Hydrogen Bonding and the Varying Sweetness of the Sugars[a]

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SUMMARY

Sugar sweetness appears to vary with hydrogen bonding. When hydroxyl groups, which elicit sweet taste, are hydrogen bonded, ability to cause sweet taste appears to be restricted. The thesis is based upon consideration of molecular models, hydrogen-bonding measurements, and taste tests. The varying sweetness of different sugars, and the apparent anomalous sweetness of sugar anomers may be largely resolved by considering hydroxyl group bonding.

INTRODUCTION

Varying sweetness of sugars. Investigators have long been concerned with the varying and anomalous sweetness of the naturally occurring sugars. Although sweetness scores vary with method and physical state of the compounds, common sugars can be listed (Biester *et al.,* 1925; Cameron, 1947; Schutz and Pilgrim, 1957) in order of decreasing sweetness as fructose, sucrose, glucose, galactose, mannose, lactose, and raffinose.

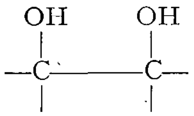
Fructose, the sweetest sugar, is 1.15–1.75 times as sweet as sucrose. Low values apparently correspond to mutarotated solutions, and high values to freshly prepared solutions, or to crystalline material. Raffinose in solution is only about 20% as sweet as sucrose.

The α-anomers of glucose, galactose and mannose are sweeter than the β-anomers. On the other hand, β-fructose and β-lactose are sweeter than their α-isomers (Tsuzuki and Yamazaki, 1953; Pangborn and Gee, 1961; Steinhardt *et al.,* 1962). Consequently phenomena which alter the equilibrium

$$\alpha \rightleftharpoons \beta$$

will also alter the apparent sugar sweetness. These include concentration and temperature (Cameron, 1947; Tsuzuki and Yamazaki, 1953). Tsuzuki (1947) pointed out that sweeter sugar anomers have a *cis* configuration between the anomeric and adjacent OH groups, but the rule does not hold for lactose. Böeseken (1949) assigned β-lactose the *trans* configuration.

The sugar —OH radical is recognized (Moncrieff, 1951) to be related to sugar sweetness. More specifically, the saporific group appears to be



$$\begin{matrix} \mathrm{OH} & & \mathrm{OH} \\ | & & | \\ -\mathrm{C} & - & \mathrm{C}- \\ | & & | \end{matrix}$$

Attempts to relate molecular and physical parameters to sugar sweetness include resonance energy (Tsuzuki *et al.*, 1954), vibratory hydrogen (Kodama, 1920) and solubility (Loginov, 1941). Carr *et al.* (1936) could find no relation between the number of carbon atoms, hydroxyl groups, molecular arrangement or spacial configuration and the sweet taste of sugar alcohols.

Physiological explanations for varying sugar sweetness include rate of diffusion into taste-bud receptors (Schutz and Pilgrim, 1957) and taste-bud receptor stereospecificity (Steinhardt *et al.,* 1962).

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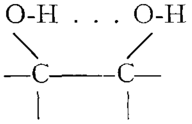
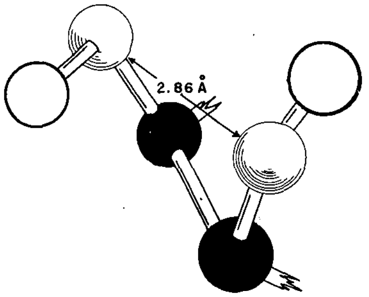
Recognizing that adjacent alcohol —OH groups may hydrogen bond (Kuhn, 1952),



it was postulated that the occurrence of the hydrogen bond might restrict the ability of the sugar saporific group to elicit the sweet taste response, and that the varying sweetness of the sugars could be largely resolved on the basis of this consideration. Evidence to support this hypothesis serves as the basis of this report.

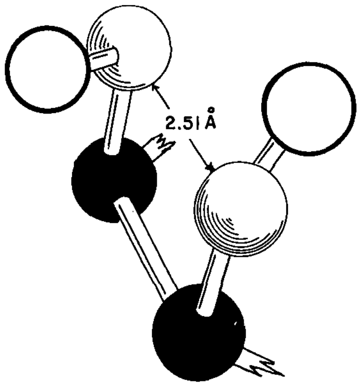
Hydrogen bonding in sugars. When the distance between two oxygen atoms is between 2.50 and 2.80 Å, a substituent hydrogen atom would be attracted to and, due to delocalization of charge, "bond" the second oxygen atom, O—H . . . O (Pauling, 1960). Certain sugar OH groups may bond in this manner. Reeves (1951) calculated that adjacent OH groups in five-membered planar or six-membered strainless rings have an O . . . O distance of 2.86 Å when the groups are *gauche*.



PROJECTED ANGLE, 60°

When the adjacent OH groups are *eclipsed*, the O . . . O distance is 2.51 Å.

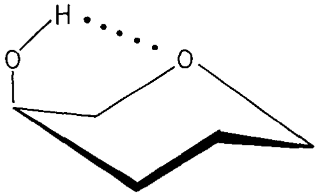
It would be expected, therefore, that adjacent *gauche* sugar OH groups would hydrogen bond when the ring conformation or ring distortions cause the projected angle between OH groups to decrease; or if the adjacent groups exist in true *cis* or *eclipsed* arrangement.



PROJECTED ANGLE, 0°

Infrared studies indicate that hydrogen bonding does occur in sugars. The strong composite OH absorption band occurring at about 3222 cm^{-1} is associated (Kuhn, 1950) with O—H stretch. Konkin *et al.* (1958) showed that the OH groups of carbohydrates may be bonded singly, O—H . . . O, or doubly bonded, O . . . H—O . . . H. Correlation (Marrinan and Mann, 1954) of infrared with X-ray diffraction data showed that α-D-glucose has one singly bonded, and four doubly bonded hydroxyl groups.

Stereochemical studies (Brimacombe *et al.*, 1958; Barker *et al.*, 1959) based, for example, on infrared analysis of sugar-related tetrahydropyran-3-ol, have led Foster (1961) to suggest that the axial hydroxyl substituents on carbon atom No. 4 in α-galactopyranoside, and on carbon No. 2 in α-mannopyranoside (C-1 conformations) are sterically located to bond the ring oxygen.



GALACTOSE

METHODS

Molecular models. To determine probable sites of hydrogen bonding in sugars, structural molecular models (Brode and Boord) were consulted. Particular attention was paid to conformations and distortions that would result in diminishing 60° projected angles between adjacent *cis* hydroxyl groups, and also conformations leading to 0° projected angles between adjacent hydroxyl groups.

Infrared studies. Sugars were dried for 2 hr over phosphorus oxide at 3 mm Hg and 100°C. After preparing powders in a dental amalgamator, nujol mulls were prepared, and the near infrared spectra recorded with a Beckman IR-7 double-beam spectrophotometer equipped with a sodium chloride prism. Air was used as the reference cell, and a scanning speed of 40 cm^{-1}/min was employed.

Sharp infrared absorption bands in the region 3400–3600 cm^{-1} were assigned to free —OH absorption, as has been done with diols (Brimacombe *et al.*, 1958) and sucrose (Marrinan and Mann, 1954). Composite bands in the region 3200–3400 cm^{-1} were assigned to hydrogen-bonded —OH groups. The quantitative strength of the hydrogen bond was estimated as the arithmetic difference, $\Delta\nu$ (cm^{-1}), between ν (cm^{-1}) for the free —OH groups and ν (cm^{-1}) for the bonded —OH groups (Kuhn, 1952; Cole and Jefferies, 1956; Brimacombe *et al.*, 1958).

Taste tests. To compare crystalline sugars, panel members placed a few mg of one sugar on the tongue, and shortly thereafter a few mg of a second sugar. The members were then asked to score the relative sweetness on an unnumbered 10-point scale. After the tests had been randomly conducted, scores were assigned to the ratings, and "average" sweetness scores obtained. Ten to 15 persons participated in each test.

When sugar sweetness comparisons were conducted with solutions at various temperatures, the tests were again conducted as described. Care was taken, however, to ensure that reducing sugars were fully mutarotated. Sugar solution concentrations were 3%.

RESULTS

Since the β-anomer is the only known crystalline form of fructose, estimates as to why the "α-anomer" is less sweet were made from molecular models. The mutarotation of β-fructose consists mainly of a pyranose to furanose ring conversion (Isbell and Pigman, 1938). At equilibrium, the mixture is composed of 31.6% furanose form and 68.4% pyranose form (Anderson and Degn, 1962). In the furanose form, two hydroxyl groups are in a true *cis (eclipsed)* configuration. If these two OH groups should hydrogen bond, the sweetness of the compound would presumably be lowered. That they are closer is in evidence from consideration of sugar reaction rate with chemicals where the rate of reaction is governed by the proximity of the OH groups. Thus, the reaction of furanose compounds with lead tetraacetate is instantaneous (Barton and Cookson, 1956).

The chair (C-1) conformation of the pyranose ring is preferred (Barton and Cookson, 1956) either in solution, or in the crystalline lattice. As mentioned previously, axial OH groups on α-D-galacto- and mannopyranoside are sterically located to bond the ring oxygen. Should this bonding restrict the ability of the saporific groups to elicit sweet taste, it would be expected that these sugars would be less sweet than their epimer, glucose.

α-D-glucose presumably exists in a near true chair (C-1) conformation, and adjacent OH groups are *gauche*. β-D-glucose, however, exists in a couch (C-1) conformation (Lentz and Heeschen, 1961). Possibly, two OH groups approach an *eclipsed* arrangement, and should they bond, it would be predicted that β-glucose is not as sweet as α-glucose. A similar argument may hold for galactose and mannose. Interestingly, β-anomers of methylgluco- and galactopyranosides react more rapidly than the α-anomers toward cuprammonium solution (Reeves, 1951). This reaction also requires the close approach of hydroxyl groups.

Infrared studies. Infrared studies of hydrogen-bonding intensity confirm predictions based upon molecular models. Where studies were not possible with molecular models, infrared analyses indicate stronger hydrogen-bonding in the less-sweet sugars. Characteristic hydroxyl absorption spectra of sugars studied are shown in Figs. 1–3. Band positions for free and bonded OH, and the estimate of hydrogen-bonding strength, $\Delta\nu$, are shown in Table 1 where comparisons may be made to relative sweetness values. Qualitatively, the bands for the least-sweet sugars are less distinct,

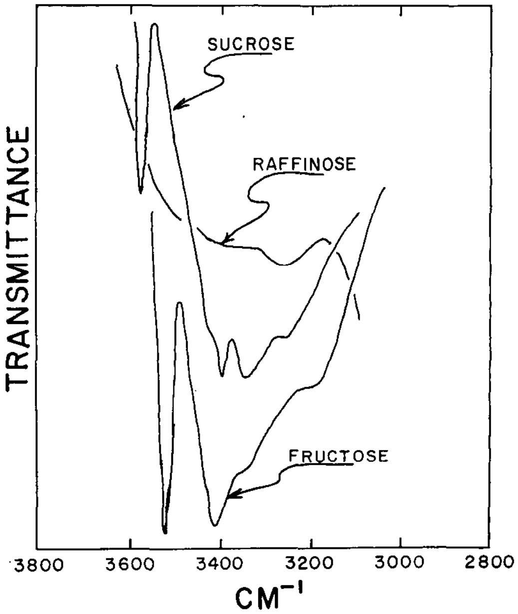


Fig. 1. Infrared spectra of the hydroxyl region of a fructose series of saccharides.

Table 1. Infrared hydroxyl band positions, ν (cm^{-1}), and hydrogen bonding strength, $\Delta\nu$ (cm^{-1}), for various crystalline sugars, and relative sweetness scores.

				Relative sugar sweetness	
Sugar	Free-OH	Bonded-OH	$\Delta\nu$	In solution [a]	"Solid" state [b]
β-Fructose	3520	3400	120	115–175	180
Sucrose	3570	3395	175	100	100
Raffinose	....	3180	(390)[c]	23	1
α-Glucose	3410	3315	95	64–74	74
β-Glucose	3545	3340	205	61	82
α-Galactose	3380	3210	170	32–67	32
α-Mannose	3450	3340	210	59	32
α-Lactose	3530	3360	170	16–38	16
β-Lactose	3460	3380	80	48	32

[a] Literature values; see especially Schutz and Pilgrim (1957) and Biester *et al.* (1925).
[b] Author's data.
[c] Estimated from sucrose-free OH position.

and displaced toward lower wave numbers, suggesting stronger hydrogen-bonding (Pimentel and McClellan, 1960), and $\Delta\nu$ is generally larger. The sweetest sugar, β-fructopyranose, has a very distinct free OH band. The least-sweet sugar, raffinose, apparently does not have a free OH band suggesting that all OH groups are bonded. The sucrose-free OH band position, 3570 cm^{-1}, corresponds well with the literature assignment (Marrinan and Mann, 1954).

In Fig. 2, α- and β-glucose may be compared. As indicated by the general nature of the spectra and $\Delta\nu$, it appears that the β-anomer is more strongly bonded. Since it is generally agreed that β-glucose is not as sweet as α-glucose, results with "solid" sugar (Table 1) appear contradictory. Possibly, the rapid rate of dissolution of crystalline β-glucose on the tongue makes it appear nearly as sweet as sucrose, but that final sweetness intensity is lower than that of even α-glucose.

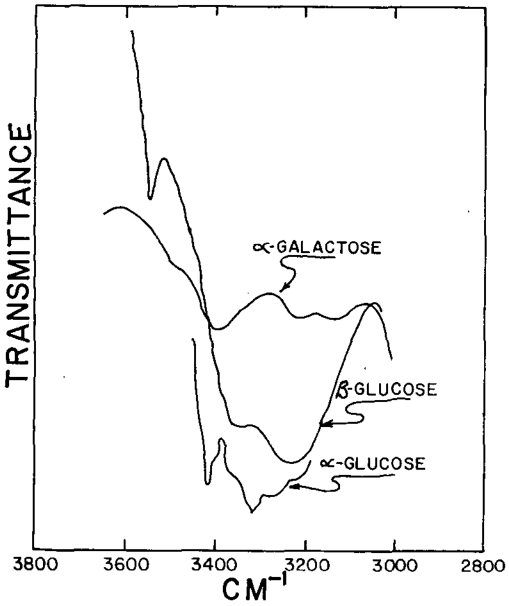


Fig. 2. Infrared spectra of the hydroxyl region of an aldose series of saccharides.

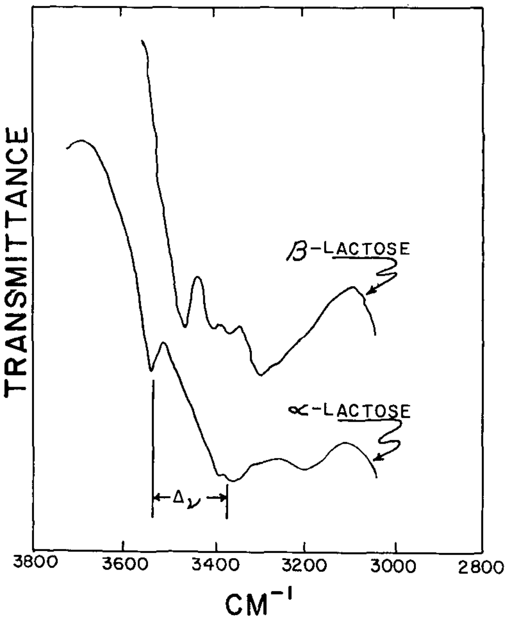


Fig. 3. Infrared spectra of the hydroxyl region of lactose anomers.

α-Galactose gives spectral evidence of being much more strongly bonded than α-glucose. This is also true of α-mannose. Fig. 3 compares α- and β-lactose. Again the spectra suggest that the less-sweet α-form is more strongly bonded.

An empirical correlation between $\Delta\nu$ and relative sugar sweetness appears to exist. As shown in Fig. 4, the logarithm of relative sweetness scores

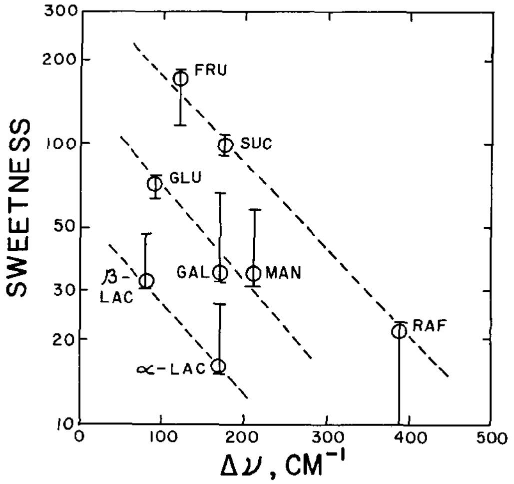


Fig. 4. Relation between the logarithm of relative sugar sweetness values and hydrogen bonding strength, Δν. Bars represent range of sugar sweetness values cited.

is approximately inversely proportionate to Δν where comparison of one infrared spectra with another appears valid. For the fructose-series of sugars, the data of Biester *et al.* (1925) were used, whereas the author's were used for the aldohexose and the lactose-series. Substitution of other data—for example, that of Schutz and Pilgrim (1957), or the author's for the fructose-series—changes the slope of the curves.

Taste tests. It was possible to substantiate the thesis being developed with taste tests. Hydrogen bonds are severed at elevated temperatures. Therefore, a sugar that is not as sweet as a second sugar should approach the sweetness of the second sugar at elevated solution temperatures. Many comparisons were made between glucose and galactose, over the range 20–60°C. Highly significant regression equations fitted to average panel sweetness scores yielded

$$s\text{, glucose} = 0.027\,t + 3.6$$

and

$$s\text{, galactose} = 0.048\,t + 1.6$$

where s equals average sweetness score, and t equals temperature. These data suggest that the sweetness of glucose increases with increasing temperature, but that the sweetness of galactose, with reference to glucose, increased twice as fast. Both the ratio of the slopes of the curves, and the intercepts suggest that glucose is about twice as sweet as galactose.

DISCUSSION

Evidence presented suggests that the varying sweetness of different sugars and sugar anomers may be resolved by consideration of hydrogen-bonded hydroxyl groups. The most perplexing instances, nearly covering the sweetness-range of the naturally occurring sugars, have been discussed. While the concept of *intramolecular* hydrogen-bonding was the major basis of the argument presented, the role of *intermolecular* hydrogen-bonding cannot be excluded. Δν for β-glucose seems much too large to be a measure of intramolecular bonding only, and there is a discrepancy concerning the sweetness of this sugar. It is possible that intermolecular hydrogen-bonding affects the rapidity with which sweetness is perceived, and that intramolecular hydrogen-bonding influences sweetness intensity.

The basis for assuming that Δν is primarily a measure of intramolecular bonding is that a multiplicity of bonded OH absorption bands are not evident in the sugar spectra. Marrinan and Mann (1954) interpret carbohydrate OH spectra in this manner, with caution, however. If the OH spectra recorded were primarily inter O—H strain, raffinose pentahydrate should, perhaps, yield a very distinct OH absorption spectrum. As shown in Fig. 1, it does not.

Finally, the thesis that sugar sweetness varies with hydrogen bonding is not at variance with suggestions of others as to why sugars differ in sweetness. For example, resonance energy, solubility, and rate of diffusion into taste bud receptor sites, are probably influenced, in turn, by hydrogen bonding.

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