

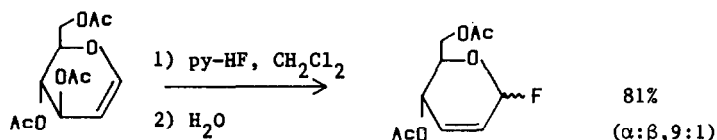
REACTION OF GLYCALs WITH PYRIDINIUM POLY(HYDROGEN FLUORIDE)
GIVING FERRIER REARRANGED SUGAR FLUORIDES

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Summary: Treatment of certain glycols with pyridinium poly(hydrogen fluoride) afford Ferrier rearranged fluorides, which have been characterized by their ^{19}F n.m.r. spectra and the preparation of derivatives.

The study of fluorinated carbohydrates has recently commanded considerable attention,¹ resulting in numerous methods of preparation² and an increasing awareness of their value as synthetic intermediates³ (e.g. in the preparation of C-glycosides⁴). In this letter it is reported that treatment of appropriate glycols with pyridinium poly(hydrogen fluoride) (py-HF) give the Ferrier rearranged⁵ products in good yield (Scheme), whose stereochemistry we have

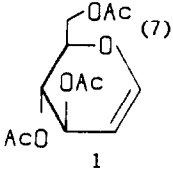
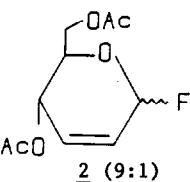
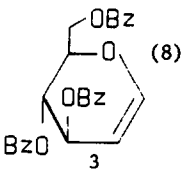
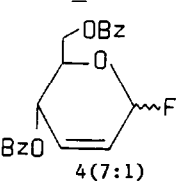
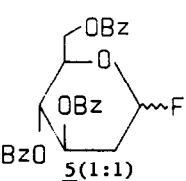
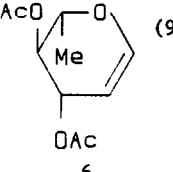
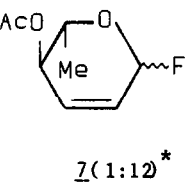
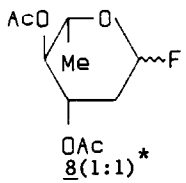
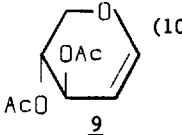
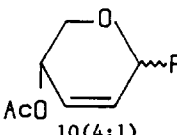
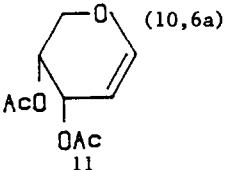
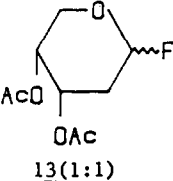
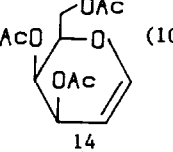


Scheme

determined through the use of ^{19}F n.m.r. Previous reagents used for this reaction (liquid HF and saturated solutions of HF in benzene)⁶ yield unstable products, whereas py-HF yields products that are stable enough to become useful synthetic intermediates. Also py-HF is readily available, cheap, and considerably easier and safer to handle than liquid HF.

Examples of the rearrangement are shown in Table 1. It will be noted that only when the ester protecting groups at C-3 and C-4 are trans does the rearrangement proceed.¹¹ When the groups at C-3 and C-4 are cis, other reactions predominate. These results are in accord with Pedersen's classical work⁶ on the Ferrier rearrangement.

TABLE 1

Unsaturated Sugar (Reference)	Retention Time	Products (α : β ratio)	Yield (of mixture)
 <p>(7) <u>1</u></p>	30 min	 <p><u>2</u> (9:1)</p>	81%
 <p>(8) <u>3</u></p>	15 min	 <p><u>4</u> (7:1) 20:1</p>	 <p><u>5</u> (1:1) 78%</p>
 <p>(9) <u>6</u></p>	30 min	 <p><u>7</u> (1:12)* 7:1</p>	 <p><u>8</u> (1:1)* 79%</p>
 <p>(10) <u>9</u></p>	5 min	 <p><u>10</u> (4:1)</p>	80%
 <p>(10,6a) <u>11</u></p>	45 min	<p>unknown 10:1</p> <p><u>12</u></p>	 <p><u>13</u> (1:1) --</p>
 <p>(10b) <u>14</u></p>	2½ h.	<p>unknown</p> <p><u>15</u></p>	--

* Following the convention that for an L-sugar β is down and α is up.

The ^{19}F n.m.r. data is shown in Table 2 and the following points have been noted. (1) Anomeric assignments have been made according to Hall et al.¹² that the resonance for the equatorial fluoride generally appears downfield of that for the axial fluoride. (2) All geminal couplings are between 50–56Hz.

TABLE 2 ^{19}F NMR Data

Compound	δ^* (J in Hz)	Compound	δ^* (J in Hz)
2 α	-120.75($J_1=53.6$, $J_2=9.4$, $J_3=2.4$)	2 β	-109.25($J_1=54.2$, $J_2=6.6$)
4 α	-119.65($J_1=53.8$, $J_2=8.9$, $J_3=2.5$)	4 β	-107.15($J_1=55.1$, $J_2=4.9$)
5 α	-129.5($J_1=50.8$, $J_2=4.7$)	5 β	-129.3($J_1=50.7$, $J_2=4.8$)
7 α	-110.95($J_1=55.5$, $J_2=4.6$)	7 β	-119.55($J_1=53.9$, $J_2=9.0$)
8 α	-130.2($J_1=51.3$, $J_2=4.5$)	8 β	-129.8($J_1=51.4$, $J_2=4.7$)
10 α	-122.55($J=53.5$)	10 β	-121.80($J_1=54.0$, $J_2=9.5$)
13 α	-127.12($J_1=51.3$, $J_2=7.3$)	13 β	-126.95($J_1=51.1$, $J_2=7.0$)
12	unknown compound(s) with two doublets at -132.15 (J=51.5) and -132.37, (J=51.4)		
15	unknown compound(s) with two doublets at -129.88 (J=51.1) and -130.14, (J=51.3)		

Obtained on a NT 200 Nicolet (200 MHz)

* values quoted with reference to Freon 11 (CFCl_3) set at $\delta=0$ ppm.

(3) Products arising from addition of HF across the C1-C2 double bond (with no stereoselectivity) (5, 8 and 13) give a characteristic pattern of overlapping double doublets. They always appear upfield of the rearranged products at -130 with geminal couplings of 51Hz.

In our hands, compounds 2 and 4 are stable enough to be rapidly chromatographed with ~50% loss of product; however pure material kept at 0°C decomposes within 2-3 days (compound 7 is less stable and 10 decomposes within 2 h). Solutions of 2,4 and 7 in CH_2Cl_2 or PhMe (over molecular sieves at 0°C) are storable for 1-2 weeks. Compounds 2, 4, 7 and 10 have been characterized spectroscopically. Derivatives of these compounds have also been prepared and characterized. For example, treatment of 2 with $\text{BF}_3 \cdot \text{OEt}_2/\text{MeOH}$ gave the corresponding methyl glycoside.^{6c}

A typical reaction procedure is as follows.

A solution of the unsaturated sugar (2.5 mmol) in dry CH_2Cl_2 (5 cm³) in a screw-cap teflon bottle was cooled to 0°C with vigorous stirring. Py-HF⁷

(8 drops, 1.5-2.5 eq) was then added and the reaction followed by tlc (the mixture often becoming red/brown in colour). On consumption of starting material the mixture was quenched with solid dry NaF and diluted with CH_2Cl_2 . After filtration through Celite, the filtrate was washed with water (X5) and dried (NaF). After solvent removal and analysis, the material was redissolved in dry CH_2Cl_2 and stored over molecular sieves at 0°C .

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