

SYNTHESES WITH ANHYDRO SUGARS. XVIII.*

AMINODIDEOXYFLUORINE DERIVATIVES OF D-GLUCOSE

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On cleavage of fluoroepoxide *I* and *VII* with ammonia 4-amino-1,6-anhydro-2,4-dideoxy-2-fluoro- β -D-glucose (*II*) and 2-amino-1,6-anhydro-2,4-dideoxy-4-fluoro- β -D-glucose (*VIII*) was obtained. The structures of both substances follow from the PMR spectra of acetates *III* and *IX*. Acetolysis of compound *II* and subsequent deacetylation gave 4-acetamido-2,4-dideoxy-2-fluoro-D-glucose (*VI*).

In preceding papers we prepared isomeric fluoroepoxides 1,6 : 3,4-dianhydro-2-deoxy-2-fluoro- β -D-galactose¹ (*I*) and 1,6 : 2,3-dianhydro-4-deoxy-4-fluoro- β -D-mannose² (*VII*). Compound *VII* was described for the first time by Barford and coworkers³.

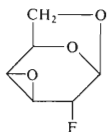
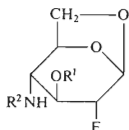
In this paper we describe the cleavage of both fluoroepoxides *I* and *VII* with ammonia⁴, during which 4-amino-1,6-anhydro-2,4-dideoxy-2-fluoro- β -D-glucose (*II*) or 2-amino-1,6-anhydro-2,4-dideoxy-4-fluoro- β -D-glucose (*VIII*) are formed in accordance to the Fürst-Plattner rule. The structures of both compounds, *II* and *VIII* followed from ¹H—NMR spectra of acetates *III* and *IX* (Table I). On partial acetylation of compound *II* with acetic anhydride in methanol 4-acetamido-1,6-anhydro-2,4-dideoxy-2-fluoro- β -D-glucose (*IV*) was obtained. Very close $[\alpha]_D$ values of compounds *II*, *VIII* and 1,6-anhydro- β -D-glucopyranose ($[\alpha]_D -66.2^\circ$ (2.8; water)⁵) also corroborate the configurational relationship of all these compounds. As follows from the literature the substitution of the hydroxyl group on the rigid 1,6-anhydro- β -D-hexopyranose system by an amino group⁶ or by a fluorine atom¹ — while retaining the configuration — should not lead to any substantial change in optical rotation.

On acetolysis of compound *II* with acetic anhydride, under catalysis with perchloric

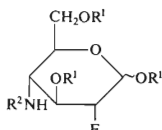
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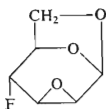
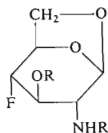
acid, 4-acetamido-1,3,6-tri-O-acetyl-2,4-dideoxy-2-fluoro-D-glucose (*V*) is formed which on deacetylation with sodium methoxide in methanol affords 4-acetamido-2,4-dideoxy-2-fluoro-D-glucose (*VI*). The structure of the latter compound was confirmed by infrared and mass spectra. Acetolysis of compound *VIII* under the same conditions gave a mixture of products which could not be identified with certainty.

*I*

II; $R^1 = R^2 = H$
III; $R^1 = R^2 = Ac$
IV; $R^1 = H, R^2 = Ac$



V; $R^1 = R^2 = Ac$
VI; $R^1 = H, R^2 = Ac$

*VII*

VIII; $R = H$
IX; $R = Ac$

EXPERIMENTAL

The melting points were determined on a Boetius micromelting point apparatus, optical rotations on an automatic Bendix Ericsson UK Ltd. polarimeter, type 143 A, at 20°C.

4-Amino-1,6-anhydro-2,4-dideoxy-2-fluoro-β-D-glucose (*II*)

500 mg of *I* were heated in an autoclave with 7 ml of methanol saturated with ammonia (at -15°C) for 8 hours at 100°C. After distilling off the solvent the residue was crystallised from methanol. Yield 400 mg (72%) of compound *II*, m.p. 159–162°, $[\alpha]_D -69^\circ$ (0.7; water). For $C_6H_{10}FNO_3$ (163.2) calculated: 44.20% C, 6.17% H, 11.63% F, 8.57% N; found: 43.75% C, 6.34% H, 11.58% F, 8.53% N.

2-Amino-1,6-anhydro-2,4-dideoxy-4-fluoro-β-D-glucose (*VIII*)

Using the same method as above compound *VII* (600 mg) gave 470 mg (70%) of compound *VIII*, m.p. 178–182°C (at 170°C sublimation begins), $[\alpha]_D -67^\circ$ (0.6; water). For $C_6H_{10}FNO_3$ (163.2) calculated: 44.20% C, 6.17% H, 11.63% F, 8.57% N; found: 43.95% C, 6.27% H, 11.65% F, 8.43% N.

TABLE I

PMR Spectra of Compounds *III* and *IX*

The spectra were measured on a Varian HA-100 (100 MHz) apparatus. Chemical shifts are given in δ (p.p.m.) values and tetramethylsilane was used as internal standard. J values are given in Hz and were determined with a ± 0.5 Hz accuracy. The assignment of the signals of single protons was carried out by the method of double resonance.

Proton	<i>III</i> ^a	<i>IX</i> ^b
H-1	5.52 ($J_{1,2} = 2.5, J_{1,3} = 1.5, J_{1,F} = 1$)	5.34 ($J_{1,2} \leq 1.5, J_{1,3} \leq 1.5, J_{1,5} \leq 1$)
H-2	4.27 ($J_{2,1} = 2.5, J_{2,3} = 1.5, J_{2,4} = 1, J_{2,F} = 43$)	3.99 ($J_{2,1} \leq 1.5, J_{2,3} = 1.5, J_{2,NH} = 8, J_{2,F} \leq 1.5$)
H-3	4.84 ($J_{3,1} = 1.5, J_{3,2} = 1.5, J_{3,4} = 1.5, J_{3,5} = 1.5, J_{3,F} = 15$)	4.86 ($J_{3,1} \leq 1.5, J_{3,2} = 1.5, J_{3,4} = 1.5, J_{3,F} = 15.5$)
H-4	4.10 ($J_{4,2} = 1, J_{4,3} = 1.5, J_{4,5} = 2.5, J_{4,NH} = 7$)	4.29 ($J_{4,3} = 1.5, J_{4,5} = 1.5, J_{4,F} = 45$)
H-5	4.50 ($J_{5,3} = 1.5, J_{5,4} = 2.5, J_{5,6en} = 1, J_{5,6ex} = 6$)	4.56 ($J_{5,1} \leq 1, J_{5,4} = 1.5, J_{5,6en} \leq 1.5, J_{5,6ex} = 5, J_{5,F} = 11$)
H-6 endo	4.19 ($J_{6en,6ex} = 8, J_{6en,5} = 1.5$)	3.89 ($J_{6en,6ex} = 8, J_{6en,5} \leq 1.5, J_{6en,F} \leq 1.5$)
H-6 exo	3.80 ($J_{6ex,6en} = 8, J_{6ex,5} = 6, J_{6ex,F} = 1.5$)	3.65 ($J_{6ex,6en} = 8, J_{6ex,5} = 5, J_{6ex,F} = 5$)
N-H	6.30 ($J_{NH,4} = 7$)	7.09 ($J_{NH,2} = 8$)
O-Ac	2.09	1.96
N-Ac	2.02	1.89

^a In deuteriochloroform; ^b in a $CDCl_3$ - CD_3SOCD_3 - C_6D_6 mixture 5 : 1 : 1.

4-Acetamido-3-O-acetyl-1,6-anhydro-2,4-dideoxy-2-fluoro- β -D-glucose (*III*)

Acetylation of 100 mg of *II* with acetic anhydride in pyridine gave, after crystallisation from chloroform, 100 mg (66%) of compound *III*, m.p. 130–131°C [α]_D –49° (0.7; chloroform). For $C_{10}H_{14}FNO_5$ (247.2) calculated: 48.57% C, 5.71% H, 7.69% F, 5.67% N; found: 48.30% C, 5.68% H, 7.68% F, 5.99% N.

2-Acetamido-3-O-acetyl-1,6-anhydro-2,4-dideoxy-4-fluoro- β -D-glucose (*IX*)

Acetylation of 100 mg of *VIII* with acetic anhydride in pyridine gave, after crystallisation from a methanol-ether mixture, 90 mg (60%) of compound *IX*, m.p. 211–212°C, [α]_D –68° (0.6; chloroform). For $C_{10}H_{14}FNO_5$ (247.2) calculated: 48.57% C, 5.71% H, 7.69% F, 5.67% N; found: 48.32% C, 5.72% H, 7.36% F, 5.71% N.

4-Acetamido-1,6-anhydro-2,4-dideoxy-2-fluoro- β -D-glucose (*IV*)

A mixture of 75 mg of *II*, 0.5 ml acetic anhydride and 2.5 ml methanol was allowed to stand at room temperature for 48 hours. After evaporation of the solvent the residue was dissolved several times in methanol and the solvent distilled off. Crystallisation from benzene-ethanol (1 : 1) mixture gave 70 mg (76%) of compound *IV*, m.p. 184–185°C, $[\alpha]_D -52^\circ$ (0.7; methanol). According to the IR spectrum of *IV* it contains an N-acetyl group (Nujol, 1560, 1660 and 3380 cm^{-1}). For $\text{C}_8\text{H}_{12}\text{FNO}_4$ (205.2) calculated: 46.83% C, 5.89% H, 9.26% F, 6.82% N; found: 46.84% C, 5.95% H, 9.15% F, 6.78% N.

4-Acetamido-1,3,6-tri-O-acetyl-2,4-dideoxy-2-fluoro-D-glucose (*V*)

A solution of 100 mg of *II* in 10 ml of acetic anhydride, containing 0.2 ml of 70% perchloric acid, was allowed to stand at room temperature for 60 hours. Working up of the reaction mixture gave (after crystallisation of the crude product from chloroform) 60 mg (28%) of compound *V*, m.p. 219–220°C, $[\alpha]_D +160^\circ$ (0.4; chloroform). For $\text{C}_{14}\text{H}_{20}\text{FNO}_8$ (349.3) calculated: 48.13% C, 5.77% H, 5.44% F, 4.01% N; found: 47.89% C, 5.69% H, 4.95% F, 4.24% N.

4-Acetamido-2,4-dideoxy-2-fluoro-D-glucose (*VI*)

50 mg of *V* were deacetylated with sodium methoxide in methanol. After crystallisation of the crude product from methanol 24 mg (75%) of *VI* were obtained, m.p. 210–216°C (under decomposition), $[\alpha]_D +85 \rightarrow +70^\circ$ (equilibrium, 3 hours). The IR spectrum confirms the presence of an N-acetyl group (Nujol, 1559, 1631 and 3290 cm^{-1}). Paper chromatography (Whatman 1, 1-butanol saturated with water, detection with $\text{Ag}(\text{NH}_3)_2^+$ after heating at 110°C): $R_F = 0.35$. Detection of *VI*, when compared with that of 2-deoxy-2-fluoro-D-glucose, is less distinct. For $\text{C}_8\text{H}_{14}\text{FNO}_5$ (223.2) calculated: 43.05% C, 6.32% H, 8.51% F, 6.27% N; found: 42.75% C, 6.15% H, 8.45% F, 5.81% N.

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