Nucleophilic Addition of Amines to Silyl- and Germyl-Substituted Thiophene 1,1-Dioxides

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Nucleophilic addition of secondary amines to *tert*-butyl-, trimethylsilyl- and trimethylgermyl-2,5-disubstituted thiophene 1,1-dioxides has been studied. It has been shown that the reactivity and reaction pathway depend strongly on the thiophene 1,1-dioxide structure, the basicity of the amine and the nature of the solvent. Addition of amines to 2,5-bis(*tert*-butyl)thiophene 1,1-dioxide does not occur either in organic or in aqueous media. In organic solvents, 2,5-bis(trimethylsilyl)-, 2-trimethylsilyl-5-trimethylgermyl- and 2,5-bis(trimethylgermyl)thiophene 1,1-dioxides add one piperidine molecule, the vinylsilane fragment being more active than the vinylgermane one. The corresponding reactions of thiophene 1,1-dioxides with morpholine and diethylamine failed to occur. In water, the addition of morpholine and diethylamine (one molecule in each case) or dimethylamine and piperidine (two molecules in each case) was accompanied by concomitant demetallation. The molecular structure of 3-piperidino-5-trimethylgermyl-2,3-dihydrothiophene 1,1-dioxide was confirmed by X-ray analysis.

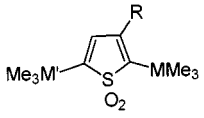
Introduction

The interest in silyl-substituted thiophene 1,1-dioxides stems from the fact that they undergo a wide variety of reactions as unsaturated cyclic sulfones and hence have attracted much attention for the synthesis of different organic compounds.[1] It has been shown that silyl- and germyl-substituted thiophene 1,1-dioxides easily react with nitrile oxides to give the products of [2+3] cycloaddition. Only one fused isoxazoline resulted in each case from the cycloaddition reaction of acetonitrile oxide and benzonitrile oxide with sulfones, indicating the high regiospecificity of these processes.[2] Different bis- and tris(trimethylsilyl)thiophene 1,1-dioxides gave adducts in high yields in the Diels−Alder reaction with *N*-phenylmaleimide.[3] The coupling of 2-dimethyl(*tert*-butyl)silyl-5-bromothiophene 1,1-dioxide with thienylstannanes in the presence of a palladium(0) catalyst enabled the easy and selective insertion of thiophene 1,1-dioxide units into the skeleton of bi-, ter-, quater- and quinquethiophenes.[4] 2,5-Dibromo- and diiodothiophene 1,1-dioxides were prepared from 2,5-bis(trimethylsilyl)thiophene 1,1-dioxide by the action of bromine or iodine in the presence of $AgBF_4$.[5]

The amine-induced ring-opening reaction of silyl-substituted thiophene 1,1-dioxides bearing methyl groups in position 2 of the heterocycle proceeds with high regio- and stereoselectivity[6] to yield *transoid* butadiene derivatives.

Results and Discussion

As molecules of 2,5-disubstituted thiophene 1,1-dioxides **1a−e** are very convenient models for comparison of the influence of different groups on the reactivity of vinyl bonds in various reactions, the nucleophilic addition of secondary amines to the C=C double bonds of sulfones **1** was investigated.



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a: M = M′ = C, R = H; **b:** M = M′ = Si, R = H; **c:** M = Si, M′ = Ge, R = H; **d:** M = M′ = Ge, R = H; **e:** M = M′ = Si, R = Me

The reaction pathway strongly depends on the thiophene 1,1-dioxide structure, the basicity of the amine and the nature of the solvent. It has been shown that the silyl- and germyl-substituted thiophene 1,1-dioxides **1b−e** react easily with piperidine (fivefold excess) in THF and benzene to give the addition products in 50−62% yields. Unlike those in organosilicon and organogermanium sulfones, the double bonds of 2,5-bis(*tert*-butyl)thiophene 1,1-dioxide **(1a)** were inactive in the reaction with piperidine in organic solvents. A similar deactivation was also observed in the [2+3] dipolar cycloaddition of acetonitrile and benzonitrile oxides[2] to 2,5-bis(*tert*-butyl)thiophene 1,1-dioxide **(1a)**. The piperidine addition to silyl- and germyl-substituted thiophene 1,1-dioxides **1b−d** proceeded in THF or benzene, with heating over 5−6 h, leading to formation of 2,5-bis(trimethylsilyl)- **(2b)**, 2-trimethylsilyl-5-trimethylgermyl- **(2c)** and 3-piperidino-2,5-bis(trimethylgermyl)-2,3-dihydrothiophene 1,1-dioxides **(2d)** (Scheme 1). In the case of the unsymmetrical sulfone **1c**, containing both trimethylsilyl and trimethylgermyl groups, reaction occurred regioselectively: only one double bond, that bearing the silyl substituent, added a piperidine molecule. In spite of the excess of piperidine,

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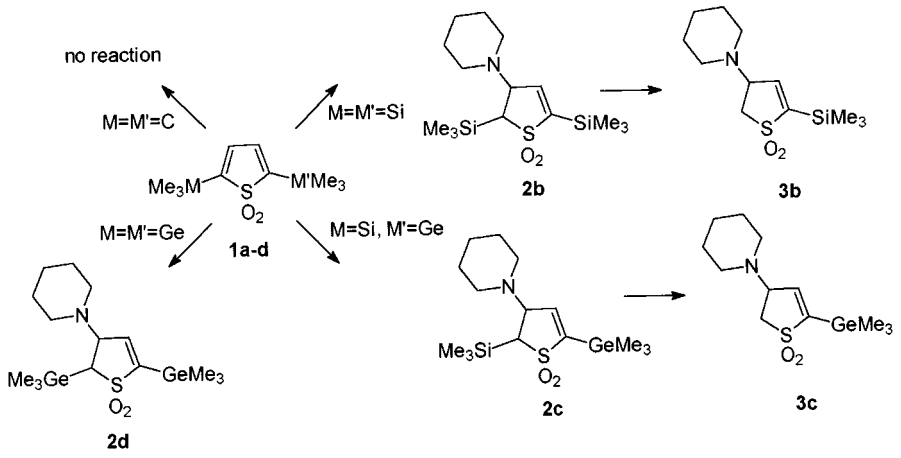
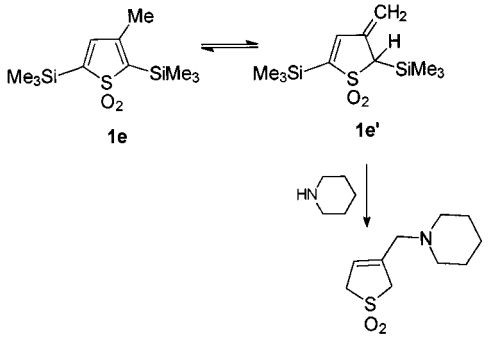


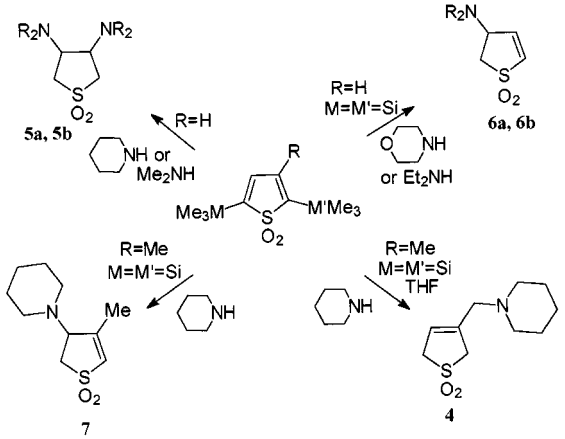
Scheme 1

the second double bond of sulfones **1b–d** did not enter into the interaction. During purification by chromatography on silica gel, desilylation of compound **2c** to 3-piperidino-5-trimethylgermyl-2,3-dihydrothiophene 1,1-dioxide **3c** was detected. Sulfone **2b** is more stable, however, and was separated, without desilylation, by chromatography on silica gel, although partial cleavage of the $Me_3Si-C_{sp}^3$ bond and the formation of a mixture of products **2b** and **3b** were observed on storage. At the same time, degermylation of 3-piperidino-2,5-bis(trimethylgermyl)-2,3-dihydrothiophene 1,1-dioxide **(2d)** did not occur. Addition failed to occur between less basic morpholine and diethylamine to thiophene 1,1-dioxide **1b** in THF and benzene. Introduction of a methyl group at position 3 of 2,5-bis(trimethylsilyl)thiophene 1,1-dioxide **(1b)** completely changed the reaction pathway. Heating of 3-methyl-2,5-bis(trimethylsilyl)thiophene 1,1-dioxide **(1e)** with a fivefold excess of piperidine in organic aprotic solvents gave 3-(piperidinomethyl)-2,5-dihydrothiophene 1,1-dioxide **(4)**. Its formation could be explained by tautomeric equilibration in compound **1e**. The addition of piperidine to tautomeric *exo*-butadiene form **1e′** proceeds in 1,4-fashion, with subsequent desilylation of the intermediate to give 2,5-dihydrothiophene 1,1-dioxide (**4**, Scheme 2). It should be noted that, in this case, the amine-induced ring-opening of thiophene 1,1-dioxide did not occur, contrary to the reaction with secondary amines of 2,5-dimethyl-3-trimethylsilyl-, 2-methyl-5-dimethylbutylsilyl-[5] and 3-bromo-2,5-dimethylthiophene 1,1-dioxides[7] and other sulfones containing methyl groups in positions 2 and 5 of the thiophene 1,1-dioxide rings.[8]

In aqueous medium, both double bonds of 2,5-disubstituted thiophene 1,1-dioxides **1b–d** interact with dimethylamine and piperidine. However, simultaneous desilylation or degermylation accompanied the addition of two amine molecules. As a result, 3,4-bis(dimethylamino)sulfolane **(5a)** and 3,4-bis(piperidino)sulfolane **(5b)** were obtained from sulfones **1b–d** in almost quantitative yield. The less basic diethylamine and morpholine also reacted with 2,5-bis(trimethylsilyl)thiophene 1,1-dioxide **(1b)** in water with desilylation, but, unlike with dimethylamine and piperidine, only one amine molecule added to one double bond of sulfone **1b**, with formation of the 3-amino-2,3-dihydrothiophene 1,1-dioxides **6a** and 6**b.** 3-Methyl-2,5-bis(trimethylsilyl)thiophene 1,1-dioxide **(1e)** also reacted with only one piperidine molecule in aqueous medium, to produce 4-methyl-3-piperidino-2,3-dihydrothiophene 1,1-dioxide **(7)** (Scheme 3). This compound is isomeric with 3-(piperidinomethyl)-2,5-dihydrothiophene 1,1-dioxide **(4)**, which was obtained from the same sulfone **1e** in organic solvents. The nucleophilic addition of amines to 2,5-bis(*tert*-butyl)thiophene 1,1-dioxide **(1a)** in aqueous medium also failed to occur.



Scheme 2



Scheme 3

X-ray Crystallography

The reaction pathway of piperidine addition to unsymmetrical 2-trimethylsilyl-5-trimethylgermylthiophene 1,1-dioxide **(1c)** in organic solvents was unambiguously confirmed by X-ray diffraction. Crystals of 3-piperidino-5-trimethylgermyl-2,3-dihydrothiophene 1,1-dioxide **(3c)** suitable for X-ray analysis were obtained from the original oil by crystallization over 12 weeks at room temperature. The colourless crystals were of size up to 0.70 × 0.50 × 0.30 mm. Crystallographic data and refinement parameters are given in Table 1. Atomic labelling and the view of the molecule **3c** are presented in Figure 1, together with selected bond lengths and angles. The 2,3-dihydrothiophene 1,1-dioxide ring has a planar structure, and the trimethylgermyl substituent is connected with a C_{sp}^2 carbon atom [r(Ge−C_{sp}^2) = 1.914 Å]. This fact clearly indicates that only the vinylsilane side of the sulfone **3c** adds a piperidine molecule.

Table 1. Crystal data and measurement conditions for compound **3c**

Molecular formula	$C_{12}H_{23}GeNO_2S$
Molecular weight	317.96
Crystal size	0.70 × 0.50 × 0.30
Crystal system	monoclinic
Space group	$P2_1/c$
Lattice parameters	
a (Å)	22.652(3)
b (Å)	6.0898(8)
c (Å)	11.418(2)
β (deg.)	103.93(1)
Cell volume V(Å^3)	1528.6(4)
Molecular multiplicity Z	4
$D_{calcd.}$ (g cm^{-3})	1.382(1)
F (000)	664
Absorption coefficient μ (mm^{-1})	2.132
Radiation type	Mo-K_α
Radiation wavelength (Å)	0.71073
$2\theta_{max}$	50.0
Miller index ranges	
h_{min}	−26
h_{max}	26
k_{min}	−7
k_{max}	0
l_{min}	0
l_{max}	13
Number of measured reflections	2665
Number of unique reflections	2512
Number of observed [$I > 2\sigma(I)$] reflections	1731
Number of parameters	154
R-factor [for $I > 2\sigma(I)$]	0.0947
Goodness of fit	1.047
Structure solution method	SHELXS-86[10]
Structure refinement method	SHELXL-93[10]

Conclusions

A general synthetic strategy allows simple access to different 2,3-dihydro- and 2,5-dihydrothiophene 1,1-dioxides and sulfolanes from the readily available silyl-substituted thiophene 1,1-dioxides as starting materials. Nucleophilic addition of amines seems sufficiently flexible to be useful for the synthesis of these heterocyclic compounds. Preliminary results on the cytotoxic activity of fused 2,3-dihydrothiophene 1,1-dioxides show that they exhibit high in vitro tumour growth inhibition on MG-22A (mouse hepatoma), HT-1080 (human fibrosarcoma), B16 (mouse melanoma) and Neuro 2A (mouse neuroblastoma) tumour cell lines.[9]

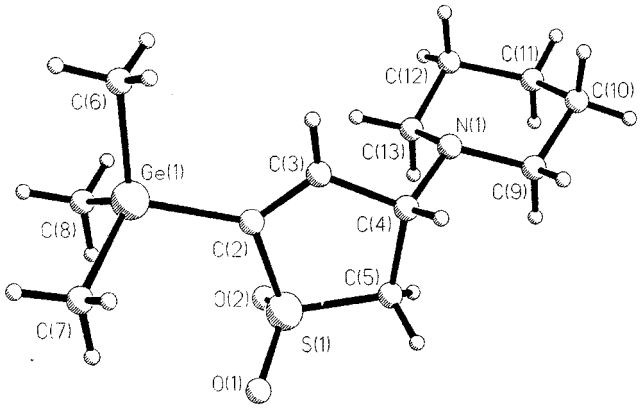


Figure 1. Molecular structure of 3-piperidino-5-trimethylgermyl-2,3-dihydrothiophene 1,1-dioxide **(3c)**; selected bond lengths (Å) and angles (deg): S(1)−C(2) 1.7580(9), C(2)−C(3) 1.3250(14), C(3)−C(4) 1.5266(15), C(4)−C(5) 1.5545(16), C(5)−S(1) 1.7605(12), Ge(1)−C(2) 1.9413(10), N(1)−C(4) 1.4664(12); C(2)−S(1)−C(5), 96.96(6)

Experimental Section

Instrumental: ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 200 spectrometer at 200.06 and 50.31 MHz, respectively, at 303 K. The chemical shifts are given relative to TMS from the solvent impurity ($CHCl_3$ in $CDCl_3$) signal (δ_H = 7.25). Mass spectra were recorded on a Hewlett Packard apparatus (70 eV). − The melting points were determined on a "Digital melting point analyser" (Fisher); the results are given without correction. − Thiophene, 3-methylthiophene, trimethylchlorosilane, piperidine, morpholine, *m*-chloroperbenzoic acid and 2.5 N *n*BuLi in hexanes were purchased from Acros. 2,5-Disubstituted thiophene 1,1-dioxides were prepared according to a previously published method.[2]

3-Methyl-2,5-bis(trimethylsilyl)thiophene: To a solution of 3-methylthiophene (2.45 g, 0.025 mol) in ether (50 mL) was added dropwise 2.5 N *n*BuLi in hexane (22 mL, 0.055 mol), at room temperature. After 30 min, Me_3SiCl (5.43 g, 0.05 mol) was added. The reaction mixture was refluxed for 1 h, hydrolysed with a saturated solution of ammonium chloride, extracted with ether, dried over Na_2SO_4 and evaporated. The residue was distilled to give 4.9 g (81% yield) of the pure product as a colourless liquid (b.p. 110 °C, 5 Torr). − ^{1}H NMR ($CDCl_3$): δ = 0.29 (s, 9 H), 0.32 (s, 9 H), 2.35 (s, 3 H), 7.10 (s, 1 H). − ^{13}C NMR ($CDCl_3$,): δ = −0.03, 0.03, 16.1, 138.5, 139.0, 144.4, 145.7. − MS; *m*/*z*: 242 [M$^+$]. − $C_{11}H_{22}SSi_2$ (242.57): calcd. C 54.45, H 9.14, S 13.22; found C 54.41, H 9.16, S 13.20.

3-Methyl-2,5-bis(trimethylsilyl)thiophene 1,1-Dioxide (1e): A solution of 3-methyl-2,5-bis(trimethylsilyl)thiophene (1.21 g, 5 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a solution of 70% *m*-CPBA (2.47 g, 10 mmol) in CH_2Cl_2. After being stirred for 4 h at room temperature, the reaction mixture was cooled to −50 °C, and the precipitate of *m*-chlorobenzoic acid was filtered off. After evaporation of the solvent, the residue was chromatographed on silica gel, using CH_2Cl_2 as the eluent, to give thiophene 1,1-dioxide **1e** (1.02 g, 74%) as a colourless oil. After some weeks this crystallised,

m.p. 41−43 °C. − ^{1}H NMR ($CDCl_3$): δ = 0.33 (s, 9 H), 0.36 (s, 9 H), 2.08 (s, 3 H), 6.52 (s, 1 H). − ^{13}C NMR ($CDCl_3$): δ = −1.8, −1.1, 17.5, 140.7, 141.0, 147.6, 150.2. − MS; *m/z*: 274 [M^+]. − $C_{11}H_{22}O_2SSi_2$ (274.55): calcd. C 48.13, H 8.08, S 11.68; found C 48.03, H 8.13, S 11.81.

Addition of Piperidine to 2,5-Disubstituted Thiophene 1,1-Dioxides in Organic Solvents. − General Procedure: A mixture of 2,5-disubstituted thiophene 1,1-dioxide **1a−d** (1 mmol) and piperidine (5 mmol) in benzene or THF (5 mL) was refluxed for 5 h. Solvent and the excess of piperidine were evaporated, and the residue was chromatographed on silica gel with CH_2Cl_2 as the eluent. Products were separated as oils. Some of them crystallised after several weeks.

3-Piperidino-2,5-bis(trimethylsilyl)-2,3-dihydrothiophene 1,1-Dioxide (2b): Yield 0.21 g (62%). − ^{1}H NMR ($CDCl_3$): δ = 0.23 (s, 9 H), 0.31 (s, 9 H), 1.47−1.41 (m, 6 H), 2.48 (dqui, *J* = 5.2 Hz, *J* = 18.0 Hz, 4 H), 2.70 (d, *J* = 4.5 Hz, 1 H), 3.95 (dd, *J* = 3.0 Hz, *J* = 4.5 Hz, 1 H), 6.73 (d, *J* = 3.0.Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = −2.3, −1.4, 24.2, 26.2, 48.0, 50.4, 69.9, 146.4, 147.8. − MS; *m/z*: 345 [M^+]. − $C_{15}H_{31}NO_2SSi_2$ (343.34): calcd. C 52.12, H 9.04, N 4.05, S 9.28; found C 52.21, H 8.95, N 4.08, S 9.34.

3-Piperidino-5-trimethylgermyl-2-trimethylsilyl-2,3-dihydrothiophene 1,1-Dioxide (2c): ^{1}H NMR (from the 1:1 mixture with **3c**, $CDCl_3$): δ = 0.20 (s, 9 H), 0.47 (s, 9 H), 1.58−1.44 (m, 6 H), 2.45 (dqui, , *J* = 5.6 Hz, *J* = 17.8 Hz 4 H), 2.72 (d, *J* = 4 Hz, 1 H), 3.96 (dd, *J* = 2.8 Hz, *J* = 4.0 Hz, 1 H), 6.52 (d, *J* = 2.8 Hz, 1 H). − MS; *m/z*: 391 [M^+].

3-Piperidino-2,5-bis(trimethylgermyl)-2,3-dihydrothiophene 1,1-Dioxide (2d): Yield 0.24 g (56%). M.p. 78−79 °C. − ^{1}H NMR ($CDCl_3$): δ = 0.37 (s, 9 H), 0.47 (s, 9 H), 1.58−1.44 (m, 6 H), 2.45 (dqui, *J* = 5.6 Hz, *J* = 17.8 Hz, 4 H), 2.88 (d, *J* = 4 Hz, 1 H), 3.97 (dd, *J* = 2.8 Hz, *J* = 4.0 Hz, 1 H), 6.56 (d, *J* = 2.8 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = −2.0, −1.1, 24.3, 26.3, 49.8, 50.4, 70.7, 144.7, 150.4. − MS; *m/z*: 437 [M^+]. − $C_{15}H_{31}Ge_2NO_2S$ (434.52): calcd. C 41.45, H 7.19, N 3.22, S 7.38; found C 41.52, H 7.23, N 3.15, S 7.32.

3-Piperidino-5-trimethylsilyl-2,3-dihydrothiophene 1,1-Dioxide (3b): ^{1}H NMR (from the 1:1 mixture with **2b**, $CDCl_3$): δ = 0.33 (s, 9 H), 1.61−1.49 (m, 6 H), 2.42 (dqui, *J* = 5 Hz, *J* = 13.4 Hz, 4 H), 3.16 (dd, *J* = 8 Hz, *J* = 13.4 Hz, 1 H), 3.26 (dd, *J* = 5.2 Hz, *J* = 13.4 Hz, 1 H), 4.25 (m, 1 H), 6.62 (d, *J* = 2.4 Hz, 1 H). − MS; *m/z*: 273 [M^+].

3-Piperidino-5-trimethylgermyl-2,3-dihydrothiophene 1,1-Dioxide (3c): Yield 0.16 g (50%). M.p. 74−75 °C. − ^{1}H NMR ($CDCl_3$): δ = 0.49 (s, 9 H), 1.52 (m, 6 H), 2.42 (dqui, *J* = 5 Hz, *J* = 13.4 Hz, 4 H), 3.13 (dd, *J* = 8 Hz, *J* = 13.4 Hz, 1 H), 3.24 (dd, *J* = 5 Hz, *J* = 13.4 Hz, 1 H), 4.25 (m, 1 H), 6.54 (d, *J* = 2.6 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = −1.3, 24.1, 25.9, 47.8, 50.1, 66.1, 145.7, 149.4. − MS; *m/z*: 319 [M^+]. − $C_{12}H_{23}GeNO_2S$ (318.13): calcd. C 45.33, H 7.29, N 4.41, S 10.08; found C 45.07, H 7.03, N 4.47, S 9.91.

3-Piperidinomethyl-2,5-dihydrothiophene 1,1-Dioxide (4): A mixture of 3-methyl-2,5-bis(trimethylsilyl)thiophene 1,1-dioxide **(1e)** (0.274 g, 1 mmol), piperidine (0.43 g, 5 mmol) and benzene (6 mL) was refluxed for 6 h. Solvent and excess piperidine were evaporated, and the residue was chromatographed on silica gel using CH_2Cl_2 as the eluent. The product (0.082 g, 38%) was separated as an oil. − ^{1}H NMR ($CDCl_3$): δ = 1.50 (m, 6 H), 2.32 (m, 4 H), 3.01 (s, 2 H), 3.80−3.77 (m, 4 H), 5.86 (d, *J* = 2 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 24.0, 25.7, 54.4, 56.8, 57.1, 60.9, 119.5, 136.9. − MS; *m/z*: 215 [M^+]. − $C_{10}H_{17}NO_2S$ (215.36): calcd. C 55.78, H 7.96, N 6.51, S 14.89; found C 55.89, H 7.86, N 6.45, S 14.65.

3,4-Bis(dimethylamino)sulfolane (5a): To a 30% solution of dimethylamine in water (2 mL) was added thiophene 1,1-dioxide **1b−d** (0.5 mmol). After 1 h, the sulfone was completely dissolved. The product was extracted with CH_2Cl_2, and the organic layer was separated and dried (sodium sulfate). Pure product was obtained after solvent evaporation. Yield 0.084 g (82%) from **1b**, 0.088 g (85%) from **1c** and 0.082 g (80%) from **1d.** M.p. 45−46 °C. − ^{1}H NMR ($CDCl_3$): δ = 2.34 (s, 12 H), 3.25−3.06 (m, 4 H), 3.53 (tt, *J* = 2.6 Hz, *J* = 5.6 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 40.7, 47.6, 62.9. − MS; *m/z*: 191 [M^+ − 15]. − $C_8H_{18}N_2O_2S$ (207.56): calcd. C 46.58, H 8.79, N 13.58, S 15.54; found C 46.52, H 8.84, N 13.43, S 15.45.

3,4-Bis(piperidino)sulfolane (5b): To a mixture of 2,5-disubstituted thiophene 1,1-dioxide **1b−d** (0.5 mmol) and piperidine (2.5 mmol) was added water (5 mL). The reaction was exothermic. After 2 h, the precipitate was filtered, washed with cold water and dried. Yield 0.124 g (87%) from **1b**, 0.129 g (90%) from **1c** and 0.134 g (94%) from **1d.** M.p: 152 °C. − ^{1}H NMR ($CDCl_3$): δ = 1.57−1.45 (m, 12 H), 2.57 (dd, *J* = 4.4 Hz, *J* = 5.4 Hz, 8 H), 3.20−3.04 (m, 4 H), 3.52 (tt, *J* = 1.6 Hz, 5.8 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 24.5, 26.3, 50.4, 50.8, 63.1. − MS; *m/z:* 286 [M^+]. − $C_{14}H_{26}N_2O_2S$ (286.58): calcd. C 58.70, H 9.14, N 9.78, S 11.19; found C 58.65, H 9.32, N 9.48, S 10.98.

3-Amino-2,3-dihydrothiophene 1,1-Dioxides (6): Water (5 mL) was added to a mixture of 2,5-bis(trimethylsilyl)thiophene 1,1-dioxide **(1b)** (0.130 g, 0.5 mmol) and amine [diethylamine, morpholine (2.5 mmol)]. The mixture was kept overnight and then the product was extracted with CH_2Cl_2. The organic layer was separated, dried and evaporated. The products were obtained as an oil **(6a)** or a white powder **(6b)**.

3-Diethylamino-2,3-dihydrothiophene 1,1-Dioxide (6a): Yield 0.077 g (82%). − ^{1}H NMR ($CDCl_3$): δ = 0.79 (t, *J* = 7 Hz, 6 H), 2.15 (q, *J* = 7 Hz, 4 H), 2.34−2.20 (m, 1 H), 2.82 (dd, *J* = 4.8 Hz, *J* = 13.6 Hz, 1 H), 3.01 (dd, *J* = 9.6 Hz, *J* = 13.6 Hz, 1 H), 4.22 (dd, *J* = 4.8 Hz, *J* = 9.6 Hz, 1 H), 6.39 (d, *J* = 4.8 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 13.7, 44.3, 48.5, 60.5, 132.9, 142.5,. − MS; *m/z*: 189 [M^+]. − $C_8H_{15}NO_2S$ (189.30): calcd. C 50.76, H 7.99, N 7.40, S 16.94; found C 50.50, H 7.83, N 7.30, S 16.76.

3-Morpholino-2,3-dihydrothiophene 1,1-Dioxide (6b): Yield 0.089 g (88%). M.p. 128 °C. − MS; *m/z*: (M^+) 203. − ^{1}H NMR ($CDCl_3$): δ = 2.62 (dd, *J* = 4.6 Hz, 7 Hz, 4 H), 3.27 (dd, *J* = 1.2 Hz, 5.6 Hz, 2 H), 3.70 (dd, *J* = 4.6 Hz, 7 Hz, 4 H), 4.32−4.25 (m, 1 H), 6.69 (dd, *J* = 2.2 Hz, 6.8 Hz, 1 H), 6.75 (dd, *J* = 1.8 Hz, 6.8 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 47.5, 49.7, 62.4, 67.0, 134.2, 139.7. − $C_8H_{13}NO_3S$: calcd. C 47.27, H 6.45, N 6.89, S 15.78; found C 47.34, H 6.48, N 6.77, S 15.62.

4-Methyl-3-piperidino-2,3-dihydrothiophene 1,1-Dioxide (7): Water (5 mL) was added to a mixture of 3-methyl-2,5-bis(trimethylsilyl)-thiophene 1,1-dioxide **(1e)** (0.137 g, 0.5 mmol) and piperidine (0.22 g, 2.5 mmol). After 2 h, the precipitate was filtered, washed with cold water and dried. Yield: 0.089 g (83%). − ^{1}H NMR ($CDCl_3$): δ = 1.58−1.42 (m, 6 H), 1.98 (s, 3 H), 2.37−2.29 (m, 4 H), 3.10 (dd, *J* = 8.2 Hz, *J* = 12.2 Hz, 1 H), 3.35 (dd, *J* = 3.8 Hz, *J* = 12.2 Hz, 1 H), 4.08−4.02 (m, 1 H), 6.37 (t, *J* = 1.4 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 15.8, 24.1, 25.8, 29.6, 46.3, 49.6, 67.0, 128.4, 152.8. − MS; *m/z:* 215 [M^+]. − $C_{10}H_{17}NO_2S$ (215.36): calcd. C 55.78, H 7.96, N 6.51, S 14.89; found C 55.83, H 7.85, N 6.45, S 14.67.

Crystal Structure Determinations: The crystals were measured on a Syntex $P2_1$, four-circle computer-controlled single-crystal diffractometer. Crystal data and details of structure determination and refinement are collected in Table 1.

Crystallographic data (excluding structure factors) for the structure(s) included in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-142832 **(3c)**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; Email: deposit@ccdc.cam.ac.uk].

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