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THE BEHAVIOUR OF D-FRUCTOSE AND INULIN TOWARDS ANHYDROUS HYDROGEN FLUORIDE*

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ABSTRACT

Inulin and D-fructose are quantitatively converted into a mixture of D-fructose dianhydrides on treatment with anhydrous hydrogen fluoride. Of the six dianhydrides isolated, five are known compounds, whereas one, β-D-fructofuranose β-D-fructopyranose 2,1′:3,2′-dianhydride, has not been described hitherto. The structures of two of the known dianhydrides have been revised. The relative amounts of dianhydrides obtained depend on the reaction conditions. The reaction of D-fructose with hydrogen fluoride is shown, using ^{13}C-n.m.r. spectroscopy, to involve D-fructofuranosyl fluoride as a probable intermediate. Dianhydrides are also formed when D-fructose is treated with methanol and sulfuric acid under Fischer glycosidation conditions or with trifluoroacetic acid.

INTRODUCTION

In studying the hydrolysis of polysaccharides and their subsequent extraction from lignocellulosic materials, the reaction of cellulose, amylose, xylan, D-glucose, and D-xylose with anhydrous hydrogen fluoride (HF) has been investigated[2]. The results have been applied to the extraction of carbohydrates from wood[1]. The solubilisation properties of HF with respect to highly hydrogen-bond-associated polysaccharides and the probable enhanced stabilisation of glycosyloxycarbonium ions by this reagent may account for the remarkable hydrolytic and extractive properties of HF towards lignocellulosic materials. Due to the tertiary structure at their anomeric carbon atoms, such reactivity and associated properties, for example, reversion, may be expected to be enhanced with ketosans and ketoses.

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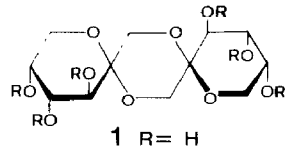
The reaction of D-fructose and inulin with strong acids[3–6], particularly hydrochloric acid, yielded mixtures of dianhydrides, in overall yields that do not exceed 50%. The reaction mixtures contained large proportions of unreacted D-fructose, even after 3 days, and their dark colour was caused by decomposition products[5]. The reaction of D-fructose with hydrogen fluoride gave[7] 50% of fructose dianhydrides. We have found reaction conditions where D-fructose and the fructosan constituent of inulin were quantitatively converted into D-fructose dianhydrides on treatment with HF and now report on these products.

RESULTS AND DISCUSSION

Storage of solutions of inulin or D-fructose in liquid hydrogen fluoride under various conditions of temperature, time, and concentration gave D-fructose dianhydrides (**1, 4, 7, 10, 13,** and **16**) by precipitation with excess of ether, or evaporation of the HF. The yields and product mixtures obtained by either procedure were almost identical. Similar behaviour was previously found with xylan and D-xylose, whereas glucans and D-glucose yielded mainly α-D-glucopyranosyl fluoride by the first, and reversion oligosaccharides by the second, procedure[2]. Since D-fructose and inulin gave the same mixture of products, most of the subsequent experiments were carried out with D-fructose.

The composition of the product mixture was dependent, to some extent, on the initial concentration of the solution in HF and the temperature and duration of the reaction (Table I). Thus, for reactions at low temperature and for a few minutes, there were small proportions of unreacted D-fructose. When the reaction



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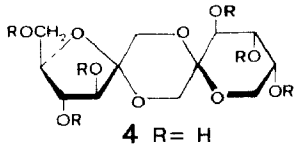

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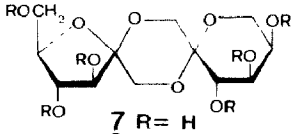

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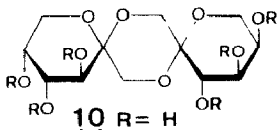

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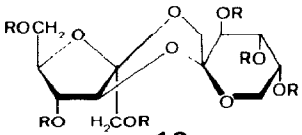

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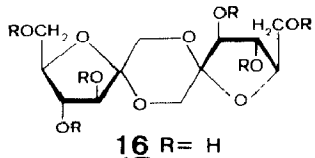


16 R= H
17 R= Ac
18 R= Me

TABLE I

PRODUCTS FORMED BY THE ACTION OF ANHYDROUS HYDROGEN FLUORIDE ON EITHER D-FRUCTOSE OR INULIN

D-Fructose (F) or inulin (I) (g)	*HF (mL)/ SO_2 (mL)*	*Reaction temp. (degrees)*	*Reaction time*	*Mode of recovery*[a]	*Products*[b] *(%)*						
					1	**4**	**7**	**10**	**13**	**16**	D-*Fructose*
I (5)	10/0	0	15 min	P	18	27	9	10	14		
I (5)	10/0	20	45 min	E	14 (12)	38 (45)	6 (4)	17 (15)	16 (18)		
F (5)	10/0	20	45 min	E	14 (12)	46 (45)	3 (4)	17 (15)	16 (18)		
F (10)	40/0	20	5 h	E	14	42		29	16		
F (10)	20/0	−25	22 h	P	20	35		23	22		
F (10)	20/0	−10	3–4 min	P	17	35	5	17	9	9	10
F (10)	20/0	−78	3 min	P	19 (17)	40 (37)	8 (8)	8 (21)	9 (10)		
F (10)	10/0	20	5 h	E	11	33	4	29	23		
F (50)	50/0	20	2 h	E	12 (10)	35 (37)	(3.7)	31 (17)	22 (28)		
F (10)	10/0	−25	24 h	P	14	30	7	32	8		9
F (50)	50/50	−25	24 h	P	10 (13)	36 (39)	4 (1)	42 (41)	4 (2.5)		6
F (10)	10/30	−25	24 h	P	4	40	4	48	4		4
F (10)	10/20	−10	5 min	P	35 (47)	19 (21)		(15)		18 (12)	28
F (20)	10/0	−10	3 min	P	19	35	13	19			
F (50)	25/50	−25	24 h	P	46 (41)	30 (30)	5 (2.5)	5 (9)	6	8 (11.5)	
F (10)	5/20	−25	20 h	P	49	38				13	
F (10)	5/20	−10	5 min	P	21	13	4			8	54

[a]P, Precipitation with ether; E, evaporation of HF. [b]Values in parentheses were obtained by g.l.c. of the methylated products; the other values were estimated from ^{13}C-n.m.r. spectra, using peak heights of the signals for the anomeric carbon atoms.

mixtures were diluted with liquid sulfur dioxide, large proportions of starting material were recovered. Thus, the comparatively low yield of D-fructose dianhydrides reported by Sattler *et al.*[7] may be ascribed to non-homogeneous reaction conditions [the 1:4.75 (v/w) ratio of HF to D-fructose used would not result in complete dissolution]. When the reaction of D-fructose with HF was for <1 h at 20° or for 20 h at −25°, the crude product mixture obtained was colourless and the yield was almost quantitative. After reaction for 24 h at 20°, the crude product mixture was black and only partially soluble in water.

Fractional crystallisation of the product mixture from methanol and then from aqueous ethanol gave **1, 10**, and **4**. Acetylation of the residue followed by chromatography gave the acetylated derivatives **8, 14**, and **17**. Chromatography was also applied to the whole product mixture after acetylation. Four of the products (**1, 4, 7,** and **10**) isolated corresponded to the diheterolevulosans I–IV[8–11] (m.p., $[\alpha]_D$, and ^{13}C-n.m.r. spectra[12]); **13** apparently has not been previously described hitherto and **16**, formed under mild conditions (Table I), was identical with the so-called[13] difructose anhydride I.

The dianhydrides have been investigated by ^{13}C-n.m.r. spectroscopy and not all of the structures originally assigned appear to be correct. Difructose anhydride I[13] (**16**) is undoubtedly α-D-fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride as confirmed[14] by the ^{1}H-n.m.r. data for its hexa-acetate. The signals for C-3,4,5 and C-3′,4′,5′, which are found at rather low field (Table II), show that it contains two different furanose rings. The signals of the anomeric carbon atoms (C-2α 103.3, C-2β 99.7 p.p.m.) are found at high field relative to those of fructofuranose[15] (C-2α 105.5, and C-2β 102.5 p.p.m.) or α-D-fructofuranose β-D-fructofuranose 1,2′:2,3′-dianhydride[16] (C-2α 106.0, C-2β 103.8 p.p.m.). However, this discrepancy is not serious in view of the dispirodioxolane disposition of these carbon atoms. Diheterolevulosan IV[11] (**10**) is the only isomer which shows only six ^{13}C signals, and the structure proposed (di-β-D-fructopyranose 1,2′:2,1′-dianhydride) on the basis of n.m.r. data[12,17] is correct. The chemical shifts of the ^{13}C signals of diheterolevulosan I[8] (**1**) are similar to those of **10** and are in agreement with a dipyranose structure. However, 12 signals are given by **1** and its hexa-acetate **2** (Table II). The structure proposed[12] (di-α-D-fructopyranose 1,2′:2,1′-dianhydride) for this compound is therefore unlikely. An X-ray analysis* showed the structure to be α-D-fructopyranose β-D-fructopyranose 1,2′:2,1′-dianhydride, in good agreement with the ^{1}H-n.m.r. data which indicate two pyranose rings in $^1C_4$ and $^4C_1$ conformations[17].

Diheterolevulosan II[9] (**4**) was assigned the structure β-D-fructofuranose α-D-fructopyranose 1,2′:2,1′-dianhydride on the basis of the ^{13}C-n.m.r. chemical shifts of the signals for the anomeric carbon atoms[12]. However, the signals for the furanose carbon atoms C-3,4,5 (84.3, 82.8, and 78.6 p.p.m., respectively) agree

*Kindly performed by Professor R Norrestam (University of Technology of Denmark); the detailed results will be published elsewhere.

TABLE II

^{13}C-N M R CHEMICAL SHIFTS AND PHYSICAL CONSTANTS OF D-FRUCTOSE DIANHYDRIDES AND OF THEIR HEXA-ACETATES

Compound (trivial name)	*Ref.*	*^{13}C Chemical shifts*[a]			*M.p. (degrees)*	$[\alpha]_D^{20}$ *(degrees)*
		C-2,2'	*C-3,4,5,3',4',5'*	*C-1,6,1',6'*		
Dianhydrides						
α-D-Fru*p* β-D-Fru*p* 1,2':2,1' (Diheterolevulosan I, **1**)	8	95.3 96.4	71.5 (C-4), 71.4 (C-4'), 69.9 (C-3, C-5'), 69.4 (C-3'), 64.8 (C-5)	64.4 (C-1'), 61.7 (C-1), 61.5 (C-6'), 60.5 (C-6)	290	−45 (*c* 6)[b]
α-D-Fru*f* β-D-Fru*p* 1,2':2,1' (Diheterolevulosan II, **4**)	9	103.1 96.5	84.3, 82.8, 78.6, 69.8 (2C), 69.4	64.3, 62.3, 62.1 (2C)	257–259	−38 (*c* 3.7)
β-D-Fru*f* β-D-Fru*p* 1,2':2,1' (Diheterolevulosan III, **7**)	10	101.5 97.6	82.8, 80.8, 76.0, 72.0, 70.6, 69.9	65.7, 65.1, 63.4, 63.2	240	−182 (*c* 0.5)
β-D-Fru*p* β-D-Fru*p* 1,2':2,1' (Diheterolevulosan IV, **10**)	11	97.8 97.8	73.1, 70.3, 69.8	65.3, 64.3	275–277	−313 (*c* 3.5)
β-D-Fru*f* β-D-Fru*p* 2,1':3,2' (**13**)	—	104.3 95.7	85.6, 77.0, 73.9, 69.9, 69.7 (2C)	64.7, 64.3, 63.2, 62.1	206–207	−58.5 (*c* 1.03)
α-D-Fru*f* β-D-Fru*f* 1,2':2,1' (Difructose anhydride I, **16**)	13	103.3 99.7	84.3, 82.7, 82.1, 78.6, 77.8, 75.4	63.5, 63.4, 62.6, 62.0	160–162	+27 (*c* 1.2)
Hexa-acetates						
α-D-Fru*p* β-D-Fru*p* 1,2':2,1' (**2**)	8	92.8 94.7	69.2, 68.9, 67.5, 67.2, 67.1, 64 8	61.4, 61.1, 60.9, 57.8	171–173	−57 (*c* 3.5)
α-D-Fru*f* β-D-Fru*p* 1,2':2,1' (**5**)	9	101.5 95.0	81.2, 79.7, 77.9, 69.0, 67.5, 67.3	63.2 (2C), 61.5, 61.1	124–125	−38 (*c* 1.4)
β-D-Fru*f* β-D-Fru*p* 1,2':2,1' (**8**)	10	101.4 96.6	78.5, 77.4, 75.4, 70.0, 69.0, 67.4	65.1, 63.8, 62.3, 61.0	127.5–129	−155 (*c* 1 1)
β-D-Fru*p* β-D-Fru*p* 1,2':2,1' (**11**)	11	97.1 97.1	70.4, 69.0, 66.9	63.1, 62.4	269–270	−195 (*c* 1.1)
β-D-Fru*f* β-D-Fru*p* 2,1':3,2' (**14**)	—	103.1 94.5	80.7, 77.9, 70.9, 68.9, 67.8, 67.2	64 3, 64.1, 62.1, 61.5	122–123	−86 (*c* 1.4)
α-D-Fru*f* β-D-Fru*f* 1,2':2,1' (**17**)	13	101.4 99.5	81.0, 79.5, 78 6, 77.6, 76.0, 75.6	64.6, 62.8, 62.5, 61.5	124–125 or 135–136 (dimorphous)	−0.9 (*c* 5.5)

[a]Except for **1**, the signals are not assigned. The signals for **1** were assigned on the basis of a ^{13}C-n m.r spectrum recorded with a Bruker 400-MHz instrument, using selective proton decoupling. [b]In water for the dianhydrides, in chloroform for the hexa-acetates.

well with those of the corresponding carbon atoms of α-D-fructofuranose (82.9, 82.2, and 77.0 p.p.m.) but not those of β-D-fructofuranose (81.6, 76.4, and 75.4 p.p.m.)[15]. These data accord with an α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride structure for **4**. The β-D configuration of the pyranose ring in the $^1C_4$ conformation is indicated by the ^{1}H-n.m.r. data[17] for the hexa-acetate **5**.

Diheterolevulosan III[10] (**7**) is assumed to be β-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride[12], in agreement with the literature. The pyranose ring adopts the $^1C_4$ conformation[17] and the configuration must therefore be β-D; consequently, the furanose moiety must also be β-D since the compound is different from **4**.

The previously unknown isomer **13** gave, as did the other dianhydrides, a pseudomolecular ion in f.a.b.-m.s. at *m/z* 325 $(M + H)^+$.That it contains a furanose and a pyranose ring was indicated by the chemical shifts of the signals of the secondary carbon atoms (Table II). The ^{1}H-n.m.r. spectrum of the hexa-acetate **14** contained signals for only four protons at low field (δ 5–5.8), which may be assigned to acetylated secondary alcohols. It is assumed that, since the signal for H-3 of the furanose ring is at higher field (3.90 p.p.m.), there is a 2,3-linkage and the furanose moiety must be β. The ^{1}H-n.m.r. data for **14** showed that the pyranose ring has the $^1C_4$ conformation ($J_{3,4}$ 10, $J_{4,5}$ and $J_{5,6}$ 1–1.5 Hz) and is therefore β. These data accord with a β-D-fructofuranose β-D-fructopyranose 2,1′:3,2′-dianhydride structure for **13**.

In order to monitor the course of anhydride formation, the compositions of reaction mixtures listed in Table I were determined from ^{13}C-n.m.r. spectra (Fig. 1) and, in many instances, by g.l.c. of the methylated products (Fig. 2). The amounts of fructofuranose fructopyranose 1,2-dianhydrides **4** and **7** formed (Table I) are largely independent of the reaction conditions. The previously unknown β-D-fructofuranose β-D-fructopyranose 2,1′:3,2′-dianhydride (**13**) was found only after prolonged reaction at room temperature. On the other hand, the difuranose anhydride **16** was obtained only at low temperature and especially when the HF was diluted with sulfur dioxide. It is probable that **16** was the first dianhydride formed, and that it subsequently rearranged into other isomers. The relative amounts of the two dipyranoses **1** and **10** depended on the amount of HF, especially when D-fructose was treated with HF in sulfur dioxide. Thus, when two parts of D-fructose are treated with one part of HF at −25° for 24 h, ~40% of α-D-fructopyranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**1**) was formed and only a few percent of the β,β-anomer **10**. With twice the amount of HF and reaction for a few minutes, **1** was also the main product but, after 24 h, the amount of **10** had increased to ~40% at the expense of **1**.

To obtain more information about the course of the reaction, a solution of D-fructose in HF at various temperatures was monitored by ^{13}C-n.m.r. spectroscopy (Fig. 3). Spectrum A was obtained at 10° and showed that the solution contained mainly **4** and **10**. As the temperature was progressively lowered, there were increasing amounts of an additional product having two signals at 107.4 and 117.4

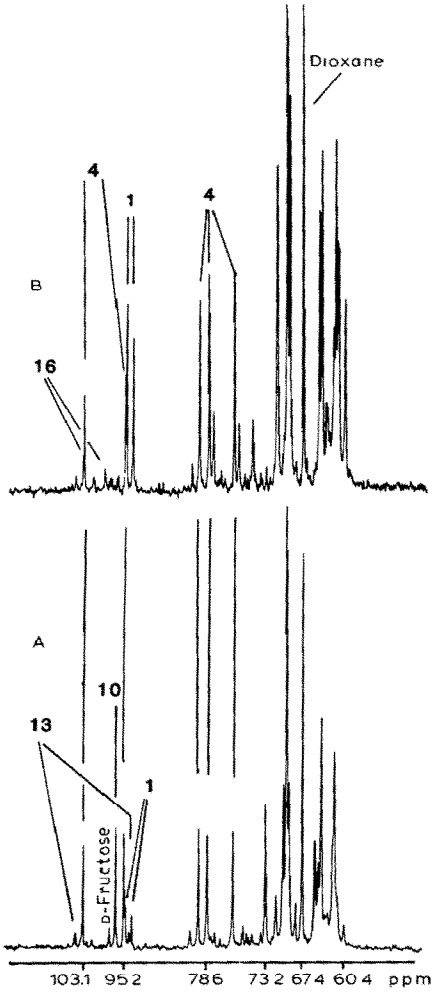


Fig. 1. ^{13}C-N.m.r. spectra of reaction mixtures after storage for 24 h at −25°: A, D-fructose (50 g), HF (50 mL), and sulfur dioxide (50 mL); B, D-fructose (50 g), HF (25 mL), and sulfur dioxide (50 mL).

p.p.m. (Fig. 3B–D). These signals probably arose from fructosyl fluoride, with the signal of C-2 centered at 112.4 p.p.m. ($J_{C\text{-}2,F}$ 236.5 Hz) suggesting it to be β-D-fructofuranosyl fluoride[18] (**19**). When the solution was again heated to 10°, it gave spectrum A, showing the existence of a reversible, temperature-dependent equilibrium between the fructofuranosyl fluoride and the mixture of dianhydrides. Since most of the experiments shown in Table I were worked-up by cooling the reaction mixture to −78° and precipitating with ether, it might be expected that the products would contain **19**. However, the presence of **19** was not observed, possibly because it was converted during the work-up procedure into dianhydrides probably *via* the oxocarbonium ion **20**, and isomerisation of dianhydrides in acid may be expected

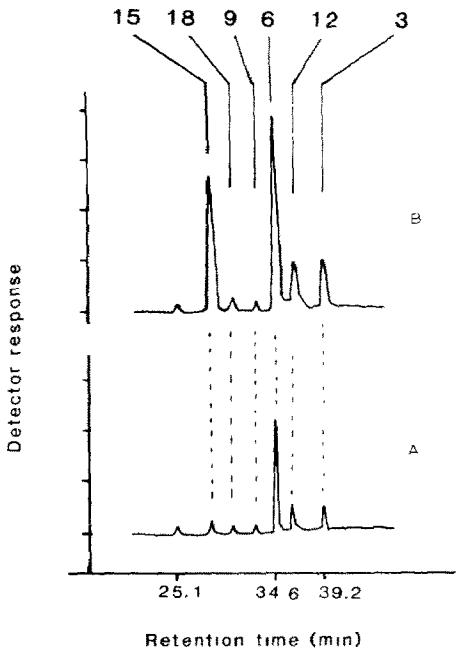
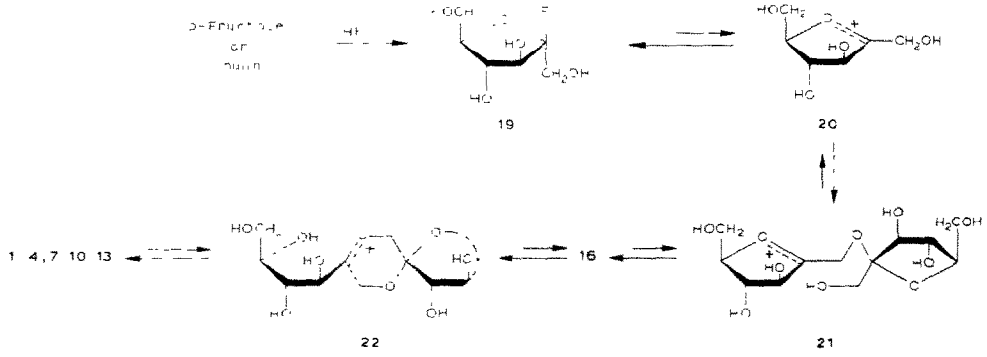


Fig. 2. G.l.c of methylated products obtained from A, D-fructose (10 g) kept in HF (10 mL) for 5 min at −10°, B, D-fructose (10 g) kept in HF (20 mL) for 5 h at +20°.



Scheme 1. Proposed mechanism for the formation of difructose dianhydrides by the action of HF on D-fructose and inulin.

to proceed *via* such ions as **21** and **22** (Scheme 1). Treatment of **1** or **10** with HF gave the same mixture of products as that obtained from D-fructose. This behaviour is in agreement with the relative stabilities that can be expected by taking into account the conflicting influences that may result from the known ring and conformational stability of D-fructose in solution[15] and the polar interactions in the dioxolane ring.

In view of the easy formation of dianhydrides from D-fructose, as

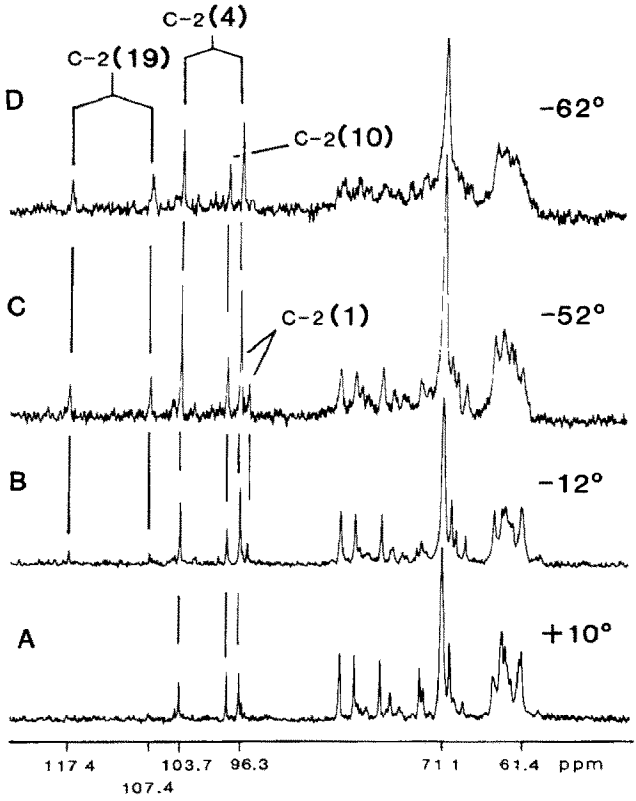


Fig. 3. ^{13}C-N.m.r. spectra of a solution of D-fructose (0.5 g) in HF (1.2 mL) containing acetone-d_6 (0.5 mL) prepared at −20°. The spectra were recorded within ~2 h at the temperature indicated.

demonstrated here and elsewhere[3,4], it might be expected that they could be formed under less acidic conditions. Treatment of D-fructose with trifluoroacetic acid gave a mixture of the dianhydrides **4**, **7**, **13**, and **16**, together with 34% of unreacted D-fructose; after acetylation, the hexa-acetate **17** could be crystallised in 15% yield. When D-fructose was treated with one part of methanolic 5% sulfuric acid, 22% of **16** and 13% of **4** were formed. As the proportion of methanol was increased, the amount of dianhydrides diminished to a few percent.

EXPERIMENTAL

General methods. — ^{13}C-N.m.r. spectra were recorded with Bruker WH-90, WP-100, HX-270, WM-400, and Cameca (Thomson CSF, Paris) 250-MHz instruments. Spectra of unacylated products were recorded for solutions in D_2O (internal 1,4-dioxane, 67.4 p.p.m.). For acetylated compounds, solutions in $CDCl_3$ were used with the central peak of the triplet (77.2 p.p.m.) as internal reference. ^{13}C-N.m.r. spectra of HF solutions (Fig. 3) were obtained using Teflon tubes which

fitted tightly inside a 10-mm glass sample tube; acetone-d_6 was used as lock substance and internal reference. Mass spectra in the f.a.b.–m.b.s.a. ionisation mode were recorded on a Devienne SM IV double-focusing instrument[19] fitted with a 1.295-T magnet, operating at the full accelerating potential (8 kV), and a Carlston–Magnuson source producing a Kr beam of 3–5 keV kinetic energy. Melting points were determined with a Zeiss microscope hot-stage and are corrected. Optical rotations were measured with a Perkin–Elmer 241 instrument.

The anhydrous hydrogen fluoride (HF) was a commercial product obtained in steel cylinders. Prior to use, it was kept in polyethylene bottles at 0°. Acetylations were effected conventionally with pyridine–acetic anhydride (1:1, 10 mL per 1 g of sample). Deacetylations were carried out, unless otherwise stated, using the Zemplén technique. T.l.c. of the hexa-acetates of the D-fructose dianhydrides was performed on silica gel 60F-254 (Merck), using hexane–ethyl acetate (1:1) and detection by u.v. light and by charring with sulfuric acid. Column chromatography was performed on silica gel 60 (70–230 mesh, Merck) with the above solvent. G.l.c. was performed with a WCOT OV17 capillary column (20 m × 0.25 mm), fitted to a Girdel 3000 instrument (Paris) which was connected to a Shimadzu (C-R1B Chromatopac) computer.

Reactions with hydrogen fluoride. — All reactions were carried out in polyethylene bottles. Either D-fructose or inulin was dissolved in the appropriate amount of HF at the temperature indicated (Table I). When the reaction was carried out below 20°, the solution was cooled (solid CO_2) and the product was precipitated by the addition of an excess of ether and triturated with ether to give an amorphous powder that was collected and dried in vacuum over potassium hydroxide. In some of the experiments carried out at 20°, the HF was evaporated in a stream of air prior to the treatment with ether. The two procedures gave virtually quantitative yields of crude product. The compositions of the product mixtures (Table I) were assessed by ^{13}C-n.m.r. spectroscopy of solutions in D_2O, using the intensities of the signals from the anomeric carbon atoms. More accurate analyses were carried out by methylation followed by g.l.c. (see below).

The dianhydrides were isolated and purified by fractional crystallisation and/or column chromatography of the hexa-acetates. Typically, a solution of the mixture (45 g) of dianhydrides in methanol (100 mL) was left for 48 h at room temperature. The resulting crystalline material, which contained **1** and **10** in proportions depending on the initial reaction conditions, was collected and the components were isolated by column chromatography of their hexa-acetates.

The methanolic mother liquors were concentrated and a solution of the residue in water (~5 mL) was diluted with ethanol (200 mL) and stored at room temperature for 24 h. The crystalline product (**4**) was recrystallised from aqueous ethanol. The mother liquors (containing **7** and **13**) were concentrated, the residue was acetylated, and the products were subjected to column chromatography to give **8** and **14** which were deacetylated to **7** and **13**. Melting points, optical rotations, and ^{13}C-n.m.r. data are reported in Table II.

Reactions of D-*fructose with hydrogen fluoride in liquid sulfur dioxide.* — Typically, to D-fructose (50 g) in a 500-mL polyethylene bottle at −78° was added liquid sulfur dioxide (50 mL) followed by HF (25 mL). The mixture was shaken whilst the temperature rose to −10° (the boiling point of SO_2). After 10 min, a homogeneous solution was obtained, which was then kept at −25° for 24 h, cooled to −78°, and stirred with ether (300 mL). The supernatant solution was removed by decantation, and the colourless precipitate was washed several times with ether, collected, and dried *in vacuo*. A ^{13}C-n.m.r. spectrum (Fig. 1B) and a methylation analysis gave the composition shown in Table I. A solution of the product (~45 g) in water (40 mL) was diluted with ethanol (300 mL), seeded with **1**, and stored overnight at room temperature. The crystals were collected, washed with methanol, and dried, giving a product (19.5 g, 43%) which contained 84% of **1** and 16% of **4** (^{13}C-n.m.r.). Two recrystallisations from water–ethanol gave **1** (14.5 g, 32%), m.p. 285–290°. Two further recrystallisations gave a product having the physical data listed in Table II. The mother liquors from the first crystallisation were concentrated, and methanol was twice evaporated from the residue (~25 g) which was then crystallised from methanol (~100 mL) for 2 days at room temperature to give almost pure **4** (3.0 g, 6.7%). Two recrystallisations from water (~2 mL) and ethanol (~40 mL) gave **4** (1.5 g) having the physical data shown in Table II.

Acetylation of the material in the main mother liquors gave a product (36 g) which crystallised from ether (~300 mL) to give α-D-fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride hexa-acetate (**17**), m.p. 118–120°. Two recrystallisations from ethanol gave **17** (2.5 g) having the properties shown in Table II. Deacetylation[14] of **17** and recrystallisation of the product from ethanol gave **16** having the physical properties shown in Table II. Deacetylation of the product in the mother liquors remaining after crystallisation of **17** gave a product which contained (^{13}C-n.m.r.) **1** (13%), **4** (48%), **7** (7%), **10** (12%), **13** (7%), **16** (12%), and small amounts of several other components. Crystallisation from methanol gave impure **4** (3.2 g).

In another experiment, a mixture of D-fructose (50 g), liquid SO_2 (50 mL), and HF (50 mL) was kept at −25° for 24 h and then worked-up as described above. A ^{13}C-n.m.r. spectrum (Fig. 2A) and a methylation analysis of the product mixture gave the composition shown in Table I. Crystallisation of the product from water (40 mL) and ethanol (300 mL) yielded material (14.5 g) which was recrystallised from water (~15 mL) and ethanol (~15 mL), to give **10** (7.4 g, 16%), m.p. 270–272°. Recrystallisation from water gave a product having the physical constants shown in Table II. ^{1}H-N.m.r. data (D_2O, 400 MHz): δ 3.71 (H-1a), 3.86 (H-1b), 3.80 (H-3), 3.90 (H-4), 4.05 (H-5), 3.77 (H-6a), and 3.70 (H-6b); $J_{1,1}$ 12.4, $J_{3,4}$ 4.7, $J_{4,5}$ 3.6, $J_{5,6a}$ 9.0, $J_{5,6b}$ 4.8, and $J_{6,6}$ 12.0 Hz; δ 3.50 (H-1′a), 4.17 (H-1′b), 3.56 (H-3′), 3.89 (H-4′), 4.01 (H-5′), 3.73 (H-6′a), and 3.84 (H-6′b); $J_{1',1'}$ 12.2, $J_{3',4'}$ 10.2, $J_{4',5'}$ 3.6, $J_{5',6'a}$ 1.5, $J_{5',6'b}$ 1.2, and $J_{6',6'}$ 12.9 Hz.

The main mother liquor was concentrated, and methanol was twice distilled from the residue which was then crystallised from methanol (~100 mL) to give

almost pure **4** (9.4 g, 21%). Recrystallisation gave a product which was identical with that described above.

Methylation analysis. — The crude product mixtures resulting from the action of HF on either inulin or D-fructose (500 mg) were dissolved in methyl sulfoxide (10 mL). Sodium hydride (1 g) and methyl sulfoxide (10 mL) were added, and the mixture was stirred overnight. Methyl iodide (2 × 3 mL) was then added with a 1-h interval, and, after being stirred for 2 h, the mixture was concentrated, the residue was extracted with chloroform (50 mL), and the extract was washed with water (2 × 10 mL), dried (Na_2SO_4), and concentrated. The products were analysed by g.l.c. Standards (**3, 6, 9, 12, 15,** and **18**) were prepared from **1, 4, 7, 10, 13,** and **16**, respectively, in the same way. The results of the analyses are shown in Table I and Fig. 2.

Separation of di-D-fructose dianhydride hexa-acetates. — The crude product mixtures resulting from the action of HF on either inulin or D-fructose (2 g) were acetylated. The product (4 g), which contained at least 4 main components (t.l.c.), was subjected to column chromatography (160 g). Further column chromatography was usually required to obtain almost pure compounds, but in low yields, which were recrystallised from ethanol. The order of elution was **11, 8, 17, 14, 2,** and **5**. The physical constants are given in Table II.

1,4,6-Tri-*O*-acetyl-β-D-fructofuranose 3,4,6-tri-*O*-acetyl-β-D-fructopyranose 2,1′:3,2′-dianhydride (**14**) gave the following ^{1}H-n.m.r. data ($CDCl_3$, 250 MHz): δ 4.33, 4.17, 3.92, 3.61 (H-1,1′), 4.04 (H-3), 4.98 (H-4), 4.24 (H-5), 4.47 (H-6a), 4.24 (H-6b), 5.40 (H-3′), 5.26 (H-4′), 5.35 (H-5′), 3.92 (H-6′a), 3.88 (H-6′b), 2.11 (OAc), 2.10 (2 OAc), 2.07 (2 OAc), and 1.96 (OAc); $J_{1,1}$ and $J_{1',1'}$ 12.0, $J_{3,4}$ ~0, $J_{4,5}$ ~0, $J_{5,6a}$ 9.3, $J_{5,6b}$ 5.5, $J_{6,6}$ 12.5, $J_{3',4'}$ ~10.2, $J_{4',5'}$ 1.5, $J_{5',6'a}$ ~1, $J_{5',6'b}$ 1.5, and $J_{6',6'}$ 12 Hz.

Anal. Calc. for $C_{24}H_{32}O_{16}$: C, 50.00; H, 5.60. Found: C, 49.89; H, 5.32.

Reaction of D-fructose with trifluoroacetic acid. — A mixture of D-fructose (5 g) and trifluoroacetic acid (50 mL) was kept for 20 h at room temperature and then concentrated under reduced pressure, and water was twice distilled from the residue. A ^{13}C-n.m.r. spectrum showed (intensities of anomeric carbon atoms) that the residue contained **4** (18%), **7** (9%), **13** (9%), **16** (30%), and D-fructose (34%). The crude product was acetylated and the resulting mixture of acetates (7.8 g) was crystallised from ether to give **17** (1.2 g), m.p. 120–122°, which, on recrystallisation from ethanol, gave a product identical with that described above.

Reaction of D-fructose with methanolic sulfuric acid. — To a mixture of D-fructose (10 g) and methanol (10 mL) was added sulfuric acid (sp. gr. 1.83, 2 mL), and the solution was stirred for 18 h at room temperature, neutralised ($CaCO_3$), filtered, and concentrated. The syrupy residue contained (intensities of ^{13}C signals of the anomeric carbon atoms) methyl α-D-fructofuranoside[20] (8%), methyl β-D-fructofuranoside[20] (13%), methyl β-D-fructopyranoside[20] (34%), D-fructose (9%), **16** (22%), and **4** (13%). The crude mixture was acetylated and the product (12.4 g) was crystallised from ether (50 mL) to give **17** (0.8 g, 5%), m.p. 119–121°. After

recrystallisation of **17** from ethanol, the physical constants in Table II were obtained.

When D-fructose (10 g) was similarly treated with methanol (40 mL) and sulfuric acid (sp. gr. 1.83, 2 mL), the products contained methyl α-D-fructofuranoside (19%), methyl β-D-fructofuranoside (20%), methyl β-D-fructopyranoside (38%), D-fructose (4%), **4** (6%), and **16** (14%).

When D-fructose (10 g) was similarly treated with methanol (100 mL) and sulfuric acid (1 mL), the product consisted mainly of the above methyl fructosides and a few percent of **16**.

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