

## A mediated hydrogen bond in an $\alpha$ -hydroxycarboxyl group: X-ray structure of (*R,R*)-*N*-methyltartramic acid monohydrate and an *ab initio* study of model systems

URSZULA RYCHLEWSKA,<sup>a,\*</sup> AGNIESZKA SZARECKA,<sup>b</sup> JACEK RYCHLEWSKI<sup>b,c</sup> AND RAFAŁ MOTALEA<sup>a</sup>

<sup>a</sup>Department of Crystallography, Faculty of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland, <sup>b</sup>Quantum Chemistry Group, Faculty of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland, and <sup>c</sup>Institute of Bioorganic Chemistry, Polish Academy of Sciences, PCS, Noskowskiego 12/14, 61-704 Poznań, Poland. E-mail: urszula@krystal.amu.edu.pl

(Received 9 December 1998; accepted 8 April 1999)

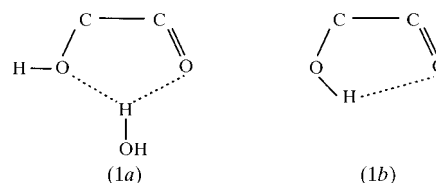
### Abstract

The crystal structure of (*R,R*)-*N*-methyltartramic acid monohydrate is presented and compared with that of the parent compound, (*R,R*)-tartaric acid. Despite some conformational differences between the two molecules the packing is very similar, as it is dictated by the carboxyl rather than the amide function. Particular attention is paid to a mediated three-centre hydrogen bond as one of the packing motifs involving the  $\alpha$ -hydroxycarboxyl moiety. The stability and geometry of such structures in the gas phase and in solution are examined *via* theoretical *ab initio* methods using the RHF/6-311++G\*\* and RHF/6-311++G\*\*/Onsager models, respectively. Liquid media, in particular those of high polarity, are found to stabilize the structures considerably.

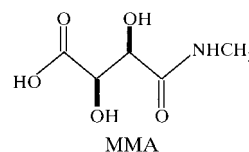
### 1. Introduction

One of many interesting structural features of (*R,R*)-tartaric acid, its esters, amides and salts is the observation that the preference for a planar T conformation of the four-atom carbon chain is accompanied by the planarity of the  $\alpha$ -hydroxycarboxylate or  $\alpha$ -hydroxyamide moieties (Gawroński *et al.*, 1997, and references therein). The planarity of these fragments is, to some extent, stabilized by intramolecular hydrogen bonding involving proximal groups, in which a hydroxyl group plays either the role of a donor in a hydrogen bond to O atoms from proximal acid, ester or tertiary amide groups or the role of an acceptor of a proton from the neighbouring primary or secondary amide function (Szczepeńska & Rychlewska, 1994; Rychlewska *et al.*, 1997). Usually, although not always, these intramolecular interactions occur in crystals as minor components of three- or four-centre hydrogen bonds with other components being intermolecular. However, as has been noted previously (Kroon, 1982), in many crystal structures hydroxyl H atoms of  $\alpha$ -hydroxycarboxylic acids are involved solely in intermolecular interactions, yet the planarity of this fragment is preserved. Analysis of

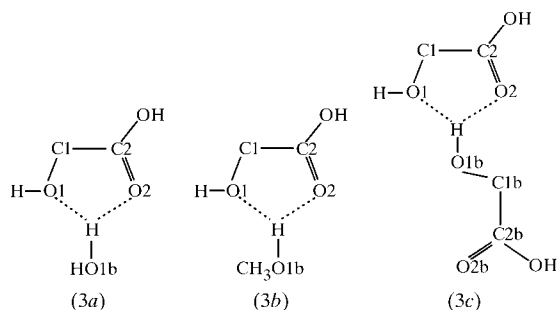
such systems has led us to the observation that O atoms from the  $\alpha$ -hydroxycarboxyl group that are *syn* to each other are joined by hydrogen bonds in which the hydroxyl OH group from the neighbouring molecule is a donor. This leads to the formation of a three-centre hydrogen bond instead of a typical intramolecular linkage. This type of bonding has been described by Jeffrey & Saenger (1991) as a mediated intramolecular hydrogen bond. Mediated (1*a*) and 'typical' (1*b*) hydrogen bonds are shown schematically below.



The pattern designator for the motif formed is  $R_1^2(5)$  while that for its intramolecular analogue is  $S(5)$  (for a description of pattern designators see, for example, Bernstein *et al.*, 1995; Etter, 1990; Bernstein *et al.*, 1990; Etter *et al.*, 1990; Bernstein *et al.*, 1994). The motif is not only common among tartaric acid derivatives and salts (for example, see Bootsma & Schoone, 1967; Carlström, 1973; Duesler *et al.*, 1984*a,b*) but is also present in other systems containing either the  $\alpha$ -hydroxycarboxylate moiety (Flippen, 1973; Larsen & Marthi, 1994; Foster *et al.*, 1983; Schouten *et al.*, 1994) or the dicarboxylate moiety as in oxalic acid (Bernstein *et al.*, 1994). In some of the cases cited above the role of the mediator is played by the solvent water molecule (Flippen, 1973) or by a hydroxyl group from a cation (Carlström, 1973). In this study, we present the results of an X-ray analysis of the mono-*N*-methylamide derivative of (*R,R*)-tartaric acid, MMA, as an example of the occurrence of a mediated type of internal hydrogen bonding.



In the case presented here, a water molecule mediates between both functions of the  $\alpha$ -hydroxycarboxyl group, *i.e.* between the  $\alpha$ -hydroxyl and carbonyl groups, instead of a typical direct linkage between these two groups. Also reported are high-accuracy *ab initio* Hartree–Fock studies of the model systems shown below. These were carried out for the isolated state and in the presence of both polar and nonpolar solvents.



Detailed *ab initio* studies of the structure and both inter- and typical intramolecular hydrogen bonding involving the  $\alpha$ -COX group, X being OH, OCH<sub>3</sub>, NH<sub>2</sub> or N(CH<sub>3</sub>)<sub>2</sub>, have been recently carried out (Szarecka *et al.*, 1996, 1998, 1999a,b; Hoffmann *et al.*, 1998).

## 2. Experimental

### 2.1. Synthesis

(*R,R*)-*N*-Methyltartramic acid (MMA) was prepared in the Laboratory of Natural Products, Department of Chemistry, Adam Mickiewicz University, Poznań, Poland (Gawroński *et al.*, 1997).

### 2.2. X-ray crystallography

Crystals of MMA·H<sub>2</sub>O suitable for X-ray analysis were grown from aqueous solution. Reflection intensities were measured on a four-circle KUMA Diffraction KM-4 diffractometer equipped with a graphite mono-

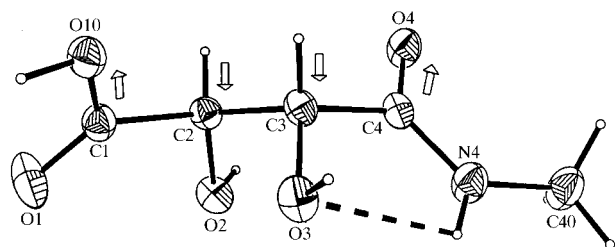


Fig. 1. An illustration of the T(s,a) conformation of the MMA molecule and the atom-numbering scheme. Note the change of conformation around the C–C\* bond caused by replacement of carboxyl by an amide group. Arrows indicate CO/C $\beta$ H dipole–dipole interactions. Displacement ellipsoids are drawn at the 40% probability level and H atoms are drawn as spheres of arbitrary radii.

Table 1. *Experimental details for MMA·H<sub>2</sub>O*

Crystal data	
Chemical formula	C <sub>5</sub> H <sub>9</sub> NO <sub>5</sub> ·H <sub>2</sub> O
Chemical formula weight	181.15
Cell setting	Orthorhombic
Space group	<i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
<i>a</i> (Å)	7.3010 (10)
<i>b</i> (Å)	7.658 (2)
<i>c</i> (Å)	13.855 (3)
<i>V</i> (Å <sup>3</sup> )	774.6 (3)
<i>Z</i>	4
<i>D<sub>x</sub></i> (Mg m <sup>-3</sup> )	1.553
<i>D<sub>m</sub></i> (Mg m <sup>-3</sup> )	1.533
Density measured by	Flotation in KI
Radiation type	Mo K $\alpha$
Wavelength (Å)	0.71073
No. of reflections for cell parameters	36
$\theta$ range (°)	8.42–14.825
$\mu$ (mm <sup>-1</sup> )	0.144
Temperature (K)	293 (2)
<i>F</i> (000)	384
Crystal form	Prism
Crystal size (mm)	0.6 × 0.25 × 0.2
Crystal colour	Colourless
Data collection	
Diffractometer	KM-4
Data collection method	$\theta$ – $2\theta$ scans
Absorption correction	None
No. of measured reflections	2066
No. of independent reflections	1875
No. of observed reflections	1485
Criterion for observed reflections	$I > 2\sigma(I)$
<i>R</i> <sub>int</sub>	0.0211
$\theta_{\max}$ (°)	28.06
Range of <i>h, k, l</i>	–9 → <i>h</i> → 9 0 → <i>k</i> → 10 0 → <i>l</i> → 18
No. of standard reflections	2
Frequency of standard reflections	Every 100 reflections
Intensity decay (%)	0
Refinement	
Refinement on	<i>F</i> <sup>2</sup>
$R[F^2 > 2\sigma(F^2)]$	0.0310
$wR(F^2)$	0.0737
<i>S</i>	1.063
No. of reflections used in refinement	1874
No. of restraints used	0
No. of parameters used	129
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0445P)^2 + 0.0586P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max}$	0.000
$\Delta\rho_{\max}$ (e Å <sup>-3</sup> )	0.183
$\Delta\rho_{\min}$ (e Å <sup>-3</sup> )	–0.165
Extinction method	None
Source of atomic scattering factors	<i>International Tables for Crystallography</i> (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Computer programs	
Data collection	KM-4 (Kuma Diffraction, 1991)
Cell refinement	KM-4
Data reduction	DATAPROC (Galdecki <i>et al.</i> , 1995)
Structure solution	SHELXS86 (Sheldrick, 1990)
Structure refinement	SHELXL93 (Sheldrick, 1993)

chromator. The intensities were corrected for Lorentz and polarization effects. The structure was solved by direct methods using *SHELXS86* (Sheldrick, 1990) and refined against  $F^2$  using *SHELXL93* (Sheldrick, 1993). Heavy atoms (C, O, N) were refined anisotropically. The positions of the H atoms attached to the C and N atoms were calculated and refined using a riding model and their isotropic displacement parameters were given a value 20% higher than the isotropic equivalent for the atom to which the H atom was bonded. The coordinates of the hydroxyl H atoms were determined from a difference Fourier map and refined, together with their isotropic displacement parameters, in the least-squares process. The absolute structure of the crystals was assumed from the known absolute configuration of (*R,R*)-tartaric acid. The value of the corresponding Flack parameter is  $-0.7(13)$ . *Stereochemical Workstation* (Siemens, 1989) was used to prepare the figures. Experimental details are summarized in Table 1.† A perspective view of the MMA molecule showing its conformation and the numbering system is shown in Fig. 1.

### 2.3. Molecular-orbital calculations

We considered three structures with a mediated three-centre bond, namely a hydroxyacetic acid (glycolic acid)/water complex (*3a*), a hydroxyacetic acid (glycolic acid)/methanol complex (*3b*) and a hydroxyacetic acid dimer (*3c*). They are designated HA–W, HA–M and HA–HA, respectively.

All calculations were carried out at the Restricted Hartree–Fock (RHF) level of theory (Pople & Beveridge, 1970) with a 6-311++G\*\* basis set, *i.e.* a large split-valence 6-311G basis set additionally augmented by two sets of polarization and two sets of diffuse functions (Krishnan *et al.*, 1980; Clark *et al.*, 1983; Frisch *et al.*, 1984). Starting geometries were built based on the structures observed in the crystalline state, although we have used standard values of bond lengths and angles (Rademacher, 1987). Solvation energies were computed with the aid of the Self-Consistent Reaction Field approach–Onsager model (Onsager, 1936; Wong *et al.*, 1991). All structures were optimized fully (both in the isolated state and in solution) and converged to stable local energy minima. We considered both polar (dielectric constant  $\epsilon = 80.0$ ) and nonpolar (dielectric constant  $\epsilon = 2.0$ ) media. Onsager cavity radii for the systems studied were derived from the respective molecular volumes calculated *via* Monte Carlo integration of molecular electron density (Foresman & Frisch, 1996). We used the *GAUSSIAN94* package (Frisch *et al.*, 1995) for all the computations.

† Supplementary data for this paper are available from the IUCr electronic archives (Reference: CF0006). Services for accessing these data are described at the back of the journal.

Table 2. Selected torsion angles ( $^\circ$ ) for *MMA*·*H*<sub>2</sub>*O*

O1–C1–C2–O2	–15.7 (2)
O10–C1–C2–O2	165.1 (1)
O1–C1–C2–C3	–138.9 (2)
O10–C1–C2–C3	41.8 (2)
O2–C2–C3–O3	–69.9 (2)
C1–C2–C3–O3	51.3 (2)
O2–C2–C3–C4	52.8 (2)
C1–C2–C3–C4	173.9 (1)
O3–C3–C4–O4	176.3 (1)
C2–C3–C4–O4	55.0 (2)
O3–C3–C4–N4	–5.1 (2)
C2–C3–C4–N4	–126.4 (2)
O4–C4–N4–C40	4.77 (3)
C3–C4–N4–C40	–173.8 (2)

## 3. Results and discussion

### 3.1. X-ray crystallography

In *MMA*, as in the optically active tartaric acid (Okaya *et al.*, 1966) and the majority of crystalline (*R,R*)-tartramides (Dobashi *et al.*, 1988; Gawroński *et al.*, 1997; Molander *et al.*, 1997; Singh *et al.*, 1990; Szarecka *et al.*, 1996; Szczepańska & Rychlewska, 1994; Williams *et al.*, 1984), the conformation around the C\*–C\* bond linking the two chiral centres is staggered such that the two carboxyl groups are *trans* (T) and the two adjacent C–OH bonds are *gauche minus*. The reported exceptions among (*R,R*)-tartramides are (*R,R*)-*N,N,N',N'*-tetramethyltartramide and its dibenzoyl derivative (Gawroński *et al.*, 1989; Rychlewska, 1992) and (*R,R*)-*N,N,N',N'*-tetracyclohexyldimethoxy-succinamide (*S*)-2,2'-dihydroxy-1,1'-binaphthyl clathrate (Toda *et al.*, 1988), in which two amide groups are in a *gauche plus* orientation and, consequently, the four-atom carbon chain is bent. The value of the C\*–C\*–C\*–C\* torsion angle in *MMA* is 173.9 (1) $^\circ$ , while the O–C\*–C\*–O torsion angle is  $-69.9(2)^\circ$  (selected torsion angles are listed in Table 2). The conformation around the C\*–C bond is such that the hydroxyl O atoms O2 and O3 lie nearly in the plane defined by the carboxy and amide groups, respectively. However, while at the carboxyl end of the molecule the  $\alpha$ -hydroxyl O atom nearly eclipses the carbonyl O atom, at the amide end the carbonyl O atom is on the opposite side to the  $\alpha$ -hydroxyl O atom, which now eclipses the amide N atom. The corresponding O=C–C\*–OH torsion angles of  $-15.7(2)^\circ$  and  $176.3(1)^\circ$  describe synplanar 's' and antipolar 'a' conformations. The overall conformation of the molecule can thus be described as T(s,a). In our previous reports on a related subject (Rychlewska *et al.*, 1997; Gawroński *et al.*, 1997) we pointed out that such a conformation of optically active tartaric acid derivatives might be stabilized by attractive interactions of local dipoles, illustrated by arrows in Fig. 1. Moreover, the planarity of the  $\alpha$ -hydroxyamide moiety is stabilized by an intramolecular hydrogen bond (indicated by a dashed line in Fig. 1) in which the amide group acts as a proton

Table 3. Hydrogen-bond parameters ( $\text{\AA}$ ,  $^\circ$ ) for  $\text{MMA}\cdot\text{H}_2\text{O}$ 

$D-H$  distances for  $N-H$  and  $O-H$  bonds have been normalized to values of 1.03 and 0.97  $\text{\AA}$ , respectively.

$D-H\cdots A$	$D\cdots A$	$H\cdots A$	$D-H\cdots A$
$\text{O2}-\text{H2O}\cdots\text{OW}^{\text{i}}$	2.640 (2)	1.67	178
$\text{O3}-\text{H3O}\cdots\text{O2}^{\text{ii}}$	2.859 (2)	1.90	171
$\text{O10}-\text{H10}\cdots\text{O4}^{\text{iii}}$	2.571 (2)	1.61	170
$\text{OW}-\text{H1W}\cdots\text{O1}^{\text{iv}}$	2.903 (2)	1.94	171
$\text{OW}-\text{H2W}\cdots\text{O1}^{\text{v}}$	2.851 (2)	2.03	141
$\text{OW}-\text{H2W}\cdots\text{O2}^{\text{v}}$	2.983 (2)	2.19	139
$\text{N4}-\text{H4}\cdots\text{OW}^{\text{vi}}$	3.105 (2)	2.23	141
$\text{N4}-\text{H4}\cdots\text{O3}$	2.632 (2)	2.15	107

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

donor to the neighbouring hydroxyl O atom. At the C1 end of the molecule, however, there is no indication of the presence of an analogous intramolecular hydrogen bond, despite the presence of two hydroxyl groups (one being a part of the carboxyl group) as potential donors. Instead, we observe the presence of what has been called (Jeffrey & Saenger, 1991) a mediated intramolecular hydrogen bond. The mediating group is the water molecule present in the crystal structure of this compound. One of the water H atoms [H2W] is used in the formation of a three-centre hydrogen bond. The two acceptors are carbonyl and hydroxyl O atoms from the same  $\alpha$ -hydroxycarboxyl group (Fig. 2a). In this way an  $R_2^2(5)$  motif is formed, which is topologically very similar to the  $S(5)$  motifs observed in the majority of (*R,R*)-tartaric acid derivatives (Gawroński *et al.*, 1997; Szczeptańska & Rychlewska, 1994; Szarecka *et al.*, 1996; Rychlewska *et al.*, 1997) and present in the isolated molecule of (*R,R*)-tartaric acid in its energetically preferred conformation (Polavarapu *et al.*, 1987).

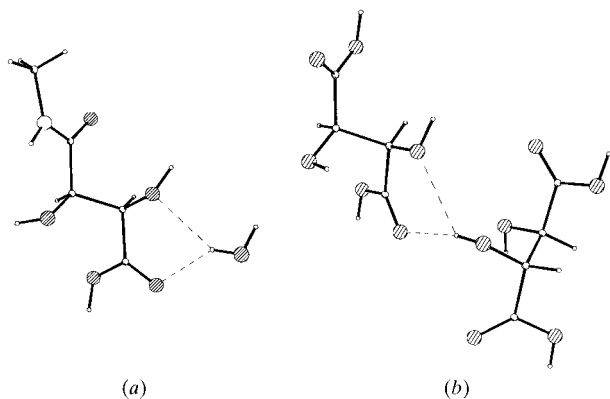


Fig. 2. (a) The mediated (through a water molecule) intramolecular hydrogen bond present in the crystal structure of  $\text{MMA}\cdot\text{H}_2\text{O}$ . (b) The analogous bond (through a hydroxyl substituent) in the parent (*R,R*)-tartaric acid.

Geometrical parameters for this and other types of hydrogen bond observed in the crystal are listed in Table 3.

Interestingly, this type of mediated intramolecular hydrogen bond is also present in the crystal structure of (*R,R*)-tartaric acid (Okaya *et al.*, 1966), although with one of the hydroxyl substituents as the mediating group (Fig. 2b).

### 3.2. Crystal structure

As in crystals of the parent (*R,R*)-tartaric acid (Okaya *et al.*, 1966), in crystals of  $\text{MMA}\cdot\text{H}_2\text{O}$  we observe hydrogen bonds linking translationally related molecules head-to-tail into infinite chains described by a  $C(7)$  pattern designator (Fig. 3). The chains are parallel to one of the crystallographic axes ( $x$ ) with a length of 7.301 (1)  $\text{\AA}$  in  $\text{MMA}\cdot\text{H}_2\text{O}$  and 7.715 (3)  $\text{\AA}$  in the crystal structure of (*R,R*)-tartaric acid (Okaya *et al.*, 1966). However, while in  $\text{MMA}\cdot\text{H}_2\text{O}$  the chains are formed *via* hydrogen bonds between carboxyl and amide groups, in

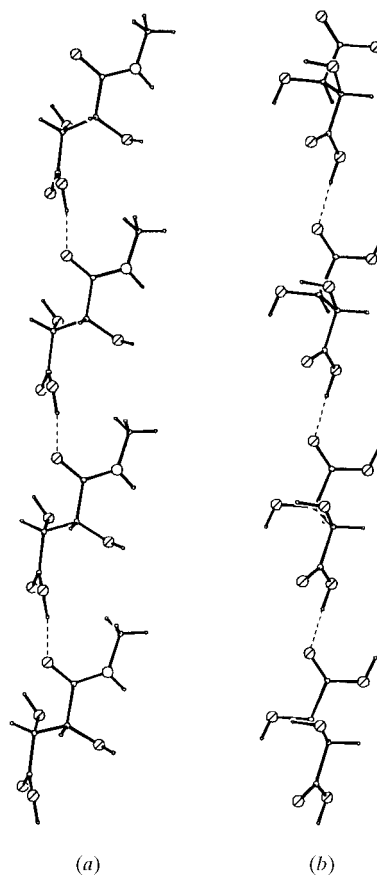


Fig. 3.  $C(7)$  chains formed by translationally related molecules hydrogen bonded in a head-to-tail fashion (a) in  $\text{MMA}\cdot\text{H}_2\text{O}$  and (b) in (*R,R*)-tartaric acid. Note that in (a) the chains are formed between carboxylic and *N*-methylamide groups, while in (b) they are formed between two carboxylic groups.

the parent tartaric acid only carboxyl groups are involved. The motif described here appears not only in the crystals of (*R,R*)-tartaric acid but is characteristic of the mode of packing of hydrogen tartrate anions (Marthi *et al.*, 1995, and references therein). On the other hand, in the crystal structures of (*R,R*)-tartaric acid diamides the *C*(7) motif, if present, involves screw-axis-related molecules (Rychlewska, 1999). It follows from the above that in MMA·H<sub>2</sub>O the packing is dictated by carboxyl rather than amide functions. The combination of one of the strongest proton donor groups, such as the carboxylic group, with one of the strongest proton acceptors, such as the amide carbonyl group, leads to the formation of a very short intermolecular hydrogen bond of length 2.571 (2) Å, the shortest one in this crystal structure. The corresponding donor-acceptor distance in (*R,R*)-tartaric acid is 2.695 Å. The *C*(7) chains are additionally supported by water molecules which, by accepting a proton from one of the hydroxyl groups (O2) and by donating one proton to the carboxyl carbonyl group of a translationally related molecule, form *C*<sub>2</sub><sup>2</sup>(7) chains propagating along *x*. Combination of *C*(7) and *C*<sub>2</sub><sup>2</sup>(7) motifs generates an *R*<sub>3</sub><sup>3</sup>(12) motif. As a result, molecules related by translation along the *x* direction form ribbons consisting of *R*<sub>3</sub><sup>3</sup>(12) and *R*<sub>2</sub><sup>1</sup>(5) rings. Exactly the same pattern is

observed in the crystal structure of (*R,R*)-tartaric acid, as shown in Fig. 4. Ribbons that are neighbours along *z* run in opposite directions and are connected by N—H···OW hydrogen bonds. In this way an infinite (010) layer is formed (Fig. 5). Moreover, ribbons that are neighbours along *y* are connected *via* water molecules in such a way that the H2W H atom is a donor in a three-centre hydrogen bond joining neighbouring  $\alpha$ -hydroxy-carboxyl moieties. In this way water molecules join proximal *xy* layers, as do the O3—H3O···O2(1 - *x*, *y* -  $\frac{1}{2}$ ,  $\frac{1}{2}$  - *z*) hydrogen bonds. The crystal structure viewed along the *y* and *z* directions is illustrated in Figs. 5 and 6, respectively.

### 3.3. Theoretical results

Structures with a mediated intramolecular three-centre hydrogen bond proved stable in the isolated state and also in solution. The fully optimized structures of the hydroxyacetic acid/water, hydroxyacetic acid/methanol and hydroxyacetic acid/hydroxyacetic acid complexes are presented in Figs. 7, 8 and 9, respectively, and the mediated hydrogen-bond parameters in these systems are given in Tables 4, 5 and 6, respectively.

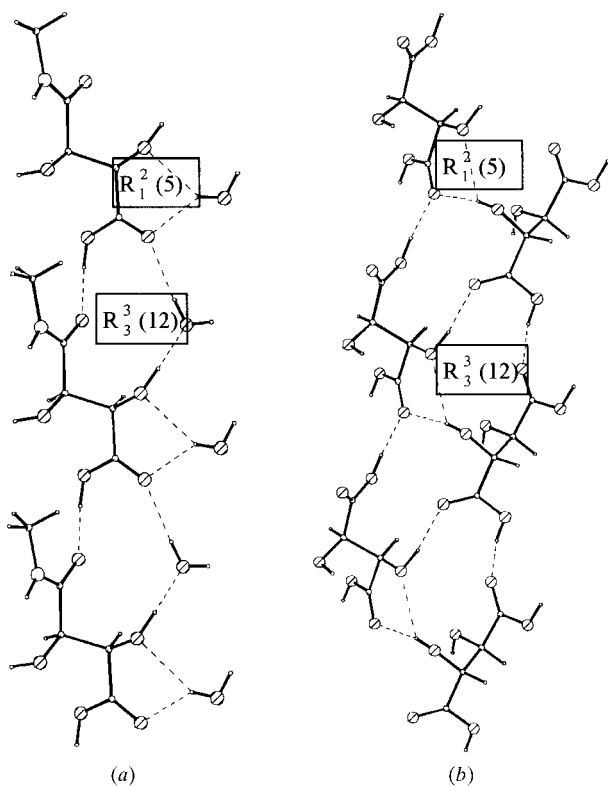


Fig. 4. An illustration of the similarity in packing along *x* in (a) MMA·H<sub>2</sub>O and (b) in (*R,R*)-tartaric acid.

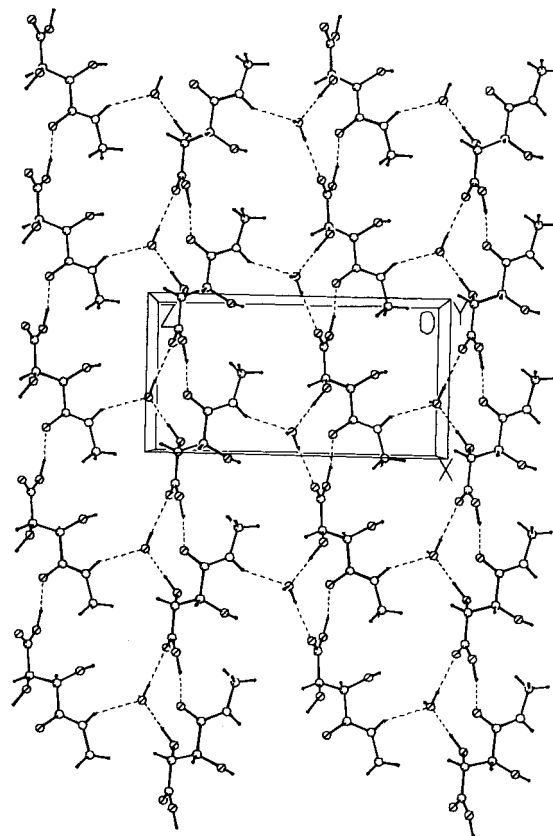


Fig. 5. The packing of MMA·H<sub>2</sub>O along *y*.

Table 4. *Hydrogen-bond parameters* ( $\text{\AA}$ ,  $^\circ$ ) *for HA-W*Hydrogen bond 1 is  $\text{O1b-H}\cdots\text{O1}$  ( $\text{OH}\cdots\text{OH}$ ); hydrogen bond 2 is  $\text{O1b-H}\cdots\text{O2}$  ( $\text{OH}\cdots\text{O=C}$ ).

Hydrogen bond	Dipole moment	Donor-acceptor distance		Proton-acceptor distance		Hydrogen-bond angle	
		1	2	1	2	1	2
Isolated state	5.389	3.0796	3.2636	2.1436	2.6647	170.60	121.86
Nonpolar solvent	5.668	3.0916	3.2276	2.1487	2.6793	175.49	117.61
Polar solvent	5.978	3.1059	3.1812	2.1618	2.7117	177.34	111.45

In the gas-phase optimized geometries of the structures studied we observe a surprising tendency for the  $\text{OH(m)}\cdots\text{O(H)}$  ( $m$  designates a mediating hydroxyl group) bond to be significantly shorter than the  $\text{OH(m)}\cdots\text{O=C}$  bond. Moreover, the hydrogen-bond angles for the  $\text{OH}\cdots\text{OH(m)}$  bonds are significantly more favourable than those for the  $\text{C=O}\cdots\text{HO(m)}$  bonds. It is worth noticing that in the case of both the HA-HA and HA-M complexes the hydrogen-bond angles are about  $150\text{--}160^\circ$  and  $130\text{--}140^\circ$ , respectively, while in the case of the HA-W complex the difference between the  $(\text{H})\text{O}\cdots\text{HO}$  and  $(\text{C=O})\cdots\text{HO}$  angles is significantly larger and much more in favour of the

hydroxyl-hydroxyl bond (the angles are about  $170$  and  $122^\circ$ , respectively). This strongly asymmetric case has been described by Newton *et al.* (1979). It is interesting to note that in the crystal structure of  $\text{MMA}\cdot\text{H}_2\text{O}$  the three-centre bond is symmetrical while in the crystal structure of (*R,R*)-tartaric acid it is markedly asymmetric. The corresponding values are  $\text{O-H(m)}\cdots\text{O=C}$   $2.03\text{ \AA}$ ,  $141^\circ$  and  $1.95\text{ \AA}$ ,  $169^\circ$ ,  $\text{O-H(m)}\cdots\text{OH}$   $2.19\text{ \AA}$ ,  $139^\circ$  and  $2.48\text{ \AA}$ ,  $114^\circ$  for  $\text{MMA}\cdot\text{H}_2\text{O}$  and (*R,R*)-tartaric acid, respectively.

The deviation from planarity of the  $\alpha$ -hydroxyacetic acid molecule is about  $3.4$  (HA-W) and  $5.7^\circ$  (HA-M). In HA-HA both  $\alpha$ -hydroxyacid molecules are nearly planar (*i.e.* the  $\text{O1-C1-C2-O2}$  and  $\text{O1b-C1b-C2b-O2b}$  angles are  $5.34$  and  $2.01^\circ$ , respectively). The degree of planarity of the  $\alpha$ -hydroxyacid moiety is therefore higher than that in the crystalline state.

Solvation affects all three structures in a similar way. We observe an increase in the dipole moments and changes in hydrogen-bond parameters, namely elongation of both PA (proton-acceptor) distances, particularly in a polar solvent, and significant changes in hydrogen-bond angles, *i.e.* further increase in the  $\text{OH}\cdots\text{OH}$  angle and decrease in the  $\text{C=O}\cdots\text{HO}$  angle, resulting from the O atom (from the mediating group) moving towards the carboxylic end of the molecule. This effect is most pronounced in HA-W where the 'free' H atom approaches the carbonyl O atom and its distance

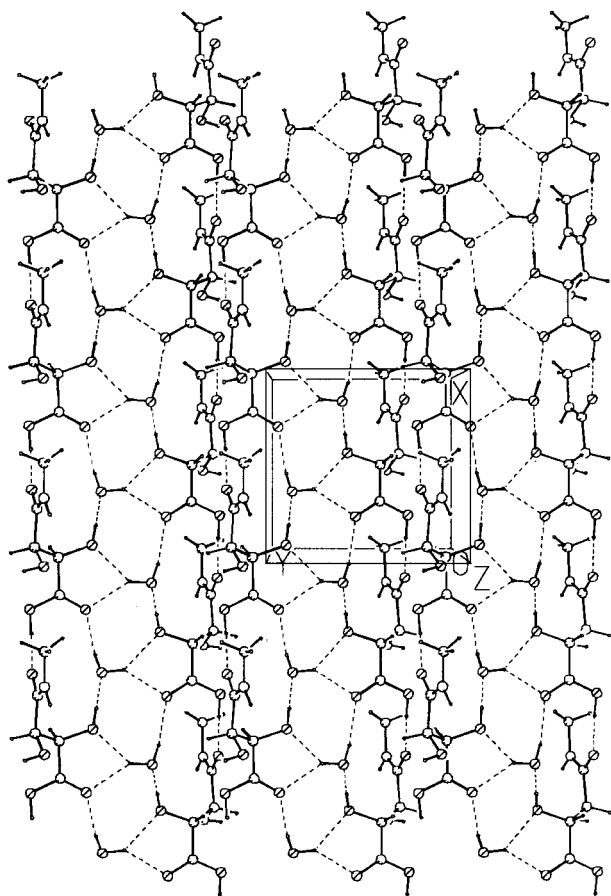
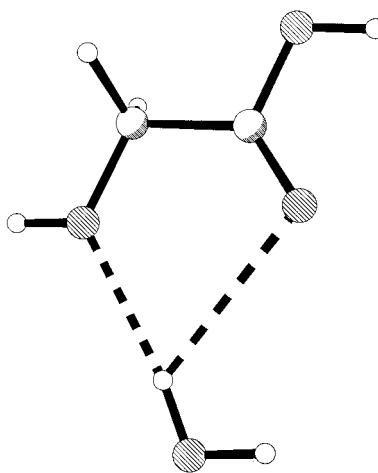
Fig. 6. An extension of the constitutional motifs along  $y$  by means of water molecules in the crystal of  $\text{MMA}\cdot\text{H}_2\text{O}$ .

Fig. 7. The optimized structure of HA-W.

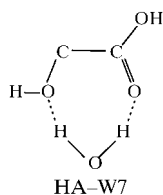
Table 5. *Hydrogen-bond parameters* ( $\text{\AA}$ ,  $^\circ$ ) for HA-MHydrogen bond 1 is O1b-H $\cdots$ O1 (OH $\cdots$ OH); hydrogen bond 2 is O1b-H $\cdots$ O2 (OH $\cdots$ O=C).

Hydrogen bond	Dipole moment	Donor-acceptor distance		Proton-acceptor distance		Hydrogen-bond angle	
		1	2	1	2	1	2
Isolated state	4.353	3.0478	3.4109	2.1876	2.6335	151.12	140.07
Nonpolar solvent	4.614	3.0561	3.4104	2.1864	2.6369	152.81	139.58
Polar solvent	4.9074	3.0687	3.4004	2.1907	2.6335	154.35	138.75

Table 6. *Hydrogen-bond parameters* ( $\text{\AA}$ ,  $^\circ$ ) for HA-HAHydrogen bond 1 is O1b-H $\cdots$ O1 (OH $\cdots$ OH); hydrogen bond 2 is O1b-H $\cdots$ O2 (OH $\cdots$ O=C).

Hydrogen bond	Dipole moment	Donor-acceptor distance		Proton-acceptor distance		Hydrogen-bond angle	
		1	2	1	2	1	2
Isolated state	5.819	3.0018	3.3105	2.1266	2.5641	153.60	136.17
Nonpolar solvent	6.550	3.0187	3.3112	2.1272	2.5776	156.84	134.74
Polar solvent	7.234	3.0400	3.2989	2.1350	2.5880	159.83	132.26

from the carbonyl O atom, being nearly 3  $\text{\AA}$  in the gas phase, decreases to about 2.70  $\text{\AA}$  in a polar environment. This tendency seems to be characteristic of changes which the HA-W structure undergoes when solvated. We have found that the test structure HA-W7 (see below) with a symmetrical seven-membered hydrogen-bonded ring is unstable in the isolated state and optimizes again to the HA-W structure, as shown in Fig. 7.



However, when the same starting structure HA-W7 is optimized in solution it does retain the seven-membered-ring arrangement in both polar and nonpolar

surroundings, although the polarity of the solvent affects the symmetry of the ring. That is, in a nonpolar solvent the OH $\cdots$ OH PA distance is shorter than that in the OH $\cdots$ O=C bond (2.2468 and 2.3910  $\text{\AA}$ , respectively). The OH $\cdots$ OH hydrogen-bond angle is also more favourable than that of OH $\cdots$ O=C (159 and 130 $^\circ$ , respectively). In polar surroundings it is the C=O $\cdots$ HO bond which becomes stronger: HO $\cdots$ O=C and OH $\cdots$ OH PA distances are 2.0808 and 2.5550  $\text{\AA}$ , respectively, and angles are 160 and 131 $^\circ$ , respectively. The energies of solvation of the HA-W7 complex are also lower than their HA-W counterparts by 8.8 ( $\epsilon = 2.00$ ) and 27.6  $\text{kJ mol}^{-1}$  ( $\epsilon = 80.00$ ).

Solvent also seems to affect the planarity of the  $\alpha$ -hydroxycarboxyl moiety in such a way that the OCCO torsion angles in all structures decrease, again, particularly in polar solvent as shown in Table 7.

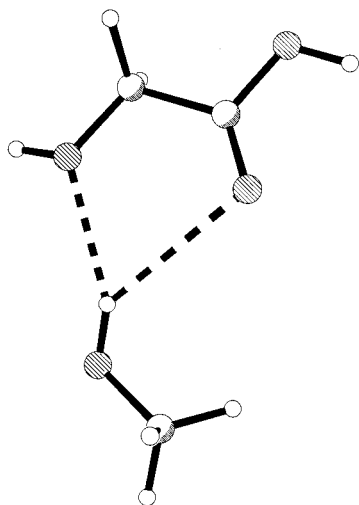


Fig. 8. The optimized structure of HA-M.

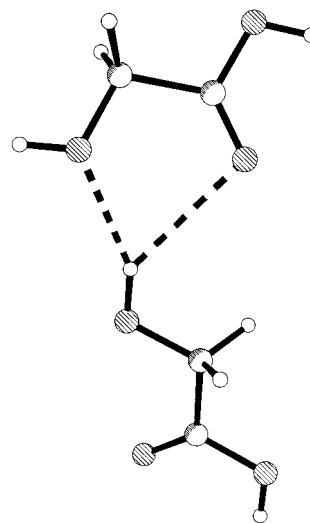


Fig. 9. The optimized structure of HA-HA.

Table 7.  $O1-C1-C2-O2$  angles ( $^\circ$ ) in HA-W, HA-M and HA-HA in the gas phase and in solution

	HA-W	HA-M	HA-HA
Gas phase	3.39	5.66	5.34
Nonpolar solvent	2.16	4.79	3.43
Polar solvent	-0.33	3.81	1.07

Table 8. Relative energies ( $\text{kJ mol}^{-1}$ ) of HA-W, HA-M and HA-HA in solution

Values given in parentheses correspond to PCM solvation energies.

	HA-W	HA-M	HA-HA
Nonpolar solvent	1.42 (30.14)	0.84	2.76
Polar solvent	3.85 (93.63)	2.22	7.69

The relative energies  $E_i$  of the  $i$ th structure (*i.e.* the differences between Onsager solute energy for low and high dielectric constant, respectively, and the isolated state energy of the  $i$ th structure) are given in Table 8. As can be seen from the data collected in Table 8 solvent stabilizes the complexes. However, the degree of stabilization depends markedly on the polarity of the solvent and is rather low: in a polar solvent it amounts to about 2.1, 4.2 and 7.5  $\text{kJ mol}^{-1}$  for HA-M, HA-W and HA-HA, respectively. We have performed test calculations for HA-W with the aid of the Polarizable Continuum Model (PCM) (Miertuš *et al.*, 1981), in which solute-solvent interactions are taken into account *via* a charge distribution much more complex than a simple dipole. Importantly, the PCM also predicts stabilization of the HA-W structure, which increases with the rising polarity of the solvent. There are, however, significant quantitative differences since PCM solvation energies are much higher, and amount to about 30 and 94  $\text{kJ mol}^{-1}$  for nonpolar and polar solvents, respectively.

### 3.4. Conclusions

In conclusion we would like to emphasize that a mediated intramolecular hydrogen bond,  $R_1^2(5)$ , is observed as one of the packing motifs in crystal lattices of (*R,R*)-*N*-methyltartramic acid monohydrate. The  $R_1^2(5)$  motif can be regarded as a typical association unit in systems with an  $\alpha$ -hydroxycarboxyl group, in particular in crystals containing solvent water molecules. Selected structures with this type of hydrogen bond are stable according to the *ab initio* RHF method. Interactions with solvent (according to the Onsager model) additionally stabilize the structures considered – the higher polarity of the solvent, the bigger this effect becomes.

We gratefully acknowledge KBN for supporting us with grant 8 T11F 29 15 and Poznań Supercomputing

and Networking Centre for access to Cray Y M-PL and Cray J916 machines. We are also grateful to Professor Jacek Gawroński for valuable discussions.

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