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Cycloaddition Reactions of Nitrile Oxides to Silyl- and Germyl-Substituted Thiophene-1,1-dioxides

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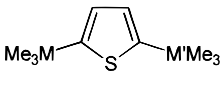
Silyl- and-germyl substituted thiophene-1,1-dioxides were prepared from the corresponding thiophenes by oxidation with m-CPBA in CH_2Cl_2 at room temperature. The [2+3] dipolar cycloaddition of nitrile oxides to the double C=C bonds of thiophene-1,1-dioxides has been investigated. It was shown that the reaction pathway strongly depends on the substituents M and M′ in the heterocycle and the method of nitrile oxide generation. The molecular structures of 2-*tert*-butyl-5-trimethylsilylthiophene-1,1-dioxide, 2-trimethylsilyl-5-trimethylgermylthiophene-1,1-dioxide, 2,5-bis(trimethylgermyl)thiophene-1,1-dioxide, and the mixture of 4,4-dioxo-3-phenyl-5-*tert*-butyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 with 4,4-dioxo-3-phenyl-5-trimethylgermyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (92:8) were studied by X-ray diffraction.

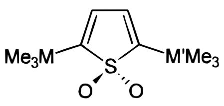
Introduction

The interest in silyl-substituted thiophene-1,1-dioxides stems from the fact that they are useful synthetic intermediates for the preparation of various types of organic compounds.[1] It has been reported that different bis- and tris(trimethylsilyl)thiophene-1,1-dioxides gave adducts in high yield in the Diels−Alder reaction with *N*-phenylmaleimide.[2] 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 $AgBF_4$.[3] It has been shown that the amine-induced ring-opening reaction of silyl-substituted methylthiophene-1,1-dioxides proceeds with high regio- and stereoselectivity.[4] The coupling of 2-dimethyl(*tert*-butyl)silyl-5-bromothiophene-1,1-dioxide with thienyl stannanes in the presence of a palladium(0) catalyst allowed the easy and selective insertion of thiophene-1,1-dioxide units into the skeleton of bi-, ter-, quater-, and quinquethiophenes.[5] The functionalization of the thienyl sulfur to the *S*,*S*-dioxide in oligothophene chains increases dramatically the electron delocalization and the electron affinity of the molecules[6]

It has been shown that unsubstituted thiophene-1,1-dioxide prepared in situ is a quite reactive dipolarophile in the [2+3] cycloaddition reactions with *N*,α-diphenylnitrone,[7] benzonitrile,[7,8] and mesitonitrile[7,8] oxides yielding mono- and diisoxazolines-2 and N-substituted isoxazolidines. The introduction of *tert*-butyl, trimethylsilyl, and trimethylgermyl substituents into thiophene-1,1-dioxide heterocycle made it possible to investigate the cycloaddition reactivity of the double C=C bonds with respect to the nature of the group IVa element. Moreover, our recent studies indicate that silyl- and germyl-containing isoxazolines have gained a great deal of attention as compounds possessing a wide spectrum of biological properties.[9] Therefore, we present here the synthesis of 2,5-disubstituted thiophenes **1**, their 1,1-dioxides **2,** and the results of [2+3] dipolar cycloaddition of acetonitrile and benzonitrile oxides to sulfones **2**, which reveal a marked difference in reactivity of *tert*-butyl, trimethylsilyl, and trimethylgermyl derivatives.



1a-f



2a-f

a (M=M'=C); **b** (M=C, M'=Si); **c** (M=C, M'=Ge);
d (M=M'=Si); **e** (M=Si, M'=Ge); **f** (M=M'=Ge)

Results and Discussion

Preparation of Thiophene-1,1-dioxides. Silyl- and germyl-substituted thiophenes **1** were obtained using the reactions of thienylmagnesium bromide or thienyllithium derivatives with trimethylsilyl or trimethylgermyl chlorides. 2-*tert*-Butyl derivatives **1b,c** were pre-

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10.1021/om9902129 CCC: $18.00

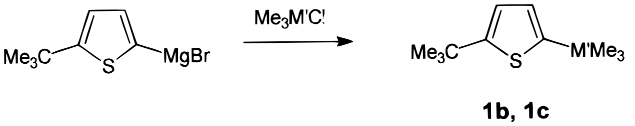
Table 1. ^{1}H, ^{13}C, and ^{29}Si NMR Spectra of Thiophenes 1a−f

			δ M,	δ ^{1}H, ppm				δ ^{13}C, ppm					
	M	M′	ppm	H^3	H^4	MMe$_3$	M′Me$_3$	C^2	C^3	C^4	C^5	MMe$_3$	M′Me$_3$
1a	C	C	34.4	6.60 (s)	6.60 (s)	1.36 (s)	1.36 (s)	154.2	120.2	120.2	154.2	32.5	32.5
1b	C	Si	34.7	7.08 (d, 2.4 Hz)	6.91 (d, 2.4 Hz)	1.41 (s)	0.31 (s)	163.1	133.7	122.8	136.8	32.9	0.03
1c	C	Ge	34.8	6.97 (d, 2.1 Hz)	6.88 (d, 2.1 Hz)	1.39 (s)	0.43 (s)	162.2	132.5	122.7	133.7	33.0	−0.2
1d	Si	Si	−6.56	7.31 (s)	7.31 (s)	0.32 (s)	0.32 (s)	146.0	135.1	135.1	146.0	0.3	0.3
1e	Si	Ge	−6.94	7.33 (d, 2.8 Hz)	7.27 (d, 2.8 Hz)	0.32 (s)	0.45 (s)	146.7	134.8	133.7	144.8	0.2	−0.2
1f	Ge	Ge		7.25 (s)	7.25 (s)	0.43 (s)	0.43 (s)	145.7	133.5	133.5	145.7	−0.3	−0.3

Table 2. ^{1} H, ^{13}C, and ^{29}Si NMR Spectra of Thiophene-1,1-dioxides 2

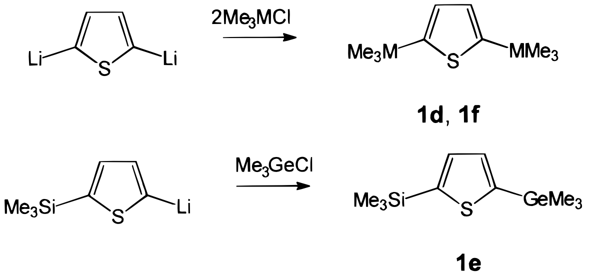
			δ M,	δ ^{1}H, ppm				δ ^{13}C, ppm					
	M	M′	ppm	H^3	H^4	MMe$_3$	M′Me$_3$	C^2	C^3	C^4	C^5	MMe$_3$	M′Me$_3$
2a	C	C	34.5	6.25 (s)	6.25 (s)	1.34 (s)	1.34 (s)	151.2	120.1	120.1	151.2	29.1	29.1
2b	C	Si	34.8 −6.30	6.73 (d, 4 Hz)	6.28 (d, 4 Hz)	1.37 (s)	0.33 (s)	154.5	135.7	120.8	150.4	29.1	−1.67
2c	C	Ge	34.8	6.63 (d, 4 Hz)	6.27 (d, 4 Hz)	1.37 (s)	0.49 (s)	154.3	133.89	121.01	151.3	29.04	−1.68
2d	Si	Si	−5.85	6.74 (s)	6.74 (s)	0.34 (s)	0.34 (s)	150.6	135.9	135.9	150.6	−1.74	−1.74
2e	Si	Ge	−6.15	6.73 (d, 3.6 Hz)	6.66 (d, 3.6 Hz)	0.34 (s)	0.5 (s)	151.8	136.1	134.2	150.0	−1.65	−1.66
2f	Ge	Ge		6.66 (s)	6.66 (s)	0.5 (s)	0.5 (s)	151.3	134.4	134.4	151.3	−1.65	−1.65

Scheme 1



1b, 1c

Scheme 2



1d, **1f**

1e

pared via Grignard reaction from 2-*tert*-butylthiophene-5-magnesium bromide in dry ether with 54 and 57% yields, respectively (Scheme 1).

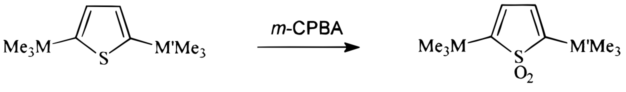
Symmetrical 2,5-bis(trimethylsilyl)-**1d**[2,10] and 2,5-bis(trimethylgermyl)thiophenes **1f** are more convenient to prepare from 2,5-dilithiothiophene and following silylation or germylation with Me$_3$MCl (yields 90%). The dilithium compound was obtained by direct hydrogen−lithium exchange[10] from thiophene using *n*-butyllithium in a mixture of ether/hexane at room temperature. Unsymmetrical 2-trimethylsilyl-5-trimethylgermylthiophene **1e** can be prepared by sequential silylation and germylation of thienyllithium derivatives; the second lithiation step involving the treatment of 2-trimethylsilyl-5-lithiothiophene by trimethylgermyl chloride proceeds with 74% yield (Scheme 2).

Oxidation of thiophenes to thiophene-1,1-dioxides is more difficult than oxidation of normal sulfides. Participation of the sulfur electrons in aromatic resonance decreases the electron density of the sulfur and diminishes its reactivity. Once the aromacity is destroyed by oxidation, the resulting diene is susceptible to further reactions. *tert*-Butyl-, trimethylsilyl-, and trimethylgermyl-substituted thiophenes **1a**−**f** are readily oxidized to corresponding thiophene-1,1-dioxides by *m*-chloroperbenzoic acid (m-CPBA) in methylene chloride at room temperature without displacement of the silyl and germyl groups (Scheme 3). These substituents are also bulky enough to prevent dimerization. Sulfones **2a**−**f** prepared from moderate to good (48−63%) yields are colorless crystalline solids which are thermally and moisture stable compounds.

Table 3. UV Spectra of Thiophenes 1a−f and Corresponding Thiophene-1,1-dioxides 2a−f

		λ$_{max}$, nm (in ethanol)	
Me$_3$M	Me$_3$M′	**1**	**2**
Me$_3$C	Me$_3$C	252	222, 294
Me$_3$C	Me$_3$Si	254	222, 304
Me$_3$C	Me$_3$Ge	260	222, 307
Me$_3$Si	Me$_3$Si	256	228, 312
Me$_3$Si	Me$_3$Ge	260	228, 312
Me$_3$Ge	Me$_3$Ge	255	228, 312

Scheme 3



1a-f **2a-f**

NMR spectroscopy was used to study the influence of the oxidation of the sulfur atom on the ^{1}H, ^{13}C, and ^{29}Si chemical shifts (Tables 1, 2). The UV−visible absorption data for thiophene-1,1-dioxides **2a**−**f** and parent thiophenes **1a**−**f** are summarized in Table 3.

X-ray Diffraction of Thiophene-1,1-dioxides 2b, 2e, and 2f. The molecular structures of thiophene-1,1-dioxides **2b**, **2e,** and **2f** are studied by X-ray diffraction (Figure 1). In the crystal the molecules of sulfones **2b**, **2e,** and **2f** lie in special positions. The molecules of 2-*tert*-butyl-5-trimethylsilylthiophene-1,1-dioxide **2b** are placed in two axes (Figure 2). The crystals of 2-trimethylsilyl-5-trimethylgermylthiophene-1,1-dioxide **2e** and 2,5-bis(trimethylgermyl)thiophene-1,1-dioxide **2f** are isomorphous. Both crystallographically independent molecules in the crystals **2e** and **2f** lie in mutually perpendicular mirror planes *m*. Molecules **A** pack perpendicularly to the *y* crystallographic axis, while molecules **B** are perpendicular to the *z* axis (Figure 3). Structure disorder is observed in the crystals of unsym-

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Table 4. Geometric Parameters of Thiophene-1,1-dioxides

	bond distances, Å				valent angles, deg		
compd	At(1)–C(2)	C(2)–C(3)	C(3a)–C(3b)	C(2)–S(1)	C(2a)–S(1)–C(2b)	S(1)–C(2)–C(3)	C(2)–C(3a)–C(3b)
2a[11]	1.47	1.34	1.46	1.79	90	112	113
2b	1.698(4)	1.319(5)	1.469(6)	1.773(3)	96.2(2)	105.5(3)	116.3(3)
2c[3]		1.323	1.480	1.761	96.1		
2e[a]	1.892(6)	1.329(9)	1.478(12)	1.777(6)	95.6(4)	105.9(5)	116.3(4)
	1.926(6)	1.303(9)	1.472(12)	1.778(6)	96.9(4)	105.0(4)	116.6(4)
2f[a]	1.962(12)	1.326(17)	1.48(2)	1.769(12)	96.2(7)	106.1(9)	115.8(7)
	1.944(11)	1.352(16)	1.47(2)	1.757(11)	97.5(7)	105.4(8)	115.9(7)

[a] For two independent molecules.

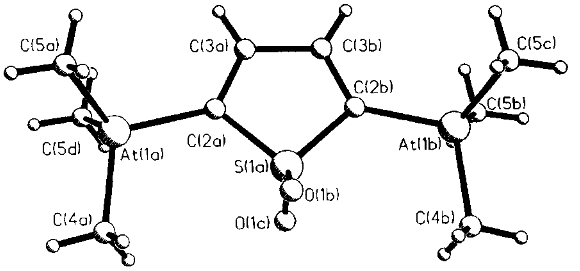

Figure 1. Molecular structure of 2,5-disubstituted thiophene-1,1-dioxides **2b** [At1 = C (g = 0.5), Si (g = 0.5)], **2e** [At1 = Si (g = 0.5), Ge (g = 0.5)], and **2f** [At1 = Ge (g = 1.0)].

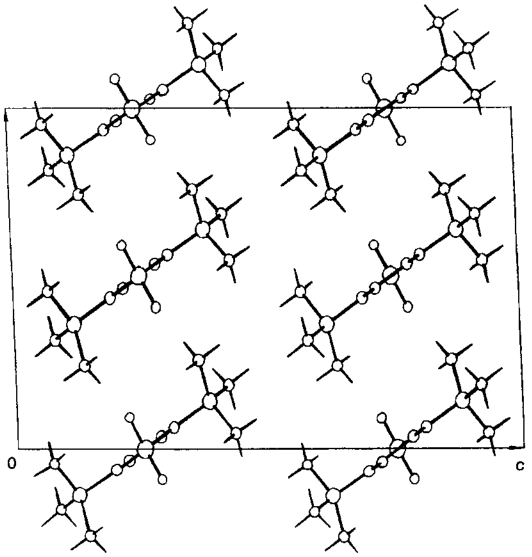

Figure 2. Molecular packing (projection on *xz*-plane) of sulfone **2b**.

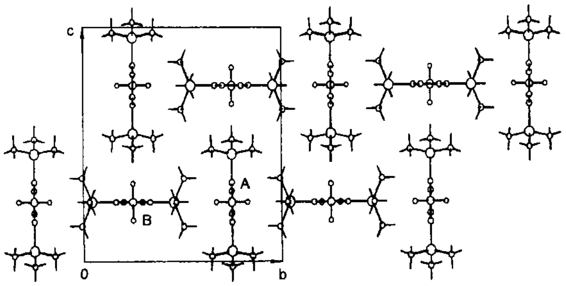

Figure 3. Molecular packing of sulfones **2e**,**f**.

metric molecules **2b** and **2e.** The five-membered heterocycle of all compounds is planar. The oxygen atoms of the SO_2 unit lie roughly at the same distance above and below the five-membered ring. The loss of the aromatic conjugation in thiophene-1,1-dioxide fragment implies S–C(2) and C(3a)–C(3b) bond lengthening (Table 4) with respect to the thiophene molecules. The main geometric parameters of studied sulfones are in good agreement with those previously found for the 2,5-di(*tert*-butyl)thiophene-1,1-dioxide[11] and 2,5-bis(trimethylsilyl)thiophene-1,1-dioxide.[3]

Synthesis of Fused Isoxazolines. The [2+3] dipolar cycloaddition of nitrile oxides to the double C=C bonds of thiophene-1,1-dioxides **2a–f** has been investigated. It has been shown that silyl- and germyl-substituted thiophene-1,1-dioxides **2b–f** easily react with nitrile oxides to give the products of [2+3] cycloaddition in 40–90% yields. Contrary to organosilicon and organogermanium sulfones, the double C=C bonds of 2,5-bis(*tert*-butyl)thiophene-1,1-dioxide **2a** were inactive in the cycloaddition process. The reaction pathway for compounds **2b–f** strongly depends on the substituents M and M′ in the thiophene-1,1-dioxide heterocycle and the method of nitrile oxide generation. The cycloaddition proceeds with high regioselectivity to give only one fused isoxazoline-2. It should be noted that only one double C=C bond of thiophene-1,1-dioxides is involved in the interaction.

Acetonitrile oxide prepared in situ by the Mukaiyama–Hoshito method[12] reacts with 2-*tert*-butyl-5-trimethylsilylthiophene-1,1-dioxide **2b** and 2,5-bis(trimethysilyl)thiophene-1,1-dioxide **2d** to yield desilylated cycloadducts **3b** and **3d,** respectively (Scheme 4). Contrary to organosilicon sulfones **2b** and **2d,** germyl-substituted thiophene-1,1-dioxides **2c** and **2f** under the same reaction conditions gave fused isoxazolines **3c** and **3f,** containing the trimethylgermyl group in position 3^a. This fact confirms higher stability of the Ge–C bonds as compared with Si–C. For unsymmetric thiophene-1,1-dioxides **2b** and **2c** the double C=C bonds bearing a *tert*-butyl group were completely inactivated and cycloaddition proceeded regioselectively with the participation of the C=C bonds bearing trimethylsilyl or trimethylgermyl substituents.

As the molecule of 2-trimethylsilyl-5-trimethylgermylthiophene-1,1-dioxide **2e** simultaneously contains vinylsilane and vinylgermane fragments, it is a very convenient model to compare the reactivity of these groups in [2+3] dipolar cycloaddition reactions. This compound interacts with acetonitrile oxide to give the bicyclic product **3e** only with the vinylgermyl side of the molecule. Besides, in this case the demetalation does not occur. It may be concluded that the reactivity of the C=C double bonds in thiophene-1,1-dioxides **2a–f** with

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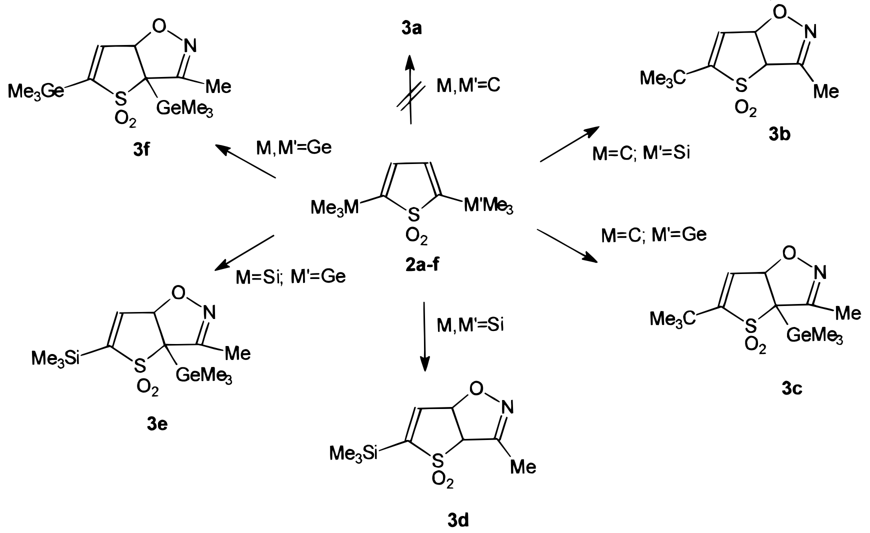
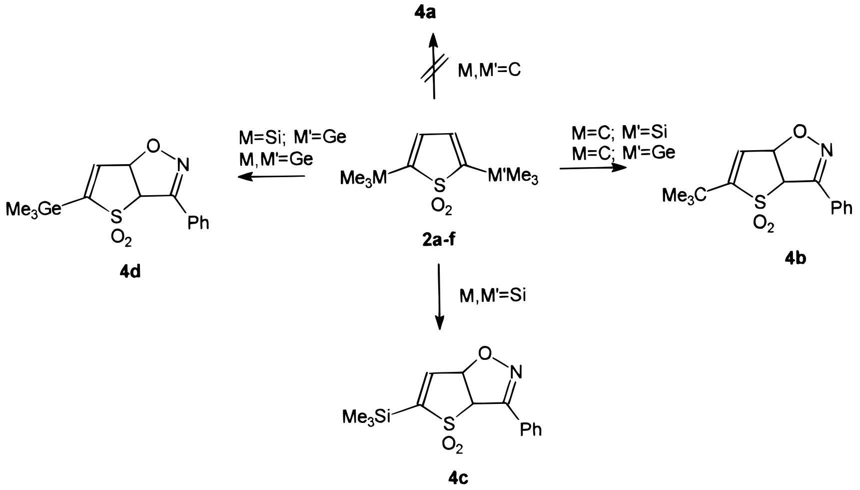
Scheme 4



Scheme 5



the acetonitrile oxide depends on the substituents in the heterocycle decreasing in the following order: Ge > Si ≫ C.

Table 5. Results of Cycloaddition of Nitrile Oxides to Sulfones 2a–f

compd	M	M′	R	yield, % with M′Me$_3$	yield, % without M′Me$_3$
3a	C	C	Me		
3b	C	Si	Me		80
3c	C	Ge	Me	58	
3d	Si	Si	Me	traces	65
3e	Si	Ge	Me	45	
3f	Ge	Ge	Me	67	
4a	C	C	Ph	traces	
4b	C	Si, Ge	Ph		84, 93
4c	Si	Si	Ph	traces	77
4d	Ge	Si, Ge	Ph		85, 87

The regioselectivity of the benzonitrile oxide cycloaddition to thiophene-1,1-dioxides **2a**–**f** has also been studied (Scheme 5). The benzonitrile oxide[13] was generated in situ, by dehydrohalogenation of the benzhydroxamic acid chloride[14] with triethylamine. Only traces of bicyclic 4,4-dioxo-3-phenyl-3a,5-di(*tert*-butyl)-3a,6a-dihydrothieno[2,3-d]isoxazoline-2 **4a** were detected in the reaction mixture of 2,5-bis(*tert*-butyl)thiophene-1,1-dioxide **2a** and benzonitrile oxide by mass spectrometry. The substitution of at least one of the *tert*-butyl groups by trimethylsilyl or trimethylgermyl leads to considerable increasing of reactivity. 2-*tert*-Butyl-5-trimethylsilylthiophene-1,1-dioxide **2b** and 2-*tert*-butyl-5-trimethylgermylthiophene-1,1-dioxide **2c** in the reaction with benzonitrile oxide gave bicyclic product **4b** with 84 and 93% yields, respectively. It should be noted that in both cases the double C═C bond bearing organometallic substituents participated in the cycloaddition reaction. The cyclization process was accompanied by desilylation of the sulfone **2b** and degermylation of **2c**. Demetalation of one group was observed also during the reaction of benzonitrile oxide with 2,5-bis(trimethylsilyl)thiophene-1,1-dioxide **2d**, 2-trimethylsilyl-5-trimethylgermylthiophene-1,1-dioxide **2e,** and 2,5-bis(trimethylgermyl)thiophene-1,1-dioxide **2f**. Moreover, contrary to acetonitrile oxide, the cycloaddition of benzonitrile oxide to unsymmetrical sulfone **2e** resulted in the formation of the fused isoxazoline **4d**, which indicates the participation

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Table 6. ^{1}H NMR Spectra of Fused Isoxazolines 3 and 4

	δ ^{1}H, ppm				
	H^6	H^{6a}	H^{3a} or Me$_3$Ge	MMe$_3$	Me or Ph
3b	6.30 (d, 3.3 Hz)	5.70 (dd, 3.3, 9.3 Hz)	4.54 (d, 9.3 Hz)	1.34 (s)	2.23 (s)
4b	6.45 (d, 2.7 Hz)	5.88 (dd, 2.7, 9.8 Hz)	5.11 (d, 9.8 Hz)	1.36 (s)	7.43−7.5 (m); 7.74−7.77 (m)
3c	6.30 (d, 2.7 Hz)	5.70 (d, 2.7 Hz)	0.46 (s)	1.40 (s)	2.21 (s)
3d	6.64 (d, 2.9 Hz)	6.00 (dd, 2.9, 9.6 Hz)	5.02 (d, 9.6 Hz)	0.29 (s)	2.03 (s)
4c	6.78 (d, 2.2 Hz)	6.02 (dd, 2.2, 10 Hz)	5.09 (d, 10 Hz)	0.34 (s)	7.25−7.46 (m); 7.76−7.81 (m)
3e	6.60 (d, 2.6 Hz)	5.94 (d, 2.6 Hz)	0.50 (s)	0.36 (s)	2.18 (s)
4d	6.68 (d, 2.2 Hz)	5.99 (dd, 2.2, 10 Hz)	5.03 (d, 10 Hz)	0.50 (s)	7.41−7.49 (m); 7.75−7.8 (m)
3f	6.58 (d, 2.1 Hz)	5.84 (dd, 2.1 Hz)	0.51 (s)	0.48 (s)	2.16 (s)

Table 7. ^{13}C and ^{29}Si NMR Spectra of Fused Isoxazolines 3 and 4

		δ ^{13}C, ppm							
	δ ^{29}Si, ppm ($J_{\text{Si-H}}$, Hz)	C^3	C^5	C^{3a}	C^{6a}	C^6	Me$_3$Ge	MMe$_3$	Me or Ph
3b		154.5	150.0	72.2	79.0	127.3		29.5, 34.2	12.3
4b		158.4	149.6	70.1	85.8	139.8		27.3, 32.8	126.4−132.1
3c		157.8	141.8	70.5	88.4	140.6	−2.3	26.9, 32.5	12.6
3d	−3.58 [6.9 (Si−Me)]	151.0	140.4	70.4	86.8	140.2		−1.14	12.7
4c	−3.67 [6.8 (Si−Me); 9.4 (Si−H^{6a}); 3.2 (Si−H^6)]	152.0	148.5	69.5	85.2	140.1		−1.53	127.2−130.8
3e	−3.95 [6.7 (Si−Me); 2.2 (Si−H^6)]	153.7	149.3	70.2	80.6	136.5	−2.06	−1.33	12.5
4d		152.0	149.5	69.3	85.6	138.4		−1.39	127.2−130.9
3f		150.2	141.3	71.5	87.8	139.8	−2.02	−1.38	12.3

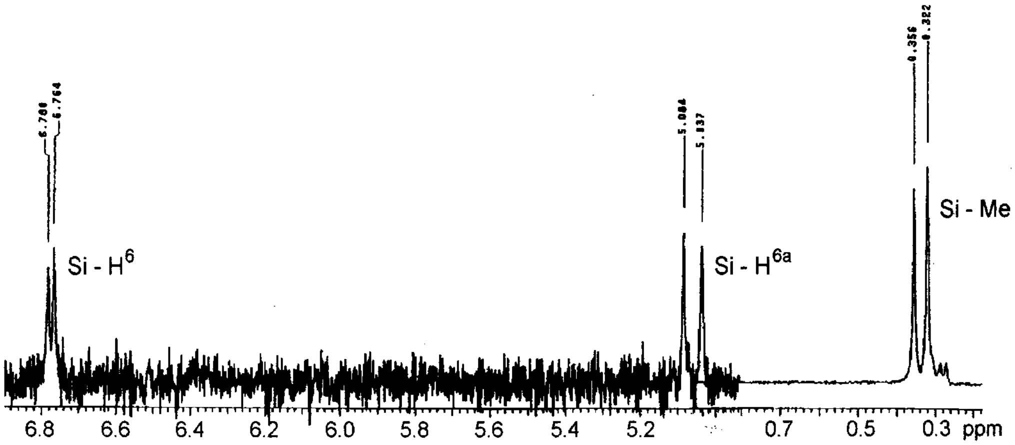

Figure 4. Si−H heteronuclear multiple-quantum coherence spectra of **4c**.

of the vinylsilane side of the molecule in this reaction. The regioselectivity of benzonitrile oxide cycloaddition is determined by the ease of the demetalation process. The leaving group ability increases in the order Si > Ge ≫ C. Yields of the cycloaddition products are presented in Table 5.

The polarization of sulfonyl-substituted double bond $SO_2C^{\alpha}{=}C^{\beta}$ directs the oxygen of the nitrile oxide to the β-carbon atom.[15] The cycloaddition of nitrile oxides to thiophene-1,1-dioxide[7] and benzothiophene-1,1-dioxide[7,16] also gave a regioisomer where the oxygen atom of nitrile oxide is bonded to carbon C^{6a}.

According to our results, only one product resulted from [2+3] cycloaddition reactions of aceto- and benzonitrile oxides to sulfones **2b**−**f**, indicating the high regiospecifity of these processes. The ^{1}H and ^{13}C NMR data confirm the formation of fused isoxazolines (Tables 6 and 7). In accordance with Si−H heteronuclear multiple quantum coherence spectrum data of fused isoxazolines **3e** and **4c** (Figure 4) the silicon atom interacts with the proton in position 6 with spin−spin constants of 2.2 and 3.2 Hz, respectively. From these results it can be concluded that the trimethylsilyl group is connected with the $C_{(5)}{=}C_{(6)}$ double bond of the biheterocyclic system.

X-ray Diffraction of the 4,4-Dioxo-3-phenyl-5-*tert*-butyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (4b) and 4,4-Dioxo-3-phenyl-5-trimethylgermyl-3a,6a-dihydrothieno[2,3-*d*] isoxazoline-2 (4d) Mixture (92:8). To confirm the direction of [2+3] dipolar cycloaddition, the molecular structure of the 4,4-dioxo-3-phenyl-5-*tert*-butyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (**4b**) and 4,4-dioxo-3-phenyl-5-trimethylgermyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (**4d**) mixture (92:8) was investigated by X-ray diffraction (Figure 5). Single crystals suitable for X-ray structure determinations were obtained from hexane only for the mixture, not for clean products **4b** and **4d**. This mixture was obtained from the mixture of thiophene-1,1-dioxides **2c** and **2f** (92:8) by cycloaddition with benzonitrile oxide.

Two five-membered rings of fused isoxazoline **4b** are planar and form a dihedral angle of 63.2°. The dihedral angle between the phenyl group and isoxazoline heterocycle is 13.7°. Molecules of the compound **4b** are in general position of the unit cell (Figure 6). The molecules of germanium analogue **4d** exist in the same

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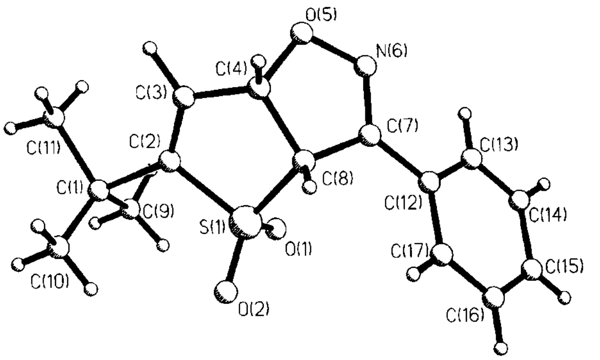

Figure 5. Molecular structure of fuxed isoxazoline **4b**. Selected bond distances (Å) and angles (deg): C(1)−C(2), 1.515(15); C(2)−C(3), 1.333(9); C(3)−C(4), 1.495(13); C(4)−C(8), 1.518(11); C(8)−S(1), 1.809(8); C(2)−S(1), 1.774(8); C(4)−O(5), 1.448(8); O(5)−N(6), 1.389(9); N(6)−C(7), 1.290(8); C(7)−C(8), 1.517(10); S(1)−C(2)−C(3), 109.5(6); C(2)−C(3)−C(4), 118.6(7); C(3)−C(4)−C(8), 109.6(6); C(4)−C(8)−S(1), 106.2(6); C(8)−S(1)−C(2), 95.7(3).

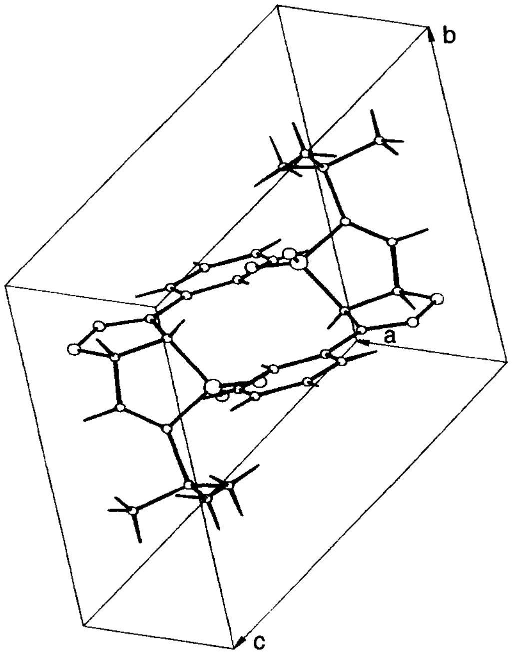

Figure 6. Molecular packing of the fused isoxazoline **4b**.

crystallographic positions; therefore the occupation *g*-factor of the C(1) atom is less than 1 and equals 0.85.

Experimental Section

Instrumental. ^{1}H, ^{13}C, and ^{29}Si NMR spectra were recorded on a Varian Mercury 200 spectrometer at 200.06, 50.31, and 39.74 MHz correspondingly at 303 K. The chemical shifts are given relative to TMS from solvent ($CDCl_3$) signal ($\delta_H = 7.25$). Mass spectra were recorded on a Hewlett-Packard apparatus (70 eV). GLC analysis was performed on a Varian 3700 instrument equipped with flame-ionizing detector using a capillary column of 5 m × 0.53 mm, df = 2.65 μ, HP-1, carrier gas nitrogen. The melting points were determined on a "Digital melting point analyzer" (Fisher); the results are given without correction.

Thiophene, trimethylchlorosilane, nitroethane, phenylisocyanate, and 2.5 N *n*-BuLi in hexanes were purchased from Acros.

2-*tert*-Butyl-5-trimethylsilylthiophene (1b). To a solution of 2-*tert*-butylthienyl-5-magnesium bromide prepared from 2-*tert*-butyl-5-bromothiophene (5 g, 0.023 mol) and magnesium (0.54 g, 0.023 mol) in 50 mL of ethyl ether was added 2.46 g (0.023 mol) of trimethylchlorosilane. The mixture was refluxed for 2 h, then hydrolyzed using ammonium chloride, extracted with ethyl ether, dried over Na_2SO_4, and evaporated. The residue was distilled (108−110 °C, 15 mmHg), and 2.6 g (54% yield) of pure **1b** as a colorless liquid was obtained. MS: *m*/*e* 244 ($M^{\bullet+}$).

2-*tert*-Butyl-5-trimethylgermylthiophene (1c). To a solution of 2-*tert*-butylthienyl-5-magnesium bromide prepared from 2-*tert*-butyl-5-bromothiophene (5 g, 0.023 mol) and magnesium (0.54 g, 0.023 mol) in 50 mL of ether was added 3.48 g (0.023 mol) of trimethylchlorogermane. The mixture was refluxed for 2 h, then hydrolyzed using a saturated solution of ammonium chloride, extracted with ethyl ether, dried over Na_2SO_4, and evaporated. The residue was distilled (118−120 °C, 15 mmHg), and 3.37 g of **1c** as a colorless liquid was obtained. **1c**, yield: 57%. MS: *m*/*e* 258 ($M^{\bullet+}$).

2-Trimethylsilyl-5-trimethylgermylthiophene (1e). To a solution of 2-trimethylsilylthiophene[17] (8.55 g, 0.055 mol) in 60 mL of ethyl ether was added 22 mL of 2.5 N *n*-BuLi in hexanes (0.055 mol) at room temperature. After 1 h, 8.41 g (0.055 mol) of trimethylchlorogermane was added dropwise. The reaction mixture was refluxed for 2 h, hydrolyzed with a saturated solution of ammonium chloride, extracted with ether, dried over Na_2SO_4, and evaporated. The residue was distilled (144−145 °C, 15 mmHg, mp 39−40 °C), and 10 g (66% yield) of pure **1e** as a colorless liquid was obtained. MS: *m*/*e* 274 ($M^{\bullet+}$). Anal. Calcd for $C_{10}H_{20}GeSSi$: C, 43.99; H, 7.38; S, 11.74. Found: C, 44.10; H, 7.69; S, 11.47.

2,5-Bis(trimethylgermyl)thiophene (1f). To a solution of 2.74 g (0.033 mol) of thiophene in 50 mL of ether was added dropwise 26 mL (0.066 mol) of 2.5 N *n*-BuLi at room temperature. After 30 min 10 g (0.066 mol) of Me_3GeCl was added. The reaction mixture was refluxed for 1 h, hydrolyzed with a saturated solution of ammonium chloride, extracted with ether, dried over Na_2SO_4, and evaporated. The residue was distilled to give 11.6 g (80% yield) of pure **1f** as a colorless liquid (bp 144−145 °C, 15 mmHg; mp 48−49 °C). MS: *m*/*e* 318 ($M^{\bullet+}$). Anal. Calcd for $C_{10}H_{20}Ge_2S$: C, 37.83; H, 6.35; S, 10.10. Found: C, 37.26; H, 6.43; S, 10.06.

Oxidation of 2,5-Disubstituted Thiophenes. The solution of 2,5-disubstituted thiophene **1b**,**e**,**f** (5 mmol) in 10 mL of CH_2Cl_2 was added dropwise to a solution of 2.47 g (10 mmol) of 70% *m*-CPBA 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 recrystallized from hexanes−ether (2:1) mixture to yield 2,5-disubstituted thiophene-1,1-dioxide **2b**,**e**,**f** as a white crystalline solid.

2-*tert*-Butyl-5-trimethylsilylthiophene-1,1-dioxide (2b). Mp: 127 °C. Yield: 48%. MS: *m*/*e* 244 ($M^{\bullet+}$). Anal. Calcd for $C_{11}H_{20}O_2SSi$: C, 54.05; H, 8.29; S, 13.12. Found: C, 54.24; H, 8.29; S, 13.09.

2-*tert*-Butyl-5-trimethylgermylthiophene-1,1-dioxide (2c). Mp: 125 °C. Yield: 54%. MS: *m*/*e* 275 ($M^{\bullet+} - Me$). Anal. Calcd for $C_{11}H_{20}GeO_2S$: C, 45.73; H, 6.98; S, 11.10. Found: C, 45.61; H, 7.05; S, 11.02.

2-Trimethylsilyl-5-trimethylgermylthiophene-1,1-dioxide (2e). Mp: 158 °C. Yield: 63%. MS: *m*/*e* 291 ($M^{\bullet+} - Me$). Anal. Calcd for $C_{10}H_{20}GeO_2SSi$: C, 39.38; H, 6.61; S, 10.51. Found: C, 40.14; H, 6.61; S, 10.45.

2,5-Bis(trimethylgermyl)thiophene-1,1-dioxide (2f). Mp: 172 °C. Yield: 60%. MS: *m*/*e* 337 ($M^{\bullet+} - Me$). Anal. Calcd for $C_{10}H_{20}Ge_2O_2S$: C, 34.36; H, 5.77; S, 9.18. Found: C, 34.12; H, 5.54; S, 9.09.

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Table 8. Crystal Data and Measurement Conditions for Compounds 2b,e,f and 4b

	2b	**2e**	**2f**	**4b**, **4d** (92:8)
molecular weight	244.5	305.1	349.6	291.4
crystal system	monoclinic	orthorhombic	orthorhombic	triclinic
space group	$C2/c$	$Pnmm$	$Pnmm$	$P\bar{1}$
cell length a [Å]	11.257(1)	6.513	6.525(1)	6.373(1)
cell length b [Å]	6.4391(7)	15.406	15.505(3)	10.794(3)
cell length c [Å]	19.735(2)	15.556	15.600(4)	12.007(3)
cell angle α [deg]	90	90	90	111.36(2)
cell angle β [deg]	92.68(1)	90	90	97.92(2)
cell angle γ [deg]	90	90	90	95.08(2)
cell volume V [Å^3]	1428.9(5)	1560.8(9)	1578.3(9)	753.1(6)
molecular multiplicity Z	4	4	4	2
D_x [g cm^{-3}]	1.136	1.298	1.471	1.285
$F(000)$	528	632	704	308
radiation	Mo Kα graphite monochromated			
wavelength λ [Å]	0.71069			
absorption coeff μ (mm^{-1})	0.29	2.26	4.14	0.22
crystal size (mm)	0.10 × 0.25 × 0.40	0.4 × 0.5 × 0.70	0.15 × 0.20 × 0.80	0.20 × 0.30 × 0.75
scan technique	$\theta/2\theta$			
$2\theta_{\max}$ [deg]	53	50	50	45
Miller index ranges:				
$h_{\min}$	0	0	0	0
$h_{\max}$	14	7	7	7
$k_{\min}$	0	0	0	−12
$k_{\max}$	8	18	18	12
$l_{\min}$	−24	0	0	−13
$l_{\max}$	23	18	18	12
no. of ind reflns collected	1493	1495	1512	1950
no. of obsd ($I > 2\sigma(I)$) reflns collected	954	1000	947	1264
goodness of fit	0.865	1.053	0.994	1.095
R-factor	0.0708	0.0534	0.0688	0.0894
structure solution method	SHELXS-86[18]			
structure refinement method	AREN[19]			

Synthesis of Isoxazolines. Interaction of Acetonitrile Oxide with Thiophen-1,1-dioxides 2a−f. Nitroethane (0.02 mol) and triethylamine (2 drops) in dry benzene (40 mL) were added dropwise during 4 h to the mixture of thiophene-1,1-dioxide (0.02 mol) and phenylisocyanate (0.04 mol) in dry benzene at room temperature. After some minutes CO_2 began to release and diphenylurea precipitated. The mixture was heated for 4 h at 70−80 °C. After cooling to room temperature diphenylurea was filtered and the solvent was evaporated. The residue was chromatographed on neutral Al_2O_3 using hexane as eluent. All fused isoxazolines **3b**−**f** were separated as colorless oils. Some of them crystallized after 3−10 days.

4,4-Dioxo-3-methyl-5-*tert*-butyl-3a,6a-dihydrothieno-[2,3-*d*]isoxazoline-2 (3b). Yield: 80%. Mp: 71−72 °C. MS: *m*/*e* 229 ($M^{\bullet+}$). Anal. Calcd for $C_{10}H_{15}NO_3S$: C, 52.38; H, 5.05; N, 4.68; S, 10.71. Found: C, 52.45; H, 5.12; N, 4.61; S, 10.63.

4,4-Dioxo-3-methyl-3a-trimethylgermyl-5-*tert*-butyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (3c). Yield: 58%. MS: *m*/*e* 347 ($M^{\bullet+}$). Anal. Calcd for $C_{13}H_{23}GeNO_3S$: C, 45.13; H, 6.70; N, 4.05; S, 9.27. Found: C, 45.04; H, 6.77; N, 4.11; S, 9.40.

4,4-Dioxo-3-methyl-5-trimethylsilyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (3d). Yield: 65%. MS: *m*/*e* 245 ($M^{\bullet+}$). Anal. Calcd for $C_9H_{15}NO_3SSi$: C, 44.05; H, 6.16; N, 5.71; S, 13.07. Found: C, 44.00; H, 6.11; N, 5.84; S, 13.20.

4,4-Dioxo-3-methyl-3a-trimethylgermyl-5-trimethylsilyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (3e). Yield: 45%. Mp: 68−69 °C. MS: *m*/*e* 363 ($M^{\bullet+}$). Anal. Calcd for $C_{12}H_{23}GeNO_3SSi$: C, 45.89; H, 7.38; N, 4.46; S, 10.21. Found: C, 45.78; H, 7.45; N, 4.51; S, 10.33.

4,4-Dioxo-3-methyl-3a,5-bis(trimethylgermyl)-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (3f). Yield: 67%. Mp: 93−95 °C. MS: *m*/*e* 407 ($M^{\bullet+}$). Anal. Calcd for $C_{12}H_{23}Ge_2NO_3S$: C, 35.45; H, 5.70; N, 3.45; S, 7.89. Found: C, 35.05; H, 5.37; N, 3.34; S, 8.06.

Interaction of Benzonitrile Oxide with Thiophene-1,1-dioxides 2a−f. Benzohydroxamic chloride (0.02 mol) in dry ether (30 mL) was added dropwise during 2 h to the mixture of an equimolar amount of thiophene-1,1-dioxide (0.02 mol) and triethylamine (0.02 mol) in ether (30 mL) at room temperature. After the addition of the benzohydroxamic chloride the mixture was stirred for 4 h at room temperature. Triethylamine hydrochloride was filtered, the solvent was evaporated, and the residue was chromatographed on neutral Al_2O_3 using hexane as eluent. All fused isoxazolines **4b**−**d** were separated as colorless oils, which were crystallized after 3−10 days.

4,4-Dioxo-3-phenyl-5-*tert*-butyl-3a,6a-dihydrothieno-[2,3-*d*]isoxazoline-2 (4b) was prepared from **2b** or **2c** with 84% and 93% yields, respectively. Mp: 134 °C. MS: *m*/*e* 291 ($M^{\bullet+}$). Anal. Calcd for $C_{14}H_{17}NO_3S$: C, 60.19; H, 6.13; N, 5.02; S, 11.48. Found: C, 60.09; H, 6.15; N, 5.08; S, 11.55. From the mixture of thiophene-1,1-dioxides **2c** and **2f** **4b** was prepared with 90% yield as a mixture of **4b** and **4d** (92:8). Single crystals suitable for X-ray structure determinations were obtained for this mixture from hexane.

4,4-Dioxo-3-phenyl-5-trimethylsilyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (4c). Yield: 77%. Mp: 162 °C. MS: *m*/*e* 307 ($M^{\bullet+}$). Anal. Calcd for $C_{14}H_{17}NO_3SSi$: C, 54.69; H, 5.57; N, 4.56; S, 10.43. Found: C, 54.27; H, 5.43; N, 4.22; S, 10.61.

4,4-Dioxo-3-phenyl-5-trimethylgermyl-3a,6a-dihydrothieno[2,3-*d*]isoxazoline-2 (4d). Yield: 85% (from **2e**), 87% (from **2f**). Mp: 57−58 °C. MS: *m*/*e* 353 ($M^{\bullet+}$). Anal. Calcd for $C_{14}H_{17}GeNO_3S$ C, 47.38; H, 4.43; N, 3.96; S, 9.53. Found: C, 47.38; H, 4.43; N, 3.96; S, 9.53.

Crystal Structure Determinations. The crystals were measured on a Syntex *2P*$_1$, four-circle computer-controlled single-crystal difractometer. Crystal data and details of structure determination and refinement are collected in Table 8.

Supporting Information Available: This material is available free of charge via the Internet at http://pubs.acs.org.

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