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Glycinium semi-malonate and a glutaric acid–glycine cocrystal: new structures with short O—H···O hydrogen bonds

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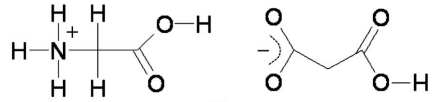
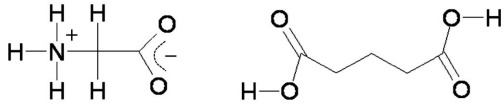
Glycinium semi-malonate, $C_2H_6NO_2^+\cdot C_3H_3O_4^-$, (I), and glutaric acid–glycine (1/1), $C_2H_5NO_2\cdot C_5H_8O_4$, (II), are new examples of two-component crystal structures containing glycine and carboxylic acids. (II) is the first example of a glycine cocrystal which cannot be classified as a salt, as glutaric acid remains completely protonated. In the structure of (I), there are chains formed exclusively by glycinium cations, or exclusively by malonate anions, and these chains are linked with each other. Two types of very short O—H···O hydrogen bonds are present in the structure of (I), one linking glycinium cations with malonate anions, and the other linking malonate anions with each other. In contrast to (I), no direct linkages between molecules of the same type can be found in (II); all the hydrogen-bonded chains are heteromolecular, with molecules of neutral glutaric acid alternating with glycine zwitterions, linked by two types of short O—H···O hydrogen bonds.

Comment

Crystalline amino acids and their salts are widely used as biologically active compounds or molecular materials. Studies of the crystal structures of salts of amino acids with carboxylic acids are also of interest for crystal engineering. Amino and carboxylic groups, and in many cases also the side chains of amino acids, are capable of forming hydrogen bonds with the carboxyl groups of carboxylic acids, giving rise to a variety of crystal structures. It is of special interest to see in which cases homomolecular fragments (chains, layers, *etc.*) are preserved in these mixed crystal structures, and when the contacts between molecules of the same type are completely substituted by heteromolecular contacts. This problem seems to be related to understanding the mechanisms of the formation of mixed crystals (cocrystals), as well as to attempts at using mixed crystals as more soluble forms compared to the individual components.


(I)


(II)

Glycine is the simplest amino acid (and is optically inactive) but it gives rise to multiple polymorphs as a pure compound and to a rich variety of crystalline salts. The majority of glycine salts described up to now are formed with inorganic anions [141 compounds in the Cambridge Structural Database (CSD), Version of 2011; Allen, 2002]. For the salts with carboxylic acids, the structures of two polymorphs of glycinium semi-oxalate (Subha Nandhini *et al.*, 2001; Tumanov *et al.*, 2010), of bis-glycinium oxalate (Chitra *et al.*, 2006) and its solvate (Tumanov *et al.*, 2010), of glycinium hydrogen maleate (Rajagopal *et al.*, 2001) and of glycinium fumarate monohydrate (Natarajan *et al.*, 2009) have been described. In the present paper, we report the structures of new two-component crystals of glycine with carboxylic acids [a salt, (I), and a cocrystal, (II)], which have interesting structural features.

The asymmetric unit of (I) contains a glycinium cation and a malonate anion, whereas the asymmetric unit of (II) contains a neutral glutaric acid molecule and a glycine zwitterion (Figs. 1*a* and 1*b*). The intramolecular geometry of glycine in (II) and in the three polymorphs of pure glycine is similar. Glycinium cations in semi-malonate are also similar to those in glycinium oxalate, hydrogen maleate and semi-oxalate (polymorphs I and II). The molecular conformation of glutaric acid

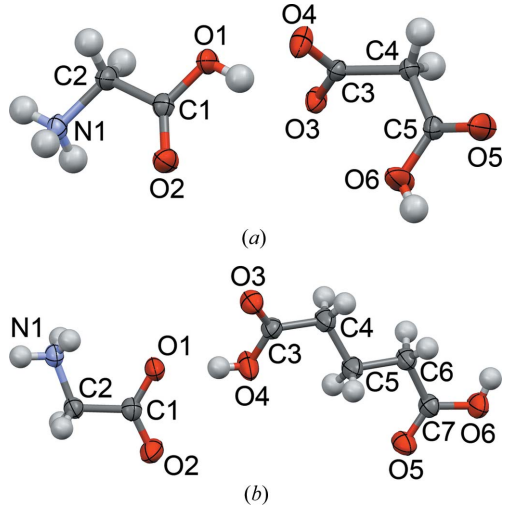


Figure 1
Displacement ellipsoid plots for (*a*) (I) and (*b*) (II), showing the atom-numbering schemes and drawn with 50% probability displacement ellipsoids for non-H atoms. H atoms are shown as arbitrary spheres.

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in (II) is similar to that in the crystals of pure glutaric acid (Thalladi *et al.*, 2000). (II) is not a salt, since glutaric acid remains completely protonated, and this is the first example of a cocrystal between glycine and this acid. There are 57 structures with glutaric acid in the CSD (Version of 2011), and glutaric acid exists in a diprotonated form in 48%, in a monoprotonated form in 33% and in the form of a doubly charged anion in 19% of them. Five cocrystals of glutaric acid with amino acids were described and glutaric acid was monoprotonated in four of those (cocrystals with histidine and lysine) and present as a dianion in the case of bis(L-arginium) glutarate dihydrate. Thus, the mixed glutaric acid–glycine crystal is the first example of a cocrystal of an amino acid with glutaric acid in which glutaric acid is present in the non-ionized form.

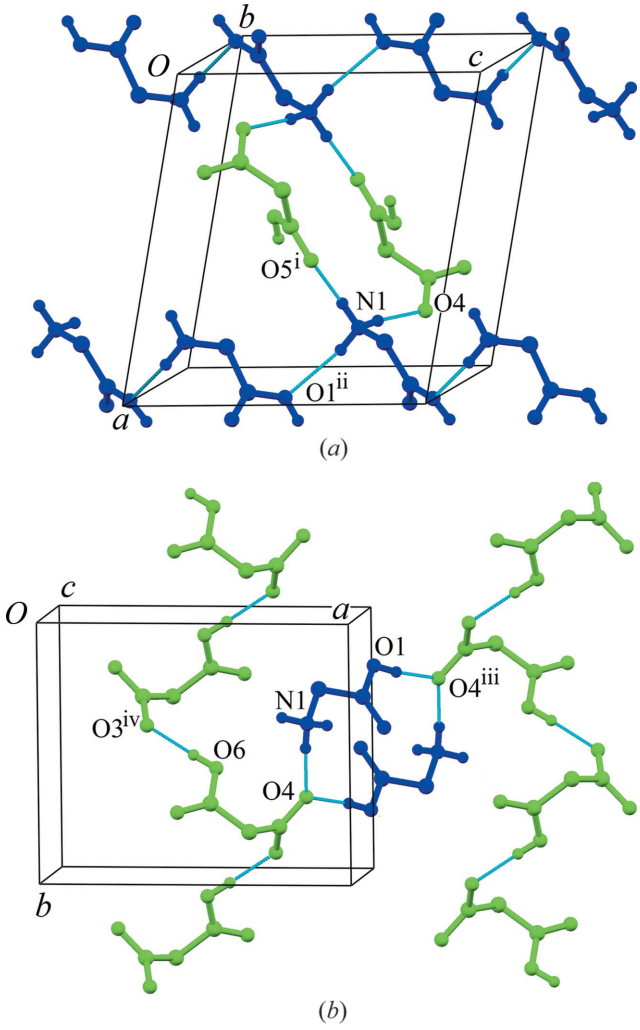

Figure 2
The components of the crystal structure of (I), showing (*a*) homomolecular chains of glycinium cations (blue in the electronic version of the paper) stretching along the *c* axis and (*b*) chains of semi-malonate anions (green) stretching along the *b* axis, with heteromolecular four-membered rings. Hydrogen bonds are shown by thin lines and H atoms not involved in hydrogen bonding have been omitted. [Symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $x, -y+\frac{1}{2}, z-\frac{1}{2}$; (iii) $-x+2, -y+1, -z+2$; (iv) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$.]

The crystal packing in (I) and (II) is substantially different. In the structure of (I), head-to-tail chains are formed exclusively by glycinium cations [$C(5)$, running along the *c* axis], or exclusively by malonate anions [$C(6)$, running along the *b* axis], and these chains are linked with each other to form mixed heteromolecular chains [$C_2^2(11)$, running along the [101] direction] and heteromolecular four-membered rings [$R_4^4(16)$ and $R_4^2(14)$] (Fig. 2) (Bernstein, 2002). Two types of very short O—H···O hydrogen bonds are present in the structure of (I), one [with an O···O distance of 2.5289 (18) Å] linking glycinium cations with malonate anions and the other [with an O···O distance of 2.5465 (19) Å] linking malonate anions with each other (Table 1). The short O—H···O hydrogen bonds linking malonate anions within the chains are similar to those in other crystal structures containing malonate chains [butane-1,4-diammonium bis(hydrogen malonate) (Babu *et al.*, 1997), methylammonium hydrogen malonate (Djinović & Golič, 1991) and malonic acid (Thalladi *et al.*, 2000)]. This motif is rather rare for compounds containing malonic acid, semi-malonate or malonate anions (eight structures out of 53 entries in the CSD have this motif), and glycinium semi-malonate is the first example of an amino acid malonate in which semi-malonate anions form chains. Comparing the glycinium semi-malonate structure with other salts of glycine, one can conclude that the chains of semi-oxalate anions are also present in the structure of glycinium semi-oxalate, polymorphs I (Subha Nandhini *et al.*, 2001) and II (Tumanov *et al.*, 2010), but that they are absent in the structure of glycinium hydrogen maleate (Rajagopal *et al.*, 2001).

In contrast to (I), no direct linkages between the molecules of the same type can be found in (II); all the hydrogen-bonded

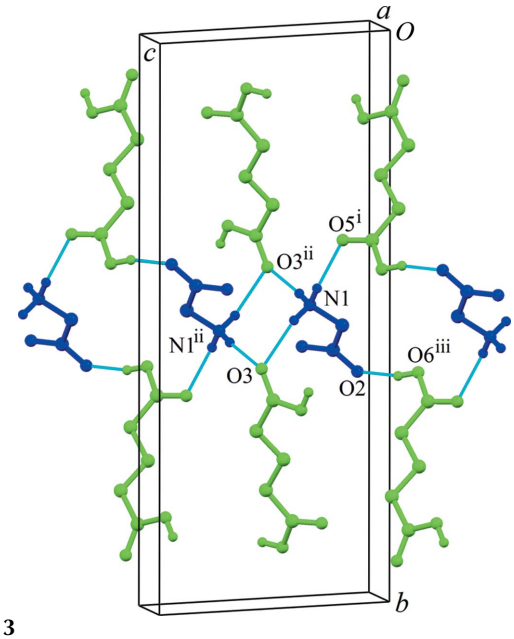

Figure 3
The components of the crystal structure of (II), showing heteromolecular chains and ring motifs. Hydrogen bonds are shown by thin lines. H atoms not involved in hydrogen bonding have been omitted. (In the electronic version of the paper, glycine molecules are blue and glutaric acid molecules are green.) [Symmetry codes: (i) $-x, y-\frac{1}{2}, -z+\frac{1}{2}$; (ii) $-x+1, -y+1, -z+1$; (iii) $x-1, -y+\frac{3}{2}, z-\frac{1}{2}$.]

chains are heteromolecular, with molecules of neutral glutaric acid alternating with glycine zwitterions, linked *via* two types of short O—H···O hydrogen bonds with O···O distances of 2.5377 (17) and 2.5671 (16) Å [$C_2^2(9)$, $C_2^2(11)$, $C_2^2(12)$ and $C_2^2(13)$] (Fig. 3 and Table 2). These heteromolecular chains are further linked with each other, to form four-membered rings [$R_4^2(8)$ and $R_4^4(18)$] (Fig. 3). This is the first example of a mixed crystal of an amino acid and a carboxylic acid which has only heteromolecular contacts.

Experimental

Crystals of glycinium semi-malonate and glutaric acid–glycine (1/1) were obtained by slow evaporation at 298 K from aqueous solutions (*ca* 3–4 ml) containing 1:1 ratios of glycine and the corresponding carboxylic acid.

Compound (I)

Crystal data

$C_2H_6NO_2^+\cdot C_3H_3O_4^-$
M_r = 179.13
Monoclinic, $P2_1/c$
a = 10.1431 (19) Å
b = 8.1729 (11) Å
c = 9.260 (2) Å
β = 101.879 (16)°
V = 751.2 (2) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.15 mm^{-1}
T = 297 K
0.40 × 0.25 × 0.15 mm

Data collection

Stoe IPDS 2 diffractometer
10879 measured reflections
1522 independent reflections
1295 reflections with $I > 2\sigma(I)$
R_{int} = 0.038

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.094
S = 1.07
1522 reflections
113 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Compound (II)

Crystal data

$C_2H_5NO_2\cdot C_5H_8O_4$
M_r = 207.18
Monoclinic, $P2_1/c$
a = 4.8954 (4) Å
b = 20.8944 (14) Å
c = 10.8462 (8) Å
β = 120.648 (6)°
V = 954.45 (14) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.13 mm^{-1}
T = 297 K
0.22 × 0.15 × 0.07 mm

Table 1
Hydrogen-bond geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O4^{i}	0.82	1.72	2.5289 (18)	167
O6—H6···O3^{ii}	0.82	1.73	2.5465 (19)	178
N1—H1A···O5^{iii}	0.89	2.03	2.859 (2)	154
N1—H1B···O1^{iv}	0.89	2.27	3.041 (2)	144
N1—H1C···O4	0.89	1.91	2.7926 (19)	171

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

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O5^{i}	0.89	2.00	2.7643 (17)	143
N1—H1B···O3	0.89	2.13	2.9581 (17)	155
N1—H1C···O3^{ii}	0.89	1.99	2.8727 (17)	169
O6—H6···O2^{iii}	0.82	1.74	2.5377 (17)	165
O4—H4···O1^{iv}	0.82	1.75	2.5671 (16)	175

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

Data collection

Oxford Gemini R Ultra CCD diffractometer
Absorption correction: multi-scan (*CrysAlis PRO*; Oxford Diffraction, 2008)
T_{min} = 0.882, T_{max} = 0.991
14842 measured reflections
1953 independent reflections
1543 reflections with $I > 2\sigma(I)$
R_{int} = 0.037

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.102
S = 1.03
1953 reflections
131 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}

All H atoms were initially located in a difference Fourier map. The positions of all H atoms were subsequently geometrically optimized and refined using a riding model, with N—H = 0.89 Å, O—H = 0.82 Å and C—H = 0.97 Å, and with U_{iso}(H) = 1.5U_{eq}(N,O) and 1.2U_{eq}(C). The tetrahedral ammonium groups were allowed to rotate but not to tip.

Data collection: *X-AREA* (Stoe & Cie, 2006) for (I); *CrysAlis PRO* (Oxford Diffraction, 2008) for (II). Cell refinement: *X-AREA* for (I); *CrysAlis PRO* for (II). Data reduction: *X-RED32* (Stoe & Cie, 2006) for (I); *CrysAlis PRO* for (II). For both compounds, program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008) and *X-STEP32* (Stoe & Cie, 2000); molecular graphics: *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *Mercury*, *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2010).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DT3003). Services for accessing these data are described at the back of the journal.

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