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Hydrogen-bonding features in the 1:2 adduct of 4-aminobenzoic acid and L-proline

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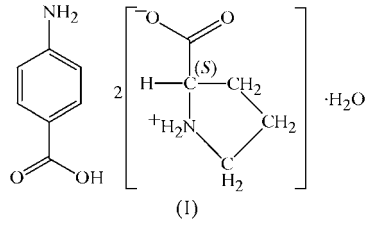
The title adduct, 4-aminobenzoic acid–L-proline–water (1/2/1), $C_7H_7NO_2\cdot 2C_5H_9NO_2\cdot H_2O$, contains two independent proline chains with a $C(5)$ motif, each of the head-to-tail type and each held together by N—H···O hydrogen bonds, propagated parallel to the *b* and *c* axes of the unit cell. Thus, the proline residues aggregate parallel to the *ac* plane. 4-Aminobenzoic acid (PABA) residues are arranged on both sides of the proline aggregate and are connected through water O atoms, which act as acceptors for PABA and as hydrogen-bond donors to the amino acids. The characteristic features of PABA, *viz.* twisting of the carboxyl plane from the aromatic ring and the formation of a head-to-tail chain motif $[C(8)]$ along the *b* axis, are observed. A distinct feature of the structure is that no proton transfer occurs between proline and PABA.

Comment

4-Aminobenzoic acid (PABA), a member of the vitamin B family, is a starting material in the manufacture of target esters, salts, folic acid, azo dyes and other organic compounds. It acts as a bacterial cofactor involved in the synthesis of folic acid (Robinson, 1966) and as an antagonist to the action of the drug sulfonilamide in competition for essential growth metabolites (Pauling & Hayward, 1964). PABA has proved to be a versatile reagent for structure extension by linear and cyclic hydrogen-bonding associations, through both its carboxyl and amine functional groups. As a simple organic molecule which promotes the extension of hydrogen-bonded network structures it has no equal, forming associations with neutral molecules such as 4-nitropyridine *N*-oxide (Moreno Fuquen *et al.*, 1996), 1,3-dimethylimidazolidin-2-one (Ueda *et al.*, 1986) and urea (Smith, Baldry *et al.*, 1997), with Lewis bases such as 4-(4-nitrobenzyl)pyridine (Smith, Lynch *et al.*, 1997), and with carboxylic acids such as 2,4,6-trinitrobenzoic acid (Lynch *et al.*, 1992*a*), (2,4-dichlorophenoxy)acetic acid (Lynch *et al.*, 1992*b*), 2-(carboxyphenoxy)acetic acid (Byriel *et al.*, 1991) and 3,5-dinitrosalicylic acid (Smith *et al.*, 1995). This property of extension was recognized as a possible tool for promoting cocrystallization, with the aim of designing noncentrosymmetric organic materials (Etter & Frankenbach, 1989). However, among the many reported cocrystals of PABA, only a few have been found to crystallize in noncentrosymmetric space groups (Allen, 2002), the title adduct, (I), being another such case.



(I)

Crystallographic studies of the nonproton transfer adducts of amino acids are scarce in the literature (Allen, 2002). Proline is a very important amino acid due to its unique conformation, which may affect the structure of proteins, in particular collagen. Investigations have shown that proline extracted and pulverized from the dehydrated fruit skin of *Lonsium domesticum* possesses antiplasmoidal and antimalarial activity (Yapp *et al.*, 2002). The structure of proline differs sharply from that of the other amino acids, as its side chain is bonded back to the N atom as well as to the C^{α} atom. Because of the bond to nitrogen, proline is technically called an imino (–NH–) acid rather than an amino ($–NH_2–$) acid. This secondary amino acid containing a cyclic structure markedly influences protein architecture. Proline has already been investigated in our laboratory in order to understand conformation and hydrogen-bonding interactions in inorganic or organic acid environments (Anitha *et al.*, 2006; Pandiarajan *et al.*, 2002). Disorder in one of the side-chain C atoms is very common in proline complexes and is also found in the present structure. In continuation of our investigations of proline-containing structures, PABA was crystallized with the amino acid L-proline to give the title monohydrate adduct, (I), and its structural features are presented here.

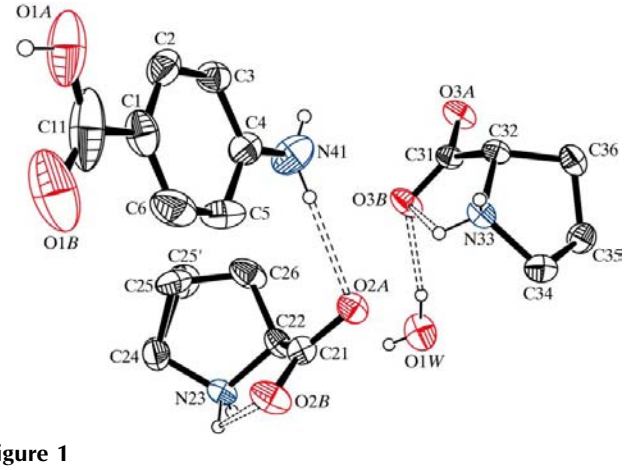


Figure 1
The asymmetric unit of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. H atoms not involved in hydrogen bonding (dashed lines) have been omitted for clarity. The primed atom is the minor disorder component of L-proline.

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The molecular structure of (I), which contains one 4-aminobenzoic acid molecule, two L-proline zwitterions and one lattice water molecule in the asymmetric unit, is shown in Fig. 1. The carboxyl plane of the vitamin is twisted from the plane of the aromatic ring through an angle of 8.9 (1)°, which is a characteristic feature found in almost all PABA complexes. The zwitterionic nature of the proline residues is confirmed by the C—O and C—N bond lengths (Table 1). The backbone conformation angles about the $C'-C^{\alpha}$ bond, Ψ^1 and Ψ^2, reveal that, in contrast with the observation of Lakshminarayanan *et al.* (1967), twisting of the carboxyl plane away from the C—N bond is not observed in the present structure. The side-chain conformation angles χ^1, χ^2, χ^3, χ^4 and θ of the pyrrolidine ring (Prasad & Vijayan, 1993) in the disordered proline are 35.2 (6) [−6.1 (10)], −39.9 (8) [25.6 (13)], 28.2 (8) [−6.1 (10)], −5.4 (6) [34.1 (9)] and −18.6 (5)°, respectively, for the disordered proline (values in square brackets are for the minor component), and 36.6 (4), −42.1 (4), 30.4 (5), −7.7 (5) and −17.9 (4)°, respectively, for the nondisordered proline residue. The major and minor conformers of the pyrrolidine ring in the disordered proline residue adopt a near-envelope conformation, as indicated by puckering analysis [q_2 = 0.378 (7)/0.361 (1) Å and φ_2 = 80.1 (8)/315.8 (17)°; Cremer & Pople, 1975]. For the nondisordered proline residue, the pyrrolidine ring adopts a twisted conformation, as indicated by puckering analysis [q_2 = 0.404 (5) Å and φ_2 = 82.6 (6)°].

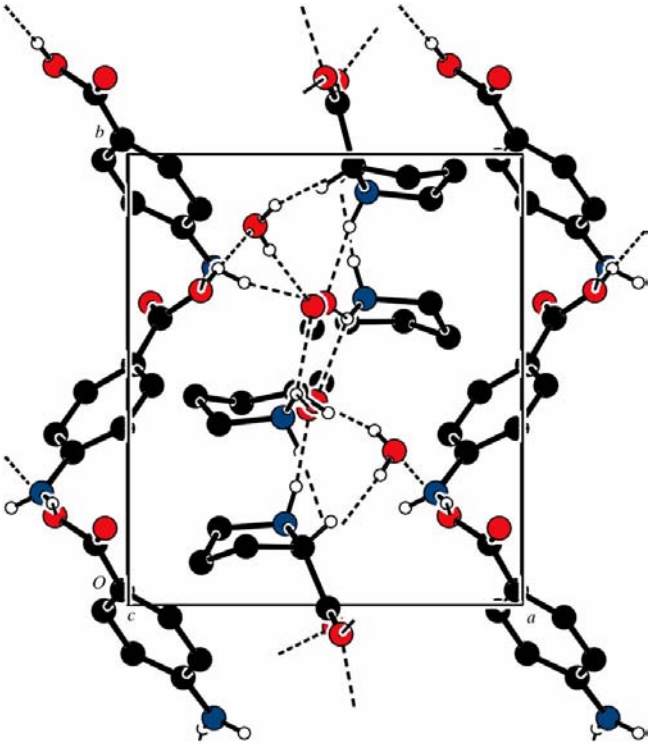

Figure 2
Packing diagram for (I), viewed down the *c* axis. Hydrogen bonds are shown as dashed lines. H atoms not involved in the hydrogen bonding and the minor components of the disordered proline are not shown.

As discussed above, PABA is widely known as a structure extension synthon in supramolecular systems. The most elegant aspect of the present work is found not in the molecular structure but in the crystal packing *via* hydrogen bonds (Fig. 2). The imino groups (NH_2^+) of each proline residue are involved in one two-centred and one three-centred hydrogen-bond interaction (Table 2). Both the amino acid zwitterions form *Z*2 head-to-tail chains (Suresh & Vijayan, 1983) or a *C*(5) hydrogen-bonding motif (Etter *et al.*, 1990; Bernstein *et al.*, 1995) parallel to the *b* axis of the unit cell. Interestingly, these ribbons (zigzag chains) are interconnected through another weak N—H···O hydrogen bond between the two different zwitterions, forming a straight *S*1 head-to-tail chain (Suresh & Vijayan, 1983) or another *C*(5) hydrogen-bonding motif along the *c* axis. The combination of these two primary motifs results

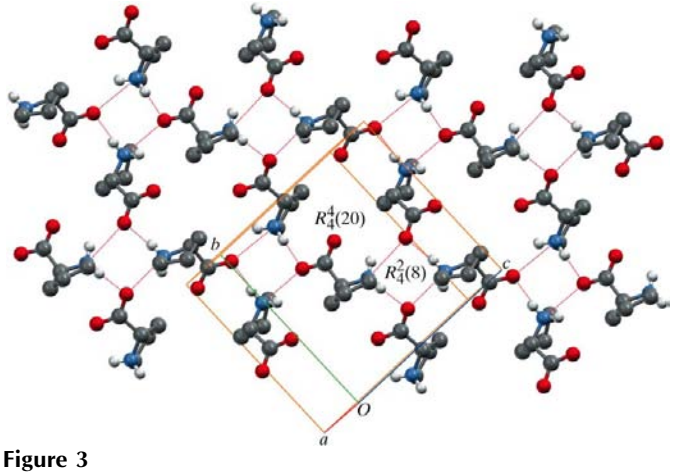

Figure 3
A view of the primary *C*(5) proline graph-set motifs, *viz*. 'head-to-tail' (*Z*1 and *S*1) chains, and secondary $R_4^2(8)$ and $R_4^4(20)$ motifs. Hydrogen bonds are shown as dashed lines. H atoms not involved in hydrogen bonding have been omitted for clarity.

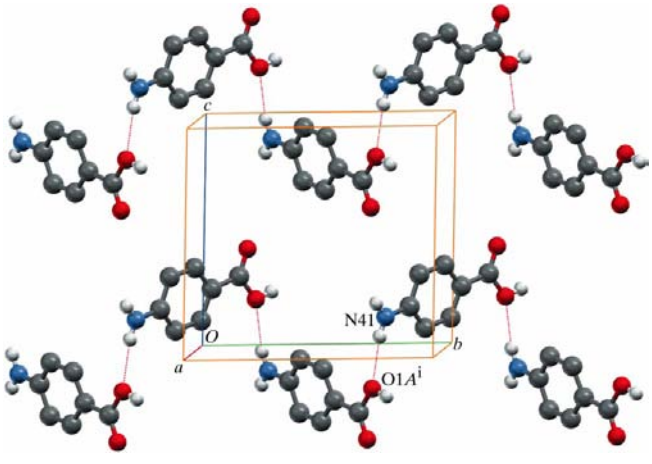

Figure 4
Head-to-tail *C*(8) graph-set motifs of PABA forming chains running along the *b* axis. Hydrogen bonds are shown as dashed lines. H atoms not involved in hydrogen bonding have been omitted for clarity. [Symmetry code: (i) $-x, -\frac{1}{2}+y, -z$.]

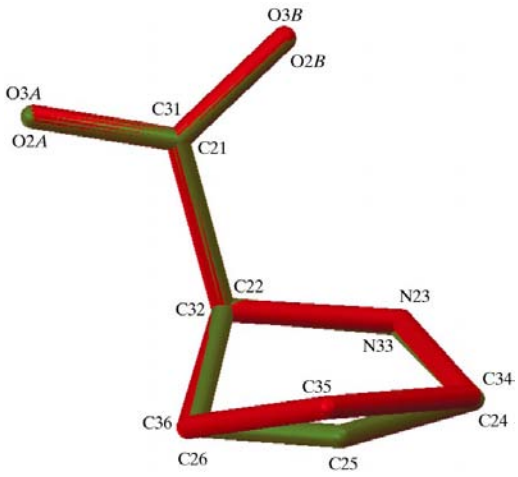

Figure 5
Overlay of the major component of the disordered proline (involving atom C25) and the ordered proline residue (atom C35), showing the slight difference in side-chain conformation. H atoms have been omitted for clarity.

in two secondary ring motifs, *viz*. $R_4^2(8)$ and $R_4^4(20)$ (Fig. 3). This forms an aggregation of prolines parallel to the *ac* plane of the unit cell. The water O atom acts as acceptor for the carboxyl O atom of the PABA and as donor for the carboxylate O atom of the amino acid, thus connecting PABA and L-proline. Generally, the structure extension of PABA is classified into two types, namely a 'head-to-tail' interaction (head = NH_2 and tail = COOH) and a carboxyl dimerization. The latter is not observed here, whereas the former feature is observed in the present structure, leading to the formation of a $C(8)$ graph-set motif extending along the *b* axis of the unit cell through the weak N—H···O hydrogen bond (Fig. 4).

Fig. 5 shows an overlay of the two proline residues (only the major component of the disordered moiety is shown) in the asymmetric unit, indicating the consistency between the conformations, except for the small deviation in the C^{γ} atom of the side chain.

Experimental

The title compound, (I), was crystallized from an aqueous mixture of 4-aminobenzoic acid and L-proline in a 2:1 stoichiometric ratio at room temperature by slow evaporation.

Crystal data

$C_7H_7NO_2{\cdot}2C_5H_9NO_2{\cdot}H_2O$
M_r = 385.42
Monoclinic, $P2_1$
a = 9.8171 (6) Å
b = 10.4167 (11) Å
c = 10.1713 (12) Å
β = 112.078 (9)°
V = 963.87 (16) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 293 (2) K
0.21 × 0.16 × 0.14 mm

Data collection

Nonius MACH3 diffractometer
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.965, T_{max} = 0.981
2117 measured reflections
1794 independent reflections
1573 reflections with $I > 2\sigma(I)$
R_{int} = 0.014
3 standard reflections
frequency: 60 min
intensity decay: none

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.115
S = 1.09
1794 reflections
263 parameters
3 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.35 e Å^{-3}
Absolute structure: by known absolute configuration of a chiral reference molecule

Table 1
Selected geometric parameters (Å, °).

C11—O1*B*	1.220 (13)	C22—N23	1.491 (5)
C11—O1*A*	1.326 (13)	C31—O3*B*	1.245 (5)
C4—N41	1.357 (7)	C31—O3*A*	1.251 (5)
C21—O2*B*	1.241 (5)	C32—N33	1.505 (5)
C21—O2*A*	1.263 (5)		
O2*B*—C21—C22—N23	0.2 (6)	N23—C22—C26—C25′	−6.0 (11)
O2*A*—C21—C22—N23	179.7 (3)	N23—C22—C26—C25	35.5 (6)
C26—C22—N23—C24	−18.8 (5)	O3*B*—C31—C32—N33	4.6 (5)
C22—N23—C24—C25	−5.5 (6)	O3*A*—C31—C32—N33	−175.7 (4)
C22—N23—C24—C25′	34.2 (9)	C36—C32—N33—C34	−18.1 (4)
N23—C24—C25—C26	28.3 (8)	C32—N33—C34—C35	−7.4 (5)
N23—C24—C25′—C26	−35.1 (12)	N33—C34—C35—C36	30.2 (5)
C24—C25′—C26—C22	25.5 (14)	C34—C35—C36—C32	−42.1 (5)
C24—C25—C26—C22	−40.1 (8)	N33—C32—C36—C35	36.6 (4)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*A*—H1*A*···O1*W*^{i}	0.82	1.94	2.746 (6)	170
N41—H41*B*···O1*A*^{ii}	0.86	2.27	3.100 (9)	162
N41—H41*A*···O2*A*	0.86	2.19	3.040 (6)	168
N23—H23*A*···O2*A*^{iii}	0.90	1.87	2.761 (5)	172
N23—H23*B*···O3*A*^{iv}	0.90	2.17	2.846 (4)	132
N23—H23*B*···O2*B*	0.90	2.19	2.659 (5)	112
N33—H33*A*···O3*B*	0.90	2.15	2.633 (5)	113
N33—H33*A*···O2*A*	0.90	2.32	3.035 (4)	136
N33—H33*B*···O3*A*^{v}	0.90	1.85	2.746 (4)	172
O1*W*—H1*W*···O2*B*^{iii}	0.80 (4)	1.97 (4)	2.762 (6)	173 (6)
O1*W*—H2*W*···O3*B*	0.84 (5)	1.92 (6)	2.740 (6)	164 (14)

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

The H atoms of the water molecule were located in a difference Fourier map and refined isotropically. All other H atoms were positioned geometrically and refined using a riding model, with C—H = 0.93 (aromatic), 0.97 (CH_2) or 0.98 Å (CH), O—H = 0.82 Å and N—H = 0.86 (NH_2 in PABA) or 0.90 Å (NH_2 in proline), and with U_{iso}(H) = 1.2U_{eq}(parent) for CH, CH_2, NH_2 and aromatic CH groups, or 1.5U_{eq}(OH). In one of the proline residues, the C^{γ} atom (C25) is disordered over two positions with site occupancies of 0.65 and 0.35. In addition to the 1794 unique reflections, 203 Friedel pairs were measured. However, owing to the absence of atoms with significant anomalous dispersion effects, these data were merged.

Data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD-4 EXPRESS*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXTL/PC* (Bruker, 2000); program(s) used to refine structure: *SHELXTL/PC*; molecular graphics: *ORTEP-3* (Farrugia, 1997), *Mercury* (Version 1.4.1; Macrae *et al.*, 2006) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXTL/PC*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA3080). Services for accessing these data are described at the back of the journal.

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