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Crystal structure of a hydrated N-glycoprotein linkage region model and its analogue: Hydrogen bonding and π–π stacking driven molecular assembly

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Abstract

X-Ray diffraction analysis of a hydrated N-glycoprotein linkage region model, N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)acetamide (**1**) and its N^1-benzamido analogue **2** reveals very interesting molecular architecture involving seven hydrogen bonds in both compounds and further stabilization of packing in **2** due to π–π stacking. The crystal structure has a two dimensional network of hydrogen bonds formed by infinite chains running along the *b*-axis and homodromic cycles, intersecting at the water oxygens.

1. Introduction

The oligosaccharide (glycan) components of glycoproteins play vital roles in cellular recognition and protein targeting [1]. Protein-linked glycans can also modulate various physiological attributes of proteins including folding of nascent peptide chains [2]. Knowledge of the structure and conformation of the linkage region in glycoproteins is fundamental to a better understanding of both intermolecular and intramolecular carbohydrate–protein interactions. Though crystal structures of several glycoproteins have been reported, the resolution currently achieved is not sufficient to provide the finer details of the atomic architecture and precise conformation of the linkage region. Structural investigation of the model compounds would prove to be very useful in this regard. Moreover, the high-resolution X-ray crystallographic analysis of such small molecules would reveal the details of packing driven by molecular recognition.

As part of our systematic study aimed at determining the three-dimensional structure of the N-glycoprotein linkage region, we determined the crystal structure of N^1-(β-D-glucopyranosyl)acetamide [3]. We now report the crystal structure and molecular assembly of hydrated N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)acetamide (**1**), a model compound, and that of an analog, N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)benzamide (**2**).

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The hydrate of **1** was chosen for the present work, keeping in mind that the solid-state structure so determined would be close to the biologically important solution structure. We believe that it would also enable the examination of hydrogen bonding that plays key role in protein–carbohydrate interactions [4] as well as in molecular recognition occurring before and during crystal nucleation [5]. The hydrated benzamido analogue **2** was included in an effort to identify the possible hydrophobic interactions [4].

2. Experimental

Synthesis.—Compound **1** was prepared according to a literature procedure [6] starting from 2-acetamido-2-deoxy-β-D-glucopyranosylamine [7]. Compound **2** was synthesized by perbenzoylation of the amine using benzoyl chloride and pyridine, followed by O-debenzoylation of the resultant product using sodium methoxide in methanol.

Physical and spectroscopic data for compound **1**.—mp 238–239 °C {Lit. 232–233 °C [6]}; ^{1}H NMR (400 MHz, D_2O): δ 2.03 (s, ^{3}H, CH_3), 2.24 (s, ^{3}H, CH_3), 3.48–3.52 (m, ^{1}H, H-5), 3.51 (t, ^{1}H, H-4), 3.63 (t, ^{1}H, H-3), 3.77 (dd, ^{1}H, $J_{6b,5}$ 4.4, $J_{6a,6b}$ 12.4, H-6b), 3.90 (d, ^{1}H, $J_{6a,6b}$ 12.4, H-6a), 3.82 (t, ^{1}H, H-2), 5.07 (d, ^{1}H, $J_{1,2}$ 9.8 Hz, H-1); ^{13}C NMR: δ 24.7 (CH_3),24.8 (CH_3), 57.1 (C-2), 63.3 (C-6), 72.2, 77.0, 80.3, 81.1 (C-1), 177.6 (CH_3-CO), 177.7 (CH_3-CO).

Physical and spectroscopic data for compound **2**.—mp 192 °C (dec); $[\alpha]_D^{27}$ −9.8° (*c* 1, CH_3OH); ^{1}H NMR (400 MHz, D_2O): δ 2.05 (s, ^{3}H, CH_3), 3.55 (t, ^{1}H, H-4), 3.55–3.65 (m, ^{1}H, H-5), 3.70 (t, ^{1}H, H-3), 3.79 (dd, ^{1}H, $J_{6b,5}$ 4.4, $J_{6a,6b}$ 12.5, H-6b), 3.92 (d, ^{1}H, $J_{6a,6b}$ 12.5, H-6a), 3.99 (t, ^{1}H, *J* 9.8, H-2), 5.27 (d, ^{1}H, $J_{1,2}$ 9.8, H-1), 7.52 (t, 2H, H-4′,H-6′), 7.63 (t, ^{1}H, H-5′), 7.74 (d, 2H, *J*7.8 Hz, H-2′, H-7′); ^{13}C NMR: δ 24.7 (C-2″), 57.3 (C-2), 63.3 (C-6), 72.3, 76.7, 80.5, 82.2 (C-1), 130.1(C-4′, C-6′), 131.6 (C-3′, C-7′), 135.2 (C-2′), 135.6 (C-5′), 174.0 (C-1′), 177.7 (C-1″).

Preparation of single crystals.—Single crystals of the compounds were obtained from their solutions in water by a slow evaporation method. X-ray diffraction data were collected at room temperature in the $\omega - 2\theta$ scan mode on an Enraf–Nonius CAD4 diffractometer. The crystal structures were solved by the direct methods using SHELXS86 [8]. The structures were refined by a full matrix least-squares method using SHELXL93 [9]. Water of crystallization was located from the difference Fourier maps. All the hydrogens were located from the difference Fourier maps during the various stages of refinement.

3. Results and discussion

The details of the crystal data, intensity data collection, and structure refinement for **1** and **2** are given in Tables 1 and 2, respectively. The crystal structure of compound **2** has two molecules (A and B) in the asymmetric unit. The fractional atomic coordinates with equivalent isotropic temperature factors for **1** and **2** are given in Tables 3 and 4, respectively.

The ORTEP diagrams for **1** and molecules A and B for **2** with the numbering schemes are shown in Fig. 1–3, respectively. Selected bond lengths and bond angles for **1** and **2** are listed in Table 5. The dimensions of the glycosidic bond in **1** and molecules A and B of **2** namely, distance C-1–N-1 and angles, O-5–C-1–N-1, C-2–C-1–N-1 and C-1–N-1–C-1′ agree well with each other and also with the values of 1.441(6) Å, 106.8(3), 111.1(4) and 121.4(4)°, respectively reported for the carbohydrate–peptide linkage region in the trihydrate of N^4-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-*N*-asparagine [(GlcNAc-)Asn] [10]. The crystal structure of the anhydrous form of **1** which was solved earlier [11] in the space group $P2_12_12_1$ had some unusual features. The bond lengths of C-2–C-3 and C-1–N-1 were both 0.05 Å shorter and the angle of C-3–C-4–O4 was 5° shorter than those of (GlcNAc-)Asn.

Table 1
Crystal data, structure determination and refinement data for N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)acetamide (**1**)

Crystal data
$C_{10}H_{16}N_2O_6 \cdot H_2O$, mol. wt. 280.28, Monoclinic, $P2_1$, $Z = 2$
Cell dimensions: $a = 4.941(1)$, $b = 7.879(4)$, $c = 17.674(4)$ Å, $\beta = 91.41(1)°$ $V = 687.8(4)$ Å^3, $D_{calc} = 1.353$ g cm^{-3}
Structure determination and refinement data
Crystal description: colourless and flaky, dimensions (mm) 0.22×0.38×0.42 1425 intensities are measured on a CAD4 diffractometer, by $\omega - 2\theta$ scan $\theta < 68°$; 1247 with $I > 2\sigma(I)$
Radiation: *MoKα*($\lambda = 0.7107$ Å), μ(*MoKα*) = 0.115 cm^{-1} 233 parameters; refinement using SHELXL93 weighting factor $w = 1/[\sigma^2F_o^2 + (aP)^2 + bP]$
Reflections to parameter ratio: 6.1 $(shift/e.s.d)_{max} = 0.06$; Largest difference peak and hole: 0.118 and −0.122 (e Å^{-3})
Final agreement indices: $R(F) = 0.025$ $Rw = 0.062$

The ORTEP diagrams of **1** (Fig. 1) and molecules A and B of **2** (Fig. 2 and 3 respectively) and their puckering parameters (Table 6) confirm the $^4C_1$ conformation of the pyranose rings in the solid state. The adoption of same conformation in solution (D_2O) is supported by the anomeric proton coupling constant ($J_{1,2}$) of 9.8 Hz observed for both **1** and **2**. Selected torsion angles are given in Table 6. The conformation at the N-glycosidic linkage turns out to be *trans* as revealed by the torsion angle H-C-1–C-1–N-1–H-N-1 of −162(2), −167(4) and −155(4)° observed for **1** and molecules A and B of **2**, respectively. These values are close to −160.7°, reported for the (GlcNAc-)Asn trihydrate [10]. The preference of the N-glycosidic bond to take up *trans* conformation in solution has been demonstrated for various asparaginyl oligosaccharides [12] based on NMR data. The torsion angles about the C-2–N-2 bond for **1** and **2** (Table 6) also indicate a *trans* conformation. The *Z*-conformation of both the amide groups in **1** and **2** is clearly evident from the dihedral angles about the H–N-1–N-1–C-1′–O-1′ and H-N-2–N-2–C-1″–O-1″ (Table 6).

The orientation of the primary hydroxyl group is *gauche* (*gg*) [13], the torsion angle O-5–C-5–C-6–O-6 being −66.4(2) for **1** and −68.2(4) and −69.3(4)° for molecules A and B for **2**, respectively. These agree well with the value of −59.8° reported for (GlcNAc-)Asn [14]. The observed vicinal coupling constants, namely, $J_{5,6a}$ and $J_{5,6b}$ of < 1 and 4.4 Hz for both **1** and **2**, respectively, also imply the adoption of *gg* conformation in solution. The amide planes formed by N-1, C-1′, O-1′ and C-2′, and N-2, C-1″, O-1″ and C-2″ tend to orient at right angles to each other as well as to the mean plane of the sugar ring (Table 6).

Hydrogen bonding and π–π stacking.—The packing of the molecules in the unit cell of **1** and **2** are shown in Fig. 4 and 5, respectively. The molecular packing is stabilized by a number of N–H···O and O–H···O hydrogen bonds, with water molecules being involved exclusively in the latter. All the hydroxyl groups are involved in hydrogen bonding. The hydrogen bonding pattern of **1** and **2**, are similar with minor differences in the geometry (Tables 7 and 8 for **1** and **2**, respectively).

Neighboring sugar molecules generated through unit translations along the *a*-axis are linked also by

Table 2
Crystal data, structure determination and refinement data for N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)benzamide (**2**)

Crystal data
$C_{15}H_{18}N_2O_6.H_2O$, mol. wt. 342.35, Triclinic, $P1$, $Z = 2$
Cell dimensions: $a = 5.090(1)$, $b = 7.868(2)$, $c = 20.263(3)$ Å
$V = 810.5(3)$ Å^3, $D_{calc} = 1.403$ g cm^{-3}

Structure determination and refinement data
Crystal description: colourless and prismatic, dimensions (mm) 0.37×0.42×0.49 3128 intensities are measured on a CAD4 diffractometer, by $\omega - 2\theta$ scan $\theta < 68°$; 3009 with $I > 2\sigma(I)$
Radiation: $CuK\alpha(\lambda = 1.5418$Å$)$, $\mu(CuK\alpha) = 0.947$ cm^{-1}
560 parameters; refinement using SHELXL93 weighting factor $w = 1/[\sigma^2F_o^2 + (aP)^2 + bP]$
Reflections to parameter ratio: 5.0 $(\text{shift/e.s.d})_{max} = 0.04$;
Largest difference peak and hole: 0.201 and −0.199 (e Å^{-3})
Final agreement indices: $R(F) = 0.033$, $R_w = 0.084$

Table 3
Fractional atomic coordinates (×10^4) with equivalent temperature factors (×10^3 Å^2) for **1**

Atoms	*x*	*y*	*z*	U_{eq}
O-1′[a]	7402(3)	3204(3)	4178(1)	63(1)
O-1″	1900(3)	−883(2)	2949(2)	74(1)
O-3	1737(4)	−101(2)	1250(1)	55(1)
O-4	4599(4)	2610(2)	598(1)	52(1)
O-5	3926(3)	4010(2)	2558(1)	35(1)
O-6	2375(4)	6444(2)	1404(1)	46(1)
N-1	3239(4)	2662(2)	3692(1)	33(1)
N-2	2579(3)	−546(2)	2870(1)	32(1)
C-1	4136(4)	2416(3)	2940(1)	29(1)
C-1′	4954(4)	3114(3)	4259(1)	41(1)
C-2′	3675(7)	3492(6)	4998(2)	62(1)
C-2	2460(4)	1096(2)	2503(1)	30(1)
C-1″	403(4)	−1415(3)	3073(1)	37(1)
C-2″	902(6)	−3078(3)	3453(2)	50(1)
C-3	3455(5)	979(3)	1687(1)	35(1)
C-4	3436(5)	2726(3)	1326(1)	35(1)
C-5	5029(4)	3978(3)	1820(1)	34(1)
C-6	5028(5)	5783(3)	1529(1)	42(1)
O-W	−1870(4)	271(3)	68(1)	51(1)
H-N-1	1722(48)	2680(33)	3773(12)	26(6)
H-N-2	4138(58)	−955(38)	2948(15)	50(8)
H-C-1	5979(43)	2076(29)	2968(11)	26(5)
H-1–C-2′	4809(85)	3909(62)	5350(25)	101(14)
H-2–C-2′	1904(86)	3859(58)	4985(21)	90(11)
H-3–C-2′	3410(118)	2452(106)	5260(36)	165(23)
H-C-2	658(51)	1408(36)	2489(13)	44(6)
H-1–C-2″	2793(77)	−3509(51)	3411(20)	85(11)
H-2–C-2″	−540(103)	−3859(78)	3372(29)	135(18)
H-3–C-2″	778(78)	−2934(62)	4004(25)	107(14)
H-C-3	5238(50)	507(33)	1714(13)	35(6)
H-C-4	−2863(59)	983(47)	256(17)	56(9)
H-C-5	6863(45)	3616(32)	1857(12)	30(6)
Ha-C-6	5872(51)	6548(36)	1900(15)	44(6)
Hb-C-6	6040(44)	5810(34)	1032(14)	40(6)
H-1–O-W	−557(62)	157(48)	377(18)	68(9)
H-2–O-W	1581(49)	3110(34)	1256(13)	37(6)
H-O-3	1931(64)	−1003(46)	1383(18)	57(9)
H-O-4	4044(64)	3355(56)	284(18)	75(10)
H-O-6	1867(59)	6147(45)	960(18)	57(8)

[a](′) Represents substituents on C-1 while (″) represents substituents on C-2.

Table 4
Fractional atomic coordinates ($\times 10^4$) with equivalent temperature factors ($\times 10^3$ Å^2) for molecules A and B of compound **2**

Atoms	x	y	z	U_{eq}
Molecule A				
O-1′	4091(6)	−992(5)	8577(2)	52(1)
O-1′	14152(6)	−4520(4)	9505(2)	56(1)
O-3	10912(7)	−3547(4)	10906(1)	48(1)
O-4	8179(7)	−895(4)	11536(1)	47(1)
O-5	8246(5)	353(3)	9809(1)	30(1)
O-6	10064(7)	2948(3)	10781(2)	46(1)
N-1	8407(6)	−1125(4)	8810(1)	28(1)
N-2	9766(6)	−4168(4)	9514(1)	27(1)
C-1	7959(7)	−1307(4)	9496(2)	25(1)
C-1′	6385(7)	−929(5)	8388(2)	30(1)
C-2′	7039(8)	−668(5)	7684(2)	30(1)
C-3′	9268(8)	237(5)	7475(2)	36(1)
C-4′	9694(10)	453(6)	6810(2)	47(1)
C-5′	7993(10)	−258(6)	6345(2)	47(1)
C-6′	5802(10)	−1187(6)	6547(2)	49(1)
C-7′	5289(9)	−1351(6)	7213(2)	41(1)
C-2	9858(7)	−2479(4)	9826(2)	26(1)
C-1″	11902(8)	−5067(5)	9376(2)	32(1)
C-2″	11415(10)	−6790(5)	9054(2)	42(1)
C-3	9115(8)	−2560(4)	10559(2)	31(1)
C-4	9131(8)	−777(4)	10875(2)	31(1)
C-5	7416(8)	372(5)	10481(2)	30(1)
C-6	7491(10)	2221(5)	10729(2)	42(1)
O-W-1	720(8)	1951(4)	2073(2)	49(1)
H-N-1	10051(88)	−1021(49)	8634(19)	28(10)
H-N-2	8254(89)	−4640(51)	9424(19)	29(11)
H-C-1	6180(80)	−1658(45)	9567(17)	21(9)
H-C-3′	10500(97)	710(54)	7810(23)	42(12)
H-C-4′	11384(153)	956(84)	6592(34)	96(21)
H-C-5′	8407(92)	−147(55)	5817(21)	42(12)
H-C-6′	4635(128)	−1692(74)	6236(31)	74(17)
H-C-7′	3801(107)	−2058(64)	7373(25)	55(14)
H-C-2	11554(83)	−1984(50)	9803(18)	26(10)
H-1–C-2″	11788(105)	−6769(63)	8551(26)	60(15)
H-2–C-2″	9475(173)	−7299(99)	9027(38)	125(27)
H-3–C-2″	12758(194)	−7591(114)	9148(44)	151(35)
H-C-3	7338(75)	−3126(43)	10595(16)	13(8)
H-C-4	10950(95)	−259(55)	10859(21)	38(11)
H-C-5	5654(100)	−39(59)	10531(21)	44(12)
Ha-C-6	6622(85)	2217(52)	11217(21)	34(10)
Hb-C-6	6487(106)	2943(63)	10441(24)	56(14)
H-O-3	10697(114)	−4545(71)	10771(26)	62(17)
H-O-4	8844(100)	0(63)	11799(24)	50(13)
H-O-6	10598(79)	2667(46)	11204(20)	25(10)
H-1–O-W-1	13083(118)	−3238(68)	11700(26)	59(17)
H-2–O-W-1	5688(155)	−2485(93)	11778(35)	99(24)
Molecule B				
O-1′	10863(5)	4686(4)	5461(1)	43(1)
O-1″	629(5)	864(4)	4481(2)	55(1)
O-3	4217(7)	1565(4)	3077(1)	48(1)
O-4	7064(7)	4263(4)	2489(1)	48(1)
O-5	6782(5)	5728(3)	4221(1)	29(1)
O-6	4996(6)	8091(3)	3229(1)	43(1)
N-1	6553(6)	4316(4)	5211(1)	27(1)
N-2	5044(6)	1191(4)	4472(2)	27(1)
C-1	7042(7)	4119(4)	4518(2)	26(1)
C-1′	8566(7)	4549(5)	5644(2)	27(1)
C-2′	7880(7)	4578(4)	6362(2)	28(1)
C-3′	9631(8)	5398(5)	6803(2)	35(1)
C-4′	9175(9)	5403(6)	7473(2)	42(1)
C-5′	6938(9)	4581(6)	7710(2)	44(1)

(continued)

Table 4—*contd*

Atoms	*x*	*y*	*z*	U_{eq}
C-6′	5214(9)	3740(6)	7280(2)	43(1)
C-7′	5657(8)	3747(5)	6606(2)	36(1)
C-2	5121(7)	2841(4)	4167(2)	28(1)
C-1″	2811(7)	309(5)	4589(2)	32(1)
C-2″	3057(10)	−1434(5)	4854(2)	40(1)
C-3	5961(8)	2680(4)	3447(2)	30(1)
C-4	6016(8)	4407(4)	3134(2)	30(1)
C-5	7674(8)	5700(5)	3551(2)	31(1)
C-6	7595(9)	7500(5)	3308(2)	39(1)
O-W-2	4377(8)	6860(4)	1946(2)	48(1)
H-N-1	5075(89)	4277(48)	5345(19)	24(10)
H-N-2	6518(99)	665(59)	4519(22)	40(12)
H-C-1	8812(81)	3696(48)	4426(18)	27(10)
H-C-3′	11179(108)	5822(60)	6629(23)	46(13)
H-C-4′	10414(125)	5853(73)	7813(29)	75(18)
H-C-5′	6786(93)	4627(55)	8192(23)	43(12)
H-C-6′	3716(89)	3146(53)	7402(20)	31(11)
H-C-7′	4555(100)	3168(58)	6294(23)	45(13)
H-C-2	3337(73)	3243(43)	4202(16)	15(8)
H-C-2″	1857(115)	−1529(67)	5284(27)	69(16)
H-C-2″	4766(154)	−1836(90)	4998(34)	105(24)
H-C-2″	2787(108)	−2199(66)	4513(26)	57(15)
H-C-3	7640(81)	2210(46)	3438(18)	21(9)
H-C-4	4269(87)	4762(49)	3112(18)	22(9)
H-C-5	9524(88)	5444(53)	3557(19)	33(10)
Ha-C-6	8619(97)	8262(56)	3625(23)	45(12)
Hb-C-6	8551(92)	7453(56)	2844(22)	43(12)
H-O-3	4475(105)	620(65)	3180(23)	48(14)
H-O-4	6378(102)	4903(65)	2212(24)	52(14)
H-O-6	4452(94)	7826(56)	2816(23)	43(12)
H-1-O-W-2	1880(98)	1882(55)	2359(23)	40(13)
H-2-O-W-2	−232(141)	2612(83)	2228(31)	80(22)

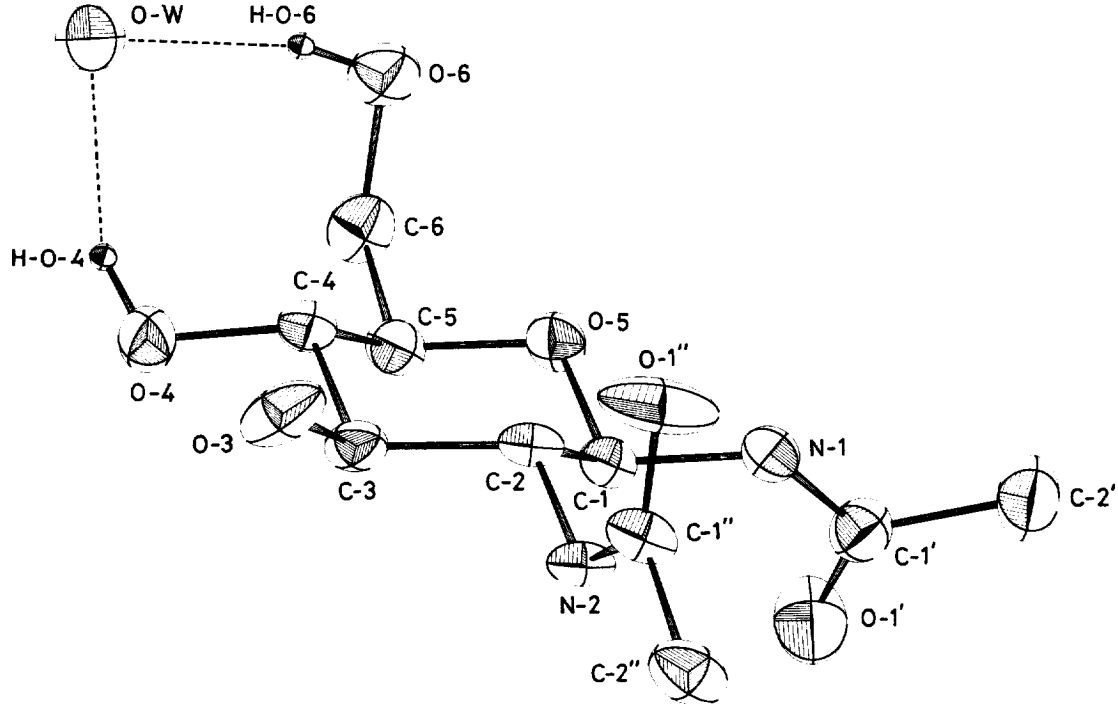

Fig. 1. ORTEP of N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)acetamide (**1**) with atomic notations and thermal ellipsoids drawn at 50% probability level.

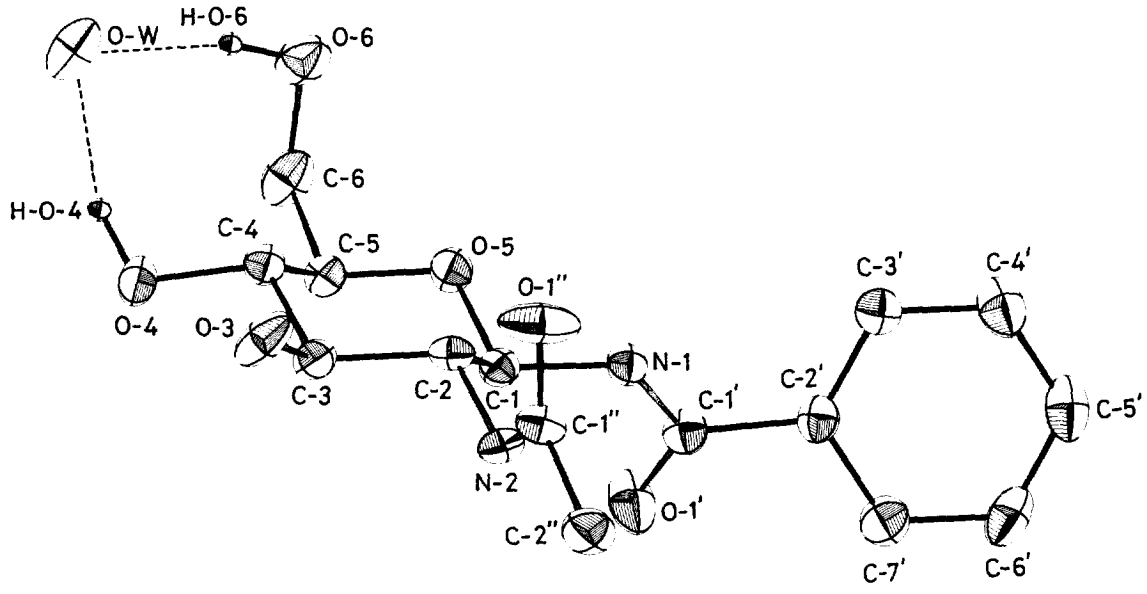

Fig. 2. ORTEP of N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)benzamide (**2**) (molecule A) with atomic notations and thermal ellipsoids drawn at 50% probability level.

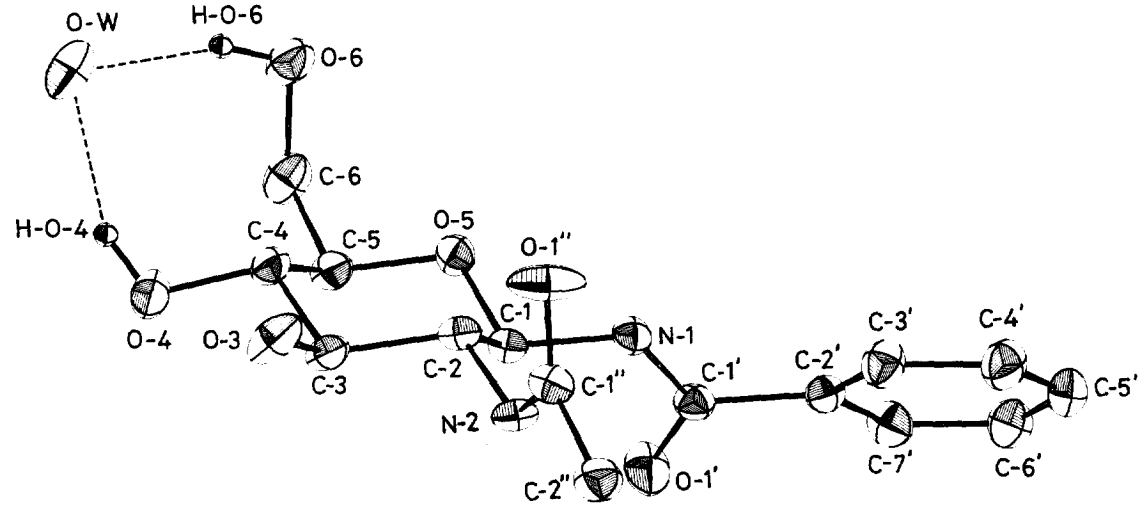

Fig. 3. ORTEP N^1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)benzamide (**2**) (molecule B) with atomic notations and thermal ellipsoids drawn at 50% probability level.

two N–H···O=C hydrogen bonds. On the other hand, such neighbors along the *b*-axis are connected through O-3–H-O-3···O-6 hydrogen bonds. Van der Waals contacts stabilize the molecules along the *c*-axis. The water molecule, acting as a donor, forms an O-W···H-O bond with the oxygens O-4 and O-6 of one of its neighbors. This facilitates the formation of a loop consisting of water oxygen, H-O-4, O-4, C-4, C-5, C-6, O-6 and H-O-6 (Fig. 1–3). Acting as a bridge, the water molecule also donates one hydrogen each to two sugar molecules that are translation equivalents along the *a*-axis.

The packing is marked by an infinite chain of hydrogen bonds, O-W(1 555)···O-3(1 555)···O-6(1 545)···O-W(2,545)···O-3(2 545)···O-6(2 535)···O-W(1 545) which propagates along the screw axis (crystallographic *b*-direction) in the form of a helix as shown in Fig. 6. In the other two coordinations, the water molecule is bonded to O-4, in one of which it is an acceptor while in the other it is a donor. This forms a four-linked homodromic cycle [15] (O-W···O-4···O-W···O-4) as shown in Fig. 7. Thus the parallel infinite chain(s) traversing the *b*-axis are connected by cyclic hydrogen bonds with the water oxygens as the nodes.

Table 5
Selected bond lengths and bond angles for the two compounds

Atoms	1	Anhydrous form of 1 [11][a]	2	
			Molecule A	Molecule B
Bond lengths (Å)				
C-1–N-1	1.425(3)	1.39	1.421(4)	1.430(4)
C-2–N-2	1.448(3)	1.44	1.451(4)	1.454(4)
C-1–C-2	1.527(3)	1.55	1.528(4)	1.535(5)
C-2–C-3	1.538(3)	1.47	1.537(5)	1.524(5)
C-3–C-4	1.517(3)	1.53	1.523(5)	1.517(4)
C-4–C-5	1.524(3)	1.54	1.523(5)	1.515(5)
C-5–O-5	1.426(3)	1.40	1.424(4)	1.431(4)
N-1–C-1′	1.344(3)	1.36	1.354(4)	1.352(4)
C-1′–O-1′	1.223(3)	1.23	1.229(4)	1.228(4)
C-1′–C-2′	1.496(3)	1.50	1.485(5)	1.496(5)
N-2–C-1″	1.331(3)	1.35	1.344(4)	1.335(5)
C-1″–O-1″	1.228(3)	1.22	1.234(4)	1.231(4)
C-1″–C-2″	1.490(3)	1.53	1.498(5)	1.498(4)
C-3–O-3	1.418(3)	1.46	1.420(4)	1.421(4)
C-4–O-4	1.424(3)	1.40	1.428(4)	1.414(4)
C-5–C-6	1.513(3)	1.51	1.523(5)	1.531(5)
C-6–O-6	1.423(3)	1.41	1.413(5)	1.429(3)
Bond angles (deg)				
C-1–C-2–C-3	109.4(2)	109.8	107.9(3)	107.6(3)
C-2–C-3–C-4	110.0(2)	111.9	110.3(3)	110.4(3)
C-3–C-4–C-5	110.4(2)	108.0	110.5(3)	110.5(3)
C-4–C-5–O-5	109.4(2)	110.8	109.6(3)	110.2(3)
C-5–O-5–C-1	113.1(2)	113.2	112.6(2)	111.9(2)
O-5–C-1–C-2	109.2(2)	108.2	108.3(2)	107.7(2)
O-5–C-1–N-1	107.5(2)	109.0	107.7(3)	108.8(2)
C-2–C-1–N-1	112.7(2)	113.6	114.0(3)	113.2(3)
C-1–N-1–C-1′	121.8(2)	123.6	121.0(3)	120.7(3)
N-1–C-1′–O-1′	122.4(2)	120.9	121.5(3)	122.0(3)
N-1–C-1′–C-2′	115.6(2)	117.1	117.4(3)	116.9(3)
C-1–C-2–N-2	111.5(2)	109.8	111.5(3)	112.3(3)
C-3–C-2–N-2	110.8(2)	112.6	110.8(3)	110.9(3)
C-2–N-2–C-1″	123.8(2)	123.5	124.0(3)	123.1(3)
N-2–C-1″–O-1″	121.8(2)	122.9	122.5(3)	122.7(3)
N-2–C-1″–C-2″	116.6(2)	114.5	116.3(3)	116.9(3)
C-4–C-5–C-6	114.7(2)	112.8	114.1(3)	113.6(3)
O-5–C-5–C-6	107.3(2)	107.8	107.4(3)	107.6(3)
C-5–C-6–O-6	112.9(2)	111.8	113.3(3)	113.8(3)
C-3–C-4–O-4	108.9(2)	112.8	108.4(3)	109.5(3)
C-2′–C-1′–N-1	115.6(2)	117.1	117.4(3)	116.9(3)
C-2–N-2–C-1″	123.8(2)	123.5	124.0(3)	123.1(3)

[a] The esds for bond lengths and bond angles are less than 0.016 and 1.0, respectively.

The two independent sugar molecules in compound **2** in the asymmetric unit show a remarkable difference in the phenyl ring orientation as seen from the N-1–C-1′–C-2′–C-3′/C-7′ torsion angles (Table 6). The close π–π stacking of the two phenyl rings, which are coplanar within ~5° and closest separation = 3.328 Å [between C-2′ (molecule A) and C-4′ (molecule B)], is an interesting feature. This distance compares with the value of 3.35 Å observed in graphite indicating the strong π–π interaction between molecules A and B of **2**. Similar π–π stacking was noticed recently in the crystal structure of a dimetallocyclophane [16].

In conclusion, a total of seven hydrogen bonds representing different patterns including the infinite chain and homodromic cycle are observed for the first time for **1**. It is interesting that identical hydrogen-bonding patterns are observed in the crystal structure of the benzamido analogue **2** as well. In addition, π–π stacking stabilizes the packing in **2**. In view of the fact that a general function of glycans is to stabilize the glycoprotein structure [17], these observations warrant a detailed investigation of the larger models of the linkage region.

Table 6
Selected torsion angles, ring puckering parameters and orientation of the amide planes with each other and with the sugar ring

Atoms	1	Anhydrous form of 1 [11]	2	
			Molecule A	Molecule B
Torsion Angle (deg)				
C-1–C-2–C-3–C-4	−54.0(2)	−54.9	−55.8(4)	−57.1(3)
C-2–C-3–C-4–C-5	53.6(2)	52.5	53.1(4)	52.5(3)
C-3–C-4–C-5–O-5	−56.6(2)	−54.3	−54.8(4)	−53.2(4)
C-4–C-5–O-5–C-1	62.7(2)	62.1	62.5(3)	61.8(3)
C-5–O-5–C-1–C-2	−63.5(2)	−62.6	−66.1(3)	−66.9(3)
O-5–C-1–C-2–C-3	57.5(2)	57.8	60.7(3)	63.0(3)
O-5–C-5–C-6–O-6	−66.4(2)	−70.1	−68.2(4)	−69.3(4)
C-4–C-5–C-6–O-6	55.4(3)	52.6	53.5(4)	53.0(4)
N-1–C-1′–C-2′–C-3′	—	—	145.9(3)	−157.1(3)
N-1–C-1′–C-2′–C-7′	—	—	−35.2(5)	26.5(5)
C-2–C-1–N-1–C-1′	149.8(2)	122.2	146.0(3)	143.4(3)
C-1–C-2–N-2–C-1″	124.8(2)	116.6	137.3(3)	135.9(3)
H-C-1–C-1–N-1–H-N-1	−162(2)	—	−167(4)	−155(4)
H-N-1–N-1–C-1′–O-1′	−177(2)	—	−178(3)	−177(3)
H-C-2–C-2–N-2–H-N-2	−176(3)	—	−166(4)	−175(4)
H-N-2–N-2–C-1″–O-1″	−178(3)	—	−178(3)	−173(4)
Cremer-Pople puckering parameters				
$Q=0.583(2)$, $\theta=177.4(2)$, $\phi=141(4)$ for **1**				
$Q=0.596(3)$, $\theta=174.9(3)$, $\phi=177(3)$ for molecule A of **2**				
$Q=0.602(3)$, $\theta=172.9(3)$, $\phi=-174(2)$ for molecule B of **2**				
Dihedral angles between mean plane of the sugar ring and C-1 and C-2 amide planes				
C-1 amide and sugar ring	66.6(1)	—	68.0(2)	64.6(2)
C-2 amide and sugar ring	84.3(2)	—	74.7(2)	79.3(2)
C-1 amide and C-2 amide	78.2(1)	—	74.7(2)	70.0(2)

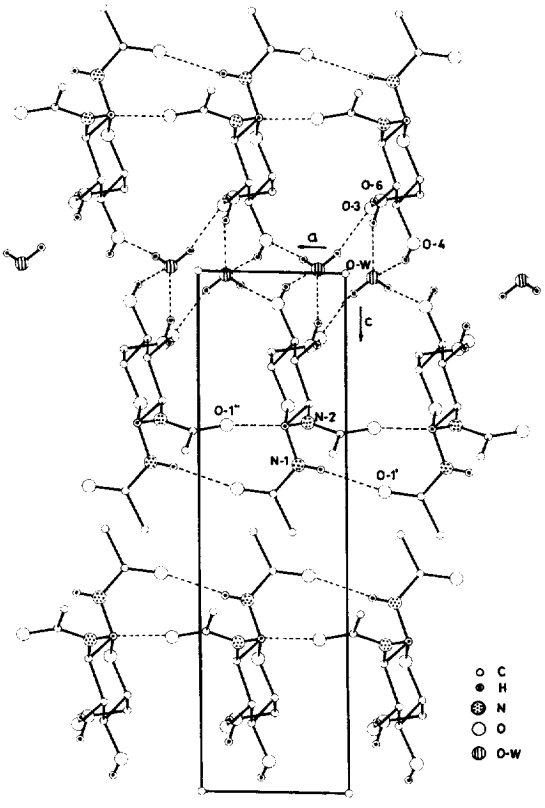

Fig. 4. Packing of molecules in the unit cell down the *b*-axis for **1**, depicting various hydrogen bonds.

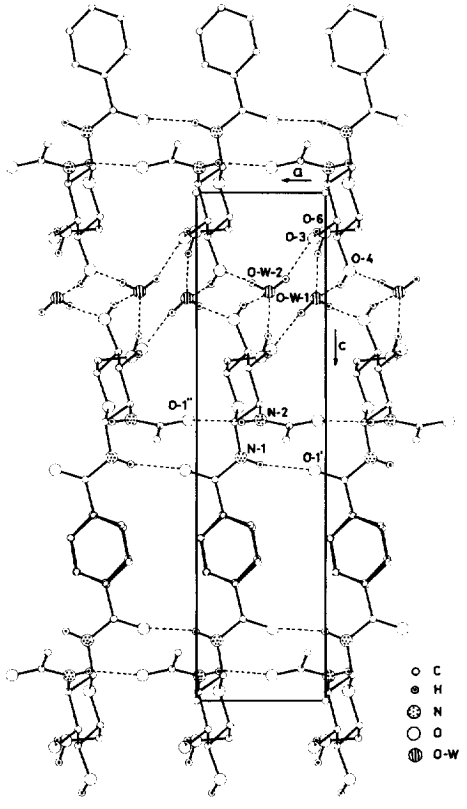

Fig. 5. Packing of molecules in the unit cell down the *b*-axis for **2**, depicting various hydrogen bonds.

Table 7
Hydrogen bonds in compound **1**

Donor D–H	Acceptor A (sym oper)	D–H (Å)	H····A′ (Å)	∠ D–H····A′(°)
O-W–H-1-O-W	O-3 (1 555)	0.843(30)	1.902(30)	166(3)
O-W–H-2-O-W	O-4 (1 655)	0.821(33)	1.903(33)	174(3)
N-1–H-N-1	O-1′ (1 455)	0.767(23)	2.305(23)	168(2)
N-2–H-N-2	O-1″ (1 655)	0.843(29)	1.958(29)	154(3)
O-3–H-O-3	O-6 (1 545)	0.755(36)	2.023(36)	163(4)
O-4–H-O-4	O-W (2 555)	0.849(38)	1.946(39)	156(4)
O-6–H-O-6	O-W (2 555)	0.850(32)	1.944(32)	162(3)

Table 8
Hydrogen bonds in compound **2**[a]

Donor D–H	Acceptor A (sym oper)	D-H (Å)	H····A′ (Å)	∠ D–H····A′(°)
O-W-1–H-1-O-W-1	'O-3 (454)	0.901(45)	1.872(47)	171(4)
O-W-1–H-2-O-W-1	'O-4 (555)	0.826(40)	1.956(52)	162(4)
'N-1–H-N-1	'O-1′ (655)	0.911(43)	2.059(44)	160(4)
'N-2–H-N-2	'O-1″ (455)	0.860(44)	2.100(45)	147(4)
'O-3–H-O-3	'O-6 (545)	0.827(54)	1.988(55)	160(5)
'O-4–H-O-4	O-W-1 (656)	0.925(48)	1.848(49)	161(5)
'O-6–H-O-6	O-W-1 (656)	0.934(41)	1.867(41)	165(4)
O-W-2–H-1-O-W-2	O-3 (555)	0.832(45)	1.909(40)	173(4)
O-W-2–H-2-O-W-2	O-4 (455)	0.782(51)	1.987(48)	171(4)
N-1–H-N-1	O-1′ (455)	0.800(44)	2.191(45)	163(4)
N-2–H-N-2	O-1″ (655)	0.877(50)	2.094(50)	146(5)
O-3–H-O-3	O-6 (545)	0.793(52)	2.022(52)	168(5)
O-4–H-O-4	O-W (555)	0.849(51)	1.967(52)	155(5)
O-6–H-O-6	O-W (555)	0.899(46)	1.897(46)	161(4)

[a] Atoms of molecule A have a preceding'.

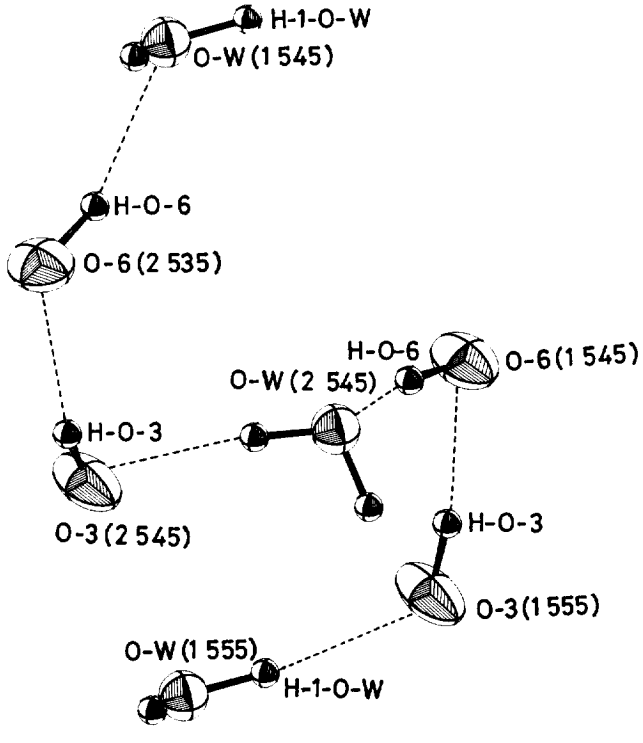

Fig. 6. The symmetry relations in the infinite hydrogen bond chain along the *b* axis for **1**.

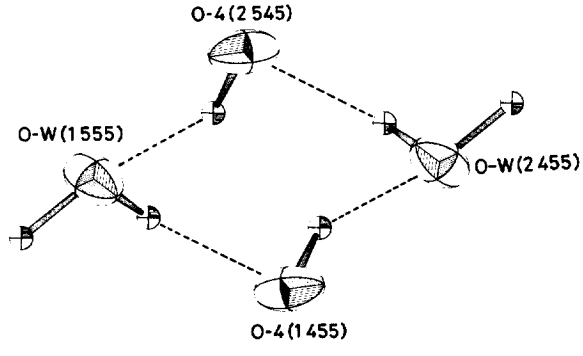

Fig. 7. The geometry of the four-membered homodromic cycle in **1**.

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