Reactions of 2-Cyano-2-dimethylamino-1,3-dithiolane[1)]

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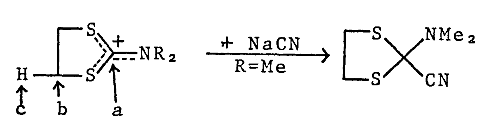
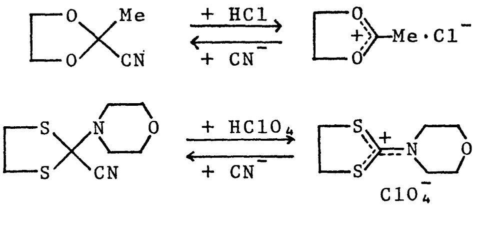
The reactions of 2-cyano-2-dimethylamino-1,3-dithiolane (**2**) with electrophiles (organic halides and perchloric acid) and nucleophiles were investigated. It was found that **2** dissociated partially to 2-dimethylamino-1,3-dithiolan-2-ylium (**1**) and cyanide ions in polar solvents. In the reactions of **2** with electrophiles, nitriles were obtained along with the formation of salts of **1**. The reactions of **2** with nucleophiles were studied since **2** was expected to be a precursor of the cation **1**. In some cases, its reactivity differs from that of perchlorate of **1**. A mechanism was discussed in which the cyanide ion might behave as a base to abstract a proton from the nucleophiles.

In a previous paper[2)] it was reported that 2-dialkylamino-1,3-dithiolan-2-ylium ions (**1**) were ambident electrophiles capable of undergoing reactions with nucleophiles at three sites, a, b, and c. In the case of the reaction of perchlorate of **1** (R=Me) with cyanide ion as a nucleophile, 2-cyano-2-dimethylamino-1,3-dithiolane (**2**) was obtained in a good yield.[3)] In this work the reactions of **2** with various electrophiles and nucleophiles have been studied.



1 **2**

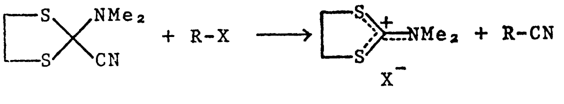
Little information has been given on the reactions of α-cyanoacetal and α-cyanoorthoester derivatives. It has only been reported that treatment of 2-cyano-2-methyl 1,3-dioxolane[4)] and 2-cyano-2-morpholino-1,3-dithiolane[5)] with acids gives 2-methyl-1,3-dioxolan-2-ylium ion and 2-morpholino-1,3-dithiolan-2-ylium ion, respectively.



Thus, compound **2** is expected to be capable of cyanogenating electrophiles along with the formation of the cation **1**. On the other hand, **2** is expected to behave as a precursor of **1** in the reaction with nucleophiles. The limitation of the use of **2** in this reaction was also studied by comparing the reactivity of **2** with that of perchlorate of **1**.

Results and Discussion

Reactions of 2 with Electrophiles. The reactions of **2** with the following electrophiles were studied: methyl iodide, *n*-butyl iodide, benzyl bromide, benzoyl chloride, phenacyl bromide, and perchloric acid. Firstly, in order to find the influence of solvent on the reactions of **2** with electrophiles, the reaction of **2** with methyl iodide was carried out in ethyl ether, acetonitrile, and nitromethane[6)] to obtain iodide of **1** in all cases. It was found that the yield of iodide of **1** was higher in polar solvents (acetonitrile and nitromethane) than in nonpolar one (ethyl ether). Thus, the reactions of **2** with other electrophiles were carried out in polar solvents. The yields of salts of **1** and nitrile **3** obtained simultaneously are summarized in Table 1. These products were found to be identical with authentic samples.[7)]



2 **1** **3**

Thus, electrophile can react with **2** giving nitrile along with the formation of salt of **1**. It should be noted that **2** is useful as a precursor of cyanide ion which is soluble in organic solvents and product **3** can readily be isolated from another product, salt of **1**.

The fact that the yield of salts of **1** increases with the increase in polarity of solvent as observed in the case of the reaction of **2** with methyl iodide suggests that **2** dissociates first to cation **1** and cyanide ion, and then cyanide ion attacks methyl iodide giving acetonitrile and iodide of **1**. In order to investigate the influence of solvents on the dissociation of **2** to cation **1** and cyanide ion, the UV spectrum of **2** was measured in the following solvents: cyclohexane, tetrahydrofuran, chloroform (containing 1% ethanol), 99% etha-

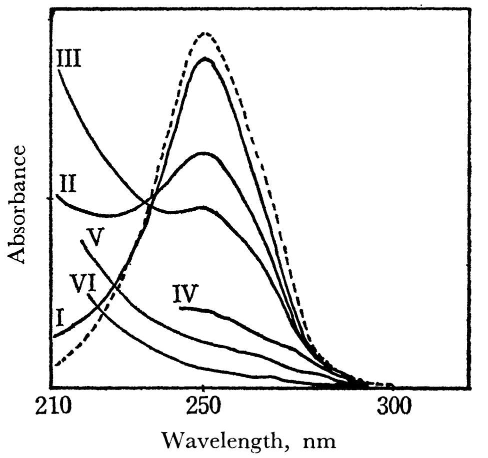
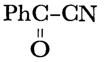
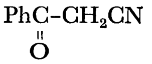


Fig. 1. Ultraviolet spectra of **2** and salt **1**.
……: **1** [ClO_4^-] in MeOH, ——: **2**
I: MeOH, II: EtOH[99%], III: MeCN, IV: $CHCl_3$-[Containing 1% EtOH], V: THF, XI: C_6H_{12}.

Table 1. Reactions of **2** with electrophiles

Electrophile	Conditions			Products			
	Solvent	Temp. °C	Time hr (day)	**1** X	**1** Yield, %[b)]	**3**[c)]	Yield, %[b)]
Methyl iodide	Et_2O	reflux	4	I	5	(MeCN)	—
	MeCN	40	3	I	35	(MeCN)	—
	$MeNO_2$	rt	(2)	I	53	(MeCN)	—
n-Butyl iodide	$MeNO_2$	rt	(2)	I	22	*n*-BuCN	15
Benzyl bromide	$MeNO_2$	rt	(2)	Br[a)]	41	$PhCH_2CN$	36
Benzoyl chloride	MeCN	reflux	3	Cl[a)]	97	 $PhC(=O)-CN$	63
Phenacyl bromide	MeCN	50	2	Br[a)]	73	 $PhC(=O)-CH_2CN$	57
Perchloric acid	EtOH	rt	1	ClO_4	80	(HCN)	—

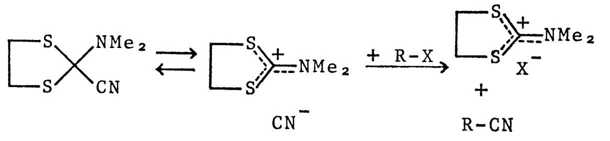
a) Cation **1** was isolated as perchlorate which was more stable than the bromide and chloride. b) Based upon **2**. c) In the cases of methyl iodide and perchloric acid, acetonitrile and hydrogen cyanide, respectively, were formed but not identified.

Table 2. Ultraviolet spectra of **2** and salt, **1**

	Solvent	λ_{max}, nm	ε[b)]
2	MeOH	250.5	1.09×10^4
	EtOH (99%)	250	2.70×10^3
	MeCN	250 (sh)[c)]	$<1.54\times10^3$
	$CHCl_3$[a)]	250 (sh)[c)]	$\ll10^2$
	THF	—	—
	C_6H_{12}	—	—
1 (ClO_4^-)	MeOH	250.5	1.30×10^4
	MeCN	250	0.94×10^4

a) Containing 1% ethanol. b) The apparent molecular extinction coefficient at absorption maxima. c) Shoulder band.

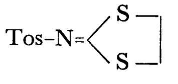
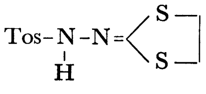
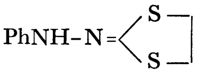
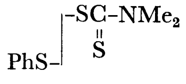
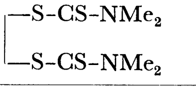
nol, acetonitrile, and methanol (Fig. 1). The absorption maxima (λ_{max}) and the molecular extinction coefficients (ε) of **2** and perchlorate of **1** in various solvents are given in Table 2. The absorption band (λ_{max}~250 nm) in Fig. 1 is evidently assigned to the cation **1** since salts (iodide, perchlorate, and tetrafluoroborate) of **1** show the same absorption band as that of **2** in the same solvents. It was observed that the values of the apparent molecular extinction coefficient (ε) at λ_{max} (~250 nm) of **2** were larger in polar solvents than in nonpolar solvents. The values of apparent ε at λmax of **2** in acetonitrile and methanol are smaller than those of perchlorate of **1** in the same solvents (Table 2). Thus it can be concluded that **2** dissociates partially to the cation **1** and cyanide ion in polar solvents. The reactions of **2** with electrophiles can be interpreted by the following scheme.



*Reactions of **2** with Nucleophiles.* Compound **2**, soluble in organic solvents, is expected to be useful as a precursor of cation **1** since **2** can dissociate partially to cation **1** and cyanide ion in polar solvents. The reactions of **2** with the following nucleophiles were studied: aniline, *p*-nitroaniline, 2,4-dinitroaniline, benzamide, *p*-toluenesulfonylamide (tosylamide), phenylhydrazine, *p*-toluenesulfonylhydrazide (tosylhydrazide), sodium thiophenoxide, and sodium *N*,*N*-dimethyldithiocarbamate. The difference in the reactivity of **2** from that of perchlorate of **1** was also investigated.

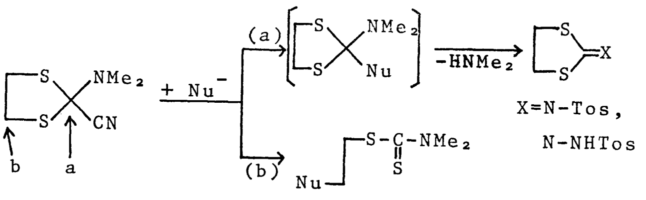
The equimolar reaction of **1** with nucleophiles was carried out in benzene or acetonitrile at refluxing temperature for 5 hr giving the products shown in Table 3. In the cases of aniline, *p*-nitroaniline, 2,4-dinitroaniline, and benzamide, the reactants were recovered unchanged. Treatment of **2** with tosylamide, phenylhydrazine, and tosylhydrazide gave 2-tosylimino-1,3-dithiolane, 2-phenylhydrazo-1,3-dithiolane, and 2-tosylhydrazo-1,3-

Table 3. Reactions of **2** with nucleophiles

Nucleophile	Product	Yield[a)] %	Mp °C
Aniline *p*-Nitroaniline 2,4-Dinitroaniline Benzamide	No reaction		
Tosylamide		70[b)] 47[c)]	121—123
Tosylhydrazide		47[b)] 28[c)]	193—195
Phenylhydrazine		88	90— 92
Sodium thiophenoxide		84	liq.
Sodium *N*,*N*-Dimethyldithiocarbamate		17	187—190

a) For reaction conditions, see Experimental. b) In acetonitrile. c) In benzene.

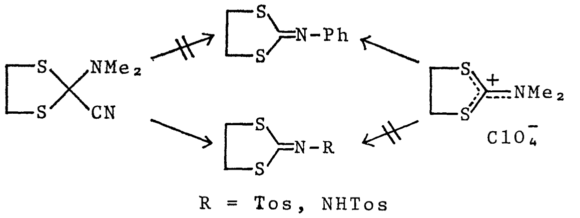
dithiolane, respectively, in moderate yields (path a). On the other hand, treatment of **2** with sodium thiophenoxide and sodium *N*,*N*-dimethyldithiocarbamate gave *β*-(phenylthio)ethyl-*N*,*N*-dimethyldithiocarbamate and ethylenebis(*N*,*N*-dimethyldithiocarbamate), respectively (path b). The structures of the products were elucidated by elemental analysis and spectroscopic methods. The yield and melting point of the products are summarized in Table 3.



2

The salt of **1** reacts with aniline, sodium thiophenoxide, and sodium *N*,*N*-dimethyldithiocarbamate giving 2-phenylimino-1,3-dithiolane, *β*-(phenylthio)ethyl-*N*,*N*-dimethyldithiocarbamate, and ethylenebis(*N*,*N*-dimethyldithiocarbamate), respectively.[2] On the other hand, perchlorate of **1** does not react with tosylamide and tosylhydrazide at all.

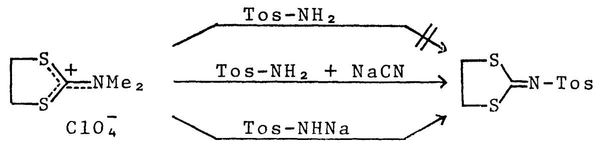
From these results it was found that i) compound **2** reacted with some nucleophiles along with the elimination of cyanide ion; ii) it reacted with nucleophiles at two sites, a and b, in formula (**2**); iii) in the case of sodium thiophenoxide and sodium *N*,*N*-dimethyldithiocarbamate as nucleophile, both **2** and perchlorate of **1** reacted with them giving the same products; and iv) **2** reacted with nucleophiles such as tosylamide and tosylhydrazide, with which perchlorate of **1** did not react, but it did not react at all with nucleophiles such as aniline with which perchlorate of **1** reacted to give 2-phenylimino-1,3-dithiolane.[2]



It is to be noted that the reactivity of **2** differs from that of salt of **1**. It is considered that cyanide ion participates in the reaction of **2** with nucleophiles. In order to clarify the difference in reactivity between **2** and salt of **1**, the following reactions were attempted with tosylamide and tosylhydrazide as nucleophiles.

The equimolar reaction of **2** with tosylhydrazide at refluxing temperature for 5 hr in a polar solvent (acetonitrile) and a nonpolar solvent (benzene) gave 2-tosylhydrazo-1,3-dithiolane in 47 and 28% yields, respectively. Under the same conditions, the reaction of **2** with tosylamide in acetonitrile and benzene gave 2-tosylimino-1,3-dithiolane in 70 and 47% yields, respectively (Table 3). The reaction seems to be more favorable in a polar solvent than in a nonpolar one.

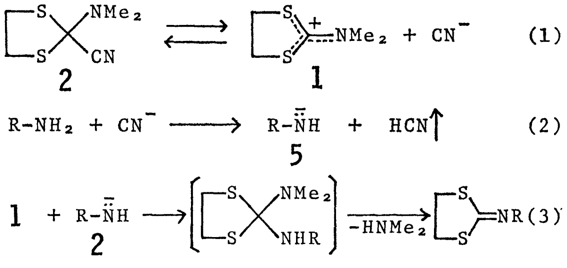
The reactants were quantitatively recovered unchanged in the reaction of perchlorate of **1** with tosylhydrazide at refluxing temperature for 5 hr in acetonitrile and dimethylformamide and also in the case of tosylamide in acetonitrile. The reaction of salt of **1** with tosylamide including sodium cyanide was attempted. The reactions in the presence of equimolar, 0.6 molar, and 0.4 molar of sodium cyanide at refluxing temperature for 5 hr in acetonitrile gave 2-tosylimino-1,3-dithiolane in 34, 25, and 14% yields, respectively. The reaction of salt of **1** with sodium tosylamide prepared by the treatment of tosylamide with sodium hydride in tetrahydrofuran, at refluxing temperature for 5 hr in the mixture of acetonitrile and tetrahydrofuran also gave 2-tosylimino-1,3-dithiolane in 17% yield.



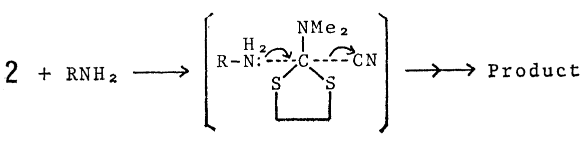
1

It can thus be concluded that cyanide ion evidently participates in the reaction of **2** with tosylamide. The result of the reaction of salt of **1** with sodium tosylamide suggests that cyanide ion behaves as a base in the reaction of **2** with tosylamide to abstract a proton from the amide. This assumption may be supported by the fact that compound **2** tends to react with tosylamide ($pK_a=10.2$)[8] which has a smaller basicity than aniline ($pK_a=27$).[9]

The reaction of **2** with tosylamide and tosylhydrazide can be interpreted by the following processes: i) compound **2** dissociates partially to 2-dimethylamino-1,3-dithiolan-2-ylium ion (**1**) and cyanide ion in solution (Eq. 1); ii) cyanide ion abstracts a proton from the nucleophiles to give anion **5** and hydrogen cyanide (Eq. 2); and iii) the cation **1** reacts with the anion **5** to afford the corresponding product (Eq. 3). An important point in this reaction seems to be that the hydrogen cyanide formed is removed from the reaction mixture to displace the equilibrium (Eq. 2).



An alternative formation of the product arising from the direct reaction of **2** with nucleophiles ($R-NH_2$) *via* S_N2 type mechanism might be disregarded since the reaction was slow in nonpolar solvent and nucleophiles having small nucleophilicity reacted preferentially with **2**.



Thus, it was proved that cyanide ion behaved as a base, and **2** could react with nucleophiles having small nucleophilicity with which salt of **1** did not react.

Experimental

General. All melting and boiling points are uncorrected. IR and UV spectra were recorded with Hitachi EPI-S2 and EPS-3T spectrophotometers, respectively. NMR spectra were obtained with Japan Electron Optics JNN PS-100 and MH-60 spectrometers. Chemical shifts are given in ppm from tetramethylsilane as an internal standard.

*2-Cyano-2-dimethylamino-1,3-dithiolane (**2**).* Dithiolane **2** was prepared by the procedure previously reported:[2] bp 119—121 °C/2.0 mmHg, yield 74%.

*Reaction of **2** with Methyl Iodide. a) In Acetonitrile.* In a 50-ml round-bottomed flask equipped with reflux condenser was placed 0.58 g (3.3 mmol) of **2** and 2.0 g (14 mmol) of methyl iodide in 20 ml of acetonitrile (MeCN). The solution was stirred for 4 hr at 40 °C. After MeCN was removed by distillation, the residue (white precipitates) was washed with ether and dried *in vacuo*. Recrystallization of the precipitates from ethanol gave 0.32 g (35%) of 2-dimethylamino-1,3-dithiolan-2-ylium iodide; mp 191—192 °C. NMR (DMSO-d_6); δ 3.47(s, 6H, NCH_3) and 3.98 (s, 4H, SCH_2).

b) In Ether. In a similar manner, the reaction of **2** (0.58 g) with methyl iodide (2.0 g) in 20 ml of ether at refluxing temperature for 4 hr gave 0.05 g (5%) of iodide of **1**.

c) In Nitromethane. In a similar manner, the reaction of **2** (1.9 g) with methyl iodide (4.0 g) in 50 ml of $MeNO_2$ at room temperature for 2 days gave 1.6 g (53%) of iodide of **1**.

*Reactions of **2** with Other Electrophiles.* In a similar manner, the reaction of **2** with equimolar electorphile under the conditions shown in Table 1 gave salt of **1** in a moderate yield along with nitrile **3**. The products were identified by spectroscopic methods and comparison of their physical properties with those of authentic samples.

*Reaction of **2** with Perchloric Acid.* To a solution of **2** (1.74 g, 10 mmol) in 20 ml of ethanol with stirring at room temperature was added dropwise 70% aqueous perchloric acid (1.5 g, 15 mmol), and the solution was stirred for 1 hr at room temperature. The precipitates formed were filtered off and washed with cooled ethanol. 2.0 g (80%) of perchlorate of **1** was obtained and recrystallized with ethanol. The IR spectrum of the product was in complete agreement with that of an authentic sample.

*Reaction of **2** with* p-*Toluenesulfonylhydrazide.* In a 100-ml flask was placed a solution of 1.74 g (10 mmol) of **2** and 1.86 g (10 mmol) of *p*-toluenesulfonylhydrazide (tosylhydrazide) in 40 ml of MeCN. The reaction mixture was refluxed for 8 hr. After removal of MeCN, a small amount of chloroform was added to the liquid residue. The white precipitates were filtered off and recrystallized from benzene giving 0.45 g of 2-tosylhydrazo-1,3-dithiolane. The filtrate was subjected to chromatography on silica gel with chloroform. The first eluent gave 0.24 g of a pale yellow liquid (unidentified). The second eluent gave 0.23 g of 2-tosylhydrazo-1,3-dithiolane:[10] total yield 0.68 g (47%); mp 193—195 °C. UV (EtOH): λ_{max} 225 and 254 (sh.)nm; NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), 3.43 (s, 4H, S–CH_2), 7.22 (d, 2H, aromatic-H), 7.51 (d, 2H, aromatic-H), and 10.05 (s, 1H, N–H).

Found: C, 41.72; H, 3.99; N, 10.09%. Calcd for $C_{10}H_{12}NS_3O_2$: C, 41.67; H, 4.06; N, 9.92%.

In the case of benzene as solvent, 2-tosylhydrazo-1,3-dithiolane was obtained in 28% yield.

*Reaction of **2** with Phenylhydrazine.* In a similar manner, the reaction of **2** (0.35 g, 2.0 mmol) with phenylhydrazine (0.22 g, 2.0 mmol) in 20 ml of benzene at refluxing temperature for 5 hr gave 0.37 g (88%) of 2-phenylhydrazo-1,3-dithiolane which was isolated by means of column chromatography (alumina, chloroform) and recrystallized from ethanol: 90—92 °C (lit,[11] 91 °C). UV (EtOH): λ_{max}=242, 288, and 315 (sh.)nm; NMR ($CDCl_3$): δ 3.16—3.56 (m, 4H, S–CH_2), 6.53(s, 1H, N–H), and 6.70—7.30 (m, 5H, aromatic-H).

Found: C, 50.56; H, 4.95; N, 13.12%. Calcd for $C_9H_{10}N_2S_2$: C, 51.42; H, 4.76; N, 13.33%.

*Reaction of **2** with* p-*Toluenesulfonylamide. a) In MeCN*: In a similar manner, the reaction of **2** (0.58 g, 3.3 mmol) with *p*-toluenesulfonylamide (tosylamide) (0.57 g, 3.3 mmol) in 20 ml of MeCN at refluxing temperature for 5 hr gave 0.64 g (70%) of 2-tosylimino-1,3-dithiolane which was recrystallized from the mixture of benzene and cyclohexane; mp 121—123 °C (lit,[12] 126—127 °C). UV (EtOH): λ_{max}=228 and 268 nm; NMR ($CDCl_3$): δ 2.42 (s, 3H, CH_3), 3.58 (s, 4H, S–CH_2), 7.47 (d, 2H, aromatic-H), and 7.87 (d, 2H, aromatic-H).

Found: C, 44.56; H, 4.21; N, 5.43%. Calcd for $C_{10}H_{11}NO_2S_3$: C, 43.96; H, 4.03; N, 5.13%.

b) In Benzene: In a similar manner, the reaction of **2** (0.30 g, 1.7 mmol) with tosylamide (0.30 g, 1.7 mmol) in 20 ml of benzene at refluxing temperature for 5 hr gave 0.22 g (47%) of 2-tosylimino-1,3-dithiolane. The IR spectrum of the product was in complete agreement with that of an authentic sample.

*Reaction of **2** with Sodium* N,N-*Dimethyldithiocarbamate.* In a similar manner, the reaction of **2** (0.35 g, 2.0 mmol) with sodium *N,N*-dimethyldithiocarbamate (0.50 g, 2.8 mmol) in 20 ml of MeCN at refluxing temperature for 5 hr gave 0.09 g (17%) of ethylenebis(*N,N*-dimethyldithiocarbamate) which was recrystallized from ethanol giving colorless crystals, mp 187—190 °C (lit,[2] 188—189 °C). The IR spectrum was in complete agreement with that of an authentic sample.

*Reaction of **2** with Sodium Thiophenoxide.* In a similar manner, the reaction of **2** (0.35 g, 2.0 mmol) with sodium thiophenoxide (0.40 g, 3.0 mmol) in 20 ml of MeCN at refluxing temperature for 5 hr gave 0.43 g (84%) of β-phenylthioethyl-*N,N*-dimethyldithiocarbamate which was purified by means of column chromatography (alumina, $CHCl_3$) giving a pale yellow liquid. NMR (CCl_4): δ 3.15 and 3.35 (s, 6H, N–CH_3), 2.96—3.56 (m, 4H, SCH_2), and 6.94—7.44 (m, 5H, aromatic-H).

*Reaction of Perchlorate of **1** with Tosylhydrazide.* A mixture of **1** (2.48 g, 0.01 mol) and tosylhydrazide (1.86 g, 0.01 mol) in 40 ml of MeCN was refluxed for 8 hr. After removal of MeCN, the residual solid was dried (weight: 4.30 g). It was then poured into water and the white precipitates were filtered and dried *in vacuo*. The product (1.80 g) was identified to be tosylhydrazide by comparison of the IR spectrum with that of an authentic sample.

In a similar manner, the reaction of **1** with tosylhydrazide in dimethylformamide (DMF) was attempted. The reactants were recovered unchanged.

*Reaction of Perchlorate of **1** with Tosylamide.* The reaction of perchlorate of **1** (1.24 g, 5.0 mmol) with tosylamide (0.86 g, 5.0 mmol) in 20 ml of MeCN at refluxing temperature for 5 hr resulted in the recovery of perchlorate of **1** (1.16 g) and tosylamide (0.83 g).

*Reaction of Perchlorate of **1** with Tosylamide and Sodium Cyanide.* In a 50-ml round-bottomed flask equipped with reflux condenser was placed a solution of perchlorate of **1** (1.24 g, 5.0 ml), tosylamide (0.86 g, 5.0 mmol), and sodium cyanide (0.25 g, 5.0 mmol) in 20 ml of MeCN. After the solution was refluxed for 5 hr, the solvent was removed by distillation. The residue was subjected to chromatography on alumina with chloroform. The first eluent gave 0.46 g (34%) of 2-tosylimino-1,3-dithiolane. The second eluent contained 0.46 g of the starting material, tosylamide. The IR spectrum of the product was in complete agreement with that of an authentic sample.

In a similar manner, the reaction of perchlorate of **1** (1.24 g) with tosylamide (0.86 g) and sodium cyanide (0.15 g, 3.0 mmol) gave 0.34 g (25%) of 2-tosylimino-1,3-dithiolane. On addition of 0.10 g (2.0 mmol) of sodium cyanide, the product was obtained in 14% yield.

*Reaction of Perchlorate of **1** with Sodium Tosylamide.* To a suspension of sodium tosylamide prepared *in situ* by the treatment of 0.83 g (4.8 mmol) of tosylamide with 0.15 g of 50% sodium hydride in 50 ml of tetrahydrofuran, was added 1.24 g (5.0 mmol) of perchlorate of **1** in 20 ml of MeCN. The mixture was stirred at 60—70 °C for 5 hr. After removal of the solvents by distillation, water was added to the residue. White precipitates separated were filtered off and washed with a small amount of ether. 2-Tosylimino-1,3-dithiolane (0.23 g, 17%) was obtained and recrystallized from the mixture of benzene and cyclohexane. The IR spectrum of the product was in complete agreement with that of an authentic sample.

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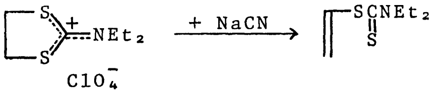
2) T. Nakai and M. Okawara, This Bulletin, **43**, 1864 (1970).

3) The reaction of perchlorate of **1** (R = Et) with cyanide ion unexpectedly gave *S*-vinyl-*N*,*N*-diethyldithiocarbamate, identical with an authentic sample.[2] The same reaction gave a yellow oil unconfirmed which was proved not to be 2-cyano-2-diethylamino-1,3-dithiolane.[2]



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6) Protic solvents, ethanol and methanol, were not used in this reaction since **2** might be subjected to solvolysis in protic solvents.[2]

7) For the preparation and physical properties of salt of **1**, see T. Nakai, Y. Ueno, and M. Okawara, This Bulletin, **43**, 156 (1970).

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