C2—N1—C6	122.5 (2)	C4—C3—C2	119.5 (2)
C2′—N1′—C6′	121.9 (2)	C4′—C3′—C2′	119.3 (2)
C2—C1—C2′	108.57 (13)	C5—C4—C3	119.9 (2)
C2—C1—O1*a*	111.90 (13)	C5′—C4′—C3′	120.0 (2)
C2—C1—O1*b*	105.95 (14)	C6—C5—C4	119.2 (2)
C2′—C1—O1*a*	106.15 (14)	C6′—C5′—C4′	119.0 (2)
C2′—C1—O1*b*	110.31 (13)	N1—C6—C5	119.9 (2)
O1*a*—C1—O1*b*	113.89 (14)	N1′—C6′—C5′	120.3 (2)
C3—C2—N1	119.0 (2)	O1′—N′—O2′	120.2 (2)
C3—C2—C1	123.0 (2)	O2′—N′—O3′	121.0 (2)
N1—C2—C1	117.95 (14)	O3′—N′—O1′	118.8 (2)
C3′—C2′—N1′	119.4 (2)	O1—N—O2	122.7 (2)
C3′—C2′—C1	122.6 (2)	O2—N—O3	119.4 (2)
N1′—C2′—C1	117.95 (15)	O3—N—O1	117.90 (14)
C2—C1—C2′—N1′	114.6 (2)	O1*a*—C1—C2′—N1′	−5.9 (2)
C2′—C1—C2—N1	120.0 (2)	O1*b*—C1—C2—N1	1.5 (2)
O1*a*—C1—C2—N1	−123.2 (2)	O1*b*—C1—C2′—N1′	−129.8 (2)

The ω-scan width was symmetrical over 1.2° about the $K\alpha_{1,2}$ maximum of each peak with the background offset by 1.0 and −1.0° in ω from the $K\alpha_{1,2}$ maximum. The scan speed varied between 3 and 6° min^{-1} depending upon intensity. The structure was solved by direct methods. All of the non-H atoms were refined with anistropic displacement parameters. The H atoms were located from a difference Fourier map and were refined without constraints. The linear absorption coefficent was calculated using values from *International Tables for X-ray Crystallography* (1974). Anomalous-dispersion corrections were taken from Cromer & Liberman (1970).

Cell refinement, data collection, data reduction, structure solution and molecular graphics: *SHELXTL-Plus* (Sheldrick, 1990). Structure refinement (by a full-matrix least-squares method): *SHELX*76 (Sheldrick, 1976). Geometric calculations and preparation of material for publication: *FUER* (Larson, 1993).

This research was supported by an award from Research Corporation, Tucson, Arizona, USA.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, bond distances and angles involving H atoms and hydrogen-bond data have been deposited with the IUCr (Reference: CR1106). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Cromer, D. T. & Liberman, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.

Cromer, D. T. & Mann, J. B. (1968). *Acta Cryst.* A**24**, 321–324.

Larson, S. B. (1993). *FUER. Program for Generating Positional and Thermal Parameters and Geometrical Quantities*. Univ. of Texas, Austin, USA.

March, J. (1985). *Advanced Organic Chemistry*, pp. 783–784, and references cited therein. New York: John Wiley.

Sheldrick, G. M. (1976). *SHELX*76. *Program for Crystal Structure Determination*. Univ. of Cambridge, England.

Sheldrick, G. M. (1990). *SHELXTL-Plus*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Sommerer, S. O. & Abboud, K. A. (1993). *Acta Cryst.* C**49**, 1152–1154.

Sommerer, S. O., Baker, J. D., Jensen, W. P., Hamza, A. & Jacobson, R. A. (1993). *Inorg. Chim. Acta*, **210**, 173–176.

Sommerer, S. O., Jensen, W. P. & Jacobson, R. A. (1990). *Inorg. Chim. Acta*, **172**, 3–11.

Sommerer, S. O., Westcott, B. L. & Abboud, K. A. (1994). *Acta Cryst.* C**50**, 48–52.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Wang, S. L., Richardson, J. W., Briggs, S. J., Jacobson, R. A. & Jensen, W. P. (1986). *Inorg. Chim. Acta*, **111**, 67–72.

Acta Cryst. (1994). C**50**, 2015–2017

Structure of Ascidiacyclamide as the Ethanol Water Solvate, a Cytotoxic Cyclic Peptide from *Ascidian*

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* 16 *September* 1993; *accepted* 19 *January* 1994)

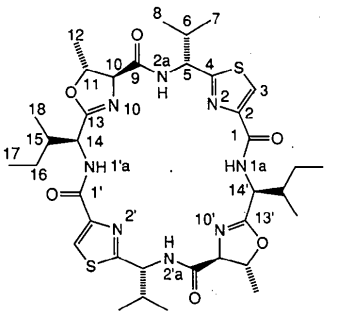
Abstract

The X-ray crystal structure determination of the $C_2H_5OH.H_2O$ solvate of ascidiacyclamide ($C_{36}H_{52}N_8O_6S_2$), a cytotoxic cyclic peptide from marine tunicate *Ascidian*, revealed a C_2-symmetric saddle-shaped rectangular conformation of the molecule. The water and ethanol molecules are located on the crystallographic diad axis and are held by hydrogen bonds and van der Waals contacts with the polar ring N atoms and nonpolar D-Val side-chain atoms, respectively. The molecular conformation and the interaction with solvent molecules are nearly the same as those of the compound with $C_2H_5OH.2H_2O$ [Ishida, In, Doi, Inoue, Hamada & Shioiri (1992). *Biopolymers*, **32**, 131–143].

Comment

In a series of investigations into the relationship between the chemical structural symmetry and the molecular conformation in cyclic peptides from marine tunicate, several crystal forms of ascidiacylamide, (1), a cytotoxic cyclic peptide from *Ascidian*, have been determined by X-ray crystal analyses (Ishida, Tanaka, Nabae, Inoue, Kato, Hamada & Shioiri, 1988; Ishida, In, Doi, Inoue, Hamada & Shioiri, 1992). The conformational analysis of (1) appears to be important for considering the 'active conformation' of cytotoxic cyclic peptides from tunicate, because most of them have a common or related

ring structure (Rinehart, Kishore, Bible, Sakai, Sullins & Li, 1988).



(1)

The crystals obtained from 50% aqueous ethanol solution containing equimolar (1) and β-phenetylamine belong to the $C2$ space group with $Z = 2$, indicating that they consist of C_2-symmetric ascidiacyclamide alone and the symmetry axis coincides with the crystallographic diad axis in the unit cell. The molecular conformation is shown in Fig. 1. Ascidiacyclamide assumes a saddle-shaped rectangular conformation, where respective side chains of isoleucine and valine protrude above and below the ring chain with four heterocyclic rings at the corners. The molecule has a cylindrically curved conformation with a depth of 2.552 (7) Å. Some distances defining this molecular conformation are: $N(1a)\cdots N(1a)' = 5.298\,(4)$, $N(2a)\cdots N(2a)' = 7.187\,(8)$, $N(2)\cdots N(2)' = 6.783\,(8)$, $N(10)\cdots N(10)' = 6.168\,(8)$, $N(1a)\cdots N(2) = 2.793\,(7)$, $N(2)\cdots N(2a) = 2.812\,(8)$, $N(2a)\cdots N(10) = 2.723\,(8)$, $N(10)\cdots N(1a)' = 2.858\,(6)$ Å; the angle intersecting the $N(1a)\cdots N(1a)'$ and $N(2a)\cdots N(2a)'$ contacts is 91.4 (2)°. These conformational features are very similar to those of ascidiacyclamide crystallized from different solvents such as nonpolar benzene (Ishida, Tanaka, Nabae, Inoue, Kato, Hamada & Shioiri, 1988), polar ethanol or aqueous ethanol (Ishida, In, Doi, Inoue, Hamada & Shioiri, 1992), indicating the energetic stability of this conformation.

The water and methanol molecules are located on a C_2 symmetry axis of ascidiacyclamide and are 'wrapped up' in the peptide molecule *via* hydrogen bonds and van der Waals interactions, as shown in Fig. 2; the O atom of ethanol could be disordered in the two C_2-related positions with an occupancy of 0.5, as judged from possible hydrogen bonds with neighboring polar atoms. Possible hydrogen bonds and short contacts (less than 3.4 Å) in which the solvent molecules participate are: $O(1)Et^{i}\cdots O(1)^{ii} = 2.85\,(2)$, $O(1)Et^{i}\cdots N(2a)^{i} = 3.38\,(2)$, $O(1)Et^{i}\cdots N(10)^{i} = 3.39\,(2)$, $O(1)Et^{i,iii}\cdots O(1)W^{i} = 2.82\,(2)$, $O(1)W^{i}\cdots N(1a)^{i,iii} = 3.177\,(4)$, $O(1)W^{i}\cdots N(10)^{i,iii} = 3.085\,(6)$ Å [symmetry codes: (i) x, y, z; (ii) $x - \frac{1}{2}, y + \frac{1}{2}, z$; (iii) $1 - x, y, -z$].

In the crystal structure, ascidiacyclamide molecules pile up along the diad axis and form a 'mid-air' column; the water and ethanol molecules are located in the column. Two intermolecular hydrogen bonds are formed [$N(1a)^{i}\cdots N(10)^{iii} = 2.858\,(6)$ Å and its C_2-related one] and the crystal structure is mainly stabilized by van der Waals contacts among neighboring columns.

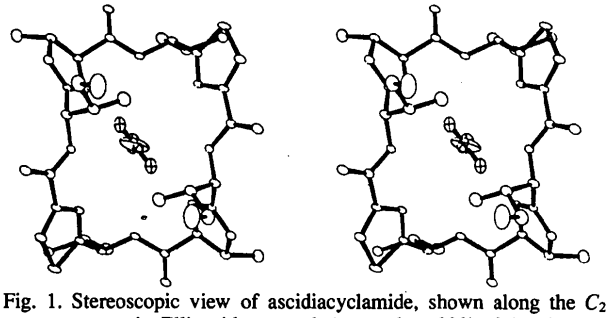


Fig. 1. Stereoscopic view of ascidiacyclamide, shown along the C_2 symmetry axis. Ellipsoids are scaled to enclose 30% of the electron density. The solvent ethanol and water molecules are shown with the crossed ellipsoids.

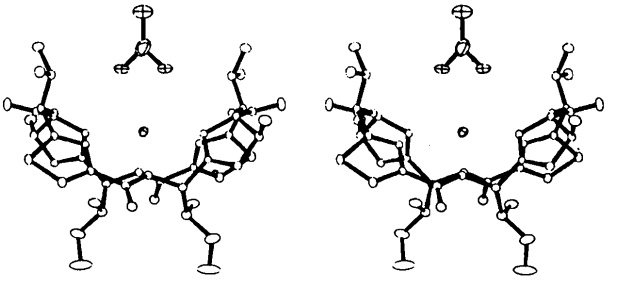


Fig. 2. Stereoscopic view of ascidiacyclamide wrapping H_2O and C_2H_5OH solvent molecules (crossed ellipsoids), shown perpendicular to the C_2 symmetry axis.

Experimental

Single crystals were obtained from the aqueous ethanol solution containing equimolar ascidiacyclamide and β-phenetylamine by slow evaporation at room temperature.

Crystal data

$C_{36}H_{52}N_8O_6S_2.C_2H_6O.H_2O$
$M_r = 821.073$
Monoclinic
$C2$
$a = 14.360\,(2)$ Å
$b = 13.369\,(2)$ Å
$c = 12.905\,(2)$ Å
$\beta = 99.95\,(1)°$
$V = 2440.2\,(5)$ Å^3
$Z = 2$
$D_x = 1.117$ Mg m^{-3}
$D_m = 1.115$ Mg m^{-3}
Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å
Cell parameters from 25 reflections
$\theta = 18.4$–$21.5°$
$\mu = 1.374$ mm^{-1}
$T = 293$ K
Plates
0.25 × 0.25 × 0.15 mm
Transparent colorless

Data collection

Rigaku AFC-5 diffractometer
ω–2θ scans
Absorption correction: none
$R_{int} = 0.018$
$\theta_{max} = 62°$
$h = 0 \rightarrow 16$
$k = 0 \rightarrow 15$
$l = -14 \rightarrow 14$

2201 measured reflections
2021 independent reflections
1960 observed reflections
$[F > 2\sigma(F)]$

4 standard reflections
monitored every 100
reflections
intensity variation: ±1%

Refinement

Refinement on F
$R = 0.055$
$wR = 0.080$
$S = 1.285$
1828 reflections
264 parameters
$w = 1/\sigma^2(F)$
$(\Delta/\sigma)_{max} = 0.52$

$\Delta\rho_{max} = 0.38$ e Å^{-3}
$\Delta\rho_{min} = -0.42$ e Å^{-3}
Extinction correction: none
Atomic scattering factors
from *International Tables for X-ray Crystallography* (1974, Vol. IV)

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*)	0.6867 (3)	0.0556	0.0524 (4)	0.077 (2)
C(1)	0.7384 (5)	0.0255 (6)	0.1416 (5)	0.084 (3)
O(1)	0.8051 (5)	−0.0337 (6)	0.1467 (5)	0.114 (4)
C(2)	0.7134 (5)	0.0698 (6)	0.2402 (5)	0.083 (3)
N(2)	0.6491 (4)	0.1485 (5)	0.2346 (4)	0.079 (3)
C(3)	0.7490 (7)	0.0367 (9)	0.3393 (6)	0.113 (5)
S(3)	0.7047 (2)	0.1049 (4)	0.4274 (1)	0.126 (2)
C(4)	0.6396 (5)	0.1760 (7)	0.3271 (5)	0.083 (3)
C(5)	0.5756 (5)	0.2612 (7)	0.3478 (4)	0.087 (3)
C(6)	0.6202 (6)	0.3621 (7)	0.3296 (6)	0.102 (5)
C(7)	0.7197 (6)	0.369 (1)	0.3979 (8)	0.122 (6)
C(8)	0.555 (1)	0.4466 (8)	0.349 (1)	0.138 (8)
N(2*a*)	0.4859 (4)	0.2465 (6)	0.2753 (4)	0.084 (3)
C(9)	0.4010 (5)	0.2513 (7)	0.3067 (5)	0.091 (4)
O(9)	0.3909 (4)	0.2745 (8)	0.3937 (3)	0.130 (4)
C(10)	0.3164 (5)	0.2357 (6)	0.2212 (4)	0.082 (3)
N(10)	0.3383 (4)	0.1817 (5)	0.1292 (4)	0.078 (3)
C(11)	0.2377 (5)	0.1745 (7)	0.2603 (5)	0.093 (4)
O(11)	0.2344 (3)	0.0852 (5)	0.1933 (3)	0.087 (2)
C(12)	0.1443 (8)	0.223 (1)	0.241 (1)	0.143 (8)
C(13)	0.2910 (4)	0.1023 (6)	0.1238 (4)	0.069 (3)
C(14)	0.2937 (6)	0.0188 (6)	0.0455 (6)	0.093 (4)
C(15)	0.3621 (7)	−0.0667 (8)	0.0830 (7)	0.114 (6)
C(16)	0.316 (1)	−0.138 (1)	0.147 (2)	0.18 (1)
C(17)	0.364 (2)	−0.231 (1)	0.153 (4)	0.31 (3)
C(18)	0.443 (1)	−0.0345 (9)	0.134 (1)	0.15 (1)
O(1)*W*†	1/2	0.1868 (7)	0	0.109 (5)
O(1)Et†	0.452 (1)	0.383 (1)	0.051 (2)	0.17 (1)
C(1)Et†	1/2	0.553 (4)	0	0.29 (4)
C(2)Et†	1/2	0.446 (2)	0	0.51 (7)

† *W* and Et denote water and ethanol molecules, respectively. The occupancy factor of O(1)Et is 0.5.

Table 2. *Selected torsion angles* (°)

Thiazole	
N(1*a*)—C(1)—C(2)—N(2)	−9.2 (6)
C(14)′—N(1*a*)—C(1)—C(2)	178.9 (8)
Valine	
C(9)—N(2*a*)—C(5)—C(4)	132.3 (7)
N(2*a*)—C(5)—C(4)—N(2)	45.7 (5)
N(2*a*)—C(5)—C(6)—C(7)	−173.3 (8)
N(2*a*)—C(5)—C(6)—C(8)	61.1 (7)
Oxazoline	
N(10)—C(10)—C(9)—N(2*a*)	21.9 (6)
C(10)—C(9)—N(2*a*)—C(5)	179.1 (8)
Isoleucine	
C(1)′—N(1*a*)′—C(14)—C(13)	−133.0 (6)
N(1*a*)′—C(14)—C(13)—N(10)	−31.1 (9)
N(1*a*)′—C(14)—C(15)—C(16)	−151 (1)
N(1*a*)′—C(14)—C(15)—C(18)	85 (1)
C(14)—C(15)—C(16)—C(17)	161 (2)

The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1985). The structure refinement by full-matrix least-squares methods was carried out using *SHELX*76 (Sheldrick, 1976). During the last stage of refinement, all H atoms, except those of solvents, were placed at assumed positions and included in the refinement. The y coordinate of N(1*a*) was fixed to define the origin during the refinement. The molecular conformation was drawn using *ORTEP*II (Johnson, 1971).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: AS1088). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Ishida, T., In, Y., Doi, M., Inoue, M., Hamada, Y. & Shioiri, T. (1992). *Biopolymers*, **32**, 131–143.

Ishida, T., Tanaka, M., Nabae, M., Inoue, M., Kato, S., Hamada, Y. & Shioiri, T. (1988). *J. Org. Chem.* **53**, 107–112.

Johnson, C. K. (1971). *ORTEPII*. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee, USA.

Rinehart, K. L., Kishore, V., Bible, K. C., Sakai, R., Sullins, D. W. & Li, K. M. (1988). *J. Nat. Prod.* **51**, 1–21.

Sheldrick, G. M. (1976). *SHELX*76. *Program for Crystal Structure Determination*. Univ. of Cambridge, England.

Sheldrick, G. M. (1985). *SHELXS*86. *Program for the Solution of Crystal Structures*. Univ. of Göttingen, Germany.

Acta Cryst. (1994). C**50**, 2017–2019

Dimethyl Cubane-1,4-dicarboxylate

HERMANN IRNGARTINGER AND STEFAN STRACK

Organisch-Chemisches Institut der Universität Heidelberg Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany

(*Received* 8 *December* 1993; *accepted* 28 *April* 1994)

Abstract

In the crystal, dimethyl pentacyclo[4.2.0.0^{2,5}.0^{3,8}.0^{4,7}]-octane-1,4-dicarboxylate, $C_{12}H_{12}O_4$, has crystallographic 2/*m* symmetry. The carbonyl group takes an eclipsed orientation with respect to the skeleton bond C1—C3, as well as to the methoxy O2—C5 bond. The ester group is tilted in the direction of the opposite C atom C3″ about its staggered orientation relative to the skele-