

**PREPARATION OF 1,6-ANHYDRO DERIVATIVES
OF 2,4-DIDEOXY-2-FLUORO- β -D-*xylo*-HEXOPYRANOSE
AND 2,3-DIDEOXY-2-FLUORO- β -D-*ribo*-HEXOPYRANOSE
AND CORRESPONDING REDUCING SUGARS***

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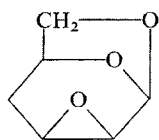
Starting from 1,6-anhydro-4-O-benzyl-2-deoxy-2-fluoro- β -D-glucopyranose (*III*) 1,6 : 3,4-dianhydro-2-deoxy-2-fluoro- β -D-galactopyranose (*VII*) and 1,6 : 3,4-dianhydro-2-deoxy-2-fluoro- β -D-allopyranose (*X*) were prepared. Both 2-fluoro epoxides *VII* and *X* were submitted to reductive cleavage with Raney nickel and with lithium aluminum hydride, under formation of 4- or 3-deoxy derivatives of 1,6-anhydro-2-deoxy-2-fluoro- β -D-hexopyranose of *xylo*- (*XI*) and *ribo*- (*XII*) configuration. On acetolysis of dideoxy derivatives *XI* and *XII* tri-O-acetyl derivatives *XV* and *XVII* were obtained which on deacetylation afforded 2,4-dideoxy-2-fluoro-D-*xylo*-hexose (*XVI*) and 2,3-dideoxy-2-fluoro-D-*ribo*-hexose (*XVIII*).

In connection with the studies dealing with the synthesis of fluoro derivatives of hexoses we also started to prepare deoxy derivatives of 2-deoxy-2-fluoro-D-hexopyranoses. Compounds of this type have not been described in the literature so far, with the exception of 2,6-dideoxy-2-fluoro-D-glucose¹. Taking into consideration the importance of deoxy sugars in natural substances, their fluoro derivatives are also of great interest, because the fluorine on carbon atom C₍₂₎ of aldoses affects their properties distinctly by impairing the cleaving of the glycoside bond^{1,2}.

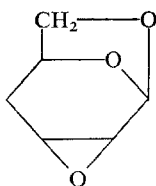
For the preparation of 3- or 4-deoxy derivatives of 2-deoxy-2-fluoro-D-glucose we considered two methods³: *a*) introduction of fluorine into the molecule of 1,6 : 2,3-dianhydro-4-deoxy- β -D-*lyxo*-hexopyranose (*I*) or of the corresponding D-*ribo*-derivative *II*, by cleaving their oxirane ring with potassium hydrogen fluoride in boiling ethylene glycol, and *b*) reductive cleavage of the oxirane ring of 1,6 : 3,4-dianhydro-2-deoxy-2-fluoro- β -D-*galacto*-pyranose (*VII*) or the similar D-*allo*-derivative *X*. The starting 4-deoxy-dianhydro derivatives *I* and *II* were prepared from 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl- β -D-galactopyranose⁴ according to literature^{5,6}, while 2-fluorodianhydro derivatives *VII* and *X* were obtained from 1,6-anhydro-4-O-benzyl-2-deoxy-2-fluoro- β -D-glucopyranose⁷ (*III*) in the following manner:

* Part XXVI in the series Syntheses with Anhydro Sugars; Part XXV: This Journal 40, 3038 (1975).

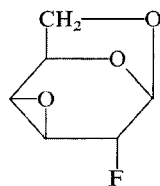
Benzyl ether *III* was reacted with acetic anhydride to give 3-O-acetyl-1,6-anhydro-4-O-benzyl-2-deoxy-2-fluoro- β -D-glucopyranose (*IV*) which was debenzylated on palladium on charcoal to 3-O-acetyl-1,6-anhydro-2-deoxy-2-fluoro- β -D-glucopyranose (*V*). From the compound *V* 3-O-acetyl-1,6-anhydro-2-deoxy-2-fluoro-4-O-*p*-toluenesulfonyl- β -D-glucopyranose (*VI*) was prepared on reaction with *p*-toluenesulfonyl chloride in pyridine, which was then converted to 2-fluoro-*galacto*-epoxide *VII* (ref.⁷) under the effect of sodium methoxide in chloroform. 2-Fluoro-*allo*-epoxide *X* was obtained from benzyl ether *III* which was converted first to 1,6-anhydro-4-O-benzyl-2-deoxy-2-fluoro-3-O-methanesulfonyl- β -D-glucopyranose (*VIII*) and then debenzylated catalytically to 1,6-anhydro-2-deoxy-2-fluoro-3-O-methanesulfonyl- β -D-glucopyranose (*IX*) and submitted to reaction with sodium methoxide.



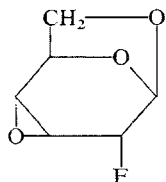
I



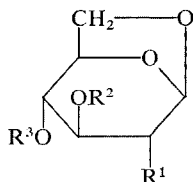
II



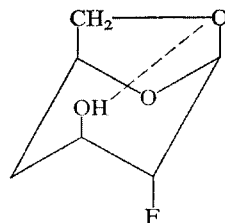
VII



X

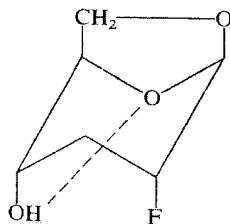


VIII

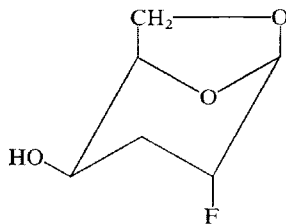


XI

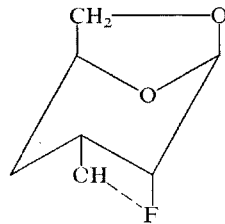
- III*; R¹ = F; R² = H; R³ = CH₂C₆H₅
IV; R¹ = F; R² = COCH₃; R³ = CH₂C₆H₅
V; R¹ = F; R² = COCH₃; R³ = H
VI; R¹ = F; R² = COCH₃; R³ = CH₃C₆H₄SO₂
VIII; R¹ = F; R² = CH₃SO₂; R³ = CH₂C₆H₅
IX; R¹ = F; R² = CH₃SO₂; R³ = H



XII

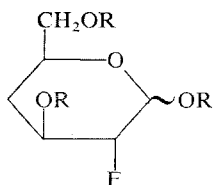


XIII

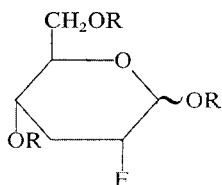


XIV

In orienting experiments aiming at the preparation of deoxyfluorohydrins *XI* and *XII* by cleavage of 4-deoxy epoxides *I* and *II* with potassium hydrogen fluoride in ethylene glycol we always found that the required products are indeed formed, but that the reaction is unexpectedly complicated⁷ by the formation of a considerable amount of by-products formed through the attack of ethylene glycol on the oxirane ring of 4-deoxy epoxides *I* and *II*. In contrast to this, for the preparation of deoxyfluorohydrins *XI* and *XII* reductive procedures were found suitable. Thus, in the case of 2-fluoro-*galacto*-epoxide *VII* catalytic reduction on Raney nickel in ethanol afforded 1,6-anhydro-2,4-dideoxy-2-fluoro- β -D-*xylo*-hexopyranose (*XI*) as the sole product, in 84% yield. The same compound *XI* was also formed as the main product during the reduction of derivative *VII* with lithium aluminum hydride in tetrahydrofuran. Catalytic reduction of 2-fluoro-*allo*-epoxide *X* took place very slowly, partly under simultaneous dehalogenation. From the reaction mixture 1,6-anhydro-2,3-dideoxy-2-fluoro- β -D-*ribo*-hexopyranose (*XII*) and 1,6-anhydro-2,3-dideoxy- β -D-*erythro*-hexopyranose (*XXIV*) were isolated in addition to the unreacted substance *X*; when lithium aluminum hydride was used 3-deoxyfluorohydrin *XII* was formed as the only product.



XV, R = COCH₃
XVI, R = H



XVII, R = COCH₃ (α -anomer)
XVIII, R = H

Acetylation of 1,6-anhydro derivatives *XI* and *XII* catalysed with perchloric acid gave tri-*O*-acetyl derivatives of *xylo*-*XV* and *ribo*-*XVII* configuration; the first was syrupy, while the second was crystalline α -anomer. Both were deacetylated to 2,4-dideoxy-2-fluoro-D-xylose (*XVI*) and 2,3-dideoxy-2-fluoro-D-ribose (*XVIII*). Deacetylation took place stepwise under formation of partially deacetylated products.

As the structures of fluorohydrins *XII* and *XIV* had been derived on the basis of the knowledge of the structure of 4-deoxyfluorohydrin *XI*, the greatest attention was devoted to the structure proof of compound *XI*. The measurement of hydrogen bonds in 4-deoxyfluorohydrin *XI* in tetrachloromethane demonstrated the existence of an intramolecular hydrogen bond which according to its properties was very similar to the hydrogen bond in 1,6-anhydro-2,4-dideoxy- β -D-*threo*-hexopyranose⁸ (*XXII*). The second isomeric fluoro derivative which might come into consideration, 1,6-anhydro-2,3-dideoxy-2-fluoro- β -D-*xylo*-hexopyranose (*XIII*), which would be formed by

a diequatorial cleavage of 2-fluoro-*galacto*-epoxide *VII*, cannot form an intramolecular bond, the same as 1,6-anhydro-2,3-dideoxy- β -D-*threo*-hexopyranose⁸ (*XXIII*) (Table I). The value $[\alpha]_D - 40^\circ$ (water), which is close to the value $[\alpha]_D - 39^\circ$ (water) of 1,6-anhydro-4-deoxy- β -D-*xyl*o-hexopyranose⁵ also corresponds to the structure of compound *XI*. This is in agreement with the view that the substitution of fluorine

TABLE I

Intramolecular Hydrogen Bonds in Deoxy Derivatives of 1,6-Anhydro- β -D-hexopyranoses

The measurement of hydrogen bonds was carried out in 2 and 4 cm thick cells at concentrations of about $3 \cdot 10^{-3} M$ in tetrachloromethane.

Substance	$\nu_{(\text{OH})}$ bound cm^{-1}	$\nu_{(\text{OH})}$ free cm^{-1}	$\Delta\nu_{(\text{OH})}$ cm^{-1}	Reference
<i>XI</i>	3 581	3 622	41	this paper
<i>XXII</i>	3 576	3 624	48	8
<i>XXIII</i>	—	3 626	0	8
<i>XII</i>	3 589	—	35 ^a	this paper
<i>XXIV</i>	3 585	3 626	41	8
<i>XIV</i>	3 601	—	23 ^a	this paper
<i>XXV</i>	—	3 624	0	8

^a Referred to the value $\nu_{(\text{OH})\text{free}} 3624 \text{ cm}^{-1}$.

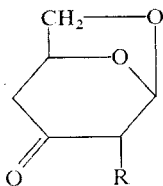
TABLE II

Optical Properties of 3-Keto Derivatives *XIX*–*XXI*

Compound	IR $\nu_{(\text{CO})}$ CHCl_3	CD ($\Delta\epsilon$) (λ_{max} , nm)	$[\alpha]_D^{25}$ CHCl_3	Reference
<i>XIX</i>	1 730	–0.273 (295) dioxane	–103°	8, 10
		–0.156 (298) cyclohexane	(<i>c</i> 0.8)	
<i>XX</i>	1 745	–1.32 (308) dioxane	–106°	this paper
		–1.62 (310) cyclohexane	(<i>c</i> 0.79)	
<i>XXI</i>	1 745	–0.58 ^a (307) dioxane	–13.5° (<i>c</i> 1.04)	11

^a This paper.

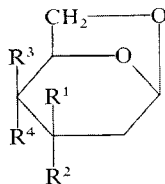
for the hydroxyl group does not cause a change in optical rotation⁹. On oxidation of 4-deoxyfluorohydrin *XI* with chromium trioxide in acetic acid 1,6-anhydro-2,4-dideoxy-2-fluoro- β -D-erythro-hexopyranos-3-ulose (*XX*) was obtained in 76% yield. The properties of this substance, the structure of which was proved by ¹H-NMR spectrometry, are similar, to a certain extent, to those of 1,6-anhydro-4-deoxy-2-O-*p*-toluenesulfonyl- β -D-erythro-hexopyranos-3-ulose (*XXI*), see Table II. Keto derivative *XX* gives a high Cotton effect in CD measurements, similarly as tosyl ketone *XXI*, which is in both cases in contradiction to the octant rule. An independent chemical proof of the structure of 4-deoxyfluorohydrin *XI* follows from the fact that this compounds is formed both on reduction of 2-fluoro-*galacto*-epoxide *VII*, and on reaction of 4-deoxy-*lyxo*-epoxide *I* with potassium hydrogen fluoride.



XIX, R = H

XX, R = F

XXI, R = OSO₂C₆H₄CH₃



XXII, R¹ = OH; R² = R³ = R⁴ = H

XXIII, R³ = OH; R¹ = R² = R⁴ = H

XXIV, R⁴ = OH; R¹ = R² = R³ = H

XXV, R² = OH; R¹ = R³ = R⁴ = H

The structure of 4-deoxyfluorohydrin *XIV* follows from its formation from fluorohydrin *XI* by oxidation and subsequent reduction of fluoro ketone *XX* with sodium borohydride. The correctness of the structure proposed for 3-deoxyfluorohydrin (*XII*) is supported by the fact that this compound was formed by diaxial cleavage of dianhydro derivative *X*, and the 3-deoxyfluorohydrin (*XII*) formed possesses different properties from those of the second isomer considered, *XIV*, which would be formed by the less probable diequatorial cleavage. After acetolysis of 3-deoxyfluorohydrin *XII* we isolated triacetyl derivative *XVII* the ¹H-NMR spectrum of which was in accordance with the supposed structure. The results of the measurements of hydrogen bond and of optical rotation also supported the above considered structures of fluorohydrins *XII* and *XIV*.

EXPERIMENTAL

The melting points were determined on a micromelting point Boëtius apparatus. Optical rotation was measured at 23–25°C on an automatic polarimeter Bendix-Ericsson, type 143 A. ¹H-NMR spectra were measured on a Varian HA 100 instrument, infrared spectra on a Zeiss UR 20 spectrophotometer, and CD spectra on the Roussel-Jouan Dichrograph. The hydrogen bonds were measured on a Unicam SP 700 apparatus. Thin layer chromatography was carried out on silica gel with 7% gypsum, in benzene-acetone (9 : 1), unless stated otherwise; detection

was carried out by spraying the chromatograms with 50% sulfuric acid and heating. For gas chromatography a Chrom II apparatus (Laboratorní přístroje) with a column 182 cm long and 4 mm i.d., packed with Chromosorb W-AW, 60–80 mesh, coated with 10% Carbowax 20 M was used. The solutions were concentrated under reduced pressure on a rotatory evaporator, and the samples for analysis were dried over phosphorus pentoxide.

3-O-Acetyl-1,6-anhydro-4-O-benzyl-2-deoxy-2-fluoro- β -D-glucopyranose (IV)

A mixture of 8 g of benzyl ether *III* (ref.⁷), 8 g of anhydrous sodium acetate, and 100 ml of acetic anhydride was refluxed for 15 minutes, then decomposed with water and the aqueous solution was extracted repeatedly with chloroform. The combined chloroform extracts were washed with sodium hydrogen carbonate solution and water; the chloroform extract was dried over magnesium sulfate, filtered, and concentrated. After addition of ether 7.7 g (83%) of product was obtained, m.p. 68–69°C, $[\alpha]_D -20^\circ$ (*c* 0.77, CHCl₃). For C₁₅H₁₇FO₅ (296.3) calculated: 60.80% C, 5.78% H, 6.14% F; found: 61.05% C, 5.95% H, 6.15% F.

3-O-Acetyl-1,6-anhydro-2-deoxy-2-fluoro- β -D-glucopyranose (V)

Benzyl ether *IV* (7.5 g) and 1.6 g of 10% palladium on charcoal were suspended in 80 ml of ethanol and hydrogenated at 50°C. When hydrogen absorption ceased the catalyst was filtered off and washed with ethanol and the filtrate was concentrated. 5.2 g (99%) of product were isolated, which was recrystallized from acetone–ether, m.p. 102–105°C, $[\alpha]_D -67^\circ$ (*c* 0.71, chloroform). For C₈H₁₁FO₅ (206.1) calculated: 46.60% C, 5.38% H, 9.22% F; found: 46.81% C, 5.42% H, 9.20% F.

3-O-Acetyl-1,6-anhydro-2-deoxy-2-fluoro-4-O-*p*-toluenesulfonyl- β -D-glucopyranose (VI)

p-Toluenesulfonyl chloride (5 g) was added to a solution of 5 g of acetate *V* in 35 ml of pyridine under stirring and cooling with ice. After 72 hours the mixture was poured into water under stirring. The solid precipitate was filtered off and dried in air. Yield, 7.3 g (84%) of product which was crystallized from ethanol–water, m.p. 109–110°C, $[\alpha]_D -72^\circ$ (*c* 0.77, chloroform). For C₁₅H₁₇FO₇S (360.4) calculated: 49.99% C, 4.76% H, 5.27% F, 8.90% S; found: 50.24% C, 4.83% H, 5.47% F, 8.75% S.

1,6 : 3,4-Dianhydro-2-deoxy-2-fluoro- β -D-galactopyranose (VII)

Methanol containing 1 g of dissolved sodium (20 ml) was added dropwise under stirring and cooling to a solution of 7 g of tosyl ester *VI* in 30 ml of chloroform and the mixture was allowed to stand at room temperature for 18 hours. It was poured into water, the chloroform layer was separated and the aqueous layer extracted with 6 small portions of chloroform. The extract was washed with water, dried over magnesium sulfate and filtered, and the solvent distilled off. Yield, 2.7 g (95%) of product, which was crystallized from a mixture of ether and light petroleum, m.p. 26–29°C, $[\alpha]_D -61^\circ$ (*c* 0.77, chloroform). Literature⁷ gives m.p. 26–28°C, $[\alpha]_D -63^\circ$ (*c* 0.8, chloroform).

1,6-Anhydro-4-O-benzyl-2-deoxy-2-fluoro-3-O-methanesulfonyl- β -D-glucopyranose (VIII)

Methanesulfonyl chloride (6 ml) was added dropwise under stirring at –20°C to a solution of 9.5 g of benzyl ether *III* in 35 ml of pyridine and the reaction mixture was allowed to stand in a refrigerator for 18 hours. After pouring into a water–ice mixture 11.8 g (94%) of a product

has separated which was crystallized from a mixture of ethanol and water, m.p. 65–66°C, $[\alpha]_D + 4^\circ$ (*c* 0.75, chloroform). For $C_{14}H_{17}FO_6S$ (322.3) calculated: 50.59% C, 5.15% H, 5.72% F, 9.65% S; found: 50.85% C, 5.45% H, 5.49% F, 9.66% S.

1,6-Anhydro-2-deoxy-2-fluoro-3-O-methanesulfonyl- β -D-glucopyranose (IX)

Four grams of 10% palladium on charcoal were added to a solution of 11 g of mesyl ester VIII in 110 ml of ethanol and the mixture was hydrogenated at 50°C to completion. The catalyst was filtered off and the solvent evaporated. The residue (8 g; 97%) was crystallized from a mixture of ethanol and light petroleum, m.p. 66–67°C, $[\alpha]_D - 45^\circ$ (*c* 0.75, chloroform). For $C_7H_{11}FO_6S$ (242.2) calculated: 34.71% C, 4.85% H, 7.84% F, 13.24% S; found: 34.96% C, 4.55% H, 7.51% F, 13.45% S.

1,6 : 3,4-Dianhydro-2-deoxy-2-fluoro- β -D-allopyranose (X)

A solution of 1.5 g of sodium in 20 ml of methanol was added dropwise under stirring and cooling with ice to a solution of 7.5 g of mesyl ester IX in 60 ml of chloroform. The mixture was allowed to stand at room temperature for 18 hours and then poured into water. The chloroform layer was separated and the aqueous layer extracted several times with chloroform. The chloroform extracts were washed, dried and evaporated, to yield 3.75 g (83%) of a product which after crystallization from ether–light petroleum had m.p. 92–94°C, $[\alpha]_D - 118^\circ$ (*c* 0.79, chloroform). For $C_6H_7FO_3$ (146.1) calculated: 49.32% C, 4.83% H, 13.00% F; found: 49.35% C, 4.87% H, 13.04% F.

1,6-Anhydro-2,4-dideoxy-2-fluoro- β -D-xylo-hexopyranose (XI)

a) A solution of 250 mg of 2-fluoro-*galacto*-epoxide VII in 5 ml of ethanol, and 5 ml of a suspension of Raney nickel T 1¹² in ethanol were hydrogenated at about 50°C for 20 hours. Thin layer chromatography indicated that the reaction mixture contained in addition to traces of the unreacted starting material (VII; R_F 0.58) only substance XI (R_F 0.27). Gas chromatography ($T_c = 175^\circ C$, $T_i = 220^\circ C$, carrier gas N_2 50 ml/min) demonstrated the presence of 4-deoxy-fluorohydrin XI, $t_r = 10.3$ min. The catalyst was filtered off through a small column of charcoal and the filtrate was concentrated. Yield 213 mg (84%) of product XI which after crystallization from ether–light petroleum melted at 91–94°C, $[\alpha]_D - 40^\circ$ (*c* 0.79, water). For $C_6H_9FO_3$ (148.1) calculated: 48.65% C, 6.12% H, 12.83% F; found: 48.74% C, 6.04% H, 12.83% F.

b) Lithium aluminum hydride (110 mg) in 4 ml of tetrahydrofuran was added to a solution of 250 mg of 2-fluoro-*galacto*-epoxide VII in 4 ml of tetrahydrofuran and the mixture was heated at 40°C. Thin layer chromatography in chloroform–ether (4 : 1) showed that after 3.5 hours' reaction time the spot corresponding to the starting substance had disappeared (R_F 0.85) and that the mixture contained substance XI (R_F 0.37) as the main product, and further a substance of R_F 0.21. Gas chromatography ($T_c = 175^\circ C$, $T_i = 220^\circ C$, carrier gas N_2 50 ml/min) indicated that the crude reaction mixture contained small amounts of three substances in addition to the main product XI (t_r 10.2 min). These three substances were not identified ($t_r = 3.75, 4.1, 5.5$ min). The reaction mixture was decomposed with water and concentrated in a flask. The residue was extracted with five 5 ml portions of chloroform, the extract was dried over calcium chloride, filtered and concentrated. The residue, 230 mg, was chromatographed on a column of silica gel with chloroform–ether (85 : 15). Combination of corresponding fractions gave 131 mg (52%) of 4-deoxyfluorohydrin XI, m.p. 91–98°C, $[\alpha]_D - 41^\circ$ (*c* 0.7, water).

c) A mixture of 5 g of 4-deoxy-*lyxo*-epoxide *I* (ref.⁵), 19 g of potassium hydrogen fluoride, and 170 ml of ethylene glycol was refluxed for two hours under nitrogen. On standing in a refrigerator inorganic salts separated which were filtered off and washed with a mixture of ethanol and acetone. The filtrate was concentrated under reduced pressure, the residue was extracted with ethanol-acetone and the precipitated inorganic salts were again filtered off. The filtrate was concentrated to give 5.8 g of product. Thin layer chromatography in ethanol-dioxane-benzene-ammonia (8 : 40 : 50 : 5) proved the presence of a compound of R_F 0.8 and another of R_F 0.5 in the mixture, while the starting compound *VII* could not be proved. Chromatography of 4.5 g of this product in 100 g of silica gel in chloroform with 3% of methanol afforded 400 mg of the substance of R_F 0.8, which crystallized out after several weeks' standing. After decoloration with charcoal and recrystallization from ether-light petroleum 4-deoxyfluorohydrin *XI*, m.p. 90–94°C, $[\alpha]_D -42^\circ$ (c 0.84, water) was obtained.

1,6-Anhydro-2,3-dideoxy-2-fluoro- β -D-*ribo*-hexopyranose (*XII*)

a) A suspension of 110 mg of lithium aluminum hydride in 3 ml of tetrahydrofuran was added to a solution of 250 mg of 2-fluoro-*allo*-epoxide *X* in 3 ml of tetrahydrofuran and the mixture was heated at 40°C. The reaction course was followed by thin layer chromatography. After 25 minutes only the spot belonging to the product *XII* (R_F 0.29) could be detected. In gas chromatography ($T_c = 175^\circ\text{C}$, $T_i = 220^\circ\text{C}$, carrier gas N_2 50 ml/min) it had $t_r = 5.2$ min. The mixture was decomposed with water, the solution evaporated and extracted with five 5 ml portions of chloroform. After drying the chloroform solution and distilling it off 220 mg (86%) of an oil were obtained. After distillation at 55°C/0.1 Torr it gave a product which crystallized out, m.p. 91–93°C (at about 50°C it sublimes), $[\alpha]_D -80^\circ$ (c 0.7, water). For $\text{C}_6\text{H}_9\text{FO}_3$ (148.1) calculated: 48.65% C, 6.12% H, 12.83% F; found: 48.43% C, 6.09% H, 12.89% F.

b) Raney nickel T 1 suspension (7 g; ref.¹²) was added to a solution of 250 mg of 2-fluoro-*allo*-epoxide *X* in 5 ml of ethanol and the mixture was hydrogenated at about 50°C. Thin layer chromatography indicated that after 20 hours the reaction mixture contained the starting compound *X* (R_F 0.55), 1,6-anhydro-2,3-dideoxy-2-fluoro- β -D-*ribo*-hexopyranose (*XII*) (R_F 0.35) and compound of R_F 0.22 which appears first on detection. The catalyst was filtered off using a small column of celite and the filtrate was evaporated affording 202 mg of crude mixture. This was chromatographed on 24 g of silica gel in benzene-acetone (95 : 5), giving 85 mg of epoxide *X*, 38 mg of 3-deoxyfluorohydrin *XII* and 34 mg of 1,6-anhydro-2,3-dideoxy- β -D-*erythro*-hexopyranose (*XXIV*). The optical rotations of dideoxy alcohol *XXIV*, $[\alpha]_D -117^\circ$ (c 0.66, chloroform), and its IR spectrum (chloroform) were identical with those of an authentic specimen⁸. Quantitative analysis of the reaction mixture by gas chromatography ($T_c = 172^\circ\text{C}$, $T_i = 230^\circ\text{C}$, carrier gas N_2 50 ml/min) gave the following: 1,6-anhydro-2,3-dideoxy-2-fluoro- β -D-*ribo*-hexopyranose (*XII*) 23%, 1,6-anhydro-2,3-dideoxy- β -D-*erythro*-hexopyranose (*XXIV*) 32.6%, 1,6 : 3,4-dianhydro-2-deoxy-2-fluoro- β -D-allopyranose (*X*) 44.5%.

1,6-Anhydro-2,4-dideoxy-2-fluoro- β -D-*ribo*-hexopyranose (*XIV*)

A solution of 0.47 g of fluoro ketone *XX* in 6 ml of ethanol was added under stirring to a suspension of 179 mg of sodium borohydride in 10 ml ethanol. Thin layer chromatography showed that a substance of R_F 0.18 was formed as the main product, containing a very small amount of an impurity of R_F 0.29. The starting compound could not be detected. The solution was demineralized by addition of Amberlite IR 120, concentrated, and the residue dissolved in methanol and the solution was again concentrated. Yield, 360 mg of a syrup (75%) which was purified with charcoal and crystallized from a mixture of ether and light petroleum giving 276 mg (58%)

of compound *XIV*, m.p. 85–88°C, sublimes, $[\alpha]_D -23^\circ$ (*c* 0.77, water). For $C_6H_9FO_3$ (148.1) calculated: 48.65% C, 6.12% H, 12.83% F; found: 48.56% C, 6.13% H, 13.05% F. Gas chromatography ($T_c = 176^\circ C$, $T_i = 190^\circ C$, carrier gas N_2 35 ml/min) $t_r = 12.2$ min.

1,3,6-Tri-O-acetyl-2,4-dideoxy-2-fluoro-D-xylo-hexopyranose (*XV*)

A solution of 0.64 g of 4-deoxyfluorohydrin *XI* in 10 ml of acetic anhydride containing 0.1 ml of 70% perchloric acid was allowed to stand at room temperature and the reaction course was followed by gas chromatography. After 24 hours' standing the mixture was diluted with water under cooling, then extracted with several portions of chloroform and the extracts were washed with a sodium hydrogen carbonate solution and water. After drying over calcium chloride and filtration the filtrate was evaporated to yield 1.24 g (94%) of syrupy triacetyl derivative *XV*.

2,4-Dideoxy-2-fluoro-D-xylo-hexopyranose (*XVI*)

Sodium (20 mg) dissolved in 7 ml of ethanol was added dropwise to a solution of 1.22 g of triacetyl derivative *XV* in 10 ml of ethanol and after 10 minutes another portion of sodium (20 mg) in 7 ml of ethanol was added to it. The mixture was allowed to stand for 6 hours and then analysed by thin-layer chromatography. At the beginning of the reaction in addition to product *XVI* (R_F 0.07) another substance is also formed, with R_F 0.3, which is probably the partly deacetylated intermediate and which gradually disappears. The neutralization was carried out by addition of Amberlite IR 120. The ion exchanger was filtered off, the filtrate was decolorized with charcoal and concentrated. The syrupy residue weighed 0.84 g and it was chromatographed on a cellulose column (about 300 g) with 1-butanol saturated with water. Combination and evaporation of corresponding fractions gave 320 mg (45%) of syrupy 2,4-dideoxy-2-fluoro-D-xylo-hexopyranose (*XVI*). Paper chromatography was carried out on paper Whatman No 1 in 1-butanol-acetic acid-water (4 : 1 : 5), for detection ammoniacal silver nitrate was used. R_{rel} (with respect to 2-deoxy-D-ribose) was 1.08.

1,4,6-Tri-O-acetyl-2,3-dideoxy-2-fluoro- α -D-ribo-hexopyranose (*XVII*)

A solution of 0.75 g of 3-deoxyfluorohydrin *XII* in 11 ml of acetic anhydride, containing 1 ml of 70% perchloric acid, was allowed to stand at room temperature for 24 hours. When the mixture was poured onto ice substance *XVII* precipitated partly and it was filtered off under suction. The filtrate was extracted with chloroform and the extract was washed with sodium hydrogen carbonate and water, then dried over calcium chloride and the solvent was distilled off. Both parts were combined to give 1.2 g (81%) of crude product *XVII*, m.p. 55–85°C, which increased after crystallization from ether-light petroleum to m.p. 85–88°C, $[\alpha]_D +116^\circ$ (*c* 0.73, chloroform). For $C_{12}H_{17}FO_7$ (292.1) calculated: 49.31% C, 5.86% H, 6.50% F; found: 49.36% C, 5.80% H, 6.40% F. 1H -NMR spectrum (in $CDCl_3$, chemical shifts in δ -values (p.p.m.), tetramethylsilane as internal reference; *J* in Hz): 6.28 (H-1, $J_{1,2} = 3.7$, $J_{1,F} = 0$) 4.86 (H-4, $J_{4,3} = 11.4 + 5.0$, $J_{4,5} = 10.5$, $J_{4,F} = 1.4$), 4.73 (H-2, $J_{2,F} = 47$, $J_{2,1} = 3.7$, $J_{2,3} = 12.2 + 5.3$), 4.27 (H-6, $J_{6,6} = 12.3$, $J_{6,5} = 4.6$), 4.09 (H-6, $J_{6,6} = 12.3$, $J_{6,5} = 2.5$), 3.95 (H-5, $J_{5,6} = 2.5 + 4.6$, $J_{5,4} = 10.5$), 2.18 (1 \times $OCOCH_3$), 2.07 (2 \times $OCOCH_3$), 1.95–2.75 (2 \times H-3) partly overlapped with $-OCOCH_3$ signals.

2,3-Dideoxy-2-fluoro-D-ribo-hexopyranose (*XVIII*)

Sodium (30 mg) dissolved in 10 ml of ethanol was added dropwise to a solution of 0.63 g of acetyl derivative *XVII* in 12 ml of ethanol and the reaction was followed by thin layer chromatography.

graphy in tetrachloromethane-ether (3 : 2). After one hour's standing at room temperature it was found that in addition to the product *XVIII* (R_F 0.09) the mixture also contained a substance of R_F 0.33, probably the partly deacetylated intermediary product. After several hours' standing the mixture was neutralized with Amberlite IR 120 and concentrated, giving 400 mg of a syrup. Paper chromatography (Whatman No 1; 1-butanol-acetic acid-water 4 : 1 : 5; for detection ammoniacal silver nitrate was used): R_{rel} (with respect to 2-deoxy-D-ribose) 1:37.

1,6-Anhydro-2,4-dideoxy-2-fluoro- β -D-erythro-hexopyranos-3-ulose (*XX*)

Chromium trioxide (0.6 g) in water (0.9 ml) was added to a solution of 0.6 g of 4-deoxyfluorohydrin *XI* in 4.5 ml of glacial acetic acid, and the mixture was allowed to react at room temperature. Its course was followed by thin-layer chromatography. After 5 hours of oxidation the starting compound *XI* disappeared. The mixture was poured into water and extracted four times with chloroform. The extract was washed with sodium hydrogen carbonate and water, dried over calcium chloride, and the solvent was distilled off. The residue (0.47 g; 76%) was ketone *XX* which was distilled, b.p. 45°C/0.07 Torr; $[\alpha]_D - 106^\circ$ (c 0.79, chloroform). For $C_6H_7FO_3$ (146.1) calculated: 49.32% C, 4.83% H, 13.00% F; found: 49.39% C, 4.83% H, 12.78% F. IR spectrum (chloroform): ν_{CO} 1745 cm^{-1} ; CD: see Table II; gas chromatography ($T_c = 176^\circ C$, $T_i = 204^\circ C$, carrier gas N_2 31 ml/min): t_r 5.7 min. 1H -NMR spectrum (deuterioacetonitrile, hexamethyl-disiloxan as internal standard, chemical shifts in δ -values (p.p.m.), J in Hz): 5.63 (H-1, $J_{1,2} = 1.9$, $J_{1,F} = 2.0$), 4.83 (H-5, $J_{4ax,5} = 5.6$, $J_{4eq,5} = 1.3$, $J_{5,6endo} = 0.5$, $J_{5,6exo} = 4.0$), 4.20 (H-2, $J_{1,2} = 1.9$, $J_{2,F} = 49.0$), 3.75 (H-6 $_{endo}$, $J_{6,6} = 7.8$, $J_{5,6endo} = 0.5$), 3.64 (H-6 $_{exo}$, $J_{6,6} = 7.8$, $J_{5,6exo} = 4.0$), 2.91 (H-4 $_{ax}$, $J_{4,4} = 17.7$, $J_{4ax,5} = 5.6$), 2.40 (H-4 $_{eq}$, $J_{4,4} = 17.7$, $J_{4eq,5} = 1.3$).

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