This article was downloaded by:

On: 26 January 2011

Access details: Access Details: Free Access

Publisher Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-

41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information: http://www.informaworld.com/smpp/title~content=t713597286

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

Hideki Umetania; Hiroshi Sonodab; Hironori Komatsua

^a Catalysis Science Laboratory, Mitsui Chemicals Inc., Sodegaura-shi, Chiba, Japan ^b Process Technology Laboratory, Mitsui Chemicals Inc., Omuta-shi, Fukuoka, Japan

Online publication date: 09 August 2003

To cite this Article Umetani, Hideki , Sonoda, Hiroshi and Komatsu, Hironori(2003) 'A New Approach for Syntheses of 2',3'-Dideoxy-2',3'-dehydronucleosides Using 2,2-Difluoro-1,3-dimethylimidazolidine (DFI) as a Dehydrating Reagent', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 667-669

To link to this Article: DOI: 10.1081/NCN-120022607 URL: http://dx.doi.org/10.1081/NCN-120022607

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS Vol. 22, Nos. 5–8, pp. 667–669, 2003

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

Hideki Umetani,1,* Hiroshi Sonoda,2 and Hironori Komatsu1

¹Catalysis Science Laboratory, Mitsui Chemicals Inc., Sodegaura-shi, Chiba, Japan ²Process Technology Laboratory, Mitsui Chemicals Inc., Omuta-shi, Fukuoka, Japan

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.

667

DOI: 10.1081/NCN-120022607 Copyright © 2003 by Marcel Dekker, Inc.

www.dekker.com

1525-7770 (Print); 1532-2335 (Online)



^{*}Correspondence: Hideki Umetani, Catalysis Science Laboratory, Mitsui Chemicals Inc., 580-32 Nagaura, 299-0265 Sodegaura-shi, Chiba, Japan; Fax: +81 43 864 2371; E-mail: hideki.umetani@mitsui-chem.co.jp.

Downloaded At: 11:02 26 January 2011

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, CHCl₃, CH₃CN and THF was examined to increase the ratio of 2a. Using CH₃CN 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 CH₃CN or DMI were superior to the non-polar solvents such as PhMe or CHCl₃. 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-deoxyribose 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.

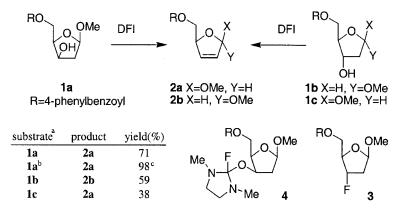


Figure 1. Reaction of various stereoisomers. ^aConditions: 2.2 equiv DFI, CH₃CN, 4 h, 85°C. ^bIn the presence of 17 equiv KF. ^cDetermined by HPLC.

Downloaded At: 11:02 26 January 2011

Copyright © 2003 by Marcel Dekker, Inc. All rights reserved.

REFERENCES

- 1. Hayashi, H.; Sonoda, H.; Fukumura, K.; Nagata, T. 2,2-Difluoro-1,3-dimethylimidazolidine (DFI). A new fluorinating agent. Chem. Commun. **2002**, 1618–1619.
- 2. Motawia, M.S.; Pedersen, E.B. A short route to 3'-deoxy-3'-fluorothymidine. Liebigs Ann. Chem. **1990**, 1137–1139.