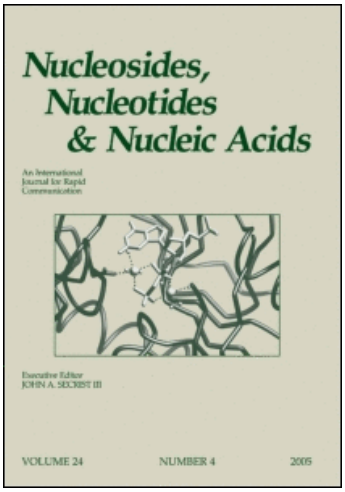

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Epimerization at C2 of Methyl 5-*O*-Benzyl-2-deoxy-2-fluoro-α-D-pentofuranosides upon Oxidation

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EPIMERIZATION AT C2 OF METHYL 5-*O*-BENZYL-2-DEOXY-2-FLUORO-α-D-PENTOFURANOSIDES UPON OXIDATION

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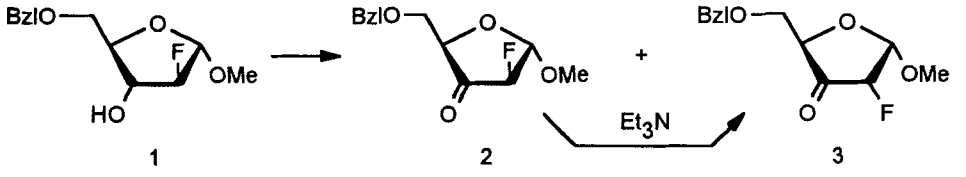
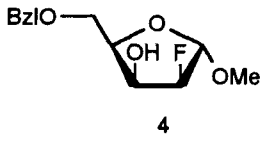
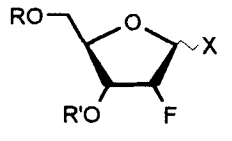
Abstract. Oxidation of **1** with DMSO-acetic anhydride resulted in the formation of a mixture of epimeric ketones **2** and **3** in the ratio of ≈3:1 in high combined yield. Acetolysis of methyl glycoside **5** afforded 1-O-acetyl-3,5-di-O-benzoyl-2-deoxy-2-fluoro-β-D-ribofuranoside (**6**)(83%). The latter was reacted with silylated N^6-benzoyladenine to give α- and β-ribosides (1:3.7; 61%, combined).

The present study was undertaken to develop a practical method for the synthesis of universal glycosylating derivative of 2-deoxy-2-fluoro-D-ribofuranose for the subsequent coupling with silylated bases in the presence of Friedel-Crafts catalysts.

We have found that oxidation of **1** with DMSO-acetic anhydride resulted in the formation of a mixture of epimeric ketones **2** and **3** in the ratio of ≈3:1 (^{1}H and ^{13}C NMR) in high combined yield. The **2** and **3** were inseparable by silica gel column chromatography. At the same time, we have observed the **2** → **3** isomerization upon column chromatography affording the mixture in ratios of 1:2 to 1:4.







	R	R'	X	
5	Bzl	H	α	OMe
6	Bz	Bz	β	OAc
7	H	H	β	Ade
8	H	H	α	Ade

Reduction of primary crude mixture of **2** and **3** with $NaBH_4$ in ethanol followed by column chromatography gave lyxoside **4** (23%), starting arabinoside **1** (44%), and riboside **5** (20%) implying pre-

dominant attack by BH_4^- anion at the β-face of the sugar ring of ketone **2** and stereoselective reduction of ketone **3** furnishing **5**. The latter was confirmed by quantitative reduction of pure **3** to **5**.

Since under many conditions investigated the predominant product was the undesired *arabino*-ketone **2**, it was of interest to attempt the equilibration of the **2/3** mixture to the *ribo*-isomer **3**. Fortunately, we have found that treatment of methanolic solution of the crude mixture of **2** and **3** with NEt_3 at room temperature for 3.5 h resulted in the **2** → **3** conversion in a yield of *ca.* 90% (^{1}H NMR). As expected, reduction of this product with sodium borohydride followed by chromatographic purification gave riboside **5** in a 85% yield.

Glycoside **5** was converted to crystalline β-acetate **6** (83%) essentially as described previously[1]. It is interesting to note that acetolysis of **5** under conditions employed in the present work [AcOH/Ac_2O/H_2SO_4 (14.7:1.75:1.0, v/v)] was readily accomplished giving crystalline **6** in 83% yield (*cf.* [2]). Acetate **6** was reacted with persilylated N^6-benzoyladenine in the presence of excess $SnCl_4$ [ratio of the reagents (mol) 1.0:1.5:2.9][3] in refluxing 1,2-dichloroethane-acetonitrile (1:2.5, v/v) mixture for 3 h to afford, after deblocking and silica gel column chromatography, 9-(2-deoxy-2-fluoro-β-D-ribofuranosyl)adenine (**7**) and its α-anomer **8** in 48 and 13% isolated yield, respectively. The assignments of anomeric configuration for **7** and **8** were based primarily upon ^{1}H NMR spectroscopy. Diagnostic of the α-anomeric configuration of the latter is long-range coupling of H8 to fluorine exhibited in its ^{1}H NMR spectrum. This coupling is generally indicative of a physical proximity of the nuclei involved[4] and is not observed in the β-anomer. The CD spectrum of **7** displays, like that of adenosine[5], negative long-wavelength envelope near 260 nm and, in contrast to adenosine, the transition centered at 217 nm is negative.

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