Synthesis and Characterization of Thiophene 1-Oxides Kinetically Stabilized by Bulky Substituents at the 3- and 4-Positions

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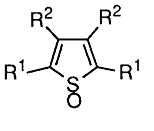
Oxidation of 3,4-di-*t*-butyl- and 3,4-di-1-adamantyl-, and 2,4-di-*t*-butylthiophenes with an equimolar amount of *m*-chloroperbenzoic acid in the presence of $BF_3{\bullet}Et_2O$ gave the corresponding thiophene 1-oxides in good yields, which are stable enough to be isolated in pure crystalline form. An X-ray single crystal structure analysis led to the conclusion that thiophene 1-oxides would not be aromatic.

We report here the preparation and characterization of stable thiophene 1-oxides which are kinetically stabilized by bulky substituents on the 3- and 4-positions.

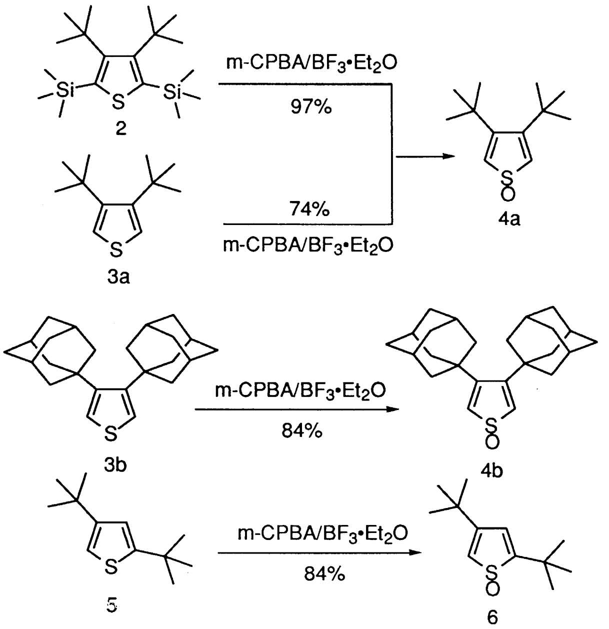
Preparation and isolation of thiophene 1-oxides are difficult mainly because of the following two reasons:[1] a) monocyclic thiophene 1-oxides readily dimerize in a Diels-Alder manner and b) oxidation of thiophenes generally produces the corresponding thiophene 1,1-dioxides because further oxidation of thiophene 1-oxides takes place very quickly. Therefore, well-characterized thiophene 1-oxides are limited. Peracid oxidation allowed Mock the first synthesis of kinetically stabilized thiophene 1-oxides (**1a,b**) in low yields.[2] Tetraphenylthiophene 1-oxide (**1c**) is another stable compound that was synthesized by reaction of a zirconium metallacycle with thionyl chloride.[3] Recently, 2,5-diphenylthiophene 1-oxide (**1d**), which is stable at –25 °C, was prepared in a moderate yield by oxidation of 2,5-diphenylthiophene with H_2O_2/CF_3CO_2H and characterized by an X-ray single crystal structure analysis.[4] More recently, Furukawa et al. developed a new method that made possible to stop the oxidation at the 1-oxide stage. Thus, the oxidation of 2,5-bis(trimethylsilyl)thiophene and the related thiophenes with *m*-chloroperbenzoic acid (m-CPBA) in the presence of $Et_2O{\bullet}BF_3$ gave the corresponding 1-oxides (**1e-g**) in good yields.[5] Thus, only 2,5-disubstituted or tetrasubstituted thiophene 1-oxides have been isolated and characterized.



1a: R^1 = CMe_3, R^2 = H
1b: R^1 = CMe_2Bu^t, R^2 = H
1c: R^1 = R^2 = Ph
1d: R^1 = Ph, R^2 = H
1e: R^1 = $SiMe_3$, R^2 = H
1f: R1 = $SiMe_2Ph$, R^2 = H
1g: R^1 = $SiMePh_2$, R^2 = H

In our continuing interest in the chemistry of highly congested thiophenes, we have examined the oxidation of 3,4-di-*t*-butyl-2,5-bis(trimethylsilyl)thiophene (**2**)[6] with an equimolar amount of m-CPBA in the presence of $Et_2O{\bullet}BF_3$ in dichloromethane. The oxidation unexpectedly resulted in the formation of crystalline 3,4-di-*t*-butylthiophene 1-oxide (**4a**)[7,8] in high yield (97%) with elimination of trimethylsilyl groups.[9] This indicates that two bulky substituents at the 3- and 4-positions make thiophene 1-oxides isolably stable. Indeed, even after heating in refluxing chlorobenzene for 24 h, **4a** was recovered in 90% yield with formation of 3,4-di-*t*-butylthiophene (**3a**) in 8% yield. Encouraged at this finding, we have examined the oxidation of **3a** and obtained **4a** in 74% yield.

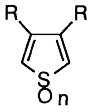
Similar oxidation of 3,4-di-1-adamantylthiophene (**3b**) gave the corresponding thiophene 1-oxide (**4b**)[8] in 84% yield. 2,4-Di-*t*-butylthiophene 1-oxide (**6**)[8] was also stable enough and was obtained in 84% yield by oxidation of 2,4-di-*t*-butylthiophene (**5**).[10]



Although X-ray structure analyses of thiophene 1-oxides **1c**[3c] and **1d**[4] were reported, precise structure determination was done satisfactorily only for **1d**.[11] We then carried out an X-ray strucure analysis of **4a** at –120 °C.[12] An ORTEP drawing structure is given in Figure 1 along with the relevant bond lengths and angles data. The sulfur atom presents pyramidalization and lies outside the quasi-plane formed by four carbon atoms of the ring by 0.26 Å, while the oxygen atom lies outside this plane in the opposite direction by 0.75 Å. The C2-C3 bond length is as long as 1.53 Å and is very close to those of common carbon-carbon single bonds. This bond length is also considerably longer than that (1.48 Å) of **1d**.[4] This should be mainly ascribed to the repulsive interactions between two bulky *t*-butyl groups. Meanwhile, C1-C2 (C3-C4) bond length (1.34 Å) is nearly equal to those of common carbon-carbon double bonds. Aromaticity problem of thiophene 1-oxides has been a matter of keen interest.[1] The pyramidal configuration of the sulfur atom and the bond lengths data make **4a** unlikely to be aromatic.

Comparison of ^{1}H-NMR chemical shift values of the thiophenes **3a** and **3b** and their corresponding 1-oxides and 1,1-

Table 1. ^{1}H-NMR chemical shift data (δ) of α-hydrogens of the thiophenes **3a** and **3b** and their corresponding 1-oxides and 1,1-dioxides



R/n	0	1	2
t-butyl	7.16	6.93	6.40
1-adamantyl	7.20	6.92	6.41

dioxides is of some interest (Table 1). Chemical shift values of the α-hydrogens of the 1-oxides **4a** and **4b** are rather close to those of the corresponding thiophenes **3a** and **3b** and are much lower than the corresponding 1,1-dioxides, although electron-withdrawing properties of the sufonyl group is greater than that of the sufinyl group. This reversion of the chemical shift values would be attributed to the anisotropic effect of the sulfinyl group.[2,13] The ring current effect of the five-membered ring would be very small, if any, since thiophene 1-oxides would not be aromatic from X-ray analysis results, and it cannot explain the observed large deshielding.

In conclusion, we have succeeded in the preparation of thiophene 1-oxides in which α-positions are unsubstitued and also in the precise structure determination of the thiophene 1-oxide **4a**.

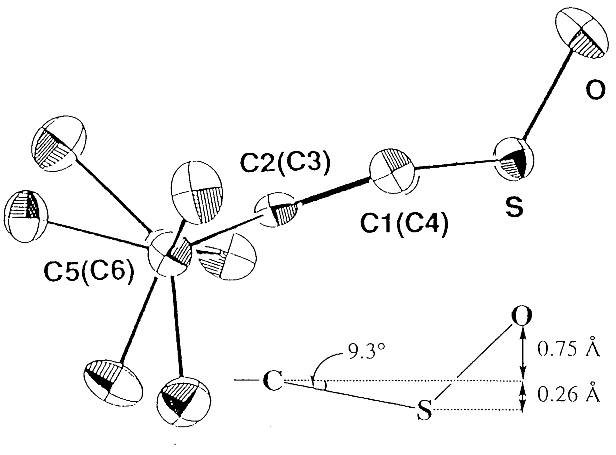


Figure 1. Molecular structure of thiophene 1-oxide **4a**. Bond lengths (Å): C1-C2, 1.340(2); C3-C4, 1.344(2); C2-C3, 1.527(2); C1-S, 1.747(2); C4-S, 1.740(1); S-O, 1.494(1); C2-C5, 1.547(1); C3-C6, 1.539(2). Bond angles (°): C1-S-C4, 89.8(1); S-C1-C2, 113.5(1); C1-C2-C3, 110.8(1); C2-C3-C4, 110.1(1); C3-C4-S, 113.9(1); C1-C2-C5, 117.8(1); C3-C2-C5, 131.3(1); C2-C3-C6, 130.7(1); C4-C3-C6, 119.2(2). Torsion angle (°) C5-C2-C3-C6, 6.0.

References and Notes

1 For a review, see J. Nakayama and Y. Sugihara, *Sulfur Reports*, **19**, 349 (1997).

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5 N. Furukawa, S. Zang, S. Sato, and M. Higaki, *Heterocycles*, **44**, 61 (1997). See also M. Higaki and N. Furukawa, 24th Congress of Heterocyclic Chemistry, Osaka, November, 1993, Book of Abstracts, p. 277.

6 Prepared by treatment of 3,4-di-*t*-butyl-2,5-dilithiothiophene with trimethylsilyl chloride.

7 Satisfactory elemental analyses were obtained for all new compounds.

8 Selected properties of the thiophene 1-oxides. **4a**: mp 114-115 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.40 (18H, s), 6.93 (2H, s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 31.9, 35.8, 134.4, 158.4; IR (KBr) 1034 cm^{-1} (SO); MS *m/z* 212 (M$^+$). **4b**: mp 194-196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68-80 (12H, m), 2.06 (12H, m), 2.12 (6H, broad s), 6.92 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.7, 36.3, 38.9, 42.5, 134.5, 159.9; IR (KBr) 1042 cm^{-1} (SO); MS *m/z* 368 (M$^+$). **6**: mp 64-66 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18 (9H, s), 1.41 (9H, s), 6.37 (1H, d, J = 1.3 Hz), 6.49 (1H, d, J = 1.3 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.4, 30.3, 33.6, 35.4, 122.5, 125.3, 154.8, 166.4; IR 1024 cm^{-1} (SO); MS *m/z* 212 (M$^+$).

9 Such desililation was previously encountered in the oxidation of trimethylsilyl substituted thiophenes with m-CPBA: see S. Gronowitz, G. Nikitidis, and A. Hallberg, *Acta Chem. Scand.*, **45**, 632 (1991); S. Gronowitz, G. Nikitidis, A. Hallberg, and C. Stalhandske, *Acta Chem. Scand.*, **45**, 636 (1991).

10 The neopentyl group is not bulky enough to stabilize the thiophene 1-oxide isolable. The oxidation of 3,4-dineo-pentylthiophene gave the corresponding 1-oxide whose formation was detected by ^{1}H NMR (α-hydrogen signal, δ 6.75), but its isolation in pure form was unsatisfactory.

11 For structure prediction of the parent thiophene 1-oxide by calculations, see: J. A. Hashmall, V. Horak, L. E. Khoo, C. Q. Quicksall, and M. K. Sun, *J. Am. Chem. Soc.*, **103**, 289 (1981); I. Rozas, *J. Phys. Org. Chem.*, **5**, 74 (1992).

12 Crystal data for **4a**: triclinic, $P1$, Dc = 1.190 gdm^{-3}, a = 8.873(7) Å, b = 11.589(1) Å, c = 11.736(1) Å, α = 97.244(6)°, β = 90.002(6)°, γ = 90.001(5)°, V = 1185.0(2) Å^3, Z = 4, R = 0.044, wR = 0.051, 4242 independent reflections.

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