Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.046$
$wR(F^2) = 0.126$
$S = 0.788$
3600 reflections
267 parameters
All H atoms refined
$w = 1/[\sigma^2(F_o^2) + (0.0476P)^2]$
  where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.14$ e Å^{-3}
$\Delta\rho_{min} = -0.13$ e Å^{-3}
Extinction correction:
SHELXL93 (Sheldrick, 1993)
Extinction coefficient: 0.0249 (18)
Scattering factors from International Tables for Crystallography (Vol. C)

Table 1. Selected geometric parameters (Å, °)

O—C7	1.230 (2)	N3—C15	1.428 (4)
N1—C7	1.344 (3)	N3—C16	1.455 (4)
N1—N2	1.388 (2)	C6—C7	1.497 (3)
N2—C8	1.283 (3)	C8—C9	1.461 (3)
N3—C12	1.362 (3)		
C7—N1—N2	118.9 (2)	O—C7—C6	121.6 (2)
C8—N2—N1	113.8 (2)	N1—C7—C6	114.7 (2)
O—C7—N1	123.7 (2)	N2—C8—C9	122.1 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
O1W—H2W···O	0.84 (3)	2.14 (3)	2.898 (2)	149 (2)
O1W—H2W···N2	0.84 (3)	2.50 (3)	3.148 (3)	134 (2)
C8—H8···O1W^i	0.96 (2)	2.57 (2)	3.366 (3)	141 (1)
N1—H1N1···O1W^i	0.94 (3)	1.97 (3)	2.892 (3)	170 (2)
O1W—H1W···O^{ii}	0.90 (2)	1.98 (2)	2.881 (3)	170 (2)

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

The structure was solved by direct methods and refined by full-matrix least-squares techniques. All H atoms were located from difference Fourier maps and refined isotropically.

Data collection: XSCANS (Siemens, 1994). Cell refinement: XSCANS. Data reduction: XSCANS. Program(s) used to solve structure: SHELXTL/PC (Sheldrick, 1990). Program(s) used to refine structure: SHELXL93 (Sheldrick, 1993). Molecular graphics: SHELXTL/PC. Program used for geometrical calculations: PARST (Nardelli, 1983). Software used to prepare material for publication: SHELXL93.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: MU1326). Services for accessing these data are described at the back of the journal.

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The Chelating Agent N,N,N',N'',N''',N'''-Triethylenetetraminehexacetic Acid (TTHA)

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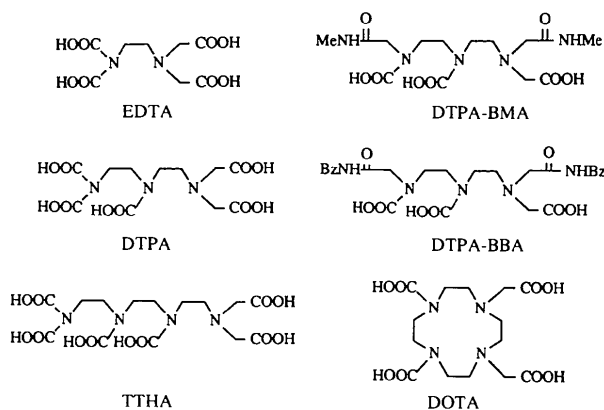
Abstract

The title compound, $C_{18}H_{30}N_4O_{12}$, exists as an unsymmetrical tri-zwitterion. The protonated N atoms form intramolecular hydrogen bonds to carboxylate O atoms. The molecules are linked by strong intermolecular hydrogen bonds formed by three COOH groups at one end of the molecule and three carboxylates at the negative ends of the two nearest neighbors [O···H 1.45 (3) Å]. The C—N bond lengths are clearly differentiated with respect to the charge on the N atom [C—N 1.459 (6) and C—NH$^+$ 1.502 (9) Å].

Comment

Metal complexes of polyaminocarboxylates have been studied widely by coordination chemists since the preparation of ethylenediaminetetracetic acid (EDTA); the equilibria and species involved in metal ion/EDTA systems are well understood (Schwarzenbach, 1960). In recent years, there has been a resurgence of interest in this area of chemistry, firstly to provide treatment for heavy-metal intoxication (e.g. Tandon & Srivastava, 1985), secondly to model metal-ion sites in biomolecules (Finnen, Pinkerton, Dunham, Sands & Funk, 1991) and thirdly to prepare contrast agents for magnetic resonance imaging (MRI) (Lauffer, 1987; Tweedle, 1989). The search for new and better chelating agents led to linear extension of flexible molecules,

e.g. to diethylenediaminepentacetic acid (DTPA) (Sievers & Bailar, 1962; Shkolnikova, Polyanchuk, Dyatlova & Polyakova, 1984), or to macrocyclic analogs, *e.g.* 1,4,7,10-tetrazacyclodecane-N,N',N'',N'''-tetracetic acid (DOTA) (Stetter & Frank, 1976; Desreux, 1980). More recently, these compounds have been fine-tuned, in particular for MRI applications, by replacing some of the carboxylates by amido groups, *e.g.* DTPA–bis(methylamide) (DTPA–BMA) or DTPA–bis(benzylamide) (DTPA–BBA) (Ehnebom, Pedersen & Klaveness, 1993). Similar approaches have also been applied to macrocyclic ligands (Kumar, Chang, Francesconi, Dischino, Malley, Gougoutas & Tweedle, 1994).

EDTA

DTPA–BMA

DTPA

DTPA–BBA

TTHA

DOTA

We have recently turned our attention to the compound N,N,N',N'',N''',N'''-triethylenetetraminehexacetic acid (TTHA). Only a few complexes with this ligand have been structurally characterized (Fallon & Gatehouse, 1974, 1976; Hu & Xie, 1991; Leverett, 1974; Jin, Li, Li, Xu & Zhang, 1994) and we have begun our study with the determination of the structure of the free acid.

The free molecule (Fig. 1) exists in the crystal as an unsymmetrical tri-zwitterion similar to the di-zwitterion observed for DTPA (Shkolnikova, Polyanchuk, Dyatlova & Polyakova, 1984). One end of the molecule carries three COOH groups and one protonated NH group. The other end of the molecule carries two protonated NH groups and all of the acid groups are deprotonated. All of the NH H atoms form strong intramolecular hydrogen bonds with carboxylate O atoms, the hydrogen bond carried by N4 being bifurcated.

All of the O—H bonds are long [1.08 (3) Å] and form strong intermolecular hydrogen bonds to the carboxylate O atoms of the deprotonated ends of the two closest neighboring molecules [O· · ·H 1.45 (3) Å].

As expected, the deprotonated carboxylate groups have symmetrical C—O bonds [C—O 1.250 (12) Å]; those with an acid group have C—O bonds that differ by ∼0.1 Å [C=O 1.206 (5) and C—OH 1.305 (3) Å]. C—N bonds involving neutral N atoms are ∼0.05 Å shorter than those which involve protonated N atoms [C—N 1.459 (6) and C—NH$^+$ 1.502 (9) Å]. We also note that the C—N bonds are shorter when the C atom carries a carboxylate group than when it is attached to an aliphatic C atom [1.495 (5) *versus* 1.510 (3) Å, excluding the unique neutral N atom from the average]. All angles fall in the range expected for sp^2 C atoms and sp^3 C and N atoms.

The observed open form of this flexible polycarboxylate molecule is in accord with its behavior as a bridging ligand in its known complexes (Fallon & Gatehouse, 1974, 1976; Hu & Xie, 1991; Leverett, 1974; Jin, Li, Li, Xu & Zhang, 1994), each end having three carboxylates and two N atoms able to complex a metal ion.
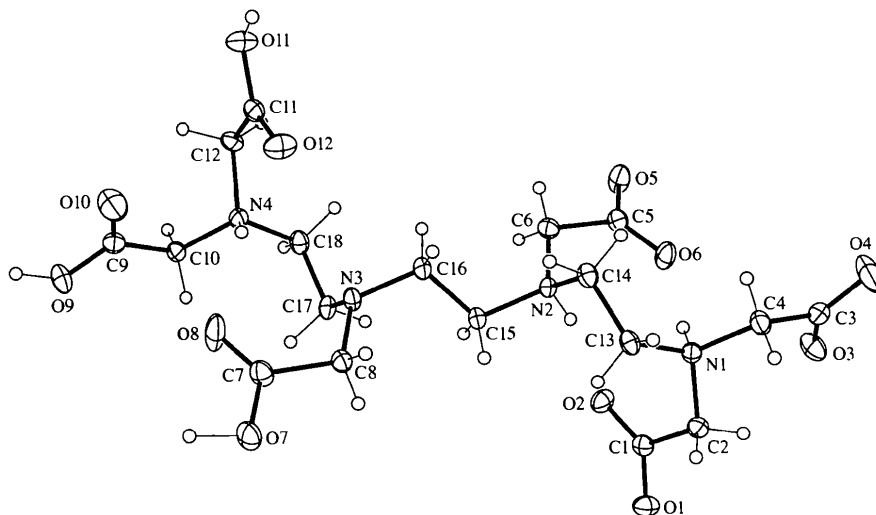

Fig. 1. The TTHA tri-zwitterion. Displacement ellipsoids for non-H atoms are drawn at the 50% probability level.

Experimental

The title compound was obtained from Aldrich and crystallized from ethanol.

Crystal data

$C_{18}H_{30}N_4O_{12}$	Mo $K\alpha$ radiation
$M_r = 494.46$	$\lambda = 0.71073$ Å
Triclinic	Cell parameters from 25
$P\bar{1}$	reflections
$a = 8.528\,(2)$ Å	$\theta = 7-12°$
$b = 11.565\,(2)$ Å	$\mu = 0.121$ mm^{-1}
$c = 11.993\,(3)$ Å	$T = 173$ K
$\alpha = 71.34\,(2)°$	Plate
$\beta = 74.77\,(2)°$	$0.32 \times 0.14 \times 0.07$ mm
$\gamma = 79.26\,(2)°$	Colorless
$V = 1074.5\,(5)$ Å^3	
$Z = 2$	
$D_x = 1.53$ Mg m^{-3}	
D_m not measured	

Data collection

Enraf–Nonius CAD-4 diffractometer	2683 reflections with $I > 2\sigma(I)$
$\theta/2\theta$ scans	$R_{int} = 0.027$
Absorption correction:	$\theta_{max} = 25.98°$
ψ scans (North, Phillips & Mathews, 1968)	$h = 0 \rightarrow 10$
	$k = -13 \rightarrow 14$
$T_{min} = 0.979$, $T_{max} = 0.999$	$l = -14 \rightarrow 14$
4480 measured reflections	3 standard reflections
4182 independent reflections	frequency: 50 min
	intensity decay: 0.48%

Refinement

Refinement on F	$w = 4F_o^2/[\sigma^2(F_o^2)$
$R = 0.043$	$+ 0.0009F_o^4]$
$wR = 0.049$	$(\Delta/\sigma)_{max} = 0.019$
$S = 1.390$	$\Delta\rho_{max} = 0.27$ e Å^{-3}
2683 reflections	$\Delta\rho_{min} = -0.17$ e Å^{-3}
397 parameters	Extinction correction: none
H atoms refined with $U =$	Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)
1.3U of bonding atom	

Table 1. *Selected geometric parameters (Å)*

O1—C1	1.260 (3)	N1—C2	1.490 (3)
O2—C1	1.249 (3)	N1—C4	1.499 (3)
O3—C3	1.256 (4)	N1—C13	1.513 (3)
O4—C3	1.231 (3)	N2—C6	1.499 (3)
O5—C5	1.262 (3)	N2—C14	1.512 (4)
O6—C5	1.240 (3)	N2—C15	1.506 (3)
O7—C7	1.309 (3)	N3—C8	1.452 (3)
O8—C7	1.211 (3)	N3—C16	1.464 (3)
O9—C9	1.304 (3)	N3—C17	1.462 (4)
O10—C9	1.201 (4)	N4—C10	1.489 (3)
O11—C11	1.303 (3)	N4—C12	1.500 (3)
O12—C11	1.207 (3)	N4—C18	1.508 (3)

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

D—H$\cdots$$A$	D—H	H$\cdots$$A$	D—H$\cdots$$A$
O7—H25$\cdots$O3^i	1.11 (2)	1.46 (2)	162 (2)
O9—H26$\cdots$O5^i	1.05 (3)	1.48 (2)	158 (3)
O11—H27$\cdots$O1^{ii}	1.08 (3)	1.42 (3)	180 (3)
N1—H28$\cdots$O6	0.87 (3)	1.88 (2)	164 (2)
N2—H29$\cdots$O2	0.85 (2)	1.92 (2)	167 (2)
N4—H30$\cdots$O8	0.85 (3)	2.23 (2)	135 (2)
N4—H30$\cdots$O12	0.85 (3)	2.24 (3)	114 (2)

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

Backgrounds were obtained from analysis of the scan profile (Blessing, Coppens & Becker, 1974).

Data collection: *CAD-4 Operations Manual* (Enraf–Nonius, 1977). Cell refinement: *CAD-4 Operations Manual*. Data reduction: *PROCESS* in *MolEN* (Fair, 1990). Program(s) used to solve structure: direct methods *MULTAN*80 (Main *et al.*, 1980). Program(s) used to refine structure: *LSFM* in *MolEN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *CIF VAX* in *MolEN*.

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