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Difructose dianhydrides from sucrose and fructo-oligosaccharides and their use as building blocks for the preparation of amphiphiles, liquid crystals, and polymers ☆

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Abstract

Controlled selective protonic activation of the fructosyl moiety in sucrose and fructo-oligosaccharides, with pyridinium poly(hydrogen fluoride) at 20°C, yielded either the kinetic product α-D-fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride (**1**), or its thermodynamically more stable isomer α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**2**), depending on the hydrogen fluoride–pyridine ratio. A similar reaction was performed with 6,6′-dichloro-6,6′-dideoxysucrose, or 6,6′-dideoxy-6,6′-diiodosucrose, using a slightly higher ratio of HF, resulting in the corresponding 6-deoxy-6-halo-α-D-fructofuranose 6′-deoxy-6′-halo-β-D-fructofuranose 1,2′:2,1′-dianhydride derivatives. Both 6,6′-dihalides were converted, upon action of the appropriate nucleophile, into the difructofuranose dianhydride derivatives bearing the 6,6′-di-*S*-heptyl-6,6′-dithio, 6,6′-diazido-6,6′-dideoxy and then 6,6′-diamino-6,6′-dideoxy functionalities. 6-Chloro-6-deoxy and 6-deoxy-6-iodo derivatives of **2** were also prepared by direct halogenation, and further converted into the 6-*S*-heptyl-6-thio, 6-azido-6-deoxy and then 6-amino-6-deoxy derivatives of **2**. Reaction of chloromethyloxirane with **1** or **2** yielded hydrophilic polymers. The 6,6′-di-*S*-heptyl-6,6′-dithio derivative of **1** displayed liquid crystal properties. The 6,6′-dideoxy-6,6′-diiodosucrose precursor was prepared by the reaction of Garegg's iodine–imidazole–triphenylphosphine reagent with sucrose in *N*,*N*-dimethylformamide solution.

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1. Introduction

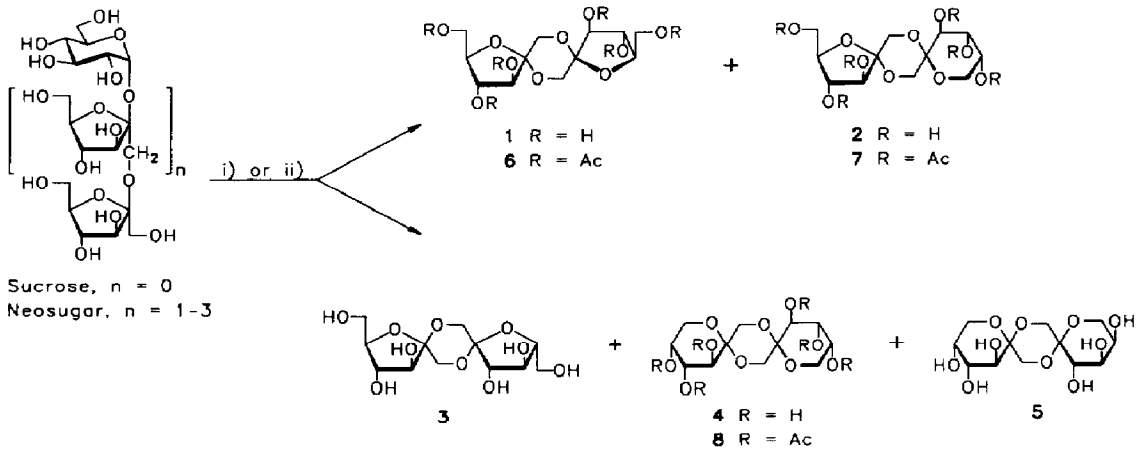
The major characteristic of difructose dianhydrides is the presence of a central spirodioxane system, which results in a rigid framework for these molecules. An improved stability to heat is also to be expected from their mode of formation which involves protonic and thermal activation of ketoses and ketosans [2–4]. Both features, which bear some similarity to anhydrohexitols [5], make them attractive building blocks for the preparation of amphiphiles, liquid crystals, and polymers from readily available D-fructose-containing agricultural feedstocks. A main limitation however for such new channels lies in the fact that, because of the stereochemical control involved in their formation, difructose dianhydrides are usually obtained as complex mixtures of isomers [3,4,6]. Acyl protecting groups have been successfully used in order to enhance the selectivity in the formation of the ring system and, interestingly, α-D-fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride hexa-acetate (**6**) has already been obtained as the main component from the hydrogen fluoride protonic activation of acetylated inulin in liquid sulfur dioxide [7].

In a recent report from this laboratory [8], pyridinium poly(hydrogen fluoride) was found to behave as a versatile protonating reagent for the preparation of glycosylated difructose dianhydrides from isomeric glycosylfructoses. Variations in the acidity of the reagent proved especially effective in controlling the kinetic steps of formation of the spirodioxane system. It was thus of interest to apply this reagent to readily available raw materials such as sucrose and fructo-oligosaccharides, in order to achieve a direct access to difructofuranose dianhydrides, keeping in mind that the five-membered fructofuranose heterocycle, present in the starting material, might be preserved using these smooth protonating conditions.

2. Results and discussion

Storage of solutions of sucrose or neosugar [2] in pyridinium poly(hydrogen fluoride) at 20°C for various conditions of time, substrate, and relative concentration of hydrogen fluoride in pyridine followed by precipitation of the reaction product by the addition of acetone or ether gave, in almost quantitative yield, difructose dianhydrides **1–5** (Scheme 1 and Table 1), together with D-glucose. Glucosyl difructose dianhydrides were not detected, in agreement with previous results in the glycosylfructose series [8] which showed that protonic activation involving pyridinium poly(hydrogen fluoride) is restricted to the more reactive tertiary anomeric carbon atom of the D-fructose moiety. A further interesting selectivity was also observed from the distinct change in the dianhydride components

[2] Neosugar, commercialised under the trademark name Actilight P® by Béghin-Meiji Ind., Paris, is a mixture of the fructo-oligosaccharides kestose, nystose, and 1-*O*-β-D-fructofuranosylnystose.



Scheme 1. (i) 4:3 HF–pyridine, 20 min, 20°C; (ii) 7:3 HF–pyridine, 90 min, 20°C.

according to the acidity of the reagent, which suggested that some of them could be obtained preferentially.

For a 4:3 hydrogen fluoride–pyridine ratio and a residence time of 20 min at 20°C, α-D-fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride (**1**) was the major product of the reaction (Table 1), with isolated yields of 35 and 52%, respectively, from sucrose or neosugar (~ 70% based on the D-fructose component). Conversely, when hydrogen fluoride in pyridine in a 7:3 ratio was used with a residence time of 90 min at 20°C, the thermodynamic α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**2**) became

Table 1
Products formed [a] by the action of pyridinium poly(hydrogen fluoride) on sucrose (Suc), neosugar, or D-fructose. The reaction temperature was 20°C in all experiments

Experiment No.	Substrate (g) [b]	HF–Py (mL)	Reaction time (min)	Products formed (%)					Residual substrate (%)
				1	**2**	**3**	**4**	**5**	
1	Suc (1)	4:3 (5)	10	59	6	17	10		8
2	Suc (1)	4:3 (5)	20	69	14	8	9		
3	Suc (2)	4:3 (5)	20	76	8	10	6		
4	Suc (5)	4:3 (12.5)	20	74	10	9	7		
5	Suc (1)	4:3 (5)	40	50	30	5	12	3	
6	Neosugar (5)	4:3 (12.5)	20	74	11	9	6		
7	D-Fru (Me_2SO) (5)	4:3 (12.5)	20	43	20	9	23		5
8	D-Fru (5)	4:3 (12.5)	20	28	31	6	25		10
9	Suc (2)	7:3 (7)	30	10	51	5	30	4	
10	Suc (5)	7:3 (18)	90	5	63	2	27	3	
11	Suc (2)	7:3 (7)	120	5	53		24	18	
12	Neosugar (5)	7:3 (18)	90	7	64	2	23	4	
13	D-Fru (5)	7:3 (18)	90	4	35	2	45	9	7

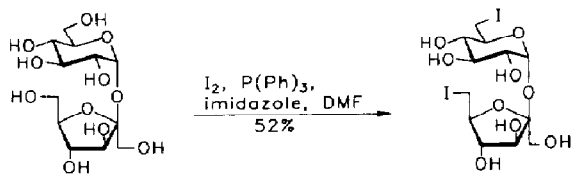
[a] In the cases of sucrose and neosugar, D-glucose and/or D-glucopyranosyl fluorides were also present in the mixtures. The proportion of dianhydrides was confirmed on the peracetylated mixtures after separation of the D-glucose derivatives.

[b] D-Fru (Me_2SO): commercial D-fructose previously equilibrated in Me_2SO.

the major product of the reaction (isolated yields of 20 and 28%, respectively, i.e., ~40% based on the D-fructose component), with traces of α-D-glucopyranosyl fluoride indicating that fluorolysis of the D-glucose by-product had begun. Minor products were, in both reactions, di-β-D-fructofuranose 1,2′:2,1′-dianhydride (**3**), α-D-fructopyranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**4**), and di-β-D-fructopyranose 1,2′:2,1′-dianhydride (**5**). Both dianhydrides **1** and **2** were obtained on a preparative scale, with overall yields which compare favorably with previous syntheses [3,7], after in situ acetylation by addition of acetic anhydride to the pyridinium poly(hydrogen fluoride) solution and isolation by flash chromatography of the acetylated derivatives **6** and **7**.

The changes observed in the relative proportion of dianhydrides **1–5**, according to the protonation conditions (Table 1), are in agreement with the order of stability previously found and rationalised on the basis of stereoelectronic factors for the formation of the spirodioxane system in diketose dianhydrides [3,4,6]. In order to improve the access to dianhydrides **1** and **2**, it was of interest to investigate the significance of the fructofuranose structure in the starting materials sucrose or neosugar on the outcome of the reaction and on the yield of **1** and **2**. Commercial crystalline D-fructose, which is known to be exclusively in the β-D-fructopyranose form, was dissolved in a 4:3 hydrogen fluoride–pyridine mixture and kept for 20 min at 20°C, conditions which already produced the kinetic difructofuranose dianhydride **1** from sucrose and neosugar in an optimal yield. A comparative assay, which used D-fructose previously equilibrated for 30 days in dimethyl sulfoxide [9] and was shown to contain >50% of fructofuranose forms by ^{13}C NMR spectroscopy, was run at the same time. Interestingly, the relative proportion of dianhydrides **1** and **2** differed drastically in the two experiments, the difuranose dianhydride **1** being predominant (48%) when D-fructose equilibrated in dimethyl sulfoxide was used as starting material while **2** was the major product of the reaction with crystalline D-fructose (31%, Table 1). This result is then in support of our previous hypothesis [10] which assumes that glycosidation in hydrogen fluoride and related reagents may involve cationisation of the cyclic form of the sugar in the kinetic step of the protonation reaction. It confirms the importance of the preformed fructofuranose ring structure in sucrose and neosugar oligosaccharides for the preparation of **1** and **2**.

The above results suggested that selective functionalisation of difructose dianhydrides **1** and **2** might be achieved by extension of a similar protonic activation scheme to 6,6′-dideoxy-6,6′-dihalosucrose precursors such as the 6,6′-dichloro derivative [11] or its 6,6′-diiodo analogue **9**. Per-*O*-acyl 6,6′-dideoxy-6,6′-diiodosucrose derivatives have already been prepared by nucleophilic displacement by I^- of acylated 6,6′-disulfonates [12] or of a C-6,6′ selectively activated sucrose in the form of a bis(alkoxyphosphonium salt) followed by an acylation step in order to isolate the diiodo derivative in a rather low yield



Sucrose **9**

Scheme 2.

Table 2
Products formed by the action of pyridinium poly(hydrogen fluoride) on 6,6′-dideoxy-6,6′-diiodosucrose (**9**) [a]. The experiments were carried out at 0°C

Experiment No.	**11** (g)	HF–Py (mL)	Reaction time (min)	Products formed (%) [b]			Residual substrate (%)
				10	**14**	**18**	
1	5.0	7:3 (10)	20	74	11	15	
2	0.2	7:3 (0.4)	30	69	8	23	

[a] The mixtures were neutralised and the pyridine was evaporated as described for the preparation of **10** from **9** (see Experimental).
[b] 6-Deoxy-6-iodo-D-glucose and 6-deoxy-6-iodo-D-glucopyranosyl fluorides were also present in the mixtures.

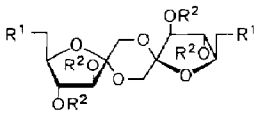
[13]. Deacylation was apparently not attempted in either example. Direct iodination of sucrose using iodine and triphenylphosphine in *N,N*-dimethylformamide, by analogy with the methodology successfully used for the preparation of per-6-deoxy-6-iodocyclomaltooligosaccharides [14], did not succeed in our hands. Application of Garegg's iodine–imidazole–triphenylphosphine procedure [15] to sucrose was no more successful. However, we found that iodination of sucrose was effective in 1.5 h at 80°C when Garegg's reagent was added to a solution of sucrose in *N,N*-dimethylformamide, resulting in crystalline 6,6′-dideoxy-6,6′-diiodosucrose (**9**) in 52% yield (Scheme 2).

Storage of solutions of 6,6′-dideoxy-6,6′-diiodosucrose (**9**), or the 6,6′-dichloro-6,6′-dideoxy analogue [11], in 7:3 hydrogen fluoride–pyridine resulted in the predominant formation of the corresponding 6,6′-dideoxy-6,6′-dihalo α,β-difructofuranose dianhydrides **10** and **12**, in 73 and 85% yield, respectively, based on the 6-deoxy-6-halo-D-fructose component of the dihalosucrose precursor, after a 20-min reaction time at 0°C. A minor proportion of 6,6′-dideoxy-6,6′-dihalo-di-β-D-fructofuranose dianhydrides **14** and **16** was simultaneously formed, which decreased to the benefit of the 1,2′:2,3′-dianhydrides **18** and **20** as the reaction proceeded (Table 2 and Table 3). Concomitant formation of 6-deoxy-6-halo-D-glucose derivatives also occurred under these conditions, together with a small proportion of the corresponding α-D-glucosyl fluorides.

Table 3
Products formed by the action of pyridinium poly(hydrogen fluoride) on 6,6′-dichloro-6,6′-dideoxysucrose [11] [a]. All experiments were carried out at 0°C

Experiment No.	Substrate (g)	HF–Py (mL)	Reaction time (min)	Products formed (%)			Residual substrate (%)
				12	**16**	**20**	
1	0.2	7:3 (0.6)	10	66	19	5	10
2 [b]	0.6	7:3 (1.2)	20	85	6	9	
3 [b]	5.0	7:3 (15)	20	87	4	11	
4 [b]	0.3	7:3 (1.2)	30	83	2	15	
5 [b]	0.3	7:3 (1.2)	60	65		35	

[a] The mixtures were neutralised and the pyridine was evaporated as described for the preparation of **12** from 6,6′-dichloro-6,6′-dideoxysucrose (see Experimental).
[b] 6-Chloro-6-deoxy-D-glucose and 6-chloro-6-deoxy-D-glucopyranosyl fluorides were also present in the mixtures.

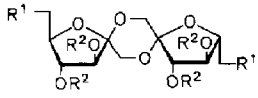


10 R^1 = I, R^2 = H
11 R^1 = I, R^2 = Ac
12 R^1 = Cl, R^2 = H
13 R^1 = Cl, R^2 = Ac

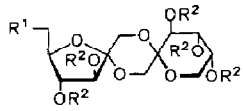
26 R^1 = $S(CH_2)_6CH_3$, R^2 = Ac
27 R^1 = $S(CH_2)_6CH_3$, R^2 = H

31 R^1 = N_3, R^2 = Ac
32 R^1 = N_3, R^2 = H

36 R^1 = NH_2, R^2 = H
37 R^1 = NHAc, R^2 = H
38 R^1 = NHAc, R^2 = Ac



14 R^1 = I, R^2 = H
15 R^1 = I, R^2 = Ac
16 R^1 = Cl, R^2 = H
17 R^1 = Cl, R^2 = Ac

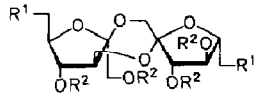


22 R^1 = I, R^2 = H
23 R^1 = I, R^2 = Ac
24 R^1 = Cl, R^2 = H
25 R^1 = Cl, R^2 = Ac

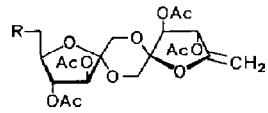
28 R^1 = $S(CH_2)_6CH_3$, R^2 = Ac
29 R^1 = $S(CH_2)_6CH_3$, R^2 = H

33 R^1 = N_3, R^2 = Ac
34 R^1 = N_3, R^2 = H

39 R^1 = NH_2, R^2 = H
40 R^1 = NHAc, R^2 = H
41 R^1 = NHAc, R^2 = Ac



18 R^1 = I, R^2 = H
19 R^1 = I, R^2 = Ac
20 R^1 = Cl, R^2 = H
21 R^1 = Cl, R^2 = Ac



30 R = $S(CH_2)_5(CH)_3$
35 R = N_3

The structure of both major difructose dianhydrides **10** and **12** was confirmed on the basis of their ^{13}C NMR spectra (Table 4 and Table 6), as well as the ^{13}C (Tables 4 and 6) and ^1H NMR spectra (Table 5 and Table 7) of their peracetates **11** and **13** and comparison with the literature [3,7,8]. Noteworthy are the high-field signals for C-6,6′ at 46.2–43.4 ppm for the dichloro derivative **12** and its tetra-acetate **13**, which are found at 9.5–4.4 ppm for the corresponding dideoxy-diiodo derivatives **10** and **11**. In the latter derivatives, the signals for C-4,4′ were shifted downfield by 3–5 ppm as compared to data for **1** and **6**, in agreement [16] with the presence of an iodomethyl group at C-6.

The structures of the minor components dideoxy-dihalo-difructose dianhydrides **14**, **16**, **18**, and **20** have been principally assigned by comparison of the resonances for their anomeric carbon atoms with data for the parent difructose dianhydrides or their glucosylated derivatives [8]. Thus, the symmetrical dideoxy-diiodo derivative **14** showed only six signals in its ^{13}C NMR spectrum with a low-field signal at 105.6 ppm, closely similar to the anomeric signal of **3** [7] or its 6,6′-diglucosylated derivative [8]. Analogously, a signal at 105.5 ppm in the ^{13}C NMR spectra of the reaction mixtures arising from the action of HF–pyridine on 6,6′-dichloro-6,6′-dideoxysucrose was assigned to C-2 of **16**, although attempts to isolate pure samples of **16** or of its peracetylated derivative **17** failed. Using the same approach, a 2,1′:3,2′-dianhydride structure was assigned to **18** and **20**, based on the comparison of the resonances for the anomeric carbon atoms with corresponding data for 6,6′-diglucosylated derivatives [8]. The ^{13}C NMR spectra for the peracetates **19** and **21**, and particularly the low-field signals at δ 81.8 and 82.4 for C-3, confirmed the involvement of this position in the acetal linkage.

The change in the relative proportions of the dihalogenated difructose dianhydrides **10**, **12**, **14**, **16**, **18**, and **20**, according to the reaction time in pyridinium poly(hydrogen fluoride)

Table 4
^{13}C NMR chemical shifts (50.3 MHz) for some unprotected (**10**, **12**, **27**, **32**, **36**, and **37**) and peracetylated (**11**, **13**, **26**, **31**, **38**, and **30**, **35**) α-D,β-D-difructofuranose 1,2′:2,1′-dianhydride derivatives

Compound	^{13}C Chemical shifts											
	C-2	C-2′	C-3	C-4	C-5	C-3′	C-4′	C-5′	C-6	C-6′	C-1	C-1′
Dianhydrides												
10 [b]	103.2	100.1	82.9	82.8	84.5	80.4 [d]	80.2 [d]	82.1	7.6	9.5	63.7 [e]	63.8 [e]
12 [a]	103.6	100.1	82.3	79.8	83.5	78.0	76.8	81.4	44.8	46.2	62.7	63.5
27 [b]	103.0	100.0	83.8	82.5	84.5	80.2 [f]	80.0 [f]	82.3	35.1	37.2	63.5 [g]	63.8 [g]
32 [b]	103.3	100.1	82.6	80.6	84.2	79.6	77.4	81.1	52.6	54.6	63.5 [h]	63.8 [h]
36 [a]	103.3	99.8	82.6	80.0	85.0	78.0	76.5	82.6	43.0	44.8	62.7	63.4
37 [a]	103.4	99.9	82.9	80.0	80.3	77.8	76.6	82.6	41.6	42.9	62.7	63.4
Peracetates [c]												
11	101.2	99.7	81.0	80.6	81.8	76.5	78.7	80.8	4.4	6.0	62.0	62.5
13	101.3	99.4	81.1 [i]	78.9	81.2 [i]	76.9	75.7	80.4	43.4	44.6	61.1	62.2
26	101.0	99.6	81.4	79.9	81.5	76.2	78.8	80.2	33.8	36.0	61.7	62.5
31	101.5	99.4	81.0	78.1	81.6	76.3	75.4	79.6	51.0	53.6	61.4	62.6
38	101.5	99.7	80.4	78.8	81.3	77.4	76.3	80.0	40.6	42.7	61.6	62.8
30	101.1	99.9	81.5	81.5	80.0	74.3	73.0	154.8	33.9	87.0	61.8	62.3
35	101.8	98.9	81.0	78.5	81.9	74.3	72.9	154.8	51.1	87.0	62.0	62.3

[a] In D_2O.
[b] In acetone-d_6.
[c] In $CDCl_3$.
[d–i] Assignments may have to be reversed.

of the 6,6′-dideoxy-6,6′-dihalosucrose precursor (Tables 2 and 3), is in agreement with previous results for the formation of 6,6′-diglucosylated difructose dianhydrides from palatinose in HF–pyridine reagents [8] and probably reflects their relative stability in protonating conditions. Thus, transient di-β-D-fructofuranose 1,2′:2,1′-dianhydrides **14** and **16** are formed in the kinetic step of the reaction and readily isomerise into the more stable α,β anomers **10** and **12** in agreement with expectation from the anomeric effect. More strenuous conditions result in the isomerisation of **10** and **12** into the partially fused spirodioxanes **18** and **20**.

6-Deoxy-6-halo-α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydrides **22** and **24**, of interest for the preparation of monofunctionalised derivatives of D-fructose dianhydrides, have been conveniently prepared by direct halogenation of **2** with Garegg's iodine–triphenylphosphine–imidazole reagent [15] in *N*,*N*-dimethylformamide or with tetrachloromethane–triphenylphosphine in pyridine, respectively. Alternatively, the halogenation processes have been applied to the crude mixture of dianhydrides **2** and **4**, avoiding a purification step for a large-scale preparation of **22** and **24** from sucrose and neosugar.

The reaction of the acylated 6,6′-dichloro-6,6′-dideoxy difructose dianhydride derivative **13** with 1-heptanethiol in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) led to the corresponding diheptyl dithioether **26** in almost quantitative yield. However, when the diiodo analogue **11** was used as the electrophile, a competition between substitution and elimination was observed in the β-fructofuranose moiety, resulting in the formation of the

Table 5
^{1}H NMR data ($CDCl_3$; δ, ppm; J, Hz) for peracetylated α-D,β-D-difructofuranose 1,2′:2,1′-dianhydride derivatives (**11**, **13**, **26**, **31**, **38**, and **30**, **35**)

Compound	H-1a	H-1b	H-3	H-4	H-5	H-6a	H-6b	H-1′a	H-1′b	H-3′	H-4′	H-5′	H-6′a	H-6′b
11 [a]	4.08d	3.71d	5.18d	4.77dd	3.95dd	3.45dd	3.36dd	3.99d	3.54d	5.10d	5.31dd	4.18ddd	3.43dd	3.32dd
13 [a]	4.08d	3.73d	5.14d	4.93dd	4.15td	3.77dd	3.71dd	4.02d	3.58d	5.13d	5.35dd	4.18ddd	3.74dd	3.65dd
26 [a]	4.00d	3.61d	5.08d	4.90dd	4.08td	⟵2.80m⟶		3.98d	3.49d	5.03d	5.32dd	4.09td	⟵2.80m⟶	
31 [b]	4.05d	3.73d	5.14d	4.84dd	4.08td	3.53dd	3.39dd	4.02d	3.55d	5.12d	5.26dd	4.07ddd	3.54dd	3.46dd
38 [b]	4.07d	3.64d	5.18d	4.77dd	4.05q	3.62dt	3.50dt	3.99d	3.56d	5.10d	5.22dd	4.04ddd	3.66dt	3.41ddd
30 [a]	3.98d	3.67d	5.13d	4.91dd	4.08td	⟵2.71m⟶		4.05d	3.58d	5.05d	5.92ddd		4.54dd	4.14dd
35 [b]	4.02d	3.75d	5.17d	4.85dd	4.10td	3.56dd	3.41dd	4.06d	3.60d	5.06d	5.92ddd		4.55dd	4.17dd
	$J_{1a,1b}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{1'a,1'b}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$		
11	11.8	1.9	5.6	4.5	5.6	12.1	11.8	6.5	4.7	6.5	7.9	10.3		
13	11.8	1.5	5.1	4.6	5.1	12.5	11.8	6.5	4.8	5.6	7.3	12.1		
26	11.8	2.0	5.9	2.7	5.9		11.8	6.3	4.7	4.7	7.4			
31	11.9	1.7	5.3	2.7	5.3	13.4	11.9	6.9	5.4	4.1	7.7	13.1		
38	11.9	1.7	5.3	5.3	5.3	13.6	11.8	6.3	4.9	5.3	7.7	13.6		
										$J_{4',6'a}$	$J_{4',6'b}$			
30	11.9	1.9	5.9	2.8	5.9		12.1	7.4		2.2	1.8	2.8		
35	12.1	1.5	5.3	2.6	5.3	13.4	12.0	7.5		2.2	1.8	2.7		

[a] At 200 MHz.
[b] At 400 MHz.

Table 6
^{13}C NMR chemical shifts (50.3 MHz) for some unprotected (**22**, **24**, **29**, **34**, **39**, and **40**) and peracetylated (**23**, **25**, **28**, **33**, and **41**) α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride derivatives

Compound	^{13}C Chemical shifts											
	C-2	C-2′	C-3	C-4	C-5	C-3′	C-4′	C-5′	C-6	C-6′	C-1	C-1′
Dianhydrides												
22 [a]	103.2	96.4	82.8	79.6	83.1	69.4	69.8	69.8	44.7	61.9	62.4	64.3
24 [b]	102.9	96.3	82.4	82.0	83.1	69.3	69.7	69.7	6.4	62.0	62.3	64.2
29 [b]	103.2	97.1	83.7	82.8	84.5	70.7 [d]	70.9 [d]	71.0 [d]	35.3	63.1	63.1	64.7
34 [b]	103.1	96.3	82.5	79.4	82.7	69.3	69.7	69.7	51.0	61.9	62.3	64.2
39 [a]	103.1	96.5	82.6	80.0	84.7	69.4	69.8	69.8	42.9	62.1	62.3	64.3
40 [a]	103.6	96.5	82.4	80.1	80.3	69.3	69.8	69.8	42.1	62.0	62.5	64.4
Peracetates [c]												
23	101.2	94.6	81.1 [e]	78.6	81.2 [e]	66.9	68.6	67.2	43.6	61.2	61.2	60.6
25	100.8	94.7	80.9	80.5	81.7	66.9	68.7	67.2	3.7	61.4	61.2	60.7
28	100.9	94.7	81.0	80.2	81.5	67.0	68.7	67.4	34.1	61.2	61.2	61.0
33	101.4	94.7	81.0	78.3	81.5	67.0	68.7	67.3	51.1	61.4 [f]	61.2 [f]	60.7
41	101.2	94.9	80.7	78.7	81.1	67.2	68.8	67.3	40.4	61.4	61.4	61.0

[a] In D_2O.
[b] In methanol-d_4.
[c] In $CDCl_3$.
[d–f] Assignments may have to be reversed.

hex-5′-enofuranose derivative **30** as by-product in the reaction. This unexpected selectivity in the elimination process in **11** has obviously to be related to a difference in conformation of the two furanoid rings in α-D-fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride derivative, as already noticed by Lemieux and Nagarajan [17] for the hexa-acetate **6** and ascribed to the anomeric effect. Such a side reaction was conclusively not found in the reaction of monohalo derivatives of **2**, which led exclusively to the 6-*S*-heptyl-6-thio derivative **28** starting from the 6-deoxy-6-iodo peracetate precursor **23** or its 6-chloro-6-deoxy analogue **25**.

Zemplén deacetylation of **26** and **28** resulted in the amphiphilic derivatives **27** and **29**. Interestingly, **27** exhibited thermotropic liquid crystal properties at room temperature on observation in the polarising microscope, probably as a result of alternation between the flexible heptyl chains and the rigid difructose dianhydride core. It was enantiotropic, i.e., a mesophase was observed upon heating and cooling, and a clearing point was found at 52.4°C. Hitherto, few carbohydrate liquid crystals have been reported [18] and carbohydrate mesogens with more than one alkyl chain are still rare [19–21].

The acetylated 6,6′-dichloro-6,6′-dideoxy difructofuranose dianhydride **13**, and the mono-6-deoxy-6-iodo and mono-6-chloro-6-deoxy derivatives **23** and **25** as well, reacted smoothly with sodium azide in *N*,*N*-dimethylformamide to afford the corresponding 6,6′-diazido-6,6′-dideoxy (**31**) and 6-azido-6-deoxy (**33**) derivatives, respectively, in good yield. However, when the reaction was performed with the 6,6′-dideoxy-6,6′-diiodo difructofuranose dianhydride derivative **11**, a competition with the formation of the elimination product **35** was also observed. Both diazide **31** and monoazide **33** were converted in almost quantitative yield into the corresponding free amines **36** and **39** by the Staudinger reaction

Table 7
^{1}H NMR data (C_6D_6; δ, ppm; *J*, Hz) for peracetylated α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride derivatives (**23**, **25**, **28**, **33**, and **41**)

Compound	H-1a	H-1b	H-3	H-4	H-5	H-6a	H-6b	H-1′a	H-1′b	H-3′	H-4′	H-5′	H-6′a	H-6′b
23 [a]	4.27d	3.89d	5.55d	5.29dd	4.16q	←3.79d→		3.99d	3.93d	5.77d	5.98dd	5.64ddd	3.69dd	3.57dd
25 [a]	4.30d	3.89d	5.59d	5.11dd	4.02ddd	3.47dd	3.35dd	←3.94s→		5.78d	6.00dd	5.64ddd	3.65dd	3.52dd
28 [a]	4.34d	3.89d	5.61d	5.40dd	4.42ddd	3.14dd	3.04dd	4.04d	3.93d	5.74d	5.93dd	5.64ddd	3.72dd	3.63dd
33 [a]	4.25d	3.88d	5.53d	5.22dd	4.11td	3.49dd	3.36dd	←3.98s→		5.73d	5.91dd	5.64ddd	3.72dd	3.63dd
41 [b]	4.29d	3.90d	5.64d	5.37dd	4.27q	←3.70m→		4.09d	3.95d	5.79d	5.94dd	5.67m	←3.70m→	
	$J_{1a,1b}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{1'a,1'b}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$		
23	11.7	1.6	5.5	4.2	4.2		11.7	10.6	3.4	1.7	1.4	13.0		
25	11.7	1.8	5.8	3.7	6.9	10.8		10.6	3.4	1.7	1.4	13.0		
28	11.7	1.9	5.2	4.4	6.8	13.9	11.7	10.6	3.4	2.0	1.4			
33	11.7	1.4	6.0	2.7	5.2	13.5		10.6	3.4	1.6	1.3	13.0		
41	11.7	1.8	5.2	5.2	5.2		11.7	10.6	3.4					

[a] At 200 MHz.
[b] At 400 MHz.

[22] of the deacetylated azides **32** and **34** with triphenylphosphine in purified dioxane, followed by hydrolysis with concentrated ammonium hydroxide of the phosphinimine intermediates. *N*-Acetylation in both amines **36** and **39** with acetic anhydride in methanol yielded the 6,6′-diacetamido-6,6′-dideoxy (**37**) or 6-acetamido-6-deoxy (**40**) derivative, whereas acetylation in pyridine afforded the corresponding peracetates **38** and **41**.

The ^{13}C NMR data (Tables 4 and 6) for *O*-unprotected derivatives and the ^{13}C (Tables 4 and 6) and ^{1}H NMR data (Tables 5 and 7) for the corresponding peracetates agreed with the proposed structures for both 6,6′-dideoxy-6,6′-disubstituted α,β-di-D-fructofuranose (**26**, **27**, **31**, **32**, and **36–38**) and 6-deoxy-6-monosubstituted α-D-fructofuranose-β-D-fructopyranose (**28**, **29**, **33**, **34**, and **39–41**) 1,2′:2,1′-dianhydride series. Of diagnostic value were the resonances of the primary C-6(6′) carbon atoms, which showed the expected [16] shielding or deshielding effects caused by substitution of the halogen atoms in **10–13** or **22–25** by alkylthio, azido, amino, or acetamido groups, respectively.

The 6-deoxy-β-D-*threo*-hex-5-enofuranose structure for compounds **30** and **35** was confirmed by the ^{13}C chemical shifts (Table 4) of the unsaturated carbon atoms C-5′ (154.8 ppm) and C-6′ (87.0 ppm), which agreed with expected [16] values for exocyclic vinyl ethers. In particular, the ^{1}H NMR spectra (Table 5) showed the well known [23] allylic coupling between the protons at C-4′ and C-6′.

The potential of difructose dianhydrides **1** and **2** as precursors of hydrophilic polymers was ascertained by their reaction with chloromethyloxirane in the presence of base. As reported [24] for the copolymerisation reaction of sucrose under similar reaction conditions, the properties of the ether copolymerisates obtained depended drastically on the relative proportion of the cross-linking reagents. Thus, for a 1:2.2 difructose dianhydride **1** or **2**–chloromethyloxirane molar equiv ratio, the copolymers formed were found to be almost insoluble in water and organic solvents, behaving as hydrophilic gels. With a 1:1.5 molar equiv ratio, water-soluble oligomers of low average molecular weight [~ 1000 with reference to poly(ethyleneoxide)] were obtained. In both cases, the difructose dianhydride–chloromethyloxirane copolymerisates showed a high thermal stability, since no decomposition was observed at ~ 200°C.

3. Experimental

Material and methods.—Unless stated otherwise, these were the same as those described previously [8]. ^{13}C NMR spectra of unacetylated products were recorded for solutions in D_2O (internal acetone, 31.1 ppm), acetone-d_6 (central peak at 29.8 ppm), or methanol-d_4 (central peak for the CD_3 signal at 49.0 ppm). ^{1}H NMR spectra of acetylated products were recorded with Bruker AC-200 and Bruker AMX-400 instruments for solutions in $CDCl_3$ or C_6D_6 (internal tetramethyl silane).

Transmission optical observation of thin films of material were made using a Leitz polarising microscope fitted with a Mettler FP-82 hot stage. Differential scanning colorimetric measurements were performed using a Perkin–Elmer DSC-2C instrument. Contained in aluminium pans, the sample was heated or cooled in a temperature range from 298 to 343 K at a scanning rate of 10 K min^{-1}.

Molecular weight determinations for the water-soluble copolymerisates of **1** or **2** with chloromethyloxirane were carried out with a Knauer 5560 apparatus using a TSK 3000 PW column fitted to a refractometric detector, with water as eluent. The calibration curve was obtained using poly(ethylene oxide).

Reactions in pyridinium poly(hydrogen fluoride).—All reactions were carried out in poly(ethylene) bottles. The reactant was dissolved in the appropriate amount of HF in pyridine and then kept at the indicated temperature (Tables 1–3). Except where otherwise stated, the product was precipitated by addition of an excess of ether, triturated with acetone, collected, and dried. The composition of the product mixtures was assessed by ^{13}C NMR spectroscopy, using the intensities of the signals for anomeric carbon atoms.

α-D-Fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride (**1**).—*(a) From sucrose.* The mixture resulting from the action of 4:3 HF–pyridine (12.5 mL) on sucrose (5 g, 14.6 mmol) after 20 min at 20°C (Table 1, Expt No. 4) was acetylated (1:1 Ac_2O–pyridine, 50 mL, 24 h). The peracetylated mixture showed two main spots in TLC (1:1 EtOAc–hexane). Flash chromatography with the above eluent gave a first fraction (5.13 g, 45%) consisting of a mixture of penta-*O*-acetyl-α- and -β-D-glucopyranose (^{13}C NMR) [25], and a second fraction which crystallised from EtOH to give 3,4,6-tri-*O*-acetyl-α-D-fructofuranose 3,4,6-tri-*O*-acetyl-β-D-fructofuranose 1,2′:2,1′-dianhydride (**6**; 3.27 g, 39%). Deacetylation (Zemplén) of **6** yielded **1** (1.66 g, 35% from sucrose). The physical constants and ^{13}C NMR data for **1** and **6** were identical with those reported [3,8].

(b) From fructo-oligosaccharides. Neosugar (5 g) was treated with 4:3 HF–pyridine (12.5 mL) (Table 1, Expt No. 6) and the mixture acetylated and processed as above to give penta-*O*-acetyl-α- and -β-D-glucopyranose (3.36 g, 31%) and **6** (5.06 g, 57%). Deacetylation of **6** yielded **1** (2.6 g, 52% relative to the starting fructo-oligosaccharide mixture).

α-D-Fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**2**).—*(a) From sucrose.* The mixture arising from the action of 7:3 HF–pyridine (18 mL) on sucrose (5 g, 14.6 mmol) after 90 min at 20°C (Table 1, Expt No. 10) was acetylated (1:1 Ac_2O–pyridine, 50 mL, 24 h). TLC (1:1 EtOAc–hexane) of the peracetylated mixture showed one main spot and some minor components having higher R_f. Flash chromatography with the above eluent gave a first fraction consisting of a mixture of α- and β-penta-*O*-acetylglucose and tetra-*O*-acetylglucosyl fluorides (^{13}C NMR) [25,26]. A second fraction (3.95 g, 44%) contained a mixture of 3,4,6-tri-*O*-acetyl-α-D-fructofuranose 3,4,5-tri-*O*-acetyl-β-D-fructopyranose 1,2′:2,1′-dianhydride (**7**) and 3,4,5-tri-*O*-acetyl-α-D-fructopyranose 3,4,5-tri-*O*-acetyl-β-D-fructopyranose 1,2′:2,1′-dianhydride (**8**) in a ~3:1 ratio (^{13}C NMR). Deacetylation of this mixture of hexaacetates led to the corresponding mixture of difructose dianhydrides **2** and **4** (2.2 g, 44%). Crystallisation from MeOH at room temperature yielded α-D-fructopyranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**4**; 0.4 g, 8% from sucrose). Evaporation of the mother liquor led to an amorphous powder which crystallised from EtOH–water to give **2** (1 g, 20%). The physical constants and ^{13}C NMR spectra for **2** and **4** were identical with those already reported [3,8].

(b) From fructo-oligosaccharides. Neosugar (5 g) was treated with 7:3 HF–pyridine (18 mL) (Table 1, Expt No. 12) and the mixture processed as above to give a mixture of **7** and **8** (~3:1, 3.05 g, 61%), which was deacetylated. Fractional crystallisation then yielded pure **2** (1.4 g, 28%) and **4** (0.55 g, 11%).

Reaction of D-*fructose in pyridinium poly(hydrogen fluoride).*—Crystalline β-D-fructopyranose (10 g, 55.5 mmol) was dissolved in dry Me_2SO (150 mL) and the solution was stored at 20°C for 30 days. Evaporation of the solvent under reduced pressure yielded a syrup which showed, in its ^{13}C NMR spectrum (Me_2SO-d_6, 200 MHz), signals at δ 104.9, 102.7, and 98.8 for C-2 of α-D-fructofuranose, β-D-fructofuranose, and β-D-fructopyranose, respectively [9], in ~1:2.5:1.5 ratios. Both crystalline β-D-fructopyranose and the D-fructose syrup so obtained were used as substrates in reactions in pyridinium poly(hydrogen fluoride) (Table 1), following the general protocol described above.

6,6'-Dideoxy-6,6'-diiodosucrose (**9**).—To a solution of sucrose (1.8 g, 5.45 mmol) in DMF (60 mL) were added Ph_3P (6.04 g, 23 mmol), imidazole (3.18 g, 46.7 mmol), and I_2 (5.4 g, 21.4 mmol). The mixture was heated at 80°C for 1.5 h, then concentrated to a residue under reduced pressure (<40°C). Water (50 mL) and toluene (50 mL) were added, and the aqueous phase was decanted, washed with additional toluene (2×50 mL), and concentrated. A solution of the residue in H_2O (150 mL) was cooled in an ice–water bath, and stirred with Duolite MB-6113 (H^+, OH^-) mixed resin (100 mL) for 15 min. The resin was filtered off and washed with MeOH (100 mL), and the combined filtrates were filtered through charcoal, concentrated, and dissolved in H_2O (100 mL). The residual Ph_3P and Ph_3PO were then eliminated by washing the aqueous solution with $CHCl_3$ (2×30 mL). Evaporation of water yielded **9** (1.6 g, 52%); mp 107–108°C (from 2-butanone); $[\alpha]_D$ +40° (*c* 1, H_2O). FABMS: *m/z* 585 (100%, $[M+Na]^+$), 563 (3, $[M+H]^+$). ^{13}C NMR (50.3 MHz, acetone-d_6): 105.6 (C-1'), 93.3 (C-1), 83.7, 80.5, 80.1 (C-3'–C-5'), 75.2, 73.9, 73.0, 71.8 (C-2–C-5), 9.6, 8.6 (C-6,6'). Anal. Calcd for $C_{12}H_{20}I_2O_9$: C, 25.63; H, 3.59; I, 45.17. Found: C, 25.47; H, 3.65; I, 44.89.

*6-Deoxy-6-iodo-α-*D-*fructofuranose 6-deoxy-6-iodo-β-*D-*fructofuranose 1,2':2,1'-dianhydride* (**10**) *by reaction of 6,6'-dideoxy-6,6'-diodosucrose* (**9**) *in pyridinium poly(hydrogen fluoride).*—The mixture arising from the action of 7:3 HF–pyridine (10 mL) on **9** (5 g, 8.9 mmol) after 20 min at 20°C (Table 2, Expt No. 1) was quenched (liquid N_2). Acetone (20 mL) and CH_2Cl_2 (20 mL) were added, and the mixture was neutralised by addition of solid $NaHCO_3$, filtered, and concentrated. Traces of pyridine were eliminated by co-evaporation with toluene. TLC (7:1 $CHCl_3$–MeOH) of the syrupy residue showed two main spots. Flash chromatography with the above eluent yielded successively Fractions 1–3.

Fraction 1 (1.76 g, 36%) consisted of pure, syrupy **10**; $[\alpha]_D^{20}$ +34° (*c* 1, EtOH). FABMS: *m/z* 567 (100%, $[M+Na]^+$), 545 (18, $[M+H]^+$). ^{13}C NMR (50.3 MHz, acetone-d_6): Table 4. Anal. Calcd for $C_{12}H_{18}I_2O_8$: C, 26.48; H, 3.33; I, 46.67. Found: C, 26.40; H, 3.21; I, 46.40.

Fraction 2 (0.8 g) contained minor dianhydrides (**14** and **18**) and 6-deoxy-6-iodo-α-D-glucopyranosyl fluoride (^{13}C NMR). Conventional acetylation of this fraction and column chromatography (2:5 EtOAc–hexane) of the peracetylated mixture yielded first: 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranosyl fluoride (0.69 g, 9%), syrup; $[\alpha]_D^{20}$ +94° (*c* 0.7, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), δ 103.3 (d, $J_{1,F}$ 230.1 Hz, C-1), 71.5 (C-4), 70.1 (d, $J_{2,F}$ 25.0 Hz, C-2), 70.0 (d, $J_{5,F}$ 4.6 Hz, C-5), 68.8 (C-3), 2.9 (C-6); ^1H (200 MHz), δ 5.71 (dd, 1 H, $J_{1,F}$ 52.8, $J_{1,2}$ 2.8 Hz, H-1), 5.44 (dd, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 9.5 Hz, H-3), 4.98 (*t*, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.90 (ddd, 1 H, $J_{2,F}$ 23.3 Hz, H-2), 3.84 (ddd, 1 H, $J_{5,6a}$ 3.0, $J_{5,6b}$ 5.8 Hz, H-5), 3.33 (dd, 1 H, $J_{6a,6b}$ 11.4 Hz, H-6a), 3.15 (dd, 1 H, H-

6b), 2.06, 2.02, 1.98 (3 s, each 3 H, 3 Ac). Anal. Calcd for $C_{12}H_{16}FIO_7$: C, 34.46; H, 3.86. Found: C, 34.34; H, 3.90.

Further elution gave: 1,4-di-*O*-acetyl-6-deoxy-6-iodo-β-D-fructofuranose 3,4-di-*O*-acetyl-6-deoxy-6-iodo-β-D-fructofuranose 2,1′:3,2′-dianhydride (**19**; 65 mg, 1%) as a syrup; $[\alpha]_D^{20}$ −17° (*c* 0.6, $CHCl_3$). FABMS: *m/z* 735 (100%, $[M+Na]^+$), 713 (13, $[M+H]^+$). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 103.6 (C-2′), 99.1 (C-2), 82.4 (C-3), 81.8 (C-5′), 79.3 (C-4), 78.6 (C-4′), 76.9 (C-3′), 72.1 (C-5), 64.2 (C-1), 62.5 (C-1′), 6.1 (C-6′), 3.9 (C-6). Anal. Calcd for $C_{20}H_{26}I_2O_{12}$: C, 33.72; H, 3.68; I, 35.65. Found: C, 33.53; H, 3.31; I, 35.49.

Finally, impure 3,4,3′,4′-tetra-*O*-acetyl-6,6′-dideoxy-6,6′-diiodo-di-β-D-fructofuranose 1,2′:2,1′-dianhydride (**15**) was eluted (^{13}C NMR). Deacetylation (Zemplén) and crystallisation from EtOH–H_2O yielded: 6,6′-dideoxy-6,6′-diiodo-di-β-D-fructofuranose 1,2′:2,1′-dianhydride (**14**; 75 mg, 2%); mp 146–147°C (dec); $[\alpha]_D^{20}$ +88° (*c* 0.7, MeOH). FABMS: *m/z* 567 (100%, $[M+Na]^+$), 545 (23, $[M+H]^+$). ^{13}C NMR (50.3 MHz, acetone-d_6): δ 105.6 (C-2), 82.3 (C-3), 81.9, 81,8 (C-4,5), 61.3 (C-1), 7.9 (C-6). Anal. Calcd for $C_{12}H_{18}I_2O_8$: C, 26.48; H, 3.33; I, 46.67. Found: C, 26.51; H, 3.27; I, 46.64.

Fraction 3 (1.8 g, 36%) was a hygroscopic syrup consisting of: 6-deoxy-6-iodo-D-glucopyranose; ^{13}C NMR (50.3 MHz, acetone-d_6): δ 97.5 (C-1 β anomer), 93.4 (C-1 α anomer), 76.9, 75.9, 75.4, 74.8 (C-2–C-5 β anomer), 75.2, 74.1, 73.3, 70.7 (C-2–C-5 α anomer), 10.1 (C-6 α anomer), 8.7 (C-6 β anomer). This compound (0.5 g, 1.7 mmol) was converted into its known [26] α-tetraacetate by treatment with concd H_2SO_4 (16 drops) in a mixture of Ac_2O (14 mL) and glacial AcOH (7 mL) at 0°C. The resulting 1,2,3,4-tetra-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranose (0.12 g, 15%) had mp 178–179°C (from MeOH); $[\alpha]_D^{20}$ +101° (*c* 0.8, $CHCl_3$). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 88.9 (C-1), 72.4, 72.1, 70.6, 69.3 (C-2–C-5), 3.6 (C-6); lit. [27] mp 177.5–178°C; lit. [28] mp 180°C, $[\alpha]_D^{20}$ +102°.

*3,4-Di-*O*-acetyl-6-deoxy-6-iodo-α-D-fructofuranose 3,4-di-*O*-acetyl-6-deoxy-6-iodo-β-D-fructofuranose 1,2′:2,1′-dianhydride* (**11**).—Acetylation of **10** (1 g, 1.84 mmol) gave **11** (1.25 g, 96%); mp 191–192°C (from EtOH); $[\alpha]_D^{20}$ 0° (*c* 1, $CHCl_3$). FABMS: *m/z* 735 (100%, $[M+Na]^+$), 713 (63, $[M+H]^+$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), Table 4; ^1H (200 MHz), Table 5 and δ 2.13, 2.07, 2.05, 2.04 (4 s, each 3 H, 3 Ac). Anal. Calcd for $C_{20}H_{26}I_2O_{12}$: C, 33.72; H, 3.68; I, 35.65. Found: C, 33.99; H, 3.68; I, 35.59.

6-Chloro-6-deoxy-α-D-fructofuranose 6-chloro-6-deoxy-β-D-fructofuranose 1,2′:2,1′-dianhydride (**12**) *by reaction of 6,6′-dichloro-6,6′-dideoxysucrose in pyridinium poly(hydrogen fluoride).*—The mixture arising from the action of 7:3 HF–pyridine (15 mL) on 6,6′-dichloro-6,6′-dideoxysucrose [11] (5 g, 13.2 mmol) after 20 min at 20°C (Table 3, Expt No. 3) was quenched (liquid N_2), and ether (3×30 mL) was added and decanted after vigorous stirring. Acetone (3×30 mL) was then added and evaporated under reduced pressure. Traces of pyridine were eliminated by co-evaporation with toluene. TLC (45:5:3 EtOAc–EtOH–H_2O) of the resulting syrupy residue showed two main spots. Flash chromatography using EtOAc as eluent gave a first fraction which crystallised from EtOAc–hexane, yielding **12** (2.0 g, 42%); mp 155–156°C (dec); $[\alpha]_D^{20}$ +21° (*c* 1, H_2O). FABMS: *m/z* 387 (8%), 385 (66), 383 (100, $[M+Na]^+$), 365 (2), 363 (14), 361 (23, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 4. Anal. Calcd for $C_{12}H_{18}Cl_2O_8$: C, 39.90; H, 5.02; Cl, 19.63. Found: C, 39.82; H, 5.01; Cl, 19.63.

The eluent was then changed to 45:5:3 EtOAc–EtOH–H_2O and 6-chloro-6-deoxy-D-glucose (2.3 g, 44%) was eluted (^{13}C NMR) [29]. Crystallisation from acetone yielded 6-chloro-6-deoxy-α-D-glucopyranose (1.4 g, 27%); mp 134–136°C; $[\alpha]_D^{20}$ +91 → +51° (24 h, *c* 1, H_2O); lit. [11] mp 137°C, $[\alpha]_D^{25}$ +96 → +51°.

The material in the mother liquor from the crystallisation of **12** was acetylated. TLC (1:2 EtOAc–hexane) of the peracetylated mixture showed two main spots. Column chromatography with the above eluent first gave: 2,3,4-tri-*O*-acetyl-6-chloro-6-deoxy-α-D-glucopyranosyl fluoride (0.17 g, 2%); mp 149–150°C (from $CHCl_3$–hexane); $[\alpha]_D^{20}$ +105° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), δ 103.5 (d, $J_{1,F}$ 229.9 Hz, C-1), 70.7 (d, $J_{5,F}$ 4.7 Hz, C-5), 70.0 (d, $J_{2,F}$ 24.3 Hz, C-2), 69.2 (C-3), 68.6 (C-4), 42.6 (C-6); ^1H (200 MHz), δ 5.76 (dd, 1 H, $J_{1,F}$ 52.8, $J_{1,2}$ 1.8 Hz, H-1), 5.47 (t, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 9.8 Hz, H-3), 5.17 (t, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 4.93 (ddd, 1 H, $J_{2,F}$ 24.2 Hz, H-2), 4.23 (ddd, 1 H, $J_{5,6a}$ 2.8, $J_{5,6b}$ 4.6 Hz, H-5), 3.68 (dd, 1 H, $J_{6a,6b}$ 12.4 Hz, H-6a), 3.56 (dd, 1 H, H-6b), 2.08, 2.04, 2.00 (3 s, each 3 H, 3 Ac); lit. [30] mp 151–152°C, $[\alpha]_D^{20}$ +106.95°.

Further elution yielded: 1,4-di-*O*-acetyl-6-chloro-6-deoxy-β-D-fructofuranose 3,4-di-*O*-acetyl-6-chloro-6-deoxy-β-D-fructofuranose 2,1′:3,2′-dianhydride (**21**; 0.21 g, 3%) as a syrup; $[\alpha]_D^{20}$ −10° (*c* 0.6, $CHCl_3$). FABMS: *m/z* 555 (11%), 553 (65), 551 (100, $[M+Na]^+$), 533 (3), 531 (12), 529 (18, $[M+H]^+$). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 103.2 (C-2′), 99.2 (C-2), 81.8 (C-3), 81.2 (C-5′), 78.2 (C-4), 77.2 (C-3′), 76.2 (C-4′), 71.5 (C-5), 63.9 (C-1), 60.2 (C-1′), 45.0 (C-6′), 43.1 (C-6). Anal. Calcd for $C_{20}H_{26}Cl_2O_{12}$: C, 45.38; H, 4.95; Cl, 13.39. Found: C, 45.10; H, 4.79; Cl, 13.40.

3,4-Di-O-acetyl-6-chloro-6-deoxy-α-D-fructofuranose 3,4-di-O-acetyl-6-chloro-6-deoxy-β-D-fructofuranose 1,2′:2,1′-dianhydride (**13**).—Conventional acetylation of **12** (1 g, 2.77 mmol) gave **13** (1.42 g, 97%); mp 197–198°C (from EtOH); $[\alpha]_D^{20}$ −8° (*c* 1, $CHCl_3$). FABMS: *m/z* 555 (1%), 553 (4), 551 (6, $[M+Na]^+$), 533 (12), 531 (65), 529 (100, $[M+H]^+$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), Table 4; ^1H (200 MHz), Table 5 and δ 2.12, 2.07, 2.06, 2.05 (4 s, each 3 H, 4 Ac). Anal. Calcd for $C_{20}H_{26}Cl_2O_{12}$: C, 45.38; H, 4.95; Cl, 13.39. Found: C, 45.05; H, 4.99; Cl, 13.36.

6-Deoxy-6-iodo-α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**22**).—*(a)* To a solution of **2** (3.24 mmol, 10 mmol) in DMF (70 mL) were added Ph_3P (6.7 g, 25 mmol) and I_2 (5.17 g, 20 mmol), and the mixture was heated at 80°C for 1.5 h. The solvent was then evaporated under reduced pressure to ~1/3 of the initial volume. Methanol (100 mL) was added, and the resulting solution was adjusted to pH 9 with 3 M NaOMe. After 30 min, the mixture was neutralised using Amberlite IRN-77 (H^+) resin, filtered, and concentrated. The residue was triturated with water (2×50 mL) and filtered, the combined aqueous filtrates were washed with toluene (2×50 mL), evaporated, and a solution of the yellow residue MeOH (75 mL) was decolourised by passing it through a layer of charcoal. The resulting syrupy residue showed a main spot in TLC, using 3:1 $CHCl_3$–MeOH as eluent. Flash chromatography with the same eluent yielded **22** (3.43 g, 79%); mp 163–164°C (dec, from EtOH); $[\alpha]_D^{20}$ −34° (*c* 1, H_2O). FABMS: *m/z* 457 (60%, $[M+Na]^+$), 435 (100, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 6. Anal. Calcd for $C_{12}H_{19}IO_9$: C, 33.19; H, 4.41; I, 29.24. Found: C, 33.21; H, 4.58; I, 28.90.

(b) Compound **22** was also obtained directly starting from the mixture of difructose dianhydrides **2** and **4** (~3:1, 1 g), without previous purification, using the above protocol (DMF, 20 mL; Ph_3P, 1.45 g, 5.4 mmol; I_2, 1.12 g, 4.32 mmol). In this case, the crude

product showed the presence of two components (TLC). Flash chromatography (3:1 $CHCl_3$–MeOH) yielded **22** (0.67 g, 50% relative to the total starting mixture) and unreacted **4** (0.2 g, 20%).

3,4-Di-O-acetyl-6-deoxy-6-iodo-α-D-fructofuranose 3,4,5-tri-O-acetyl-β-D-fructopyranose 1,2′:2,1′-dianhydride (**23**).—Conventional acetylation of **22** (1 g, 2.3 mmol) gave **23** (1.44 g, 97%) as a syrup having $[\alpha]_D^{20}$ −29.5° (*c* 1.4, $CHCl_3$). FABMS: *m/z* 667 (98%, $[M+Na]^+$), 645 (100, $[M+H]^+$). NMR data: ^{13}C (50.3 MHz, $CDCl_3$), Table 6; ^1H (200 MHz, C_6D_6), Table 7 and δ 2.03, 1.95, 1.88, 1.77, 1.76 (5 s, each 3 H, 3 Ac). Anal. Calcd for $C_{22}H_{29}IO_{14}$: C, 41.00; H, 4.54; I, 19.71. Found: C, 40.67; H, 4.30; I, 19.50.

6-Chloro-6-deoxy-α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**24**).—*(a)* To a solution of α-D-fructofuranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**2**, 2 g, 6.17 mmol) in pyridine (120 mL) were added Ph_3P (24 g, 12.34 mmol) and CCl_4 (9.8 mL), and the mixture was heated at 65–70°C for 0.5 h. Methanol (9.8 mL) was then added and, after 1 h at 50°C, the mixture was evaporated to a residue which was triturated with water (3×30 mL) and filtered. The combined aqueous filtrates were evaporated and the residue, which showed a main spot in TLC (3:1 $CHCl_3$–MeOH), was subjected to flash chromatography with the above eluent to give **24** (1.84 g, 87%); mp 181–182°C (dec, from MeOH); $[\alpha]_D^{20}$ −43° (*c* 1.2, H_2O). FABMS: *m/z* 367 (40%), 365 (100, $[M+Na]^+$), 345 (4), 343 (10, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 6. Anal. Calcd for $C_{12}H_{19}ClO_9$: C, 42.01; H, 5.59; Cl, 10.22. Found: C, 42.00; H, 5.50; Cl, 10.22.

(b) Compound **24** was also obtained directly from the mixture of difructose dianhydrides **2** and **4** (~3:1, 1 g), without previous purification, using the above protocol (pyridine, 60 mL; Ph_3P, 8.4 g, 4.32 mmol; CCl_4, 3.5 mL). In this case, the crude product showed the presence of two components (TLC). Flash chromatography (3:1 $CHCl_3$–MeOH) yielded **24** (0.62 g, 58% relative to the total starting mixture) and unreacted **4** (0.22 g, 22%).

3,4-Di-O-acetyl-6-chloro-6-deoxy-α-D-fructofuranose 3,4,5-tri-O-acetyl-β-D-fructopyranose 1,2′:2,1′-dianhydride (**25**).—Conventional acetylation of **24** (1 g, 2.92 mmol) gave **25** (1.55 g, 97%) as a syrup having $[\alpha]_D^{20}$ −53° (c 1.2, $CHCl_3$). FABMS: *m/z* 577 (30%), 575 (70, $[M+Na]^+$), 555 (40), 553 (100, $[M+H]^+$). NMR data: ^{13}C (50.3 MHz, $CDCl_3$), Table 6; ^1H (200 MHz, C_6D_6), Table 7 and δ 1.98, 1.95, 1.89, 1.77, 1.76 (5 s, each 3 H, 5 Ac). Anal. Calcd for $C_{22}H_{29}ClO_{14}$: C, 47.78; H, 5.28; Cl, 6.42. Found: C, 47.60; H, 5.28; Cl, 6.21.

3,4-Di-O-acetyl-6-S-heptyl-6-thio-α-D-fructofuranose 3,4-di-O-acetyl-6-S-heptyl-6-thio-β-D-fructofuranose 1,2′:2,1′-dianhydride (**26**).—*(a) From 3,4-di-O-acetyl-6-chloro-6-deoxy-α-D-fructofuranose 3,4-di-O-acetyl-6-chloro-6-deoxy-β-D-fructofuranose 1,2′:2,1′-dianhydride* (**13**). To a solution of **13** (0.2 g, 0.56 mmol) in DMPU (5 mL) were added 1-heptanethiol (0.35 mL, 0.29 g, 2.2 mmol) and Na_2CO_3 (0.237 g, 2.2 mmol), and the mixture was heated at 90°C for 16 h. Additional 1-heptanethiol (0.35 mL, 0.29 g, 2.2 mmol) and Na_2CO_3 (0.237 g, 2.2 mmol) were then added and the mixture was kept at 125°C for 24 h. The solvent was then evaporated under vacuum at 65–70°C and the residue was acetylated (1:1 Ac_2O–pyridine, 5 mL, 15 h). The peracetylated mixture showed a main spot in TLC (1:2 EtOAc–hexane). Flash chromatography with the above eluent and crystallisation from EtOH yielded **26** (0.27 g, 68%); mp 86–87°C; $[\alpha]_D^{20}$ +2° (*c* 1.1, $CHCl_3$). FABMS: *m/z* 743 (100%, $[M+Na]^+$), 721 (10, $[M+H]^+$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), Table 4 and δ 32.8, 32.1, 31.4 (2 C), 29.3 (2 C), 28.6 (2 C), 28.4 (2 C),

22.3 (2 C), 13.8 (2 C) (heptyl chains); ^{1}H (200 MHz), Table 5 and δ 2.50 (m, 4 H, 2 SCH_2), 2.07, 2.02, 2.01, 2.00 (4 s, each 3 H, 4 Ac), 1.6–1.1 (m, 20 H, 10 CH_2), 0.81 (m, 6 H, 2 CH_3). Anal. Calcd for $C_{34}H_{56}O_{12}S_2$: C, 56.50; H, 7.81; S, 8.73. Found: C, 56.50; H, 7.81; S, 8.73.

(*b*) *From 3,4-di-*O*-acetyl-6-deoxy-6-iodo-α-*D*-fructofuranose 3,4-di-*O*-acetyl-6-deoxy-6-iodo-β-*D*-fructofuranose 1,2':2,1'-dianhydride* (**11**). To a solution of **11** (0.5 g, 0.7 mmol) in DMPU (10 mL) were added 1-heptanethiol (0.44 mL, 0.37 g, 2.8 mmol) and Na_2CO_3 (0.297 g, 2.8 mmol). The mixture was heated at 70°C for 24 h and then concentrated under vacuum at 55–60°C. The residue was dissolved in CH_2Cl_2 (30 mL), and the solution was washed with water (2×30 mL), dried (Na_2SO_4), and evaporated to a residue which showed two components in TLC (1:2 EtOAc–hexane). Column chromatography using 2:5 EtOAc–hexane as eluent yielded **26** (0.31 g, 62%, higher R_f) and then: 3,4-di-*O*-acetyl-6-*S*-heptyl-6-thio-α-D-fructofuranose 3,4-di-*O*-acetyl-6-deoxy-β-D-*threo*-hex-5-enofuranose 1,2':2,1'-dianhydride (**30**; 90 mg, 22%, lower R_f); mp 95–96°C (from EtOH); $[\alpha]_D^{20}$ +1° (*c* 0.65, $CHCl_3$). FABMS: *m/z* 612 (100%, $[M+Na]^+$), 589 (25, $[M+H]^+$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), Table 4 and δ 32.9, 31.5, 29.4, 28.7, 28.5, 22.3, 13.8 (heptyl chain); ^{1}H (200 MHz), Table 5 and δ 2.54 (m, 2 H, SCH_2), 2.08, 2.05, 2.03, 2.01 (4 s, each 3 H, 4 Ac), 1.6–1.1 (m, 10 H, 5 CH_2), 0.81 (m, 3 H, CH_3). Anal. Calcd for $C_{27}H_{40}O_{12}S$: C, 55.09; H, 6.85; S, 5.45. Found: C, 54.93; H, 6.93; S, 5.42.

6-S-Heptyl-6-thio-α-D-fructofuranose 6-S-heptyl-6-thio-β-D-fructofuranose 1,2':2,1'-dianhydride (**27**).—Deacetylation (Zemplén) of the tetraacetate **26** (0.2 g, 0.28 mmol), with monitoring by TLC (45:5:3 EtOAc–EtOH–H_2O), yielded **27** (0.15 g, 98%) as a viscous, enantiotropic liquid crystal having cp 52.4°C (ΔH 1.7 kJ mol^{-1}); $[\alpha]_D^{20}$ +21° (*c* 0.8, EtOH). FABMS: *m/z* 575 (100%, $[M+Na]^+$), 553 (20, $[M+H]^+$). ^{13}C NMR (50.3 MHz, acetone-d_6): Table 4 and δ 33.4, 32.9, 32.5 (2 C), 30.5 (2 C), 29.6 (2 C), 29.5 (2 C), 23.2 (2 C), 14.4 (2 C) (heptyl chains). Anal. Calcd for $C_{26}H_{48}S_2O_8$: C, 56.49; H, 8.75; S, 11.60. Found: C, 56.20; H, 8.90; S, 11.23.

*3,4-Di-*O*-acetyl-6-S-heptyl-6-thio-α-D-fructofuranose 3,4,5-tri-*O*-acetyl-β-D-fructopyranose 1,2':2,1'-dianhydride* (**28**).—*(a) From 3,4-di-*O*-acetyl-6-chloro-6-deoxy-α-D-fructofuranose 3,4,5-tri-*O*-acetyl-β-D-fructopyranose 1,2':2,1'-dianhydride* (**25**). The procedure described for the preparation of the diheptylthio derivative **26** (*a*) was followed starting from **25** (0.5 g, 0.9 mmol); DMPU (10 mL); 1-heptanethiol (2×0.57 mL, 0.48 g, 3.6 mmol); Na_2CO_3 (2×0.38 g, 3.6 mmol). Flash chromatography using 1:2 EtOAc–hexane as eluent yielded **28** (0.5 g, 67%) as a syrup having $[\alpha]_D^{20}$ −31° (*c* 1.2, $CHCl_3$). FABMS: *m/z* 671 (100%, $[M+Na]^+$), 649 (25, $[M+H]^+$). NMR data: ^{13}C (50.3 MHz, $CDCl_3$), Table 6 and δ 32.9, 31.4, 29.3, 28.6, 28.5, 22.3, 13.8 (heptyl chain); ^{1}H (200 MHz, C_6D_6), Table 7 and δ 2.67 (m, 2 H, SCH_2), 2.06, 1.94, 1.89, 1.84, 1.82 (5 s, each 3 H, 5 Ac), 1.75–1.25 (m, 10 H, 5 CH_2), 1.06 (m, 3 H, CH_3). Anal. Calcd for $C_{29}H_{44}O_{14}S$: C, 53.69; H, 6.84; S, 4.94. Found: C, 53.37; H, 6.72; S, 4.60.

*(b) From 3,4-di-*O*-acetyl-6-deoxy-6-iodo-α-D-fructofuranose 3,4,5-tri-*O*-acetyl-β-D-fructopyranose 1,2':2,1'-dianhydride* (**23**). The procedure described for the preparation of the diheptylthio derivative **26** (*b*) was followed starting from **23** (0.74 g, 1.15 mmol); DMPU (12 mL); 1-heptanethiol (0.34 mL, 0.284 g, 2.3 mmol); Na_2CO_3 (0.244 g, 2.3 mmol). TLC (1:2 EtOAc–hexane) of the crude product showed only one component. Flash chromatography with the above eluent yielded **28** (0.686 g, 92%).

6-S-Heptyl-6-thio-α-D-fructofuranose β-D-fructopyranose 1,2':2,1'-dianhydride (**29**).—Deacetylation of the pentaacetate **28** (0.5 g, 0.77 mmol) yielded **29** (0.334 g, 99%); mp 201–203° (from H_2O); $[\alpha]_D^{20}$ −33° (*c* 1, MeOH). FABMS: *m/z* 461 (100%, $[M+Na]^+$), 639 (2, $[M+H]^+$). ^{13}C NMR (50.3 MHz, methanol-d_4): Table 6 and δ 33.6, 32.9, 30.7, 30.0, 29.7, 23.6, 14.4 (heptyl chain). Anal. Calcd for $C_{19}H_{34}O_9S$: C, 52.04; H, 7.81; S, 7.31. Found: C, 51.83; H, 7.80; S, 7.23.

3,4-Di-O-acetyl-6-azido-6-deoxy-α-D-fructofuranose 3,4-di-O-acetyl-6-azido-6-deoxy-β-D-fructofuranose 1,2':2,1'-dianhydride (**31**).—*(a) From 3,4-di-O-acetyl-6-chloro-6-deoxy-α-D-fructofuranose 3,4-di-O-acetyl-6-chloro-6-deoxy-β-D-fructofuranose 1,2':2,1'-dianhydride* (**13**). To a solution of **13** (0.94 g, 0.34 mmol) in DMF (6 mL) was added NaN_3 (0.203 g, 3.12 mmol). The mixture was heated at 125°C for 24 h, then concentrated under reduced pressure (40–50°C), and the residue acetylated (1:1 Ac_2O–pyridine, 10 mL, 24 h). The peracetylated product showed a single spot in TLC (1:2 EtOAc–hexane). Crystallisation from EtOH yielded **31** (0.413 g, 81%); mp 124–125°C; $[\alpha]_D^{20}$ +32° (*c* 1, $CHCl_3$). FABMS: *m/z* 565 (80%, $[M+Na]^+$), 589 (100, $[M+H]^+$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), Table 4; ^1H (400 MHz), Table 5 and δ 2.06, 2.05 2.02, 2.00 (4 s, each 3 H, 4 Ac). Anal. Calcd for $C_{20}H_{26}N_6O_{12}$: C, 44.28; H, 4.83; N, 15.49. Found: C, 44.40; H, 4.86; N, 15.42.

(b) From 3,4-Di-O-acetyl-6-deoxy-6-iodo-α-D-fructofuranose 3,4-di-O-acetyl-6-deoxy-6-iodo-β-D-fructofuranose 1,2':2,1'-dianhydride (**11**). To a solution of **11** (0.5 g, 0.7 mmol) in DMF (8 mL) was added NaN_3 (0.274 g, 4.2 mmol). The mixture was heated at 80°C for 24 h and then concentrated under vacuum (45–50°C). The residue was triturated with ice–water (25 mL) to give a white solid which was collected and dried. TLC (1:2 EtOAc–hexane) of this crude product showed two components which crystallised simultaneously from EtOH. Column chromatography with the above eluent yielded, first, 3,4-di-*O*-acetyl-6-azido-6-deoxy-α-D-fructofuranose 3,4-di-*O*-acetyl-6-deoxy-β-D-*threo*-hex-5-enofuranose 1,2':2,1'-dianhydride (**35**; 90 mg, 26%); mp 116–117°C (from EtOH); $[\alpha]_D^{20}$ +15° (*c* 1, $CHCl_3$). FABMS: *m/z* 522 (50%, $[M+Na]^+$), 500 (100, $[M+H]^+$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), Table 4; ^1H (400 MHz), Table 5 and δ 2.09, 2.06, 2.05, 2.03 (4 s, each 3 H, 3 Ac). Anal. Calcd for $C_{20}H_{25}N_3O_{12}$: C, 48.10; H, 5.05; N, 8.41. Found: C, 48.27; H, 4.95; N, 8.51.

Further elution provided the peracetyl diazide **31** (0.25 g, 66%).

6-Azido-6-deoxy-α-D-fructofuranose 6-azido-6-deoxy-β-D-fructofuranose 1,2':2,1'-dianhydride (**32**).—Deacetylation of the tetraacetate **31** (0.5 g, 0.92 mmol), with monitoring by TLC (45:5:3 EtOAc–EtOH–H_2O), yielded **32** (0.338 g, 98%); mp 144–145°C (from EtOAc); $[\alpha]_D^{20}$ +52° (*c* 0.75, acetone). FABMS: *m/z* 397 (100%, $[M+Na]^+$), 375 (5, $[M+H]^+$). ^{13}C NMR (50.3 MHz, acetone-d_6): Table 4. Anal. Calcd for $C_{12}H_{18}N_6O_8$: C, 38.50; H, 4.85; N, 22.45. Found: C, 38.44; H, 4.71; N, 22.57.

3,4-Di-O-acetyl-6-azido-6-deoxy-α-D-fructofuranose 3,4,5-tri-O-acetyl-β-D-fructopyranose 1,2':2,1'-dianhydride (**33**).—*(a) From 3,4-di-O-acetyl-6-chloro-6-deoxy-α-D-fructofuranose 3,4,5-tri-O-acetyl-β-D-fructopyranose 1,2':2,1'-dianhydride* (**25**). The procedure described for the preparation of the diazide **31** (*a*) was followed starting from **25** (2.76 g, 5 mmol); DMF (30 mL); NaN_3 (0.97 g, 15 mmol). Flash chromatography using 1:1 EtOAc–hexane as eluent yielded **33** (2.57 g, 92%) as a syrup having $[\alpha]_D^{20}$ −30° (*c* 1, $CHCl_3$). FABMS: *m/z* 582 (100%, $[M+Na]^+$), 560 (65, $[M+H]^+$). NMR data:

^{13}C (50.3 MHz, $CDCl_3$), Table 6; ^1H (200 MHz, C_6D_6), Table 7 and δ 1.99, 1.94, 1.90, 1.84, 1.79 (5 s, each 3 H, 5 Ac). Anal. Calcd for $C_{22}H_{29}N_3O_{14}$: C, 47.23; H, 5.22; N, 7.51. Found: C, 47.48; H, 5.05; N, 7.34.

(b) From 3,4-di-O-acetyl-6-deoxy-6-iodo-α-D-fructofuranose 3,4,5-tri-O-acetyl-β-D-fructopyranose 1,2':2,1'-dianhydride (**23**). The procedure described for the preparation of the diazido derivative **31** (*b*) was followed starting from **23** (0.5 g, 0.77 mmol); DMF (7 mL); NaN_3 (0.15 g, 2.31 mmol). TLC (1:1 EtOAc–hexane) of the crude product showed only one component. Flash chromatography with the above eluent yielded **36** (0.41 g, 95%).

6-Azido-6-deoxy-α-D-fructofuranose β-D-fructopyranose 1,2':2,1'-dianhydride (**34**).—Deacetylation of the pentaacetate **33** (2 g, 3.57 mmol), with monitoring by TLC (3:1 $CHCl_3$–MeOH), yielded **34** (1.25 g, 99%) as a syrup having $[\alpha]_D^{20}$ −28° (*c* 1, H_2O). FABMS: *m/z* 372 (100%, $[M+Na]^+$), 350 (15, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 6. Anal. Calcd for $C_{12}H_{19}N_3O_9$: C, 41.26; H, 5.49; N, 12.03. Found: C, 40.98; H, 5.48; N, 12.13.

6-Amino-6-deoxy-α-D-fructofuranose 6-amino-6-deoxy-β-D-fructofuranose 1,2':2,1'-dianhydride (**36**).—To a solution of the diazide **32** (0.3 g, 0.8 mmol) in a mixture of dioxane (23 mL) and MeOH (4.6 mL) was gradually added Ph_3P (1.22 g, 4.6 mmol) while stirring under N_2, and the mixture was stored for 1 h at room temperature. Concentrated NH_4OH (28%, 1.2 mL) was then added. After 16 h, the solvent was evaporated under reduced pressure (<40°C), the residue was triturated with H_2O (3×20 mL), and the excess of Ph_3P and Ph_3PO were filtered off. The combined aqueous filtrates were washed with toluene (2×20 mL) and evaporated to give **36** (0.235 g, 91%) as a syrup having $[\alpha]_D^{20}$ +29° (*c* 1, H_2O). FABMS: *m/z* 335 (18%, $[M+Na]^+$), 323 (100, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 4. Anal. Calcd for $C_{12}H_{22}N_2O_8$: C, 44.72; H, 6.88; N, 8.69. Found: C, 44.69; H, 6.50; N, 8.29.

6-Acetamido-6-deoxy-α-D-fructofuranose 6-acetamido-6-deoxy-β-D-fructofuranose 1,2':2,1'-dianhydride (**37**).—To a solution of the diamine **36** (0.1 g, 0.31 mmol) in MeOH (12 mL) was added Ac_2O (0.15 mL), and the mixture was stirred at room temperature for 24 h. The solvent was evaporated under reduced pressure, the residue was dissolved in EtOH (3×5 mL), and the EtOH was evaporated to yield **37** (0.125 g, 99%) as an amorphous, white solid having $[\alpha]_D^{20}$ +28° (*c* 0.9, EtOH). FABMS: *m/z* 429 (100%, $[M+Na]^+$), 407 (23, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 4. Anal. Calcd for $C_{16}H_{26}N_2O_{10}$: C, 47.29; H, 6.45; N, 6.89. Found: C, 47.00; H, 6.52; N, 6.61.

6-Acetamido-3,4-di-O-acetyl-6-deoxy-α-D-fructofuranose 6-acetamido-3,4-di-O-acetyl-6-deoxy-β-D-fructofuranose 1,2':2,1'-dianhydride (**38**).—Conventional acetylation of **36** (81 mg, 0.2 mmol) yielded **38** (0.11 g, 96%); mp 189–191°C (from EtOH); $[\alpha]_D^{20}$ +5° (*c* 0.8, $CHCl_3$). FABMS: *m/z* 597 (100%, $[M+Na]^+$), 575 (60, $[M+H]^+$). NMR data ($CDCl_3$): ^{13}C (50.3 MHz), Table 4; ^1H (400 MHz), Table 5 and δ 6.12 (t, 1 H, $J_{6'a,N'H}$ 5.5, $J_{6'b,N'H}$ 5.5 Hz, N'H), 6.05 (t, 1 H, $J_{6a,NH}$ 5.5, $J_{6b,NH}$ 5.5 Hz, NH), 2.12, 2.08 (2 s, each 3 H, 2 NAc), 2.05, 1.97 (2 s, each 6 H, 4 OAc). Anal. Calcd for $C_{24}H_{34}N_2O_{14}$: C, 50.17; H, 5.96; N, 4.88. Found: C, 50.00; H, 6.01; N, 4.50.

6-Amino-6-deoxy-α-D-fructofuranose β-D-fructopyranose 1,2':2,1'-dianhydride (**39**).—Reduction of the azide **34** (1 g, 2.86 mmol) with Ph_3P (2.19 g, 8.34 mmol) in a mixture of dioxane (54 mL) and MeOH (11 mL), and subsequent treatment with concen-

trated NH_4OH (28%, 20 mL), as described for the preparation of the diamine **36**, yielded **39** (0.107 g, 98%) as a syrup having $[\alpha]_D^{20}$ −41° (*c* 1, H_2O). FABMS: *m/z* 346 (15%, $[M+Na]^+$), 322 (100, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 6. Anal. Calcd for $C_{12}H_{21}NO_9$: C, 44.58; H, 6.55; N, 4.33. Found: C, 44.20; H, 6.55; N, 4.12.

6-Acetamido-6-deoxy-α-D-fructofuranose β-D-fructopyranose 1,2':2,1'-dianhydride (**40**).—*N*-Acetylation of **39** (0.1 g, 0.31 mmol) with Ac_2O (0.15 mL) in MeOH (12 mL), as described for the diacetamido derivative **37**, yielded syrupy **40** (0.107 g, 98%); $[\alpha]_D^{20}$ −33.5° (*c* 1, H_2O). FABMS: *m/z* 388 (100%, $[M+Na]^+$), 366 (28, $[M+H]^+$). ^{13}C NMR (50.3 MHz, D_2O): Table 6. Anal. Calcd for $C_{14}H_{23}NO_{10}$: C, 46.03; H, 6.35; N, 3.83. Found: C, 45.89; H, 6.60; N, 3.72.

6-Acetamido-3,4-di-O-acetyl-6-deoxy-α-D-fructofuranose 3,4,5-tri-O-acetyl-β-D-fructopyranose 1,2':2,1'-dianhydride (**41**).—Conventional acetylation of **39** (80 mg, 0.22 mmol) yielded **41** (0.116 g, 95%) as a syrup having $[\alpha]_D^{20}$ −52° (*c* 1, $CHCl_3$). FABMS: *m/z* 598 (100%, $[M+Na]^+$), 576 (65, $[M+H]^+$). NMR data: ^{13}C (50.3 MHz, $CDCl_3$), Table 6; ^1H (400 MHz, C_6D_6), Table 7 and δ 6.19 (bs, 1 H, NH), 2.03 (s, 3 H, NAc), 1.95 (6 H), 1.90 (6 H), 1.80 (3 s, 15 H, 5 Ac). Anal. Calcd for $C_{24}H_{33}NO_{14}$: C, 50.09; H, 5.78; N, 2.43. Found: C, 50.00; H, 5.63; N, 2.19.

*Preparation of difructose dianhydride (**1** or **2**)–chloromethyloxirane copolymerisates.*—*(a) Water-insoluble copolymerisates.* To a solution of the difructose dianhydride **1** or **2** (0.657 g, 2.02 mmol) and NaOH (0.2 g, 4.5 mmol) in H_2O (0.4 mL) was added chloromethyloxirane (0.42 g, 0.35 mL, 4.5 mmol), and the mixture was stirred at room temperature for 3 days. Water (30 mL) was then added to the viscous mixture and the resulting suspension was carefully neutralised by addition of 1 M and then 0.1 M HCl. The two-phase mixture was centrifuged (5000 rpm, 20 min) and an insoluble, translucent gel was decanted, washed with H_2O (2×40 mL), centrifuged, and decanted. The hydrophilic gel was precipitated by addition of acetone (2×40 mL) to give a white powder which was collected by centrifugation and dried at 90°C under low pressure (0.14 Pa) over P_4O_{10} for 3 h and then overnight at room temperature. Yield from **1**, 0.75 g; dec 240–260°C. Yield from **2**, 0.5 g; dec 270–290°C.

(b) Water-soluble copolymerizates. To a solution of the difructose dianhydride **1** or **2** (0.7 g, 2.16 mmol) and NaOH (0.136 g, 3.4 mmol) in H_2O (0.9 mL) was added chloromethyloxirane (0.29 g, 0.24 mL, 3.24 mmol), and the mixture was stirred at room temperature for 24 h. Water (10 mL) was then added and the resulting solution was neutralised by addition of 1 M and 0.1 M HCl. Addition of acetone (100 mL) resulted in the separation of an oil which was decanted by centrifugation (10000 rpm, 20 min), dissolved in H_2O (15 mL), and reprecipitated with acetone (100 mL). The oily product was precipitated with acetone (4×30 mL) and decanted to give a white powder which was dried at 80°C under low pressure (0.14 Pa) over P_4O_{10} for 1 h and then overnight at room temperature. Yield from **1**, 0.78 g; mp 180–190°C, dec 200–240°C. Yield from **2**, 0.9 g; mp 195–200°C, dec 215–250°C.

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