1,4,8,11-Tetrakis(carboxymethyl)-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazoniacyclotetradecane tetrachloride octahydrate

Shi-Fan Wang,[a] Huan-Qiu Li,[a] Ban-Feng Ruan,[a] Hai-Liang Zhu[a] and Seik Weng Ng[b]*

[a]Institute of Functional Biomolecules, State Key Laboratory of Pharmaceutical Biotechnology, Nanjing University, Nanjing 210093, People's Republic of China, and [b]Department of Chemistry, University of Malaya, 50603 Kuala Lumpur, Malaysia

Correspondence e-mail: seikweng@um.edu.my

The crystal structure of the centrosymmetric title compound, $C_{24}H_{48}N_4O_8^{4+} \cdot 4Cl^- \cdot 8H_2O$, consists of a 14-membered methyl-substituted $C_{10}N_4$ cationic ring which interacts with the chloride ions and water molecules of crystallization to give a three-dimensional hydrogen-bonded network structure.

Comment

The title compound, (I), a hydrochloride salt of an edta type of amino acid whose four amine N atoms belong to a 14-membered $C_{10}N_4$ macrocyclic ring (Fig. 1), is the methyl-substituted derivative of 1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid hexahydrate.

(I)
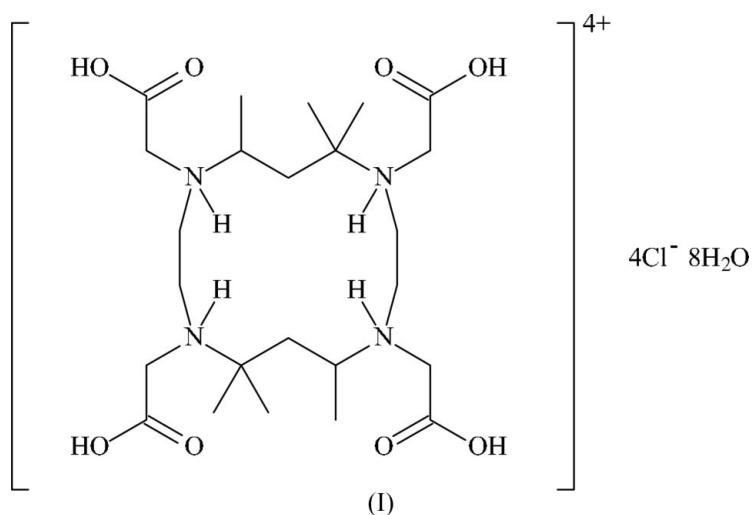
The unsubstituted parent compound exists in the zwitter-ionic form as two out of the four amine N atoms are protonated (Maurya *et al.*, 1991; Spirlet *et al.*, 1991). In the synthesis of such compounds, hydrochloric acid is usually added to precipitate the amino acid, but hydrochloric acid can be incorporated into the crystal structure, as was found in the present study.

The 14-membered macrocycle in (I) lies on a center of inversion; each N atom is linked to a carboxymethyl group, but the macrocycle carries four positive charges arising from the protonation of the N atoms. The net charge is balanced by four chloride ions; the cation and anions interact with each other and with the water molecules of crystallization to furnish a hydrogen-bonded (Table 1) network structure. Another homolog, namely 1,4,7,10-tetrakis(*N*-carboxymethyl)-1,4,7,10-tetraazacyclodecane, crystallizes as a dihydrochloride penta-hydrate; two of the four amine units of the 12-membered C_8N_4 ring are protonated (Aime *et al.*, 1999).

doi:10.1107/S1600536805020817

Experimental

The tetraazamacrocycle γ-C-*meso*-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane was synthesized according to the literature method of Hay *et al.* (1975). The macrocycle (0.28 g, 1 mmol) and five molar equivalents of ethyl bromoacetate (0.85 g, 5 mmol) were refluxed in 1 *M* sodium hydroxide for an hour. After the solution was cooled, 1 *M* hydrochloric acid was added to lower the pH to about unity. The solution was left in a refrigerator. Large colorless crystals separated and were collected and washed with water.

Crystal data

$C_{24}H_{48}N_4O_8^{4+} \cdot 4Cl^- \cdot 8H_2O$	$Z = 1$
$M_r = 806.59$	$D_x = 1.386$ Mg m^{-3}
Triclinic, $P\bar{1}$	Mo $K\alpha$ radiation
$a = 8.6283 (3)$ Å	Cell parameters from 8332
$b = 10.6995 (4)$ Å	reflections
$c = 11.0065 (4)$ Å	$\theta = 2.4$–$28.3°$
$\alpha = 100.161 (1)°$	$\mu = 0.38$ mm^{-1}
$\beta = 94.482 (1)°$	$T = 295 (2)$ K
$\gamma = 103.168 (1)°$	Block, colorless
$V = 966.42 (6)$ Å^3	$0.35 \times 0.22 \times 0.18$ mm

Data collection

Bruker APEX area-detector diffractometer	4153 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.017$
Absorption correction: none	$\theta_{max} = 27.5°$
11066 measured reflections	$h = -11 \rightarrow 11$
4351 independent reflections	$k = -13 \rightarrow 13$
	$l = -14 \rightarrow 14$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0657P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.044$	$+ 0.404P]$
$wR(F^2) = 0.121$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.05$	$(\Delta/\sigma)_{max} = 0.001$
4351 reflections	$\Delta\rho_{max} = 0.37$ e Å^{-3}
265 parameters	$\Delta\rho_{min} = -0.34$ e Å^{-3}
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Hydrogen-bond geometry (Å, °).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O1—H1o$\cdots$O1w	0.85 (1)	1.67 (1)	2.514 (2)	171 (3)
O3—H3o$\cdots$O2w^i	0.85 (1)	1.69 (1)	2.541 (2)	173 (3)
O1w—H1w1$\cdots$O4^{ii}	0.85 (1)	2.17 (3)	2.889 (2)	143 (4)
O1w—H1w2$\cdots$Cl1	0.85 (1)	2.40 (1)	3.221 (2)	163 (3)
O2w—H2w1$\cdots$O2^{iii}	0.84 (1)	2.00 (2)	2.767 (2)	152 (3)
O2w—H2w2$\cdots$Cl1^{iv}	0.84 (1)	2.25 (1)	3.087 (2)	179 (2)
O3w—H3w1$\cdots$Cl1	0.85 (1)	2.41 (2)	3.198 (2)	156 (3)
O3w—H3w2$\cdots$Cl2	0.85 (1)	2.40 (1)	3.216 (2)	163 (3)
O4w—H4w1$\cdots$Cl1^v	0.85 (1)	2.47 (1)	3.313 (2)	170 (3)
O4w—H4w2$\cdots$Cl2^v	0.85 (1)	2.38 (2)	3.172 (2)	157 (3)
N1—H1n$\cdots$O4w	0.86 (1)	2.02 (1)	2.869 (2)	174 (2)
N2—H2n$\cdots$Cl2^{vi}	0.86 (1)	2.32 (1)	3.173 (2)	170 (2)

Symmetry codes: (i) $x, y, z - 1$; (ii) $x, y, z + 1$; (iii) $-x + 1, -y, -z + 2$; (iv) $-x, -y, -z + 2$; (v) $x + 1, y, z$; (vi) $-x + 1, -y + 1, -z + 1$.
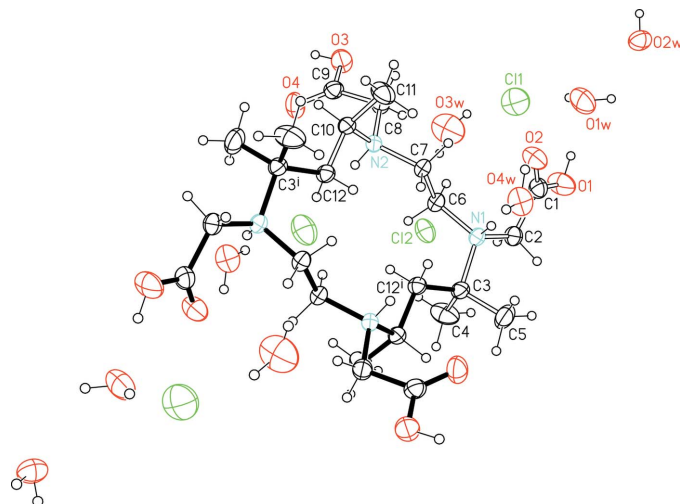

Figure 1
ORTEPII plot (Johnson, 1976) of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as spheres of arbitrary radii. [Symmetry code: (i) $2 - x, 1 - y, 1 - z$.]

The carbon-bound H atoms were positioned geometrically [C—H = 0.96–0.98 Å and $U_{iso} = 1.2U_{eq}(C)$, or $1.5U_{eq}(C)$ for methyl H atoms] and were included in the refinement in the riding-model approximation. The water, acid and amino H atoms were located in difference Fourier maps, and were refined with distance restraints of O—H = N—H = 0.85 (1) Å.

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

References

Aime, S., Barge, A., Bruce, J. I., Botta, M., Howard, J. A. K., Moloney, J. M., Parker, D., de Sousa, A. S. & Woods, M. (1999). *J. Am. Chem. Soc.* **121**, 5762–5771.

Bruker (2002). *SAINT* and *SMART*. Bruker AXS Inc., Madison, Wisconsin, USA.

Hay, R. W., Lawrence, G. A. & Curtis, N. F. (1975). *J. Chem. Soc. Perkin Trans. 1*, pp. 591–593.

Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Maurya, M. R., Zaluzec, E. J., Pavkovic, S. F. & Herlinger, A. W. (1991). *Inorg. Chem.* **30**, 3657–3662.

Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

Spirlet, M. R., Rebizant, J., Barthelemy, P. P. & Desreux, J. F. (1991). *J. Chem. Soc. Dalton Trans.* pp. 2477–2481.