Fluorinative α-cleavage of cyclic ketoximes with diethylaminosulfur trifluoride: an efficient synthesis of fluorinated carbonitriles

Masayuki Kirihara, Kanako Niimi and Takefumi Momose*

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani 2630, Toyama 930-01, Japan

Diethylaminosulfur trifluoride effects ready cleavage of cyclic ketoximes to fluorinated carbonitriles.

Fluorinated organic compounds are widely used in scientific and industrial fields. Since the preparative methods for organofluorine compounds remain limited to a few procedures, new fluorinating agents and methodology are required.[1] Since diethylaminosulfur trifluoride (DAST), a reagent converting aliphatic alcohols into alkyl fluorides, has been introduced into organic synthesis,[2] there have been several reports concerning new fluorinating methods.[3–9] Among the methods, we reported the reaction of DAST with tertiary cyclopropyl silyl ethers causing ring opening to give allylic fluorides.[10]

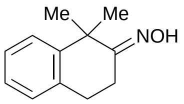
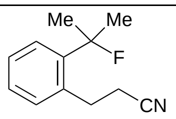
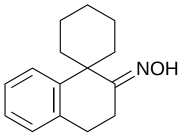
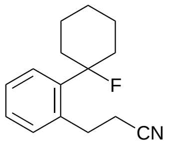
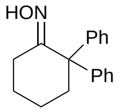
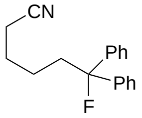
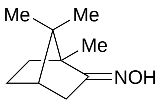
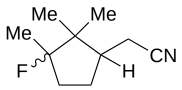
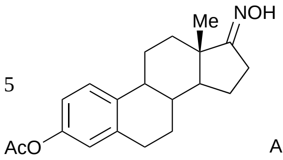
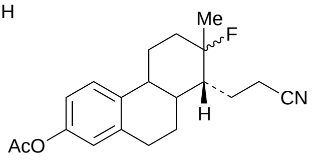
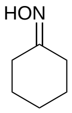
Here we describe a novel reaction involving the treatment of cyclic ketoximes **1** with DAST to cause a ring fragmentation resulting in the formation of fluorinated carbonitriles **2**.† The methodology has also provided an efficient route to tertiary fluorides or fluoroalkenes. The results are summarized in Table 1.

The presence of substituent(s) capable of stabilising a carbocation at the position α to the oximino carbon is essential to obtain fluorinated carbonitriles. An oxime lacking such substituents afforded a complex mixture (*e.g.* run 6 in Table 1). In the cases of runs 4 and 5, the products were a 1 : 1 mixture of stereoisomers. The results suggest that the reaction is a kind of Beckmann fragmentation (abnormal Beckmann rearrangement)[11] involving a carbocation intermediate.

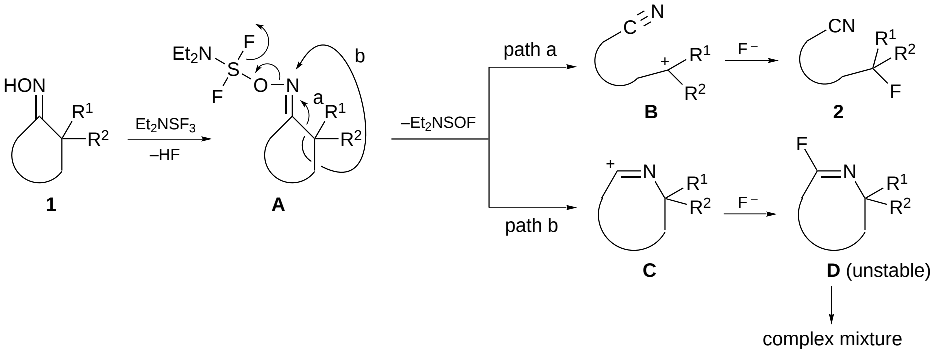
A postulated reaction mechanism is depicted in Scheme 1. The first step is the nucleophilic displacement of a fluorine in DAST by the oxygen of the oximino substrate **1** with elimination of hydrogen fluoride. Next, the elimination of diethylaminosulfino fluoride from the intermediate **A** causes the bond cleavage and gives a carbocation intermediate **B**. Finally, the fluoride ion attacks **B** to afford the fluorinated carbonitrile **2** (path a). In the case of compounds lacking substituents to stabilise the α-carbocation, the reaction proceeds through a mechanism similar to that of the 'normal' Beckmann rearrangement. The carbon–carbon bond *anti* to the oximino leaving group in the intermediate **A** migrates to the nitrogen atom to afford the carbocation **C**. The fluoride ion attacks **C** to give an unstable compound **D**, which leads to a complex mixture (path b).

Compounds bearing a sulfur functionality **3** at the position α to the oximino carbon reacted with DAST to cause the fragmentation efficiently leading to α-fluoro sulfides **4**. Since α-fluoro sulfides **4** were not stable, they were subjected, without purification, to oxidation with MCPBA. The resulting sulf-

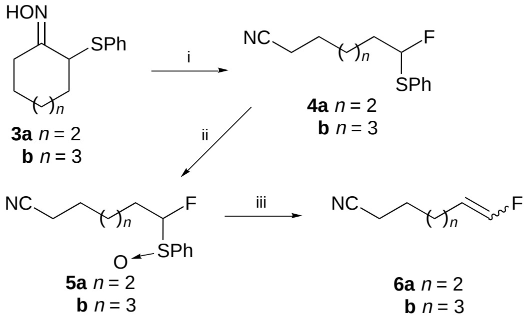
Table 1

Run	Starting material[a]	Product[b]	Yield (%)
1			77
2			91
3			75
4			69[c]
5			63[c]
6		complex mixture	—

[a] Oximes were prepared from ketones by reaction with hydroxylamine. [b] All compounds were characterised on the basis of mass, IR, ^1H and ^{19}F NMR spectral data. [c] A 1 : 1 mixture of stereoisomers.



Scheme 1



Scheme 2 *Reagents and conditions*: i, DAST, CH_2Cl_2, −78 °C, ii, MCPBA, CH_2Cl_2 (**5a** : 51%, **5b**: 75%, in 2 steps), iii, 160 °C, C_6H_6, heated in a sealed tube (**6a** : 91%, **6b** : 97%)

oxides **5** were heated in a sealed tube at 160 °C to afford fluoroalkenes **6** in high yields (Scheme 2).

Footnote

† A typical experimental procedure is as follows: to a solution of oxime (1.0 mmol) in dichloromethane (3 ml) was added DAST (1.0 mmol) at −78 °C under an inert atmosphere, and the reaction mixture was stirred for 30 min. A saturated sodium hydrogen carbonate solution was added to the reaction mixture, and the resulting mixture was extracted with dichloromethane. The extract was dried over anhydrous sodium sulfate, filtered, and evaporated to afford the crude product. Purification by chromatography (silica gel, hexane–dichloromethane) gave a pure sample.

References

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