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CRYSTAL AND MOLECULAR STRUCTURE OF 1′,2:4,6-DI-*O*-ISOPROPYLIDENESUCROSE TETRA-ACETATE: A UNIQUE EXAMPLE OF A D-FRUCTOFURANOSYL RING IN A SUCROSE DERIVATIVE PUCKERED AT OXYGEN

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ABSTRACT

Crystals of the title compound are monoclinic, space group $P2_1$, with cell dimensions: $a = 11.260(5)$, $b = 8.841(7)$, $c = 15.605(6)$ Å, $\beta = 102.25(7)°$, and $Z = 2$; 2888 independent reflections, measured on a diffractometer, have been refined to $R = 0.055$. In the molecule, the pyranosyl ring has the expected $^4C_1$ conformation. However, the conformation of the D-fructofuranosyl ring is unexpected [$P = 277.1°$] with O-2′ *exo* to C-6′ furthest from the ring plane. The reason for this conformation, previously unknown in sucrose-related molecules, is not readily apparent from the crystal structure. The eight-membered ring, however, has the expected boat-chair conformation.

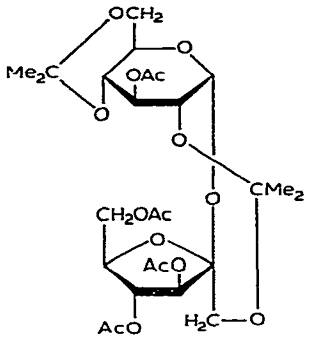
INTRODUCTION

1′,2:4,6-Di-*O*-isopropylidenesucrose tetra-acetate (**1**) is an important synthetic intermediate[1–3], and its structure has been established by chemical transformations and by ^{1}H-n.m.r. spectroscopy. Compound **1** probably constitutes the first example in carbohydrate chemistry of an eight-membered cyclic acetal (1′,2-group). Because of this additional linkage between the D-glucopyranosyl and D-fructofuranosyl residues, it was decided to determine the structure of **1** by single-crystal X-ray diffraction.

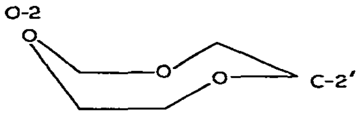
Compound **1** has been synthesised in an improved yield, and without recourse to column chromatography.

EXPERIMENTAL

*1′,2:4,6-Di-*O*-isopropylidenesucrose tetra-acetate*[1] (**1**). — A solution of sucrose (25.0 g) in anhydrous *N,N*-dimethylformamide (1.2 litres) was treated with 2,2-



1



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dimethoxypropane (150 ml) in the presence of dry toluene-*p*-sulphonic acid (2 0 g) at 40° for 1 5 h The solution was then neutralised with Amberlite IR-45 (HO^-) resin, filtered, and concentrated The syrupy residue was treated with acetic anhydride (150 ml) and pyridine (400 ml) T l c (ether–light petroleum, 6 1) showed a major product that was coincident with an authentic sample[1] The reaction mixture was concentrated by co-distillation with toluene, to afford a syrup Crystallisation from ether–light petroleum gave **1** (16 5 g, 38 3%) The physical constants and ^{1}H-n m r spectrum of **1** were identical with those of an authentic sample

Crystal data $C_{26}H_{38}O_{15}$, M = 590 3, a = 11 260(5), b = 8 841(7), c = 15 605(6) Å, β = 102 25(7)°, U = 1518 1 Å^3, Z = 2, d_m = 1 30(3), d_c = 1 29, space group $P2_1$ from systematic absences 0k0, k = 2n + 1, and the successful structure determination A crystal of approximate size 0 3 × 0 3 × 0 3 mm was mounted on an Enraf–Nonius CAD-4 diffractometer, and 3010 independent reflections ($2\theta < 140°$) were measured by the $\theta/2\theta$ scan technique, using CuKα radiation. The intensity of standard reflections dropped by 30% during the data collection, and a linear correction factor was therefore applied to the intensities of all reflections, 2888 reflections with $I > \sigma(I)$ were used in subsequent calculations Absorption and extinction corrections were not applied

STRUCTURE DETERMINATION AND REFINEMENT

The structure was determined by direct methods using the "SHELX-76" suite of programmes[4] The carbon and oxygen atoms were then refined anisotropically. The hydrogen atoms were placed in the appropriate tetrahedral positions The methyl groups were refined as rigid groups with free rotation allowed about the C–C bonds Each methyl group was given an individual, refineable thermal parameter Unit weights were used and the final R value was 0 055 The atomic scattering factors for C, O, and H atoms were taken from International Tables of X-ray Crystallography[5], and computation was done with the programmes of Sheldrick[4] on the CDC 7600 of the University of London Computer Centre In the final cycle

TABLE I

POSITIONAL PARAMETERS ($\times$ 10^4) FOR **1** WITH ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Atom	x	y	z	*Atom*	x	y	z
O-1	−3327(3)	5052(4)	7384(2)	O-5	−2340(3)	4856(4)	8842(2)
C-1	−2754(4)	5876(6)	8150(3)	O-6	−0123(3)	1804(4)	9257(2)
O-2	−2062(3)	7632(3)	7129(2)	C-7	0906(5)	2537[a]	9012(3)
C-2	−1683(4)	6783(6)	7922(3)	C-8	1731(5)	3313(9)	9779(4)
C-3	−0699(4)	5729(6)	7738(3)	C-9	1537(7)	1248(8)	8625(5)
O-3	0341(3)	6663(4)	7706(2)	C-10	0863(6)	6524(8)	7001(4)
C-4	−0350(4)	4658(6)	8496(3)	C-11	0476(5)	5729(8)	6396(4)
O-4	0488(3)	3553(5)	8298(2)	C-12	1973(7)	7519(10)	7122(6)
C-5	−1457(4)	3815(6)	8663(3)	C-13	−2909(5)	8844(6)	7126(4)
C-6	−1032(5)	2810(7)	9453(4)	C-14	−2544(6)	9901(7)	7914(5)
O-1′	−4060(3)	8246(4)	7217(2)	C-15	−2963(6)	9621(8)	6251(4)
C-1′	−4574(5)	7132(7)	6586(4)	C-16	−3480(6)	4265(9)	5365(4)
C-2′	−4521(4)	5525(7)	6963(3)	O-17	−3849(5)	5396(7)	5003(3)
O-2′	−5345(3)	5409(4)	7535(2)	C-18	−2372(7)	3386(11)	5252(5)
C-3′	−4989(4)	4375(6)	6226(3)	C-19	−7722(6)	2166(10)	6169(5)
O-3′	−4026(3)	3563(4)	5965(2)	O-20	−7450(5)	1240(7)	6703(4)
C-4′	−5771(4)	3260(7)	6611(3)	C-21	−8919(6)	2352(12)	5467(6)
O-4′	−6960(3)	3335(6)	6034(2)	C-22	−4468(6)	2752(9)	9758(4)
C-5′	−5794(5)	3876(7)	7522(4)	O-23	−3800(4)	1741(6)	9680(3)
C-6′	−5052(5)	2888(7)	8211(3)	C-24	−4652(7)	3417(12)	10608(4)
O-6′	−5161(3)	3472(5)	9050(2)				

[a] Parameter fixed

of refinement, all shifts were less than 0.2σ and the final, difference Fourier map showed no significant features.

Final atomic parameters are given in Table I, and bond lengths and angles in Table II. The anisotropic thermal parameters, hydrogen positions, and structure factors are deposited with, and can be obtained from, Elsevier Scientific Publishing Company, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/105/*Carbohydr. Res.*, 71 (1979) 35–42.

DISCUSSION

Fig. 1 shows the numbering system used for **1**. This corresponds to the convention for sucrose, in that the atoms in the D-glucopyranosyl moiety are unprimed and those in the D-fructofuranosyl moiety are primed. Torsion angles for the four rings in the molecule are shown in Table III. Those for the α-D-glucopyranosyl unit of the molecule, which has the normal $^4C_1$ conformation, are unexceptional. The conformation of the other six-membered ring forming the cyclic acetal (sharing C-4 and C-5 with the α-D-glucopyranosyl ring) is equivalent, the two rings having parallel chair conformations.

TABLE II

INTERATOMIC DISTANCES (ÅNGSTROMS) AND ANGLES (DEGREES)[a]

O-1–C-2′	1 428(5)	C-1–O-1–C-2′	116 7(4)	O-3′–C-3′–C-4′	108 9(4)
C-1–O-1	1 431(5)	O-1–C-1–C-2	107 8(4)	C-3′–O-3′–C-16	116 3(4)
C-1–C-2	1 551(7)	O-1–C-1–O-5	109 4(4)	C-3′–C-4′–O-4′	105 1(4)
C-1–O-5	1 408(6)	C-2–C-1–O-5	111 1(3)	C-3′–C-4′–C-5′	106 2(4)
O-2–C-2	1 433(5)	C-2–O-2–C-13	118 1(4)	O-4′–C-4′–C-5′	111 5(4)
O-2–C-13	1 434(6)	C-1–C-2–O-2	111 4(3)	C-4′–O-4′–C-19	113 0(4)
C-2–C-3	1 521(7)	C-1–C-2–C-3	111 1(4)	O-2′–C-5′–C-4′	105 9(5)
C-3–O-3	1 442(6)	O-2–C-2–C-3	104 7(4)	O-2′–C-5′–C-6′	113 4(4)
C-3–C-4	1 501(7)	C-2–C-3–O-3	106 6(4)	C-4′–C-5′–C-6′	110 1(5)
O-3–C-10	1 358(8)	C-2–C-3–C-4	108 5(4)	C-5′–C-6′–O-6′	107 5(5)
C-4–O-4	1 437(6)	O-3–C-3–C-4	108 0(3)	C-6′–O-6′–C-22	115 1(5)
C-4–C-5	1 520(7)	C-3–O-3–C-10	118 0(4)	O-4–C-7–O-6	109 7(4)
O-4–C-7	1 431(5)	C-3–C-4–O-4	109 5(4)	O-4–C-7–C-8	112 1(3)
O-5–C-5	1 427(6)	C-3–C-4–C-5	110 8(3)	O-4–C-7–C-9	105 3(4)
C-5–C-6	1 516(8)	O-4–C-4–C-5	107 6(4)	O-6–C-7–C-8	112 6(4)
C-6–O-6	1 437(7)	C-4–O-4–C-7	112 5(4)	O-6–C-7–C-9	103 6(3)
O-6–C-7	1 448(6)	C-1–O-5–C-5	113 1(4)	C-8–C-7–C-9	113 0(5)
O-1′–C-1′	1 426(7)	C-4–C-5–O-5	110 4(4)	O-3–C-10–O-11	123 4(6)
O-1′–C-13	1 434(7)	C-4–C-5–C-6	107 3(4)	O-3–C-10–C-12	109 6(6)
C-1′–C-2′	1 533(9)	O-5–C-5–C-6	109 2(4)	C-11–C-10–C-12	127 0(7)
C-2′–O-2′	1 423(6)	C-5–C-6–O-6	107 7(5)	O-2–C-13–O-1′	109 8(4)
C-2′–C-3′	1 541(7)	C-6–O-6–C-7	115 2(4)	O-2–C-13–C-14	112 9(4)
O-2 –C-5	1 445(7)	C-1′–O 1′–C-13	115 4(4)	O-2–C-13–C-15	103 9(4)
C-3′–O-3′	1 430(6)	O-1′–C-1′–C-2′	113 5(5)	O-1′–C-13–C-14	103 9(5)
C-3′–C-′	1 527(8)	O-1 –C-2′–C-1′	113 8(4)	O-1′–C-13–C-15	113 0(4)
O-3′–C-16	1 373(8)	O-1′–C-2′–O-2	111 4(4)	C-14–C-13–C-15	113 5(5)
C-4′–O-4′	1 448(5)	O-1′–C-2 –C-3′	106 9(4)	O-3′–C-16–O-17	123 1(7)
C-4′–C-5′	1 528(8)	C-1′–C-2′–O-2′	109 3(4)	O-3′–C-16–C-18	110 3(6)
O-4′–C-19	1 388(9)	C-1′–C-2 –C-3′	110 3(4)	O-17–C-16–C-18	126 5(7)
C-5′–C-6	1 495(8)	O-2 –C-2 –C-3′	104 8(4)	O-4′–C-19–O-20	123 8(6)
C-6′–O-6	1 437(6)	C-2 –O-2′–C-5′	109 3(4)	O-4′–C-19–C-21	106 6(6)
O-6′–C-22	1 367(7)	C-2 –C-3′–O-3′	112 6(3)	O-20–C-19–C-21	129 6(8)
C-7–C-8	1 515(7)	C-2′–C-3′–C-4′	105 5(4)	O-6′–C-22–O-23	122 2(6)
C-7–C-9	1 533(8)			O-6′–C-22–C-24	111 6(6)
C-10–O-11	1 183(8)			O-23–C-22–C 24	126 2(6)
C-10–C-12	1 506(11)				
C-13–C-14	1 530(9)				
C-13–C-15	1 518(9)				
C-16–O-17	1 180(9)				
C-16–C-18	1 511(11)				
C-19–O-20	1 162(10)				
C-19–C-21	1 555(10)				
C-22–O-23	1 191(9)				
C-22–C-24	1 505(10)				

[a]Standard deviations in parentheses

The conformation of the eight-membered ring is a boat-chair Torsion angles (Table III) are compared with those found for this conformation *via* strain-energy calculations[6 7] The mirror plane located in this conformation passes through C-2′ and O-2, with the latter as the boat This boat-chair conformation has the lowest

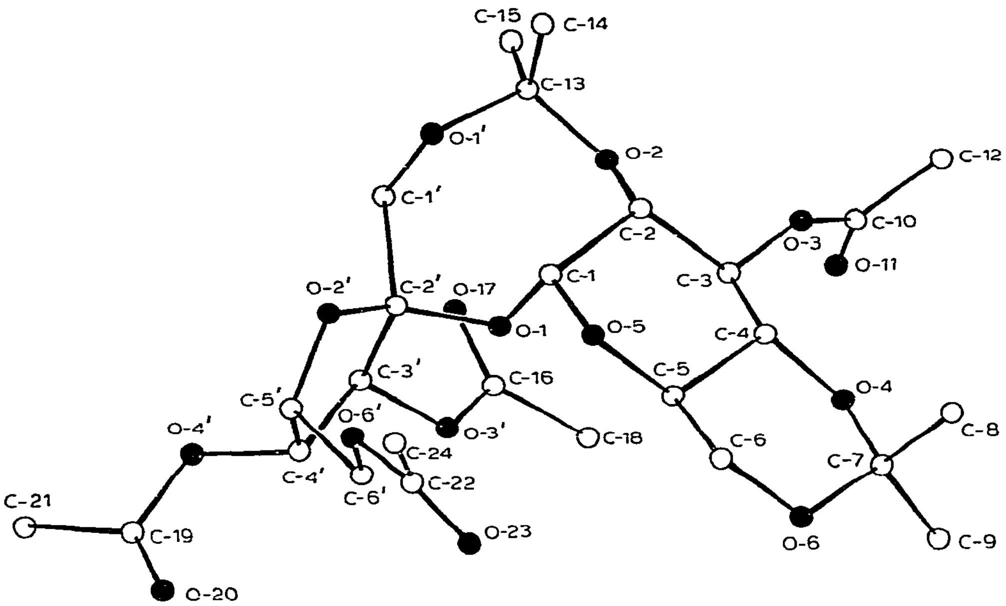

Fig 1 Numbering system used for compound **1**

energy of all of the eight-membered ring conformations of cyclo-octane[6] Clearly, the conformational analysis of the 1,3,6-trioxo analogue might give a different series of energy preferences, because of the smaller size of oxygen and the lack of many H H repulsions Anet[7] has suggested an interpretation of ^{1}H-n m r results for 1,3,6-trioxocane in terms of the boat-chair conformation In **1**, we have this conformation with O-2 as the boat and C-2' as the chair end (**2**) However, in spite of the replacement of three CH_2-groups by oxygen, the conformation of the twist boat is very close to that predicted by strain-energy calculations (Table III)

The geometry of the D-fructofuranosyl ring is compared (Table III) with values for other sucrose-type molecules which have been investigated by X-ray diffraction The conformation of the ring is analysed in the way suggested by Altona and Sundaralingham[14] All examples prior to the present work have P values[14] close to 0 or 180°, with C-3' and C-4' furthest from the ring plane* This is not the case in the present molecule, which has O-2' and C-2' furthest from the plane Least-squares calculations on C-3', C-4', and C-5' show that O-2' is 0 34 Å *exo* to C-6' and C-2' is 0 10 Å *endo* to C-6' (Table IV) The conformation of the present ring can therefore be called E_o with a slight distortion towards $_oT^2$

The geometry is unique among compounds containing the sucrose moiety However, one precedent for an unusual conformation is found in 2,6-anhydro-β-

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*These $_3T^4$ conformations are equivalent to the $_2T^3$ conformations of Ref 14, noting that the furanoid rings are numbered O-1', C-1', C-2', C-3', and C-4', compared to our fructofuranose numbering-scheme O 2', C-2', C-3', C-4', and C-5' Then, in **1**, the conformation $_oT^2$ corresponds to a $_oT^1$ conformation The E_o conformation is named the same for both types of ring

TABLE III

TORSION ANGLES (DEGREES) FOR **1**

(*a*) α-D-*Glucopyranosyl ring*

C-5–O-5–C-1–C-2	−57 5
O-5–C-1–C-2–C-3	53 9
C-1–C-2–C-3–C-4	−52 8
C-2–C-3–C-4–C-5	55 6
C-3–C-4–C-5–O-5	−59 0
C-4–C-5–O-5–C-1	60 1

(*b*) *Six-membered cyclic acetal (4,6-ring)*

O-6–C-6–C-5–C-4	−58 9
C-6–C-5–C-4–O-4	62 5
C-5–C-4–O-4–C-7	−62 4
C-4–O-4–C-7–O-6	56 5
O-4–C-7–O-6–C-6	−54 3
C-7–O-6–C-6–C-5	56 5

(*c*) *Eight-membered cyclic acetal (1′,2-ring)*

	In **1**	*Calc*[6]
O-2–C-2–C-1–O-1	50 3	44 7
C-2–C-1–O-1–C-2′	−111 1	−102 2
C-1–O-1–C-2′–C-1′	63 9	65 0
O-1–C-2′–C-1′–O-1′	−55 0	−65 0
C-2 –C-1 –O-1′–C-13	107 2	102 2
C-1′–O-1′–C-13–O-2	−55 0	−44 7
O-1′–C-13–O-2–C-2	−66 7	−65 0
C-13–O-2–C-2–C-1	66 0	65 0

(*d*) β-D-*Fructofuranosyl ring*[a]

	1	*1-Kestose*[8]	*Planteose*[9]	*Raffinose*[10]	*Sucrose*[11,12]	*Melezitose*[16] [b]
C-3′–C-2′–O-2′–C-5	31 5	−3 7	15 9	−9 4	14 6	8 5
C-2′–O-2′–C-5′–C-4′	−29 2	−15 2	9 0	−16 2	8 1	16 6
O-2′–C-5′–C-4 –C-3′	14 3	28 0	−29 8	33 5	−27 2	−34 1
C-5 –C-4′–C-3′–C-2	3 9	−29 3	38 9	−38 6	35 0	38 2
C-4′–C-3 –C-2 –O-2′	−21 0	21 1	−34 5	30 6	−31 2	−29 5
P[14]	277 1	191 5	−5 5	184 7	−5 6	6 2
Conformation	E_0	E_4 or $_4T^3$	$_3T^4$	$^4T_3$	$_3T^4$	$^4T_3$

(*e*) *Glycosidic linkage between five- and six-membered rings*

	Reference					
	1	*8*	*9*	*10*	*11, 12*	*16*
O-1–C-1–C-2–C-3	−65 9	−72 3	−62 6	−66 9	−67 7	−57 9
C-2–C-1–O-1–C-2′	−111 1	−152 9	−130 5	−157 5	−129 3	−142 1
C-1–O-1–C-2′–C-3′	−174 1	177 4	−141 5	−105 5	−159 8	−145 8
O-1–C-2′–C-3′–C-4′	97 3	140 8	85 1	90 0	87 6	89 3
O-1–C-2′–C-3′–O-3′	−21 3	20 5	−39 6	−32 5	−38 7	−27 9

[a] Stachyose[13] has the $_3T^4$ conformation, but torsion angles are not available [b] There is another crystal form of melezitose[17], this has the E^3 conformation

TABLE IV

DISTANCES (Å) OF ATOMS FROM THE C-3′, C-4′, C-5′ PLANE

C-2′ 0 10, O-2′ −0 34, C-1′ −0 84, O-1 1 48, O-3′ 1 11, C-6′ 1 33, O-4′ −1 24

D-fructofuranose[15], in which C-3′ and C-4′ are both in *exo* positions (with respect to C-6′), but this is due to the fact that the furanosyl ring is part of a bicyclic system It is a conformation not as unexpected as the one found in the present molecule

The cyclic acetal (1′,2) linkage between the D-glucopyranosyl and D-fructofuranosyl rings is characterised by the torsion angles shown in Table III It is apparent that the angles in **1** are very close to those in sucrose, indeed, more so than for the majority of other molecules Thus, it is apparent that the formation of the second linkage between these two rings, *via* C-1′, O-1′, C-13, and O-2, has made little difference to the spatial relationship between the two rings Sucrose, of course, is somewhat special, in that there is an intramolecular hydrogen bond between O-6′ and O-5, and another between O-1′ and O-2

It remains to consider the unusual conformation of the D-fructofuranosyl ring Clearly, a conformation in which the oxygen remains in the ring plane and carbon atoms are puckered is the most likely on the basis of substituent interactions As O-2′ has no substituents, it is the most likely atom to remain in the plane In all seven examples (Table III), we find that C-3′ and C-4′ are the atoms most puckered from the ring plane There are clearly three possible causes, not necessarily independent, for the unusual conformation of **1** (*a*) the acetate groups, (*b*) the eight-membered ring formation, and (*c*) intermolecular forces However, there seems to be no evidence in favour of any of these explanations Of the acetates, only that on C-3′ (see Fig 1) appears close to any groups in the rest of the molecule We also note that the C-3′–O-3′–C-16–O-17 torsion angle is −8 0°, whereas the equivalent angles of the other three acetates are all less than 3 6°, there does not seem to be any good reason for this, as O-17 and C-18 are also far away from other atoms The only close contacts involving this acetate group are the unexceptional O-3′ O-1 2 55, and C-16 O-1′ 3 20 Å Indeed, we find that the O-1–C-2′–C-3′–O-3′ torsion angle is quite small compared to that found in the other molecules in Table III, suggesting that the steric effects involving this acetate group are unimportant C-6′ O-1 is 3 18 Å, but again this is not unreasonable The formation of the eight-membered ring has also not led to any awkward steric effects The ring formation ensures that C-2–C-1–O-1–C-2′ is smaller than other examples, but this can have little effect on the geometry of the five-membered ring A study of intermolecular distances likewise shows no obvious reasons for the unusual geometry Unlike other examples, **1** contains no molecular hydrogen bonds that could cause the surprising conformation Clearly, it would be necessary to determine the crystal structures of other related acetate derivatives before deciding on the reason for the unusual conformation of the present compound

An analogy could be drawn with the furanoid rings of nucleosides, where structures have been determined by X-ray crystallography Of these, nearly all have P ~ 0 or 180°, *i e*, with oxygen in the ring plane There are a few exceptions (for example, those listed by Narayanan and Berman[18]) with P ~ 90°, for the majority of such compounds, however, there is no obvious reason for the unusual conformation

The bond length and angles in **1** show no unusual features It is noticeable that C-1–O-5 at 1.408(6) Å is the shortest C–O bond. This is often found and has been shown to be consistent with molecular orbital calculations[19].

It is of interest to mention here the selective de-esterification reaction of **1**, in which the reaction occurs predominantly at the D-fructofuranosyl moiety[2] This can be attributed, in addition to the steric factors, to the unusual conformation ($E_0 \rightarrow {}_0T^2$) of the D-fructofuranosyl ring In view of the rigidity of the molecule, it is likely that the same conformation would exist in solution

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REFERENCES

1 R KHAN AND K S MUFTI, *Carbohydr Res* , 43 (1975) 247–253
2 R. KHAN, M R. JENNER, AND H LINDSETH, *Carbohydr Res* , 65 (1978) 99–108
3 R KHAN AND H LINDSETH, *Carbohydr Res* , 71 (1979) 327–330
4 G M SHELDRICK, University of Cambridge, 1976, SHELX-76
5 International Tables for X-Ray Crystallography, Vol IV, Kynoch Press, Birmingham, 1975
6 J B HENDRICKSON, *J Am Chem Soc* , 89 (1967) 7036–7043
7 F A L ANET, *Fortschr Chem Forsch* , 45 (1974) 169–220
8 G A. JEFFREY AND Y. J PARK, *Acta Crystallogr* , *Sect B*, 28 (1972) 257–267
9 D C ROHRER, *Acta Crystallogr* , *Sect B*, 28 (1972) 425–433
10 H M BERMAN, *Acta Crystallogr* , *Sect B*, 26 (1970) 290–299
11 G M BROWN AND H A LEVY, *Acta Crystallogr* , *Sect B*, 29 (1973) 790–797
12 J. C. HANSON, L C SIEKER, AND L H JENSEN, *Acta Crystallogr* , *Sect B*, 29 (1973) 797–808
13 R D GILARDI AND J L FLIPPEN, *J Am Chem Soc* , 97 (1975) 6264–6266
14 C ALTONA AND M SUNDARALINGHAM, *J Am Chem Soc* , 94 (1972) 8205–8212
15 W. DREISSIG AND P LUGER, *Acta Crystallogr* , *Sect B*, 29 (1973) 1409–1416
16 D AVENEL, A NEUMAN, AND H GILLIER-PANDRAUD, *Acta Crystallogr* , *Sect B*, 32 (1976) 2598–2605
17 K HIROTSU AND A SHIMADA, *Chem Lett* , (1973) 83–84
18 P NARAYANAN AND H. M BERMAN, *Carbohydr Res* , 44 (1975) 169–180
19 G A JEFFREY, J A POPLE, AND L RADOM, *Carbohydr Res* , 38 (1974) 81–95