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Reaction of Sugar Esters with Hydrogen Fluoride. XIV. Rearrangement of D-Xylose and D-Lyxose Derivatives

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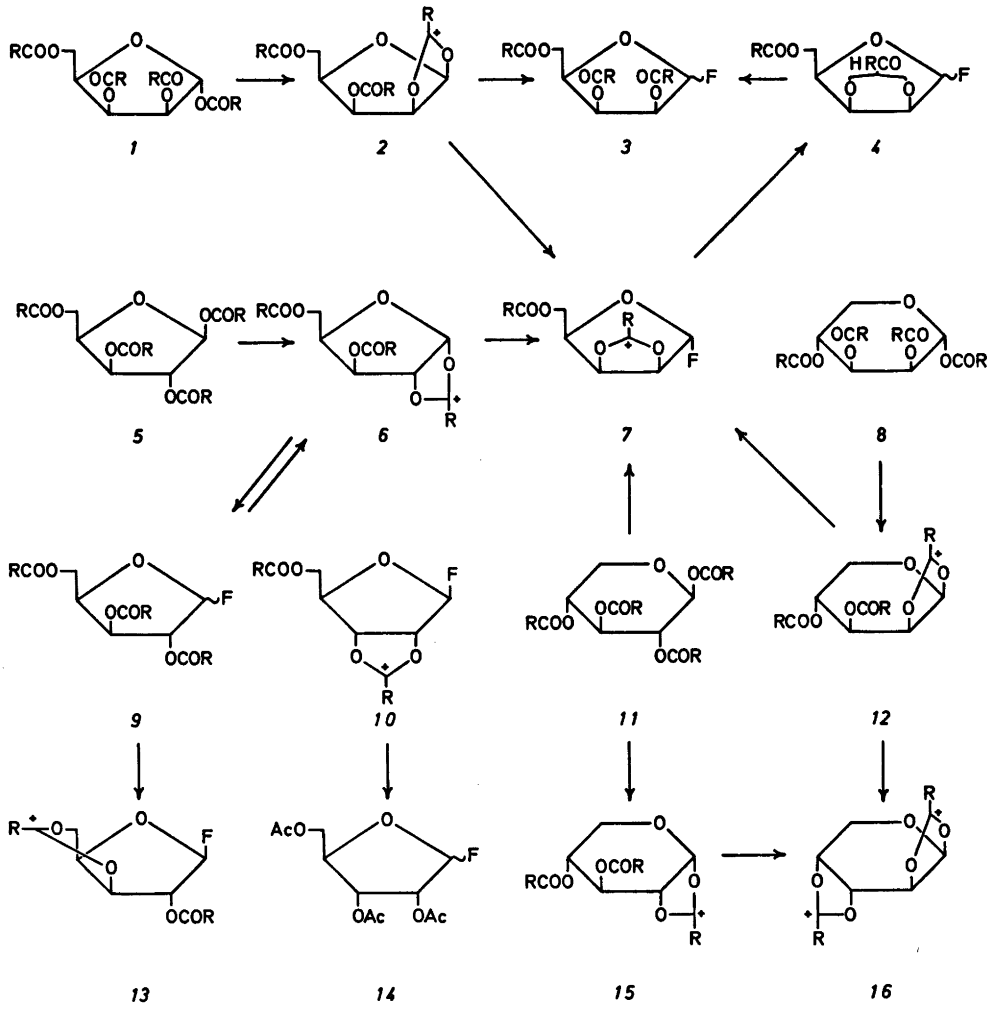
Prolonged treatment of tetra-*O*-benzoyl-α-D-xylofuranose with anhydrous hydrogen fluoride gave tri-*O*-benzoyl-α-D-lyxofuranosyl fluoride. Reaction of the tetraacetates of D-xylofuranose, D-lyxofuranose, D-xylopyranose, and D-lyxopyranose with hydrogen fluoride yielded complicated mixtures of products, which were analyzed by ^{19}F NMR spectroscopy. ^{13}C NMR spectra of some dioxolanylium ions have been measured in hydrogen fluoride solution.

In previous papers the reaction of benzoylated xylo- and lyxo-pyranoses with anhydrous hydrogen fluoride (HF) was described.[1,2] Tetra-O-benzoyl-β-D-xylopyranose (*11b*) was completely converted into a dibenzoxonium ion (*16b*) derived from D-arabinopyranose.[1] Tetra-*O*-benzoyl-α-D-lyxopyranose (*8b*) gave the same ion; but in addition it underwent ring-contraction to a lyxofuranose derivative.[2] Benzoylated and acetylated ribo- and arabino-pyranoses were converted to ribofuranose derivatives on prolonged treatment with HF.[3] In order to get a complete picture of the behaviour of pentose esters towards HF the reactions of some additional derivatives of xylose and lyxose have now been investigated.

A solution of tetra-*O*-benzoyl-α-D-lyxofuranose (*1b*) in anhydrous HF was kept at +5 °C and ^1H NMR spectra were measured at intervals. The tetrabenzoate (*1b*) reacted immediately in HF to form a product the ^1H NMR spectrum of which could not be analyzed. A ^{13}C NMR spectrum (Table 3), however, showed that it must be the 1,2-benzoxonium ion (*2b*).[4] Hydrolysis of the HF solution after 15 min gave a good yield of tri-*O*-benzoyl-α-D-lyxofuranosyl fluoride (α-*3b*). When (*1b*) was kept in HF for 4 days at +5 °C, or for *ca.* 24 h at room temperature, the initially formed ion (*2b*) disappeared and the 2,3-benzoxonium ion (*7b*) was formed as the sole product as seen from NMR spectra (Tables 1 and 3). When this solution was hydrolysed it gave a mixture of dibenzoylated lyxofuranosyl fluorides (*4b*). Benzoylation yielded (α-*3b*) and a small amount of the corresponding β-anomer (β-*3b*).

When tetra-*O*-benzoyl-β-D-xylofuranose (*5b*) was dissolved in HF at 0 °C it reacted at once and gave the 1,2-benzoxonium ion (*6b*). The ^1H NMR spectrum of this ion could not be analyzed, but ^{13}C NMR data are presented in Table 3. Hydrolysis gave a good yield of tri-*O*-benzoyl-β-D-xylofuranosyl fluoride (β-*9b*). When (*5b*) was kept in HF it underwent further reaction and after *ca.* 24 h at room temperature it was completely converted into a product which, as seen from ^1H NMR spectra of the solution, contained the 2,3-benzoxonium ion (*7b*), identical with the ion described above. However, hydrolysis and subsequent benzoylation gave a mixture of tri-*O*-benzoyl-α-D-lyxofuranosyl fluoride (α-*3b*) and tri-*O*-benzoyl-β-D-xylofuranosyl fluoride (β-*9b*) in a ratio of 2.3:1. The two products could not be separated but were identified through their ^1H and ^{19}F NMR spectra. The xylofuranosyl fluoride is not formed from unreacted (*6b*). Probably some 3,5-benzoxonium ion (*13b*) is formed together with the 2,3-ion (*7b*). Hydrolysis and benzoylation of (*13b*) will then give the tribenzoylated fluoride (β-*9b*).

The reaction of tetrabenzoyl-α-D-lyxopyranose (*8b*) with HF, which has been investigated previously,[2] has now been followed by NMR spectroscopy. A solution of (*8b*) in HF immedi-



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a, R= CH_3

b, R= C_6H_5

ately formed a compound which was different from the known tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride.[2] Its spectrum could not be analyzed, but it is assumed to be the 1,2-benzoxonium ion (*12b*). On further reaction with HF for *ca.* 200 h at +5 °C (*12b*) was converted into a mixture of the 2,3-benzoxonium ion (*7b*) and the dibenzoxonium ion (*16b*). Hydrolysis at this stage has been shown to give products that may be derived from these ions.[2]

Thus the reaction of benzoylated xylo- and lyxo-furanoses, with HF is similar to the reaction of benzoylated or acetylated arabino- and ribofuranoses, which give the 2,3-dioxolanylium ion (*10*).[5] This ribofuranose ion is also formed as the only detectable product when acetylated or benzoylated arabino- and ribo-pyranoses are subjected to prolonged treatment with HF.[3] The benzoylated xylo- and lyxo-pyranoses react differently, the former giving no furanose derivative at all.[1]

Table 1. ^{1}H and ^{19}F chemical shifts and observed first order coupling constants of some pentofuranose derivatives. The pentosyl fluorides were measured in deuteriochloroform solution, the ions (*6* and *7*) in anhydrous HF.

Compound	H1	H2	H3	H4	H5, H5′	Φ_F	J_{1F}	J_{2F}	J_{4F}	J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	
α-3a						−122	63.0	10.0	0						
β-3a						−128.7	67.0	22.5	6.5						
α-3b	6.03	5.83	6.09	5.06	4.6−4.8	−121.0	61.0	8.5	2.2	0.8	5.4	6.0	6.0	6.0	$J_{13}=0.6$
β-3b	6.10	5.48	6.21	5.00	4.6−4.8	−133.8	67.0	21.5	6.0	3.5	5.8	5.8	6.0	6.0	
α-9a	5.95	5.13	5.56	4.74	4.31,4.13	−134.8	61.8	17.2	1.4	3.6	6.5	6.5	4.8	4.1	$J_{55'}=-12.4$
β-9b	5.96	5.67	5.95	5.09	4.5−4.8	−118.5	61.5	4.5	6.0			5.8	6.0	6.0	
α-14a						−133.1	67.7	20.7							
β-14a						−116.6	61.8	4.2	6.9						$J_{3F}=2.3$
6a	7.42	6.08	5.90							4.8	≃0	3.6			$H_3C-C^+=2.90$
7a	6.27	6.1−6.6		5	4.5−4.8		55			≃0					$H_3C-C^+=2.90$
7b	6.58	6.3−6.8		5.6	5.1−5.3		55			≃0					

In view of this it was of interest also to study the reaction of acetylated xyloses and lyxoses with HF.

Treatment of these acetates with HF for 48 h followed by acetylation gave complex mixtures of products which were not separated. ^{1}H NMR spectra of these mixtures were very complex; but since most of the products were glycosyl fluorides they could be conveniently analysed by ^{19}F NMR spectroscopy. Glycosyl fluorides give simple ^{19}F spectra with a wide range of chemical shifts,[6,7] and signals do therefore usually not overlap. Furthermore, the ^{19}F spectra were measured by pulsed Fourier technique allowing the detection of small amounts of products. In Fig. 1 is shown the ^{19}F NMR spectrum of the mixture of acetylated glycosyl fluorides which was obtained when tetra-*O*-acetyl-α-D-lyxopyranose was treated with anhydrous HF for 48 h.

When tri-*O*-acetyl-α-D-xylofuranosyl fluoride (*9a*) was dissolved in HF at +5 °C it gave at once the 1,2-acetoxonium ion (*6a*) as seen from an NMR spectrum of the solution (Table 1). When the HF solution was kept at +5 °C or at room temperature further reactions took place. When the reaction was finished after *ca.* 24 h a rather complex ^{1}H NMR spectrum was obtained. It indicated, however, that the 2,3-acetonium ions (*7a* and *10a*) were present; their signals are given in Table 1. Hydrolysis of the HF solution after 48 h reaction and acetylation of the product gave a mixture of tri-*O*-acetyl-pentosyl fluorides, which were analyzed by ^{19}F NMR spectroscopy.

It was found (Table 2) that almost equal amounts of lyxo-(*3a*) and ribo-furanosyl fluorides (*14a*) were obtained. The formation of lyxofuranosyl fluorides is analogous to the behaviour of tetra-*O*-benzoyl-D-xylofuranose (see above) and may be explained through a mechanism similar to that proposed for the rearrangement of arabinofuranose into ribofuranose derivatives.[5] The rearrangement of *9a* into a ribofuranosyl fluoride, involving an inversion at C3 and formation of the ion *10a*, was unexpected and is not in agreement with the behaviour of other sugar esters towards HF.

Treatment of tetra-*O*-acetyl-α-D-lyxofuranose (*1a*) with HF for 48 h gave a similar result, however, smaller amounts of ribofuranosyl fluorides were found (Table 2). The acetylated

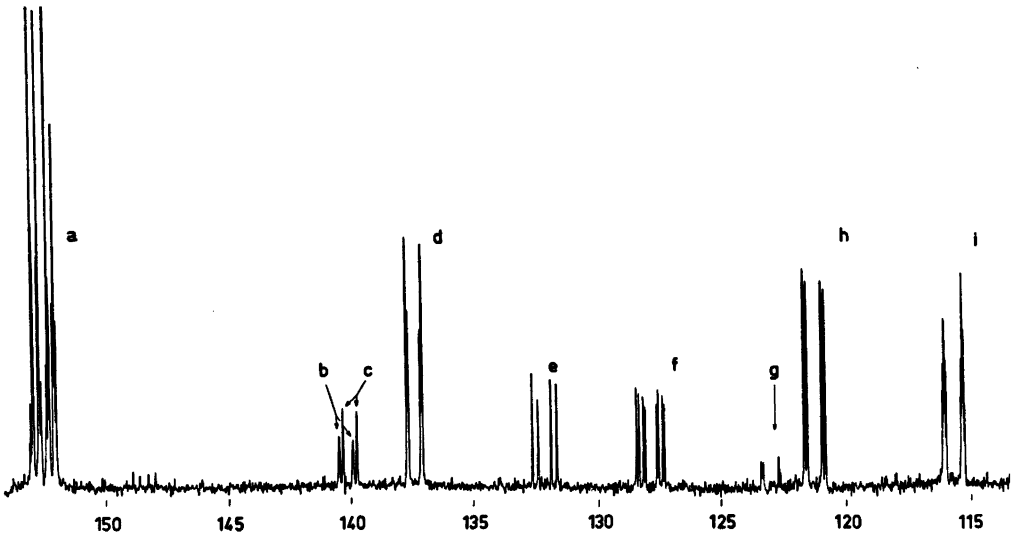

Fig. 1. ^{19}F NMR spectrum of a mixture of acetylated pentosyl fluorides. *a*, β-Ara*p*; b, β-Rib*p*; c, α-Lyx*p*; d, α-Ara*p*; e, α-Rib*f*; f, β-Lyx*f*; g, β-Ara*f*; h, α-Lyx*f*; i, β-Rib*f*.

xylo- and lyxo-pyranoses (*8a* and *11a*) were treated with HF for 48 h. This gave a very complex mixture of glycosyl fluorides (Table 2). In both cases considerable amounts of tri-*O*-acetyl-ribofuranosyl fluorides were formed, showing that the two acetates (*8a* and *11a*) react to some extent differently from the corresponding benzoates.

In view of the unexpected formation of ribofuranosyl fluorides from the acetates of xylose and lyxose it was decided to reinvestigate the reaction of acetylated arabinose and ribose with HF, using the rather sensitive ^{19}F NMR spectroscopy to analyse the products. The results (Table 2) are in agreement with those found previously [3,5] and show that both the acetylated pyranoses and furanoses give ribofuranosyl fluorides on prolonged treatment with HF. Small amounts of lyxofuranosyl fluorides were, however, also detected.

It should be pointed out that since the reaction mixtures resulting from the treatment of acetylated pentoses with HF, were analysed by ^{19}F NMR spectroscopy (Table 2) only fluorine containing products were found. Compounds which do not contain fluorine are also present.

Table 2. Relative yields (%) of acetylated pentosyl fluorides obtained by prolonged reaction of acetylated pentoses with anhydrous HF. Products were analyzed by ^{19}F NMR spectroscopy.

Starting compound (acetylated D-pentoses)	Products Pyranosyl fluorides				Furanosyl fluorides			
	β-Ara	α-Ara	α-Lyx	β-Rib	α-Rib α-*14a*	β-Rib β-*14a*	α-Lyx α-*3a*	β-Lyx β-*3a*
α-Lyxofuranose (*1a*)					8	10	72	10
Xylofuranosyl fluoride (α,β-*9a*)				4	20	31	30	15
α-Lyxopyranose (*8a*)	20	14	2	1	12	24	15	12
β-Xylopyranose (*11a*)	4	3	2		15	41	26	9
β-Ribofuranose				2	21	71	4	trace
α-Arabinofuranose	3	2		1	22	71	1	trace
β-Ribopyranose				3	21	76	trace	
β-Arabinopyranose	57	20			10	13		

The reaction shown in Table 2 were carried out with acetylated D-pentoses and the products probably belong to the D-series. However, since they were identified by NMR spectroscopy only, this has not been proved.

The ^{19}F NMR spectra of some of the glycosyl fluorides shown in Table 2 are known.[6,7] Previously unreported spectral data are presented in Table 1. Tri-*O*-acetyl-α- and -β-D-xylofuranosyl fluoride (*9a*) were obtained by brief treatment of 3,5-di-*O*-acetyl-1,2-*O*-isopropylidene-α-D-xylofuranose with HF at −70 °C followed by acetylation. Brief treatment of tetra-*O*-acetyl-β-D-ribofuranose with HF gave a mixture of the anomeric tri-*O*-acetyl-D-ribofuranosyl fluorides (α- and *β-14a*). The two anomers could not be separated, but their ^{19}F NMR data could be obtained from the mixture and are very similar to those of the corresponding benzoates.[7] Analogous treatment of tetra-*O*-acetyl-D-lyxofuranose (*1a*) gave a mixture of α- and *β-3a* from which ^{19}F NMR data were obtained.

Proton NMR spectra of a number of dioxolanylium ions in hydrogen fluoride have been measured in the course of the present and previous work.[3,4,5] ^{13}C NMR spectra have now been measured on a series of dioxolanylium ions in hydrogen fluoride solution and spectral data of ions derived from pentoses are shown in Table 3. The cationic carbon of benzoxonium ions is found at *ca.* 187 ppm, in agreement with results found for other phenylsubstituted onium ions.[8,9] The corresponding carbon in acetoxonium ions resonates at *ca.* 198 ppm (*17a* and *10a*, Table 3). The other two carbon atoms of the dioxolanylium ring are in most cases shifted downfield *ca.* 20 ppm relative to the carbon atoms of acylated sugars. A few $^{13}C-^{19}F$ coupling constants were also measured (Tables 3); they are in agreement with values found previously for glycosyl fluorides.[10]

EXPERIMENTAL

^{1}H NMR spectra and thin layer chromatography was performed as described previously.[4] ^{19}F NMR spectra were obtained at 84.68 MHz on a Bruker HX-90E instrument using pulsed Fourier technique. Position of signals (*Φ*F) are in ppm relative to internal trichlorofluoromethane. ^{13}C NMR spectra were measured at 0 °C on a Bruker WH-90 instrument. Hydrogen fluoride containing 10 % deuterium fluoride (for the deuterium lock) was used as solvent, which was contained in a Teflon sample tube. Position of signals are in ppm relative to internal $(CH_3)_3SiCH_2CH_2CH_2SO_3Na$.

*Reaction of tetra-*O*-benzoyl-α-D-lyxofuranose (1b) with HF. For 15 min.* A solution of *1b*[11] (1.16 g) in anhydrous HF (4 ml) was kept at 0 °C for 15 min. Dichloromethane was then added and the mixture was poured on ice. The organic phase was washed with aqueous $NaHCO_3$, dried and evaporated. The product (1.1 g) was purified by preparative TLC with ether-pentane (1:1) as eluent. The main fraction gave 771 mg (81 %) of pure tri-*O*-benzoyl-α-D-lyxofuranosyl fluoride (*α-3b*) as a syrup,

Table 3. ^{13}C NMR spectral data of dioxolanylium ions in anhydrous hydrogen fluoride containing 10 % deuterium fluoride.

Dioxolanylium ions	Chemical shifts (ppm) and $J^{19}F-^{13}C$) values (Hz) C1	C2	C3	C4	C5	R−C(=O)+	H_3C-C^+
2b	124.0	90.27	75.13	87.28	68.18	186.98	
7b	114.19	97.10	95.47	84.29	66.68	187.13	
	229.4	47.1					
6b	121.60	95.08	79.35	85.27	67.66	187.56	
17a[5]	122.31	89.75	74.48	83.12	67.14	198.37	18.13
17b[5]	121.08	89.82	75.91	83.12	67.72	187.50	
10a[5]	115.46	98.07	97.03	88.52	69.60	197.77	17.74
	230.9	47.10		2.9			
15b[3]	116.01	82.73	71.55	70.90	67.14	186.76	
16[3]	112.50	86.83	80.72	77.47	64.46	187.37	
						186.85	

$[\alpha]_D^{20}$ −15.5° (*c* 0.46, $CHCl_3$). Anal. $C_{26}H_{21}FO_7$: C, H. NMR data are shown in Table 1.

For 4 days. Treatment of *1b* (1.05 g) with HF for 4 d at +5 °C as described above gave 875 mg of a product which was benzoylated in the usual manner with benzoyl chloride (0.5 ml) in pyridine (5 ml). The product thus obtained (875 mg) was separated into two fractions by preparative TLC (ether-pentane 1:1). The fast moving fraction gave 483 mg (58 %) of *α-3b*, $[\alpha]_D^{20}$ −17.0° (*c* 7, $CHCl_3$). ^1H and ^{19}F NMR spectra proved its identity with the product described above. The next fraction gave 296 mg of a mixture of tri-*O*-benzoyl-*β*-D-lyxofuranosyl fluoride (*β-3b*) and the tetrabenzoate (*1b*). Crystallization from ether and recrystallization gave the pure *β*-fluoride (*β-3b*), m.p. 62–63 °C, $[\alpha]_D^{20}$ −14.13° (*c* 0.72, $CHCl_3$). Anal. $C_{26}H_{21}FO_7$: C, H. NMR data are in Table 1.

Reaction of tetra-O-benzoyl-β-D-xylofuranose (5b) with HF. For 10 min. Treatment of *5b* [12] (1.63 g) with HF (5 ml) for 10 min. at 0 °C as described above gave 1.47 g of crude product. Purification by preparative TLC (ether-pentane 1:1) gave 1.007 g (75 %) of pure tri-*O*-benzoyl-*β*-D-xylofuranosyl fluoride (*β-9b*) as a syrup, $[\alpha]_D^{22}$ +61.5° (*c* 11, $CHCl_3$). Anal. $C_{26}H_{21}FO_7$: C, H. NMR data are given in Table 1.

For 4 days. Reaction of *5b* (2.0 g) with HF (5 ml) for 4 d at +5 °C gave a crude product (1.7 g) which was benzoylated immediately. The product (1.82 g) was purified by preparative TLC (ether-pentane 1:1). The main fraction (1.113 g, 68 %) was a mixture of tri-*O*-benzoyl-α-D-lyxofuranosyl fluoride (*α-3b*) and tri-*O*-benzoyl-*β*-D-xylofuranosyl fluoride (*β-9b*) in a ratio 2.3:1 as seen from a ^{19}F NMR spectrum. ^1H and ^{13}C NMR spectra further confirmed that these two products were present. All attempts to separate them were unsuccessful.

Treatment of acetylated pentoses with anhydrous HF. The acetylated pentose (500 mg) was dissolved in HF (1 ml) and the solution was kept at room temperature for 48 h. It was then diluted with chloroform and poured on ice. The organic phase was dried ($MgSO_4$) and the solvent was evaporated. The rather unstable product was immediately acetylated with acetic anhydride in pyridine. Work up in the usual way gave a syrupy product which was analyzed by ^{19}F NMR spectroscopy. The results are shown in Table 2. ^1H NMR spectra were also measured but were in most cases too complicated to be analyzed.

Tri-O-acetyl-α- and β-D-xylofuranosyl fluoride (α- and β-9a). 3,5-Di-O-acetyl-1,2-*O*-isopropylidene-α-D-xylofuranose [13] (810 mg) was dissolved in anhydrous HF (2 ml) at −78 °C and the solution was kept for 30 min. Work up as described above followed by acetylation with acetic anhydride in pyridine gave 690 mg (84 %) of a product which was a mixture of α- and *β-9a* in a 1.4:1.0 ratio as seen from ^1H and ^{19}F NMR spectra.

The two anomers were separated by preparative TLC using ether-pentane (3:1) as eluent. The fast-moving fraction gave 240 mg (30 %) of *α-9a* as a syrup, $[\alpha]_D^{22}$ +52.5° (*c* 7.4, $CHCl_3$). Anal. $C_{11}H_{15}FO_7$: C, H. Spectral data are shown in Table 1.

The next fraction gave 180 mg (22 %) of syrupy *β-9a*, $[\alpha]_D^{22}$ +8.4° (*c* 3.9, $CHCl_3$). Anal. $C_{11}H_{15}FO_7$: C, H. NMR data were in agreement with those reported previously.[7]

Tri-O-acetyl-α- and -β-D-ribofuranosyl fluoride (α- and β-14) were obtained as a 1:3 mixture by treatment of tetra-*O*-acetyl-*β*-D-ribofuranose with HF for 10 min at room temperature as described above. ^{19}F NMR data were measured on the mixture (Table 1).

Tri-O-acetyl-α- and -β-D-lyxofuranosyl fluoride (α- and β-3a) were obtained in the same way as a mixture by brief treatment of *1a* [14] with HF.

Microanalyses were performed by NOVO analytical laboratory. The Bruker WH-90 instrument was provided by The Danish National Science Research Council.

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