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LETTERS

A facile route to thiophene-1,1-dioxides bearing electron-withdrawing groups

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Abstract—No commonly available synthetic method for thiophene-1,1-dioxides with strong EWGs has been described to date. Trifluoroperacetic acid in acetonitrile in the absence of water is shown to oxidise thiophenes, including examples possessing an electron-withdrawing group such as sulfonyl or alkoxycarbonyl. An easy and ready for scale-up procedure is developed, some formerly unknown thiophene-1,1-dioxides are obtained. © 2001 Published by Elsevier Science Ltd.

Thiophene-1,1-dioxides serve as intermediates in the synthesis of numerous classes of organic compounds via cycloaddition reactions[1] or nucleophilic ring-opening.[2] Their chemistry has been thoroughly reviewed.[3–5] Recently, these compounds have attracted growing interest as starting materials for the development of new conducting polymers for optical and electronic devices.[6] Nevertheless, their chemistry is significantly underdeveloped and their synthetic potential is relatively low due to the lack of general synthetic methods permitting the preparation of thiophene-1,1-dioxides with a wide range of substituents.

The introduction of an electron-withdrawing group into a thiophene ring substantially decreases the propensity of the sulfur atom to undergo oxidation. Although a number of reagents have been used for the oxidation of thiophenes, only a few thiophene-1,1-dioxides bearing an electron withdrawing group are known[7,8] and no representatives with two such substituents are known. These compounds would be especially interesting as strained dienes with very low electron density and presumably high reactivity toward cycloaddition reactions and nucleophilic attack. Hence, the development of an oxidizing method for EWG-bearing thiophenes seems to be a worthy task.

During our studies of alkenes containing several strong electron-withdrawing groups, we found trifluoroperacetic acid in non-aqueous media to be an excellent oxidant for electron-deficient sulfur.[9] Therefore, it seemed interesting to investigate the application of this reagent for the oxidation of thiophenes. The employment of systems containing trifluoroacetic acid or its anhydride and aqueous hydrogen peroxide for this purpose was previously reported[10–12] and its higher oxidative ability in comparison with the commonly used *m*CPBA was demonstrated. However, as was shown for 2-(4-chlorobenzoyl)-thiophenedioxide,[11] water easily adds to the electron-deficient double bonds of such compounds even in strongly acidic media. Hence, the absence of water in the oxidizing system is necessary. A significant merit of this reagent is that all the reaction products except thiophenedioxides are volatile and can be easily removed ensuring a convenient workup. Herein, we report results of our efforts to use trifluoroperacetic acid for the oxidation of substituted thiophenes.

Solutions of the reagent were prepared by cautious addition of trifluoroacetic anhydride to an ice-cold mixture of the appropriate solvent and 98–99% hydrogen peroxide.[15] Typically, molar ratios of oxidant–substrate 2.5:1 were used and reactions were carried out at rt. Preliminary investigation of solvents showed that in the case of 2,5-dichlorothiophene, a very slow reaction takes place in chloroform, dichloromethane and dichloroethane. No reaction occurs in these solvents for 2-chloro-5-methylsulfonyl- and 2-methyl-5-carboethoxythiophenes even after several days at 20°C and the starting materials were recovered. However, in acetonitrile rapid formation of the oxidized product from 2,5-dichlorothiophene was observed and the reaction was completed within hours. The isolated product was identical to the formerly described 2,5-dichlorothiophene-1,1-dioxide according to its spectral data and

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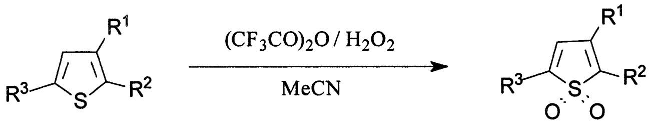
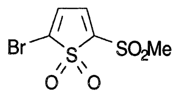
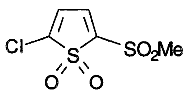
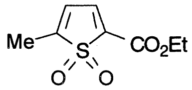
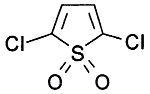
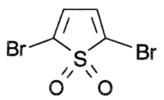
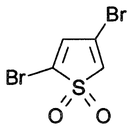
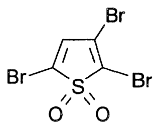
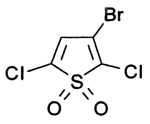
Table 1.



Entry	Thiophene-1,1-dioxide	Yield (%)	Entry	Thiophene-1,1-dioxide	Yield (%)
1		72[13]	**5**		66[13]
2		75[7]	**6**		76[7,8]
3		82[8]	**7**		42[7]
4		85[14]	**8**		81[13]

melting point.[7] The structures and yields of some thiophene-1,1-dioxides obtained by this method are given in Table 1.

Oxidation of thiophenes containing methylsulfonyl or carboethoxy groups proceeds much more slowly and takes up to 2–3 days at rt for completion of the reaction. Under these conditions we were not able to oxidize thiophenes with two electron-withdrawing groups such as 2,5-di-(methylsulfonyl)- or 2,5-dicarboethoxythiophene. Increase of the oxidant–substrate ratio (5:1) gave less satisfactory results in the oxidation of polyhalogenothiophenes, giving higher amounts of by-products, though it somehow accelerates the reaction in the cases of carboethoxy- or methylsulfonylthiophenes. The double bond in thiophene-1,1-dioxides is known to be susceptible to epoxidation, and the oxiranes so formed rearrange under acidic conditions into thiete-1,1-dioxides.[5] We presumed these reactions were occurring in the presence of an excess of trifluoroperacetic acid. Also, the reactions run at higher temperatures gave less pure products although in shorter times. Trifluoroperacetic acid solutions above 35–40°C start to decompose evolving oxygen, complicating the work at higher temperatures.

In the case of 2-chloro-5-nitrothiophene and 2,5-dichloro-3-nitrothiophene, we detected the formation of a new product by TLC only after several days; indeed, the oxidation rate was so low that we were unable to isolate the desired products in pure form.

This method permits the preparation of thiophene-1,1-dioxides containing halogen substituents and/or at least one strong electron-withdrawing group. The procedure is extremely simple and can be easily scaled-up. Our results allow us to hope that the method can be extended to the oxidation of more electron-deficient thiophenes. This work is in process in our laboratory and the results will be reported in due course.

Acknowledgements

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13. *Typical procedure*: An equimolar quantity of trifluoroacetic anhydride (26.2 g, 17.5 ml) was cautiously added to an ice-cold solution of H_2O_2[15] (0.125 mol) in 100 ml of CH_3CN. After 1 h, 12.1 g (0.05 mol) of 2,5-dibromothiophene was added at 0°C. The mixture was allowed to stand at rt until the substrate was consumed (TLC). All volatile materials were evaporated in vacuo, finally at 0.5–1 mmHg, and the residue was recrystallized from hexane–CH_2Cl_2, yielding 12.5 g (82%) of 2,5-dibromothiophene-1,1-dioxide.

   The NMR spectra and melting points for all known substances are in accordance with literature data.

   1: White crystals, mp 147–150°C (dec.). ^{1}H NMR (400 MHz, $CDCl_3$) 3.25 (s, 3H, SO_2CH_3); 7.25 (d, 1H, $J=5.0$ Hz); 7.65 (d, 1H, $J=5.0$ Hz); ^{13}C NMR (400 MHz, $CDCl_3$) 45.05 (CH_3), 118.08 (CH), 123.46 (CH), 127.32 (C), 141.16 (C). Found: C, 21.96; H, 1.89. Anal. calcd for $C_5H_5O_4SBr$: C, 21.99; H, 1.85%.

   5: White crystals, mp 123–124°C. ^{1}H NMR ($CDCl_3$) 3.25 (s, 3H); 7.08 (d, 1H, $J=8.0$ Hz); 7.70 (d, 1H, $J=8.0$ Hz); ^{13}C NMR 45.53 (CH_3), 118.52 (CH), 123.58 (CH), 138.36 (C), 140.98 (C). Found: C, 26.18; H, 2.16%. Anal. calcd for $C_5H_5O_4SCl$: C, 26.26; H, 2.20%.

   8: Pale yellow crystals, mp 60–62°C. ^{1}H NMR ($CDCl_3$) 7.11 (s, 1H); ^{13}C NMR 118.40 (CH), 121.67 (C), 129.03 (C), 131.44 (C). Found: C, 18.25; H, 0.35%. Anal. calcd for C_4HCl_2Br: C, 18.20; H, 0.38%.
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15. Highly concentrated H_2O_2 was obtained according to: Giguere, P. A. *Bull. Chem. Soc. Fr.* **1954**, 720, and stored at −20°C as a 5 M solution in CH_3CN. This solution seems to be quite stable at this temperature and did not show any signs of decomposition while being kept even at room temperature. Special care should be taken while handling anhydrous H_2O_2 and we recommend minimizing the time of storing it in the pure form.