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Oxidation-Reduction Sequence for the Synthesis of Peracylated Fluorodeoxy Pentofuranosides

Igor A. Mikhailopulo^a; Nicolai E. Poopeiko^a; Grigorii G. Sivets^a; Natalia B. Khripach^a

^a Institute of Bioorganic Chemistry, Byelorussian Academy of Sciences, Minsk, Zhodinskaya, Byelorussia

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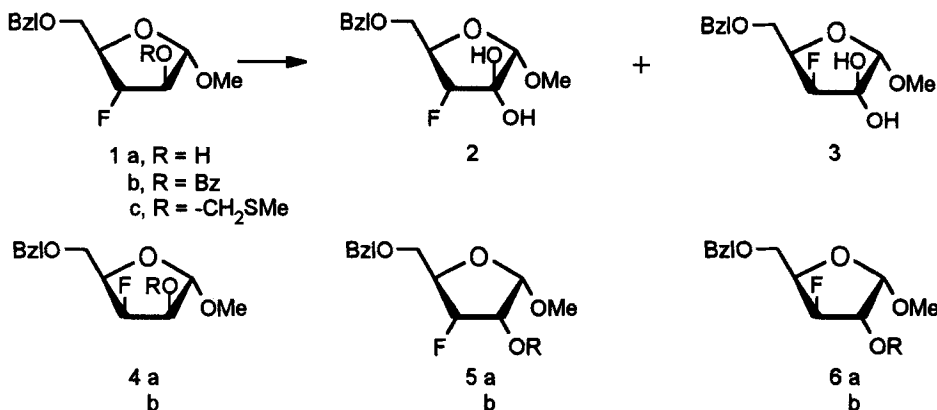
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OXIDATION-REDUCTION SEQUENCE FOR THE SYNTHESIS OF PERACETYLATED FLUORODEOXY PENTOFURANOSIDES

Igor A. Mikhailopulo*, Nicolai E. Poopeiko, Grigori G. Sivets, Natalia B. Khripach
Institute of Bioorganic Chemistry, Byelorussian Academy of Sciences, 220141 Minsk, Zhodinskaya 5/2,
Byelorussia

Abstract. Oxidation of 1a with DMSO-acetic or trifluoroacetic anhydride led to the formation of a mixture of epimeric *gem*-diols 2 and 3 in the ratios of $\approx 3:1$ and $\approx 7:1$, respectively. Reduction of this mixture with NaBH_4 followed by benzylation and chromatography afforded 4a and 5a.

A careful study of oxidation of 1a with DMSO-acetic anhydride at room temperature showed that a mixture of epimeric *gem*-diols 2 and 3 is formed in ratios of 2:1 to 4:1 (^1H and ^{13}C NMR) (*cf.* ¹). Reduction of the crude 2 and 3 with NaBH_4 in benzene-ethanol mixture (4:1 to 1:1) followed by benzylation and chromatography afforded pure riboside 5b (43-52%) and lyxoside 4b (9-15%); in some experiments, arabinoside 1b, 2-O-methylthiomethyl derivative 1c, and xylosides 6a/b were also isolated.



The use of sodium borodeuteride as a reducing agent at the second step of the reaction sequence afforded 2(R)- and 2(S)-deuterio derivatives of 4b and 5b, respectively. No deuterium was found according to ^1H NMR data in compound 1a that was isolated from the reaction mixture; xyloside 6a was not isolated in this experiment. From these results, it may be reasonably concluded that reduction of ketone 2 proceeds stereoselectively *via* attack by BH_4^- at the less hindered β -face of the sugar ring leading to

exclusive formation of riboside 5a (isolated as benzoate 5b). Surprisingly, isomeric ketone 3 undergoes predominant attack at the α -face of the sugar ring suggesting negligible steric and/or electronic hindrance of methoxy group.

Oxidation of arabinoside 1a with DMSO-trifluoroacetic anhydride² in CH_2Cl_2 followed by quenching with triethylamine at -78°C afforded the mixture of *gem*-diols 2 and 3 in ratios of 6:1 to 8:1. Thus, the tendency toward epimerization at C3 was reduced under these oxidation conditions. Reduction of the crude 2 and 3 with NaBH_4 led to the isolation of 5b in 75% yield. There was not observed a decrease in the yield of 5b in larger scale preparations (*ca.* 5 g of 1a). None of the corresponding β -anomers of 1-6 was detected in mixtures of *gem*-diols as well as in either of the purified products under all oxidation-reduction conditions investigated. Thus, this oxidation-reduction sequence offers a useful alternative to the previously described two-step route for the preparation of 5b³.

It should be pointed out that a mixture of *gem*-diols 2 and 3 was also obtained upon oxidation of lyxoside 4a.

The assignments of configuration for all the compounds that were synthesized were based primarily upon ^{13}C NMR data, taking into account previous empirical correlations of the effect of configuration of vicinal substituents in the furanose ring on the $\delta^{13}\text{C}$ values of the atoms bearing these groups⁴.

Starting from 4b, 9-(α -D-lyxofuranosyl)adenine (α -lyxo-A) was prepared (47%; combined) essentially as described earlier³. The structure of α -lyxo-A was proved by UV, CD, and ^1H NMR data. As reported for 9-(α -D-lyxofuranosyl)adenine⁵, α -lyxo-A displays the positive B_{2u} Cotton effect; in contrast, envelope centered at 212 nm is negative.

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