(*DENZO*; Otwinowski & Minor, 1994) employing all reflections observed. H atoms in compounds (I) and (II) were placed at calculated positions (C—H 0.96 Å), except for the hydroxyl-H atoms which were found from difference Fourier maps. In compound (I), all H atoms were refined isotropically using a riding model, while H1 was refined with an isotropic displacement parameter. In the final cycle of refinement, isotropic displacement parameters of the methyl H atoms on C12 and C13 were fixed to their values equal to those obtained from the previous cycle. All H atoms in (II) were refined isotropically. In the final cycle of refinement, all H parameters of methyl C14 and C16 were held fixed to those obtained from the previous cycle.

For both compounds, data collection: *XDIP* (Mac Science, 1996); data reduction: *DENZO* (Otwinowski & Minor, 1994); program(s) used to solve structures: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structures: *CRYSTAN-GM* (Edwards *et al.*, 1996); molecular graphics: *ORTEP* (Johnson, 1970); software used to prepare material for publication: *CRYSTAN-GM* (Edwards *et al.*, 1996).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: OA1055). Services for accessing these data are described at the back of the journal.

References

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Bläser, D., Boese, R., Billups, W. E., Halley, M. M., Maulitz, A. H., Mohler, D. L. & Volhardt, K. P. C. (1994). *Angew. Chem. Int. Ed. Engl.* **33**, 313–305.

Bläser, D., Boese, R., Brett, W. A., Rademacher, P., Schwager, H., Stanger, M. & Volhardt, K. P. C. (1989). *Angew. Chem. Int. Ed. Engl.* **28**, 206–208.

Boese, R. & Bläser, D. (1988). *Angew. Chem. Int. Ed. Engl.* **27**, 304–305.

Cambridge Structural Database (1996). *QUEST3D User's Manual.* Version 2.3.7. Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, England.

Courtois, A., Carré, M. C., Caubère, P. & Grégoire, B. (1987). *Acta Cryst.* C**43**, 501–503.

Courtois, A., Protas, J., Mourad, M. S. & Caubère, P. (1975). *Acta Cryst.* B**31**, 1907–1912.

Courtois, A., Protas, J., Mourad, M. S. & Caubère, P. (1977). *Acta Cryst.* B**33**, 208–210.

Edwards, C., Gilmore, C. J., Mackey, S. & Stewart, N. (1996). *CRYSTAN-GM. Program for the Solution and Refinement of Crystal Structures.* Version 6.3.3. University of Glasgow, Scotland, and MacScience Co. Ltd, Yokohama, Japan.

Frisch, M. J., Trucks, G. W., Schlegel, H. B., Gill, P. M. W., Johnson, B. G., Robb, M. A., Cheeseman, J. R., Keith, T., Petersson, G. A., Montgomery, J. A., Raghavachari, K., Al-laham, M. A., Zakrewski, V. G., Ortiz, J. V., Foresman, J. B., Cioslowski, J., Stefanof, B. B., Nannayakkara, A., Challacombe, M., Peng, C. Y., Ayala, P. Y., Chen, W., Wong, M. W., Andres, J. L., Replogle, E. S., Gomperts, R., Martin, R. L., Fox, D. J., Binskley, J. S., Defrees, D. J., Baker, J., Stewart, J. P., Head-Gordon, M., Gonzalez, C. & Pople, J. A. (1996). *GAUSSIAN*94, Revision D.3. Gaussian Inc., Pittsburgh, Pennsylvania, USA.

Ianelli, S., Nardelli, M., Belletti, D., Geoffroy, P., Carré, M. C., Mouaddib, A. & Caubère, P. (1990). *Acta Cryst.* C**46**, 1318–1324.

Ianelli, S., Nardelli, M., Belletti, D., Jamart-Grègoire, B., Mouaddib, A. & Caubère, P. (1992*a*). *Acta Cryst.* B**48**, 178–185.

Ianelli, S., Nardelli, M., Belletti, D., Jamart-Grègoire, B., Mouaddib, A. & Caubère, P. (1992*b*). *Acta Cryst.* B**48**, 687–695.

Ianelli, S., Nardelli, M., Belletti, D., Jamart-Grègoire, B., Mouaddib, A., Zouaoui, M. A. & Caubère, P. (1992). *Acta Cryst.* C**48**, 1730–1733.

Johnson, C. K. (1970). *ORTEP.* Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

Kammermeier, S., Jones, P. G. & Herges, R. (1997). *Angew. Chem. Int. Ed. Engl.* **36**, 1757–1760.

Kaupp, G. & Boy, J. (1997). *Angew. Chem. Int. Ed. Engl.* **36**, 48–49.

Mac Science (1996). *XDIP. DIP3000 Diffractometer Control Software.* Mac Science Co. Ltd, Yokohama, Japan.

Otwinowski, Z. & Minor, W. (1994). *DENZO. An Oscillation Data Processing Suite for Macromolecular Crystallography.* Yale University and the Howard Hughes Medical Institute, New Haven, USA.

Toda, F., Tanaka, K., Stein, Z. & Goldberg, I. (1996). *Acta Cryst.* C**52**, 177–180.

Yoshioka, M., Iida, K., Kawata, E., Maeda, K., Kumakura, S. & Hasegawa, T. (1997). *J. Org. Chem.* **62**, 2655–2657.

Yoshioka, M., Miyazoe, S. & Hasegawa, T. (1993). *J. Chem. Soc. Perkin Trans.* 1, pp. 2781–2786.

Yoshioka, M., Momose, S., Nishizawa, K. & Hasegawa, T. (1992). *J. Chem. Soc. Perkin Trans.* 1, pp. 499–503.

Yoshioka, M., Nishizawa, K., Arai, K. & Hasegawa, T. (1991). *J. Chem. Soc. Perkin Trans.* 1, pp. 541–547.

Acta Cryst. (1998). C**54**, 1941–1943

A Cytosine and Tryptophan Hybrid Dipeptide: Cytosinyl-L-tryptophan–Water (2/6)

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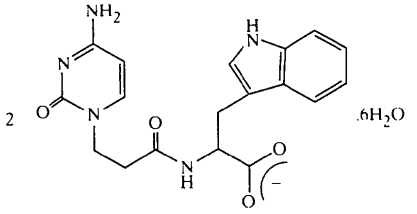
Abstract

The hybrid dipeptide of the title compound, $2C_{18}H_{19}N_5O_4.6H_2O$, containing cytosine base and L-tryptophan was crystallized in hexahydrated form; the solvent occupies 12% by weight of the asymmetric unit. Two independent molecules were distinguished by the different directions of their indole rings. All polar atoms of the title compound participate in hydrogen-bond formation, and a tight network is built by combination with solvent-mediated hydrogen bonds. A π–π electron interaction was observed between the indole and nucleic base; it is facilitated by hydrogen bonds.

Comment

The title compound, C-Trp, was designed in order to investigate the cooperative interactions between the nucleic acid and polypeptide molecules (Ishida *et al.*,

1990); hydrogen bonding and π–π stacking between the nucleic base and the functional group of the peptide was expected (Hélène & Maurizot, 1981). The properties of its chemical structure are similar to those of peptide nucleic acid (PNA). It is known that if the indole ring is hybridized with nucleic base it has high affinity against N7-quarternized guanine (Kamiichi *et al.*, 1986, 1987). In this paper, we report the interaction between indole and cytosine stabilized by water-mediated hydrogen bonds in the title compound, C-Trp.



C-Trp

The crystals of C-Trp are in the hexahydrated form and contain two crystallographically independent dipeptide molecules. All water atoms participate in hydrogen-bond formation with the dipeptide. In the case of the C-Trp complex with 7-methylated guanine, a pentahydrate has been reported (C-Trp:guanine:water = 1:1:5; Ishida *et al.*, 1993). Solvation may be necessary for the crystallization of this type of hybrid molecule. The two crystallographically independent molecules are mainly characterized by the orientation of the indole ring: the torsion angles φ (C9/29—N10/30—C10/30—C11/31) and χ (N10/30—C10/30—C12/32—C13/33) are $-159.7(5)/-122.1(4)$ and $82.9(4)/-66.8(4)°$, respectively. Both molecules contain carboxylate groups because there is no significant difference in the C—O bond lengths [C11/31—O11/31 = 1.24(4)/1.25(2) and C11/31—O12/32 = 1.27(13)/1.26(17) Å, respectively]. The acceptor O12/32 atoms of the carbonyl groups are located within hydrogen-bonding distance of the N23/3 and N24/4 atoms of cytosine in both molecules [2.734(5)–2.913(5) Å]. These possible interactions suggest an amino–imino tautomerism in the cytosine base, although the $\Delta\rho$ maps showed no clear H atom bonded to the N3/23 atom. Therefore, the chemical structure of the cytosine base is treated as the amino tautomer in this report.

The indole and cytosine rings are in parallel and overlapped arrangements; the ring–ring distance is shorter than expected from the van der Waals radii, the shortest distance being C4···C38($x-1$, y, $z-1$) = 3.370(7) Å. It has been suggested that the highest occupied molecular orbital (HOMO) of the indole ring prefers an interaction with the lowest unoccupied molecular orbital (LUMO) of the nucleic base (Ishida *et al.*, 1993). A π–π electron interaction is also suggested between the cytosine base and the indole ring in this crystal. Furthermore, the N atom of indole is hydrogen bonded to the carbonyl O atom of cytosine [N34···O22($x+1$, y, z) = 3.073(6) Å], and also to the carboxyl O atom [N14···O31(x, $y-1$, $z-1$) = 2.958(5) Å]. Interactions

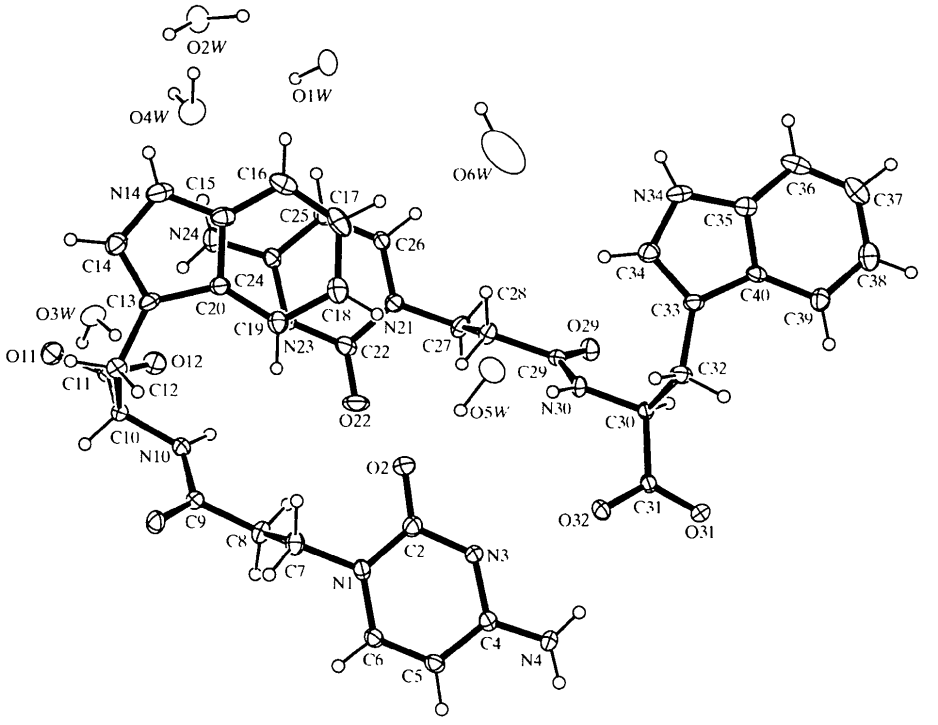


Fig. 1. A view of the title compound with displacement ellipsoids drawn at the 50% probability level.

of this type have been observed both in natural peptides (Hélène & Maurizot, 1981; Niu & Black, 1979) and in synthetic models (Hamilton & Little, 1990), and they work cooperatively in the selective recognition between the side chain of aromatic amino acids and nucleic bases (Kamiichi *et al.*, 1987). In C-Trp, the hydrogen bonds formed between the indole ring and neighbouring O atom may facilitate $\pi-\pi$ electron interaction between the aromatic side chain of the amino acid and the nucleic base.

Experimental

C-Trp was synthesized from 1-ethylcarboxycytosine and tryptophan methyl ester according to a previous report (Kamiichi *et al.*, 1987). An aqueous methanol solution yielded crystals of the hexahydrated form.

Crystal data

$2C_{18}H_{19}N_5O_4.6H_2O$
M_r = 846.85
Triclinic
$P\bar{1}$
a = 9.2032 (8) Å
b = 14.792 (4) Å
c = 7.483 (2) Å
α = 101.15 (2)°
β = 96.175 (14)°
γ = 88.701 (13)°
V = 993.6 (4) Å^3
Z = 1
D_x = 1.415 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 18 reflections
θ = 19.87–20.53°
μ = 0.931 mm^{-1}
T = 293 (2) K
Needle
0.78 × 0.11 × 0.10 mm
Colourless

Data collection

Rigaku AFC-5*R* diffractometer
2θ–ω scans
Absorption correction: none
6799 measured reflections
6774 independent reflections (including Friedel pairs)
6397 reflections with $I > 2\sigma(I)$

R_{int} = 0.023
θ_{max} = 65.09°
$h = -10 \rightarrow 10$
$k = -17 \rightarrow 17$
$l = -8 \rightarrow 8$
4 standard reflections
every 100 reflections
intensity decay: 4.4%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.168
S = 0.966
6774 reflections
542 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.0792P)^2 + 1.7713P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.005
$\Delta\rho_{max}$ = 0.557 e Å^{-3}
$\Delta\rho_{min}$ = −0.408 e Å^{-3}

Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0309 (15)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.1 (3)

Table 1. *Hydrogen-bonding geometry (Å, °)*

D—H···A	D—H	H···A	D···A	D—H···A
N3—H···O32			2.734 (5)	
N4—H4A···O32	0.86	2.101	2.837 (5)	143.3
N14—H14···O31^{i}	0.86	2.140	2.958 (5)	158.6
N23—H···O12			2.913 (5)	
N24—H241···O12	0.86	2.116	2.891 (5)	149.7
N34—H34···O22^{ii}	0.86	2.213	3.073 (6)	178.6

Symmetry codes: (i) $x, y-1, z-1$; (ii) $1+x, y, z$.

Scan widths were $(1.732 + 0.3\tan\theta)°$ in ω with a background/scan time ratio of 0.5. H atoms were geometrically located and refined as riding with fixed isotropic displacement parameters ($U_{iso} = 1.2U_{eq}$ for the associated C atom, or $U_{iso} = 1.5U_{eq}$ for methyl C atoms). H atoms of water molecules were picked up from the difference Fourier map, except for those of O1*W* and O5*W*. No clear peaks were found for O1*W* or O5*W* from the map.

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* (Miller *et al.*, 1994). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997). Molecular graphics: *ORTEP*III (Burnett & Johnson, 1996). Software used to prepare material for publication: *PARST* (Nardelli, 1983).

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References

Burnett, M. N. & Johnson, C. K. (1996). *ORTEP*III. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Hamilton, A. D. & Little, D. (1990). *J. Chem. Soc. Chem. Commun.* pp. 297–298.
Hélène, C. & Maurizot, J. C. (1981). *CRC Crit. Rev. Biochem.* **10**, 213–258.
Ishida, T., Iyo, H., Ueda, H., Doi, M. & Inoue, M. (1990). *J. Chem. Soc. Chem. Commun.* pp. 217–218.
Ishida, T., Tarui, M., In, Y., Ogiyama, M., Doi, M. & Inoue, M. (1993). *FEBS Lett.* **333**, 214–216.
Kamiichi, K., Danshita, M., Minamino, N., Doi, M., Ishida, T. & Inoue, M. (1986). *FEBS Lett.* **195**, 57–60.
Kamiichi, K., Doi, M., Nabae, M., Ishida, T. & Inoue, M. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. 1739–1745.
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.
Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.
Niu, C. H. & Black, S. (1979). *J. Biol. Chem.* **254**, 265–269.
Sheldrick, G. M. (1997). *SHELXL*97. *Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.