pass through Cl^- (Fig. 2): $Cl^-\cdots H(11W)-O(1)-H(12W)\cdots Cl^-\cdots H(21)-N(2)-H(22)\cdots Cl^-$ (two such rings at each Cl^- ion), $Cl^-\cdots H(22W)-O(2)-H(21W)\cdots N(3)-C(2)-N(2)-H(21)\cdots Cl^-$, $Cl^-\cdots H(22W)-O(2)\cdots H(9)-N(9)-C(8)-H(8)\cdots O(1)-H(11W)\cdots Cl^-$ and $O(2)-H(21W)\cdots N(3)-C(4)-N(9)-H(9)\cdots O(2)-H(21W)\cdots N(3)-C(4)-N(9)-H(9)\cdots O(2)$.

The authors are indebted to Professors Maciej Wiewiórowski and Stefan Paszyc for their interest in this work. This work was partly supported by project RP II 13.12.13 and Polish Academy of Sciences project 3.14.4.2.1.

References

ADAMIAK, R. W., BIAŁA, E., GDANIEC, Z., MIELEWCZYK, S. & SKALSKI, B. (1986*a*). *Chem. Scr.* **26**, 3–7.

ADAMIAK, R. W., BIAŁA, E., GDANIEC, Z., MIELEWCZYK, S. & SKALSKI, B. (1986*b*). *Chem. Scr.* **26**, 7–11.

ADAMIAK, R. W., BIAŁA, E. & SKALSKI, B. (1985*a*). *Angew. Chem. Int. Ed. Engl.* **24**, 1054–1055.

ADAMIAK, R. W., BIAŁA, E. & SKALSKI, B. (1985*b*). *Nucleic Acids Res.* **13**, 2989–3003.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

JASKÓLSKI, M. (1982*a*). *Collected Abstracts of the Fourth Symposium on Organic Crystal Chemistry*, Poznań, September 1982, edited by Z. KAŁUSKI, pp. 70–71. A. Mickiewicz Univ., Poznań.

JASKÓLSKI, M. (1982*b*). *Proc. 4th Symp. Organic Crystal Chemistry*, Poznań, September 1982, edited by Z. KAŁUSKI, pp. 221–245. A. Mickiewicz Univ., Poznań.

JOHNSON, C. K. (1976). *ORTEP*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

LEHMANN, M. S. & LARSEN, F. K. (1974). *Acta Cryst.* A**30**, 580–584.

MOTHERWELL, W. D. S. & CLEGG, W. (1978). *PLUTO*. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.

NEWKOME, G. R., THERIOT, K. J. & FRONCZEK, F. R. (1985). *Acta Cryst.* C**41**, 1642–1644.

SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.

SKALSKI, B., ADAMIAK, R. W. & PASZYC, S. (1984). *Nucleic Acids. Symp. Ser.* **14**, 293–295.

TAYLOR, R. & KENNARD, O. (1982*a*). *J. Am. Chem. Soc.* **104**, 5063–5070.

TAYLOR, R. & KENNARD, O. (1982*b*). *J. Mol. Struct.* **78**, 1–28.

Acta Cryst. (1987). C**43**, 2113–2117

Dopaminergic 3-Benzazepines: SKF 87516 (II) and SKF 82526 (III)

BY DRAKE S. EGGLESTON

Department of Physical and Structural Chemistry, Smith Kline & French Laboratories, L-950, PO Box 7929, Philadelphia, PA 19101, USA

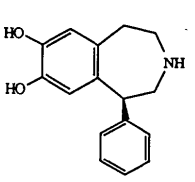
(*Received* 31 *December* 1986; *accepted* 8 *June* 1987)

Abstract. (II): (1*R*)-6-Fluoro-2,3,4,5-tetrahydro-1-(*p*-hydroxyphenyl)-1*H*-3-benzazepine-7,8-diol hydrobromide, $C_{16}H_{17}FNO_3^+.Br^-$, $M_r = 370{\cdot}23$, orthorhombic, $P2_12_12_1$, $a = 9{\cdot}293\ (2)$, $b = 10{\cdot}309\ (1)$, $c = 16{\cdot}479\ (4)$ Å, $V = 1578{\cdot}7\ (6)$ Å^3, $Z = 4$, D_m (flotation in $CHCl_3/C_2H_4Cl_2$) $= 1{\cdot}54\ (2)$, $D_x = 1{\cdot}558$ Mg m^{-3}, λ(Mo $K\bar{\alpha}$) $= 0{\cdot}71073$ Å, $\mu = 2{\cdot}5973$ mm^{-1}, $F(000) = 752$, $T = 293$ K, $R = 0{\cdot}039$, $wR = 0{\cdot}043$ for 1282 observations. (III): (1*R*)-6-Chloro-2,3,4,5-tetrahydro-1-(*p*-hydroxyphenyl)-1*H*-3-benzazepine-7,8-diol hydrobromide, $C_{16}H_{17}ClNO_3^+.Br^-$, $M_r = 386{\cdot}68$, orthorhombic, $P2_12_12_1$, $a = 9{\cdot}254\ (1)$, $b = 10{\cdot}011\ (2)$, $c = 17{\cdot}555\ (4)$ Å, $V = 1626{\cdot}3\ (6)$ Å^3, $Z = 4$, D_m not measured, $D_x = 1{\cdot}58$ Mg m^{-3}, λ(Cu $K\alpha$) $= 1{\cdot}54184$ Å, $\mu = 5{\cdot}41$ mm^{-1}, $F(000) = 784$, $T = 296$ K, $R = 0{\cdot}034$, $wR = 0{\cdot}046$ for 1693 observations. (II) and (III), members of a novel class of dopamine receptor agonists, incorporate the phenethylamine skeleton of dopamine in a moderately constrained fashion and differ only in the halogen substituent attached to the catechol ring. Both molecules crystallize with the seven-membered azepine ring adopting a chair conformation; the 1-(*p*-hydroxyphenyl) substituent sits in an equatorial orientation relative to the benzazepine ring with the phenyl ring also perpendicular to the catechol nucleus. Significant differences in catechol C—O bond lengths are observed in both structures with the bond *ortho* to the halogen substituent 0·18 Å shorter. Observed bond-angle distortions about the catechol ring are also consistent with the σ-withdrawing ability of the halo substituents at C(6). Intermolecular hydrogen bonding involves all available donors in both structures. The bromide ions are 'coordinated' in a distorted square-planar fashion by four H-bonding interactions. The possibility of a three-center interaction involving the catechol group adjacent to the halo substituent is also noted.

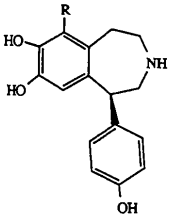
Introduction. The observations of Goldberg (1972), that low doses of dopamine increased renal blood flow

0108-2701/87/112113-05$01.50

and reduced renal vascular resistance, stimulated a search for peripherally acting dopamine agonists useful for the therapeutic treatment of hypertension. 2,-3,4,5-Tetrahydro-1-phenyl-1*H*-3-benzazepine-7,8-diol, SKF 38393 (I), was identified as a lead compound (Pendelton, Samler, Kaiser & Ridley, 1978). This molecule incorporates the phenethylamine skeleton of dopamine in a moderately constrained manner by precluding the *trans*-extended spatial relationship between the N atom and the fused aromatic ring. SKF 87516 (II) and SKF 82526 (III) are prototypes of a large series of molecules which have been investigated as dopamine agonists and antagonists (Weinstock *et al.*, 1983).



(I) SKF 38393



(II) R = F SKF 87516
(III) R = Cl SKF 82526

Compound (III), approximately ten times as potent a renal vasodilator as dopamine, decreases blood pressure in anesthetized dogs. Activity resides solely in the (*R*) isomer. The seemingly trivial substitution of chlorine by fluorine leads to a markedly different pharmacological profile for (II) characterized by enhanced diuretic activity and introduction of a substantial peripheral presynaptic D_2 activity compared to (III) while retaining essentially equivalent D_1-related α2 and renal vasodilator potency (Weinstock *et al.*, 1983). Such dramatic pharmacological differences might reflect any number of physicochemical differences between (II) and (III) at the D_1 and D_2 receptors, one of which might be conformational in origin. To examine the possibility that (III) might adopt a conformation distinct from that of (II) and to confirm the absolute configuration of the active isomer for both molecules, the crystal and molecular structures of (II) and (III) have been determined.

Experimental. For (II): colorless tabloid from methanol, approximate dimensions 0·30 × 0·30 × 0·40 mm, mounted with epoxy on a glass fiber. Cell constants from a least-squares analysis of 25 reflections [$30 \le 2\theta(\text{Mo}) \le 35°$] measured on the diffractometer. Data collection on an Enraf–Nonius CAD-4 diffractometer equipped with a graphite monochromator at SKF Laboratories; variable-speed ω–θ scans. Systematic absences: *h*00, 0*k*0, 00*l*, for *h*, *k*, *l* odd, respectively. 2070 measured intensities, $2\theta \le 55°$, $0 \le h \le 13$, $0 \le k \le 12$, $0 \le l \le 21$; Lorentz–polarization correction, no systematic fluctuation in reflections $6\bar{4}\bar{1}$, $\bar{1}76$ or 0,0,12 monitored at the beginning, end and each 3h during data collection (11 times); max. deviations in $|F|$ 1·3, 0·7 and 1·0%, respectively; mean values of $|F|$ 191·3 (9), 236·3 (8) and 313·0 (1·2), respectively; absorption correction based on ψ scans of eight strong reflections with $80 \le \chi \le 90°$, transmission coefficients range from 99·98 to 58·26%. Programs in the Enraf–Nonius (1979) CAD-4 *SDP*; structure solution from a Patterson map and subsequent difference Fourier maps; anisotropic least-squares refinement (on *F*) of positions led to $wR = 0{\cdot}074$; weights $4F_o^2/\sigma^2(I)$ with $\sigma(I) = [\sigma(I)^2 + (pF_o)^2]^{1/2}$ and *p*, a small percentage value which dampens the weights of large intensities to prevent them from biasing the refinement, was assigned a value of 0·05. Difference Fourier syntheses revealed positions for all H atoms; all H-atom positions and thermal parameters (except those attached to the *p*-hydroxyphenyl ring C atoms) were allowed to vary in the final cycles. An extinction coefficient of the type defined by Zachariasen (1963) included in the later stages refined to 2·69 (2) × 10^{-7}, final $wR = 0{\cdot}043$, $R = 0{\cdot}039$, $S = 1{\cdot}203$, 1282 observations with $I \ge 3{\cdot}0\sigma(I)$, 252 variables; convergence indicated by max. $\Delta/\sigma = 0{\cdot}05$; final difference map showed maximum positive and minimum excursions of 0·472 and −0·389 e Å^{-3}, respectively, in the vicinity of the bromide ion. Atomic coordinates were inverted and additional refinement cycles led to $R = 0{\cdot}060$, $wR = 0{\cdot}071$ indicating substantial confidence in the assignment of the absolute configuration based on the *R*-factor-ratio test (Hamilton, 1965). For the correct enantiomer refinement using 1780 observations with $I \ge 0{\cdot}01\sigma(I)$ gave $R = 0{\cdot}062$, $wR = 0{\cdot}049$. Neutral-atom scattering factors from *International Tables for X-ray Crystallography* (1974), for H from Stewart, Davidson & Simpson (1965).

For (III): data collected as a service by Molecular Structure Corporation. Colorless prism, 0·15 × 0·25 × 0·25 mm, mounted on a glass fiber with the long axis parallel to φ. Enraf–Nonius CAD-4 diffractometer, graphite monochromator, systematic absences: *h*00, 0*k*0, 00*l* for *h*, *k*, *l* odd, respectively. Cell constants from least-squares analyses of 25 reflections [$24 \le 2\theta(\text{Cu}) \le 122°$] measured on the diffractometer. Intensity data collected with variable-speed ω–θ scans, 1921 unique non-systematically absent reflections, $2\theta \le 150{\cdot}0°$, $0 \le h \le 11$, $0 \le k \le 12$, $0 \le l \le 21$; Lorentz–polarization correction, linear decay correction (correction factors on *I* from 1·00 to 1·02), absorption correction based on ψ scans (transmission coefficients 68·3 to 99·6%). A secondary-extinction correction of the type described by Zachariasen (1963) was applied and refined to 6·0 (1) × 10^{-7}. Structure solution from a Patterson map, which revealed the Br position, and subsequent difference Fourier maps.

Least-squares refinement (on F) of non-H atoms with anisotropic thermal parameters and of H atoms with isotropic thermal parameters converged at $R = 0{\cdot}0341$, $wR = 0{\cdot}0457$, where the function minimized was $\sum w(|F_o| - |F_c|)^2$ and the weights $w = 4F_o^2/\sigma^2(I)$ with $\sigma^2(I) = [\sigma(I)^2 + (pF_o)^2]^{1/2}$ and p, a small percentage value which dampens the weights of large intensities to prevent them from biasing the refinement, was assigned a value of 0·05. 1693 observations with $I \geq 3\sigma(I)$. The final refinement cycle included 268 variables, max. $\Delta/\sigma = 0{\cdot}29$; final difference map showed maximum positive excursion of 0·45 e Å^{-3}, $S = 1{\cdot}394$. Refinement of the other enantiomer yielded significantly higher $R = 0{\cdot}0426$ and $wR = 0{\cdot}0584$. The agreement factor for all data was $R = 0{\cdot}042$.

The optical rotation of a sample of (II) in its methanesulfonic acid salt form, prepared from the same batch of free base as the hydrobromide salt reported here, is $[\alpha]_D^{25°C} = +19{\cdot}4°$ (c 1·00, MeOH); for the methanesulfonic acid salt of (III) the optical rotation is $[\alpha]_D^{25°C} = +10{\cdot}1°$ (c 1·00, MeOH).

Discussion. Crystals of the hydrobromide salts of (II) and (III) are isomorphous. Tables 1 and 2 present the positional parameters and their standard deviations as estimated from the inverse least-squares matrix.* Figs. 1 and 2 display the structures of (II) and (III), respectively, from a common viewpoint. As may be seen from these figures, (II) and (III) adopt nearly identical conformations in the solid state characterized by a chair conformation for the seven-membered azepine ring and an equatorial orientation for the 'dangling' p-hydroxyphenyl group very nearly perpendicular to the plane of the fused aromatic ring. The C(1a)–C(1)–C(10)–C(11) and C(1a)–C(1)–C(10)–C(15) torsion angles are 78 (1) and −101 (1)°, respectively, for (II), 84 (1) and −95 (1)°, respectively, for (III). Alternatively, this orientation may be described by the dihedral angles between the aromatic rings which are 106·0 and 102·5° for (III).

Intramolecular bond distances and angles are similar in the two structures and well within expected ranges. The asymmetry in C–O bond distances for the catechol ring is noteworthy; the C(7)–O(1) distances of 1·356 (7) and 1·367 (4) Å in (II) and (III), respectively, are 0·18 Å shorter than the C(8)–O(2) distances of 1·374 (7) and 1·385 (4) Å owing to their proximity to the halogen substituent attached at C(6). A second interesting feature involving the halogen substituent is an asymmetry in the exocyclic bond angles at C(6). The

Table 1. *Positional and thermal parameters for* (II)

$B_{eq} = \frac{4}{3}[B_{11} + B_{22} + B_{33}]$.

	x	y	z	B_{eq}(Å^2)
Br	0·20250 (7)	−0·35572 (6)	0·50367 (4)	4·57 (1)
F	0·1869 (4)	0·1085 (3)	0·8252 (2)	4·40 (8)
O(1)	0·1468 (5)	0·3711 (4)	0·8192 (2)	4·4 (1)
O(2)	0·1417 (4)	0·4921 (3)	0·6768 (2)	3·55 (8)
O(3)	0·1164 (5)	0·3904 (4)	0·2494 (2)	3·84 (9)
N	0·3787 (5)	−0·1045 (4)	0·5689 (3)	3·1 (1)
C(1)	0·2091 (6)	0·0796 (5)	0·5277 (3)	2·5 (1)
C(1a)	0·1883 (5)	0·1554 (5)	0·6074 (3)	2·3 (1)
C(2)	0·3592 (6)	0·0178 (5)	0·5227 (3)	2·7 (1)
C(4)	0·3675 (7)	−0·0980 (5)	0·6594 (3)	3·4 (1)
C(5)	0·2192 (7)	−0·0544 (6)	0·6877 (3)	3·4 (1)
C(5a)	0·1934 (6)	0·0897 (5)	0·6814 (3)	2·6 (1)
C(6)	0·1791 (6)	0·1640 (5)	0·7510 (3)	3·0 (1)
C(7)	0·1604 (6)	0·2981 (5)	0·7512 (3)	2·9 (1)
C(8)	0·1563 (5)	0·3594 (5)	0·6760 (3)	2·7 (1)
C(9)	0·1692 (5)	0·2885 (5)	0·6055 (3)	2·5 (1)
C(10)	0·1862 (6)	0·1601 (5)	0·4525 (3)	2·4 (1)
C(11)	0·2911 (6)	0·2451 (5)	0·4257 (3)	2·9 (1)
C(12)	0·2716 (6)	0·3227 (5)	0·3577 (3)	3·1 (1)
C(13)	0·1426 (6)	0·3162 (5)	0·3161 (3)	2·5 (1)
C(14)	0·0374 (6)	0·2302 (6)	0·3417 (3)	3·0 (1)
C(15)	0·0600 (6)	0·1538 (6)	0·4092 (3)	2·7 (1)

Table 2. *Positional and thermal parameters for* (III)

$B_{eq} = \frac{4}{3}[B_{11} + B_{22} + B_{33}]$.

	x	y	z	B_{eq}(Å^2)
Br	0·27517 (6)	0·36392 (5)	0·01572 (3)	4·57 (1)
Cl	0·1897 (2)	−0·0940 (1)	−0·31430 (6)	5·60 (3)
O(1)	0·1573 (4)	−0·3831 (3)	−0·2841 (2)	4·7 (1)
O(2)	0·1778 (4)	−0·5036 (3)	−0·1509 (1)	4·0 (1)
O(3)	0·1265 (4)	−0·3705 (3)	0·2499 (2)	4·1 (1)
N	0·4312 (4)	0·1035 (3)	−0·0623 (2)	3·4 (1)
C(1)	0·2548 (4)	−0·0727 (3)	−0·0173 (2)	2·9 (1)
C(1a)	0·2241 (4)	−0·1537 (3)	−0·0894 (2)	2·7 (1)
C(2)	0·4106 (5)	−0·0204 (4)	−0·0164 (2)	3·2 (1)
C(4)	0·4025 (5)	0·0975 (4)	−0·1461 (2)	3·9 (1)
C(5)	0·2457 (5)	0·0607 (4)	−0·1651 (2)	3·7 (1)
C(5a)	0·2185 (5)	−0·0887 (4)	−0·1596 (2)	3·1 (1)
C(6)	0·1946 (5)	−0·1647 (4)	−0·2239 (2)	3·3 (1)
C(7)	0·1790 (5)	−0·3041 (4)	−0·2216 (2)	3·2 (1)
C(8)	0·1880 (4)	−0·3655 (4)	−0·1511 (2)	3·0 (1)
C(9)	0·2090 (4)	−0·2915 (3)	−0·0861 (2)	2·7 (1)
C(10)	0·2258 (4)	−0·1519 (3)	0·0551 (2)	2·9 (1)
C(11)	0·3272 (5)	−0·2388 (4)	0·0862 (2)	3·3 (1)
C(12)	0·2984 (5)	−0·3121 (4)	0·1510 (2)	3·4 (1)
C(13)	0·1644 (5)	−0·2998 (4)	0·1861 (2)	3·0 (1)
C(14)	0·0629 (5)	−0·2130 (4)	0·1564 (2)	3·3 (1)
C(15)	0·0926 (4)	−0·1403 (4)	0·0913 (2)	3·1 (1)

C(7)–C(6)–X angles of 115·1 (5)° (X = F) and 115·3 (3)° (X = Cl) are remarkably narrowed compared to the ideal 120° angle and compared to their counterpart angles C(5a)–C(6)–X of 120·6 (5)° (X = F) and 121·8 (3)° (X = Cl). An asymmetric pattern of exocyclic bond angles is also observed around C(7) and C(8).

Of the endocyclic angles in the fused aromatic ring the angle about the halo-substituted C atom, C(5a)–C(6)–C(7), is consistently the widest [124·2 (5)° in (II) and 122·8 (3)° in (III)] while the angles about each C atom *ortho* to the halogen substituent are consistently narrowed from the ideal 120° value and in comparison

* Lists of structure factors, H-atom positions, torsion angles, anisotropic librational parameters and complete bond lengths and angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44151 (40 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

to the other endocyclic angles [*i.e.* C(6)–C(5a)–C(1a) = 116·8 (5), C(6)–C(7)–C(8) = 116·9 (5)°. in (II), 118·1 (3) and 117·4 (3)° in (III), respectively]. The observed angular distortions about C(6) and the *ortho* C atoms may be attributed to the σ-withdrawing capabilities of the halogen substituents and are in qualitative agreement with the observations of Domenicano & Murray-Rust (1979), particularly in that fluoro-containing (II) shows a much larger endocyclic widening at C(6) than does the chloro analog.

The chair conformation for the seven-membered heterocyclic ring in both structures is defined by both the coplanarity of atoms C(1)–C(2)···C(4)–C(5), which show maximum deviations from the four-atom least-squares plane of 0·004 (6) Å in (II) and 0·002 (4) Å in (III), and by the deviations of N, C(1a) and C(5a) from this plane [0·636 (4), −1·102 (5) and −1·076 (5) Å, respectively, for (II); 0·622 (4), −1·152 (4) and −1·136 (5) Å, respectively, for (III)]. Alternatively, this chair conformation may be described by the ring torsion angles which are listed together with idealized torsion angles for the chair form of cycloheptene as derived from Ermer & Lifson (1973) (Table 3). Thus, the well established postulate (Kaiser, 1984; Liptak, Kusiak & Pitha, 1985) on the importance of a location for N approximately in the plane of the catechol ring for dopamine agonist activity can not be confirmed for these dopaminergic 3-benzazepines if the crystal structures represent a biologically active conformation. Such coplanarity can be achieved if the heterocyclic ring adopts a higher energy twist conformation (Eggleston & Wise, 1986) such as was observed in the structure of the methiodide of the *N*-methyl dimethyl ether of (I) (Kaiser, Dandridge, Garvey, Hahn, Sarau, Setler, Bass & Clardy, 1982).

The crystal structures display intermolecular H-bonding patterns (Fig. 3) which are identical in terms of donor–acceptor interactions but which differ slightly in metric detail. The bromide ion is an acceptor for four hydrogen bonds, two from N and one from each of the

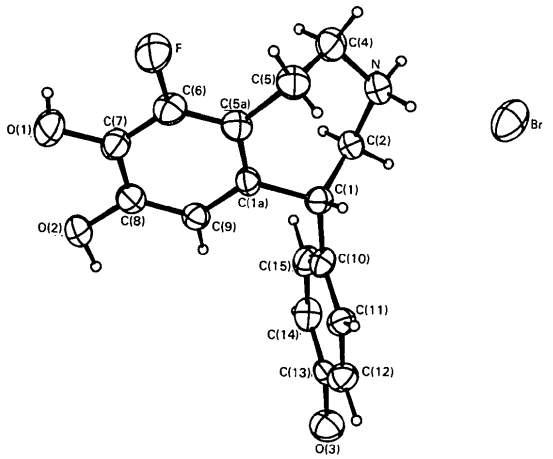


Fig. 1. View of molecule (II) with non-H atoms depicted as primary ellipsoids at the 50% probability level; H atoms as small spheres of arbitrary size.

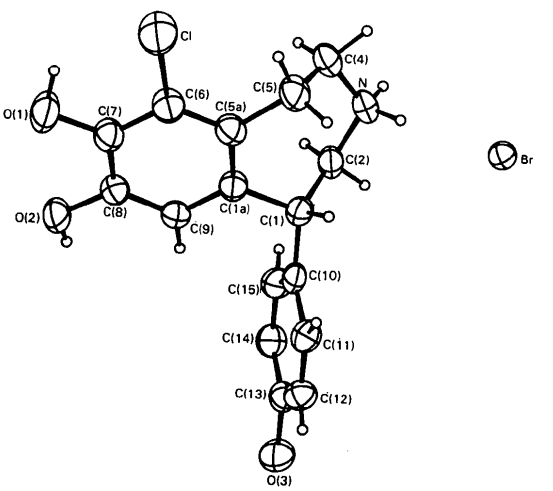


Fig. 2. View of molecule (III) with non-H atoms depicted as primary ellipsoids at the 50% probability level; H atoms as small spheres of arbitrary size.

Table 3. *Selected torsion angles* (°)

	(II)	(III)	Theory*
C(1a)–C(1)–C(2)–N	79·5	81·4	+74·9
C(1)–C(2)–N–C(4)	−64·9	−61·9	−67·6
C(2)–N–C(4)–C(5)	62·3	61·2	67·6
N–C(4)–C(5)–C(5a)	−78·3	−80·3	−74·9
C(4)–C(5)–C(5a)–C(1a)	65·4	67·1	+58·5
C(5)–C(5a)–C(1a)–C(1)	0·2	1·4	0·0
C(5a)–C(1a)–C(1)–C(2)	−62·9	68·8	−58·5

* Derived from Ermer & Lifson (1973).

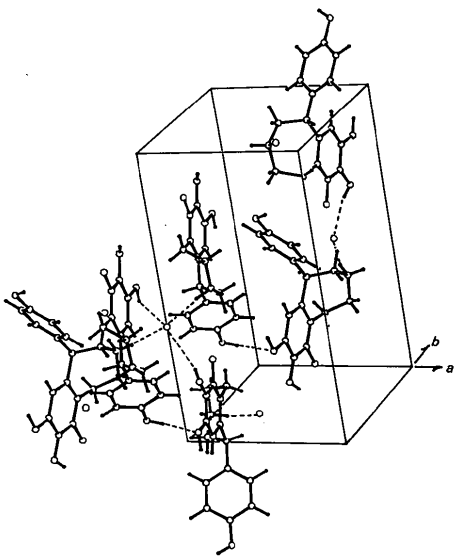


Fig. 3. View of the unit-cell packing for (II). Dashed lines indicate hydrogen bonds. Axial directions are as labeled.

catechol O atoms with Br···N distances of 3·247 (5), 3·264 (6) Å for (II), 3·280 (3), 3·303 (4) Å for (III) and Br···O distances of 3·351 (5), 3·305 (4) Å for (II), 3·336 (3), 3·574 (4) Å for (III). Angles at H range from 145 (7) to 161 (4)° for (II) and 127 to 166° for (III). These interactions describe a distorted square-planar 'coordination geometry' about the bromide ion. The hydroxyl group on the *p*-hydroxyphenyl substituent O(3) acts as a donor to atom O(2) in both structures with an O···O separation of 2·820 (6) Å for (II) and 2·811 (4) Å for (III); the angle at H is 173 (7)° for (II) and 157 (6)° for (III). In both (II) and (III) the catechol H(O1) atom may participate in a three-center interaction involving the adjacent halogen. Angles about H(O1), [O(1)–H(O)···Cl = 126 (5), O(1)–H(O1)···Br = 127 (5)°] are equivalent for (III), whereas angles for (II) [O(1)–H(O1)···F = 112 (6), O(1)–H(O1)···Br = 145 (7)°] show a polarization away from F towards the Br ion.

References

DOMENICANO, A. & MURRAY-RUST, P. (1979). *Tetrahedron Lett.* pp. 2283–2286.

EGGLESTON, D. S. & WISE, M. W. (1986). *Proc. Am. Crystallogr. Assoc. Meet. Abstr.* **14**, A55.

Enraf–Nonius (1979). *Structure Determination Package.* Enraf–Nonius, Delft, The Netherlands.

ERMER, O. & LIFSON, S. (1973). *J. Am. Chem. Soc.* **95**, 4121–4132.

GOLDBERG, L. I. (1972). *Pharmacol. Rev.* **24**, 1–29.

HAMILTON, W. C. (1965). *Acta Cryst.* **18**, 502–510.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

KAISER, C. (1984). *Proceedings of Smith Kline & French First Annual Research Symposium: Dopamine Receptor Agonists,* edited by G. POSTE & S. T. CROOKE, pp. 81–137. New York: Plenum.

KAISER, C., DANDRIDGE, P. A., GARVEY, E., HAHN, R. A., SARAU, H. M., SETLER, P. E., BASS, L. S. & CLARDY, J. (1982). *J. Med. Chem.* **25**, 697–703.

LIPTAK, A., KUSIAK, J. W. & PITHA, J. (1985). *J. Med. Chem.* **28**, 1699–1703.

PENDELTON, R. G., SAMLER, L., KAISER, C. & RIDLEY, P. T. (1978). *Eur. J. Pharmacol.* **51**, 19–28.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

WEINSTOCK, J., WILSON, J. W., LADD, D. L., BRENNER, M., ACKERMAN, D. M., BLUMBERG, A. L., HAHN, R. A., HIEBLE, J. P., SARAU, H. M. & WIEBELHAUS, V. D. (1983). *ACS Symposium Series* No. 224, edited by C. KAISER & J. W. KEBABIAN, pp. 157–169. Washington, DC: American Chemical Society.

ZACHARIASEN, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.

Acta Cryst. (1987). C**43**, 2117–2120

Structure of 1-Methyladenosine Trihydrate

BY YURIKO YAMAGATA AND KEN-ICHI TOMITA

Faculty of Pharmaceutical Sciences, Osaka University, Suita 565, *Japan*

(*Received* 23 *February* 1987; *accepted* 1 *June* 1987)

Abstract. N^6-Didehydro-1,6-dihydro-1-methyladenosine trihydrate, $C_{11}H_{15}N_5O_4.3H_2O$, $M_r = 335·3$, monoclinic, space group $P2_1$, $a = 6·726$ (1), $b = 20·090$ (3), $c = 11·496$ (11) Å, $\beta = 91·22$ (6)°, $V = 1553$ (1) Å^3, $Z = 4$, $D_m = 1·427$ (3), $D_x = 1·434$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54184 Å, $\mu = 0·995$ mm^{-1}, $F(000) = 712$, $T = 296$ K, $R = 0·049$ for 2687 observed reflections. The molecular conformations of the two independent nucleosides in the asymmetric unit are quite different. The conformation around the glycosidic bond is *syn* in molecule (*a*), whereas it is *anti* in molecule (*b*). The conformation of the exocyclic C(4′)–C(5′) bond is *gauche-gauche* in molecule (*a*) and *trans-gauche* in molecule (*b*). On the other hand, the sugar puckerings of both molecules are the C(2′)-*endo* type. The most pronounced feature of the crystal structure is the alternating parallel stacking of the two independent purine bases to form columns parallel to the *a* axis.

0108-2701/87/112117-04$01.50

Introduction. A number of alkylated nucleosides occur in nature or are obtained by chemical modification. Among these, 1-methyladenosine is one of the minor nucleosides isolated from transfer RNA in many eukaryotes and some microorganisms (Nishimura, 1978). According to the three-dimensional structure reported for yeast $tRNA^{Phe}$ (Landner *et al.*, 1975; Quigley *et al.*, 1975; Stout *et al.*, 1978), 1-methyladenosine (m^1A58) is located at the $T\psi C$ loop and forms a reverse Hoogsteen-type base pairing with a thymine base (T54). It is also stacked on the paired bases between G18 of the *D* loop and $\psi 55$. These structural features seem to be necessary for retaining the sharp bend in the $T\psi C$ loop and for stabilizing the interaction between the $T\psi C$ and *D* loops. In addition, 1-methyladenine base can be produced when single-strand DNA and RNA are treated with alkylating agents which are mutagenic or carcinogenic. The