Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: TA1119). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–S19.
Chemla, D. S. & Zyss, T. (1987). *Nonlinear Properties of Organic Molecules and Crystals*, Vols. 1 and 2. New York: Academic Press.
Cheng, L. T., Tam, W., Stevenson, S. H. & Meredith, G. R. (1991). *J. Phys. Chem.* **95**, 10631–10643.
Enraf–Nonius (1988). *CAD-4 VAX/PC Operators Manual*. Enraf–Nonius, Delft, The Netherlands.
Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.
Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
Sheldrick, G. M. (1990*a*). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1990*b*). *SHELXTL/PC. Structure Determination Software Programs*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

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Methylxanthines. I. Anhydrous Theophylline

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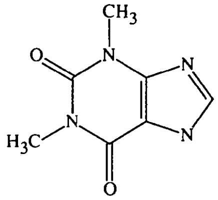
Abstract

Clear crystals of anhydrous theophylline (3,7-dihydro-1,3-dimethyl-1*H*-purine-2,6-dione), $C_7H_8N_4O_2$, were grown by sublimation and the X-ray structure determined. The planar molecules are stacked in columns along [010] and are inclined at an angle of 26.05 (10)° relative to (010). The melting point has been determined to be 548.8 (5) K.

Comment

There is considerable interest in the structures of methylxanthines such as theophylline owing to their pharmacological use. Theophylline is often used as a muscle relaxant or vasodilator. However, the X-ray structure of pure theophylline has not been reported since it is difficult to obtain crystals not containing solvent or other complexing agents. As part of our research on the methylxanthines, we report the structure of anhydrous theophylline, (I).



(I)

The unit-cell dimensions and space-group assignment determined in the present work agree well with crystal data from previously reported powder diffraction data (Naqvi & Bhattacharyya, 1981).

The numbering scheme is shown in Fig. 1. Bond lengths and angles (Table 1) agree well with previously reported theophylline-complex structures (Aoki & Ichikawa, 1978; Karczmarzyk, Karolak-Wojciechowska & Pawłowski, 1995; Sutor, 1958; Zaitu, Miwa & Taga, 1995*a*,*b*; Nakao, Fujii, Sakaki & Tomita, 1977). The molecular packing and the hydrogen-bonding scheme can be seen in Fig. 2. The planar molecules are stacked in columns along [010]. The molecular plane is inclined at an angle of 26.05 (10)° relative to (010). The mean separation between molecular planes is 3.425 (7) Å.

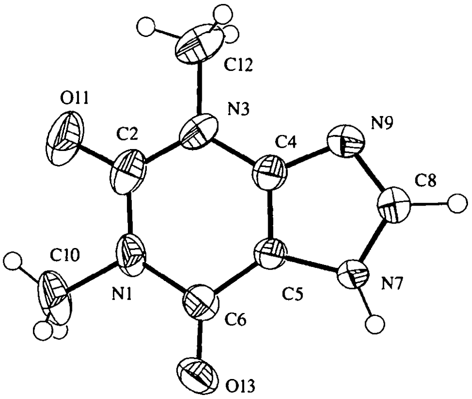


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of theophylline showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are drawn as spheres with arbitrary radii.

The theophylline molecules form hydrogen-bonded networks as shown in Fig. 2. The networks are composed of one N—H···N hydrogen bond and two (bifurcated) C—H···O hydrogen bonds. The values for these interactions are given in Table 2. As would be expected from hydrogen-bonding rules (Etter, 1990), the best pro-

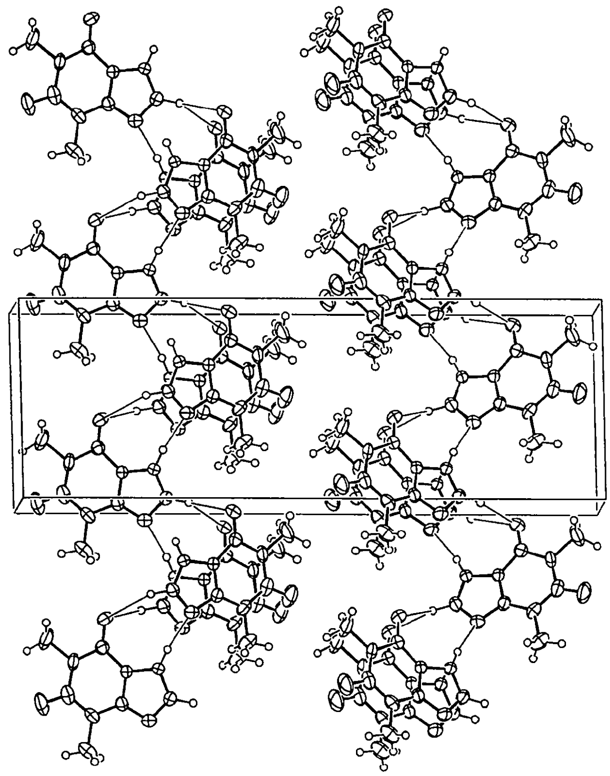


Fig. 2. *ORTEP*II (Johnson, 1976) drawing showing the hydrogen-bonding networks. Projection is approximately down the [0$\bar{1}$0] axis. Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as spheres with arbitrary radii.

ton donor (N7) is hydrogen bonded to the best proton acceptor (N9). Graph-set characterization (Etter, MacDonald & Bernstein, 1990; Bernstein, Davis, Shimoni & Chang, 1995) of the hydrogen bonding at the lowest degree may be described as a first-level $C(6)C(6)C(4)$ set. While it is beyond the scope of this report to present a full graph-set analysis, it is worth pointing out the existence of a second-level $R^2_2(8)$ network comprised of the N—H···H hydrogen bond and the longer C—H···O hydrogen bond.

It is also of interest to analyze the hydrogen-bonding geometry around the acceptor atom O13. The C6—O13···H8($\frac{3}{2}-x$, $y+\frac{1}{2}$, $z-\frac{1}{2}$) angle is 96.4 (16)° and the H8 position deviates by 2.241 (6) Å from the N1, C5, C6, O13 plane, giving an angular deviation of approximately 68°. The C6—O13···H8($\frac{3}{2}-x$, $y-\frac{1}{2}$, $z-\frac{1}{2}$) angle is 120.1 (13)° and this H8 position deviates by 1.174 (11) Å from the N1, C5, C6, O13 plane, giving an angular deviation of approximately 24°. The longer C—H···O interaction has the H atom pointing to where one of the lone pairs on O13 would be positioned. This observation is in accordance with previously observed directionality of hydrogen bonds involving sp^2-hybridized O atoms (Murray-Rust & Glusker, 1984).

Experimental

Commercial theophylline (Aldrich) was recrystallized several times using water and ethanol. The solvent was removed under vacuum and the theophylline sublimed several times before use. Anhydrous crystals employed in the melting-point determinations and in the X-ray study were grown in a vacuum sublimation tube. Colorless optically clear crystals of theophylline appeared in the tube when the temperature was 503–508 K. Crystals grew as thin plates, with the plate normal approximately parallel to [100].

Crystal data

$C_7H_8N_4O_2$
$M_r = 180.16$
Orthorhombic
$Pna2_1$
$a = 24.612(2)$ Å
$b = 3.8302(4)$ Å
$c = 8.5010(5)$ Å
$V = 801.38(12)$ Å^3
$Z = 4$
$D_x = 1.493$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 12$–$20°$
$\mu = 0.11$ mm^{-1}
$T = 293$ K
Thin plate
$0.45 \times 0.30 \times 0.03$ mm
Colorless

Data collection

Nonius CAD-4 diffractometer
ω scans
Absorption correction: none
752 measured reflections
752 independent reflections
646 reflections with $I_{net} > 0.5\sigma(I_{net})$

$\theta_{max} = 25°$
$h = 0 \rightarrow 29$
$k = 0 \rightarrow 4$
$l = 0 \rightarrow 10$
3 standard reflections
frequency: 80 min
intensity decay: <1%

Refinement

Refinement on F
$R = 0.053$
$wR = 0.056$
$S = 1.65$
646 reflections
126 parameters
H atoms: see below
$w = 1/[\sigma^2(F) + 0.0005F^2]$
$(\Delta/\sigma)_{max} = 0.001$

$\Delta\rho_{max} = 0.25$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}
Extinction correction: Larson (1970)
Extinction coefficient: $4.2(14) \times 10^{-1}$
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Table 1. *Selected geometric parameters (Å, °)*

N1—C2	1.413 (9)	C4—N9	1.350 (6)
N1—C6	1.418 (7)	C5—C6	1.430 (7)
N1—C10	1.488 (8)	C5—N7	1.388 (5)
C2—N3	1.360 (8)	C6—O13	1.213 (6)
C2—O11	1.221 (6)	N7—C8	1.327 (8)
N3—C4	1.384 (6)	N7—H7	0.90 (7)
N3—C12	1.469 (8)	C8—N9	1.316 (7)
C4—C5	1.349 (8)	C8—H8	1.02 (6)
C2—N1—C6	126.6 (4)	C4—C5—N7	105.4 (4)
C2—N1—C10	117.1 (5)	C6—C5—N7	129.8 (5)
C6—N1—C10	116.3 (5)	N1—C6—C5	110.1 (5)
N1—C2—N3	117.4 (4)	N1—C6—O13	122.0 (5)
N1—C2—O11	120.2 (6)	C5—C6—O13	127.9 (4)
N3—C2—O11	122.4 (6)	C5—N7—C8	105.7 (5)
C2—N3—C4	119.7 (5)	C5—N7—H7	128 (4)
C2—N3—C12	120.1 (5)	C8—N7—H7	126 (4)
C4—N3—C12	120.2 (5)	N7—C8—N9	113.4 (4)

N3—C4—C5	121.4 (5)	N7—C8—H8	121 (4)
N3—C4—N9	127.3 (5)	N9—C8—H8	125 (4)
C5—C4—N9	111.3 (4)	C4—N9—C8	104.2 (5)
C4—C5—C6	124.8 (4)		

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	H···*A*	*D*—H···*A*
N7—H7···N9^{i}	1.93 (7)	179 (5)
C8—H8···O13^{ii}	2.42 (6)	149 (4)
C8—H8···O13^{iii}	2.85 (6)	116 (4)

Symmetry codes: (i) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{1}{2} + z$; (ii) $\frac{3}{2} - x, \frac{1}{2} + y, z - \frac{1}{2}$; (iii) $\frac{3}{2} - x, y - \frac{1}{2}, z - \frac{1}{2}$.

The intensity data were corrected for Lorentz and polarization effects, but not for absorption. All non-H-atom positions were recovered from the initial *E* map. Although subsequent difference Fourier maps yielded peaks suggestive of H-atom positions, the H atoms were placed at idealized positions. The atomic positions and anisotropic displacement parameters (ADPs) for the non-H atoms refined smoothly. The positional and isotropic displacement parameters for H atoms H7 and H8 were included in the least-squares refinement. The methyl H atoms were included in the structure-factor calculation, but not refined. These C—H distances were fixed to 0.96 Å and the isotropic displacement [*U*(H)] was set according to the expression, *U*(H) = *U*(C) + 0.01 Å^2. These parameters were updated every second cycle of the least-squares refinement. The calculated structure factors included corrections for anomalous dispersion from the usual tabulation (Cromer, 1974). The final cycles of refinement included an extinction correction (Larson, 1970). Intermolecular geometries were analyzed using *PLATON* (Spek, 1990).

Data reduction: *NRCVAX DATRD*2 (Gabe, Le Page, Charland, Lee & White, 1989). Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994). Program(s) used to refine structure: *NRCVAX LSTSQ*. Molecular graphics: *NRCVAX* and *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *NRCVAX TABLES* (version of January 1994).

The comments of a referee are gratefully acknowledged.

Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: BK1284). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435–436.

Aoki, K. & Ichikawa, T. (1978). *Acta Cryst.* B**34**, 2333–2336.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Cromer, D. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, Table 2.3, pp. 72–98. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.

Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* B**46**, 256–262.

Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.

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

Karczmarzyk, Z., Karolak-Wojciechowska, J. & Pawłowski, M. (1995). *Acta Cryst.* C**51**, 2121–2123.

Larson, A. C. (1970). *Crystallographic Computing*, edited by F. R. Ahmed, S. R. Hall & C. P. Huber, pp. 291–294. Copenhagen: Munksgaard.

Murray-Rust, P. & Glusker, J. P. (1984). *J. Am. Chem. Soc.* **106**, 1018–1025.

Nakao, S., Fujii, S., Sakaki, T. & Tomita, K. (1977). *Acta Cryst.* B**33**, 1373–1378.

Naqvi, A. A. & Bhattacharyya, G. C. (1981). *J. Appl. Cryst.* **14**, 464.

Spek, A. L. (1990). *Acta Cryst.* A**46**, C-34.

Sutor, D. J. (1958). *Acta Cryst.* **11**, 83–87.

Zaitu, S., Miwa, Y. & Taga, T. (1995*a*). *Acta Cryst.* C**51**, 1857–1859.

Zaitu, S., Miwa, Y. & Taga, T. (1995*b*). *Acta Cryst.* C**51**, 2390–2392.

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Dicyclohexylammonium (*N*,*N*-Dicyclohexylthiocarbamoylthio)acetate

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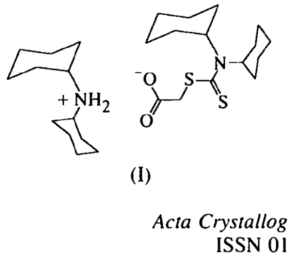
Abstract

The unit cell of dicyclohexylammonium (*N*,*N*-dicyclohexylthiocarbamoylthio)acetate contains two $C_{12}H_{24}N^+.C_{15}H_{24}NO_2S_2^-$ ion pairs in the $P2_1/c$ space group. The ammonium N atom is hydrogen bonded to the carboxyl and carbonyl O atoms, forming a O—C—O···N···O—C—O···N ring. The N-bonded cyclohexyl rings are disordered.

Comment

Dicyclohexylammonium (*N*,*N*-dimethylthiocarbamoylthio)acetate crystallizes as a monohydrate having a hydrogen-bonded network structure (Ng, 1992), whereas the present cyclohexyl analog, $[(cyclo\text{-}C_6H_{11})_2NH_2]^+.[(cyclo\text{-}C_6H_{11})_2NCS_2CH_2CO_2]^-$, (I), contains no water. Two ion pairs are held across a center of inversion by two strong hydrogen bonds [N···O 2.706 (2) and 2.757 (2) Å]. The hydrogen-bond distances are similar to those found in dicyclohexylammonium bis(*N*,*N*-dimethylthiocarbamoylthio)acetate [N···O 2.698 (2) and 2.837 (3) Å; Ng, 1996], which also exists as an ion pair.



(I)

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