Synthesis, reactions, and crystal structure of 5-azido-6-Obenzoyl-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -Dglucofuranose*

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ABSTRACT

5-Bromo-6-*O-tert*-butyldiphenylsilyl-5-deoxy-1,2-*O*-isopropylidene- β -L-talofuranose (7) was obtained by treatment of 3,5-*O*-benzylidene-6-*O-tert*-butyldiphenylsilyl-1,2-*O*-isopropylidene- α -D-glucofuranose (3) with *N*-bromosuccinimide followed by Zemplén *O*-deacylation and an oxidation-reduction sequence. Nucleophilic displacement of the bromide in 7 with potassium azide readily gave the corresponding 5-azido-5-deoxy-*allo* derivative 8. Treatment of the 3-trifluoromethanesulphonate of 8 with tris(dimethylamino)sulphonium difluorotrimethylsilicate gave 5-azido-6-*O-tert*-butyldiphenylsilyl-3,5-dideoxy-3-fluoro-1,2-*O*-isopropylidene- α -D-glucofuranose (17). The configuration at C-3 in 17 was confirmed by X-ray crystallography of the 6-benzoate 19.

INTRODUCTION

Fluorinated carbohydrates are of continuing interest because of their potential biological activity^{2,3}. Such compounds are inhibitors⁴ of DNA and RNA synthesis, and are potential antiviral and antitumour agents^{3,5}. Moreover ¹⁸F-labelled carbohydrates, for example, 2-deoxy-2-[¹⁸F]fluoro-D-glucose, have been used in the study of regional-organ metabolism by positron emission tomography^{3,6}. Derivatives of mono- and bi-cyclic polyhydroxylated alkaloids isolated from plants show considerable promise as chemotherapeutic agents⁷. Fluorinated analogues of these alkaloids could show interesting properties and a potential intermediate in their synthesis is 5-azido-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -D-glucofuranose. We now describe the synthesis and reactions of this compound and the crystal structure of its 6-benzoate.

RESULTS AND DISCUSSION

The synthesis of 3-O-benzoyl-5-bromo-6-O-tert-butyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- β -L-talofuranose (1) by bromide ion displacement of the corresponding 5-methanesulphonate has been reported¹. The reaction also gave the 5-bromo-5-

^{* 5-}Azido-3,5-didepxy-3-fluoro-1,2-O-isopropylidene-α-D-glucofuranose derivatives, Part 4. For Part 3, see ref. 1.

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deoxy-D-glucose derivative 2, probably as a result of the drastic reaction conditions and steric hindrance due to the tert-butyldiphenylsilyl group. Moreover, the separation of the isomers by column chromatography was difficult since their $R_{\rm F}$ values were very similar.

A more convenient route to 1 was via 3,5-O-benzylidene-6-O-tert-butyldiphenylsilv1.2-*O*-isopropylidene- α -D-glucofuranose (3), obtained by *tert*-butyldiphenylsilvlation⁸ of 1,2-O-isopropylidene- α -D-glucofuranose at C-6 (4) followed by zinc chloridecatalysed benzylidenation⁹. Reaction of 3 with N-bromosuccinimide¹⁰ gave only 3-Obenzovl-5-bromo-6-O-tert-butyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- β -L-idofuranose (5), which was O-debenzoylated with methanolic sodium methoxide (\rightarrow 6), then subjected to an oxidation-reduction sequence at position 3 (\rightarrow 7), and benzoylated

1

1

1 1







2
$$R^{1} = OBz$$
, $R^{2} = H$, $R^{3} = Br$, $R^{4} = {}^{t}BuPh_{2}Si$
4 $R^{1} = H$, $R^{2} = R^{3} = OH$, $R^{4} = {}^{t}BuPh_{2}Si$
8 $R^{1} = OH$, $R^{2} = H$, $R^{3} = N_{3}$, $R^{4} = {}^{t}BuPh_{2}Si$
9 $R^{1} = OBz$, $R^{2} = H$, $R^{3} = N_{3}$, $R^{4} = {}^{t}BuPh_{2}Si$
12 $R^{1} = H$, $R^{2} = OBz$, $R^{3} = N_{3}$, $R^{4} = {}^{t}BuPh_{2}Si$
13 $R^{1} = H$, $R^{2} = OBz$, $R^{3} = N_{3}$, $R^{4} = {}^{t}BuPh_{2}Si$
13 $R^{1} = H$, $R^{2} = OBz$, $R^{3} = N_{3}$, $R^{4} = {}^{t}BuPh_{2}Si$
13 $R^{1} = H$, $R^{2} = F$, $R^{3} = N_{3}$, $R^{4} = {}^{t}BuPh_{2}Si$
17 $R^{1} = H$, $R^{2} = F$, $R^{3} = N_{3}$, $R^{4} = {}^{t}BuPh_{2}Si$
18 $R^{1} = H$, $R^{2} = F$, $R^{3} = N_{3}$, $R^{4} = H$
19 $R^{1} = H$, $R^{2} = F$, $R^{3} = N_{3}$, $R^{4} = Rz$



100

to give 1 (~ 29% from 3). Displacement of Br-5 in 7 with potassium azide in N,N-dimethylformamide gave the 5-azido-5-deoxy-D-glucose derivative 8 characterised as the 3-benzoate 9^1 .

The structure of 5 was supported by its n.m.r. and mass spectral data. The presence of bromine at C-5 was evident from the $M^+ - 15$ and $M^+ - 58$ fragments at m/z 609 and 611 (1:1 ratio) and m/z 567 and 569 (1:1 ratio) in the mass spectrum and an upfield shift of the C-5 resonance by ~19 p.p.m. compared to that of the C-5 resonance in 3,5,6-tri-O-benzoyl-1,2-O-isopropylidene- β -L-idofuranose¹¹. The configuration at C-5 of 5 was confirmed by desilylation to give 10, using tetrabutylammonium fluoride⁸, followed by Purdie methylation to give the known 6-methyl ether¹⁰. Benzoylation of 10 gave the 3-benzoate 11.

Reaction of the 5-bromo-5-deoxy-L-idose derivatives 5 and 11 with sodium azide in N,N-dimethylformamide for 24 h at ~90° gave a 1:1 mixture of 5-azido-5-deoxy- α -Dglucofuranose derivatives (12 and 13, respectively) and the corresponding 4-enofuranose (14 and 15, respectively). Only the unsaturated products were formed (in ~63.2%) when the reaction mixtures were boiled under reflux. The ¹H-n.m.r. spectra of 12-15 agree with the structures proposed. The large $J_{4,5}$ values (9.5 Hz for 12, 11.5 Hz for 13) confirmed the gluco configuration¹¹. The structures of 14 and 15 were also evident from their ¹H- and ¹³C-n.m.r. spectra. The H-3 signal appeared as a singlet, whereas that due to H-5 was a triplet. Moreover, the C-4,5 signals showed large downfield shifts (151.2 and ~106 p.p.m. for 14, 155 and 107 p.p.m. for 15), clearly indicative of unsaturation at C-4,5.

Doboszewski *et al.*¹² reported that a fluorine substituent could be introduced at C-3 of 1,2-O-isopropylidene- α -D-glucofuranose derivatives by displacement of the 3-trifluoromethanesulphonate (triflate) group with tris(dimethylamino)sulphonium difluorotrimethylsilicate (TASF). Thus, the 3-triflate (16) of the D-allose derivative **8** reacted with TASF for ~0.5 h in cold dichloromethane to give 5-azido-6-O-tert-butyldiphenylsilyl-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -D-glucofuranose (17). Prolonged reaction caused desilylation to give 18, which could also be obtained when 17 was treated with tetrabutylammonium fluoride in tetrahydrofuran.

The structure of 17 was supported by its ¹H-, ¹³C-, and ¹⁹F-n.m.r. spectra. The most significant ¹H signal was that (δ 5.04) of H-3, which was deshielded (~1.1 p.p.m.) by F-3. The J values ($J_{F,3}$ 49.5, $J_{3,4} \sim 2.2$, $J_{F,2} \sim 10$, and $J_{F,4} \sim 29$ Hz) confirm¹² the location of the fluorine substituent at position 3 and the D-gluco configuration.

The structure of 17 was further confirmed by X-ray crystallography of the 6-benzoate (19) of 18. The structure and numbering system of 19 are shown in Fig. 1, and the bond lengths and bond angles are given in Tables I and II. Torsion angles for the two rings in the molecules are shown in Table III. The unit cell contained discrete molecules of 19 (Fig. 2), a single molecule comprising the asymmetric unit. The furanose ring adopted a near ${}^{3}T_{4}$ conformation (ϕ 68.8°, Q 36 pm). However, the $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ values (3.5, ~0, and 2.1 Hz, respectively) were consistent with the ${}^{3}T_{2}$ conformation, which is that normally found in 1,2-O-isopropylidene and 1,2-O-ethylidene furanoid derivatives in solution¹³. The dioxolane ring is closer to the ⁷E conformation (ϕ 106.7°, Q



Fig. 1. Numbering system used for 5-azido-6-O-benzoyl-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -D-glucofuranose (19).



Fig. 2. Molecular packing in 5-azido-6-O-benzoyl-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -D-glucofuranose (19).



Fig. 3. Newman projection, viewed along $C-5 \rightarrow N-1$.

TABLE I

$\begin{array}{c ccccccccccccccccccccccccccccccccccc$					
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0-1-C-1	1.427(15)	O-1–C-8	1.409(15)	
O-4-C-1 $1.416(13)$ $O-4-C-4$ $1.429(12)$ $O-6-C-6$ $1.461(13)$ $O-6-C-7$ $1.304(16)$ $O-7-C-7$ $1.213(17)$ $F-1-C-3$ $1.375(14)$ $N-1-N-2$ $1.201(18)$ $N-1-C-5$ $1.479(14)$ $N-2-N-3$ $1.123(21)$ $C-1-C-2$ $1.480(17)$ $C-2-C-3$ $1.535(15)$ $C-3-C-4$ $1.506(16)$ $C-4-C-5$ $1.539(14)$ $C-5-C-6$ $1.498(18)$ $C-7-C-71$ $1.507(16)$ $C-8-C-9$ $1.480(20)$ $C-8-C-10$ $1.495(18)$ $C-71-C-72$ $1.362(19)$ $C-71-C-76$ $1.366(20)$ $C-72-C-73$ $1.403(17)$ $C-73-C-74$ $1.362(23)$ $C-74-C-75$ $1.374(23)$ $C-75-C-76$ $1.403(20)$ $C-74-C-75$ $1.374(23)$	O-2-C-2	1.432(14)	O-2-C-8	1.427(16)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0-4-C-1	1.416(13)	0-4-C-4	1.429(12)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	O-6-C-6	1.461(13)	O-6-C-7	1.304(16)	
N-1-N-21.201(18)N-1-C-51.479(14)N-2-N-31.123(21)C-1-C-21.480(17)C-2-C-31.535(15)C-3-C-41.506(16)C-4-C-51.539(14)C-5-C-61.498(18)C-7-C-711.507(16)C-8-C-91.480(20)C-8-C-101.495(18)C-71-C-721.362(19)C-71-C-761.366(20)C-72-C-731.403(17)C-73-C-741.362(23)C-74-C-751.374(23)C-75-C-761.403(20)C-74-C-751.374(23)	O-7-C-7	1.213(17)	F-1-C-3	1.375(14)	
N-2-N-3 $1.123(21)$ C-1-C-2 $1.480(17)$ C-2-C-3 $1.535(15)$ C-3-C-4 $1.506(16)$ C-4-C-5 $1.539(14)$ C-5-C-6 $1.498(18)$ C-7-C-71 $1.507(16)$ C-8-C-9 $1.480(20)$ C-8-C-10 $1.495(18)$ C-71-C-72 $1.362(19)$ C-71-C-76 $1.366(20)$ C-72-C-73 $1.403(17)$ C-73-C-74 $1.362(23)$ C-74-C-75 $1.374(23)$ C-75-C-76 $1.403(20)$ C-74-C-75 $1.374(23)$	N-1-N-2	1.201(18)	N-1-C-5	1.479(14)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	N-2-N-3	1.123(21)	C-1-C-2	1.480(17)	
C-4-C-5 $1.539(14)$ $C-5-C-6$ $1.498(18)$ $C-7-C-71$ $1.507(16)$ $C-8-C-9$ $1.480(20)$ $C-8-C-10$ $1.495(18)$ $C-71-C-72$ $1.362(19)$ $C-71-C-76$ $1.366(20)$ $C-72-C-73$ $1.403(17)$ $C-73-C-74$ $1.362(23)$ $C-74-C-75$ $1.374(23)$ $C-75-C-76$ $1.403(20)$ $C-74-C-75$ $C-74-C-75$	C-2-C-3	1.535(15)	C-3-C-4	1.506(16)	
C-7-C-71 1.507(16) C-8-C-9 1.480(20) C-8-C-10 1.495(18) C-71-C-72 1.362(19) C-71-C-76 1.366(20) C-72-C-73 1.403(17) C-73-C-74 1.362(23) C-74-C-75 1.374(23) C-75-C-76 1.403(20) C-74-C-75 C-74(23)	C-4C-5	1.539(14)	C-5-C-6	1.498(18)	
C-8-C-10 1.495(18) C-71-C-72 1.362(19) C-71-C-76 1.366(20) C-72-C-73 1.403(17) C-73-C-74 1.362(23) C-74-C-75 1.374(23) C-75-C-76 1.403(20) C-74-C-75 1.374(23)	C-7-C-71	1.507(16)	C-8–C-9	1.480(20)	
C-71-C-76 1.366(20) C-72-C-73 1.403(17) C-73-C-74 1.362(23) C-74-C-75 1.374(23) C-75-C-76 1.403(20) C-74-C-75 1.374(23)	C-8-C-10	1.495(18)	C-71–C-72	1.362(19)	
C-73-C-74 1.362(23) C-74-C-75 1.374(23) C-75-C-76 1.403(20)	C-71-C-76	1.366(20)	C-72–C-73	1.403(17)	
C-75-C-76 1.403(20)	C-73-C-74	1.362(23)	C-74-C-75	1.374(23)	
	C-75-C-76	1.403(20)		. ,	

Bond lengths (Å) for 19

TABLE II

Bond angles (°) for 19

109.5(10)	C-2-O-2-C-8	107.2(8)	
106.4(7)	C-6-O-6C-7	116.4(9)	
115.5(11)	N-1N-2N-3	170.3(17)	
107.9(10)	0-1-C-1-C-2	104.2(9)	
108.4(9)	O-2-C-2-C-1	106.5(10)	
108.1(9)	C-1-C-2-C-3	105.5(9)	
108.7(9)	F-1C-3C-4	110.1(9)	
101.0(9)	0-4-C-4-C-3	105.7(8)	
107.0(8)	C-3-C-4-C-5	114.8(9)	
106.0(8)	N-1-C-5-C-6	107.4(9)	
110.5(9)	O-6-C-6-C-5	105.7(9)	
123.7(10)	O-6-C-7-C-7 1	111.8(11)	
124.9(12)	O-1-C-8-O-2	104.1(13)	
109.3(12)	O-2-C-8-C-9	107.9(10)	
112.4(10)	O-2-C-8-C-10	108.4(12)	
114.2(11)	O-71-C-72-C-73	120.2(12)	
117.5(14)	O-73-C-74-C-75	123.8(13)	
117.0(14)	C-71C-76C-75	120.4(13)	
122.3(12)	C-7-C-71-C-76	116.7(12)	
121.0(11)			
	$109.5(10) \\106.4(7) \\115.5(11) \\107.9(10) \\108.4(9) \\108.1(9) \\108.7(9) \\101.0(9) \\107.0(8) \\106.0(8) \\110.5(9) \\123.7(10) \\124.9(12) \\109.3(12) \\112.4(10) \\114.2(11) \\117.5(14) \\117.0(14) \\122.3(12) \\121.0(11) \\117.0($	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

24 pm) (the notation is taken clockwise with O-1 as atom 1 in the Cremer–Pople programme¹⁴, and C-8 is the isopropylidene acetal carbon). The angle between the two five-membered rings, defined by the torsion angle O-4–C-1–C-2–O-2, was 114.4° (*cf.* 101° for 1,2-*O*-isopropylidene- α -D-glucofuranose¹⁵ and 98° for 5-azido-3-*O*-benzoyl-6-*O-tert*-butyldiphenylsilyl-5-deoxy-1,2-*O*-isopropylidene- β -L-talofuranose¹. As expected^{2,16}, the acetal moiety C-8–O-1–C-1–O-4–C-4 showed the variations in bond lengths characteristic of methyl pyranosides and predicted from theoretical calculations¹⁶. However, the C-4–O-4–C-1–O-1 and C-8–O-1–C-1–O-4 torsion angles (+90.4 and

TABLE III

C-1-C-2C-3-C-4	20.7(1.1)	C-3-C-4C-5-C-6	- 179.3(0.9)
C-2-C-3C-4-O-4	-34.3(1.0)	C-3-C-4C-5-N-1	- 63.2(1.2)
C-3-C-4O-4-C-1	35.8(1.1)	C-4-C-5N-1-N-2	115.4(1.2)
C-4-O-4C-1-C-2	-21.9(1.2)	C-4-C-5C-6-O-6	179.6(0.8)
O-4-C-1C-2-C-3	0.3(1.2)	C-4-C-5C-6-H-6A	- 60.1(0.9)
O-1-C-1C-2-O-2	-0.3(1.1)	C-4-C-5C-6-H-6B	60.2(0.8)
O-2-C-2C-3-F-1	- 151.2(0.9)	O-4-C-4C-5-N-1	- 179.9(0.9)
O-1-C-1C-2-C-3	-115.1(1.0)	H-4-C-4C-5-N-1	63.1(0.9)
O-2-C-2C-3-C-4	- 93.0(1.0)	C-5-C-6O-6-O-7	- 177.1(0.9)
0-4-C-4C-3-F-1	80.5(0.9)	C-6-O-6C-7-O-7	-2.4(1.7)
F-1-C-3C-2-C-1	-95.2(1.1)	C-6-O-6C-7-O-71	179.1(0.9)
F-1-C-3C-4-C-5	-37.1(1.2)	N-1-C-5C-6-O-6	64.3(1.1)
F-1-C-3C-2-H-2	24.7(0.9)	N-1-C-5C-6-H-6A	- 175.3(0.6)
F-1-C-3C-4-H-4	- 161.3(0.6)	N-1-C-5C-6-H-6B	- 55.0(0.8)
C-2-C-3C-4-C-5	- 151.9(0.9)	N-3-N-2N-1-C-5	175.4(***)
H-1-C-1C-2-H-2	4.5(0.5)	N-2-N-1C-5-H-5	-6.7(1.2)
H-2-C-2C-3-H-3	- 99.5(0.3)	N-2-N-1C-5-C-6	- 126.5(1.2)
H-3-C-3C-4-H-4	- 35.2(0.4)		
H-4-C-4C-5-H-5	-172.9(0.0)		

Torsion angles (°) for 19

132.7°, respectively) are different from those (~60 and ~180°) observed for the acetal moiety of the pyranosides¹⁵. The azido group was nearly linear (the bond angle N-1–N-2–N-3 of 170.3° agrees well with reported values^{1,17}) and the N-2–N-1–C-5–C-4 torsion angle was -115.4° (Fig. 3). The C–F bond length (1.375 Å) was normal¹⁸.

EXPERIMENTAL

For general experimental details, see ref. 19. The n.m.r. data are given in Tables IV and V.

6-O-tert-Butyldiphenylsilyl-1,2-O-isopropylidene-α-D-glucofuranose (4). — A solution of 1,2-O-isopropylidene-α-D-glucofuranose (42.4 g) in dry pyridine (450 mL) was stirred with 4-dimethylaminopyridine (1.7 g) and *tert*-butyldiphenylsilyl chloride (73.9 mL, 1.58 equiv.) for ~20 h at room temperature when t.l.c. (1:1 toluene–EtOAc) showed only one fast-moving product. The mixture was poured into ice–water and extracted with EtOAc, the extract was dried (Na₂SO₄), and the solvent was evaporated. Short-column chromatography (2:1 hexane–EtOAc) gave 4 (88.0 g, 99.7%), [α]_D - 72° (c 1.0, CHCl₃).

Anal. Calc. for C₂₅H₃₄O₆Si: C, 65.5; H, 7.5. Found: C, 64.7; H, 7.5.

3,5-O-Benzylidene-6-O-tert-butyldiphenylsilyl-1,2-O-isopropylidene- α -D-glucofuranose (3). — A mixture of 4 (2.8 g), fused zinc chloride (6.0 g), and freshly distilled benzaldehyde (17 mL) was stirred vigorously for ~ 22 h at room temperature, when t.l.c. (3:1 toluene-EtOAc) showed a faster moving product. The solution was poured into ice-cold saturated aq. sodium hydrogencarbonate and extracted with CH₂Cl₂. Barium carbonate (~5 g) was added to the extract which was steam-distilled to remove the excess of benzaldehyde. The aqueous suspension was filtered hot, cooled, and extracted with CH_2Cl_2 , and the extract was washed with water, dried (Na₂SO₄), and concentrated. Short-column chromatography (9:1 hexane-EtOAc) of the residue gave 3 (3.15 g, 94.4%), $[\alpha]_p + 25^\circ$ (c 1.05, CHCl₃).

Anal. Calc. for C₃₂H₃₈O₆Si: C, 70.3; H, 7.0. Found: C, 71.0; H, 7.0.

3-O-Benzoyl-5-bromo-6-O-tert-butyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- β -L-idofuranose (5). — To a solution of 4 (5.8 g) in CCl₄ (130 mL) were added freshly recrystallised N-bromosuccinimide (2.0 g) and barium carbonate (15.7 g). The mixture was stirred efficiently and boiled under reflux for 4 h. T.1.c. (toluene) then showed one slightly faster-moving product. The suspension was filtered and concentrated. Shortcolumn chromatography (9:1 hexanc-EtOAc) of the syrupy product gave 5 (4.92 g, 74.1%), [α]_p +4° (c 1.05, CHCl₃).

Anal. Calc. for C₃₂H₃₇BrO₆Si: C, 61.4; H, 6.0; Br, 12.8. Found: C, 61.3; H, 5.5; Br, 12.2.

5-Bromo-6-O-tert-butyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- β -L-idofuranose (6). — A methanolic solution of 5 (2.3 g) was treated with methanolic M sodium methoxide (1.0 mL) for 4 h at room temperature, then deionised with Duolite MB 5113 mixed-bed resin, filtered, and concentrated, to give 6 (1.25 g, 65.5%), $[\alpha]_{p}$ +4° (c 1.0, CHCl₃).

Anal. Calc. for $C_{25}H_{33}BrO_5Si: C, 57.6; H, 6.4; Br, 15.3$. Found: C, 57.6; H, 6.6; Br, 14.3.

3-O-Benzoyl-5-bromo-5-deoxy-1,2-O-isopropylidene- β -L-idofuranose (10). — A solution of 5 (0.96 g) in tetrahydrofuran (20 mL) was stirred with tetrabutylammonium fluoride (0.48 g) for ~6 h at room temperature. The solution was concentrated, a solution of the residue in dichloromethane was washed with water and dried (Na₂SO₄), and the solvent was evaporated. Short-column chromatography (5:1 hexane–EtOAc) of the syrupy residue gave 10 (0.4 g, 67.3%), m.p. 116–117° (from ether), $[\alpha]_{\rm p} = 15^{\circ}$ (c 1.05, CHCl₃).

Anal. Calc. for C₁₆H₁₉BrO: C, 49.6; H, 4.9; Br, 20.6. Found: C, 49.9; H, 4.9; Br, 20.7.

3,6-Di-O-benzoyl-5-bromo-5-deoxy-1,2-O-isopropylidene- β -L-idofuranose (11). — Conventional benzoylation of 10 (0.2 g) with pyridine (2.0 mL) and benzoyl chloride (0.1 mL) gave 11 (0.21 g, 90.6%), m.p. 158.5–159.5° (from EtOAc-hexane), $[\alpha]_{D} - 39^{\circ}$ (c 1.0, CHCl₃).

Anal. Calc. for C₂₃H₂₃BrO₇: C, 56.2; H, 4.7; Br, 16.3. Found: C, 56.2; H, 4.7; Br, 16.55.

Reaction of 5 and 11 with sodium azide. — A solution of 5 (0.65 g) in N,Ndimethylformamide (16 mL) was heated with sodium azide (0.65 g) for 24 h at ~ 90°. T.l.c. (9:1 hexane-EtOAc) then showed 2 faster-moving spots with similar R_F values. The solution was poured into ice-water and extracted with ether, and the extract was washed with water, dried (MgSO₄), filtered, and concentrated. Flash-column chromatography (twice; 9:1 hexane-EtOAc) of the residue gave, first, 3-O-benzoyl-6-O-tert-bu-

¹ H-N.m.r. (90) MHz) data ^a i	(CDCI ₃)							
Compound	І-Н	Н-2	Н-3	Н-4	Н-5	Н-ба	Н-бЪ	CMe2	Other signals
å	6.05(d)	4.68(d)	4.31(d)	4.59(d)	4.34(1)	4.13(dd)	3.95(dd)	1.35, 1.55	1.10(CMe ₃) 6.08(CHPh)
4	5.93(d)	4.52(d)		-3.9-4.4(m)-		9. 0	-3.9(m)	1.29, 1.46	1.07(CM ₃) 3.24(OH)
¥0	6.01(d)	4.67(d)	5.48(d)	4.68(dd)	4.2-4.4(m)	3.8	4.1(m)	1.32, 1.57	$1.06(CMe_3)$
e,	5.97(d)	4.63(d)			<u> </u>			1.38, 1.55	1.08(CMe ₃) 3.29(OH)
7	5.85(d)	4.60(t)		3.9	4.8(m)			-1.38, 1.55	1.06(CMe ₃) 2.90(OH)
*	5.74(d)	4.52(t)			<u>3.8-4.1(m</u>			1.32, 1.52	1.08(CMe ₃) 2.77(OH)
6	5.85(d)	49-5.	.1(m)	4.4-4.5(m)		<u> </u>		1.30, 1.51	1.08(CMe ₃)
10	5.98(d)	4.94(d)			-4.3-4.8(m			1.31, 1.51	2.99(OH)
11	6.01(d)	4.6-5.0(m)	5.50(s)		4.6	-5.0(m)		1.33, 1.57	
12	5.88(d)	4.95(d)	5.56(d)	4.47(dd)		<u>3.7-4.1(m</u>		1.27, 1.48	1.05(CMe ₃)
13	6.00(d)	4.68(d)	5.61(d)	4.91(dd)		<u>3.8-4.6(m</u>		1.33, 1.54	
14	6.07(d)	4.63(d)	5.71(s)		5.12(t)	4.47(dd)	4.28(dd)	1.37, 1.44	1.06(CMe ₃)
15	6.25(d)	4.72(d)	5.78(s)		5.14(t)	4.8	-5.0(m)	1.42, 1.50	
17	5.91(d)	4.68(dd)	5.04(dd)	4.20(qd)	4.05(dd)	3.6	-3.9(m)	1.31, 1.44	1.08(CMe ₃)
18	5.97(d)	4.73(dd)	5.06(dd)	4.15(qd)	3.89(td)	3.6	-3.9(m)	1.33, 1.49	2.17(OH)
61	5.98(d)	4.72(dd)	5.13(dd)	4.26(qd)	4.33(dd)	4.0	-4.2(m)	1.32, 1.48	

TABLE IV

106

Compound	J,,2	$J_{2,3}$	$\mathbf{J}_{2,F}$	J _{3,4}	$\mathbf{J}_{3,F}$	J _{4,5}	$J_{4,F}$	J 5,6a	$J_{5,6b}$	J _{6a,6b}
3	3.7	0		2.0		0		4.4	4.5	11.2
4	3.9								1	1
ŝ	3.9	0		2.9		8.3				
9	3.7	0								
7	3.7	4.4								
00	3.7	4.2								
6	3.7									
10	3.7	0								
11	3.9	0		0						
12	3.7	0		2.9		9.5				
13	3.7	0		2.7		11.7				
14	3.4	0						6.3	6.3	8.1
15	3.4	0		0		0		6.6	7.5	
17	3.9	0	9.6	2.0	49.5	9.8	28.1	1.7		
18	3.9	0	10.4	2.0	49.9	9.5	27.6	2.0	5.2	
19	3.5	0	6.6	2.0	41.7	11.4	31.7	4.1		
" Chemical sl	hifts in p.p.m	1 J in Hz. ⁶	At 300 MHz							

¹³ C-N.m.	r. chemical shil	fts ^e (CDCl ₃)	-												
Compour	ıd C-I	C-2	C-3	C-4	C-5	C-6	CMe2	CMe ₂	CMe3	CMe3	CPh	J _{2.F}	$J_{3,F}$	J, F	J _{5.F}
6	104.8	84.0	74.1	78.2	73.2	65.4	111.7	26.2, 26.8	19.2	26.8	95.5				
4	104.9	85.2	75.5	79.3	70.3	65.0	111.6	26.2, 26.6	19.2	26.9					
ŝ	104.2	84.0	76.7	79.5	50.65	65.55	112.5	26.8, 26.8	19.0	26.9					
9	104.3	85.5	75.1	83.9	49.4	65.7	111.8	26.3, 26.3	19.2	26.8					
2	104.0	78.7/78.0	73.8	78.0/78.7	53.5	65.0	112.8	26.7, 26.7	19.2	26.7					
90	103.7	79.0/78.9	71.9	78.9/19.0	63.7/64	4.0	112.8	26.5, 26.5	19.1	26.7					
6	104.5	78.0	73:6	76.55	63.8/6	4.3	113.3	26.7, 26.7	19.2	26.9					
10	104.2	85.7	74.8	81.75	47.2	62.9	112.1	26.2, 26.8							
II	104.2	83.9	76.8	80.1	45.7	65.5	112.6	26.3, 26.7							
12	105.0	83.2	76.77	6.8	60.8	64.5	112.5	26.2, 26.8	19.0	26.7					
13	105.2	83.15	76.4 <i>D</i>	6.6	58.8	65.4	112.7	26.8, 26.8							
14	106.5/106.2	82.7	76.1	151.2	106.5/106.2	58.7	114.2	26.3, 26.8	19.0	26.55					
15	107.0	82.7	76.0	155.0	100.3	59.4	114.6	27.3, 27.9							
17	105.1	82.2(d)	93.9(d)	77.5(d)	60.2(d)	64.5	112.4	26.2, 26.2	19.2	26.7		31.7	185.6	22.0	7.3
18	105.0	82.2(d)	93.9(d)	78.4(d)	60.4(d)	62.9	112.6	26.1, 26.1				33.0	185.6	18.3	6.1
19	104.4	82.6(d)	93.2(d)	81.1(d)	55.3(d)	65.1	112.5	26.1, 26.6				34.5	185.5	20.0	5.0

" Downfield from DSS, p.p.m.

108

TABLE V

tyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- β -L-threo-hex-4-enofuranose (14; 0.22 g, 38.9%), $[\alpha]_p = 21^\circ$ (c 1.0, CHCl₃).

Anal. Calc. for C₃₂H₃₆O₆Si: C, 70.6; H, 6.7. Found: C, 70.3; H, 6.9.

Eluted second was 5-azido-3-O-benzoyl-6-O-tert-butyldiphenylsilyl-5-deoxy- α -D-glucofuranose (12; 0.21 g, 36.6%), $[\alpha]_n = 10.5^\circ$ (c 1.0, CHCl₃).

Anal. Calc. for C₃₂H₃₇N₃O₆Si: C, 65.4; H, 6.35; N, 7.15. Found: C, 65.5; H, 6.6; N, 6.9.

When the reaction mixture was heated under reflux, 63% of 14 was obtained. Treatment of 11, as described for 5, gave, first 3,6-di-O-benzoyl-5-deoxy-1,2-O-

isopropylidene- β -L-threo-hex-4-enofuranose (15, 59.9%), $[\alpha]_{D} = 49^{\circ}$ (c 1.0, CHCl₃).

Anal. Calc. for C₂₃H₂₂O₇: C, 67.3; H, 5.4. Found: C, 67.1; H, 5.55.

Eluted second was 5-azido-3,6-di-O-benzoyl-5-deoxy-1,2-O-isopropylidene- α -D-glucofuranose (13, 30.1%), $[\alpha]_{p} = -63^{\circ}$ (c 1.0, CHCl₃).

Anal. Calc. for $C_{23}H_{23}N_3O_7Si$: C, 60.9; H, 5.1; N, 9.3. Found: C, 61.3; H, 4.6; N, 8.4.

5-Bromo-6-O-tert-butyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- β -L-talofuranose (7). — A solution of **6** (0.56 g) in methyl sulphoxide (0.47 mL) and N,Ndimethylformamide (2.0 mL) was stirred for ~3.5 h at 65–70° with phosphorus pentaoxide (0.66 g) under N₂. T.I.c. (5:2 hexane–EtOAc) then showed a major and a minor fast-moving product. The mixture was poured into ice–water and extracted with ethyl acetate, and the extract was dried (MgSO₄) and concentrated. A solution of the syrupy residue in MeOH (20 mL) was treated with sodium borohydride (40 mg) during 10 min at 0°. The mixture was stirred for 45 min at room temperature, then treated with Duolite MB 5113 mixed-bed resin, and concentrated. Flash-column chromatography (5:1 hexane–EtOAc) of the residue gave 7 (0.34 g, 60.7%), [α]_p +9° (c 1.0, CHCl₃).

Anal. Calc. for C₂₅H₃₃BrO₅Si: C, 57.6; H, 6.4; Br, 15.3. Found: C, 56.9; H, 6.7; Br, 15.7.

3-O-Benzoyl-5-bromo-6-O-tert-butyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- β -L-talofuranose (1). — Conventional treatment of 7 with pyridine and benzoyl chloride gave 1 (89%), $[\alpha]_p$ + 76° (c 1.0, CHCl₃); lit.¹ $[\alpha]_p$ + 76° (CHCl₃).

5-Azido-6-O-tert-butyldiphenylsilyl-5-deoxy-1,2-O-isopropylidene- α -D-allofuranose (8). — A solution of 7 (2.97 g) in N,N-dimethylformamide (150 mL) was stirred with sodium azide (3.0 g) under N₂ for 17 h at ~90°, when t.l.c. (4:1 hexane–EtOAc) showed a major and a trace of another faster-moving product. The mixture was poured into ice-water and extracted with EtOAc, and the extract was dried (MgSO₄) and concentrated. Short-column chromatography (10:1 hexane–EtOAc) of the residue gave 8 (1.98 g, 71.9%), [α]_D - 4° (c 1.0, CHCl₃).

Anal. Calc. for $C_{25}H_{33}N_3O_5Si$: C, 62.1; H, 5.2; N, 8.7. Found: C, 62.4; H, 5.1; N, 8.3.

Conventional treatment of 8 with pyridine and benzoyl chloride gave the 3-benzoate 9 (85%), $[\alpha]_{p}$ + 80° (c 1.0, CHCl₃).

Anal. Calc. for C₃₂H₃₇N₃O₆Si: C, 65.4; H, 6.35; N, 7.15. Found: C, 65.1; H, 6.3; N, 7.2.

5-Azido-6-O-tert-butyldiphenylsilyl-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -D-glucofuranose (17) and 5-azido-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -D-gluco-furanose (18). — A solution of 8 (3.89 g) in dry CH₂Cl₂ (200 mL) and pyridine (3.2 mL) was treated with triflic anhydride (5.0 mL) during 25 min at -5° . After 1 h, t.l.c. (5:1 hexane-EtOAc) showed only a faster-moving product. The solution was washed with ice-water, dilute aq. HCl, and saturated aq. NaCl, dried (MgSO₄), and concentrated at $\sim 30^{\circ}$.

A solution of the syrupy residue in dry CH_2Cl_2 (200 mL) was treated with TASF (9.12 g) under N₂ for ~1 h at -3°, when t.l.c. (5:1 hexane-EtOAc) showed only one faster-moving product. The reaction was washed with cold saturated aq. NaCl, dried (MgSO₄), and concentrated. Short-column chromatography (20:1 hexane-EtOAc) of the syrupy residue gave 17 (2.64 g, 67.4%), $[\alpha]_p - 41^\circ$ (c 1.0, CHCl₃).

Anal. Calc. for C₂₅H₃₂FN₃O₄Si: C, 61.8; H, 6.6; F, 3.9; N, 8.65. Found: C, 61.9; H, 6.8; F, 3.8; N, 8.3.

When the mixture was stirred overnight at room temperature, t.l.c. showed only one slower-moving product. Work-up, as for 17, gave 18 (0.1 g, 71.1%), $[\alpha]_D = 9^\circ$ (c 1.0, CHCl₃).

Anal. Calc. for C₉H₁₄FN₃O₄: C, 43.7; H, 5.7; F, 7.6; N, 16.9. Found: C, 43.3; H, 5.4; F, 7.4; N, 17.4.

Treatment of a solution of 17 (0.14 g) in dry tetrahydrofuran (10 mL) with tetrabutylammonium fluoride (0.12 g) for ~ 5 h at room temperature and work-up as for 10, but using EtOAc for extraction, gave 18 (59.5 mg, 82.7%).

5-Azido-6-O-benzoyl-3,5-dideoxy-3-fluoro-1,2-O-isopropylidene- α -D-glucofuranose (19). — Conventional treatment of 18 with pyridine and benzoyl chloride gave 19 (99%), m.p. 117–119° (from MeOH), $[\alpha]_p = -14^\circ$ (c 1.0, CHCl₃).

Anal. Calc. for: C₁₆H₁₈FN₃O₅: C, 54.7; H, 5.1; F, 5.4; N, 12.0. Found: C, 55.1; H, 5.2; F, 5.7; N, 11.6.

Crystal data for 19. — $C_{16}H_{18}FN_3O_5$, M_r 351.3, a = 11.025(3), b = 26.889(9), c = 5.851(2) Å, orthorhombic space group $P2_12_12$, U = 1734.4 Å³, Z = 4, $D_x = 1.345$, $\mu = 0.101$ mm⁻¹, and F(000) = 736. A single crystal of approximate size $0.3 \times 0.3 \times 0.4$ mm was studied using a Siemens R3m/v diffractometer, with Mo radiation (graphite monochromator). The cell parameters were determined from 25 reflections by a least-squares procedure. Intensity data were collected in the range $\theta = 3-50^{\circ}$ (h = 0-13, k = 0-29, l = 0-7). Two standard reflections were measured every 98 reflections. A total of 2257 reflections was measured and 957 with $I > 3\sigma(I)$ were used in subsequent calculations.

Structure determination and refinement*. — The structure was determined by the direct method and refined by a full-matrix least-squares procedure, using SHELXTL PLUS on a Micro Vax 2000 computer. The carbon, fluorine, nitrogen, and oxygen

^{*} Lists of final atomic parameters, anisotropic thermal parameters, and hydrogen positions are deposited with, and can be obtained from, Elsevier Science Publishers, B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/488/Carbohydr. Res., 225 (1992) 99–111.

atoms were then refined anisotropically. The hydrogen atoms were included with isotropic temperature factors in the final R calculation, but their positions were not refined. The final refinement gave R = 0.088, wR = 0.072, max $\Delta/\sigma = 0.86$ with a goodness-of-fit = 1.50, and largest difference peak = 0.37 e.Å^{-3} . The weighting scheme used was:

 $\mathbf{w}^{-1} = \sigma^2(F) + 0.0006F^2.$

The bond lengths and angles are given in Tables I and II, and the torsion angles in Table III.

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