Cycloaddition in Synthesis of Sulfonamide Derivatives. IV.[1] One-Pot Synthesis of 3-Dimethylamino-4,1,2-benzoxathiazine 1,1-Dioxides, 3-Methoxy-4-methyl-1,2,4-benzothiadiazine 1,1-Dioxide and 3-Dimethylamino-1,4,2-benzodithiazine 1,1-Dioxides

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A novel, one-pot synthesis of 3-dimethylamino-4,1,2-benzoxathiazine 1,1-dioxides (7), 3-methoxy-4-methyl-1,2,4-benzothiadiazine 1,1-dioxide (9) and 3-dimethylamino-1,4,2-benzodithiazine 1,1-dioxides (11) is described. The procedure in the case of 7 involves [2+2] cycloaddition reaction of chlorosulfonyl isocyanate (CSI) with thiocarbamates with subsequent loss of carbonyl sulfide, followed by cyclization of the resulting *N*-chlorosulfonyl isothioureas under Friedel–Crafts conditions. Synthesis of 9 was achieved similarly. Also, by using dithiocarbamates instead of thiocarbamates, the 1,4,2-benzodithiazines 11 were synthesized.

Keywords [2+2] cycloaddition; chlorosulfonyl isocyanate; dithiocarbamate; thiocarbamate; Friedel–Crafts cyclization; 3-dimethylamino-4,1,2-benzoxathiazine 1,1-dioxide; 3-methoxy-4-methyl-1,2,4-benzothiadiazine 1,1-dioxide; 3-dimethylamino-1,4,2-benzodithiazine 1,1-dioxide

In a previous paper of this series, we reported the synthesis of *N*-(*C*-amino-alkylthiomethylene)benzenesulfonamides (A)[2] and *N*-arylsulfonylethoxyalamides (B)[3] by means of a novel [2+2] cycloaddition reaction of benzenesulfonyl isocyanate with dithiocarbamate and ethyl oxamate, respectively. In the course of our study on the preparation of heterocyclic compounds which bear the sulfonamide moiety, we developed a one-pot synthesis of 3-alkylthio-4*H*-1,2,4-benzothiadiazine 1,1-dioxide (C) which involves [2+2] cycloaddition reaction of chlorosulfonyl isocyanate (CSI) with dithiocarbamate as a key step.[1]

To explore further the utility of the [2+2] cycloaddition reaction of sulfonyl isocyanate in organic synthesis, we became interested in the synthesis of the title compounds, which have been comparatively little explored. In the present paper, we describe a new and facile synthesis of the title compounds, which is superior in simplicity and/or yield to the procedures used thus far.

Reaction of *p*-Toluenesulfonyl Isocyanate (TSI) with Carbamate, Thiocarbamate, Urea and Thiourea Derivatives To accomplish our aim, we first investigated the generality of the [2+2] cycloaddition reaction of sulfonyl isocyanate. Four compounds **1**—**4** were used as model compounds (Chart 2). The conditions and results of this reaction of TSI with **1**—**4** are summarized in Table I.

The reaction of **3** with TSI did not proceed under reflux in toluene for 3 h, resulting in quantitative recovery of **3**. The reaction of **4** with TSI gave similar results. However, interestingly, **1** and **2** under the same reaction conditions gave the corresponding **5** and **6**, in each case as a single stereoisomer, in 80% and 78% yields, respectively. When **1** and **2** were treated with TSI at room temperature for 24 h, the corresponding **5** and **6** were obtained in 65% and 70% yields, respectively. The structures of **5** and **6** were confirmed by elemental analyses and examination of the infrared (IR) absorption and proton nuclear magnetic resonance (^{1}H-NMR) spectra (see Experimental). These findings encouraged us to try to prepare the title compounds.

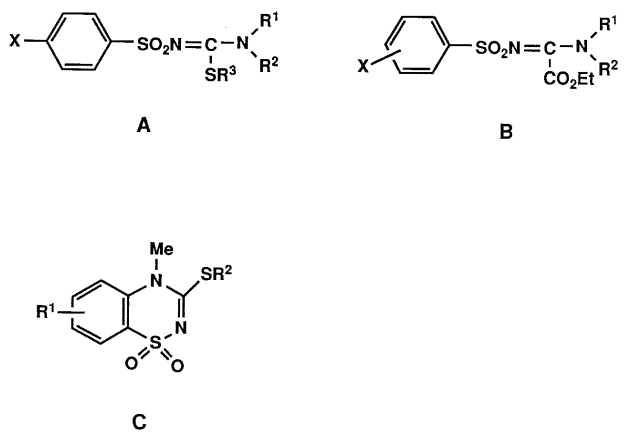


Chart 1

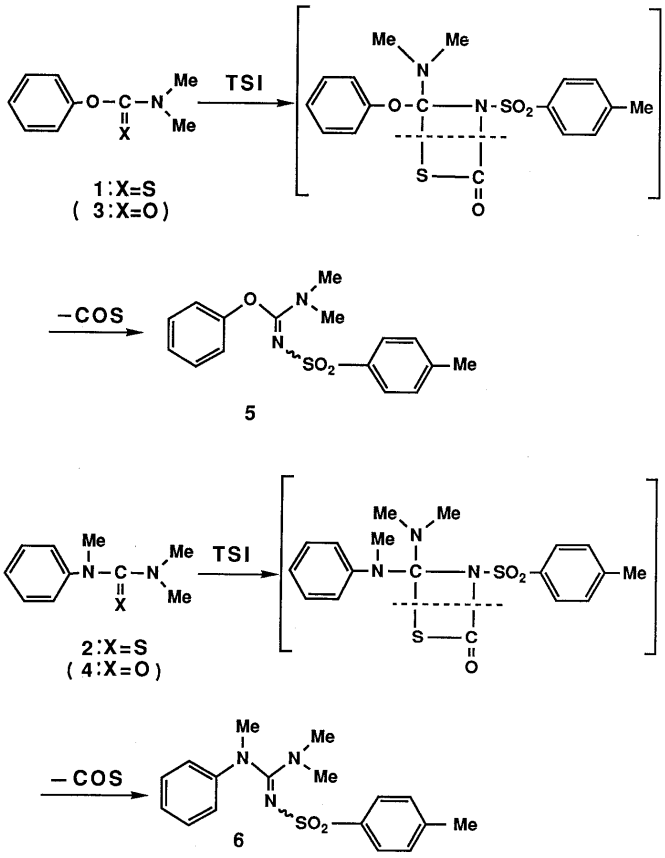


Chart 2

TABLE I. Reaction of TSI with **1**—**4**

S.M.	Reaction conditions	Product	Yield (%)
1	Reflux, 3 h	**5**	80
1	r.t., 24 h	**5**	65
2	Reflux, 3 h	**6**	78
2	r.t., 24 h	**6**	70
3	Reflux, 3 h	**5**	0
4	Reflux, 3 h	**6**	Trace

TSI = *p*-toluenesulfonyl isocyanate. S.M. = starting material. r.t. = room temperature.

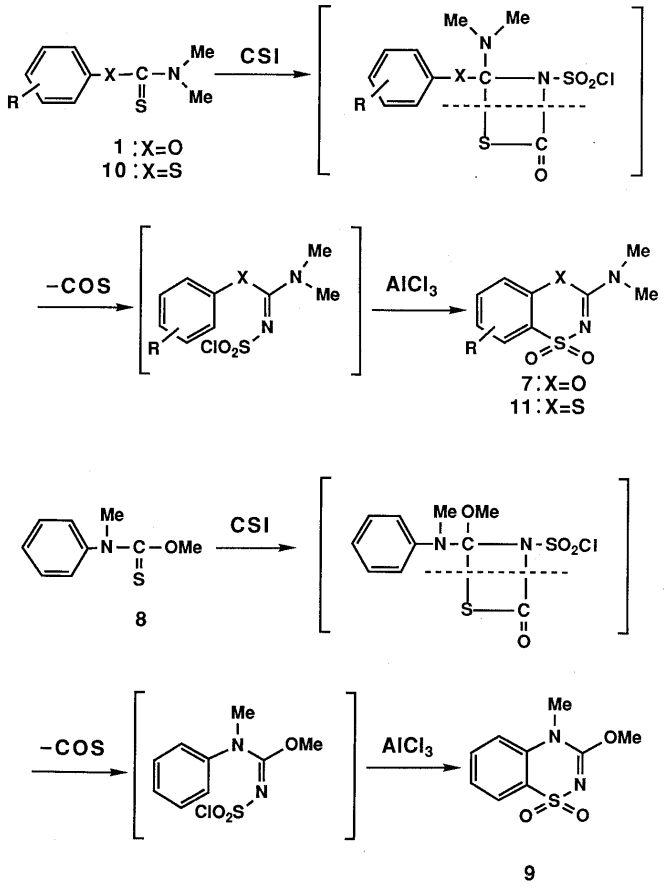


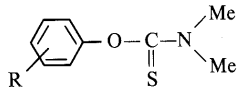
Chart 3

Numerous studies have been done on the [2+2] cycloaddition reaction of sylfonyl isocyanate,[4] but there has been no previous report of a [2+2] cycloaddition reaction of sulfonyl isocyanate with thiocarbamate or thiourea.

Synthesis of 3-Dimethylamino-4,1,2-benzoxathiazine 1,1-Dioxides (7) Literature survey yielded only one method for the preparation of **7**.[5] However, this procedure, involving the reaction of 2-hydroxyphenylsulfonylureas with phosphorus oxychloride, requires multiple steps and uncommon starting materials. Moreover, the yields are low. To overcome these problems, we investigated an alternative method for the preparation of **7**. As starting materials, *O*-phenyl *N*,*N*-dimethylthiocarbamates (**1a**—**e**) were easily prepared by the standard method (Tables II and IV).[6] Compound **1a** was treated with CSI in dry CH_2Cl_2 under stirring at room temperature for 30 min, then the solvent was replaced with dry CH_3NO_2, and the mixture was treated with $AlCl_3$ at room temperature for 2 h, giving **7a** in 76% yield. The other compounds (**7b**—**e**) were similarly obtained in 30—68% yields (Tables III and V).

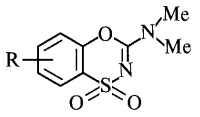
Synthesis of 3-Methoxy-4-methyl-1,2,4-benzothiadiazine 1,1-Dioxide (9) To examine the scope of the above method, we applied it to the synthesis of **9**. The starting material, *O*-methyl *N*-methyl-*N*-phenylthiocarbamate (**8**), was prepared by a previously reported method.[7] Use of **8**, instead of **1**, afforded the desired compound **9** in 75% yield, by the same procedure as that described for the preparation of **7**.

TABLE II. *O*-Phenyl *N*,*N*-Dimethylthiocarbamates (**1a**—**e**)



	R	mp (°C)	Formula	*Anal.* (%) Calcd (Found)		
				C	H	N
1a	H	Oil	$C_9H_{11}NOS$	59.64	6.12	7.73
				(59.53	6.10	7.71)
1b	2-Me	Oil	$C_{10}H_{13}NOS$	61.50	6.71	7.17
				(61.38	6.78	7.22)
1c	4-Me	91—92	$C_{10}H_{13}NOS$	61.50	6.71	7.17
				(61.46	6.70	7.09)
1d	2-Cl	Oil	$C_9H_{10}ClNOS$	50.12	4.67	6.49
				(49.94	4.72	6.59)
1e	4-Cl	51—53	$C_9H_{10}ClNOS$	50.12	4.67	6.49
				(49.95	4.65	6.54)

TABLE III. 3-Dimethylamino-4,1,2-benzoxathiazine 1,1-Dioxides(**7a**—**e**)



	R	Yield (%)	mp (°C)	Formula	*Anal.* (%) Calcd (Found)		
					C	H	N
7a	H	76	248—250	$C_9H_{10}N_2O_3S$	47.78	4.46	12.38
					(47.40	4.46	12.23)
7b	5-Me	30	227—229	$C_{10}H_{12}N_2O_3S$	49.99	5.03	11.66
					(50.31	5.04	11.74)
7c	7-Me	57	240—241	$C_{10}H_{12}N_2O_3S$	49.99	5.03	11.66
					(49.95	4.96	11.61)
7d	5-Cl	50	239—240	$C_9H_9ClN_2O_3S$	41.47	3.48	10.75
					(41.17	3.50	10.65)
7e	7-Cl	68	204—206	$C_9H_9ClN_2O_3S$	41.47	3.48	10.75
					(41.31	3.48	10.75)

TABLE IV. Spectral Data for *O*-Phenyl *N*,*N*-Dimethylthiocarbamates (**1a**—**e**)

	IR $\nu_{max}^{CHCl_3}$ cm^{-1} (ν-N···C···S)	^{1}H-NMR ($CDCl_3$) δ (ppm)
1a	1495	3.35 (3H, s), 3.46 (3H, s), 7.04—7.08 (2H, m), 7.22—7.28 (1H, m), 7.36—7.42 (2H, m)
1b	1495	2.20 (3H, s), 3.37 (3H, s), 3.47 (3H, s), 6.99 (1H, d, J=8 Hz), 7.13—7.26 (3H, m)
1c	1500	2.36 (3H, s), 3.34 (3H, s), 3.46 (3H, s), 6.94 (2H, d, J=8 Hz), 7.18 (2H, d, J=8 Hz)
1d	1490	3.39 (3H, s), 3.47 (3H, s), 7.14—7.23 (2H, m), 7.30 (1H, ddd, J=8, 8, 2 Hz), 7.43 (1H, dd, J=8, 2 Hz)
1e	1490	3.34 (3H, s), 3.45 (3H, s), 7.01 (2H, d, J=9 Hz), 7.34 (2H, d, J=9 Hz)

Thus, [2+2] cycloaddition of CSI with **8** with subsequent loss of carbonylsulfide is followed by Friedel–Crafts cyclization of the resulting *N*-chlorosulfonyl isothiourea (Chart 3).

Attempted Synthesis of 3-Dimethylamino-4-methyl-1,2,4-benzothiadiazine 1,1-Dioxide (12) We next turned our attention to the conversion of *N*,*N*-dimethyl-*N'*-methyl-*N'*-phenylthiourea (**2**) to the corresponding **12** by means of a reaction analogous to those shown in Chart 3. However, the desired product could not be obtained, probably due to the lability of the intermediate 1-methyl-1-phenyl-3,3-dimethyl-2-chlorosulfonylguanidine under the reaction conditions employed.

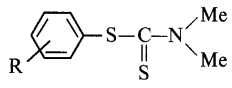
Synthesis of 3-Dimethylamino-1,4,2-benzodithiazine 1,1-Dioxides (11) In general, **11** have been prepared by cyclization of 2-halogenobenzenesulfonamides with CS_2 followed by alkylation and subsequent treatment of the reaction products with dimethylamine.[8] However, this method is not entirely satisfactory because of the complicated procedure. Moreover, the preparation of the starting 2-halogenobenzenesulfonamide derivatives is somewhat troublesome.[9] Therefore, we became interested in finding a new and facile method for the synthesis of **11**. In a previous paper,[1] we reported the synthesis of C and here tried applying the method to the synthsis of **11**.

As shown in Chart 3, a similar reaction occurred and the desired compounds (**11a—f**) were obtained when we used the corresponding *S*-phenyl *N*,*N*-dimethyldithiocarbamates (**10a—f**) (Tables VI and VIII) as the starting material instead of the *S*-alkyl *N*-methyl-*N*-phenyldithiocarbamates. The results are summarized in Tables VII and IX. When **10f** was used as the starting material, no 8-methyl

TABLE V. Spectral Data for 3-Dimethylamino-4,1,2-benzoxathiazine 1,1-Dioxides (**7a—e**)

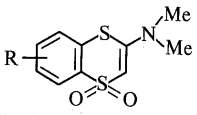
	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ (ppm)
7a	1160, 1170, 1275, 1635	3.19 (3H, s), 3.22 (3H, s), 7.20 (1H, d, J=8 Hz), 7.40 (1H, dd, J=8, 8 Hz), 7.57 (1H, ddd, J=8, 8, 2 Hz), 7.92 (1H, dd, J=8, 2 Hz)
7b	1155, 1310, 1610, 1635	2.39 (3H, s), 3.20 (3H, s), 3.23 (3H, s), 7.28 (1H, dd, J=8, 8 Hz), 7.41 (1H, d, J=8 Hz), 7.75 (1H, d, J=8 Hz)
7c	1160, 1280, 1310, 1640	2.41 (3H, s), 3.18 (3H, s), 3.20 (3H, s), 7.09 (1H, d, J=9 Hz), 7.35 (1H, dd, J=9, 2 Hz), 7.72 (1H, d, J=2 Hz)
7d	1360, 1375, 1320, 1640	3.21 (3H, s), 3.30 (3H, s), 7.35 (1H, dd, J=8, 8 Hz), 7.62 (1H, dd, J=8, 2 Hz), 7.83 (1H, dd, J=8, 2 Hz)
7e	1170, 1265, 1320, 1640	3.19 (3H, s), 3.21 (3H, s), 7.17 (1H, d, J=9 Hz), 7.52 (1H, dd, J=9, 3 Hz), 7.88 (1H, d, J=3 Hz)

TABLE VI. *S*-Phenyl *N*,*N*-Dimethyldithiocarbamates (**10a—f**)



	R	mp (°C)	Formula	*Anal.* (%) Calcd (Found)		
				C	H	N
10a	H	90—91	$C_9H_{11}NS_2$	54.78 (54.62	5.62 5.56	7.10 7.04)
10b	2-Me	78—80	$C_{10}H_{13}NS_2$	56.83 (56.74	6.20 6.20	6.63 6.76)
10c	4-Me	110—112	$C_{10}H_{13}NS_2$	56.83 (56.77	6.20 6.11	6.63 6.68)
10d	2-Cl	100—101	$C_9H_{10}ClNS_2$	46.64 (46.38	4.35 4.37	6.04 6.18)
10e	4-Cl	96—97	$C_9H_{10}ClNS_2$	46.64 (46.56	4.35 4.38	6.04 6.15)
10f	3-Me	Oil	$C_{10}H_{13}NS_2$	56.83 (56.49	6.20 6.39	6.63 6.81)

TABLE VII. 3-Dimethylamino-1,4,2-benzodithiazine 1,1-Dioxides(**11a—f**)



	R	Yield (%)	mp (°C)	Formula	*Anal.* (%) Calcd (Found)		
					C	H	N
11a	H	43	152—154	$C_9H_{10}N_2O_2S_2$	44.61 (44.43	4.16 4.13	11.56 11.54)
11b	5-Me	15	202—203	$C_{10}H_{12}N_2O_2S_2$	46.85 (46.77	4.72 4.69	10.93 10.99)
11c	7-Me	36	196—197	$C_{10}H_{12}N_2O_2S_2$	46.85 (46.70	4.72 4.68	10.93 10.75)
11d	5-Cl	11	139—141	$C_9H_9ClN_2O_2S_2$	39.05 (39.10	3.28 3.39	10.12 10.00)
11e	7-Cl	12	158—161	$C_9H_9ClN_2O_2S_2$	39.05 (38.70	3.28 3.42	10.12 10.24)
11f	6-Me	18	249—250	$C_{10}H_{12}N_2O_2S_2$	46.85 (46.72	4.72 4.74	10.93 10.85)

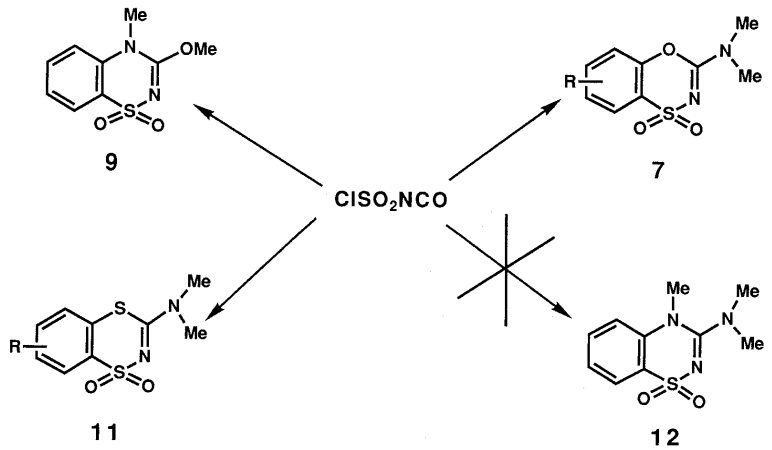


Chart 4

TABLE VIII. Spectral Data for *S*-Phenyl *N,N*-Dimethyldithiocarbamates (**10a—f**)

	IR $\nu_{max}^{CHCl_3}$ cm^{-1} (ν-N···C···S)	^{1}H-NMR ($CDCl_3$) δ (ppm)
10a	1500	3.50 (3H, s), 3.56 (3H, s), 7.30—7.60 (5H, m)
10b	1500	2.41 (3H, s), 3.52 (3H, s), 3.56 (3H, s), 7.23—7.44 (4H, m)
10c	1490	2.40 (3H, s), 3.50 (3H, s), 3.56 (3H, s), 7.26 (2H, d, J=7.8 Hz), 7.35 (2H, d, J=7.8 Hz)
10d	1495	3.53 (3H, s), 3.55 (3H, s), 7.31—7.57 (4H, m)
10e	1495	3.50 (3H, s), 3.55 (3H, s), 7.40 (4H, s)
10f	1500	2.39 (3H, s), 3.50 (3H, s), 3.56 (3H, s) 7.26—7.35 (4H, m)

TABLE IX. Spectral Data for 3-Dimethylamino-1,4,2-benzodithiazine 1,1-Dioxides (**11a—f**)

	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ (ppm)
11a	860, 1165, 1315, 1565, 1575	3.30 (3H, s), 3.33 (3H, s), 7.41—7.58 (3H, m), 8.12—8.18 (1H, m)
11b	860, 955, 1135, 1310, 1565	2.46 (3H, s), 3.34 (6H, s), 7.38—7.48 (2H, m), 8.05 (1H, dd, J=6.8, 2.0 Hz)
11c	860, 955, 1155, 1315, 1570	2.44 (3H, s), 3.29 (3H, s), 3.33 (3H, s), 7.33 (2H, s), 7.98 (1H, s)
11d	860, 950, 1165, 1315, 1570	3.36 (6H, s), 7.50 (1H, dd, J=7.8, 6.8 Hz), 7.61 (1H, d, J=6.8 Hz), 8.10 (1H, d, J=7.8 Hz)
11e	855, 950, 1160, 1310, 1560	3.30 (3H, s), 3.35 (3H, s), 7.39 (1H, d, J=8.8 Hz), 7.50 (1H, dd, J=8.8, 2.0 Hz), 8.15 (1H, d, J=2.0 Hz)
11f	860, 1115, 1165, 1315, 1565	2.43 (3H, s), 3.29 (3H, s), 3.31 (3H, s), 7.24 (1H, s), 7.33 (1H, d, J=7.8 Hz), 8.03 (1H, d, J=7.8 Hz)

congener was obtained, probably because of the steric hindrance of the methyl group.

Biological Results Some 1,4,2-benzodithiazine 1,1-dioxide derivatives have been reported to show fungicidal activity.[8] Thus, fungicidal activity testing of **11a—e** was carried out. From the viewpoint of molecular modification based on the concept of bioisosterism,[10] we also tested the fungicidal activity of **7a—e**, which can be viewed as bioisosteres of **11**. Contrary to our expectation, none of the compounds tested showed significant activity.

Conclusion We have newly developed practical and convenient synthetic methods for the title compounds by utilizing the novel [2+2] cycloaddition reaction of CSI with thiocarbamate or dithiocarbamate derivatives. Since CSI is commercially available and the starting thiocarbamate or dithiocarbamate derivatives are easy to prepare, the present method should be useful for the synthesis of heterocyclic compounds which bear the sulfonamide moiety.

Experimental

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were recorded with a Hitachi 260-10 spectrometer. ^{1}H-NMR spectra were determined with a JEOL JNM-PMX 60 or JEOL JNM-GSX 270 spectrometer, and δ values are quoted relative to tetramethylsilane. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad, dd=double doublet, ddd=double double doublet.

General Procedure for Preparation of Thiocarbamates (1a—e) NaH (60%, 64 mmol) was added in portions to a solution of phenol (53 mmol) in dry dimethylformamide (DMF) (50 ml) with stirring below 15 °C. Then, the reaction mixture was stirred at room temperature for 1 h, and dimethylthiocarbamoyl chloride (53 mmol) was added at 0 °C. After further stirring for 2 h at room temperature, the mixture was poured onto ice and extracted with ether. The ethereal solution was washed with brine, then dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (hexane–CH_2Cl_2, 2:1).

***N,N*-Dimethyl-*N'*-methyl-*N'*-phenylthiourea (2)** *N*-Methylaniline (18.7 mmol) and Et_3N (18.7 mmol) were added to a solution of dimethylthiocarbamoyl chloride (18.7 mmol) in toluene. Then the toluene solution was refluxed for 18 h and treated with water. The mixture was extracted with AcOEt. The organic layer was washed with brine, then dried over Na_2SO_4. The solution was concentrated under reduced pressure and the residue was subjected to column chromatography on silica gel with hexane–CH_2Cl_2 (2:3) as an eluent to give **2** (2.9 g, 81% yield). Oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1495, 1385, 1340, 1325, 1100. ^{1}H-NMR ($CDCl_3$) δ: 3.01 (6H, s), 3.54 (3H, s), 7.03 (2H, d, J=8 Hz), 7.12 (1H, dd, J=8, 8 Hz), 7.34 (2H, dd, J=8, 8 Hz). *Anal.* Calcd for $C_{10}H_{14}N_2S$: C, 61.82; H, 7.26; N, 14.42. Found: C, 61.81; H, 7.26; N, 14.57.

***O*-Phenyl-*N,N'*-dimethylcarbamate (3)** NaH (60%, 24.3 mmol) was added to a solution of phenol (18.7 mmol) in DMF, and the mixture was stirred for 15 min at room temperature. Then dimethylcarbamoyl chloride (18.7 mmol) was added and the whole mixture was stirred for 30 min at room temperature and treated with ice. The mixture was extracted with ether. The organic layer was washed with brine, then dried over Na_2SO_4. The solution was concentrated under reduced pressure and the residue was chromatographed on silica gel with hexane–CH_2Cl_2 (1:1) as an eluent to give **3** (2.3 g, 74% yield). Oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710, 1490, 1390, 1170. ^{1}H-NMR ($CDCl_3$) δ: 3.00 (3H, s), 3.09 (3H, s), 7.11 (2H, d, J=8, 8 Hz), 7.18 (1H, dd, J=8, 8 Hz), 7.35 (2H, dd, J=8, 8 Hz). *Anal.* Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.41; H, 6.81; N, 8.48.

***N,N*-Dimethyl-*N'*-methyl-*N'*-phenylurea (4)** The same procedure as described for the preparation of 2 was employed. Yield 95%. Oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630, 1595, 1490, 1380, 1130. ^{1}H-NMR ($CDCl_3$) δ: 2.69 (6H, s), 3.22 (3H, s), 7.02—7.13 (3H, m), 7.32 (2H, dd, J=8, 8 Hz). *Anal.* Calcd for $C_{10}H_{14}N_2O$: C, 67.39; H, 7.92; N, 15.72. Found: C, 67.00; H, 7.93; N, 15.38.

1,1-Dimethyl-2-phenyl-3-toluenesulfonylisourea (5) mp 80—82 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1610, 1440, 1150, 1095. ^{1}H-NMR ($CDCl_3$) δ: 2.34 (3H, s), 3.05 (6H, br s), 6.87 (2H, d, J=8 Hz), 7.05—7.15 (3H, m), 7.26 (2H, dd, J=8, 8 Hz), 7.63 (2H, d, J=8 Hz). *Anal.* Calcd for $C_{16}H_{18}N_2O_3S$: C, 60.36; H, 5.70; N, 8.80. Found: C, 60.25; H, 5.68; N, 8.91.

1,1-Dimethyl-3-phenyl-2-toluenesulfonylguanidine (6) mp 120—121 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1555, 1490, 1395, 1145, 1085. ^{1}H-NMR ($CDCl_3$) δ: 2.39 (3H, s), 2.79 (6H, s), 3.31 (3H, s), 6.95 (2H, d, J=9 Hz), 7.09 (1H, dd, J=8, 8 Hz), 7.23 (2H, d, J=8 Hz), 7.31 (2H, dd, J=8, 8 Hz), 7.82 (2H, d, J=9 Hz). *Anal.* Calcd for $C_{17}H_{21}N_3O_2S$: C, 61.61; H, 6.39; N, 12.68. Found: C, 61.32; H, 6.20; N, 12.43.

General Procedure for Preparation of 3-Dimethylamino-4,1,2-benzoxathiazine 1,1-Dioxides (7a—e) Chlorosulfonyl isocyanate (7.2 mmol) was added dropwise to an ice-cooled solution of thiocarbamate (5.5 mmol) in CH_2Cl_2. The mixture was stirred at room temperature for 30 min. After removal of the solvent, the residue was dissolved in nitromethane (10 ml), then anhydrous aluminum chloride (8.3 mmol) was added. The reaction mixture was stirred at room temperature for 2 h, cooled, diluted with water and extracted with CH_2Cl_2. The extract was washed with brine, then dried. The solvent was removed under reduced pressure and the residue was crystallized from CH_2ClCH_2Cl.

***O*-Methyl *N*-Methyl-*N*-phenylthiocarbamate (8)** NaOMe (28%, 8.7 mmol) was added to a solution of thiophosgene (13 mmol) in dry tetrahydrofuran (THF) (10 ml) in portions with stirring below −45 °C. Then, the reaction mixture was stirred at −45 °C for 10 min, and *N*-methylaniline (8.7 mmol) was added at −45 °C. The mixture was stirred for 30 min below 0 °C, poured into water and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel silica gel with hexane–CH_2Cl_2 (3:1) as an eluent to give **8** (200 mg, 13% yield). Oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1500, 1480, 1450, 1390, 1295. ^{1}H-NMR ($CDCl_3$) δ: 3.61 (3H, br s), 3.95 (3H, br s), 7.05—7.52 (5H, m). *Anal.* Calcd for $C_9H_{11}NOS$: C, 59.64; H, 6.12; N, 7.73. Found: C, 59.79; H, 6.18; N, 7.76.

3-Methoxy-4-methyl-1,2,4-benzothiadiazine 1,1-Dioxide (9) Chlorosulfonyl isocyanate (1.3 mmol) was added dropwise to an ice-cooled solution of the thiocarbamate (**8**) (0.9 mmol) in dry CH_2Cl_2 (4 ml). The mixture was stirred at room temperature for 40 min. After removal of the solvent, the residue was dissolved in nitromethane (4 ml), then anhydrous

aluminum chloride (1.1 mmol) was added. The reaction mixture was stirred at room temperature for 12 h, diluted with water and extracted with CH_2Cl_2. The extract was washed with brine, then dried. The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel with hexane–AcOEt (2 : 1) as an eluent to give **9** (150 mg, 75% yield). mp 202—204 °C (lit[11] mp 200—202 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1615, 1460, 1385, 1310, 1170. ^{1}H-NMR ($CDCl_3$) δ:3.55 (3H, s), 4.08 (3H, s), 7.26 (1H, d, J=8 Hz), 7.41 (1H, dd, J=8, 8 Hz), 7.64 (1H, dd, J=8, 8 Hz), 8.01 (1H, d, J=8 Hz). *Anal.* Calcd for $C_9H_{10}N_2O_3S$: C, 47.78; H, 4.46; N, 12.38. Found: C, 47. 64; H, 4.43; N, 12.34.

General Procedure for Preparation of Dithiocarbamates (10a—f) A mixture of a thiophenol (36.3 mmol), dimethylthiocarbamoyl chloride (48.5 mmol), potassium *tert*-butoxide (43.7 mmol) and DMF (40 ml) was stirred at room temperature for 20 min and then at 90 °C for 30 min. The reaction mixture was diluted with water and extracted with ether. The ethereal solution was washed with saturated brine, then dried. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (hexane : CH_2Cl_2 = 2 : 1), followed by recrystallization (hexane–AcOEt).

General Procedure for Preparation of 3-(*N*,*N*-Dimethylamino)-1,4,2-benzodithiazine 1,1-Dioxides (11a—f) Chlorosulfonyl isocyanate (6.1 mmol) was added dropwise to a solution of dithiocarbamate (5.1 mmol) in toluene (10 mmol). The mixture was stirred at 100 °C for 20 min. After removal of the solvent, the residue was dissolved in nitromethane (10 ml), then anhydrous aluminum chloride (5.6 mmol) was added all at once. The reaction mixture was stirred at 100 °C for 20 min, cooled, diluted with water and extracted with CH_2Cl_2.

The extract was washed with saturated brine, then dried. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (CH_2Cl_2 : AcOEt = 9 : 1).

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