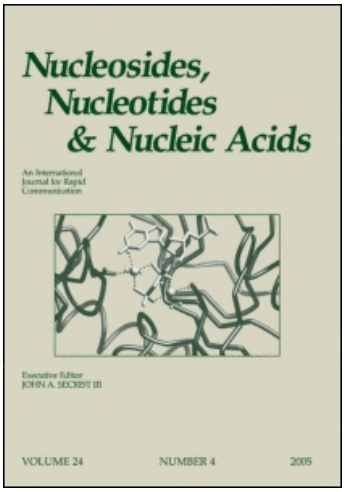

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A New Approach for Syntheses of 2′,3′-Dideoxy-2′,3′-dehydronucleosides Using 2,2-Difluoro-1,3-dimethylimidazolidine (DFI) as a Dehydrating Reagent

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ABSTRACT

We found that 2,2-difluoro-1,3-dimethylimidazolidine (DFI) is useful for not only fluorination but also dehydrating reactions. This dehydrating ability of DFI was applied to the syntheses of dihydrofurans (**2**) that are possible starting materials for various anticancer or antiviral drugs.

Key Words: DFI; Dehydrating reactions; Dihydrofurans.

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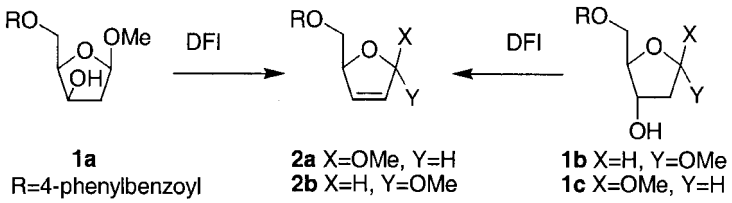
INTRODUCTION

We have recently developed a new fluorinating agent, DFI.[1] DFI is commercially available and advantageous with respect to cost, safe handling, accessibility, and possible to be recycled. In the course of studies on DFI, we have found that it is useful for not only fluorination but also dehydrating reactions. We have focused on the dehydrating ability of DFI and applied it to the syntheses of dihydrofurans (**2**) that would be possible key compounds for the preparation of various anticancer or antiviral drugs.

RESULTS AND DISCUSSION

The reaction of sugar[2] (**1a**) with DFI was performed at rt in DMI or PhMe. DFI-adduct (**4**) was unexpectedly observed as a main product. In attempt to enhance the conversion into **2a**, raising the temperature to 85°C in DMI resulted in disappearance of **4** and **2a** was obtained as a main product in 77% yield. Fluorinated sugar (**3**) derived by inversion at C3-position was also observed as a by-product. Furthermore, effect of solvents such as DMI, PhMe, $CHCl_3$, CH_3CN and THF was examined to increase the ratio of **2a**. Using CH_3CN as a solvent resulted in the highest ratio of **2a**:**3** (84:17). In contrast, the reaction in PhMe ended in the lowest ratio of **2a**:**3** (64:37). To generate **2a** efficiently, the polar solvents such as CH_3CN or DMI were superior to the non-polar solvents such as PhMe or $CHCl_3$. Finally, the reactions of various stereoisomers of **1** with DFI were examined (Fig. 1). Consequently, a hydroxyl group of each stereoisomer was dehydrated by DFI regardless of the configuration at the C1- or the C3-position of the substrates (**1a-c**). However, 2-deoxy-ribose derivatives (**1b**,**c**) demonstrated lower yields than 2-deoxy-xylose derivative (**1a**). The low yield was attributable to the formation of 2-deoxy-3-*O*-(4-phenylbenzoyl)xylose derivative resulting from the acyl transfer from C5- to C3-position.

We showed a new synthesis for dehydrated sugars using DFI. We will apply this synthesis to other nucleosides in the future to come.



substrate[a]	product	yield(%)
1a	**2a**	71
1a[b]	**2a**	98[c]
1b	**2b**	59
1c	**2a**	38

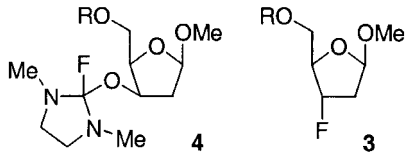


Figure 1. Reaction of various stereoisomers. [a]Conditions: 2.2 equiv DFI, CH_3CN, 4 h, 85°C. [b]In the presence of 17 equiv KF. [c]Determined by HPLC.

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