Preparation of *N*-(Substituted formyl) dialkylamino(thioxo)-methanesulfenamides

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Synopsis. *N*-(Substituted formyl)dialkylamino(thioxo)-methanesulfenamides ($R_2NCSSNHCOR'$, **2**), anti-foggants for silver halide photographic materials as well as potential precursors for 1,4,2-dithiazolium salts, were prepared in good yields in two "one-pot" procedures. Various amide-type compounds ($R'CONH_2$, **1**) were treated successively with NaH and I_2 and then condensed with dialkyldithiocarbamates (Method A); or **1** were reacted with tetraalkylthiuram disulfides after treatment with NaH (Method B). These methods allowed a wide variation of substituents R′ in **2**: R′=H, dialkylamino, alkoxy, aryl, alkyl, and heterocyclic substituent.

The syntheses of 1,4,2-dithiazolium salts (**3**) were recently established by three research groups independently. 3-Aryl-5-methylthio,[1a] 3-aryl-5-dialkylamino,[1b,c,e] 3,5-diaryl,[1d,g] and 3,5-bis(dialkylamino)[1e] derivatives and parent ring systems[1f] have been prepared so far. Systematic studies on the reactivity of **3** have also been performed.[2]

Our approach for preparation of 1,4,2-dithiazolium salts have been the cyclization of *S*-dialkylthiocarbamoyl and *S*-thioaroyl-*N*-acylsulfenamides with dehydration in strong acidic media.[1b] As an extension of this strategy, we used amide-type compounds (**1**) ($R'CONH_2$: R′=H, dialkylamino, alkoxy, aryl, alkyl, heterocyclic substiluent) as starting materials to prepare various *N*-(substituted formyl)dialkyl(thioxo)methanesulfenamides (**2**), the potential precursors for **3**.

Recently we found that both the sulfenamides (**2**) and the 1,4,2-dithiazolium salts were new types of lead compounds with high fog restraining ability for silver halide photographic materials, e.g., commercial color films.[3] In particular, several derivatives among **2** have been found to show far superior efficacy to the conventional ones only with a little amount of addition.

We now report two alternative methods for successful preparation of **2**, by means of direct formation of S–N bond in the sulfenamide moiety, the methods of which allow a wide variation of substituents R′ in **2**.

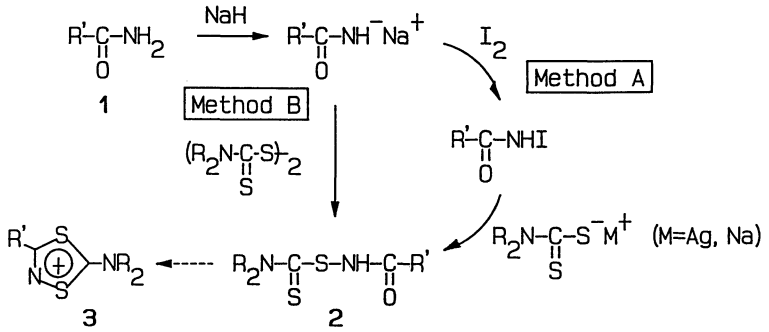
Results and Discussion

Our initial approach for preparation of *N*-acyl or *N*-

Table 1. Preparation of Sulfenamides **2**

Entry	Product			Method[a]	Yield[b]
	No.	R′	R_2N		%
1	**2a**	*t*-Bu	Et_2N	A(Ag)	41
2	**2a**	*t*-Bu	Et_2N	B	80
3	**2b**	*t*-Bu	Me_2N	B	84
4	**2c**	*t*-Bu	Piperidino	B	69
5	**2d**	Me	Morpholino	A(Na)	22
6	**2e**	Et_2N	Me_2N	A(Ag)	16
7	**2e**	Et_2N	Me_2N	B	80
8	**2f**	Et_2N	Et_2N	A(Ag)	8
9	**2g**	Me_2N	Et_2N	B	81
10	**2h**	MeO	Et_2N	A(Ag)	89
11	**2i**	MeO	Me_2N	A(Na)	67
12	**2j**	MeO	Piperidino	A(Na)	85
13	**2k**	*i*-PrO	Et_2N	A(Na)	75
14	**2k**	*i*-PrO	Et_2N	B	60
15	**2l**	$4\text{-}MeOC_6H_4$	Et_2N	A(Ag)	39
16	**2m**	$4\text{-}MeC_6H_4$	Et_2N	B	65
17	**2n**	$4\text{-}ClC_6H_4$	Et_2N	A(Ag)	7
18	**2n**	$4\text{-}ClC_6H_4$	Et_2N	B	88
19	**2o**	3-Pyridyl	Et_2N	A(Ag)	37
20	**2p**	3-Pyridyl	Me_2N	B	21
21	**2q**	2-Thienyl	Et_2N	A(Ag)	26
22	**2r**	2-Thienyl	Me_2N	B	81
23	**2s**	H	Piperidino	B	76
24	**2t**	PhCH=CH	Me_2N	B	64

a) Atomic symbols "Ag" and "Na" in parentheses correspond to "M" in $R_2NCSS^-M^+$. b) Isolated yields based on dialkyldithiocarbamates and **1** for Methods A and B, respectively.



Scheme.

aroyldialkylamino(thioxo)methanesulfenamides (**2**) was the acylation or aroylation of the corresponding *N*-unsubstituted sulfenamides by treating with the corresponding acyl or aroyl chlorides, respectively.[1b] As far as this method was employed, however, variation of substituents R′ in **2** was limited to alkyl (including hydrogen) and aryl groups because of limited availability or poor reactivity of R′COCl (or $(R'CO)_2O$ as substitute) bearing other substituents R′.

In order to extend the variation of the substituents in **2**, we chose the amide-type compounds **1** as starting materials because of a wide variation of substituents R′ in **1**. Consequently, our alternative strategy for preparation of **2** was the introduction of dialkylthiocarbamoylthio group on N-atom in **1** to form a sulfenamide S–N bond directly.[4]

When dialkyldithiocarbamates are used as a substrate, the reaction requires involvement of umpolung of amino reactivity. From this standpoint, we carried out the following "one-pot" procedure including an oxidative process, denoted "Method A" for convenience. After treatment with NaH, **1** were iodinated by I_2-oxidation leading to *N*-iodoamide-type intermediates, which subsequently reacted with dialkyldithiocarbamates to afford **2**. As shown in Table 1, good yields were obtained only when alkyl carbamates were employed (Entries 10—14). The lower yields obtained in many cases are attributable to the formation of considerable amounts of tetraalkylthiuram disulfides as a side reaction. It is most likely that $(R_2NCSS)_2$ is formed by condensation of unreacted $R_2NCSS^-M^+$ with R_2NCSSI which temporarily arises from $R_2NCSS^-M^+$ by oxida-

Table 2. Characterization Data of Sulfenamides **2**

Compd	Mp (solv.) °C	^{1}H NMR[a]	^{13}C NMR[a] C=S, C=O	IR[b]/cm^{-1} NH, C=O	MS (rel intensity) *m/z*
2a	145.5—146.5 (Benzene)	1.3 (6H, br. t), 1.33 (9H, s), 3.4—4.3 (4H, br.), 7.1 (NH, br. s)	196.09 179.63	3296 1674	250 (M^+, 0.4) 116 (100)
2b	119.0—120.0 (Benzene–Hexane)	1.32 (9H, s), 3.2—3.6 (6H, br. s), 7.2 (NH, br. s)	197.34 179.41	3264 1696	220 (M^+, 4) 88 (100)
2c	146.0—147.0 (CH_2Cl_2–Pentane)	1.33 (9H, s), 1.6—1.8 (6H, br.), 3.8—4.2 (4H, br.), 7.2 (NH, br. s)	196.07 179.44	3248 1696	260 (M^+, 3) 128 (100)
2d	156.0—157.0 (CH_2Cl_2–Pentane)	2.27 (3H, br. s), 3.7—3.9 (4H, m), 3.9—4.1 (4H, m), 7.3 (NH, br. s)	198.10 172.23	3248 1681	220 (M^+, 8) 130 (90)
2e	99.0—100.0 (CH_2Cl_2–Pentane)	1.23 (6H, t, *J*=7.2 Hz), 3.44 (4H, q, *J*=7.2 Hz), 3.2—3.6 (6H, br. s), 6.3 (NH, br. s)	200.13 155.54	3296 1668	235 (M^+, 3) 88 (100)
2f	132.5—133.5 (CH_2Cl_2–Pentane)	1.25 (6H, t, *J*=7.2 Hz), 1.3 (6H, br. t), 3.45 (4H, q, *J*=7.2 Hz), 3.4—4.3 (4H, br.), 6.0 (NH, br. s)	199.25 156.10	3220 1645	263 (M^+, 4) 116 (100)
2g	152.0—153.5 (CH_2Cl_2–Hexane)	1.3 (6H, br. t), 3.10 (6H, s), 3.5—4.2 (4H, br.), 6.1 (NH, br. s)	198.96 157.35	3228 1651	235 (M^+, 6) 116 (88)
2h	66.0— 67.0 (Ether–Pentane)	1.3 (6H, br. t), 3.4—4.3 (4H, br.), 3.80 (3H, s), 6.4 (NH, br. s)	197.07 157.22	3228 1735	222 (M^+, 13) 116 (100)
2i	150.5—151.5 (CH_2Cl_2–Hexane)	3.2—3.6 (6H, br, s), 3.78 (3H, s), 6.1 (NH, br. s)	198.51 157.17	3176 1717	194 (M^+, 8) 88 (100)
2j	115.0—116.0 (CH_2Cl_2–Pentane)	1.6—1.8 (6H, br.), 3.80 (3H, s), 3.8—4.2 (4H, br.), 6.1 (NH, br. s)	197.25 157.32	3212 1721	234 (M^+, 8) 128 (100)
2k	90.0— 90.5 (CH_2Cl_2–Pentane)	1.28 (6H, d, *J*=6 Hz), 1.3 (6H, br. t), 3.4—4.3 (4H, br.), 5.00 (1H, m), 6.4 (NH, br. s)	197.07 156.09	3216 1703	250 (M^+, 4) 116 (100)
2o	134.0—135.0 (CH_2Cl_2–Hexane)	1.3 (6H, br. t), 3.5—4.2 (4H, br.), 7.35—7.5 (1H, m), 8.25—8.4 (1H, m and NH), 8.7—8.85 (1H, m), 9.2—9.3 (1H, m)	195.36 167.41	—[c] 1691	269 (M^+, 2) 116 (100)
2p	127.0—127.5 (CH_2Cl_2–Pentane)	3.3—3.6 (6H, br. s), 7.3—7.5 (1H, m), 8.2—8.4 (1H, m and NH), 8.7—8.85 (1H, m), 9.2—9.3 (1H, m)	—[d]	3444 1662	241 (M^+, 5) 88 (100)
2q	116.0—117.0 (Benzene)	1.3 (6H, br. t), 3.5—4.2 (4H, br. t), 7.1—7.2 (1H, m), 7.55—7.65 (1H, m and NH), 7.8—7.9 (1H, m)	195.93 162.91	3268 1658	274 (M^+, 4) 116 (100)
2r	92.0— 93.5 (CH_2Cl_2–Pentane)	3.3—3.6 (6H, br. s), 7.1—7.2 (1H, m), 7.4 (NH, br. s), 7.55—7.65 (1H, m), 7.8—7.9 (1H, m)	—[d]	3212 1646	246 (M^+, 4) 88 (100)
2t	127.0—127.5 (MeCN–Ether)	3.3—3.6 (6H, br. s), 6.76 (1H, d, *J*=16 Hz), 7.1 (NH, br. s), 7.3—7.45 (3H, m), 7.5—7.6 (2H, m), 7.79 (1H, d, *J*=16 Hz)	—[d]	3128 1666	103 (38) 88 (100)

a) In $CDCl_3$, ppm from TMS. No *J* values were often given because the resonances were unresolved. b) Using KBr disks. c) No distinct N–H band was observed. d) Low solubility in ordinary deuterated solvents.

tion with the *N*-iodoamide as a competing pathway.

It is well-known that thiuram disulfides are liable to suffer from cleavage of the S–S bond homolytically[5a] and heterolytically.[5b] Therefore an umpolung synthon R_2NCSS^+ is expected to be produced from $(R_2NCSS)_2$ by the attack of a nucleophile. On the other hand, a convenient method for synthesis of sulfenamides from disulfides and lithium amides has been reported.[6] From this viewpoint, we examined another method, "Method B", using tetraalkylthiuram disulfides as substrates instead of dialkyldithiocarbamates. When **1** were treated with NaH followed by the reaction with $(R_2NCSS)_2$, successful formation of **2** was observed. As seen in Table 1, for R′=alkyl (Entries 1—5), dialkylamino (Entries 6—9), and aryl groups (Entries 15—18), Method B gave far better results than Method A. Furthermore, for R′=heterocyclic substitutent, hydrogen, and PhCH=CH, **2** were also prepared by Method B in moderate to good yields.

Davis et al. have developed a one-step synthesis of sulfenamides from disulfides and amines in the presence of silver salts.[7] The mechanism is believed to involve the complexation of Ag^+ with one of the disulfide sulfurs, followed by nucleophilic attack on the other sulfur by the amine. We attempted some application of this method to our system; but no satisfactory results were obtained. It may be attributable to the lower nucleophilicity of **1** and the instability of products **2** in the presence of Ag^+.

Some attempts to convert **2** into **3** were also carried out according to the same procedure as described in our previous report.[1b] When 40% tetrafluoroboric acid was added dropwise to an acetic anhydride solution of **2b**, **e**, and **r**, respectively, a pale yellow precipitate was immediately deposited in each case. It was found that the three precipitated products were not the corresponding 1,4,2-dithiazolium salts but identical with one another, by means of IR, ^1H NMR, and elemental analysis. The common product was identified with 3,5-bis(dimethyliminio)-1,2,4-trithiolane bis(tetrafluoroborate) by direct comparison with the authentic one which was prepared by the treatment of tetramethylthiuram monosulfide with mCPBA in HBF_4/Ac_2O.[8] Further attempts to prepare **3**, for instance by use of other strong acids or Lewis acids, are currently under way.

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. Mass spectra were taken on a Hewlett Packard 5995A spectrometer by electron impact ionizing technique at 70 eV. IR spectra were measured on a JASCO A-302 spectrometer. The substrates, i.e., dialkyldithiocarbamates,[9] tetraalkylthiuram disulfides,[10] and the amide-type compounds, are readily obtainable according to literatures or commercially.

Preparation of Sulfenamides 2: Method A: General Procedure. Sodium hydride (ca. 60% in oil) (60 mg; 1.5 mmol) was added to a dry THF solution (10 ml) of the amide-type compounds **1** (2 mmol). The reaction mixture was stirred for ca. 15 min at room temperature or, if necessary, by short heating at 60 °C. After the evolution of hydrogen ceased, iodine (254 mg; 1 mmol) was added to the cooled suspension, which was stirred for ca. 15 min at room temperature. Finally, sodium or silver dialkyldithiocarbamates (often hydrated) (1 mmol) were added to the dark red suspension. After the initial dark red color faded, the resulting pale yellow solution was stirred for 1 h. The crude product was extracted with dichloromethane after addition of an aqueous sodium hydrogencarbonate. After the solvent was removed in vacuo, the residue was purified by column chromatography on silica gel and/or recrystallized from appropriate solvents.

Method B: General Procedure. After the amide-type compounds **1** were treated with NaH in the same manner as Method A, tetraalkylthiuram disulfides were added to the reaction suspension, which was stirred for 1 h at room temperature. It should be noted that prolonged standing on the reaction mixture is apt to decrease the yields of **2**. Subsequent work-up and purification were accomplished by a procedure similar to Method A.

The yields of sulfenamides **2** are presented in Table 1, and their melting points and spectral data are listed in Table 2. Characterization of **2l**, **m**, **n**,[1b] and **2r**[1f] have been reported in the literatures. The results of elemental analyses of several representative sulfenamides, i.e., **2b** (R′=alkyl), **2g** (R′=dialkylamino), **2h** (R′=alkoxy), **2p**, **q** (R′=heterocyclic), and **2t** (R′=PhCH=CH), are shown below.

2b: Found: C, 43.50; H, 7.12; N, 12.58%. Calcd for $C_8H_{16}N_2S_2O$: C, 43.61; H, 7.32; N, 12.71%.

2g: Found: C, 40.97; H, 7.14; N, 17.95%. Calcd for $C_8H_{17}N_3S_2O$: C, 40.82; H, 7.28; N,17.85%.

2h: Found: C, 37.82; H, 6.27; N, 12.50; S, 28.73%. Calcd for $C_7H_{14}N_2S_2O_2$: C, 37.82; H, 6.35; N, 12.60; S, 28.85%.

2p: Found: C, 44.48; H, 4.43; N, 17.18; S, 26.57%. Calcd for $C_9H_{11}N_3S_2O$: C, 44.79; H, 4.59; N, 17.41; S, 26.64%.

2q: Found: C, 43.72; H, 5.07; N, 10.12; S, 34.72%. Calcd for $C_{10}H_{14}N_2S_3O$: C, 43.77; H, 5.14; N, 10.21; S, 35.05%.

2t: Found: C, 53.84; H, 5.32; N, 10.85; S, 24.07%. Calcd for $C_{12}H_{14}N_2S_2O$: C, 54.11; H, 5.30; N, 10.52; S, 23.84%.

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