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THE SYNTHESIS OF 3-ACETAMIDO-2,3,5,6-TETRADEOXY-5-FLUORO-D,L-*ribo*-HEXOFURANOSE BY THE DIRECT FLUORINATION OF METHYL 3-ACETAMIDO-2,3,6-TRIDEOXY-D,L-*arabino*-HEXOPYRANOSIDE (METHYL *N*-ACETYL-D,L-ACOSAMINIDE)*

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ABSTRACT

3-Acetamido-2,3,5,6-tetradeoxy-5-fluoro-D,L-*ribo*-hexofuranose was synthesized by direct, fluorinative dehydroxylation of methyl 3-acetamido-2,3,6-trideoxy-D,L-*arabino*-hexopyranoside with sulfur tetrafluoride–hydrogen fluoride. The furanose form and the *ribo* configuration, indicated by ^{13}C- and ^{1}H-n.m.r. spectroscopy, respectively, were confirmed by a single-crystal, X-ray diffraction study.

INTRODUCTION

The preparation of fluorinated carbohydrates has received considerable attention as a result of the growing recognition of the utility of fluoro sugars as biochemical or metabolic probes, as well as in defining structure–activity relationships. However, as has been reported elsewhere, the synthesis of such compounds can be both tedious and difficult[1]. Recent advances in fluorination with such reagents as diethylamino sulfur trifluoride[2] or acetyl hypofluorite[3] have made the preparation of new fluorinated sugars increasingly easy. In spite of these developments, there has been only little attention paid to the preparation of aminofluoro sugars by traditional synthetic approaches[4] or more recent methods.

The broad-spectrum and outstanding antitumor activity of the anthracycline antibiotics has been limited by the accompanying cumulative-dose-related cardiotoxicity[5]. Extensive research aimed at the synthesis of analogs that by subtle structural alteration modifies the therapeutic activity has led to the synthesis of numerous pyranose[6] and furanose[7,8] analogs of daunosamine, an amino sugar component of these drugs. Fluorination would be predicted to have a minimal steric effect on the sugar molecule and a maximal electronic effect, and the reaction of 4-

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epidaunosamine (acosamine) with sulfur tetrafluoride in hydrogen fluoride is described herein. Although sulfur tetrafluoride–hydrogen fluoride has been used to effect fluorinative dehydroxylation of hydroxy-amino acids, where dialkylamino sulfur trifluoride reagents failed[9], this reagent has not been previously employed in the fluorinative dehydroxylation of amino sugars. In our hands, attempted fluorinative dehydroxylation with diethylamino sulfur trifluoride did not lead to fluorinated products.

RESULTS AND DISCUSSION

The known methyl 4,5-*O*-isopropylidene-*erythro*-hex-2-enoate[10] (**1**) was treated with anhydrous ammonia in methanol to give 3-amino-4,5-*O*-isopropylidene-D,L-*ribo*- and -*arabino*-hexanamide (**2**). The crude amide was heated with hydrochloric acid, and the resulting amino-1,5- and -1,4-lactones* **3** and **5** were acetylated to afford the corresponding acetamidolactones **4** and **6**. Although both lactones were characterized by ^{13}C-n.m.r. spectroscopy (Table I) and were purified by column chromatography, only the 1,4-lactone **6** crystallized. The purified lactones were treated with a 1.5-fold excess of diisobutylaluminum hydride, and chromatography of the crude reduction-product yielded an ~1:1 anomeric mixture of **7** and **9** as determined by ^{13}C-n.m.r. spectroscopy. The anomers failed to separate under the conditions of t.l.c. employed. In the ^{1}H-n.m.r. spectrum at 90 MHz

TABLE I

^{13}C-N M.R. DATA FOR COMPOUNDS **4**, **6–12**, AND **14**[a]

Compounds	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*CH_3CO*	*CH_3CO*	*OCH_3*
4	172.4	36.9	47.8	67.0	76.5	16.6	22.1	174.2	
6	179.9	36.3	47.0	90.3	67.8	17.7	23.1	174.8	
		(138.6)[b]	(143.4)[b]	(149.5)[b]	(145.8)[b]	(125.7)[b]	(128.7)[b]		
7	91.7	36.9	48.8	75.6	69.6	18.3	22.4	175.2	
8	98.3	35.7	48.8	75.0	69.4	17.7	22.9	174.7	55.2
9	94.6	38.8	51.8	74.3	75.0	18.3	22.4	175.2	
10	101.7	37.1	51.4	75.0	74.8	17.7	22.9	174.7	57.4
11[c]	105.6	39.3	50.7	88.3	90.3	16.8	23.3	170.3	55.0
				$J_{C\text{-}4,F}$ 20.7[d]	$J_{C\text{-}5,F}$ 180.7[d]	$J_{C\text{-}6,F}$ 22.0[d]			
12[c]	99.8	40.2	49.6	85.3	91.7	16.3	22.9	174.5	
	(178.0)[b]	(130.6)[b]	(146.5)[b]	$J_{C\text{-}4,F}$ 20.8[d]	$J_{C\text{-}5,F}$ 167.2[d]	$J_{C\text{-}6,F}$ 22.0[d]	(128.7)[b]		
				(156.3)[b]	(165.7)[b]	(128.2)[b]			
14[c]	103.6	39.3	48.4	86.1	90.3	16.8	23.3	169.2	55.0
				$J_{C\text{-}4,F}$ 43.9[d]	$J_{C\text{-}5,F}$ 180.7[d]	$J_{C\text{-}6,F}$ 22.0[d]			

[a]For solutions in D_2O unless otherwise noted; 90-MHz Fourier-transform spectra; chemical shifts (δ) reported from signal of Me_4Si. [b]$J_{C,H}$ between H and C, in Hz. [c]For solutions in $CDCl_3$. [d]In Hz.

*For simplification, only the D form of the structures is given in the Scheme.

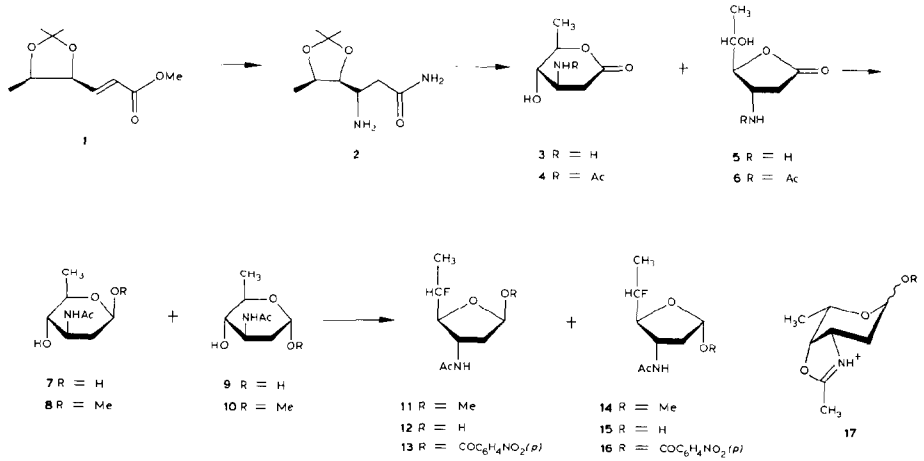
TABLE II

^{1}H-N.M.R. DATA FOR COMPOUNDS **7–11, 13, 14,** AND **16**[a]

Compounds[b]	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*Ac*	*NH*	*Other*
7 and **9**[c]	5.14 $J_{1,2a}$ 3.4 $J_{1,2e}$ 1.2 4.79 $J_{1,2a}$ 9.2 $J_{1,2e}$ 2.0	1.65(2*a*) 2.08 (2*e*)	4.14 $J_{2a,3}$ 12.3 $J_{2e,3}$ 4.6	2.98 $J_{3,4}$ 9.5	3.97 $J_{4,5}$ 9.2	1.18 $J_{5,6}$ 6.1	1.9		
8 and **10**	4.62 $J_{1,2a}$ 2.44	1.63(2*a*) 2.04(2*e*)	4.19 $J_{2a,3}$ 12.45	2.97 $J_{3,4}$ 8.0	3.58 $J_{4,5}$ 7.0	1.2 $J_{5,6}$ 5.4	1.92	6.76 $J_{NH,3}$ 7.08	OMe 3.24
11 and **14**	5.14	1.65–2.33	4.55	3.86 $J_{3,4}$ 2.0 $J_{4,F}$ 24.7	4.71 $J_{4,5}$ 3.0 $J_{5,F}$ 56.0	1.34 $J_{5,6}$ 6.4 $J_{6,F}$ 24.17	1.97	5.9	OMe 3.39
	5.09								OMe 3.34
13 and **16**[d]	6.65 $J_{1,2a}$ 4.9	2.66(2*a*) 2.16(2*e*) $J_{2a,2e}$ 14.1	4.70 $J_{2a,3}$ 8.0	4.13 $J_{3,4}$ 2.0 $J_{4,F}$ 24.6	4.75 $J_{4,5}$ 2.7 $J_{5,F}$ 48.7	1.43 $J_{5,6}$ 6.6 $J_{6,F}$ 23.9	2.0	5.95 $J_{NH,3}$ 6.7	Aryl 8.22

[a]For solutions in $CDCl_3$ unless otherwise noted; chemical shifts (δ) reported from signal of Me_4Si, and coupling constants in Hz. [b]Mixtures of anomers. [c]For a solution in $(CD_3)_2CO$–D_2O. [d]Measured at 400 MHz.

(Table II) of an ~1:2 mixture of the α and β anomer, the resonances assignable to protons other than H-1 were not clearly defined for the α anomer. The chemical shifts and coupling constants observed for the β anomer were in good agreement with the reported[11] values. However, the large, geminal coupling-constant, $J_{2e,a}$ −13.5 Hz, reported in the literature[11], was not observed. The lack of interaction was verified by simulation[12] of the spectra with LAOCN3. The mixture of anomers **7** and **9** was converted into a mixture of the methyl glycosides **8** and **10** by the method of Bollenback[13] in 73% yield. Treatment of the mixture **8** and **10**, dissolved in anhydrous hydrogen fluoride, at −78° with sulfur tetrafluoride yielded a crude product which, on inspection of the ^{1}H-n.m.r. spectrum, had lost the methyl glycoside group by hydrolysis. Glycosidification with methanol gave methyl 3-acetamido-2,3,5,6-tetradeoxy-5-fluoro-β- (**11**) and -α-D,L-*ribo*-hexofuranosides (**14**). Chromatography of the crude product yielded an oil which did not crystallize. E.i.–mass spectroscopy failed to show the molecular ion, but formed a fragment-ion of *m/z* 185 ($M^+ - 20$), *via* the loss of hydrogen fluoride. The fragmentation followed the typical pathways described for a furanose according to the nomenclature of Kochetkov and Chizhov[14]. Processes leading to ions of the A and C series are initiated by cleavage of the glycosidic bond (A_1, *m/z* 173; and C_1, *m/z* 174). Formation of the ions of the E series occurs by loss of the C-5–C-6 fragment (E_1, *m/z* 158), a process that occurs with increased facility in the furanose series resulting in the greater intensity of E type fragments. Rupture of the furanose ring between C-



1 and O-4, followed by cleavage of the C-3–C-4 bond leads to ions of the F series (F_1, *m/z* 129). Ions of the G family may arise from initial cleavage of C-3–C-4 followed by cleavage of the C-1–C-2 bond (G_1, *m/z* 86). Precedent for this fragmentation may be found in the mass spectral analyses of daunosamine[15] and acosamine[11]. ^{1}H- and ^{13}C-N.m.r. spectroscopy supported the structure of the fluorinated product as a furanose. The fluorinative dehydroxylation, at C-5 of a furanose sugar,

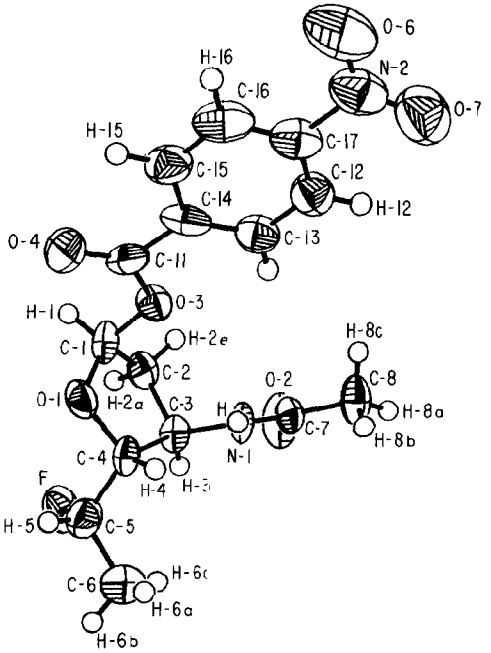


Fig. 1. Perspective view of **16** showing atom numbering and 50%-thermal ellipsoids for the anisotropic atoms.

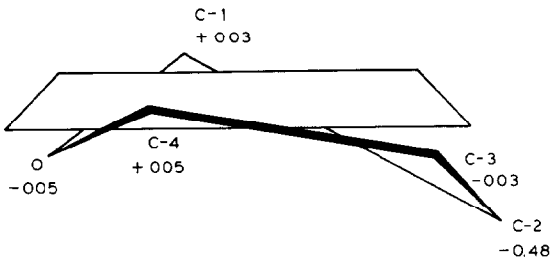


Fig. 2. V_2 Conformation of furanose ring with deviation from the least-squares plane given in angstroms.

under the acidic reaction conditions is in agreement with the frequent failure of SN2-type displacement reactions at C-4 of mannose derivatives[16]. As the inhibition of these displacements is generally attributed to the steric hindrance of an axial OH-2, it was not predictable that the 2-deoxy series would show similar reluctance toward displacement. As the methyl glycosides **11** and **14** failed to crystallize, they were hydrolyzed to give the free sugars **12** and **15**, respectively, and 4-nitrobenzoylated to give the highly crystalline **13** and **16**, respectively. The choice of derivative

TABLE III

ATOM COORDINATES × 10^4 AND TEMPERATURE FACTORS (Å × 10^3)

Atom	*x*	*y*	*z*	U_{eq}[a]
F	9310(2)	2394(4)	729(4)	83(2)
C-1	7600(4)	3489(8)	1669(7)	51(3)
C-2	7876(4)	4299(8)	408(7)	47(3)
C-3	8509(4)	5097(8)	996(7)	40(3)
C-4	8708(4)	4049(8)	2238(7)	45(3)
C-5	9341(4)	3089(8)	2069(7)	62(3)
C-6	9981(4)	3995(9)	2175(9)	92(4)
N-1	8378(3)	6691(6)	1468(5)	39(2)
C-7	8313(4)	7832(8)	568(9)	47(3)
C-8	8141(4)	9372(7)	1200(7)	64(3)
O-1	8148(2)	3012(5)	2472(4)	53(2)
O-2	8389(3)	7658(6)	−684(5)	74(2)
O-3	7209(3)	4636(5)	2422(5)	50(2)
O-4	6742(3)	2739(7)	3718(6)	79(3)
O-5	5584(3)	10288(7)	6121(6)	108(3)
O-6	4945(3)	8508(8)	7038(6)	134(3)
C-11	6808(4)	4103(11)	3431(9)	53(4)
C-12	6218(3)	8114(9)	4538(7)	65(3)
C-13	6564(3)	6960(8)	3836(7)	59(3)
N-2	5401(3)	8945(8)	6295(6)	86(3)
C-14	6454(3)	5392(9)	4166(7)	60(3)
C-15	6001(3)	5028(7)	5181(7)	68(3)
C-16	5651(4)	6198(11)	5881(9)	78(4)
C-17	5778(4)	7715(11)	5534(9)	67(4)

[a]Equivalent isotropic U defined as one-third of the trace of the orthogonalized U tensor.

TABLE IV

TORSION ANGLES

Torsion angles[a]	*Degrees*
H-1–C-1–H-2*a*–C-2	36.8
H-1–C-1–H-2*e*–C-2	85.6
H-3–C-3–H-2*a*–C-2	31.3
H-3–C-3–H-2*e*–C-2	91.2
H-3–C-3–H-4–C-4	103.8
H-2*a*–C-2–H-2*e*–C-2	122.4

[a]Angle as viewed down the carbon–carbon bond.

was predicated on the utility of **13** and **16** in the glycosidation reaction with an anthracyclinone[17].

Crystals suitable for single-crystal, X-ray diffraction were grown from a solution of diethyl ether–acetone. A perspective view of the structure is shown in Fig. 1. From the structure (see Tables III–VI)*, it is clear that the furanose ring adopts the V_2 conformation[18] with C-2 lying below (0.5 Å) (Fig. 2) the least-squares plane determined by the remaining atoms of the furanose ring. This results in the substituents at C-1 being pseudo-axial and at C-3 and -4 being nearly equally above and below the plane, respectively. The torsional angle between H-2*e* and H-2*a* was determined to be 122.4° corresponding to a geminal coupling-constant ($J_{2e,a}$) of 14.1 Hz, as determined from the ^{1}H-n.m.r. spectroscopy at 400 MHz, in agreement with literature values for 2-deoxyfuranoses[8]. The sign of the observed coupling constant was not determined. It is also apparent from the crystal structure that an inversion of configuration had occurred at C-4 in order for the sugar molecule to have a *ribo* configuration. An alternative explanation would require a *ribo* configuration for the starting sugar, *i.e.*, *N*-acetylristosamine. This is ruled out by the ^{1}H-n.m.r. spectrum of **7** and **9**. The large values $J_{3,4}$ 9.5 and $J_{4,5}$ 9.2 Hz are not in agreement with those reported for the *ribo* conformation[19], $J_{3,4}$ 4.5 and $J_{4,5}$ 9.5 Hz. The inversion at C-4 may be explained by the known[20] neighboring-group participation of the acetamido group in the displacement of OH-4 to form the protonated oxazoline **17**. Protolytically assisted cleavage of the oxazoline[21] would, on further reaction and hydrolysis, form furanoses **12** and **15**.

EXPERIMENTAL

General methods. — Melting points were determined in open capillaries and

*Fig. 3, showing the packing diagram of the unit cell, and Tables VII–IX, of anisotropic thermal parameters, hydrogen coordinates, and observed and calculated structure factors, are deposited with, and may be obtained from the Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/289/*Carbohydr. Res.*, 132 (1984) 221–231.

TABLE V

BOND DISTANCES (Å)[a]

F–C-5	1.420(8)	C-1–C-2	1.506(9)
C-1–O-1	1.380(8)	C-1–O-3	1.452(8)
C-2–C-3	1.525(10)	C-3–C-4	1.541(10)
C-3–N-1	1.468(9)	C-4–C-5	1.506(11)
C-4–O-1	1.439(9)	C-5–C-6	1.486(10)
N-1–H	0.960	N-1–C-7	1.313(10)
C-7–C-8	1.499(10)	C-7–O-2	1.223(10)
O-3–C-11	1.340(10)	O-4–C-11	1.213(11)
O-5–N-2	1.222(9)	O-6–N-2	1.217(9)
C-11–C-14	1.493(12)	C-12–C-13	1.385(10)
C-12–C-17	1.346(11)	C-13–C-14	1.403(10)
N-2–C-17	1.490(11)	C-14–C-15	1.368(10)
C-15–C-16	1.397(12)	C-16–C-17	1.371(14)

[a]Estimated standard deviations in parentheses.

TABLE VI

BOND ANGLES (DEGREES)[a]

C-2–C-1–O-1	107.3(6)	C-2–C-1–O-3	106.6(5)
O-1–C-1–O-3	110.0(5)	C-1–C-2–C-3	102.3(5)
C-2–C-3–C-4	102.8(6)	C-2–C-3–N-1	112.8(6)
C-4–C-3–N-1	110.6(5)	C-3–C-4–C-5	116.1(6)
C-3–N-1–C-7	107.2(6)	C-5–C-4–O-1	108.3(5)
F–C-5–C-4	107.7(6)	F–C-5–C-6	107.9(6)
N-1–C-7–C-8	114.5(7)	N-1–C-7–O-2	122.9(7)
C-8–C-7–O-2	122.6(7)	C-1–O-1–C-4	108.9(5)
C-1–O-3–C-11	116.8(6)	O-3–C-11–O-4	124.2(8)
O-3–C-11–C-14	111.9(7)	O-4–C-11–C-14	123.9(7)
C-13–C-12–C-17	119.4(7)	C-12–C-13–C-14	120.0(6)
O-5–N-2–O-6	126.4(7)	O-5–N-2–C-17	117.1(6)
O-6–N-2–C-17	116.5(7)	C-11–C-14–C-13	122.2(6)
C-11–C-14–C-15	118.8(7)	C-13–C-14–C-15	119.0(7)
C-14–C-15–C-16	120.7(8)	C-15–C-16–C-17	118.4(8)
C-12–C-17–N-2	119.9(8)	C-12–C-17–C-16	122.5(8)
N-2–C-17–C-16	117.6(7)		

[a]Estimated standard deviations in parentheses.

are reported uncorrected. I.r. spectra were recorded with a Perkin–Elmer Model 283 infrared spectrometer. ^{1}H-N.m.r. spectra were determined with Varian EM-360A and Bruker WH 90D spectrometers, and ^{13}C-n.m.r. spectra were determined with a Bruker WH 90D spectrometer. Chemical shifts (δ) are reported relative to the signal of tetramethylsilane. M.s. were determined with an AEI 902 CI mass spectrometer at an ionization potential of 70 V under the supervision of Mr. A. E. Wolf. Analytical t.l.c. was performed with Silica gel F_{254} (E. Merck) as the adsorbent in 0.20-mm layers. The spots were detected by spraying with a solution

of 5% phosphomolybdic acid in ethanol, and then heating in an oven for 4–5 min at 140° or by staining with iodine. Preparative l.c. (0.85 MPa) was performed with Li Chroprep Si 60, 25–40-μm particle size. Chromatography on silica gel otherwise refers to Silica gel 60 (E. Merck, 40–63 μm).

3-Acetamido-2,3,6-trideoxy-arabino- *and* -ribo-D,L-*hexono-1,5-* (**4**) *and -1,4-lactone* (**6**). — A modification of the published procedure[10] was used. To anhydrous ammonia (0.6 g, 40 mmol) in methanol (20 mL), freshly distilled from calcium hydride, was added in a thick-walled glass tube 4,5-*O*-isopropylidene-*erythro*-hex-2-enoic acid methyl ester[10] (**1**) (2.0 g, 10 mmol). The tube was sealed and heated at 95° in a thermostated water-bath for three days. The contents of two such tubes were transferred to a round-bottom flask and evaporated *in vacuo*. To the residue was added 4M HCl (60 mL) and the mixture heated under reflux for 2 h. The cooled solution was extracted twice with diethyl ether. The acid, aqueous phase was evaporated *in vacuo,* and the residue dissolved in aqueous methanol. The methanolic solution was passed through a column of strongly-basic, ion-exchange resin (Amberlite CG-400, AcO^-), which was eluted with methanol. The volume of the eluent was reduced to 50 mL and acetic anhydride (10 mL, 50 mmol) added at 0°, and the mixture stirred overnight at room temperature. An equivalent volume of toluene was added and the solution evaporated to dryness. This process was repeated twice to give a crude product showing three spots on t.l.c. (R_F 0.73, 0.46, and 0.31, in 10:1 ethyl acetate–ethanol). Chromatography on silica gel (20:1 ethyl acetate–ethanol) yielded, on evaporation of the solvent, an oil (2.4 g, 64% yield). A portion of this material crystallized, m.p. 140–144°; it was identified as the 1,4-lactone **6**; ν_{max}^{KBr} 3435, 3320, 3005, 1770, 1665, 1560, 1390, 1200, and 1015 cm^{-1}; ^1H-n.m.r.: see Table II.

Anal. Calc. for $C_8H_{13}O_4N$: C, 51.33; H, 7.03. Found: C, 51.18; H, 6.85.

3-Acetamido-2,3,6-trideoxy-arabino-β- *and* -α-D,L-*hexoses* (**7, 9**). — The published procedure[10] was modified as follows. A cold (−78°) solution of the mixture of **4** and **6** (2.2 g 12 mmol) in anhydrous oxolane (100 mL) was stirred under argon while diisobutylaluminum hydride (25% in toluene; 37 mL, 9.24 g, 65 mmol) was added dropwise over 2.5 h. After stirring for 3 h at −78°, methanol (25 mL) was added, and the solution was allowed to warm to room temperature. The solid salts formed were separated by filtration. Evaporation of the filtrate yielded a crude product (2.11 g), which was treated with water. Filtration of insoluble salts and evaporation of the aqueous filtrate resulted in the isolation of crude **7, 9** (1.27 g, 56%) which showed 5 spots on t.l.c. (R_F 0.11, 0.23, 0.40, 0.51, and 0.60, in 5:1 ethyl acetate–ethanol). Chromatography on silica gel (70 g; gradient elution from ethyl acetate to 5:1 ethyl acetate–ethanol) yielded **7, 9** (0.40 g, 18%) showing one spot by t.l.c. (R_F 0.23, in 5:1 ethyl acetate–ethanol), m.p. 164–166°; ν_{max}^{KBr} 3360, 3280, 2970, 2880, 1640, 1560, 1370, 1310, 1110, 1070, 1050, and 990 cm^{-1}; ^1H- and ^{13}C-n.m.r.: see Tables II and I.

Anal. Calc. for $C_8H_{15}NO_4$: C, 50.78; H, 7.99. Found: C, 50.71; H, 8.14.

Methyl 3-acetamido-2,3,6-trideoxy-β- *and* -α-D,L-arabino-*hexopyranosides* (**8,**

10). — A mixture of **7, 9** (0.39 g, 2.1 mmol) and Amberlite IR-120 (H^+ C.P.) ion-exchange resin (4 g) in methanol (40 mL) was stirred for 24 h at room temperature. Removal of the resin by filtration and evaporation of the solvent yielded the methyl glycosides **8** and **10** (0.30 g, 73%), one spot by t.l.c. (R_F 0.33, in 5:1 ethyl acetate–ethanol), m.p. 126–130°; ^{1}H- and ^{13}C-n.m.r.: see Tables II and I.

*Methyl 3-acetamido-2,3,5,6-tetradeoxy-5-fluoro-β- and -α-*D,L-ribo-*hexofuranosides* (**11, 14**). — To a solution of the methyl glycosides **8, 10** (0.5 g, 2 mmol) in anhydrous hydrogen fluoride (5 mL) in a TFE tube at −78° under an argon atmosphere was added sulfur tetrafluoride (0.5 g, 5 mmol). The solution was stirred overnight at −78°. Evaporation of the volatile reaction products and hydrogen fluoride solvent yielded a yellow, solid product, which was dissolved in methanol (~40 mL) and stirred with Amberlite IR-120 (H^+) ion-exchange resin (3 g). Removal of the resin by filtration and evaporation of the solvent yielded a crude material (0.45 g) showing one spot with tailing by t.l.c. in 10:1 ethyl acetate–ethanol. The purification of this material was attempted by medium-pressure l.c. (gradient elution with 99:1 to 5:1 ethyl acetate–ethanol). The purified oil (0.32 g, 63%) gave one spot by t.l.c. (10:1 ethyl acetate–ethanol), but failed to crystallize; ^{1}H- and ^{13}C-n.m.r.: see Tables II and I; m.s.: *m/z* (rel. int.): 185 (M − HF, 16), 174 (9) [C_1], 173 (13) [A_1], 158 (13) [E_1], 154 (5) [C_2], 153 (16) [A_2], 138 (28) [A_3], 129 (62) [F_1], 128 (35) [F_1 − H], 126 (40) [E_1 − CH_3OH], 116 (37) [E_1 − CH_2=C=O], 115 (35) [E_2], 114 (53) [F_2], 99 (60) [*m/z* 126 − C_2H_3], 96 (35) [A_4], 95 (30) [C_3], 94 (40), 86 (58) [G_1], 84 (100) [E_3], 72 (60) [F_3], and 68 (23) [C_4].

*3-Acetamido-2,3,5,6-tetradeoxy-5-fluoro-β- and -α-*D,L-ribo-*hexofuranoses* (**12, 15**). — A suspension of **11** and **14** (0.30 g, 1.5 mmol) was stirred with 0.2M HCl (10 mL) for 2 h at 90°. The cooled solution was passed through a strongly basic, ion-exchange column (Amberlite CG-400, AcO^-). After washing the column with methanol, evaporation of the combined aqueous and methanolic eluants yielded a colorless syrup (0.26 g, 93%); ^{13}C-n.m.r.: see Table I.

*3-Acetamido-2,3,5,6-tetradeoxy-5-fluoro-1-*O*-(4-nitrobenzoyl)-β- and -α-*D,L-ribo-*hexofuranoses* (**13, 16**). — To a solution of **12, 15** (0.26 g, 1.4 mmol) in anhydrous pyridine (4 mL) was added at 0° 4-nitrobenzoyl chloride (0.40 g, 2.2 mmol), freshly recrystallized from carbon tetrachloride). After being stirred for 3 h, the mixture was poured onto ice and extracted with chloroform. The extract was washed with water, 0.5M HCl, and saturated $NaHCO_3$, and evaporated *in vacuo* to give a colorless oil (0.25 g, 55% yield), which solidified. Recrystallization yielded crystals (0.08 g, 17% yield), m.p. 150–160°, giving two spots on t.l.c. (R_F 0.45 and 0.32, ethyl acetate). Continuous extraction of the combined aqueous phases with ethyl acetate yielded additional material (0.20 g), giving two spots on t.l.c. (R_F 0.45 and 0.32, ethyl acetate). Recrystallization of the solids isolated from this extraction from acetone–diethyl ether yielded crystals, one spot on t.l.c. (R_F 0.35, ethyl acetate), m.p. 157–158°, suitable for single crystal X-ray diffraction.

Anal. Calc. for $C_{15}H_{17}FN_2O_6 \cdot 1.5\ H_2O$: C, 49.05; H, 5.49. Found: C, 48.58; H, 5.63.

X-Ray structural determination of 3-acetamido-2,3,5,6-tetradeoxy-5-fluoro-4-nitrobenzoyl-D,L-ribo-*hexofuranose* (**16**). — A single crystal of **13, 16** was obtained by recrystallization from acetone–diethyl ether. X-Ray data collection was performed with a Nicolet R3m automated diffractometer equipped with a MoKα target tube (λ 0.710730 Å) and a graphite-crystal monochromator. The crystal data are: space group $P2_1/c$; a = 19.7105(88), b = 8.6013(35), and c = 9.6051(39) Å; β = 90.83(3)°, and Z = 4. The absorption coefficient was μ(Mo) = 1.2 cm^{-1}. The X-ray intensity data were measured for a total of 920 independent observed reflections with $I \geq 0.75\,\sigma(I)$. The structure was solved by direct methods which revealed the locations of all nonhydrogen atoms on the initial E map. The structure was refined down to a final value of R_1 = 7.4% and R_2 = 5.5% by full-matrix, least-squares techniques with anisotropic-thermal parameters for all nonhydrogen atoms. Hydrogen atoms were placed in idealized positions with isotropic thermal parameters set to 1.2 times the attached-carbon thermal parameter. All structural determinations and refinement calculations were carried out with the SHELXTL package on the Nicolet R3m Nova 3 crystallographic system*. On the basis of four molecules of $C_{15}H_{17}FN_2O_6$ in a unit cell of volume of 1628.4 $Å^3$, the calculated density was 1.39 g/cm^3. The final difference-map revealed no abnormal features (final difference-Fourier, map peak equals 0.25 electrons/$Å^3$).

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