

SYNLETT Spotlight 160

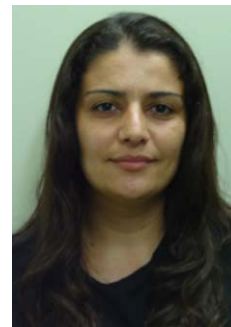
Diethylaminosulfur Trifluoride (DAST)

Compiled by Sabrina Baptista Ferreira

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

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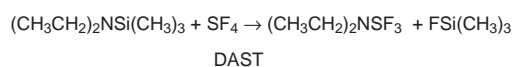
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Introduction

Fluorination is an important structural modification for diverse classes of bioactive organic molecules. The introduction of a fluorine atom or fluorinated group into organic molecules often changes their physical, chemical and physiological properties, resulting in greater stability and lipophilicity of the molecule.¹ Diethylaminosulfur trifluoride (DAST) is a widely used fluorinating reagent,²⁻⁶ which is very effective for converting alcohols, ketones, aldehydes and carboxylic acids into their corresponding fluoro derivatives. This reagent has its origins in the pioneering work of Middleton et al. at DuPont.⁷ DAST is synthesized via the substitution of a fluorine atom of sulfur tetrafluoride (SF₄) by a diethylamino group, result-

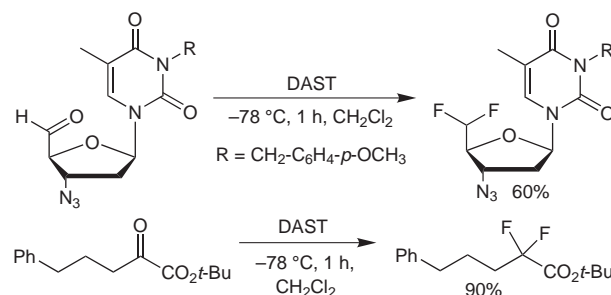
ing in a powerful fluorination agent (Scheme 1). DAST presents the following advantages: the product is relatively easy to handle and shows good selectivity, consequently being less prone to formation of olefins in elimination reactions and/or rearrangement reactions. This reagent is commercially available as liquid that can be handled at room temperature and in common laboratory glassware. However, DAST is unstable above 70 °C.



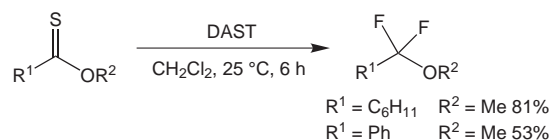
Scheme 1

Abstracts

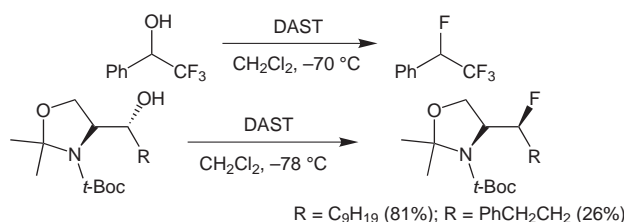
(A) A variety of aldehydes and ketones can be easily transformed into the corresponding difluoro compounds through reaction with DAST. The reactions are conducted in dichloromethane in the presence of catalytic amounts of HF, generated in situ, by adding trace amounts of EtOH to the reaction mixture.^{7,8}



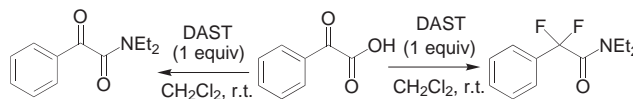
(B) Carboxylic esters are unreactive toward DAST. However, thioesters are more electrophilic and can lead to fluorodesulfurization reaction more easily (substitution of a thiocarbonyl moiety by two fluorine atoms).⁹



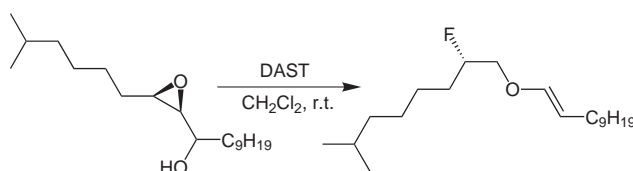
(C) Simple alcohols, such as primary, secondary, tertiary, allylic and benzylic alcohols, are readily converted to the corresponding monofluorides using DAST. Moderate to excellent yields were obtained with a variety of structurally diverse substrates.^{10,11}



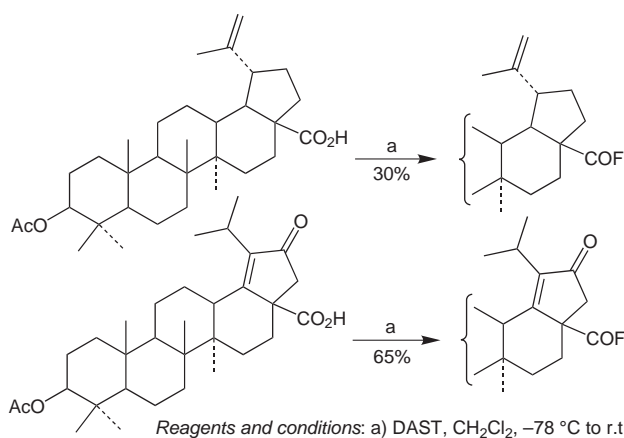
(D) The synthesis of α,α -difluoroamides from 1,2-dicarbonyl compounds via direct fluorination using DAST as the fluorinating reagent in a one-pot reaction was recently reported.¹²



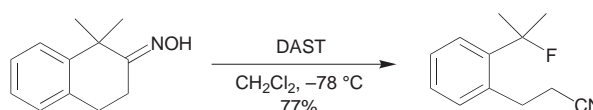
(E) Lakshmipathi et al. showed that DAST promotes an unusually easy C-C bond cleavage when epoxy alcohols are used, leading exclusively to monofluoro vinyl ethers.¹³



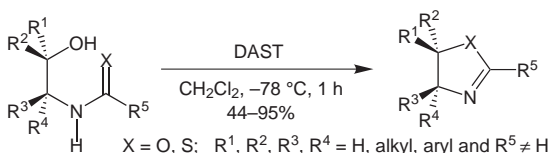
(F) Biedermann et al. reported that DAST is the convenient reagent for the synthesis of acyl fluorides from the corresponding carboxylic acids under very mild conditions. The experimental procedure is analogous to the procedure used for fluorination of alcohols. The yields of this reaction are good (60–70%) and by-products were not observed.¹⁴



(G) Kiriara et al. showed that cyclic ketoximes reacted with DAST affording fluorinated carbonitriles in good yields.¹⁵



(H) DAST is a nucleophilic fluorination reagent but under appropriate conditions it can also serve as a catalyst. For instance, Lafarge et al. reported that DAST can induce intramolecular cyclization of (1,2)-amido-alcohols to 2-oxazolines.¹⁶



References

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