

2,489 Å correspondant à une liaison hydrogène très courte. Par ailleurs on remarque que l'oxygène du pont intervient dans la cohésion de la structure en formant une liaison électrostatique avec un atome de potassium. Les polyèdres de coordination de ions  $K^+$  présentent des déformations importantes et chaque molécule d'eau est lié à trois atomes de potassium.

Nous remercions Monsieur le Professeur Maurin de nous avoir suggéré cette étude.

#### Références

- BAUR, W. H. (1970). *Trans. Amer. Cryst. Assoc.* **6**, 129–155.  
 BRUN, L. (1967). *Rev. Chim. Minér. Fr.* **4**, 839–897.  
 BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). *ORFLS*. ORNL-TM-305, Oak Ridge National Laboratory, Oak Ridge, Tennessee.  
 COLLIN, R. L. & WILLIS, M. (1971). *Acta Cryst.* **B27**, 291–302.  
 CRUICKSHANK, D. W. J. (1961). In *Computing Methods and the Phase Problem in X-ray Crystal Analysis*, p. 45. Oxford: Pergamon Press.  
 CRUICKSHANK, D. W. J. (1964). *Acta Cryst.* **17**, 672–673.  
 CRUICKSHANK, D. W. J. & ROBERTSON, A. P. (1953). *Acta Cryst.* **6**, 698–705.  
 DICKENS, J., BOWEN, J. S. & BROWN, W. E. (1972). *Acta Cryst.* **B28**, 797–806.  
 DOYLE, P. A. & TURNER, P. S. (1968). *Acta Cryst.* **A24**, 390–397.  
 GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1970). *Acta Cryst.* **B26**, 274–285.  
 HAMILTON, W. C. & IBERS, J. A. (1968). *Hydrogen Bonding in Solids*, pp. 15–18. New York: Benjamin.  
 IBERS, J. A., HAMILTON, W. C. & MACKENZIE, D. R. (1964). *Inorg. Chem.* **3**, 1412–1418.  
*International Tables for X-ray Crystallography* (1959). Vol. II, pp. 291–294. Birmingham: Kynoch Press.  
*International Tables for X-ray Crystallography* (1962). Vol. III. p. 214. Birmingham: Kynoch Press.  
 KARLE, J. & KARLE, I. L. (1966). *Acta Cryst.* **21**, 849–859.  
 LAPASSET, J. (1972). Thèse, Montpellier.  
 LYNTON, H. & TRUTER, M. R. (1960). *J. Chem. Soc.* pp. 5112–5118.  
 MACARTHUR, D. M. & BEEVERS, C. A. (1957). *Acta Cryst.* **10**, 428–432.  
 McDONALD, W. S. & CRUICKSHANK, D. W. J. (1967). *Acta Cryst.* **22**, 43–48.  
 NORBERT, A., MAURIN, M. & LARBOT, A. (1972). *Bull. Soc. Fr. Minér. Crist.* **95**, 401–404.  
 PAULING, L. (1960). *The Nature of the Chemical Bond*. 3rd ed., p. 559. Ithaca: Cornell Univ. Press.  
 STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.  
 VIDAL, J. P., LAPASSET, J. & FALGUEIRETTES, J. (1970). *Rev. Chim. Minér.* **7**, 611–622.

*Acta Cryst.* (1973). **B29**, 1630

## The Crystal and Molecular Structure of Morphine Hydrochloride Trihydrate

BY LEIF GYLBERT

*Department of Medical Physics, Karolinska Institutet, Stockholm, S-104 01 Sweden*

(Received 19 March 1973; accepted 22 March 1973)

The alkaloid morphine crystallizes as hydrochloride trihydrate in the orthorhombic space group  $P2_12_12_1$  with the unit-cell dimensions  $a = 13.019$ ,  $b = 20.750$ ,  $c = 6.941$  Å. Three-dimensional data were collected on an automatic linear diffractometer. The structure was determined by the heavy-atom technique and the positions of the hydrogen atoms were established by difference syntheses. Refinement by full-matrix least-squares methods resulted in a final  $R$  value of 0.046 for 1089 observed reflexions. The morphine molecules, connected by  $N-H \cdots O$  hydrogen bonds, form chains about the  $2_1$  axes parallel to  $\mathbf{a}$  and the chains are connected *via* water molecules and chloride ions. The packing of the molecules and the hydrogen bonding system are very similar to those earlier found in the structures of morphine hydroiodide dihydrate and codeine hydrobromide dihydrate.

### Introduction

The chemical structure of morphine, which is the principal alkaloid of opium, was established by Gates & Tschudi (1952), who succeeded in synthesizing the complete molecule. Gulland & Robinson (1925) had already proposed exactly the same structure but were unable to confirm it. The molecular structure of morphine was determined from two projections of the hydroiodide dihydrate by Mackay & Hodgkin (1955)

and the chemical structure was thereby verified. The absolute configuration of the morphine skeleton was established by Kartha, Ahmed & Barnes (1962), who made a full three-dimensional crystal structure determination of codeine (3-methoxymorphine) hydrobromide dihydrate. Since several attempts have been made to explain the pharmacological effects of morphine in terms of its stereochemical structure it was considered valuable to determine the three-dimensional structure of morphine in more detail.

### Experimental

Crystals of morphine hydrochloride trihydrate in the form of orthorhombic colourless needles were obtained from an aqueous solution by slow evaporation. In spite of considerable efforts it was not possible to grow crystals much wider than 0.1 mm. Preliminary unit-cell dimensions and systematic absences were determined from rotation and Weissenberg photographs while accurate cell parameters were derived from diffractometer measurements. The density was measured by flotation in a chloroform-xylene mixture.

#### Crystal data

Morphine [(−)-7,8-didehydro-4,5 $\alpha$ -epoxy-17-methylmorphinon-3,6 $\alpha$ -diol] hydrochloride trihydrate, C<sub>17</sub>H<sub>19</sub>O<sub>3</sub>N.HCl.3H<sub>2</sub>O

F.W. 375.85  $V = 1875.07 \text{ \AA}^3$   
 $a = 13.019 \pm 0.007 \text{ \AA}$ ;  $D_m = 1.31 \text{ g cm}^{-3}$   
 $b = 20.750 \pm 0.010$ ;  $D_x(Z=4) = 1.33 \text{ g cm}^{-3}$   
 $c = 6.941 \pm 0.004$ ;  $\mu(\text{Mo } K\alpha) = 2.41 \text{ cm}^{-1}$ .

Systematic extinctions:  $h00$  when  $h = 2n + 1$ ,  $0k0$  when  $k = 2n + 1$  and  $00l$  when  $l = 2n + 1$ .

Space group  $P2_12_12_1$ .

A crystal having the dimensions  $0.12 \times 0.12 \times 0.25$  mm was mounted with its long dimension ( $c$  axis) parallel to the  $\omega$  axis of an automatic linear diffractometer (PAILRED). Intensities of 1207 symmetry independent reflexions were measured for the layers  $hk0$  through  $hk7$  within  $\sin \theta/\lambda < 0.65$  using graphite monochromated Mo  $K\alpha$  radiation. Depending on the

intensities the reflexions were scanned from 1 up to 3 times. There were 118 reflexions not significantly different from the background intensity, corresponding to 9.8% of the total. The net intensities were corrected for polarization and Lorentz effects but not for absorption, owing to the low absorbance of the crystal ( $\mu R \approx 0.025$ ). The corrected structure amplitudes were placed on an approximately absolute scale by Wilson statistics. All calculations were performed on an IBM 360/75 computer with the program system of Bergin (1971).

#### Determination and refinement of the structure

In the three-dimensional Patterson maps it was easy to identify the Cl-Cl rotation peak. The chlorine atom alone was used for phasing the reflexions in the first electron density calculation. By iterated Fourier calculations with inclusion of an increasing number of maxima found in the electron density maps, all non-hydrogen atoms could be located after four cycles. The conventional  $R$  index ( $R = \sum ||F_o| - |F_c|| / \sum |F_o|$ ) had then decreased from an initial value of 0.58 to 0.20.

The structure was refined by using a full-matrix least-squares program. Unit weights were applied throughout and the atomic scattering factors were those of *International Tables for X-ray Crystallography* (1962) except for that of hydrogen which was taken from Stewart, Davidson & Simpson (1965). After several cycles of refinement of the non-hydrogen atoms, with the inclusion of anisotropic temperature factors, three-dimensional difference maps disclosed the positions of 18 hydrogen atoms. The positional coor-

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

E.s.d.'s in parentheses are in units of the last digit. The temperature expression is of the form:  
 $\exp[-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + hk\beta_{12} + hl\beta_{13} + kl\beta_{23}) \times 10^{-4}]$ .

	$x$	$y$	$z$	$\beta_{11}$	$\beta_{22}$	$\beta_{33}$	$\beta_{12}$	$\beta_{13}$	$\beta_{23}$
C(1)	3229 (5)	418 (3)	364 (11)	58 (5)	19 (2)	179 (24)	-9 (5)	44 (19)	-11 (10)
C(2)	2180 (5)	570 (3)	191 (11)	51 (5)	19 (2)	211 (26)	-20 (5)	-23 (18)	-2 (10)
C(3)	1068 (5)	1158 (3)	835 (10)	37 (5)	21 (2)	179 (24)	-4 (5)	-20 (19)	1 (10)
C(4)	2506 (5)	1584 (3)	1621 (10)	39 (5)	12 (2)	131 (22)	-7 (5)	-18 (14)	7 (9)
C(5)	3189 (5)	2347 (3)	3607 (10)	34 (4)	16 (2)	195 (25)	-2 (5)	-1 (17)	-14 (9)
C(6)	3069 (5)	2186 (3)	5729 (11)	30 (4)	27 (2)	185 (26)	5 (5)	29 (17)	-39 (11)
C(7)	3419 (5)	1528 (3)	6286 (11)	45 (5)	27 (2)	148 (23)	-3 (6)	-22 (17)	9 (10)
C(8)	4297 (5)	1279 (3)	5545 (10)	45 (5)	22 (2)	154 (24)	7 (5)	-24 (17)	14 (10)
C(9)	5571 (5)	1229 (3)	2807 (10)	33 (4)	21 (2)	183 (24)	10 (5)	1 (16)	23 (10)
C(10)	5029 (5)	702 (3)	1624 (11)	41 (4)	22 (2)	211 (26)	-2 (5)	37 (17)	-18 (11)
C(11)	3921 (4)	857 (3)	1127 (9)	41 (4)	13 (2)	153 (24)	-6 (5)	-12 (15)	-17 (9)
C(12)	3533 (5)	1437 (3)	1658 (10)	38 (5)	14 (2)	161 (23)	-18 (5)	-19 (14)	1 (9)
C(13)	4089 (4)	1978 (3)	2640 (10)	30 (4)	13 (2)	125 (22)	4 (4)	13 (14)	4 (8)
C(14)	4867 (4)	1664 (3)	4053 (10)	30 (4)	14 (2)	177 (24)	10 (4)	-1 (15)	14 (10)
C(15)	4675 (4)	2415 (3)	1220 (11)	33 (4)	19 (2)	174 (24)	-5 (5)	7 (16)	31 (9)
C(16)	5492 (5)	2047 (3)	103 (10)	34 (4)	28 (2)	137 (23)	-14 (5)	-6 (15)	12 (10)
C(17)	7069 (5)	1394 (3)	513 (13)	34 (4)	34 (2)	274 (29)	5 (5)	54 (19)	-43 (14)
O(1)	792 (3)	1333 (2)	800 (8)	33 (3)	30 (1)	275 (23)	-1 (3)	-37 (12)	-8 (8)
O(2)	2016 (3)	2288 (2)	6371 (8)	46 (3)	23 (1)	273 (23)	16 (4)	55 (12)	-24 (7)
O(3)	2270 (3)	2154 (2)	2506 (7)	32 (3)	16 (1)	194 (21)	5 (3)	-20 (10)	-21 (7)
O(W1)	324 (5)	1678 (3)	4632 (11)	84 (5)	69 (2)	450 (30)	-95 (6)	132 (19)	-181 (14)
O(W2)	-582 (4)	607 (2)	-689 (10)	73 (4)	44 (2)	302 (25)	-45 (5)	-84 (17)	-44 (10)
O(W3)	-1364 (4)	-132 (3)	2151 (10)	88 (4)	38 (2)	380 (26)	-29 (5)	-64 (16)	16 (11)
N	6177 (4)	1692 (2)	1511 (8)	31 (3)	21 (1)	190 (22)	-2 (4)	40 (13)	-12 (8)
Cl	-1774 (2)	884 (1)	5439 (4)	76 (1)	31 (1)	307 (17)	-21 (2)	-10 (6)	3 (3)

dinates of the remaining 8 hydrogen atoms were later found from further difference analyses. All the hydrogen atoms were given isotropic temperature factors of  $3.0 \text{ \AA}^2$ . The final refinement cycle involving 309 parameters resulted in an  $R$  value of 0.046 and gave the positional coordinates and thermal parameters listed in Tables 1 and 2.\*

Table 2. Final coordinates for hydrogen atoms having a temperature factor  $B$  of  $3.0 \text{ \AA}^2$

E.s.d.'s in parentheses are in units of the last digit.

	$x$	$y$	$z$
H(C1)	0.346 (3)	0.003 (5)	-0.002 (12)
H(C2)	0.169 (3)	0.021 (5)	-0.032 (12)
H(C5)	0.326 (3)	0.280 (5)	0.340 (12)
H(C6)	0.349 (3)	0.253 (5)	0.645 (12)
H(C7)	0.311 (3)	0.132 (5)	0.741 (11)
H(C8)	0.452 (3)	0.089 (5)	0.586 (12)
H(C9)	0.612 (3)	0.103 (5)	0.379 (12)
H(C10) <i>A</i>	0.547 (3)	0.063 (5)	0.059 (11)
H(C10) <i>B</i>	0.504 (3)	0.027 (5)	0.238 (13)
H(C14)	0.530 (3)	0.201 (5)	0.477 (11)
H(C15) <i>A</i>	0.414 (3)	0.256 (5)	0.032 (12)
H(C15) <i>B</i>	0.503 (3)	0.280 (5)	0.193 (12)
H(C16) <i>A</i>	0.603 (3)	0.233 (5)	-0.065 (12)
H(C16) <i>B</i>	0.523 (3)	0.175 (5)	-0.074 (12)
H(C17) <i>A</i>	0.739 (3)	0.180 (5)	-0.018 (12)
H(C17) <i>B</i>	0.749 (3)	0.121 (5)	0.131 (12)
H(C17) <i>C</i>	0.681 (3)	0.109 (5)	-0.048 (13)
H(O1)	0.067 (3)	0.143 (5)	0.219 (11)
H(O2)	0.183 (3)	0.224 (5)	0.521 (12)
H(N)	0.641 (3)	0.199 (5)	0.225 (12)
H(W1) <i>A</i>	0.088 (3)	0.190 (5)	0.538 (12)
H(W1) <i>B</i>	-0.036 (3)	0.144 (5)	0.497 (12)
H(W2) <i>A</i>	-0.018 (3)	0.082 (5)	0.022 (12)
H(W2) <i>B</i>	-0.082 (3)	0.070 (5)	-0.202 (12)
H(W3) <i>A</i>	-0.111 (3)	0.018 (5)	0.073 (12)
H(W3) <i>B</i>	-0.192 (3)	-0.027 (5)	0.168 (12)

## Description and discussion of the structure

### Configuration and geometry of the molecule

The numbering system of the non-hydrogen atoms of the morphine molecule is that generally accepted (Fig. 1). The over-all configuration of the molecule is seen in Fig. 2, which shows the correct absolute configuration of the natural (-) form. From this figure it is evident that the molecule consists of two roughly planar parts. The first plane (I) involves the atoms C(1) through C(5), C(9) through C(14), O(1) and O(3) comprising the benzene ring (*A*), the oxide ring (*B*) and the carbocyclic ring (*C*). The second plane (II) contains the carbocyclic ring (*D*) and the ethenamine ring (*E*) and includes the atoms C(5) through C(9), C(13) through C(17), O(2) and N. The deviations of respective atoms from planes I and II are given in Table 3. The two planes are nearly perpendicular ( $90.9^\circ$ ) and the morphine molecule thus has the T-shape already

described by Mackay & Hodgkin (1955). The same T-shape has been found in codeine (Lindsay & Barnes, 1955; Kartha, Ahmed & Barnes, 1962). The atoms of the benzene ring (*A*) are nearly coplanar (Table 3) whereas the five membered *B*-ring is distorted. The ethenamine ring (*E*) has a typical chair form while the *D*-ring has a boat form. This is caused by the 4,5-ether bridge which also is responsible for the rigidity of the morphine structure. In morphinans which lack this ether bridge the corresponding *D*-ring has a chair form (Beckett & Casy, 1954).

Table 3. Least-squares planes and deviations in  $\text{\AA}$  of individual atoms

Each plane is described by the equation  $aX + bY + cZ = d$  where  $X, Y, Z$  are the coordinates in orthogonal Ångström space.

Plane I			
$a$	$b$	$c$	$d$
-0.2330	-0.4669	0.8531	-1.2161
C(1)	0.0478	C(11)	-0.1356
C(2)	0.1162	C(12)	-0.2653
C(3)	0.0408	C(13)	-0.3773
C(4)	-0.1184	C(14)	0.5269
C(5)	0.1114	O(1)	0.1584
C(9)	-0.0025	O(3)	-0.0745
C(10)	-0.0277		
Plane II			
$a$	$b$	$c$	$d$
-0.5296	-0.6652	-0.5264	-6.8629
C(5)	0.1089	C(14)	-0.2696
C(6)	-0.3624	C(15)	-0.1388
C(7)	0.1016	C(16)	0.2147
C(8)	0.1107	C(17)	-0.1215
C(9)	0.3000	O(2)	-0.0110
C(13)	0.3502	N	-0.2829

Plane of benzene ring			
$a$	$b$	$c$	$d$
-0.1483	-0.3805	0.9128	-0.7333
C(1)	0.0107	C(4)	0.0258
C(2)	-0.0166	C(11)	0.0138
C(3)	-0.0010	C(12)	-0.0327

The bond lengths and bond angles for the non-hydrogen atoms are shown in Fig. 1. The average e.s.d.'s for the C-C, C-O and C-H bonds and C-C-C angles are 0.009, 0.008, 0.09 Å and  $0.6^\circ$  respectively.

The bond distances of the benzene ring are all normal with an average value of 1.38 Å. There is a good agreement with corresponding bonds in codeine hydrobromide (Kartha, Ahmed & Barnes, 1962) except for the C(11)-C(12) bond which in morphine is 0.04 Å shorter than in codeine. Outside the benzene ring the carbon-carbon single bonds are all of normal lengths. As could be expected, the two bonds adjacent to the C(7)-C(8) double bond are slightly shortened and so are the C-O bond and the two C-C bonds attached to the benzene ring. The three carbon-

\* The structure factor table has been deposited with the National Lending Library, England, as Supplementary Publication No. SUP 30110. Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

nitrogen bonds having an average length of 1.51 Å are normal for a C-N<sup>+</sup> bond.

The mean value for the C-H and N-H bond lengths is 0.99 Å. The positional coordinates of the hydrogen atoms of the three water molecules, which were the ones most difficult to locate, show larger e.s.d.'s than those of the hydrogen atoms of the morphine molecule. The three H-O-H angles of the water molecules thus range from 95 to 136° with e.s.d.'s of ±9°. The angles involving non-hydrogen atoms are all in good agreement with corresponding ones in the codeine structure.

#### *Molecular packing and hydrogen bonds*

The packing of the molecules in morphine hydrochloride trihydrate is very similar to that in morphine hydroiodide dihydrate (Mackay & Hodgkin, 1955)

and codeine hydrobromide dihydrate (Karth, Ahmed & Barnes, 1962). This is evident from Fig. 3, which shows the three structures projected onto the 001 plane. The molecules have almost the same orientation and relation to the screw axes and as the three structures belong to the same space group and have roughly identical unit-cell dimensions they are nearly isostructural. The small differences, obvious from Fig. 3, consist mainly of displacements along the axes. In relation to the present structure the atoms of the morphine hydroiodide molecule show average displacements of -0.26 Å along *a*, -0.08 Å along *b* and 0.00 Å along *c*. Corresponding figures for the codeine molecules are +0.57, -0.09 and -0.05 Å. The water molecules and the halogen ions occupy likewise nearly the same sites in the three structures. The oxygen atoms

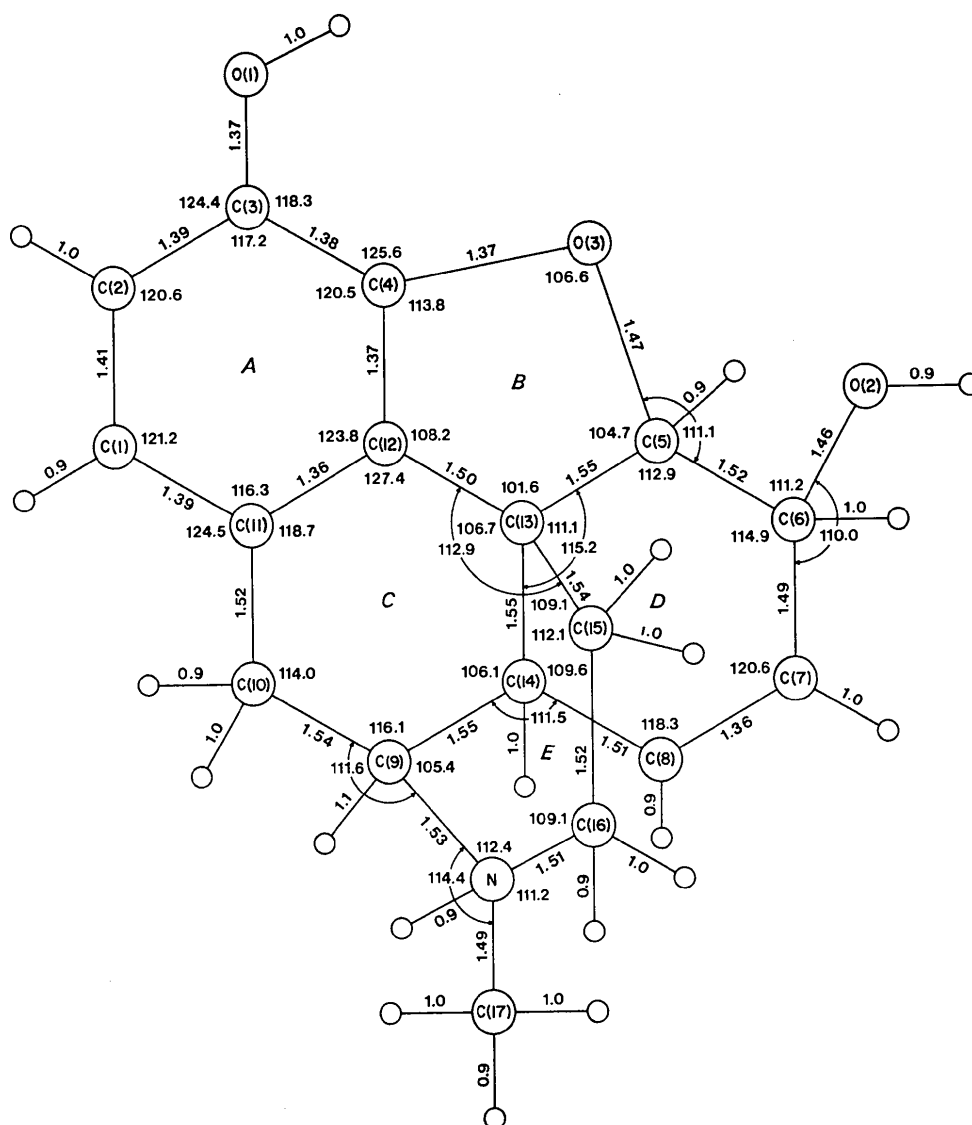


Fig. 1. Interatomic distances (Å) and interbond angles (°) in the morphine molecule.

of the two water molecules in the morphine hydroiodide structure thus correspond to O(W1) and O(W2) and those of the codeine structure to O(W1) and O(W3). The volume occupied by the oxygen atom O(W2) of the present structure is, in codeine, filled to the same extent by the methyl group on O(1). The halide ions are within  $\pm 0.3 \text{ \AA}$  of the same position.

Because of the similar packing in the three structures the hydrogen bonding systems are very much the same. In each of the structures the molecules form infinite zigzag chains about the  $2_1$  axes parallel to *a*. The molecules of the chains are linked together by N-H...O hydrogen bonds (Fig. 3). Since the positions of the hydrogen atoms were not determined in the

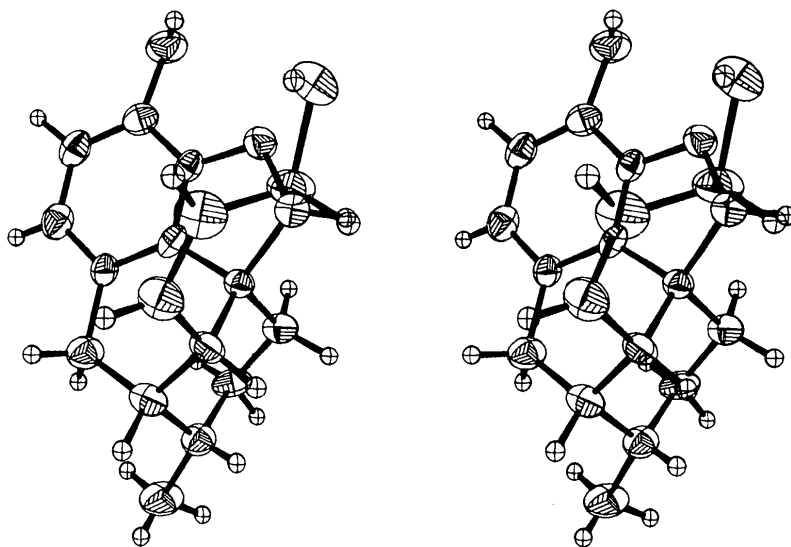


Fig. 2. Stereogram of the (-)-morphine molecule. The thermal ellipsoids are drawn at the 50% probability level. The drawing was performed using the program *ORTEP* (Johnson, 1965).

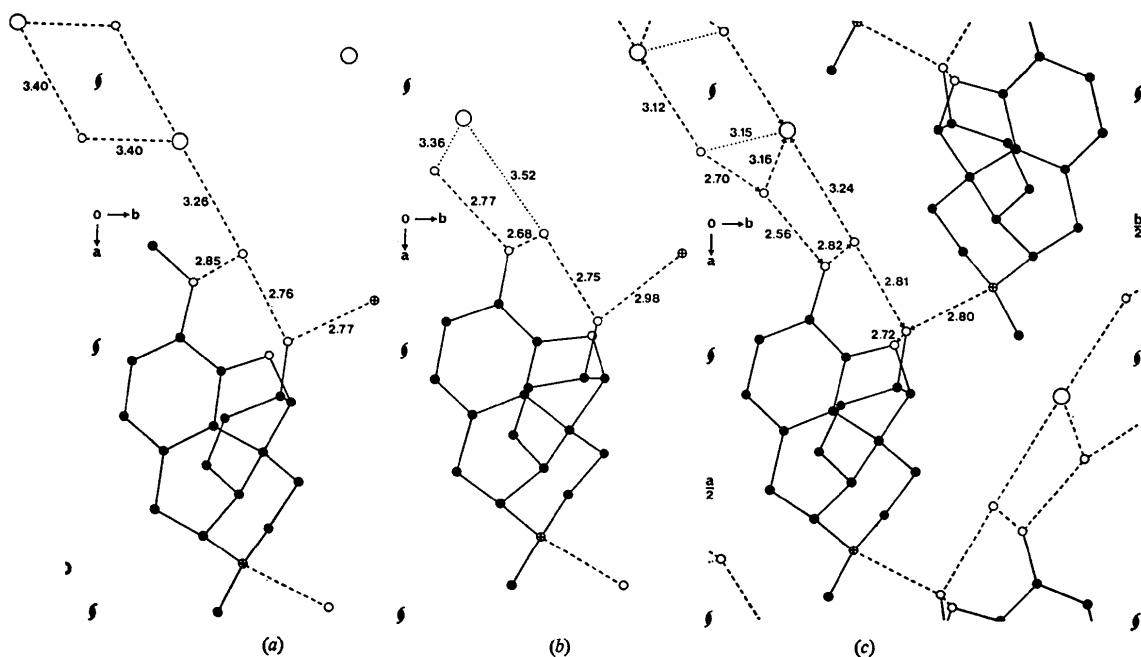


Fig. 3. A comparison between the molecular arrangements and hydrogen bonding systems in (a) codeine hydrobromide dihydrate, (b) morphine hydroiodide dihydrate and (c) morphine hydrochloride trihydrate. Filled, open and crossed small circles represent carbon, oxygen and nitrogen atoms respectively. Large circles represent halide ions. Projection onto (001). Hydrogen bonds are indicated by dashed lines, short distances by dotted lines. Distances in  $\text{\AA}$ .

Table 4. *Hydrogen bonded interactions X-H...Y'*

The column labelled  $x', y', z'$  gives the symmetry code of the acceptor atom  $Y'$ . Reference molecule in  $x, y, z$ .

$X$	H	$Y'$	$x'$	$y'$	$z'$	$X \cdots Y'$	$H \cdots Y'$	$X-H \cdots Y'$
O(1)	H(O1)	O(W1)	$x$	$y$	$z$	2.82 Å	1.83 Å	173°
O(2)	H(O2)	O(3)	$x$	$y$	$z$	2.72	1.97	142
O(W1)	H(W1)A	O(2)	$x$	$y$	$z$	2.81	1.84	170
O(W1)	H(W1)B	Cl	$x$	$y$	$z$	3.24	2.19	175
O(W2)	H(W2)A	O(1)	$x$	$y$	$z$	2.56	1.71	151
O(W2)	H(W2)B	Cl	$x$	$y$	$z-1$	3.16	2.20	160
O(W3)	H(W3)A	O(W2)	$x$	$y$	$z$	2.70	1.50	165
O(W3)	H(W3)B	Cl	$\bar{x}-\frac{1}{2}$	$\bar{y}$	$z-\frac{1}{2}$	3.12	2.30	165
N	H(N)	O(2)	$x+\frac{1}{2}$	$\bar{y}+\frac{1}{2}$	$\bar{z}+1$	2.80	1.95	180

earlier structure determinations this bond was interpreted as an O-H...N bond. The chains of morphine molecules are interconnected *via* water molecules and halide ions by a well developed hydrogen bonding system of similar construction in the three structures. However, in the present structure it is more elaborate due to the presence of an extra water molecule (Fig. 3). Data about these hydrogen bonds are given in Table 4. Only one hydrogen donor atom, H(O2), does not participate in the intermolecular network of hydrogen bonds. This hydrogen atom points towards O(3) and it is probable that there exists an intramolecular hydrogen bond O(2)-H...O(3) although the geometry of the atoms involved is not quite ideal. There is a short distance (3.15 Å) between the oxygen atom O(W3) of a water molecule and the chloride ion. The hydrogen atoms of this water molecule are however involved in hydrogen bonds to O(W2) (2.70 Å) and to a symmetry-related chlorine atom (3.12 Å) but in the codeine structure, where O(W2) is missing, this short distance certainly represents a genuine hydrogen bond. Apart from this short distance there are no exceptionally short contacts in the present structure; the shortest distances are given in Table 5.

I wish to express my gratitude to Professor Diego Carlström for his support and patient guidance. My thanks are also due to Mrs Ingrid Hacksell for preparing the manuscript and drawings.

This work has been supported by the Swedish Medical Research Council (Project No 13X-144).

#### References

BECKETT, A. H. & CASY, A. F. (1954). *J. Pharm. Pharmacol.* **6**, 986-1001.

Table 5. *Some short intermolecular distances*

All heavy-atom distances less than 3.40 Å and all C...H and O...H distances less than 2.70 Å.

Second atom at ( $x, y, z$ )

O(1).....O(3)	2.83	O(3).....O(W1)	3.09
O(W3).....Cl	3.15		

Second atom at ( $x-\frac{1}{2}, \frac{1}{2}-y, \bar{z}$ )

O(1).....C(15)	3.29	O(3).....C(16)	3.38
O(3).....H(C16)A	2.33		

Second atom at ( $\frac{1}{2}-x, \bar{y}, z-\frac{1}{2}$ )

O(W2).....C(10)	3.37	O(W2).....H(C10)B	2.37
-----------------	------	-------------------	------

Second atom at ( $x-\frac{1}{2}, \frac{1}{2}-y, 1-z$ )

O(W1).....H(C15)B	2.66
-------------------	------

Second atom at ( $\frac{1}{2}-x, \bar{y}, \frac{1}{2}+z$ )

O(W3).....H(C17)C	2.64
-------------------	------

- BERGIN, R. (1971). Internal Report I/71. Department of Medical Physics, Karolinska Institutet, Stockholm.
- GATES, M. & TSCHUDI, G. (1952). *J. Amer. Chem. Soc.* **74**, 1109-1110.
- GULLAND, J. M. & ROBINSON, R. (1924/25). *Mem. Proc. Manchester Lit. Phil. Soc.* **69**, 79-86.
- International Tables for X-ray Crystallography* (1962). Vol. III. Birmingham: Kynoch Press.
- JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tennessee.
- KARTHA, G., AHMED, F. R. & BARNES, W. H. (1962). *Acta Cryst.* **15**, 326-333.
- LINDSAY, J. M. & BARNES, W. H. (1955). *Acta Cryst.* **8**, 227-232.
- MACKAY, M. & HODGKIN, D. C. (1955). *J. Chem. Soc.* pp. 3261-3267.
- STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175-3187.