Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Conformation of cationic *N*,*N*-dimethylglycine in dimethylglycinium trifluoroacetate

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Received 19 December 2000
Accepted 2 January 2001

In the title compound, $C_4H_{10}NO_2^+\cdot C_2F_3O_2^-$, the main N—C—COOH skeleton of the protonated amino acid is nearly planar. The C═O/C—N and C═O/O—H bonds are *syn* and the two methyl groups are *gauche* to the methylene H atoms. The conformation of the cation in the crystal is compared to that given by *ab initio* calculations (Hartree–Fock, self-consistent field molecular-orbital theory). The trifluoroacetate anion has the typical staggered conformation with usual bond distances and angles. The cation and anion form dimers through a strong O—H···O hydrogen bond which are further interconnected in infinite zigzag chains running parallel to the *a* axis by N—H···O bonds. Weaker C—H···O interactions involving the methyl groups and the carboxy O atoms of the cation occur between the chains.

Comment

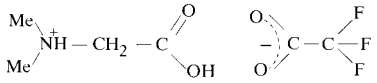
N,*N*-Dimethylglycine [DMG; IUPAC name: 2-(*N*,*N*-dimethylamino)acetic acid] is a sweet-tasting substance legally considered as a nutrient and freely available in health-food stores. It is a popular ingredient of supplementary diet tablets and 'energetic drinks' for sportsmen. In living cells, DMG is present as a product of the metabolic pathways of choline and methionine. DMG has been used to improve situations of mental disturbance, like autism, seizures and aging, and of physical and athletic performance in humans and animals (*e.g.* racehorses), but the therapeutic value of DMG is still the subject of much controversy (Tonda & Hart, 1992; Kendall, 1994; Bolman & Richmond, 1999). Some studies claim that DMG can significantly enhance, at least temporarily, the immune system (Graber *et al.*, 1981; Reap & Lawson, 1990).

From a chemical point of view, DMG belongs to the family of *N*-methylated derivatives of glycine which also includes sarcosine (*N*-methylglycine) and betaine (*N*,*N*,*N*-trimethylglycine) as members (Meister, 1965). Compounds of the parent molecule, glycine, first attracted attention when ferroelectric behaviour was discovered in isomorphous triglycine sulfate (Matthias *et al.*, 1956), selenate and trifluoroberyllate (Pepinsky *et al.*, 1957), and in diglycine nitrate (Pepinsky *et al.*, 1958). Later, several compounds of sarcosine and betaine were also found to have interesting physical properties, like ferroelastic (Zobetz & Preisinger, 1989), ferroelectric or antiferroelectric behaviour, often associated with structural phase transitions to commensurate or incommensurate superstructures (Pepinsky & Makita, 1962; Ashida *et al.*, 1972; Mishima *et al.*, 1984; Shildkamp & Spilker, 1984; Haussühl, 1984, 1988; Almeida *et al.*, 1992). Although an impressive number of structural studies on glycine, sarcosine and betaine compounds triggered by these discoveries has been reported, very few crystallographic studies of dimethylglycine compounds have been undertaken.

The DMG molecule has an amphoteric character and can exist in an anionic or a cationic form, as well as in the two uncharged tautomeric forms, one of which, with neutral amino and carboxylic acid groups, is thought to be the more stable form in the gas phase; in the dipolar zwitterionic form, stable in aqueous solution, the molecule has a positively charged dimethylammonium group and a negatively charged carboxylate group. When the molecule acts as an acid, an H atom is released from the former group, forming the dimethylglycinate anion. The cation is formed when the molecule acts as a base by accepting a proton at the negatively charged carboxylate group of the zwitterion. Due to this amphoteric character, a large number of DMG salts and adducts can be formed. In the anionic form, it is known that DMG is a good complexation agent of *p*- and *d*-metals, a property that is shared with the parent molecule (glycine), sarcosine and betaine. Chelation occurs commonly *via* the carboxylate group, but metal binding to the N atom may also occur (Darensbourg *et al.*, 1994). According to a recent survey of the Cambridge Structural Database (October 2000 release; Allen & Kennard, 1993), there is only one reported crystal structure where DMG is in the cationic form, that of dimethylglycinium chloride (Santarsiero & Marsh, 1983). The crystal structure of pure DMG itself has not yet been reported, which is certainly due to the fact that the pure substance is highly hygroscopic and deliquescent, a property common to several salts of DMG with organic acids. Recently, a theoretical *ab initio* study of the molecular conformations of DMG and sarcosine has been carried out by Headley & Starnes (1996). It was found that the molecule has some conformational flexibility, due to the rotational freedom of the 'rigid' dimethylammonium and carboxylate groups around the N—C and C—C bonds, respectively, and of the hydroxyl group around the C—O bond. For DMG, Headley & Starnes identified five distinct stable conformers.

We are presently engaged in a systematic study of the structural and dielectric properties of simple salts and adducts of *N*-methylated amino acids in order to find other compounds with ferro- or antiferroelectric order which might possibly induce structural phase transitions at low temperature. By varying the acid strength of the counter-ion, we aim at getting a deeper understanding of the role of the intermolecular interactions, in particular of the different patterns of hydrogen bonding between the anion and the cation *via* the carboxy and

amino groups, on the unusual physical properties of this family of compounds. Trifluoroacetic acid (TFA) is a very strong carboxylic acid due to the charge-withdrawing effect of the F atoms on the C_α atom, with a dissociation constant K = 0.66 mol dm^{-3} determined by Raman spectroscopy (Strehlow & Hildebrandt, 1990). Phase transitions at low temperature of crystalline trifluoroacetic acid tetrahydrate have been found in both undeuterated and deuterated samples (Mootz & Schilling, 1992). Dimethylglycinium trifluoroacetate, (I), is thus expected to be a good candidate to exhibit phase transitions and superstructures. The present study, performed at room temperature, will be completed by further work, including calorimetric, spectroscopic and dielectric measurements at low temperature.



(I)

The ionization states of the DMG and TFA molecules were determined from the objective localization of the H atoms bonded to the carboxylic acid groups on a difference Fourier synthesis but could also be inferred from the bond distances within these groups. The DMG molecule exists in the cationic form, with a mono-positively charged amino group and a neutral carboxylic acid group, in agreement with the large asymmetry between the C—O bond lengths of this functional group. The TFA molecules are ionized, as expected from the strength of the acid and the required charge neutrality of the salt. The DMG carboxy skeleton, which includes atoms O1, O2, C1 and C2, is planar within 0.0069 (16) Å. The N atom is slightly displaced out of this plane by −0.055 (4) Å, corresponding to a small rotation around the single C1—C2 bond. The relevant torsion angles are O1—C1—C2—N [178.09 (16)°] and O2—C1—C2—N [−3.2 (3)°], which should be compared with the respective values in dimethylglycinium chloride [177.3 (2) and −2.2 (3)°; Santarsiero & Marsh, 1983] and in the closely related compound sarcosinium trifluoroacetate [177.71 (14) and −2.5 (2)°; Rodrigues *et al.*, 2000]. The other relevant torsion angle is C1—C2—N—C4 [161.49 (19)°], describing the rotation around the central C—N bond and defining the arrangement of the methyl groups with respect to the methylene H atoms. The corresponding values in DMG chloride and in sarcosinium trifluoroacetate are 166.9 (2) and 172.39 (14)°. In the two DMG compounds, the methyl groups are almost *gauche* with respect to the methylene H atoms. In the three compounds, there is a *syn* arrangement of the C═O/C—N and C═O/O—H bonds.

It is interesting to compare the conformation of the DMG moiety with that of the isolated molecule as given by *ab initio* calculations, in order to elucidate the effect of intermolecular interactions in stabilizing a particular conformation. Headley & Starnes (1996) have reported an *ab initio* study of neutral *N*-methyl- and *N*,*N*-dimethylglycine, where they have found that an intramolecular O—H···N bond favours a *trans* arrangement of the C═O/C—N and C═O/O—H bonds in the most stable conformer, whereas these bonds are *syn* in the lowest energy conformers of glycine and *N*-methylglycine. The O2—C1—C2—N and C1—C2—N—C4 torsion angles are calculated as 157.8 and 151.9°, respectively. We have performed similar *ab initio* calculations for the protonated molecule, using the same basis set and Hamiltonian (MP2/6–311++G**//RHF/6–311++G**) as Headley & Starnes. The calculations were performed with the computer program *GAMESS* (Schmidt *et al.*, 1993). The geometry of the isolated cation was optimized starting from the X-ray geometry using tight constraints for SCF (self-consistent field) convergence and location of the equilibrium geometry, the final electron-density variation and maximum energy gradient being 10^{-6} and 10^{-5} atomic units, respectively. At the end of the geometry optimization, the Hessian matrix was calculated at the RHF/6–311++G** level to confirm that the stationary point is a true minimum and not a saddle point, and indeed, positive frequencies were obtained for every vibrational normal mode. The calculation gave values for the bond distances and valence angles in good agreement with the X-ray data, the r.m.s. deviation from the experimental values being 0.0096 Å and 1.09°, respectively, and the largest deviations being those related to the C1—O2 bond distance [calculated: 1.180 Å; experimental: 1.198 (2) Å] and N—C2—C1 angle [calculated: 109.0°; experimental: 111.21 (15)°]. Bonds involving H atoms were excluded from these average deviations. The main torsion angles defining the conformation of the molecule are calculated as O1—C1—C2—N (171.1°) and C1—C2—N—C4 (150.7°), and can be compared with the experimental values given above. The conformation of the carboxylic acid group is *syn*, in agreement with the X-ray data, as shown by the calculated torsion angle O2—C1—O1—H1 (−1.1°). It can be concluded that the calculated conformation of the isolated cation is close to that observed in the crystal, although intermolecular interactions are important in the title compound (see below). After application of second-order Møller–Plesset perturbation theory to the RHF (Roothaan Hartree-Fock) values to partially correct for electronic correlation, the values of the dipole moment and energy are 4.749 D and −362.5447539 hartree, respectively. The harmonic (unscaled) zero-point energy calculated at the RHF/6–311++G** level was 0.161522 hartree per molecule (424.076 kJ mol^{-1}). We have also performed an optimization of the charged low-energy conformer starting from the molecular geometry of the most stable conformer found by Headley & Starnes (1996) for the neutral molecule, which has *trans* C═O/C—N and C═O/O—H bonds. This conformation was not stable, as expected, due to the repulsion of the hydroxyl and amine H atoms, and reverted to a *trans*–C═O/C—N, *syn*–C═O/O—H conformation in the course of the geometry optimization. This conformer is 14.13 kJ mol^{-1} (calculated at the MP2 level, including zero-point energy correction) higher in energy compared with the *syn*/*syn* conformer, which was optimized starting from the coordinates given by the X-ray data.

The trifluoroacetate anion has a staggered conformation, as indicated by the value of the torsion angle O4—C5—C6—F2 [17.3 (3)°]. The geometry of the CF_3 group is similar to that

found in other structures (Nahringbauer *et al.*, 1979), with an average C—F bond length and F—C—F angle of 1.323 (1) Å and 106.4 (3)°, respectively. The average F—C—C angle is 112 (1)°. The carboxylate group of the anion is planar within 0.0144 (19) Å; the C5—C6 bond length [1.530 (3) Å] is longer than the average Csp^3—Csp^2 bond, but is within the normal range of values found in trifluoroacetic acid and trifluoroacetate compounds (Lundgren, 1976).

The cation and anion interact directly *via* a strong hydrogen bond between their carboxylic acid groups [O1···O4^{i} 2.593 (2) Å; symmetry code: (i) $\frac{1}{2}+x$, $\frac{3}{2}-y$, $1-z$]. These dimers are interconnected in zigzag chains running parallel to the *a* axis *via* a moderately strong hydrogen bond between the amino N—H group and the carboxy O4 atom of the anion [N···O 2.836 (2) Å]. Parallel chains are further linked by weaker C—H···O interactions involving the methyl groups and the carboxy O atoms of the amino acid cation, as depicted in Fig. 2. It is remarkable that the two bare O atoms of the anion have such a distinct role in hydrogen bonding; O4 acts twice as an acceptor, whereas atom O3 does not participate in any hydrogen bond. Also, no hydrogen bonds can be ascribed to the F atoms, which seem to have a passive role in the network of intermolecular interactions. However, this is not an exceptional occurance. A recent statistical survey of the Cambridge Structural Database (Allen & Kennard, 1993) has shown that the neutral F atom exhibits an anomalously small number of short contacts with strong hydrogen donors, such as the O—H and N—H groups, in contrast with the much larger number of contacts found for the F^- anion (Dunitz & Taylor, 1997). The notable exceptions are F···π interactions, for which a statistically significant number of short contacts with appropriate directional characteristics was disclosed (Prasanna & Guru Row, 2000).

It should be pointed out that the atomic displacement tensors of the F atoms have an enhanced anisotropic character which might indicate a slight disorder, probably of a dynamic nature, of these atoms. It is plausible that at room temperature, the CF_3 groups rotate, undergoing small angular oscillations around the single C—C bond, particularly taking into account that the F atoms do not engage in hydrogen bonding with neighbouring molecules. The more anisotropic character of the atomic displacement tensor of the O3 atom compared with that of O4 may also reflect the fact that the former atom does not participate in the hydrogen-bond network.

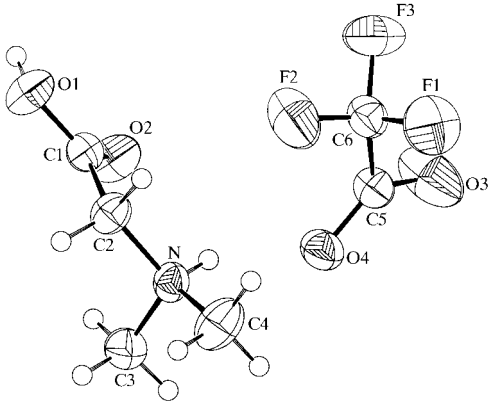


Figure 1
*ORTEP*II (Johnson, 1976) plot of the title compound. Displacement ellipsoids are drawn at the 50% probability level.

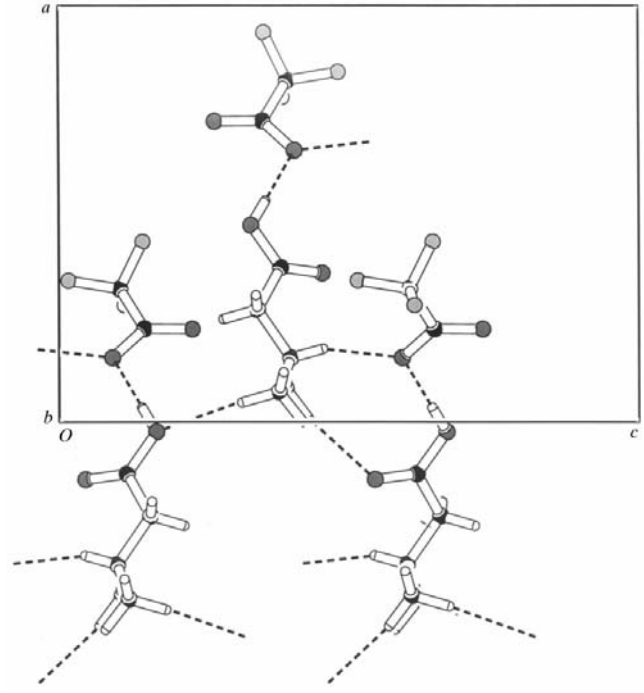


Figure 2
Projection of the title structure along the *b* axis showing the hydrogen-bonded chains.

Experimental

Small colourless crystals of block form were obtained after several weeks evaporation of the solution obtained from adding an excess of trifluoroacetic acid (Aldrich, 99%) directly to 1 g of pure dimethylglycine, as purchased from Aldrich (98%). A small single crystal was enclosed in a sealed glass capillary and checked prior to data collection by photographic methods.

Crystal data

$C_4H_{10}NO_2^+\cdot C_2F_3O_2^-$
M_r = 217.15
Orthorhombic, *Pbca*
a = 10.4286 (5) Å
b = 12.1213 (12) Å
c = 14.6271 (18) Å
V = 1849.0 (3) Å^3
Z = 8
D_x = 1.560 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 7.60–15.18°
μ = 0.164 mm^{-1}
T = 293 (2) K
Block, colourless
0.36 × 0.28 × 0.26 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile data from ω–2θ scans
2039 measured reflections
1631 independent reflections
1313 reflections with $I > 2\sigma(I)$
R_{int} = 0.026
θ_{max} = 25.03°
$h = 0 \rightarrow 12$
$k = 0 \rightarrow 14$
$l = -17 \rightarrow 17$
3 standard reflections
frequency: 180 min
intensity decay: 6%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0432P)^2 + 1.2200P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.037$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.105$	$\Delta\rho_{max} = 0.32$ e Å^{-3}
$S = 1.038$	$\Delta\rho_{min} = -0.22$ e Å^{-3}
1631 reflections	Extinction correction: *SHELXL*97
158 parameters	Extinction coefficient: 0.0037 (8)
Only coordinates of H atoms refined	

Table 1
Selected geometric parameters (Å, °).

C1—O2	1.198 (2)	C5—C6	1.530 (3)
C1—O1	1.301 (2)		
O2—C1—C2—N	−3.2 (3)	C1—C2—N—C3	−73.7 (2)
O1—C1—C2—N	178.09 (16)	C1—C2—N—C4	161.49 (19)

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O4^{i}	0.89 (3)	1.71 (3)	2.593 (2)	175 (3)
N—H4···O4	0.84 (2)	2.04 (2)	2.836 (2)	158 (2)
C3—H5···O2^{ii}	0.96 (3)	2.37 (3)	3.302 (3)	163 (2)
C3—H7···O1^{iii}	0.97 (3)	2.52 (3)	3.470 (3)	166 (2)

Symmetry codes: (i) $\frac{1}{2}+x, \frac{3}{2}-y, 1-z$; (ii) $x-\frac{1}{2}, \frac{3}{2}-y, 1-z$; (iii) $x-\frac{1}{2}, y, \frac{1}{2}-z$.

All H atoms were located on a difference Fourier map and were refined isotropically [C—H = 0.96 (3)–0.97 (3) Å], with U_{iso} values constrained to that of the parent atom using *SHELXL* defaults. Examination of the crystal structure with *PLATON* (Spek, 1995) showed that there are no solvent-accessible voids in the crystal lattice.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *PLATON* (Spek, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

This work was supported by Fundação para a Ciência e a Tecnologia (FCT) and FEDER under project SAPIENS-POCTI/33495/QUI/00.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1450). Services for accessing these data are described at the back of the journal.

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