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Reaction of Disulfide and Trisulfide with N-Chlorocarboxamide

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The reactions of diaryl disulfide with N-chlorosuccinimide, N-chloroacetamide and N-chlorosaccharine were attempted. When diaryl disulfide was allowed to react with N-chlorosuccinimide in the presence of pyridine, N-arylsulfensuccinimide was obtained in moderate yield. The reaction of di(*p*- and *m*-nitrophenyl) disulfide with N-chloroacetamide in the similar conditions was also successfully carried out to yield the corresponding N-sulfenacetamide, though dibenzyl disulfide reacted to give exclusively N-sulphidobisacetamide. In the reaction with N-chlorosaccharine, N-sulfensaccharine was successful to isolate only in the case of di(*o*-nitrophenyl) disulfide. Dibenzyl trisulfides also reacted with N-chlorosuccinimide under the similar conditions to give N-phenylmethanesulfensuccinimides.

The reaction between benzyl sulfides and N-chlorosuccinimide[2] (NCS) in carbon tetrachloride has been shown to yield α-chloro sulfides, with no cleavage or ring halogenation.[3] We attempted, on the other hand, α-chlorination of dibenzyl disulfide with NCS under the similar reaction condition and found to obtain N-phenylmethanesulfensuccinimide, without isolation of any α-chlorinated dibenzyl disulfide. Thus, in order to extend this reaction, several disulfides and trisulfides were examined to react with some N-chlorocarboxamides. This paper deals with the reaction of disulfides and trisulfides with NCS, N-chloroacetamide and N-chlorosaccharine.

Although the reaction of disulfide with N-bromosuccinimide (NBS) is first reported by Oda[4] and later a few investigations[5,6] are attempted, little has been made relating to the reaction between disulfide or trisulfide and NCS. Disulfides employed in the reaction were as follows: dibenzyl disulfide, bis(4-tolyl)disulfide, bis(2- or 4-nitrophenyl)disulfide and bis-(2-naphthyl)disulfide. Among them, dibenzyl disulfide and bis(2-or 4-nitrophenyl)disulfide were successfully synthesized by refluxing benzyl chloride and 2- or 4-nitrochlorobenzene with sodium disulfide in ethanol.[7] Bis(4-tolyl)disulfide and bis(2-naphthyl)disulfide were prepared by the reduction of the corresponding sulfonylchloride[8,9] with red phosphorus in the presence of iodine as catalyst at 80—90°.[10] When one mole of these disulfides and 2 moles of NCS in benzene were stirred in the presence of pyridine as catalyst at 30—40°, the corresponding sulfensuccinimides were obtained in 50—60% yields, whose structures were established by the infrared (IR) spectra and elemental analyses.

Regarding the reaction of disulfide with NBS, Oda,[4] Groebel[5] and Büchel[6] have proposed the radical mechanism, which involved the cleavage of NBS to succinimide radical and

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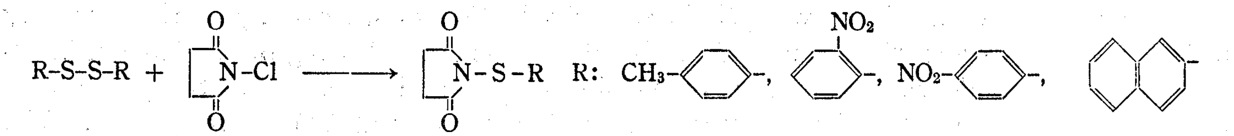
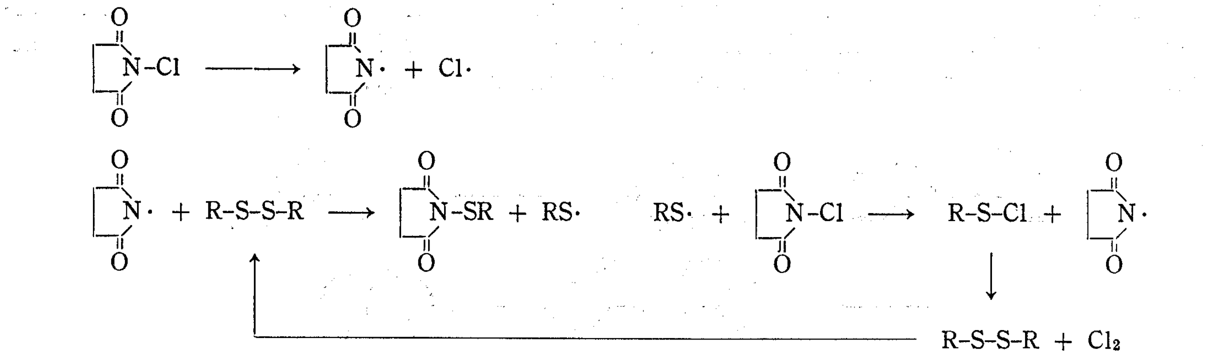
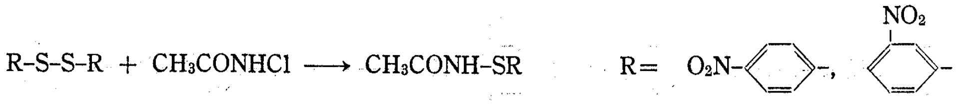
[1] Location: *Oe-hon-machi, Kumamoto.*
[2] J. Tscherniac. *Chem. Ber.*, **34**, 4209 (1901).
[3] D.L. Tuleen, *J. Org. Chem.*, **32**, 4006 (1967).
[4] H. Miyoshi and R. Oda, *Kogyo Kagaku Zasshi*, **59**, 224 (1956).
[5] W. Groebel, *Chem. Ber.*, **93**, 284 (1960).
[6] K.H. Büchel and A. Conte, *Chem. Ber.*, **100**, 1248 (1967).
[7] Org. Synth., Coll. Vol., **I**, 220.
[8] H. Erdman and C. Süvern, *Ann.*, **275**, 233 (1893).
[9] R. Schuloff, R. Pollak, and E. Riez, *Chem. Ber.*, **62**, 1851 (1929).
[10] K. Kawahara, *Yakugaku Zasshi*, **77**, 959, 963 (1957).



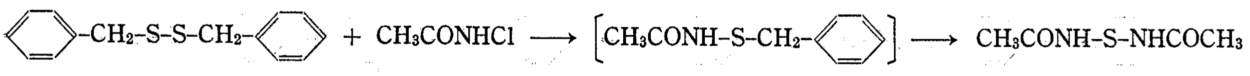
chlor radical at the first step. The reaction between disulfide and NCS would also proceed similarly through the initial formation of succinimide radical, though any evidence was not given.



The reaction of disulfide with N-chloroacetamide[11] was carried out under the reaction condition similar to the case of NCS. When one mole of disulfides described above was stirred with two moles of N-chloroacetamide in benzene in the presence of pyridine as catalyst at 40°, the expected N-sulfenacetamide was successfully obtained only in the case of bis(4-nitrophenyl)disulfide in 85% yield. Treating of bis(3-nitrophenyl)disulfide with N-chloroacetamide also gave N-(3-nitrobenzenesulfen)acetamide in 30% yield. Probably, only



stable sulfenacetamide would be possible to isolate. The structure of the sulfenacetamide obtained was confirmed by the elemental analyses and IR spectra which exhibited absorptions assignable to the amide group at near 3100 cm^{-1} and 1700 cm^{-1} and the nitro group at near 1350 cm^{-1}. On the other hand, it is of interest that in the reaction of benzyl disulfide with N-chloroacetamide under the similar condition, the different behavior was observed. Treating one mole of dibenzyl disulfide with two moles of N-chloroacetamide in benzene in the presence or absence of pyridine gave a product melting at 185° in 70% yield, which was assumed to be N-sulphidoacetamide by the IR spectrum and elemental analysis. The product was identified by comparison with N-sulphidobisacetamide[12] which prepared from acetamide and sulfur monochloride. The reaction would probably involve the initial formation



of unstable intermediate of N-sulfenacetamide followed by the cleavage of C-S bond.

In order to examine whether the condensation of disulfide with N-chloroacetamide proceeds through the radical mechanism or not, the reaction between bis(3-nitrophenyl) disulfide and N-chloroacetamide in the presence of styrene was examined under the similar conditions. N-(3-Nitrobenzenesulfen)acetamide was analogously obtained, but no polymerization of styrene was observed. Therefore, the reaction would not proceed through a radical mechanism, which is initiated by the formation of acetamide radical, different from the case of N-chlorosuccinimide.

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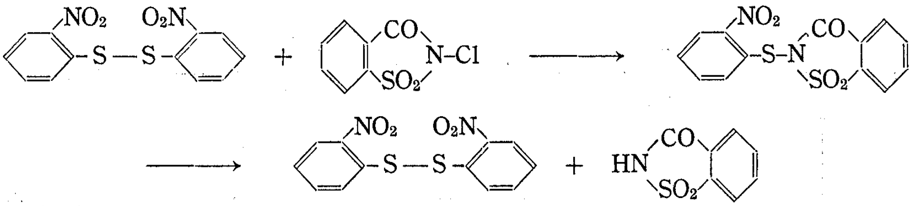
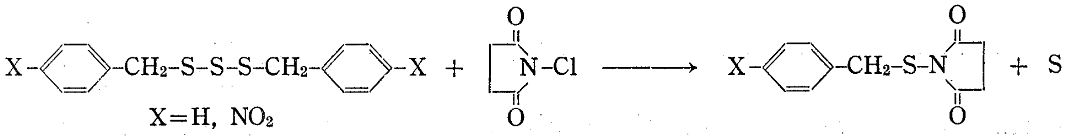
11) K.J.P. Orton and A.E. Bradfield, *J. Chem. Soc.*, **1927**, 993.
12) K.G. Naik, *J. Chem. Soc.*, **1921**, 1166.

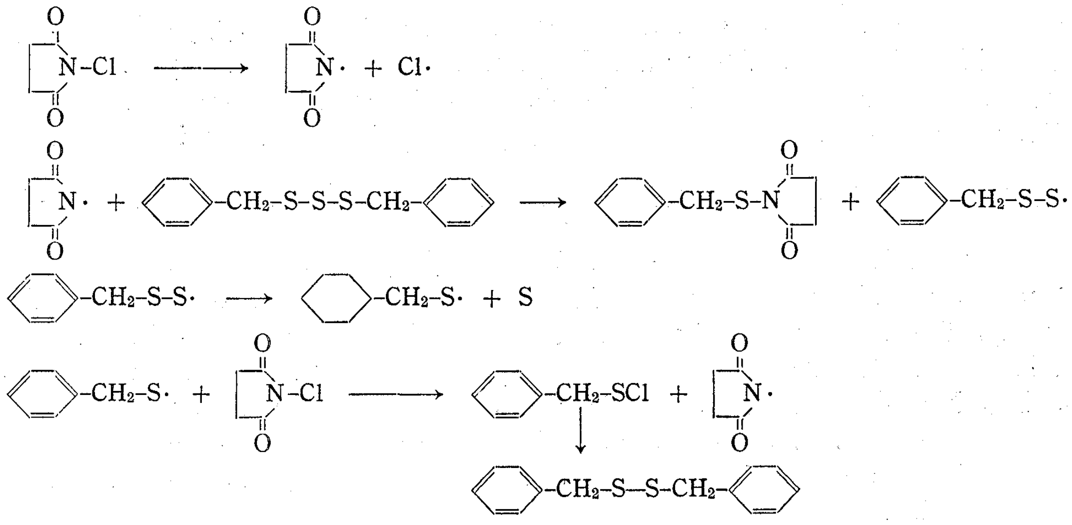
The reaction of disulfides with N-chlorosaccharine[13] was successfully carried out only in the case of bis(2-nitrophenyl)disulfide to isolate a product. Heating of one mole of bis(2-nitrophenyl) disulfide with two moles of N-chlorosaccharine in benzene in the presence of pyridine for seven hours under reflux gave a product melting at 195° in 78% yield. The structure of the product was established to be N-(2-nitrobenzenesulfen)saccharine by the elemental analysis and IR spectrum which exhibited absorption assignable to the ring carbonyl group at 1725 cm^{-1}, ring sulfonyl group at 1350 cm^{-1} and 1180 cm^{-1}, and nitro group at 1520 cm^{-1} and 1335 cm^{-1}. This compound was unstable and easily converted into bis(2-nitrophenyl)disulfide and saccharine on recrystallization from benzene. Probably it is presumed that N-sulfensaccharines formed in the case of another disulfide were readily decomposed and therefore not isolated, due to the extreme unstability.



The reaction of trisulfide with NCS was also examined. Treating of one mole of dibenzyl trisulfide[14] with three moles of NCS in benzene in the presence of pyridine for thirty two hours at room temperature gave N-phenylmethanesulfensuccinimide in 41% yield, which was confirmed by identification with the authentic sample obtained by the reaction of dibenzyl disulfide with NCS. Isolation of sulfur was also observed in this reaction.



The reaction would proceed by the radical mechanism through the initial formation of succinimide radical similarly to the reaction of disulfide with NCS. Dibenzyl disulfide formed in the course of the reaction would also react with an excess of NCS. Therefore, no dibenzyl



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13) F.D. Chattaway, *J. Chem. Soc.*, **1905**, 1884.

14) B. Milligan, B. Saville and J.M. Swan, *J. Chem. Soc.*, **1963**, 3608.

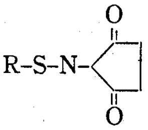
disulfide was isolated. Bis(4-nitrobenzyl)trisulfide also reacted more readily with NCS under the similar condition to give N-(4-nitrophenyl)methanesulfensuccinimide in 53% yield.

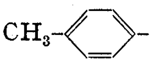
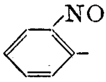
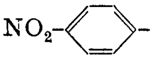
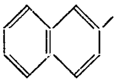
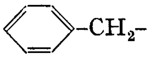
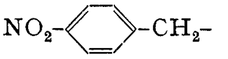
Progress is being made to establish the reaction mechanism.

Experimental

Reaction of Disulfide with NCS——A mixture of 0.01 mole of disulfide, 0.02 mole of NCS and 0.02 mole of dry pyridine in 50 ml of dry benzene was stirred for 2—3 hr at 30—40°. The mixture was poured into H_2O and the benzene layer was separated. The benzene layer was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness under reduced pressure. The residue was recrystallized from EtOH to give the corresponding N-sulfensuccinimide. The details of the data were shown in Table I.

Table I. N-Substituted Sulfensuccinimide

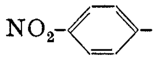
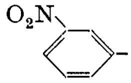


R	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N	IR ν_{max}^{KBr} cm^{-1} (C=O)	(NO$_2$)	
	58.8	113.5	$C_{11}H_{11}O_2NS$	59.70	5.01	6.33	59.38	4.95	5.89	1715		
	59.5	210	$C_{10}H_8O_4N_2S$	47.62	3.20	11.11	47.41	3.23	10.90	1725	1567	1335
	16.0	169.5—171.5	$C_{10}H_8O_4N_2S$	47.62	3.20	11.11	47.49	3.09	10.90	1730	1580	1340
	51.0	154	$C_{14}H_{11}O_2NS$	65.31	4.31	5.44	65.59	4.37	5.59	1715		
	41.0	159—161.5	$C_{11}H_{11}O_2NS$	59.72	5.01	6.33	59.77	5.04	6.25	1715		
	53.0	145—147	$C_{11}H_{10}O_4N_2S$	49.63	3.79	10.52	49.42	3.55	10.60	1726	1517	1349

Reaction of Disulfide with N-Chloroacetamide——A mixture of 0.01 mole of disulfide, 0.02 mole of N-chloroacetamide and 0.02 mole of dry pyridine in 50 ml of dry benzene was stirred for 3 hr at 40°. The mixture was poured into H_2O and the benzene layer separated was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness under reduced pressure. The residue was recrystallized from EtOAc to give the corresponding N-sulfenacetamide. The details of the data were shwon in Table II.

Table II. N-Substituted Sulfenacetamide

R-S-NHCOCH$_3$

R	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
	85	177—179	$C_8H_8O_3N_2S$	45.25	3.80	13.21	44.99	4.10	13.65
	30	144—145	$C_8H_8O_3N_2S$	45.25	3.80	13.21	45.22	3.92	13.14

Reaction of Dibenzyl Disulfide with N-Chloroacetamide——A solution of 2.46 g (0.01 mole) of dibenzyl disulfide and 1.87 g (0.02 mole) of N-chloroacetamide in 50 ml of dry benzene was stirred for 30 min at room temperature. The precipitates deposited from the solution were collected by filtration and recrystallized from EtOH to give 1.03 g (70%) of colorless needles melting at 185°. *Anal.* Calcd. for $C_4H_8O_2N_2S$: C, 32.43; H, 5.44; N, 18.91. Found: C, 32.58; H, 5.55; N, 18.56. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3230, 1680 (CONH).

This compound was identified with an authentic sample of N-sulphidobisacetamide by comparison of the IR spectrum and mixed melting point determination.

Reaction of Bis(2-nitrophenyl) Disulfide with N-Chlorosaccharine——A mixture of 3.08 g (0.01 mole) of bis(2-nitrophenyl) disulfide, 4.35 g (0.02 mole) of N-colorosaccharine and 1.58 g (0.02 mole) of dry pyridine in 50 ml of dry benzene was heated with stirring for 7 hr under reflux. The precipitates deposited were collected by filtration to give 5.2 g (77.6%) of N-(2-nitrobenzenesulfenyl)saccharine melting at 195°. *Anal.* Calcd. for $C_{13}H_8O_5N_2S_2$: C, 46.44; H, 2.40; N, 8.33. Found: C, 46.37; H, 2.50; N, 8.27. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1725 (CO); 1520, 1335 (NO_2); 1350, 1180 (SO_2).

Reaction of Dibenzyl Trisulfide with NCS——A mixture of 1.4 g (0.005 mole) of dibenzyl trisulfide, 1.9 g (0.015 mole) of NCS and 1.2 g (0.015 mole) of dry pyridine in 30 ml of dry benzene was stirred for 32 hr at room temperature. The mixture was poured into H_2O and the benzene layer separated was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness. The residue was recrystallized from EtOH to give 0.90 g (41%) of needles, N-phenylmethanesulfensuccinimide, melting at 159—161.5°, which was confirmed by identification with an authentic sample prepared from dibenzyl disulfide and NCS. *Anal.* Calcd. for $C_{11}H_{11}ON_2S$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.77; H, 5.04; N, 6.25. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1720 (CO). From the water layer, succinimide and sulfur were isolated.

Reaction of Bis(4-nitrobenzyl) Trisulfide with NCS——A mixture of 1.84 g (0.005 mole) of bis(4-nitrobenzyl) trisulfide, 1.9 g (0.015 mole) of NCS and 1.2 g (0.015 mole) of dry pyridine in 75 ml of dry benzene was stirred for 3 hr at room temperature. The precipitates separated were filtered off and the filtrate was poured into H_2O and the benzene layer was washed with H_2O, dried over Na_2SO_4 and concentrated. The precipitates deposited on standing were recrystallized from benzene to give 1.40 g (53%) of pale yellow prisms, N-(4-nitrophenyl) methanesulfensuccinimide, melting at 145—147°, which was confirmed by identification with an authentic sample. *Anal.* Calcd. for $C_{11}H_{10}O_4N_2S$: C, 49.63; H, 3.79; N, 10.52. Found: C, 49.42; H, 3.55; N, 10.60. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1720 (CO), 1350 (NO_2).

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