C10	0.3478 (6)	0.1926 (4)	0.3635 (5)	4.5 (1)
C11	0.4698 (6)	0.2601 (4)	0.3749 (4)	4.5 (1)
C12	0.6168 (5)	0.2375 (4)	0.3299 (4)	3.5 (1)
C13	0.7412 (6)	0.3190 (4)	0.3434 (5)	4.9 (1)

Table 2. *Selected geometric parameters* (Å, °)

O1—C2	1.412 (5)	C3—C4	1.480 (7)
O1—C3	1.437 (5)	C7—C8	1.415 (6)
O2—C2	1.406 (5)	C7—C12	1.387 (7)
N—C1	1.524 (5)	C8—C9	1.377 (6)
N—C4	1.504 (6)	C9—C10	1.355 (8)
N—C5	1.507 (5)	C10—C11	1.357 (7)
N—C6	1.492 (6)	C11—C12	1.423 (7)
C1—C2	1.501 (6)	C12—C13	1.488 (7)
C2—C7	1.543 (6)		
C2—O1—C3	112.8 (3)	C1—C2—C7	108.5 (3)
C1—N—C4	108.1 (3)	O1—C3—C4	110.5 (4)
C1—N—C5	111.4 (3)	N—C4—C3	111.8 (4)
C1—N—C6	108.8 (3)	C2—C7—C8	117.5 (4)
C4—N—C5	111.2 (3)	C2—C7—C12	122.5 (4)
C4—N—C6	109.3 (4)	C8—C7—C12	119.9 (4)
C5—N—C6	108.1 (3)	C7—C8—C9	120.2 (4)
N—C1—C2	114.4 (3)	C8—C9—C10	120.6 (5)
O1—C2—O2	109.5 (3)	C9—C10—C11	119.9 (5)
O1—C2—C1	111.4 (4)	C10—C11—C12	122.7 (5)
O1—C2—C7	105.5 (3)	C7—C12—C11	116.6 (4)
O2—C2—C1	109.2 (3)	C7—C12—C13	125.0 (4)
O2—C2—C7	112.8 (3)	C11—C12—C13	118.4 (4)
C2—O1—C3—C4	−60.7 (5)	N—C1—C2—O2	70.7 (4)
C4—N—C1—C2	48.3 (4)	O2—C2—C7—C12	37.6 (6)
N—C1—C2—O1	−50.3 (4)	H2OH—O2—C2—O1	−29.6 (31)

Refinement of the inversion-related structure under identical conditions yielded: $R = 0.060$, $wR = 0.069$, $S = 2.828$. Thus, the absolute configuration of the sample was determined. Programs used were *MolEN* (Fair, 1990) and *ORTEP* (Johnson, 1965).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71435 (23 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HH1076]

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Acta Cryst. (1994). C**50**, 432–434

Patellamide A, a Cytotoxic Cyclic Peptide from the Ascidian *Lissoclinum patella*

YASUKO IN, MITSUNOBU DOI, MASATOSHI INOUE AND TOSHIMASA ISHIDA*

Osaka University of Pharmaceutical Sciences, 2-10-65 Kawai, Matsubara, Osaka 580, Japan

YASUMASA HAMADA AND TAKAYUKI SHIOIRI

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

(*Received* 22 *March* 1993; *accepted* 17 *September* 1993)

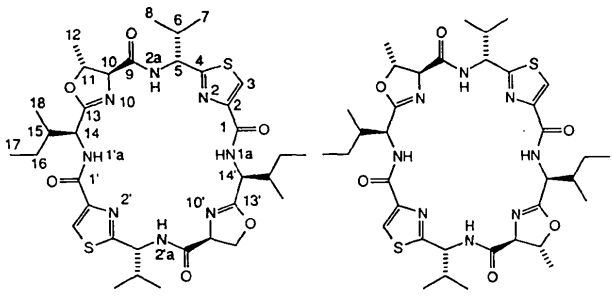
Abstract

The structure of crystals of patellamide A {13-methyl-9,23-bis(1-methylethyl)-2,16-bis(1-methylpropyl)-14,-28-dioxa-7,21-dithia-3,10,17,24,29,30,31,32-octaaza-pentacyclo[24.2.1.1^{5,8}.1^{12,15}.1^{19,22}]dotriaconta-1(29),5,-8(30),15(31),19,22(32)-hexaene-4,11,18,25-tetraone methanol solvate monohydrate, $C_{35}H_{49}N_8O_6S_2.CH_4O.H_2O$}, a cytotoxic cyclic peptide having a non-C_2-symmetric methyl group, shows the C_2-symmetric and saddle-shaped rectangular conformation where the methyl group is disordered into two C_2-symmetric positions. The water and methanol solvents were located on the crystallographic diad axis and were held by hydrogen bonds and van der Waals contacts with the polar ring N atoms and non-polar D-Val side-chain atoms, respectively.

Comment

As part of a series of studies on the relationship between the chemical structural symmetry and the molecular conformation in cyclic peptides from marine ascidian, the crystal structure of patellamide A (1), a cytotoxic cyclic peptide from *Lissoclinum patella* (Ireland, Durso, Newman & Hacker, 1982) was determined by X-ray single-crystal analysis. The conformational analysis of this molecule, which has a non-C_2-symmetric methyl group on one side of two C_2-symmetric dihydro oxazole rings, appears to be important in considering the 'active conformation' of cytotoxic cyclic peptides from ascidian, as seen from the C_2-symmetric ascidiacyclamide (2) which takes a rectangular conformation (Ishida, Tanaka, Nabae, Inoue, Kato, Hamada & Shioiri, 1988; Ishida, In, Doi, Inoue, Hamada & Shioiri, 1992). The non-C_2-symmetric patellamide D, in which a benzyl group is attached to only one side, shows a twisted and folded conformation stabilized by four intramolecular

hydrogen bonds (Schmitz, Ksebati, Chang, Wang, Hossain, van der Helm, Engel, Serban & Silfer, 1989).



(1) (2)

The space group $C2$ and $Z = 2$ indicate that the non-C_2-symmetric patellamide A itself has a crystallographic C_2 symmetry axis within the molecule, implying that the C(12) atom is disordered into two C_2-symmetric positions at 12 and 12′ with occupancies of 50%. The molecular conformation is shown in Fig. 1. Patellamide A assumes a saddle-shaped rectangular conformation, where respective side chains of isoleucine and valine protrude over and down the ring chain with four heterocyclic rings at the corner. The molecular conformation is cylindrically curved and has a depth of 2.387 Å. The distances characterizing the molecular conformation are as follows: N(1*a*)···N(1′*a*) = 5.172 (8), N(2*a*)···N(2′*a*) = 7.336 (9), N(2)···N(2′) = 6.530 (9), N(10)···N(10′) = 6.666 (9), N(1*a*)···N(2) = 2.820 (9), N(2)···N(2*a*) = 2.868 (9), N(2*a*)···N(10) = 2.684 (9), N(10)···N(1′*a*) = 2.786 (9) Å; the angle intersecting the N(1*a*)···N(1′*a*) and N(2*a*)···N(2′*a*) vectors is 86.5 . These conformational features are similar to those of the patellamide A polymorph with the space group $P1$ (In, Doi, Inoue, Ishida, Hamada & Shioiri, 1993) and to those of ascidiacyclamide (Ishida, In, Doi, Inoue, Hamada & Shiori, 1992).

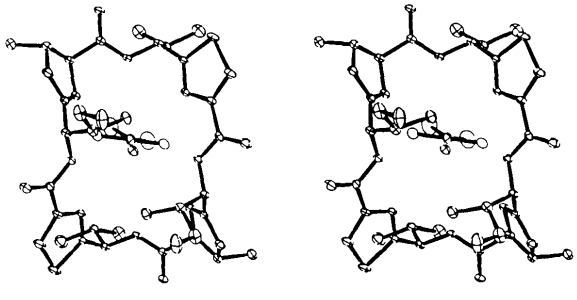


Fig. 1. Stereoscopic view of patellamide A, viewed perpendicular to the C_2-symmetry axis. Ellipsoids are scaled to enclose 30% of the electron density. The disordered O atoms of methanol are shown with open circles.

Water and methanol solvent molecules are located on a C_2-symmetric axis of patellamide A and are wrapped up in the molecule with hydrogen bonds and van der Waals interactions, as shown in Fig. 2; the O atom of methanol, although not definitive, appears to be disordered into four different positions [O(1*a*)Me, O(1*b*)Me and their atoms translated by C_2 symmetry], as judged from possible hydrogen bonds with neighboring polar atoms. The bond distances less than 3.4 Å are as follows: O(1)*W*···N(1*a*) = 3.146 (7), O(1)*W*···N(2) = 3.301 (7), O(1)*W*···N(10) = 3.344 (7) and O(1)*W*···O(1*a*)Me = 2.69 (2) Å.

In the crystal structure, patellamide A molecules pile up in the *b* direction to form columns with the water and methanol solvent molecules inside. No intermolecular hydrogen bonds are formed and the crystal structure is stabilized by van der Waals contacts among these neighboring columns.

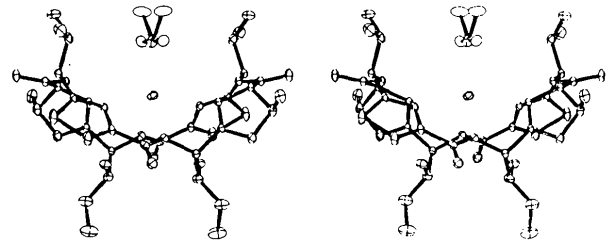


Fig. 2. Stereoscopic view of patellamide A, along the C_2-symmetry axis. Ellipsoids are scaled to enclose 30% of the electron density.

Experimental

Crystal data

$C_{35}H_{49}N_8O_6S_2.CH_4O.H_2O$
M_r = 792.01
Monoclinic
$C2$
a = 15.773 (9) Å
b = 12.402 (15) Å
c = 12.989 (6) Å
β = 102.72 (6)°
V = 2478.4 (36) Å^3
Z = 2
D_x = 1.061 Mg m^{-3}
Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 21-27°
μ = 1.322 mm^{-1}
T = 293 K
Plates
0.25 × 0.25 × 0.10 mm
Transparent

Data collection

Rigaku AFC-5 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2342 measured reflections
2231 independent reflections
1852 observed reflections [$F \geq 2\sigma(F)$]
R_{int} = 0.022
θ_{max} = 65°
h = 0 → 19
k = 0 → 15
l = −15 → 15
4 standard reflections monitored every 100 reflections
intensity variation: ±1%

Refinement

Refinement on F	$w = 1/\sigma^2(F)$
$R = 0.064$	$(\Delta/\sigma)_{max} = 0.84$
$wR = 0.088$	$\Delta\rho_{max} = 0.48$ e Å^{-3}
$S = 0.7885$	$\Delta\rho_{min} = -0.43$ e Å^{-3}
1839 reflections	Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)
266 parameters	
H-atom parameters not refined	

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

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
N(1*a*)	0.3322 (4)	0.2882 (6)	0.4444 (4)	0.071 (3)
C(1)	0.2810 (5)	0.2674 (8)	0.3517 (6)	0.074 (4)
O(1)	0.2167 (5)	0.2072 (8)	0.3402 (5)	0.112 (5)
C(2)	0.3049 (6)	0.3184 (9)	0.2591 (6)	0.082 (4)
N(2)	0.3693 (4)	0.3937 (6)	0.2670 (4)	0.067 (3)
C(3)	0.2622 (8)	0.291 (1)	0.1579 (7)	0.126 (8)
S(3)	0.3069 (2)	0.3631	0.0711 (2)	0.140 (2)
C(4)	0.3789 (5)	0.4252 (8)	0.1749 (5)	0.072 (4)
C(5)	0.4435 (5)	0.5077 (7)	0.1573 (5)	0.074 (4)
C(6)	0.4158 (6)	0.6246 (9)	0.1778 (6)	0.093 (5)
C(7)	0.328 (1)	0.649 (1)	0.105 (1)	0.15 (1)
C(8)	0.488 (1)	0.706 (1)	0.167 (1)	0.14 (1)
N(2*a*)	0.5273 (4)	0.4808 (7)	0.2268 (4)	0.070 (3)
C(9)	0.6007 (5)	0.4805 (7)	0.1958 (5)	0.075 (4)
O(9)	0.6087 (4)	0.5015 (8)	0.1046 (4)	0.106 (4)
C(10)	0.6829 (5)	0.4610 (7)	0.2792 (5)	0.073 (4)
N(10)	0.6629 (4)	0.4105 (6)	0.3745 (4)	0.065 (3)
C(11)	0.7450 (5)	0.383 (1)	0.2435 (6)	0.094 (5)
O(11)	0.7419 (4)	0.2888 (7)	0.3095 (4)	0.093 (3)
C(12)†	0.839 (1)	0.431 (2)	0.275 (2)	0.12 (1)
C(13)	0.6938 (4)	0.3191 (7)	0.3820 (5)	0.062 (3)
C(14)	0.6874 (5)	0.2352 (7)	0.4635 (5)	0.071 (4)
C(15)	0.6214 (6)	0.1470 (8)	0.4189 (8)	0.090 (5)
C(16)	0.6581 (9)	0.064 (1)	0.361 (2)	0.14 (1)
C(17)	0.604 (1)	−0.039 (2)	0.344 (3)	0.19 (2)
C(18)	0.5332 (7)	0.193 (1)	0.362 (1)	0.105 (6)
O(1)*W*	0.5000	0.4327 (8)	0.5000	0.085 (5)
C(1)Me	0.5000	0.6162 (9)	0.5000	0.104 (7)
O(1*a*)Me‡	0.593 (1)	0.617 (2)	0.515 (2)	0.10 (1)
O(1*b*)Me‡	0.552 (3)	0.718 (2)	0.494 (4)	0.20 (3)

† Occupancy 0.5.
‡ Occupancy 0.25.

Table 2. *Selected torsion angles* (°)

Thiazole	
N(1*a*)—C(1)—C(2)—N(2)	−7.9 (7)
C(14′)—N(1*a*)—C(1)—C(2)	−177.2 (7)
Valine	
C(9)—N(2*a*)—C(5)—C(4)	134.6 (8)
N(2*a*)—C(5)—C(4)—N(2)	47.0 (6)
N(2*a*)—C(5)—C(6)—C(7)	−179.0 (1)
N(2*a*)—C(5)—C(6)—C(8)	55.0 (9)
Oxazoline	
N(10)—C(10)—C(9)—N(2*a*)	18.8 (6)
C(10)—C(9)—N(2*a*)—C(5)	174.5 (9)
Isoleucine	
C(1′)—N(1′*a*)—C(14)—C(13)	−127.1 (7)
N(1′*a*)—C(14)—C(13)—N(10)	−21.2 (6)
N(1′*a*)—C(14)—C(15)—C(16)	−154.0 (1)
N(1′*a*)—C(14)—C(15)—C(18)	72.9 (8)
C(14)—C(15)—C(16)—C(17)	163.0 (2)

Crystals were obtained from aqueous methanol solution by slow evaporation at room temperature. The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1985). Refinement was by full-matrix least-squares methods using *SHELX*76 (Sheldrick, 1976). During the last stage of the refinement, all H atoms, except for those of the solvents, were placed in assumed positions and included only for the calculation of structure factors. The y coordinate of S(3) was fixed to define the origin during refinement. The molecular conformation was depicted using *ORTEP* (Johnson, 1971).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry and a stereoscopic drawing of crystal packing, viewed down the b axis, have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71549 (14 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AS1063]

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Acta Cryst. (1994). C**50**, 434–438

A Steroid Derivative that Crystallizes with Three Molecules in the Asymmetric Unit

CAROLYN PRATT BROCK, IVAN STOILOV AND DAVID S. WATT

Department of Chemistry, University of Kentucky, Lexington, KY 40506-0055, USA

(*Received* 13 *January* 1993; *accepted* 31 *August* 1993)

Abstract

Crystals of (20*R*,23*S*,24*R*)-5α-dinosteran-29-ol, $C_{30}H_{54}O$, grow as blades elongated in the direction of hydrogen-bonded chains of OH groups and thin in the direction of the 50 Å c axis. There are three independent molecules in the unit cell. Hydrogen-bonding requirements dictate that the OH group of each molecule be within a few ångströms