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cis,cis-Ceratospongamide monohydrate

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Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.006 Å
R factor = 0.056
wR factor = 0.141
Data-to-parameter ratio = 16.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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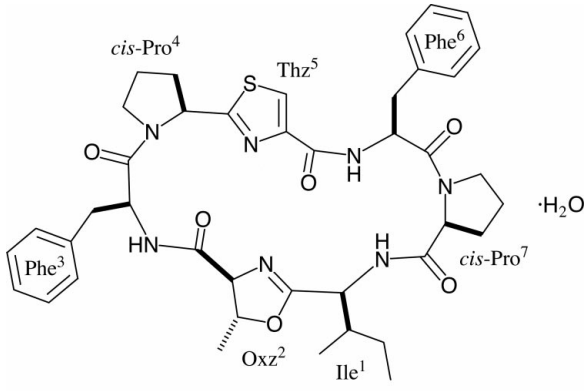
In the title compound, $C_{41}H_{49}N_7O_6S\cdot H_2O$, a water molecule is located close to the peptide ring and forms hydrogen bonds with the carboxyl groups of two Phe residues. The peptide structure is folded and the thiazole ring is stacked above an amide bond.

Comment

Ceratospongamide (CS) is a cyclic heptapeptide containing oxazoline (Oxz) and thiazole (Thz) (Tan *et al.*, 2000). Two isomers of CS, *cis,cis*-CS and *trans,trans*-CS, are known, relating to the *cis*- and *trans*-rotamers of proline, and each isomer shows different bioactivities. *cis,cis*-CS is partially converted to the *trans,trans*-isomer by heat at 423–433 K (Tan *et al.*, 2000). Very careful strategies (Yokokawa *et al.*, 2001; Kutsumura *et al.*, 2002) and kinetic control (Deng & Taunton, 2002) are necessary for the chemical synthesis of each isomer. Tetragonal crystals of the stable isomer, *cis,cis*-CS, were grown from an aqueous methanol solution (Doi *et al.*, 2002). Here, we report the structure of a monoclinic crystal grown from aqueous hexylene glycol, *cis,cis*-CS monohydrate, (I).



(I)

The molecule of *cis,cis*-CS is folded, and the water molecule (W^8) is cocrystallized (Fig. 1). The *cis*-amide rotamers are confirmed for Pro^4 and Pro^7: $\omega_3 = -11.6$ (6) and $\omega_6 = -4.6$ (6); these are the torsion angles of the amido bonds between Phe^3–Pro^4 and Phe^6–Pro^7, respectively. The peptide ring turns at two Pro residues, and the Thz^5 ring faces the amide bond of Oxz^2–Phe^3. The W^8 molecule is located close to the peptide ring and interacts with Phe^3 O and Phe^6 O atoms: $O(W^8)\cdots Phe^3\text{-}O$ = 2.920 (5) and $O(W^8)\cdots Phe^6\text{-}O$ = 2.866 (5) Å. Fig. 1 shows the peptide structure and also the accessible surface of the peptide, calculated by *MSMS* (Sanner *et al.*, 1996). A small cavity is observed on the peptide surface, and the W^8 molecule

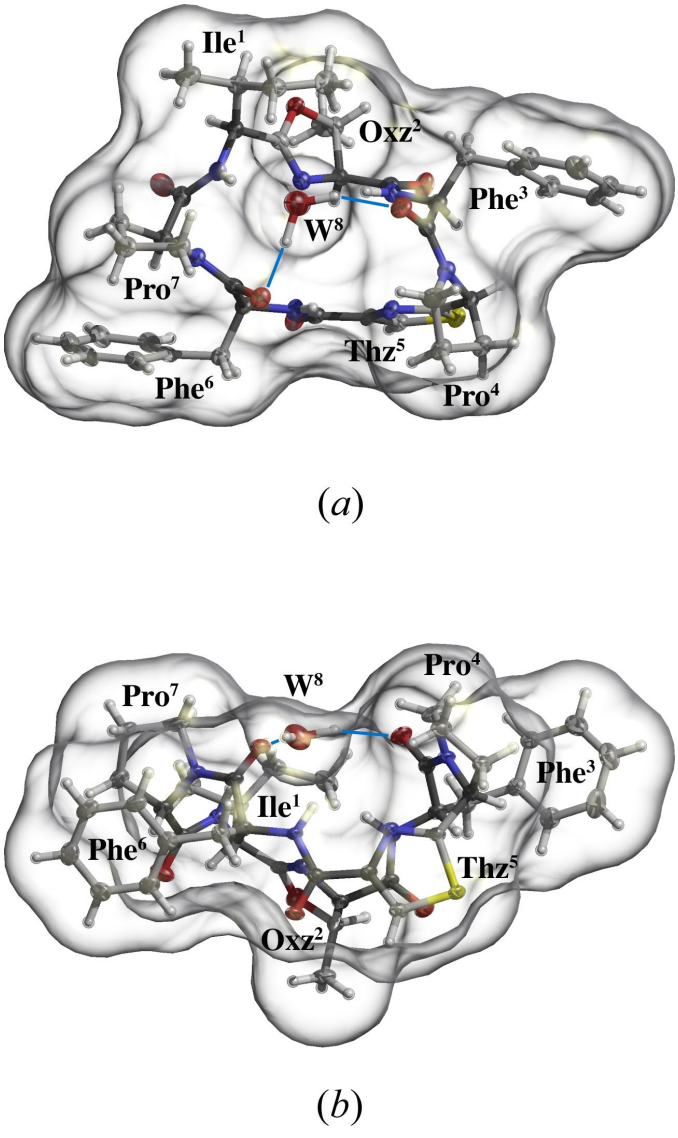


Figure 1
Structure of *cis,cis*-CS (*Raster3D*; Merritt & Bacon, 1997), showing (*a*) top and (*b*) side views. Thin lines represent hydrogen bonds. The transparent shell represents the accessible surface of the peptide, calculated by *MSMS* (Sanner *et al.*, 1996).

is located in it. The peptide conformation is likely to be affected by hydration, but a least-squares fit shows that the structures of the anhydrous and the title monohydrate crystals are very similar to each other, with an r.m.s. deviation of 0.086 Å (Fig. 2). It seems that the small cavity accepted the water molecule, and no significant conformational change resulted from the hydration.

Experimental

cis,cis-CS (5–8 mg) was dissolved in 0.3 ml hexylene glycol, and water was added to the solution, up to 5–10% (*v*/*v*). Crystals were grown after 30–40 days at room temperature. A crystal was mounted on a nylon loop (Hampton Res., USA) with glycerol and was flash-frozen under a nitrogen stream at 100 K.

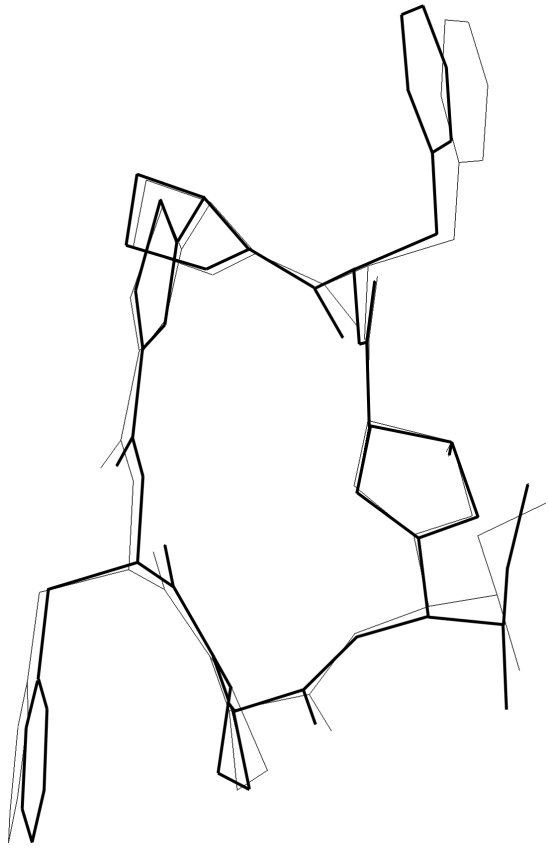


Figure 2
Superposition of the structures of *cis,cis*-CS (*Swiss-PDBviewer*; Guex & Peitsch, 1997). Thin and bold lines represent the structures of the tetragonal (anhydrous crystal) and monoclinic (title monohydrate crystal) forms.

Crystal data

$C_{41}H_{49}N_7O_6S\cdot H_2O$
M_r = 785.95
Monoclinic, $P2_1$
a = 12.037 (3) Å
b = 13.239 (3) Å
c = 14.158 (3) Å
β = 113.728 (4)°
V = 2065.5 (8) Å^3
Z = 2
D_x = 1.264 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 15361 reflections
θ = 2.2–19.9°
μ = 0.14 mm^{-1}
T = 100 (2) K
Needle, colourless
0.45 × 0.03 × 0.03 mm

Data collection

Bruker SMART APEX CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.814, T_{max} = 0.997
13044 measured reflections
8394 independent reflections
5679 reflections with $I > 2\sigma(I)$
R_{int} = 0.050
θ_{max} = 28.3°
$h = -15 \rightarrow 12$
$k = -17 \rightarrow 16$
$l = -18 \rightarrow 18$
52 standard reflections
every 13044 reflections
intensity decay: 0.1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.141
S = 1.00
8394 reflections
513 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0509P)^2 + 0.3572P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.37 e Å^{-3}
$\Delta\rho_{min}$ = −0.43 e Å^{-3}
Absolute structure: (Flack, 1983), 3058 Friedel pairs
Flack parameter = 0.00 (10)

H atoms of the peptide were positioned at calculated positions and constrained during the refinement. The H atoms of the water molecule were found from a difference Fourier map and refined. The O—H bond lengths are 1.09 (7) and 1.16 (11) Å.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: SAINT-*Plus* (Bruker, 1998); program(s) used to solve structure: *SHELXD* (Sheldrick & Gould, 1996); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *Raster*3*D* (Merritt & Bacon, 1997); software used to prepare material for publication: *PARST* (Nardelli, 1995).

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