SYNLETT
Spotlight 111

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

HOF·CH_3CN Complex

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Introduction

HOF was originally synthesized by Appelman[1] in 1971, but was found to be a very unstable substance and of little use in synthetic chemistry as it was difficult to prepare and could be generated only in very minute amounts. A few years ago, Rozen developed a new way to prepare and stabilize it through complexation with acetonitrile.[2] Whereas neat HOF can be unpredictably explosive at temperatures above –40 °C, its acetonitrile complex (HOF·CH_3CN) is much more stable.

HOF·CH_3CN complex is a potent oxygen-transfer reagent for a variety of reactions, some of which are occasionally difficult on certain substrates. It reacts very efficiently with a large variety of organic compounds, resulting in either an oxidation or a transfer of an oxygen atom from the reagent to the substrate. This reagent can be applied to the synthesis of epoxides from various olefins, ketones from methyl ethers, esters by the Baeyer–Villiger reaction, sulfones from sulfides, nitro compounds from amines and amino acids, N-oxides from tertiary amines, and other conversions. More recently, HOF·CH_3CN complex has been used in the direct oxidation of aliphatic and selected aromatic azides to nitro compounds, both very efficiently and in excellent yields.

Its uniqueness is based on its oxygen, which becomes a strongly electrophilic species because of it being bonded to highly electronegative fluorine. Its reactions have been shown to be ionic in nature and are usually complete in a few minutes at temperatures ranging from 0 °C to 25 °C.

Preparation:

HOF·CH_3CN complex is simply prepared in a glass reactor by bubbling nitrogen-diluted fluorine (10–15%) into aqueous acetonitrile (10% H_2O in CH_3CN) at 0 °C. The product is stable at 0 °C for a few hours.[2]

$$F_2 + H_2O + CH_3CN \longrightarrow HOF\cdot CH_3CN + HF$$

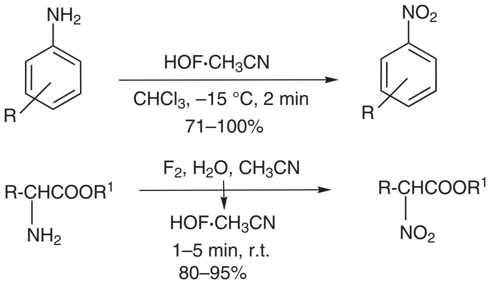
Scheme 1 Preparation of HOF·CH_3CN complex

Abstracts

(A) Rozen and coworkers reported the first direct oxidation of aliphatic and aromatic azides into nitro compounds with HOF·CH_3CN complex in excellent yields.[3]

$$RN_3 \xrightarrow[CH_2Cl_2,\ 0\ °C]{HOF\cdot CH_3CN} RNO_2$$

(B) As a strong oxidant, HOF·CH_3CN complex can oxidize aromatic amines to nitroarenes in high yields.[4] It can also oxidize the amino group of α-amino esters to α-nitro esters without affecting the aromatic ring.[5]



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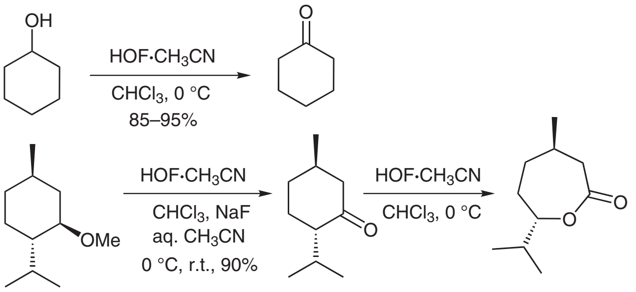
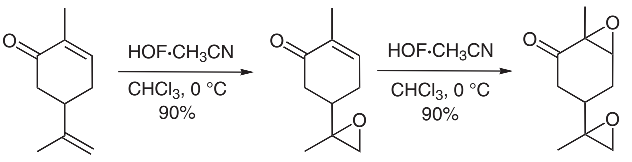
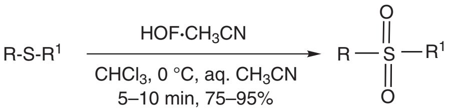
(C) HOF·CH_3CN complex is an ecologically friendly oxidizing agent and can oxidize alcohols[6] and methyl ethers to ketones. Ketones also undergo Baeyer–Villiger oxidation to give esters under the same reaction conditions.[7] All these reactions are ionic in nature.



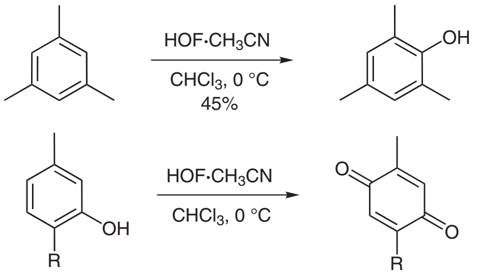
(D) With its strong electrophilic oxygen, HOF·CH_3CN complex is an excellent oxygen transfer agent[8] that epoxidizes a wide variety of alkenes and alkynes, including very deactivated ones that cannot be directly epoxidized by other methods.



(E) HOF·CH_3CN complex can oxidize all types of sulfides to sulfones in excellent yields in only a few minutes at or below room temperature.[9] The reaction proceeds through the formation of sulfoxides which, at low temperatures of around –78 °C, can be isolated in good yields.



(F) HOF·CH_3CN complex can also hydroxylate[10] and otherwise oxidize many aromatic compounds, though yields are moderate.



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