SYNLETT
Spotlight 174

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Deoxo-Fluor [Bis(2-methoxyethyl)aminosulfur Trifluoride]: An Advanced Nucleophilic Fluorinating Reagent in Organic Synthesis

Compiled by Xihe Bi

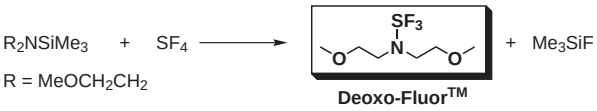
Xihe Bi was born in 1977 in Jilin Province (P. R. of China). He studied Chemistry at the Northeast Normal University where he has completed his Ph.D. work under the supervision of Professor Qun Liu. His research interest is mainly focused on developing new synthetic methods for biologically interesting carbo- and heterocycles. He has just started working in the field of Chemical Biology in the group of Professor Michael Famulok at the University of Bonn, Germany, with a fellowship of the Alexander von Humbold Foundation.

Department of Chemistry, Northeast Normal University, Changchun 130024, P. R. of China
E-mail: drxhbi@gmail.com

Introduction

Organofluorine compounds have had a marked impact on medical and organochemical fields and the number of applications continues to grow.[1] These significant contributions arise from the unique changes that occur in the physical and chemical properties of ordinary organic compounds due to the presence of a fluorine-containing group. The use of Deoxo-Fluor™ [$N(MeOCH_2CH_2)_2SF_3$] as a nucleophilic fluorinating reagent is gaining popularity.[2] Compared with DAST (Et_2NSF_3), the traditional deoxofluorinating agent, Deoxo-Fluor™ is thermally less instable and thus more amenable to large-scale use. So far, it has been predominantly applied to convert alcohols,[3–5] aldehydes, ketones,[3a,6] glyoxalates[8] and carboxylic acids[9] into the corresponding monofluoromethyl and difluoromethylene derivatives. Also, conversion of thiocarbonyl derivatives to fluorinated products has been achieved.[7] In addition to its role as fluorinating reagent, Deoxo-Fluor™ played an important role in inducing cyclizations of β-hydroxy amides (thioamides) to corresponding oxazolines (thiazolines).[10]

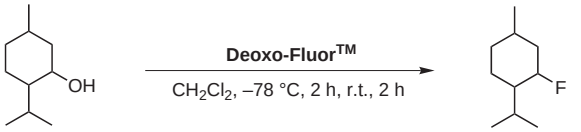
Deoxo-Fluor™ can be obtained by reacting the *N*-trimethylsilyl derivative of bis(2-methoxyethyl)amine with SF_4 in Et_2O at –30 °C (Scheme 1).[3]



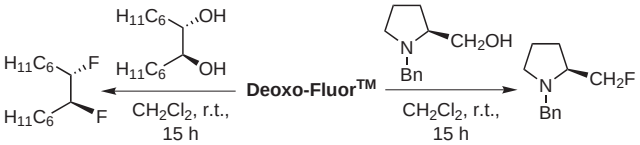
Scheme 1 Preparation of Deoxo-Fluor™

Abstracts

(A) Simple alcohols are readily converted into the corresponding monofluorides using Deoxo-Fluor™. Moderate to excellent yields were obtained with a variety of structurally diverse substrates, such as primary, secondary, tertiary, allylic and benzylic alcohols. For most of the compounds, fluorination proceeds below room temperature, sometimes as low as –78 °C.[3]



(B) Shreeve et al. found that when Deoxo-Fluor™ was reacted with various chiral amino alcohols, the corresponding chiral fluorinated compounds were produced in good yields. Under similar reaction conditions, diols reacted with Deoxo-Fluor™ to give good yields of the corresponding difluorinated products.[4]



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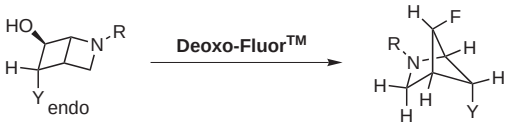
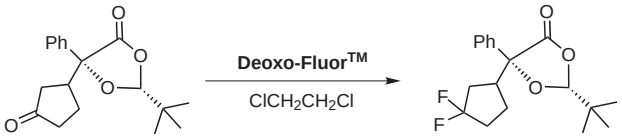
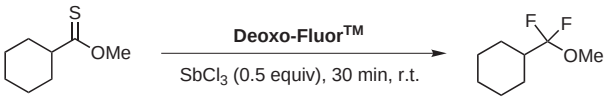
(C) Rearrangement of 5-*endo*-methyl-6-*exo*-alcohols to 6-*syn*-methyl-5-*anti*-fluorides was initiated using Deoxo-Fluor™.[5]



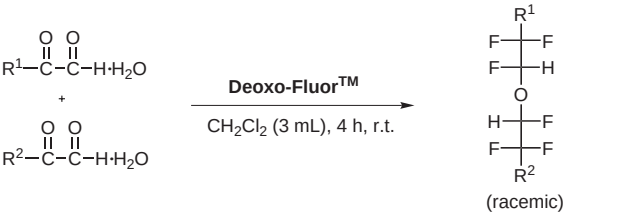
(D) Reactions of structurally different aldehydes and ketones with Deoxo-Fluor™ have been utilized in order to prepare geminal difluoro compounds. The fluorination of aldehydes and ketones was conducted in the presence of catalytic amounts of HF, generated in situ, by adding trace amounts of EtOH to the reaction mixture.[3a,6]



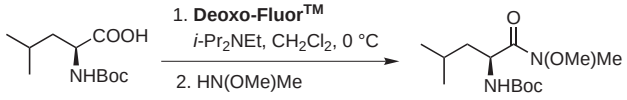
(E) A variety of thiocarbonyl derivatives (thioketone, thioester, thioamide, dithioester, and dithiocarbamate) were converted to the corresponding *gem*-difluorides in excellent yields on reaction with the fluorinating agent, Deoxo-Fluor™, in the presence of $SbCl_3$.[7]



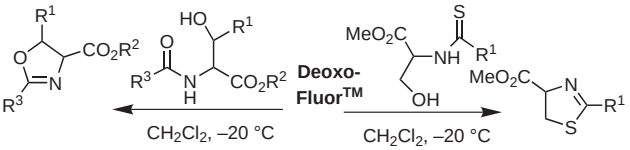
(F) Shreeve and coworkers reported the reactions of various glyoxal hydrates with Deoxo-Fluor™. In concentrated solutions of dichloromethane, Deoxo-Fluor™ efficiently fluorinates a variety of glyoxal hydrates, RCOCHO·H_2O (R = 4-methoxyphenyl, 3,4-methylenedioxyphenyl, 4-methylphenyl, 4-fluorophenyl, phenyl, 2-thienyl, methyl) to form polyfluoroethers as meso and racemic mixtures (~1:1) in good yields. When the reactant comprised two different glyoxal hydrates, mixed polyfluoroethers were observed as the major products.[8]



(G) The Deoxo-Fluor™ reagent converts carboxylic acids to the corresponding acid fluorides, which then react with *N*,*O*-dimethylhydroxylamine to give the corresponding Weinreb amides in high yields. The reaction proceeds without racemization when optically active acids are used as starting material. This method is operationally simple and provides the products in high purity.[9]



(I) A mild and highly efficient cyclization of α-hydroxy amides (thioamides) to oxazolines (thiazolines) using the Deoxo-Fluor™ reagent has been developed.[10]



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