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The Crystal and Molecular Structure of Apomorphine Hydrochloride Hydrate

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Apomorphine (aporphine-10,11-diol, CA Registry Number 58004) was crystallized as the hydrochloride and hydrobromide. The crystals are isomorphous, space group $P2_12_12_1$, with eight formula units in cells having the dimensions $a=13{\cdot}279$, $b=20{\cdot}317$, $c=11{\cdot}562$ Å and $a=13{\cdot}17$, $b=20{\cdot}57$, $c=11{\cdot}76$ Å respectively. The structure of the hydrobromide was first determined from photographic data. Three-dimensional data for the hydrochloride were then collected on an automatic linear diffractometer, and this structure was refined by full-matrix least-squares methods to a final R value of 4·5% for 1539 observed reflexions. The two molecules of the asymmetric unit are slightly different. The structure is stabilized by a network of hydrogen bonds with chloride ions as acceptors. Crystal water molecules seem to appear at different sites in different cells.

Introduction

Apomorphine is easily obtained from morphine, either by heating to 150°C or by cracking with strong acids. The substance totally lacks the narcotic properties of morphine, but it has long been used in medicine as a most powerful vomitory. It has also long been known to mimic the effect of the endogenous transmitter substance dopamine on the central nervous system. This has been shown by *inter alios* Fuxe & Ungerstedt (1970), and apomorphine is in fact used in research on the brain in lieu of dopamine as it can pass the blood–brain barrier, which the dopamine cannot. Furthermore there is a high probability (Ernst, 1969) that apomorphine acts directly on the dopamine receptor sites and not on any other stage in the neural transmission.

Apomorphine is not usually included in the group of substances to which dopamine belongs, the catecholamines, but in Fig. 1 it can be seen that such a molecule is hidden in the apomorphine skeleton. What makes apomorphine so interesting from a stereochemical point of view is the fact that this compound, unlike the catecholamines previously examined at this department, has a rigid 'side chain', supported by three carbon rings. This is important because it has often been argued that psychoactive substances with a free side chain do not necessarily act as transmitter substances in the conformation they prefer in crystals; and therefore it has been suggested by Bergin (1971*b*) that the stable architecture of apomorphine makes this substance most appropriate for a comparison with the dopamine and its relatives.

Experimental

In a preliminary study, forming the basis of an examination paper at the Royal Institute of Technology in Stockholm, the crystal and molecular structure of apomorphine hydrobromide was determined. There is no need to make a detailed account of this structure determination here, but some of its results will be given below.

Transparent, colourless crystals of both the hydrobromide and hydrochloride of apomorphine were quite easily obtained from aqueous solutions, although some of them apparently oxidized in the process, the former turning brown, the latter green. In order to lessen the effects of oxidation, the water was in both cases evaporated at 10 mm Hg. The crystal data for the two salts can be found in Table 1. The systematic absences in both crystals were: $h00$ when h is odd, $0k0$ when k is odd, and $00l$ when l is odd, indicating the space group $P2_12_12_1$. Since this space group has only four equivalent positions it was concluded that the asymmetric unit contained two molecules of apomorphine in both salts. The water content of the crystal varies, but the difference between D_m and D_x found in apomorphine hydrochloride was assumed to correspond to about $\frac{3}{4}H_2O$ per asymmetric unit.

Intensity data for the bromide was collected with the multiple-film Weissenberg technique. 863 independent reflexions were measured in a microdensitometer.

In the subsequent investigation of the chloride a crystal measuring 0·3 × 0·2 × 0·4 mm was mounted along **c**. The integrated intensities were measured on the automatic linear diffractometer PAILRED, using graphite monochromated Mo $K\alpha$ radiation ($\lambda=0{\cdot}71069$. The layers $hk0$ through $hk8$ were recorded, giving 3142 reflexions. Owing to the symmetry of the crystal only about half of these were symmetry independent and the average of each pair of reflexions was used in the calculations. The fainter reflexions were scanned up to three times, and the backgound was measured for one minute on each side. Standard reflexions, measured continuously during the collection of data, showed no significant change in intensity. When the usual physical and statistical corrections had been applied 1612 independent reflexions remained. Of these 66 had an intensity not statistically different from the background intensity.

Structure determination

The structure of apomorphine hydrobromide was determined from a three-dimensional Patterson calculation. By giving the bromide atoms anisotropic thermal parameters but keeping the other atoms isotropic the structure was then refined to a conventional R value of 8%. No hydrogen atoms were located, nor were any crystal water molecules. When it came to determining the structure of apomorphine hydrochloride it was initially assumed that the crystals of the two salts were isomorphous.

Refinement procedure

When the coordinates of the bromide were applied to the intensity data of the chloride the original R value was 35%, but after only one cycle of refinement it dropped to 19·7% and it was concluded that the assumption had been right. The structure was refined isotropically to $R = 12{\cdot}5\%$. It was decided to exclude from further full-matrix least-squares refinement all non-observed reflexions. In addition, seven reflexions which had obviously not been correctly measured, partly due to their low sin θ values, were excluded. The introduction of anisotropic temperature factors then reduced the R value to 10·7%. A subsequent difference synthesis did not show the expected water molecule as one distinct peak, but instead showed three prominent peaks that were definitely not hydrogen atoms. It was obvious that the water molecules occupied different sites in different unit cells. The three peaks would then correspond to $\frac{1}{2}$, $\frac{1}{4}$, and $\frac{1}{8}$ of an oxygen atom respectively. Oxygen atoms with these weights were included in the refinement, each with anisotropic temperature factors, and their parameters are given with those of the other atoms in Table 2 under the designations O(W1), O(W2) and O(W3) respectively. It is not entirely certain that these three peaks really represent oxygen atoms. However, there is space enough in the cell for the water molecules, the shortest distance from any of them to a non-hydrogen atom in an apomorphine molecule being 2·95 Å. It should be noted, though, that O(W1) and O(W3) cannot occupy the same asymmetric unit simultaneously, since they are much too close (1·24 Å).

When these water oxygen atoms were included in a refinement it was quite easy to find in a difference synthesis all but one of the 34 hydrogen atoms belonging to the two apomorphine molecules. The positional parameters of these hydrogen atoms were then refined in one cycle, but the thermal parameters were kept constant at 4·0 Å^2. Since the crystal water molecules were only fractional no attempt was made to locate their hydrogen atoms.

A final cycle of refinement of the non-hydrogen atoms yielded an R value of 4·5%.

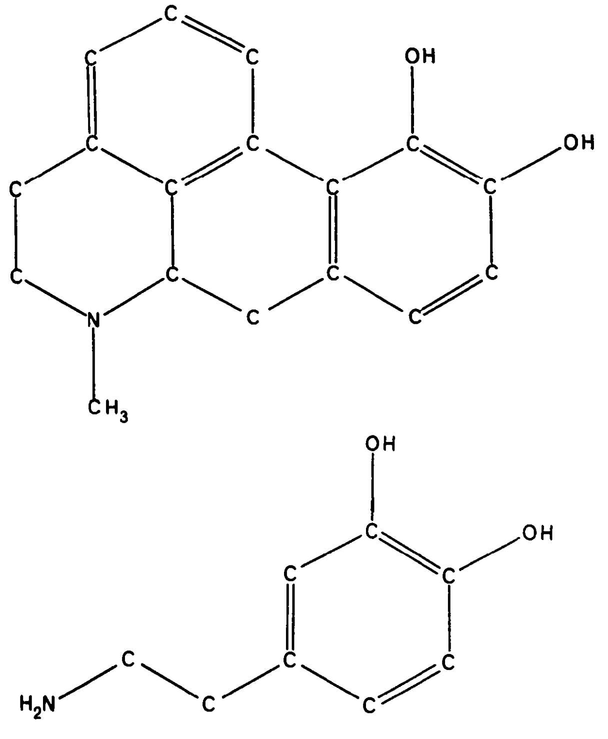

Fig. 1. A comparison of the apomorphine molecule (top) and the dopamine molecule (bottom).

Table 1. *Crystal data*

	Apomorphine hydrochloride	Apomorphine hydrobromide
Empirical formula	$C_{17}H_{17}O_2N.HCl$, aq	$C_{17}H_{17}O_2N.HBr$, aq
M.W.	303·79	348·26
Crystal system	Orthorhombic	Orthorhombic
Unit-cell dimensions	$a = 13{\cdot}279 \pm 0{\cdot}004$ Å	$a = 13{\cdot}17 \pm 0{\cdot}03$ Å
	$b = 20{\cdot}317 \pm 0{\cdot}005$	$b = 20{\cdot}57 \pm 0{\cdot}05$
	$c = 11{\cdot}562 \pm 0{\cdot}005$	$c = 11{\cdot}76 \pm 0{\cdot}02$
	$V = 3115$ Å^3	$V = 3185$ Å^3
D_m	$1{\cdot}318 \pm 0{\cdot}005$ g.cm^{-3}	$1{\cdot}48 \pm 0{\cdot}01$ g.cm^{-3}
D_x (without any water)	1·295	1·452
Molecules per unit cell	8	8
Electrons per unit cell	1280	1424

The scattering factors for the neutral non-hydrogen atoms and Cl$^-$ were those given in *International Tables for X-ray Crystallography*, that for N$^+$ was interpolated from the tables for O$^+$ and B$^+$, and that for hydrogen was the one given by Stewart, Davidson & Simpson (1965). All structure factors were given unit weight. The computations were carried out on an IBM 360/75 computer using our program system (Bergin, 1971*a*). The final non-hydrogen and hydrogen parameters are given in Tables 2 and 3 respectively.*

Description and discussion of the structure

The asymmetric unit of the crystal contains two molecules of apomorphine hydrochloride, *A* and *B*, which are shown in Fig. 2(*a*) and (*b*). The upper value in the drawings and the first value in the text always refer to molecule *A*. The atoms of the catecholamine part are numbered according to Bergin (1971*b*), while the others are numbered in logical continuation. This numbering scheme does not correspond to the generally approved system; it has however been chosen to facilitate comparison with dopamine and related substances.

From the stereoscopic pair in Fig. 3 (showing the *A*-molecule) it can be seen that the apomorphine molecule is rather flat. It consists of two aromatic rings

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* The observed and calculated structure factors have been deposited with the National Lending Library, England, as Supplementary Publication No. SUP 30113. Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Final positional and thermal parameters for non-hydrogen atoms* (× 10^4)

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

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl(1)*A*	9980 (2)	3453 (1)	3607 (2)	74 (1)	35 (1)	89 (2)	−17 (3)	−20 (4)	−4 (2)
C(1)*A*	5719 (5)	3366 (3)	5127 (7)	71 (6)	24 (2)	57 (9)	−21 (6)	8 (12)	2 (7)
C(2)*A*	4815 (6)	3643 (4)	5515 (8)	61 (5)	35 (2)	87 (11)	−14 (6)	38 (13)	10 (8)
C(3)*A*	4405 (5)	4175 (4)	4973 (8)	46 (5)	43 (3)	56 (10)	13 (6)	4 (12)	−8 (9)
C(4)*A*	4891 (5)	4471 (4)	4038 (7)	48 (5)	38 (2)	50 (10)	6 (6)	20 (11)	−3 (8)
C(5)*A*	5823 (4)	4225 (3)	3637 (7)	47 (4)	24 (2)	33 (8)	9 (5)	−13 (10)	−2 (7)
C(6)*A*	6210 (5)	3663 (3)	4193 (7)	54 (5)	25 (2)	50 (9)	−11 (5)	−23 (11)	−17 (7)
C(7)*A*	7201 (5)	3378 (3)	3782 (8)	54 (5)	24 (2)	70 (12)	6 (5)	5 (11)	6 (7)
C(8)*A*	7264 (5)	3458 (3)	2467 (8)	40 (4)	26 (2)	64 (11)	6 (5)	11 (10)	−10 (7)
C(9)*A*	8228 (6)	2433 (3)	2111 (9)	89 (6)	16 (2)	139 (12)	13 (5)	10 (15)	−7 (8)
C(10)*A*	8359 (5)	3347 (4)	763 (9)	59 (5)	36 (3)	98 (13)	34 (6)	12 (13)	−24 (9)
C(11)*A*	8570 (6)	4081 (4)	671 (9)	64 (5)	31 (2)	143 (13)	19 (6)	59 (14)	37 (9)
C(12)*A*	7794 (5)	4466 (3)	1324 (7)	52 (5)	26 (2)	56 (9)	−0 (5)	7 (12)	16 (7)
C(13)*A*	7173 (4)	4172 (3)	2153 (7)	43 (4)	18 (2)	50 (8)	−5 (4)	−25 (10)	−3 (6)
C(14)*A*	6427 (4)	4547 (3)	2736 (7)	40 (4)	22 (2)	53 (8)	5 (5)	−5 (10)	−8 (7)
C(15)*A*	6337 (5)	5223 (3)	2464 (7)	50 (4)	26 (2)	70 (10)	−2 (5)	−13 (11)	−10 (7)
C(16)*A*	6955 (6)	5509 (3)	1670 (8)	62 (5)	24 (2)	103 (12)	−3 (6)	−23 (13)	17 (8)
C(17)*A*	7674 (5)	5134 (4)	1079 (7)	56 (5)	31 (2)	80 (10)	−11 (6)	−0 (11)	27 (8)
N(1)*A*	8217 (4)	3160 (2)	1996 (6)	53 (4)	21 (1)	72 (9)	−1 (4)	5 (9)	−1 (6)
O(1)*A*	3519 (4)	4460 (3)	5309 (6)	66 (4)	79 (3)	101 (8)	57 (6)	67 (9)	47 (8)
O(2)*A*	4442 (4)	4994 (3)	3494 (5)	66 (4)	50 (2)	91 (7)	53 (5)	35 (8)	47 (6)
Cl(1)*B*	7867 (1)	720 (1)	2153 (2)	55 (1)	31 (1)	69 (2)	14 (1)	11 (3)	10 (2)
C(1)*B*	8694 (6)	2159 (3)	−2903 (10)	63 (5)	25 (2)	65 (12)	7 (6)	−11 (15)	1 (9)
C(2)*B*	9065 (6)	2665 (4)	−3575 (9)	82 (6)	27 (2)	71 (11)	15 (7)	−3 (14)	6 (9)
C(3)*B*	9850 (7)	3033 (4)	−3144 (10)	71 (6)	25 (2)	82 (14)	5 (7)	33 (16)	7 (9)
C(4)*B*	10257 (6)	2915 (4)	−2068 (10)	56 (6)	25 (2)	66 (11)	18 (6)	2 (14)	12 (9)
C(5)*B*	9898 (5)	2399 (3)	−1381 (8)	45 (5)	17 (2)	69 (10)	5 (5)	30 (13)	−2 (7)
C(6)*B*	9088 (5)	2035 (3)	−1830 (8)	49 (5)	24 (2)	56 (12)	11 (6)	5 (12)	0 (8)
C(7)*B*	8714 (5)	1462 (3)	−1103 (8)	43 (4)	25 (2)	66 (10)	−10 (5)	4 (11)	−21 (7)
C(8)*B*	9615 (5)	1095 (3)	−631 (7)	42 (4)	19 (2)	48 (9)	−8 (5)	21 (10)	9 (6)
C(9)*B*	8724 (6)	19 (4)	−621 (9)	68 (6)	26 (2)	129 (12)	−17 (6)	22 (14)	−24 (9)
C(10)*B*	10211 (6)	185 (3)	587 (8)	62 (5)	23 (2)	81 (10)	7 (6)	13 (12)	7 (8)
C(11)*B*	10682 (5)	634 (4)	1493 (9)	58 (5)	32 (3)	102 (11)	17 (6)	8 (13)	37 (9)
C(12)*B*	10759 (5)	1329 (4)	1076 (8)	48 (5)	28 (2)	71 (11)	4 (6)	5 (13)	11 (8)
C(13)*B*	10265 (5)	1548 (3)	103 (8)	37 (4)	22 (2)	62 (10)	5 (5)	35 (11)	−2 (8)
C(14)*B*	10363 (5)	2209 (3)	−278 (8)	34 (4)	24 (2)	62 (11)	2 (5)	−0 (11)	5 (8)
C(15)*B*	10918 (6)	2639 (3)	425 (9)	51 (5)	21 (2)	117 (13)	−5 (6)	36 (14)	−17 (9)
C(16)*B*	11352 (6)	2428 (4)	1444 (10)	52 (6)	39 (3)	91 (12)	−5 (7)	−26 (15)	−24 (10)
C(17)*B*	11291 (6)	1783 (4)	1757 (8)	59 (5)	32 (3)	70 (11)	−1 (6)	−21 (12)	1 (9)
N(1)*B*	9304 (4)	502 (2)	81 (6)	48 (3)	20 (1)	68 (8)	−2 (4)	17 (9)	−1 (6)
O(1)*B*	10274 (5)	3556 (3)	−3776 (6)	120 (5)	26 (2)	120 (9)	−21 (5)	23 (12)	34 (6)
O(2)*B*	11044 (4)	3297 (3)	−1706 (6)	67 (4)	31 (2)	136 (9)	−39 (4)	−16 (9)	26 (6)
O(*W*1)	11568 (13)	4195 (5)	2111 (19)	234 (18)	21 (3)	496 (38)	−55 (12)	613 (47)	−102 (18)
O(*W*2)	12194 (18)	3190 (13)	5124 (29)	83 (18)	60 (10)	159 (41)	29 (23)	35 (48)	49 (34)
O(*W*3)	12024 (20)	4141 (13)	3043 (30)	25 (18)	41 (8)	176 (38)	14 (20)	−81 (43)	11 (28)

Table 3. *Final coordinates for hydrogen atoms (temperature factors* =4·0 Å^3)

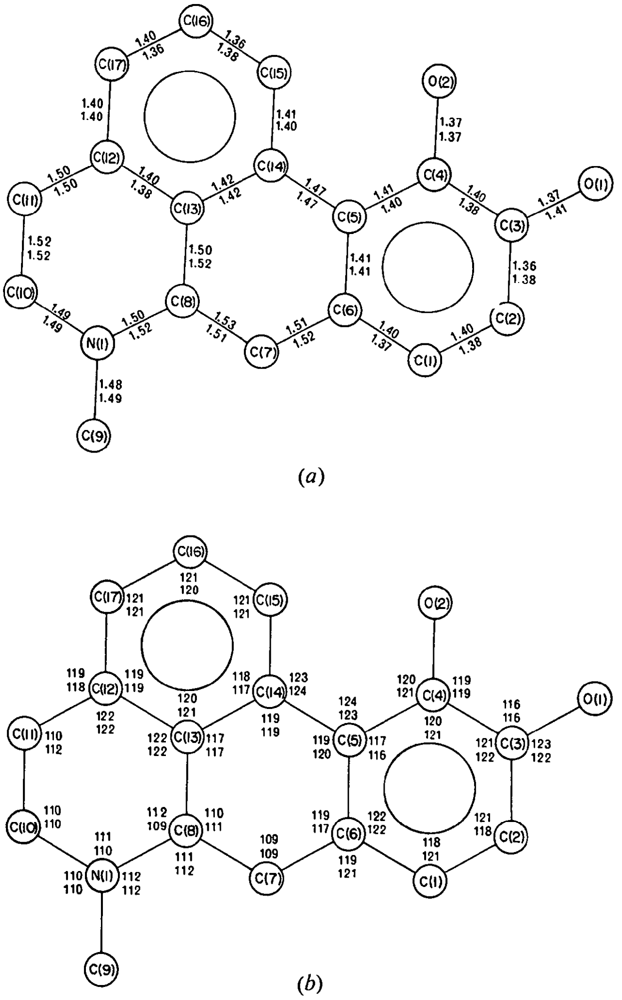
	x	*y*	*z*
H(1)*A*	0·3928 (39)	0·3002 (25)	0·4533 (54)
H(2)*A*	0·5567 (38)	0·3466 (25)	0·3895 (56)
H(7*A*)*A*	0·2216 (40)	0·3616 (25)	0·5834 (54)
H(7*B*)*A*	0·2666 (39)	0·2915 (25)	0·5922 (54)
H(8)*A*	0·3322 (40)	0·3196 (25)	0·7815 (56)
H(9*A*)*A*	0·1100 (40)	0·2270 (25)	0·8191 (54)
H(9B)*A*	0·2303 (39)	0·2268 (25)	0·8258 (55)
H(9C)*A*	0·1848 (40)	0·2273 (25)	0·7139 (58)
H(10*A*)*A*	0·1047 (40)	0·3144 (26)	0·9564 (55)
H(10*B*)*A*	0·2221 (40)	0·3251 (25)	0·9692 (56)
H(11*A*)*A*	0·0732 (40)	0·4164 (26)	0·9064 (55)
H(11*B*)*A*	0·1368 (40)	0·4219 (25)	1·0150 (55)
H(15)*A*	0·4200 (39)	0·5531 (25)	0·7088 (56)
H(16)*A*	0·3136 (40)	0·5949 (25)	0·8435 (56)
H(17)*A*	0·1902 (40)	0·5296 (25)	0·9541 (56)
H(N1)*A*	0·1257 (39)	0·3312 (25)	0·7534 (51)
H(O1)*A*	0·6648 (39)	0·4390 (25)	0·3963 (54)
H(O2)*A*	0·6345 (37)	0·5042 (23)	0·5993 (47)
H(1)*B*	0·1848 (40)	0·1916 (25)	1·3215 (54)
H(2)*B*	0·1239 (39)	0·2798 (25)	1·4344 (54)
H(7*A*)*B*	0·1638 (39)	0·1567 (26)	1·0408 (56)
H(7*B*)*B*	0·1747 (40)	0·1188 (26)	1·1435 (56)
H(8)*B*	−0·0007 (40)	0·0905 (24)	1·1353 (55)
H(9*A*)*B*	0·1496 (41)	−0·0404 (25)	1·0091 (56)
H(9*B*)*B*	0·0862 (39)	−0·0188 (25)	1·1224 (56)
H(9*C*)*B*	0·1829 (39)	0·0228 (25)	1·0892 (54)
H(10*A*)*B*	−0·0034 (41)	−0·0169 (24)	0·9098 (53)
H(10*B*)*B*	−0·0678 (39)	0·0092 (26)	1·0023 (55)
H(11*A*)*B*	−0·0251 (39)	0·0619 (24)	0·7921 (55)
H(11*B*)*B*	−0·1344 (40)	0·0468 (25)	0·8262 (52)
H(15)*B*	−0·0995 (38)	0·3023 (25)	0·9732 (56)
H(16)*B*	−0·1695 (39)	0·2758 (25)	0·7903 (58)
H(17)*B*	−0·1659 (40)	0·1611 (25)	0·7623 (53)
H(N1)*B*	0·1074 (40)	0·0640 (25)	0·9354 (54)
H(O2)*B*	−0·1566 (40)	0·3654 (25)	1·1937 (55)

joined to two non-aromatic rings, one of which contains a nitrogen atom. The catechol ring, made up from the atoms C(1) through C(6), is quite planar in both molecules (see Table 4). However, some of the other atoms that would be expected to lie in this same plane deviate from it somewhat: notably C(14) of both molecules. As can also be seen in Table 4 there is a marked difference between the planarity of the benzene rings, C(12) through C(17), of the two molecules, the deviations in *A* being much smaller. The angle between the two aromatic rings of the apomorphine molecule is 24·3° (26·7°).

For the sake of brevity the values for intramolecular distances and angles are given in Fig. 2 only. The full table of these figures can be obtained from the author.

None of the distances between the non-hydrogen atoms found in apomorphine differs by more than 0·03 Å from the values for dopamine given by Bergin & Carlström (1968). The bond lengths also compare very well with the values for other catechol derivatives (Bergin, 1971*b*). The mean aromatic C–C bond length in apomorphine is 1·397 Å (1·388 Å), while the corresponding value for single C–C bonds is 1·506 Å (1·507 Å). The mean standard deviation for the C–C bonds is 0·011 Å (0·012 Å). The fact that the single bonds are slightly shorter than a standard C–C single bond could be explained by the resonance from nearby double bonds. For example, the C(5)–C(14) distance is only 1·47 Å in both molecules and this bond thus has a rather pronounced double bond character, a fact that is further stressed by the reduction of the angles C(4)–C(5)–C(6) and C(13)–C(14)–C(15). The mean value for C–O distances is 1·370 Å (1·387Å) with mean standard deviation 0·009 Å (0·011 Å). The corresponding values for C–N bonds are 1·491 Å (1·497 Å) and 0·010 Å (0·011 Å) respectively. These values do not differ from those expected.

Excluding the hydrogen atoms the maximum deviation from theoretical values is 3° (3°) for the tetrahedral and 4° (4°) for the trigonal angles. The standard deviations for both types of angle lie around 0·8° (0·9°). It is interesting to note that atom O(1) is dis-



(*a*)

(*b*)

Fig. 2(*a*) Bond distances (Å) for non-hydrogen atoms in the apomorphine molecule. The upper value refers to the *A*-molecule. (*b*) angles (°) between non-hydrogen atoms in the apomorphine molecule. The upper value refers to the *A*-molecule.

Table 4. *Least-squares planes and deviations in* Å *of individual atoms*

Equations of planes are written as $aX+bY+cZ=d$, where X, Y, Z are coordinates in orthogonal Ångström space. Asterisks indicate atoms included in the calculation of the planes.

Catechol ring	*a*	*b*	*c*	*d*
Molecule *A*	0·4965	0·5964	0·6307	11·5963
Molecule *B*	0·6574	−0·6314	−0·4156	6·1797
Benzene ring				
Molecule *A*	0·6644	0·2200	0·7143	9·9658
Molecule *B*	0·8284	−0·2154	−0·5170	10·5860

Catechol ring	Molecule *A*	Molecule *B*
C(1)*	0·0085	0·0030
C(2)*	−0·0151	0·0004
C(3)*	0·0061	0·0027
C(4)*	0·0089	−0·0088
C(5)*	−0·0147	0·0118
C(6)*	0·0062	−0·0091
C(7)	−0·0027	0·0503
C(14)	−0·1461	0·1298
O(1)	0·0004	0·0046
O(2)	0·0675	0·0113
Benzene ring		
C(12)*	0·0007	−0·0243
C(13)*	0·0057	0·0331
C(14)*	−0·0035	−0·0135
C(15)*	−0·0052	−0·0145
C(16)*	0·0118	0·0235
C(17)*	−0·0095	−0·0043
C(8)	0·0264	0·1114
C(11)	−0·0263	0·0050

placed 3° (2°) making the C(2)–C(3)–O(1) angle larger than 120°, for this is also the case in all the catecholamines mentioned by Bergin (1971*b*), as well as in the adrenaline molecule recently studied by Carlström (1973).

The bonds involving hydrogen atoms range from 0·88 Å (0·81 Å) to 1·21 Å (1·11 Å) with an average of 0·98 Å (0·96 Å) (mean standard deviation 0·06 Å in both molecules) and the angles differ in no case by more than 10° (10°) from the expected value.

Although molecules *A* and *B* are very similar they do not have exactly the same conformation. This is perhaps most easy to see when comparing the torsion angles τ_1 and τ_2 in the two molecules. The angle τ_1, C(1)–C(6)–C(7)–C(8), is that between the catechol ring plane and the plane through the ethylamine side chain C(7)–C(8)–N, which is about −90° for most catechol derivatives, while τ_2, C(6)–C(7)–C(8)–N, describes the conformation of the side chain. A maximally extended chain corresponds to a τ_2 value of ± 180°. The difference in τ_1 between the two apomorphine molecules is quite large: 146° and 133° for *A* and *B* respectively. The other torsion angle, τ_2, is −178° in both molecules which is in good agreement with all phenethylamines studied so far. The height of the nitrogen atom over the catechol ring is 0·89 Å (1·23 Å), compared to 1·61 Å for dopamine, but the distance from this atom to the centre of the ring is almost the same as for dopamine: 5·12 Å (5·09 Å) and 5·14 Å respectively.

To make a detailed comparison between the conformations of apomorphine hydrobromide and apomorphine hydrochloride would not be profitable since the former structure determination was less precise. There are however no large discrepancies between the two structures, as may be exemplified by the torsion angles: the bromide has a τ_1 angle of 147° (137°) and a τ_2 angle of −179° (179°).

Hydrogen bonds and molecular packing

The packing of the molecules and the hydrogen bonds involving chloride ions are depicted in the stereogram in Fig. 4. Numerical values for hydrogen bonds and short distances are given in Tables 5 and 6 respectively. The crystal water molecules are not included in the drawing, but values of interest involving these molecules are given in the tables.

Each asymmetric unit contains one *A*- and one *B*-molecule stacked almost parallel to each other. There are however no hydrogen bonds between these two, the shortest intermolecular distance between them being 3·29 Å from C(9)*A* to O(2)*B*. Instead each chloride ion forms a bridge from the head of one molecule to the tail of the opposite member of an adjacent pair. These are quite short hydrogen bonds, the distance from N(1)*B* to Cl(1)*B* being 3·09 Å and from Cl(1)*B* to O(1)*A* 3·08 Å. Similarly, the distance from N(1)*A* to Cl(1)*A* is 3·05 Å and from Cl(1)*A* to O(1)*B* 3·06 Å. Unfortunately the hydrogen atom belonging to O(1)*B* was the one that could not be found in the structure determination. However, the short O(1)···Cl(1)*A* distance and the favourable C(3)*B*–O(1)*B*···Cl(1)*A* angle of 114° both strongly

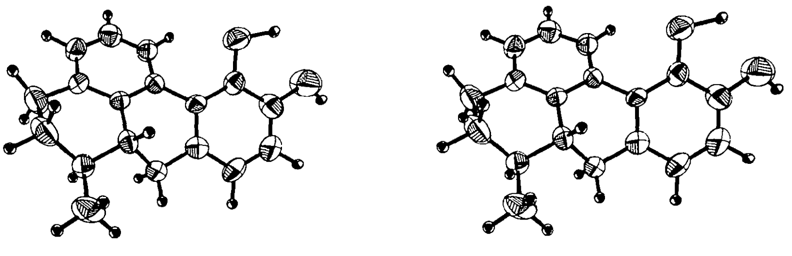


Fig. 3. Stereoscopic pair showing the *A*-molecule. Thermal ellipsoids for non-hydrogen atoms scaled to 50% probability.

indicate that there is a O(1)*B*–H(O1)*B*···Cl(1)*A* bond. Cl(1)*B* also forms a bridge between the head of one *B*-molecule and the tail of another, with a O(2)*B*···Cl(1)*B* distance of 3·18 Å. The only hydrogen atom belonging to an oxygen or nitrogen atom in the apomorphine molecules that does not form an intermolecular hydrogen bond is H(O2)*A*. This could be the ideal case for the intramolecular hydrogen bond O(2)*A*–H(O2)*A*···O(1)*A* postulated for catechol by Pauling (1960), especially as H(O1)*A* is attracted by Cl(1)*B*. However, the value of 115° for the O(2)*A*–H(O2)*A*···O(1)*A* angle makes such an assumption unlikely.

The oxygen atoms of the crystal water molecules do not seem to act as acceptors for any hydrogen bonds from the apomorphine molecules, but the water hydrogen atoms may form a few bonds, *e.g.* O(*W*3) to Cl(1)*A*, 3·12 Å and O(*W*2) to O(1)*B*, 2·95 Å.

The author wishes to thank Mrs I. Hacksell for preparing the drawings. Thanks are also due to Professor D. Carlström for valuable help and discussions.

Table 5. *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*···*Y*′	H···*Y*′	*X*–H···*Y*′
N(1)*A*	H(N1)*A*	Cl(1)*A*	x	y	z	3·05 Å	2·13 Å	169°
O(1)*A*	H(O1)*A*	Cl(1)*B*	$x-\frac{1}{2}$	$\frac{1}{2}-y$	$1-z$	3·08	2·20	176
N(1)*B*	H(N1)*B*	Cl(1)*B*	x	y	z	3·09	2·25	165
O(2)*B*	H(O2)*B*	Cl(1)*B*	$\frac{1}{2}+x$	$\frac{1}{2}-y$	$-z$	3·18	2·16	167

Table 6. *Some short intermolecular distances*

All heavy-atom distances less than 3·40 Å.

Second atom at (x,y,z)				
	Cl(1)*A*···O(*W*3)	3·12 Å	O(*W*1)···O(*W*3)	1·24 Å*
Second atom at $(x,y,z-1)$				
	O(1)*B*···Cl(1)*A*	3·06 Å	O(1)*B*···O(*W*2)	2·95 Å
Second atom at $(x-1,y,z)$				
	O(1)*A*···O(*W*2)	3·13 Å	O(1)*A*···O(*W*3)	3·35 Å
Second atom at $(\frac{1}{2}+x,\frac{1}{2}-y,-z)$				
	O(*W*1)···C(7)*B*	3·36 Å	O(*W*2)···C(1)*B*	3·33 Å
Second atom at $(x-\frac{1}{2},\frac{1}{2}-y,-z)$				
	C(9)*A*···O(2)*B*	3·29 Å		
Second atom at $(2-x,y-\frac{1}{2},\frac{1}{2}-z)$				
	Cl(1)*B*···O(*W*1)	3·30 Å	Cl(1)*B*···O(*W*3)	3·22 Å
	C(9)*B*···O(1)*B*	3·33		

* As O(*W*1) and O(*W*3) cannot occupy the same unit cell simultaneously this is no real distance.

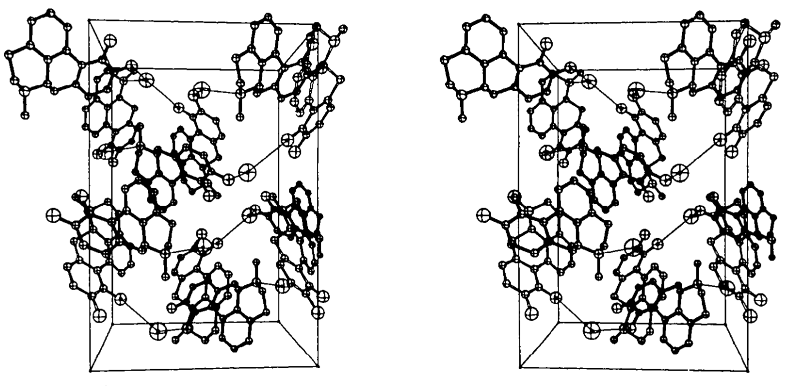


Fig. 4. Stereoscopic drawing of one unit cell in the apomorphine hydrochloride crystal. The cell is viewed in the negative *z* direction, with the *x* axis to the right and *y* axis upwards. Origin in lower left, far corner. Bonds in the *A*-molecules are drawn in heavy black lines. Hydrogen bonds are shown as thin lines. The plotting program *ORTEP* (Johnson, 1965) was used for both this figure and Fig. 3.

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Crystal Structures of Six New Polytypes of Cadmium Iodide

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Crystal structures of six newly discovered polytypes, $16H_4$, $18H_4$, $28H_2$, $28H_3$, $36H_1$ and $40H_1$, have been determined. The structures are represented by $(22)_31111$, (222122121111), $(22)_411222211$, $(22)_5112211$, $(22221111)_211112222$ and $(22)_721122211$ in Zhdanov symbols. They all belong to the space group $P3m1$. The two cell dimensions, $a=b=4{\cdot}24$ Å, are identical for all the polytypes while the c dimensions are 54·68, 61·52, 95·69, 123·03 and 136·70 Å for the polytypes, $16H_4$, $18H_4$, $28H_2$ or $28H_3$, $36H_1$ and $40H_1$, respectively. All six polytypes were found to have grown in syntactic coalescence with other polytypes, showing a transformation of structure during growth. To date, polytype $40H_1$ is the largest hexagonal cadmium iodide polytype for which the structure has been determined. The mode of growth of these polytypes is discussed.

During the course of study of polytype growth in cadmium iodide crystals by successively cleaving the crystals parallel to their basal plane (Gyaneshwar & Trigunayat, 1972), six new polytypes have been discovered, for which it has been possible to determine the complete crystal structures. The crystals show structural transformation during growth and provide information regarding the process of polytype formation and the role played by the stacking faults therein.

Experimental methods

The crystals were grown from solution. A suitable range of oscillation, *viz.* the one in which the angle between the incident beam and the c axis varied between 25 and 40°, was chosen to record a large succession of 10.*l* reflexions on the X-ray film (Chadha & Trigunayat, 1967). These reflexions were employed to compare the calculated intensities with those observed, for structure analysis.

Structure of polytypes

(i) *Polytype* $16H_4$*

This polytype [Fig. 1(*a*)] was discovered in a well developed thin crystal. It occurred in syntactic coalescense with the common type $4H$. Three other 16-layered polytypes have already been reported (Lal, Chadha & Trigunayat, 1971). Although a stupendously vast number of possiblities exist for such a large unit cell, nevertheless the task of postulating the correct crystal structure was facilitated by the observation that the intensity sequence of 10.*l* spots closely simulated those of known polytypes of the series $(22)_n1111$. Four members of this series, *viz.* $(22)1111$, $(22)_21111$, $(22)_41111$ and $(22)_61111$, have been reported earlier. Thus the possible structure of the present polytype could be $(22)_31111$. The intensity calculations were made for the

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* The polytype representation in this paper follows the scheme of notation suggested by Trigunayat & Chadha (1971)