lar compound, 1-methyl-4-[2-(4-hydroxyphenyl)vinyl]-pyridinium 4-toluenesulfonate (Okada *et al.*, 1990), crystallizing in space group $P\overline{1}$, is non-linear optical; it differs from the monomer of the title compound only in the position of the hydroxy substituent, indicating the important role of the group *ortho* to the central vinyl group in the monomeric cation. We are currently studying the actual mechanism for the photochemical dimerization.

Experimental

1,4-Dimethylpyridinium iodide (7.05 g, 30 mmol) (prepared from CH_3I and 4-methylpyridine) and 5.2 ml (49 mmol) of 2-hydroxybenzaldehyde in methanol (10 ml) were heated to 353 K for 12 h. The product was recrystallized twice from water, dissolved in water again (0.68 g in 100 ml) and treated with a saturated solution of silver *p*-tolylsulfonate added dropwise with stirring at 363 K over 20 min. The title compound was separated, recrystallized twice and finally crystals suitable for X-ray analysis were grown from methanol–water (10:1) by slow evaporation.

Crystal data

$C_{28}H_{28}N_2O_2^{2+}.2C_7H_7SO_3^-.2H_2O$
$M_r = 802.92$
Triclinic
$P\overline{1}$
$a = 8.704\ (1)$ Å
$b = 9.116\ (1)$ Å
$c = 12.968\ (2)$ Å
$\alpha = 84.69\ (1)°$
$\beta = 76.63\ (1)°$
$\gamma = 80.35°$
$V = 985.3\ (2)$ Å^3
$Z = 1$
$D_x = 1.353$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 27 reflections
$\theta = 3.06–15.88°$
$\mu = 0.197$ mm^{-1}
$T = 295\ (2)$ K
Block
0.46 × 0.46 × 0.37 mm
Pale yellow

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction: none
3723 measured reflections
3475 independent reflections
2531 reflections with $I > 2\sigma(I)$
$R_{int} = 0.010$

$\theta_{max} = 24.99°$
$h = 0 \rightarrow 10$
$k = -10 \rightarrow 10$
$l = -14 \rightarrow 15$
3 standard reflections
every 97 reflections
intensity decay: 3.0%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.112$
$S = 0.981$
3474 reflections
345 parameters
H atoms refined isotropically
$w = 1/[\sigma^2(F_o^2) + (0.066P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.004$
$\Delta\rho_{max} = 0.230$ e Å^{-3}
$\Delta\rho_{min} = -0.344$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

C(14)—C(15^i)	1.553 (2)	C(14)—C(15)	1.583 (2)
C(13)—C(14)—C(15^i)	120.52 (15)	C(16)—C(15)—C(14^i)	117.21 (15)
C(13)—C(14)—C(15)	116.49 (14)	C(16)—C(15)—C(14)	116.16 (14)
C(15^i)—C(14)—C(15)	90.43 (13)	C(14^i)—C(15)—C(14)	89.57 (13)

Symmetry code: (i) $-x, -y, 1-z$.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O(4)—H(4O)···O(5^i)	0.81 (3)	1.85 (3)	2.653 (2)	171 (3)
O(5)—H(5O*B*)···O(2^{ii})	0.88 (3)	1.86 (3)	2.733 (2)	171 (3)
O(5)—H(5O*A*)···O(2)	0.79 (3)	2.01 (3)	2.802 (3)	177 (3)

Symmetry codes: (i) $x, y-1, z$; (ii) $-x, 1-y, 2-z$.

Data collection: *XSCANS* (Siemens, 1994). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Software used to prepare material for publication: *PARST* (Nardelli, 1983).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: CF1158). Services for accessing these data are described at the back of the journal.

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8-Amino-7-(4-morpholinobutyl)theophylline

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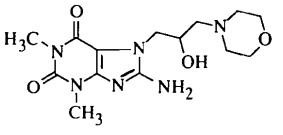
Abstract

The crystal structure of the title compound, 8-amino-1,3-dimethyl-7-(4-morpholinobutyl)-3,7-dihydro-1*H*-purine-2,6-dione, $C_{15}H_{24}N_6O_3$, (III), is described and com-

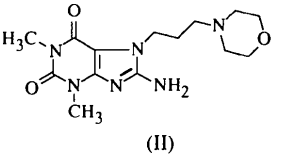
pared with that of 8-amino-7-(2-hydroxy-3-morpholinopropyl)theophylline, (I). The molecules of (III) have typical geometry. In the purine fused-ring system, the six-membered ring is planar to within 0.006 (2) Å, the five-membered ring is planar to within 0.011 (2) Å and the two rings are inclined at 0.72 (8)°. The aminoalkyl side chain at the 7 position of the theophylline has a *gauche-trans-gauche-gauche-gauche* conformation which may be influenced by a weak N—H···N intramolecular hydrogen bond. The morpholine ring adopts a chair conformation with puckering parameters Q = 0.560 (2) Å and θ = 178.5 (2)° [Cremer & Pople (1975). *J. Am. Chem. Soc.* **97**, 1354–1358]. The molecules in the crystal are joined in chains parallel to the [010] direction by N—H···O intermolecular hydrogen bonds. Inversion-related purine moieties overlap each other with a mean separation between the molecular planes of 3.46 (1) Å.

Comment

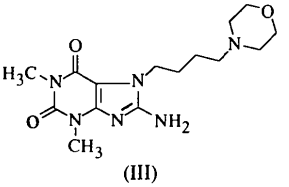
We report here the results of the X-ray structure determination of the title compound, (III), as part of a larger structural and pharmacological study on 7,8-disubstituted theophylline derivatives. The addition of selected substituents at the 7 and 8 positions of theophylline modifies the pharmacological profile of the new derivatives in comparison with the parent compound. The pharmacological investigation of a series of synthesized 7,8-disubstituted derivatives of theophylline showed that some have antihypertensive and vasodilatory activity (Łucka-Sobstel *et al.*, 1985; Gorczyca, Pawłowski, Mrozikiewicz, Kozłowska & Wasik, 1986; Olejnik *et al.*, 1989). Of particular interest with respect to pharmacological properties [*e.g.* circulatory effects, mainly antihypertensive activity, the beneficial effect on cerebral blood-flow autoregulation and low toxicity in comparison with its mother compound theophylline (Kozłowska *et al.*, 1989)] is 8-amino-7-(2-hydroxy-3-morpholinopropyl)theophylline, (I) (Karczmarzyk, Karolak-Wojciechowska & Pawłowski, 1995*a*), which was chosen as a pharmacophore system for other 7,8-disubstituted derivatives in structure–activity relationship studies.



(I)



(II)



(III)

In order to know whether the presence of the chiral centre and the length of an aminoalkyl chain at position 7 determine the cardiovascular activity of 8-aminotheophylline, the 7-(3-morpholinopropyl)-, (II), and 7-(4-morpholinobutyl)-, (III), analogues of (I) were synthesized. This seems to be a useful method for resolving the structure requirements needed to propose possible mechanisms for activity on the basis of pharmacological tests, *e.g.* β-receptor blocking action. The results of the pharmacological screening of 8-amino-7-(3-morpholinopropyl)theophylline, (II), directed at the circulatory effects showed its low hypotensive activity (Pawłowski, Gorczyca & Bobkiewicz-Kozłowska, 1997). Replacement of the trimethylene spacer by tetramethylene between morpholine and 8-aminotheophylline causes a dramatic loss of antihypertensive activity (Pawłowski, Gorczyca & Bobkiewicz-Kozłowska, 1997), but weak adenosine deaminase inhibition *in vitro* was observed. These results prompted us to perform a structure determination of compound (III) to obtain the conformational and electronic requirements for enzyme-binding properties.

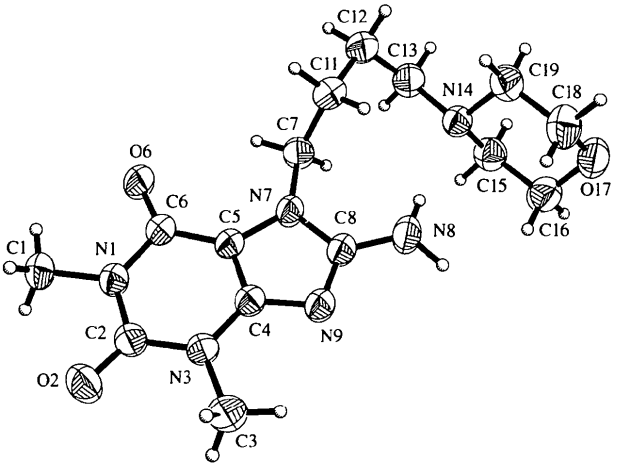


Fig. 1. A view of the molecule with the atomic labelling. Non-H atoms are represented by displacement ellipsoids of 50% probability.

The bond lengths, angles, planarity and conformations of the rings in molecules (III) and (I) are very similar and the geometries of the theophylline skeletons do not differ significantly from that reported for theophylline (Sutor, 1958). The significant differences occur only in the conformations of the substituents at position 7 of theophylline. The torsion angles C8—N7—C7—C11 −68.6 (3), N7—C7—C11—C12 157.6 (2), C7—C11—C12—C13 −52.6 (3), C11—C12—C13—N14 −48.8 (3) and C12—C13—N14—C19 −67.6 (3)° indicate a *gauche-trans-gauche-gauche-gauche* conformation of the aminobutyl side chain in (III), while the conformation of the 2-hydroxyaminopropyl side chain in (I) is *gauche-gauche-trans-*

gauche [the torsion angles being −77.0 (3), −73.2 (3), −179.7 (3) and −77.7 (4)°, respectively]. The major conformation-determining feature for substituents at the 7-positions of the molecules (III) and (I) is the presence of intramolecular hydrogen bonds: the N atom of the morpholine ring of each structure acts as an acceptor, while the amino group in (III) and hydroxy group in (I) exhibit donor capabilities [N8—H82···N14: N8···N14 3.059 (3), H82···N14 2.16 (3) Å and N8—H82···N14 173 (3)°]. The molecules in the crystal are joined in chains parallel to [010] by N8—H81···O6(x, $y+1$, z) intermolecular hydrogen bonds: N8···O6 2.969 (3), H81···O6 2.08 (3) Å and N8—H81···O6 166 (3)°. The differences in the side-chain conformations observed in (III), (I) and other described 7,8-disubstituted theophylline derivatives (Karczmarzyk, Karolak-Wojciechowska & Pawłowski, 1995*b*,*c*) indicate a large flexibility and a strong influence of the intra- and intermolecular hydrogen bonds on the conformation of the substituent. This suggests that differences in the pharmacological activities of 7,8-disubstituted theophylline derivatives are connected with the electronic properties of the molecules rather than the conformations observed in crystals.

Experimental

Preparation of the title compound involved several synthetic steps starting from 8-dibenzylaminotheophylline (Pawłowski & Gorczyca, 1980), which was alkylated at the 7-position with dibromobutane. Non-reductive debenzylation followed by substitution with morpholine led to the final product with 7-(4-morpholinobutyl) and deprotected 8-NH_2 substituents (Pawłowski, Gorczyca & Bobkiewicz-Kozłowska, 1997). Crystals were obtained by slow evaporation of a toluene solution at room temperature.

Crystal data

$C_{15}H_{24}N_6O_3$
M_r = 336.40
Monoclinic
$P2_1/c$
a = 10.211 (2) Å
b = 8.285 (1) Å
c = 19.539 (3) Å
β = 99.32 (1)°
V = 1631.1 (5) Å^3
Z = 4
D_x = 1.370 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54184 Å
Cell parameters from 25 reflections
θ = 10–50°
μ = 0.813 mm^{-1}
T = 293 (2) K
Prism
0.30 × 0.22 × 0.20 mm
Colourless

Data collection

Kuma KM-4 four-circle diffractometer
ω–2θ scans
Absorption correction: none
2409 measured reflections
2325 independent reflections
2053 reflections with $I > 2\sigma(I)$
R_{int} = 0.023

θ_{max} = 60.01°
$h = -11 \rightarrow 11$
$k = 0 \rightarrow 9$
$l = -21 \rightarrow 0$
2 standard reflections every 100 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.151
S = 1.007
2325 reflections
224 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.1017P)^2 + 0.6782P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max}$ = 0.348 e Å^{-3}
$\Delta\rho_{min}$ = −0.248 e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0071 (8)
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

N1—C2	1.390 (3)	N8—C8	1.333 (3)
N1—C6	1.407 (3)	N9—C8	1.333 (3)
N1—C1	1.466 (3)	N9—C4	1.342 (3)
N3—C4	1.362 (3)	O2—C2	1.213 (3)
N3—C2	1.372 (3)	O6—C6	1.237 (3)
N3—C3	1.454 (3)	C4—C5	1.364 (3)
N7—C8	1.357 (3)	C5—C6	1.402 (3)
N7—C5	1.396 (3)		
C8—N7—C5	105.7 (2)	O2—C2—N1	122.2 (2)
C8—N7—C7	124.7 (2)	N3—C2—N1	116.2 (2)
C5—N7—C7	129.5 (2)	O6—C6—C5	127.5 (2)
C8—N9—C4	103.7 (2)	O6—C6—N1	120.3 (2)
O2—C2—N3	121.6 (2)	C5—C6—N1	112.2 (2)

The positions of the H atoms of the amino group were located from difference electron-density maps and refined; all other H atoms were placed in calculated positions and refined using a riding model. Isotropic displacement parameters of 1.5U_{eq} of their respective carrier atoms were used for all H atoms.

Data collection: Kuma KM-4 diffractometer software. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *XP* in *SHELXTL-Plus* (Sheldrick, 1989). Software used to prepare material for publication: *SHELXL*93. Geometrical calculations: *PARST* (Nardelli, 1983).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1110). Services for accessing these data are described at the back of the journal.

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2,6-Dibenzoyl-1,4-benzoquinone

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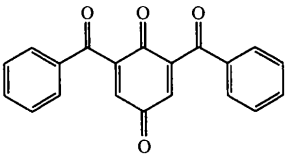
Abstract

In contrast to the stacking characteristic of quinones, the title compound, $C_{20}H_{12}O_4$, forms a two-dimensional network of C—H···O hydrogen bonds. The molecule has an unsymmetrical butterfly shape with the two benzoyl O atoms lying out of the plane of the quinonoid ring. The unusual conformation is a result of the crystal packing and the numerous weak hydrogen bonds.

Comment

C—H···O hydrogen bonds play an important role in the crystal structures of many organic compounds (Desiraju, 1996). It is well known that the strength of C—H···O hydrogen bonds depends on the acidity of the relevant C—H group. In this context, the title compound, 2,6-dibenzoyl-1,4-benzoquinone, (I), is of interest because it has a profusion of potential C—H···O hydrogen-bond donors (quinone and phenyl C—H) and acceptors (quinone and benzoyl C=O) in the molecular skeleton. The molecule can exist in three different conformations: the quinone ring and benzoyl carbonyl groups coplanar; the benzoyl carbonyl groups twisted out of the quinonoid plane and on the same face; the benzoyl carbonyl groups twisted out of the quinonoid plane but on opposite faces. The crystal structure of the title compound was undertaken to ascertain if there is any connection between the molecular conformation in the crystal and the intermolecular C—H···O hydrogen-bonding pattern.



(I)

In the crystal structure of the title quinone, both the benzoyl O atoms are out of the plane of the quinonoid ring; O7 is twisted out of the plane by 112.2 (4)° and O14 by −77.0 (4)°. The quinonoid H11 atom forms a C—H···O hydrogen bond with the benzoyl O14 atom of the [100]-translated molecule [C···O 3.154 (4) Å]. These molecules form another C—H···O bond between the quinonoid H9 and the benzoyl O7 atom [C···O 3.406 (4) Å]. The phenyl H18 and H19 atoms form C—H···O hydrogen bonds with quinonoid O10 atoms of distinct *b*-glide related molecules [C···O 3.368 (5) and 3.602 (5) Å]. Additional C—H···O bonds are formed between the phenyl H atoms, H2 and H3, and the benzoyl O7 atom of the screw-axis related molecule along [100] [C···O 3.502 (5) and 3.539 (5) Å]. In effect, the structure is two-dimensionally C—H···O hydrogen bonded. Short C20···H20 contacts of 2.744 (5) Å are present between phenyl rings in *a*-glide related molecules. The unsymmetrical butterfly shape of the molecule is unexpected and may be attributed to the numerous C—H···O hydrogen bonds that determine the molecular conformation in the crystal. The characteristic stacking, typical of quinones (Bernstein, Cohen & Leiserowitz, 1974), is not found here.

Crystal structures where the two- and three-dimensional networks are supported solely by C—H···O hydrogen bonding have not been generally discussed in detail, perhaps because of the supposed weakness of this interaction; the crystal structure of trimethylisocyanurate has such a complex three-dimensional network. Its structure was originally determined without H-atom positions (Belaj & Nachbaur, 1987). We subsequently redetermined the structure with the H atoms included (Thalladi, Panneerselvam, Carrell, Carrell & Desiraju, 1995). Although the C—H···O hydrogen bond is definitely weak, the phenomenon may be significant when several such hydrogen bonds are found in a crystal and when factors such as cooperativity and polarization become important.

When crystal-packing forces and hydrogen bonding are important, changes in the molecular conformation are likely. In order to rationalize the skewed conformation of the molecule in the crystal, *AM*1 semi-empirical