Dialkylaminodifluorosulfinium Salts: XtalFluor-E and XtalFluor-M

Compiled by Antonio Franconetti

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Introduction

Fluorination is an important reaction in medicinal chemistry.¹ Fluorinated analogues of biomolecules frequently show increased biological power, lipidic permeability and metabolic stability. Diethylaminosulfur trifluoride (DAST) has been widely used for directly replacing a hydroxyl group by fluorine under very mild conditions.²,³ Nevertheless, the corrosive properties of DAST make it unsuitable for high-scale usage.

In this context, commercially available aminodifluorosulfinium salts,⁴ such as XtalFluor-E (1) or XtalFluor-M (2), are efficient alternatives. These fluorinating agents are crystalline, more selective and significantly more stable⁵ than Deoxo-Fluor or DAST and do not react violently with water.⁶

Abstracts

(A) Failure of Hydrocinnamyl Alcohol with XtalFluor-M:
The reaction of hydrocinnamyl alcohol with 2 or 1 in acetonitrile provided an intractable mixture. For this reaction to proceed, the addition of exogenous sources of fluoride, such as Et₃N·3HF or Et₃N·2HF, was necessary.⁵

(B) Halogenation of Alcohols with XtalFluor Reagents:
Reaction of primary, secondary and tertiary alcohols with 1 using Et₃N·3HF as a promoter gave the fluorinated nucleophilic substitution products. The addition order was a key parameter in this reaction. To obtain good selectivity and stereochemical integrity, 1,8-diazabicycloundec-7-ene (DBU) had to be used together with the fluorination agents.⁵ A mixture of fluorinated bridged biphenyl systems has been obtained from 3-hydroxyspirodienones by means of a XtalFluor-E-promoted rearrangement. When compound 2 was used instead of compound 1, substrate decomposition was observed.⁵ Chlorination, bromination and iodination reaction of primary alcohols in good yield has been described using a combination of tetraethylammonium halide and XtalFluor-E.⁷

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## References