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Senecivernine Dihydrate

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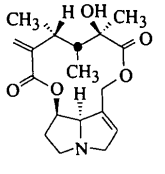
Abstract

12-Hydroxy-14-methyl-21-norsenecionan-11,16-dione dihydrate, $C_{18}H_{25}NO_5.2H_2O$, has two independent molecules of the alkaloid and four water molecules in the asymmetric unit. In both alkaloid molecules, one of the five-membered rings is *exo* buckled and the conformations of the two molecules are very similar with no major differences in the torsion angles. The structure is stabilized by a network of hydrogen bonds involving N and hydroxy (including water) O atoms with O···O and N···O separations in the range 2.73 (1)–2.93 (1) Å.

Comment

Senecivernine, (I), was obtained from *Senecio moorei R. E. Fr.* (Benn & Mathenge, 1994). This alkaloid was first isolated from *Senecio vernalis Walkstein et Kit.* (Röder, Wiedenfeld & Pastewka, 1979) and assigned the structure (I) without stereochemistry. Crystallization of our material from aqueous methanol afforded crystals suitable for X-ray analysis, which resulted in the relative configurations shown in Fig. 1.



(I)

The absolute stereochemistry (7*R*,8*R*,12*R*,13*R*,14*R*) may be inferred from that known for the retronecine portion of (I) (Fridrichsons, Mathieson & Sutor, 1963; Leonard, 1960).

The bond distances and angles in the two molecules are equivalent to within 3σ limits except the angles O23*a*—C12*a*—C18*a* [113.8 (9)°] and O23*b*—C12*b*—C18*b* [109.0 (10)°]. The average bond distances are C_{sp^3}—C_{sp^3} 1.54 (2), C_{sp^3}—C_{sp^2} 1.51 (2), C_{sp^3}—O 1.44 (1), C_{sp^2}—O 1.36 (1), C—N 1.49 (2), C=C 1.33 (2) and C=O 1.20 (1) Å. There are no outstanding conformational differences in the two independent molecules. In the pyrrolizidine moieties, the five-membered rings C1*a*, C2*a*, C3*a*, N4*a*, C8*a* and C1*b*, C2*b*, C3*b*, N4*b*, C8*b* are essentially planar with maximum deviations of 0.050 (10) and 0.092 (15) Å, respectively, while the other five-membered rings have C6*a*- and C6*b*-envelope conformations with these atoms 0.650 (12) and 0.579 (13) Å, respectively, out of the planes of the remaining atoms in the rings.

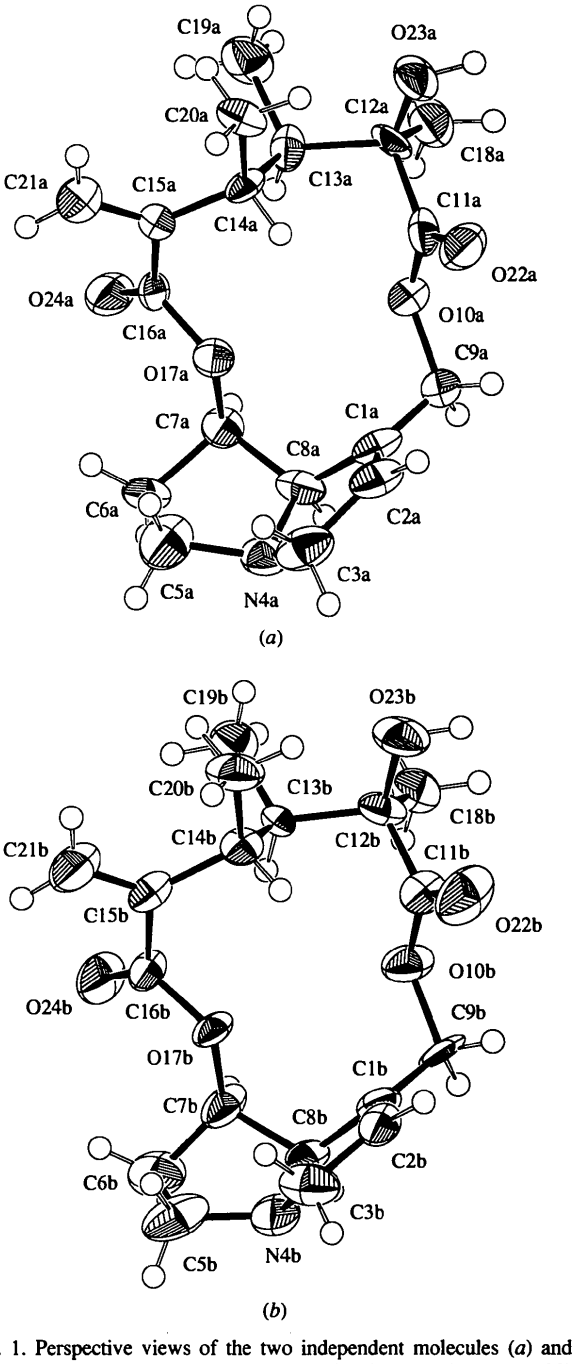


Fig. 1. Perspective views of the two independent molecules (*a*) and (*b*) of senecivernine. Displacement ellipsoids are shown at 50% probability levels; H atoms were assigned arbitrary radii.

Experimental

The natural product (I) was crystallized from an aqueous methanol solution.

Crystal data

$C_{18}H_{25}NO_5.2H_2O$	Mo $K\alpha$ radiation
M_r = 371.43	λ = 0.71069 Å
Triclinic	Cell parameters from 18 reflections
$P\bar{1}$	θ = 9.0–15.0°
a = 10.232 (3) Å	μ = 0.095 mm^{-1}
b = 14.964 (7) Å	T = 295 (1) K
c = 6.826 (4) Å	Large needle
α = 93.81 (4)°	0.80 × 0.37 × 0.30 mm
β = 98.02 (3)°	Colourless
γ = 104.37 (3)°	
V = 997.0 (8) Å^3	
Z = 2	
D_x = 1.237 Mg m^{-3}	

Data collection

Rigaku AFC-6*S* diffractometer	R_{int} = 0.041
ω–2θ scans	θ_{max} = 25°
Absorption correction: none	$h = 0 \rightarrow 12$
3742 measured reflections	$k = -17 \rightarrow 17$
3525 independent reflections	$l = -7 \rightarrow 7$
1864 observed reflections [$I > 2\sigma(I)$]	3 standard reflections frequency: 100 min intensity decay: 36.1%

Refinement

Refinement on F	$\Delta\rho_{max}$ = 0.33 e Å^{-3}
R = 0.0802	$\Delta\rho_{min}$ = −0.28 e Å^{-3}
wR = 0.0804	Extinction correction: none
S = 3.43	Atomic scattering factors from Cromer & Mann (1968) and Stewart, Davidson & Simpson (1965)
1864 reflections	
488 parameters	
$w = 1/[\sigma^2(F_o) + 0.019F_o^2]$	
$(\Delta/\sigma)_{max}$ = 0.02	

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
O1	0.6292	0.6472	0.2677	11.7 (5)
O2	0.6468 (10)	0.6587 (6)	0.8545 (12)	6.5 (3)
O3	−0.2825 (9)	0.4869 (5)	0.739 (2)	6.8 (4)
O4	−0.2299 (16)	0.5154 (10)	0.346 (2)	12.9 (5)
C1*a*	0.0502 (15)	0.7023 (11)	0.726 (2)	5.7 (4)
C2*a*	0.0602 (17)	0.6766 (12)	0.908 (2)	6.8 (4)
C3*a*	−0.0190 (18)	0.7226 (12)	1.034 (2)	8.2 (5)
N4*a*	−0.0883 (13)	0.7734 (9)	0.896 (2)	6.4 (4)
C5*a*	−0.0654 (18)	0.8742 (14)	0.962 (3)	8.9 (6)
C6*a*	−0.0602 (15)	0.9214 (11)	0.776 (2)	6.9 (5)
C7*a*	0.0203 (15)	0.8674 (10)	0.666 (2)	5.1 (4)
C8*a*	−0.0415 (15)	0.7667 (11)	0.706 (2)	5.9 (4)
C9*a*	0.0999 (15)	0.6600 (10)	0.556 (2)	5.5 (5)
O10*a*	0.2105 (12)	0.7266 (8)	0.4836 (18)	5.9 (3)
C11*a*	0.3394 (16)	0.7251 (10)	0.552 (2)	5.0 (4)
C12*a*	0.4419 (15)	0.7928 (10)	0.451 (2)	5.2 (4)
C13*a*	0.4333 (16)	0.8949 (10)	0.525 (2)	5.1 (4)
C14*a*	0.4477 (14)	0.9121 (9)	0.759 (2)	4.0 (3)
C15*a*	0.3863 (15)	0.9885 (9)	0.806 (2)	4.8 (3)
C16*a*	0.2416 (14)	0.9762 (9)	0.717 (2)	4.2 (3)
O17*a*	0.1650 (12)	0.8932 (8)	0.7533 (17)	4.9 (3)
C18*a*	0.3993 (18)	0.7750 (12)	0.230 (2)	7.7 (4)
C19*a*	0.5387 (19)	0.9677 (12)	0.444 (2)	8.2 (5)
C20*a*	0.5967 (14)	0.9255 (11)	0.869 (2)	5.9 (4)
C21*a*	0.4459 (18)	1.0690 (11)	0.919 (3)	7.8 (5)
O22*a*	0.3673 (13)	0.6736 (9)	0.667 (2)	7.0 (4)
O23*a*	0.5711 (12)	0.7829 (8)	0.5163 (19)	6.4 (4)
O24*a*	0.1961 (13)	1.0284 (9)	0.622 (2)	7.1 (4)
C1*b*	0.3377 (15)	0.4382 (10)	0.410 (2)	5.3 (5)
C2*b*	0.3237 (15)	0.4541 (10)	0.602 (3)	5.9 (5)
C3*b*	0.3850 (17)	0.3997 (14)	0.736 (2)	8.4 (5)
N4*b*	0.4716 (13)	0.3602 (10)	0.615 (2)	6.9 (4)
C5*b*	0.4606 (18)	0.2603 (12)	0.631 (3)	7.9 (5)
C6*b*	0.4406 (19)	0.2182 (15)	0.416 (4)	9.7 (6)
C7*b*	0.3601 (15)	0.2712 (10)	0.302 (3)	6.0 (5)
C8*b*	0.4251 (14)	0.3713 (10)	0.401 (2)	5.3 (5)
C9*b*	0.3009 (16)	0.4863 (11)	0.243 (2)	7.0 (4)
O10*b*	0.1850 (12)	0.4249 (9)	0.1023 (19)	6.5 (4)
C11*b*	0.0590 (15)	0.4290 (10)	0.119 (2)	5.2 (4)
C12*b*	−0.0469 (15)	0.3647 (11)	−0.035 (2)	5.4 (5)
C13*b*	−0.0465 (15)	0.2609 (9)	−0.002 (2)	4.2 (4)
C14*b*	−0.0640 (14)	0.2401 (10)	0.216 (2)	4.5 (4)
C15*b*	−0.0056 (15)	0.1577 (9)	0.263 (2)	5.2 (4)
C16*b*	0.1370 (14)	0.1667 (9)	0.237 (2)	4.6 (4)
O17*b*	0.2200 (11)	0.2490 (8)	0.3339 (18)	4.6 (3)
C18*b*	−0.0207 (16)	0.3854 (11)	−0.245 (2)	6.7 (4)
C19*b*	−0.1426 (16)	0.1898 (11)	−0.155 (2)	6.8 (4)
C20*b*	−0.2058 (16)	0.2268 (13)	0.259 (3)	8.0 (5)
C21*b*	−0.0747 (18)	0.0775 (12)	0.313 (3)	9.1 (5)
O22*b*	0.0326 (15)	0.4830 (9)	0.240 (2)	10.0 (4)
O23*b*	−0.1809 (13)	0.3736 (9)	−0.013 (2)	7.6 (4)
O24*b*	0.1784 (13)	0.1126 (8)	0.138 (2)	7.8 (4)

Based on a statistical analysis of intensity distribution and the successful solution and refinement of the structure, the space group was determined to be $P\bar{1}$. Lorentz–polarization and linear decay corrections were applied. The structure was solved by direct methods using *SIR*92 (Altomare *et al.*, 1994) and refined by full-matrix least-squares calculations with the non-H atoms isotropic. Allowance was made for anomalous dispersion (Ibers & Hamilton, 1964). H atoms were located from the ΔF map and those attached to C atoms were included at geometrically idealized positions (C—H, O—H 0.95 Å). All calculations were performed using the *TEXSAN* (Molecular Structure Corporation, 1992) crystallographic package and *SHELX*76 (Sheldrick, 1976), installed on a Silicon Graphics Personal Iris D/35 computer. Molecular graphics were obtained using *ORTEP*II (Johnson, 1976). We attribute the relatively high final R factor (0.080) to the substantial decay of the crystal during data collection.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: FG1006). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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An Unusual C6-Spiro-Fused Cyclouridine Derivative

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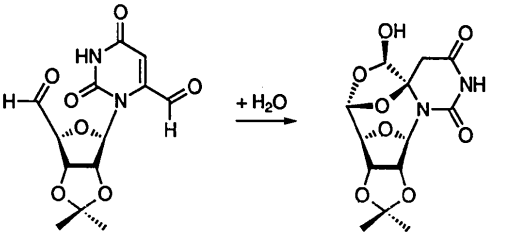
Abstract

The title compound, [3*S*,4*S*,5*R*-(1β,3β,4aα,7aα,13aβ)]-1,4,4a,7a,8,13a-hexahydro-1-hydroxy-6,6-dimethyl-3,-13a:4,8-diepoxy-3*H*,6*H*-dioxolano[4,5-*f*]pyrimido[6,1-*c*][1,4]oxazonine-10,12(11*H*,13*H*)-dione, $C_{13}H_{16}N_2O_8$, is a structurally unusual C6-spiro-fused *anti*-locked dihydrouridine nucleoside derivative arising from the monohydration and subsequent two-step cyclization of a uridine-6,5′-dicarboxaldehyde. The torsion angle O4′—C1′—N1—C6 of the glycosidic linkage is 42.7 (4)°.

Comment

Uridine-6-carboxaldehyde was prepared recently and shown to exhibit a strong tendency towards undergoing hydration and 7,5′-cyclic hemiacetal formation in solution (Groziak & Koohang, 1992). The findings of a detailed investigation (Groziak, Koohang, Stevens & Robinson, 1993) of this ribonucleoside and its 2′-deoxyribofuranose and arabinofuranose counterparts have encouraged us to undertake the development of several new classes of uridine-based cyclonucleosides based upon the 6-formyluridine framework. Among these is a new class of cyclonucleosides expected to arise from hydration reactions involving both formyl groups present in certain uridine-6,5′-dicarboxaldehydes. In the first example of such a cyclonucleoside-forming hydration process, we report that 2′,3′-*O*-isopropylideneuridine-6,5′-dicarboxaldehyde, (1), hydrates in, and crystallizes out of, aqueous solution as the title compound (2). The enantiomorphic identity of (2) was established through its method of synthesis, which did not alter that of the commercially available starting material uridine, known to possess a β-glycosidic linkage and a ribofuranosyl moiety of the D configuration.



(1) (2)

An *ORTEP* (Johnson, 1965) view of (2), together with the standard uridine atom numbering, is provided in Fig. 1. The molecular structure of (2) is a unique blend of some of the structural features determined for certain 6,5′-methano-bridged uridines (Yamagata, Tomita, Usui, Sano & Ueda, 1989), for a 2,5′:2,6′-dianhydro derivative of a 4-*N*-acetylcytosine talofuranoside (David, de Sennyey, Pascard & Guilhem, 1981) and for a 6,3′:6,5′-dianhydro derivative of a 5,5-dibromo-5,6-dihydro-6,6-dihydroxyuracil xylofuranoside (Honjo, Maruyama, Wada & Kamiya, 1984). It is useful to view the cyclonucleoside (2), formally the (6*R*,7*R*,5′S)-6,5′:7,5′-dianhydro version of 5,6-dihydro-6,5′-dihydroxy-6-(dihydroxymethyl)-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)uracil, as simply a monohydrate of (1) arising from a three-step kinetic sequence that involves initially a hydration of the C6-formyl substituent, followed by a 1,2-addition of a hydroxyl group of the resultant 6-hydrate moiety onto the ribofuranose 5′-carboxaldehyde, and finally a Michael-type addition of the hydroxyl group of the resultant 5′-hemiacetal moiety onto the C6 position of the uracil ring. The 7*R* stereochemical configuration in (2) is identical to that found in the 7,5′-cyclic hemiacetal structure of uridine-6-carboxaldehyde (Groziak, Koohang, Stevens & Robinson, 1993), while the 5′*S* and 6*R* configurations can be viewed as the outcomes of stereofacially specific hydroxyl-group addition reactions to the *si* face of the 5′-carbonyl C atom and to the *re* face of the C6 trigonal C atom, respectively. The stereofacial intramolecular 1,2-addition to a nucleoside 5′-carboxaldehyde producing 5′*S* stereochemistry is well precedented (Rabi & Fox, 1972).