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The Structure of the Catecholamines.
IV. The Crystal Structure of (—)-Adrenaline Hydrogen (+)-Tartrate

BY DIEGO CARLSTRÖM

Department of Medical Physics, Karolinska Institutet, S-104 01 Stockholm 60, Sweden

The hormone adrenaline (epinephrine) crystallizes as the bitartrate in the orthorhombic space group $P2_12_12_1$, with unit-cell constants $a = 7\cdot402$, $b = 28\cdot202$, $c = 6\cdot995$ Å. Three-dimensional data were collected on an automatic linear diffractometer. The structure was determined by direct methods and all hydrogen atoms were located in a difference electron synthesis. Refinement by full-matrix least-squares methods resulted in a final R-value of $3\cdot1$ % for 1618 observed reflexions. The hydrogen tartrate ions, bound head to tail by a strong O–H$\cdots$O hydrogen bond ($2\cdot49$ Å), form infinite chains along the a axis. The almost planar adrenaline cations having maximally extended ethylamine side chains are tilted about $11°$ relative to the (100) plane and are firmly bound to the tartrate ions by a network of N–H$\cdots$O and O–H$\cdots$O hydrogen bonds. The configuration of (—)-adrenaline is R.

Introduction

Adrenaline (epinephrine) was the very first hormone to be discovered and it was obtained in pure form in 1901. The levorotatory natural isomer is about 100 times more active than the (+)-isomer. Adrenaline is a sympathomimetic catecholamine with a direct mode of action on both α- and β-receptors. Its main function in the body is to increase the activity of the heart, the blood pressure by vasoconstriction and the rate of glycogenolysis in liver and muscle.

The present study forms part of a research project on catecholamines and other bioactive phenethylamines. Owing to the biological importance of (—)-adrenaline it was considered of interest to be able to compare the characteristics of the adrenaline molecule with those of related compounds. The easily crystallized (—)-adrenaline hydrogen (+)-tartrate was selected for the structure determination as attempts to grow suitable crystals of adrenaline or adrenaline hydrochloride were unsuccessful. Since the absolute configuration of (+)-tartaric acid is known, this choice also made it possible to find the correct enantiomorph of natural adrenaline.

Experimental

Reagent-pure (—)-adrenaline hydrogen (+)-tartrate was recrystallized in water by slow evaporation at room temperature. The orthorhombic crystals were six-sided prisms bounded by {011} (predominant) and {010} and terminated by {100}. They were biaxial negative and highly birefringent. Optical data are: $\alpha_D = 1\cdot537$, $\beta_D = 1\cdot599$, $\gamma_D = 1\cdot655$, $V = 41\cdot9°$ (calculated) $\alpha = a$, $\beta = c$, $\gamma = b$. Preliminary unit-cell dimensions and systematic absences were determined from Weissenberg photographs while accurate cell parameters were derived from diffractometer measurements. The density was measured by flotation in a chloroform–bromoform mixture.

Crystal data

(—)-Adrenaline [2-methylamino-1-(3,4-dihydroxyphenyl)ethanol] hydrogen (+)-tartrate

$C_9H_{13}O_3N \cdot C_4H_6O_6$ F.W. 333·29

$a = 7\cdot402$ (3) Å $V = 1460\cdot2$ Å^3

$b = 28\cdot202$ (15) $D_m = 1\cdot507 \pm 0\cdot004$ g cm^{-3}

$c = 6\cdot995$ (5) D_x ($Z = 4$) $= 1\cdot515$

μ(Mo $K\alpha$) $= 1\cdot39$ cm^{-1} $F(000) = 704$

Systematic extinctions: $h00$ absent with h odd, $0k0$ absent with k odd, $00l$ absent with l odd indicating the space group $P2_12_12_1$.

An optically perfect crystal was trimmed to a sphere of 0·35 mm in diameter and was mounted about **a**. Integrated intensities were recorded using a linear diffractometer (PAILRED) with graphite crystal monochromated Mo $K\alpha$ radiation (0·7107 Å) for the layers $0kl$ through $8kl$ within $\sin\theta/\lambda \leq 0·65$. The ω scan technique was employed. Standard reflexions showed no systematic fluctuation. Altogether 3803 reflexions were recorded within a quarter-sphere resulting in 1937 symmetry-independent intensities. Of these, 318 did not differ significantly from the background. The net intensities were not corrected for absorption owing to the low μ-value ($\mu R = 0·024$). The observed structure amplitudes were brought on to an absolute scale by Wilson statistics and normalized structure factors, $|E(hkl)|$, were calculated.

Determination and refinement of the structure

From optical data and the unit-cell dimensions it seemed plausible that the adrenaline molecules should extend along the b axis and be more or less parallel to the (100) plane. However, all attempts to solve the structure by Patterson methods using this information failed. The structure was finally determined by direct methods with the multiple solution technique using the automatic phasing program *MULTAN* of Germain, Main & Woolfson (1971). The solution of the structure presented no difficulties; of the 16 sets of phases for the 195 strongest $|E|$ values ($\geq 1·51$) two sets were identical and superior to the others. An E map was calculated and the 23 highest peaks corresponded to all non-hydrogen atoms. A comparison between the phase angles calculated by *MULTAN* and the final refined phase values showed that 70% of the calculated phase angles were within $\pm 10°$ and 92% within $\pm 20°$ of the true values. The refinement was carried out by a full-matrix least-squares procedure. After two cycles of isotropic refinement of all non-hydrogen atoms and one cycle of anisotropic refinement of these atoms the residual $R = \sum||F_o| - |F_c||/\sum|F_o|$ was 6·7%. In a difference synthesis prepared at this stage all 19 hydrogen atoms were easily located. Two further refinement cycles with the hydrogen atoms introduced reduced the R value to 3·8%.

Five reflexions with $|F_o| > 85$ were excluded from further refinements because of secondary extinction. The positional and isotropic thermal parameters for the hydrogen atoms were then refined and a final cycle of refinement of the non-hydrogen atoms yielded an R value of 3·1% for the 1614 observed reflexions.

Unit weight was applied throughout and the scattering factors were those of *International Tables for X-ray Crystallography* (1962) except for that of the hydrogen atoms, which was taken from the data of Stewart, Davidson & Simpson (1965). The computations were performed on IBM 360/75 using our program system (Bergin, 1971a). The final non-hydrogen

Table 1. *Final positional and thermal parameters* ($\times 10^5$) *for non-hydrogen atoms*

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

Adrenaline ion

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	36038 (42)	22556 (9)	7094 (36)	1448 (58)	79 (3)	822 (46)	−1 (22)	271 (97)	−1 (20)
C(2)	36369 (44)	17832 (9)	12465 (36)	1521 (63)	75 (3)	938 (49)	21 (23)	204 (98)	−59 (21)
C(3)	33413 (43)	16583 (9)	31353 (36)	1216 (55)	75 (3)	1058 (49)	−39 (23)	−275 (96)	53 (20)
C(4)	30003 (41)	20102 (10)	44954 (36)	1317 (60)	100 (3)	887 (51)	−9 (24)	142 (93)	28 (22)
C(5)	29624 (45)	24761 (9)	39391 (37)	1698 (69)	85 (3)	966 (51)	89 (24)	179 (98)	−109 (22)
C(6)	32562 (41)	26077 (8)	20365 (35)	1205 (55)	68 (3)	1035 (50)	58 (21)	−70 (91)	−25 (19)
C(7)	31071 (42)	31294 (8)	15125 (35)	1384 (59)	68 (3)	1021 (50)	83 (21)	−125 (93)	−70 (20)
C(8)	34831 (43)	32193 (8)	−5867 (36)	1353 (53)	64 (3)	1103 (51)	52 (21)	−209 (99)	−11 (21)
C(9)	34784 (48)	38319 (10)	−31241 (38)	1833 (64)	91 (3)	999 (52)	81 (26)	53 (105)	50 (23)
N(1)	33398 (33)	37355 (7)	−10259 (29)	1244 (43)	68 (2)	964 (41)	7 (18)	−201 (79)	−48 (17)
O(1)	33512 (35)	11984 (6)	37680 (27)	2406 (53)	74 (2)	1190 (40)	−27 (20)	−373 (87)	105 (16)
O(2)	28054 (35)	18868 (7)	63936 (26)	2405 (60)	141 (3)	744 (36)	−28 (22)	171 (77)	84 (18)
O(3)	43394 (32)	33938 (6)	26724 (30)	2507 (55)	70 (2)	1537 (46)	84 (18)	−1491 (95)	−144 (18)

Hydrogen tartrate ion

C(10)	72374 (35)	3711 (8)	74119 (38)	823 (47)	83 (3)	1000 (48)	12 (19)	134 (89)	−67 (22)
C(11)	53112 (35)	5578 (8)	74436 (42)	843 (47)	63 (3)	1158 (52)	34 (19)	−135 (91)	−32 (22)
C(12)	44014 (35)	3991 (8)	93052 (38)	842 (47)	55 (3)	1143 (52)	11 (18)	−26 (86)	−20 (20)
C(13)	24121 (35)	5268 (8)	92301 (43)	802 (48)	67 (3)	1509 (59)	−49 (19)	122 (92)	−50 (22)
O(4)	74252 (28)	−632 (6)	75073 (36)	1200 (38)	62 (2)	2929 (60)	85 (15)	1468 (93)	−46 (20)
O(5)	85320 (26)	6667 (6)	73140 (30)	805 (33)	81 (2)	1996 (49)	−23 (14)	−91 (78)	−36 (18)
O(6)	52989 (27)	10614 (6)	73595 (31)	1354 (40)	64 (2)	1913 (47)	96 (15)	−359 (82)	210 (17)
O(7)	52195 (24)	6219 (6)	108995 (26)	1001 (35)	69 (2)	1115 (37)	96 (14)	−538 (62)	22 (15)
O(8)	16131 (29)	3330 (7)	77701 (34)	792 (37)	150 (3)	2584 (60)	118 (18)	−549 (90)	−689 (24)
O(9)	16839 (28)	7853 (7)	103829 (28)	994 (37)	106 (3)	1757 (46)	126 (17)	117 (74)	−288 (19)

parameters are given in Table 1 and the parameters for the hydrogen atoms are listed in Table 2. The observed and calculated structure factors are available by request from the authors.

Table 2. *Final fractional coordinates* ($\times 10^3$) *and isotropic temperature factors* (Å^2) *for hydrogen atoms*

	x	y	z	B
H(1)	390 (5)	233 (1)	−59 (4)	2·8
H(2)	395 (5)	156 (1)	18 (4)	3·4
H(O1)	341 (5)	101 (1)	286 (4)	5·4
H(O2)	177 (5)	173 (1)	662 (5)	6·3
H(5)	280 (5)	272 (1)	486 (5)	3·9
H(7)	189 (5)	325 (1)	173 (4)	3·5
H(O3)	400 (5)	365 (1)	282 (5)	5·2
H(8A)	465 (5)	312 (1)	−99 (5)	3·4
H(8B)	260 (5)	306 (1)	−140 (4)	3·3
H(NA)	216 (4)	387 (1)	−43 (5)	3·0
H(NB)	430 (5)	389 (1)	−40 (5)	4·9
H(9A)	452 (5)	371 (1)	−355 (5)	4·2
H(9B)	352 (5)	417 (1)	−329 (5)	5·2
H(9C)	240 (5)	369 (1)	−376 (5)	3·9
H(11)	455 (5)	43 (1)	618 (5)	2·8
H(O6)	460 (5)	114 (1)	651 (5)	4·5
H(12)	443 (5)	4 (1)	944 (5)	1·9
H(O7)	585 (5)	45 (1)	1148 (5)	3·0
H(O8)	30 (5)	47 (1)	758 (5)	6·4

Description and discussion of the structure

The adrenaline molecule

The adrenaline molecule is shown in Fig. 1 in which the numbering of the atoms is also indicated. This figure depicts the absolute configuration of the (−)-form relative to the known absolute configuration of (+)-tartaric acid (Peerdeman, van Bommel & Bijvoet, 1951). Since (−)-adrenaline is synthesized from (−)-noradrenaline in the body, it is natural that it has the *R* configuration of noradrenaline (Carlström & Bergin, 1967). Like other catecholamines the adrenaline molecule consists of two planar parts; the catechol nucleus and the maximally extended ethylamine side chain. The six-membered aromatic ring of the catechol nucleus is highly planar (see Table 3) but some of the exocyclic atoms are significantly out-of-plane. The ethylamine side chain is likewise planar within ± 0.004 Å and makes an angle of only 2·8° with the benzene ring of the catechol nucleus. The torsion angle τ_1, C(1)–C(6)–C(7)–C(8), is −3·2°; τ_2, C(5)–C(6)–C(7)–C(8), is 179·2° and τ_3, C(6)–C(7)–C(8)–N(1), is −179·4°, that is, none of the atoms C(1) to C(8), N(1), O(1) and O(2) deviates more than 0·036 Å from a common plane defined by these atoms. This is a situation quite different from comparable structures which have the plane of the ethylamine side chain more or less perpendicular to the plane of the catechol nucleus corresponding to a τ_1 angle close to −90°. The difference between the conformation of the adrenaline molecule and the preferred one found in other bioactive phenethylamines is thus restricted to the τ_1 angle. It may be assumed that the conformation here found does not represent an absolute energy minimum. There

are certainly barriers against free rotation about the C(6)–C(7) bond but the magnitudes and angular positions of these barriers are not known. However, it is probable that the torsion angle τ_1 here found is at a local minimum as the hydrogen atom H(1) is equidistant, at 2·32 and 2·34 Å, from H(8A) and H(8B). The dense packing of the structure and the hydrogen bonding system in the solid state (see below) may cause the adrenaline molecule to assume another conformation than that usually encountered among related compounds.

Table 3. *Least-squares planes and deviations in* Å *of individual atoms*

Each plane is represented by $AX + BY + CZ = D$ where X, Y, Z are coordinates in orthogonal Ångström space referred to crystallographic axes. Asterisks indicate atoms not included in the calculation of the plane.

Plane of benzene ring. Equation:
$$0.9801X + 0.0747Y + 0.1838Z = 3.1770 .$$

C(1)	0·0043	C(7)*	−0·0689
C(2)	−0·0024	O(1)*	−0·0087
C(3)	−0·0004	O(2)*	0·0779
C(4)	0·0013	H(1)*	0·064
C(5)	0·0005	H(2)*	0·037
C(6)	−0·0033	H(5)*	0·053

Plane of side chain. Equation:
$$0.9716X + 0.1189Y + 0.2045Z = 3.5038 .$$

C(6)	0·0036	N(1)	0·0036
C(7)	−0·0037	C(9)*	−0·1645
C(8)	−0·0035		

Plane I of tartrate ion. Equation:
$$0.0336X + 0.0491Y + 0.9982Z = 5.4120 .$$

C(10)	−0·0053	O(5)	−0·0006
C(11)	−0·0053	O(6)	0·0054
O(4)	0·0058		

Plane II of tartrate ion. Equation:
$$-0.2185X - 0.7965Y + 0.5637Z = 2.0592 .$$

C(12)	0·0015	O(8)	−0·0042
C(13)	0·0068	O(9)	−0·0015
O(7)	−0·0027		

The intramolecular bond distances and valency angles, uncorrected for thermal vibration, of the adrenaline molecule are given in Tables 4 and 5. The C–C bonds and the C–O bonds of the catechol nucleus with average lengths of 1·387 and 1·375 Å respectively are in good agreement with values observed for other catecholamines (Carlström & Bergin, 1967; Bergin & Carlström, 1968; Bergin, 1971b). In all catechol derivatives hitherto investigated the oxygen atom O(1) is displaced from the C(6)–C(3) axis so that the C(2)–C(3)–O(1) angle is larger than 120°. This is also the case in the adrenaline molecule. The other exocyclic oxygen atom O(2) is nearly symmetric with respect to the ring. The C–C distances of the side chain are normal and so are the C–N distances when considering the charged state of the nitrogen atom. The valency angles around the carbon atoms and the nitrogen atom of the side chain are all close to the expected tetrahedral value. The anisotropic thermal parameters of

the non-hydrogen atoms are given in Table 1 and visualized in Fig. 1. The oxygen atoms and the methyl carbon atom, C(9), exhibit the largest thermal movements. This is also reflected by the isotropic thermal parameters of the hydrogen atoms (Table 2). Thus, the hydrogen atoms attached to the carbon atoms of the benzene ring and to C(7) and C(8) have B values ranging between 2·8 and 3·9 Å² whereas those of the hydroxyl groups range between 5·2 and 6·3 Å². The hydrogen atoms of the methyl group have intermediate B values.

The hydrogen tartrate ion

The configuration of the hydrogen (+)-tartrate ion is shown in Fig. 2. As in the crystal structures of tartaric acid and most tartrates the molecule consists of two essentially planar halves. The angle between the planes I and II comprised of the atoms C(11), O(6), C(10), O(4), O(5) and C(12), O(7), C(13), O(8), O(9) respectively is 58·9°. The corresponding angle in ammonium hydrogen (+)-tartrate, calculated from the coordinates of van Bommel & Bijvoet (1958), is 62·6° and values around 60° are also reported for tartaric acid and most tartrates. From the intramolecular bond lengths and bond angles (Tables 4 and 5) it is evident that the two carboxyl groups are different. The non-ionized end of the molecule is, as could be expected,

Table 4. *Intramolecular bond distances in* Å *with estimated standard deviations in parentheses*

Adrenaline ion

C(1)–C(2)	1·387 (3)	C(1)–H(1)	0·96 (3)
C(2)–C(3)	1·385 (4)	C(2)–H(2)	1·01 (3)
C(3)–O(1)	1·370 (3)	O(1)–H(O1)	0·83 (3)
C(3)–C(4)	1·398 (4)	O(2)–H(O2)	0·90 (4)
C(4)–O(2)	1·380 (3)	C(5)–H(5)	0·95 (3)
C(4)–C(5)	1·371 (4)	C(7)–H(7)	0·97 (4)
C(5)–C(6)	1·399 (4)	O(3)–H(O3)	0·78 (3)
C(6)–C(1)	1·381 (3)	C(8)–H(8A)	0·95 (3)
C(6)–C(7)	1·520 (3)	C(8)–H(8B)	0·98 (3)
C(7)–O(3)	1·431 (3)	N(1)–H(NA)	1·04 (3)
C(7)–C(8)	1·516 (4)	N(1)–H(NB)	0·95 (4)
C(8)–N(1)	1·491 (3)	C(9)–H(9A)	0·90 (4)
N(1)–C(9)	1·496 (3)	C(9)–H(9B)	0·97 (3)
		C(9)–H(9C)	0·99 (3)

Hydrogen tartrate ion

C(10)–O(4)	1·234 (3)	C(13)–O(8)	1·301 (4)
C(10)–O(5)	1·272 (3)	C(13)–O(9)	1·213 (3)
C(10)–C(11)	1·520 (4)	C(11)–H(11)	1·11 (4)
C(11)–O(6)	1·421 (3)	O(6)–H(O6)	0·82 (3)
C(11)–C(12)	1·533 (4)	C(12)–H(12)	1·01 (3)
C(12)–O(7)	1·416 (3)	O(7)–H(O7)	0·79 (3)
C(12)–C(13)	1·517 (4)	O(8)–H(O8)	1·05 (3)

quite unsymmetrical and the distances and angles are in excellent agreement with the values reported for tartaric acid (Okaya, Stemple & Kay, 1966), hydrate racemic acid (Parry, 1951) and ammonium hydrogen
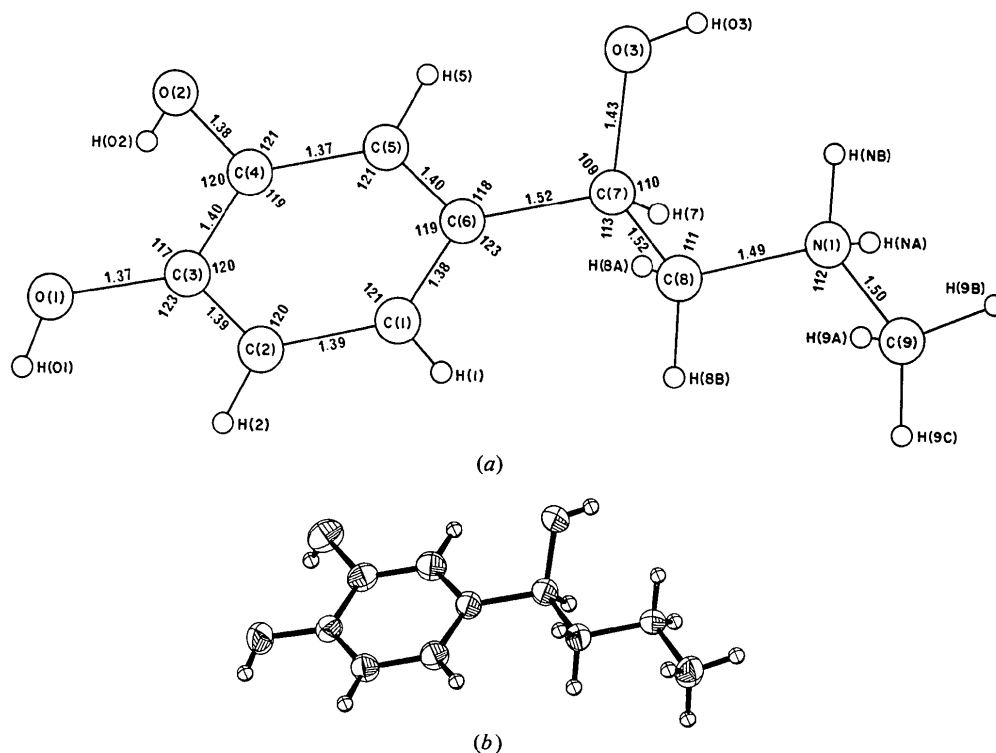

Fig. 1. (a) The numbering of the atoms and major bond distances and bond angles in the (−)-adrenaline molecule. (b) The thermal ellipsoids for the non-hydrogen atoms, scaled to 50% probability (bottom) were drawn using the plotting program ORTEP (Johnson, 1965).

tartrate (van Bommel & Bijvoet, 1958). It is perhaps surprising to find that the ionized end of the tartrate molecule is not as symmetrical as in ammonium hydrogen tartrate (van Bommel & Bijvoet, 1958) and sodium tartrate dihydrate (Ambady & Kartha, 1968). Thus, the C(10)–O(4) bond has an appreciably stronger double bond character than the C(10)–O(5) bond and the angles C(11)–C(10)–O(4) and C(11)–C(10)–O(5) differ by 2·1°. This distortion of the ionized carboxyl group certainly depends on the hydrogen-bonding system in the solid state. The oxygen atom O(5) is the acceptor for a very strong hydrogen bond, 2·49 Å, (see below) and the situation is equivalent to that in lithium hydrogen oxalate monohydrate (Thomas, 1972)

where an equally short bond influences the bond distances and angles of a carboxyl group. The rest of the hydrogen tartrate molecule is fully symmetrical with average C–C and C–O distances of 1·523 Å and 1·419 Å respectively.

Hydrogen bonds and molecular packing

The arrangement of the molecules in the crystal and the hydrogen bonding scheme are shown in Fig. 3. Intermolecular distances and angles of interest are given in Tables 6 and 7. The hydrogen tartrate molecules extend along **a** and are bound head to tail by a strong hydrogen bond, 2·49 Å, thereby forming infinite chains along **a**. The screw-axis-related tartrate

Table 5. Intramolecular bond angles in degrees with estimated standard deviations in parentheses

Adrenaline ion

C(6)–C(1)–C(2)	120·7 (3)	C(4)——O(2)–H(O2)	112 (2)
C(1)–C(2)–C(3)	120·0 (3)	C(4)——C(5)–H(5)	120 (2)
C(2)–C(3)–C(4)	119·8 (3)	C(6)——C(5)–H(5)	118 (2)
C(2)–C(3)–O(1)	123·2 (3)	C(6)——C(7)–H(7)	111 (2)
C(4)–C(3)–O(1)	116·9 (3)	C(8)——C(7)–H(7)	105 (2)
C(3)–C(4)–C(5)	119·4 (3)	O(3)——C(7)–H(7)	109 (2)
C(3)–C(4)–O(2)	119·7 (3)	C(7)——O(3)–H(O3)	111 (3)
C(5)–C(4)–O(2)	120·8 (3)	C(7)——C(8)–H(8A)	114 (2)
C(4)–C(5)–C(6)	121·4 (3)	N(1)——C(8)–H(8A)	107 (2)
C(5)–C(6)–C(1)	118·6 (3)	C(7)——C(8)–H(8B)	111 (2)
C(5)–C(6)–C(7)	118·4 (3)	N(1)——C(8)–H(8B)	107 (2)
C(1)–C(6)–C(7)	123·0 (3)	H(8A)–C(8)–H(8B)	107 (3)
C(6)–C(7)–C(8)	112·5 (3)	C(8)——N(1)–H(NA)	110 (2)
C(6)–C(7)–O(3)	108·8 (2)	C(9)——N(1)–H(NA)	113 (2)
C(8)–C(7)–O(3)	110·2 (2)	C(8)——N(1)–H(NB)	108 (2)
C(7)–C(8)–N(1)	110·5 (2)	C(9)——N(1)–H(NB)	108 (2)
C(8)–N(1)–C(9)	112·0 (2)	H(NA)–N(1)–H(NB)	106 (3)
C(6)–C(1)–H(1)	122 (2)	N(1)——C(9)–H(9A)	108 (2)
C(2)–C(1)–H(1)	117 (2)	N(1)——C(9)–H(9B)	108 (2)
C(1)–C(2)–H(2)	114 (2)	N(1)——C(9)–H(9C)	108 (2)
C(3)–C(2)–H(2)	126 (2)	H(9A)–C(9)–H(9B)	109 (3)
C(3)–O(1)–H(O1)	111 (3)	H(9A)–C(9)–H(9C)	112 (3)
		H(9B)–C(9)–H(9C)	111 (3)

Hydrogen tartrate ion

O(4)——C(10)–O(5)	124·6 (3)	O(9)——C(13)–C(12)	123·4 (3)
O(4)——C(10)–C(11)	116·6 (2)	O(8)——C(13)–O(9)	124·9 (3)
O(5)——C(10)–C(11)	118·7 (2)	C(10)–C(11)–H(11)	111 (2)
C(10)–C(11)–C(12)	108·9 (2)	C(12)–C(11)–H(11)	111 (2)
C(10)–C(11)–O(6)	110·6 (2)	O(6)——C(11)–H(11)	107 (2)
C(12)–C(11)–O(6)	108·9 (2)	C(11)–O(6)——H(O6)	107 (3)
C(11)–C(12)–C(13)	109·1 (2)	C(11)–C(12)–H(12)	111 (2)
C(11)–C(12)–O(7)	110·6 (2)	C(13)–C(12)–H(12)	105 (2)
C(13)–C(12)–O(7)	109·7 (2)	O(7)——C(12)–H(12)	111 (2)
O(8)——C(13)–C(12)	111·6 (2)	C(12)–O(7)——H(O7)	112 (3)
		C(13)–O(8)——H(O8)	111 (2)

Table 6. 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'
O(1)	H(O1)	O(7)	x	y	$z-1$	2·93 Å	2·21 Å	146°
O(1)	H(O1)	O(9)	x	y	$z-1$	2·91	2·24	138
O(2)	H(O2)	O(3)	$x-\frac{1}{2}$	$\frac{1}{2}-y$	$1-z$	2·76	1·90	160
O(3)	H(O3)	O(5)	$x-\frac{1}{2}$	$\frac{1}{2}-y$	$1-z$	2·72	1·96	166
N(1)	H(NA)	O(7)	$x-\frac{1}{2}$	$\frac{1}{2}-y$	$1-z$	2·94	2·05	141
N(1)	H(NB)	O(9)	$\frac{1}{2}+x$	$\frac{1}{2}-y$	$1-z$	2·86	1·98	153
O(6)	H(O6)	O(1)	x	y	z	2·92	2·13	162
O(7)	H(O7)	O(4)	$\frac{3}{2}-x$	$-y$	$\frac{1}{2}+z$	2·61	1·82	171
O(8)	H(O8)	O(5)	$x-1$	y	z	2·49	1·43	178

chains, running in opposite directions, are sideways connected by O–H⋯O hydrogen bonds, 2·61 Å long. Between the rows of negatively charged tartrate chains the adrenaline ions are suspended by a network of hydrogen bonds. The oxygen atom O(1) is equally far from O(7) and O(9) of an adjacent tartrate ion. Its hydrogen atom H(O1) is likewise at the same distance (2·21 and 2·24 Å) from the two acceptor atoms and the O–H⋯O angles involved are very much the same, 146 and 138° respectively. It thus seems likely that this is a genuine bifurcated hydrogen bond. The hydrogen atom H(O3) of the hydroxyl group of the side chain is involved in a hydrogen bond to a tartrate ion and so are the two hydrogens of the nitrogen atom. The adrenaline molecules which are tilted 10·8° to the (100) plane form rows connected by O(2)–H(O2)⋯O(3) hydrogen bonds.

The strong hydrogen bond O(8)–H(8)⋯O(5) between the tartrate ions, with the hydrogen atom only 0·2 Å from being midway between the two oxygen atoms, does not only influence the bond lengths of the accepting carboxyl group but it does also create some short intermolecular contacts. The atoms C(13) and O(9) of one tartrate ion will both be 3·19 Å from the O(5) atom of another tartrate molecule and H(8) will be 2·29 and 2·60 Å from C(10) and O(4) respectively. The hydrogen bonds connecting the charged end of

Table 7. *Some short intermolecular distances*

All heavy-atom distances less than 3·20 Å and all C⋯H and O⋯H distances less than 2·70 Å.

O(2)⋯O(6)	3·05	O(2)⋯H(O6)	2·50
O(2)⋯H(1^i)	2·57	O(6)⋯H(2^i)	2·62
C(10)⋯H(O8^{ii})	2·29	O(5)⋯C(13^{ii})	3·19
O(4)⋯H(O8^{ii})	2·60	O(5)⋯O(9^{ii})	3·19
O(8)⋯H(12^{iii})	2·67	O(4)⋯H(9B^v)	2·33
O(5)⋯H(NB^{iv})	2·56	O(6)⋯H(7^{iv})	2·36
O(5)⋯N(1^{iv})	3·10	O(6)⋯H(N4^{iv})	2·56
O(6)⋯C(7^{iv})	3·19		

Symmetry code

Superscript	Transformation		
None	x	y	z
i	x	y	$1+z$
ii	$1+x$	y	z
iii	$\frac{1}{2}-x$	$-y$	$z-\frac{1}{2}$
iv	$\frac{1}{2}+x$	$\frac{1}{2}-y$	$1-z$
v	$1-x$	$y-\frac{1}{2}$	$\frac{1}{2}-z$

the adrenaline molecule to the tartrate ions also create short intermolecular contacts. The distance between N(1) and O(5) is 3·10 Å and the hydrogen atoms on N(1) will be 2·56 Å from oxygen atoms of tartrate molecules. These contacts, however, do not represent hydrogen bonds because of the unfavourable N–H⋯O angles. Another short distance, 3·05 Å, indicative of a hydrogen bond between O(2) and O(6) is also unlikely to represent such a bond, as H(O6) is already involved
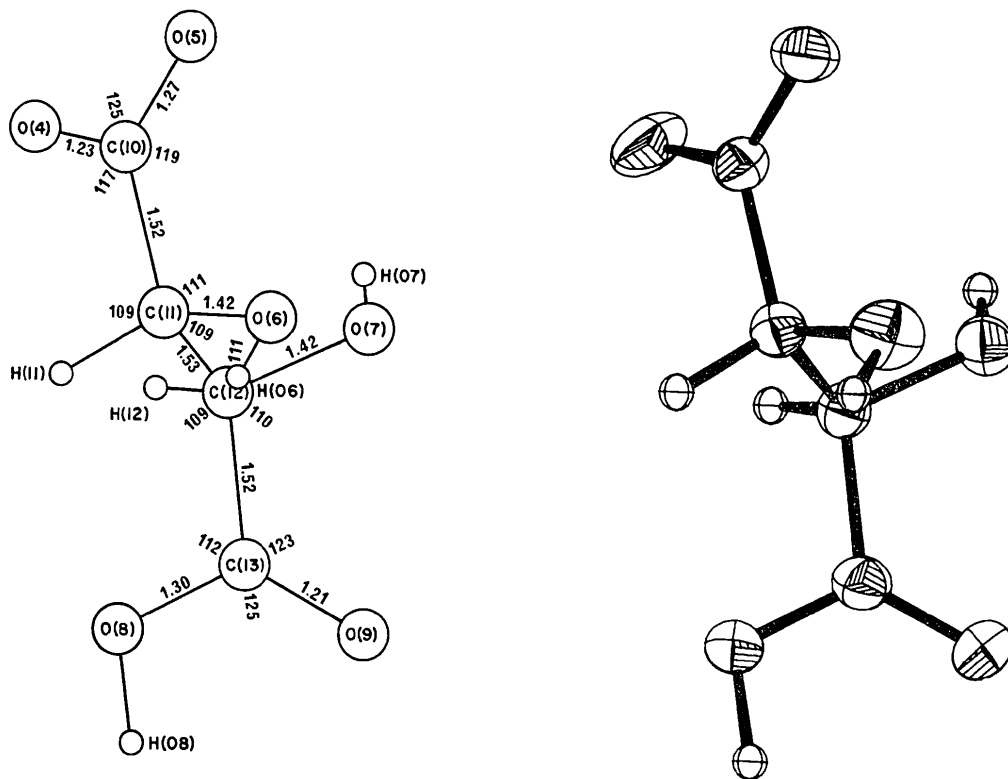

Fig. 2. The numbering of the atoms and major bond distances and bond angles in the hydrogen (+)-tartrate ion (left). The thermal ellipsoids for the non-hydrogen atoms, scaled to 50% probability (right) were drawn using the plotting program *ORTEP* (Johnson, 1965).
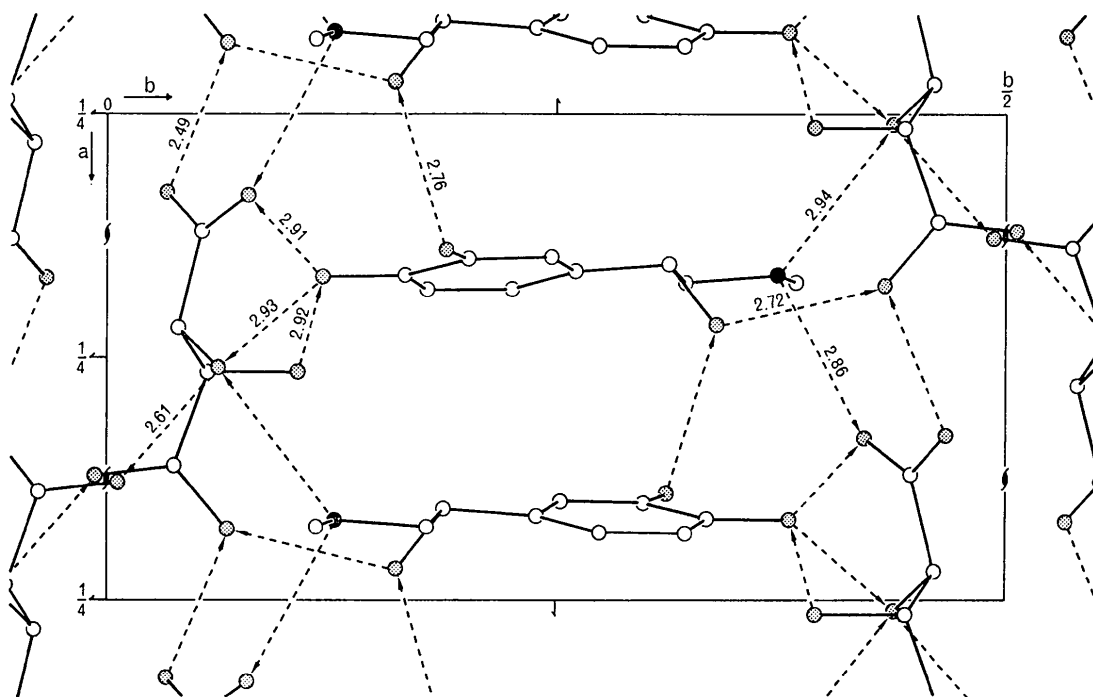
Fig. 3. Projection of half a unit cell of the crystal structure of (−)-adrenaline hydrogen (+)-tartrate. Open, filled and shaded circles represent carbon, nitrogen and oxygen respectively. Hydrogen bonds are indicated by broken lines and the arrow-heads indicate the acceptor atoms. Distances in Å. The positive direction of c is towards the viewer.

in a hydrogen bond and the $O(6)-H(O6)\cdots O(2)$ angle, 125°, is far from ideal. On the whole, the crystal structure of adrenaline hydrogen tartrate is densely packed which is also evident from the high density (1·51 g cm^{-3}) of the crystals.

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