The Crystal Structure of a Disaccharide, α-Melibiose Monohydrate
(O-α-D-Galactopyranosyl-(1→6)-α-D-glucopyranoside)

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α-Melibiose is a disaccharide of α-D-glucose and α-D-galactose, linked α-1 → 6, with glucose as the reducing unit. The crystal data are $a = 8.878$ (5), $b = 10.920$ (6), $c = 15.730$ (10) Å; space group $P2_12_12_1$; $Z = 4$, $D_m = 1.552$, $D_x = 1.570$ g cm^{-3}. The structure analysis was performed with 1921 independent reflexions, collected on a Nonius CAD-4 diffractometer, by applying the tangent formula. The H atoms were located on difference syntheses. Final difference syntheses showed a partial (19.6%) substitution of α-melibiose by the β-anomer. After anisotropic least-squares refinement for non-hydrogen and isotropic refinement for H atoms the final R was 0.046. Both rings have the usual $^4C_1$ chair conformation. The conformation of the α-1 → 6 linkage is similar to that in the trisaccharide raffinose, which contains the melibiose disaccharide moiety. All hydroxyl groups are involved in intermolecular hydrogen bonds. With the exception of the αO(1) anomeric hydroxyl group all other groups function as hydrogen-bond acceptors. The ring O atom of the glucose residue takes part in hydrogen bonding; in the β-anomer the ring O of the galactose residue also acts as an acceptor. The melibiose molecules are linked by an intricate three-dimensional network of hydrogen bonds, in which the water molecule plays a central part by donating and accepting two hydrogen bonds.

Introduction

α-Melibiose, O-α-D-galactopyranosyl-(1 → 6)-α-D-glucopyranoside, is a reducing disaccharide occurring in many plant exudates and in honey. It consists of a galactose and glucose moiety connected by an α-1 → 6 linkage. Apart from interest in the conformation of α-melibiose, a primary purpose of this study was to compare this conformation with that of the melibiose unit in the trisaccharide raffinose pentahydrate (Berman, 1970) and also to provide more information on the hydrogen-bonding scheme and on the conformation of the 1 → 6 glycosidic bond so far only observed in raffinose (Berman, 1970), the disaccharide isomaltulose (Dreissig & Luger, 1973) and the trisaccharide planteose dihydrate (Rohrer, 1972). Since the structure of α-D-galactose has recently been reported (Sheldrick, 1976), it is of interest to look into the effect on the conformation of α-D-galactose and α-D-glucose (Brown & Levy, 1965) when these monosaccharides are constituents of the disaccharide α-melibiose and the trisaccharide raffinose (Berman, 1970).

Experimental

Crystals were grown by slow evaporation from an aqueous ethanolic solution. A crystal, $0.8 \times 0.5 \times 0.1$ mm, was used for photographic measurements and for collection of the automatic diffractometer data. Photographs showed that the crystal is orthorhombic. The systematically absent reflexions, $h00$ for $h = 2n + 1$, $0k0$ for $k = 2n + 1$ and $00l$ for $l = 2n + 1$, indicate that the space group is $P2_12_12_1$. Accurate cell dimensions were measured on a Nonius CAD-4 diffractometer.

The crystal data are summarized in Table 1. 4956 reflexions were measured with the θ–2θ scan technique and Zr-filtered Mo radiation (λMo $K\alpha = 0.7107$ Å). The upper limit for sin θ/λ was 0.70. After the application of the Lorentz–polarization correction, equivalent reflexions were averaged to give 2541 independent reflexions. Of these 1921 were above the $3\sigma(I)$ level. No corrections for absorption were made.

Table 1. *Crystal data for α-melibiose monohydrate*

Molecular formula	$C_{12}H_{22}O_{11} \cdot H_2O$
Formula weight	360.3
Crystal system	Orthorhombic
a	8.878 (5) Å
b	10.920 (6)
c	15.730 (10)
Systematic absences	$h00$, $h = 2n + 1$
	$0k0$, $k = 2n + 1$
	$00l$, $l = 2n + 1$
Space group	$P2_12_12_1$
V	1524.98 Å^3
Z	4
D_m	1.552 g cm^{-3}
D_x	1.570
μ(Mo $K\alpha$)	1.53 cm^{-1}
Crystal dimensions	$0.8 \times 0.5 \times 0.1$ mm
λ(Mo $K\alpha$)	0.7107 Å

Determination and refinement of the structure

The observed structure factors were scaled and normalized to E values by means of a Wilson plot.

The structure was solved by direct phasing methods with the tangent formula (Karle & Hauptman, 1956). For the phase determination the *MULTAN* program of the X-RAY system (1972) was employed. In the

structure analysis 381 $|E|$ values $>1\cdot40$ were used. A solution was achieved with the origin and enantiomorph defining phases given in Table 2, where n refers to the position of the reflexion in a list sorted on $|E|$ values.

Table 2. *Origin and enantiomorph defining phases*

n	Reflexion	$|E|$	Starting phase	Type	Final phase
2	0 2 13	4·04	2π	Origin	—
5	0 3 12	3·24	$\pi/2$	Origin	—
27	1 5 3	2·40	$\pi/4$	Origin	59·8°
27	1 5 3	2·40	$\pi/4$	Enantiomorph	59·8

Other reflexions in the starting set were 626 ($n=15$) and 718 ($n=6$), to which the arbitrary starting phases of $\pi/4, 3\pi/4, 5\pi/4, 7\pi/4$ were assigned. The phasing was then extended to include the 381 $|E|$ values $>1\cdot40$. The set of phases with $\varphi_{626}=7\pi/4$ and $\varphi_{718}=7\pi/4$ appeared to be significantly better than the other sets. An E map calculated on the basis of these phases clearly showed all C and O atoms. Isotropic block-diagonal least-squares refinement [*CRYLSQ* program of the X-RAY system (1972)] followed by anisotropic refinement reduced R to 0·070.

Standard tabulations of atomic scattering factors were used for C and O (Cromer & Mann, 1968) and H (Stewart, Davidson & Simpson, 1965). The function minimized was $\sum w(|F_o|-k|F_c|)^2$. The weights were initially set at $w=1$ for all observed reflexions; in the final stage the weights $w=\sigma^{-2}(F_o)$ were introduced.

In a difference synthesis 23 of the 24 H atoms could be located. The electron density ranged from 0·25 to 0·69 e Å^{-3} with a peak near C(1) which showed a density of $1\cdot36$ e Å^{-3}. The H atoms were given isotropic thermal factors equal to those of the carrier atom. After refinement of the anisotropic thermal parameters of the non-hydrogen atoms and positional parameters of the 23 H atoms a difference synthesis showed a residual electron density of 0·97 e Å^{-3} near the position assigned to H(C1). This is indicative of the presence of a small amount of the β-anomer of melibiose which has the anomeric O atom in the $^4C_1$ chair form in the equatorial position.

The large C(1)–H(C1) distance of 1·39 Å also points to the presence of the β-anomer, so the residual density was assigned to the β-oxygen atom with an initial population parameter of 0·20. The position of H(C1) was calculated from a molecular model because its detection proved to be impossible owing to the nearby presence of the β-anomeric O atom. The parameters of this H atom were kept fixed during refinement.

Three cycles of anisotropic refinement of the non-hydrogen atoms and refinement of the positional parameters of the H atoms for 1921 observed reflexions reduced R to 0·046 and R_w to 0·041. The 'goodness-of-fit' was 0·52. A final difference map showed no electron density above 0·29 e Å^{-3}. The occupancy parameter of αO(1) converged to 0·873 (9) and that of βO(1) to 0·213 (9). Since these two parameters must add up to unity they were normalized to 0·804 and 0·196 respectively.

Table 3. *Fractional coordinates ($\times 10^4$) and anisotropic thermal parameters ($\times 10^4$) of the non-hydrogen atoms*

The estimated standard deviations are in parentheses and refer to the last decimal position. The anisotropic temperature factor is of the form $\exp[-2\pi^2(a^{*2}h^2U_{11}+\ldots+2b^*c^*klU_{23})]$.

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	4153 (4)	7122 (3)	−98 (2)	293 (16)	447 (20)	212 (14)	−55 (16)	16 (13)	−19 (14)
C(2)	4282 (3)	8435 (3)	172 (2)	198 (13)	382 (18)	231 (14)	3 (14)	29 (12)	60 (14)
C(3)	4889 (3)	8586 (3)	1067 (2)	191 (14)	339 (16)	248 (14)	21 (14)	−1 (12)	−26 (13)
C(4)	4103 (3)	7732 (3)	1686 (2)	205 (14)	391 (18)	189 (13)	47 (15)	1 (12)	−10 (13)
C(5)	4096 (3)	6441 (3)	1332 (2)	184 (13)	400 (17)	196 (13)	46 (14)	−6 (11)	16 (13)
C(6)	3368 (3)	5492 (3)	1878 (2)	252 (15)	336 (18)	270 (14)	27 (14)	9 (13)	51 (14)
O(1)	5552 (3)	6671 (3)	−255 (2)	322 (15)	504 (19)	408 (16)	−45 (14)	124 (12)	−124 (14)
O(2)	5184 (3)	9125 (2)	−407 (1)	340 (12)	442 (14)	303 (11)	23 (12)	103 (10)	115 (11)
O(3)	4727 (3)	9813 (2)	1343 (1)	357 (12)	333 (12)	368 (12)	−34 (11)	10 (10)	−31 (11)
O(4)	4816 (3)	7757 (2)	2499 (1)	449 (14)	510 (15)	208 (10)	88 (13)	−81 (10)	−39 (11)
O(5)	3355 (2)	6438 (2)	523 (1)	250 (10)	431 (13)	187 (9)	−51 (11)	4 (9)	−4 (10)
O(6)	1822 (2)	5773 (2)	2048 (1)	228 (11)	363 (12)	220 (10)	−5 (10)	28 (9)	71 (9)
C(1')	1194 (3)	4948 (3)	2630 (2)	302 (16)	306 (16)	216 (13)	−39 (14)	−16 (12)	−2 (13)
C(2')	−524 (3)	5020 (3)	2562 (2)	275 (15)	426 (18)	221 (14)	−105 (15)	−11 (13)	54 (14)
C(3')	−1086 (3)	6258 (3)	2852 (2)	229 (15)	426 (20)	360 (17)	−2 (15)	4 (14)	165 (15)
C(4')	−489 (4)	6528 (3)	3745 (2)	343 (18)	318 (17)	327 (17)	11 (16)	61 (14)	2 (15)
C(5')	1221 (4)	6395 (3)	3752 (2)	324 (17)	308 (16)	250 (14)	−35 (15)	25 (13)	−7 (14)
C(6')	1893 (4)	6552 (4)	4628 (2)	420 (19)	514 (22)	291 (16)	−94 (19)	11 (15)	−66 (17)
O(2')	−971 (3)	4687 (3)	1729 (1)	430 (15)	705 (19)	313 (12)	−223 (15)	−78 (11)	16 (13)
O(3')	−2675 (3)	6337 (3)	2822 (2)	245 (12)	802 (20)	531 (15)	38 (14)	12 (12)	284 (15)
O(4')	−1179 (3)	5652 (2)	4300 (1)	383 (13)	583 (17)	267 (11)	−30 (13)	72 (10)	19 (12)
O(5')	1655 (2)	5192 (2)	3473 (1)	289 (11)	381 (13)	201 (10)	12 (11)	−7 (9)	27 (10)
O(6')	3498 (3)	6561 (3)	4592 (2)	415 (15)	720 (20)	470 (15)	−37 (15)	−103 (12)	−105 (16)
O(W)	3703 (4)	8977 (4)	3907 (2)	408 (14)	533 (17)	412 (14)	−15 (13)	62 (12)	−7 (12)
βO(1)	3679 (17)	7039 (14)	−859 (8)	543 (75)	574 (80)	204 (51)	0 (65)	−39 (48)	−134 (52)

Table 4. *Fractional coordinates* (×10³) *and isotropic thermal parameters of the hydrogen atoms*

	x	y	z	B (Å²)
H(C1)	350	700	−50	2·3
H(C2)	328 (3)	878 (2)	13 (2)	2·2
H(C3)	597 (3)	828 (3)	103 (2)	2·1
H(C4)	299 (3)	794 (3)	176 (2)	2·1
H(C5)	509 (3)	616 (3)	127 (2)	2·1
H(C6)	402 (3)	549 (3)	239 (2)	2·2
H'(C6)	347 (3)	476 (3)	163 (2)	2·2
H(O1)	554 (4)	586 (4)	−46 (3)	4·1
H(O2)	588 (3)	848 (3)	−49 (2)	2·8
H(O3)	514 (4)	1025 (3)	114 (2)	2·9
H(O4)	568 (3)	736 (3)	247 (2)	3·0
H(C1')	148 (3)	405 (3)	252 (2)	2·3
H(C2')	−88 (3)	430 (3)	295 (2)	2·5
H(C3')	−75 (3)	705 (3)	250 (2)	2·7
H(C4')	−70 (4)	742 (3)	387 (2)	2·8
H(C5')	160 (3)	720 (3)	334 (2)	2·4
H(C6')	162 (4)	578 (3)	500 (2)	3·3
H'(C6')	145 (4)	748 (3)	487 (2)	3·3
H(O2')	−84 (4)	539 (3)	151 (2)	3·6
H(O3')	−316 (4)	581 (3)	310 (2)	4·2
H(O4')	−115 (3)	596 (3)	465 (2)	3·0
H(O6')	364 (4)	738 (3)	434 (2)	4·2
H(OW)	277 (5)	943 (4)	366 (3)	3·6
H'(OW)	408 (5)	837 (4)	351 (3)	3·6

The positional and anisotropic thermal parameters of the non-hydrogen atoms are listed in Table 3, the parameters of the H atoms in Table 4.*

Molecular geometry

The structural and conformational features of α-melibiose monohydrate are illustrated in Fig. 1. The glucose and galactose moieties are denoted by unprimed and single-primed atom designators respectively. The melibiose molecule is the α-anomer with the two pyranose rings in the ⁴C₁ chair conformation. Bond lengths and

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angles involving non-hydrogen atoms are given in Tables 5 and 6 respectively, with the values of corresponding distances and angles of the melibiose residue in raffinose pentahydrate (Berman, 1970).

The C–C lengths range from 1·493 to 1·530 Å with a mean of 1·515 Å, the smallest being associated with the C(5)–C(6) bridge bond. This shortening of C(5)–C(6) is absent in raffinose pentahydrate (Berman, 1970).

The exocyclic C–O lengths, excluding the anomeric C(1)–O(1) and C(1)–βO(1), range from 1·414 to 1·432 Å with a mean of 1·422 Å, in good agreement with previous observations (Jeffrey & Rosenstein, 1964; Berman, Chu & Jeffrey, 1967; Arnott & Scott, 1972). The α-glucosyl C(1)–O(1) bond (1·359 Å) is shortened by 16σ from the mean value. This is the shortest anomeric C–O distance observed in pyranose rings
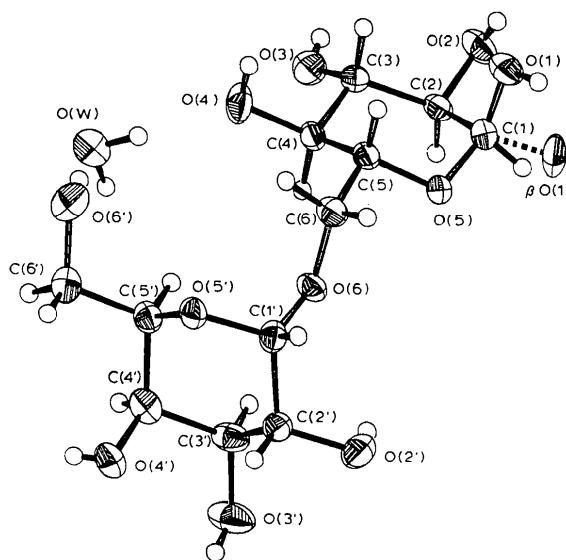

Fig. 1. Molecular conformation and atomic numbering in α-melibiose monohydrate. The carbon and oxygen atoms are represented by thermal ellipsoids at the 50% level (Johnson, 1965). The βO(1) atom represents the β-anomer of melibiose that is also present in this partially disordered structure.

Table 5. *Bond distances* (Å) *involving the non-hydrogen atoms with the corresponding values for raffinose*

The e.s.d.'s for the bond distances in α-melibiose are 0·005 Å, with the exception of bond distances involving βO(1) where the e.s.d.'s are 0·010 Å. The e.s.d.'s in the raffinose bond distances are 0·008 Å.

	Glucose moiety				Galactose moiety	
	α-Melibiose	Raffinose			α-Melibiose	Raffinose
C(1)–C(2)	1·500	1·514		C(1')–C(2')	1·530	1·518
C(2)–C(3)	1·518	1·536		C(2')–C(3')	1·512	1·513
C(3)–C(4)	1·518	1·516		C(3')–C(4')	1·530	1·531
C(4)–C(5)	1·515	1·515		C(4')–C(5')	1·525	1·514
C(1)–O(5)	1·419	1·419		C(1')–O(5')	1·412	1·422
C(5)–O(5)	1·433	1·433		C(5')–O(5')	1·439	1·435
C(5)–C(6)	1·493	1·520		C(1')–O(6)	1·401	1·428
C(6)–O(6)	1·431	1·442		C(5')–C(6')	1·511	1·520
C(2)–O(2)	1·428	1·424		C(2')–O(2')	1·416	1·424
C(3)–O(3)	1·415	1·440		C(3')–O(3')	1·414	1·442
C(4)–O(4)	1·427	1·430		C(4')–O(4')	1·432	1·426
C(1)–O(1)	1·359	1·402		C(6')–O(6')	1·426	1·425
C(1)–βO(1)	1·272					

and this extreme shortening must be ascribed to both the anomeric effect (Durette & Horton, 1971) and the disorder (19·6%) of the O atom attached to C(1). This is corroborated by the short C(1')–O(1') in α-lactose monohydrate (Fries, Rao & Sundaralingam, 1971) of 1·387 Å in which O(1') is disordered to a degree of 7%.

The significant difference observed in endocyclic C–O lengths when the anomeric C atom is involved in the glycosidic link (Berman, Chu & Jeffrey, 1967) is also encountered in α-melibiose in which C(5')–O(5') is 0·027 Å longer than C(1')–O(5'). The difference in the corresponding bonds in the glucose moiety in which O(1), attached to the anomeric C atom, is not involved in a glycosidic link is less striking (0·014 Å). The average value of the fourteen C–H bonds is 1·01 (5), that of the ten O–H bonds 0·88 (5) Å.

The internal C–C–C ring angles are close to tetrahedral (mean 110·7°) and range from 109·5 to 113·2°. The exocyclic C–C–O angles range from 106·4 to 114·6°, with an average of 110·5°. Both ring O angles

glucose　　　　　　　*galactose*

Fig. 2. The conformation of the 1 → 6 linkage in α-melibiose and raffinose (Berman, 1970).

are 112·4°. Normal internal valence angles at the ring O in pyranosides range from 110 to 116° (Jeffrey & Rosenstein, 1964).

All pairs of exocyclic angles are unequal, the greatest difference occurring at C(5') and C(5); the C–C–C angle is consistently larger than the O–C–C angle in both rings, in accordance with observations in α-lactose (Fries, Rao & Sundaralingam, 1971), raffinose (Berman, 1970), α,α-trehalose (Brown, Rohrer, Berkin, Beevers, Gould & Simpson, 1972) and β-lactose (Hirotsu & Shimada, 1974).

In Table 7 the C–O–C bridge angles in some di- and trisaccharides and C–O–C angles in methylglycosides are shown. In three of the four compounds with a 1 → 6 linkage the bridge angle is at a minimum (average 111·9°). In isomaltulose (Dreissig & Luger, 1973) the bridge angle is 115·5°. However, in this disaccharide the conformation of the 1 → 6 bridge deviates largely from the antiperiplanar arrangement (143°), whereas in the other di- and trisaccharides with a 1 → 6 linkage the conformation is nearly antiperiplanar (Table 8). In 1 → 1, 1 → 2, 1 → 3, and 1 → 4 linkages the corresponding C–O–C angle is consistently larger (average 115·8, 117·6, 116·8 and 116·1°, respectively). The C–O–C angle in methylglycosides shows a striking constancy (average 113·3°) with a value intermediate between the values found for compounds with a 1 → 6 linkage and oligosaccharides having other types of linkage.

The bond angles involving H atoms have mean values, distributed as follows over the different classes: H–C–C (21 contributors) 112; H–C–O (nine) 109; H–O–C (eight) 105; H–C–H (two) 108; and H–O–H (one) 111°.
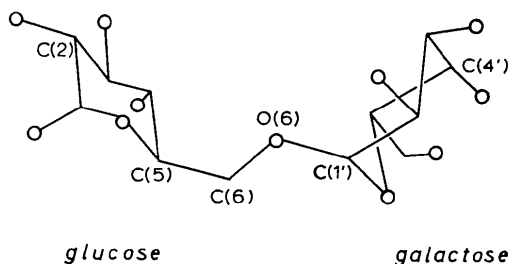
Table 6. *Bond angles* (°) *involving the non-hydrogen atoms with the corresponding values for raffinose*

The e.s.d.'s for the bond angles in α-melibiose are 0·3°, with the exception of bond angles involving βO(1) where the e.s.d.'s are 0·6°. The e.s.d.'s in all bond angles of raffinose are 0·5°.

| | | Glucose moiety | | | | Galactose moiety | |
		α-Melibiose	Raffinose			α-Melibiose	Raffinose
	C(1)–C(2)–C(3)	113·2	110·8		C(1')–C(2')–C(3')	110·7	111·4
	C(2)–C(3)–C(4)	111·4	109·9		C(2')–C(3')–C(4')	109·6	109·9
	C(3)–C(4)–C(5)	109·8	110·5		C(3')–C(4')–C(5')	109·5	107·9
	C(4)–C(5)–O(5)	109·3	110·9		C(4')–C(5')–O(5')	110·6	110·3
	C(5)–O(5)–C(1)	112·4	114·5		C(5')–O(5')–C(1')	112·4	113·2
	O(5)–C(1)–C(2)	110·3	109·8		O(5')–C(1')–C(2')	110·2	110·4
	O(5)–C(1)–O(1)	113·0	112·7		O(5')–C(1')–O(6)	112·2	111·2
	C(2)–C(1)–O(1)	109·1	106·9		C(2')–C(1')–O(6)	108·6	106·8
	C(1)–C(2)–O(2)	111·5	111·8		C(1')–C(2')–O(2')	109·3	111·7
	C(3)–C(2)–O(2)	109·6	112·2		C(3')–C(2')–O(2')	114·6	112·3
	C(2)–C(3)–O(3)	110·6	111·1		C(2')–C(3')–O(3')	112·0	110·2
	C(4)–C(3)–O(3)	109·8	107·3		C(4')–C(3')–O(3')	111·4	108·2
	C(3)–C(4)–O(4)	111·1	111·9		C(3')–C(4')–O(4')	106·4	112·0
	C(5)–C(4)–O(4)	110·4	106·7		C(5')–C(4')–O(4')	111·0	112·1
	C(4)–C(5)–C(6)	115·9	113·8		C(4')–C(5')–C(6')	112·9	113·6
	O(5)–C(5)–C(6)	108·1	107·4		O(5')–C(5')–C(6')	106·1	104·4
					C(5')–C(6')–O(6')	111·1	112·9
Bridge	C(5)–C(6)–O(6)	111·9	108·0		C(1')–O(6)–C(6)	111·5	111·4
	O(5)–C(1)–βO(1)	116·4					
	C(2)–C(1)–βO(1)	111·1					
	O(1)–C(1)–βO(1)	96·1					

Molecular conformation

Endocyclic torsion angles of the glucose and galactose parts of α-melibiose and raffinose (Berman, 1970) are given in Table 9. For comparison the corresponding angles of α-D-glucose (Brown & Levy, 1965) and α-D-galactose (Sheldrick, 1976) are also tabulated.

The smallest values for the torsion angles about the ring bonds in α-melibiose are −46·8 about C(2)–C(3) and −54·0° about C(2')–C(3'); the largest values are 65·3 about C(5)–O(5) and 61·6° about C(5')–O(5'). The mean values for the glucose and galactose units are 55·4 and 57·4° respectively. All torsion angles are within the ranges reported in previous tabulations (Arnott & Scott, 1972).

In comparison with the ring torsion angles of 55°

Table 7. C–O–C *bridge angles* (°) *in oligosaccharides with different types of linkage and* C–O–C *angles in methylglycosides*

E.s.d.'s are in parentheses.

α,α-Trehalose.2H₂O	115·8 (2)	1 → 1	Brown, Rohrer, Berkin, Beevers, Gould & Simpson (1972)
Sucrose	114·3 (8)	1 → 2	Brown & Levy (1973)
1-Kestose	119·4 (3)	1 → 2	Jeffrey & Park (1972)
	116·4 (3)	1 → 2	
Planteose.2H₂O	118·9 (2)	1 → 2	Rohrer (1972)
Raffinose.5H₂O	122·1 (5)	1 → 2	Berman (1970)
Melezitose.1H₂O	116·0	1 → 2	Hirotsu & Shimada (1973)
	116·8	1 → 3	
Cellobiose	116·1 (2)	1 → 4	Chu & Jeffrey (1968)
α-Lactose.1H₂O	117·1 (2)	1 → 4	Fries, Rao & Sundaralingam (1971)
Maltose.1H₂O	117·2 (11)	1 → 4	Quigley, Sarko & Marchessault (1970)
Methyl β-cellobioside–methanol	115·8 (4)	1 → 4	Ham & Williams (1970)
β-Lactose	116·5 (4)	1 → 4	Hirotsu & Shimada (1974)
Aldotriouronic acid.3H₂O	113·8 (4)	1 → 4	Moran & Richards (1973)
Isomaltulose	115·5 (3)	1 → 6	Dreissig & Luger (1973)
α-Melibiose.1H₂O	111·5 (2)	1 → 6	This paper
Planteose.2H₂O	111·2 (2)	1 → 6	Rohrer (1972)
Raffinose.5H₂O	111·4 (5)	1 → 6	Berman (1970)
Methyl α-D-altropyranoside	113·2 (3)		Gatehouse & Poppleton (1971a)
Methyl α-D-galactopyranoside	113·0 (3)		Gatehouse & Poppleton (1971b)
Methyl α-D-glucopyranoside	113·0 (2)		Berman & Kim (1968)
Methyl β-maltopyranoside	113·2 (6)		Chu & Jeffrey (1967)
Methyl α-D-mannopyranoside	113·4		Gatehouse & Poppleton (1970)
Methyl β-D-ribopyranoside	113·8 (2)		James & Stevens (1971)
Methyl β-xyloside	113·4 (3)		Brown, Cox & Llewellyn (1966)

Table 8. *Exocyclic torsion angles* (°) *of* α-*melibiose and raffinose, including the bridge torsion angles*

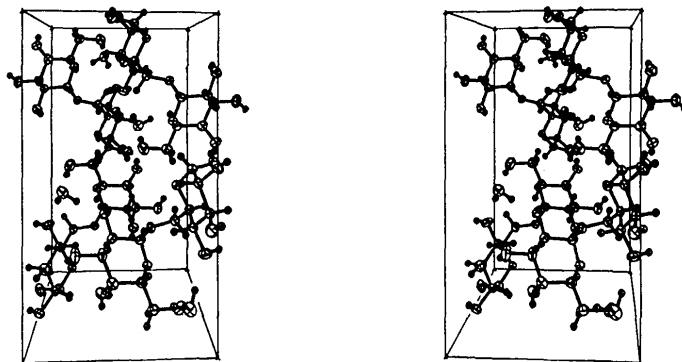|	Glucose moiety			Galactose moiety	
	α-Melibiose	Raffinose		α-Melibiose	Raffinose
O(1)–C(1)–C(2)–O(2)	50·6	59·1	O(6)–C(1')–C(2')–O(2')	61·0	58·9
O(2)–C(2)–C(3)–O(3)	65·6	62·0	O(2')–C(2')–C(3')–O(3')	57·7	61·0
O(3)–C(3)–C(4)–O(4)	−65·2	−67·8	O(3')–C(3')–C(4')–O(4')	58·4	52·5
O(4)–C(4)–C(5)–C(6)	56·7	62·5	O(4')–C(4')–C(5')–C(6')	−58·4	−52·6
O(5)–C(5)–C(6)–O(6)	−63·8	−64·7	O(5')–C(5')–C(6')–O(6')	65·4	172·5
C(4) –C(5)–C(6)–O(6)	59·2	58·5	C(4')–C(5')–C(6')–O(6')	−173·3	−67·4
C(5) –C(6)–O(6)–C(1')	−173·9	−169·6			
O(5')–C(1')–O(6)–C(6)	76·5	71·9			
C(2')–C(1')–O(6)–C(6)	−161·4	−167·6			

Fig. 3. A stereo view of the unit-cell contents of α-melibiose monohydrate as seen along **b**; **c** is down the page.

in cyclohexane the glucose ring shows a greater puckering about C(1)–O(5), C(5)–O(5) and C(4)–C(5) and a smaller puckering about C(1)–C(2), C(2)–C(3) and C(3)–C(4). For the galactose unit the puckering pattern is not identical to that of the glucose moiety. An
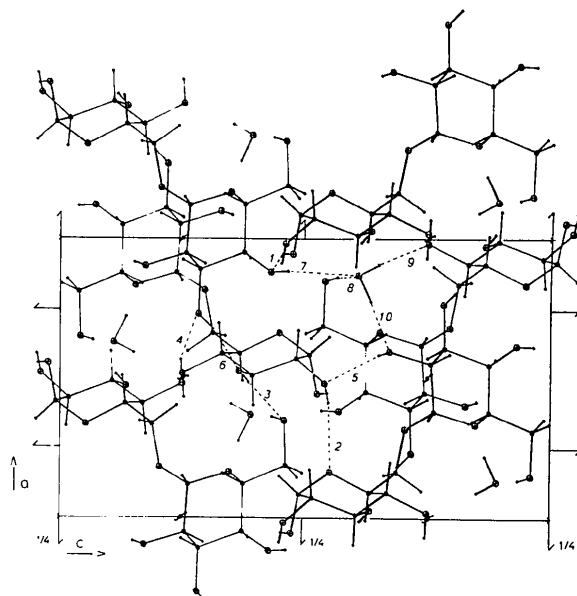

Fig. 4. A view of the molecular packing and hydrogen bonds in α-melibiose monohydrate down the *b* axis. The hydrogen bonds, numbered according to Table 12, are indicated by dashed lines.
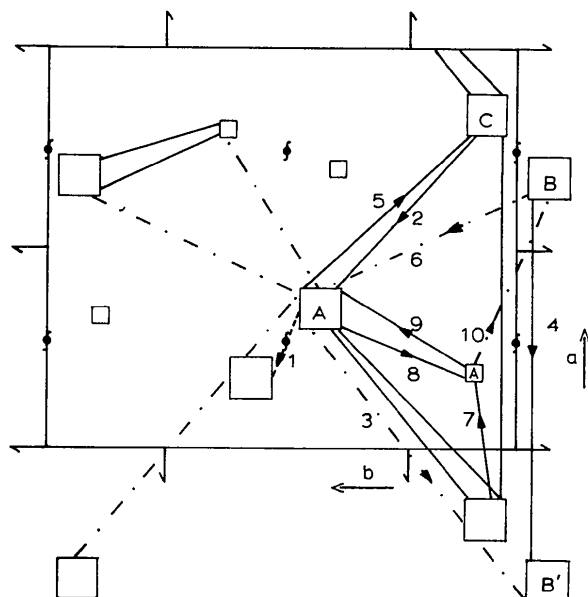

Fig. 5. Schematic diagram representing the network of hydrogen bonds in α-melibiose monohydrate viewed along **c**. The numbering of the hydrogen bonds is according to Table 12. The unit consisting of α-melibiose and water is denoted by two squares, marked *A*, the smaller one referring to the water molecule. ——— indicates the chain along **a**, –·–·–· the chain along **b** and – – – – – depicts the hydrogen bond along **c**.

Table 9. *Ring torsion angles* (°) *in α-melibiose, raffinose, α-D-glucose and α-D-galactose*

Torsion angle $A(1)$–$A(2)$–$A(3)$–$A(4)$ is viewed down $A(2)$–$A(3)$ with a clockwise rotation of $A(1)$ to $A(4)$ taken to be positive.

| | Glucose moiety | | α-D-Glu- |
	α-Melibiose	Raffinose	cose
O(5)–C(1)–C(2)–C(3)	51·1	55·6	54·1
C(1)–C(2)–C(3)–C(4)	−46·8	−53·6	−51·3
C(2)–C(3)–C(4)–C(5)	49·7	52·4	53·3
C(3)–C(4)–C(5)–O(5)	−58·2	−54·3	−57·5
C(4)–C(5)–O(5)–C(1)	65·3	59·1	62·2
C(5)–O(5)–C(1)–C(2)	−61·0	−59·4	−60·9
Average	55·4	55·7	56·6

| | Galactose moiety | | α-D-Gal- |
	α-Melibiose	Raffinose	actose
O(5′)–C(1′)–C(2′)–C(3′)	57·0	53·6	59·1
C(1′)–C(2′)–C(3′)–C(4′)	−54·0	−53·8	−58·6
C(2′)–C(3′)–C(4′)–C(5′)	53·9	56·0	55·7
C(3′)–C(4′)–C(5′)–O(5′)	−57·0	−59·6	−55·8
C(4′)–C(5′)–O(5′)–C(1′)	61·6	62·4	61·5
C(5′)–O(5′)–C(1′)–C(2′)	−60·8	−58·1	−61·4
Average	57·4	57·2	58·7

identical behaviour was found in raffinose (Berman, 1970) in contrast to α-lactose (Fries, Rao & Sundaralingam, 1971) where the puckering patterns are the same for the glucose and galactose units.

Table 8 shows the exocyclic torsion angles in α-melibiose and raffinose (Berman, 1970), including the bridge torsion angles.

The conformation of the exocyclic galactoside C(6′)–O(6′) bond is *gauche–trans*, whereas the conformation of the glucosidic C(6)–O(6) bond, participating in the 1 → 6 link, is *gauche–gauche*. According to Sundaralingam (1968) the *gauche–trans* form is the most favoured form of the non-eclipsing conformations *gauche–trans*, *gauche–gauche* and *trans–gauche*. For 42 known structures the *gauche–trans* form shows a slight preference over the *gauche–gauche* form (Longchambon, Ohannessian, Avenel & Neuman, 1975). The *trans–gauche* form is the least favoured arrangement because of the interaction between O(6) and O(4). This conformation has been observed in only two galactosides *viz.* raffinose (Berman, 1970) and α-D-galactose (Sheldrick, 1976) and in none of the glucosides. However, it should be noted that the *gauche–gauche* form is less likely than the *gauche–trans* form in galactosides owing to the interaction between O(6) and the axially oriented O(4). Therefore the *gauche–trans* form is predominant in galactosides, whereas in glucosides the *gauche–trans* and *gauche–gauche* forms are nearly equally distributed (Longchambon, Ohannessian, Avenel & Neuman, 1975).

The conformation around C(5)–C(6) and C(6)–O(6) in α-melibiose and raffinose (Berman, 1970) is identical (Table 8). However, in the Berman (1970) paper on raffinose the bridge torsion angle C(1′)–O(6), tabulated as 72°, corresponds to the torsion angle O(5′)–C(1′)–O(6)–C(6), whereas according to convention the conformation is characterized by the torsion angle C(2′)–

C(1')–O(6)–C(6). This angle has a value of −167·6° indicating a *trans–gauche* conformation of the C(1')–O(6) bond. Bearing in mind that the conformation around C(5)–C(6) is *gauche–gauche* (Table 8), it follows from Table 10 and Fig. 2 that the best plane of the four atoms constituting the melibiose bridge and C(2) only bisects the mean plane of the glucose ring and not the mean planes of both pyranose rings as was reported in the raffinose paper (Berman, 1970). In α-melibiose the 1 → 6 linkage has the antiperiplanar

Table 10. *Displacements* (Å) *from the least-squares plane calculated for the four atoms constituting the* 1 → 6 *linkage and* C(2) *in α-melibiose and in raffinose*

	α-Melibiose	Raffinose
C(5)	0·059	0·065
C(6)	−0·056	−0·061
O(6)	−0·010	−0·063
C(1')	0·021	0·062
C(2)	−0·013	−0·003
C(4')*	2·016	2·180

* C(4') was excluded from the calculation of the best plane.

Table 11. *Torsion angles* (°) *involving the hydrogen atoms in α-melibiose*

Glucose moiety		Galactose moiety	
H(C1)···H(C2)*	35·0	H(C1')···H(C2')	49·5
H(C2)···H(C3)	−175·0	H(C2')···H(C3')	178·2
H(C3)···H(C4)	−178·3	H(C3')···H(C4')	41·6
H(C4)···H(C5)	−177·4	H(C4')···H(C5')	−51·2
H(C5)···H(C6)	57·2	H(C5')···H(C6')	−172·3
H(C5)···H'(C6)	−56·3	H(C5')···H'(C6')	61·7
H(C1)···H(O1)†	−47·6		
H(C2)···H(O2)	153·8	H(C2') ···H(O2')	166·3
H(C3)···H(O3)	51·2	H(C3')···H(O3')	−175·7
H(C4)···H(O4)	162·2	H(C4') ···H(O4')	−34·0
		H(C6') ···H(O6')	−171·0
		H'(C6')···H(O6')	−43·2

* Refers to the torsion angle H(C1)–C(1)–C(2)–H(C2).
† Refers to the torsion angle H(C1)–C(1)–O(1)–H(O1).

arrangement (torsion angle −173·9°) as in raffinose (Berman, 1970) and planteose (Rohrer, 1972) with torsion angles of − 169·6 and 172·5° respectively, whereas in isomaltulose (Dreissig & Luger, 1973) the torsion angle is +143·5°.

The H atoms on adjacent C atoms of the pyranose systems have the *trans* or *gauche* orientation (Table 11). The preference for the *gauche* conformation of the OH groups with respect to the C–H bonds as previously observed (Fries, Rao & Sundaralingam, 1971) is not confirmed in α-melibiose.

Molecular packing and hydrogen bonding

The molecular packing and hydrogen bonds are shown in Figs. 3 and 4, respectively.

All OH groups participate in intermolecular hydrogen bonding, each, with the exception of O(1)–H, acting as a donor and as an acceptor; the ring O of the glucose moiety is an acceptor and the water molecule twice a donor and acceptor. There is only indirect intramolecular hydrogen bonding *via* the water molecule.

The geometry of the hydrogen bonds with some short intermolecular contacts is summarized in Table 12. The mean O···O distance is 2·788 Å and the spread is from 2·657 to 2·887 Å. The bridge O atom is not involved in hydrogen bonding, although it has a close intermolecular O···O contact of 2·96 Å with O(2). In view of the short intermolecular O···O contact between βO(1) and O(5') it is conjectured that this contact is also a hydrogen bond; thus the eventual loss of lattice energy by α/β disorder might be compensated for. The intriguing observation that accommodation of the β-anomer in the structure occurs without sacrifice in the number of hydrogen bonds was also made in the disordered structure of α-lactose monohydrate (Fries, Rao & Sundaralingam, 1971).

The ten hydrogen bonds constitute an intricate three-dimensional system, in which the water molecule

Table 12. *Geometry of the hydrogen bonds in α-melibiose and some short intermolecular contacts*

No.	Atom j	Atom k	Atom l*	R_{jl}	R_{kj}	R_{kl}	$\angle j$-k-l	Symmetry operation†
1	O(1)	H(O1)	O(4')	2·690 Å	0·941 Å	1·788 Å	159·6°	564·2
2	O(2)	H(O2)	O(5)	2·887	0·939	2·204	128·8	565·3
3	O(3)	H(O3)	O(6')	2·880	0·678	2·203	176·5	655·4
4	O(4)	H(O4)	O(3')	2·762	0·882	1·922	158·6	655·1
5	O(2')	H(O2')	O(2)	2·657	0·851	2·023	130·7	465·3
6	O(3')	H(O3')	O(3)	2·796	0·842	1·973	165·4	545·4
7	O(4')	H(O4')	O(W)	2·852	0·639	2·283	149·5	466·3
8	O(6')	H(O6')	O(W)	2·856	0·983	1·877	173·6	555·1
9	O(W)	H'(OW)	O(4)	2·767	0·972	1·841	158·2	555·1
10	O(W)	H(OW)	O(2')	2·736	1·039	1·736	160·1	555·4

Intermolecular oxygen–oxygen distances less than 3·300 Å

O(1)····O(5)	3·261 Å		O(2)···O(6)	2·965 Å
O(6')···O(2)	3·176		O(3)···O(5')	3·252
βO(1)···O(5')	2·670			

* The symmetry operation is performed on atom *l*.
† The first set of numbers specifies the lattice translations, *e.g.* 564·2 is +*b*–*c* from 555·2. The last digit indicates one of the following symmetry operations: (1) x, y, z; (2) $\frac{1}{2}-x, -y, \frac{1}{2}+z$; (3) $\frac{1}{2}+x, \frac{1}{2}-y, -z$; (4) $-x, \frac{1}{2}+y, \frac{1}{2}-z$.

plays a central part. The hydrogen-bond network is schematically represented in Fig. 5, in which for reasons of clarity the α-melibiose and water molecules are denoted by squares. Two hydrogen bonds (8 and 9) are involved in a type of indirect intramolecular hydrogen bonding, similar to that found in many other oligosaccharides, such as raffinose pentahydrate (Berman, 1970), planteose dihydrate (Rohrer, 1972) and trehalose dihydrate (Brown, Rohrer, Berkin, Beevers, Gould & Simpson, 1972). The water molecule further donates a hydrogen bond (10) to molecule B, related to the unit melibiose + water (A) by the 2_1 axis in the **b** direction. Molecule B back-donates a hydrogen bond (6) to α-melibiose in unit A, thus constituting a double chain in which the donor–acceptor directions are opposite. Molecule A also donates a hydrogen bond (3) to molecule B', related to B by the **a** translation and related to A by the 2_1 axis in the **b** direction, thus intersecting the above described system at the common molecule. The hydrogen bond (4) between the molecules B and B' completes this part of the scheme. Another branch of the hydrogen-bond scheme is formed by means of the 2_1 axis along **a**, interrelating molecules A and C through two hydrogen bonds (2 and 5) in opposite directions. The hydrogen-bond chain along **a** is completed by a fourth hydrogen bond (7) of water linking molecule A to the chain of water molecules in that direction. The last hydrogen bond (1) involves α-melibiose molecules related by the 2_1 axis along **c**.

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