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Das Reagenz · The Reagent

Ruppert's Reagent: Trifluoromethyltrimethylsilane

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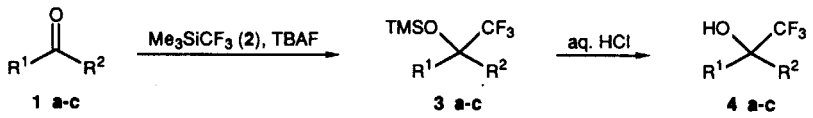
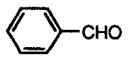
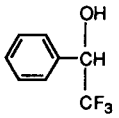
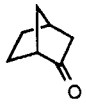
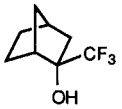
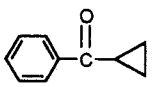
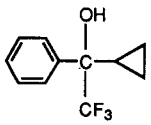
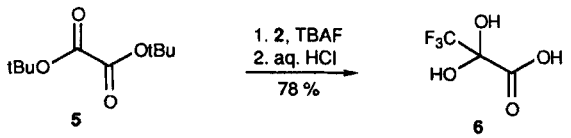
Despite the comparable size of fluorine and hydrogen, the exchange of a hydrogen atom by fluorine often results in a significant shift of the compound's physical properties, chemical behaviour and physiological activity. These changes are due to the high electronegativity of fluorine, the high C-F bond energy leading to enhanced thermal stability of the molecule and finally the increased lipid solubility of fluorine organic compounds, facilitating the transport of bio-active compounds across lipid membranes [1]. As a consequence, in a host-guest complex a molecule and its fluoro analog would be sterically almost indistinguishable but their chemical behaviour could be different from one another. The fact, that many modern pharmaceuticals and agrochemicals, like the ophthalmic antiviral agent trifluridine [2] and the pyrethroid insecticide fluvalinate [3], bear trifluoromethyl groups demonstrates the value of this substitution pattern and the need for appropriate synthetic methods for the easy introduction of this function. In this regard, trifluoromethyltrimethylsilane (**2**) is a valuable reagent for the trifluoromethylation of various electrophilic substrates under mild conditions. It acts as a stable *in situ* equivalent for the trifluoromethide carbanion (CF_3^-) and its metalloorganic derivatives, which generally show great tendency for the formation of difluorocarbene by α-elimination. Ruppert's reagent adds readily to a wide range of aldehydes, ketones and enones under fluoride catalysis or initation. The resulting trimethylsilyl ethers **3** are hydrolysed by aqueous acid to afford the trifluoromethyl carbinols **4** in excellent yield [1]. In most



	Educt (1)	Product (4)	Yield (%)
a			85
b			92
c			81

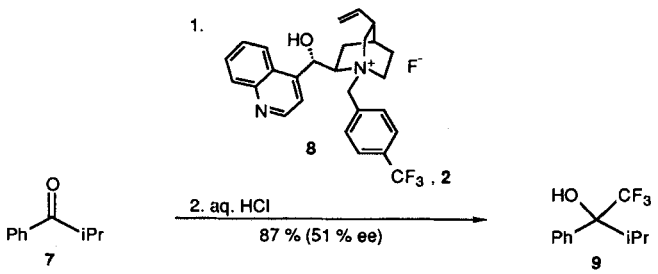
cases, tetra-*n*-butylammonium fluoride (TBAF) serves as a source of fluoride anion, tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) is also used. The formation of silyl enol ethers with enolizable aldehydes and ketones is not observed. In the case of enones 1,2-addition predominates.

The trifluoromethylation of carbonyl functions has been successfully applied to natural products, for instance steroids [1, 4], amino acids [5] and carbohydrates [6]. In contrast to aldehydes and ketones, simple unactivated esters and amides do not react with trifluoromethyltrimethylsilane. However, activated and cyclic carboxylic acid derivatives are transformed with Ruppert's reagent into trifluoromethylated hemiketals or hemiaminals, respectively. An efficient and simple synthesis of trifluoropyruvic acid monohydrate (**6**) has been developed from di-*t*-butyl oxalate (**5**) [7].



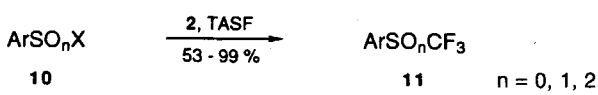
5 **6**

Also one example for an asymmetric trifluoromethylation with Ruppert's reagent is known. Herein the application of the chiral quarternary ammonium fluoride **8** as catalyst leads to an enantioselective addition of trifluoromethyltrimethylsilane to different aldehydes and ketones [8].



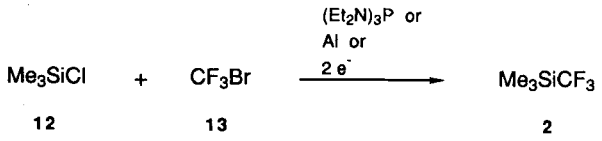
8 **7** **9**

Further use of Ruppert's reagent was reported in the synthesis of aryltrifluoromethylsulfides, -sulfoxides and -sulfones from the corresponding arylsulfenyl-, sulfinyl- and sulfonyl chlorides and fluorides (**10** —> **11**) [9].



10 **11**

Reactions with Ruppert's reagent are generally unaffected by moisture and easy to perform. Trifluoromethyltrimethylsilane is usually prepared from chlorotrimethylsilane (**12**) and bromo- trifluoromethane (**13**) either with the aid of hex ıyl-phosphorous triamide [10] or aluminum powder, respectively [11], or even electrochemically [12]. In our days, Ruppert's reagent is commercially available from major chemical suppliers.



12 **13** **2**

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