Carbohydrate Research, 87 (1980) 209–217
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

THERMOLYSIS OF SUCROSE IN DIMETHYL SULPHOXIDE SOLUTION

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(Received April 14th, 1980; accepted for publication, May 20th, 1980)

ABSTRACT

The kinetics of thermolysis of sucrose in solution in anhydrous dimethyl sulphoxide have been studied. The reaction appears to be facilitated by intramolecular hydrogen-bonding and is inhibited by intermolecular hydrogen-bonding to water or alcohols. The thermolysis yields α-D-glucopyranose (which then anomerises) and the fructofuranosyl carbonium ion which can react with benzyl alcohol to yield benzyl α- and β-D-fructofuranosides. This fructosyl cation is probably also the precursor for the formation of 2,6-anhydrofructofuranose in the thermolysis of sucrose.

INTRODUCTION

For the thermal degradation of sucrose at about its melting temperature (190°), it was concluded[1] that the first step was a first-order, intramolecular displacement, yielding D-glucose and a reactive D-fructose derivative (Fru*). The latter species reacted either with excess of sucrose or with an added alcohol (erythritol) to yield trisaccharides or fructofuranosides of the alcohol. The kinetic conclusions from this work were extremely tentative, because of the difficulties in measuring the rate of disappearance of sucrose from the melt. We have now found that similar thermolysis of sucrose will occur in solution in dry dimethyl sulphoxide (and probably in other aprotic solvents). In this system, the reaction is no longer restricted to temperatures above the melting point, as was the case with crystalline sucrose. Lower temperatures can therefore be used, leading to lower and more accurately measurable rates.

RESULTS AND DISCUSSION

The logarithmic plot of sucrose remaining *versus* time for heated solutions in Me_2SO was linear to at least 80% conversion. The degradation is therefore first order in sucrose, but the rate also showed some dependence on the initial concentration of sucrose (Table I). The reaction was almost completely inhibited by the addition of 5% of water to the system, and (with allowance for temperature differences) the reaction occurred much more readily in dry Me_2SO than in the melt. We interpret

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TABLE I

RATE OF DEGRADATION OF SUCROSE IN Me_2SO SOLUTION AT 90°

Sucrose concentration (%)	$k_{obs} \times 10^6$ *(sec^{-1})*
2	672 ±26
4	479 ±17
10	344 ±18
4[a]	3 ±2

[a]Water (5%) added to Me_2SO.

all of these observations to indicate that intermolecular hydrogen-bonding of the sucrose molecule slows the thermolysis reaction. This hydrogen bonding can be with water or with another sucrose molecule, and the latter type will increase with increase in the initial concentration of sucrose in Me_2SO and will be particularly important in the sucrose melt. In accordance with these observations, it has been recorded[2] that solutions of sucrose in high-boiling alcohols are particularly stable, and our subsequent work with benzyl alcohol added to the sucrose solution in Me_2SO has confirmed that the alcohol slows the reaction (see below).

A possible explanation of the inhibition of the thermolysis reaction by intermolecular hydrogen-bonding is that the thermolysis is favoured by intramolecular hydrogen-bonds and that the latter are decreased or prevented by intermolecular hydrogen-bonding. This situation might require that thermolysis proceeds *via* one or more specific and relatively ordered, intramolecularly hydrogen-bonded structures. To investigate this possibility, we have determined k_{obs} for loss of sucrose in Me_2SO at various temperatures (Table II). From the rates shown, the Arrhenius plot gave a value of 86 × 10^3 J.mole^{-1} for the energy of activation and hence a value of 81 J.mole^{-1}.deg^{-1} for the entropy of activation. The latter value is quite significantly negative and hence confirms that the transition state in the rate-determining step is relatively highly ordered. The bonding of the glycosidic oxygen with hydrogen from either or both of HO-1′ and HO-3′, and possibly also HO-6′, would be sterically

TABLE II

RATE OF DEGRADATION OF SUCROSE IN Me_2SO (4% SOLUTION)

Temperature (degrees)	$k_{obs} \times 10^6$ *(sec^{-1})*
80	151 ±24
85	280 ±13
90	479 ±17
100	934 ±7
110	1852 ±29

favoured and would assist the mechanism proposed below for the thermolysis reaction. We are currently investigating such bonding by thermolysis studies of sucrose derivatives, and preliminary results are compatible with such an effect.

The products of the thermolysis of sucrose in solution in Me_2SO have been investigated by g.l.c. of the trimethylsilyl ethers, using *myo*-inositol and α,α-trehalose as internal standards. A typical profile of the variation of the products with the course of the reaction is shown in Fig. 1, which clearly shows that the α anomer of D-glucopyranose is first produced and then mutarotates to an equilibrium mixture with the β form. It has been reported[3] that mutarotation of D-glucose in Me_2SO does not occur, or is very slow; in this study by n.m.r. spectroscopy, the probe temperature was not specified, but it may be assumed that it was about room temperature. We have confirmed this result by keeping a solution of α-D-glucopyranose in Me_2SO at room temperature for 4 days, and the solution then showed only a trace of the β-D anomer (g.l.c. of the Me_3Si ether). However, on heating the same solution at 90° for 2 h, an equilibrium mixture of the α and β anomers was formed (ratio 43:57). Evidently, therefore, mutarotation occurs slowly at 90°.

The total, molar yield of D-glucose from thermolysis of sucrose is almost theoretical up to ~50 min (Fig. 1) when related to sucrose lost. Evidently, therefore, α-D-glucopyranose is produced almost quantitatively in the thermolysis. The molar yield of D-fructose is much lower (~20% after 50 min) and that of the anhydrofructose is even less (~5%). These two products certainly undergo secondary thermal decomposition more rapidly than D-glucose, but there is no doubt that D-glucose is the

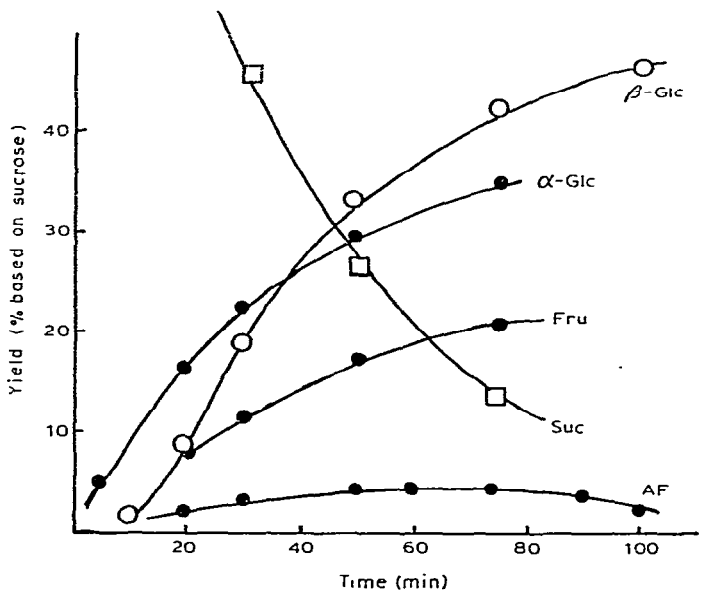


Fig. 1. Products formed on heating a 2% solution of sucrose in Me_2SO at 90°: β-Glc, β-D-glucopyranose; α-Glc, α-D-glucopyranose; Fru, D-fructose; Suc, sucrose; AF, 2,6-anhydro-D-fructofuranose.

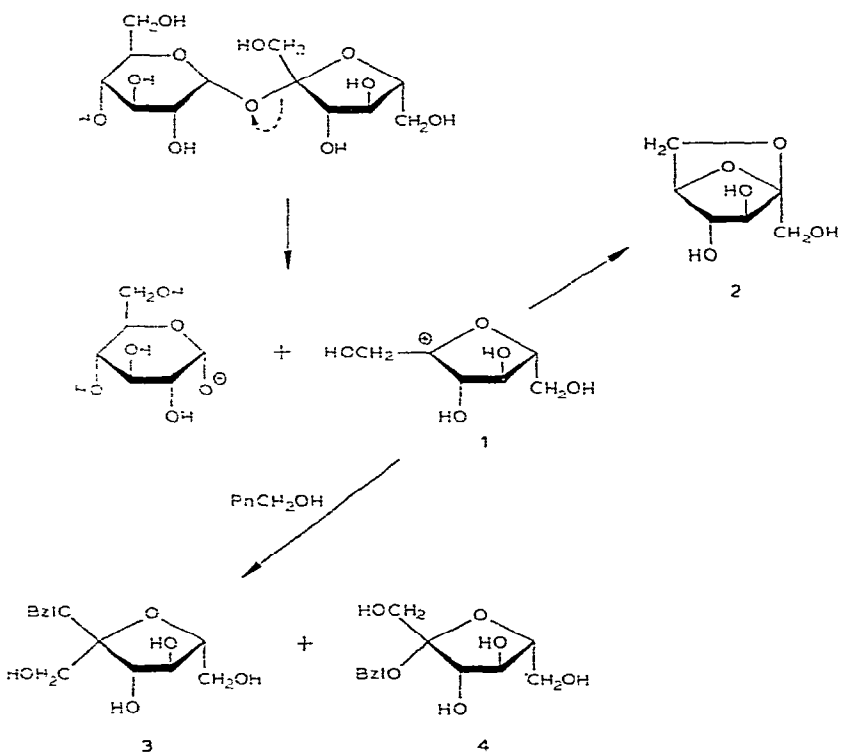
preponderant primary product. These results therefore support the general mechanism previously postulated[1] as a major pathway for thermolysis:

Glc-Fru→α-Glc + Fru*,

but give no evidence of the nature of Fru* nor of its ultimate fate.

It has been tentatively suggested[3,4] that the fructosyl carbocation **1** (Scheme 1) may be an intermediate in the thermal degradation of sucrose (*i.e.*, that Fru* is **1**). This suggestion was first based on the observed formation[4] of 2,6-anhydro-β-D-fructofuranose (**2**) and the ethyl α- and β-D-fructofuranosides in high-temperature hydrogenolysis of sucrose in ethanol. The conclusion was that the fructosides "may be produced by solvolysis of the (first-formed) anhydride, as well as *via* a carbonium-ion intermediate such as **1**". This suggestion was used[5] to explain the formation of ketoses (fructosylsucroses) when powdered sucrose was heated at 170° for 15 min, but no more definite evidence was available that **1** or **2** is an intermediate in thermolysis of sucrose. We therefore attempted to resolve this question.

The thermolysis of sucrose in Me_2SO was performed in the presence of benzyl alcohol, and the g.l.c. profile of the products is illustrated in Fig. 2 (with yields shown in Table III). The yields of the fructosides **3** and **4** were calculated *via* α,α-trehalose



Scheme 1. Thermal decomposition of sucrose

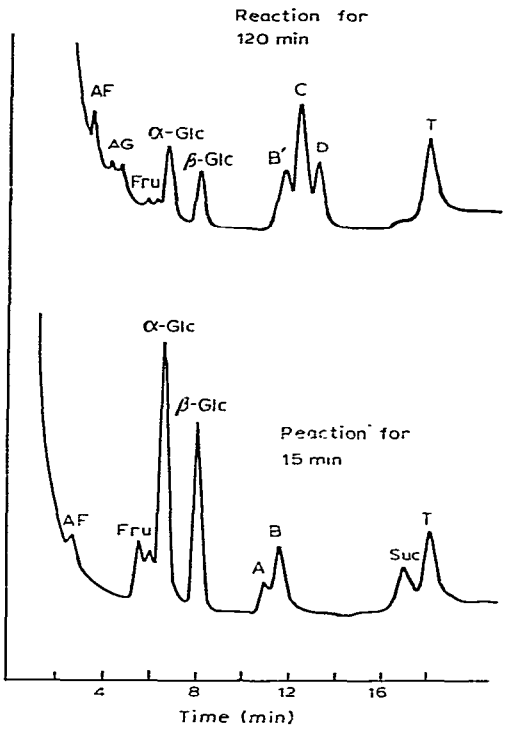


Fig. 2. Gas chromatogram of Me_3Si ethers of products formed when a solution of sucrose and benzyl alcohol in Me_2SO was kept at 130°: AF, 2,6-anhydro-D-fructofuranose; AG, 1,6-anhydro-D-glucoses; Fru, D-fructose; α-Glc, α-D-glucopyranose; β-Glc, β-D-glucopyranose; A, benzyl β-D-fructofuranoside; B, benzyl α-D-fructofuranoside; B', C, D, benzyl glucosides; Suc, sucrose; T, α,α-trehalose (internal standard).

TABLE III

MOLAR YIELDS (%) OF PRODUCTS FROM HEATING SUCROSE WITH Me_2SO AND BENZYL ALCOHOL (130°)

Compound	*Time (min)*			
	15	*30*	*45*	*120*
D-Glucose	80	103	106	17
Benzyl β-D-fructofuranoside	6	4	4	N.d.[c]
Benzyl α-D-fructofuranoside[a]	20	21	19	14
Benzyl glucoside (C)[b]	N.d.[c]	N.d.	N.d.	27
Benzyl glucoside (D)[b]	N.d.	N.d.	N.d.	14

[a]Includes increasing amounts of benzyl glucoside B' (Fig. 2). [b]See Fig. 2. [c]N.d. = Not detected.

as the internal standard, using a calibration factor derived from the relative g.l.c. responses of trehalose and phenyl β-D-glucopyranoside, on the assumption that the latter has a response similar to that of **3** and **4**. The products yielding peaks B'

(coincident with B), C, and D were benzyl glucosides formed slowly by the reaction of benzyl alcohol with the first-formed glucose. The same g.l.c. profile (B′, C, and D) was obtained by heating a solution of D-glucose and benzyl alcohol in Me_2SO. The benzyl fructosides are themselves subject to non-specific, thermal degradation on further heating.

The benzyl fructofuranosides **3** and **4** were isolated, and their structures verified by n.m.r. and mass spectrometry (m.s.), and by acid hydrolysis to fructose under mild conditions. The ^{13}C-n.m.r. assignments are based on previous assignment of fructosides[6], and the mass spectrum showed scission on both sides of the glycosidic oxygen and between C-1′ and C-2′. The isolation of benzyl α- and β-D-fructofuranosides is compatible with the reaction of benzyl alcohol with the fructosyl carbonium-ion intermediate **1**, but the possibility remained that they could also have arisen by alcoholysis of the anhydrofructose **2**, since Goldschmid and Perlin[5] have shown that **2** undergoes ethanolysis to yield both anomeric furanosides. It was therefore necessary to isolate **2** and to study its reactivity under our conditions.

The anhydrofructose **2** has previously been isolated (4% yield) after high-pressure catalytic hydrogenolysis of sucrose in ethanol[4] and, in unstated yield, by heating[5] crystalline sucrose at 170° for 15 min. In both cases, extensive chromatography was required for purification. However, we found that the stated thermal treatment of pure, finely powdered sucrose gave no reaction after 15 min at 170°. Commercial "raw" sugar (purity ~98%) reacted more rapidly and gave a maximum 1.5% yield of **2** after 50 min at 170°, as determined by g.l.c. of Me_3Si ethers with *myo*-inositol as the internal standard and 1,6-anhydro-D-glucopyranose as the reference for g.l.c. response. Only low yields (<1%) of **2** could be obtained by molecular distillation (at 170° or 180°) of the products from crystalline or amorphous sucrose. When dibenzyl ether was used as an inert liquid to improve the thermal contact with powdered sucrose, heating at 170° for 15 min gave an apparently optimised yield of **2**, which was purified by chromatography (0.3% final yield). This product did not crystallise, but was homogeneous by t.l.c. and by g.l.c. (Me_3Si ether) and had the anticipated ^{13}C-n.m.r. and mass spectra (after g.l.c. of the Me_3Si ether). The large abundance of a fragment of *m/z* 217 and the failure to detect a fragment having *m/z* 204 confirm the presence of the furanoid rather than the pyranoid ring in the Me_3Si ether of the anhydride[7].

When **2** was treated with benzyl alcohol in Me_2SO at 130° under the exact conditions used for the benzyl fructoside preparation, ~10% of **2** had been lost (measured by g.l.c. of the Me_3Si ethers) after 15 min, presumably by non-specific, thermal degradation. No formation of benzyl fructosides was detected. Thus, **2** was not the reactive intermediate in the conversion of sucrose into benzyl fructosides, and we conclude that the mechanism of the thermolysis is predominantly as shown in Scheme 1. There is no likely mechanism whereby **2** could arise directly from sucrose by an intramolecular displacement, and it is therefore concluded that the most likely source of **2** is a cyclisation of **1**. This process would provide a source of protons for the glucosyl anion (see below).

The fructosyl-carbocation **1** can react with excess of sucrose to produce trisaccharides, or with other alcohols to produce fructofuranosides as shown, but other, non-specific, thermal-degradation reactions probably compete with such processes. The sources of the fructose, which is always found in small yield, and also of the proton required by the glucosyl anion, are not known with certainty. However, the non-specific, thermal degradations that are postulated to account for the fate of some of **1** will certainly include some condensation reactions which yield water, thus accounting for some hydrolysis of sucrose to D-glucose and D-fructose, and for some protons. One such important chain of reactions results in the formation of 5-hydroxymethyl 2-furaldehyde, which can always be detected after such thermolyses.

It is also possible that fructose could arise by thermolytic scission of the glucose–oxygen bond, analogous to the fructose–oxygen scission shown in Scheme 1. However, if it occurs, such a reaction must be relatively minor and we conclude that the former type of scission is preferred, at least partly because of the greater stability of the fructosyl carbocation. The question of the facilitation of the scission by intramolecular hydrogen-bonding (see above) will be further investigated, as will the use of other nucleophiles to react with the intermediate carbonium ion.

EXPERIMENTAL

Determination of the rate of degradation of sucrose. — Finely ground, dry sucrose was weighed into a glass test-tube and sealed with a rubber septum. Redistilled, dry Me_2SO was added by syringe and measured by weight. The tube was ultrasonicated until dissolution was complete and then placed in an oil bath at the required temperature (±0.1°). Samples of ~10 µl were transferred at intervals, by syringe, to a reaction vial and weighed. A weighed amount of a solution of α,α-trehalose in dry Me_2SO was added as the internal standard, followed by 150 µl of a 2:1 (v/v) mixture of dry pyridine and *N*-trimethylsilylimidazole. After the mixture had been kept at room temperature for 1 h, 0.5-µl samples were analysed by g.l.c. (isothermally at 230° on a column of 3% SE30 as described earlier[2]); monosaccharide products were analysed at 130 + 10°.min^{-1} with *myo*-inositol as the internal standard. The rate of disappearance of sucrose (k_{obs}) was determined by a linear least-squares plot of log (sucrose remaining) against time, and the results are shown in Table I.

*Isolation of 2,6-anhydro-β-*D*-fructofuranose.* — Finely ground, dry sucrose (10 g) was dispersed by ultrasonication in redistilled, dry dibenzyl ether (50 ml) in a test-tube. The mixture was heated in an oil bath at 170° with occasional stirring for 15 min and then cooled, and as much as possible of the dibenzyl ether was removed by decantation. The sticky, amber-coloured, solid residue was washed by decantation with diethyl ether (3 × 100 ml), and then dissolved in water (25 ml) and washed with chloroform (25 ml). The aqueous phase was diluted with acetone (90 ml), in order to precipitate oligo- and poly-saccharides. The remaining solution was evaporated to dryness, and the residue was subjected to recycling dry-column chromatography on

silica gel with butanone. The anhydrofructose was obtained as a colourless syrup (28 mg; single component by t.l.c. and g.l.c.) that could not be induced to crystallise; $[\alpha]_D^{25}$ −105.7° (*c* 1, water); lit.[+] m.p. 118–119°, $[\alpha]_D^{25}$ −107° (water). ^{13}C-N.m.r. data [$(CD_3)_2SO$]: δ 60.5 (C-1), 68.8 (C-6), 81.2 (C-4), 84.2 (C-3), 85.5 (C-5), and 111.2 (C-2). E.i.-mass spectrum (by g.l.c. of trimethylsilyl ether): *m/z* 363 (2%), 273 (3), 260 (3), 245 (3), 243 (4), 230 (49), 217 (64), 215 (45), 191 (9), 147 (58), 121 (21), 103 (20), and 73 (100).

Anal. Calc. for $C_6H_{10}O_5$: C, 57.12; H, 4.80. Found: C, 56.83; H, 5.02.

Reaction of sucrose and benzyl alcohol in Me_2SO. — Dry, powdered sucrose (10.0 g) and dry, redistilled Me_2SO (35 ml) were sonicated in a flask sealed with a rubber septum until dissolution was complete. Dry, redistilled benzyl alcohol (35 ml) was added by syringe, and the mixture was kept in an oil bath at 130° for 15 min. A sample then gave the gas chromatogram shown in Fig. 2. Water (100 ml) was added and the mixture extracted with chloroform (5 × 100 ml). The chloroform extract contained benzyl alcohol and 5-hydroxymethyl-2-furaldehyde, the latter being detected by t.l.c. and as its 2,4-dinitrophenylhydrazone. The aqueous phase was adjusted to pH 7 with ammonia and evaporated to dryness. Fractionation by recycling dry-column chromatography on silica gel with dichloromethane and ethyl acetate was incomplete, but the following fractions were found to be homogeneous by t.l.c. and g.l.c. (as trimethylsilyl ethers).

(*i*) 2,6-Anhydro-β-D-fructofuranose (13 mg); properties as described above.

(*ii*) Benzyl α-D-fructofuranoside (38 mg), m.p. 91–92°, $[\alpha]_D^{25}$ +45.8° (*c* 2, water); lit.[8] m.p. 88–89°, $[\alpha]_D^{25}$ +44.9° (water). ^{13}C-N.m.r. data [$(CD_3)_2SO$]: δ 59.11 (C-1); 61.06 (benzyl); 63.69 (C-6); 76.94 (C-4); 80.94 (C-3); 82.45 (C-5); 128.01, 128.26, and 128.59 (aromatic). E.i.-mass spectrum of trimethylsilyl ether: *inter alia*, *m/z* 455 (38%), 451 (19%), and 91 (100%).

(*iii*) Benzyl β-D-fructofuranoside (38 mg), colourless syrup, $[\alpha]_D^{25}$ −21.5° (*c* 2, water), ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 3.25–4.01 (broad-peak m, 8 H), 4.21–4.73 (m, 4 H, OH), 4.91–5.20 (m, 1 H), and 7.27 (s, 5 H, aromatic). ^{13}C-N.m.r. data [$(CD_3)_2SO$]: 60.13 (C-1); 61.16 (benzyl); 62.38 (C-6); 76.94 (C-4); 81.58 (C-3); 82.60 (C-5); 107.50 (C-2); 126.80, 127.19, and 127.87 (aromatic). The e.i.-mass spectrum of the trimethylsilyl ether was indistinguishable from that of the α anomer (above).

Anal. Calc. for $C_{13}H_{18}O_6$: C, 57.75; H, 6.72. Found: C, 57.46; H, 6.95.

Acid hydrolysis of benzyl fructofuranosides. — A sample (1 mg) of each anomer (*i* and *ii* above) was dissolved in water (50 μl) and heated with 5 beads of Amberlite IR-120(H^+) resin at 100° for 30 min. The solution was then evaporated to dryness, and the residue was trimethylsilylated and examined by g.l.c. In each case, the fructoside was completely hydrolysed and fructose was the only product detected.

ACKNOWLEDGMENTS

The authors thank Dr. G. Meehan for helpful discussion. Financial support was provided by the Sugar Research Institute, Mackay, Australia.

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