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The Synthesis of 1,3-Dithiolane-2-thione Derivatives

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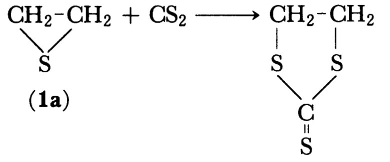
The reaction of 2,2-dimethylthiirane with carbon disulfide in the presence of triethylamine was accelerated under high pressure to give 4,4-dimethyl-1,3-dithiolane-2-thione nearly quantitatively. The activation volume of this reaction at 40 °C was estimated to be −41 ml mol^{-1}. The rate of the reaction was proportional to the amount of triethylamine when a limited amount of triethylamine was used. The reaction of 2-methylthiirane, 2-hexylthiirane, 1,2-epithiocyclohexane, and 2-phenylthiirane with carbon disulfide gave the corresponding 1,3-dithiolane-2-thione derivatives in good yields. 2-Chloromethylthiirane was less reactive to carbon disulfide than other thiiranes under high pressure. Tertiary amines such as *N*,*N*-dimethylethylamine, pyridine, and *N*-methylmorpholine were good catalysts of the reaction.

Thiiranes react with various compounds to form the open-ring products.[1,2] It has been known that five-membered heterocyclic compounds are obtained by the reaction of thiiranes with methyl cyanoacetate,[3] malononitrile,[4] acetonitrile,[5] diethyl malonate,[6] and ethyl acetoacetate.[6] Although the reaction of thiirane (**1a**) with carbon disulfide gave 1,3-dithiolane-2-thione in a good yield, the reaction of substituted thiiranes with carbon disulfide showed lower yield.[7] On the other hand, high pressure accelerates many organic reactions[8] including those of carbon disulfide.[9,10] However, there has been no report on the reaction of thiiranes under high pressure.

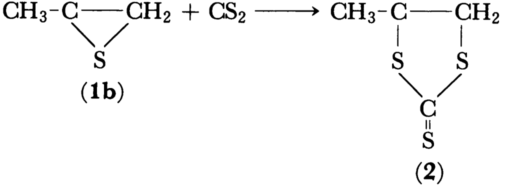


(**1a**)

We will report that the reaction of substituted thiiranes with carbon disulfide is accelerated under high pressure to give the corresponding 1,3-dithiolane-2-thione derivatives in good yields. The effects of pressure, reaction temperature, and amount and kind of catalysts on the reaction of 2,2-dimethylthiirane (**1b**) with carbon disulfide were investigated and the reactions of various thiiranes with carbon disulfide attempted.

Results and Discussion

Under 1 kg cm^{-2} pressure, the reaction of **1b** with carbon disulfide at 80—100 °C in the presence of triethylamine as a catalyst gave 4,4-dimethyl-1,3-dithiolane-2-thione (**2**) in 2—12% yield. At a higher temperature (120 °C) the yield was still lower (10%) and various by-products were contained in **2** (Table 1, Runs 1—3). When the reaction was carried out under high pressures (2000—8000 kg cm^{-2}), the yield of **2** increased to over 90% (Runs 4—7). As the pressure was increased to 5000 kg cm^{-2}, the rate of the formation of **2** was enhanced satisfactorily even at 40 °C (Run 4).



(**1b**)

(**2**)

Table 1. Effect of Reaction Conditions on the Reaction of **1b** with CS_2[a)]

Run	Temp	Press.[b)]	Yield
	°C	kg cm^{-2}	%
1	80	1	2
2	100	1	12
3	120	1	10
4	40	5000	92
5	70	2000	96
6	100	2000	87
7	100	8000	91

a) **1b**: 10 mmol, CS_2: 50 mmol, Et_3N: 0.10 g, reaction time: 20 h. b) 1 kg cm^{-2}=0.9806×10^{5}Pa.

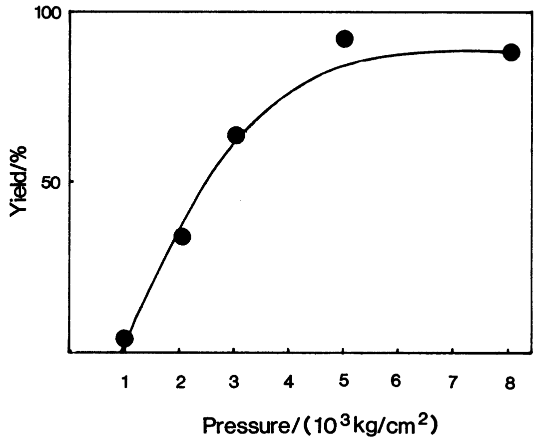


Fig. 1. Effect of pressure on the reaction of **1b** with CS_2; Reaction temperature: 40°C, reaction time: 20 h, **1b**: 10 mmol, CS_2: 50 mmol, Et_3N: 1 mmol.

The effect of pressure on the reaction of **1b** with carbon disulfide is shown in Fig. 1. The reaction is regarded as a first-order reaction with respect to **1b**, because carbon disulfide is excessive. The reaction-velocity constant *k* is calculated from the data in Fig. 1.

The activation volume $\Delta V^{\neq}$ at 40 °C estimated by Eq. 1 was -41 ml mol^{-1}. This value suggests that the reaction is considerably accelerated by the pressure.

$$\Delta V^{\neq} = RT(\partial \ln k/\partial P)_{T} \qquad (1)$$

Figure 2 shows that the rate of reaction of **1b** with carbon disulfide is proportional to the amount of triethyamine catalyst when a limited amount of triethylamine is used.

Table 2 shows the products and yields of reactions of various thiiranes with carbon disulfide. The reaction of 2-methylthiirane, 2,2-dimethythiirane, 2-hexylthiirane, 2-phenylthiirane, and 1,2-epithiocyclohexane with carbon disulfide gave the corresponding 1,3-dithiolane-2-thiones in good yields. The yield of the reaction of **1a** with carbon disulfide was 53%. This fact is considered to be due to a tendency of **1a** to polymerize. 2-Chloromethylthiirane showed low reactivity and selectivity toward carbon disulfide in comparison with other thiiranes.

Table 3 shows the effects of various catalysts on the reaction of **1b** with carbon disulfide. *N,N*-Dimethylethylamine, triethylamine, *N*-methylmorpholine, and pyridine were good catalysts under high pressure, the catalytic activity decreasing in this order. *N,N*-Dimethylaniline had no catalytic activity even under high pressure. The catalytic activity of tertiary amines, therefore, would be influenced by basicity as well as steric factor. Tetramethylammonium bromide, which has been reported to have catalytic activity on the reaction of oxiranes with carbon disulfide,[7] showed low activity under 8000 kg cm^{-2}. Lithium chloride was used as a catalyst of the reaction of thiiranes or oxiranes with various heterocumulenes,[8,11,12] but it had no catalytic activity on the reaction of **1b** with carbon disulfide under 8000 kg cm^{-2} at 100 °C.

The reaction of thiiranes or oxiranes with various heterocumulenes under ordinary pressure has been reported to give five-membered products.[8,11,12] The reactions of **1b** with methyl isothiocyanate, phenyl

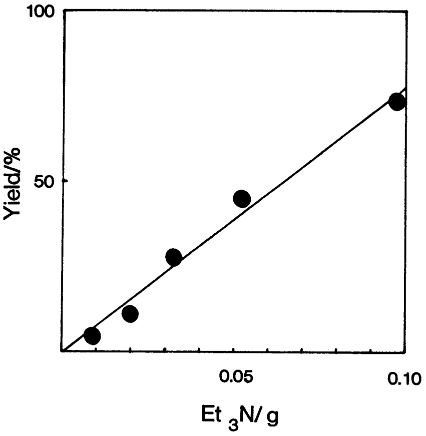
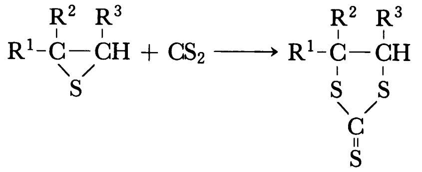


Fig. 2. Effect of amount of Et$_3$N on the reaction of **1b** with CS$_2$; Reaction temperature: 40°C, reaction time: 20 h, pressure: 3000 kg cm^{-2}, **1b**: 10 mmol, CS$_2$: 50 mmol.

Table 2. The Reaction of Various Thiiranes with CS$_2$[a]



Run	Thiiranes R^1	R^2	R^3	Temp °C	Press. kg cm^{-2}	Yield %
1	H	H	H	40	8000	53
2	CH$_3$	H	H	40	8000	97
3	CH$_3$	CH$_3$	H	40	5000	92
4	C$_6$H$_{13}$	H	H	40	8000	94
5	C$_6$H$_{13}$	H	H	70	2000	94
6	C$_6$H$_5$	H	H	100	8000	91
7	ClCH$_2$	H	H	40	8000	6
8	ClCH$_2$	H	H	100	8000	32[b]
9	H	$(CH_2)_4$		40	8000	92

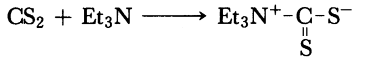
a) thiirane: 10 mmol, CS$_2$: 50 mmol, Et$_3$N: 0.10 g, reaction time: 20 h. b) 0.30 g of Et$_3$N was used as catalyst.

Table 3. Effect of Various Catalysts on the Reaction of **1b** with CS$_2$[a]

Run	Catalyst	Press. kg cm^{-2}	Temp °C	Yield %
1	Triethylamine	3000	40	74
2	*N,N*-Dimethylethylamine	3000	40	83
3	*N*-Methylmorpholine	3000	40	2
4	Pyridine	3000	40	trace
5	*N,N*-Dimethylaniline	3000	40	trace
6	*N*-Methylmorpholine	8000	40	100
7	Pyridine	8000	40	99
8	*N,N*-Dimethylaniline	8000	40	trace
9	Pyridine	8000	100	100
10	Et$_4$NBr	8000	40	7
11	Et$_4$NBr	8000	100	10
12	LiCl	8000	100	trace
13	None	2000	100	trace

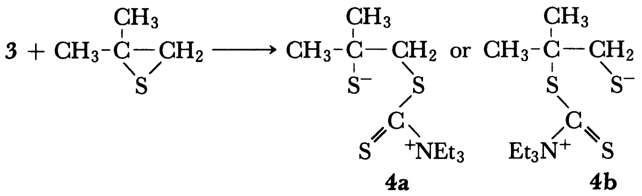
a) **1b**: 10 mmol, CS$_2$: 50 mmol, catalyst: 1 mmol, reaction time: 20 h.

isocyanate, and dicyclohexylcarbodiimide under high pressure were tried, but no effect of the compression appeared in any cases. Accordingly, highly selective reaction of thiiranes under high pressure seems to be characteristic of carbon disulfide; it is carbon disulfide that is activated under high pressure but not **1b**. On the other hand, the reaction of **1b** with carbon disulfide without catalyst under high pressure gave various by-products and only a trace of **2** (Table 3, Run 13). It is well-known that carbon disulfide reacts with amines easily.[14]

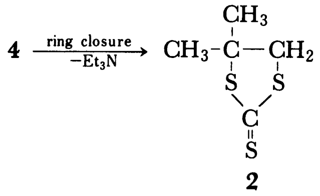


$$CS_2 + Et_3N \longrightarrow Et_3N^+\text{-}\underset{\underset{S}{\|}}{C}\text{-}S^- \qquad (2)$$

3



(3)



(4)

The reaction of **1b** with carbon disulfide in the presence of triethylamine seems to proceed succesively with the first step of adduct **3** formation from carbon disulfide and triethylamine (Eq. 2), then addition of **3** to **1b** yielding **4** (Eq. 3), and ring closing of **4** (Eq. 4). Whether the structure of **4** is **4a** or **4b** is ambiguous, because both **4a** and **4b** lead to the same product **2** by rapidly succeeding ring closure. But **4a** is more likely, because active methylene compounds[6] and secondary amines[15] are apt to attack the less-hindered carbon atom of thiirane ring. Equation 4 is a reaction in which two molecules (**2** and Et_3N) are formed from one molecule, and it is unlikely that compression accelerates such a reaction. Therefore, the compression seemes to be effective on a step of Eq. 2 or 3.

Experimental

Apparatus. The apparatus used for the reaction under high pressure was the same as that described previousyl.[16]

Measurement. GLC was carried out by a JEOL 20KF chromatograph with 20% SE-30 columns. ^{1}H NMR spectra were measured by a Hitachi R-40 spectrometer. Mass spectra were measured by a JEOL D-300 GC-MS spectrometer using the CI (chemical ion) method with isobutane. IR spectra were obtained by a JASCO A-302 spectrophotometer.

Materials. Thiirane and 2-methylthiirane were purchased from Aldrich Chem. Co. 2,2-Dimethylthiirane, 2-hexylthiirane, 2-phenylthiirane, and 1,2-epithiocyclohexane were prepared as previously described.[6] 2-Chloromethylthiirane was obtained by the method of Culvenor.[17]

Reaction of Thiiranes with Carbon Disulfide. A typical procedure is as follows: A homogeneous mixture of **1b** (10 mmol), carbon disulfide (50 mmol), and triethylamine (1 mmol) in a sealed teflon tube was compressed to 5000 kg cm^{-2}, heated at 40 °C, and maintained for 20 h in a high pressure equipment. The resulting mixture was subjected to evaporation and the residue was purified by distillation with Kugelrohr to give 1.50 g (92%) of **2**. IR: 1054, 1089 cm^{-1}; ^{1}H NMR δ=1.74 (s, 6H, 2CH$_3$), 3.76 (s, 2H, CH$_2$); QM$^+$: 165.

Thiirane, 2-methylthiirane, 2-hexylthiirane, 1,2-epithiocyclohexane, 2-phenylthiirane, and 2-chloromethylthiirane were treated with carbon disulfide in a similar manner to the reaction of **lb** with carbon disulfide. The spectral data of products of these reactions are as follows:

1,3-dithiolane-2-thione. IR: 1057 cm^{-1}; ^{1}H NMR δ=4.00 (s, 4H, 2CH$_2$); QM$^+$: 137.

4-methyl-1,3-dithiolane-2-thione. IR: 1076, 1050, 1033 cm^{-1}; ^{1}H NMR δ=1.64 (d, 3H, CH$_3$), 3.55—3.85 (dd, 1H, one proton of CH$_2$), 3.95—4.20 (dd, 1H, one proton of CH$_2$), 4.35—4.75 (m, 1H, CH); QM$^+$: 151.

4-hexyl-1,3-dithiolane-2-thione. IR: 1064 cm^{-1}; ^{1}H NMR δ=0.88 (t, 3H, CH$_3$), 1.34 (s, 8H, $\leftarrow$CH$_2\rightarrow_4$), 1.70—2.10 (m, 2H, CH$_2$), 4.25—4.60 (m, 1H, CH); QM$^+$: 221.

4,5-Tetramethylene-1,3-dithiolane-2-thione. IR: 1033, 1058 cm^{-1}; ^{1}H NMR δ=1.00—2.40 (m, 8H, $\leftarrow$CH$_2\rightarrow_4$), 3.90—4.40 (m, 2H, CH$_2$); QM$^+$: 191.

4-Phenyl-1,3-dithiolane-2-thione. IR: 1047 cm^{-1}; ^{1}H NMR δ=3.90—4.40 (m, 2H, CH$_2$), 5.55—5.80 (dd, 1H, CH), 7.25—7.70 (m, 5H, C$_6$H$_5$); QM$^+$: 213.

4-Chloromethyl-1,3-dithiolane-2-thione was purified by column chromatography on silica gel using a mixture of hexane and chloroform (7 : 3 v/v) as an eluent. IR: 1067, 1039 cm^{-1}, ^{1}H NMR δ=3.55—4.05 (m, 2H, CH$_2$), 4.05—4.30 (m, 2H, CH$_2$), 4.30—4.65 (m, 1H, CH); QM$^+$: 185.

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