

A Novel Oxidation of Thiophenes using HOF·MeCN

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The complex, HOF·MeCN made directly by bubbling fluorine through aqueous MeCN, oxidizes various types of thiophenes to the corresponding *S,S*-dioxides, including ones which could not be oxidized by any other method.

The HOF·MeCN complex is rapidly evolving as the best possible oxygen transfer agent, since it contains a truly electrophilic oxygen. Its easy preparation only requires bubbling of nitrogen diluted fluorine¹ through aqueous acetonitrile. Its moderate reaction conditions with substrates make it an excellent epoxidizing agent² and unique oxidizer of many functional groups among them amines,³ alcohols, ketones,⁴ amino acids⁵ and sulfides.⁶ The last reaction prompted us to explore its potential to oxidize the sulfur atom in thiophenes to the corresponding *S,S*-dioxides. These derivatives have long been recognized as precursors for azulenes and participants in various cycloadditions including Diels–Alder reactions with inverse electron demands.⁷ However, their synthesis up till now has met with difficulties. The main obstacle to the oxidation of a thiophene arises from the difficulty in overcoming the aromatic stabilization and once this is achieved the reaction conditions encourage dimerizations and other secondary reactions.

Benzothiophene **1** served as the first example for the reaction with HOF·MeCN. One gram (7.5 mmol) was dissolved in about 20 ml CHCl₃ and cooled down to –10 °C. This solution was then added in one portion to a MeCN solution containing 22.5 mmol (50% excess) of the oxidizing complex. After 20 min the reaction was terminated by adding saturated NaHCO₃ solution and the benzothiophene *S,S*-dioxide **2**, mp 140 °C,⁸ was obtained in quantitative yield. While in this case our method shows mainly improvement in the reaction time (minutes vs. hours with perborate^{8a} or MoO₅·HMPA^{8b}), with 2,5-dimethylthiophene **3** the yield of the *S,S*-dioxide **4**, mp 88 °C, was also considerably improved

(95% vs. 52% with MCPBA⁹), although when employing dimethyl dioxirane as oxidant the yield was also over 90%.¹⁰ In 2,5-dibromothiophene **5** the bromine atoms cause electron deficiency around the sulfur atom and peracids no longer oxidize it efficiently. Only dimethyl dioxirane was able to convert **5** into the *S,S*-dioxide derivative **6**, but in the low yield of 27%¹⁰ and this with reaction time of several days. The reaction with HOF·MeCN was performed in this case at room temp. during 20 min and **6**, mp 128 °C, was obtained in 95%.

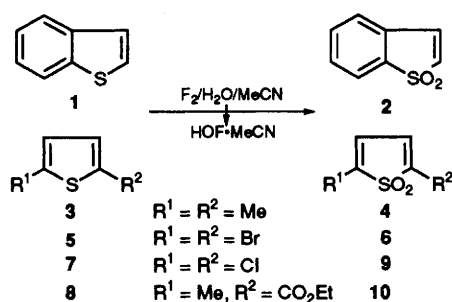
Thiophenes with stronger electron-withdrawing groups are usually beyond the oxidizing power of common oxidizers, since under the harsh conditions required the dioxides undergo various secondary reactions. For example, 2,5-dichlorothiophene **7** or ethyl 5-methyl-2-thiophene carboxylate **8** have never yet been oxidized, but the use of 4 equiv. (twofold excess) of HOF·MeCN at room temp. for 20 min was sufficient to transform each of them into the corresponding *S,S*-dioxide [**9**, mp 103 °C (ethanol) and **10** mp 140 °C (ethanol)] in 70 and 90% yield, respectively.

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Scheme 1