived from the structure analysis ( $U_{\text{obs}}$ ), a comparatively good agreement can be obtained if the two parts of the molecule, namely the stock and arms of the T-shape are separately assumed to be rigid bodies (Table 8). The translational and librational tensors of these parts assumed as rigid bodies are given in Table 9. In Table 10 the principal axes of the translational and librational tensor ellipsoids of the two assumed rigid bodies can be seen and can also be compared with the vibrational ellipsoids of the individual atoms (Table 7).

## Discussion of the structure

The framework of the azidomorphine molecule, composed of five rings, has the same composition and T-conformation as morphine (Mackay & Hodgkin, 1955) and codeine (Lindsey & Barnes, 1955; Kartha, Ahmed & Barnes, 1962). The left and right arms of the T-shape are formed in all three molecules by the piperidine ring *D* and carbocyclic ring *C*, respectively. The only significant deviation in the framework of azidomorphine compared with morphine and codeine can be found in the ring *C*. In azidomorphine it becomes saturated at the C(7)–C(8) bond (1.542 Å) and consequently ring *C* changes its conformation from boat to chair (*P2* in Table 4). This chair is rather flattened and distorted. The distortion is especially pronounced at the bond C(5)–C(13) which is shared with the five-membered oxide ring *E*, where the molecule is most probably strained.

The deviations of the atoms from the planes of the T-shape, given in Table 4, agree fairly well with the corresponding deviations in the codeine molecule if one disregards the *C* ring. Accordingly the dihedral

angles of ring *D* agree with the corresponding angles in codeine with deviations less than  $3.6^\circ$ .

In azidomorphine the angles C(1)–C(11)–C(10), C(11)–C(12)–C(13), C(3)–C(4)–O(18) and C(5)–C(13)–C(12) show significant deviations from the normal values and exactly the same distortions can be found for the four corresponding angles in codeine (Table 6). These equal distortions may originate from the strain caused in both molecules by the five-membered oxide ring. This assumption is supported by the fact that no such distortions of the corresponding angles ( $118.5$ ,  $119.3$ ) are present in *D,L*-cyclazocine (Karle, Gilardi, Fratini & Karle, 1969), where the five-membered ring is absent.

The two N–N bond lengths of the azido group ( $1.210$ ,  $1.147$  Å) deviate only slightly from those found earlier in hydrogen azide ( $1.24$ ,  $1.134$  Å) and methyl azide ( $1.24$ ,  $1.12$  Å). The latter values were determined by electron diffraction, microwave and infrared spectroscopy [Eyster, 1940 (IR); Schomaker & Spurr, 1942 (ED); Amble & Dailey, 1950 (MW+IR); Pauling & Brockway, 1937 (ED)]. In determining the N–N bonds of the  $N_3$  group of  $HN_3$  and  $H_3CN_3$  the authors in both cases assumed that the  $N_3$  group is linear. For

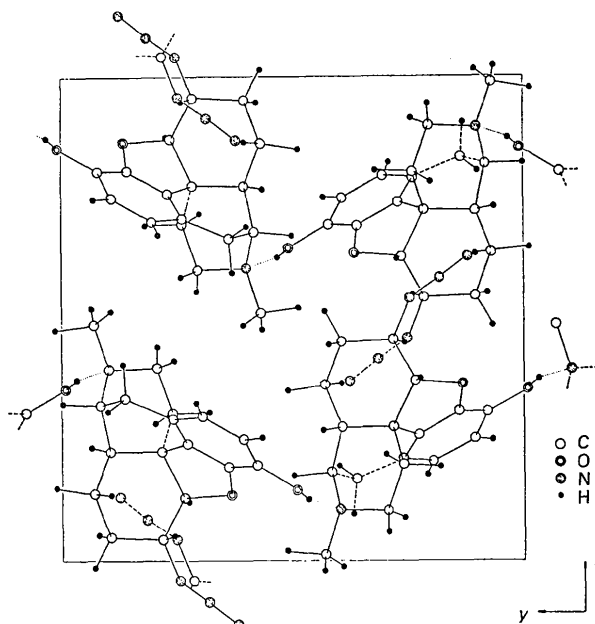


Fig. 3. Packing of the molecule in the crystal lattice shown in orthogonal projection on the plane (100).

Table 8. Observed and calculated components of *U* tensors of individual atoms referred to an orthogonalized axial system (in  $10^{-2}$  Å)

Data are given for two groups of atoms forming in the molecule the stock and arms, respectively, of the T-shape, considered as two separate rigid bodies.

	$U_{11}$		$U_{22}$		$U_{33}$		$U_{12}$		$U_{13}$		$U_{23}$	
	obs	calc	obs	calc	obs	calc	obs	calc	obs	calc	obs	calc
C(1)	3.68	3.67	4.15	4.55	5.43	5.47	-0.26	-0.01	0.38	0.56	-1.04	1.16
C(2)	3.48	3.69	5.09	4.26	6.54	6.27	0.64	0.56	-0.13	-0.19	-1.54	-1.16
C(3)	4.45	3.93	3.27	3.65	4.95	5.18	0.10	0.42	-0.96	-0.79	-0.38	-0.45
C(4)	3.46	3.52	4.07	3.37	4.39	4.31	-0.26	0.04	-0.11	-0.33	0.01	-0.25
C(10)	4.37	4.52	4.22	4.28	5.37	5.37	-0.66	-0.78	0.23	0.31	0.48	0.23
C(11)	3.80	3.52	3.66	4.87	4.18	4.25	-0.12	-0.32	0.21	0.09	-0.50	-0.55
C(12)	3.15	3.15	3.12	3.33	4.21	4.19	0.17	-0.11	-0.39	-0.25	-0.77	-0.33
O(18)	3.93	4.33	3.62	3.89	5.58	5.61	0.06	-0.13	0.79	0.63	0.40	0.34
C(5)	3.45	3.16	4.30	4.42	5.14	4.95	0.56	0.50	0.25	0.40	0.13	0.50
C(6)	4.05	4.10	6.56	6.02	3.84	4.07	0.72	0.81	0.78	0.46	0.22	0.33
C(7)	5.90	6.13	5.50	5.93	4.24	4.09	0.57	0.71	-0.16	-0.02	-1.15	-0.95
C(8)	5.47	5.23	5.06	4.72	4.29	4.37	-0.23	-0.49	-0.99	-0.82	-0.24	-0.70
C(9)	4.32	4.34	4.16	4.22	4.30	4.23	0.05	-0.33	-0.34	-0.41	-0.16	0.20
C(13)	2.72	3.06	3.36	3.41	4.13	4.23	0.10	0.40	0.02	-0.11	-0.27	-0.22
C(14)	3.84	3.65	3.01	3.47	4.22	4.09	0.22	0.15	-0.74	-0.38	-0.36	-0.43
C(15)	4.13	4.35	3.70	3.66	5.48	5.42	-0.26	0.19	-1.06	-1.16	-0.02	-0.33
C(16)	6.26	6.16	3.68	4.24	4.90	4.54	0.07	0.11	-1.65	-1.38	-0.50	-0.69
N(17)	5.41	5.38	5.02	4.26	3.68	4.24	0.01	0.13	-0.51	-0.98	0.09	0.04

Table 9. Translational *T* ( $10^{-2}$  Å<sup>2</sup>) and librational  $\omega$  ( $10^{-2}$  rad<sup>2</sup>) tensors of the two groups of atoms (as in Table 8), assumed as separate rigid bodies of the molecule, referred to an orthogonalized axial system

The e.s.d.'s given in parentheses refer to the last two digits.

$T_1 =$ (stock)	$\begin{pmatrix} 3.22 (17) & 0.00 (15) & -0.29 (17) \\ & 3.50 (16) & -0.66 (17) \\ & & 4.03 (21) \end{pmatrix}$	$T_2 =$ (arms)	$\begin{pmatrix} 3.07 (24) & 0.33 (18) & -0.19 (12) \\ & 3.43 (17) & -0.34 (11) \\ & & 4.01 (11) \end{pmatrix}$
$\omega_1 =$ (stock)	$\begin{pmatrix} 0.31 (08) & 0.08 (10) & 0.00 (07) \\ & 0.55 (10) & -0.04 (10) \\ & & 0.16 (10) \end{pmatrix}$	$\omega_2 =$ (arms)	$\begin{pmatrix} 0.28 (04) & -0.04 (04) & 0.05 (05) \\ & 0.35 (04) & -0.20 (03) \\ & & 0.50 (15) \end{pmatrix}$

Table 10. *Principal axes of the translational T and librational ω tensors of the two group of atoms (as in Table 8), assumed as separate rigid bodies*

The principal axes are given by their lengths (in Å and radians respectively) and their unit vectors referred to an orthogonalized axial system.

Tensor	<i>i</i>	( <i>u</i> <sup>2</sup> ) <sup>1/2</sup>	<i>x</i>	<i>y</i>	<i>z</i>
T <sub>1</sub> (stock)	1	0.213 (Å)	-0.186	-0.532	0.827
	2	0.181	-0.804	0.566	0.184
	3	0.172	-0.566	-0.630	-0.532
T <sub>2</sub> (arms)	1	0.206	0.269	0.460	-0.846
	2	0.184	0.436	0.725	0.533
	3	0.169	0.859	-0.512	-0.006
ω <sub>1</sub> (stock)	1	0.076 (rad)	0.280	0.956	-0.092
	2	0.054	0.960	-0.276	0.055
	3	0.039	0.027	-0.104	-0.994
ω <sub>2</sub> (arms)	1	0.081	0.186	-0.563	0.806
	2	0.052	0.979	0.036	-0.201
	3	0.046	0.084	0.825	0.558

azidomorphine, however, this angle was found to be 173.0°.

It follows from the above that the framework common to the azidomorphine and codeine molecules is identical in both and the deviations are due only to alterations within the carbocyclic ring *C* caused by intramolecular forces. Thus the intermolecular forces, which must be somewhat different in the two crystal lattices, have no special effect on the conformation.

In the spatial packing each molecule is linked to two neighbouring molecules by O(30)–H(3)···N(17) hydrogen bonds to form endless linear molecular chains parallel to the *b* crystal axis, as can be seen in Fig. 3. The hydrogen-bond distance O(30)···N(17) is 2.785 Å with O(30)–H(3)=0.968 Å and H(3)···N(17)=1.829 Å. The angle O(30)–H(3)–N(17) is 169.1°. The linear molecular chains are held together by van der Waals forces. The shortest intermolecular H···H distances are listed in Table 11, together with the mean value compared with the sum of the van der Waals radii, which is given in parentheses.

Table 11. *The shortest intermolecular H···H distances*

The sum of the van der Waals radii is given in parentheses.

From atom at <i>x, y, z</i>	To atom	At position	Distance (Å)
H(1)	H(151)	1 + <i>x</i> <i>y</i> <i>z</i>	2.526
H(2)	H(101)	1 - <i>x</i> -½ + <i>y</i> ½ - <i>z</i>	2.572
H(3)	H(14)	- <i>x</i> -½ + <i>y</i> ½ - <i>z</i>	2.254
H(3)	H(151)	- <i>x</i> -½ + <i>y</i> ½ - <i>z</i>	2.622
H(3)	H(162)	- <i>x</i> -½ + <i>y</i> ½ - <i>z</i>	2.569
H(3)	H(172)	- <i>x</i> -½ + <i>y</i> ½ - <i>z</i>	2.443
H(81)	H(152)	- <i>x</i> ½ + <i>y</i> ½ - <i>z</i>	2.403

Mean: 2.484 (2.54)

The same endless linear molecular chains linked by OH···N hydrogen bonds can be found in D,L-cyclazocine, with the same hydrogen-bond length (2.79 Å). The bonds around the N(17) atom, included

in the hydrogen bond, as in D,L-cyclazocine, are directed according to the tetrahedral coordination. The angles H(3)–N(17)–C(*X*) with *X*=170, 9 and 16, not included in Table 6, are 104.5°, 112.1° and 103.8°, respectively.

*Note:*—Immediately after the completion of the present paper the structure of morphine hydrochloride trihydrate was published (Gylbert, 1973). In this molecule the five rings as well as their overall configuration compare very well with those in the morphine and codeine molecules, while maintaining the boat form in the carbocyclic *C* ring (*D* ring in Gylbert's paper). Based on Beckett & Casy's (1954) conclusion, the boat form has been assumed by Gylbert to be due to the presence of the 4,5-ether bridge. In azidomorphine, however, it was found that after saturation, the *C* ring changed its form from a boat to a chair, in spite of the presence of the 4,5-ether bridge. Thus it does not seem that the boat form is caused directly by the 4,5-ether bridge, but is most probably a consequence of the double bond in the *C* ring.

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