

The crystal structure of the ammonium salt of 2-aminomalonic acid

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This article is dedicated to the memory of Professor Dr Andreas J. Kornath who passed away in March 2024.

† Deceased

Keywords: crystal structure; 2-aminomalonic acid; Raman; NMR; peptide synthesis.

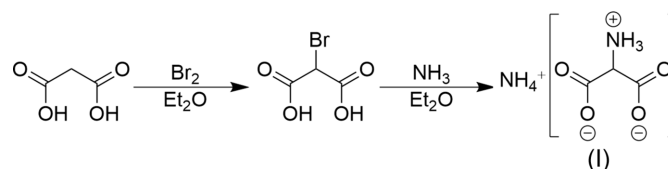
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The salt ammonium 2-aminomalonate (systematic name: ammonium 2-azaniumylpropanedioate), $\text{NH}_4^+\cdot\text{C}_3\text{H}_4\text{NO}_4^-$, was synthesized in diethyl ether from the starting materials malonic acid, ammonia and bromine. The salt was recrystallized from water as colourless blocks. In the solid state, intramolecular medium–strong $\text{N}-\text{H}\cdots\text{O}$, weak $\text{C}-\text{H}\cdots\text{O}$ and weak $\text{C}-\text{H}\cdots\text{N}$ hydrogen bonds build a three-dimensional network.

1. Introduction

The first synthesis of 2-aminomalonic acid was in 1864 and described by Bayer (Beaujon & Hartung, 1953). In 1902, Ruhemann and Orton investigated the preparation with nitromalonamide as a starting material and a reduction with amalgam (Beaujon & Hartung, 1953). In 1902, Lütz used halogenated malonic acid and ammonia as the starting materials to obtain 2-aminomalonic acid as the product (Beaujon & Hartung, 1953). To obtain a much purer product, Hartung invented in 1952 a distillation in a vacuum with a palladium–charcoal catalyst. 2-Aminomalonic acid was obtained in a yield of 80–90% (Beaujon & Hartung, 1953).



2-Aminomalonic acid is used as a complexone in medicine, environmental technology and chemistry due to it being a member of the amino polycarboxylic acid group of substances (Anderegg *et al.*, 2005). In 1945, G. Schwarzenbach introduced the name ‘complexones’ for laboratory-synthesized compounds which are close to amino acids (Anderegg *et al.*, 2005). Well-known representatives of complexones are, for example, EDTA (ethylenediaminetetraacetic acid), DTPA (diethylenetriamine pentaacetate) or TETA (triethylenetetramine) (Anderegg *et al.*, 2005). These compounds are built with a nitrogen-containing moiety which enables their use as ligands.

The corresponding acids of 2-aminomalonic acid and its salts are of particular interest because of their two carboxyl groups, one of which can be decarboxylated to form a chiral centre (Zheng *et al.*, 2023). Like other complexones, 2-aminomalonic has a nitrogen moiety and other functional groups that are very suitable for binding complexes (Anderegg *et al.*, 2005). The zwitterionic character is similar to that of amino acids and makes it possible to use it as a ligand at different pH values.

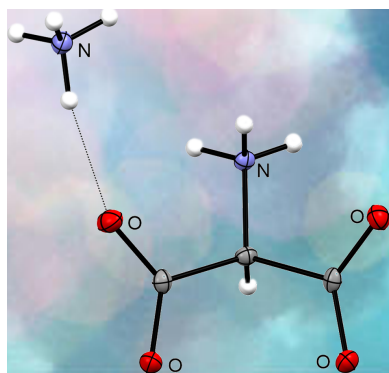


Table 1
Experimental details.

Crystal data	
Chemical formula	$\text{NH}_4^+ \cdot \text{C}_3\text{H}_4\text{NO}_4^-$
M_r	136.11
Crystal system, space group	Orthorhombic, <i>Pbca</i>
Temperature (K)	101
a, b, c (Å)	9.9714 (4), 9.8671 (3), 11.1884 (4)
V (Å ³)	1100.81 (7)
Z	8
Radiation type	Mo $K\alpha$
μ (mm ⁻¹)	0.15
Crystal size (mm)	0.73 × 0.60 × 0.51
Data collection	
Diffractometer	Rigaku Xcalibur Sapphire3
Absorption correction	Multi-scan (<i>CrysAlis PRO</i> ; Rigaku OD, 2020)
T_{\min}, T_{\max}	0.847, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	18831, 1483, 1391
R_{int}	0.021
$(\sin \theta/\lambda)_{\text{max}}$ (Å ⁻¹)	0.685
Refinement	
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.039, 0.113, 1.20
No. of reflections	1483
No. of parameters	114
H-atom treatment	All H-atom parameters refined
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$ (e Å ⁻³)	0.49, -0.21

Computer programs: *CrysAlis PRO* (Rigaku OD, 2020), *SHELXT2018* (Sheldrick, 2015a), *SHELXL2019* (Sheldrick, 2015b), *ORTEP-3* (Farrugia, 2012) and *PLATON* (Spek, 2020).

2. Experimental

2.1. Synthesis and crystallization

Malonic acid (10.4 g, 0.1 mmol) and diethyl ether (100 ml) were added to a dried Schlenk flask. The mixture was cooled to 273 K and bromine (16.0 g, 0.1 mol) was added under stirring over a period of 40 min. The mixture was warmed to room temperature and stirred for a further 40 min. Aqueous ammonia (100 ml, 25%) was added slowly under stirring. The solvent was removed in a vacuum. The product was obtained as a white-to-light-yellow solid product. The synthesis route is shown in Scheme 1.

2.2. Analysis (X-ray, Raman and NMR)

We investigated and characterized salt (I) by single-crystal X-ray diffraction, Raman spectroscopy and NMR spectroscopy. Complete data and devices for the X-ray measurements are listed in the CIF in the supporting information. Low-temperature Raman spectroscopic studies were performed using a Bruker MultiRAM FT-Raman spectrometer with an Nd:YAG laser excitation ($\lambda = 1064 \text{ cm}^{-1}$) under vacuum at 77 K. For a measurement, the synthesized compound was transferred to a cooled glass cell. A Bruker AV400TR spectrometer was used for the ¹H, ¹³C and ¹⁴N NMR measurements.

2.3. Refinement

Crystal data, data collection, and structure refinement details are summarized in Table 1.

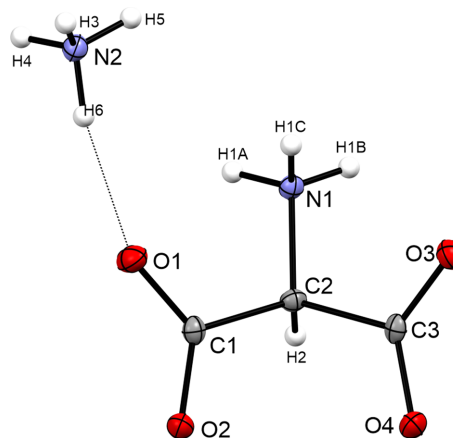


Figure 1
The asymmetric unit of salt (I), with displacement ellipsoids drawn at the 50% probability level.

3. Results and discussion

3.1. Single-crystal X-ray diffraction

Herein, we present the first single-crystal X-ray diffraction analysis of the salt ammonium 2-aminomalonic acid, $\text{NH}_4^+ \cdot \text{C}_3\text{H}_4\text{NO}_4^-$, (I), as a zwitterion. The salt crystallizes in the orthorhombic space group *Pbca* with eight formula units per unit cell. The asymmetric unit is shown in Fig. 1. The C—C bonds are 1.5394 (18) (C1—C2) and 1.5485 (18) Å (C2—C3). The C—C bonds are significantly elongated compared to the median of the average $\text{Csp}^2\text{—Csp}^3$ hybridized bond (1.475–1.522 Å) determined by X-ray diffraction (Allen *et al.*, 1987). The C2—N1 bond [1.4821 (16) Å] is in the same range as the median of an average $\text{Csp}^3\text{—Nsp}^3$ hybridized bond (1.488 Å) and that of glycine (1.484 Å) (Allen *et al.*, 1987; Itaka, 1960). The shorter C—O bond lengths of 1.2483 (16) (C1—O1) and 1.2462 (17) Å (C3—O3) are significantly elongated by approximately 0.015 Å compared to the shorter C—O bond in

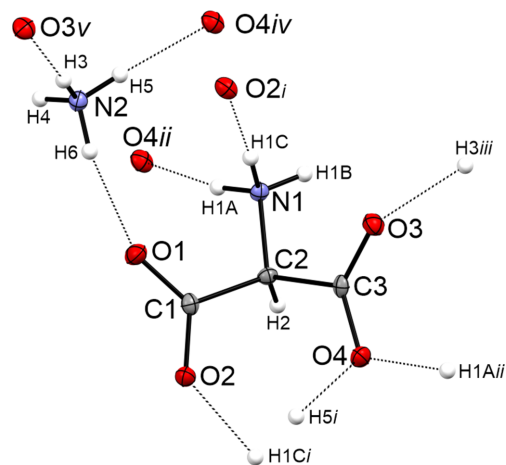


Figure 2
Hydrogen bonds in the crystal structure of salt (I), with displacement ellipsoids drawn at the 50% probability level. [Symmetry codes: (i) $x + \frac{1}{2}, y, -z + \frac{3}{2}$; (ii) $-x + \frac{3}{2}, -y + 1, z - \frac{1}{2}$; (iii) $-x + 1, y + \frac{1}{2}, -z + \frac{3}{2}$; (iv) $x - \frac{1}{2}, y, -z + \frac{3}{2}$; (v) $-x + 1, y - \frac{1}{2}, -z + \frac{3}{2}$]

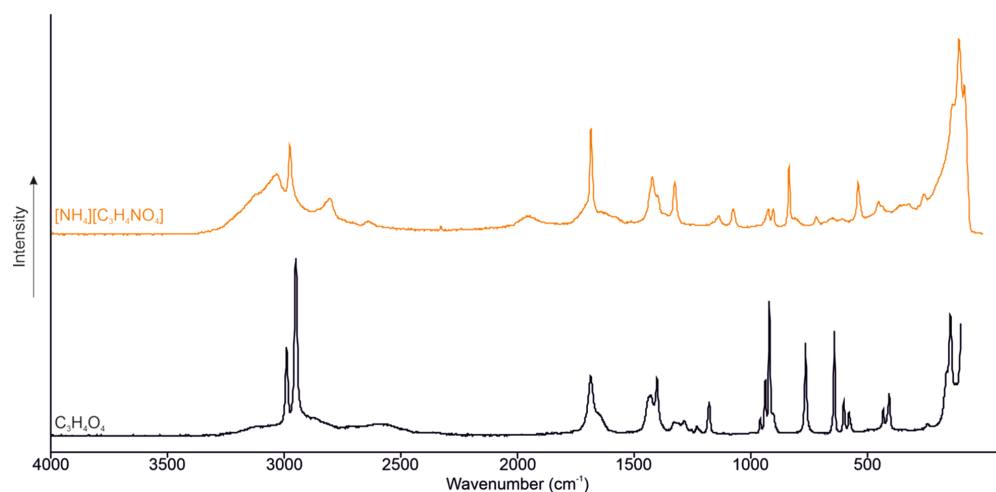


Figure 3
The low-temperature Raman spectrum of malonic acid and (I).

β -glycine (1.233 Å) (Iitaka, 1960). The longer C—O bonds are 1.2657 (16) (C1—O2) and 1.2597 (16) Å (C3—O4). In comparison to β -glycine (1.257 Å), the C1—O2 bond is slightly elongated (Iitaka, 1960).

The carbon chain has a C1—C2—C3 angle of 113.00 (10) $^\circ$ and is only slightly magnified compared to the starting material [111.3 (1) $^\circ$; Jagannathan *et al.*, 1994]. The O1—C1—O2 [124.87 (12) $^\circ$] and O3—C3—O4 [127.55 (12) $^\circ$] angles are only slightly influenced by the NH₃ moiety compared to the starting material [O1—C1—O2 = 124.8 (1) $^\circ$ and O1—C1—O2 = 123.3 (2) $^\circ$]. The N1—C2—C1 angle is 109.56 (10) $^\circ$ and the N1—C2—C3 angle is 109.98 (10) $^\circ$. The torsion angles are -2.96 (16) (O1—C1—C2—N1), 175.49 (11) (O2—C1—

C2—N1), 10.44 (15) (O3—C3—C2—N1) and -169.89 (10) $^\circ$ (O4—C3—C2—N1).

The crystal structure of salt (I) displays a three-dimensional network built of moderate N—H \cdots O hydrogen bonds, according to the classification of Jeffrey (1997). Fig. 2 shows the hydrogen bonds in the crystal structure. The hydrogen bonds are listed in the CIF in the supporting information. The strongest hydrogen bond, N2—H6 \cdots O1, is in the asymmetric unit with an N \cdots O distance of 2.803 (2) Å. The crystal structure builds chains *via* N1—H1C \cdots O2ⁱ [2.928 (1) Å] and N2—H5 \cdots O4^{iv} [2.908 (2) Å] hydrogen bonds. The chains are connected *via* N2—H3 \cdots O3^v [2.832 (2) Å] and N1—H1A \cdots O4ⁱⁱ [2.822 (2) Å] hydrogen bonds.

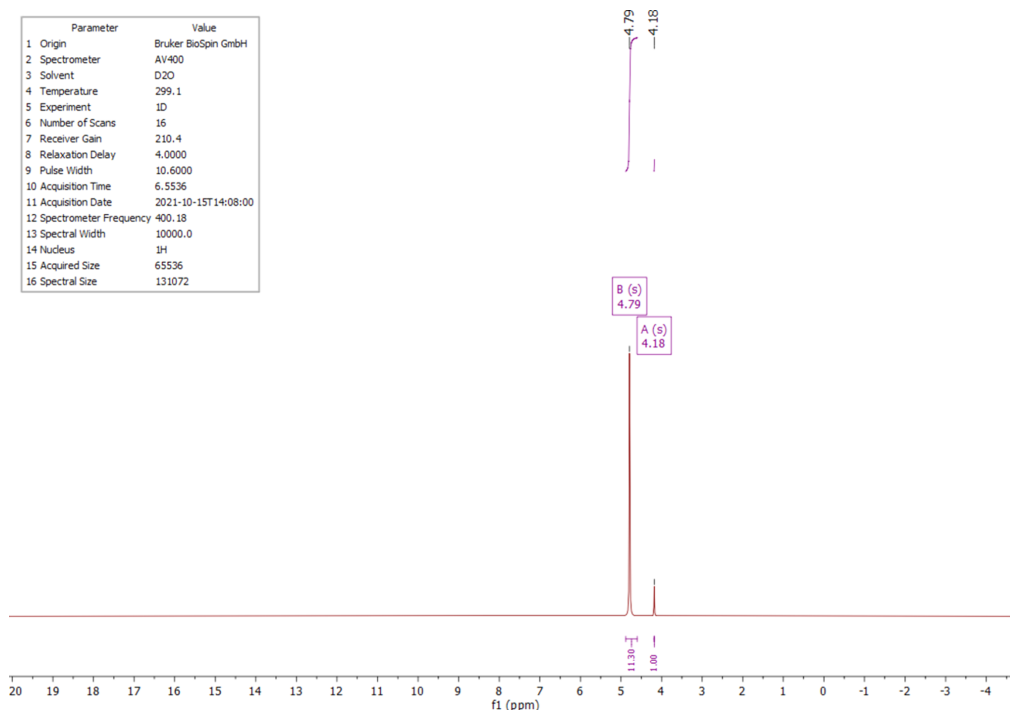


Figure 4
The ¹H NMR spectrum of (I) in D₂O.

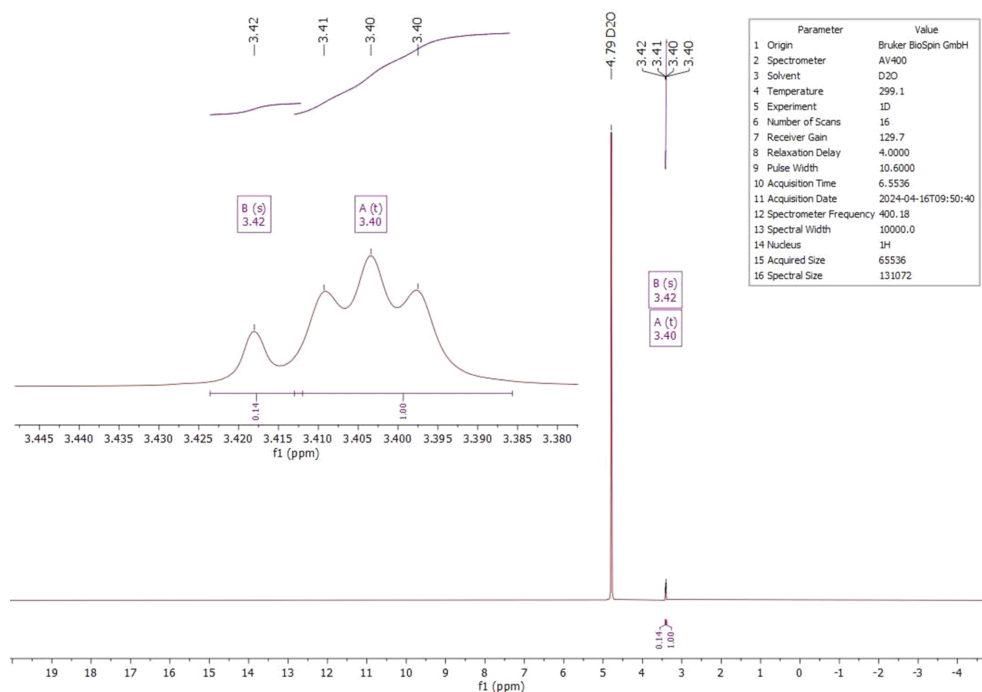


Figure 5
The ^1H NMR spectrum of malonic acid ($\text{C}_3\text{H}_4\text{O}_4$) in D_2O .

3.2. Raman spectroscopy

The Raman spectrum of (I) is shown in Fig. 3, together with that of the starting material malonic acid. The N–H stretching vibrations are detected at 3032 and 2809 cm^{-1} . The C–H stretching vibration is observed at 2977 cm^{-1} . The polarized C=O stretching vibration is detected at 1684 cm^{-1} and that of C–O at 1328 cm^{-1} .

3.3. NMR spectroscopy

The ^1H , ^{13}C and ^{14}N NMR spectra of salt (I) were measured in D_2O at room temperature. The ^1H NMR spectrum (Fig. 4) shows one singlet at 4.18 ppm (*s*, CH). Compared to the starting material, the proton is significantly less acidic and deshielded by 0.76 ppm . The starting material has an H/D exchange in D_2O , which is recognizable by the triplet at

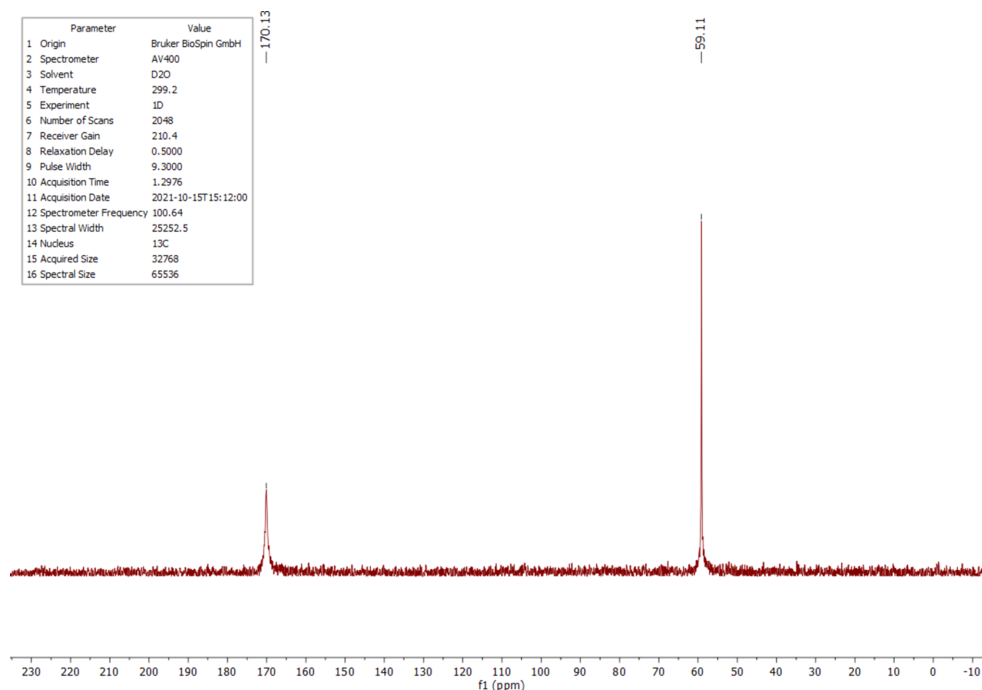


Figure 6
The ^{13}C NMR spectrum of (I) in D_2O .

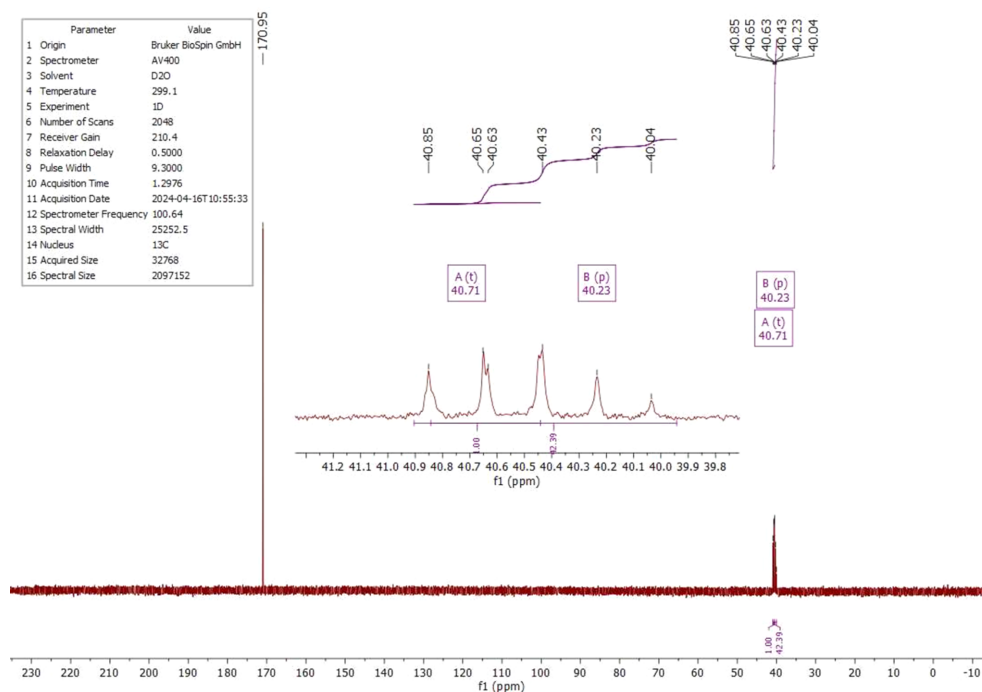


Figure 7
The ¹³C NMR spectrum of malonic acid (C₃H₄O₄) in D₂O.

3.40 ppm and the singlet at 3.42 ppm (Fig. 5). The ¹³C NMR analysis of (I) detected the carboxyl C atom at 170.1 ppm and the C2 atom at 59.1 ppm (Fig. 6); compared to the starting material, the carboxy moieties are not significantly shifted (Fig. 7). The protons of atom C2 of the malonic acid are much more acidic, resulting in the ¹³C NMR spectrum in a triplet at 40.7 ppm (*t*, *J* = 20.0 Hz) and a quintet at 40.2 ppm (*p*, *J* = 20.3 Hz) splitting. In salt (I), the C2 carbon is much more deshielded and a singlet is seen at 59.1 ppm. The ¹⁴N NMR

spectrum (Fig. 8) shows the ammonium cation at −340.6 ppm and the −NH₃⁺ moiety at −361.5 ppm as singlets.

4. Conclusion

Herein we present the first single-crystal X-ray diffraction and Raman and NMR spectroscopy study of the salt ammonium 2-aminomalionate. For 2-aminomalonic acid, only the ¹H NMR spectrum is known in the literature (Callahan & Wolfenden,

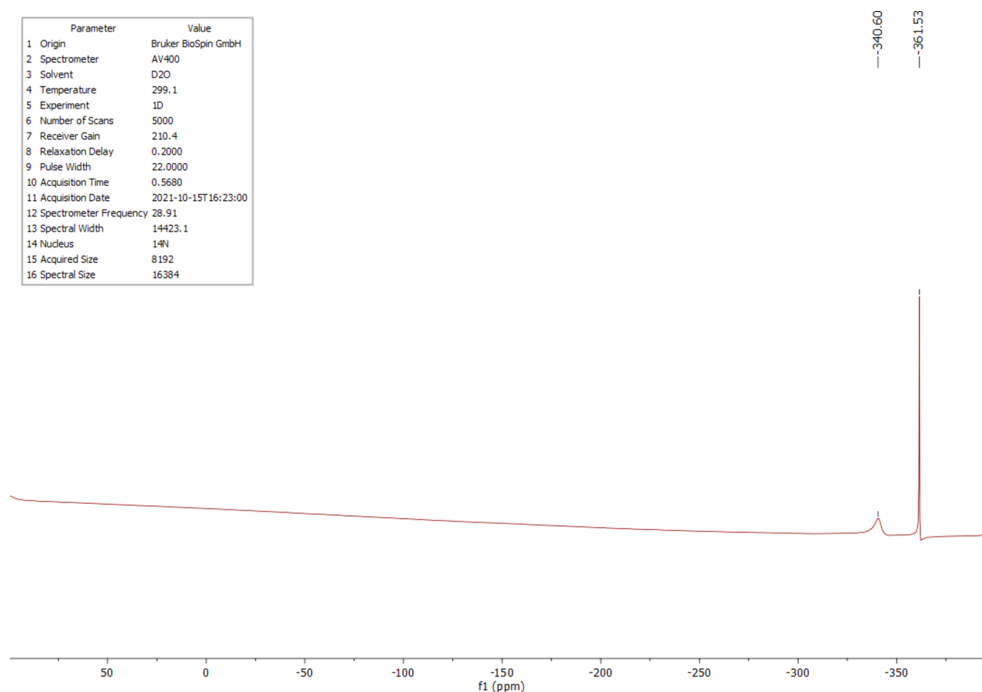


Figure 8
The ¹⁴N NMR spectrum of (I) in D₂O.

2004). Also, we describe the H/D exchange of the CH₂ moiety in D₂O of malonic acid for the first time.

Acknowledgements

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supporting information

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Computing details

Ammonium 2-azaniumylpropanedioate

Crystal data

$\text{NH}_4^+\cdot\text{C}_3\text{H}_4\text{NO}_4^-$

$M_r = 136.11$

Orthorhombic, *Pbca*

$a = 9.9714$ (4) Å

$b = 9.8671$ (3) Å

$c = 11.1884$ (4) Å

$V = 1100.81$ (7) Å³

$Z = 8$

$F(000) = 576$

$D_x = 1.643$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 7376 reflections

$\theta = 2.1\text{--}32.3^\circ$

$\mu = 0.15$ mm⁻¹

$T = 101$ K

Block, colorless

$0.73 \times 0.60 \times 0.51$ mm

Data collection

Rigaku Xcalibur Sapphire3
diffractometer

Radiation source: Enhance (Mo) X-ray Source

Graphite monochromator

Detector resolution: 15.9809 pixels mm⁻¹

ω scans

Absorption correction: multi-scan

(CrysAlis PRO; Rigaku OD, 2020)

$T_{\min} = 0.847$, $T_{\max} = 1.000$

18831 measured reflections

1483 independent reflections

1391 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.021$

$\theta_{\max} = 29.1^\circ$, $\theta_{\min} = 3.4^\circ$

$h = -13 \rightarrow 13$

$k = -13 \rightarrow 13$

$l = -15 \rightarrow 15$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.039$

$wR(F^2) = 0.113$

$S = 1.20$

1483 reflections

114 parameters

0 restraints

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier
map

Hydrogen site location: difference Fourier map

All H-atom parameters refined

$w = 1/[\sigma^2(F_o^2) + (0.0446P)^2 + 0.912P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.49$ e Å⁻³

$\Delta\rho_{\min} = -0.21$ e Å⁻³

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2 , conventional R-factors R are based on F, with F set to zero for negative F^2 . The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Hydrogen atoms were located in the residual electron density map and their coordinates were freely refined. The thermal parameters of the hydrogens on N1 were constrained to 1.5x that of N1, while all other hydrogen atoms were refined isotropically. Reflections were merged by SHELXL according to the crystal class for the calculation of statistics and refinement.

reflns Friedel fraction is defined as the number of unique Friedel pairs measured divided by the number that would be possible theoretically, ignoring centric projections and systematic absences.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
N2	0.50374 (12)	0.23766 (12)	0.51186 (11)	0.0124 (2)
H4	0.515 (2)	0.233 (2)	0.438 (2)	0.027 (5)*
H3	0.461 (2)	0.167 (2)	0.5344 (19)	0.024 (5)*
H5	0.456 (2)	0.308 (2)	0.534 (2)	0.026 (5)*
H6	0.584 (2)	0.238 (2)	0.545 (2)	0.024 (5)*
O3	0.64253 (10)	0.50248 (10)	0.92457 (9)	0.0151 (2)
O4	0.86733 (10)	0.49144 (10)	0.93630 (9)	0.0145 (2)
O2	0.93388 (10)	0.29895 (10)	0.74002 (9)	0.0136 (2)
O1	0.74231 (10)	0.26216 (10)	0.64267 (10)	0.0165 (2)
C3	0.75713 (13)	0.49122 (12)	0.88125 (11)	0.0102 (3)
C1	0.81752 (13)	0.33305 (13)	0.70628 (11)	0.0109 (3)
C2	0.76674 (13)	0.47406 (13)	0.74394 (11)	0.0103 (3)
H2	0.8249 (18)	0.541 (2)	0.7165 (17)	0.012 (4)*
N1	0.63426 (11)	0.50005 (11)	0.68844 (10)	0.0103 (2)
H1A	0.643 (2)	0.4967 (19)	0.605 (2)	0.019 (5)*
H1B	0.602 (2)	0.584 (2)	0.7085 (18)	0.023 (5)*
H1C	0.568 (2)	0.438 (2)	0.7126 (19)	0.022 (5)*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N2	0.0136 (5)	0.0122 (5)	0.0115 (5)	−0.0001 (4)	−0.0005 (4)	−0.0014 (4)
O3	0.0145 (5)	0.0172 (5)	0.0136 (5)	0.0014 (3)	0.0025 (4)	−0.0009 (3)
O4	0.0145 (5)	0.0176 (5)	0.0114 (4)	0.0018 (3)	−0.0022 (3)	−0.0020 (3)
O2	0.0131 (5)	0.0144 (4)	0.0132 (4)	0.0026 (3)	−0.0016 (3)	−0.0019 (3)
O1	0.0154 (5)	0.0135 (5)	0.0207 (5)	0.0000 (4)	−0.0054 (4)	−0.0032 (4)
C3	0.0151 (6)	0.0064 (5)	0.0092 (5)	0.0006 (4)	−0.0001 (4)	0.0002 (4)
C1	0.0134 (6)	0.0107 (6)	0.0087 (5)	0.0002 (4)	0.0016 (4)	0.0007 (4)
C2	0.0100 (5)	0.0113 (5)	0.0096 (5)	−0.0002 (4)	−0.0011 (4)	0.0010 (4)
N1	0.0120 (5)	0.0098 (5)	0.0092 (5)	0.0012 (4)	−0.0015 (4)	0.0005 (4)

Geometric parameters (Å, °)

N2—H4	0.83 (3)	C3—C2	1.5485 (18)
N2—H3	0.85 (2)	C1—C2	1.5394 (18)
N2—H5	0.88 (2)	C2—N1	1.4821 (16)
N2—H6	0.89 (2)	C2—H2	0.93 (2)
O3—C3	1.2462 (17)	N1—H1A	0.93 (2)
O4—C3	1.2597 (16)	N1—H1B	0.91 (2)
O2—C1	1.2657 (16)	N1—H1C	0.94 (2)
O1—C1	1.2483 (16)		
H4—N2—H3	108 (2)	N1—C2—C1	109.56 (10)
H4—N2—H5	113 (2)	N1—C2—C3	109.98 (10)
H3—N2—H5	107 (2)	C1—C2—C3	113.00 (10)
H4—N2—H6	107 (2)	N1—C2—H2	107.1 (11)
H3—N2—H6	109.4 (19)	C1—C2—H2	110.1 (12)
H5—N2—H6	111.5 (19)	C3—C2—H2	106.8 (12)
O3—C3—O4	127.55 (12)	C2—N1—H1A	109.2 (13)
O3—C3—C2	116.89 (11)	C2—N1—H1B	111.4 (13)
O4—C3—C2	115.55 (11)	H1A—N1—H1B	108.0 (17)
O1—C1—O2	124.87 (12)	C2—N1—H1C	113.2 (12)
O1—C1—C2	117.71 (11)	H1A—N1—H1C	109.0 (18)
O2—C1—C2	117.40 (11)	H1B—N1—H1C	105.9 (18)
O1—C1—C2—N1	-2.96 (16)	O3—C3—C2—N1	10.44 (15)
O2—C1—C2—N1	175.49 (11)	O4—C3—C2—N1	-169.89 (10)
O1—C1—C2—C3	120.05 (13)	O3—C3—C2—C1	-112.34 (12)
O2—C1—C2—C3	-61.50 (15)	O4—C3—C2—C1	67.33 (14)
