SIMPLE PROCEDURE FOR THE SYNTHESIS OF 2,5-BIS(SILYLATED) THIOPHENE *S*-OXIDES WITH *m*-CHLORO-PERBENZOIC ACID IN THE PRESENCE OF $BF_3(Et_2O)$

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Abstract– Oxidation of 2,5-bis(silyl)thiophenes (**1**) with *m*-chloroperbenzoic acid (*m*-CPBA) in the presence of $BF_3(Et_2O)$ gave the corresponding *S*-oxides (**2**) in moderate yields, while, without $BF_3(Et_2O)$, the oxidation gave solely the corresponding thiophene *S*-dioxides (**3**) and no *S*-oxide was obtained at all. This procedure was successfully applied to the synthesis of other 2,5-bis-substituted thiophene monooxides.

Although thiophene *S*-oxides are unstable species and only a few derivatives have been reported, they are of great interest in view of the reactivity, structure and biological behavior in toxicology.[1] Oxidation of thiophenes with *m*-CPBA (*m*-chloroperbenzoic acid) and other oxidants gives the corresponding *S*-dioxides[2] except that a few thiophenes bearing bulky 2,5-bis-substituents afford the *S*-oxides in low yields. In the first examples of this reaction, 2,5-di-*tert*-butyl and 2,5-di-*tert*-octylthiophenes were oxidized to give the corresponding *S*-oxides only in 5% yields even at low temperature; these compounds were characterized by uv and nmr spectroscopy in solution.[3] Recently, Weiss *et al.* have reported the preparation of 2,3,4,5-tetraphenylthiophene *S*-oxide in 59% yield by the reaction of

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Dedicated to Prof. Shigeru Oae on the occasion of his 77th birthday.

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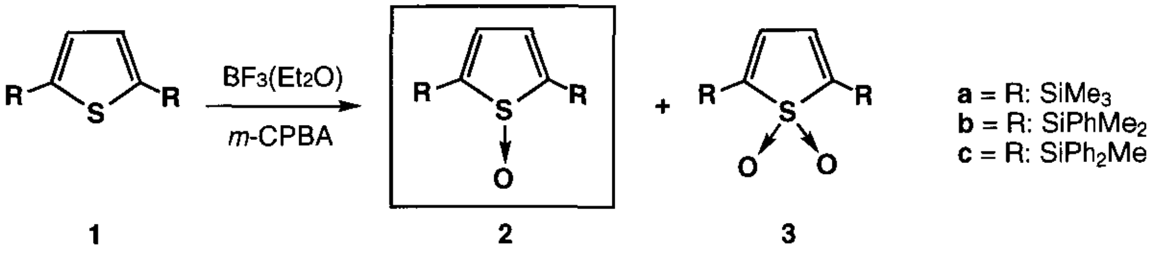
bis(η^5-cyclopentadienyl)-2,3,4,5-tetraphenyl-1-zirconacyclopentadiene with thionylchloride.[4] However, precise determination of the ring conformation and of the S-O and S-C distances was not achievable in that case because of the structural disorder. Recently, Mansuy *et al.* have reported the preparation of 2,5-diphenythiophene *S*-oxide in 25% yield.[5] This compound is stable at -20 °C, but slowly decomposes in solution over a few days at room temperature. Furthermore, the oxidation of η^4 metal complex of thiophene has been reported to afford successfully the corresponding *S*-oxide with molecular oxygen.[6] It can be inferred from these results that the stabilization of thiophene monooxide requires protection by the bulky 2,5-disubstituents. We have attempted preparation of 2,5-bis(silylated) thiophene *S*-oxide with *m*-CPBA; however, in the preliminary experiments, the products were found to be solely the *S*-dioxides and the corresponding thiophene *S*-oxides were not obtained at all.[7] Apparently, thiophenes would be oxidized to the *S*-dioxides *via* an initial formation of the *S*-oxide which should be more reactive than thiophenes; hence, *S*-oxides are readily oxidized to the *S*-dioxides unless either the thiophenes have bulky substituents at the 2,5-positions or one lone electron pair is blocked by the formation of a coordination complex with metals. These results suggest that the activation energy for the oxidation of thiophene to the *S*-oxide should be higher than that of the oxidation of the *S*-oxide to the *S*-dioxide. If the oxidation steps could be controlled to lower the activation energy in the first phase, the reaction could give the *S*-oxide. With this aim in mind, we undertook the oxidation of 2,5-bis-substituted thiophenes with *m*-CPBA in the presence of a Lewis acid, i.e., boron trifluoride etherate: $BF_3(Et_2O)$. Indeed, the thiophene derivatives bearing bulky silyl-substituents at the 2,5-positions provided the *S*-oxides in moderate yields together with a small amount of *S*-dioxides. We wish to report that 2,5-bis(trimethylsilyl)- (**2a**), 2,5-bis(dimethylphenylsilyl)- (**2b**), and 2,5-bis(diphenylmethylsilyl)thiophene *S*-oxides (**2c**) were selectively obtained by oxidation of the corresponding thiophenes (**1**) with *m*-CPBA in the presence of $BF_3(Et_2O)$.

$BF_3(Et_2O)$ was employed as the Lewis acid in the present reactions in order to decelerate the oxidation of the sulfur atom on the thiophene ring and to prevent production of the corresponding *S*-dioxide (**3a**). The oxidation of **1a** with *m*-CPBA was performed in various reaction conditions. The results are summarized in Table 1. The oxidation of **1a** with *m*-CPBA in the absence of $BF_3(Et_2O)$ afforded solely the corresponding *S*-dioxide (**3a**), together with the recovered **1a**. On the other hand, the oxidation of **1a** with *m*-CPBA in the presence of more than 3 eq. of $BF_3(Et_2O)$ afforded predominantly the corresponding *S*-oxide (**2a**) and the yield of **2a** increased up to 62% on oxidation at low temperature.

Scheme 1



It is expected from comparison of the reaction time and product ratio that $BF_3(Et_2O)$ plays a role not only in preventing further oxidation of the thiophene *S*-oxide once formed to the *S*-dioxide (**3a**), but also in increasing the reactivity of *m*-CPBA, probably through coordination onto both the sulfinyl oxygen of **2a** and the peracid oxygen. Although the starting thiophene (**1a**) was consumed completely, the yield of **2a** was found to be around 62% indicating that the *S*-oxide (**2a**) may undergo a Diels-Alder type self-condensation to afford unidentified products.

Table 1. Oxidation of 2,5-bis(trimethylsilyl)thiophene (**1a**) with 1.0 eq. *m*-CPBA in the presence of $BF_3(Et_2O)$ in CH_2Cl_2

				Yield (%)			Product ratio	
Run	$BF_3(Et_2O)$ (eq.)	Time (h)	Temp (°C)	**1a**[a]	**2a**	**3a**	**2a** :	**3a**
1	-	2.5	25	30	0	27	0	100
2	0.5	1.5	25	0	19	13	60	40
3	1.0	1.0	25	0	30	7	81	19
4	2.0	<0.5	25	0	25	4	86	14
5	3.0	<0.5	25	0	26	3	90	10
6	3.0	<1	0	0	26	3	90	10
7	3.0	2	-20	0	62	3	95	5

A typical experimental procedure (run 7) is shown in Experimental. The ^1H-nmr signals of the hydrogens at the 3 and 4 positions of **2a** appear at higher field (6.82 ppm) than those of **1a** (7.31 ppm). These results suggest that the aromaticity on the thiophene ring of *S*-oxide (**2a**) first disappears to be oxidized at once to the corresponding dioxides. The observed chemical shifts of **2a** are similar to those of *S*-dioxide (**3a**).

Additionally, we tried to synthesize thiophene *S*-oxide derivatives having more bulky substituents in order to obtain more stable compounds as shown in Scheme 1. The thiophene derivative (**1b**) or (**1c**) having dimethylphenylsilyl or diphenylmethylsilyl groups was oxidized in the same manner to isolate the corresponding thiophene *S*-oxide (**2b**) or (**2c**) in 45% or 15% yield, respectively. On the other hand, though 2,5-bis(triphenylsilyl)thiophene (**1d**) was also oxidized under the same conditions, neither the corresponding *S*-oxide (**2d**) nor *S*-dioxide (**3d**) could be isolated at all. These results indicate that the oxidative capability of the sulfur atom on the thiophenes (**1b-d**) is reduced by the steric hindrance of the two larger substituents attached at 2 and 5 positions. Another conceivable reason for these results would be the steric hindrance on the formation of the $BF_3 \cdot$*m*-CPBA complex, since the thiophene *S*-dioxide (**3d**) could be synthesized from the reaction of thiophene (**1d**) with *m*-CPBA without $BF_3(Et_2O)$ quantitatively. The spectral data of the isolated *S*-oxides (**2a-c**) are summarized in Table 2.

Table 2. The spectral data of thiophene *S*-oxides (**2a-c**)

Compd	**2a**	**2b**	**2c**
Yield (%)	62	45	15
mp (decomp., °C)	128	73-74	157
^{1}H-Nmr data (270 MHz, ppm)	0.35 (s, 18H, CH_3) 6.82 (s, 2H, ThH)	0.64 (s, 12H, CH_3) 6.71 (s, 2H, ThH) 7.38-7.40 (m, 6H, PhH) 7.58-7.61 (m, 4H, PhH)	0.93 (s, 6H, CH_3) 6.76 (s, 2H, ThH) 7.34-7.37 (m, 12H, PhH) 7.54-7.56 (m, 8H, PhH)
^{13}C-Nmr data (68 MHz, ppm)	0.8, 137.9, 161.5	-2.5, 128.1, 129.8, 133.9, 135.8, 137.7, 158.8	-3.61, 128.1, 130.0, 134.0, 135.0, 139.4, 158.1
Ir (KBr, cm^{-1})	1048 (SO)	1046 (SO)	1058 (SO)
Ms (m/z)	244(M^+)	368(M^+)	492(M^+)
Elemental Analysis			
Anal. Calcd for	$C_{10}H_{20}OSSi_2$ C, 49.12; H, 8.24	$C_{20}H_{24}OSSi_2$ C, 65.16; H, 6.56	$C_{30}H_{28}OSSi_2$ C, 73.12; H, 5.73
Found	C, 48.96; H, 8.61	C, 64.89; H, 6.45	C, 72.69; H, 5.63

The present reaction represents a simple method for selective preparation of thiophene *S*-oxides from the corresponding thiophene derivatives. Application to other thiophene derivatives bearing bulky substituents and study on the mechanistic aspect of the reactions are currently under way in the laboratory.

Preparation of thiophene monooxides

2,5-bis(Trimethylsilyl)thiophene *S*-Oxide (2a). Boron trifluoride-etherate $BF_3(Et_2O)$ (0.19 ml, 1.5 mmol) was added to a solution of thiophene (**1a**) (114 mg, 0.5 mmol) in dry CH_2Cl_2 (4 ml) at -20 °C under an argon atmosphere, and *m*-CPBA (104 mg, 0.6 mmol) in dry CH_2Cl_2 (2ml) was added to the solution. The reaction was monitored occasionally by tlc analysis on silica gel. After the reaction, saturated aqueous sodium carbonate was added to the reaction mixture, and the organic layer was extracted with chloroform (3 x 50 ml). The combined organic layer was washed with brine (3 x 50 ml) and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was subjected to column chromatography on silica gel (hexane : ethylacetate = 3 : 1 v/v) to afford the *S*-oxide (**2a**). Recrystallization from hexane gave colorless crystals (50 mg, yield 62%).

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REFERENCES

1. D. Mansuy, P. Valadon, I. Erdelmeier, P. Lopez-Garcia, C. Amar, J. P. Girault, and P. M. Dansette, *J. Am. Chem. Soc*, 1991, **113**, 7825; P. M. Dansette, T. Do Cao, H. El Amri, and D. Mansuy, *Biochem. Biophys. Res. Commun.*, 1992, **186**, 1624; P. Lopez-Garcia, P. M. Dansette, P. Valadon, C. Amar, P. Beaune, F. Guengerich, and D. Mansuy, *Eur. J. Biochem.*, 1993, **213**, 223; P. Lopez-Garcia, P. Dansette, and D. Mansuy, *Biochemistry*, 1994, **33**, 166.
2. S. Gronowitz, *Heterocycles*, 1963, **1**, 1; W. J. M. van Tilborg, *Synth. Commun.*, 1976, **6**, 583; J. Nakayama, S. Yamaoka, and M. Hoshino, *Tetrahedron Lett.*, 1988, **29**, 1161; J. Nakayama and R. Hasemi, *J. Am. Chem. Soc.*, 1990, **112**, 5654; J. Nakayama and H. Kamiyama, *Tetrahedron Lett.*, 1992, **33**, 7539.

3. W. L. Mock, *J. Am. Chem. Soc.*, 1970, **92**, 7610,

4. F. Meier-Brocks and E. Weiss, *J. Organomet. Chem.*, 1993, **453**, 33.

5. P. Pouzet, I. Erdelmeier, D. Ginderow, J.-P. Morson, P. Dansette, and D. Mansuy, *J. Chem. Soc., Chem. Commun.*, 1995, 473.

6. A. E. Skaugest, T. B. Rauchfuss, and C. L. Stern, *J. Am. Chem. Soc.*, 1990, **112**, 2432.

7. N. Furukawa, H. Hoshiai, T. Shibutani, M. Higaki, F. Iwasaki, and H. Fujihara, *Heterocycles*, 1992, **34**, 1085.

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