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Crystal structure of an Amadori compound, *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine ("D-fructose-glycine") ☆

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Abstract

The first crystal structure data on an Amadori compound, *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine, are reported. The space group is $P2_1$ with $Z=2$ and cell parameters $a=7.246(1)$, $b=10.009(1)$, $c=7.060(1)$ Å, and $\beta=101.085(6)°$. The structure was solved by direct methods and refined to a final R of 2.9% and R_W of 3.8% for 1385 reflections to give esd's of 0.002 Å in bond lengths and 0.2° in angles. The conformation of the carbohydrate is the normal $^2C_5$ pyranose chair. Bond lengths and valence angles compare well with average values from a number of pyranose structures. The molecule of the Amadori compound exists in the zwitterion form and has the C-6–O-6–C-2–C-1–N–C-2′–C-1′–O-1′ chain in a zig-zag conformation, that is (together with O-2′) substantionally planar. All hydroxyl, carboxyl, and ring oxygen atoms, and the secondary ammonuim group are involved in hydrogen bonding, which forms a three-dimensional network of two infinite chains that have an ammonium group as a common segment. The shortest intra- and inter-molecular hydrogen bonds involve donors of the pyranosyl moiety and acceptors of the amino acid portion, and vice versa.

Keywords: Crystal structure of an Amadori compound; Amadori compound; *N*-(1-Deoxy-β-D-fructopyranos-1-yl)-glycine; Fructose-glycine, D-

1. Introduction

Amadori compounds (1-amino-1-deoxy-2-ketoses) arise during the initial stages of the Maillard reaction as the result of reactions between aldose sugars and amino groups (for

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example, amino acids or proteins) [1]. The initial condensation leads to the formation of Schiff bases, or glycosylamines, which are unstable and, in the presence of hydrogen ions, undergo either hydrolysis or irreversible rearrangement to give Amadori compounds. Amadori compounds have been isolated from numerous baked, dried, and stored [2] foodstuffs where they play a role as key precursors of substances responsible for food aroma, taste, and color compounds [3]. More recently the initial stages of the Maillard reaction have been shown to be an important in vivo reaction, possibly participating in undesired protein cross-linking in diabetes and aging [4], and in the modification of cancer cell aggregation, adhesion, and metastasis [5]. Amadori compounds derived from amino acids show considerable biological activity as cell growth stimulants [6], analgesics [7], and precursors of mutagenic compounds [8].

The solution properties of some Amadori compounds derived from the reaction of D-glucose and amino acids have been examined by ^{1}H and ^{13}C NMR spectroscopy [9,10]. For these compounds, all four ring forms (α- and β-pyranose and -furanose) are present. At room temperature ca. 60–70% of the population consists of the β-pyranose form and ca. 5% of the α-pyranose form, with the remainder of the population being a mixture of furanose forms. In aqueous solution, only a small amount (up to 2%) can be detected as the open chain form [9]. Infrared studies of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine [11] in the solid, amorphous state shows a predominance of a pyranose form together with lesser amounts of the furanose isomers. The IR spectrum is very similar to that of amorphous D-fructose itself, which also exists largely in the β-pyranose form.

More than three decades ago, Anet [12] assumed that crystalline D-fructose-glycine exists in the β-pyranose configuration. This modification was used as a model for studies on the thermal degradation of Amadori compounds [13]. Surprisingly, and in spite of the numerous studies involving this compound, no crystallographic data have been obtained for it. Mester et al. [14] claim to have investigated Amadori compounds derived from serotonin by X-ray analysis, but the data appear not to have been reported. In this paper, we present the first X-ray analysis data on a crystalline Amadori compound, *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine. Calculated bond distances, valence angles, and torsion angles are compared with corresponding values for β-D-fructopyranose, which is structurally similar to the sugar portion of the Amadori compound, and to *N*-methylglycine (sarcosine) which is a structural analogue for the amino acid part of the molecule.

2. Experimental

N-(1-Deoxy-D-fructopyranos-1-yl)-glycine [15] was crystallized from a 1:3 water–MeOH solution over a period of 4 days at room temperature. The crystals were obtained as colorless prisms.

Crystal data and experimental details of the crystallographic studies are given in Table 1. The crystal structure was solved with the direct methods program SHELX86 [16] and refined by full-matrix least squares techniques with the NRCVAX [17] suite of programs. Data were corrected for Lorentz and polarization effects, but not for absorption. Nonhydrogen atoms were refined with anisotropic thermal parameters. Hydroxyl and secondary ammonium hydrogen atoms were located in difference Fourier maps and were refined with

Table 1
Crystal data, structure determination, and refinement data for *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine

Formula	$C_8H_{18}NO_7$
M_W (amu)	237.21
Space group	$P2_1$
a (Å)	7.2456(11)
b (Å)	10.0092(14)
c (Å)	7.0595(11)
β (°)	101.085(6)
U (Å^3)	502.42(13)
Z	2
D_c (g cm^{-3})	1.57
μ (cm^{-1})	1.3
$F(000)$	258
Radiation Mo$K\alpha$, graphite monochromator	$\lambda = 0.71073$Å
Diffractometer	Enraf–Nonius CAD4
Orienting reflections, range	25, $11 < \theta < 15°$
Temperature (°C)	22 ± 1
Scan method	$\omega - 2\theta$
Data collection range	$2.0 < 2\theta < 46°$
No. of unique data	1385
No. of observed data ($I > 2.0\sigma(I)$), N	1314
No. of parameters, P	162
R [a]	2.9%
R_w [b]	3.8%
S, goodness of fit [c]	1.33
Maximum shift/error, final	0.038
Largest positive peak (e/Å^3)	0.15
Largest negative hole (e/Å^3)	−0.16

[a] $R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|$. [b] $R_w = \{\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2\}^{1/2}$; $w = 1/[(\sigma F_o)^2 + 0.0005^* F_o^2]$.
[c] $S = [\Sigma w(|F_o| - |F_c|)^2/(N-P)]^{1/2}$.

fixed isotropic thermal parameters. The remaining H-atoms were placed at calculated positions. Atomic scattering factors and anomalous-dispersion corrections are taken from Ref. [18]. Positional and thermal parameters are listed in Table 2.

3. Results and discussion

The resulting ORTEP view of the molecule and numbering of atoms are shown in Fig. 1. A molecule of the Amadori compound may be considered as a hybrid of an amino sugar and an amino acid conjugated via the amino group. The amino sugar is a 1-amino-1-deoxyfructose derivative, and the amino acid is glycine in the zwitterion form with a positively charged tetrahedral secondary ammonium nitrogen and a negatively charged deprotonated carboxyl group. The β-D-pyranose ring form of the crystalline Amadori compound exists in the $^2C_5$ or $1C(D)$ chair conformation, with puckering parameters [19] of $Q = 0.562$ Å, $\theta = 177.73$, and $\phi = 197.49$. The same conformation was reported for the major component of an equilibrium mixture of the tautomeric forms of Amadori compounds

Table 2
Atomic positional parameters[a] for *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine

	x	*y*	*z*	B_{eq} [b]
C-1	1277(4)	4518(3)	6809(4)	2.39(10)
C-2	2350(3)	3475(3)	5866(3)	2.07(9)
O-2	1179(2)	2393(3)	5182(2)	2.36(6)
C-3	4071(3)	2934(3)	7275(3)	2.28(9)
O-3	3495(2)	2270(3)	8846(2)	2.85(8)
C-4	5257(3)	2066(3)	6210(3)	2.44(9)
O-4	6933(3)	1700(3)	7492(3)	3.39(8)
C-5	5719(3)	2814(3)	4485(3)	2.63(10)
O-5	6983(2)	3863(3)	5199(2)	3.16(8)
C-6	3961(3)	3356(3)	3217(3)	2.73(10)
O-6	2931(2)	4175(3)	4349(2)	2.33(7)
N	160(3)	3851(3)	8108(3)	2.28(9)
C-1′	−1154(3)	4125(3)	11075(3)	2.42(10)
C-2′	−717(4)	4796(3)	9292(4)	2.70(10)
O-1′	−2089(3)	4804 [c]	12021(3)	4.33(10)
O-2′	−508(2)	2988(3)	11490(2)	2.90(7)
HO-2	51(4)	256(3)	429(4)	3.2
HO-3	309(4)	146(3)	852(4)	3.8
HO-4	729(5)	112(4)	718(5)	4.1
HO-5	735(5)	411(4)	438(4)	4.1
H-NA	90(4)	331(3)	881(4)	3.2
H-NB	−84(4)	341(3)	739(4)	3.2
H-1A	34	507	570	3.3
H-1B	228	519	765	3.3
H-3	492	379	785	3.1
H-4	446	119	569	3.3
H-5	637	213	363	3.5
H-6A	308	254	263	3.6
H-6B	431	394	205	3.6
H-2′A	24	563	972	3.6
H-2′B	−201	517	844	3.6

[a] All coordinate values are $\times 10^3$ for hydrogen atoms and $\times 10^4$ for nonhydrogens. The esd's refer to the last digit printed. B_{eq} is the mean of the principal axes of the thermal ellipsoids. [b] The *B* values for H atoms were fixed at 1.3 times the value for the atom to which they are attached. [c] The *y* coordinate of O-1′ was not refined in order to fix the origin.

in aqueous solutions, based on ^{1}H NMR measurements [9,10,15]. In related studies, it has been shown that in crystalline forms of hydrated calcium halide complexes of D-fructose and an anhydrous D-fructose, the pyranose rings assume the same conformations [20].

Bond distances.—Bond distances in the sugar moiety of the Amadori compound are similar (in the esd range) to the corresponding values for β-D-fructopyranose (Table 3) and to the average values for a number of crystalline pyranose structures [21]. The mean values of C–C and C–O bond lengths in the β-D-fructopyranosyl portion of the Amadori compound (1.523 and 1.420 Å, respectively) agree well with the corresponding values for β-pyranoses (See Ref. [19] and references therein). Differences were observed with respect to the carboxyl–oxygen bond lengths for the Amadori compound and sarcosine (*N*-methyl

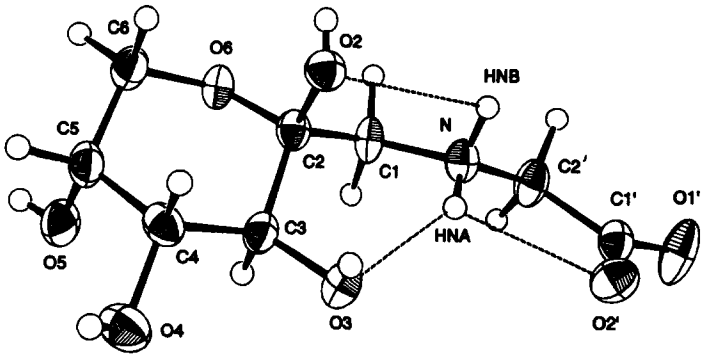

Fig. 1. Atomic numbering and thermal ellipsoids (50% probability) for molecular conformation of crystalline *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine. Intramolecular hydrogen bonds are shown as dotted lines.

glycine). For sarcosine [22], one of the bonds is much longer than the other, while, for the Amadori compound, both were approximately equal (Table 3). The elongation of one of the two carboxyl bonds in sarcosine has been ascribed to participation of O-1′ in strong hydrogen bonding [22].

Valence angles.—Differences in values of valence angles for the Amadori compound and β-D-fructopyranose are larger than 1° for the O–C–C angle type where O = O-2, O-3, and O-5. All these oxygens are involved in strong intermolecular hydrogen bonding, both in the Amadori compound (see below) and in β-D-fructopyranose [20]. All other valence angles in both β-D-fructopyranosyl rings are very close to the average values [21] of 110–110.5° for a tetrahedral structure. There is also a great deal of similarity in the valence angles for sarcosine and the amino acid portion of the Amadori compound (Table 3). Both carboxyl groups show small dissymmetry due to participation of the groups in strong hydrogen bonding (see below).

Torsion angles.—The endocyclic torsion angles of the Amadori compound differ from the corresponding angles for β-D-fructopyranose (Table 4) by not more than 5.3° (mean 2.4°) and range from 52.5 to 60.9°. Again, the pyranose ring of the Amadori compound appears to be closer conformationally to the "standard" pyranosides [21] which show C–C–C–C (ring) torsion angles of 53°, C–C–C–O (ring) of 56–57°, and C–C–O–C of 60–64°.

The Amadori compound shows the exocyclic angles around ring bonds to be close to the corresponding torsion angles of β-D-fructopyranose (Table 4). However, the Amadori compound shows ranges and mean deviations from "ideal" 180° or 60° of values for these torsion angles which are closer to the average value than corresponding values of the β-D-fructopyranose: compare 171.5–178.9° (4.7°) and 169.6–177.1° (6.0°) or 51.5–69.2° (4.3°) and 52.5–69.1° (5.8°), respectively.

An evident difference between the two structures (Amadori compound vis-a-vis β-D-fructopyranose) arises when comparing the corresponding torsion angles around the C-1–C-2 bond (Table 4). The Amadori compound has the *trans–gauche* conformation (distorted by 15° relative to a staggered conformation) in contrast to the *gauche–gauche* relationship around C-1–C-2 found in crystalline anhydrous β-D-fructopyranose [20] or the *gauche–trans* conformation in β-D-fructopyranose–calcium halide complexes. Such a shifted *trans–gauche* (*tg*) conformation is rarely observed in pyranose carbohydrate structures. Probably,

Table 3
Bond distances (Å) and angles (°) of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine and related β-D-fructopyranose and sarcosine

	Amadori [a]	β-D-Fructopyranose [b]	*N*-Methylglycine [c]
Bond distance			
C-1–C-2	1.529(4)	1.520(4)	
C-1–N	1.492(3)		1.484(2)
C-2–O-2	1.403(4)	1.411(4)	
C-2–C-3	1.537(3)	1.540(4)	
C-2–O-6	1.410(3)	1.413(3)	
C-3–O-3	1.423(3)	1.425(4)	
C-3–C-4	1.519(4)	1.518(4)	
C-4–O-4	1.416(3)	1.415(4)	
C-4–C-5	1.520(4)	1.524(4)	
C-5–O-5	1.420(4)	1.423(4)	
C-5–C-6	1.510(4)	1.494(5)	
C-6–O-6	1.448(3)	1.436(4)	
N–C-2′	1.484(4)		1.481(2)
C-1′–C-2′	1.512(4)		1.525(2)
C-1′–O-1′	1.242(3)		1.271(2)
C-1′–O-2′	1.244(4)		1.239(2)
Bond angle			
C-2–C-1–N	110.1(2)		111.4(2)
C-1–C-2–O-2	110.6(2)	110.8(2)	
C-1–C-2–C-3	112.1(2)	112.3(2)	
C-1–C-2–O-6	104.1(2)	104.6(2)	
O-2–C-2–C-3	108.2(2)	106.8(2)	
O-2–C-2–O-6	111.8(2)	111.2(2)	
C-3–C-2–O-6	110.1(2)	111.2(2)	
C-2–C-3–O-3	110.3(2)	111.1(2)	
C-2–C-3–C-4	110.3(2)	111.2(2)	
O-3–C-3–C-4	113.4(3)	108.8(2)	
C-3–C-4–O-4	109.2(2)	110.2(2)	
C-3–C-4–C-5	110.3(3)	109.3(2)	
O-4–C-4–C-5	110.2(2)	109.6(2)	
C-4–C-5–O-5	107.8(2)	110.8(2)	
C-4–C-5–C-6	111.2(2)	111.1(2)	
O-5–C-5–C-6	111.0(3)	107.3(2)	
C-5–C-6–O-6	110.0(2)	111.0(2)	
C-2–O-6–C-6	113.5(2)	114.6(2)	
C-1–N–C-2′	113.8(3)		112.9(2)
C-2′–C-1′–O-1′	115.3(3)		115.2(2)
C-2′–C-1′–O-2′	118.2(2)		118.7(2)
O-1′–C-1′–O-2′	126.4(2)		126.1(2)
N–C-2′–C-1′	111.5(3)		111.4(2)

[a] This work. [b] Ref. [19]. [c] Ref. [21].

for the Amadori compound, the unusual conformation is caused by the amino acid portion of the molecule. It forms a *trans* conformation around the C-1–N bond; *trans* conformations can also be found around N–C-2′ (distorted by 22° relative to the staggered structure) and

Table 4
Torsion angles (°) of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine and related β-D-fructopyranose and sarcosine

	Amadori [a]	β-D-Fructopyranose [b]	*N*-Methylglycine [c]
Endocyclic			
O-6–C-2–C-3–C-4	−56.2(2) [d]	−52.7	
C-2–C-3–C-4–C-5	+52.5(2)	+52.2	
C-3–C-4–C-5–C-6	−52.7(2)	−54.7	
C-4–C-5–C-6–O-6	+55.0(2)	+56.5	
C-5–C-6–O-6–C-2	−60.5(2)	−58.0	
C-3–C-2–O-6–C-6	+60.9(2)	+55.6	
Exocyclic			
N–C-1–C-2–C-3	−75.6(2)	+58.4 [e]	
N–C-1–C-2–O-2	+45.3(2)	+177.7 [e]	
N–C-1–C-2–O-6	+165.5(3)	−62.4 [e]	
C-1–C-2–C-3–C-4	−171.5(3)	−169.6	
C-1–C-2–C-3–O-3	+62.6(2)	+69.1	
O-2–C-2–C-3–C-4	+66.3(2)	+68.8	
O-2–C-2–C-3–O-3	−59.7(2)	−52.5	
O-6–C-2–C-3–O-3	+177.9(3)	−174.0	
C-2–C-3–C-4–O-4	+173.7(3)	+172.7	
O-3–C-3–C-4–C-5	+176.6(3)	+174.9	
O-3–C-3–C-4–O-4	−62.1(2)	−64.7	
C-3–C-4–C-5–O-5	+69.2(2)	+64.5	
O-4–C-4–C-5–C-6	−173.3(3)	−175.5	
O-4–C-4–C-5–O-5	−51.5(2)	−56.3	
O-5–C-5–C-6–O-6	−65.0(2)	−64.8	
C-1–C-2–O-6–C-6	−178.9(3)	+177.1	
O-2–C-2–O-6–C-6	−59.4(2)	−63.3	
C-2–C-1–N–C-2′	+172.0(3)		
Amino acid			
C-1–N–C-2′–C-1′	−157.5(3)		−166.3
O-1′–C-1′–C-2′–N	−171.9(3)		+173.7
O-2′–C-1′–C-2′–N	+10.4(1)		−6.8

[a] This work. [b] Ref. [20]. [c] Ref. [22]. [d] The esd's refer to the last digit printed. [e] In β-D-fructopyranose, O-1 must be taken in place of N.

C-1′–C-2′ (if the dihedral angle is formed with the O-1′ carboxyl atom) bonds as in crystalline sarcosine (Table 4). Thus, the C-6–O-6–C-2–C-1–N–C-2′–C-1′–O-1′ chain of atoms forms a zig-zag conformation and, together with another carboxyl oxygen, O-2′, lie in a plane, i.e., this part of the molecule is nearly planar.

Hydrogen bonding.—Carbohydrates and amino acids can participate in strong intermolecular hydrogen bonding because of the large number of protonated electronegative heteroatoms. Since Amadori compounds are sugar–amino acid conjugates they would be expected to exhibit the same behavior. In fact, Amadori compounds readily form aggregates in solutions, as were detected by fast atom bombardment mass spectrometry (FABMS) [15]. Such aggregates are probably stabilized by multicentered hydrogen bonding between the polar molecules of the Amadori compounds.

In the crystal structure of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine we have found nine pairs of heteroatom contacts (distance <3.20 Å) which form an intra- and inter-

Table 5
Intra- and inter-molecular hydrogen-bonding network of *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine [a]

D–H···A	D···A (Å)	D–H (Å)	H···A (Å)	<(D–H···A) (°)
O-2–HO-2···O-2′ [b]	2.724(3)	0.74(3)	2.02(3)	161(2)
O-3–HO-3···O-1′ [c]	2.695(3)	0.88(3)	1.81(3)	175(2)
O-4–HO-4···O-6 [d]	2.852(3)	0.69(3)	2.22(3)	154(2)
O-5–HO-5···O-1′ [e]	2.637(3)	0.73(3)	1.92(3)	171(2)
N–HNA···O-3	2.852(3)	0.86(3)	2.14(3)	140(2)
N–HNA···O-2′	2.669(3)	0.86(3)	2.34(3)	104(2)
N–HNB···O-2	2.743(3)	0.91(3)	2.54(3)	93(2)
N–HNB···O-5 [f]	2.774(3)	0.91(3)	2.03(3)	137(2)
N–HNB···O-4 [f]	3.147(3)	0.91(3)	2.37(3)	143(2)

[a] The esd's refer to the last digit printed. Symmetry codes: [b] $x,y,-1+z$; [c] $-x,-1/2+y,2-z$; [d] $1-x,-1/2+y,1-z$; [e] $1+x,y,-1+z$; [f] $-1+x,y,z$

molecular hydrogen bonding network (Table 5). All hydroxyl groups act as hydrogen donors and the ammonium nitrogen donates two hydrogen atoms to the network. In accordance with geometric criteria for hydrogen bonds (for D···O and H···O distances less than 3.00 and 2.40 Å, respectively, a contact can be assumed to be a hydrogen bond) we excluded O-2 as a strong acceptor of a hydrogen bond, whereas for crystalline β-D-fructopyranose, this atom appears to be the acceptor of two protons [20,23]. Jeffrey and Lewis [24] have previously noted that anomeric hydroxyl groups are strong hydrogen bond donors, but weak acceptors. Each of two carboxyl oxygen atoms (which are equivalent and carry effective charges of $-1/2$ each) participate in hydrogen bonding, twice as acceptors. The interactions involving ammonium hydrogens, HA and HB, are of the asymmetrical bifurcated [23,25] type. Since the interactions N–HA···O2′ and N–HB···O4 have H···O distances close to the 2.40 Å criterion, these H-bonds should be considered as weak. The short N···O-2 contact distance allows a third interaction that involves the HB atom. However, the HB···O-2 distance is long (2.54 Å) and the angle N–HB···O-2 is far from linearity (93°), so that this is at most a weak interaction. Counting this latter contact as a hydrogen bond leads to an unusual asymmetrical four-center hydrogen bond at HB (Table 5).

IR spectra of crystalline organic molecules, such as carbohydrates, can provide useful information concerning the participation of a definite number of heteroatom-bonded hydrogens in hydrogen bonding. D-Fructopyranose, which is structurally similar to an Amadori compound, affords an IR spectrum [20,26] which, in the region of O–H stretching vibrations (3100–3600 cm^{-1}), has two peaks, one of which is sharp and shifted to a short-wave region (3520 cm^{-1}) relative to a broad absorption at ca. 3400 cm^{-1}. The latter was split into a triplet when the sample was cooled to 100 K [26]. Since vibrational stretching increases linearly with O–H bond shortening, and the width of the corresponding band becomes wider as the proton participates in hydrogen bonding, it was concluded that the sharp peak corresponds to a vibration of the O–H group of the weak hydrogen bonded O-4–H···O-2 sequence in crystalline β-D-fructopyranose. The 3000–3600 cm^{-1} region in the IR spectrum of crystalline *N*-(1-deoxy-β-D-fructosyl)-glycine [2b] also shows a sharp peak at 3500 cm^{-1} and a broad band at 3100 cm^{-1}. This result suggests that at least one of the X–H

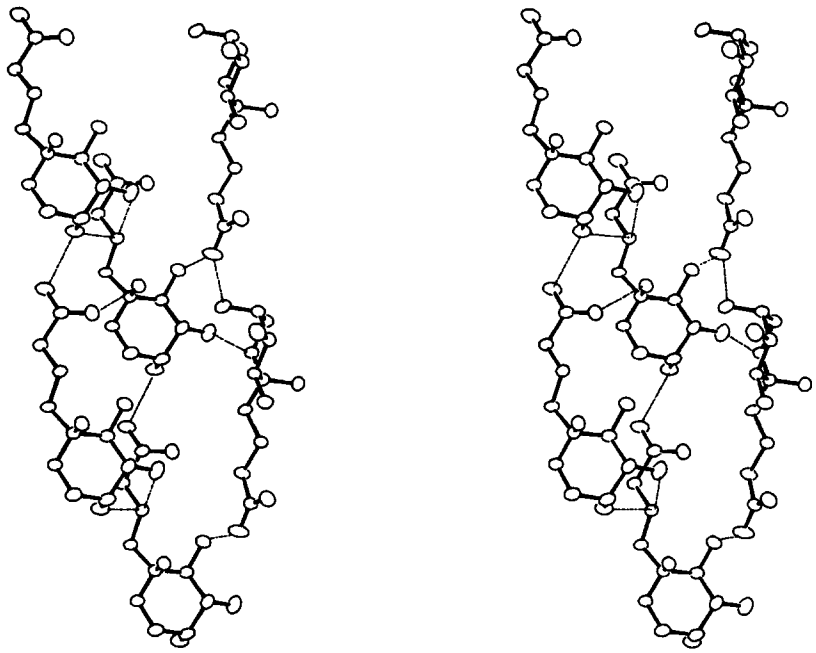

Fig. 2. A stereo view of the intermolecular hydrogen bonding scheme and packing in *N*-(1-deoxy-β-D-fructopyranos-1-yl)-glycine.

groups (X = N or O), most likely O-4–H, interacts weakly with a hydrogen bond acceptor.

Intramolecular hydrogen bonding in the crystalline Amadori compound is represented by the above mentioned bifurcated type for ammonium HA which interacts with the sugar (O-3) and the amino acid (O-2′) oxygen atoms forming two conjugated pseudocycles, one six-membered with sugar atoms and another five-membered with amino acid atoms (Fig. 1). Another ammonium hydrogen, HB, also appears to participate in intramolecular hydrogen bonding with the sugar O-2, but this bond (as mentioned above) is probably weak, and stabilization of the planar (zig-zag) part of the molecule may be due to HA providing intramolecular bonds.

In the hydrogen bonded network of the crystalline Amadori compound (Figs. 1 and 2), the strongest intra- and inter-molecular hydrogen bonds involve donors on the pyranosyl moiety for acceptors on the amino acid portion and vice versa. This arrangement determines the packing of the molecules (Fig. 2), forming infinite head-to-tail strings with molecules linked by O-5–H···O-1′ interactions. These strings are then cross-linked to parallel strings via the N–HB···O-4 and O-2–H···O-2′ intermolecular hydrogen bonds, and to anti-parallel strings via the O-3–H···O1′ and O-4–H···O6 hydrogen bonds.

Taken together, the intra- and inter-molecular hydrogen bonds form a three-dimensional network of two infinite chains that have an ammonium group as a common segment. One of them is an antidromic chain, ···O-2′···HA–N–HB···O-2–H···O-2′···, which lies along the string. All strings are intersected by other antidromic chains, ···O-1′···H–O-3···HA–N–HB···O-5–H···O-1′···. Short lines formed by weak hydrogen bonds at O-4 are attached to the nitrogen intersections of the infinite chains via the four-centered hydrogen bond at HB.

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