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2-(4-Methylbenzoyloxymethyl)-5-(5-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)-tetrahydrofuran-3-yl 4-methylbenzoate

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.003 Å
R factor = 0.041
wR factor = 0.109
Data-to-parameter ratio = 9.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The title compound, $C_{26}H_{26}N_2O_7$, is a thiamidine derivative. Geometric parameters are in the usual ranges. The crystal packing is stabilized by a classical N—H···O hydrogen bond, several weak C—H···O hydrogen bonds and a π–π stacking interaction.

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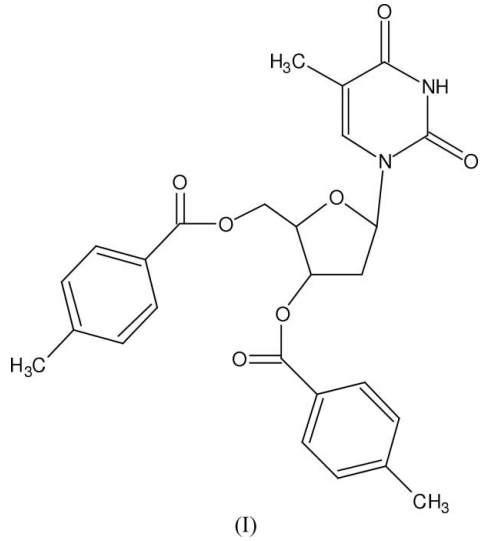
Comment

The title compound, (I), is a derivative of thiamidine, an intermediate in the preparation of zidovudine (AZT), the first drug approved for the treatment of AIDS and HIV infection (Mitsuya *et al.*, 1990; De Clercq, 1994). It contains a ribose unit, a pentose (five-carbon sugar) that is a component of ribonucleic acid (RNA), where it alternates with phosphate groups to form the back-bone of the RNA polymer and binds to nitrogenous bases. It also contains thymine, a pyrimidine base, linked to deoxyribose to form the nucleoside deoxythymidine in animal cells. Thymidine is significant because of its involvement in the biosynthesis of DNA and in the preservation and transfer of genetic information. Nucleoside derivatives are involved in important functions in cellular metabolism and are used to synthesize enzyme inhibitors, antiviral agents and anticancer agents (Yarchoan *et al.*, 1989). The present reaction is used to protect the hydroxyl groups during the preparation of AZT. Recently, we reported the crystal structure of a derivative of pyrimidine (Yathirajan *et al.*, 2007), and as a continuation of our research work on the structures of bioactive molecules and drug intermediates, we now report the crystal structure of (I), a new derivative of thiamidine.



(I)

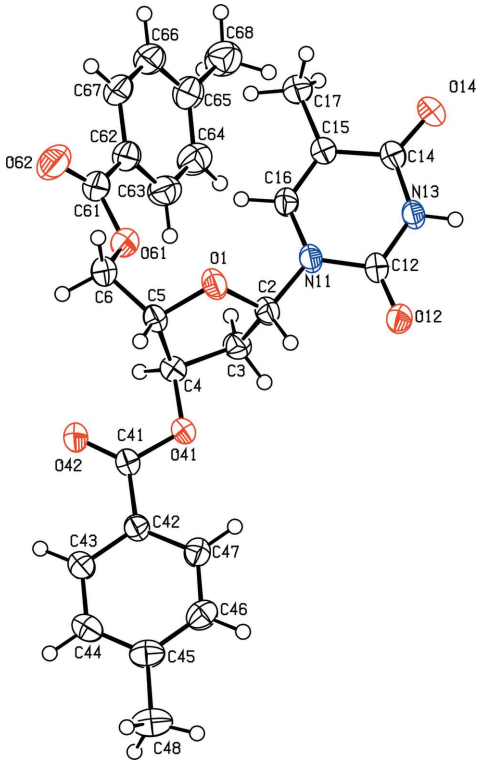


Figure 1
The molecular structure of the title compound, with the atom numbering. Displacement ellipsoids are drawn at the 50% probability level.

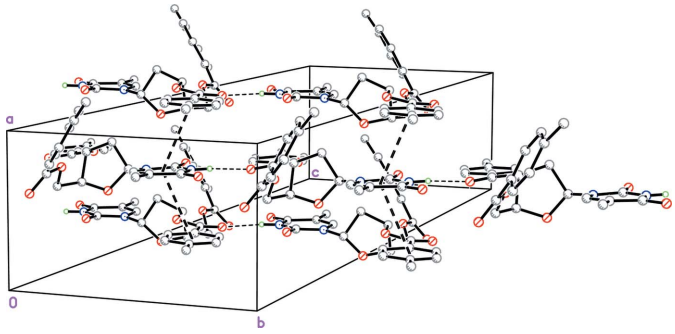


Figure 2
A packing diagram of the title compound. Only H atoms bonded to N are shown. Hydrogen bonds are shown as dashed lines and π–π stacking interactions as open dashed bonds.

A perspective view of compound (I) is shown in Fig. 1. Bond lengths and angles can be regarded as normal (Cambridge Structural Database, Version 5.28, November 2006; *MOGUL* Version 1.1; Allen, 2002; Bruno *et al.*, 2004). The tetrahydrofuran ring adopts an envelope conformation (Table 1), with atoms C2, O1 C5 and C4 in a common plane and atom C3 deviating by 0.497 (3) Å from this plane. Both carboxylate groups are only slightly twisted out of the plane of the *para*-methylphenyl ring to which they are attached (Table 1).

An intermolecular N—H···O hydrogen bond (Table 2) links the molecules into chains running along the *b* axis. The crystal packing is further stabilized by weak C—H···O hydrogen bonds (Table 2). In addition to these *X*—H···O bonds, there is a π–π stacking interaction between the dihydropyrimidine ring and the aromatic rings comprising atoms C42–C47 at $(-\frac{1}{2}+x, \frac{3}{2}-y, 1-z)$ (centroid-to-centroid distance 3.478 Å) and at $(\frac{1}{2}+x, \frac{3}{2}-y, 1-z)$ (centroid-to-centroid distance 3.508 Å). The N—H···O hydrogen bond and the π–π stacking interaction are illustrated in Fig. 2.

Experimental

Toluoyl chloride (680 mg, 4.4 mmol) was added to a solution of thymidine (485 mg, 2 mmol) in dry pyridine (10 ml). The solution was stirred at room temperature for 2 h. The mixture was partitioned between $CHCl_3$ (50 ml) and 5% $NaHCO_3$ (50 ml), and the organic layer was collected, washed with 5% $NaHCO_3$ (50 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The compound was crystallized from a solution in chloroform (m.p. 471–473 K). Analysis for $C_{26}H_{26}N_2O_7$, found (calculated): C 65.16 (65.26), H 5.39 (5.48), N: 5.76% (5.85%).

Crystal data

$C_{26}H_{26}N_2O_7$
M_r = 478.49
Orthorhombic, $P2_12_12_1$
a = 6.4353 (4) Å
b = 10.6994 (7) Å
c = 34.373 (2) Å
V = 2366.7 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 173 (2) K
0.41 × 0.37 × 0.21 mm

Data collection

Stoe IPDS II two-circle diffractometer
Absorption correction: none
14101 measured reflections
2915 independent reflections
2617 reflections with $I > 2\sigma(I)$
R_{int} = 0.059

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.109
S = 1.01
2915 reflections
324 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.21 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

Table 1
Selected torsion angles (°).

C5—O1—C2—C3	22.2 (2)	O41—C41—C42—C47	7.2 (3)
O1—C2—C3—C4	−32.4 (2)	O42—C41—C42—C43	7.1 (3)
C2—C3—C4—C5	30.0 (2)	O61—C61—C62—C63	18.8 (3)
C2—O1—C5—C4	−2.8 (2)	O62—C61—C62—C67	17.3 (4)
C3—C4—C5—O1	−17.7 (2)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N13—H13···O42^{i}	0.88 (3)	1.96 (3)	2.842 (2)	175 (3)
C2—H2···O12	1.00	2.34	2.751 (2)	104
C6—H6A···O14^{ii}	0.99	2.41	3.353 (2)	159
C16—H16···O61	0.95	2.59	3.473 (2)	156
C43—H43···O12^{ii}	0.95	2.44	3.373 (2)	168
C68—H68B···O62^{iii}	0.98	2.55	3.453 (4)	153

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

In the absence of significant anomalous scattering effects, Friedel pairs were merged. The absolute configuration was assigned arbitrarily. Carbon-bound H atoms were found in a difference map, but they were refined using a riding model, with C—H = 0.95–1.00 Å and U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(C_{methyl}). The methyl groups were allowed to rotate but not to tip. The amino H atom was freely refined.

Data collection: *X-AREA* (Stoe & Cie, 2001); cell refinement: *X-AREA*; data reduction: *X-AREA*; program(s) used to solve structure: *SIR2002* (Burla *et al.*, 2003); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003) and *XP* in *SHELXTL-Plus* (Sheldrick, 1991); software used to prepare material for publication: *SHELXL97*.

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