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FORMATION AND EQUILIBRATION OF D-FRUCTOSIDES AND 2-THIO-D-FRUCTOSIDES IN ACIDIFIED DIMETHYL SULFOXIDE: SYNTHETIC AND MECHANISTIC ASPECTS

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ABSTRACT

A kinetic study of the reaction of ketoses and ketosides under catalysis with very dilute acid to produce the ketosyl carbonium ion is reported, and the subsequent reaction of this ion with alcohol and thiol nucleophiles has been studied. The relative reactivity of D-fructosides and 2-thio-D-fructosides is discussed, and some tentative conclusions have been reached on the mechanisms of their furanoside–pyranoside equilibration. The change in ring size in such systems probably proceeds *via* an anhydro-D-fructose intermediate, rather than an acyclic intermediate. The synthetic applications of the system have been explored, and it has been shown that both D-fructosides and 2-thio-D-fructosides may be synthesized in good yield. The D-fructofuranosides are best obtained from sucrose as the starting material, whereas the pyranosides are obtained from any readily available D-fructopyranoside (*e.g.*, methyl β) by use of the desired alcohol or thiol, only the β anomers being obtained. Three new 2-thio-D-fructosides are reported.

INTRODUCTION

It has previously been demonstrated that, in acid solution, sucrose is degraded *via* cleavage of the D-fructosidic bond[1–3]. If suitable nucleophiles are introduced into the reaction mixture, D-fructosides are produced[4]. The reaction, which is very similar to the Fischer process of glycoside formation, is an example of transglycosidation, and is a general reaction of glycosides[5]. Although the reaction is, in general, much faster for ketosides than for aldosides, the former have been relatively little investigated[6,7]. In view of the synthetic possibilities of using sucrose in this way as a convenient source of D-fructosides, the process has now been examined in more detail, and, to this end, the behavior of a variety of D-fructosides has been examined.

As an example of the synthetic possibilities that exist in this regard, the reaction has been used to produce three new 2-thio-D-fructosides. The behavior of the 2-thio-D-fructosides in acid-catalyzed alcoholysis has also been studied, in an at-

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tempt to elucidate the mechanism by which the products of alcoholysis equilibrate.

RESULTS AND DISCUSSION

The advent of liquid chromatography (l.c.) under elevated pressure has proved especially useful in this area of carbohydrate chemistry, in that it does not require derivatization, and can usually be extended to preparative as well as to analytical separations. In most cases, the analytical determination of the compounds in question was performed by 10-MPa l.c. on a column of an aminopropyl-bonded phase eluted with suitable water–acetonitrile mixtures. Several general conclusions may be drawn from the behavior of the compounds in question, and of various model compounds, in this system. Thus, the retention time decreases as the number of free hydroxyl groups in the molecule is decreased (*i.e.*, sucrose > D-fructose >D-fructosides). For the methyl, ethyl, and benzyl D-fructosides and benzyl 2-thio-D-fructosides, the pyranosides are eluted more slowly than the furanosides. The retention time of a D-fructoside decreases with increasing hydrophobic nature of the aglycon (Me > Et > Bn). In all cases studied, α-D-fructofuranosides were eluted slightly faster than β-D-fructofuranosides. Thus, for a given experiment, the retention times were invariably D-fructose > β-pyranoside >

TABLE I

RATES OF ACID-CATALYZED GLYCOSIDATION OF VARIOUS SUGARS[a,b]

Sugar	$k \times 10^4$ (s^{-1})
D-Fructose	4.1 ±0.1
L-Sorbose	1.1 ±0.1
D-Arabinose	0.05 ±0.005
Sucrose	2.0 ±0.1

[a]In 1:1 MeOH–Me_2SO containing 830μM H_2SO_4 at 60°. [b]Measured as rate of loss of starting material.

TABLE II

RATES OF ACID-CATALYZED GLYCOSIDATION OF VARIOUS D-FRUCTOSIDES[a,b]

Compound	$k \times 10^4$ (s^{-1})
D-Fructose	1.32 ±0.05
Sucrose	0.96 ±0.05
Methyl α-D-fructofuranoside	2.38 ±0.10
Methyl β-D-fructofuranoside	2.07 ±0.07
Benzyl α-D-fructofuranoside	2.83 ±0.07
Benzyl β-D-fructofuranoside	2.53 ±0.01
Methyl β-D-fructopyranoside	0.32 ±0.01
Benzyl β-D-fructopyranoside	0.40 ±0.02

[a]Performed in 1:1 EtOH–Me_2SO containing 830μM H_2SO_4 at 60°. [b]Measured as rate of disappearance of starting material.

β-furanoside > α-furanoside. At no time in any experiment involving the reaction of D-fructose with various alcohols was there any evidence of α-pyranoside formation, which is highly disfavored[8].

From Table I, the rates of glycosidation of the ketoses (D-fructose and L-sorbose) and the ketoside (sucrose) are much greater than that of the aldose (D-arabinose), reflecting the greater ease of formation of the carbonium-ion intermediate at a tertiary than at a secondary carbon atom. Consequently, ketosides can conveniently be produced at acid concentrations much lower (mM) than those for aldosides (~0.1–1M). This is important, because, as well as the (trans)glycosidation reaction, there exist competing reaction-pathways by which the starting material and products are degraded to such compounds as[1] 5-(hydroxymethyl)-2-furaldehyde. Such degradations are much more important for ketoses than for aldoses, and are favored by high concentrations of acid and high temperature. Under the mild conditions used here, such side reactions are usually negligible.

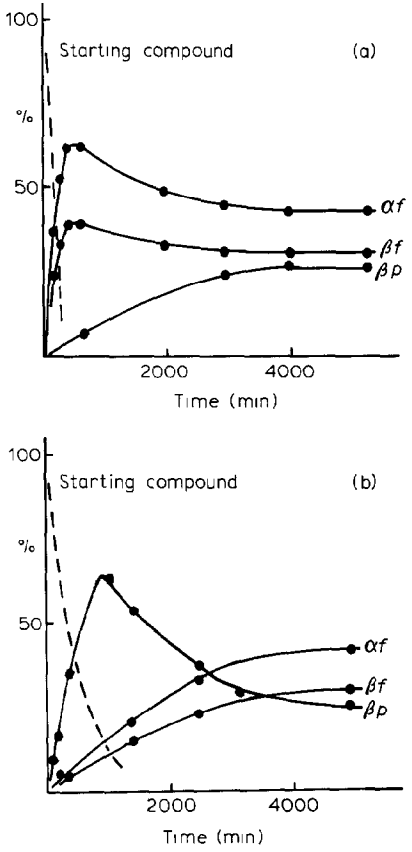


Fig. 1. Formation of ethyl D-fructosides from the reaction of (a) benzyl α-D-fructofuranoside and (b) benzyl β-D-fructopyranoside at 60° in 1:1 ethanol–Me_2SO containing mM sulfuric acid.

The reactions were performed on ~0.1M solutions of the various starting-materials (see Table II) in a 1:1 mixture of the alcohol and dimethyl sulfoxide (Me_2SO), the latter being used to overcome some solubility problems, and the alcohol being chosen to be different from the aglycon of the starting material. Thus, the reaction of a methyl D-fructoside was examined in ethanol–Me_2SO, and ethyl D-fructosides were produced. The general profiles of the reactions initially show predominant formation of an anomeric mixture of D-fructosides having the same ring-size as the starting material (for pyranosides, only the β anomer is ever observed). These initial (kinetic) products then equilibrate at a much lower rate, to give an equilibrium mixture of the α- and β-D-fructofuranosides and the β-D-fructopyranosides (see Fig. 1). By examination of Fig. 1 and Table II, it may be seen that D-fructofuranosides react faster than D-fructopyranosides, and, as in the acid hydrolysis of aldosides[7], the nature of the aglycon has relatively little influence on the rate of reaction. Good yields of D-fructofuranosides may thus be obtained by reaction of sucrose with alcohols, whereas D-fructopyranosides are best obtained by transglycosidation of other D-fructopyranosides.

Values for the overall rate-constants for the furanoside (*f*)–pyranoside (*p*) equilibrium were obtained by the following procedure by using the data from the period after the initial transglycosidation of benzyl α-D-fructofuranoside (see Fig. 1a). Because the interconversion of the two ethyl D-fructofuranosides is fast, and their relative ratio does not change throughout, they may be treated as a single species. The process then reduces to the simple case of

$$f \underset{k_{pf}}{\overset{k_{fp}}{\rightleftharpoons}} p.$$

If the initial concentrations of *f* and *p* are $[a - x]$ and $[x]$, respectively, then

$$\frac{dx}{dt} = k_{fp}\,[a - x] - k_{pf}\,[x],$$

and, at equilibrium (E),

$$k_{fp}\,[a - x_E] = k_{pf}\,[x_E].$$

By combining these two expressions, the rate equation can be shown to be given by

$$\ln [x_E - x] = \frac{k_{fp}\,[a]t}{[x_E]} + \ln [x_E].$$

The value of $[x_E]$ is given by the final equilibrium concentration of ethyl β-D-fructopyranoside, and hence, a plot of $\ln[x_E - x]$ *versus* time yields k_{fp}. The value of k_{pf} can then be found from the equilibrium constant ($K = f/p = k_{pf}/k_{fp}$). By this procedure, values of $k_{fp} = 2 \pm 1 \times 10^{-6}$ s^{-1} and $k_{pf} = 7 \pm 1 \times 10^{-6}$ s^{-1} were obtained.

The values of the various rate-constants are combined in Table III, where k_f and k_p are rates of transglycosidation taken from Table II; although not equivalent to rates of anomerization they bear some similarity to them.

The direct, acid-catalyzed glycosidation of aldoses by thiols is unsatisfactory as a general method for the preparation of 1-thioaldosides[9]. The initial kinetic product of such reactions for aldoses is usually the dithioacetal, which subsequently equilibrates at a lower rate, to give a mixture of free aldose, the dithioacetal, and the 1-thioaldosides (usually in poor yield)[10]. The small amount of data on simple glycosides treated in this way also indicates low yields of 1-thioaldosides[11].

Ketoses are decomposed under the conditions used to convert aldoses into dithioacetals[12–14], and the preparation of 2-thio-2-ketosides is usually a lengthy process involving acetylated dithioacetal intermediates[15,16]. This is in marked contrast to the facile method reported here. Under these mild conditions, the reaction is almost identical to the alcohol-based, Fischer process of glycoside formation, producing the two anomeric 2-thio-D-fructofuranosides and the 2-thio-β-D-fructopyranoside. The use of Me_2SO is essential here, for, in its absence, D-fructose was rapidly degraded. Benzyl 2-thio-β-D-fructofuranoside is the initial, kinetically favored product, and, because the rate of anomerization is lower than the rate of its formation, very high yields of this compound may be obtained (up to 80% when only 10% of the starting D-fructose remains, employing 100mM H^+ at room temperature). At longer times, the relative amount of the α anomer increases to a maximum of ~40%, its formation being favored under conditions of high acid concentration (100mM) at 60°. Benzyl 2-thio-β-D-fructopyranoside is never a major product, but may be optimized to ~10% yield by prolonged heating with a low acid concentration (mM) at 60°.

Although thiols are normally considered to be better nucleophiles than alcohols, in the reactions considered here, the reverse appears to be the case. Thus, when D-fructose was heated in acidified Me_2SO containing equimolar amounts of

TABLE III

VALUES OF THE RATE CONSTANTS FOR REACTION OF VARIOUS D-FRUCTOSIDES[a]

Rate constant	*Value (s^{-1})*	*Aglycon involved*
k_f	1.3×10^{-4}	Me,Bn/α,β
k_p	3.4×10^{-5}	Me,Bn/β
k_{fp}	2×10^{-6}	Et/α,β
k_{pf}	7×10^{-6}	Et/β

[a]In 1:1 EtOH–Me_2SO containing 830μM H_2SO_4 at 60°.

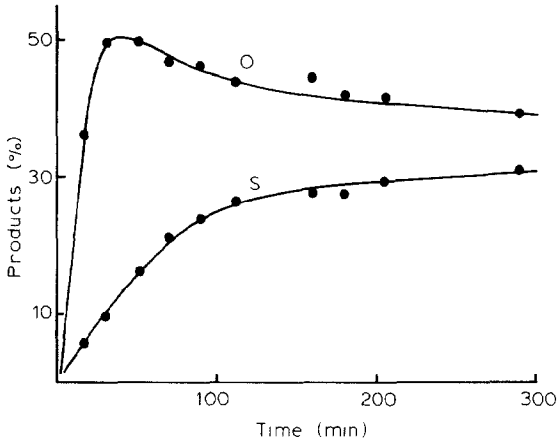


Fig. 2. Total yields of D-fructosides (O curve) and 2-thio-D-fructosides (S curve) from D-fructose in 2:1:1 Me_2SO–benzyl alcohol–α-toluenethiol containing mM sulfuric acid, at 60°.

benzyl alcohol and α-toluenethiol, it was the benzyl D-fructosides which were first formed. The corresponding 2-thio-D-fructosides were produced much more slowly, but subsequently increased in relative amount until equilibrium was reached (see Fig. 2). At the commencement of this study, it had been anticipated that these methods might yield a synthesis of thiosucrose by use of sucrose or D-fructose plus 1-thio-D-glucose under the reaction conditions already described. The foregoing experiment, however, indicates that such a reaction should yield mainly a mixture of D-fructosyl-(1-thio-D-glucose) disaccharides by reaction of the D-fructosyl carbonium ion with hydroxyl groups of the 1-thio-D-glucose. An attempt to prepare a thiosucrose derivative by reaction of D-fructose with 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose in acidified Me_2SO gave no disaccharide product.

TABLE IV

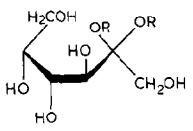
RATES OF REACTIONS FOR VARIOUS D-FRUCTOSIDES[a,b]

Compound	*Rate*[c]	*Value* (s^{-1})
Benzyl α-D-fructofuranoside	$k^O_{f\alpha}$	$7.1 \pm 0.4 \times 10^{-3}$
Benzyl β-D-fructofuranoside	$k^O_{f\beta}$	$6.4 \pm 0.2 \times 10^{-3}$
Benzyl β-D-fructopyranoside	$k^O_{p\beta}$	$9.3 \pm 0.2 \times 10^{-4}$
Benzyl 2-thio-α-D-fructofuranoside	$k^S_{f\alpha}$	$7.1 \pm 0.1 \times 10^{-6}$
Benzyl 2-thio-β-D-fructofuranoside	$k^S_{f\beta}$	$4.0 \pm 1.0 \times 10^{-5}$
Benzyl 2-thio-β-D-fructopyranoside	$k^S_{p\beta}$	$3.6 \pm 1.0 \times 10^{-6}$
Methyl α,β-D-fructofuranoside	k^O_{fp}	$2 \pm 0.3 \times 10^{-5}$ [d]
Methyl β-D-fructopyranoside	k^O_{pf}	$5 \pm 0.7 \times 10^{-5}$ [d]

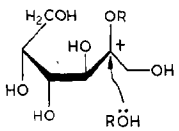
[a]In 1:1 MeOH–Me_2SO containing 10.3mM H_2SO_4 at 60°. [b]Measured as previously described. [c]Superscript O = oxygen; S = sulfur; subscript *f* = furanoside, *p* = pyranoside. [d]Found by monitoring the products of benzyl β-D-fructopyranoside to equilibrium.

The rates of glycosidation of the benzyl 2-thio-D-fructosides were examined relative to their oxygen analogs (see Table IV). The two processes show some marked differences. The thio species disappear much more slowly than the oxygen species, and only very small amounts of products are seen. It would appear, therefore, that the 2-thio-D-fructosides react so slowly that they approach the rate of degradation into other organic species already mentioned. It is not absolutely clear, therefore, that the rates given in Table IV accurately represent the rates of cleavage of the 2-thio-D-fructosyl bond; however, the appearance of small yields of the transglycosidation products expected does imply that the two rates are of the same order of magnitude.

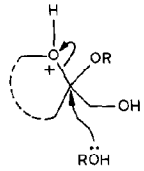
These differences between O- and S-analogs allow some tentative insight into the mechanism of the furanoside–pyranoside interconversion. This equilibration requires the formation of an intermediate that can be transformed reversibly into both furanoside and pyranoside. The major point of contention is whether this intermediate is cyclic or acyclic[17]. An acyclic mechanism involving an intermediate such as **1** has been postulated[5]. This product (D-fructose dialkyl acetal) would be expected to undergo ring closure by internal attack of either O-5 or O-6 (the former being the favored but not exclusive route). Furthermore, it seems possible that this intermediate could be formed from either a furanoid or pyranoid precursor by ring opening and nucleophilic attack by a second alcohol molecule in either a stepwise (**1a**) or concerted fashion (**1b**).



1

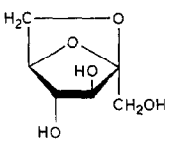


1a



1b

Alternatively, a cyclic mechanism involving bicyclic intermediates such as **2** has been proposed[5,17]. This product (2,6-anhydro-β-D-fructofuranose) has been shown[18] to undergo alcoholysis very rapidly, to form a mixture of α- and β-D-fructofuranosides. Such an intermediate could be formed from either ring system by internal nucleophilic attack of the appropriate hydroxyl group (OH-6 of the furanoid, OH-5 of the pyranoid) on the anomeric carbon atom, again by either a stepwise (**2a**) or concerted (**2b**) process.



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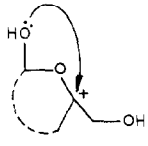
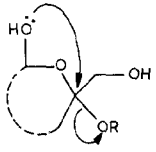


2a

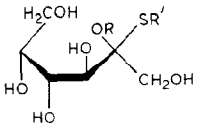


2b

It would be expected that **2**, having both a 5- and a 6-membered ring, could undergo acid-catalyzed opening of either ring, to give both furanoid and pyranoid products. Some evidence for this dual possibility may be seen in the cationic polymerization of such compounds[19].

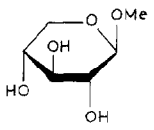
Species **2** is known to be produced in significant proportions when sucrose is heated in an inert solvent containing traces of acid (*e.g.*, in Me_2SO with mM sulfuric acid[1]) and when the D-fructosides initially formed are unstable (*e.g.*, phenyl D-fructosides)[4]. Surprisingly, **2** is also formed from sucrose in ethanol under extreme conditions[18]. On the other hand, dialkyl acetals of type similar to **1** have been found under alcoholysis conditions for several monosaccharides[20,21]. They have been found only in small yield, and it has been claimed that they are not true intermediates, but rather, kinetic by-products[22]. In an investigation into the methanolysis of D-fructose and L-sorbose, designed to examine the role played by their dimethyl acetals, no trace of these species could be detected[22]. This is surprising, in view of the greater prevalence of acyclic species in the chemistry of ketoses than in that of aldoses[23].

It may be seen that the chief mechanistic difference in the formation of the two intermediates (**1** and **2**) lies in the question of whch bond is broken. For **1**, the bond between the anomeric carbon atom and the ring-oxygen atom must be cleaved, whereas for **2**, it is the glycosidic bond that is broken. If we now examine the 2-thio-D-fructosides already discussed, the difference becomes even more extreme. An acyclic mechanism involves cleavage of a C–O bond, and the intermediate becomes **3**, whereas a cyclic mechanism involves cleavage of a C–S bond,



3

and the intermediate remains **2**. A previous study of the acid hydrolysis of methyl β-D-xylopyranoside (**4**) and methyl 5-thio-β-D-xylopyranoside (**5**) showed the latter to be hydrolyzed much the faster[24].



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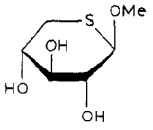
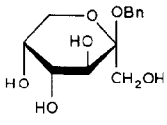


5

It thus seems that the inductive effect of the sulfur atom, or its poorer competition for the available protons, or both, causes more extensive protonation of the glycosidic oxygen atom, and hence is rate-promoting. The greater stability of

an oxygen-substituted over a sulfur-substituted carbonium ion (which would be rate-decreasing) does not seem to be so important. It is, therefore, likely that, for benzyl β-D-fructopyranoside (**6**) and benzyl 2-thio-β-D-fructopyranoside (**7**), a ring-opening mechanism involving protonation of the *ring*-oxygen atom would proceed faster for the latter (any effect of destabilization of the resulting carbonium



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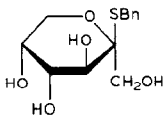
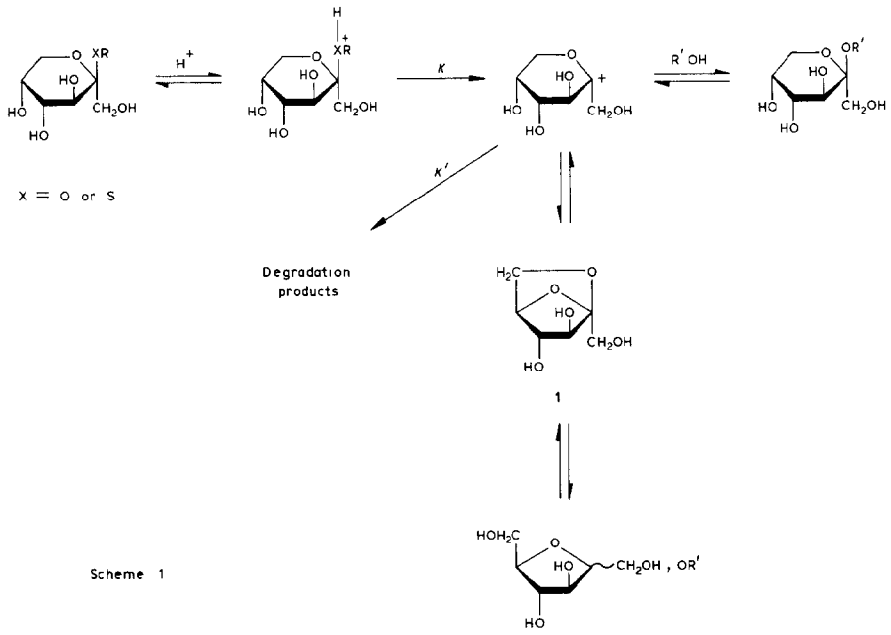


7

Bn = $PhCH_2$

ion by the sulfur substituent should be minimized by its tertiary structure). Conversely, because of the lower basicity of sulfur, the rate of cleavage of the glycosidic bond should be lower for **7** than for **6**. Examination of Fig. 1(b)and Table IV thus leads to the conclusion that, for **6**, glycosidic bond cleavage is faster than the ring-contraction mechanism, whereas, for **7**, on the reasoning just outlined, the reverse would be the case if the ring-contraction mechanism involved ring-opening. The consequence of this is that formation of significant proportions of benzyl 2-thio-β-D-fructofuranoside would be predicted when **7** is treated with acid in methanol–Me_2SO (from Table IV, the rate of cleavage of the glycosidic bond in the 2-



Scheme 1. 2,6-Anhydro-β-D-fructofuranose (**2**) as the intermediate in the ring contraction–expansion.

thiofuranosides should also be lower than the ring-opening mechanism). The fact that no sulfur-containing products are detected therefore militates against an acyclic mechanism for the ring contraction, and the extremely slow disappearance of the 2-thioketosides implies that the rate-limiting step is, indeed, the removal of the aglycon.

It thus seems that the intermediate in the ring contraction–expansion is 2,6-anhydro-D-fructose (**2**), as outlined in Scheme 1. For ketosides, the rate-determining step is the rate of equilibration of initially formed pyranosides and furanosides, whereas for the 2-thioketosides, the rate-determining step is the generation of the cyclic carbonium ion: (k), a rate so low that it is exceeded by the rate of the pathways leading to degradation (k^1).

EXPERIMENTAL

Materials. — Dimethyl sulfoxide was dried by being kept for several days over calcium hydride, and then distilling under vacuum onto fresh calcium hydride. Aliquots were filtered immediately prior to use. Ethanol and methanol were distilled, and stored over freshly dried, 3A molecular sieves. The various monosaccharides and sucrose were obtained commercially, and used as received. Chromatography solvents of HPLC grade, were filtered, and degassed.

Instrumentation. — Optical rotations were determined with a Perkin–Elmer 141 polarimeter. N.m.r. spectra were recorded with JEOL FX60Q, and JEOL FX90Q spectrometers. A Varian 5000 HPLC apparatus was used for both analytical and semi-preparative, 10-MPa liquid chromatography, using bonded-amine columns, and eluting with water–acetonitrile (usually, 5–15% of water). A Waters Associates R401 differential refractometer was used for detection, in conjunction with a Hewlett–Packard 3380S recording integrator. Rate data, subject to the assumptions discussed next, were obtained from plots of peak area with time, in a manner analogous to that used previously for g.l.c. detection[3].

Liquid chromatography. — In order to obtain the kinetic results detailed, some approximations were necessary. The concentration of a species was assumed to be represented by the peak area obtained from the 10-MPa liquid chromatograms. For rates determined by disappearance of starting material, this is unequivocal; however, for more-complex cases, where several products are formed and the concentrations of these products are compared, the further assumption of a constant-response factor has been made. Although this assumption may introduce error, this is considered to be small as the combined area of all peaks proved to be approximately constant throughout most experiments. In all instances where several products were actually isolated from a single experiment, their proportional yields were in good agreement with the relative peak-areas displayed on the chromatogram. Hence, it was considered that the rate values obtained are good representations of the true values. For only one sugar (D-arabinose) was there obviously a significantly different response-behavior, but the only datum used for this

compound was that of the rate of disappearance of starting material. The errors reported in the Tables are based on normal, statistical analysis of the rate curves, and do not take into account the foregoing assumptions.

Synthesis of D-*fructosides.* — A quantity of dry sucrose was stirred in a hot alcohol (boiling methanol under reflux, or benzyl alcohol at 90°) containing 10mM sulfuric acid, until acceptable amounts of the derived D-fructosides (as determined by 10-MPa l.c.) were present. The mixture was then cooled, made neutral with barium carbonate, filtered, and the filtrate evaporated. A crude separation of the reaction mixture was then performed by 10-MPa l.c. (1:4 H_2O–acetonitrile) by repeated injection (200 μL) until a sufficient quantity of the mixed D-fructosides had been collected. This crude fraction was then evaporated, and the process was repeated, using a water–acetonitrile mixture that afforded complete resolution of all of the D-fructoside peaks. In all cases examined, only three D-fructoside peaks were detected. The pure fractions were then evaporated, and l.c. was repeated for each compound, using a silica column in order to remove traces of basic material (probably introduced by slow leaching from the bonded-amine column) that would have interfered with acid-catalyzed rate-studies. It was found advantageous to postpone this last step if the compounds were to be kept for any extended length of time, as the furanosides, in particular, are very acid-sensitive and can be kept much longer under slightly basic conditions.

Synthesis of 2-thio-D-*fructosides.* — Some modifications were made in the foregoing procedure, because of the odor of the starting materials. D-Fructose (5 g) was dissolved in dimethyl sulfoxide (10 mL) at 60°. α-Toluenethiol (10 mL) was added, and then sulfuric acid to 100mM. The mixture was heated for 2 h, after which, barium carbonate (20 g) was added, with stirring and heating for a further 30 min. After cooling, and standing for 20 min, the solvents were removed under vacuum at room temperature during 3 days. Methanol (50 mL) was now added, and the suspension was filtered, to remove most of the remaining barium carbonate. Evaporation of the filtrate to dryness left a creamy solid which was partitioned between water (60 mL) and dichloromethane (60 mL). The dichloromethane layer, which contained only α-toluenethiol and dibenzyl disulfide (identified by ^{13}C-n.m.r. spectroscopy), was discarded. The water layer and some insoluble material were washed with more dichloromethane (30 mL), and subjected to continuous extraction with ethyl acetate for 2 h. The ethyl acetate extract was concentrated to a smaller volume, and carefully filtered to remove any final traces of barium carbonate. The filtrate was then evaporated to a pale-yellow syrup which was shown by g.l.c. and 10-MPa l.c. to contain only 2-thiofructosides (overall yield, ~60%). A portion of the syrup was dissolved in the minimal volume of methanol, and separated by l.c. similarly to the fructosides. The three components thus isolated were characterized as follows.

Benzyl 2-thio-α-D-fructofuranoside, m.p. 103.5–104.5° (from acetonitrile).

Anal. Calc. for $C_{13}H_{18}O_5S$: C, 54.53; H, 6.34; S, 11.2. Found: C, 54.28; H, 6.66; S, 11.4.

TABLE V

SOME PROPERTIES OF D-FRUCTOSIDES

Compound	^{13}*C-N.m.r assignment (p.p.m.)*[a]				$[\alpha]_D$[b] *(degrees)*
	C-1,6	*C-3,4,5*	*C-2*	*Aglycon*	
Methyl α-D-fructofuranoside	59.1, 62.3	78.4, 81.2, 84.3	109.2	49.4	+92.3 (lit.[25] +93)
Methyl β-D-fructofuranoside	60.1, 63.5	75.8, 77.7, 82.0	104.6	49.8	−52.4 (lit.[26] −50.4)
Methyl β-D-fructopyranoside	61.8, 64.7	69.3, 69.9, 70.5	101.1	49.3	−172.5 (lit.[27] −172.1)
Benzyl α-D-fructofuranoside	60.0, 61.9	78.2, 81.9, 84.3	109.0	64.6, 128.9, 129.1, 129.5, 138.4	+45.0 (lit.[2,28] +45.7)
Benzyl β-D-fructofuranoside	61.6, 63.6	75.7, 77.4, 82.1	104.9	64.4, 127.7, 128.4, 137.8	−21.5 (lit.[2] −21.5)
Benzyl β-D-fructopyranoside	62.4, 63.8	69.2, 69.9, 70.5	101.9	65.0, 128.5, 128.8, 129.5, 138.6	−131.1 (lit.[28] −130)
Benzyl 2-thio-α-D-fructofuranoside	61.2, 64.0	77.2, 81.3, 94.7	94.7	33.2, 127.8, 129.4, 129.8, 138.7	93.3
Benzyl 2-thio-β-D-fructofuranoside	64.2[c]	76.7, 77.5, 83.5	96.0	32.1, 129.9, 129.5, 129.9, 139.2	−118.4
Benzyl 2-thio-β-D-fructopyranoside[d]	65.2, 65.5	67.5, 68.9, 70.4	93.8	30.3, 126.7, 128.4, 128.9, 139.3	−214.3[e]

[a]In D_2O, using 1,4-dioxane as the internal standard (67.4 p.p.m.). [b]0.05M, in H_2O at 25°. [c]Intensity equivalent to two overlapping peaks. [d]In Me_2SO-d_6. [e]0.05M, in Me_2SO at 25°.

Benzyl 2-thio-β-D-fructofuranoside, m.p. 51.5–53.5° (from ethyl acetate).

Anal. Calc. for $C_{13}H_{18}O_5S$: C, 54.53; H, 6.34; S, 11.2. Found: C, 54.83; H, 6.63; S, 11.5.

Benzyl 2-thio-β-D-fructopyranoside, m.p. 177–178° (from 1:1 methanol–acetonitrile).

Anal. Calc. for $C_{13}H_{18}O_5S$: C, 54.53; H, 6.34; S, 11.2. Found: C, 54.30; H, 6.60; S, 11.4.

The compounds were further characterized by their ^{13}C-n.m.r. spectra and optical rotations (see Table V).

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