Formation of 1,4,2,5-Dithiadiazines as a Heterocyclic System by Reaction of 1,4,2-Dithiazolium Salts with Sulfenamides

Katsumi YONEMOTO,* Isao SHIBUYA,* and Kazumasa HONDA
National Chemical Laboratory for Industry, Tsukuba, Ibaraki 305
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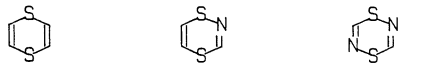
Synopsis. The first example of application of sulfenamides for ring expansion on nitrogen atom has been reported to give 1,4,2,5-dithiadiazines (**3**) from 1,4,2-dithiazolium salts (**1**). The structure of **3** was confirmed by X-ray crystallographic analysis. The similar ring expansion reaction occurred on 1,3-dithiolium salts (**5**) to afford 1,4,2-dithiazines (**6**).

The chemistry of 1,4-dithiins, an interesting 8π-electron ring system containing heteroatoms, has been extensively studied[1] and reviewed.[2] Their aza-analogues, 1,4,2-dithiazines, which were conveniently accessible by the reaction of 1,3-dithiolium salts with sodium azide,[3] have also been known and studied; much attention has been focused on their thermal decomposition reactions.[3,4] In contrast, the chemistry of 1,4,2,5-dithiadiazines, a higher aza-analogue, remains virtually unexplored, mainly because they were prepared for the first time only a few years ago by the reaction between thiobenzamide *S*-oxide and $Et_3O^+BF_4^-$.[5] Generally, 6-membered ring systems with four heteroatoms are much less known. As an extension of our studies on the reactivity of 1,4,2-dithiazolium salts (**1**) toward various kinds of amino compounds, we will report an alternative method for the preparation of unsymmetrically substituted 1,4,2,5-dithiadiazines (**3**) by the reaction of **1** with *S*-dimethylthiocarbamoyl-substituted sulfenamides (**2**).



Results and Discussion

1,4,2-Dithiazolium perchlorates **1** were allowed to react with 2 molar amount of sulfenamide **2a** in MeCN at room temperature to give 1,4,2,5-dithiadiazines **3** in good yields, whereupon tetramethylthiuram disulfide (**4**) and ammonium perchlorate were also formed.[6] The results are presented in Table 1. The products **3** were identified with spectral data and elemental analysis. However, we cannot unequivocally distinguish the spectral data between 1,4,2,5- and 1,4,2,6-dithiadiazine isomers; the structure, on the other hand, was determined by X-ray crystallographic analysis of **3f**. This analysis showed that the molecule is a 1,4,2,5-isomer and has a boat conformation similar to that of dithiins (Fig. 1).

In order to investigate the versatility of other sulfenamides for this reaction, the reaction of **1a** with sulfenamides **2b—g** was examined under the same conditions as used for **2a**. The results are presented in Table 2. The yield of **3a** was remarkably dependent on the kind of sulfenamides, ranging from 95 to 0%. From the present results, *S*-dimethylthiocarbamoyl-substituted

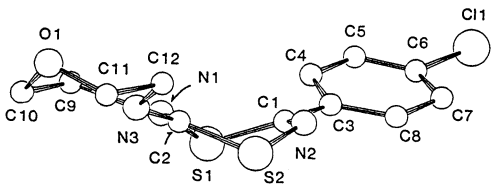
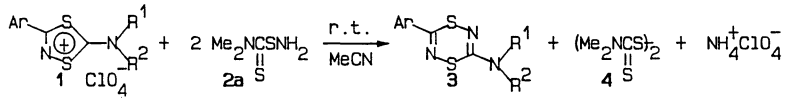


Fig. 1. The molecular structure of **3f**.

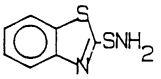
Table 1. Synthesis of 1,4,2,5-Dithiadiazines (**3a—f**)



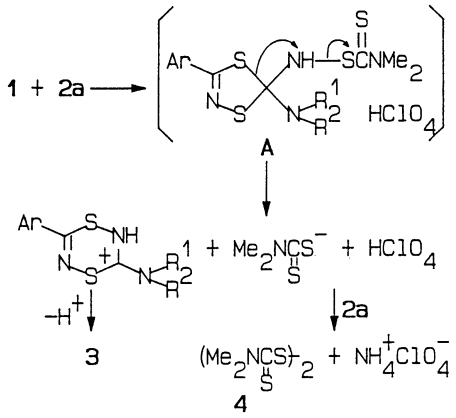
Compd	Ar	R^1R^2N	Time	Yield[a]	Mp	Found(Calcd)/%[b]			
			d	%	θ_m/°C	C	H	N	S
3a	Ph	Et_2N	2	89	71.0—71.5	54.13 (54.31)	5.67 (5.70)	15.83 (15.83)	24.07 (24.16)
3b	Ph	Me_2N	2	83	59.0—59.5				
3c	Ph	*i*-Pr_2N	3	41	125.0—125.5	57.37 (57.30)	6.54 (6.53)	14.29 (14.32)	21.79 (21.85)
3d	Ph	PhMeN	1	88	74.0—74.5	59.97 (60.17)	4.39 (4.38)	13.94 (14.03)	21.37 (21.42)
3e	4-MeC_6H_4	Et_2N	2	90	49.5—50.0				
3f	4-ClC_6H_4		3	60	157.0—158.0	45.79 (45.93)	3.84 (3.85)	13.31 (13.39)	20.34 (20.43)

a) Isolated yield. b) Elemental analyses of **3b** and **3e** were difficult due to instability in crystal form.

Table 2. Formation of **3a** by Reaction of **1a** with Various Kinds of Sulfenamides **2a—g**

	Sulfenamide	Time	Yield of **3a**[a]
		d	%
2a	$Me_2NCSSNH_2$	2	89
2b	$i\text{-}Pr_2NCSSNH_2$	2	60
2c		2	87
2d		3	10
2e	$PhN{=}C(Ph)SNH_2$	1	95
2f		4	0[b]
2g	$PhCOSNH_2$	3	0[c]

a)Isolated yield. b) No reaction. c) 5-Benzoylimino-3-phenyl-1,4,2-dithiazole **8** was formed; see Ref. 13.



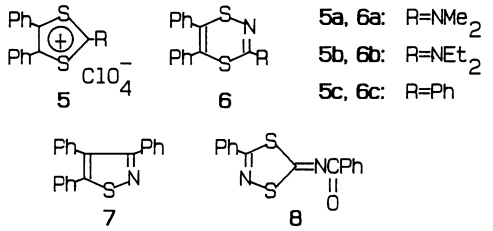
Scheme 1.

sulfenamides **2a—c** were most favorable for this reaction in terms of availability, stability, and high yields of **3**.

A mechanistic interpretation for the formation of **3** is shown in Scheme 1. Nucleophilic attack of the terminal amino group of sulfenamide **2a** on the C-5 carbon atom of dithiazolium cation leads to an intermediate **A** (Scheme 1), which is then converted into dithiadiazine **3** with liberation of dimethyldithiocarbamate followed by S-4 migration and deprotonation, although the exact timing of each step is indefinite. This mechanism is similar to that of the reaction of *N*-methylacridinium salts with hydroxylamine-*O*-sulfonic acid which gives 4-methyldibenzo-[*b*,*e*][1,4]-diazepine.[7] Furthermore, the observation in a separate experiment that disulfide **4** is formed by reaction of **2a** with sodium dimethyldithiocarbamate in the presence of *p*-toluenesulfonic acid is consistent with the proposed reaction mechanism.

Other attempts to convert **1b** into the target molecule **3b** by a ring expansion reaction using standard "*N*-expansion" reagents, such as sodium azide and *S*,*S*-diphenylsulfilimine ($Ph_2S{=}NH$), were unsuccessful. But 5-phenyl-1,2,3,4-tetrazole[8] and *N*-(dimethylthiocarbamoyl)-*S*,*S*-diphenylsulfilimine,[9] respectively, were obtained instead. It is therefore likely that the attack of nitrogen of these nucleophiles on the C-5 position in dithiazolium cation induces further ring cleavage in preference to the formation of nitrene.

In order to check the possibility of application of this reaction to other cation compounds, the reaction of 2-dialkylamino-4,5-diphenyl-1,3-dithiolium perchlorates (**5a, b**) with sulfenamide **2a** was carried out under the same conditions, from which 3-dialkylamino-5,6-diphenyl-1,4,2-dithiazines (**6a, b**) were obtained in good yields. On the other hand, treatment of **5a** with NaN_3 in refluxing toluene for 30 min did not give the expected **6a**. Furthermore, 2,4,5-triphenyl-1,3-dithiolium perchlorate (**5c**) was allowed to react with **2a** to give 3,5,6-triphenyl-1,4,2-dithiazine (**6c**) (20%) together with 3,4,5-triphenylisothiazole (**7**) (30%, mp 209 °C, lit,[3a] mp 211.5—212.5 °C), while Nakayama et al. reported that **5c** was subjected to react with NaN_3 in refluxing toluene to afford only a product **7**, which arose from **6c** by thermal elimination of sulfur.[3a]



In summary, we believe that this is the first example of the ring expansion on nitrogen atom with sulfenamides **2**. It belongs to important class of ring expansion reactions, especially because it can be smoothly carried out under mild conditions, i.e., at ambient temperature, without irradiation, and in the absence of a base. The application of this reaction to a wide range of cation compounds is currently under way.

Experimental

All the melting points were uncorrected. The ^1H NMR and ^{13}C NMR spectra were recorded on a Hitachi R-40 and a JEOL FX-90A spectrometers, respectively, in $CDCl_3$, using TMS as an internal standard. The IR spectra were measured on a JASCO A-302 spectrometer using KBr disks. The low-resolution mass spectra were taken on Hewlett Packard 5995A spectrometer by electron impact ionizing technique at 70 eV.

1,4,2-Dithiazolium salts **1** were readily prepared from disubstituted dithiocarbamate in three steps, utilizing our reported procedure.[10] 1,3-Dithiolium salts **5** were prepared from the reaction of dithiocarbamate (or dithiobenzoate) and 2-bromo-2-phenylacetophenone in a manner similar to that described in Ref. 11. Sulfenamides **2a—g** were prepared from the reaction of thiolates (RS^-) with hydroxylamine-*O*-sulfonic acid by the same method as described in literatures.[10,12]

Preparation of 1,4,2,5-Dithiadiazines 3a—f; General Procedure. 1,4,2-Dithiazolium perchlorate **1a—f** (1 mmol) was added to stirred solution (MeCN, 4 ml) of sulfenamide **2a** (2 mmol). The reaction mixture was stirred for a few days at room temperature, during which time disulfide **4** and/or ammonium perchlorate were crystallized out and filtered off.

The crude product was extracted with dichloromethane after addition of water. The residual solid was purified by column chromatography on silica gel and recrystallization from appropriate solvents (MeCN-ether, dichloromethane-hexane, etc.) to give **3a—f** as yellow powder.

3a: ^{1}H NMR δ=1.21 (6H, t, J=7.5 Hz), 3.53 (4H, q, J=7.5 Hz), 7.4—7.6 (3H, m), 7.9—8.1 (2H, m). ^{13}C NMR δ=13.65, 44.48, 127.74, 128.64, 131.67, 134.81, 162.50, 176.96. IR ν 1535, 939, 695 cm^{-1}. MS m/z (rel intensity) 265 (M^+; 20), 232 (M^+—SH; 62), 121 ($PhCS^+$; 100).

3b: ^{1}H NMR δ=3.12 (6H, s), 7.4—7.6 (3H, m), 7.9—8.1 (2H, m). ^{13}C NMR δ=39.17, 127.72, 128.64, 131.70, 134.68, 163.55, 175.96. IR ν 1546, 936, 695 cm^{-1}. MS m/z (rel intensity) 237 (M^+; 34), 204 (M^+—SH; 84), 121 ($PhCS^+$; 100), 88 (Me_2NCS^+; 97).

3c: ^{1}H NMR δ=1.32 (12H, d, J=6.9Hz), 4.07 (2H, m, J=6.9Hz), 7.4—7.6 (3H, m), 7.9—8.1 (2H, m). ^{13}C NMR δ=20.80, 49.46, 127.72, 128.61, 131.59, 134.95, 161.60, 177.45. IR ν 1527, 1286, 1030, 939, 689 cm^{-1}. MS m/z (rel intensity) 293 (M^+; 16), 260 (M^+—SH; 41), 218 (82), 121 ($PhCS^+$; 82), 103 ($PhCN^+$; 80), 69 (100).

3d: ^{1}H NMR δ=3.43 (3H, s), 7.1—7.6 (8H, m), 7.8—8.0 (2H, m). ^{13}C NMR δ=40.41, 126.09, 127.53, 127.64, 128.56, 129.53, 131.54, 134.60, 143.48, 161.06, 173.44. IR ν 1536, 1268, 935, 689 cm^{-1}. MS m/z (rel intensity) 299 (M^+; 24), 266 (M^+—SH; 12), 150 ($PhMeNCS^+$; 24), 132 ($PhMeNCN^+$; 100), 121 ($PhCS^+$; 61), 103 ($PhCN^+$; 31).

3e: ^{1}H NMR δ=1.19 (6H, t, J=7.0 Hz), 2.36 (3H, s), 3.49 (4H, q, J=7.0 Hz), 7.22 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=9.0 Hz). ^{13}C NMR δ=13.65, 21.43, 44.42, 127.64, 129.34, 132.21, 142.15, 162.60, 176.66. IR ν 1531, 1251, 931, 825, 761 cm^{-1}. MS m/z (rel intensity) 279 (M^+; 29), 246 (M^+—SH; 74), 135 ($MeC_6H_4CS^+$; 82), 117 ($MeC_6H_4CN^+$; 100).

3f: ^{1}H NMR δ=3.5—3.9 (8H, m), 7.43 (2H, d, J=9.0 Hz), 7.90 (2H, d, J=9.0 Hz). ^{13}C NMR δ=47.57, 66.28, 129.04, 129.10, 133.08, 138.28, 163.39, 175.01. IR ν 1541, 1206, 1115, 949, 825 cm^{-1}. MS m/z (rel intensity) 315 (M^++2; 15), 313 (M^+; 36), 280 (M^+—SH; 76), 155 ($ClC_6H_4CS^+$; 100), 137 ($ClC_6H_4CN^+$; 69).

Preparation of 1,4,2-Dithiazines 6a—c. The similar treatment of **5a—c** (1 mmol) with **2a** (2 mmol) gave crude products **6a—c** which were purified by the same procedure as mentioned above.

6a: Yield 81%. Mp 164.0—164.5 °C. ^{1}H NMR δ=3.18 (6H, s) 7.1—7.5 (10H, m). ^{13}C NMR δ=40.58, 123.14, 127.26, 127.96, 128.10, 128.18, 129.40, 130.32, 135.79, 138.63, 147.79, 164.47. IR ν 1553, 1358, 1243, 1117, 907, 693 cm^{-1}. MS m/z (rel intensity) 312 (M^+; 22), 242 ($(PhCS)_2^+$; 32), 178 ($PhCCPh^+$; 69), 121 ($PhCS^+$; 100). Found: C, 65.36; H, 5.16; N, 8.91; S, 20.39%. Calcd for $C_{17}H_{16}N_2S_2$: C, 65.35; H, 5.16; N, 8.97; S, 20.52%.

6b: Yield 80%. Mp 123.0—124.5 °C. ^{1}H NMR δ=1.18 (6H, t, J=7.2 Hz), 3.55 (4H, q, J=7.2 Hz), 7.1—7.5 (10H, m). ^{13}C NMR δ=13.71, 45.70, 123.14, 127.20, 127.96, 128.10, 128.69, 129.42, 130.37, 135.95, 138.82, 148.68, 163.12. IR ν 1540, 1259, 1123, 692 cm^{-1}. MS m/z (rel intensity) 340 (M^+; 13), 242 ($(PhCS)_2^+$; 36), 178 ($PhCCPh^+$; 50), 121 ($PhCS^+$; 100). Found: C, 67.00; H, 5.95; N, 8.23; S, 18.65%. Calcd for $C_{19}H_{20}N_2S_2$: C, 67.02; H, 5.92; N, 8.23; S, 18.83%.

6c: Yield 20%. Yellow oil. ^{1}H NMR δ=7.1—7.5 (13H, m) 8.0—8.2 (2H, m). ^{13}C NMR δ=123.65, 127.80, 128.12, 128.34, 128.58, 128.77, 129.64, 130.18, 131.51, 135.54, 135.65, 137.74, 140.93, 164.47. IR ν 1498, 1439, 1210, 898, 689 cm^{-1}. MS m/z (rel intensity) 345 (M^+; 13), 313 (M^+—S; 10), 242 ($(PhCS)_2^+$; 29), 178 ($PhCCPh^+$; 50), 121 ($PhCS^+$; 100). **6c** tends to decompose slowly on standing in air, so elemental analysis of **6c** has been unsuccessful.

X-Ray Analysis of 3f. Crystal data: $C_{12}H_{12}ClN_3OS_2$; MW 313.83; orthorhombic; space group $Pca2_1$; a=15.408(4), b=4.064(2), and c=42.855(9) Å; U=2686(2) Å^3; D_c=1.55 g cm^{-3} for Z=8; μ(Cu $K\alpha$)=52.6 cm^{-1}. Intensity data were collected on a Rigaku AFC-4 four-circle diffractometer by using graphite monochromated Cu $K\alpha$ radiation (λ=1.5418 Å) in the 2θ-ω scan mode with a scan width of $\Delta\omega$=(1.0+0.5 tanθ) and a scan speed of 4.0° min^{-1} over the range of 2θ values of 3 to 120°. Intensities of 2240 reflections were measured and 1310 independent reflections ($|F_o|>3.0\sigma(|F_o|)$) were used for the analysis. The structure was solved by *MULTAN* 78 program. The structural parameters were refined by a full-matrix least-squares method to the final R value of 0.130 and the R_w=0.141 in conjunction with the weighting scheme of $w=(-0.002|F_o|^2+|F_o|-1)^{-1}$. The unit cell contains two crystallographically independent molecules and they have almost similar configurations. The difficulty in convergence may be attributable to some disorders and a pseudo symmetry of the crystal. All the computations were carried out on a FACOM M-380 computer using the *UNICS* III system.[14] Lists of the atomic coordinates and other structural parameters are deposited as Document No. 8801 at the Office of the Editor of Bull. Chem. Soc. Jpn.

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13) **8** was obtained as colorless solid in 29% yield. IR(KBr) 1619, 1491, and 1281 cm^{-1}. MS m/z 298 (M^+), 195 (M^+ —PhCN), and 135 ($PhCNS^+$). Found: C, 60.18; H, 3.32; N, 9.37; S, 21.49%. Calcd for $C_{15}H_{10}N_2OS_2$: C, 60.38; H, 3.38; N, 9.39; S, 21.49%.

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