Studies of the Pyrimidine Derivatives. XXV.* The Reaction of Alkoxycarbonylthiocyanates and Related Compounds with the Sodium Salt of Thiamine

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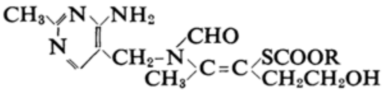
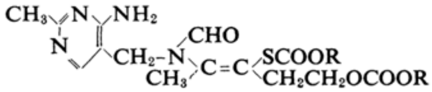
In previous papers of this series,[1,2] the syntheses of many S-alkoxycarbonylthiamine (I) and O, S-bis(alkoxycarbonyl)thiamine (II) derivatives have been reported. It has also been shown that O, S-bis(ethoxycarbonyl)thiamine (DCET) (IIa) has a thiamine activity approximately equivalent to that of thiamine hydrochloride (III) that it is highly absorbed when administered orally, and that the high thiamine level is maintained for a longer time than that of III.[3] In an attempt to obtain a reagent which can introduce the alkoxycarbonyl group into thiamine under mild conditions, the present authors first took up alkoxycarbonylthiocyanate (IV).

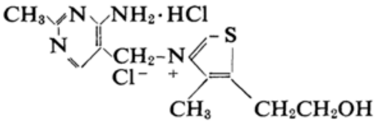
Dixon and Taylor[4] reported that potassium thiocyanate reacted with ethyl chloroformate and with acylchloride in acetone solutions to give ethoxycarbonylisothiocyanate (Va) and acylisothiocyanate (VIII) respectively. We reinvestigated the reaction of ethyl chloroformate with potassium thiocyanate and obtained two oily substances with b. p. 25.5~26.7°C/1.8 mmHg and b. p. 41.2~41.9°C/2.0 mmHg. The elementary analyses of both substances agreed with the formula $C_4H_5O_2SN$, and it was suggested that they were the isomeric each other. The infrared spectrum of the former showed absorptions at 1960~1990 cm^{-1} for the –N=C=S group and at 1750 cm^{-1} (C=O)



(I)



(II) a) $R=C_2H_5$
b) $R=C_4H_9$



(III)

$KSCN + ClCOOR \longrightarrow N{\equiv}C\text{-}S\text{-}COOR + S{=}C{=}N\text{-}COOR$

(IV) a) $R=C_2H_5$ (V) a) $R=C_2H_5$
b) $R=C_4H_9$ b) $R=C_4H_9$

$KSCN + ClCOSC_2H_5$ (VI) $\longrightarrow S{=}C{=}N\text{-}COSC_2H_5$ (VII)

$KSCN + ClCOR \longrightarrow S{=}C{=}N\text{-}COR$

(VIII) a) $R=C_6H_5$
b) $R=CH_3$

$KSCN + ClCOOCH_2CH{=}CH_2$ (IX) $\longrightarrow S{=}C{=}N\text{-}CH_2CH{=}CH_2$ (X) + $S{=}C{=}N\text{-}COOCH_2CH{=}CH_2$ (XI)

$KSCN + BrCH_2CH{=}CH_2 \longrightarrow$ (X)

Chart 1

* Part XXIV of this series: A. Takamizawa, K. Hirai, Y. Hamashima and H. Sato, submitted to *Chem. Pharm. Bull*.

1) A. Takamizawa and K. Hirai, ibid., 10, 1102 (1962).

2) A. Takamizawa, K. Hirai and Y. Hamashima, ibid., 10, 1107 (1962).

3) a) T. Minesita, M. Morita and T. Iwata, *Ann. Rep., Shionogi Research Lab.*, 12, 6 (1962); b) Vitamin B_1, New Deriv. Research Sub-Comm., Japan, *Vitamins*, 25, 516 (1962).

4) A. E. Dixon and J. Taylor, *J. Chem. Soc.*, 93, 684 (1908).

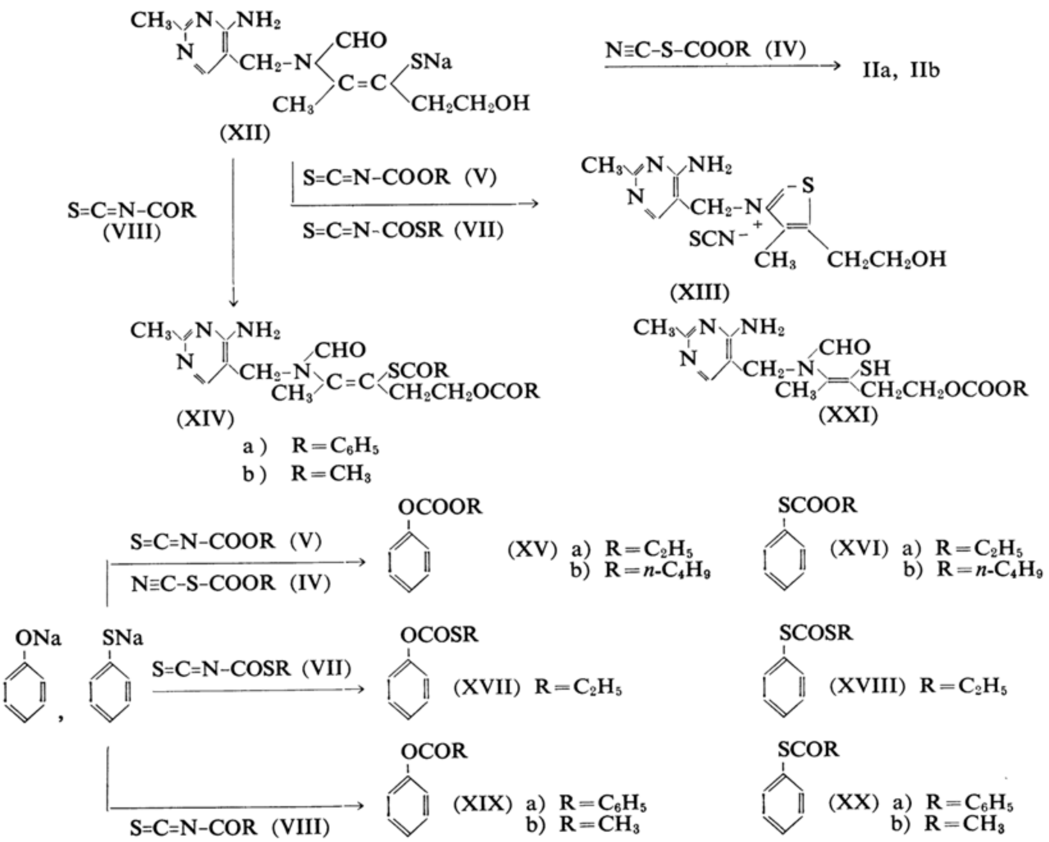


Chart 2

and at $1220\sim1260\ \mathrm{cm}^{-1}$ (C–O) respectively for the $-\mathrm{N}-\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{O}-$ group (Fig. 1). The spectrum of the latter showed the $-\mathrm{C{\equiv}N}$ band at 2190 cm^{-1}, and C=O and C–O bands at $1770\ \mathrm{cm}^{-1}$ and $1140\sim1190\ \mathrm{cm}^{-1}$ respectively for the $-\mathrm{S}-\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{O}-$ group (Fig. 4). From these results, the former should be ethoxycarbonyl isothiocyanate (Va), and the latter, ethoxycarbonylthiocyanate (IVa). These structures were also confirmed by their ultraviolet spectra. Hosoya, Tanaka and Nagakura[5] have shown that the ultraviolet spectrum of thioacetamide has the absorption maximum characteristic of the C=S group at 318 mμ (ε, 60). The ultraviolet spectrum of the former substance (isothiocyanate) showed the absorption maximum at 325 mμ (ε, 61.9). On the other hand, no absorption was found in the latter substance (thiocyanate) (Fig. 5).

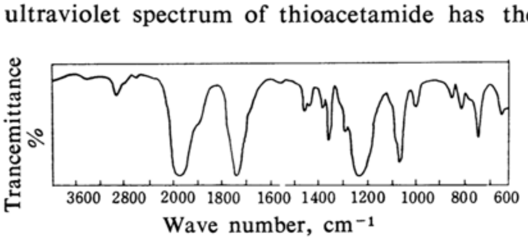


Fig. 1. Infrared spectrum of ethoxycarbonylisothiocyanate (Va). (film)

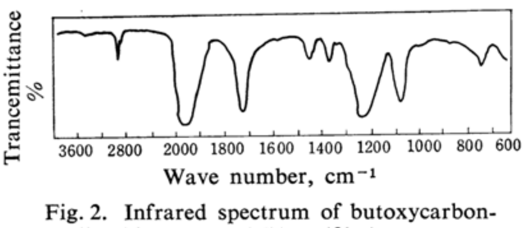


Fig. 2. Infrared spectrum of butoxycarbonylisothiocyanate (Vb). (film)

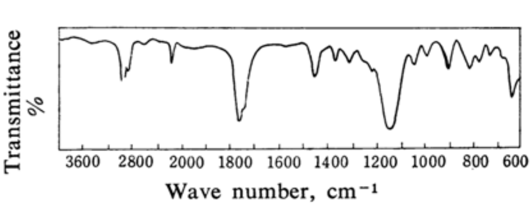


Fig. 3. Infrared spectrum of butoxycarbonylthiocyanate (IVb). (film)

5) H. Hosoya, J. Tanaka and S. Nagakura, This Bulletin, 33, 850 (1960).

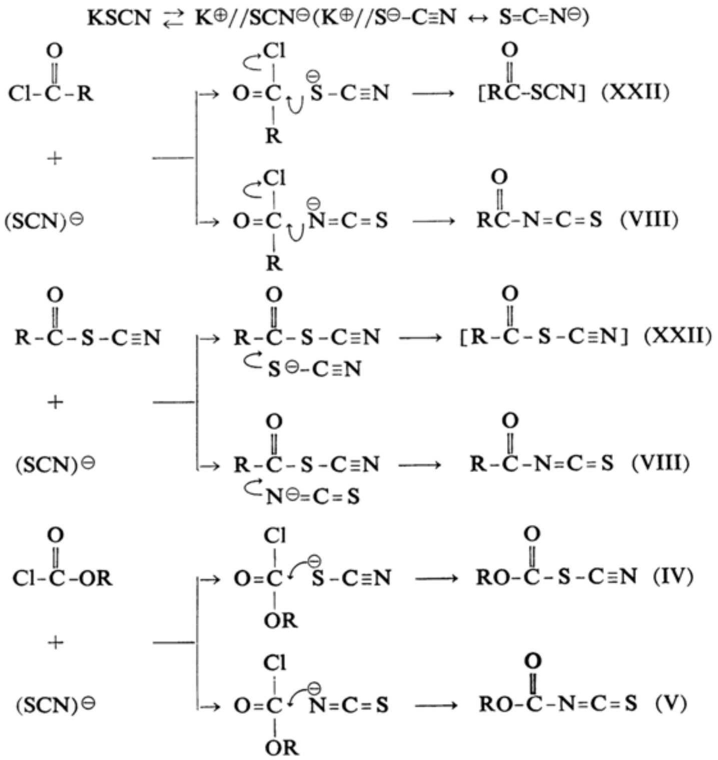


Chart 3

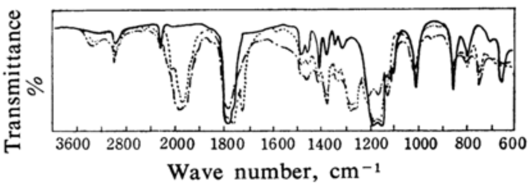


Fig. 4. Infrared spectrum of IVa and its spectral change with the left time in acetone solution in the presence of KSCN.

1. Original IVa (——)
2. After 20 min. at room temperature (------)
3. After 45 min. at room temperature (—·—·)

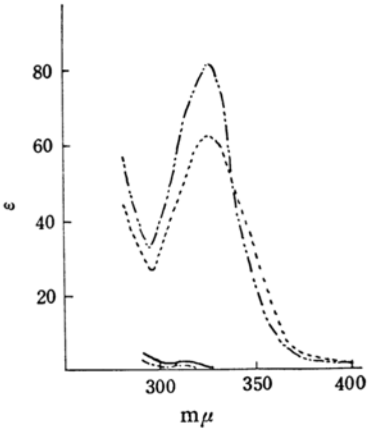


Fig. 5. Ultraviolet spectra of IVa (——), IVb (------), Va (—·—·—) and Vb (··—··—).

As it was interesting that two isomers were obtained in this reaction, investigations on analogous compounds were carried out. The reaction of butyl chloroformate with potassium thiocyanate gave two isomers, buthoxycarbonylthiocyanate (IVb) and butoxycarbonyl isothiocyanate (Vb), whose structures were confirmed by their infrared and ultraviolet spectra. The infrared spectrum of Vb showed the –N=C=S band at 1970~1990 cm^{-1}, the C=O band at 1750 cm^{-1} and the C–O band at 1240~1250 cm^{-1} for the –N–C(=O)–O– group (Fig. 2), while that of IVb showed the –C≡N band at 2190 cm^{-1}, the C=O band at 1765 cm^{-1} and the C–O band at 1155~1165 cm^{-1} for the –S–C(=O)–O– group (Fig. 3). Moreover, although the ultraviolet spectrum of Vb exhibited the absorption maximum at 323 mμ (ε, 81) no maximum was observed with IVb (Fig. 5).

Further, the reaction of potassium thiocyanate with thioethoxycarbonylchloride (VI) gave only one product, the isothiocyanate (VII). Similarly, benzoylchloride and acetylchloride did not give the thiocyanates, but only the respective isothiocyanates, VIIIa[4,6] and VIIIb[4]. Their structures were confirmed by infrared

6) J. C. Ambelang and T. B. Johnson, *J. Am. Chem. Soc.*, **61**, 632 (1939).

TABLE I. PRODUCTS OBTAINED FROM THE REACTION OF RCl WITH KSCN

RCl	Product	Yield, %	B. p., °C/mmHg	UV λ_{max}^{EtOH} mμ (ε)
$ClCOOC_2H_5$	$S=C=N-COOC_2H_5$	30	25.5∼26.7/1.8	325 (61.9)
	$N\equiv C-S-COOC_2H_5$	30	41.2∼41.9/2.0	
$ClCOOC_4H_9$	$S=C=N-COOC_4H_9$	34	59.0∼61.0/6.0	323 (81.8)
	$N\equiv C-S-COOC_4H_9$	21	54.0∼55.5/2.0	
$ClCOSC_2H_5$	$S=C=N-COSC_2H_5$	61	50.0∼50.5/3.0	328 (94.7)
	$N\equiv C-S-COSC_2H_5$	0		
$ClCOC_6H_5$	$S=C=N-COC_6H_5$	76	102∼103 /4.8	340 (133)
	$N\equiv C-S-COC_6H_5$	0		
$ClCOCH_3$	$S=C=N-COCH_3$	20	39.5∼40.5/21	333 (53.2)
	$N\equiv C-S-COCH_3$	0		
$ClCOOCH_2-CH=CH_2$	$S=C=N-CH_2CH=CH_2$	30.9	38.0∼40.8/8.0	
	$S=C=N-COOCH_2-CH=CH_2$	3.5	40.8∼50.5/7.0	325 (69.6)

TABLE II. REACTION PRODUCTS AND YIELDS

Reagent	Thiamine sodium salt		C_6H_5ONa		C_6H_5SNa	
	Product	Yield, %	Product	Yield, %	Product	Yield, %
$N\equiv C-S-COOC_2H_5$	DCET	26	$C_6H_5OCOOC_2H_5$	42	$C_6H_5SCOOC_2H_5$	52
$S=C=N-COOC_2H_5$	B_1-SCN	trace	$C_6H_5OCOOC_2H_5$	24	$C_6H_5SCOOC_2H_5$	33
$N\equiv C-S-COOC_4H_9$	IIb	21	$C_6H_5OCOOC_4H_9$	51	$C_6H_5SCOOC_4H_9$	64
$S=C=N-COOC_4H_9$	B_1-SCN	trace	$C_6H_5OCOOC_4H_9$	31	$C_6H_5SCOOC_4H_9$	47
$S=C=N-COSC_2H_5$	B_1-SCN	trace	$C_6H_5OCOSC_2H_5$	39	$C_6H_5SCOSC_2H_5$	38
$S=C=N-COCH_3$	DAT	34	$C_6H_5OCOCH_3$	42	$C_6H_5SCOCH_3$	50
$S=C=N-COC_6H_5$	DBT	26	$C_6H_5OCOC_6H_5$	56	$C_6H_5SCOC_6H_5$	60

TABLE III. BOILING POINTS AND ELEMENTAL ANALYSES OF THE PRODUCTS

	B. p., °C/mmHg (m. p., °C)	Formula	Analysis % Calcd. C	Calcd. H	Found C	Found H
$C_6H_5OCOOC_2H_5$	56∼57/2	$C_9H_{10}O_3$	65.05	6.07	65.18	6.12
$C_6H_5OCOOC_4H_9$	95∼96/2	$C_{11}H_{14}O_3$	68.02	7.63	68.57	7.34
$C_6H_5OCOSC_2H_5$	80∼85/3	$C_9H_{10}O_2S$	59.86	5.53	59.21	5.56
$C_6H_5OCOCH_3$	83∼84/14	$C_8H_8O_2$	70.57	5.92	71.04	6.29
$C_6H_5OCOC_6H_5$	(68.5∼70.5)	$C_{13}H_{10}O_2$	78.77	5.09	78.66	5.05
$C_6H_5SCOOC_2H_5$	93∼95/5	$C_9H_{10}O_2S$	59.31	5.53	58.96	5.69
$C_6H_5SCOOC_4H_9$	109∼109.5/4	$C_{11}H_{14}O_2S$	62.82	6.71	63.60	7.06
$C_6H_5SCOSC_2H_5$	100∼101/2	$C_9H_{10}OS_2$	54.51	5.08	54.47	5.25
$C_6H_5SCOCH_3$	76∼77/3	C_8H_8OS	63.12	5.23	62.98	5.41
$C_6H_5SCOC_6H_5$	(54)	$C_{13}H_{10}OS$	72.86	4.70	72.38	4.72

and ultraviolet spectra. When allyl chloroformate (IX) was used, however, besides a small amount of allyloxycarbonyl isothiocyanate (XI), allylisothiocyanate (X) was afforded, along with decarboxylation. X was identified by the infrared spectra of the product obtained by the reaction of allyl bromide with potassium thiocyanate in dimethylformamide.[7] These results are listed in Table I.

Next, the behaviors of these thiocyanate and isothiocyanate derivatives in relation to the sodium salt of thiamine (XII) were investigated. The reaction of alkoxycarbonylthiocyanate (IV) with thiamine sodium salt (XII) produced *O,S*-bis(alkoxycarbonyl)thiamine (II). However, when alkoxycarbonyl isothiocyanate (V) was used, a small amount of thiamine thiocyanate (XIII) was obtained as the only product. On the other hand, benzoylisothiocyanate (VIIIa) and acetylisothiocyanate (VIIIb) gave *O, S*-dibenzoylthiamine (XIVa)[8,9] and *O, S*-diacetylthiamine (XIVb)[8] respectively.

Analogously, IV or V reacted with simple phenol and thiophenol to give alkoxycarbonyl phenol (XV) and alkoxycarbonylthiophenol (XVI) respectively. Similarly, thioalkoxy carbonyl isothiocyanate (VII) gave thioalkoxycarbonyl phenol (XVII) or thioalkoxycarbonyl

7) S. Yoneda, H, Kitano and K. Fukui, *J. Chem. Soc. Japan, Ind. Chem. Soc.* (*Kogyo Kagaku Zasshi*), **65**, 1816 (1962).

8) T. Matsukawa and H. Kawasaki, *J. Pharm. Soc.* (*Yakugaku Zasshi*), **73**, 705, 709 (1953).

9) S. Yoshida, ibid., **74**, 993 (1954).

thiophenol (XVIII), and acylisothiocyanate (VIII) gave acylphenol (XIX) or acylthiophenol (XX). From these facts, it became clear that these thiocyanate or isothiocyanate derivatives can be used for alkoxycarbonylation or acylation reactions. These results are summarized in Table II.

Acyl- or alkoxycarbonylphenol and thiophenol are obtained in better yields than diacyl- and bis(alkoxycarbonyl)-thiamine respectively, possibly because phenol and thiophenol are much more reactive than the thiol-type thiamine. Thiocyanates gave a better yield than isothiocyanates. From Table II, the power of acylation and alkoxycarbonylation may tentatively ranked as follows:

$$\text{RCOCl} \geq (\text{RCOSCN}) > \text{ROCOCl} \geq \text{RCONCS} \geq \text{ROCOSCN} > \text{ROCONCS}$$

In the reaction with thiamine, it was noticed that IV, having reactive carbonyl, could react with thiamine, which has a relatively weak activity, and that at the first step, *S*-alkoxycarbonylthiamine (I) was formed and then a S→O rearrangement of the alkoxycarbonyl group occurred to give *O*-alkoxycarbonylthiamine (XXI) in the presence of alkali. The SH group of (XXI) was further alkoxycarbonylated to yield *O*, *S*-bis(alkoxycarbonyl)thiamine (II).[2)]

While V seemed to have no carbonyl reactive enough to interact with the SH group of thiamine, VIII was much more active and reacted with XII to give *O*, *S*-diacylthiamine (XIV).

When a 2.5 molar equivalent of alkyl chloroformate was used in the reaction with potassium thiocyanate, IV and V were given in ratio of 1 : 1; this ratio was not changed by the increase of the mole of alkyl chloroformate. When an equimolar equivalent of alkyl chloroformate was used, however, V was given predominantly. Ethoxycarbonylthiocyanate (IVa) was thermally stable and did not change upon being boiled in ethanol in the presence of acetic acid. When a small amount of potassium thiocyanate or potassium acetate was added, however, IVa was readily converted into Va, even at room temperature. This conversion was traced by the infrared spectrum of this reaction mixture. As is shown in Fig. 4, the N=C=S and $\text{N–}\underset{\text{O}}{\underset{\parallel}{\text{C}}}\text{–O}$ bands increased with the decrease in the C≡N and $\text{S–}\underset{\text{O}}{\underset{\parallel}{\text{C}}}\text{–O}$ bands. It was considered that IV would convert into V by the reaction with potassium thiocyanate.

The mechanism of these reactions may be explained as follows: In an acetone solution the thiocyanato ion takes the form of an ion pair, and the S site or N site of this ion attacks the carbonyl carbon of acylchloride to give acylthiocyanate (XXII) and acyl isothiocyanate (VIII) as the respective transient products. Since XXII was considered to be the powerful acylation agent, however, it reacted with the thiocyanato ion to yield the stable acylisothiocyanate (VIII).

In the same manner, the reaction between the thiocyanato ion and alkyl chloroformate gives alkoxycarbonylthiocyanate (IV) and isothiocyanate (V). However, as the activity of IV is considerably weaker, the excess of alkyl chloroformate consumes the thiocyanato ion and IV is not able to participate in the reaction with the thiocyanato ion. As a result, IV and V are isolated in the reaction mixture.

Experimental

Ethoxycarbonylthiocyanate (IVa) and Ethoxycarbonylisothiocyanate (Va).—Into a solution of 244 g. (2.5 mol.) of potassium thiocyanate in 2.5 l. of acetone was added 633 g. (5.75 mol.) of ethyl chloroformate dropwise with stirring at room temperature. After the solution had been stirred for 4 hr. at room temperature, the separating potassium chloride was filterd off and the filtrate was concentrated. Distillation of the residue yielded 200.5 g. of the liquid with a b. p. of 43~58°/6.0 mmHg. The fractional distillation of this liquid (119.1 g.) gave 32.1 g. of IVa and 26.5 g. of Va.

IVa; b. p. 25.5~26.7°C/1.8 mmHg. $n_D^{25.3}$ 1.4930.

Found: C, 36.79; H, 4.06; N, 10.40; S, 24.07. Calcd. for $C_4H_5O_2NS$: C, 36.63; H, 3.84; N, 10.68; S, 25.21%.

Va: b. p. 41.2~41.9°C/2.0 mmHg.*1 $n_D^{25.3}$ 1.4570.

Found: C, 36.86; H, 4.33; N, 10.13. Calcd. for $C_4H_5O_2NS$: C, 36.63; H, 3.84; N, 10.68%. λ_{max}^{EtOH} 325 mμ (ε, 61.9).

Butoxycarbonylthiocyanate (IVb) and Butoxycarbonylisothiocyanate (Vb).—To a solution of 9.8 g. (0.1 mol.) of potassium thiocyanate in 100 cc. of acetone 27.2 g. (0.2 mol.) of butyl chloroformate was added dropwise. Treating it as above gave 8.7 g. of the liquid with a b. p. of 38~74°C/4~5 mmHg. The fractional distillation of this liquid (35 g.) gave 10 g. of VIb and 6.0 g. of Vb.

IVb: b. p. 54.0~55.5°C/2.0 mmHg. $n_D^{24.5}$ 1.4545.

Found: C, 44.87; H, 5.96; N, 8.66. Calcd. for $C_5H_9O_2SN$: C, 45.25; H, 5.69; N, 8.79%.

Vb: b. p. 59.0~61.0°C/6.0 mmHg. $n_D^{24.5}$ 1.4820.

Found: C, 46.18; H, 6.22; N, 8.82. Calcd. for $C_5H_9O_2SN$: C, 45.25: H, 5.69; N, 8.79%. λ_{max}^{EtOH} 323 mμ (ε, 81).

Thioethoxycarbonyl Isothiocyanate (VII).—To a solution of 14.6 g. (0.15 mol.) of potassium thiocyanate in 150 cc. of acetone 37.4 g. (0.3 mol.) of thioethoxycarbonyl chloride was added dropwise. Treatment as above gave 9.0 g. (61.2%) of (VII); b. p. 50.0~50.5°C/3.0 mmHg. $n_D^{23.5}$ 1.5788. IR ν_{max}^{film}

*1 Ref. 4: b. p. 83°C/30 mmHg.

1930~1970 (-N=C=S), 1685 (C=O) cm^{-1}. UV: 328 mμ (ε, 94.7).

Found: C, 33.17; H, 3.60; N, 9.59; S, 43.27. Calcd. for $C_4H_5OS_2N$: C, 32.63; H, 3.42; N, 9.52; S, 43.56%.

Benzoylisothiocyanate (VIIIa).—This was obtained from 9.7 g. (0.1 mol.) of potassium thiocyanate in 100 cc. of acetone and 28.0 g. (0.2 mol.) of benzoyl chloride after treating them as described above. Yield, 12.4 g. (75.6%). B. p., 102~103°C/4.8 mmHg.*2 IR ν_{max}^{film} 1930~1970 (-N=C=S), 1690 (C=O) cm^{-1}. UV: λ_{max}^{EtOH} 340 mμ (ε, 133).

Found: C, 59.04; H, 3.21; N, 8.43; S, 19.23. Calcd. for C_8H_5ONS: C, 58.81; H, 3.09; N, 8.58; S, 19.65%.

Acetylisothiocyanate (VIIIb).—This was obtained from 9.7 g. (0.1 mol.) of potassium thiocyanate in 100 cc. of acetone and 15.7 g. (0.2 mol.) of acetyl chloride after treating them as described above. Yield, 2.0 g. (19.8%). B. p. 39.5~40.5°C/21 mmHg.*3 $n_D^{23.5}$ 1.5190. IR ν_{max}^{film}: 1950~1980 (-N=C=S), 1725 (C=O) cm^{-1}. UV: λ_{max}^{EtOH} 333 mμ (ε, 53.2).

Found: C, 36.92; H, 3.43; N, 12.66; S, 29.91. Calcd. for C_3H_3ONS: C, 35.63; H, 2.99; N, 13.85; S, 31.71%.

Allylisothiocyanate (X) and Allyloxyisothiocyanate (XI).—To a solution of 14.7 g. (0.15 mol.) of potassium thiocyanate in 150 cc. of acetone 36.2 g. (0.3 mol.) of allyl chloroformate was added dropwise and the mixture was treated as above. Fractional distillation of the yielded product gave 4.6 g. (30.9%) of X and 0.77 g. (3.5%) of XI.

X: b. p. 38~40.8°C/8 mmHg.*4

Found: C, 48.52; H, 5.28; N, 13.48. Calcd. for C_4H_5NS: C, 48.44; H, 5.08; N, 14.12%.

It was identified with the product obtained by the method of Yoneda et al.[7] by infrared spectra.

XI: b. p. 48.5~50.5°C/7 mmHg. IR ν_{max}^{film}; 1960~1990 (-N=C=S), 1750 (C=O), 1220~1250 (C-O-C) cm^{-1}. UV: λ_{max}^{EtOH} 325 mμ (ε, 69.6).

Found: C, 42.87; H, 3.81; N, 9.57. Calcd. for $C_5H_5O_2NS$: C, 41.95; H, 3.52; N, 9.78%.

***O,S*-Bis(ethoxycarbonyl)thiamine (IIa) Hydrochloride.**—Into the suspension of 3.6 g. (0.01 mol.) of the sodium salt of thiamine[10] (XII) in *n*-propyl alcohol was added 3.3 g. (0.025 mol.) of IVa dropwise with stirring. During this reaction, the reaction mixture was maintained at pH 8.8~9.0 by the addition of alcoholic sodium ethoxide. After stirring for 2 hr. at room temperature, *n*-propyl alcohol was removed by vacuum distillation. Residue was dissolved in 20% hydrochloric acid and after being washed with ether, extracted with chloroform thoroughly. This chloroform extract was dried over anhydrous magnesium sulfate, and the chloroform was removed. The sirup obtained was induced to crystallize by treating it with ether and then recrystallized from the mixture of ethyl acetate and ethanol to give 1.26 g. (26.2%) of IIa hydrochloride in the form of colorless prisms m.p. 121~123°C. This product was identified with an authentic sample of IIa hydrochloride[1] by infrared spectra.

***O,S*-Bis(butoxycarbonyl)thiamine (IIb) Hydrochloride.**—This was prepared from 3.6 g. (0.01 mol.) of the sodium salt of thiamine (XII) in EtOH and 3.2 g. (0.02 mol.) of IVb as described above. The yield of IIb hydrochloride was 1.1 g. (21.2%); m. p. 86~88°C. The infrared spectrum of this product was identical with that of an authentic sample of IIb hydrochloride.[2]

Thiamine Thiocyanate (XIII).—This compound was obtained in a trace amount from XII by the reaction of either Va, Vb, or VII after treating it as above. It was then recrystallized from water to give colorless prisms, m. p. 180~181°C (decomp.). The infrared spectrum of this product was identical with that of an authentic sample of XIII.

***O,S*-Dibenzoylthiamine (DBT) (XIVa).**—To a suspension of 2.8 g. (0.06 mol.) of XII in ethanol 2.5 g. (0.15 mol.) of VIIIa was added dropwise as described above for the preparation of II. After the removal of ethanol, the residue was dissolved in ethyl acetate and washed with water and a diluted sodium hydroxide aqueous solution. After being dried over anhydrous magnesium sulfate, ethyl acetate was removed to give colorless crystals. Recrystallization from diluted ethanol gave 0.98 g. (25.5%) of colorless prisms; m. p. 172°C. The infrared spectrum was identical with that of the sample obtained by the other method.[8,9]

Found: C, 63.58; H, 5.43; N, 11.24; S, 6.62. Calcd. for $C_{26}H_{26}O_4N_4S$: C, 63.65; H, 5.34; N, 11.42%.

***O,S*-Diacetylthiamine (DAT) (XIVb).**—To a suspension of 3.9 g. (0.11 mol.) of XII in ethanol 2.2 g. (0.22 mol.) of VIIIb was added dropwise as described above for the preparation of II. After the removal of ethanol, the residue was dissolved in water and extracted with benzene. This benzene extract was shaken with 3% acetic acid, and the acetic acid layer was thoroughly extracted with chloroform. The chloroform extract was dried over anhydrous magnesium sulfate, and the chloroform was removed. The residual sirup was treated with ether to give colorless crystals; yield 1.35 g. (34.0%). Recrystallization from benzene-petroleum benzine gave colorless prisms (m. p. 118~119.5°C), whose infrared spectrum was identical with that of the sample obtained by the other method[8].

Found: C, 52.44; H, 6.12; N, 15.00. Calcd. for $C_{16}H_{22}O_4N_4S$: C, 52.44; H, 6.05; N, 15.29%.

The Acylation and Alkoxycarbonylation of Phenol and Thiophenol.—To a suspension of 0.03 mol. of dry sodium salt of phenol or thiophenol in ethanol 0.03 mol. of various alkoxycarbonylthiocyanates, isothiocyanates or acylisothiocyanates were added. After the mixture had been stirred for 2 hr. at room temperature, the ethanol was removed ether was added to the residue, and the separated sodium thiocyanate was filtered off. The esher solution fractionally distilled.

The Infrared Spectral Change of Ethoxycarbonyl Thiocyanate (IVa) in the Presence of

*2 Ref. 4: b. p. 119°C/10 mmHg.
*3 Ref. 4: b. p. 30~32°C/9~10 mmHg.
*4 Ref. 7: b. p. 151~152°C.

10) O. Zima and R. R. Williams, *Ber.*, 73, 941 (1940).

Potassium Thiocyanate.—To a solution of 2.3 g. (0.0175 mol.) of IVa in acetone 0.34 g. (0.0035 mol.) of potassium thiocyanate was added and the mixture was stirred at room temperature. After 20 min. and 45 min., a part of the reaction mixture was taken up, the acetone was removed, and the infrared spectrum of the residual oil was taken. The results are shown in Fig. 4.

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