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Hydrogen-bonding interactions in (3,4-dimethoxyphenyl)acetic acid monohydrate

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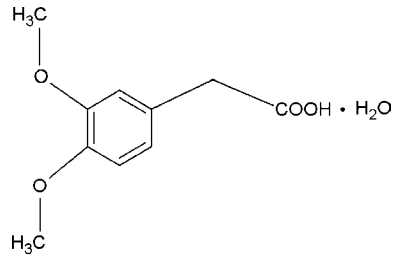
The crystal structure of the title compound, $C_{10}H_{12}O_4\cdot H_2O$, consists of (3,4-dimethoxyphenyl)acetic acid and water molecules linked by O—H···O hydrogen bonds to form cyclic structures with graph-set motifs $R_1^2(5)$ and $R_4^4(12)$. These hydrogen-bond patterns result in a three-dimensional network with graph-set motifs $R_4^4(20)$ and $R_4^4(22)$, and the formation of larger macrocycles, respectively. The C—C bond lengths and the endocyclic angles of the benzene ring show a noticeable asymmetry, which is connected with the charge-transfer interaction of the carboxyl or methoxy groups and the benzene ring. The title compound is one of the simple carboxylic acid systems that form hydrates. Thus, the significance of this study lies in the analysis of the interactions in this structure and the aggregations occurring *via* hydrogen bonds in two crystalline forms of (3,4-dimethoxyphenyl)acetic acid, namely the present hydrate and the anhydrous form [Chopra, Choudhury & Guru Row (2003). *Acta Cryst.* E**59**, o433–o434]. The correlation between the IR spectrum of this compound and its structural data are also discussed.

Comment

(3,4-Dimethoxyphenyl)acetic acid (DMPAA), also known as homoveratric acid, is the main urinary metabolite of 3,4-dimethoxyphenylethylamine (DMPEA) produced by the oxidation of DMPEA by monoamine oxidase (MAO) (Friedhoff & Van Winkle, 1963; Perry *et al.*, 1964; Kuehl *et al.*, 1966; Friedhoff & Furiya, 1967; Goto *et al.*, 1997). DMPEA is a doubly methylated metabolite of 3,4-dihydroxyphenylethylamine (dopamine) and the enzyme involved in the creation of DMPEA is catechol-*O*-methyltransferase (COMT) (Goto *et al.*, 1997; Birtwistle & Baldwin, 1998). DMPAA and DMPEA are biologically important compounds which have attracted attention in relation to neuropsychiatric diseases [*e.g.* schizophrenia (Friedhoff & Van Winkle, 1962*a*,*b*) and Parkinson's disease (Barbeau *et al.*, 1963)], for which urinary excretions were reported to be increased. DMPAA is also of great importance for the synthesis of a large number of 1,2,3,4-tetrahydroisoquinoline compounds, which are the most significant group of alkaloids [particularly the opium alkaloids, *e.g.* morphine, codeine or papaverine (Nagarajan *et al.*, 1985; Szawkało & Czarnocki, 2005)]. DMPAA can be used as the starting material to prepare 1-aryl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-ones, which are potentially useful for the treatment of epilepsy (Bevacqua *et al.*, 2001).



(I)

Carboxylic acids exhibit a remarkable range of structural diversity in their crystal structures. The carboxyl groups can be arranged as centrosymmetric dimers or catemers (Leiserowitz, 1976; Das & Desiraju, 2006). Anhydrous DMPAA, with the chain arrangement of hydrogen bonds, has been the subject of a study of the mechanism of the generation of IR spectra by hydrogen-bonded carboxylic acid crystals (Flakus & Hachuła, 2008). Measurement of the IR spectra of polycrystalline and monocrystalline samples of anhydrous DMPAA and theoretical analysis of the results focused mainly on spectroscopic effects corresponding to the intensity distribution, the influence of temperature, linear dichroism, and isotopic substitution of deuterium in the abovementioned acid molecules measured in the frequency range of the H and D stretching vibration bands, ν_{O-H} and ν_{O-D}, respectively. The crystal structure of the anhydrous form of DMPAA has been described previously (Chopra *et al.*, 2003). The molecules of this compound are linked into linear chains along the crystallographic *b* axis by intermolecular O—H···O hydrogen bonds. Hydrated crystals of DMPAA were obtained by the

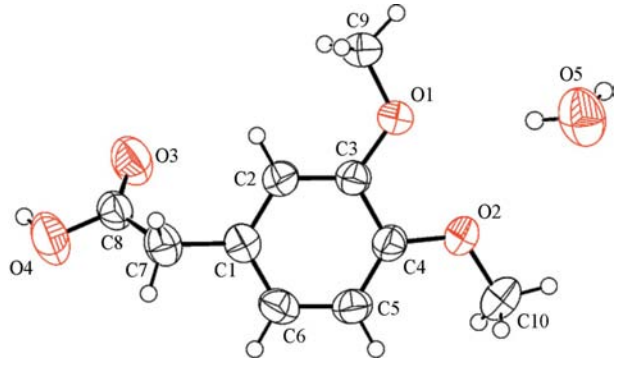


Figure 1
The asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

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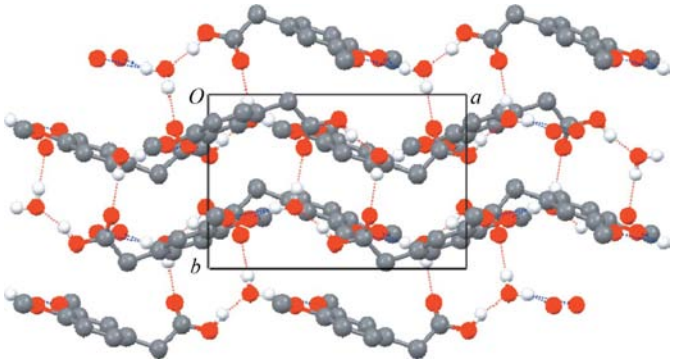

Figure 2
The molecular packing of the title compound, viewed along the *c* axis, showing the $R_4^4(12)$ rings. Dashed lines indicate the hydrogen-bonding interactions.

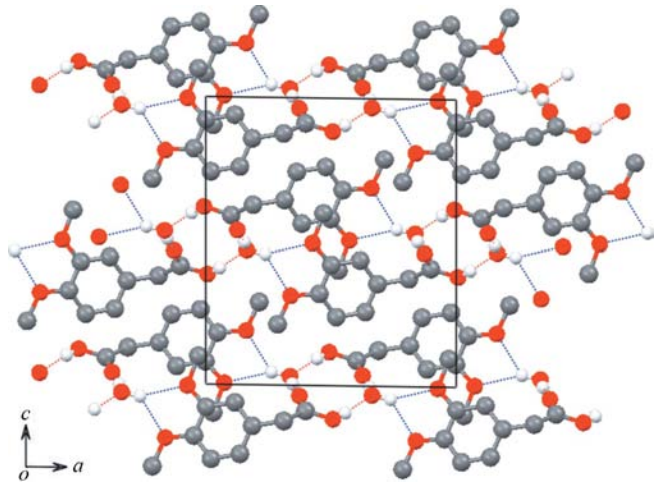

Figure 3
A fragment of molecular framework in the crystal structure of (I). Hydrogen bonds and bifurcated O—H···O interactions are shown as dashed lines (red and blue, respectively, in the electronic version of the paper).

evaporation of a solution in a mixture of water and acetone. The existence of the title hydrated form, (I), of DMPAA was identified by analysis of the IR spectrum of the compound. For this reason, the determination of the crystal structure of (I) was necessary.

The asymmetric unit of (I) contains one DMPAA molecule and one water molecule (Fig. 1). The endocyclic C—C bonds of the benzene ring show a noticeable bond-length asymmetry: the C1—C2 bond is elongated, whereas the C2—C3 bond is shortened (Table 1). The longest bond is that between atoms C3 and C4, which have the two methoxy substituents, while the shortest bond, C4—C5, is located opposite the carboxyl substituent. The C2—C1—C6 angle is significantly less than 120°, whereas the neighbouring angles, C1—C2—C3 and C1—C6—C5, are increased by 1.06 (14) and 1.01 (16)°, respectively. A similar effect is observed for C2—C3—C4 and C3—C4—C5 (reduction of the angles) and C1—C2—C3 and C4—C5—C6 (enlargement of the angles). This fact is probably connected with the charge-transfer interaction of the carboxyl or methoxy groups and the benzene ring (Domenicano *et al.*, 1975*a*,*b*). The bond distances and endocyclic angles in the title compound are comparable with the corresponding values in other ring structures (Domiano *et al.*, 1979; Allen *et al.*, 1987).

The acetic acid group is twisted out of the benzene ring plane [torsion angles C2—C1—C7—C8 = 65.7 (2)° and C6—C1—C7—C8 = −115.66 (17)°]. The dihedral angle between the plane of the benzene ring and the plane of the carboxylic acid group, O3—C8—O4, is 54.09 (14)°. The C—O bond distances and O—C—C angles are similar to those in anhydrous DMPAA [C8—O4 = 1.3104 (18) Å and C8—O3 = 1.2114 (18) Å, and O3—C8—C7 = 124.55 (14)° and O4—C8—C7 = 113.72 (14)°]. The two methoxy groups lie in the plane of the benzene ring in (I) and point away from each other, as in the anhydrous compound [torsion angles C9—O1—C3—C4 = 175.6 (1)°, C10—O2—C4—C3 = 170.4 (1)° and O1—C3—C4—O2 = 1.3 (2)°]. The geometry of the methoxy groups is governed by the repulsive interaction between the C9 and C10 methyl groups and the aromatic ring, leading to an enlargement of the O1—C3—C2 and O2—C4—C5 angles and a diminution of O1—C3—C4 and O2—C4—C3. A similar interaction between the two lone pairs on atom O4 and the neighbouring atoms causes the enlargement of the O3—C8—O4 angle and the reduction of C8—O4—H10 (Table 1). The vicinal bond lengths, C3—O1 and C4—O2, are very close to the values found in similar structures, *i.e.* DMPAA (Chopra *et al.*, 2003), 4-hydroxy-3-methoxyphenylacetic acid (Okabe *et al.*, 1991) or benzoic acid derivatives including the methoxy substituent (Bryan & White, 1982; Wallet *et al.*, 2001; Barich *et al.*, 2004), but these bond distances are slightly shorter than the value specified by Allen *et al.* (1987) for a methoxy substituent (1.424 Å).

The DMPAA molecules of (I) are linked approximately along the *b* axis by interleaving water molecules, which act as hydrogen-bond donors and acceptors to the carboxyl group O atoms. In addition, each solvent water molecule is a donor in a hydrogen bond to the methoxy group O atoms of an adjacent carboxylic acid molecule. Thus, each water molecule bridges three DMPAA molecules. In turn, each DMPAA molecule is hydrogen bonded to three water molecules. The result of these interactions is the formation of specific ring motifs with binary graph-set notation (Etter *et al.*, 1990; Bernstein *et al.*, 1995) as follows. Firstly, O4—H1O···O5($x+1$, y, z) and O5—H15O···O3($-x+1$, $-y$, $-z+1$) generate a centrosymmetric $R_4^4(12)$ motif parallel to the *c* axis containing two water and two DMPAA molecules (Fig. 2). Secondly, the bifurcated hydrogen bonding of the O5—H25O group to atoms O1 and O2 generates an $R_1^2(5)$ motif involving one water molecule and one DMPAA molecule which runs along the *a* axis (Fig. 3). These hydrogen-bond patterns result in a three-dimensional network with graph-sets $R_4^4(20)$ and $R_4^4(22)$, and the formation of larger macrocycles, respectively (Fig. 4). Judging from the bond distances, the O—H···O hydrogen bonds between water and carboxyl O atoms appears to be somewhat stronger [O3···O5 = 2.749 (2) Å and O4···O5 = 2.614 (2) Å] than the hydrogen bond involving water and methoxy O atoms [O1···O5 = 3.039 (2) Å and O2···O5 = 2.915 (2) Å]. It can also be mentioned that a similar graph set is observed in

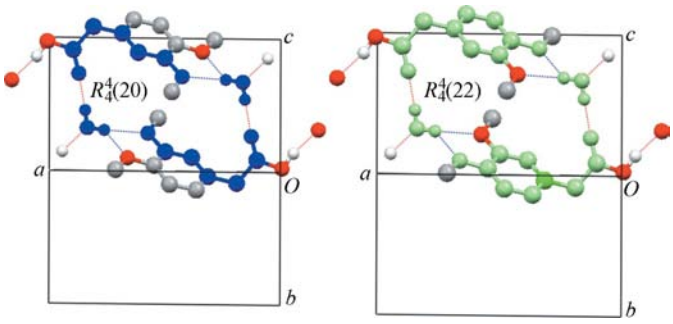

Figure 4
Part of the crystal structure of (I), showing the formation of the sheets *via* $R_4^4(20)$ and $R_4^4(22)$ motifs.

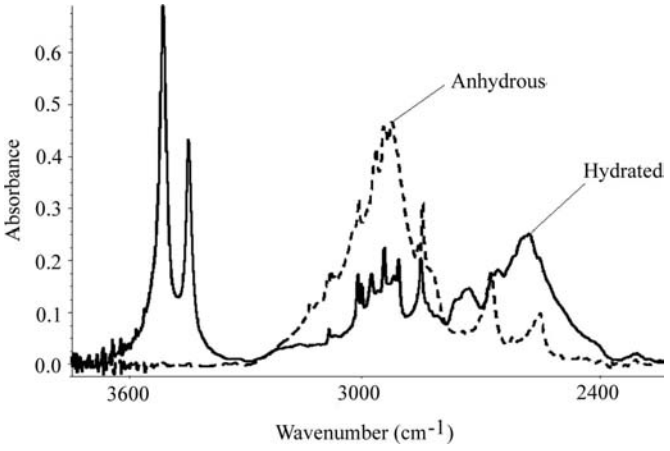

Figure 5
IR spectra of anhydrous and hydrated DMPAA samples dispersed in KBr pellets.

2-hydroxy-3-methoxybenzoic acid monohydrate (Fang *et al.*, 2008), in which the molecules are connected through O—H···O hydrogen bonds forming an $R_4^4(12)$ ring. The details of the hydrogen-bonding interactions are shown in Figs. 2–4 and given in Table 2.

A comparison of the polycrystalline spectra of both forms of DMPAA is shown in Fig. 5. The spectra differ from each other in the intensity distribution patterns, the intensity ratio of the branches and their location. For anhydrous DMPAA, the ν_{O-H} proton stretching vibration band is extended over the frequency range 2300–3300 cm^{-1}. In the case of DMPAA monohydrate, the ν_{O-H} proton–deuteron stretching band covers the range 2200–3700 cm^{-1}. In the IR spectrum of the title compound (Fig. 5), a broad absorption band with maxima at 3453 and 3519 cm^{-1} arises from the stretching vibration of the solvent water molecule. Analysis of the IR spectra shows that the ν_{O-H} band of the hydrated form of the compound is shifted towards the lower frequencies compared with the band location in the anhydrous form. This effect proves that the O—H···O hydrogen bonds are slightly stronger in the hydrated form of DMPAA than those in the anhydrous form of the compound. A familiar relation between the hydrogen-bond energy and the frequency shift of the proton (or deuteron) stretching vibration band is used to justify this statement (Schuster *et al.*, 1976; Schuster & Mikenda, 1999). A similar connection between the hydrogen-bond energies in the two forms of DMPAA can also be estimated from the O—H···O bond distances. The O—H···O bond length [O4—H1O···O5 = 2.614 (2) Å] in DMPAA monohydrate appears to be slightly shorter than that in the anhydrous form [O2—H2O···O1 = 2.651 (2) Å]. Consequently, the stronger O—H···O hydrogen bonds correspond to a larger frequency shift. Thus, the water molecules exerting an influence on the carboxyl groups noticeably stabilize the molecular structure of the title compound.

Experimental

DMPAA (98% pure) was purchased from Sigma–Aldrich. Slow crystallization from a mixture of acetone and water (1:1 *v*/*v*) over a period of several days at room temperature afforded the title crystalline monohydrate, (I). The IR spectra of polycrystalline samples of anhydrous and hydrated DMPAA dispersed in KBr were measured at the temperature of liquid nitrogen using an FT–IR Nicolet Magna 560 spectrometer operating at a resolution of 2 cm^{-1}. The IR spectra were recorded over the range 1000–4000 cm^{-1} using an Ever-Glo source, a KBr beamsplitter and a DTGS detector.

Crystal data

$C_{10}H_{12}O_4·H_2O$
M_r = 214.21
Monoclinic, $P2_1/n$
a = 11.362 (2) Å
b = 7.5474 (15) Å
c = 13.029 (3) Å
β = 90.80 (3)°
V = 1117.1 (4) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 298 (2) K
0.60 × 0.26 × 0.21 mm

Data collection

Oxford Diffraction KM-4-CCD Sapphire3 diffractometer
6748 measured reflections
2049 independent reflections
1498 reflections with $I > 2\sigma(I)$
R_{int} = 0.098

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.151
S = 1.15
2049 reflections
150 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C3	1.383 (2)	C1—C2	1.407 (2)
O2—C4	1.3871 (19)	C2—C3	1.391 (2)
O3—C8	1.207 (2)	C3—C4	1.417 (2)
O4—C8	1.321 (2)	C4—C5	1.382 (2)
C1—C6	1.390 (2)	C5—C6	1.407 (3)
C8—O4—H1O	109 (2)	O2—C4—C3	114.67 (15)
C6—C1—C2	118.45 (15)	C4—C5—C6	120.34 (15)
C3—C2—C1	121.06 (14)	C1—C6—C5	121.01 (16)
O1—C3—C2	125.71 (13)	C8—C7—C1	115.40 (13)
O1—C3—C4	114.51 (13)	O3—C8—O4	122.08 (17)
C2—C3—C4	119.77 (15)	O3—C8—C7	124.58 (16)
C5—C4—O2	125.97 (14)	O4—C8—C7	113.32 (15)
C5—C4—C3	119.36 (14)		
C9—O1—C3—C4	178.38 (14)	C6—C1—C7—C8	−115.66 (17)
C10—O2—C4—C3	−176.53 (16)	C2—C1—C7—C8	65.7 (2)
O1—C3—C4—O2	0.2 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O4—H1O···O5^{i}	0.94 (3)	1.70 (3)	2.614 (2)	162 (3)
O5—H15O···O3^{ii}	0.87 (3)	1.89 (3)	2.749 (2)	172 (2)
O5—H25O···O2	0.86 (3)	2.26 (3)	2.915 (2)	133 (2)
O5—H25O···O1	0.86 (3)	2.25 (3)	3.039 (2)	153 (2)

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

Aromatic H atoms were treated as riding on their parent C atoms, with C—H = 0.96 Å and U_{iso}(H) = 1.2U_{eq}(C). Methyl H atoms were also treated as riding on their parent C atoms, with C—H = 0.93 Å and U_{iso}(H) = 1.5U_{eq}(C). H atoms which take part in hydrogen bonding were located in a difference Fourier map and refined freely with isotropic displacement parameters.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *publCIF* (Westrip, 2008).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV3147). Services for accessing these data are described at the back of the journal.

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