Reaction of 1,3-Oxathiolium Salts with Three Types of Ring Expansion Reagents on a Nitrogen Atom

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The ring expansion reactions of 1,3-oxathiolium salts (**1**) using NaN_3 and an I_2–aq NH_3 system resulted exclusively in the formation of 1,4,2-oxathiazines (**3**) by incorporation of a nitrogen atom into the C–O bond in **1**. On the other hand, the reaction of **1** with dialkylamino(thioxo)methanesulfenamides, another type of N-expansion reagent, gave di-5-thiazolyl sulfide derivatives (**4**) in addition to **3**. The structure of **4** was confirmed by X-ray crystallographic analysis. It was speculated that the formation of **4** goes via initially-formed **3**. Furthermore, **1** reacted with another N-unsubstituted sulfenamides having a heterocyclic substituent such as a 2-pyridyl and 2-benzothiazolyl group to afford 2-pyridyl 5-thiazolyl sulfide and 2-benzothiazolyl 5-thiazolyl sulfide derivatives, respectively, together with **3**. The stability and reactivity of oxathiazines **3**, which comprise an electron-rich π-system, were also examined.

It is well known that the reaction of heterocyclic cation compounds with azides results in ring expansion by incorporation of a nitrogen atom into the heteroring.[1] While exploring the reactivity of heteroaromatic cations toward various nucleophiles, we have discovered alternative and potentially general methods for ring expansion of heterocyclic cations on a nitrogen atom.

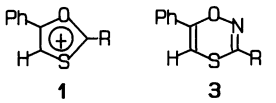
We reported the reaction of 1,4,2-dithiazolium and 1,3-dithiolium salts with N-unsubstituted sulfenamides of the general formula ($RSNH_2$) leading to 1,4,2,5-dithiadiazines and 1,4,2-dithiazines, respectively, arising from insertion of the terminal nitrogen atom of the sulfenamides into the heteroring.[2] We have also found a new method for the ring expansion reaction using an I_2–aq NH_3 system, which was applied toward a wide range of aromatic and nonaromatic five-membered heterocyclic cations to afford various types of N-expanded products.[3] We have supposed that the reaction mechanism involves two types of intermediates, i.e., a nitrene for NaN_3 and a nitrenium ion for the sulfenamides and an I_2–aq NH_3 system as shown in Scheme 1.

As a further extension of the previous studies, the behavior of 1,3-oxathiolium salts toward the three types of N-expansion reagents was investigated to clarify the scope of these reactions. Furthermore, the stability and reactivity of ring-expanded products, 1,4,2-oxathiazine derivatives, which have an intriguing 8π-electron ring system, were also examined.

Results and Discussion

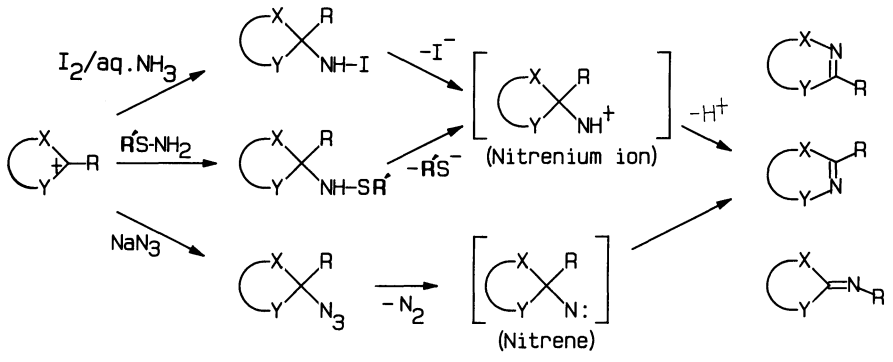
First of all, the ring expansion reaction of 1,3-oxathiolium salts (**1**) using NaN_3 and an I_2–aq NH_3 system was carried out. When 2,5-diphenyl-1,3-oxathiolium perchlorate (**1a**) was treated successively with I_2 and aqueous ammonia at room temperature or reacted with NaN_3 in refluxing acetonitrile, each reaction gave only a single product (**3a**), which was identical with each other. Similarly, 3-piperidino derivative (**1b**) was also allowed to react with I_2–aq NH_3 leading to a sole product (**3b**). However, the reaction of **1b** with NaN_3 did not proceed in refluxing acetonitrile for 1 h. The results are presented in Table 1.

On the basis of elemental analysis of **3a** and their



1 **3**

a: R=Phenyl **b**: R=Piperidino **c**: R=Morpholino



Scheme 1.

Table 1. Reaction of 1,3-Oxathiolium Perchlorate **1** with NaN_3 or I_2/aq NH_3

R in **1**	N-Source	Condition[a)]	Product yield/%
			3
Phenyl	I_2/aq NH_3	r.t./30 min	45
Phenyl	NaN_3	Reflux/10 min	41
Piperidino	I_2/aq NH_3	r.t./30 min	63
Piperidino	NaN_3	Reflux/1 h	—

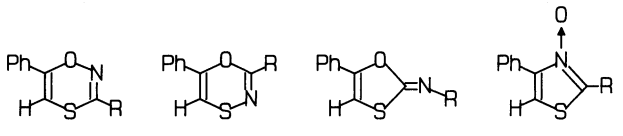
a) In acetonitrile.

Table 2. Reaction of 1,3-Oxathiolium Perchlorate **1** with Sulfenamides **2** ($R'SNH_2$)

Entry	R in **1**	R′ in **2**	Condition[a)]	Product yield/%		
			Time/h	**3**	**4**[b)]	**5**
1	Piperidino	Dimethylthiocarbamoyl	20	46	13	—
2	Piperidino	Dimethylthiocarbamoyl	72	—	25	—
3	Piperidino	Morpholinothiocarbonyl	24	16	33	—
4	Morpholino	Dimethylthiocarbamoyl	16	33	37	—
5	Phenyl	Dimethylthiocarbamoyl	15	—	—	—
6	Morpholino	1,3-Benzothiazol-2-yl	48	Low	—	39
7	Morpholino	2-Pyridyl	6	19	—	52
8	Piperidino	2-Pyridyl	2	45	—	30
9	Piperidino	2-Pyridyl	6	39	—	29
10	Piperidino	2-Pyridyl	96	15	4	30
11	Piperidino	2-Pyridyl	72[c)]	—	20	9
12	Phenyl	2-Pyridyl	20	13	—	—

a) At room temperature in MeCN. b) Conversion yield based on **1**. c) Addition of tetramethylthiuram disulfide in amounts equimolar with **1b**.

spectral data (^1H and ^{13}C NMR, and MS), oxathiazine forms (**A**, **B**) and their isomers (**C**, **D**) appear to be candidates for the structure of the products. The method for synthesis of **D** (R=piperidino) by the reaction of **1b** with hydroxylamine has been reported separately by Hirai et al.[4] On the basis of their ^1H NMR spectra, **3b** proved not to be identical with **D**: Signals of a vinyl proton are δ=6.48 for **3b** and δ=6.75 for **D**. The product **3a** was directly compared with an authentic sample of **C** (R=Ph) which was prepared by the reaction of **1b** with aniline,[5] and the possibility of **C** as **3a** was also ruled out. In order to examine the remaining possibility, i.e., 1,4,2- and 1,4,3-oxathiazine forms **A** and **B**, the deoxygenation of **3b** by treating with triphenylphosphine was carried out. The reaction afforded no isothiazole derivative from **B** but 4-phenyl-2-piperidino-1,3-thiazole together with triphenylphosphine oxide.[6] Therefore the product **3** was identified with 1,4,2-oxathiazine derivative **A**, which was produced by insertion of a nitrogen atom into the C–O bond, and not into the C–S bond, in the oxathiole ring.



A **B** **C** **D**

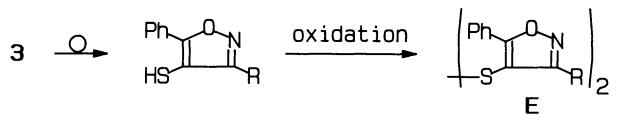
It is interesting to compare the reactivity of 1,3-oxathiolium cations with that of 1,3-dithiolium cations, a thia-analogue, and that of 1,4,2-dithiazolium cations, a higher aza-analogue, toward NaN_3 and an I_2–aq NH_3 system. The related findings have been already reported as follows. The ring expansion reaction of 2,4-diphenyl-1,3-dithiolium perchlorate using NaN_3 as well as an I_2–aq NH_3 system gives a mixture of the corresponding 1,4,2- and 1,4,3-dithiazine isomers in each case.[3,7] On the other hand, 3,5-diphenyl-1,4,2-dithiazolium perchlorate is treated with NaN_3 and an I_2–aq NH_3 system to produce the corresponding 1,4,2,6- and 1,4,2,5-dithiadiazine derivatives as a sole product, respectively.[3,8]

Subsequently we investigated the behavior of **1** toward an alternative N-expansion reagent, *N*-unsubstituted sulfenamides **2**. The oxathiolium salt **1b** was allowed to react with sulfenamide **2a** (R′=dimethylthiocarbamoyl) and sulfenamide **2b** (R′=morpholinothiocarbonyl) to afford not only **3b** but also a common oily product (**4b**) (Entries 1 and 3 in Table 2). The same reaction as in Entry 1, except for prolonged reaction time, resulted in disappearance of **3b** and improvement of the yield of **4b** (Entry 2). It is thus speculated that the formation of **4b** goes via initially-formed **3b**.

^1H and ^{13}C NMR spectra of **4b** show the presence of a piperidino, a phenyl, and a heterocyclic substituent.

Furthermore, its mass spectrum shows a molecular ion peak at m/z 518, which was about twice the value for **3b** (m/z 260). It seems therefore reasonable to propose a dimeric structure, bis(5-phenyl-3-piperidino-4-isoxazolyl) disulfide (**E**) (MW=518), as the product **4b**, which consists at least with these spectral data. On the other hand, formation of **E** can be rationalized by means of the pathway from **3** including both the rearrangement in which the ring sulfur atom becomes exocyclic and an autoxidation step, as shown in Scheme 2. A similar behavior of 1,4-dithiin derivatives is also known to form the corresponding di-3-thienyl disulfide derivatives.[9]

The reaction of 2-morpholino derivative (**1c**) with **2a** also gave the corresponding 1,4,2-oxathiazine (**3c**) and a solid product (**4c**) (Entry 4), while the same reaction of **1a** gave only 2,4-diphenylthiazole in 15% yield (Entry 5).[10] The spectral data of **4c** show a similar characteristic pattern to those of **4b**. However, elemental analysis of **4c** indicates that **4c** should contain three sulfur atoms in the molecule rather than two. In addition, the high resolution MS spectrum of **4b** shows the molecular ion peak at m/z 518.1670, which is much closer to m/z 518.1633 calculated for $C_{28}H_{30}N_4S_3$ than m/z 518.1811 for **E** ($C_{28}H_{30}N_4S_2O_2$). Since the structure of **4** could not be unequivocally determined from the present data, an X-ray crystallographic analysis of **4c** was carried out. A correct structure of **4c** thereby proved to be not disulfide **E** but bis(2-morpholino-4-phenyl-5-thiazolyl) sulfide as illustrated in Fig. 1. No plausible explanation for the mechanism of the formation of **4** has been given yet.



Scheme 2.

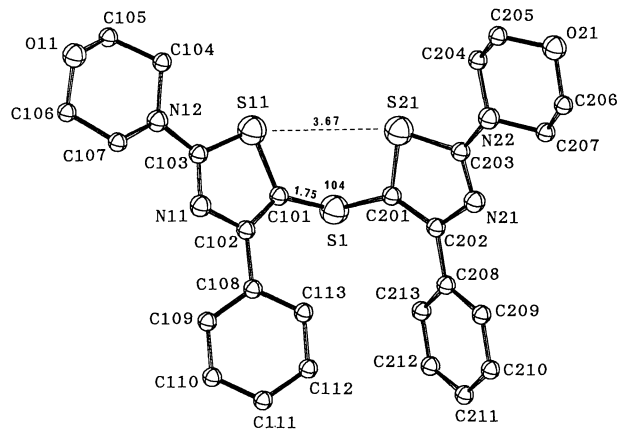
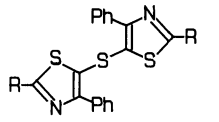
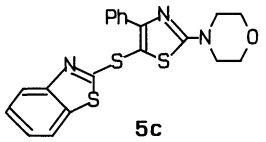


Fig. 1. Molecular structure[19] of **4c** with the numbering system for the non-hydrogen atoms. Thermal ellipsoids are drawn at 50% probability.

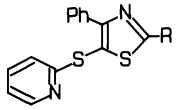
Crystal structural analysis shows a couple of characteristic features as follows. The length of the C–S bond in the sulfide moiety is 1.75 Å on the average, which is among the ordinary values of diaryl sulfides, e.g., 1.75 Å for $(p\text{-}CH_3C_6H_4)_2S$.[11] On the other hand, it is noteworthy that the C–S–C (sulfide moiety) angle of 104° is close to the value of dimethyl sulfide (105°) rather than that of diphenyl sulfide (113°).[11] It seems to be due to an intramolecular S···S contact of 3.67 Å between two thiazole rings, the value of which is approximately the sum of two sulfur van der Waals radii (3.70 Å).



4b: R=Piperidino
4c: R=Morpholino



5c



5b′: R=Piperidino
5c′: R=Morpholino

In order to obtain additional information on the reactivity, we attempted the reaction with other N-unsubstituted sulfenamides having a heterocyclic substituent such as 2-pyridinesulfenamide (**2c**) and 2-benzothiazolesulfenamide (**2d**). The reaction of **1c** with **2d** gave no **4c** but **3c** in a low yield and a new type of product (**5c**) (Entry 6). On the basis of its elemental analysis and spectral data (^1H and ^{13}C NMR and MS), 2-benzothiazolyl 2-morpholino-4-phenyl-5-thiazolyl sulfide was proposed as the product **5c**. The sulfide **5c** has the benzothiazole ring which is originated from sulfenamide **2d** and the thiazole ring which is the same group as that in **4c**. The mass spectrum of **5c** shows a characteristic pattern similar to that of **4c**. In paprticular, they show a common fragment peak at m/z 165 (relative intensity 100%) attributable to $PhCSCS^+$, which seems to result from the similarity in their sulfide structures. Although the mechanism of the reaction remains in doubt, it is apparent at least that the overall pathway for the formation of **5** is composed of entire addition of **2c** or **2d** to **1** including cleavage of the sulfenamide S–N bond and elimination of H_2O and $HClO_4$ with respect to mass balance.

In the case of using sulfenamide **2c**, the reaction of **1c** and **1b** also gave the corresponding sulfide (**5c′**) and (**5b′**) together with **3c** and **3b**, respectively (Entries 7 and 8). On the other hand, the reaction of **1a** with **2c** afforded only **3a** in 13% yield (Entry 12). Furthermore, the same reactions as in Entry 8, except for prolonged reaction time, were carried out (Entries 9 and 10). The yield of **5b′** proved to be independent on the reaction time,

whereas the yield of **3b** decreased with the elapse of time along with the formation of a small amount of **4b**. However, this tendency is not so drastic as for Entry 2. We postulate here that these phenomena are associated with the formation of tetramethylthiuram disulfide and dipyridyl disulfide which arise from the corresponding sulfenamides **2** during the ring-expansion reaction, and that the former is acting more effectively than the latter. From this viewpoint, the reaction of **1b** with **2c**, on addition of tetramethylthiuram disulfide in amounts equimolar with **1b**, was examined. The reaction resulted in complete disappearance of **3b** and remarkable appearance of **4b** along with unexpected decrease in yield of **5b'** (Entry 11). On the other hand, direct treatment of **3b** with tetramethylthiuram disulfide in MeCN at room temperature for 3 d was separately attempted; but **3b** was recovered unchanged.

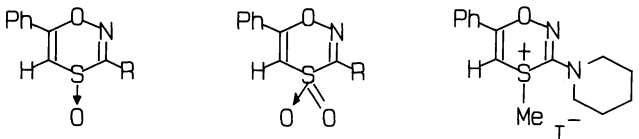
We suggested in a previous paper that the reactivity of N-expansion reagents toward heterocyclic cation compounds is controlled by the contribution of two types of intermediates, i.e., a nitrene and a nitrenium cation. However, a significant difference in the reactivity obtained in this study and the mechanisms for the formation of **4** and **5** cannot be explained at present.

1,4,2-Oxathiazines **3**, which, if planar, would show the 8π-antiaromatic character, have the electron rich π-system common to dithiadiazines, dithiazines, and dithiins. We examined their stability and some reactions which tended to reduce the electron density in the oxathiazine ring. 1,4,2-Oxathiazines **3** were stable in air at room temperature for several weeks. However, oily **3b** and **3c** completely decomposed in about one year to afford the sulfide **4b** and **4c** in moderate yields (ca. 30% for conversion), respectively. The conversion yields were calculated on the assumption that the formation of one molecule of **4** requires three molecules of **3** which serve as sources of not only two thiazole-rings but one sulfide sulfur.

The oxathiazines **3a** and **3b** were allowed to react with an equimolar or 2 molar amount of *m*-chloroperbenzoic acid in $CHCl_3$ at room temperature to afford the corresponding 4-oxide (**6a**, **b**) or 4,4-dioxide derivatives (**7a**, **b**), respectively, in moderate to good yields. It is known that benzo-fused 1,4,2- and 1,4,3-oxathiazine 4-

Table 3. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters, with Estimated Standard Deviations in Parentheses

Atom	*x*	*y*	*z*	B_{eq}	Atom	*x*	*y*	*z*	B_{eq}
S1	5516 (1)	3781 (0)	2155 (1)	4.69 (0.02)	C205	10362 (2)	1551 (2)	1846 (3)	7.8 (0.1)
S2	7848 (1)	8741 (0)	2008 (1)	5.19 (0.02)	C206	9444 (2)	276 (2)	1218 (3)	6.4 (0.1)
S11	7162 (1)	4840 (0)	3696 (1)	5.00 (0.02)	C207	8451 (2)	747 (2)	860 (2)	5.4 (0.1)
S21	7551 (1)	3020 (0)	1956 (1)	4.49 (0.02)	C208	4870 (2)	1681 (2)	1299 (2)	4.1 (0.1)
S31	7053 (1)	9826 (0)	3602 (1)	5.35 (0.02)	C209	4794 (2)	788 (2)	1298 (3)	5.9 (0.1)
S41	5683 (1)	8035 (0)	1721 (1)	4.62 (0.02)	C210	3832 (2)	390 (2)	1169 (3)	7.4 (0.1)
O11	9238 (2)	6399 (1)	7303 (2)	8.0 (0.1)	C211	2960 (2)	872 (2)	1051 (3)	6.6 (0.1)
S21	10325 (2)	780 (1)	1207 (2)	7.6 (0.1)	C212	3011 (2)	1757 (2)	1021 (2)	5.9 (0.1)
O31	6978 (2)	11371 (2)	7292 (2)	8.9 (0.1)	C213	3964 (2)	2159 (2)	1134 (2)	5.0 (0.1)
O41	2587 (1)	5805 (1)	1153 (2)	6.4 (0.1)	C301	7927 (2)	9055 (2)	3345 (2)	4.5 (0.1)
N11	6514 (2)	4372 (1)	5307 (2)	4.2 (0.1)	C302	8672 (2)	8890 (2)	4259 (2)	4.1 (0.1)
N12	7844 (2)	5406 (1)	5757 (2)	5.4 (0.1)	C303	7761 (2)	9858 (2)	4931 (2)	4.6 (0.1)
N21	6694 (2)	1545 (1)	1290 (2)	4.0 (0.1)	C304	6484 (3)	10769 (2)	5506 (3)	8.4 (0.1)
N22	8487 (2)	1569 (1)	1464 (2)	4.6 (0.1)	C305	6468 (3)	11514 (3)	6218 (3)	10.0 (0.2)
N31	8566 (2)	9349 (1)	5163 (2)	4.4 (0.1)	C306	8005 (3)	11103 (3)	7409 (3)	9.8 (0.2)
N32	7500 (2)	10401 (1)	5670 (2)	5.7 (0.1)	C307	8106 (3)	10336 (2)	6764 (3)	8.2 (0.1)
N41	6236 (2)	6521 (1)	1173 (2)	4.2 (0.1)	C308	9562 (2)	8295 (2)	4408 (2)	4.3 (0.1)
N42	4494 (2)	6592 (1)	1246 (2)	4.6 (0.1)	C309	9514 (2)	7525 (2)	3802 (2)	5.5 (0.1)
C101	6155 (2)	4085 (2)	3476 (2)	4.2 (0.1)	C310	10363 (3)	6984 (2)	3967 (3)	6.9 (0.1)
C102	5927 (2)	3923 (1)	4422 (2)	3.8 (0.1)	C311	11263 (3)	7187 (2)	4743 (3)	7.2 (0.1)
C103	7186 (2)	4878 (2)	5047 (2)	4.4 (0.1)	C312	11316 (2)	7934 (2)	5365 (3)	6.2 (0.1)
C104	8734 (3)	5797 (2)	5505 (3)	7.2 (0.1)	C313	10473 (2)	8483 (2)	5197 (2)	4.9 (0.1)
C105	9105 (3)	6540 (3)	6211 (3)	10.6 (0.2)	C401	6973 (2)	7867 (2)	1721 (2)	4.3 (0.1)
C106	8313 (3)	6098 (2)	7499 (3)	8.8 (0.2)	C402	7123 (2)	7035 (2)	1393 (2)	4.1 (0.1)
C107	7890 (3)	5340 (2)	6877 (2)	8.1 (0.1)	C403	5441 (2)	6949 (2)	1329 (2)	4.1 (0.1)
C108	5119 (2)	3335 (2)	4599 (2)	4.0 (0.1)	C404	3591 (2)	7115 (2)	1275 (2)	5.6 (0.1)
C109	4661 (2)	3519 (2)	5431 (2)	4.6 (0.1)	C405	2859 (2)	6603 (2)	1720 (3)	6.5 (0.1)
C110	3907 (2)	2982 (2)	5621 (2)	5.6 (0.1)	C406	3483 (2)	5292 (2)	1195 (3)	5.8 (0.1)
C111	3602 (2)	2252 (2)	4969 (3)	6.6 (0.1)	C407	4258 (2)	5732 (2)	741 (2)	4.9 (0.1)
C112	4047 (3)	2056 (2)	4152 (2)	6.5 (0.1)	C408	8077 (2)	6623 (2)	1246 (2)	4.5 (0.1)
C113	4820 (2)	2589 (2)	3963 (2)	5.2 (0.1)	C409	8870 (2)	7078 (2)	979 (2)	5.6 (0.1)
C201	6230 (2)	2890 (2)	1863 (2)	3.8 (0.1)	C410	9750 (2)	6657 (2)	860 (2)	6.7 (0.1)
C202	5915 (2)	2071 (2)	1484 (2)	3.8 (0.1)	C411	9871 (2)	5790 (2)	990 (3)	7.2 (0.1)
C203	7590 (2)	1940 (2)	1521 (2)	3.8 (0.1)	C412	9098 (2)	5327 (2)	1246 (3)	7.2 (0.1)
C204	9413 (2)	2078 (2)	1513 (3)	6.7 (0.1)	C413	8205 (2)	5735 (2)	1366 (2)	5.6 (0.1)



6 7 8

a: R=Phenyl b: R=Piperidino

oxide and 4,4-dioxide derivatives can be used as pesticides, herbicides, and fungicides.[12] Hence these procedures are attractive as a synthetic method for these skeletons. Furthermore, in an excess of methyl iodide at room temperature, **3b** was readily converted into 4-methyl-1,4,2-oxathiazinium iodide (**8**) in 77% yield, which easily dissociated back to **3b** and MeI when dissolved in organic solvents or heated.

Experimental

All melting points were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Hitachi R-40 and a JEOL FX-90A spectrometer using TMS as an internal standard. Mass spectra were taken on a Hewlett Packard 5995A and a JEOL D-300 spectrometer (high resolution), by electron impact ionizing technique. IR spectra were measured on a JASCO A-302 spectrometer using KBr disks.

1,3-Oxathiolium perchlorates **1**[13] and sulfenamides **2**[14] were prepared according to the procedures in literatures.

Reaction of 1,3-Oxathiolium Perchlorates 1 with NaN_3. Sodium azide (1.1 mmol) was added to an acetonitrile solution (6 ml) of **1** (1 mmol). The reaction mixture was refluxed for 10 min to 1 h. The crude products were extracted with dichloromethane after addition of aq $NaHCO_3$. After the solvent was removed in vacuo, the residue was purified by column chromatography on silica gel. The yields of products are shown in Table 1.

Reaction of 1,3-Oxathiolium Perchlorates 1 with I_2-aq NH_3. A large excess of aqueous ammonia (28%) (0.6 ml) was added to a stirred acetonitrile solution (6 ml) of **1** (1 mmol). The reaction mixture was stirred for 30 min at room temperature. Subsequent work-up and purification were accomplished by the procedure similar to that mentioned above. The yields of products are shown in Table 1.

Reaction of 1,3-Oxathiolium Perchlorates 1 with Sulfenamides 2. Sulfenamides **2** (2 mmol) were added to a stirred acetonitrile solution (6 ml) of **1** (1 mmol). The reaction mixture was stirred for 2 h to 4 d at room temperature. Subsequent work-up and purification were accomplished by the procedure mentioned above. The yield and reaction time are listed in Table 2.

3,5-Diphenyl-1,4,2-oxathiazine 3a: Orange. Mp 105.0—105.5 °C (MeCN). ^1H NMR ($CDCl_3$) δ=6.20 (1H, s), 7.3—7.6 (6H, m), 7.6—7.75 (2H, m), 8.0—8.15 (2H, m). ^{13}C NMR ($CDCl_3$) δ=101.04, 123.95, 127.39, 128.37, 128.66, 128.88, 131.05, 131.43, 132.35, 144.92, 156.35. MS *m/z* (rel intensity) 253 (M^+, 4), 150 ($PhCOCSH^+$, 21), 105 ($PhCO^+$, 100). Found: C, 71.14; H, 4.35; N, 5.51; S, 12.64%. Calcd for $C_{15}H_{11}NSO$: C, 71.12; H, 4.38; N, 5.53; S, 12.66%.

5-Phenyl-3-piperidino-1,4,2-oxathiazine 3b: Pale yellow oil. ^1H NMR ($CDCl_3$) δ=1.4—1.6 (6H, br), 3.4—3.6 (4H, br), 6.50 (1H, s), 7.3—7.5 (5H, m). ^{13}C NMR ($CDCl_3$) δ=24.25, 25.28, 46.30, 105.68, 123.61, 128.11, 128.54, 132.66, 144.60, 154.57. MS *m/z* (rel intensity) 260 (M^+, 10), 150 ($PhCOCSH^+$, 25), 105 ($PhCO^+$, 100). Found: *m/z* 260.1010. Calcd for $C_{14}H_{16}N_2SO$: M, 260.0983.

3-Morpholino-5-phenyl-1,4,2-oxathiazine 3c: Pale yellow oil. ^1H NMR ($CDCl_3$) δ=3.4—3.6 (4H, m), 3.65—3.85 (4H, m), 6.47 (1H, s), 7.3—7.6 (5H, m). ^{13}C NMR ($CDCl_3$) δ=45.40, 66.09, 104.91, 123.54, 128.31, 128.58, 132.32, 144.27, 153.72. MS *m/z* (rel intensity) 262 (M^+, 8), 150 ($PhCOCSH^+$, 35), 105 ($PhCO^+$, 100). Found: *m/z* 262.0791. Calcd for $C_{13}H_{14}N_2SO_2$: M, 262.0775.

Bis(4-phenyl-2-piperidino-5-thiazolyl) Sulfide 4b: Colorless oil. ^1H NMR ($CDCl_3$) δ=1.5—1.7 (12H, br.), 3.3—3.6 (8H, br.), 7.25—7.4 (6H, m), 7.8—7.95 (4H, m). ^{13}C NMR ($CDCl_3$) δ=24.11, 25.11, 49.00, 111.55, 127.88, 129.10, 134.57, 153.69, 170.32. MS *m/z* (rel intensity) 518 (M^+, 6), 275 (47), 244 (24), 165 ($PhCSCS^+$, 100). Found: *m/z* 518.1670. Calcd for $C_{28}H_{30}N_4S_3$: M, 518.1633.

Bis(2-morpholino-4-phenyl-5-thiazolyl) Sulfide 4c: White. Mp 180.5—181.0 °C (CH_2Cl_2–hexane). ^1H NMR ($CDCl_3$) δ=3.4—3.6 (8H, m), 3.7—3.9 (8H, m), 7.25—7.45 (6H, m), 7.8—7.95 (4H, m). ^{13}C NMR ($CDCl_3$) δ=48.00, 66.04, 112.63, 127.96, 128.15, 129.07, 134.22, 153.77, 170.30. MS *m/z* (rel intensity) 522 (M^+, 11), 277 (29), 246 (32), 165 ($PhCSCS^+$, 100). Found: C, 58.96; H, 4.96; N, 9.92; S, 18.47%. Calcd for $C_{26}H_{26}N_4S_3O_2$: C, 59.74; H, 5.01; N, 10.72; S, 18.40%.

2-Benzothiazolyl 2-Morpholino-4-phenyl-5-thiazolyl Sulfide 5c: White. Mp 133.0—134.0 °C (CH_2Cl_2–MeOH). ^1H NMR ($CDCl_3$) δ=3.5—3.7 (4H, m), 3.75—3.95 (4H, m), 7.2—8.1 (9H, m). ^{13}C NMR ($CDCl_3$) δ=47.92, 65.96, 102.47, 120.92, 121.87, 124.17, 126.09, 128.12, 128.56, 128.85, 133.54, 135.57, 154.34, 159.30, 171.60, 172.22. MS *m/z* (rel intensity) 411 (M^+, 20), 378 (15), 165 ($PhCSCS^+$, 100). Found: C, 57.93; H, 4.07; N, 10.13; S, 23.30%. Calcd for $C_{20}H_{17}N_3S_3O$: C, 57.37; H, 4.16; N, 10.21; S, 23.37%.

4-Phenyl-2-piperidino-5-thiazolyl 2-Pyridyl Sulfide 5b′: Pale yellow oil. ^1H NMR ($CDCl_3$) δ=1.5—1.8 (6H, br.), 3.4—3.7 (4H, br.), 6.9—7.1 (2H, m), 7.2—7.6 (4H, m), 7.8—8.0 (2H, m), 8.4—8.5 (1H, m). ^{13}C NMR ($CDCl_3$) δ=24.11, 25.16, 49.03, 102.88, 119.67, 119.83, 127.99, 128.31, 128.77, 134.35, 136.95, 149.52, 157.89, 162.28, 171.68. MS *m/z* (rel intensity) 353 (M^+, 49), 320 (17), 165 ($PhCSCS^+$, 100). Found: *m/z* 353.0967. Calcd for $C_{19}H_{19}N_3S_2$: M, 353.1020

2-Morpholino-4-phenyl-5-thiazolyl 2-Pyridyl Sulfide 5c′: White. Mp 158.0—158.5 °C (CH_2Cl_2–pentane). ^1H NMR ($CDCl_3$) δ=3.45—3.65 (4H, m), 3.7—3.9 (4H, m), 7.0—7.15 (1H, m), 7.25—7.4 (3H, m), 7.45—7.55 (2H, m), 7.85—8.0 (2H, m), 8.4—8.5 (1H, m). ^{13}C NMR δ=47.66, 65.67, 104.08, 119.36, 119.71, 127.67, 128.11, 128.43, 133.85, 136.64, 149.21, 157.28, 161.23, 171.31. MS *m/z* (rel intensity) 355 (M^+, 44), 165 ($PhCSCS^+$, 100). Found: C, 60.25; H, 4.97; N, 11.83; S, 17.99%. Calcd for $C_7H_{13}N_2S_2ClO_4$: C, 60.82; H, 4.82; N, 11.82; S, 18.04%.

Reaction of Oxathiazines 3 with mCPBA: *m*-Chloroperbenzoic acid (172 mg; 1 mmol or 344 mg; 2 mmol) was added to a chloroform solution (10 ml) of **3** (1 mmol). The reaction mixture was stirred for 1 to 2 h at room temperature. Subsequent work-up and purification were accomplished by the procedure used in the reaction of **1** with NaN_3.

3,5-Diphenyl-1,4,2-oxathiazine 4-Oxide 6a: Yield 85%. White. Mp 114.5—115.0 °C (CH_2Cl_2–pentane). ^1H NMR

($CDCl_3$) δ=6.60 (1H, s), 7.4—7.6 (6H, m), 7.65—7.8 (2H, m), 8.15—8.3 (2H, m). ^{13}C NMR ($CDCl_3$) δ=102.64 (-CH=). IR ν 1067 (-SO-) cm^{-1}. MS m/z (rel intensity) 105 ($PhCO^+$, 51), 103 ($PhCN^+$, 100). Found: C, 66.95; H, 4.17; N, 5.27; S, 11.93%. Calcd for $C_{15}H_{11}NSO_2$: C, 66.90; H, 4.12; N, 5.20; S, 11.91%.

5-Phenyl-3-piperidino-1,4,2-oxathiazine 4-Oxide 6b: Yield 72%. White. Mp 127.0—128.0 °C (CH_2Cl_2–hexane). ^1H NMR ($CDCl_3$) δ=1.6—1.8 (6H, br.), 3.6—3.8 (4H, br.), 6.58 (1H, s), 7.4—7.7 (5H, m). ^{13}C NMR ($CDCl_3$) δ=104.70 (-CH=). IR ν 1051 (-SO-) cm^{-1}. MS m/z (rel intensity) 228 (M^+—SO, 100). Found: C, 60.40; H, 5.83; N, 10.28; S, 11.54%. Calcd for $C_{14}H_{16}N_2SO_2$: C, 60.85; H, 5.84; N, 10.14; S, 11.60%.

3,5-Diphenyl-1,4,2-oxathiazine 4,4-Dioxide 7a: Yield 65%. White. Mp 232 °C (CH_2Cl_2–hexane). ^1H NMR ($CDCl_3$) δ=6.84 (1H, s), 7.4—7.6 (6H, m), 7.65—7.8 (2H, m), 8.15—8.3 (2H, m). ^{13}C NMR ($CDCl_3$) δ=102.42 (-CH=). IR ν 1269, 1127 (-SO_2-) cm^{-1}. MS m/z (rel intensity) 285 (M^+, 3), 221 (M^+—SO_2, 15). Found: C, 62.88; H, 3.86; N, 5.05%. Calcd for $C_{15}H_{11}NSO_3$: C, 63.14; H, 3.89; N, 4.91%.

5-Phenyl-3-piperidino-1,4,2-oxathiazine 4,4-Dioxide 7b: Yield 56%. White. Mp 192.5—193.5 °C (MeCN–ether). ^1H NMR ($CDCl_3$) δ=1.6—1.8 (6H, br.), 3.6—3.8 (4H, br.), 6.73 (1H, s), 7.4—7.7 (5H, m). ^{13}C NMR ($CDCl_3$) δ=102.78 (-CH=). IR ν 1287, 1138 (-SO_2-) cm^{-1}. MS m/z (rel intensity) 292 (M^+, 2), 228 (M^+—SO_2, 100). Found: C, 57.50; H, 5.36; N, 9.57; S, 10.92%. Calcd for $C_{14}H_{16}N_2SO_3$: C, 57.52; H, 5.52; N, 9.58; S, 10.97%.

Reaction of 3b with Methyl Iodide: Oxathiazine **3b** was dissolved in 2 ml of methyl iodide. The reaction mixture was stirred for 30 min at room temperature. After addition of pentane, the precipitate formed was collected by filtration, which was recrystallized from CH_2Cl_2–hexane.

4-Methyl-5-phenyl-3-piperidino-1,4,2-oxathiazinium Iodide 8: Yield 77%. Ivory white. Mp 106.0—108.0 °C (decomp) (CH_2Cl_2–hexane). ^1H NMR ($CDCl_3$) δ=1.6—1.9 (6H, br.), 3.45 (3H, s), 3.7—3.9 (4H, br.), 7.3—7.6 (3H, m), 7.70 (1H, s), 7.7—7.85 (2H, m). ^{13}C NMR ($CDCl_3$) δ=91.20 (-CH=). IR ν 1625, 1587, 1249, 1094 cm^{-1}. MS m/z (rel intensity) 260 (M^+—MeI, 19), 150 ($PhCOCSH^+$, 27), 105 ($PhCO^+$, 100). Found: C, 43.91; H, 4.63; N, 6.75%. Calcd for $C_{15}H_{19}N_2SOI$: C, 44.78; H, 4.76; N, 6.96%.

X-Ray Analysis of 4c. Crystal data: $C_{26}H_{26}N_4O_2S_3$; MW 522.71; triclinic; space group $P\bar{1}$; a=13.291 (4), b=15.489 (4), and c=12.949 (4) Å and α=91.94 (2), β=104.98 (2) and γ=89.58 (2) °; U=2573 (1) Å^3; D_c=1.35 g cm^{-3} for Z=4; μ(Mo $K\alpha$)=3.06 cm^{-1}. Intensity data were collected on a Entra–Nonius CAD4 four-circle diffractometer by using graphite monochromated Mo $K\alpha$ radiation in the 2θ–ω scan mode with a scan width of $\Delta\omega$=(0.6+1.5 tanθ) ° over the range of 2θ values of 2 ° up to 55 °. Intensities of 12216 reflections were measured and 7798 independent reflections ($|F_o|>3.0\sigma(|F_o|)$) were used for the analysis. The structure was solved by MULTAN 82 program.[15] Forty-eight hydrogen atoms were introduced from deferential Fourier synthesis and the remaining 4 were located at the calculated position. Anisotropic thermal parameters and isotropic thermal parameters were assumed for the non-hydrogen atoms and for the hydrogen atoms, respectively. The structural parameters were refined by a full-matrix least-squares method to the final R value of 0.050 and the R_w=0.040 in conjunction with the weighting scheme of $w=-1/\sigma^2$. All the calculations were carried out with the Enraf–Nonius SDP package and the UNICS III system.[16,17] The final atomic parameters for non-hydrogen atoms are given in Table 3 and the molecular structure with the numbering system for the non-hydrogen atoms are shown in Fig. 1.[18]

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