Carbohydrate Research, 125 (1984) 185–201
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

X-RAY ANALYSIS OF 3-*O*-(6-*O*-ACETYL-2,4-DIAZIDO-3-*O*-BENZYL-2,4-DIDEOXY-α-D-GLUCOPYRANOSYL)-1,6-ANHYDRO-2,4-DIAZIDO-2,4-DIDEOXY-β-D-GLUCOPYRANOSE, A DISACCHARIDE HAVING AN UNUSUAL α-D-(1→3) LINKAGE

MARIANNA STRUMPEL, HEINZ-JURGEN SCHMIDT, PETER LUGER,
Institut für Kristallographie, Freie Universität Berlin, D-1000 Berlin 33 (Federal Republic of Germany)

AND HANS PAULSEN
Institut für Organische Chemie und Biochemie der Universität Hamburg, D-2000, Hamburg 13 (Federal Republic of Germany)

(Received May 24th, 1983; accepted for publication, July 30th, 1983)

ABSTRACT

The crystal structure of 3-*O*-(6-*O*-acetyl-2,4-diazido-3-*O*-benzyl-2,4-dideoxy-α-D-glucopyranosyl)-1,6-anhydro-2,4-diazido-2,4-dideoxy-β-D-glucopyranose, $C_{21}H_{24}N_{12}O_7$, mol. wt. 556.5, was investigated by X-ray analysis. The disaccharide crystallizes in the triclinic space group P1, with a = 889.3(5), b = 869.6(5), and c = 999.5(6) pm, and α = 105.83(4)°, β = 116.22(4)°, γ = 88.42(4)°, Z = 1, and $\rho = 1.394$ g.cm^{-3}. Phase determination failed with direct methods, but, as the 1,6-anhydride component of the molecule was already known from a previous structure analysis, the vector-search method could be applied in solving the structure. Diffractometer data were refined to an R value of 0.063 (R_w = 0.080) for 2102 observed reflections. The anhydro-bridged system has a distorted $^1C_4$(D) conformation, in agreement with that of other anhydropyranoses so far investigated. A comparison shows that, for the specific kind of distortion, mainly the anti-reflex effect is reponsible, whereas 1,3-diaxial interactions have a minor influence. The non-bridged ring adopts an almost perfect $^4C_1$(D) conformation. The anomeric effect is observed in both of the sugar-ring systems in terms of bond-length shortening. The disaccharide has an α-D-Glc-$^4C_1$-(1*a*→3*e*)-D-Glc-$^1C_4$ glycosidic linkage. No previous X-ray investigation of a compound of this type is known. The pyranoid rings are almost perpendicular to each other. The Φ, ψ angles of the glycosidic linkage are +78.1(5) and −86.0(4)°. The magnitude of the Φ value is in agreement with the predictions of the exo-anomeric effect. The glycosidic Φ and ψ angles were very well reproduced by empirical calculations using the HSEA approach.

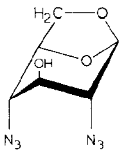
INTRODUCTION

The system of 1,6-anhydropyranoses plays an important role in the field of conformational analysis of carbohydrates. Because of the formation of the five-

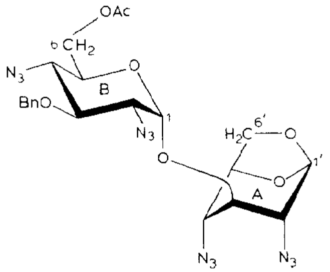
0008-6215/84/$ 03.00

membered, anhydro ring, the pyranoid ring is forced to adopt the ${}^1C_4$(D) conformation[1], producing, in the case of a β-D-*gluco* configuration (**1**), two 1,3-diaxial interactions. Several investigations of such systems have been carried out by X-ray methods[2], n.m.r. spectroscopy[3–5], and molecular-mechanics calculations[6].

We here report the structure of the disaccharide **2**. It contains the 2,4-diazido derivative (**1**) of 1,6-anhydro-β-D-glucopyranose as one monosaccharide component, the other being a substituted 2,4-diazido-α-D-glucopyranosyl group that is nonbridged, and therefore in the ${}^4C_1$(D) form. We thus had, for the first time, the chance to investigate an α-D-(1→3)-glucosidic linkage between a ${}^4C_1$(D) and a ${}^1C_4$(D) form by X-ray analysis. A further point of interest was that we had recently investigated[2] the X-ray structure of monosaccharide **1**, and had found a special arrangement of the azido groups, with close contact-distances to ring-oxygen atoms. A second analysis of this molecular fragment offered the possibility of checking these findings in a different chemical and crystallographic environment.



1



2

Bn = PhCH$_2$

EXPERIMENTAL

A colorless, almost cubic crystal of **2**, ~0.5 mm on edge, was selected for the X-ray investigations.

Precise cell-parameters (from 15 high-order reflections) and 2202 three-dimensional, intensity data of a half sphere ($2\theta_{max}$ = 129°) were measured on a DEC PDP 15 controlled Stoe diffractometer with Ni-filtered, CuKα radiation (λ = 154.178 pm), using the $\omega - 2\theta$ scan-mode. The two reference reflections used for control and scaling of the intensities in the course of the data collection showed no significant variations.

Several attempts to solve the phase problem with "Direct Methods" (MULTAN)[7] failed. We therefore decided to apply the "vector-search method"[8] to this structure.

The rigid anhydro-D-glucopyranose ring-system in **2** was expected to be similar to that in **1**. Therefore, this known, eleven-atom fragment was used in an orientation search.

TABLE I

ATOMIC PARAMETERS FOR **2** (E.S.D. VALUES IN PARENTHESIS)

Atom	*X*	*Y*	*Z*	*UEQ U*
C-1′	−0.2953(9)	−0.0326(9)	−0.3505(7)	8.6(2)
O-5′	−0.2066(6)	−0.0642(6)	−0.4410(4)	8.9(1)
C-5′	−0.0683(8)	−0.1410(7)	−0.3529(6)	8.4(2)
C-6′	−0.155(1)	−0.2545(8)	−0.3093(8)	9.5(2)
O-6′	−0.2952(6)	−0.1718(6)	−0.3030(6)	10.0(2)
C-2′	−0.2007(8)	−0.1101(7)	−0.2051(6)	7.8(2)
N-21′	−0.2096(9)	−0.2506(8)	−0.2618(6)	10.7(2)
N-22′	−0.184(1)	−0.3746(9)	−0.1734(8)	13.5(4)
N-23′	−0.176(2)	−0.502(1)	−0.106(1)	18.1(4)
C-3′	−0.0189(7)	0.0838(6)	−0.1098(6)	6.7(2)
C-4′	0.0590(7)	−0.0146(7)	−0.2127(7)	7.9(2)
N-41′	0.1201(8)	0.1021(8)	−0.2664(8)	11.5(2)
N-42′	0.2459(7)	0.0740(7)	−0.2852(5)	8.5(2)
N-43′	0.3586(9)	0.069(1)	−0.3051(8)	13.3(3)
O-10	0.0000(–)	0.0000(–)	0.0000(–)	6.6(1)
C-1	0.0167(6)	0.0950(6)	0.1453(5)	6.5(1)
O-5	−0.1365(5)	0.1414(4)	0.1422(4)	6.9(1)
C-2	0.0975(6)	0.0017(7)	0.2640(5)	6.9(2)
N-21	0.2673(6)	−0.0412(8)	0.2804(6)	9.1(2)
N-22	0.2707(7)	−0.1443(9)	0.1753(8)	10.2(2)
N-23	0.288(1)	−0.241(1)	0.081(1)	15.4(4)
C-3	−0.0230(7)	−0.1452(7)	0.2254(5)	7.2(2)
O-3	0.0403(5)	−0.2190(5)	0.3496(4)	8.1(1)
C-31	0.115(2)	−0.363(1)	0.326(1)	14.9(5)
C-311	0.1619(9)	−0.4230(7)	0.4654(7)	8.7(2)
C-312	0.052(1)	−0.5257(9)	0.4599(9)	9.8(2)
C-313	0.085(2)	−0.585(1)	0.590(5)	13.8(5)
C-314	0.220(2)	−0.528(1)	0.720(1)	13.5(4)
C-315	0.330(2)	−0.420(1)	0.731(1)	12.7(4)
C-316	0.307(7)	−0.3625(9)	0.602(1)	11.2(3)
C-4	−0.1932(7)	−0.0919(7)	0.2081(6)	7.2(2)
N-41	−0.3220(–)	−0.2315(–)	0.1406(–)	9.8(–)
N-42	−0.3262(–)	−0.3159(–)	0.2119(–)	8.2(–)
N-43	−0.347(1)	−0.393(1)	0.275(1)	17.4(4)
C-5	−0.2581(7)	0.0105(7)	0.0959(6)	7.4(2)
C-6	−0.4194(8)	0.081(1)	0.0824(6)	8.8(2)
O-60	−0.3922(5)	0.1704(6)	0.2378(4)	9.0(1)
C-61	−0.5197(7)	0.2495(8)	0.2447(7)	8.8(2)
O-61	−0.6500(6)	0.2453(9)	0.1307(6)	11.7(2)
C-62	−0.484(1)	0.337(1)	0.4057(9)	10.5(3)

A location search is superfluous in space group P1, and the origin was arbitrarily fixed at O-10. The correctly oriented, eleven-atom fragment was not sufficient to phase the structure. Additional atom-positions had to be determined, and a multiple superposition search[9] was carried out in a limited region around the origin, locating nine chemically sensible atoms as an extension of the search group. This twenty-atom fragment was sufficient to determine 20 further non-hydrogen atoms from subsequent difference-syntheses.

Full matrix, least-squares refinement[10] with isotropic thermal parameters, whereby the usual agreement factor $R = \Sigma||F_o| - k|F_c||/\Sigma|F_o|$ was minimized, led to an R value of 0.125. Further refinement with anisotropic thermal parameters brought the agreement to 0.079. At this point, 19 hydrogen atoms were located from a difference-Fourier map, while the positions of further five hydrogen atoms were calculated.

An empirical weighting scheme was introduced that allowed the quantity $w\Delta F$ to be independent both of F_o and of $\sin\theta$. This was achieved by setting $w = xy$ with $x = 1$ for $\sin\theta > 0.55$, $x = \sin\theta/0.55$ otherwise, and $y = 1$ for $F_o < 2.0$, $y = 2.0/F_o$ if $F_o > 2.0$. Unobserved reflections (100 with $I < 2\sigma$) were included in the refinement only if $|F_c| > |F_o|$.

Some difficulties were encountered in the refinement of the azido groups at C-2′ and C-4. One of the six thermal parameters, U_{11}, of N-23′ was unusually large, although the position and the rest of the thermal parameters converged normally.

In the azido group attached to C-4, atom N-42 refined to a position where the bond lengths to the neighboring atoms were chemically unreasonable. The electron density around this atom could not be interpreted as two or more disordered positions, and therefore the coordinates of N-42 were held fixed in a chemically reasonable position within the electron density. The final agreement factors were $R = 0.063$ and $R_w = 0.080$ for 2102 observed reflections. Final atomic parameters are given in Table I*.

RESULTS AND DISCUSSION

(a) Molecular geometry. — A model of the molecular structure is shown in Fig. 1, giving the numbering scheme, and the bond lengths in pm. Fig. 2 shows an ORTEP plot of the molecule[11]; bond angles and torsion angles are listed in Tables II and III. The anhydro-bridged part of the disaccharide is designated by "A", and the nonbridged part, by "B". Atoms belonging to A are denoted by single-primed numbers, and those in B, by unprimed numbers.

The anhydro-bridged system A has already been investigated in the monosaccharide 1,6-anhydro-2,4-diazido-2,4-dideoxy-β-D-glucopyranose[2]. Being part of the disaccharide, it adopts the same distorted $^1C_4$(D) conformation as it does in the free molecule. Proof consists in the similar puckering-parameters[12,13] (see Table IV). For comparison, the puckering parameters (average) of several 1,6-anhydropyranoses investigated so far are listed in Table IV. When marked on the conformational hemisphere, ring A falls half way between a perfect $^1C_4$(D) (θ

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*A complete atom list, with the temperature parameters included, and the list of observed and calculated structure-factors can be obtained on request from Elsevier Scientific Publishing Company, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/266/*Carbohydr. Res.*, 125 (1984) 185–201

TABLE II

VALENCE ANGLES OF **2** (E.S.D. VALUES IN PARENTHESES)

(a) Intracyclic angles			
Ring A			
O-5′–C-1′–C-2′	109.6(6)	C-1′–C-2′–C-3′	112.3(5)
C-2′–C-3′–C-4′	112.4(4)	C-3′–C-4′–C-5′	112.2(5)
C-4′–C-5′–O-5′	108.8(5)	C-5′–O-5′–C-1′	101.9(5)
Anhydro ring			
O-5′–C-1′–O-6′	106.0(6)	C-1′–O-6′–C-6′	107.4(7)
O-6′–C-6′–C-5′	102.8(6)	C-6′–C-5′–O-5′	102.1(6)
C-5′–O-5′–C-1′	101.6(5)	O-6′–C-1′–C-2′	108.7(5)
C-5′–C-5′–C-6′	112.8(6)		
Ring B			
O-5–C-1–C-2	109.7(5)	C-1–C-2–C-3	110.5(4)
C-2–C-3–C-4	110.3(5)	C-3–C-4–C-5	110.8(6)
C-4–C-5–O-5	110.8(4)	C-5–O-5–C-1	113.9(4)
(b) Angles of the glycosidic linkage			
C-2′–C-3′–O-10	113.2(5)	C-4′-C-3′–O-10	106.2(4)
C-3′–O-10–C-1	116.1(3)	O-10–C-1–C-2	108.1(4)
O-10–C-1–O-5	113.4(3)		
(c) Angles to the substituents			
C-1′–C-2′–N-21′	106.0(5)	C-3′–C-2′–N-21′	111.2(6)
C-3′–C-4′–N-41′	106.2(5)	C-5′–C-4′–N-41′	109.0(6)
C-1–C-2–N-21	111.2(6)	C-3–C-2–N-21	114.6(5)
C-2–C-3–O-3	110.3(4)	C-4–C-3–O-3	107.2(5)
C-3–C-4–N-41	111.2(4)	C-5–C-4–N-41	105.9(3)
C-4–C-5–C-6	114.5(6)	O-5–C-5–C-6	106.8(5)
(d) Angles of the azido groups			
C-2′–N-21′–N-22′	117.1(7)	N-21′–N-22′–N-23′	170.(1)
C-4′–N-41′–N-42′	116.7(7)	N-41′–N-42′–N-43′	170.4(9)
C-2–N-21–N-22	116.3(4)	N-21–N-22–N-23	174.3(7)
C-4–N-41–N-42	122.6(2)	N-41–N-42–N-43	172.8(6)
(e) Angles of the benzyl group			
C-3–O-3–C-3	117.3(6)	O-3–C-31–C-311	107.9(9)
C-31–C-311–C-312	119.1(7)	C-31–C-311–C-316	122.2(8)
C-316–C-311–C-312	118.6(8)	C-311–C-312–C-313	120.8(7)
C-312–C-313–C-314	121.(1)	C-313–C-314–C-315	120.(1)
C-314–C-315–C-316	122.4(9)	C-315–C-316–C-311	116.9(9)
(f) Angles of the 6-O-acetyl group			
C-5–C-6–O-60	107.6(4)	C-6–O-60–C-61	115.0(4)
O-60–C-61–O-61	122.8(6)	O-60–C-61–C-62	112.0(5)
O-61–C-61–C-62	125.1(7)		

TABLE III

SELECTED TORSION ANGLES OF **2** (E S D VALUES IN PARENTHESES)

(a) Intracyclic angles	
C-1–C-2–C-3–C-4	−52.2(6)
C-2–C-3–C-4–C-5	51.2(5)
C-3–C-4–C-5–O-5	−54.0(6)
C-4–C-5–O-5–C-1	60.6(6)
C-5–O-5–C-1–C-2	−61 2(5)
O-5–C-1–C-2–C-3	56.3(5)
C-1′–C-2′–C-3′–C-4′	33.6(8)
C-2′–C-3′–C-4′–C-5′	−34.9(8)
C-3′–C-4′–C-5′–O-5′	57.1(8)
C-4′–C-5′–O-5′–C-1′	−76.4(7)
C-5′–O-5′–C-1′–C-2′	75.3(6)
O-5′–C-1′–C-2′–C-3′	−55.5(8)
C-1′–O-5′–C-5′–C-6′	43.1(5)
O-5′–C-5′–C-6′–O-6′	−29.1(5)
C-5′–C-6′–O-6′–C-1′	4.2(5)
C-6′–O-6′–C-1′–O-5′	23.0(5)
O-6′–C-1′–O-5′–C-5′	−41.9(5)
(b) Glycosidic angles	
C-3′–O-10–C-1–C-2	−160.1(4) ($\phi^{\mathrm{C\text{-}2}}$)
C-3′–O-10–C-1–O-5	78.1(5) ($\phi^{\mathrm{O\text{-}5}}$)
C-2′–C-3′–O-10–C-1	−86.0(4) ($\psi^{\mathrm{C\text{-}2'}}$)
C-4′–C-3′–O-10–C-1	150.2(3) ($\psi^{\mathrm{C\text{-}4'}}$)
O-10–C-1–O-5–C-5	59.7(6) (θ)
(c) Glycosidic angles including hydrogen	
H-1–C-1–O-10–C-3′	−41.(4) ($\phi^{\mathrm{H\text{-}1}}$)
C-1–O-10–C-3′–H-3′	33.(3) ($\psi^{\mathrm{H\text{-}3'}}$)
H-1–C-1–C-3′–H-3′	−6.(5) (Pseudo-torsion angle)
(d) Angles to the substituents	
C-1–C-2–N-21–N-22	−74.3(8)
C-2–C-3–O-3–C-31	−103.2(8)
C-3–C-4–N-41–N-42	74.5(5)
C-4–C-5–C-6–O-60	55.0(7)
C-1′–C-2′–N-21′–N-22′	161.6(9)
C-3′C-4′–N-41′–N-42′	147.4(5)

= 180°) and a *sofa*$_0$(D) (θ= 125.3°, ψ = 180°) conformation (see letter J in Fig. 3). Ring B adopts the $^4C_1$(D) conformation. Its θ parameter [θ = 2.7(6)°] indicates an almost perfect chair form (see Table IV).

In A, the average torsion-angle of 34.3° at C-3′ indicates that the chair is flattened at this atom; this may also be seen from the different distances of C-3′ and O-5′ from the plane of the C-1′, C-2′, C-4′, and C-5′ atoms, which are 44 pm and 83 pm, respectively. In the nearly perfect $^4C_1$(D) conformer B, these distances are almost equal: 64 pm for C-3 and 63 pm for O-5. Here, the average torsion-angle at C-3 is 51.7°.

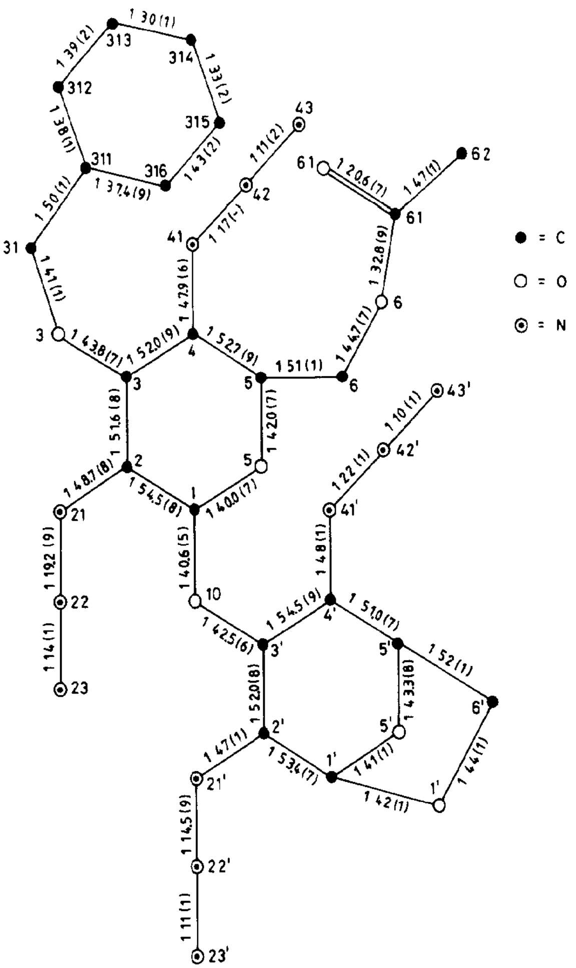


Fig. 1. Atom-numbering scheme and bond lengths (in pm) of the nonhydrogen atoms of 3-*O*-(6-*O*-acetyl-2,4-diazido-3-*O*-benzyl-2,4-dideoxy-α-D-glucopyranosyl)-1,6-anhydro-2,4-diazido-2,4-dideoxy-β-D-glucopyranose (**2**).

TABLE IV

PUCKERING PARAMETERS[12,13]

	2, *ring A* $^1C_4$ *(anhydro ring)*	*Azido compound* (**1**) *(exptl. mean)*	*Exptl. mean of 14 non-bridged 1,6-anhydro-pyranoses (B to L)*[a]	2, *ring B* $^4C_1$
Q (pm)	61.4(7)	61.1	61.9[b]	55.6(6)
φ(°)	177(1)	175.9	177.2	36(13)
θ(°)	153.5(6)	151.4	154.1	2.7(6)

[a]For references to the 1,6-anhydropyranoses B to L, see Table VI. [b]Q excl. F, Q(F) = 35.9 pm.

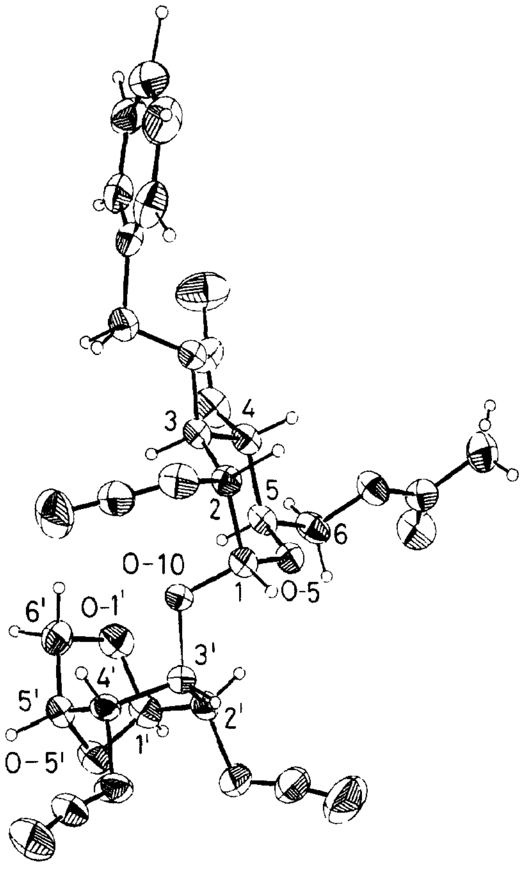


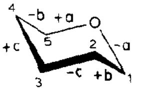
Fig. 2 Molecular model of compound **2** (ORTEP II; ref. 11).

In general, the variations among the ring torsion-angles are smaller in B than in A. There are also significant differences in the valence angles of the two rings. In A, the smallest of all of the pyranoid angles is at O-5′ [101.9(5)°], while the angles at the two bridge-head atoms, C-1′ and C-5′, are nearly tetrahedral [average of 109.2(6)°], and, at C-2′, C-3′, and C-4′, they are widened to values lying between 112.2(5) and 112.4(4)°. By comparison, in the nonbridged system B, the angle at O-5 is the largest of all of the pyranosyl angles [113.9(4)°], while the others are nearly tetrahedral [109.7(5) to 110.8(6)°].

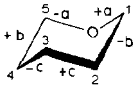
The distortion of ring-system A indicated by the facts just cited is mainly a consequence of the anti-reflex effect caused by the anhydro bridge. It may therefore be observed in all 1,6-anhydropyranoses (see Tables IV–VI, and Fig. 4). This effect also enlarges the distance of the axial substituents at C-2′ and C-4′ in **2** to 319 pm, and, in monosaccharide **1**, even to 345.2(7) pm (average of two independent molecules). Because the sum of the Van der Waals radii of nitrogen is[14] 292 pm, the repulsive forces of the partially negatively charged, N-21′ and N-41′ atoms have

TABLE V

AVERAGED TORSION ANGLES



$^4C_1$



$^1C_4$

	a	*b*	*c*	*Δθ*[a]	*References*
Ring B	60.9	55.2	51.7	2.7	this work
α-D-Glucose	62.0	56.	52.	4	23,24
Ring A	75.6	56.3	34.3	26.5	this work
Azido comp., exptl. mean	76.3	55.3	31.8	28.6	2
Exptl. mean of 14 nonbridged 1,6-anhydropyranoses[b]	76.1	56.5	34.9	25.9	1,2,16,25–33

[a] *Δθ* designates the deviation of the puckering parameter *θ* from the "north pole" (upper group, *θ* = 0°) and "south pole" (*θ* = 180°), *i.e.*, the deviation from the ideal chair. [b] Compounds B to L (see Table VI).

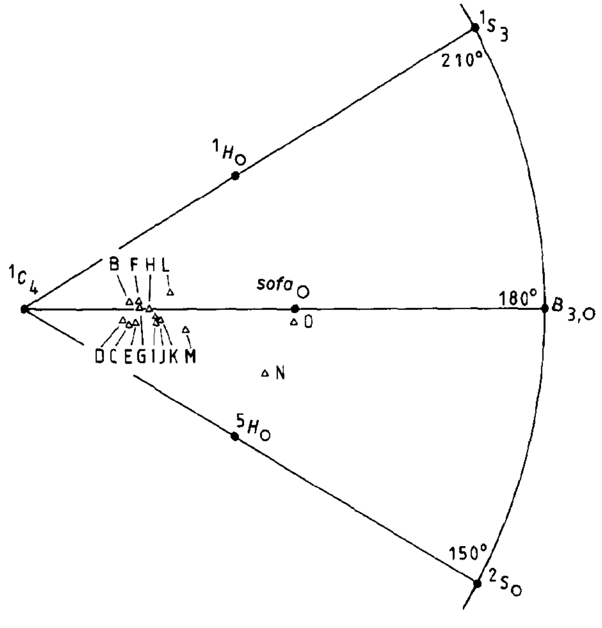


Fig. 3. Stereographic plot of the puckering parameters of the pyranoid ring for the 1,6-anhydro and dianhydro sugars given in the key to Table VI.

TABLE VI

1,6-ANHYDRO-β-D-HEXOPYRANOSES

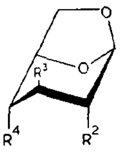
Compound[a]	*Averaged torsion-angle at C-3 (degrees)*	*θ (degrees)*	*Axial substituents at*			*Conformation*
			C-2	*C-4*	*C-3*	
A	44.2		H	OH	H	between $^1C_4$(D) and *sofa*$_O$
B	39.1	157.2	H	OH	OR	between $^1C_4$(D) and *sofa*$_O$
C	38.8	157.4	OAc	H	OAc	between $^1C_4$(D) and *sofa*$_O$
D	38.4	158.4	OH	OH	OH	between $^1C_4$(D) and *sofa*$_O$
E	38.0	155.8	OH	H	OH	between $^1C_4$(D) and *sofa*$_O$
F	36.0	154.6	H	OH	OH	between $^1C_4$(D) and *sofa*$_O$
G	35.2	154.7	OH	OH	OH	between $^1C_4$(D) and *sofa*$_O$
H	33.1	152.5	OH	OH	NH_2	between $^1C_4$(D) and *sofa*$_O$
I,J	32.6	152.1	N_3	N_3	OH	between $^1C_4$(D) and *sofa*$_O$
K	31.2	150.9	OAc	OAc	OAc	between $^1C_4$(D) and *sofa*$_O$
L	27.9	147.6	OH	OH	NH_3^+	between $^1C_4$(D) and *sofa*$_O$
M	26.6	145.6	H	H	OPr	between $^1C_4$(D) and *sofa*$_O$
N	5.5	128.7	O	H	H	between *sofa*$_O$ and ^5H_O
O	1.8	124.2	H	OR	OR	*sofa*$_O$
P	?	?	NH_3^+	NH_3^+	OH	$B_{3,O}$

[a]Letters A to O designate the structures investigated by X-ray analysis. These are 19 independent molecules of 15 types in 7 configurations. Molecule P could not be crystallized, and was investigated only in solution by n.m.r. spectroscopy.

Key (also to Tables IV, V, and VII, and Figs. 3 and 4): A, 2,6-anhydro-β-D-*altro*-heptulopyranose[25]; B, non-isopropylidene-bridged moiety[26] of 1,6-anhydro-β-D-*arabino*-hexopyranos-3-ulose dimer; C, 2,3-di-*O*-acetyl-1,6-anhydro-β-D-galactopyranose[27]; D, 1,6-anhydro-1(6)-thio-β-D-glucopyranose[28]; E, 1,6-anhydro-β-D-galactopyranose (three independent molecules)[29]; F, 2,7-anhydro-L-*glycero*-β-D-*manno*-octulopyranose[30]; G, 1,6-anhydro-β-D-glucopyranose[1]; H, 3-amino-1,6-anhydro-3-deoxy-β-D-glucopyranose[31]; I, 1,6-anhydro-2,4-diazido-2,4-dideoxy-β-D-glucopyranose (two independent molecules)[2]; J, this work; K, 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-glucopyranose[32]; L, 3-ammonio-1,6-anhydro-3-deoxy-β-D-glucopyranose, hydrochloride, monohydrate[33]; M, 1,6-anhydro-3,4-*O*-isopropylidene-β-D-talopyranose[34]; N, 1,6:2,3-dianhydro-β-D-gulopyranose (two independent molecules)[35]; O, isopropylidene-bridged moiety[26] of 1,6-anhydro-β-D-*arabino*-hexopyranos-3-ulose dimer; and P, 2,4-diammonio-1,6-anhydro-2,4-dideoxy-β-D-glucopyranose[16].

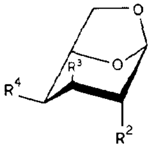
little influence on the geometry of the conformer. The anti-reflex effect also causes the distance of O-10 to the O-6′–C-6′ bridge to be enlarged to 300.3(4) and 300.4(6) pm.

If all the 1,6-anhydropyranoses already investigated are sorted into the decreasing order of averaged torsion-angle at C-3, as in Table VI, it may be seen that this is correlated with a sorting according to a declining θ parameter towards a value corresponding to the *sofa*$_O$(D) conformation (θ = 125.3°). Table VI shows that the 1,3-diaxial interactions exert a relatively small influence on the geometry of the ring, compared to the anti-reflex effect. Those molecules, G to L, which have such axial substituents as oxygen or nitrogen at both C-2 and C-4 are somewhat more flattened at C-3 than those that have a hydrogen atom in axial position on C-2 or C-4, or both (molecules A to F). The thio compound D is a special case, where the reflex effect of the large sulfur atom counterbalances the 1,3-diaxial, re-



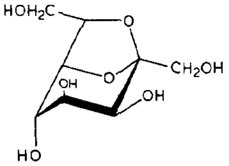
1 *gluco*

	R^2	R^3	R^4
D	OH O(1)=S	OH	OH
G	OH	OH	OH
H	OH	NH_2	OH
I,J	N_3	OH	N_3
K	OAc	OAc	OAc
L	OH	NH_3^+	OH
P	NH_3^+	OH	NH_3^+

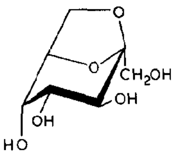


2 *galacto*

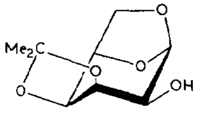
	R^2	R^3	R^4
E	OH	OH	OH
C	OAc	OAc	OH



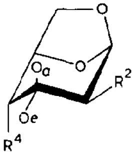
3 *manno* (F)



4 *altro* (A)

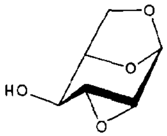


5 *talo* (M)



6 *arabino*

	R^2	*a*	*e*	R^4
B	OH	O→C-3′	O→C-4′	OH
O	*O*-Ip	*O*-Ip	O→C-3	O→C-3



7 *gulo* (N)

Fig. 4. Formula schemes for the different types of 1,6-anhydro-β-D-glycopyranoses investigated by structure analysis: 19 independent molecules, 15 sugars in 7 configurations. (The diammonia-glycopyranose P was only investigated in solution by n.m.r. spectroscopy). For the key (molecules A to P), see Table VI.

pulsive forces of the two diaxial hydroxyl groups. The molecules N to O are flattened the most, and nearly reach a sofa conformation; they are, however, tricyclic molecules. The diammonium compound P has not yet been crystallized, but, according to n.m.r.-spectral measurements, it has the $B_{3,\mathrm{O}}$(D) conformation in solution[5]. Only in the boat form do the charged 1,3-substituents reach maximal separation from each other.

The anhydro ring of system A adopts a distorted $sofa_{\mathrm{O}}$(D) conformation. The distortion is characterized best by the torsion angle around the C-6′–O-6′ bond, which is 4.2(5)°. The adjacent bonds have an average torsion-angle of 26.1(5)°, and the bonds to the O-5′ tip of the *sofa* form a torsion angle of 42.5(5)°. Whereas the valence angle at O-5′ is the smallest of all of the intracyclic angles [101.9(5)°], the angle at O-6′ is the largest [107.4(7)°].

The asymmetry in the valence angles at the sp^2-hybridized atom C-61 of the acetyl group is typical, and was also found in other structures. Thus, the angle O-61–C-61–C-62 is diminished to 112.0(5)°, mainly in favor of O-6–C-61–C-62, which is enlarged to 125.1(7)°.

(b) The azido groups. — According to several investigations[2] (references cited therein), the mesomeric structure of the azido group in which N-1 bears a negative charge and the middle N-2 atom a positive one has more weight than the other, in which N-3 is negatively charged. Therefore, the bond between N-2 and N-3 has triple-bond character, whereas the one between N-1 and N-2 is more like a single bond. The bond lengths found agree with this model. The 7–12° deviation from linearity is significant, and is found in all organic azido groups. The relatively large valence-angle of 116.3(4)–122.6(2)° at N-1 is also typical, and indicates a large proportion of sp^2-hybridization.

Although the N-21′ and N-41′ atoms are situated at a considerable distance from each other, they both come relatively close to the ring-oxygen atom (O-5′) in A, both in **2** and in the azido compound **1**. The distances observed are: N-41′–O-5′: 282.0(8) pm, N-21′–O-5′: 284.0(8) pm in **2**, and 280.1 (5) and 303.6(5) pm in the azido compound **1** (values for **1** are the average of two independent molecules). The Van der Waals distance for N · · · O should be 290 pm, according to Pauling[14], and the minimal possible contact-distance is[15] 270 pm. The partial negative charge on these nitrogen atoms might lead to a transannular repulsion with the lone-pair electrons of the ring-oxygen atom. This interaction is expected to be more powerful in the ring geometry than the 1,3-diaxial N · · · N interaction[16].

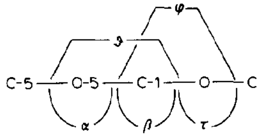
In agreement with the partial positive charge of the middle nitrogen atom, in the azido compound **1**, an orientation of the azido groups was observed that allowed the middle nitrogen atom to approach the ring-oxygen atom to contact-distances of 280–290 pm. These contacts were found to be intramolecular, as well as intermolecular. Comparable contacts are missing in compound **2**, where the azido groups spread away from the bulk of the molecule. One exception is the approach of N-22 to the glycosidic oxygen atom [N-22–O-10, 278.3(6) pm]. This azido group has no other contacts to ring A that are equal to, or smaller than, the corresponding Van der Waals radii, and that could affect its orientation.

(c) The anomeric effect. — The anhydro-D-glucose residue A adopts a distorted β-D-$^{1}C_{4}$ conformation, whereas the D-glucosyl group B adopts the α-D-$^{4}C_{1}$ conformation. In an α-D-$^{4}C_{1}$ conformation, there is a (+sc, +sc) arrangement between C-1–O-10 and O-5–C-1 bonds. In a β-D-$^{1}C_{4}$ conformer, there is a (+sc, −sc) arrangement between the C-1′–O-5′ and C-1′–O-1′ bonds. Thus, in both chairs, the anomeric effect can arise, and is, indeed, observed in terms of bond-shortening of the inner C–O bonds of the C–O–C–O–C sequence. Both bonds are shortened, because both oxygen atoms can delocate their lone-pair p-electrons into the anti-bonding σ^*-orbital of each other's C–O bond. The geometry at the anomeric carbon atom is summarized in Table VII.

Two facts should be noted in regard to Table VII. (*i*) In all of the 1,6-anhydropyranoses, the average glycosidic C-1–O-1 bond is ~0.9 pm longer than the average ring bond to the anomeric carbon atom. If this difference (obtained from 17 independent investigations) is accepted as significant, an explanation can be pro-

TABLE VII

GEOMETRY AT THE ANOMERIC CARBON ATOM



	C-5–O-5 (pm)	*O-5–C-1 (pm)*	*C-1–O (pm)*	*O–C (pm)*	*θ (degrees)*	*Φ (degrees)*	*α*	*β*	*τ*
Anhydro ring A	143.3	141.4	141.6	144.3	−41.9	23.0	101.9	106.0	107.4
Experimental mean of 17 1,6-anhydropyranoses (A–C,E,G–O)[a]	144.0	141.1	142.0	144.4	−42.7	24.0	101.8	106.2	106.6
Experimental mean of the azido-cd. (I)	144.1	140.3	142.2	144.6	−43.1	23.0	101.8	106.7	106.6
Ring B	142.0	140.0	140.6	142.5	59.7	78.1	113.9	113.4	116.1
α-Glycosidic linkages, experimental mean of 5 X-ray and 2 neutron studies[18]	143.4	141.1	141.4	143.2		99.	114.3	110.9	116.1
Methyl α-pyranosides, experimental mean of 8 X-ray and 3 neutron studies[18]	143.5	141.6	140.2	142.4		65.	113.5	112.3	113.4
Theory for (+sc, +sc) orientation[18]	144.4	142.3	(142.3)	(144.4)	60.0	60.0	115.9	113.9	(115.9)

[a] For A–O, see key to Table VI.

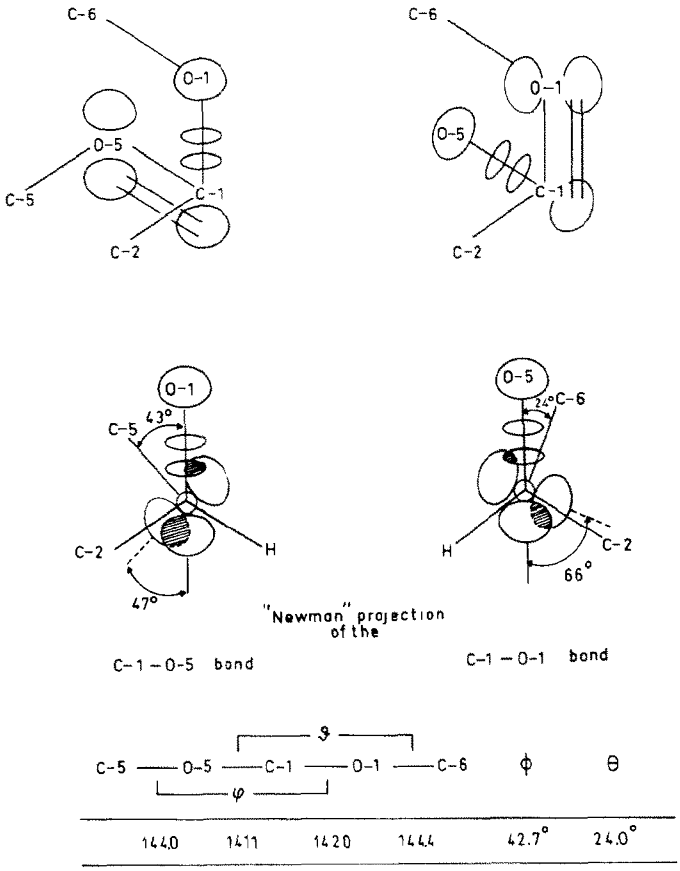


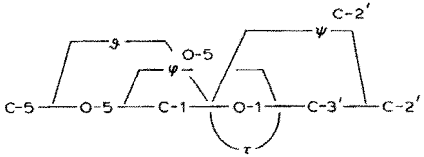
Fig. 5. Illustration of the varying orbital overlap caused by the different torsion-angles at the C-1–O-5 and C-1–O-1 bonds. Overlapping areas are shaded in both cases. The numerical values listed are averages of 17 structure investigations of anhydropyranoses.

vided by inspection of the torsion angles at the C–O bonds. Around the O-5–C-1 bond, the torsion angle is 42.7° (average), but around the C-1–O-1 bond, it is 24.0°. A torsion angle of 42.7° means a 46.3° angle between the orbitals concerned. Because the oxygen atom is expected to be sp^2-hybridized[17], these orbitals are the lone-pair p-orbital of O and the anti-bonding σ^*-orbital of the other C–O bond. A torsion angle of 24.0° means an interorbital angle of 66.0°. The smaller the angle between the orbitals, the more complete is the overlap between them, and, consequently, the double bond character of this bond increases (see Fig. 5). (*ii*) The differences in the anomeric, C–O bond-lengths tend to disappear when the torsion angle Φ around the anomeric C-1–O-1 bonds is nearer to 90° than[18] to 60°.

(d) Geometry of the glycosidic linkage. — Because of the presence of an α-(1→3) linkage between a D-*gluco* ${}^4C_1$(D) and a D-*gluco* ${}^1C_4$(D) conformer, the glycosidic, C–O bonds are axial with respect to both rings. Consequently, the

TABLE VIII

GEOMETRY OF RARE GLYCOSIDIC LINKAGES



Disaccharide[a]	*Type of linkage*	*C-1–O-1 (pm)*	*O-1–C-3′/2′ (pm)*	*θ (degrees)*	$\Phi^{O\text{-}5}$ *(degrees)*	$\psi^{C\text{-}2'}$ *(degrees)*	*τ (degrees)*
Gal-Gal[36]	β-Gal-$^4C_1$-(1*e*→3*e*)-Gal-$^4C_1$	140.7	142.4	−179.1	−71.2	−96.2	114.5
Laminarabiose[37]	β-Glc-$^4C_1$-(1*e*→3*e*)-Glc-$^4C_1$	138.7	143.1		−93.6	−161.0	118.2
β-Glycosidic linkages (experimental mean)[18]		138.9	144.1		−80.		116.4
Theory[18]		140.0	144.3	180.	60.		116.1
2	α-Glc-$^4C_1$-(1*a*→3*a*)-Glc-$^1C_4$	140.6	142.4	59.7	78.1	−86.0	116.1
Turanose[21,38] (experimental mean of 2 structures)	α-Glc-$^4C_1$-(1*a*→3*e*)-Fru-$^2C_5$	141.5	143.7	63.6	98.8	−127.8	116.2
α-Gal-Gal[39]	α-Gal-$^4C_1$-(1*a*→3*e*)-Gal-$^4C_1$	138.5	142.1		81.7	140.5	116.4
α-Glycosidic linkages[18]		141.4	143.2		99. (72–122)		116.1
Nigeroside[40]	α-Glc-$^4C_1$-(1*a*→3*e*)-Glc-$^4C_1$	140.5	143.3	59.3	99.9	−137.6	116.2
Theory[18]		142.3	144.4	60.	60.		115.9

[a] Gal-Gal, 1,2,4,6-tetra-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-galactopyranose[36]; laminarabiose, *O*-β-D-glucopyranosyl-(1→3)-β-D-glucopyranose[37]; nigeroside, methyl 3-*O*-α-D-glucopyranosyl-α-D-glucopyranoside (methyl α-nigeroside)[40]; turanose, *O*-α-D-glucopyranosyl-(1→3)-β-D-fructopyranose[21,38]; and α-Gal-Gal, 2-acetamido-3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-1,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranose[39].

monosaccharide components are almost perpendicular to one another: the angle between the planes of the C-1–C-2–C-4–C-5 and C-1′–C-2′–C-4′–C-5′ atoms is 84.7(6)°. In this regard, **2** resembles the disaccharides of the α,α-trehalose type[19]. In these sugars having an α-D-$^4C_1(1a\leftrightarrow 1a)$-$\alpha$-D-$^4C_1$ glycosidic linkage, the two moieties are linked diaxially, as in the case of **2**.

More information about the relative arrangement of the two components is provided by the torsion angles around the glycosidic bonds. The conformation angles $\Phi^{\text{O-5}}$ = O-5–C-1–O-10–C-3′, $\Phi^{\text{C-2}}$ = C-2–C-1–O-10–C-3′, and $\psi^{\text{C-2}}$ = C-1–O-10–C-3′–C-2′, $\psi^{\text{C-4}}$ = C-1–O-10–C-3′–C-4′ are used for the description of the α-D-(1→3) linkage. For these angles, the following values were obtained: $\Phi^{\text{O-5}}$ = 78.1(5)°, $\Phi^{\text{C-2}} = -160.1(4)°$, $\psi^{\text{C-2}}$ = 86.0(4)°, and $\psi^{\text{C-4}'}$ = 150.2(3)°.

The magnitudes of the Φ values show that C-3′ is almost trans with respect to C-2, and gauche to the ring-oxygen atom (O-5). This setting is found in nearly all disaccharides so far investigated, and is caused by the exo-anomeric effect. However, it has been shown[18] that the torsion angle $\Phi^{\text{O-5}}$ is ~60° (ideal gauche orientation according to the exo-anomeric effect) only in methyl pyranosides. In disaccharides, it is always found to be >60°, and even reaches 122° in β-maltose[20].

It was pointed out by Kanters *et al.*[21] that the variation in this torsion angle is influenced by intramolecular hydrogen-bonds. As **2** is a completely substituted disaccharide, no hydrogen-bonds can occur, and the torsion angle $\Phi^{\text{O-5}}$ should be mainly influenced by the exo-anomeric effect. It may be seen from Table VIII that, in agreement with this effect, the glycosidic C–O bonds are of different lengths.

To obtain more information on the glycosidic linkage, an empirical calculation using the HSEA approach[22] was executed. In a systematic variation of Φ and ψ, with the geometry of the monosaccharide components found in the structure as input, the minimal energy conformation was calculated at $\Phi^{\text{H-1}} = -44.0(5)°$ and $\psi^{\text{H-3}'} = +31.0(5)°$. The corresponding experimental values are $-41.(4)°$ and $+33.(3)°$ (see Table III). A number of additional HSEA calculations made with more-or-less incomplete monosaccharide fragments, led to the following results. If only the two six-membered rings were used, the minimum occurred at $\Phi^{\text{H-1}} = -60.(5)°$ and $\psi^{\text{H-3}'} = 0.(5)°$. The addition of the anhydro-bridge atoms C-6′ and O-6′ to residue A led to $\Phi^{\text{H-1}} = -50.(5)°$ and $\psi^{\text{H-3}'} = +20.(5)°$, which is already a good approximation of the final minimum. If the H-1, H-3, N-21, H-5, and H-2′ atoms were input as the only ring substituents, the same minimum as for the complete monosaccharide moieties was achieved. This obviously suggests that even large substituents may have little influence on the glycosidic linkage of oligosaccharides.

ACKNOWLEDGMENT

We are grateful to the Deutsche Forschungsgemeinschaft for financial support of this work.

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