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The Pummerer-Like Reaction of 2,5-Bis(trimethylsilyl)thiophene *S*-Oxide with Trifluoroacetic Anhydride: Intermediary Formation of Sulfurane [10-*S*-4(C2O2)] (λ^4-Sulfane)

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ABSTRACT: *On treatment of a 2,5-bissilylsubstituted thiophene S-oxide or dibenzothiophene S-oxide with trifluoroacetic anhydride, the equillibria between the corresponding substrates and hypervalent sulfur compounds (sulfurane or λ⁴-sulfane) have now been first detected by low temperature NMR experiments. By elevating the temperature to room temperature, in the case of the thiophene S-oxide, the sulfurane detected was converted to 3-thiolene-2-one quantitatively via a Pummerer-like reaction.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:444–450, 2001

INTRODUCTION

Although thiophene *S*-oxides are unstable species, they can have interesting reactivities [1]. Recently, new synthetic methods and structure determinations of stable thiophene *S*-oxides having bulky substituents on the thiophene ring have been reported [2]. Thiophene *S*-oxide species have mainly two reactive sites. One is the diene site on the thiophene ring. The other is the sulfinyl site (sulfoxide group). A few reaction properties of the diene site in the thiophene *S*-oxides have been reported after development of convenient synthetic methods; for example, the isolated thiophene *S*-oxides undergo [4 + 2] cycloaddition with olefins and acetylenes as dienophiles, or *cis*-1,4-addition with halogenes [3]. However, only Nakayama *et al.* [4] have reported a reaction on the sulfur atom in the thiophene *S*-oxides. In order to estimate the reactivity of the sulfinyl site in the thiophene *S*-oxide species, we tried to react the thiophene *S*-oxide derivatives with an acid anhydride. Generally, the reactions of chiral sulfoxides with acid anhydrides undergo concurrent racemization and oxygen exchange. In the case of sulfoxides having α-protons as substrates, Pummerer-type reactions can conceivably proceed via the corresponding sulfonium salts as intermediates. Detailed studies on possible reaction mechanisms were reported by Oae *et al*. [5]. They proposed that the reactions proceed via the corresponding sulfonium salts, and sulfuranes formed as unstable intermediates. However, these sulfurane intermediates were not detected directly. In this article, we wish to report the first detection of an equilibrium between thiophene *S*-oxide derivatives and the corresponding hypervalent sulfur compounds (sulfuranes or λ^4-sulfanes) as intermediates by low temperature NMR experiments in which the thiophene *S*-oxide derivatives were caused to react with acid anhydrides. Furthermore, a Pummerer-type reaction was observed involving the cor-

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Dedicated to Professor Naoki Inamoto on the occasion of his 72nd birthday.

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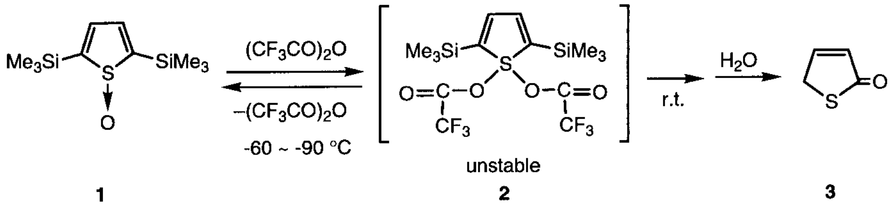


SCHEME 1

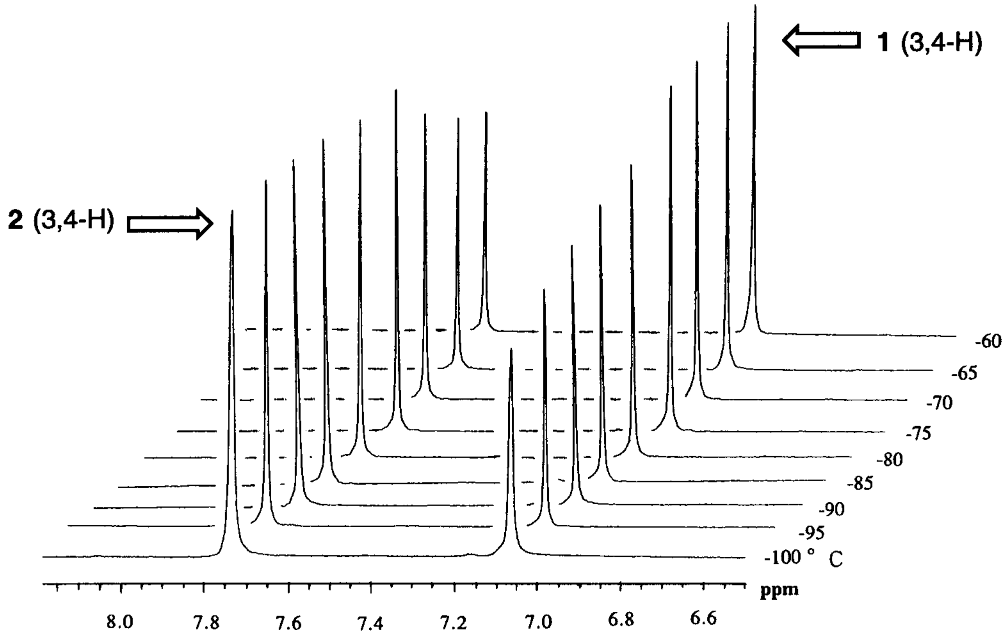


FIGURE 1 VT ^{1}H NMR spectra of the thiophene *S*-oxide with trifluoroacetic anhydride.

responding sulfurane intermediate by raising the temperature to room temperature.

RESULTS AND DISCUSSION

First, we examined the reaction of the kinetically stabilized 2,5-bis(trimethylsilyl)thiophene *S*-oxide (**1**) with trifluoroacetic anhydride, as shown in Scheme 1. The thiophene *S*-oxide **1** was treated with 1.5 equiv. of trifluoroacetic anhydride at low temperature (below −60°C) in THF-d_8, and the ^{1}H chemical shifts of both of the 3,4-protons on the thiophene ring and the protons of the trimethylsilyl groups were monitored by variable low temperature NMR spectroscopy. New signals appeared at low field (7.60 ppm (3,4-H) and at 0.37 ppm (Me_3Si)) compared with those of the substrate **1** (6.97 ppm (3,4-H) and 0.31 ppm (Me_3Si)) at −60°C. By elevating the temperature, the NMR signal intensities of a new intermediate **2** increased and those of the substrate **1** decreased, while, by lowering the temperature, the NMR observation was the opposite, as shown in Figure 1. This result suggests that an equilibrium between the thiophene *S*-oxide **1** and the corresponding intermediate **2** exists in this reaction only below −60°C and that the structure of the intermediate **2** is a symmetrical one. The intermediate **2** was also characterized by ^{19}F and ^{13}C NMR spectroscopy at −80°C. These NMR spectra also show that the intermediate **2** is a symmetrical molecule with one signal (−78.1 ppm) in the ^{19}F NMR spectrum and a set of five peaks in the ^{13}C NMR spectrum. These results indicate that the intermediate **2** is probably an unstable sulfurane having two trifluoromethylcarboxyl ligands [6]. Furthermore, the kinetic control of the reaction depends sensitively on the concentration of anhydride. When the thiophene *S*-oxide **1** was treated with more than 3.0 equiv. of trifluoroacetic anhydride at −80°C in dry THF-d_8, the NMR signals of **1** disappeared completely and only those of the corresponding intermediate **2** remained.

Based on the ^{1}H NMR spectral data observed at various temperatures, the equilibrium constants (*K*) between the thiophene *S*-oxide **1** and the corre-

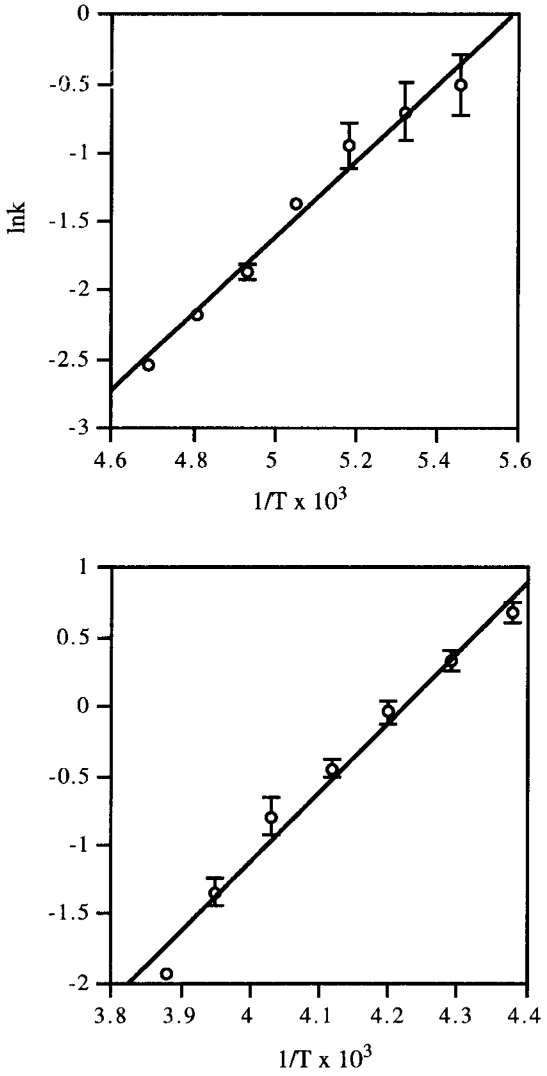


FIGURE 2 van't Hoff plots with standard deviation of equilibria between **1** and **2** (top graph) and **6** and **7** (bottom graph).

sponding sulfurane intermediate **2** were calculated, based on the second-order rate equation. By plotting ln*K* against 1/*T*, a straight line was obtained, as shown in Figure 2. The enthalpy values, $\Delta H°$ (−5.5 kcal mol^{-1}) and free energy, $\Delta G_{(198)}°$ (0.5 kcal mol^{-1}) were calculated. These parameters are summarized in Table 1.

By elevating the temperature to room temperature, the ^{1}H NMR signals due to **1** and **2** disappeared, and new signals due to the product appeared. The reaction mixture was separated, and after treatment by column chromatography, the product **3** was obtained in 95% yield (Scheme 2). The compound **3** was identified by ^{1}H, ^{13}C NMR, and mass spectroscopy to be the known compound, 3-thiolene-2-one (**3**) [7]. In order to investigate the mechanism for the formation of product **3**, this reaction system was monitored in detail by variable low temperature NMR spectroscopy. When the temperature of the solution was slowly elevated from −60 to −35°C, the signals due to both **1** and **2** disappeared gradually and one set of an AB quartet of two protons on the thiophene ring at 7.04 and 7.07 ppm (J = 7.8 Hz) and two singlets of trimethylsilyl groups at 0.32 and 0.53 ppm appeared. By elevating the temperature to room temperature, the ^{1}H NMR spectrum shows one set of an AB quartet peak of two protons on the thiophene ring at 7.02 and 7.07 ppm (J = 8.0 Hz) and a singlet of 9 protons of one trimethylsilyl group at 0.31 ppm. These results indicate that this Pummerer-like reaction proceeded via two intermediates. These final signals did not change in a closed system, even at room temperature. The intermediate **4** in the final solution was decomposed gradually by water contained in the solution or was reacted with additional water to conver it to 3-thiolene-2-one **3**. We propose the mechanism of the Pummerer-like reaction to be that shown in Scheme 2 on the basis of the aforementioned results.

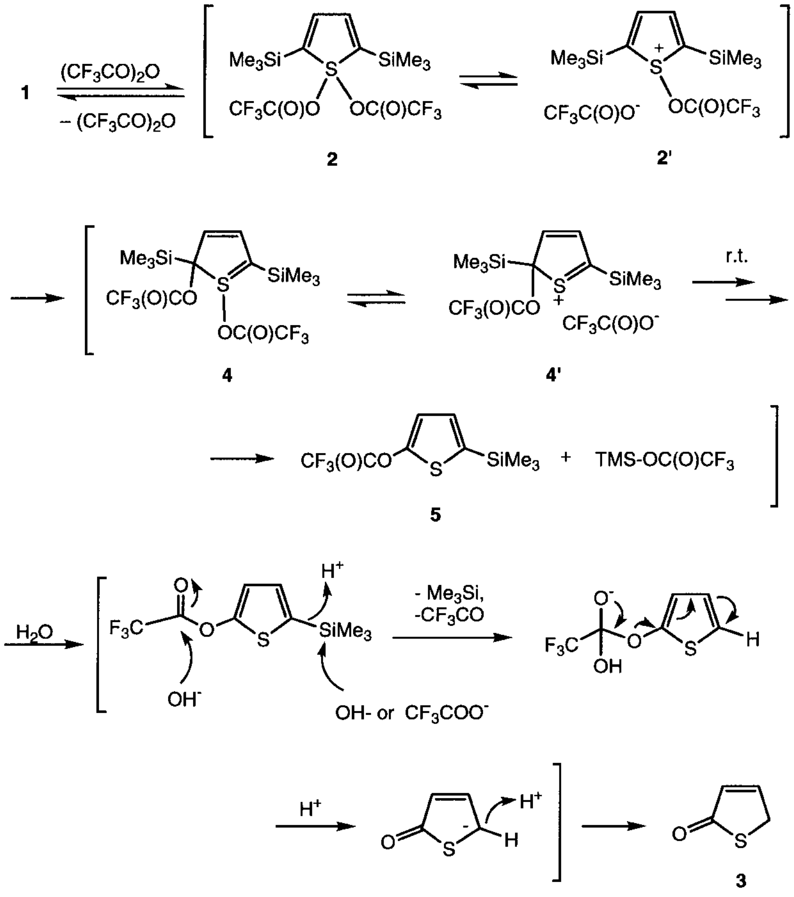
The mechanism for the present reactions may proceed initially by the Pummerer-like reaction of the intermediate **2** by formation of intermediates **4** and **5**, and then the hydrolysis of intermediate **5** could proceed. Furthermore, the reaction was quenched with D_2O or $H_2{}^{18}O$ in order to determine the source of the 5-protons and the oxygen of the carbonyl group in **3**. ^{18}O-Uptake was not observed, while D atoms were found at the 5-position of **4**. These results indicate that water is not the source of the oxygen atom but is the source of the protons in **3**. Thus, the source of theoxygen is the original carboxyl group in **3**.

Furthermore, we undertook the reaction of dibenzothiophene *S*-oxide (**6**) with trifluoroacetic anhydride, as shown in Scheme 3 [8]. The equilibrium between dibenzothiophene *S*-oxide (**6**) and the corresponding sulfurane intermediate **7** with trifluoroacetic anhydride was also observed by monitoring with variable low-temperature ^{1}H NMR spectroscopy. Only the ^{1}H NMR signals of the substrate **6** appeared at room temperature, and only those of the sulfurane intermediate **7** appeared at −78°C. The temperature dependence of this equilibrium state was observed even from −78°C to room temperature as shown in Figure 3. The intermediate **7** was also characterized by ^{19}F and ^{13}C NMR spectroscopy at −78°C. These spectra indicate that the intermediate **7** has a symmetrical structure. These results also indicate that the intermediate **7** is an unstable sulfurane compound having two trifluoromethylcarboxyl ligands. Based on this ^{1}H NMR technique, the equilibrium constants (K) at the corresponding tempera-

TABLE 1 Equilibrium Parameters for the Reactions of Thiophene *S*-Oxide Derivatives with $(CF_3CO)_2O$

Reactions[a]	K^b (s^{-1})		$\Delta H^{\circ c}$ (kcal mol^{-1})	$\Delta G^{\circ c}$ (kcal mol^{-1})
A	7.48×10^{-2} (213 K)	1.13×10^{-1} (208 K)	−5.5	0.5 (198 K)
	1.56×10^{-1} (203 K)	2.55×10^{-1} (198 K)		
	3.94×10^{-1} (193 K)	5.07×10^{-1} (188 K)		
	6.12×10^{-1} (183 K)			
B	1.46×10^{-1} (258 K)	2.62×10^{-1} (253 K)	−10.0	0.2 (243 K)
	4.53×10^{-1} (248 K)	6.40×10^{-1} (243 K)		
	9.64×10^{-1} (238 K)	1.40 (233 K)		
	1.97 (228 K)			

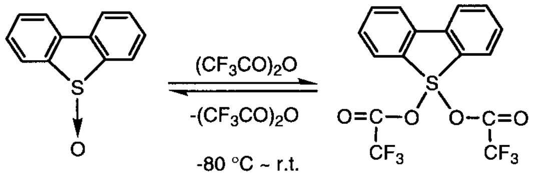
[a] Reaction **A**: reaction of **1** with 1.5 equiv $(CF_3CO)_2O$. Reaction **B**: reaction of **6** with 2.0 equiv $(CF_3CO)_2O$.
[b] Average values.
[c] These values were obtained from van't Hoff equation, $\ln K = -\Delta H^{\circ}/RT$ + const. and $-\Delta G_{(T)}^{\circ} = RT\ln K$.



SCHEME 2

tures were calculated. By plotting ln*K* against 1/*T*, a good straight line was obtained as shown in Figure 2. Furthermore, the free energy and enthalpy of the equilibrium reaction were calculated. Based on the spectral data observed at various temperatures, the equilibrium constants (*K*) between **6** and **7** were calculated by use of the second-order rate equation. The enthalpy value, ΔH° (−10.0 kcal mol^{-1}) and free energy, $\Delta G_{(243)}^{\circ}$ (0.2 kcal mol^{-1}) were also calculated. These parameters are summarized in Table 1.

We found that the ^{1}H chemical shift (7.64 ppm) of the 3,4-protons in **2** appeared at quite low field compared with those of the known 2,5-bis(trimethylsilyl)thiophene derivatives [2,5-bis(trimethylsilyl)thiophene *S*-oxide **8** (6.74 ppm), 2.5-bis(trimethylsilyl)thiophene *S*-oxide **1** (6.82 ppm), 2,5-bis(tri-



6 **7**

SCHEME 3

methylsilyl)thiophene *S*-oxide (*O*-*B*)trifluoroborane **9** (7.13 ppm), and 2,5-bis(trimethylsilyl)thiophene **10** (7.31 ppm)], as shown in Figure 4. The thiophene rings of the derivatives **1**, **8**, and **9** do not have aromatic characters due to their nonplaner structures [3a]. Therefore, these ^{1}H chemical shifts of the 3,4-protons appeared at low field compared with that of the thiophene *S*-oxide **1** in spite of the bonding of the electronegative ligands on the sulfur atom in **1**,**8**, and **9**. These results suggest that the low-field shift of the 3,4-protons in **2** is due not only to the strong electron-withdrawing character of the two trifluoroacetyl groups on the sulfur atom but also to the new aromatic character of the thiophene ring that can make use of a pair of electrons in the hypervalent bond to complete a [4*n* + 2] shell, as shown in Figure 5. The latter phenomenon had been predicted by Martin *et al.* [9].

In the present study, we showed that the equilibrium between thiophene *S*-oxide derivatives and the corresponding hypervalent sulfur compounds (sulfuranes or λ^4-sulfanes) as intermediates could be detected directly by low temperature NMR spectroscopy in the reaction of thiophene *S*-oxide derivatives with an acid anhydride, and that a Pummerer-type reaction of the corresponding sulfurane intermedi-

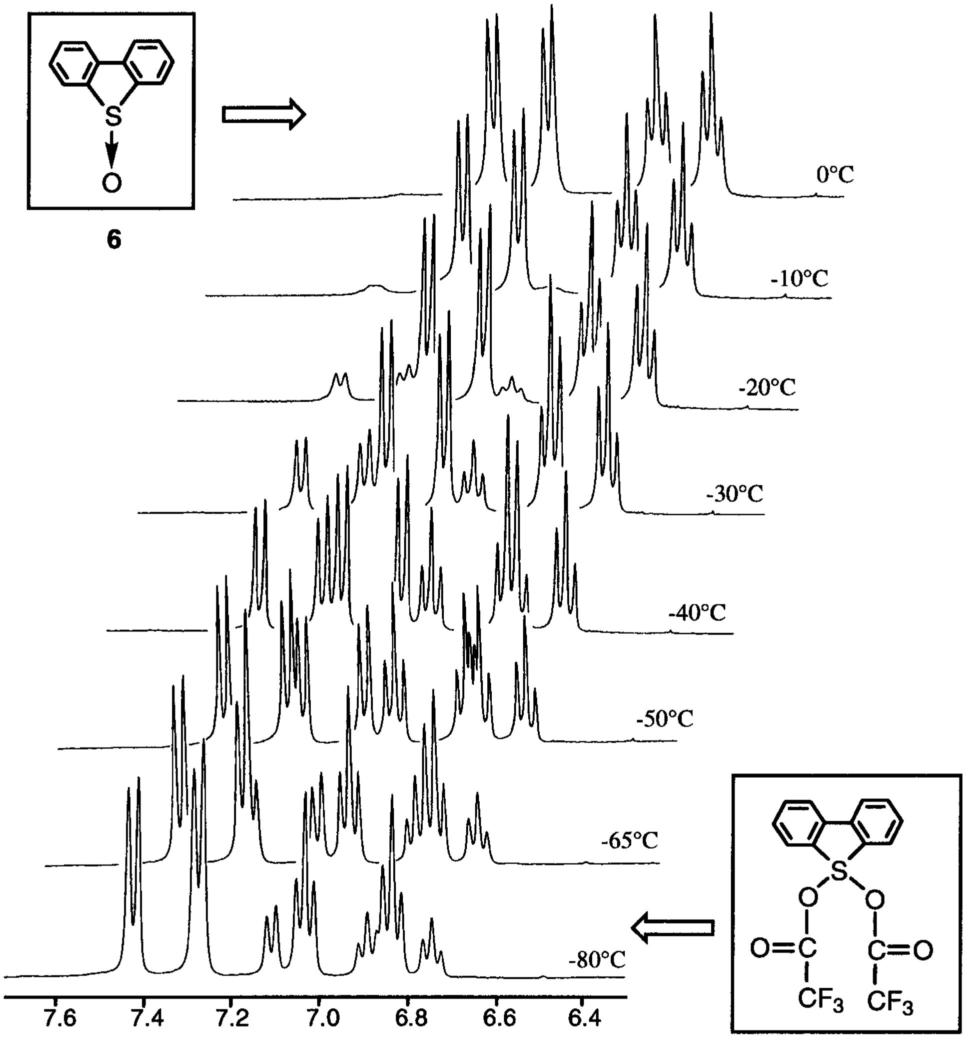


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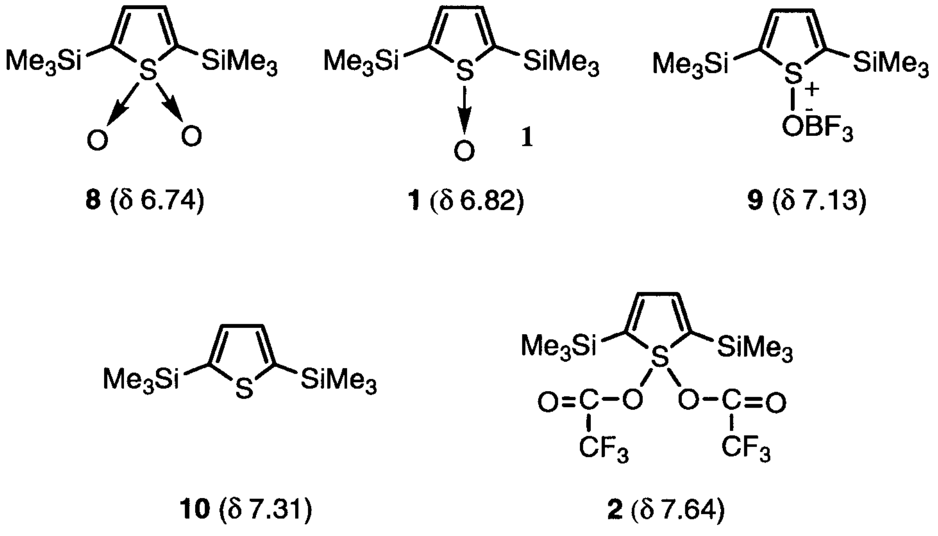
FIGURE 3 VT ^{1}H NMR spectra of dibenzothiophene *S*-oxide **6** with trifluoroacetic anhydride.



8 (δ 6.74) **1** (δ 6.82) **9** (δ 7.13)

10 (δ 7.31) **2** (δ 7.64)

FIGURE 4 ¹H NMR chemical shits of 2,5-bis(trimethylsilyl)thiophene derivatives.

ate proceeded when the temperature was elevated to room temperature. These investigations demonstrate alternative reactivities of the sulfinyl group in thiophene *S*-oxides that are unlike those of simple sulfoxides.

EXPERIMENTAL

General Data

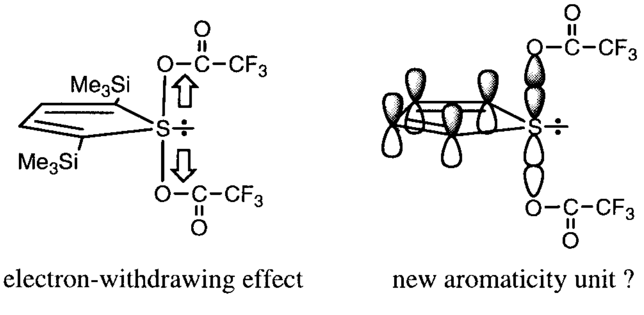
All NMR spectra were measured on a JEOL LMN-EX-270 or a Bruker ARX-400 spectrometer. Mass spectra were taken with a Shimazu QP-2000 and a JEOL JMS SX 102 mass spectrometer. All solvents and reagents were obtained from commercial sources and were further purified by general methods.

Reaction of 2,5-Bis(trimethylsilyl)thiophene S-oxide 1 with Trifluoroacetic Anhydride

2,5-Bis(trimethylsilyl)thiophene *S*-oxide **1** (0.1 mmol, 24.0 mg) was dissolved in dry THF-d_8 (0.60 mL) contained in an NMR tube, the solution was cooled to −78°C, and trifluoroacetic anhydride (0.2 mmol, 0.032 ml) was added by a microsyringe. This reaction was monitored by variable temperature ¹H NMR spectroscopy. The NMR spectra of the sulfurane intermediate **2** could be observed over the temperature range from −100 to −60°C. Sulfurane **2**: ¹H NMR (270 MHz, THF-d_8, −80°C) δ 0.34 (s, 18 H, MeH), 7.64 (s, 2 H, ThH). ^{13}C NMR (68 MHz, THF-d_8, −80°C) δ −1.28, 115.9 (q, J = 286 Hz), 149.6, 161.0 (q, J = 41 Hz), 161.8. ^{19}F NMR (254 MHz, THF-d_8, −80°C) δ −78.1 (relative to $CFCl_3$). ¹H NMR chemical shifts of **2** were shifted to high field by elevating the temperature. The scale of the chemical shift shown in Figure 1 was adapted to the NMR spectrum at −100°C.

Isolation of 3-Thiolene-2-one 3

2,5-Bis(trimethylsilyl)thiophene *S*-oxide (1.0 mmol, 240.0 mg) was dissolved in dry THF (10 mL) contained in a reactor, the solution was cooled to −78°C, and trifluoroacetic anhydride (2.0 mmol, 0.32 ml) was added by a microsyringe. The reaction vessel was warmed to room temperature slowly. After removal of the solvent, the residue was subjected to column chromatography on silica gel (hexane:dichloromethane = 1:1 v/v) to afford 3-thiolene-2-one **3** (48.0 mg, 48%). 3-Thiolene-2-one **3**: ¹H NMR (400 MHz, $CDCl_3$, r.t.) δ 4.15 (t, J = 2.5 Hz, 2H), 6.41 (sext, J = 2.0 Hz, 1H), 7.58 (quint, J = 2.9 Hz, 1H). ^{13}C NMR (270 MHz, $CDCl_3$, room temperature [r.t.]) δ 39.0, 133.5, 154.0, 210.5. MS m/z 100 (M^+). RI (NaCl) 1669 (cm^{-1}).



electron-withdrawing effect new aromaticity unit ?

FIGURE 5 The electronic structure of sulfurane **2**.

The Quenching of the Pummerer-Like Reaction by D_2O or $H_2{}^{18}O$

Reaction of 2,5-(bistrimethylsilyl)thiophene *S*-oxide **1** with trifluoroacetic anhydride was quenched by D_2O and by $H_2{}^{18}O$ at r.t. The aforementioned reaction solution was warmed gradually to r.t. and D_2O (2.0 mmol, 0.04 mg) or $H_2{}^{18}O$ (2.0 mmol, 0.04 mg) was added by a microsyringe. Each product was identified by its ^1H NMR spectra and by mass spectroscopy.

Reaction of Dibenzothiophene S-Oxide **6** *with Trifluoroacetic Anhydride*

The dibenzothiophene *S*-oxide **6** (0.05 mmol, 10.0 mg) was dissolved into dichloromethane-d_2 (0.60 ml) contained in an NMR tube. The trifluoroacetic anhydride (0.05 mmol, 0.008 mL) was added by a microsyringe at -78°C. This reaction was monitored by variable temperature ^1H NMR spectroscopy. The NMR spectra of sulfurane intermediate **7** was observed at -60°C. Sulfurane **7**: ^1H NMR (270 MHz, $CDCl_3$, -60°C) δ 7.65 (t, J = 8.3 Hz, 2 H, PhH), 7.82 (t, J = 98.3 Hz, 2 H, PhH), 8.02 (d, J = 7.7 Hz, 2 H, PhH), 8.20 (d, J = 7.7 Hz, 2 H, PhH) ^{13}C NMR (68 MHz, $CDCl_3$, -60°C) δ 113.2 (q, J_{F-C} = 286 Hz), 123.5, 125.9, 130.3, 133.8, 140.3, 159.8, 149.2 (q, J_{F-C} = 48 Hz). ^{19}F NMR (254 MHz, $CDCl_3$, -60°C) δ -76.1 (relative to $CFCl_3$).

REFERENCES

[1] Nakayama, J.; Sugihara, Y. Sulfur Reports 1997, 19, 349 (see also references therein).

[2] (a) Fagan, P. J.; Nugent, W. A. J Am Chem Soc 1988, 110, 2310; (b) Fagan, P. J.; Nugent, W. A.; Calabrese, J. C. J Am Chem Soc 1994, 116, 1880; (c) Furukawa, N.; Zhang, S.-Z.; Sato, S.; Higaki, M. Heterocycles 1997, 44, 61; (d) Nakayama, J.; Yu, T.; Sugihara, Y.; Ishii, A. Chem Lett 1997, 499.

[3] (a) Furukawa, N.; Zhang, S.-Z.; Horn, E.; Takahashi, O.; Sato, S. Heterocycles 1998, 47, 793; (b) Zhang, S.-Z.; Sato, S.; Horn, E.; Furukawa, N. Heterocycles 1998, 48, 227; In situ Diels-Alder reactions of thiophene *S*-oxides as follows: (c) Melles, J. L.; Backer, H. J. Rec Trav Chim 1953, 72, 491; (d) Davies, W.; Gamble, N. W.; James, F. C.; Savigi, W. E.; Chem Ind 1954, 804; (e) Davies, W.; James, F. C. J Chem Soc 1954, 15; (f) Okita, K.; Kambara, S. Kogyo Kagaku Zasshi 1956, 59, 547; (g) Merrill, R. E.; Sherwood, G. J. Heterocycl Chem 1977, 14, 1251; (h) Torssell, K. Acta Chem Scand B 1976, 30, 353; (i) Naperstkow, A. M.; Macaulay, J. B.; Newlands, M. J.; Fallis, A. G. Tetrahedron Lett 1989, 30, 5077; (j) Li, Y.; Matsuda, M.; Thiemann, T.; Sawada, T.; Mataka, S.; Tashiro, M. Synlett 1996, 461; (k) Girault, J.-P.; Ginderow, D.; Morson, J.-P.; Mansuy, D. J Am Chem Soc 1997, 119, 1565; (l) Zheng, H.-P.; Eguchi, S. Synlett 1997, 175.

[4] Otani, T.; Sugihara, Y.; Ishii, A.; Nakayama, J. Tetrahedron Lett 1999, 40, 5549.

[5] (a) Oae, S.; Kise, M. Tetrahedron Lett 1967, 15, 1409; (b) Kise, M.; Oae, S. Bull Chem Soc Jpn 1970, 43, 1421.

[6] (a) Akiba, K.-Y. Chemistry of Hypervalent Compounds; VCH: New York, 1999; Chapter 7; (b) Page, P. C. Organosulfur Chemistry II: Topics in Current Chemistry; Springer: U.K., 1999; Chapter 2 (see also references therein).

[7] Jakobsen, H. J.; Larsen, E. H.; Lawesson, S.-O. Tetrahedron 1963, 19, 1867.

[8] Stoss, P.; Satzinger, F. Tetradedron Lett 1974, 1973.

[9] Forbus, T. R.; Martin, J. C. J Am Chem Soc 1979, 101, 5057.