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N,*N*′,*N*″,*N*‴-Tetraethylterephthalamidinium bis(tetrazolate)

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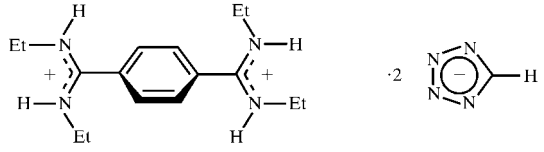
The crystal structure of the title 2:1 salt of tetrazole and a substituted terephthalamidine, $C_{16}H_{28}N_4^{2+}\cdot 2CHN_4^-$, contains an infinite network of hydrogen bonds, with short N···N distances of 2.820 (2) and 2.8585 (19) Å between the tetrazolate anion and the amidinium cation. Involvement of the lateral N atoms of the tetrazole in the hydrogen bonding appears to be a typical binding pattern for the tetrazolate anion.

Comment

Tetrazoles are acidic heterocycles that are deprotonated under physiological conditions and serve routinely as bioisosteric replacements for carboxylic acids in modern drug design. The tetrazole pharmacophore is found in several angiotensin II receptor antagonists that are currently marketed for the treatment of hypertension (Wexler *et al.*, 1996). Mutagenesis studies indicate that the tetrazolate anion in these pharmaceutical drugs interacts with a protonated lysine and a histidine at the receptor binding site (Noda *et al.*, 1995). While transmembrane receptors are notoriously difficult to study, model systems can provide further insight into non-covalent binding interactions. Earlier model complexes of tetrazoles and amidines have shown that the tetrazolate anion is a surprisingly adaptable hydrogen-bond acceptor system (Peters *et al.*, 2001). The crystal structure of the title compound, (I), presented here, gives an example of the hydrogen-bonding pattern of a tetrazolate anion in the presence of a protonated bis-amidine.

A 2:1 salt between tetrazole and *N*,*N*′,*N*″,*N*‴-tetraethylterephthalamidine (Grün, 1996; Laackmann & Friedrichsen, 1996; Peters, 2001) was obtained by dissolution of the two components in hot methanol, followed by recrystallization from acetonitrile–methanol. Crystals of the salt, (I), could be grown by slow evaporation from a methanol solution at room temperature. The crystal structure of (I) has C_i symmetry, and both amidine groups of the protonated terephthalamidine are located in the same plane (Fig. 1). The dihedral angle between the benzene ring and the amidine group (75°) is marginally larger than for a recently described 4-bromo-*N*,*N*′-diethylbenzamidinium tetrazolate (66 and 72°; Peters *et al.*, 2001). However, compared with the unsubstituted terephthalamidine (24.5°; Jokić *et al.*, 2001), the torsion angle has increased considerably, owing to the steric bulk of the *N*,*N*′-diethyl-substituted amidine group.



(I)

The C—N bond lengths of 1.31 Å for the amidine, and 1.32 and 1.29 Å for the tetrazolate (Table 1), are characteristic of partial double bonds (Barker & Powell, 1996; Palenik, 1963), confirming that an H atom has been transferred between the acidic tetrazole and the amidine base. The bond lengths in the tetrazolate are slightly shorter than those of α-tetrazole (Goddard *et al.*, 1997), but not quite as short as those of a tetrazolate anion in the presence of a non-coordinating counter-cation (Glowiak *et al.*, 1992).

Both amidine groups have an *E*,*Z* configuration, whereas the sterically more hindered *E*,*E* isomer seems to be found exclusively in the presence of strong ligands, such as carboxylates. The methyl group of the (*Z*)-ethyl substituent of the amidine is disordered. Each amidine group is hydrogen bonded to two tetrazolate anions, while each tetrazolate forms two hydrogen bonds with different terephthalamidine molecules (Fig. 2). The result is a three-dimensional hydrogen-bond network. The hydrogen-bonding distances N15···N24^{ii} (2.86 Å) and N12···N25^{i} (2.82 Å) are almost equal; H15···N24^{ii} 1.90 (2) Å and H12···N25^{i} 1.87 (2) Å [symmetry codes: (i) $\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$; (ii) $x, y-1, z$]. One of the hydrogen bonds is linear [N15—H15···N24^{ii} 177.3 (19)°], while the other is slightly bent [N12—H12···N25^{i} 161.3 (16)°]

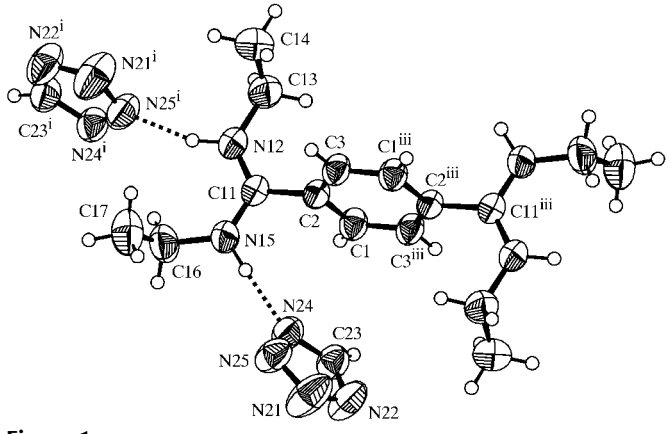


Figure 1
The molecular structure of (I), showing the hydrogen bonding between the amidinium and carboxylate groups. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small circles of arbitrary radii [symmetry codes: (i) $\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iii) $1-x, -y, -z$].

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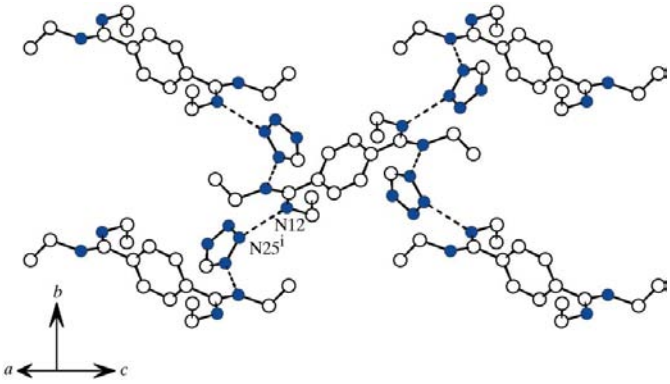

Figure 2
Part of the crystal structure of (I), showing the three-dimensional hydrogen-bonding network. N atoms are shaded [symmetry code: (i) $\frac{1}{2}-x$, $y-\frac{1}{2}$, $\frac{1}{2}-z$].

(Table 2). It is apparent that, unlike a carboxylate, the smaller tetrazolate ligand cannot bind to an amidinium group through two linear hydrogen bonds.

In the case of 4-bromo-*N*,*N*′-diethylbenzamidinium tetrazolate, only the N atoms next to the CH group of the tetrazole are involved in hydrogen bonding (Peters *et al.*, 2001), which correlates well with theoretical calculations that the charge density is highest on these N atoms (Zablocki *et al.*, 1992), while the binding mode varies in solution depending on solvent, concentration and temperature. Although the tetrazolate anions in (I) are rotated by 54 and 82° relative to the plane of the amidine groups, the binding motif is reminiscent of the crystal structure of 1,3,5-tris(4,5-dihydroimidazolium-2-yl)benzene tris(tetrazolate) tetrahydrate, in which the two N atoms on one side of the tetrazole are involved in hydrogen bonding to a heterocyclic amidine (Kraft *et al.*, 1999). The recently reported X-ray crystal structure of a tetrazole-containing inhibitor of HIV-1 integrase similarly shows hydrogen bonds between the lateral N atoms of the tetrazole and two lysines at the binding site (Goldgur *et al.*, 1999). We therefore conclude that, unless steric or crystal-packing constraints dominate, lateral binding is a favourable binding mode for tetrazolate anions.

Experimental

N,*N*′,*N*″,*N*‴-Tetraethylterephthalamidine (172 mg, 0.625 mmol) was freshly sublimed at 373 K and 10^{-4} mbar (1 mbar = 100 Pa) before being dissolved with tetrazole (87.6 mg, 1.25 mmol) in a hot acetonitrile–methanol (25:3, *v*/*v*) mixture. The solution was concentrated to about half its volume, and the crystals were collected by suction filtration and dried (yield 36%, decomposition > 523 K). Crystals of (I) were grown by slow evaporation from a methanol solution that was kept in a closed vial at room temperature. Spectroscopic analysis, ^{1}H NMR [500 MHz, $CDCl_3/CD_3OD$ (6:1), δ, p.p.m.]: 1.20 (*br s*, 6H, CH_3), 1.30 (*br s*, 6H, CH_3), 3.23 (*br s*, 4H, N-CH_2), 3.47 (*br s*, 4H, N-CH_2), 7.57 (*s*, 4H, Ar-H), 8.32 (*s*, 2H, tetrazole CH); ^{13}C NMR (125 MHz, DMSO-d_6, δ, p.p.m.): 12.8, 15.1 (CH_3), 37.7 (CH_2), 128.7, 148.2 (CH), 131.6, 161.9 (*ipso*-C, CN); IR (KBr, ν, cm^{-1}): 2980, 1642, 1440, 1152, 845. Analysis calculated for $C_{18}H_{30}N_{12}$: C 52.16, H 7.29, N 40.55%; found: C 52.11, H 7.48, N 40.51%.

Table 1
Selected geometric parameters (Å, °).

C2—C11	1.4873 (19)	N12—C13	1.463 (2)
C11—N12	1.3090 (18)	N15—C16	1.460 (2)
C11—N15	1.3126 (19)		
N12—C11—N15	123.29 (13)	C11—N12—C13	125.53 (13)
N12—C11—C2	120.85 (13)	C11—N15—C16	125.73 (14)
N15—C11—C2	115.86 (12)		
C3—C2—C11—N12	−76.46 (19)	C1—C2—C11—N15	−74.18 (19)
C1—C2—C11—N12	106.05 (17)	N15—C11—N12—C13	174.70 (17)
C3—C2—C11—N15	103.32 (17)	N12—C11—N15—C16	−0.7 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N12—H12···N25^{i}	0.98 (2)	1.87 (2)	2.820 (2)	161.3 (16)
N15—H15···N24^{ii}	0.96 (2)	1.90 (2)	2.8585 (19)	177.3 (19)

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

Crystal data

$C_{16}H_{28}N_4^{2+}\cdot 2CHN_4^-$	D_x = 1.189 Mg m^{-3}
M_r = 414.54	Cu $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 25 reflections
a = 9.818 (2) Å	θ = 40.2–46.4°
b = 9.402 (2) Å	μ = 0.64 mm^{-1}
c = 12.571 (4) Å	T = 298 (2) K
β = 93.80 (2)°	Block, colourless
V = 1157.9 (5) Å^3	0.25 × 0.20 × 0.20 mm
Z = 2	

Data collection

Enraf–Nonius CAD-4 diffractometer	R_{int} = 0.031
$\omega/2\theta$ scans	θ_{max} = 74.3°
Absorption correction: ψ scan (North *et al.*, 1968)	$h = -12 \rightarrow 12$
T_{min} = 0.856, T_{max} = 0.882	$k = 0 \rightarrow 11$
2472 measured reflections	$l = -15 \rightarrow 0$
2365 independent reflections	3 standard reflections every 250 reflections
1934 reflections with $I > 2\sigma(I)$	frequency: 120 min
	intensity decay: 1%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0712P)^2 + 0.1750P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.047	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.137	$\Delta\rho_{max}$ = 0.21 e Å^{-3}
S = 1.06	$\Delta\rho_{min}$ = −0.19 e Å^{-3}
2365 reflections	Extinction correction: *SHELXL*97 (Sheldrick, 1997)
162 parameters	Extinction coefficient: 0.0118 (13)
H atoms treated by a mixture of independent and constrained refinement	

For the H atoms attached to N atoms, the N—H distances refined to 0.96 (2) and 0.98 (2) Å, and for the tetrazole anion, C23—H refined to 0.98 (2) Å. All other H atoms attached to C atoms were treated as riding atoms using *SHELXL*97 (Sheldrick, 1997) defaults.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *MolEN* (Fair, 1990); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97; molecular graphics: *SCHAKAL* (Keller, 1997) and *DIAMOND* (Brandenburg, 1997); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1105). Services for accessing these data are described at the back of the journal.

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