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2-Amino-6,7-dihydroxytetralin Hydrobromide, $C_{10}H_{13}NO_2.HBr$*

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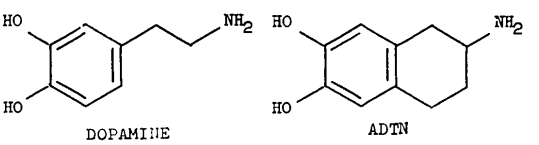
Abstract. $M_r = 260{\cdot}1$, monoclinic, $P2_1/c$, $a = 11{\cdot}061(2)$, $b = 20{\cdot}939\ (3)$, $c = 9{\cdot}420\ (1)$ Å, $\beta = 92{\cdot}81\ (1)°$, $V = 2179{\cdot}1$ Å^3, $Z = 8$, $D_m = 1{\cdot}54\ (2)$, $D_x = 1{\cdot}586$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 4{\cdot}987$ mm^{-1}, $F(000) = 1056$, $T = 295$ K. Final $R = 0{\cdot}039$ for 2934 observed reflections. There are two independent molecules in the unit cell. Molecule *A* is essentially planar, except for two C atoms of the aliphatic ring which are displaced equally 0·33 Å above and below the plane of the molecule; the N atom also lies in the molecular plane defined by the aromatic ring. Molecule *B* exhibits partial disorder of the (+)- and (−)-enantiomers.

Introduction. In neurobiology one of the most intensively studied neurotransmitters is the catecholamine dopamine. The crystal and molecular structure of dopamine was first reported by Bergin & Carlström (1968). New dopamine receptor agonists are currently being sought by the pharmaceutical industry due to their possible clinical applications in diseases such as Parkinsonism (Hornykiewicz, 1975). The tetrahydronaphthalene derivative 2-amino-6,7-dihydroxytetralin† (ADTN) has been the object of much recent pharmacological interest since it is a very potent dopamine agonist (Horn, Grol, Dijkstra & Mulder, 1978; Horn, de Kaste, Dijkstra, Rollema, Feenstra, Westerink, Grol & Westerbrink, 1978; see also references therein). ADTN is also of interest from a structural point of view, as it is a semirigid analogue of dopamine and the conformation in the crystal could yield valuable information about the receptor-site preferred conformation of dopamine.



* Contribution from the National Bureau of Standards.

† Tetralin®: 1,2,3,4-tetrahydronaphthalene.

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Experimental. ADTN.HBr crystallized from diisopropyl acetate and methanol. D_m by flotation in mixed halogenated organic solvents. 0·20 × 0·12 × 0·04 mm. Syntex $P2_1$ diffractometer, graphite-monochromated Cu $K\alpha$. Lattice parameters from refinement of setting angles of 15 reflections with $20 < 2\theta < 40°$, systematic absences $h0l$ with l odd and $0k0$ with k odd. Variable scan rate 2·0 to 29·3° min^{-1}. Standard reflections ($\bar{2}12$, 022, $\bar{2}34$, 180) stable. 4044 reflections (h 0–13, k 0–26, l −11–10) with $4 < 2\theta < 150°$, 2934 independent with $I > 3\sigma(I)$ where $\sigma^2(I) = C + (0{\cdot}0082C)^2$ (C = total count). Absorption correction by Gaussian quadrature with corrections to I of 1·18 to 1·92. Structure solved by heavy-atom technique. Anisotropic refinement on F. Isotropic extinction parameter 0·0014 (14). H atoms from difference map (—NH and —CH positions idealized). Function minimized $\sum w(|F_o| - |F_c|)^2$, $w = |\sigma(F_o)|^{-2}$; $R = 0{\cdot}039$, $R_w = 0{\cdot}040$, $S = 2{\cdot}28$. $(\Delta/\sigma)_{max} = 0{\cdot}0138$, $(\Delta/\sigma)_{av} = 0{\cdot}0021$. Final difference Fourier map showed a small amount of residual electron density [0·8 e Å^{-3} near C(2*B*) and 0·6 e Å^{-3} near C(3*B*)] which can be attributed to disorder (see *Discussion*), remaining peaks 0·3 e Å^{-3} or lower. Scattering factors for C, N, O, Br from Cromer & Mann (1968), for H from Stewart, Davidson & Simpson (1965); anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974). All computations performed with XRAY 76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976).

Discussion. Table 1* lists the final atomic parameters.

The structure analysis reveals that there are two crystallographically independent protonated molecules (*A* and *B*) of ADTN in the unit cell. A view of molecule *A* with atom labeling is presented in Fig. 1. Bond distances and angles for molecules *A* and *B* are given in Table 2.

Table 1. *Final positional and equivalent isotropic thermal parameters with e.s.d.'s in parentheses*

Atoms are numbered as in Fig. 1; a molecule label (*A* or *B*) is attached to the atom name. $B_{eq} = 8\pi^2(U_{11} + U_{22} + U_{33})/3$.

	x	y	z	B_{eq}(Å^2)
Br(1)	0·51060 (5)	0·31329 (2)	0·31994 (6)	4·62 (3)
Br(2)	0·10140 (4)	0·74188 (2)	0·25515 (6)	4·01 (2)
C(1*A*)	0·0950 (4)	0·3656 (2)	0·4297 (5)	3·4 (2)
C(2*A*)	0·1782 (4)	0·3149 (2)	0·4948 (5)	3·9 (2)
C(3*A*)	0·2307 (4)	0·3337 (2)	0·6365 (6)	4·6 (2)
C(4*A*)	0·3047 (4)	0·3946 (2)	0·6288 (6)	4·6 (2)
C(5*A*)	0·2836 (4)	0·5094 (2)	0·5501 (6)	4·4 (3)
C(6*A*)	0·2318 (4)	0·5568 (2)	0·4665 (6)	4·1 (2)
C(7*A*)	0·1362 (4)	0·5423 (2)	0·3719 (5)	3·5 (2)
C(8*A*)	0·0945 (4)	0·4807 (2)	0·3618 (5)	3·5 (2)
C(9*A*)	0·1469 (4)	0·4321 (2)	0·4442 (5)	3·2 (2)
C(10*A*)	0·2426 (4)	0·4458 (2)	0·5394 (5)	3·7 (2)
N(*A*)	0·1099 (3)	0·2534 (2)	0·5034 (4)	3·7 (2)
O(1*A*)	0·2673 (3)	0·6198 (1)	0·4714 (4)	5·8 (2)
O(2*A*)	0·0824 (3)	0·5886 (1)	0·2854 (3)	4·3 (2)
C(1*B*)	0·7579 (4)	0·1049 (2)	0·5483 (5)	4·1 (2)
C(2*B*)	0·6770 (4)	0·1479 (2)	0·4630 (6)	4·3 (2)
C(3*B*)	0·5611 (5)	0·1240 (2)	0·4144 (8)	6·8 (3)
C(4*B*)	0·5645 (4)	0·0604 (2)	0·3376 (6)	4·2 (2)
C(5*B*)	0·6552 (4)	−0·0482 (2)	0·3601 (5)	3·5 (2)
C(6*B*)	0·7396 (4)	−0·0912 (2)	0·4135 (5)	3·2 (2)
C(7*B*)	0·8323 (4)	−0·0709 (2)	0·5080 (5)	3·2 (2)
C(8*B*)	0·8365 (4)	−0·0080 (2)	0·5486 (5)	3·7 (2)
C(9*B*)	0·7500 (4)	0·0362 (2)	0·4970 (5)	3·2 (2)
C(10*B*)	0·6595 (4)	0·0159 (2)	0·4011 (5)	3·3 (2)
N(*B*)	0·6748 (3)	0·2128 (2)	0·5235 (4)	4·1 (2)
O(1*B*)	0·7356 (3)	−0·1554 (1)	0·3782 (4)	4·1 (1)
O(2*B*)	0·9153 (3)	−0·1157 (1)	0·5547 (4)	4·6 (2)

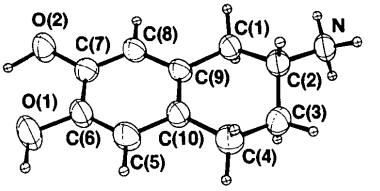

Fig. 1. Perspective view of molecule *A* showing the labeling scheme. Non-H atoms are represented by thermal ellipsoids drawn at the 50% probability level (Johnson, 1965).

* Lists of structure factors, H-atom positions, least-squares planes, and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38918 (32 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

	Molecule *A*	Molecule *B*		Molecule *A*	Molecule *B*		Molecule *A*	Molecule *B*		Molecule *A*	Molecule *B*
C(1)–C(2)	1·514 (6)	1·478 (6)*	C(3)–C(4)	1·519 (7)	1·517 (7)*	C(6)–C(7)	1·382 (7)	1·390 (6)	C(7)–O(2)	1·382 (5)	1·369 (5)
C(1)–C(9)	1·508 (6)	1·519 (6)	C(4)–C(10)	1·507 (7)	1·507 (6)	C(6)–O(1)	1·378 (5)	1·385 (5)	C(8)–C(9)	1·389 (6)	1·400 (6)
C(2)–C(3)	1·482 (7)	1·430 (7)*	C(5)–C(6)	1·374 (7)	1·373 (6)	C(7)–C(8)	1·372 (6)	1·372 (6)	C(9)–C(10)	1·384 (6)	1·382 (6)
C(2)–N	1·498 (5)	1·474 (6)*	C(5)–C(10)	1·408 (6)	1·398 (6)						

	Molecule *A*	Molecule *B*		Molecule *A*	Molecule *B*		Molecule *A*	Molecule *B*
C(2)–C(1)–C(9)	112·9 (3)	112·3 (4)*	C(5)–C(6)–C(7)	119·7 (4)	120·1 (4)	C(1)–C(9)–C(8)	118·6 (4)	119·2 (4)
C(1)–C(2)–C(3)	112·5 (4)	118·1 (4)*	C(5)–C(6)–O(1)	124·2 (4)	122·3 (4)	C(1)–C(9)–C(10)	121·7 (4)	121·8 (4)
C(1)–C(2)–N	109·1 (3)	111·8 (4)*	C(7)–C(6)–O(1)	116·1 (4)	117·6 (4)	C(8)–C(9)–C(10)	119·6 (4)	119·0 (4)
C(3)–C(2)–N	110·9 (4)	114·5 (4)*	C(6)–C(7)–C(8)	119·6 (4)	119·0 (4)	C(4)–C(10)–C(5)	119·8 (4)	118·1 (4)
C(2)–C(3)–C(4)	111·6 (4)	114·6 (4)*	C(6)–C(7)–O(2)	121·4 (4)	117·3 (4)	C(4)–C(10)–C(9)	121·8 (4)	122·6 (4)
C(3)–C(4)–C(10)	113·1 (4)	112·8 (4)*	C(8)–C(7)–O(2)	119·0 (4)	123·7 (4)	C(5)–C(10)–C(9)	118·5 (4)	119·3 (4)
C(6)–C(5)–C(10)	121·2 (4)	121·0 (4)	C(7)–C(8)–C(9)	121·4 (4)	121·6 (4)			

* Values not corrected for the partial disorder in molecule *B*.

Molecule *A* is essentially planar, except for C(2) and C(3) of the puckered aliphatic ring which are displaced equally 0·33 Å above and below the plane of the molecule; the N atom also lies in the molecular plane defined by the aromatic ring.

Molecule *B* has essentially the same geometry as molecule *A*. The small amount of residual electron density in the final difference Fourier map can be interpreted as alternative positions for the C(2) and C(3) atoms in molecule *B* owing to partial disordering of the (+)- and (−)-enantiomers on a single crystallographic site. This type of stereochemical disorder has been reported previously for 3-(*o*-chlorophenylimino)-camphor (Foulon, Baert & Fouret, 1979) and dihydrothymine (Furberg & Jensen, 1968). Further evidence of the disorder can be seen in the anisotropic thermal ellipsoids and the abnormally short C(2)–C(3) bond length of 1·430 (7) Å as compared to the value of 1·482 (7) Å found in molecule *A*.

The protonated ADTN molecules pack in hydrogen-bonded layers. One such layer is shown in Fig. 2. Hydrogen-bond distances are given in Table 3. Planar molecules of this type evidently can disorder when no strong orientation forces are present in the crystal structure. The observation that molecule *A* is ordered and molecule *B* is disordered can be attributed to the fact that only molecule *A* forms NH–O hydrogen bonds (both molecules also form weaker NH–Br bonds). It is particularly important that this type of disorder be recognized, as even a small amount of the disorder can result in significantly distorted apparent bond lengths.

When dealing with very flexible molecules of biological interest it is always difficult to reach firm conclusions regarding the relevance of the crystal conformation to that pertaining at the biological receptor site. One method of circumventing this problem is the use of rigid or semirigid analogues (Portoghese, 1970; Horn & Rodgers, 1977). Depending on the structure and conformation of the new analogue, however, this can lead to a retention or diminution of pharmacological activity; if the latter occurs it is very difficult to draw reliable conclusions about the active conformation at the receptor site. This is not the case with ADTN, as it has been shown that the racemic mixture of ADTN is as potent as dopamine in many pharmacological tests (Horn, Grol, Dijkstra & Mulder, 1978; Horn, de Kaste, Dijkstra, Rollema, Feenstra, Westerink, Grol & Westerbrink, 1978) while the (+)-enantiomer is about 100 times more potent than the (−)-enantiomer and about four times more active than dopamine itself (Andrews, Davis, Freeman, McDermed, Poat & Woodruff, 1978). Thus although ADTN is not a fully rigid molecule it is of sufficient rigidity to allow one to suggest with some degree of certainty that the parameters found in the solid state for the dopamine skeleton in ADTN may closely resemble the active form of dopamine at its receptor site.

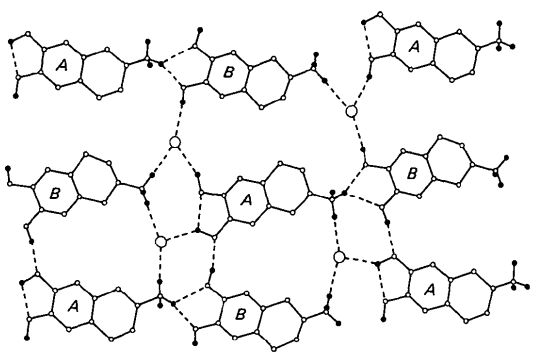

Fig. 2. Hydrogen-bonded layer of protonated ADTN molecules. The large circles represent Br atoms; NH–Br bonds to Br atoms in adjacent layers are not shown.

Table 3. *Hydrogen-bond distances* (Å) *and angles* (°) *of the type* X–H$\cdots Y$

	$X\cdots Y$	X–H	H$\cdots Y$	$\angle X$–H$\cdots Y$
N(*A*)–H(N*A*)$\cdots$O(1*B*)*	2·861 (4)	1·0†	1·99	144
N(*A*)–H(N*A*)$\cdots$O(2*B*)	2·946 (4)	1·0	2·36	116
N(*A*)–H′(N*A*)$\cdots$Br(2)	3·301 (4)	1·0	2·31	175
N(*A*)–H″(N*A*)$\cdots$Br(2)	3·342 (4)	1·0	2·40	157
N(*B*)–H(N*B*)$\cdots$Br(1)	3·326 (4)	1·0	2·40	154
N(*B*)–H′(N*B*)$\cdots$Br(1)	3·449 (4)	1·0	2·49	160
N(*B*)–H″(N*B*)$\cdots$Br(2)	3·297 (4)	1·0	2·36	156
O(1*A*)–H(O1*A*)$\cdots$Br(1)	3·374 (4)	1·09	2·34	158
O(2*A*)–H(O2*A*)$\cdots$Br(2)	3·230 (3)	1·11	2·29	142
O(2*A*)–H(O2*A*)$\cdots$O(1*A*)	2·708 (5)	1·11	2·18	106
O(1*B*)–H(O1*B*)$\cdots$Br(1)	3·291 (3)	0·89	2·41	171
O(2*B*)–H(O2*B*)$\cdots$O(2*A*)	2·840 (4)	0·94	1·94	160

* Atoms in molecule *A* are designated by (*A*) and atoms in molecule *B* are designated by (*B*).

† H-atom positions were not refined. The H atoms bonded to N atoms were idealized to give N–H = 1·0 Å.

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1′,3′-Dicyclohexylspiro[2*H*-1-benzopyran-2,4′-imidazolidine]-2′,4(3*H*),5′-trione, $C_{23}H_{28}N_2O_4$

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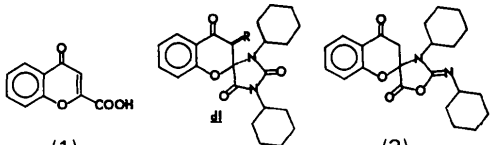
Abstract. $M_r = 396{\cdot}5$, monoclinic, $P2_1/c$, $a = 9{\cdot}935$ (4), $b = 6{\cdot}669$ (2), $c = 31{\cdot}983$ (9) Å, $\beta = 90{\cdot}51$ (3)°, $V = 2119$ (1) Å^3, $Z = 4$, $D_m = 1{\cdot}22$ (2) (flotation in aq. $ZnBr_2$), $D_x = 1{\cdot}24$ g cm^{-3}, λ (Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}80$ cm^{-1}, $F(000) = 848$, $T = 298$ K, $R = 0{\cdot}053$ for 1934 observed reflections. An unexpected product from the treatment of an α,β-unsaturated acid with *N,N′*-dicyclohexylcarbodiimide and its monochlorination product are shown to be imidazolidine-2,4-diones. There are no unusual bond distances or bond angles.

Introduction. During attempts to make esters of acid (1) with dicyclohexylcarbodiimide (DCC), we obtained not esters but instead a crystalline 1:1 adduct of (1) and DCC in good yield. Through elemental analysis and spectral data, we came to the conclusion that the adduct was either (2*a*) or (3). We now report that X-ray results conclusively establish this adduct to be (2*a*) and its monochlorination product to be (2*b*).



(1) (3)

R
(2*a*) H
(2*b*) Cl

Experimental. *Compound* (2*a*). DCC (2·06 g) in 5 mL dioxane was added in one portion to a hot solution of (1) (1·90 g) in 30 mL dioxane. After refluxing 5h and removing the solvent on a rotary evaporator, the residue was crystallized from absolute ethanol (40 mL), giving 3·0 g (75%) of (2*a*), m.p. 460–462 K. Colorless crystal, 0·70 × 0·30 × 0·35 mm. Automated four-circle Syntex $P2_1$ diffractometer, scan range $4° < 2\theta < 50°$, graphite-monochromated Mo $K\alpha$ radiation, θ–2θ scan technique. 4157 independent reflections, 1934 observed with $I > 3\sigma(I)$. Lp correction but no absorption. Three check reflections collected every 100 data points showed no crystal decay. Direct methods (*MULTAN*80, Main *et al.*, 1980). Positional and anisotropic thermal parameters for all non-H atoms were refined (on *F*) by block-diagonal least squares, H's in calculated positions. $R = 0{\cdot}053$, $R_w = 0{\cdot}060$, $S = 2{\cdot}1$. Weighting scheme of Corfield, Doedens & Ibers (1967) with $p = 0{\cdot}04$. $(\Delta/\sigma)_{max} = 0{\cdot}3$; maximum height on final difference Fourier map 0·2 e Å^{-3}. Scattering-factor tables from *International Tables for X-ray Crystallography* (1962). No correction for secondary extinction. Refinement program *NUCLS* (Doedens & Ibers); plotter program *ORTEP* (Johnson, 1965).

Compound (2*b*). (2*a*) (10 g) in 100 mL CH_2Cl_2 was treated with 10 mL SO_2Cl_2 in one portion at 298 K. After 3h, the solvent was removed on a rotary evaporator and the residue was heated with 100 mL absolute ethanol on a steam bath; on cooling, 7·7 g

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