a = 13.0786 (8) Å
b = 12.1740 (7) Å
c = 9.9027 (9) Å
β = 94.354 (8)°
V = 1572.1 (2) Å^3
Z = 4
D_x = 1.546 Mg m^{-3}
D_m not measured

μ = 1.411 mm^{-1}
T = 293 (2) K
Plate
0.540 × 0.132 × 0.036 mm
Dark green

Data collection

Enraf–Nonius CAD-4 diffractometer
ω scans
Absorption correction: ψ scans (Siemens, 1996*b*)
T_{min} = 0.516, T_{max} = 0.951
3736 measured reflections
3428 independent reflections
2787 reflections with $I > 2\sigma(I)$

R_{int} = 0.021
θ_{max} = 27°
$h = 0 \rightarrow 16$
$k = 0 \rightarrow 15$
$l = -12 \rightarrow 12$
2 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.101
S = 1.075
3428 reflections
210 parameters
H-atom parameters constrained (see below)

$w = 1/[\sigma^2(F_o^2) + (0.0562P)^2 + 0.6515P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.419 e Å^{-3}
$\Delta\rho_{min}$ = −0.805 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

Cu—O1	1.9189 (19)	Cu—O2	1.9942 (18)
Cu—N1	1.9229 (19)	Cu—O4	2.416 (2)
Cu—N2	1.992 (2)		
O1—Cu—N1	93.66 (8)	N2—Cu—O2	90.73 (7)
O1—Cu—N2	90.53 (8)	O1—Cu—O4	98.99 (8)
N1—Cu—N2	169.31 (9)	N1—Cu—O4	90.66 (8)
O1—Cu—O2	170.16 (8)	N2—Cu—O4	98.40 (7)
N1—Cu—O2	83.50 (8)	O2—Cu—O4	90.47 (8)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O4—H41···O2^{i}	0.83	2.12	2.936 (3)	167
O4—H42···O3^{ii}	0.88	2.01	2.856 (3)	159

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

The methyl group H atoms were included at calculated positions and refined as rigid groups. All other H atoms were found from difference Fourier syntheses and refined using a riding model.

Data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994). Cell refinement: *CAD-4 EXPRESS*. Data reduction: *XCAD-4* (Harms, 1997). Program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997). Molecular graphics: *XP* in *SHELXTL* (Siemens, 1996*a*). Software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1096). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1998). C**54**, 770–773

Bis(guanidinium) (Hydrogen triethylenetetraminehexaacetato)bismuthate(III) Tetrahydrate†

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Abstract

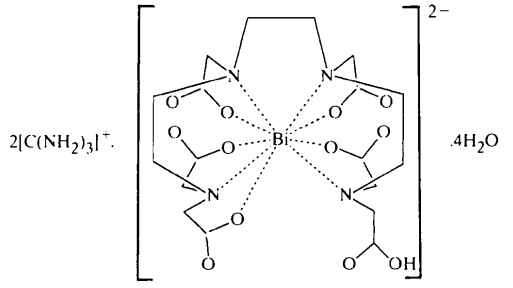
The Bi atom in the title compound, $(CH_6N_3)_2[Bi(C_{18}H_{25}N_4O_{12})].4H_2O$, is nine-coordinated through four N and five O atoms of the ttha ligand, where ttha denotes triethylenetetraminehexaacetate. The non-coordinated COOH group is involved in a strong hydrogen bond with an O atom of a neighbouring complex, thereby forming dimeric units.

† Alternative name: bis(guanidinium) [hydrogen 3,6,9,12-tetrakis(carboxylatomethyl-κO)-3,6,9,12-tetraaza-$\kappa^4 N$-tetradecanedioate-κO^1]-bismuth(III) tetrahydrate.

Comment

The use of bismuth compounds has been well known in medicine for more than two hundred years; new bismuth-based drugs (*e.g.* ranitidine bismuth citrate) are still being developed (Sun *et al.*, 1997; McColm *et al.*, 1996), and ^{212}Bi-labelled bismuth complexes are used in radiotherapy and for selective imaging. The radionuclide is attached to monoclonal antibodies *via* chelating agents such as ethylenediaminetetraacetic acid (edta) and *N,N,N′,N″,N″*-diethylenetriaminepentaacetic acid (dtpa) (Kozak *et al.*, 1986). Within this context, the development of new chelating agents able to form stable metal complexes in a biological environment is a matter of great concern. In addition to these medical applications, bismuth-based ceramics attract real interest in several fields, such as catalysis (Grasselli & Burrington, 1981), superconductivity (Maeda *et al.*, 1988) and ferroelectricity (Newnham *et al.*, 1971).

When Bi complexes are investigated from a structural viewpoint, great attention is paid to the potential stereochemical activity of the Bi 6*s* electron lone pair. Some ten years ago, bismuth coordination chemistry was still very poorly understood compared with that of transition metals, but interest in Bi complexes is now growing because of the wide applicability of this element. Against this background, we focused our attention on polyaminocarboxylates, which can form very stable complexes with a wide variety of metals. Previously, we studied the structures of $Bi(H_3ttha).3H_2O$, (2), and $Bi(HCydta).5H_2O$ (Wullens *et al.*, 1996), and discussed the crystallographic data with reference to those from other bismuth polyaminocarboxylates [nitrilotriacetic acid (nta), edta and dtpa complexes]. We report here the isolation and structure of the water-soluble Bi complex $(CH_6N_3)_2Bi(Httha).4H_2O$, (1), which presents singular differences from $Bi(H_3ttha)$, but strong similarities to the corresponding complexes of Dy^{III} and La^{III}: $(CH_6N_3)_2Dy(Httha).5H_2O$, (3), and $(CH_6N_3)_2La(Httha).3H_2O$, (4) (Ruloff *et al.*, 1996).



(1)

Although the ten coordinating sites of the ttha ligand were fully exploited in complex (2), complex (1) is characterized by a ninefold coordination (Fig. 1). The non-coordinating site is the un-ionized carboxylic acid for which the hydrogen (H101) has been located unambiguously: it corresponds to the density of the highest peak in a difference Fourier synthesis, and the C=O and C—OH distances of 1.18 (1) and 1.32 (1) Å, respectively, clearly indicate non-ionization. The coordination is quite similar to the stoichiometrically equivalent Dy^{III} complex, (3). The La^{III} equivalent complex, (4), exhibits a tenfold coordination, but one of the coordinating bonds, between the La atom and the protonated carboxylic acid group, was much longer than the other La—O bonds: the authors interpreted this situation by referring to the labilization of the carboxylic acid group (Ruloff *et al.*, 1996). The ligand conformation around the metal is analogous in complexes (1), (3) and (4). In complex (1), the proton of the non-coordinated carboxylic acid group (H101) is involved in a very strong hydrogen bond with atom O112 of a symmetry-related complex, thus forming dimeric entities. The OH conformation in the non-coordinated carboxylic acid group is antiperiplanar, the torsion angle O1—C101—O101—H101 being 173 (2)°.

Although the H atoms of the water molecules could not be localized, it appears that all four co-crystallized water molecules participate in four hydrogen bonds, two of which are between themselves. All but one of the guanidinium H atoms act as acceptors for a carboxylate O atom or for a water molecule, and so complete the hydrogen-bonding network.

When one compares the coordinating bond lengths in complexes (1), (2), (3), (4), and in an analogous Nd^{III} complex, $Na_3[Nd(ttha)].2.5NaClO_4.7.61H_2O$, (5) (Mondry & Starynowicz, 1997), in which the ttha ligand is fully deprotonated, it is obvious that the *M*—*L* distances (where *L* denotes the ligand donor atoms) vary over a smaller range in (1) than in (2). The larger range of *M*—*L* distances in (2) is not observed in the other complexes. As in the other lanthanide–ttha complexes, the mean *M*—O bonding distances in (1) are smaller than the mean *M*—N bonding distances. In all five complexes, the *M*—O distances are shorter for the carboxylates attached to the central N atoms than for carboxylates bonded to the external N atoms.

The coordination polyhedron around the Bi atom in (1) cannot reasonably be described on the basis of a square antiprism (SAP), nor of a trigonal prism. However, complex (3), in which the ligand wrapped itself around the metal in the same fashion as that observed in (1), was described as a monocapped SAP. While a first square-planar face can be defined in (1) and (3) [in (1): N3, O5, O12, O11], which is capped by an N atom [in (1): N4], the second square face [in (1): N2, N1, O2, O8] actually corresponds to a butterfly-like geometry, and the overall structure may not be described as a tricapped trigonal prism. In (1), the N1 atom is indeed located in an intermediate position between the capping position of a bicapped SAP and the site it should occupy to form a monocapped SAP. The main reason for the observed distortion is assumed

to be the presence of a non-coordinating oxygen (O1) that is strongly bonded to O112 *via* hydrogen bonding.

It is obvious from the coordination bond lengths that there is no stereochemically active lone pair in the title complex.

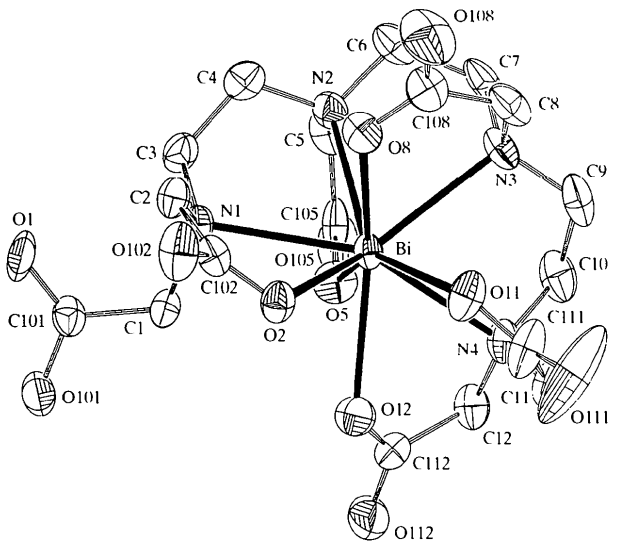


Fig. 1. View of complex (1) with the atom labelling. Ellipsoids correspond to 50% probability levels. H atoms and the guanidinium and water molecules have been omitted for clarity.

Experimental

The compound H_6ttha (1.00 g, 2.022 mmol) was dissolved in water (100 ml) by heating. Bismuth oxocarbonate, $Bi_2O_2CO_3$ (0.52 g, 1.02 mmol), was added to this solution and the mixture heated with stirring for 5 h. To the cooled suspension was added guanidinium carbonate, $(CH_6N_3)_2CO_3$ (0.36 g, 2.022 mmol). The mixture was heated with stirring for 1 h and then filtered. The clear filtrate was concentrated down to a volume of 5 ml by heating, and then cooled to 278 K. Colourless crystals suitable for X-ray analysis appeared after several days (found: C 26.90, H 5.08, N 15.58%; calculated for $C_{20}H_{45}BiN_{10}O_{16}$: C 26.97, H 5.09, N 15.73%).

Crystal data

$(CH_6N_3)_2[Bi(C_{18}H_{25}N_4O_{12})].4H_2O$
M_r = 890.66
Triclinic
$P\bar{1}$
a = 9.716 (3) Å
b = 10.447 (4) Å
c = 16.303 (6) Å
α = 87.56 (3)°
β = 89.14 (3)°
γ = 88.10 (3)°
V = 1652.2 (10) Å^3
Z = 2
D_x = 1.790 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 22 reflections
θ = 5.0–12.5°
μ = 5.420 mm^{-1}
T = 293 (2) K
Parallelepiped
0.3 × 0.2 × 0.2 mm
Colourless

Data collection

Huber four-circle diffractometer
ω scan
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.155, T_{max} = 0.303
7606 measured reflections
7606 independent reflections
5902 reflections with $F > 4\sigma(F)$
θ_{max} = 27.55°
$h = -12 \rightarrow 12$
$k = -13 \rightarrow 13$
$l = 0 \rightarrow 21$
1 standard reflection
every 50 reflections
intensity decay: 3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.119
S = 1.061
7606 reflections
428 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0732P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 3.285 e Å^{-3}
$\Delta\rho_{min}$ = −2.162 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

Bi—O2	2.554 (6)	Bi—N1	2.687 (6)
Bi—O5	2.474 (6)	Bi—N2	2.688 (7)
Bi—O8	2.327 (6)	Bi—N3	2.619 (7)
Bi—O11	2.408 (6)	Bi—N4	2.649 (7)
Bi—O12	2.560 (6)		
O8—Bi—O11	77.0 (2)	O2—Bi—N4	122.8 (2)
O8—Bi—O5	138.5 (2)	O12—Bi—N4	61.7 (2)
O11—Bi—O5	140.8 (2)	N3—Bi—N4	69.1 (2)
O8—Bi—O2	73.9 (2)	O8—Bi—N1	83.5 (2)
O11—Bi—O2	73.0 (2)	O11—Bi—N1	135.2 (2)
O5—Bi—O2	124.5 (2)	O5—Bi—N1	76.3 (2)
O8—Bi—O12	146.2 (2)	O2—Bi—N1	62.8 (2)
O11—Bi—O12	82.2 (2)	O12—Bi—N1	93.2 (2)
O5—Bi—O12	71.7 (2)	N3—Bi—N1	133.6 (2)
O2—Bi—O12	74.7 (2)	N4—Bi—N1	147.0 (2)
O8—Bi—N3	68.4 (2)	O8—Bi—N2	75.0 (2)
O11—Bi—N3	74.6 (2)	O11—Bi—N2	140.1 (2)
O5—Bi—N3	100.7 (2)	O5—Bi—N2	63.9 (2)
O2—Bi—N3	134.6 (2)	O2—Bi—N2	124.1 (2)
O12—Bi—N3	130.6 (2)	O12—Bi—N2	134.7 (2)
O8—Bi—N4	129.4 (2)	N3—Bi—N2	69.0 (2)
O11—Bi—N4	66.4 (2)	N4—Bi—N2	112.9 (2)
O5—Bi—N4	75.6 (2)	N1—Bi—N2	68.4 (2)

A suitable crystal was chosen and mounted in a glass capillary tube with mother liquor, because it was not stable in air. Numerical absorption corrections were therefore not possible, since the determination of the shape of the crystal, immersed in liquid, was extremely difficult (Kopfmann & Huber, 1968). Hence, an empirical ψ-scan correction was applied (North *et al.*, 1968). Apart from the H atom of the carboxylic acid group (H101), which was located from a difference Fourier synthesis, all the H atoms were constrained to their parent sites with *AFIX*. All the H atoms were refined with a common isotropic displacement parameter (U_{iso} = 0.051 Å^2). The largest peak in the final difference Fourier synthesis is located 1.27 Å from the Bi atom. The displacement parameters of O111 were not normal, U_{11} being three times larger than U_{22} and U_{33}; no restraint was applied.

Data collection: local program. Cell refinement: local program. Data reduction: local program. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graph-

ics: *PLATON* (Spek, 1990). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: AB1531). Services for accessing these data are described at the back of the journal.

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A Dinuclear Complex of the Thiopurine Drug Azathioprine: $[Cu_2Cl_4(\mu\text{-azathioprine})_2]$.4DMF

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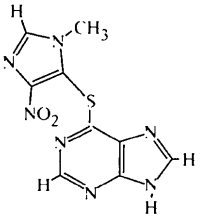
Abstract

In the title centrosymmetric dinuclear complex, bis[μ-6-(1-methyl-4-nitro-5-imidazolylthio)-7*H*-purine-N^3:N^9]-bis[dichlorocopper(II)] tetrakis(dimethylformamide) solvate, $[Cu_2Cl_4(C_9H_7N_7O_2S)_2].4C_3H_7NO$, the two Cu atoms are each coordinated by two chloro and two N3:N9-bridging neutral azathioprine ligands. The coordination geometry of each Cu atom is strongly distorted square planar. The Cu···Cu distance within the dinuclear unit is 2.939 (2) Å. Azathioprine exhibits a conformation in which there is a *trans* arrangement of the C5—C6 and S6—C10 bonds with respect to C6—S6, and in which the imidazole substituent at S6 points away from the imidazole ring of the purine moiety. The imidazole plane is approximately perpendicular to the purine plane, with a corresponding dihedral angle of 72.1 (3)°.

Comment

Azathioprine, 6-(1-methyl-4-nitro-5-imidazolylthio)-9*H*-purine, (I), was first synthesized in the early 1960s and subsequently introduced as a slow-release prodrug for the antileukemic drug 6-mercaptopurine and as an immunosuppressant by Hitchings & Elion (Elion, 1989). In addition, azathioprine is currently used for the treatment of rheumatoid arthritis.



(I)

The investigation of the formation and structure of metal complexes of azathioprine and related purines is of much interest. First, considering the well known anticancer activity of the metal complex *cis*-$PtCl_2(NH_3)_2$ (Rosenberg *et al.*, 1969) and the fact that metal complexes containing ligands which have biological activity in their own right may exhibit a somewhat greater activity than does the free ligand (Kirschner *et al.*, 1966), the activity and/or selectivity of the purine drugs might be enhanced by metal complexation. Second, the copper dependence of rheumatoid arthritis and, therefore, of the corresponding drugs has received particular attention (Jackson *et al.*, 1981). Finally, we have proposed (Zhu *et al.*, 1998) that the embedding of drug molecules like azathioprine within the framework of a polynuclear mixed-ligand metal complex molecule could represent a new method for influencing the biological properties of purine drugs.

Neutral azathioprine is found as its 9*H* tautomer in the crystal structure of azathioprine (Acharya, 1984) and of azathioprine.$2H_2O$ (Cook & Bugg, 1975). By deprotonation or tautomerization of azathioprine, all four N atoms of the purine ring become potential coordination sites for metal ions. Two different coordination modes have already been established for azathioprine by X-ray crystallography: monodentate binding of the neu-