A Novel Oxidation of Thiophenes using HOF·MeCN

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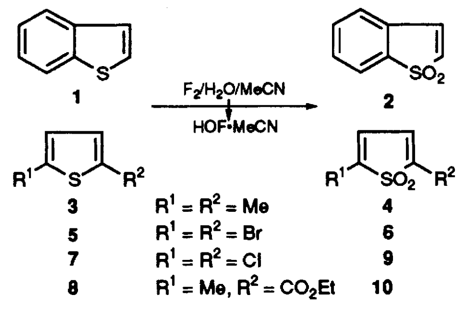
The complex, HOF·MeCN made directly by bubbling fluorine through aqueous MeCN, oxidizes various types of thiophenes to the corresponding *S,S*-dioxides, including ones which could not be oxidized by any other method.

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 fluorine[1] through aqueous acetonitrile. Its moderate reaction conditions with substrates make it an excellent epoxidizing agent[2] and unique oxidizer of many functional groups among them amines,[3] alcohols, ketones,[4] amino acids[5] 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 $CHCl_3$ 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 $NaHCO_3$ 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 MoO_5·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 MCPBA[9]), 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%.



Scheme 1

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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