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SYNTHESIS AND GLYCOSIDATION OF 1-DEOXY-1-[(2,2-DIACYLVINYL)AMINO]-D-FRUCTOSES*†

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ABSTRACT

The reactions of 1-amino-1-deoxy-D-fructose acetate (**1**) with methyl 3-methoxy-2-methoxycarbonylacrylate and 5-methoxymethylene-2,2-dimethyl-1,3-dioxane-4,6-dione in the presence of a base afforded 1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]- (**2**) and 1-deoxy-1-[(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidenemethyl)amino]-D-fructose (**3**), respectively, in high yields. 1-Deoxy-1-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-D-fructose (**4**) was obtained (85%) by a transamination reaction between **1** and 5,5-dimethyl-2-phenylaminomethylene-1,3-cyclohexanedione in the presence of Et_3N. The isomeric composition of equilibrium solutions of **1–4** was established by ^{13}C-n.m.r. spectroscopy. For all the compounds, the β-pyranose form was the main component in D_2O; the α-furanose, the β-furanose, and, for **1**, the α-pyranose forms, were also present. The major constituents of **2** in $(CD_3)_2SO$ solution were the β- and the α-furanose forms. Acetylation of **2** afforded the tetra-acetates of the α- and β-furanose forms, the 3,4,6-triacetates of the α- and β-furanose forms, the 3,4,5-triacetate of the β-pyranose form, and 2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-D-*arabino*-hex-1-enitol. Glycosidation of **2** with MeOH–HCl afforded a mixture of methyl 1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-α- (**11α**) and -β-D-fructofuranoside (**11β**), and methyl 1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)-amino]-β-D-fructopyranoside (**13**). Compounds **11α** and **13** were isolated as their tri-acetates (**12** and **14**, respectively). Deacetylation and removal of the *N*-protecting group of **12** gave methyl 1-amino-1-deoxy-α-D-fructofuranoside (~54% from **2**).

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†Protection of the Amino Group of Amino Sugars by the Acylvinyl Group, Part II. For Part I, see ref. 1.

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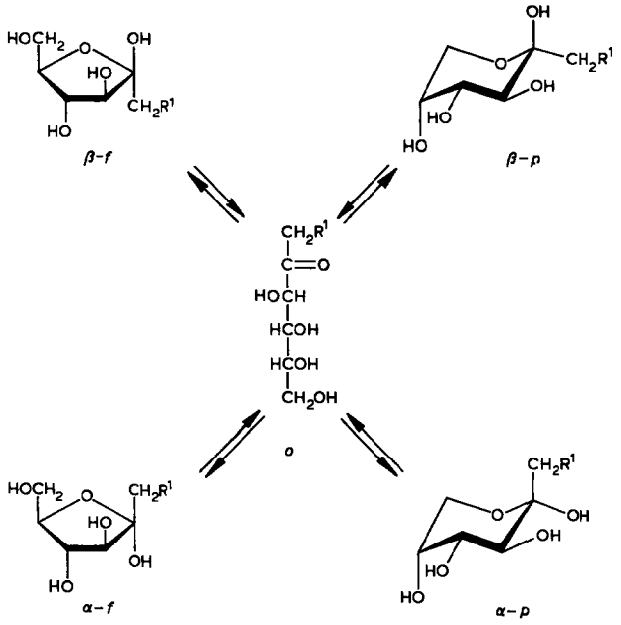
INTRODUCTION

In spite of the biological interest of some *N*-substituted 1-amino-1-deoxy-D-fructoses ("Amadori compounds")[2], few simple derivatives and no glycosides of the amino sugar are known. Previous work[3,4] has demonstrated the utility of the acylvinyl and the diacylvinyl groups for protecting the amino group of 2-amino-2-deoxy-D-glucose during the preparation of various *O*-acetylated derivatives and glycosides. We have extended this work to other amino sugars, and now report on the synthesis of several 1-deoxy-1-(diacylvinylamino)-D-fructoses, and the Fischer glycosidation of one of them. In contrast to what has been observed[3,4] with the 2-deoxy-2-(diacylvinylamino)-D-glucoses, the similar derivatives of 1-amino-1-deoxy-D-fructose exist in solution as mixtures of up to four tautomeric forms, and their acetylation leads to mixtures of tri- and tetra-acetates. These equilibria and the structures of the various acetyl derivatives and glycosides have been investigated by ^{1}H- and ^{13}C-n.m.r. spectroscopy.

RESULTS AND DISCUSSION

Preparation of 1-deoxy-1-[(2,2-diacylvinyl)amino]-D-fructoses. — Compound **2** was obtained in quantitative yield by treating an aqueous solution of 1-amino-1-deoxy-D-fructose acetate (**1**) and sodium carbonate with methyl 3-methoxy-2-methoxycarbonylacrylate. This and similar reactions can also be performed in methanolic triethylamine, as illustrated by the formation (92%) of **3** from **1** and 5-methoxymethylene-2,2-dimethyl-1,3-dioxane-4,6-dione. Compound **4** was prepared (85%) by the transamination reaction[4] between 1-amino-1-deoxy-D-fructose (prepared *in situ* from **1** and 1 mol of triethylamine in methanol) and the readily available[5] 5,5-dimethyl-2-phenylaminomethylene-1,3-cyclohexanedione. Derivatives **3** and **4** were crystalline, but **2** was amorphous.

The analytical and spectroscopic data of **2–4** were consistent with the assigned structures. Compound **2** had u.v. and i.r. absorptions due to the *N*-substituent similar to those of simple 2-alkoxycarbonyl-3-alkylaminoacrylic esters[6] and to that of the analogous derivative (**5**) of 2-amino-2-deoxy-α-D-glucopyranose[1]. Similarly, **3** and **4** had u.v. and i.r. spectra similar to those of 5-alkylamino-2,2-dimethyl-4,6-dioxo-1,3-dioxane[7] and 2-alkylaminomethylene-5,5-dimethyl-1,3-cyclohexanedione[8], respectively. The presence of the chelate structure was demonstrated by the low stretching-frequencies of *cis*-NH and C=O groups, and the large δ values for the NH protons for a solution in $(CD_3)_2SO$. They did not mutarotate in aqueous solution, and the ^{1}H-n.m.r. spectrum of a freshly prepared solution in D_2O showed a one-proton complex signal in the range δ 8.1–8.2 attributable to the olefinic protons of the *N*-deuterated species of four isomeric forms. These results indicate either that **3** and **4** exist in the solid state as a mixture of several isomeric forms or that the establishment of the isomeric equilibrium in water is too fast to be followed by polarimetry or n.m.r. spectroscopy.



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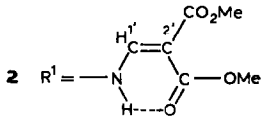

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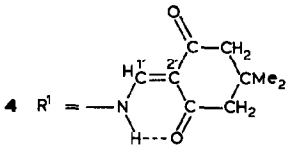

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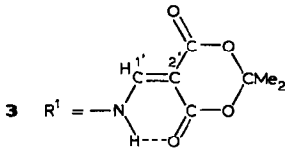

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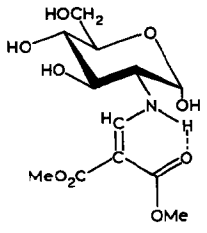

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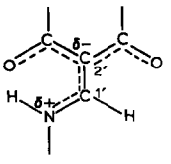

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Isomeric composition at equilibrium. — The ^{13}C-n.m.r. spectrum of a solution of **1** in D_2O and those of its derivatives **2–4** (Table I) showed, for each compound, the presence of the α- (*α-f*) and β-furanose (*β-f*) forms and the β-pyranose (*β-p*) form in the $^2C_5$ conformation; for **1** in D_2O and for **2** in $(CD_3)_2SO$, the α-pyranose (*α-p*) form in the $^2C_5$ conformation was also present. The assignment of the signals was made by comparison with those for D-fructose[9] and for the *N*-(1-deoxy-D-fructos-1-yl)amino acids[10]. The low-field shift of the signal for C-1 (~10 p.p.m.), and, to a smaller extent, for C-2 in **2–4** relative to those of **1**, is attributed to the magnetic anisotropy and the electron-delocalisation of the diacylvinylamino system (**6**) which result in an accumulation of positive charge on the amino group. The latter effect also accounts for the large difference between the chemical shifts of the signals for C-1′ and C-2′. The ratio of the isomers (Table II) at the probe temperature was deduced from the integrated intensities of the signals for C-1,6 and C-3,4,5[9]. No signals were observed at δ ~214 which could be attributed to C=O of the open-chain (*o*) form. As can be seen from the data in Table II, the *β-p* form is favoured for all the compounds in D_2O solution. In $(CD_3)_2SO$, the equilibrium for **2** is shifted to the *β-f* form as has been observed[11] for D-fructose. This effect is probably due[11] to stabilisation by intramolecular hydrogen-bonding of HO-3 with HO-6; intramolecular bonding of HO-4 with the NH in **2**, similar to that suggested between HO-4 and HO-1 in D-fructose, is unlikely as the amino group is involved in a strong hydrogen-bond with the C=O of the *N*-substituent.

The isomeric compositions of **2–4** in D_2O are similar to those observed[10] for the *N*-(1-deoxy-D-fructos-1-yl)amino acids, and contrast sharply with the results obtained for **5** and for similar *N*-monoacyl- and *N*-diacyl-vinyl derivatives of 2-amino-2-deoxy-D-glucose, which, in the solid state[12] and in solution[3], exist only in the *α-p* form.

Acetylation of **2**. — The acetylation reaction of the *N*-(diacylvinyl)amino derivatives of 1-amino-1-deoxy-D-fructose is more complex than that of the similar derivatives of 2-amino-2-deoxy-D-glucose[3]. Thus, treatment of **2** with acetic anhydride–pyridine at 0–20°, followed by column chromatography, afforded a mixture (37%) of the tetra-acetates of the *α-f* (**7α**) and *β-f* (**7β**) forms having the same chromatographic mobility, a mixture (12%) of the 3,4,6-triacetates of the *α-f* (**8α**) and *β-f* (**8β**) forms, also indistinguishable chromatographically, the penta-acetate **9** (9%) of the enol form, and the 3,4,6-triacetate **10** (5%) of the *β-p* form.

The structures of these acetates followed from their analytical data and spectroscopic properties. The ^1H- and ^{13}C-n.m.r. spectra of **7α**, **7β**, **8α**, and **8β** are summarised in Tables III and IV. In the ^{13}C-n.m.r. spectrum of the mixture **7α** + **7β**, it was not possible to detect the signals of the latter compound because of the low signal-to-noise ratio. However, a ratio of ~8.5:1.5 could be determined for these two isomers from the integrated intensities of the H-3 and H-4 signals in the ^1H-n.m.r. spectrum of the **7α** + **7β** mixture. The spectrum of a freshly prepared solution of **8α** + **8β** indicated a ~1:1 ratio, which changed to ~1:2 after several days at room temperature. The *α-f* structure for **7α** and **8α** was deduced from the

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFTS[a] FOR **1–4**

	1				**2**[b]				**3**[c]				**4**[c]			
	β-p	β-f	α-f	α-p	β-p	β-f	α-f	α-p	β-p	β-f	α-f	α-p	β-p	β-f	α-f	α-p
C-1	45.4	43.65	44.7	40.9	55.3 (55.1)	53.9 (54.25)	53.9 (53.9)		56.0		54.7		55.8	54.55		
C-2	95.6	99.1	102.1	96.3	97.4 (96.9)	100.6 (100.7)	103.8 (103.4)	(96.4)	97.1	103.55	107.9		97.1	101.1	106.2	
C-3	69.8	77.8	82.5	70.6	69.8 (69.5)	76.8 (77.2)	81.2 (81.4)	(71.25)	69.8	77.05	81.2		69.8	77.2	81.3	
C-4	69.6	74.5	76.3	71.9	69.4 (69.0)	74.4 (74.8)	76.4 (76.8)		69.6	74.4	76.05		69.65	74.5	76.0	
C-5	69.2	81.1	82.6	66.0	69.3 (68.95)	81.1 (82.3)	82.8 (83.1)		69.25	81.3	82.95		69.3	83.0	84.0	
C-6	64.1	62.2	61.0	62.9	64.0 (63.65)	62.5 (62.6)	61.3 (62.0)	(62.9)	64.15	62.5	61.15		64.15	62.5	60.95	
C-1′					162.3	162.5 (161.0)	162.1 (161.1)						162.25		162.2	
C-2′					88.4 (88.25)	88.4 (88.0)	88.0 (87.6)									

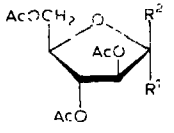
[a]At 75.43 MHz in D_2O (acetone as internal reference). [b]In brackets, in $(CD_3)_2SO$. [c]At 50.30 MHz.

TABLE II

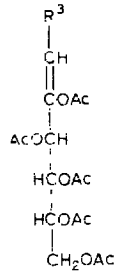
PERCENTAGE[a] OF THE ISOMERS OF **1–4** IN D_2O AND (IN PARENTHESES) IN $(CD_3)_2SO$ AT EQUILIBRIUM

Compound	*Isomer*			
	β-p	α-f	β-f	α-p
1	72	12	12	4
2	74	15	10	
	(22)	(28)	(40)	(10)
3	70	16	14	
4	70	17	13	

[a]At 30°.



7α $R^1 = OAc$, $R^2 = CH_2R^3$
8α $R^1 = OH$, $R^2 = CH_2R^3$
7β $R^1 = CH_2R^3$, $R^2 = OAc$
8β $R^1 = CH_2R^3$, $R^2 = OH$



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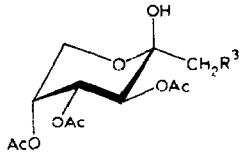

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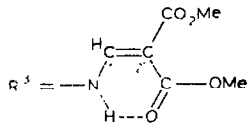


values of $J_{3,4}$ (4.0 and 2.3 Hz, respectively; lit.[13] 3.0–3.5 Hz); the corresponding anomers, **7β** and **8β** had $J_{3,4}$ values of 7.3 and 6.3 Hz, respectively (lit.[13] 6.5–7.5 Hz).

The acetate **9** was crystalline and its analytical and n.m.r. spectral data indicated the presence of five AcO groups. The ^{1}H-n.m.r. spectrum contained signals at δ 7.95 ($J_{NH,1'}$ 13.1 Hz) and 6.47 ($J_{NH,1}$ 11.3 Hz) assigned to H-1′ and H-1, respectively, and a dd at δ 10.65 due to NH. Correspondingly, the ^{13}C-n.m.r. spectrum contained signals for four olefinic carbons, two of which (at δ 154.0 and 94.8) were characteristic of C-1′ and C-2′ of the *N*-substituent. The other two, at δ 122.6 and 128.9, were assigned to C-1 and C-2, respectively, of the sugar moiety. The remaining signals of these spectra had δ values and coupling constants in accordance with structure **9**. From the $J_{NH,1'}$ and $J_{NH,1}$ values, it could be deduced that both H-1′ and H-1 are s-*trans* to the hydrogen of the amino group; the stereochemistry around the 1,2-double bond remains uncertain.

TABLE III

^{1}H-N.M.R. DATA[a] (δ, P.P.M.) FOR **7α**, **7β**, **8α**, AND **8β**

Compound	*H-1*	*H-1'*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*=CH*	*CO_2Me*	*OAc*	*NH*
7α	3.97dd	3.76dd	5.81d	5.06dd	4.49ddd	4.35dd	4.18dd	7.95d	3.79s 3.71s	2.00s 2.10s 2.10s 2.19s	9.31ddd
8α[b]			5.31d	5.00dd				7.98d			9.33ddd
7β			5.31d	5.50dd				8.05d	3.73s 3.82s		
8β[c]	3.55dd	3.48dd	5.15d	5.37dd	4.13ddd	4.48dd	4.29dd	8.05d	3.81s 3.73s	2.09s 2.11s 2.17s	9.44ddd

Coupling constants (Hz) *Compound*	$J_{NH,1}$	$J_{NH,1'}$	$J_{1,1'}$	$J_{NH=CH}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
7α	6.2	6.8	−14.2	13.8	4.0	6.6	3.3	5.4	−12.4
8α	6.8	6.9		14.1	2.3	5.0			
7β				13.8	7.3				
8β	6.6	6.7	−14.0	14.1	6.3	5.0	7.2	3.9	−11.9

[a]At 300 MHz, in $CDCl_3$. [b]δ 4.38 (s, OH). [c]δ 4.40 (s, OH).

TABLE IV

^{13}C-N.M.R. DATA[a] FOR **7α**, **8α**, AND **8β**

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1'*	*C-2'*	*CO_2Me*	*OAc*
7α	51.55	108.2	79.5	76.2	80.5	62.5	161.1	90.75	166.0; 51.2 169.05; 51.3	169.3; 20.6 169.6; 21.5 169.7 170.5
8α	53.65	103.7	76.5	76.15	79.0	63.1	161.4	89.85	166.6; 51.2 169.2; 51.3	169.3; 20.65 170.4; 20.7 171.4; 20.9
8β	54.6	101.6	79.7	77.9	81.3	64.9	161.25	90.2	166.5 169.5	170.1; 20.65 170.65; 20.7 170.7; 20.9

[a]At 75.43 MHz in $CDCl_3$.

TABLE V

^{13}C-N.M.R. DATA[a] FOR **11α**, **11β**, AND **13**

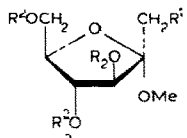
Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1'*	*C-2'*	*OMe*	*CO_2Me*
11α	51.05	106.4	80.8	76.9	82.9	61.7	160.9	87.8	48.3	165.6; 50.4 168.2; 50.4 50.45
11β	51.2	102.4	78.1	74.3	82.1	62.1	160.65	88.4	48.85	165.5; 50.4 168.25; 50.4 50.45
13	*51.1*	*99.4*	*69.7*	*69.0*	*68.7*	*64.35*	*160.45*	*88.3*	*47.85*	*165.6* 167.9

[a]At 75.43 MHz in $(CD_3)_2SO$.

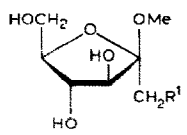
The tri-acetate **10** was also crystalline; the β configuration, suggested by its optical rotation, was confirmed by the $J_{3,4}$ value of 10.5 Hz, characteristic[13] of the β-*p* form in $^2C_5$ conformation, and by the δ values of C-3,4,5, which are close to those observed[10] for this tautomer in the *N*-(1-deoxy-D-fructos-1-yl)amino acids. The axial HO-2 resonated as a dd at δ 4.42 due to long-range coupling ($^4J_{3,OH}$ −1.1 Hz).

When **9** was further treated with acetic anhydride–pyridine, it gave a mixture of **7**α,β and **9**.

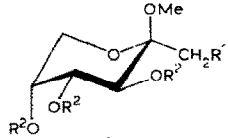
Fischer glycosidation of **2**. — Treatment of **2** with methanolic 1.25% hydrogen chloride at room temperature produced methyl 1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-α-D-fructofuranoside (**11**α), its anomer (**11**β), and methyl 1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-β-D-fructopyranoside (**13**). Compound **2** was completely transformed after ~5 h (t.l.c.), and the glycoside equilibrium ($[\alpha]_D$ constant) was reached after ~24 h. A syrupy mixture of the glycosides was then obtained in almost quantitative yield. Attempts to separate the glycosides were unsuccessful, but the identity of **11**α, **11**β, and **13**, and their ratios (~7:2:1), could be deduced from the ^{13}C-n.m.r. spectrum (Table V) of the mixture.



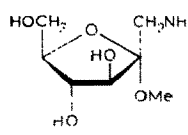
11α R^2 = H
12 R^2 = Ac



11β



13 R^2 = H
14 R^2 = Ac



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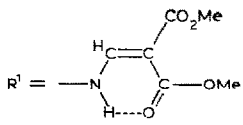

The crude glycoside, obtained (100%) after allowing 5 h for the glycoside reaction, was acetylated to afford an almost quantitative yield of **12** and **14**. Fractional crystallisation of the mixture yielded >55% of **12**, and **14** (28%) was obtained from the mother liquor.

The structure of **12** was consistent with its ^{1}H- (Table VI) and ^{13}C-n.m.r. (Table VII) data. In the ^{1}H-spectrum in $CDCl_3$, the resonances of H-5,6,6′ formed an ABC-type system which was not amenable to a first-order interpretation. However, this could be done with the spectrum for a solution in C_6D_6. From the δ and *J* values obtained for the latter solvent, the parameters of the $CDCl_3$ spectrum were obtained by simulation. The α-*f* structure **12** and the β-*p* **14** were indicated by the $J_{3,4}$ and the ^{13}C-chemical shifts (Tables VI and VII).

Zemplén deacetylation of **12** afforded a quantitative yield of **11**α, the ^{1}H-n.m.r. spectrum (Table VI) and optical rotation of which confirmed the assigned structure; its ^{13}C-n.m.r. spectrum was the same as that observed in its admixture with **11**α and **13**. Compound **11**α consumed 1 mol of periodate and did not produce formaldehyde.

TABLE VI

^{1}H-N.M.R. DATA[a] (δ, P.P.M.) FOR **11α**, **12**, AND **13**

Compound	*H-1*	*H-1'*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*=CH*	*OMe*	*CO_2Me*	*OAc*
11α[b]	3.32dd	3.34dd		3.93dd	3.54m	3.66dd	3.47dd	8.00d	3.21s	3.58s 3.62s	
12[c]	3.66dd	4.54dd	5.22d	4.99dd	4.11m	4.36m	4.14m	7.44d	3.36s	3.71s 3.78s	2.09s 2.10s 2.18s
12[d]			5.44d	5.17dd	3.96ddd	4.38dd	4.16dd	7.97d	2.86s	3.52s 3.59s	1.55s 1.70s 1.86s
14[c]	3.55dd	3.33dd	5.31d	5.34dd	5.27m	3.84m	3.80m	7.96d	3.36s	3.73s 3.82s	1.99s 2.05s 2.13s

Coupling constants (Hz)

Compound	$J_{NH,1}$	$J_{NH,1'}$	$J_{1,1'}$	$J_{NH,=CH}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
11α	5.8	6.1	−11.8	14.5	2.4	5.6	2.7	6.6	−14.3
12	5.4	7.3	−14.5	13.9	3.0	6.1	3.3	5.3	−12.1
14	7.4	5.1	−14.0	14.1	10.0	2.7	1.8	1.3	−12.8

[a]At 300 MHz. [b]In $(CD_3)_2SO$. [c]In $CDCl_3$. [d]In C_6D_6.

TABLE VII

^{13}C-N.M.R. DATA[a] FOR **12** AND **14**

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1'*	*C-2'*	*OMe*	*CO_2Me*	*OAc*
12	48.4	106.45	80.0	77.5	80.9	62.85	160.6	90.4	48.9	166.25; 51.1 169.2; 51.2	169.2; 20.6 169.9 170.4
14	50.8	99.0	68.85	68.35	68.15	61.8	160.9	90.5	49.0	166.6; 51.1 169.2; 51.2	169.9; 20.7 170.25 171.1

[a]At 75.43 MHz in $CDCl_3$.

Treatment of **11α** with Amberlite IRA-400 (HO^-) resin in aqueous acetone[1] afforded a quantitative yield of methyl 1-amino-1-deoxy-α-D-fructofuranoside (**15**) (54% from **2**) as a syrup which was characterised as its crystalline oxalate, the $[\alpha]_D$ and ^{13}C-n.m.r. spectrum of which confirmed the assigned structure.

The above results further illustrate the utility of the diacylvinyl groups in amino sugar chemistry and provide an easy route to the glycosides of 1-amino-1-deoxy-D-fructose.

EXPERIMENTAL

General methods. — Unless stated otherwise, these were as described previously[1]. N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si), unless otherwise specified, using a Varian XL-200, Varian XL-300, or Bruker AM-500 spectrometer. All reactions were monitored by t.l.c.

1-Deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-D-fructose (**2**). — To a stirred solution of **1** (2.39 g, 10 mmol) and sodium carbonate (0.35 g, 5.0 mmol) in water (7.5 mL) was added methyl 3-methoxy-2-methoxycarbonylacrylate[14] (2.09 g, 12 mmol), and stirring was continued for 4 h. The solution was then concentrated to a syrup from which methanol was evaporated. Column chromatography of the resulting, amorphous solid afforded **2** (97%) as an amorphous solid, $[\alpha]^{30}_{5461}$ −17°, $[\alpha]^{30}_{D}$ −15° (*c* 1, methanol); λ^{EtOH}_{max} 222 and 278 nm (log ε 3.96 and 4.37); $\nu^{Me_2SO}_{max}$ 3290 (OH, NH), 1705sh,s and 1690s (free CO_2Me), 1650s,br (intramolecularly bonded CO_2Me), and 1600vs cm^{-1} (C=C-NH). ^1H-N.m.r. data [200 MHz, $(CD_3)_2SO$]: δ 9.18 (m, 1 H, exchangeable with D_2O), 7.95 (m, 1 H, H-1′ of several isomeric forms). The ^{13}C-n.m.r. data are listed in Tables I and II.

Anal. Calc. for $C_{12}H_{19}NO_9$: C, 44.86; H, 5.96; N, 4.35. Found: C, 44.76; H, 5.90; N, 4.11.

1-Deoxy-1-[(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidenemethyl)amino]-D-fructose (**3**). — A solution of **1** (2.39 g, 10.0 mmol), 2,2-dimethyl-5-methoxymethylene-1,3-dioxane-4,6-dione[7] (1.86 g, 10 mmol), and triethylamine (3.5 mL) in methanol (55 mL) was heated under reflux for 0.5 h and then concentrated. Treatment of the residual syrup with ether–hexane gave a solid which was recrystallised from ethanol to give **3** (3.4 g, 92%), m.p. 173–175°, $[\alpha]^{30}_{5461}$ −22° and $[\alpha]^{30}_{D}$ −18° (*c* 1, pyridine); $\lambda^{H_2O}_{max}$ 228 and 280 nm (log ε 4.02 and 4.37); ν^{KBr}_{max} 3200s (HO, NH), 1715m (free C=O), 1665vs (intramolecularly bonded C=O), and 1610s cm^{-1} (C=C-NH). The ^{13}C-n.m.r. data are listed in Tables I and II.

Anal. Calc. for $C_{13}H_{19}NO_9$: C, 46.84; H, 5.74; N, 4.20. Found: C, 46.68; H, 5.98; N, 4.52.

1-Deoxy-1-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-D-fructose (**4**). — A solution of **1** (0.36 g, 1.5 mmol), triethylamine (0.6 mL), and 5,5-dimethyl-2-phenylaminomethylene-1,3-cyclohexanedione[5] (0.44 g, 1.8 mmol) in methanol (5.5 mL) was stirred for 6 h and then concentrated. Treatment of the residual syrup with ether gave a solid which was recrystallised from ethanol to

afford **4** (0.42 g, 85%), m.p. 176–178°, $[\alpha]_{5461}^{30}$ −43°, $[\alpha]_{D}^{30}$ −36° (*c* 1, methanol); $\lambda_{max}^{H_2O}$ 253 and 301 nm (log ε 4.21 and 4.39); λ_{max}^{KBr} 3190 (OH, NH), 1662s (free C=O), 1590s (intramolecularly bonded C=O), and 1570vs cm^{-1} (C=C-NH). The ^{13}C-n.m.r. data are listed in Tables I and II.

Anal. Calc. for $C_{15}H_{23}NO_7$: C, 54.70; H, 7.04; N, 4.25. Found: C, 54.69; H, 6.86; N, 4.10.

Acetylation of **2**. — To an ice-cold solution of **2** (5.0 g) in pyridine (20 mL) was gradually added acetic anhydride (30 mL). After 4 days at 0°, the mixture was diluted with chloroform, washed with water, 0.5M sulphuric acid, and saturated aqueous sodium hydrogencarbonate, dried (Na_2SO_4), and concentrated. T.l.c. (ether–hexane, 9:1) of the syrupy residue revealed **7*α*** + **7*β*** (R_F 0.50, major product), **9** (R_F 0.65), and **10** (R_F 0.25, minor product). Column chromatography (ether–hexane, 2:1) afforded, first, 2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-D-*arabino*-hex-1-enitol (**9**; 0.63 g, 8.5%), m.p. 106–107° (from ethanol), $[\alpha]_{5461}^{30}$ −147° (*c* 1, chloroform); $\lambda_{max}^{CHCl_3}$ 310 and 370sh nm (log ε 4.44 and 3.77); ν_{max}^{KBr} 3125w (NH), 1750vs,sh and 1740vs (AcO), 1720s and 1694m (CO_2Me), 1653s (intramolecularly bonded CO_2Me), and 1610s cm^{-1} (C=C-NH). N.m.r. data: ^1H (500 MHz), δ 10.65 (dd, 1 H, $J_{NH,1}$ 11.4, $J_{NH,1'}$ 13.1 Hz, NH), 7.95 (d, 1 H, H-1'), 6.47 (d, 1 H, H-1), 5.57 (d, 1 H, $J_{3,4}$ 5.9 Hz, H-3), 5.52 (dd, 1 H, $J_{4,5}$ 6.2 Hz, H-4), 5.19 (ddd, 1 H, $J_{5,6a}$ 2.9, $J_{5,6b}$ 6.2 Hz, H-5), 4.30 (dd, 1 H, $J_{6a,6b}$ −12.4 Hz, H-6a), 4.16 (dd, 1 H, H-6b), 3.80 (s, 3 H, CO_2Me), 3.70 (s, 3 H, CO_2Me), 2.35 (s, 3 H, AcO), 2.10 (s, 3 H, AcO), 2.06 (s, 6 H, 2 AcO), and 2.05 (s, 3 H, AcO); ^{13}C (75.43 MHz), δ 122.6 (C-1), 128.9 (C-2), 69.7 (C-3), 69.5 (C-4), 69.3 (C-5), 61.7 (C-6), 154.0 (C-1'), 94.8 (C-2'), 165.25, 167.9, 51.5, and 51.6 (2 CO_2Me), 168.8, 169.4, 169.6, 169.8, 170.45, 20.4, and 10.6 (5 AcO).

Anal. Calc. for $C_{22}H_{29}NO_{14}$: C, 49.71; H, 5.50; N, 2.63. Found: C, 49.83; H, 5.48; N, 2.38.

Eluted second was a mixture (2.76 g, 36.4%) of **7*α*** and **7*β*** in the ratio ~8.5:1.5 (^1H-n.m.r. data). The analytical sample, obtained after a second chromatography (ether–hexane, 4:1), was an amorphous solid, $[\alpha]_{5461}^{25}$ −7° (*c* 1.8, chloroform); $\lambda_{max}^{CHCl_3}$ 278 nm (log ε 4.24); $\nu_{max}^{CCl_4}$ 3270w (NH), 1740vs (AcO), 1700s (free CO_2Me), 1660s (intramolecularly bonded CO_2Me), and 1615s cm^{-1} (C=C-NH). The ^1H- and ^{13}C-n.m.r. data are listed in Tables III and IV, respectively.

Anal. Calc. for $C_{20}H_{27}NO_{13}$: C, 49.08; H, 5.56; N, 2.86. Found: C, 49.32; H, 5.51; N, 3.22.

Eluted third was 3,4,5-tri-*O*-acetyl-1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)-amino]-*β*-D-fructopyranose (**10**; 0.63 g, 5%), m.p. 161–162° (from ethanol), $[\alpha]_{5461}^{23}$ −53° (*c* 1, chloroform); $\lambda_{max}^{CHCl_3}$ 279 nm (log ε 4.38); ν_{max}^{KBr} 3390 (OH, NH), 1740vs and 1245vs (AcO), 1694vs (CO_2Me), 1664vs (intramolecularly bonded CO_2Me), and 1620s cm^{-1} (C=C-NH). N.m.r. data: ^1H (300 MHz), δ 9.40 (ddd, 1 H, $J_{NH,1a}$ 5.2, $J_{NH,1b}$ 7.8, $J_{NH,1'}$ 14.0 Hz), 7.96 (d, 1 H, H-1'), 5.41 (dd, 1 H, $J_{3,4}$ 10.5, $J_{4,5}$ 3.3 Hz, H-4), 5.31 (ddd, 1 H, $J_{5,6a}$ 2.0, $J_{5,6b}$ 1.0 Hz, H-5), 5.25 (dd, 1 H, $J_{3,OH}$ −1.1 Hz, H-3; collapsed to a d, $J_{3,4}$, on irradiation of the OH signal), 4.42 (d, 1 H, OH), 4.15

(dd, 1 H, $J_{6a,6b}$ −13.0 Hz, H-6a), 3.79 (dd, 1 H, H-6b), 3.78 (s, 3 H, CO_2Me), 3.71 (s, 3 H, CO_2Me), 3.50 (dd, 1 H, $J_{1a,1b}$ −13.9 Hz, H-1a), 3.33 (dd, 1 H, H-1b), 2.15 (s, 3 H, AcO), 2.10 (s, 3 H, AcO), and 2.00 (s, 3 H, AcO); ^{13}C (75.43 MHz), δ 55.3 (C-1), 96.4 (C-2), 69.0 (C-3), 68.35 (C-4), 68.25 (C-5), 61.4 (C-6), 161.5 (C-1'), 90.2 (C-2'), 169.1, 166.9, 51.4, and 51.3 (2 CO_2Me), 170.9, 170.4, 170.1, 20.85, 20.8, and 20.7 (3 AcO).

Anal. Calc. for $C_{18}H_{25}NO_{12}$: C, 48.32; H, 5.63; N, 3.13. Found: C, 48.78; H, 5.64; N, 3.16.

When the acetylation was performed at ~20°, the products (t.l.c.) were **7α** + **7β**, **9**, **10**, and **8α** + **8β** (R_F 0.35, ether–hexane, 9:1). Work-up and column chromatography as above yielded a mixture (0.91 g, 12%) of **8α** and **8β** in the ratio ~1:1 (^1H-n.m.r. data), which was further chromatographed to yield the analytical sample as an amorphous solid, $[\alpha]_{5461}^{23}$ −2°, $[\alpha]_D^{23}$ −3° (*c* 1.4, dichloromethane); $\lambda_{max}^{CHCl_3}$ 278 nm (log ε 4.31); ν_{max}^{film} 3350m (NH, OH), 1755vs (AcO), 1695s,sh (free CO_2Me), 1668vs (intramolecularly bonded CO_2Me), 1614s cm^{-1} (C=C-NH). The ^1H- and ^{13}C-n.m.r. data are listed in Tables III and IV, respectively.

Anal. Calc. for $C_{18}H_{25}NO_{12}$: C, 48.32; H, 5.63; N, 3.13. Found: C, 48.00; H, 5.97; N, 3.13.

Glycosidation of **2**. — A solution of **2** (2.50 g, 78 mmol) in methanol (160 mL) containing 1.25% of HCl was stirred at room temperature for 4 h. T.l.c. (chloroform–methanol, 8:1) then revealed **11α** + **11β** (R_F 0.55, major product), **13** (R_F 0.50, trace), and **2** (R_F 0.25, trace). After 24 h, the $[\alpha]_D$ value was constant, and the mixture was stirred with lead carbonate, filtered, and concentrated. Column chromatography (chloroform–methanol, 4:1) of the residue (2.73 g, 93%) yielded a mixture (0.80 g) of **11α**, **11β**, and **13** in the ratios ~7:2:1 (^{13}C-n.m.r. data).

Anal. Calc. for $C_{13}H_{21}NO_9$: C, 46.56; H, 6.31; N, 4.17. Found: C, 46.46; H, 6.41; N, 4.13.

The ^{13}C-n.m.r. data are listed in Table V.

A sample of **2** (2.50 g) was glycosidated for 5 h, and the mixture was worked-up as indicated above. Conventional acetylation (Ac_2O–pyridine, ~0°, 3 days) of the crude glycoside (2.27 g) afforded a syrupy mixture (3.70 g, 99%) of **12** (R_F 0.60, ether; major product) and **14** (R_F 0.45). Fractional crystallisation of the mixture from ethanol gave methyl 3,4,6-tri-*O*-acetyl-1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-α-D-fructofuranoside (**12**; 2.02 g, 54.6%), m.p. 95–96° (from ethanol), $[\alpha]_{5461}^{25}$ +66° (*c* 1, chloroform); $\lambda_{max}^{CHCl_3}$ 278 nm (log ε 4.83); ν_{max}^{KBr} 3260w (NH), 1745vs and 1768s (AcO), 1690s (free CO_2Me), 1638vs (intramolecularly bonded CO_2Me), and 1608s cm^{-1} (C=C-NH). The ^1H- and ^{13}C-n.m.r. data are listed in Tables VI and VII, respectively.

Anal. Calc. for $C_{19}H_{27}NO_{12}$: C, 49.45; H, 5.89; N, 3.03. Found: C, 49.25; H, 5.93; N, 3.07.

The mother liquor was concentrated and the residual syrup was chromatographed to afford methyl 3,4,5-tri-*O*-acetyl-1-deoxy-1-[(2,2-dimethoxycarbonyl-

vinyl)amino]-β-D-fructopyranoside (**14**; 1.0 g, 28%), m.p. 50–52°, $[\alpha]_{5461}^{25}$ −78° (*c* 1, dichloromethane); $\lambda_{max}^{CHCl_3}$ 278 nm (log ε 4.42); $\nu_{max}^{CHCl_3}$ 3260w (NH), 1735vs and 1745vs,sh (AcO), 1700s and 1680s (free CO_2Me), 1659vs (intramolecularly bonded CO_2Me), and 1600vs cm^{-1} (C=C-NH). The ^1H- and ^{13}C-n.m.r. data are listed in Tables VI and VII, respectively.

Anal. Calc. for $C_{19}H_{27}NO_{12}$: C, 49.45; H, 5.89; N, 3.03. Found: C, 49.10; H, 6.11; N, 3.50.

A solution of **12** (0.5 g) in methanol (10 mL) was treated with methanolic 0.2M sodium methoxide (0.3 mL) for 3 h. The mixture was deionised with Amberlite IR-120 (H^+) resin and concentrated to yield methyl 1-deoxy-1-[(2,2-dimethoxycarbonylvinyl)amino]-α-D-fructofuranoside (**11α**; 0.36 g, 100%) which, after column chromatography, was obtained as an amorphous solid, $[\alpha]_{5461}^{25}$ +62° (*c* 1, methanol); λ_{max}^{EtOH} 223 and 278 nm (log ε 4.94 and 4.36); ν_{max}^{KBr} 3380s (OH, NH), 1700s (free CO_2Me), 1670s (intramolecularly bonded CO_2Me), and 1630vs cm^{-1} (C=C-NH). The ^1H- and ^{13}C-n.m.r. data are listed in Tables VI and V, respectively.

Anal. Calc. for $C_{13}H_{21}NO_9$: C, 46.56; H, 6.31; N, 4.17. Found: C, 46.20; H, 6.14; N, 3.87.

Compound **11α** consumed[15] 1.0 mol of sodium metaperiodate and no formaldehyde was liberated.

Methyl 1-amino-1-deoxy-α-D-fructofuranoside (**15**). — A solution of **11α** (0.50 g) in acetone–water (2:1; 20 mL) was stirred for 2 h with Amberlite IRA-400 (HO^-) resin. The resin was collected and washed well with acetone–water, and the combined filtrate and washings were concentrated to remove the acetone and then freeze-dried to yield **15** (0.28 g, 97.2%) as a syrup, $[\alpha]_{5461}^{25}$ +49°, $[\alpha]_D^{25}$ +37° (*c* 1, water); R_{FruN^*} 1.42 and R_F 0.62 (p.c.; 1-butanol–pyridine–water, 1:1:1).

To a solution of **15** (0.19 g, 0.97 mmol) in methanol–1,4-dioxane (3:7; 10 mL) was added oxalic acid (0.087 g, 0.97 mmol). The solution was heated for 30 min and then cooled (~5°) overnight. Addition of ether to turbidity gave methyl 1-amino-1-deoxy-α-D-fructofuranoside oxalate (0.26 g, 94.2%), m.p. 144–146° (from ethanol), $[\alpha]_{5461}^{25}$ +69°, $[\alpha]_D^{25}$ +59° (*c* 1, water). ^{13}C-N.m.r. data (75.43 MHz): δ 40.0 (C-1), 104.95 (C-2), 79.25 (C-3), 75.8 (C-4), 83.0 (C-5), 60.2 (C-6), 48.15 (OMe), and 165.0 (2 CO_2H).

Anal. Calc. for $C_9H_{17}NO_9$: C, 38.16; H, 6.05; N, 4.96. Found: C, 38.16; H, 6.48; N, 4.87.

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