C981438-SX1064 (FO)

Acta Cryst. (1999). C**55**, 000–000

The highly solvated structure of theonellapeptolide Id, a tridecapeptide lactone from the Okinawa marine sponge *Theonella swinhoei*

MITSUNOBU DOI,[a] TOSHIMASA ISHIDA,[a] MOTOMASA KOBAYASHI,[b] JEFFREY R. DESCHAMPS[c] AND JUDITH L. FLIPPEN-ANDERSON[c]

[a]*Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahara, Takatsuki, Osaka 569-11, Japan,* [b]*Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamada-oka, Suita, Osaka 565, Japan, and* [c]*Laboratory for the Structure of Matter, Code 6030, Naval Research Laboratory, Washington DC 20375, USA. E-mail: doit@oysun01.oups.ac.jp*

(*Received 9 September 1997; accepted 4 November 1998*)

Abstract

Theonellapeptolide Id (TNLP-Id) was crystallized from an aqueous methanol solution. This crystalline cyclic tridecapeptide is solvated by 12 water molecules, which interact with the backbone. All the solvent molecules are located on one face of the hydrophobic peptide. This suggests that the molecule also has unanticipated amphipathic properties. The uniquely folded cyclic backbone is composed of short and long turn units.

Comment

Theonellapeptolide Id (TNLP-Id) is the tridecapeptide lactone isolated from the Okinawa marine sponge *Theonella swinhoei*, and it shows potent cytotoxicity (Kobayashi *et al*., 1991). The TNLP family has high hydrophobicity and is extracted by ethyl acetate with related peptides and macrolides (Kobayashi, Kanzaki *et al*., 1994; Kobayashi, Kawazoe *et al*., 1994). Their chemical structures contain unusual amino acids and most of the amide bonds are methylated. In TNLP-Id, the terminal N is capped by the methoxyacetate, and the terminal C bonds through an ester linkage to the hydroxyl group of the threonine^{13} residue.

SCHEME HERE

The highly hydrophobic title polypeptide was crystallized from aqueous methanol solution in a solvated form. The 12 independent water molecules are associated with one face of TNLP-Id. The alkyl groups of the hydrophobic residues (Val, Leu and Ile) are assembled on the opposing face, as shown in Fig. 1. Previ-

ously, only hydrophobic properties were presumed to be associated with this molecule; selective hydration of a single surface, however, suggests that TNLP-Id also has amphipathic characteristics. Solvation occurs by hydrogen-bonding with the amide bonds (Table 1) and networks are observed among the solvent molecules (not indicated). No direct interaction is observed between neighboring peptides, except for van der Waals contacts and water-mediated indirect connections that stabilize the molecular packing in the crystal. The intermolecular hydrogen bonds contribute to the formation of turn segments, which have different characteristics from some β-turns. A $1 \rightarrow 3$ turn is formed between N-3(L-Thr^3) $\rightarrow$ O-5(D-Leu^5). This type of turn leads to unfavourable steric interactions. However, in this case, the turn does not appear to be tight because it includes a β-alanine residue. The conformation of the peptide is also stabilized by two $1 \rightarrow 5$ turn units formed between N-5(D-Leu^5) $\rightarrow$ O-1(L-Val^1) and N-12(D-Leu^{12}) $\rightarrow$ O-8(D-*a*Ile^8). A *cis*-amide bond is observed between *N*-Me-L-Val^9 and *N*-Me-L-Ala^{10} (Table 2). Finally, a long loop is formed between *N*-Me-L-Ile^6 and *N*-Me-D-*a*Ile^{13}.

FIG. 1

Experimental

The title compound, TNLP-Id, was crystallized from an aqueous methanol solution.

Crystal data

$C_{70}H_{125}N_{13}O_{16}\cdot 12H_2O$	Cu $K\alpha$ radiation
M_r = 1621.0	λ = 1.54180 Å
Orthorhombic	Cell parameters from 20 reflections
$P2_12_12_1$	θ = 9.92–10.09°
a = 21.205 (4) Å	μ = 0.697 mm^{-1}
b = 37.941 (8) Å	T = 293 (2) K
c = 12.227 (2) Å	Block
V = 9837 (3) Å^3	0.8 × 0.3 × 0.2 mm
Z = 4	Colorless
D_x = 1.095 Mg m^{-3}	
D_m not measured	

Data collection

Rigaku AFC-5*R*/RU-200 diffractometer	θ_{max} = 62.89°
$2\theta/\omega$ scans	$h = 0 \rightarrow 24$
Absorption correction: none	$k = 0 \rightarrow 43$
8571 measured reflections	$l = 0 \rightarrow 13$
8571 independent reflections	4 standard reflections every 100 reflections
7490 reflections with $I > 2\sigma(I)$	intensity decay: −3.64%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.113$
$wR(F^2) = 0.287$
$S = 1.020$
8571 reflections
1001 parameters
H-atom treatment: mixed
$w = 1/[\sigma^2(F_o^2) + (0.14P)^2 + 18.50P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.074$
$\Delta\rho_{max} = 0.615$ e Å^{-3}
$\Delta\rho_{min} = -0.594$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.0 (5)

Table 1. *Selected hydrogen bonds (Å, °)*

D—H···A	D···A	D—H	H···A	D—H···A
N(L-Thr^{3})—H···O(D-Leu^{5})	2.832 (8)	0.860	1.978	171.4
N(D-Leu^{5})—H···O(L-Val^{1})	2.861 (8)	0.860	2.073	151.8
N(D-*a*Ile^{8})—H···O(D-Leu^{12})	2.900 (7)	0.860	2.058	166.2
N(D-Leu^{12})—H···O(D-*a*Ile^{8})	2.921 (8)	0.860	2.110	157.1
Peptide···water				
O(Methoxy)···O(*W*1)	2.74 (1)			
O(Methoxy)···O(*W*10)^{i}	2.95 (2)			
O(*N*-Me-D-Leu^{2})···O(*W*3)^{i}	2.84 (1)			
O(*N*-Me-D-Leu^{2})···O(*W*11)^{ii}	2.87 (1)			
O(L-Thr^{3})···O(*W*8)	2.86 (1)			
O(βAla^{4})···O(*W*2)	2.90 (1)			
O(βAla^{4})···O(*W*10)	2.69 (2)			
O(βAla^{7})···O(*W*3)	2.65 (1)			
O(*N*-Me-L-Ala^{10})···O(*W*6)	2.81 (1)			
N(βAla^{11})···O(*W*4)	2.97 (1)	0.860	2.189	150.7
O(βAla^{11})···O(*W*5)	2.78 (1)			
O(βAla^{11})···O(*W*1)^{iii}	2.86 (1)			

Symmetry codes: (i) $x, y, z+1$; (ii) $x+\frac{1}{2}, \frac{3}{2}-y, 2-z$; (iii) $x-1\frac{1}{2}, \frac{3}{2}-y, 2-z$.

Table 2. *Selected torsion angles (°)*

L-Val[1]					
φ	C1	N-1	Cα-1	C-1	−135.1 (8)
ψ	N-1	Cα-1	C-1	N-2	161.1 (7)
ω	Cα-1	C-1	N-2	Cα-2	166.6 (7)
N-Me-D-Leu[2]					
φ	C-1	N-2	Cα-2	C-2	98.9 (6)
ψ	N-2	Cα-2	C-2	N-3	−112.8 (7)
ω	Cα-2	C-2	N-3	Cα-3	175.5 (8)
L-Thr[3]					
φ	C-2	N-3	Cα-3	C-3	−125.7 (8)
ψ	N-3	Cα-3	C-3	N-4	64.6 (7)
ω	N-3	Cα-3	Cβ-3	Cγ-3	−171.7 (7)
βAla[4]					
φ	C-3	N-4	Cα-4	Cβ-4	98.6 (9)
ψ	N-4	Cα-4	Cβ-4	C-4	−74.1 (7)
ψ†	Cα-4	Cβ-4	C-4	N-5	99.6 (8)
ω	Cβ-4	C-4	N-5	Cα-5	174.9 (8)
D-Leu[5]					
φ	C-4	N-5	Cα-5	C-5	122.7 (8)
ψ	N-5	Cα-5	C-5	N-6	−158.5 (7)
ω	Cα-5	C-5	N-6	Cα-6	−179.0 (7)
N-Me-L-Ile[6]					
φ	C-5	N-6	Cα-6	C-6	−106.3 (7)
ψ	N-6	Cα-6	C-6	N-7	100.2 (8)
ω	Cα-6	C-6	N-7	Cα-7	−165.9 (9)
βAla[7]					
φ	C-6	N-7	Cα-7	Cβ-7	−131.5 (9)
ψ	N-7	Cα-7	Cβ-7	C-7	78.0 (8)
ψ†	Cα-7	Cβ-7	C-7	N-8	−137.3 (9)
ω	Cβ-7	C-7	N-8	Cα-8	−173.7 (9)
D-*a*Ile[8]					
φ	C-7	N-8	Cα-8	C-8	126.0 (9)
ψ	N-8	Cα-8	C-8	N-9	−161.6 (8)
ω	Cα-8	C-8	N-9	Cα-9	−171.3 (8)
N-Me-L-Val[9]					
φ	C-8	N-9	Cα-9	C-9	−112.7 (8)
ψ	N-9	Cα-9	C-9	N-10	100.2 (9)
ω	Cα-9	C-9	N-10	Cα-10	0.7 (9)
N-Me-L-Ala[10]					
φ	C-9	N-10	Cα-10	C-10	−109.4 (9)
ψ	N-10	Cα-10	C-10	N-11	−164.6 (8)
ω	Cα-10	C-10	N-11	Cα-11	−171.2 (8)
βAla[11]					
φ	C-10	N-11	Cα-11	Cβ-11	72.3 (7)
ψ	N-11	Cα-11	Cβ-11	C-11	68.5 (6)
ψ†	N-12	C-11	Cβ-11	Cα-11	−93.3 (7)
ω	Cβ-11	C-11	N-12	Cα-12	−173.3 (8)
D-Leu[12]					
φ	C-11	N-12	Cα-12	C-12	87.0 (7)
ψ	N-12	Cα-12	C-12	N-13	−158.1 (8)
ω	Cα-12	C-12	N-13	Cα-13	−177.2 (8)
N-Me-D-*a*Ile[13]					
φ	C-12	N-13	Cα-13	C-13	−56.3 (7)
ψ‡	N-13	Cα-13	C-13	Oγ-3	−50.1 (6)
ω‡	Cβ-3	Oγ-3	C-13	Cα-13	172.2 (8)

† The β-alanine has two torsion angles corresponding to ψ. ‡ The angle is for the ester linkage between C-13(*N*-Me-D-*a*Ile[13]) and hydroxy oxygen Oγ-3(L-Thr[3]).

Intensities were measured to a maximum 2θ value of 120°, because reflections are only poorly detected beyond this limit. Direct method trials were extensively carried out using *SHELXS*86 (Sheldrick, 1985), but no clear solution was obtained. The structure was solved by the *Shake-and-Bake* method using the program *SnB* (Miller *et al*., 1994; Chang *et al*., 1996); a single running of the program gave a solution with a default setting and 700 trial structures. Full-matrix least-squares refinement with F^2 magnitudes and anisotropic displacement parameters for non-H atoms was carried out by *SHELXL*93 (Sheldrick, 1993). The difference Fourier map showed 12 peaks, which were interpreted as solvent molecules. At the *N*-Me-Ile^6 residue, the Cδ1 atom was disordered into two parts, with probabilities of 0.69 and 0.31.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1991). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *MSC/AFC Diffractometer Control Software*. Program(s) used to solve structure: *SnB*. Program(s) used to refine structure: *SHELXL*93. Molecular graphics: *ORTEP*III (Burnett & Johnson, 1996).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1064). Services for accessing these data are described at the back of the journal.

References

Bernardinelli, G., Jefford, C. W., Sakai, R. & Higa, T. (1992). *Seventh International Symposium on Marine Natural Products*, Abstracts of Papers, pp. 29–30. Capri, Italy.

Burnett, M. N. & Johnson, C. K. (1996). *ORTEP*III. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.

Chang, C.-S., DeTitta, G. T., Gallo, S. M., Hauptman, H. A., Jones, R., Khalak, A., Khalak, H., Langs, D. A., Miller, R., Potte, S., Thuman, P. & Weeks, C. M. (1996). *SnB. A Program for Crystal Structure Determination by Shake-and-Bake.* Version 1.5.0. Hauptman-Woodward Medical Research Institute, Buffalo, New York, USA.

Flack, H. D. (1983). *Acta Cryst*. A**39**, 876–881.

Kobayashi, M., Kanzaki, K., Katayama, S., Ohashi, K., Okada, H., Ikegami, S. & Kitagawa, I. (1994). *Chem. Pharm. Bull*. **42**, 1410–1415.

Kobayashi, M., Kawazoe, K., Okamoto, T., Sasaki, T. & Kitagawa, I. (1994). *Chem. Pharm. Bull*. **42**, 19–26.

Kobayashi, M., Lee, N. K., Shibuya, H., Momose, T. & Kitagawa, I. (1991). *Chem. Pharm. Bull*. **39**, 1177–1184.

Miller, R., Gallo, S. M., Khalak, H. G. & Weeks, C. M. (1994). *J. Appl. Cryst*. **27**, 613–621.

Molecular Structure Corporation (1991). *MSC/AFC Diffractometer Control Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

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

Sheldrick, G. M. (1993). *SHELXL*93. *Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

Fig. 1. A stereoscopic drawing of TNLP-Id with the residue names. The displacement ellipsoids are drawn at 50% probablity level. H atoms have been omitted for clarity.

$C_{70}H_{125}N_{13}O_{16}\cdot 12H_2O$

MITSUNOBU DOI *et al.*

$C_{70}H_{125}N_{13}O_{16}\cdot 12H_2O$

MITSUNOBU DOI *et al.*

$C_{70}H_{125}N_{13}O_{16}\cdot 12H_2O$

Supplementary data

The data shown below are not normally printed in *Acta Cryst. Section C* but the data will be available electronically *via* the online contents pages of the journal at

http://www.iucr.org/journals/acta/tocs/actac/actac.html

Table *S*1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²)*

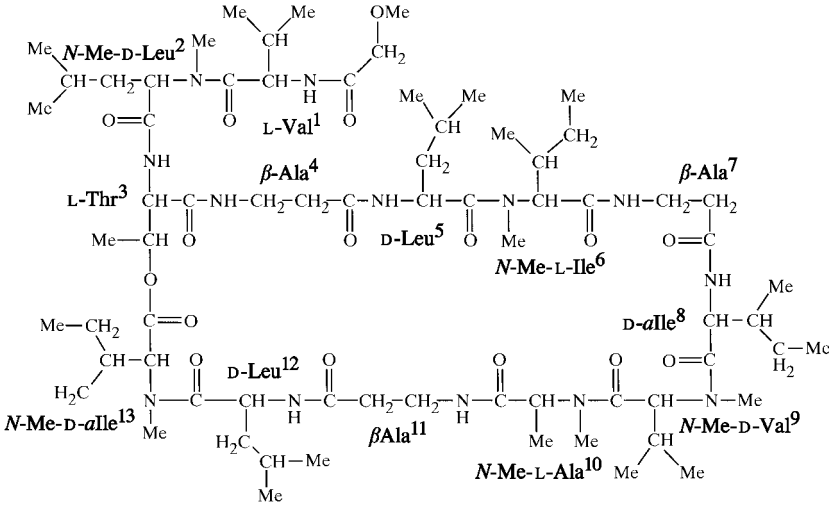
$U_{eq} = (1/3)\sum_i \sum_j U^{ij} a^i a^j \mathbf{a}_i . \mathbf{a}_j .$

	x	*y*	*z*	U_{eq}
O	0.8363 (4)	0.8527 (2)	1.2845 (7)	0.111 (2)
C1	0.8383 (4)	0.8637 (3)	1.1909 (10)	0.079 (2)
C2	0.8912 (5)	0.8536 (4)	1.1132 (13)	0.111 (4)
O3	0.8817 (4)	0.8684 (3)	1.0101 (8)	0.144 (4)
C4	0.9295 (8)	0.8602 (7)	0.9324 (19)	0.242 (13)
N-1	0.7948 (3)	0.88547 (18)	1.1478 (6)	0.0694 (17)
Cα-1	0.7368 (3)	0.8949 (2)	1.2064 (7)	0.0633 (18)
C-1	0.6824 (3)	0.89233 (19)	1.1253 (6)	0.0540 (16)
O-1	0.6935 (3)	0.89692 (16)	1.0272 (4)	0.0678 (14)
Cβ-1	0.7406 (5)	0.9323 (3)	1.2533 (9)	0.091 (3)
Cγ1-1	0.7526 (6)	0.9602 (3)	1.1620 (13)	0.116 (4)
Cγ2-1	0.7920 (6)	0.9337 (4)	1.3432 (11)	0.132 (5)
N-2	0.6237 (3)	0.88975 (16)	1.1659 (5)	0.0555 (14)
Cα-2	0.5695 (3)	0.89518 (18)	1.0901 (6)	0.0551 (16)
C-2	0.5438 (3)	0.8596 (2)	1.0535 (6)	0.0573 (17)
O-2	0.5175 (3)	0.83891 (16)	1.1161 (5)	0.0768 (15)
Cβ-2	0.5173 (4)	0.9185 (2)	1.1405 (8)	0.074 (2)
Cγ-2	0.5385 (5)	0.9557 (3)	1.1671 (11)	0.096 (3)
Cδ1-2	0.5608 (8)	0.9758 (3)	1.0729 (15)	0.141 (6)
Cδ2-2	0.4862 (7)	0.9749 (4)	1.2263 (11)	0.135 (6)
C1*N*-2	0.6101 (4)	0.8781 (2)	1.2766 (7)	0.068 (2)
N-3	0.5521 (3)	0.85250 (15)	0.9475 (5)	0.0561 (14)
Cα-3	0.5360 (3)	0.81993 (18)	0.8949 (7)	0.0580 (17)
C-3	0.5946 (4)	0.8058 (2)	0.8353 (7)	0.0643 (19)
O-3	0.5966 (3)	0.8051 (2)	0.7361 (6)	0.097 (2)
Cβ-3	0.4793 (4)	0.8232 (2)	0.8184 (8)	0.068 (2)
Cγ-3	0.4569 (5)	0.7885 (3)	0.7709 (11)	0.106 (4)
Oγ-3	0.4262 (2)	0.83740 (13)	0.8813 (5)	0.0669 (14)
N-4	0.6426 (3)	0.79701 (18)	0.8989 (6)	0.0718 (18)
Cα-4	0.7061 (4)	0.7873 (2)	0.8579 (9)	0.076 (2)
Cβ-4	0.7528 (4)	0.8169 (2)	0.8623 (8)	0.073 (2)
C-4	0.7432 (4)	0.8448 (2)	0.7760 (7)	0.0635 (19)
O-4	0.7620 (4)	0.8397 (2)	0.6832 (5)	0.098 (2)
N-5	0.7132 (3)	0.87428 (15)	0.8067 (5)	0.0586 (14)
Cα-5	0.7039 (4)	0.9050 (2)	0.7385 (6)	0.0606 (18)
C-5	0.6338 (3)	0.91335 (19)	0.7288 (6)	0.0566 (17)
O-5	0.5966 (2)	0.90412 (17)	0.7990 (5)	0.0745 (16)
Cβ-5	0.7381 (4)	0.9366 (2)	0.7889 (7)	0.070 (2)
Cγ-5	0.8108 (4)	0.9332 (3)	0.7965 (10)	0.092 (3)
Cδ1-5	0.8396 (6)	0.9642 (4)	0.8601 (12)	0.130 (5)
Cδ2-5	0.8421 (5)	0.9301 (5)	0.6880 (14)	0.145 (6)
N-6	0.6154 (3)	0.93323 (17)	0.6412 (5)	0.0619 (15)
Cα-6	0.5461 (4)	0.9423 (2)	0.6307 (7)	0.0654 (19)
C-6	0.5196 (4)	0.9202 (2)	0.5397 (7)	0.066 (2)
O-6	0.5321 (4)	0.92668 (19)	0.4428 (5)	0.094 (2)
Cβ-6	0.5351 (4)	0.9815 (2)	0.6107 (9)	0.078 (2)
Cγ1-6	0.5626 (6)	1.0060 (3)	0.6953 (12)	0.105 (4)
Cγ2-6	0.4635 (5)	0.9882 (3)	0.6035 (14)	0.120 (5)
Cδ1-6*A*†	0.5549 (10)	1.0442 (5)	0.6740 (18)	0.132 (7)
Cδ1-6*B*‡	0.555 (2)	0.9998 (11)	0.809 (4)	0.080 (13)
C1*N*-6	0.6565 (4)	0.9429 (3)	0.5503 (7)	0.077 (2)
N-7	0.4874 (3)	0.89124 (17)	0.5689 (6)	0.0691 (17)
Cα-7	0.4701 (4)	0.8629 (2)	0.4955 (10)	0.082 (3)
Cβ-7	0.4005 (4)	0.8520 (2)	0.5037 (9)	0.073 (2)
C-7	0.3560 (4)	0.8762 (2)	0.4465 (8)	0.075 (2)
O-7	0.3676 (4)	0.8886 (2)	0.3553 (6)	0.109 (2)
N-8	0.3025 (3)	0.88417 (18)	0.4996 (6)	0.0674 (17)
Cα-8	0.2514 (4)	0.9048 (2)	0.4492 (8)	0.075 (2)
C-8	0.1892 (3)	0.8843 (2)	0.4577 (7)	0.0617 (19)
O-8	0.1832 (2)	0.86075 (14)	0.5258 (5)	0.0698 (14)
Cβ-8	0.2442 (5)	0.9414 (2)	0.5038 (13)	0.101 (4)
Cγ1-8	0.2296 (8)	0.9376 (3)	0.6256 (14)	0.142 (6)

Cγ2-8	0.3024 (7)	0.9640 (4)	0.485 (2)	0.167 (8)
Cδ-8	0.3125 (8)	0.9758 (4)	0.368 (3)	0.237 (16)
N-9	0.1417 (3)	0.89395 (17)	0.3907 (7)	0.075 (2)
Cα-9	0.0784 (4)	0.8780 (2)	0.4084 (9)	0.075 (2)
C-9	0.0629 (4)	0.8543 (2)	0.3111 (9)	0.082 (3)
O-9	0.0446 (4)	0.8673 (2)	0.2257 (7)	0.110 (3)
Cβ-9	0.0252 (5)	0.9054 (2)	0.4269 (12)	0.099 (4)
Cγ1-9	−0.0371 (5)	0.8861 (4)	0.4475 (15)	0.128 (5)
Cγ2-9	0.0417 (6)	0.9298 (3)	0.5205 (15)	0.134 (6)
C1*N*-9	0.1493 (6)	0.9187 (3)	0.3012 (12)	0.124 (5)
N-10	0.0704 (4)	0.81855 (18)	0.3175 (7)	0.083 (2)
Cα-10	0.0923 (4)	0.7992 (2)	0.4139 (8)	0.071 (2)
C-10	0.1591 (4)	0.7848 (2)	0.3921 (8)	0.064 (2)
O-10	0.1926 (3)	0.79725 (17)	0.3177 (6)	0.0841 (17)
Cβ-10	0.0446 (5)	0.7719 (3)	0.4542 (12)	0.100 (3)
C1*N*-10	0.0555 (7)	0.7980 (3)	0.2199 (11)	0.120 (4)
N-11	0.1790 (3)	0.76012 (16)	0.4603 (6)	0.0658 (17)
Cα-11	0.2446 (4)	0.74741 (19)	0.4592 (7)	0.0630 (18)
C-11	0.2811 (3)	0.78030 (18)	0.6256 (6)	0.0542 (17)
O-11	0.3074 (3)	0.76078 (16)	0.6933 (5)	0.0835 (17)
Cβ-11	0.2903 (4)	0.7750 (2)	0.5063 (6)	0.0614 (18)
N-12	0.2430 (3)	0.80595 (16)	0.6577 (5)	0.0608 (15)
Cα-12	0.2342 (4)	0.8167 (2)	0.7692 (7)	0.0635 (19)
C-12	0.2844 (4)	0.8441 (2)	0.7992 (7)	0.0604 (18)
O-12	0.3097 (3)	0.86136 (15)	0.7256 (5)	0.0703 (14)
Cβ-12	0.1678 (4)	0.8328 (3)	0.7842 (9)	0.078 (2)
Cγ-12	0.1141 (5)	0.8067 (3)	0.7747 (11)	0.106 (4)
Cδ1-12	0.0513 (5)	0.8275 (6)	0.7534 (16)	0.169 (8)
Cδ2-12	0.1057 (8)	0.7843 (5)	0.8719 (18)	0.173 (7)
N-13	0.2993 (3)	0.84950 (18)	0.9040 (5)	0.0610 (15)
Cα-13	0.3462 (4)	0.8777 (2)	0.9271 (7)	0.067 (2)
C-13	0.4078 (4)	0.8705 (2)	0.8638 (7)	0.0624 (19)
O-13	0.4354 (3)	0.89116 (16)	0.8072 (6)	0.0799 (16)
Cβ-13	0.3225 (4)	0.9154 (2)	0.9117 (10)	0.082 (3)
Cγ1-13	0.3638 (6)	0.9417 (3)	0.9691 (13)	0.114 (4)
Cγ2-13	0.2533 (6)	0.9193 (3)	0.9464 (17)	0.145 (6)
Cδ-13	0.3565 (8)	0.9784 (3)	0.942 (2)	0.182 (9)
C1*N*-13	0.2765 (6)	0.8283 (3)	0.9926 (8)	0.098 (3)
O1*S*-14	0.8852 (3)	0.79486 (18)	1.3890 (7)	0.099 (2)
O2*S*-14	0.8812 (4)	0.8102 (2)	0.6122 (8)	0.122 (3)
O3*S*-14	0.3904 (4)	0.8487 (3)	0.1817 (7)	0.123 (3)
O4*S*-14	0.1315 (4)	0.7146 (2)	0.6398 (7)	0.116 (3)
O5*S*-14	0.3002 (6)	0.7315 (3)	0.9010 (9)	0.153 (4)
O6*S*-14	0.3157 (4)	0.7892 (3)	0.2361 (9)	0.145 (4)
O7*S*-14	0.9099 (5)	0.7570 (4)	0.7459 (12)	0.175 (5)
O8*S*-14	0.6305 (6)	0.8360 (3)	0.5309 (9)	0.153 (4)
O9*S*-14	0.1835 (5)	0.6934 (3)	0.8642 (8)	0.132 (3)
O10*S*-14	0.7488 (6)	0.8581 (4)	0.4717 (10)	0.191 (6)
O11*S*-14	0.0098 (6)	0.7119 (4)	0.7105 (13)	0.186 (5)
O12*S*-14§	0.9077 (15)	0.7531 (8)	0.9624 (16)	0.251 (13)

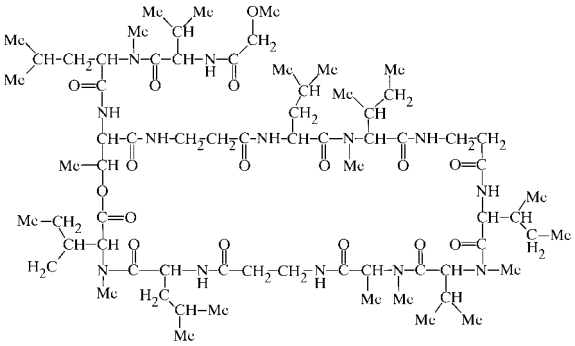
† Site occupancy = 0.78 (2). ‡ Site occupancy = 0.22 (2).
§ Site occupancy = 0.65.

SX1064.Scheme

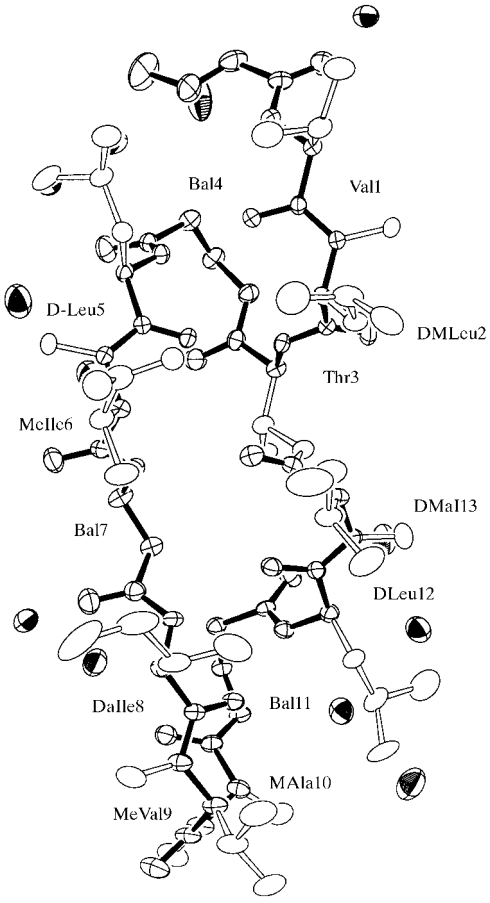


TNLP-Id

SX1064.Contents



SX1064.Fig. 1



INTERNATIONAL UNION OF CRYSTALLOGRAPHY

Electronic Proof Instructions

These proofs should be returned **within 14 days of January 27 1999**. After this period, the Editors reserve the right to publish articles with only the Managing Editor's corrections.

Please

(1) Read the proofs and indicate corrections on the proof (see next page for details).

(2) Check that the references are correct and complete.

(3) Return one copy of the proofs immediately

(a) by e-mail, giving a full description of all corrections required, to

sc@iucr.org

The subject line of the e-mail should contain the reference number of the paper. A copy of the corrected proofs should also be mailed to Chester.

(b) via facsimile machine (corrections should be clearly marked in black ink, not pencil) by dialling

44 1244 314888

It is recommended that authors check that the transmission has been successful and also send the corrected proofs by mail.

or (c) by mail to

Mr P. STRICKLAND
MANAGING EDITOR,
INTERNATIONAL UNION OF CRYSTALLOGRAPHY,
5 ABBEY SQUARE,
CHESTER CH1 2HU,
ENGLAND

TELEPHONE: 44 1244 342878

Substantial alterations, apart from occasioning delay in publication, are much more expensive than many authors would suppose. Authors may therefore be required to pay for any major alterations from their original copy, and it may sometimes be necessary to disallow such changes. Where alterations are unavoidable every effort should be made to substitute words or phrases equal in length to those deleted.

Please note that in order to save postal expenses and clerical work, the typescript, drawings and photographs of articles are normally destroyed after publication. Drawings and photographs will only be returned to authors if their return is specifically requested.

Authors wishing to obtain the publication details of their paper should refer to the status information service on the IUCr web pages (http://www.iucr.org/iucr-top/docs/status.html).

Proof Corrections

Please indicate your corrections on the enclosed proofs. The Managing Editor will then mark the corrections on a second proof which will be sent to the printer. It is therefore important to make clear to the Managing Editor what correction is needed, but it is not important how this is done. Corrections may be made in the text and margin in any of the commonly used systems (Continental European, American or Russian, as well as English). The main points of the system recommended by the printer are given below.

(1) Each place in the text where a correction is needed should be indicated either by crossing out the characters to be corrected or by an insert mark (/) if an insertion is needed.
(2) The correct character, word, instruction or insertion should be shown in the margin at one end of the line and should be terminated with a long slash mark (/).
(3) The corrections in the margins (both left and right margins may be used) should be arranged in the same sequence as they are required in the line of text.
(4) Characters to be printed in the superior position, such as superscripts, apostrophes and quotation marks, are to be so identified by the symbol ∨ under them, e.g. $\sqrt{2}$ or $\sqrt{''}$. Characters to be printed in the inferior position, such as subscripts, are to be identified by the symbol ∧ over them, e.g. A_2.
(5) Instructions written in the margins should be encircled. This indicates that this text is not to be printed. This does not apply to the full stop (period), the colon and the solidus (slash mark), which are circled for clarity.
(6) Some instructions are needed so frequently that it is convenient to indicate them simply with special symbols or abbreviations. The symbols are recognized as instructions without being circled. Some frequently used instructions are given in the following list.

Alteration	Marginal mark	Mark in text
Insert or substitute:		
Space	#	/ (for an insertion) or delete material to be replaced
Full stop (period)	⊙	
Colon	:⊙	
Solidus (slash mark)	/⊙	
Hyphen	-⊙	
Rule	⊙	
Chemical bond	bond	
Superior (e.g. superscript 2 or apostrophe	$\sqrt{2}$ or $\sqrt{'}$	
Inferior (e.g. subscript 2)	A_2	
Change to:		
Capitals	caps	≡ under characters
Small capitals	s c	= under characters
Italic type	ital	– under characters
Bold type	bold	~ under characters
Lower case letters	l c	Circle characters
Roman type	Rom	Circle characters
Delete	⌒	Cross out unwanted material
Delete and close up	⌒	Cross out unwanted material and surround with ⌒
Close up	⌒	⌒ around space to be closed up
Invert type	⊙	Circle inverted characters
Transpose	tr	⌐¬ between letters or words
Faulty setting (e.g. broken type)	X	Circle defective characters
Leave as printed	stet	..... under material to be left
New paragraph	n p	⊏ before first word of new paragraph
No new paragraph or line	run on	⌒ between lines

Please note
(a) No correction should be made in the text without an accompanying mark in the margin, or the correction may be easily missed.
(b) Complicated corrections can be explained in a covering letter.

Acta Crystallographica Section C

PAID OFFPRINT ORDER FORM
Return within 14 days of January 27 1999

PLEASE NOTE THAT 25 FREE OFFPRINTS WILL AUTOMATICALLY BE SENT TO THE ADDRESS GIVEN BELOW. ONLY RETURN THIS FORM IF YOU REQUIRE ADDITIONAL PAID OFFPRINTS

Please keep a copy of this order and send the original to:

MANAGING EDITOR
International Union of Crystallography
5 Abbey Square
Chester CH1 2HU, England

Article No.: C981438-SX1064

Author(s) Mitsunobu Doi, Toshimasa Ishida, Motomasa Kobayashi, Jeffrey R. Deschamps and Judith L. Flippen-Anderson

Title of article The highly solvated structure of theonellapeptolide Id, a tridecapeptide lactone from the Okinawa marine sponge ***Theonella swinhoei***

I wish to order . . . . . paid offprints

These offprints should be sent to

Name Dr. Mitsunobu Doi

Address Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahata, Takatsuki, Osaka 569-11, Japan,

If the above address is not correct, please indicate an alternative:

Date | Signature

Payments to MUNKSGAARD may take place directly by cheque or by transfer to postal account No. 8162050, Copenhagen, Denmark.

(please help us to identify your payment by marking your remittance "Payment of Acta Crystallographica Section C offprints, art. No. SX1064")

A remittance for . . . . . payable to MUNKSGAARD ☐ is enclosed ☐ has been transferred to MUNKSGAARD's postal account No. 8162050, Copenhagen, Denmark.

☐ An official purchase order ☐ is enclosed ☐ will follow

Purchase order No.

Spaces below for the use of MUNKSGAARD, Copenhagen

Date of despatch	Number of parcels	Weight	Postage	Invoice, date, No.

OFFPRINTS

Offprints are printed exactly as the article appears in the journal. Extracts of the preceding or subsequent article will not be "blanked out". Offprints of articles which do not commence at the top of a right-hand page in the journal will include the last part of the preceding article, whilst offprints of articles which do not finish at the bottom of a left-hand page in the journal will include the first part of the subsequent article.

Twenty-five offprints are supplied free. Do not return this form if you only require the free offprints.

Further offprints without limit of number may be purchased at the prices given in the table below. the requirements of all joint authors, if any, and of their laboratories should be included in a single order, specifically ordered on the form overleaf, which must be accompanied by a remittance payable to MUNKSGAARD unless an official purchase order is sent. All orders must be submitted promptly; it will not be possible to supply reprints for orders received after the journal is printed.

Please note that normally offprints are sent about one month after publication of the article, and normally by surface mail. If offprints are wanted by air mail additional costs will be invoiced.

Orders should be forwarded to:

MANAGING EDITOR
International Union of Crystallography
5 Abbey Square
Chester CH1 2HU, England

PRICE LIST OF OFFPRINTS

Prices are given in danish kroner and include postage.

Offprints with covers are only available by special order. Please contact the Managing Editor (at the address given above) for a quotation.

	Size of paper (in printed pages)				
Number of additional offprints required	1–2	3–4	5–8	9–16	Additional 8's
50	297	425	587	890	394
100	429	601	839	1276	519
150	565	777	1092	1663	649
200	700	965	1345	2052	808
Additional 50's	134	176	253	387	130

IMPORTANT:
European Union residents: Please add your local VAT to the price in DKK.