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Note

Crystal structure of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-L-proline—an Amadori compound

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Abstract—Here we report the crystal structure data on *N*-(1-deoxy-β-D-fructopyranos-1-yl)-L-proline (Fru-Pro)—an Amadori compound. X-ray crystal and molecular structures of its two isomorphous crystalline forms, (Fru-Pro)·MeOH, $C_{11}H_{19}NO_7{\cdot}CH_4O$ (**1a**) and (Fru-Pro)·$2H_2O$, $C_{11}H_{19}NO_7{\cdot}2H_2O$ (**1b**) were determined. In **1a** and **1b** the compound crystallizes as the β-anomer with the overall geometry of Fru-Pro zwitterions being very similar. Fructose ring adopts the chair $^2C_5$ conformation with the proline moiety bonded to equatorial C-1 atom and remaining in a *trans–gauche* (*tg*) orientation with respect to the sugar ring. The five-membered pyrrolidine ring adopts an envelope conformation, with the Cβ atom puckered. Fructosyl and carboxylate groups are in bisectional and axial positions of pyrrolidine ring, respectively. The overall molecular geometry of Fru-Pro zwitterions, especially the relative orientation of sugar and amino acid moieties, is stabilized by intramolecular, three-centred N–H···O_{Fru}/O_{Pro} hydrogen bonds (with bifurcated acceptor) formed between aminium and hydroxyl/carboxylate groups. The packing diagrams are very similar in both **1a** and **1b** with the adjacent zwitterions linked to each other by the extensive network of O–H···O and C–H···O hydrogen bonds to form channels along the *a*-axis, filled up with solvent molecules.

Keywords: Amadori compound; Fructosyl-proline; Fru-Pro; X-ray crystal structure

Amadori compounds are N-substituted (1-deoxy-ketos-1-yl)-amines representing an important class of relatively stable Maillard intermediates.[1] They are formed in the early stage of the Maillard reaction, called non-enzymatic browning,[2,3] by condensation of an amino acid with an aldose followed by Amadori rearrangement of the corresponding *N*-glycosylamine derivative.[4] The Amadori compounds play a significant role in the initial phase of the Maillard reaction—they can decompose and initiate a cascade of further reactions that finally result in formation of very complex mixtures.[5,6] These reactions take place during food processing and storage, as well as under physiological conditions, and may be involved in the pathology of diabetes and ageing. The Amadori compounds have been identified in naturally occurring materials such as fruit and vegetables.[7,8] They are also responsible for flavour and colour formation in processed foods. Additionally the Amadori compounds are present in peat extract (Tołpa® Peat Preparation)[9,10] and are responsible for its immunomodulatory effects. In this study the X-ray crystal and molecular structures of the *N*-(1-deoxy-β-D-fructopyranos-1-yl)-L-proline (Fru-Pro) were determined for its two crystalline forms: methanol monosolvate, (Fru-Pro)·MeOH, $C_{11}H_{19}NO_7{\cdot}CH_4O$ (**1a**) and dihydrate, (Fru-Pro)·$2H_2O$, $C_{11}H_{19}NO_7{\cdot}2H_2O$ (**1b**).

1-Deoxy-1-substituted fructose derivatives, especially sugar–amino acid compounds, have been poorly explored as regards their solid-state structures. The only X-ray data deposited so far with the Cambridge Structural Database[11] are five crystal structures: one of phosphate ester and four of N-substituted derivatives, viz.

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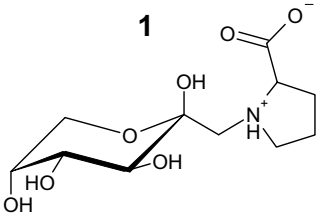
disodium β-D-fructopyranose 1-phosphate pentahydrate, $Na_2(Fru\text{-}OPO_3)\cdot 5H_2O$[12] [CSD refcode TARBIX], *N*-benzyl-*N*-methyl-(1-deoxy-β-D-fructopyranos-1-yl)-amine, Fru-N(Me)CH_2Ph[13] [CSD refcode BMAAHP10], *N*-(1-deoxy-β-D-fructopyranos-1-yl)-*p*-toluidine, Fru-NH(*p*Tol)[14] [CSD refcode ZIVTON], *N*,*N*-dibenzyl-(1-deoxy-β-D-fructopyranos-1-yl)-amine, Fru-$N(CH_2Ph)_2$[15] [CSD refcode UDEVUU] and *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine, Fru-Gly[16] [CSD refcode YUXCUP]. Only the latter of these crystal structures is a sugar–amino acid compound. Very recently, another Amadori compound has been reported (Fru-L-His·H_2O).[17] Therefore we present the results of our single-crystal X-ray study of the title compound, Fru-Pro, in two crystalline forms: methanol monosolvate (**1a**) and dihydrate (**1b**), together with a comparison of the results with those previously reported for Fru-Gly, Fru-His and other Fru derivatives as well as fructose itself. The analysis of intermolecular interactions in the crystal network of **1a** and **1b** is also presented.

Molecular geometry of Fru-Pro zwitterions in **1a** *and* **1b** *crystals*

N-(1-Deoxy-β-D-fructopyranos-1-yl)-L-proline (Fru-Pro, **1**)



was formed in the Amadori rearrangement of D-glucose and L-proline. The compound was obtained in two crystalline forms, as methanol monosolvate, (Fru-Pro)·MeOH, $C_{11}H_{19}NO_7\cdot CH_4O$ (**1a**) and dihydrate, (Fru-Pro)·$2H_2O$, $C_{11}H_{19}NO_7\cdot 2H_2O$ (**1b**). In both crystals the compound is shown to crystallize as the β-anomer, which is the only anomeric form so far observed in all the crystal structures of fructopyranose and its simple complexes, with the coordinates deposited with the CSD.[11] In **1a** and **1b** crystal forms, Fru-Pro is present as a zwitterion (analogous to that observed in Fru-Gly and Fru-His·H_2O crystals) with the carboxylic group deprotonated and the pyrrolidine ring N atom protonated. Structures **1a** and **1b** crystallize in the same space groups and are isomorphous. Both methanol in **1a** and water molecules in **1b** are disordered into two positions (see Section 1). The molecular geometry of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-L-proline zwitterion is very similar in both **1a** and **1b** (Fig. 1). The pyranosyl carbohydrate moiety adopts the chair $^2C_5$ conformation with Cremer and Pople[18] puckering parameters for **1a** and **1b** given in Table 1. It should be noted that the chair $^2C_5$ is the only conformation observed in the known

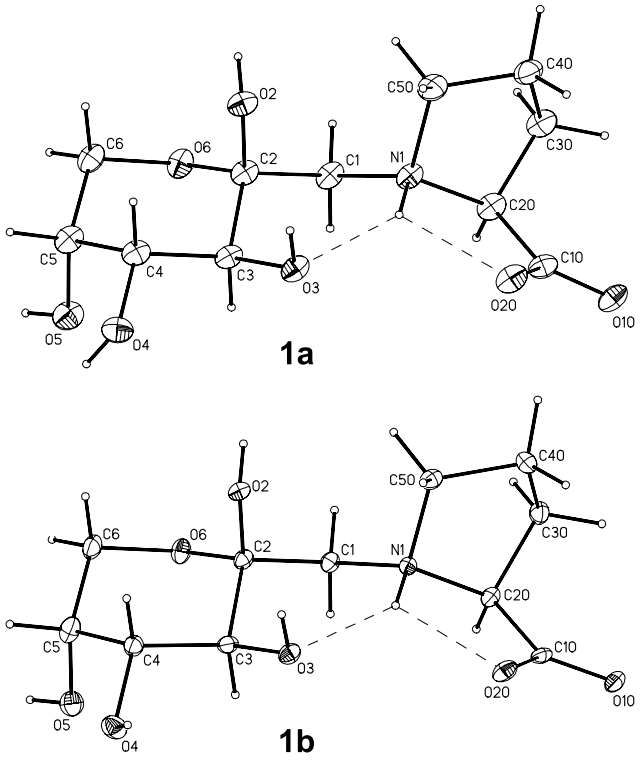


Figure 1. The molecular structures of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-L-proline zwitterions in **1a** and **1b** showing the atom numbering scheme and the intramolecular bifurcated N1–H1···O3 and N1–H1···O20 hydrogen bonds forming *S*(6) and *S*(5) motifs, respectively (dashed line). Displacement ellipsoids are shown at the 30% probability level.

Table 1. Cremer and Pople[18] puckering parameters for fructopyranose ring and pseudorotation parameters[19] *P* and τ_m for proline (reference bond N1–C20) in **1a** and **1b**

	1a	**1b**	
Fructose ring			
Q (Å)	0.579(4)	0.567(4)	$^2C_5$
Θ (°)	178.8(4)	178.9(4)	
Φ (°)	294(12)	171(14)	
Proline ring			
P (°)	237.6(3)	233.5(3)	*E* (Cβ puckered)
τ_m (°)	43.5(3)	44.9(2)	

solid-state structures of fructopyranose and its complexes.[1111]

The exocyclic, anomeric C2–O2 distances in both **1a** and **1b** are significantly shorter (see the relevant values in Table 2), which was previously observed for β-D-fructose itself and β-D-fructose moieties in its derivatives: hydrated calcium chloride, calcium bromide and strontium chloride complexes and 1-substituted β-D-fructopyranose derivatives such as $Na_2(Fru\text{-}OPO_3)\cdot 5H_2O$[12] [CSD refcode TARBIX], Fru-N(Me)CH_2Ph[13] [CSD refcode BMAAHP10], Fru-$N(CH_2Ph)_2$[15] [CSD refcode UDEVUU] and Fru-Gly[16] [CSD refcode YUXCUP]. In both **1a** and **1b**, the anomeric shortening is accompanied by a slight shortening of the adjacent ring C2–O6