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Thiocyanoacetate. I. Reactions of Thiocyanoacetic Esters with Aldehydes[1]

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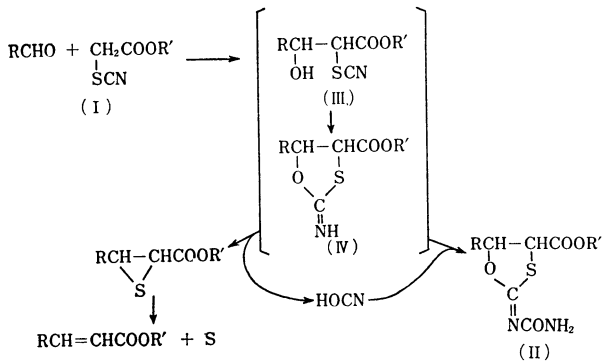
Thiocyanoacetic esters (I) and aldehydes reacted in the presence of potassium fluoride or carbonate to give α,β-unsaturated ester as a major product and an unexpected solid product (II) as a minor one, which was determined to be *N*-carbamoyl-2-imino-5-substituted 1,3-oxathiolane-4-carboxylic esters.

The thiocyanato group which is often referred to as "pseudohalogen," is strongly electron-attractive. The thiocyanoacetic esters (I) would thus be expected to have an active methylene group.[3] I is structurally similar to chloroacetic and cyanoacetic esters, which easily react with carbonyl compounds. However, little is known so far about the reactions of **I** with carbonyl compounds. This might be ascribed to the fact that the thiocyanato group is extremely sensitive to the bases usually used as a catalyst, giving cyclization compounds[4] or resinous matters. However, if a suitable catalyst is found, I is expected to react with carbonyl compounds. The purpose of this investigation is to find the possibility of I as an active methylene compound.



Scheme 1

Results and Discussion

Equimolecular reactions of thiocyanoacetic ester (I) with an aldehyde in the presence of potassium fluoride or carbonate were carried out in moist ether at low temperatures. The reaction consistently gave liquid products as major ones, and an unexpected, solid product (II) as a minor one and elemental sulfur. Glpc analysis and NMR spectra showed that the liquid products contain a stereoisomeric mixture of *cis*- and *trans*- α,β-unsaturated esters and two other components which could not be identified. In the case of the

1) Presented in part at the 22nd Annual Meeting of the Chemical Society of Japan, Tokyo, April 2nd, 1969.
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3) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y. (1955), p. 55.
4) Unpublished Results.

TABLE 1. PROPERTIES OF THE PRODUCTS

Compound	R	R	Mp °C[a]	Yield % b)	Yield % c)	Formula	Analysis % Found (Calcd) C	H	N	S
IIa	C_6H_5	C_2H_5	190—191	18	42	$C_{13}H_{14}O_4N_2S$	52.42 (53.06)	4.87 (4.76)	9.50 (9.52)	10.88 (10.88)
IIb	C_6H_5	CH_3	188—189	13	26	$C_{12}H_{12}O_4N_2S$	53.46 (53.43)	4.21 (4.14)	9.63 (9.59)	11.04 (10.94)
IIc	*p*-$CH_3OC_6H_4$	C_2H_5	179—180	17	31	$C_{14}H_{16}O_5N_2S$	51.97 (51.85)	4.95 (4.97)	8.66 (8.64)	9.82 (9.86)
IId	*p*-$CH_3OC_6H_4$	CH_3	161—162	14	29	$C_{13}H_{14}O_5N_2S$	50.43 (50.35)	4.58 (4.55)	9.07 (9.03)	10.11 (10.31)
IIe	CH_3	C_2H_5	128—129	13	27	$C_8H_{12}O_4N_2S$	41.37 (41.37)	5.19 (5.17)	12.02 (12.06)	13.81 (13.79)
IIf	C_2H_5	C_2H_5	147—148	15	32	$C_9H_{14}O_4N_2S$	43.82 (43.90)	5.60 (5.69)	11.49 (11.39)	13.02 (13.00)
IIg	*n*-C_3H_7	C_2H_5	176—177	12	20	$C_{10}H_{16}O_4N_2S$	46.80 (46.15)	5.97 (6.15)	10.78 (10.76)	12.06 (12.30)
IIh	*iso*-C_3H_7	C_2H_5	149—150	9	13	$C_{10}H_{16}O_4N_2S$	46.00 (46.15)	6.26 (6.15)	10.81 (10.76)	12.23 (12.30)
IIi	*n*-C_4H_5	C_2H_5	218—219	8	10	$C_{11}H_{18}O_4N_2S$	48.00 (48.17)	6.59 (6.62)	10.25 (10.21)	11.60 (11.58)

a) All melting points are uncorrected.
b) Potassium fluoride was used as a catalyst.
c) Potassium carbonate was used as a catalyst.

TABLE 2. IR DATA OF PRODUCT II (cm^{-1})

Compd	NH stretching				C=O stretching		C=N and carbamoyl C=O stretching		NH deformation
a	3300m		3180m		1743s		1681s		1575s
b	3320m	3290m	3220m	3190m	1752s	1737s	1680s	1660m	1580s
c	3450m	3390m	3242m	3200m	1748s		1687s	1620m	1587s
d	3300m		3190m		1748s		1688s	1620m	1587s
e	3450m	3370m	3280m	3200m	1737sh	1730s	1680s	1645m	1586s
f	3360m	3290m	3240m	3200m	1738sh	1731s	1678s		1573s
g	3300m		3180m		1724s		1676s	1615m	1578s
h	3420m		3200m		1743s		1676s	1630m	1570s
i	3310m		3180m		1740s		1680s		1580s

All spectra were measured in KBr pellets.

TABLE 3. NMR DATA OF PRODUCT II (ppm downfield from TMS)

Compd	H_α[a]	H_β[a]	J	COOR		NH_2		Other signals	
a	4.83	5.97	6.3	0.72[b]	3.96[c]	7.02	7.30	7.40[d]	
b	4.87	5.97	6.3	3.25[e]		7.04	7.30	7.40[d]	
c	4.76	5.89	6.3	0.78[b]	3.75[c]	not located		3.75[f]	
d	4.76	5.88	6.3	3.28[e]		not located		3.74[f]	
e	4.41	4.95	6.0	1.19[b]	4.14[c]	6.93	7.16	1.37[g]	
f	4.40	4.88	6.0	1.21[b]	4.15[c]	6.91	7.16	1.78[g]	
g	4.44	4.70	6.0	1.20[b]	4.15[c]	6.93	7.16	0.93[g]	1.64[h]
h	4.45	4.74	6.0	1.20[b]	4.15[c]	6.93	7.18	0.94[g]	near 2.00[i]
i	4.45	4.77	6.0	1.20[b]	4.16[c]	6.90	7.15	0.93[g]	1.60[h]
j[j]	4.46	4.78	6.0	3.80[e]		6.75	6.93	0.95[g]	1.64[h]
e[l]	4.20	4.88	6.3	1.29[b]	4.24[c]	5.75		1.56[g]	

All spectra were measured in DMSO-d_6 solution.
a) The proton on α-position to ester group is denoted by H_α, and that on β-position by H_β.
b) Methyl protons of the ethoxy carbonyl group.
c) Methylene protons of the ethoxy carbonyl group.
d) Aromatic protons.
e) Methyl protons of the methoxycarbonyl group.
f) Methoxyl protons.
g) Methyl group.
h) Methylene group.
i) Methine group.
j) Methyl *N*-carbamoyl-2-imino-1,3-oxathiolane-5-ethyl-4-carboxylate.
l) Measured in a $CDCl_3$ solution.

reaction between ethyl thiocyanoacetate and benzaldehyde, the liquid products were found to be only a mixture of *cis*- and *trans*-cinnamic esters (*cis*:*trans*= 25:75).

The structural elucidation of the solid product (II) is based on elemental analysis, spectral studies, and chemical reactivity. Product (IIa), for example, was white needles having a structural formula $C_{13}H_{14}N_2O_4S$, *m/e* 294, and mp 190—191°C. All the solid product (II) obtained have the general formula $RC_4H_5N_2O_2COOR'$ which corresponds formally to an addition compound between β-substituted β-hydroxy

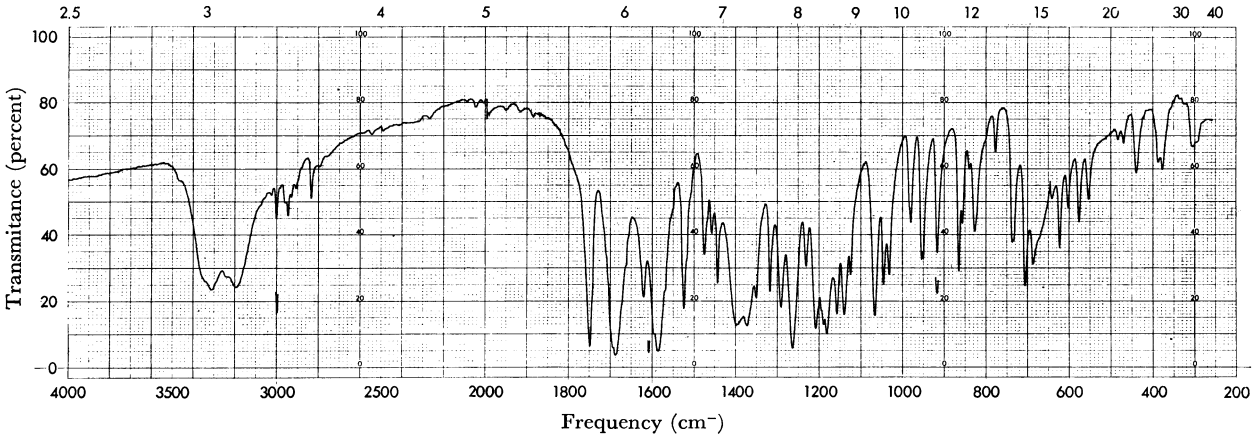


Fig. 1. IR spectrum of IIc (KBr pellet).

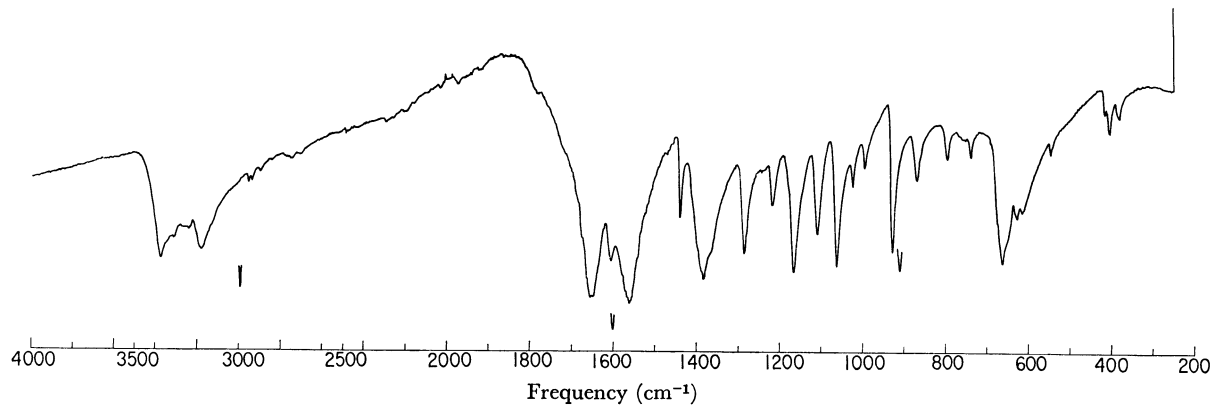


Fig. 2. IR spectrum of *N*-carbamoyl-2-imino-1,3-oxathiolane.

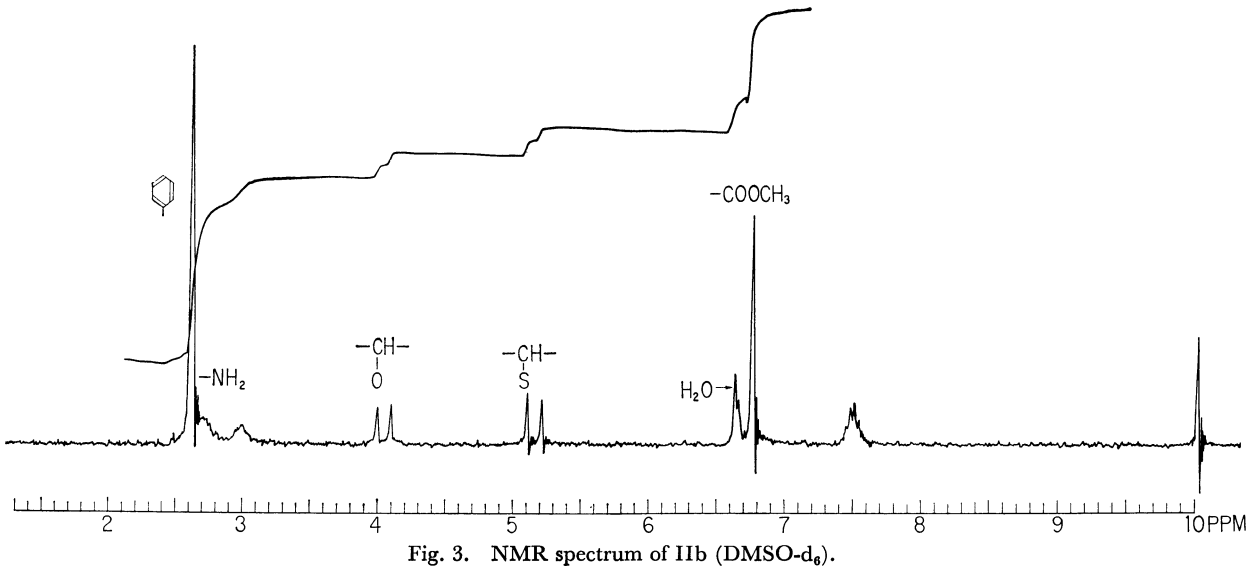


Fig. 3. NMR spectrum of IIb (DMSO-d_6).

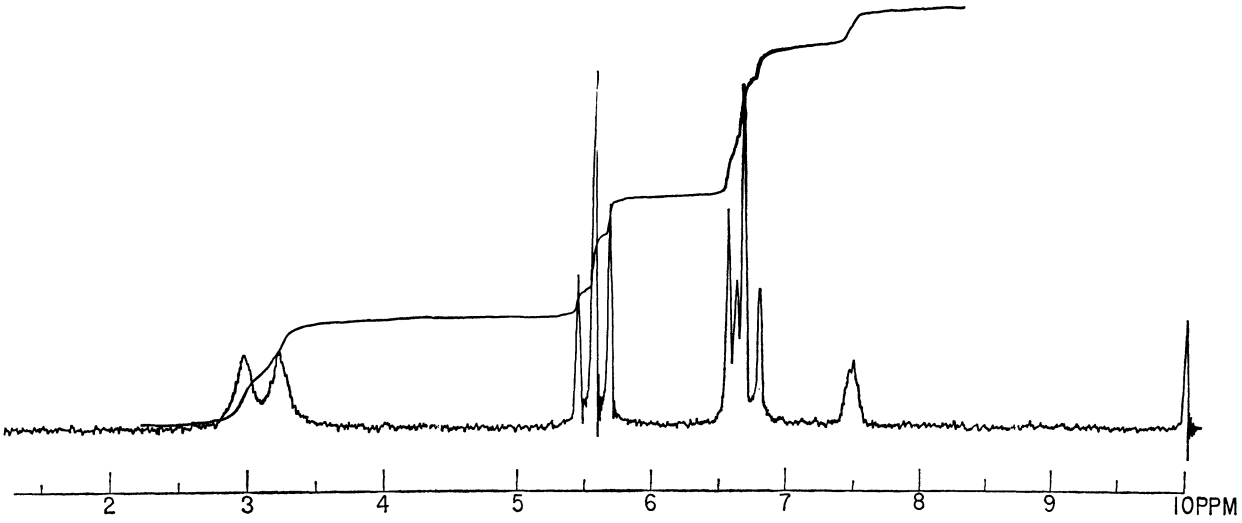


Fig. 4. NMR spectrum of *N*-carbamoyl-2-imino-1,3-oxathiolane (DMSO-d_6).

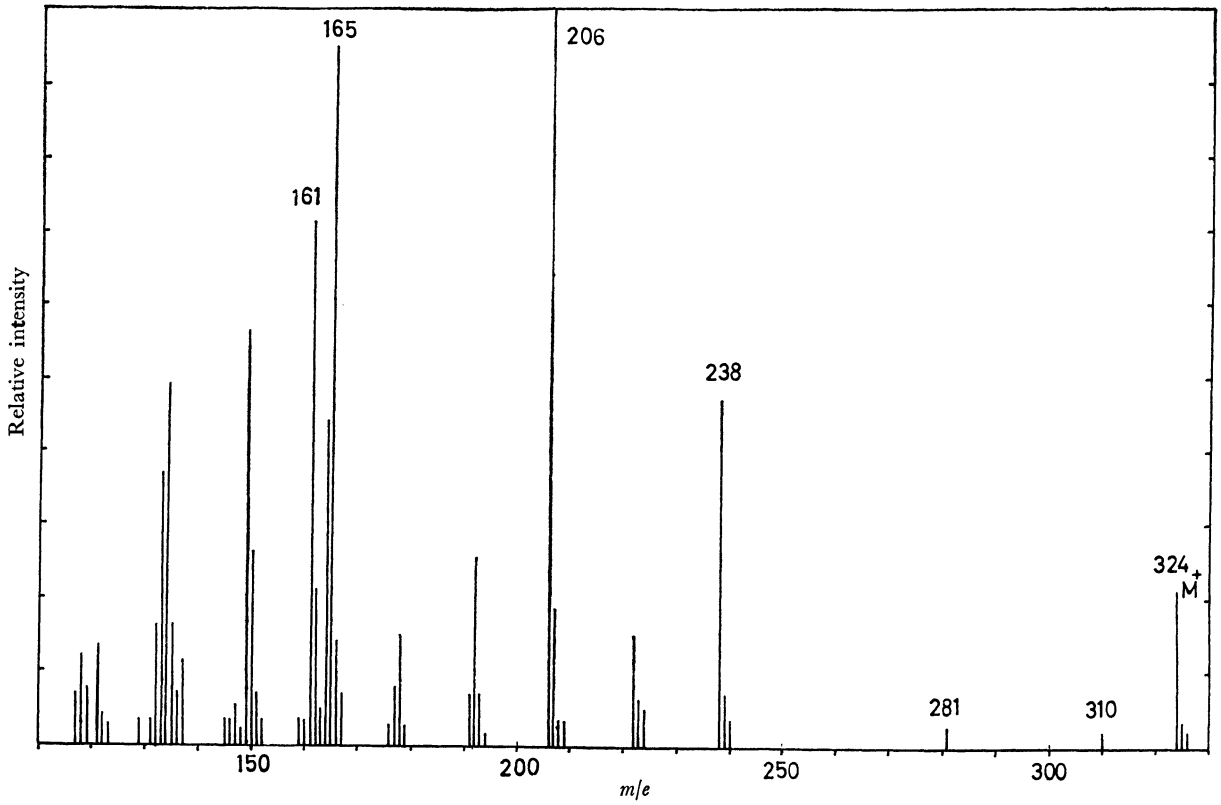


Fig. 5. Mass spectrum of IIc.

α-thiocyano-propionic ester (III) and cyanic acid. II, when treated with ethanol solution of sodium hyroxide, gives rise to α,β-unsaturated ester. We see from Table 2 that the IR spectra of II (KBr pellet) exhibit broad stretching bands in the range 3450—3180 cm^{-1}, the ester C=O band near 1740 cm^{-1}, and the C=N and carbamoyl C=O bands in the range 1688—1615 cm^{-1}. As shown in Figs. 1 and 2, the spectra in the region between 1700 and 1550 cm^{-1} are very similar in position and shape to those of *N*-carbamoyl-2-imino-1,3-oxathiolane. The NMR spectra of II (DMSO-d_6) also revealed that the signals of the NH_2 protons in II are similar in position and shape to those of the carbamoyl NH_2 protons in *N*-carbamoyl-2-imino-1,3-oxathiolane (Figs. 3 and 4). The doublet of the NH_2 protons near 7.00 ppm in a DMSO-d_6 solution coalesces into one broad signal near 5.75 ppm in a $CDCl_3$ solution (Table 3). However, the reason why the NH_2 signal splits into doublet in a DMSO-d_6 solution, could not be elucidated. The mass spectra of II also suggested the presence of *N*-carbamoyl-2-imino-1,3-oxathiolane system (Figs. 5

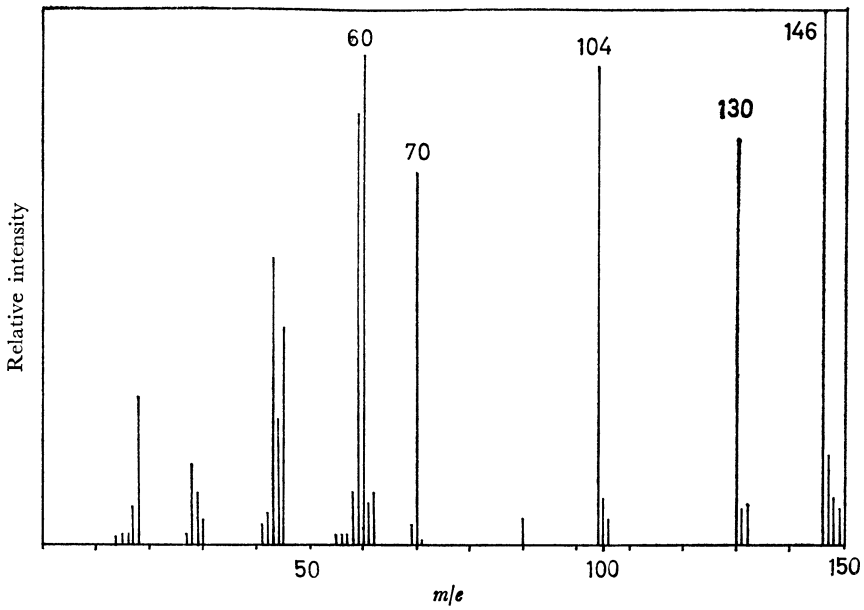
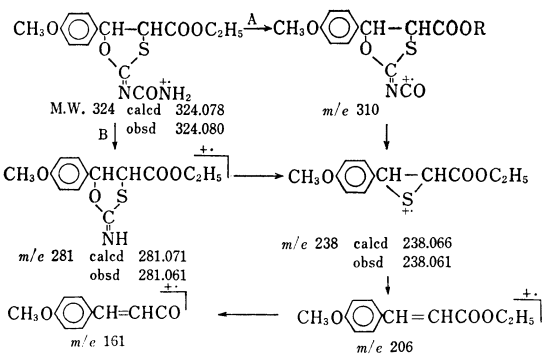
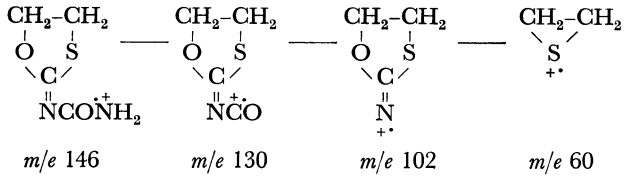


Fig. 6. Mass spectrum of *N*-carbamoyl-2-imino-1,3-oxathiolane.



Scheme 2



Scheme 3

and 6, and Scheme 2). Although the fragmentation of II proceeds in two ways A and B as shown in Scheme 3, route A is similar to the fragmentation of the oxathiolane. We have determined the structure of II to be *N*-carbamoyl-2-imino-5-substituted 1,3-oxathiolane-4-carboxylic ester.

A plausible reaction pathway is postulated in Scheme 1. Wagner-Jauregg *et al.*[5] and Price and Kirk[6] found that 2-thio-cyanoethanols are slowly converted into thiirane and *N*-carbamoyl-2-imino-1,3-oxathiolane at room temperature. Intermediate III which is produced initially from I and aldehyde, would be converted into II and thioglycidic ester by the same mechanism. Owen *et al.*[7] reported that the thioglycidic esters are unstable and lose sulfur, forming unsaturated esters. The reason why II is obtained as a minor product might be ascribed to slowness of reaction by which liberated cyanic acid is added to III, because II once formed is stable against potassium carbonate in ether.

NMR spectra suggest that II obtained in the present work is all in the same configuration. However, without isolation of any isomeric form, the configuration cannot be determined by means of NMR technique.

Experimental

NMR spectra were obtained on a JNM-C-60 high-resolution NMR spectrometer at temperatures 19—20°C. Tetramethylsilane was used as an internal reference standard. IR spectra were determined in the KBr pellet using a Perkin-Elmer 521 spectrophotometer. Mass spectra were measured with a JMS-01S instrument operating at 75 eV.

Reaction of Thiocyanoacetic Ester (I) with Aldehyde. General Procedure. Thiocyanoacetic ester (0.05 mol) was added dropwise below 10°C to a mechanically stirred solution of potassium carbonate or fluoride (0.05 mol) and aldehyde (0.05 mol) in 20 m*l* of moist ether. Stirring was continued for 10 hr, and the solution was allowed to stand overnight. The catalyst was removed by filtration, and the precipitated solid product was collected on a filter, washed with a small amount of water and then dried. Repeated recrystallization yielded pure *N*-carbamoyl-2-imino-5-substituted 1,3-oxathiolane-4-carboxylic ester (II). The filtrate was subjected to Glpc analysis.

Conversion of IIa into Ethyl Cinnamate. A solution which contained 1.0 g of IIa and 1.0 g of sodium hydroxide in 15 m*l* of ethanol was refluxed for an hour. After ethanol was removed with a vacuum evaporator, the remaining liquid was subjected to glpc and NMR analysis.

5) Th. Wagner-Jauregg, *Ann. Chem.*, **561**, 87 (1949): H. D. Hogelsang, Th. Wagner-Jauregg, and R. Rebling, *ibid.*, **569**, 183 (1950); Th. Wagner-Jauregg and M. Maring, *Helv. Chim. Acta*, **41**, 377 (1958).

6) C. C. Price and P. F. Kirk, *J. Amer. Chem. Soc.*, **75**, 2396 (1953).

7) T. C. Owen, C. L. Gladys, and L. Field, *J. Chem. Soc.*, **1962**, 656.