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RELATIONSHIP BETWEEN THE STRUCTURE AND THE PROPERTIES OF CARBOHYDRATES IN AQUEOUS SOLUTIONS*: SWEETNESS OF CHLORINATED SUGARS

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ABSTRACT

The structural basis of the sweet taste of D-galactose, D-glucose, D-mannose, sucrose, and some of their chlorinated derivatives has been derived from an interpretation of their F.t.-i.r. spectra. AH–B glucophores are proposed in the light of the observed OH vibrations, and an explanation of the differences in sweetness of the monosaccharides is proposed. The hydrophobic character of the CH_2Cl, "γ" centre in the tripartite template does not seem to play the same role in monosaccharides and 4,1′,6′-trichloro-4,1′,6′-trideoxy-*galacto*-sucrose. The enhancement of sweetness in the disaccharide derivative is due to the enhanced hydrophobicity of the CH_2Cl groups as well as to specific interactions with water. A sharp i.r. absorption characteristic of free hydroxyl is found in the spectra of most of the very sweet polyhydroxy compounds.

INTRODUCTION

The recent discovery[2,3] of the enhanced sweetness of chlorodeoxy derivatives of sucrose, especially 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (4,1′,6′-trichloro-4,1′,6′-trideoxy-*galacto*-sucrose) and 4,6,1′,6′-tetrachloro-4,6,1′,6′-tetradeoxy-*galacto*-sucrose, raised the question of the structure–sweetness enhancement relationship for chlorodeoxy sugars. This question was partially answered by the synthesis and sensory evaluation of a range of chlorodeoxy derivatives of sucrose and *galacto*-sucrose. Tripartite glycophores were proposed[3] according to the theories[4,5] of sweetness for carbohydrate derivatives.

The same theories[4,5] were applied[6] to interpret the taste of chlorodeoxy

*Part III. For Part II, see ref. 1.

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derivatives of monosaccharides, their alditols, trehalose, and maltose. Although AH–B hydrogen-bonding to the receptor site seems unquestionable, the role of the chlorine substituent as a "γ" lipophilic centre in the enhancement of the sweetness does not emerge clearly from sensory analysis[6]. Recently, we interpreted[1] the sweetness of D-fructose, D-glucose, and sucrose by reference to their interactions with water. The hydrophobic effect of the "γ" centre plays a major role in stabilising the AH···B hydrogen bond between the sweetener and the receptor site and the mobility of water could extend the duration of the sweet taste sensation.

However, in order for there to be a specific effect of the "γ" unit on the AH···B bond, favouring the resonance between AH···B and A^-···$H\text{-}B^+$, the AH donor and the AH–B pair have to be unique; however, in some sugars, more than one pair is possible. Some hydroxyl groups are sometimes excluded[7] from the glucophore because they may be engaged in hydrogen bonding with the ring oxygen. I.r. spectra have been used[8] to interpret the differences in sweetness between sucrose and *galacto*-sucrose. Whereas the i.r. spectrum of sucrose shows a strong vibration at 3560 cm^{-1} characteristic of a free hydroxyl group and assigned to the equatorial HO-4, no such vibration is seen in the i.r. spectrum of *galacto*-sucrose. The relationships between hydrogen bonding and the sweetness of D-fructose and L-sorbose were derived[9] from their Raman and i.r. spectra.

In order to interpret the differences in the sweetness of chlorodeoxy sugars, we have studied their F.t.-i.r. spectra in the region 2800–3800 cm^{-1} for the solid forms and for aqueous solutions.

EXPERIMENTAL

The sugars studied were commercially available or synthesised (chlorodeoxy derivatives) according to methods previously[6,10] reported.

F.t.-i.r. spectra were recorded with a Nicolet Fourier-Transform Infrared spectrometer Model 7199 for KBr pellets for solid samples, and between AgCl windows for aqueous solutions. Wave numbers are accurate to within ± 2 cm^{-1}.

RESULTS AND DISCUSSION

The F.t.-i.r. spectra of α-D-glucose, α-D-galactose, α-D-mannose, sucrose, and their chlorodeoxy derivatives, in the solid state and in aqueous solution, are shown in Figs. 1–4. The region (3800–2800 cm^{-1}) explored is characteristic of C-H and O-H stretching. The observed bands are listed in Table I for α-D-glucopyranose and 6-chloro-6-deoxy-D-glucose, in Table II for α-D-galactose and 6-chloro-6-deoxy-D-galactose, in Table III for α-D-mannose and 6-chloro-6-deoxy-D-mannose, and in Table IV for sucrose and 4,1′,6′-trichloro-4,1′,6′-trideoxy-*galacto*-sucrose (TGS). Assignments of the observed frequencies are proposed. Hydroxyl vibrations are broad in aqueous solutions because of hydrogen bonding.

Hydroxyl vibrations. — The only solid samples which showed strong, sharp

TABLE I

F.T.-I.R. BANDS[a] FOR α-D-GLUCOSE AND 6-CHLORO-6-DEOXY-D-GLUCOSE

α-D-Glucose						*6-Chloro-6-deoxy-D-glucose*		
Solid			*Aqueous solution*			*Solid*		
ν(cm⁻¹)	*I*	*Assignment*	*ν(cm⁻¹)*	*I*	*Assignment*	*ν(cm⁻¹)*	*I*	*Assignment*
			3600	shl,br	H_2O			
						3435	s,br	ν(O-3-H)
3410	s	ν(O-3-H) and ν(O-6-H)						
			3400	s,br	ν(O-H)			
						3390	vs,br	ν(O-4-H) and ν(O-2-H)
3350	shl,s	ν(O-4-H)						
						3335	shl,s	ν(O-1-H)
3310	br,s	ν(O-2-H)						
3320	shl,br	ν(O-1-H)						
			3050	s,br	ν(O-H)			
						3025	vw	—
						2975	m,sh	ν_s(C-H-6)
2945	m,sh	ν_s(C-6-H)						
						2940	m,sh	ν_a(C-H-6)
2913	m,sh	ν_a(C-6-H)						
						2928	m,sh	ν(C-H)
						2905	shl,w	ν(C-H)
2892	m,sh	ν(C-H)						
2878	w	ν(C-H)						
						2855	shl,br	—
2850	vw	—						

[a]Key: I, intensity; s, strong; m, medium; w, weak; sh, sharp; br, broad; shl, shoulder; v, very.

absorptions typical of free hydroxyl groups were sucrose and TGS. The i.r. spectra of crystalline monosaccharides do not contain bands characteristic of free hydroxyl groups[11]. These sharp vibrations (at 3565 cm^{-1} for sucrose and 3460 cm^{-1} for TGS) correspond to hydroxyl groups that do not take part in the hydrogen bonding in the crystal.

The proposed assignments are based on literature[12–14] data for hydrogen bonds in the crystalline forms of the sugars studied. Likewise, correlations between hydrogen-bond distances in the crystal and vibrational properties (frequencies, intensities, shifts) of OH stretchings were taken into account. Although the O···O distance is not decisive in determining the hydrogen-bond interaction, it could be taken as a reference mark to differentiate the OH vibrations. Moreover, shifts in frequencies may be observed for hydrogen-bonded hydroxyl groups. In general, free-OH stretching occurs at a frequency higher than that of bonded-OH. However, increased strength of hydrogen bonding leads to increased constraint and may give rise to absorption at higher frequency because of a need of a higher energy for OH to vibrate. Hence, there are no definite rules that govern hydrogen bonding.

TABLE II

F.T.-I.R. SPECTRA BANDS[a] FOR α-D-GALACTOSE AND 6-CHLORO-6-DEOXY-D-GALACTOSE

α-D-Galactose						*6-Chloro-6-deoxy-D-galactose*					
Solid			*Aqueous solution*			*Solid*			*Aqueous solution*		
ν(cm⁻¹)	*I*	*Assignment*	*ν(cm⁻¹)*	*I*	*Assignment*	*ν(cm⁻¹)*	*I*	*Assignment*	*ν(cm⁻¹)*	*I*	*Assignment*
			3600	s,br	ν(O-H),H_2O						
						3566	sh,s	ν(O-4-H)	3570	br,s	ν(O-H)
3490	shl,m	ν(O-6-H)									
						3495	sh,s	ν(O-2-H)			
						3435	s	ν(O-3-H)			
3400	s,sh	ν(O-2-H)	3400	vbr,s	ν(O-H)						
						3390	s,br	ν(O-1-H)			
						3350	shl,br	bound OH			
3214	s	ν(O-3-H)									
						3200	shl,br	bound OH			
									3195	br,s	ν(O-H)
3136	s	ν(O-1-H), ν(O-4-H)									
			3100	br,s	ν(O-H)						
						3012	w	—			
						2990	vw	—			
2972	w	—	2972	shl	—						
						2966	w,sh	ν(C-6-H)			
						2947	m,sh				
2940	m,sh	ν(C-6-H)							2940	w,br	ν(C-6-H)
						2935	vw	ν(C-H)			
2918	w,sh	ν(C-H)				2915	m,sh	ν(C-H)			
									2900	vw	ν(C-H)
2876	vw	ν(C-H)									
						2850	w	ν(C-H)			

[a]See Table I.

TABLE III

F.T.-I.R. SPECTRA BANDS[a] FOR α-D-MANNOSE AND 6-CHLORO-6-DEOXY-D-GALACTOSE

α-D-Mannose						*6-Chloro-6-deoxy-D-galactose*					
Solid			*Aqueous solution*			*Solid*			*Aqueous solution*		
$\nu(cm^{-1})$	*I*	*Assignment*	$\nu(cm^{-1})$	*I*	*Assignment*	$\nu(cm^{-1})$	*I*	*Assignment*	$\nu(cm^{-1})$	*I*	*Assignment*
									3640	s	ν(O-H),H_2O
			3620	shl	H_2O						
3500	shl	ν(O-6-H)									
						3490	s	ν(O-2-H)			
3430	br,s	ν(O-3-H)									
						3460	shl	ν(O-H)			
			3380	br,s	ν(O-H)	3380	s,br	ν(O-H)			
3350	s	ν(O-2-H)									
3305	s	ν(O-1-H)									
3165	shl,m	ν(O-4-H)+ν(O-H), H_2O traces									
									3125	br,s	ν(O-H) bound
						2992	vw	—			
						2980	vw	—			
2977	w	—									
2950	w,sh	ν(C-H)				2952	m,sh	ν(C-H)			
2928	s,sh	ν(C-H-6)				2925	s,sh	ν(C-H-6)			
2918	s,sh					2916	shl,m				
2910	shl,s	ν(C-H)									
			2900	shl	—						
						2870	vw	ν(C-H)			
2855	vw	ν(C-H)									

[a]See Table I.

TABLE IV

F.T.-I.R. SPECTRA BANDS[a] FOR SUCROSE AND 4,1′,6′-TRICHLORO-4,1′,6′-TRIDEOXY-*galacto*-SUCROSE (TGS)

Sucrose						*TGS*		
Solid			*Aqueous solution*			*Solid*		
$\nu(cm^{-1})$	*I*	*Assignment*	$\nu(cm^{-1})$	*I*	*Assignment*	$\nu(cm^{-1})$	*I*	*Assignment*
3565	s,s	free OH ν(O-4-H)						
			3520	sh	(O-H) sucrose			
3420	shl,s	ν(O-6′-H) intra				3460	s,s	ν(O-3-H)
			3400	br,s	ν(O-H) H_2O			
3398	s	ν(O-2-H) & intra ν(O-1′-H)						
						3360	shl,s	ν(O-2-H) $\nu\nu$(O-H)
3340	s,sh	ν(O-6′-H)						
						3320	s,br	ν(O-6-H)
						3270	shl,s	ν(O-4′-H)
			3260	shl,s	ν(O-H) sucrose			
3250	shl,s	ν(O-H)						
						3025	vw	—
3018	vw	—						
3000	w	—						
2978	w,sh	—						
						2970	w	—
						2960	w	ν(C-H),CH_2 Fru moiety
2943	m,sh	ν(C-H),CH_2 Fru moiety				2940	vw	
			2930	m,br	ν(C-H),CH_2	2930	m,sh	ν(C-H-6)
2920	m,sh	ν(C-H),CH_2 Glc moiety						
						2905	w	ν(C-H)
2900	w	ν(C-H)						
			2880	shl,w	ν(C-H)			
						2975	sh,w	ν(C-H)
2840	shl,w	ν(C-H)						

[a]See Table I.

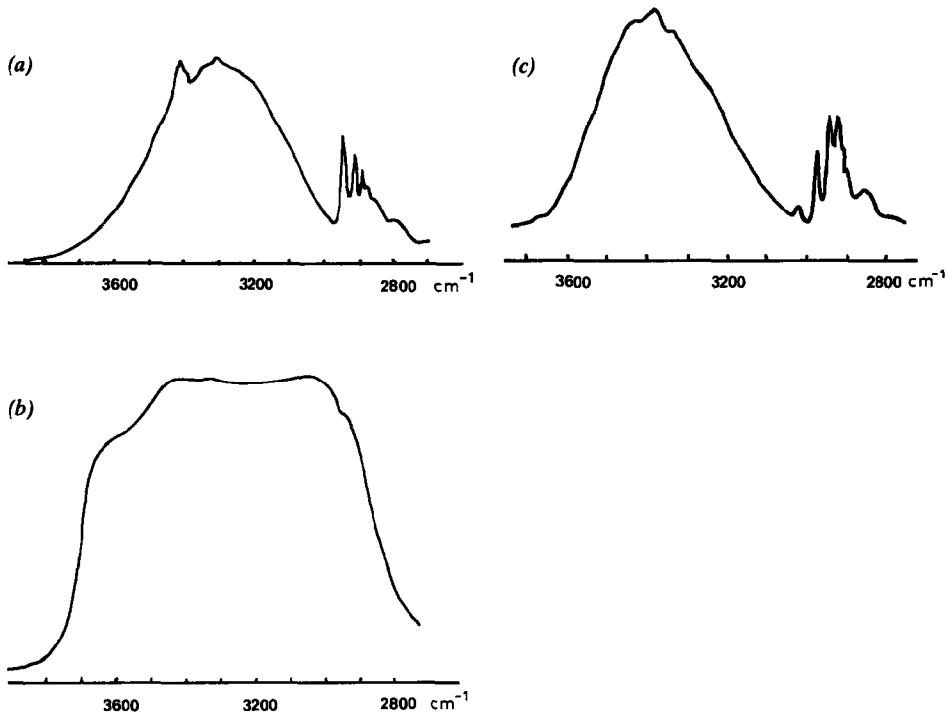

Fig. 1. F.t.-i.r. spectra of α-D-glucose (*a*), its aqueous solution (*b*), and 6-chloro-6-deoxy-D-glucose (*c*).

From intermolecular hydrogen-bond distances[13] and energies[14b] in α-D-glucopyranose, an assignment of the observed OH vibrations was derived (see Table I). The energies of intermolecular hydrogen-bonds in the α-D-glucopyranose crystal range[14b] from 9.4 (HO-1···O-5) to 14.6 kJ.mole^{-1} (HO-3···O-2). The argument adopted in our assignment, as no characteristic free-hydroxyl is apparent (see Fig. 1), is that the strongly hydrogen-bonded hydroxyl groups (HO-3 and HO-6) corresponded to the higher frequency (3410 cm^{-1}) and the weakly bonded (HO-1) to the lower frequency (3220 cm^{-1}).

Chlorination of D-glucose leads to displacement of frequencies towards higher values. Assignment of the observed OH-vibrations for 6-chloro-6-deoxy-D-glucose are derived from the preceding assignments. No absorption characteristic of free hydroxyl was observed in the spectrum of 6-chloro-6-deoxy-D-glucose (see Fig. 1).

A theoretical determination of the hydrogen-bond system in α-D-galactopyranose was recently performed[14a] and it appears that HO-6, which is a fairly good donor and acceptor of hydrogen bonds, is the most hindered in its movement. Accordingly, the highest broad absorption at 3490 cm^{-1} could be due to HO-6. The strongest i.r. absorption (see Fig. 2) is assigned to the hydroxyl group which establishes the shortest hydrogen bond (HO-2···O-3, 174 pm) in the α-D-galactopyranose crystal. The weakest hydrogen-bond involves HO-4 and corresponds to

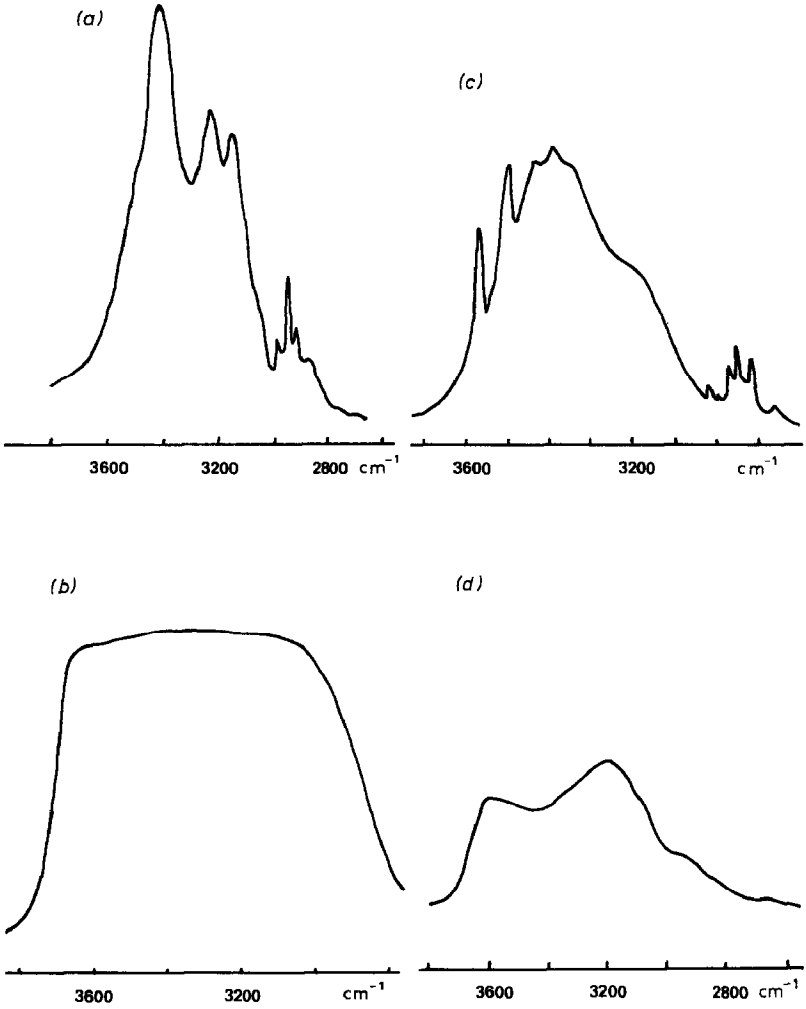

Fig. 2. F.t.-i.r. spectra of α-D-galactose (*a*), its aqueous solution (*b*), and 6-chloro-6-deoxy-D-galactose (*c*), and its aqueous solution (*d*).

the lower observed frequency, 3136 cm^{-1} (see Table II). This quasi-freedom of HO-4 is transformed into a completely free vibration, characterised by a sharp peak at 3566 cm^{-1} for 6-chloro-6-deoxy-D-galactose (see Fig. 2). Chlorination of D-galactose changes the electron density around C-6, and the closest hydroxyl group (HO-4*a*) exhibits free vibration. The other hydroxyl groups in 6-chloro-6-deoxy-D-galactose are assigned by comparison with the spectrum of α-D-galactose, with a shift towards higher frequencies. Although the observed OH-frequencies for aqueous solutions (Fig. 2) are broad, the general pattern is not the same for α-D-galactopyranose and 6-chloro-6-deoxy-D-galactose. Thus, the hydrations of galactose and its chlorodeoxy derivative are different.

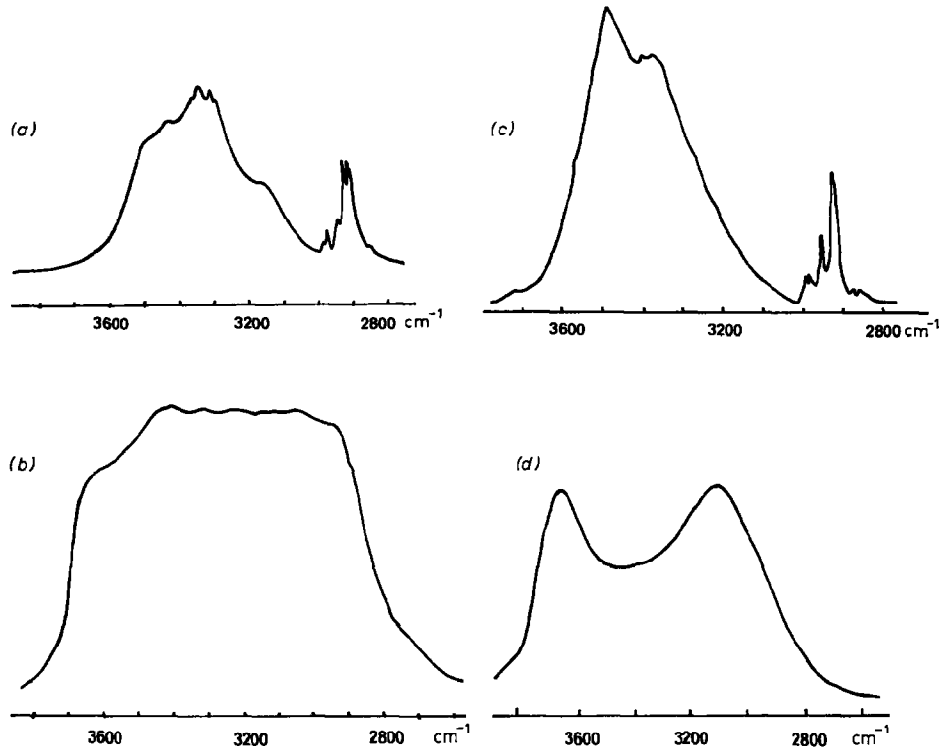

Fig. 3. F.t.-i.r. spectra of α-D-mannose (*a*), its aqueous solution (*b*), and 6-chloro-6-deoxy-D-mannose (*c*), and its aqueous solution (*d*).

Fig. 3 does not show any sharp absorption typical of free hydroxyl groups in crystalline α-D-mannose and its 6-chloro-6-deoxy derivative. Assignment of OH frequencies (see Table III) is based on hydrogen-bond data[12] for α-D-mannose and methyl α-D-mannopyranoside. The argument used for D-galactose was also used to assign the frequencies observed in the spectrum of 6-chloro-6-deoxy-D-mannose. The axial HO-2 acquires some freedom and exhibits a stronger vibration after 6-chlorination. The general appearance of the spectra of aqueous solutions (see Fig. 3) recalls that observed for D-galactose in Fig. 2. The hydrogen bonding in aqueous solutions of D-mannose does not permit differentiation of vibrations, whereas two wide bands were observed in the spectrum of the aqueous solution of 6-chloro-6-deoxy-D-mannose.

Fig. 4. shows that the sweetest molecules (sucrose and TGS) exhibit strong, sharp i.r. absorptions characteristic of free hydroxyl groups. As expected from neutron diffraction data[15] of sucrose, the hydroxyl group (HO-4) that is not engaged in hydrogen bonding is responsible for the absorption at 3565 cm^{-1}. Assignments for other OH vibrations (see Table IV) are based on bond energies and distances in the sucrose crystal[15]. Hydroxyl groups participating in both inter- and intra-molecular hydrogen bonds (HO-6, HO-2, and HO-1′) are thought to contribute to the higher frequencies in the wide band corresponding to bonded

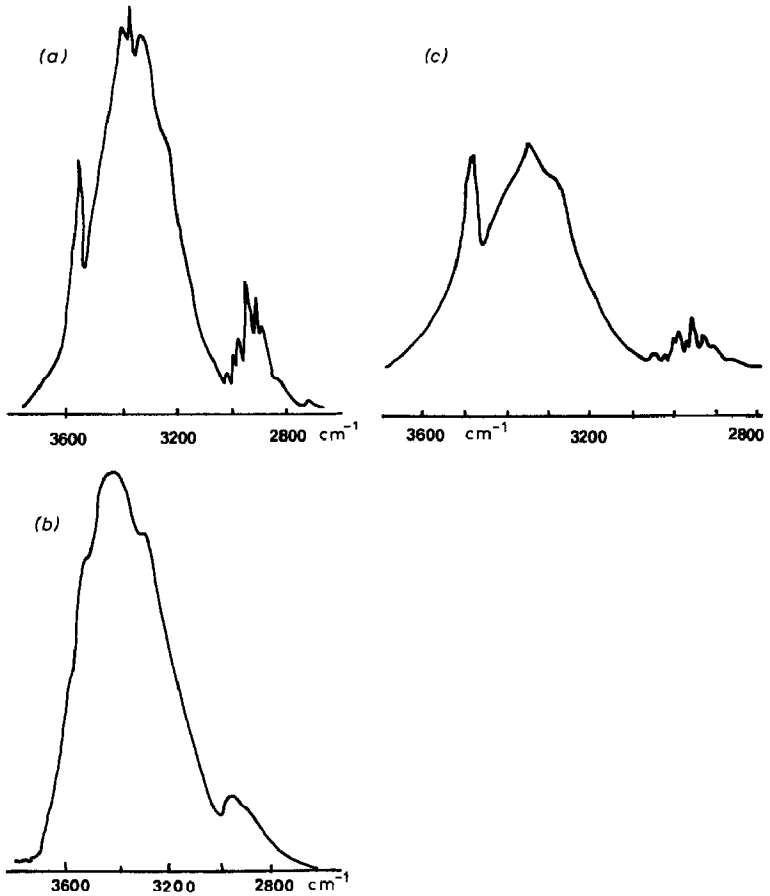

Fig. 4. F.t.-i.r. spectra of sucrose (*a*), its aqueous solution (*b*), and 4,1′,6′-trichloro-4,1′,6′-trideoxy-*galacto*-sucrose (TGS) (*c*).

hydroxyl-groups. Assignments of the observed frequencies in the spectrum of TGS are listed in Table IV. The sharp absorption could be assigned to HO-3; chlorination of sucrose and the axial position of the substituent on C-4 change the electron density around HO-3 in such a way that it is free to vibrate. Moreover, HO-3 has one of the shortest O-H bonds (95.9 pm), which gives (in sucrose) the longest O···O distance (286.2 pm) in intermolecular hydrogen-bonding. The same argument was applied[9] to β-D-fructopyranose, to support the assignment of the sharp i.r. band at 3525 cm^{-1} to HO-4. The ratio of intensities of ν(HO-3) to those of other bonded-OH vibrations is almost unity, whereas the ratio of intensities of free- to bonded-OH vibrations in sucrose is much smaller. These spectral features as well as other data relative to the conformation of the CH_2OH group may help in interpreting the sweet taste of the various molecules.

CH vibrations. — Assignments of the observed frequencies in the region 3000–2800 cm^{-1} are listed in Tables I–IV. Only the crystalline samples showed such

TABLE V

SENSORY ANALYSIS OF MONOSACCHARIDES AND THEIR CHLORINATED DERIVATIVES (FROM REF. 6)

Sugar	*Sweetness*[a]	*Bitterness*
D-Glucose	SS	0
D-Galactose	S	0
D-Mannose	S	trB
6-Chloro-6-deoxy-D-glucose	trS	trB
6-Chloro-6-deoxy-D-galactose	0	0
6-Chloro-6-deoxy-D-mannose	trS	trB

[a]Key: SS, very sweet; S, sweet; B, bitter; tr, trace.

vibrations. As a general rule, CH_2 stretchings occur at frequencies higher than those of CH. The effect of chlorination at C-6 gives rise to stronger ν(C-H) in CH_2Cl groups. These CH stretchings generally occur at frequencies higher than those of the corresponding C-H vibrations in non-chlorinated sugars. The CH_2 groups in both CH_2OH and CH_2Cl constitute the "γ" centre in the (AH–B, γ) tripartite template of sweetness.

Sweetness of the sugars. — The sweet taste of D-glucose, D-galactose, D-mannose, and their 6-chloro-6-deoxy derivatives was recently examined[6]. The results of sensory analysis are listed in Table V. None of the chlorodeoxy derivatives of simple sugars showed more than a trace of sweetness. It might have been expected that substitution of Cl for OH would increase the hydrophobic effect of the "γ" centre in the tripartite glucophore and consequently the sweetness of the molecule. However, except for TGS[2] and chlorodeoxy derivatives of D-fructofuranoses[6], no appreciable enhancement of sweetness was observed[6,16]. This finding led to the conclusion that hydrophobicity or lipophilicity should be regarded as an overall effect rather than a specific action of the chlorine substituent as a "γ" attribute. Such an overall lipophilic effect could also explain the extremely high sweetness of TGS (2000 times that of sucrose)[3]. A synergistic effect of two glucophores (AH = HO-2, B = Cl-1′, γ = Cl-4; and AH = HO-2, B = Cl-1′, γ = Cl-6′) was proposed[3] to account for the sweetness of TGS, but the exact mechanism is unclear. Chlorination of the fructose moiety seems to be important for the enhancement of sweetness, whereas replacement of HO-6 by a chlorine reduces the sweet taste.

Solute–solvent interactions and the sweetness of chlorinated sugars. — An interpretation of the sweetness of D-fructose, D-glucose, and sucrose, based on their properties in aqueous solution (viscosity, acidity, hydration) and their vibrational spectra, has been proposed[1]. It was emphasised that the rôle of the hydrophobic centre in the tripartite glucophore involves the repelling of water molecules and preventing them from sharing the hydrogen bonding with the receptor site on the tongue. Moreover, a structure-breaker effect of the sugar on the water structure is needed to facilitate Na^+/K^+ transport across the membrane and extend the sweet-

taste sensation. Comparison of the sweetness of isomers of simple sugars may help in interpreting their difference.

Whereas only one tripartite glucophore (AH = HO-2, B = O-1, γ = H-6,6) is possible for β-D-fructopyranose, the sweetest naturally occurring monosaccharide, different AH–B couples of hydrogen bonds are possible for the other sugars. From the F.t.-i.r. results listed in Tables I–III and the known physical properties of monosaccharides, the sweet or bitter taste of the sugars studied could be interpreted. The sweet taste of D-glucose has been discussed[1]. F.t.-i.r. results could help in specifying the glucophores. Although no sharp OH-vibration is present in the spectrum of the sugar (Fig. 1), two strong, wide bands assigned to ν(HO-3) and ν(HO-2) are observed. For D-glucose, the "γ" centre in the sweetness triangle is always H-6,6', whereas the AH–B donor–acceptor couple of hydrogen bonds could be either HO-4/O-3 or HO-3/O-2 (see Fig. 5). The need for a marked acidity for the AH donor does not emerge clearly from the hydroxyl groups in D-glucose since all except HO-1 are almost equivalent as donors and acceptors of hydrogen bonds. The ambiguity of the AH–B pair, together with the weaker hydrophobic character of CH_2OH compared to that of the intramolecular CH_2 in fructose, make D-glucose less sweet than β-D-fructopyranose. 6-Chloro-6-deoxy-D-glucose is slightly sweet and bitter[6]. The hydrophobic character is reinforced by chlorination which leads to an increase of the bitter taste. However, no noticeable change is observed in the hydrogen bonding, since the shape of the OH band is almost identical in α-D-glucose and its 6-chloro-6-deoxy derivative (see Fig. 1). The wide OH-band of the aqueous solution also shows the large number of equivalent hydrogen-bonds.

D-Galactose is less sweet than D-glucose (see Table V). This has been attributed to intramolecular hydrogen-bonding in galactose (HO-4···O-5). However, structural investigations[12,14b,17] led to the conclusion that there was no intramolecular hydrogen-bonding in monosaccharides. Alternatively, the effect could be due to differences in conformation of the CH_2OH group in α-D-glucose and α-D-galactose. Vibrational spectroscopy indicated that, whereas the CH_2OH only adopts the g^- and t positions in D-glucose and D-mannose, its preferred conformation in D-galactose is g^+ or, in some instances, g^- (see Fig. 6). The rotamers of CH_2OH groups, although investigated[18,19] experimentally and theoretically, are not always taken into account when evaluating the chemical reactivity or sweet taste of sugars. The g^- rotamer of the CH_2OH group in α-D-glucose and α-D-mannose corresponds to the *trans* position of the C-6–O-6 and C-4–C-5 bonds, whereas the

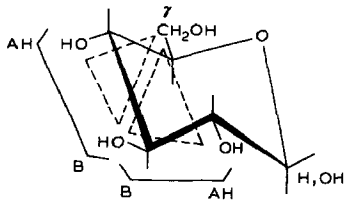

Fig. 5. Possible glucophores (4,3,6 or 3,2,6) for D-glucose.

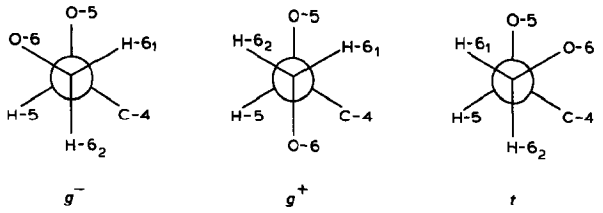

Fig. 6. Possible positions of the CH_2OH group in D-glucose, D-galactose, and D-mannose.

g^+ position in α-D-galactose corresponds to 120° rotation of the CH_2OH group around the C-5–C-6 bond. Such conformations modify the influence of HO-6 on the H-6,6 hydrophobic centre. With the hydroxyl group in the *trans*-position, the hydrophobic character is enhanced, hence the sweetness. Thus, the fact that D-glucose is sweeter than D-galactose could be due to the CH_2OH isomerism. Moreover, the overall lipophilic character may be derived from a lower intrinsic viscosity of the D-glucose solution. The chlorination of C-6 changes the conformation around the C-5–C-6 bond, and 6-chloro-6-deoxy-D-galactose is almost tasteless.

However, a trace of bitterness is observed for D-mannose (see Table V), which exhibits the same CH_2OH isomerism as D-glucose. This is probably due to the fact that there is always a trace of the β anomer in α-D-mannose, which was found[21] to be bitter. The taste of 6-chloro-6-deoxy-D-mannose could be interpreted in the same way as that of 6-chloro-6-deoxy-D-glucose. Aqueous solutions of D-mannose show a broad i.r. absorption (see Fig. 3), whereas two bands are seen in the spectrum of aqueous solutions of the 6-chloro-6-deoxy derivative, which could account for a difference in hydrogen bonding with the receptor site.

Thus, in connection with the sweet taste of 6-chloro-6-deoxy derivatives of D-glucose, D-galactose, and D-mannose, the rôle of the chlorine atom in the (AH–B, γ) tripartite glucophore is not clearly defined. However, the extremely high sweetness of TGS is probably due to the spatial disposition of the chlorine substitutents. According to Khan[22], the enhancement of sweetness could be due to the synergistic effect of two glucophore systems. Assignment of frequencies in Table IV and the hypothesis[22] of a double glucophore system allow binding to the receptor bud, as shown in Fig. 7, to be proposed. The two AH–B pairs are HO-3/O-2 and HO-2/O-3′. The lipophilicity required for enhancing the sweetness is obtained from the CH_2Cl groups. These groups are responsible for the hydrophobic–lipophilic behaviour of TGS, which may then be strongly held to two adjacent receptor sites by two pairs of hydrogen bonds. These hydrogen bonds are not shared with water because of the hydrophobic effect of the CH_2Cl groups (Fig. 7). The solute–solvent effect is manifested by a surprisingly low intrinsic viscosity for TGS ($[\eta] = 18.0 \times 10^{-3}$ dL.g^{-1}), which is lower than those of both sucrose and D-fructose ($>20.0 \times 10^{-3}$ dL.g^{-1}) in aqueous solution[20]. Thus, rather than a specific rôle in the (AH–B, γ) template, the chlorine substituents play an important part in the overall effects of TGS on water molecules, namely, hydrophobic and structure-breaking effects as in the case of β-D-fructose in solution[1].

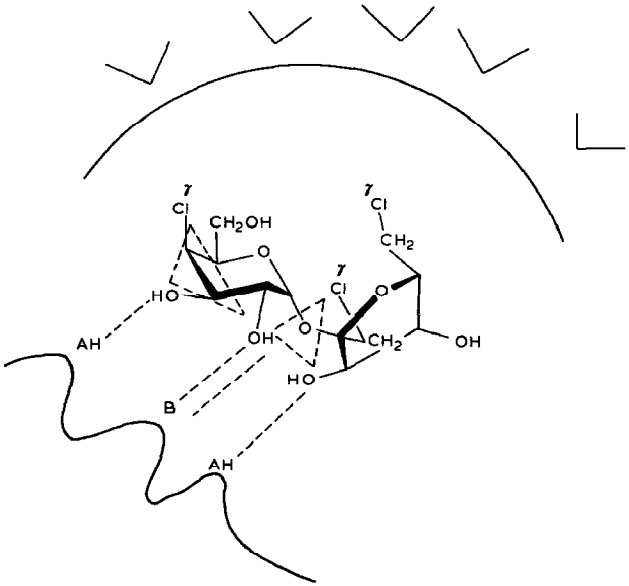

Fig. 7. Representation of the mechanism of sweetness of TGS: 3,2,4′ and 2,3′,1′ glucophores, and the overall hydrophobic effect of the three γ centres.

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