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(4*RS*,1′*RS*)-Methyl 1-Phenyl-2-piperidinoethyl 1,4-Dihydro-2,6-dimethyl-4-(2-thienyl)pyridine-3,5-dicarboxylate Methanol Solvate, $C_{27}H_{32}N_2O_4S.1.5CH_4O$

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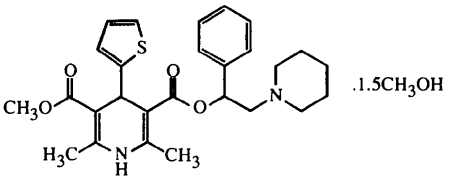
Abstract

The two independent molecules in the asymmetric unit have similar conformations. The 4-thienyl-1,4-dihydropyridine moieties adopt a flat boat conformation commonly observed for 4-aryl-1,4-dihydropyridine derivatives with the 4-thienyl group in a pseudo-axial orientation. The thienyl and phenyl rings are perpendicular to each other. The six methanol molecules in the unit cell stabilize the crystal structure through intermolecular hydrogen bonds involving the N atoms of the dihydropyridine and the piperidine rings of both molecules.

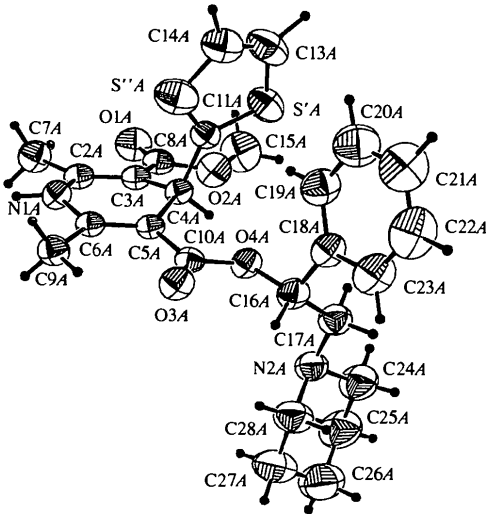
Comment

Many 1,4-dihydropyridine derivatives are well known as belonging to the most potent class of calcium channel antagonists. In the course of the development of effective antagonists, the title compound, (I), was synthesized

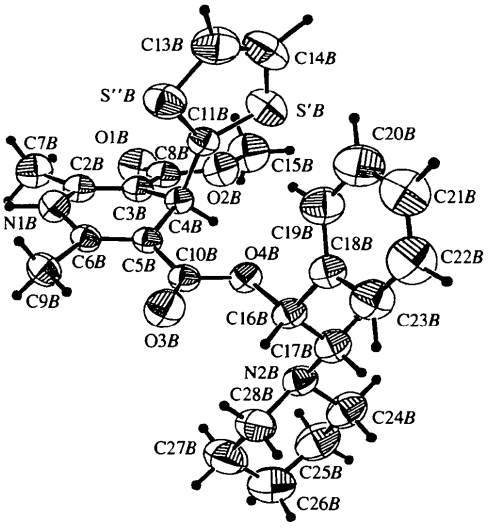


(I)

(Araki, Ao, Inui & Aihara, 1983). The structure analysis has been undertaken in order to confirm the relative configuration of the two chiral centers and to understand the three-dimensional structure.



Molecule *A*



Molecule *B*

Fig. 1. The molecular structures showing 50% probability displacement ellipsoids (*ORTEP*II; Johnson, 1976).

There are two crystallographically independent molecules (*A* and *B*) in the asymmetric unit. As shown in Fig. 1, both of the molecules have quite similar conformations. The relative configuration of the compound is (*RS*,*RS*). The 4-thienyl-1,4-dihydropyridine moiety of both molecules adopts a flat boat conformation typical of 4-aryl-1,4-dihydropyridines, with the 4-thienyl group in a pseudo-axial orientation (Triggle, Shefter & Triggle, 1980; Fossheim *et al.*, 1982, 1988). The piperidine ring of both molecules adopts a chair conformation. Bond lengths and angles, except those of the thienyl rings, are within the expected range. The thienyl rings of both molecules exhibit 180° rotational disorder.

There are four rings in the molecule: dihydropyridine (*A*), thienyl (*B*), phenyl (*C*) and piperidinyl (*D*). It is likely that the relative orientations of these rings are important for the biological activity. Ring *B* is nearly perpendicular to ring *C*, and ring *C* is nearly perpendicular to ring *D*. Both rings *C* and *D* are approximately perpendicular to the mean plane of ring *A*. There is no interaction between the two independent molecules. Three methanol molecules in the asymmetric unit stabilize the crystal structure by intermolecular hydrogen bonds. They are bonded to the N atoms of the dihydropyridine and piperidine rings of both molecules, and also to each other.

Experimental

Single crystals of (I) were obtained by slow evaporation of a methanol solution.

Crystal data

$C_{27}H_{32}N_2O_4S.1.5CH_4O$
M_r = 528.68
Triclinic
$P\bar{1}$
a = 14.074 (2) Å
b = 15.738 (2) Å
c = 13.588 (2) Å
α = 96.82 (1)°
β = 100.61 (1)°
γ = 74.63 (1)°
V = 2844.5 (7) Å^3
Z = 4
D_x = 1.23 Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
λ = 1.54184 Å
Cell parameters from 25 reflections
θ = 40–45°
μ = 1.307 mm^{-1}
T = 294 K
Prism
0.5 × 0.4 × 0.3 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
8830 measured reflections
8431 independent reflections
7366 reflections with $I > 3\sigma(I)$
R_{int} = 0.007
θ_{max} = 59.96°
h = −15 → 15
k = −17 → 17
l = 0 → 15
3 standard reflections
frequency: 120 min
intensity decay: −7.91%

Refinement

Refinement on F
R = 0.049
wR = 0.070
S = 1.884
7366 reflections
668 parameters
H atoms included but not refined
$w = 1/[\sigma^2(F) + 0.0004F^2 + 1]$
$(\Delta/\sigma)_{max}$ = 0.008
$\Delta\rho_{max}$ = 0.2812 e Å^{-3}
$\Delta\rho_{min}$ = −0.0507 e Å^{-3}
Extinction correction: isotropic (Zachariasen, 1963)
Extinction coefficient: 7.5 × 10^{-7}
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

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

O1*A*—C8*A*	1.207 (3)	O1*B*—C8*B*	1.211 (3)
O2*A*—C8*A*	1.343 (3)	O2*B*—C8*B*	1.340 (3)
O2*A*—C15*A*	1.437 (3)	O2*B*—C15*B*	1.437 (3)
O3*A*—C10*A*	1.213 (2)	O3*B*—C10*B*	1.213 (2)
O4*A*—C10*A*	1.359 (3)	O4*B*—C10*B*	1.355 (3)
O4*A*—C16*A*	1.444 (3)	O4*B*—C16*B*	1.445 (3)
N1*A*—C2*A*	1.379 (2)	N1*B*—C2*B*	1.376 (2)
N1*A*—C6*A*	1.375 (3)	N1*B*—C6*B*	1.378 (3)
N2*A*—C17*A*	1.468 (3)	N2*B*—C17*B*	1.464 (3)
N2*A*—C24*A*	1.471 (3)	N2*B*—C24*B*	1.476 (3)
N2*A*—C28*A*	1.476 (3)	N2*B*—C28*B*	1.470 (3)
C8*A*—O2*A*—C15*A*	117.4 (2)	C8*B*—O2*B*—C15*B*	116.6 (2)
C10*A*—O4*A*—C16*A*	117.8 (1)	C10*B*—O4*B*—C16*B*	116.9 (1)
C2*A*—N1*A*—C6*A*	123.4 (2)	C2*B*—N1*B*—C6*B*	123.0 (2)
C17*A*—N2*A*—C24*A*	106.8 (2)	C17*B*—N2*B*—C24*B*	108.4 (2)
C17*A*—N2*A*—C28*A*	110.7 (2)	C17*B*—N2*B*—C28*B*	113.2 (2)
C24*A*—N2*A*—C28*A*	109.7 (2)	C24*B*—N2*B*—C28*B*	109.6 (2)
N1*A*—C2*A*—C3*A*	119.6 (2)	N1*B*—C2*B*—C3*B*	119.3 (2)
N1*A*—C2*A*—C7*A*	113.8 (2)	N1*B*—C2*B*—C7*B*	112.6 (2)
N1*A*—C6*A*—C5*A*	119.6 (2)	N1*B*—C6*B*—C5*B*	119.4 (2)
N1*A*—C6*A*—C9*A*	113.6 (2)	N1*B*—C6*B*—C9*B*	112.5 (2)
O1*A*—C8*A*—O2*A*	121.2 (2)	O1*B*—C8*B*—O2*B*	120.9 (2)
O1*A*—C8*A*—C3*A*	128.4 (2)	O1*B*—C8*B*—C3*B*	127.4 (2)
O2*A*—C8*A*—C3*A*	110.5 (2)	O2*B*—C8*B*—C3*B*	111.7 (2)
O3*A*—C10*A*—O4*A*	121.5 (2)	O3*B*—C10*B*—O4*B*	121.0 (2)
O3*A*—C10*A*—C5*A*	127.7 (2)	O3*B*—C10*B*—C5*B*	126.6 (2)
O4*A*—C10*A*—C5*A*	110.8 (1)	O4*B*—C10*B*—C5*B*	112.4 (2)
O4*A*—C16*A*—C17*A*	106.4 (2)	O4*B*—C16*B*—C17*B*	107.8 (2)
O4*A*—C16*A*—C18*A*	111.7 (2)	O4*B*—C16*B*—C18*B*	110.7 (2)
N2*A*—C17*A*—C16*A*	117.1 (2)	N2*B*—C17*B*—C16*B*	115.3 (2)
N2*A*—C24*A*—C25*A*	112.3 (3)	N2*B*—C24*B*—C25*B*	112.0 (3)
N2*A*—C28A—C27A	111.6 (2)	N2*B*—C28*B*—C27*B*	111.1 (2)

The structure was solved by direct methods using *MULTAN*-11/82 (Main *et al.*, 1982) and subsequent Fourier syntheses, and refined by full-matrix least-squares techniques using *MolEN* (Fair, 1990). Electron density suggested 180° rotational disorder around the C4—C11 bond in the thienyl rings in both molecules. To account for this disorder, the two atoms connected to C11 were treated as pseudo-atoms produced by a superposition of sulfur (S) and carbon (C). The scattering factors for the pseudo-atoms were constructed using the composition: S′*A* = 0.7S + 0.3C, S″*A* = 0.3S + 0.7C and S′*B* = S″*B* = 0.5S + 0.5C. The final difference Fourier map showed no large residual peaks around the hybrid atoms. All non-H atoms were refined anisotropically. The positions of H atoms bonded to N and O atoms were located from difference Fourier maps and all other H atoms were calculated geometrically. The calculations were carried out on a VAX3900 computer.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *MolEN* (Fair, 1990). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *MolEN*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: VJ1043). Services for accessing these data are described at the back of the journal.

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Lactosylurea Dihydrate

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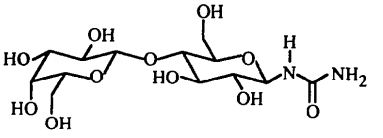
Abstract

Lactosylurea dihydrate [(4-*O*-β-D-galactopyranosyl-1-*N*-β-D-glucopyranosyl)urea], $C_{13}H_{24}N_2O_{11}.2H_2O$, crystallizes as a dihydrate in the space group $P1$. There are twelve distinct hydrogen bonds, including one intramolecular hydrogen bond joining the glucose and galactose rings. This structure determination establishes that the reaction of urea with lactose does not lead to rearrangement or to an acyclic form of lactose and that the urea forms a β-*N*-glycoside linkage.

Comment

As the major carbohydrate component of whey (Gouda, Larm & Larsson, 1980), lactose is a surplus carbohydrate which is of interest as a reusable resource. Reaction with urea to produce a lactosylurea makes it more useful as an animal feed (Merry, Smith & McAllan, 1982). Reduction of lactosylurea may also yield a cheap starting material for the manufacture of polyurethane. The structure of the urea-modified saccharide, (I), has been inferred from spectroscopy and chemical means (Benn & Jones, 1960; Segal, O'Connor & Eggerton, 1960; Shkantova, Dudkin & Grinshpun, 1967; Cerbulis, Pfeffer & Farrell, 1978), but there has been disagreement on whether or not rearrangement or ring opening occurs.



(I)

This structure determination shows that the lactosylurea has a β-*N*-glycoside linkage and that the ring structure is otherwise unchanged. There is an intramolecular hydrogen bond joining the O3′ H atom of glucose to O5 of galactose, as is also found in the structures of β-lactose (Hirotsu & Shimada, 1974) and in α-lactose monohydrate (Noordik, Beurskens, Visser & Gould, 1984). The comparable O···O distances are 2.744, 2.707 and 2.813 Å, respectively. There are eleven other relatively strong hydrogen bonds, including those to the two water molecules of hydration.

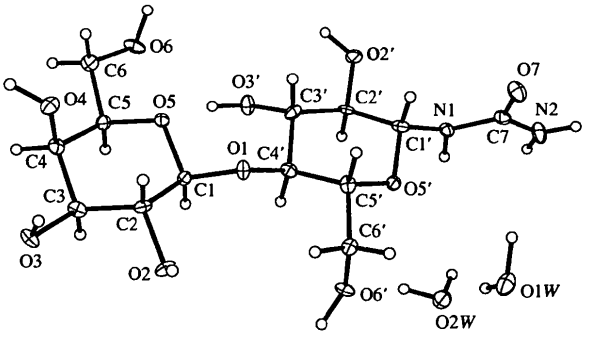


Fig. 1. The molecular structure of (I) showing 50% probability displacement ellipsoids. H atoms are shown as small circles of arbitrary radii.

Experimental

The title compound was prepared following the literature procedure of Merry, Smith & McAllan (1982).

Crystal data

$C_{13}H_{24}N_2O_{11}.2H_2O$
M_r = 420.37

Cu $K\alpha$ radiation
λ = 1.54178 Å