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9,9-Dimethoxy-7,11-diphenyl-2,4-diazaspiro[5.5]undecane-1,3,5-trione monohydrate

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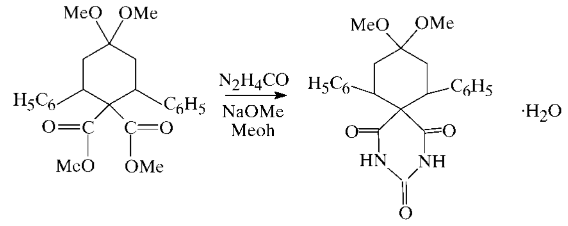
Due to steric repulsions, the cyclohexane ring in the title compound, $C_{23}H_{24}N_2O_5\cdot H_2O$, shows some bond-length abnormalities and adopts a chair conformation. The pyrimidine and cyclohexane rings are approximately perpendicular to each other, and the phenyl rings are equatorial. C—H···π and N—H···O intermolecular interactions, as well as C—H···O inter- and intramolecular interactions, occur between the molecules. In addition to van der Waals interactions, the water molecule interacts with the pyrimidinetrione ring to stabilize the structure.

Comment

Spiro compounds are biologically important because of the diverse nature of their medicinal properties. Pyrimidine derivatives are widely used in antiviral chemotherapy. A series of spiro-pyrimidine nucleoside analogues, such as 2′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-3′-spiro-5″-(4″-amino-1″,2″-oxathiole-2″,2″-dioxide)pyrimidine (TSAO), were found to inhibit human immunodeficiency virus type 1 (HIV-1) replication at a concentration of 0.06–0.8 μ*M*, but were not cytotoxic at between 1000- and 10 000-fold higher concentrations (Balzarini *et al.*, 1992). These derivatives were also found to be effective against various HIV-2, simian immunodeficiency virus, Moloney murine sarcoma virus, and other RNA or DNA viruses (Balzarini *et al.*, 1992), and they have proved to be highly specific inhibitors of the RNA-dependent DNA-polymerase function of the HIV-1 reverse transcriptase enzyme (Balzarini *et al.*, 1992).

The cyclohexane triones are a novel group of synthetic antibacterial agents, which are active against the gram-positive bacteria *Haemophilus influenzae* and *Mycobacterium smegmatis*. In general, these compounds behave in a manner similar to that of hexachlorophene, inhibiting the transport of low molecular weight hydrophilic substances into bacteria. They may express more than one type of antibacterial effect (Lloyd *et al.*, 1988).

Spiro-pyrimidinetriones containing the barbituric acid moiety exhibit a broad spectrum of chemotherapeutic properties, such as hypnotic, antitumour, antiviral, anticonvulsant, analgesic and toxic properties. They possess bacteriostatic, antidiabetic, antiarrhythmic and anti-inflammatory properties, and have been found to possess antifungal activity against *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas vulgaris* (Bhasker Reddy *et al.*, 1992). Against this background, the crystal structure of the title compound, (I), has been determined and the results are presented here.



(I)

The bond lengths in (I) involving atoms C2 and C6 are slightly abnormal, but a similar situation has been observed in related structures (Toupet & Messager, 1983). This may be due to steric repulsion between the cyclohexane ring and the phenyl substituents at the C2 and C6 positions. Other than this, the bond lengths and angles in (I) are normal (Allen *et al.*, 1987).

The cyclohexane ring adopts a chair conformation, with atoms C1 and C4 deviating from the best plane by 0.632 (3) and −0.595 (3) Å, respectively. This is confirmed by the

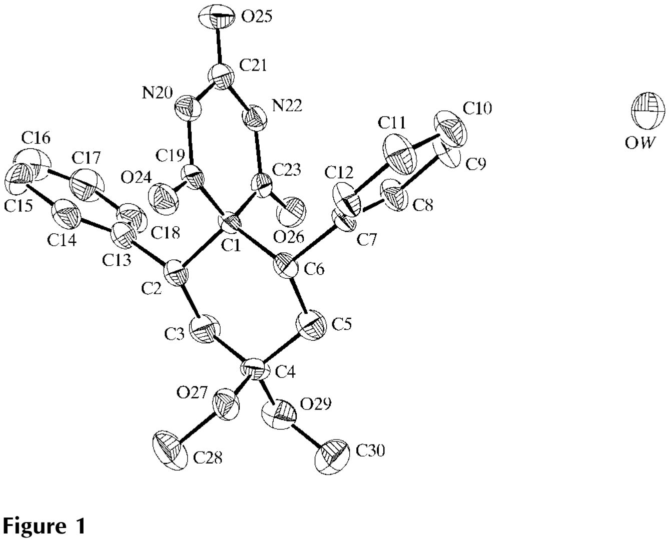


Figure 1
The molecular structure of (I), showing 30% probability displacement ellipsoids and the atomic numbering scheme. H atoms have been omitted for clarity. Ring *A* is the phenyl ring containing atoms C7–C12 and ring *B* is the phenyl ring containing atoms C13–C18.

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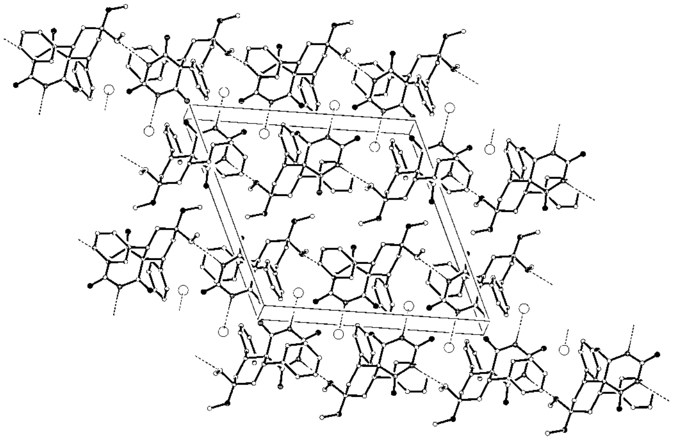

Figure 2
A packing diagram for (I), viewed down the *b* axis. C atoms are denoted by small open circles, O atoms by small dark circles and N atoms by hatched circles; the water O atom is partially shaded. The dashed lines represent the hydrogen-bonding scheme.

puckering amplitude Q_T of 0.5045 (Nardelli, 1983). The two phenyl rings (*A* and *B*) and the pyrimidine ring are planar, and the phenyl rings are oriented at an angle of 68.9 (1)° to each other. Phenyl rings *A* and *B* are oriented at angles of 65.8 (1) and 58.9 (1)°, respectively, to the mean plane of the cyclohexane ring. The pyrimidine ring and the mean plane of the cyclohexane ring are approximately perpendicular to each other, which is seen from the orientation angle of 89.0 (1)°. This is in agreement with the theoretical conclusion for most spiro compounds (Finar, 1985). The two phenyl rings have an equatorial orientation and the corresponding torsion angles are C13—C2—C3—C4 of −176.2 (3)° and C4—C5—C6—C7 of 179.0 (3)°.

Interestingly, weak intramolecular π–π interactions occur between the pyrimidine and phenyl rings, with a $Cg\cdots Cg$ distance (*Cg* is the ring centroid) of 3.9019 Å (α = 59.54°; α is the dihedral angle between the planes concerned) for ring *A* and 3.7088 Å (α = 52.03°) for ring *B* (Jorgensen & Severance, 1990; Hunter & Sanders, 1990; Desiraju, 1989). In addition to this, one of the phenyl rings also participates in an intermolecular C—H$\cdots\pi$ interaction, between atom C16 and the terminal C30 atom (Desiraju, 1989).

The water molecule of (I) interacts with the pyrimidinetrione ring, making a strong intermolecular hydrogen bond with atom N20 and intermolecular interactions with atoms O24 and O25, the contact distances of which are less than the sum of the van der Waals radii, which stabilize the crystal packing. The other N atom (N22) of the pyrimidinetrione ring is involved in an intermolecular hydrogen bond with the carboxyl O atom (O27). In addition, there are some weak C—H$\cdots$O intra- and intermolecular interactions which stabilize the structure (Table 1).

The packing of the molecule of (I), viewed down the *b* axis, is shown in Fig. 2. The molecules are packed in a discrete fashion and are stabilized by van der Waals forces in addition to the above-mentioned interactions.

Experimental

The title compound was prepared by mixing dimethyl 2,6-diphenyl-4,4-dimethoxycyclohexane-1,1-dicarboxylate (0.01 mol) with urea (0.01 mol) and methanol (10 ml), and then adding a 10% solution of sodium methoxide (5 ml). The mixture was refluxed for 12 h, then cooled and poured on to crushed ice mixed with concentrated hydrochloric acid. The product which separated out was filtered off and purified. Recrystallization was carried out from an ethyl acetate–hexane (2:3) mixture.

Crystal data

$C_{23}H_{24}N_2O_5\cdot H_2O$
M_r = 426.46
Monoclinic, $P2_1/c$
a = 14.559 (2) Å
b = 10.755 (2) Å
c = 15.346 (4) Å
β = 114.100 (10)°
V = 2193.5 (8) Å^3
Z = 4
D_x = 1.291 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5812 reflections
θ = 2.4–27.5°
μ = 0.09 mm^{-1}
T = 293 (2) K
Rectangular, colourless
0.60 × 0.55 × 0.50 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
5812 measured reflections
4726 independent reflections
1053 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.096
$\theta_{\rm max}$ = 27.5°
$h = -1 \rightarrow 15$
$k = -1 \rightarrow 13$
$l = -19 \rightarrow 18$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.067
$wR(F^2)$ = 0.192
S = 0.74
4726 reflections
282 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0589P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max}$ = 0.024
$\Delta\rho_{\rm max}$ = 0.34 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.20 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

*Cg*3 is the centroid of the C7–C12 phenyl ring.

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N20—H20$\cdots$O$W^{\rm i}$	0.86	2.10	2.897 (6)	154
N22—H22$\cdots$O27$^{\rm ii}$	0.86	2.13	2.984 (6)	170
C3—H3$A\cdots$O26	0.97	2.50	3.087 (7)	119
C30—H30$C\cdots$O26$^{\rm iii}$	0.96	2.60	3.517 (9)	160
C16—H16$\cdots Cg3^{\rm ii}$	0.93	3.06	3.51	112

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

It was not possible to locate the H atoms of the water molecule. Other H atoms were treated as riding, with C—H distances in the range 0.93–0.98 Å and an N—H distance of 0.86 Å.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1983).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: DE1191). Services for accessing these data are described at the back of the journal.

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