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Reactions of Various Thione-compounds with Epoxides. A New Method for the Transformation of the C=S Bond into the C=O*1

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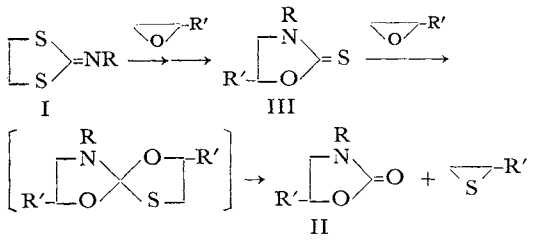
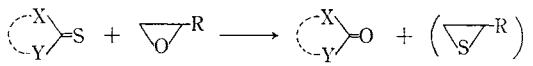
The reactions of propylene oxide (PO) with various thione-compounds containing two α-hetero atoms including dithiocarbamates, thioncarbamates, trithiocarbonates and thioureas, and their cyclic analogs were studied in the presence of triethylamine or boron trifluoride etherate as a catalyst. It was found that most of these thione-compounds reacted with PO at 170—180°C to afford the corresponding one-compounds in good yields. This type of reaction may provide a new method for the transformation of the C=S bonds in thione-compounds into the C=O bonds. Boron trifluoride etherate appeared to be more effective than triethylamine as the catalyst. The mechanism which involves initial cycloaddition of PO to the C=S bond followed by elimination of propylene sulfide was proposed for the transformation. The reactivities of these thione-compounds were significantly affected by whether they are cyclic or open-chain and by the nature of the α-hetero atoms: the cyclic thione-compounds were more reactive then the open-chain analogs except for a pair of thioureas and the enhancement by the α-hetero atoms was in the order: N,O≈N,N>N,S>S,S. Both observations may be interpreted in terms of basicity of the thione-compounds. These results also support the proposed mechanism for the formation of 2-oxazolidones from 2-substituted imino-1,3-dithiolanes with epoxides in our preceding paper.

In the preceding paper[1] we have reported that 2-substituted imino-1,3-dithiolane (I) reacted with epoxides giving the oxazolidone derivatives (II). The mechanism for the formation of II has been assumed to involve the cycloaddition of epoxide to the C=S bond of the intermediate 1,3-oxazolidine-2-thione (III) followed by elimination of episulfide, as illustrated below.



The transformation, however, of the thione-compound into the one-compound with epoxide is not found in literature. The purpose of the present study is to ascertain the proposed mechanism for the formation of II and to extend this type of reaction to a method for the transformation of the C=S bonds in various thione-compounds into the C=O bonds. Thus, the reactions of a variety of thione-compounds including the oxazolidine-2-thione (III) with epoxides were studied. This paper describes a new method for the transformation of the C=S bond in the thione-compound into the C=O bond and clarifies the scope and limitation of this method.



Results

We investigated open-chain and cyclic thione-compounds containing two α-hetero atoms including *S*-methyl *N,N*-dimethyldithiocarbamate (IV) and a cyclic analog, *N*-methyl-1,3-thiazolidine-2-thione (V) [X, Y = N and S], *O*-methyl *N,N*-dimethylthioncarbamate (VI) and a cyclic analog, *N*-piperidinomethyl-1,3-oxazolidine-2-thione (VII) [X, Y=N and O], dimethyl trithiocarbonate (VIII) and a cyclic analog, 1,3-dithiolane-2-thione (IX) [X, Y=S], and tetramethylthiourea (X) and a cyclic analog, *N,N'*-dimethyl-1,3-imidazolidine-2-thione (XI) [X, Y=N].

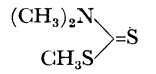
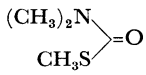
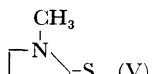
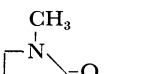
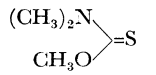
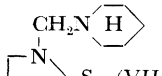
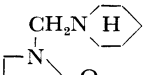
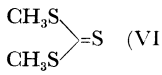
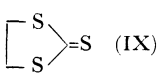
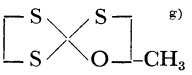
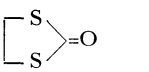
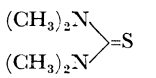
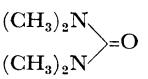
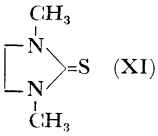
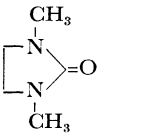
Oxazolidine-2-thione (VII) was prepared in 88% yield by the reaction of oxazolidine-2-thione with formaldehyde and piperidine. Other thione-compounds were either commerically-available materials or prepared by previously-reported methods.

The reaction of the thione-compound with propylene oxide (PO) was carried out in the presence of

*1 Presented at the 22nd Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1969.

1) Y. Ueno, T. Nakai and M. Okawara, This Bulletin, **43**, 162 (1970).

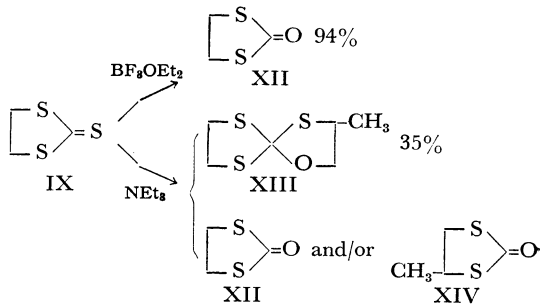
Table 1. Reactions of thione-compounds with PO[a]

	pK_a [b]	Catalyst[c]	Product	Yield, %	$\nu_{C=O}$, cm^{-1}
 (IV)	−3.3	A		30	1650
		B		53	
 (V)	−1.6[d]	A		81	1665
 (VI)		A	e)	0	
 (VII)		A		93[f]	1750
 (VIII)	−5.3	A	e)	0	
 (IX)		A	 [g]	35	
		B		94	1660
 (X)	−1.0	A		91[h]	1630
 (XI)	−2.4	A		60[h,i]	1680

a) The reaction temperature: 170—180°C; time: 6.5 hr.
b) The acidities of the conjugate acids of the thione-compounds reported by M. J. Janssen (see Ref. 4).
c) A=NEt_3; B=BF_3OEt_2.
d) The present work (see Experimental section).
e) The starting material was recovered in 92% and 64% yield for VI and VIII, respectively.
f) The reaction conditions; 130—140°C, 5 hr; based on the picrate.
g) The distillate was contaminated with a small amount of triethylamine and unidentified one-compouunds were also obtained (see the text).
h) The reaction conditions: 150°C, 6.5 hr.
i) The starting material was also recovered in 28% yield.

a small amount of triethylamine or boron trifluoride etherate at 170—180°C in a sealed tube. Products obtained were identified by elemental analyses, spectrometric methods (IR and NMR) and comparison of their physical properties with those of the authentic samples. Results obtained are summarized in Table 1.

In the case of 1,3-dithiolane-2-thione (IX) a great difference in product between BF_3OEt_2 and NEt_3 was observed; the reaction in the presence of BF_3-OEt_2 gave the expected product, 1,3-dithiolane-2-one (XII) in 94% yield, whereas the reaction in the presence of NEt_3 afforded a spirocyclic compound XIII as a major product along with one-



compounds XII and/or XIV.

The spirocyclic compound was identified by

(A) H_2C–S, S–CH_2(B); H_2C–S, O–C–CH_3(D); H(C)

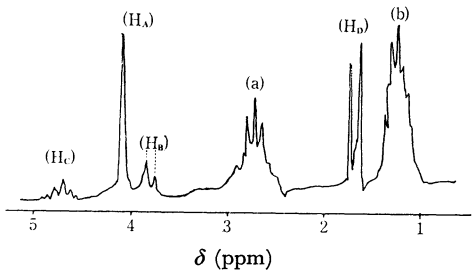


Fig. 1. The NMR spectrum of the spirocyclic compound XIII (CCl_4).
The signals (a) and (b) are due to the protons of the contaminating triethylamine (see the text).

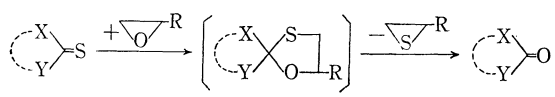
NMR spectrum (Fig. 1) which shows a singlet at δ 4.01 ppm (4H, –S–C<u>H</u>$_2$–C<u>H</u>$_2$–S–), two doublets at 1.67 (3H, –CH–C<u>H</u>$_3$) and 3.75 ppm (2H, –C<u>H</u>$_2$–CH–), a multiplet centered at 4.55 ppm (1H, –CH_2–C<u>H</u>–) and other signals assigned to the protons of the contaminated triethylamine at 1.3 (–CH_2–C<u>H</u>$_3$) and 2.8 ppm (–C<u>H</u>$_2$–CH_3) (the ratio of 3 : 2). The contamination of triethylamine was also observed in the elemental analysis (Found: N, 0.89%). The spirocyclic compound (XIII) is not very stable. After standing at room temperature for three weeks redistillation of XIII gave one-compounds.

In all cases the episulfide eliminated was detected in the distillation trap tube.

Discussion

Examination of structures of products reveals that the thione-compound is converted into the corresponding one-compound. The fact that the oxazolidine-2-thione (VII) can be easily transformed into the 2-oxazolidone supports a possibility of the proposed mecahnism for the formation of the oxazolidone (II) from the reaction of 2-substituted imino-1,3-dithiolane (I) with epoxides.[1] The results suggest that this type of reaction provides a new method for the transformation of the C=S bonds in thione-compounds into the C=O bonds.

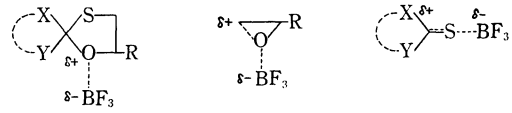
Isolation of the spirocyclic intermediate in the case of IX suggests the cycloaddition-elimination mechanism for the transformation, as illustrated below.



XV

Information on the elimination of episulfide from sulfur containing five-membered heterocycles is available.[2]

Catalytic Effect. As shown in the cases of IV and IX, boron trifluoride etherate appears to be more effective than triethylamine as a catalyst. It should be noted that in the case of IX the one-compound was obtained in the presence of BF_3OEt_2 whereas the spirocyclic intermediate was isolated in the presence of NEt_3. The results may be explained by the fact that BF_3OEt_2 enhances the elimination of episulfide from the oxothiolane (XV) by interaction with the hetero atoms in the ring (XVI) as well as the cycloaddition by interaction with both substrates (XVII and XVIII) while NEt_3 would activate only substrates but not the intermediate.



XVI XVII XVIII

Structural Effects on Reactivities. Examination of yields of products (Table 1), which might be regarded as an approximate measure of the reactivity, indicates that the reactivities of the thione-compounds studied might be significantly affected by whether these compounds are cyclic or open-chain and by the nature of the α-hetero atoms (X and Y); the cyclic thione-compounds are more reactive than the open-chain analogs except for a pair of thioureas and the enhancement by the α-hetero atoms is in the order: N,O≈N,N>N,S>S,S.

It should be noted that the yield of the one-compound appears to be parallel with the basicity (pK_a) of the thione-compound for both an open-chain and cyclic series (Table 1); the correlation was nearly linear. The fact may account for the two structural effects on the reactivities of the thione-compounds described above. The basicity of the thiocarbonyl group would be more enhanced both by the replacement of the α-hetero group (X and Y) with the stronger electron-donating group and the ring-structure. This would be due to the greater delocalization of the positive charge in structure XIX by the greater supply of electron from the α-hetero atoms.

XIX

The fact that the positive charge is more delocalized by ring-closing is in line with our observation

2) R. Feinauer, *Angew. Chem. Int. Ed. Engl*, **5**, 894 (1966).

that 2-dimethylamino-1,3-dithiolanylium ion (XX) is more stabilized than an open-chain analog XXI. This might be explained by the more developed 1,3-overlap in the ring system based upon spectral and kinetical observations.[3]

XX XXI

In comparison with other thione-compounds, it is remarkable that cyclic thiourea XI has lower basicity and less reactivity than the open-chain X. These observations might be explained by steric hindrance to the protonation at the thione-sulfur atom by the N-methyl group arising from the severely restricted rotation around the (S=) C–N bond.[4] Accordingly this effect appears to be very operative in lowering the reactivity of XI toward epoxide.

The results suggest the limitation that only thione-compounds of which pK_a is at least over -5.0 may be transformed into the corresponding one-compounds with epoxides.

Experimental

Melting and boiling points are uncorrected. Infrared and ultraviolet spectra were recorded with Hitachi EPI-S2 and recording EPS-2 spectrometers, respectively. NMR spectra were obtained with a Japan Electron Optics C-100 spectrometer. Chemical shifts are reported in part per million (ppm) from tetramethylsilane as an internal standard.*2

Materials. Propylene oxide (PO) was dried over calcium hydride and then distilled: bp 35°C. Triethylamine was dried over calcium hydride and then distilled: bp 88—89°C. Commercial boron trifluoride etherate was used without purification.

Thione-compounds. The following thione-compounds were either commercially available materials or prepared. *S*-Methyl *N,N*-dimethyldithiocarbamate (IV), mp 46—47°C; dimethyl trithiocarbonate (VIII), bp 85—88°C/5 mmHg; 1,3-dithiolane-2-thione (IX), mp 35—36°C; tetramethylthiourea (X), mp 77—78°C; *N,N'*-dimethyl-1,3-thiazolidine-2-thione (XI), mp 110—112°C.

N-Methylthiazolidine-2-thione(V) was obtained by the thermal ring-isomerization of 2-methylimino-1,3-dithiolane[1]: mp 68—69°C. *O*-Methyl *N,N*-dimethylthioncarbamate (VI) was prepared by the reaction of 2-dimethylamino-1,3-dithiolanylium perchlorate (XX) with sodium methoxide[5]: bp 81—82°C/10 mmHg.

N-Piperidinomethyl-oxazolidine-2-thione (VII) was prepared as follows. Into a stirred solution of 4.4 g (0.05 mol) of oxazolidine-2-thione in 20 m*l* of ethanol was added 7.5 m*l* of 30% formalin. 5 m*l* of piperidine was added drop by drop to the mixture below 10°C. The mixture was stirred at room temperature for 30 min, then at 40—60°C for an additional 30 min. The mixture was cooled in an ice box giving 8.2 g (88%) of precipitates of VII: mp 58—59°C (ethanol).

Found: C, 53.98; H, 8.06; N, 13.99%. Calcd for $C_9H_{16}N_2OS$: C, 53.55; H, 8.07; N, 13.71%.

A General Method for the Reactions of Thione-compounds with Propylene Oxide. The thione-compound (*ca.* 5 g), a slight molar excess of propylene oxide and a small amount of the catalyst were sealed in a hard-glass tube, and heated at 170—180°C for 6.5 hr. After cooling and carefully opening the tube the volatile materials were removed *in vacuo*. Distillation in the reduced pressure or recrystallization from an appropriate solvent of the residue gave the corresponding one-compound.

Reactions of 1,3-Dithiolane-2-thione (IX) with PO. *Triethylamine Catalyst.* 1,3-Dithiolane-2-thione (5.4 g) and PO (3.5 g, 0.05 mol) was heated at 170—180°C for 6.5 hr in the presence of triethylamine (1 m*l*). Distillation of the residue gave two distillates; bp 90—110°C/7 mmHg and bp 132—138°C/4 mmHg (2.7 g). The former showed a carbonyl band at 1650 cm^{-1}, however the latter did not show any absorption bands in the carbonyl region. The latter was a reddish liquid with an unpleasant odor, and was distilled after standing for three weeks giving a small amount of a low-boiling distillate spectrometrically identical with the former. The NMR spectrum (Fig. 1) of the latter confirms the structure and indicates that the distillate was contaminated with triethylamine used as a catalyst.

Found: S, 50.59; N, 0.86%. Calcd for $C_6H_{10}OS$: S, 49.44; N, 0%.

Boron Trifluoride Etherate Catalyst. In the presence of a few drops of BF_3OEt_2 the reaction was carried out under the same conditions. Distillation of the residue gave one distillate of 1,3-dithiolane-2-one (XII) in 94% yield: bp 82—90°C/0.23 mmHg. The distillate was solidified by standing at room temperature: mp 31—32°C (lit,[6] 31°C). The IR spectrum of the product was identical with that of the authentic sample.

Identifications of Products. Products obtained are summarized in Table 1 along with yields and infrared carbonyl bands. Products were identified by elemental analyses, the spectrophotometric methods and comparison of their physical properties with those of the authentic samples as follows.

S-Methyl N,N-dimethylthiolcarbamate: bp 87—89°C/30 mmHg; n_D 1.4938 (21°C) (lit,[7] bp 115—116°C/89 mmHg; n_D 1.4932 (30°C)). This compound was identical with the authentic sample prepared by the reaction of *O*-methyl *N,N*-dimethylthioncarbamate with methyl iodide[8] or by the hydrolysis of bis(methylthio)-dimethylaminocarbonium perchlorate (XXI).[9]

N-Methylthiazolidine-2-one. Bp 85—87°C/0.3 mmHg

3) T. Nakai, Y. Ueno and M. Okawara, Abstracts of papers presented at the 18th Symposium on Organic Reaction Mechanisms, Kyoto, October, 1967, p. 77.

4) M. J. Janssen, *Rec. Trav. Chim. Bays-Bas*, **81**, 650 (1962).

*2 Microanalysis was carried out by Mr. T. Saito.

5) T. Nakai and M. Okawara, *Tetrahedron Lett.*, **1967**, 3835.

6) H. Husemann, *Ann.*, **126**, 269 (1863).

7) H. Tilles, *J. Amer. Chem. Soc.*, **81**, 714 (1959).

8) A. F. Schöberl and A. Wagner, "Houben-Wyle: Methoden der Organischen Chemie," Vol. IX, George Thieme Verlag, Stuttgart (1955), p. 837.

9) T. Nakai, Y. Ueno and M. Okawara, Abstracts of papers presented at the 20th Annual Meeting of the Chemical Society of Japan, April, 1967, p. III-27.

(lit,[10] 84—85°C/0.2 mmHg).

Found: C, 40.66; H, 6.40%. Calcd for C_4H_7NOS: C, 41.02; H, 6.03%.

N-Piperidinomethyl-oxazolidine-2-one. The reaction of VII with PO was carried out at 130—140°C for 5 hr. An oily residue obtained was treated with picric acid giving precipitates of the picrate in 93% yield: mp 154—156°C (ethanol).

Found: C, 43.71; H, 4.79; N, 16.34%. Calcd for $C_{15}H_{19}N_5O_7S$: C, 43.58; H, 4.63; N, 16.94%.

Tetramethylurea. Bp 71—74°C/21 mmHg; n_D 1.4538 (21°C) (lit,[11] bp 63—64°C/12 mmHg; n_D 1.4495 (25°C)).

N,N'-Dimethyl-thiazolidine-2-one. Bp 80—82°C/2 mmHg (lit,[12] 106—108°C/20 mmHg); n_D 1.4770 (18°C).

pK_a Measurement. The value of pK_a of the thione-compound was obtained by the method by Janssen.[4] The molar extinction coefficients (ε) in the UV spectra of *N*-methyl-thiazolidine-2-thione (V) were measured in 98% and 15% sulfuric acid and water. The value of pK_a was calculated from the equation

$$pK_a = H_0 + \log [(\varepsilon_M - \varepsilon_B)/(\varepsilon_{BH} - \varepsilon_M)],$$

where H_0 denotes Hammett's acidity function($H_0 = -0.66$ for 15% sulfuric acid[13]) and ε_B, ε_M and ε_{BH} represent the molar extinction coefficients in water, and 15% and 98% sulfuric acid, respectively. The experimental data for V are shown in Table 2.

Table 2. Measurement of pK_a of V

Wavelength mμ	ε_B	ε_M	ε_{BH}	pK_a
235	3400	3800	9200	−1.8
237	3900	4400	9300	−1.7
240	4700	5400	8800	−1.4
			Aver.	−1.6

10) H. Eilingsfeld and L. Möbius, *Chem. Ber.*, **98**, 1293 (1965).

11) J. K. Lawson, Jr., and J. A. Croom, *J. Org. Chem.*, **28**, 232 (1963).

12) A. B. Jansen and D. J. Stokes, *J. Chem. Soc.*, **1962**, 4909 (1962).

13) M. J. Jorgenson and D. R. Hartter, *J. Amer. Chem. Soc.*, **85**, 878 (1963).