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Studies on Geometrical Isomerism by Nulear Magnetic Resonance. V.[1] Stereochemistry of 5-Substituted 4-Alkoxycarbonyl-2-carbamoylimino-1,3-oxathiolanes[2]

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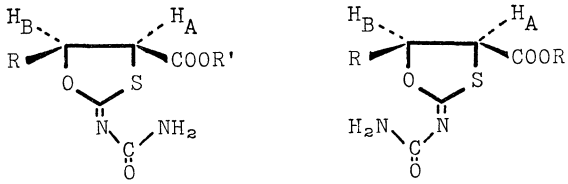
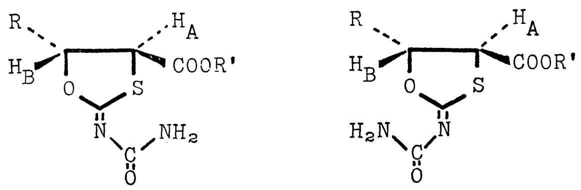
An equimolar reaction of thiocyanoacetic esters with aldehydes in the presence of potassium fluoride or carbonate leads to a stereoisomeric mixture of *cis* and *trans* isomers of 5-substituted 4-alkoxycarbonyl-2-carbamoylimino-1,3-oxathiolanes. Several of them were separated into two isomeric forms, whose geometrical configurations were determined by means of nuclear magnetic resonance technique. The vicinal coupling constant between the 4- and 5-protons is consistently larger for the *cis* forms than for the *trans*. In the case of the 5-aryl derivatives, the signals of the alkoxycarbonyl group appear at higher field for the *cis* isomers than for the *trans*. The composition ratios of *cis* and *trans* isomers of the oxathiolanes prepared are determined. Infrared data of the *cis* and *trans* oxathiolanes are also reported.

In a previous paper[3] we reported that the reaction of thiocyanoacetic esters (**1**) with aldehydes in the presence of potassium fluoride or carbonate, led to a mixture of 5-substituted 4-alkoxycarbonyl-2-carbamoylimino-1,3-oxathiolanes (**2**) and α,β-unsaturated esters. These oxathiolanes can exist in four isomeric forms, relative to arrangements of the alkoxycarbonyl group and 5-substituent about a single bond in the ring as well as to arrangement of the carbamoyl group about the C–N bond. In the course of study, it has been found that the oxathiolanes prepared in the present work consisted of *cis* and *trans* isomers, some of them being separated into two isomeric forms.[4] The present paper deals with configurational determinations of *cis* and *trans* isomers of the 1,3-oxathiolane derivatives by means of the nuclear magnetic resonance technique.



cis forms



trans forms

Results and Discussion

An equimolar reaction of methyl thiocyanoacetate (**1a**) with benzaldehyde in the presence of potassium carbonate, on standing overnight after removal of the catalyst, gave rise to predominant precipitation of the higher-melting isomer, mp 190—191°C (**6*α***).[5] The reaction mixture, on further standing, gradually deposited the lower-melting isomer, mp 138—139°C (**6*β***). The *cis* and *trans* isomers of the corresponding ethyl esters (**7*α*** and **7*β***) were isolated similarly. The isomers showed essentially the same mass spectra. With the corresponding *t*-butyl ester only one form, mp 155—156°C (**8*β***) was isolated pure.[6] The reaction of **1** with *p*-anisaldehyde, and *p*-chloro- and *p*-bromo-benzaldehydes gave exclusively one isomer. The physical properties of the oxathiolanes are summarized in Table 1. The NMR data for the *cis* and

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[1] Part IV: T. Hayashi, I. Hori, H. Baba, and H. Midorikawa, This Bulletin, **40**, 2160 (1967).

[2] Presented in part at the 23rd Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1970.

[3] S. Kambe, T. Hayashi, H. Yasuda, and H. Midorikawa, This Bulletin, **44**, 1357 (1971).

[4] Geometrical isomers of several imines were first isolated by Curtin and Hausser.[4a] This was the first unequivocal demonstration of the existence of stereoisomeric compounds in which a carbon atom was bonded to the imino nitrogen. Later, Marullo and Wagner[4b] showed that the isomerization rates of iminocarbonates were so fast that the stereoisomers could not be isolated. However, it was also shown that the isomerization rates are very sensitive to the group on the imino nitrogen. At present we prefer the explanation that the observed separation of the NH_2 signals in the 2-carbamoylimino-1,3-oxathiolanes (Figs. 2 and 3) is due to the existence of *syn* and *anti* isomers, and that the isomerization rates are too fast for isolation. This problem is now under investigation. a) D. Y. Curtin and J. W. Hausser, *J. Amer. Chem. Soc.*, **83**, 3474 (1961); b) N. P. Marullo and E. H. Wagner, *ibid.*, **88**, 5034 (1966).

[5] The higher-melting isomers are denoted as α, and the lower-melting isomer, β. In the case where only one isomer was obtained, the isomer having the alkoxycarbonyl signals at higher field than those of the ordinary esters is denoted by C, while the isomer having the alkoxycarbonyl at almost the same field as the ordinary esters is denoted by T. Form C has *cis* configuration, and form T, *trans*.

[6] The yield of the α-form was too low for purification. However, the stereoisomeric mixture which contained the α-form predominantly had a melting point higher than the β-form.

TABLE 1. PHYSICAL PROPERTIES OF *N*-CARBAMOYL-2-IMINO-4-ALKOXYCARBONYL-5-SUBSTITUTED 1,3-OXATHIOLANES

Compound			Form	Mp (°C)	Formula	Calcd				Found			
						C%	H%	N%	S%	C%	H%	N%	S%
6	C_6H_5	CH_3	α	190—191	$C_{12}H_{12}N_2O_4S$	51.46	4.21	10.63	11.04	51.58	4.35	10.91	11.35
			β	138—139	$C_{12}H_{12}N_2O_4S$	51.46	4.21	10.63	11.04	51.38	4.31	10.14	11.33
7	C_6H_5	C_2H_5	α	190—191	$C_{13}H_{14}N_2O_4S$	53.06	4.80	9.52	10.87	53.42	4.87	9.50	10.88
			β	159—160	$C_{13}H_{14}N_2O_4S$	53.06	4.80	9.52	10.87	53.48	4.62	9.54	10.87
8	C_6H_5	*t*-Bu	β	155—156	$C_{15}H_{18}N_2O_4S$	55.88	5.63	8.69	9.95	55.81	5.67	8.62	9.58
9	*p*-$CH_3OC_6H_4$	CH_3	C	161—162	$C_{13}H_{14}N_2O_5S$	50.35	4.55	9.03	10.31	50.43	4.58	9.07	10.11
10	*p*-$CH_3OC_6H_4$	C_2H_5	C	179—180	$C_{14}H_{16}N_2O_5S$	51.85	4.97	8.64	9.86	51.97	4.95	8.66	9.82
11	*o*-$CH_3OC_6H_4$	C_2H_5	T	197—198	$C_{14}H_{16}N_2O_5S$	51.85	4.97	8.64	9.86	51.83	4.99	8.64	9.89
12	*p*-ClC_6H_4	C_2H_5	T	174—175	$C_{13}H_{13}N_2O_4SCl$	47.50	3.99	8.56	9.74[a)]	47.48	3.98	5.56	9.76
13	*o*-ClC_6H_4	CH_3	C	189—191	$C_{12}H_{11}N_2O_4SCl$	45.79	3.52	8.90	10.19[b)]	45.68	3.51	8.84	10.27
14	*p*-BrC_6H_4	C_2H_5	T	176	$C_{13}H_{13}N_2O_4SBr$	41.83	3.51	7.51	8.59[c)]	41.81	3.51	7.53	8.63
15	*p*-$N{\equiv}CC_6H_4$	C_2H_5	α+β[d)]	175—179	$C_{14}H_{13}N_3O_4S$	52.66	4.10	13.16	10.02	52.61	4.10	13.23	9.79
16	CH_3	CH_3	α+β[d)]	140—141	$C_7H_{10}N_2O_4S$	38.53	4.62	12.84	14.67	38.74	4.52	12.89	14.69
17	C_2H_5	CH_3	T	145—146	$C_8H_{12}N_2O_4S$	41.38	5.21	12.07	13.78	41.35	5.20	12.11	13.81
18	C_2H_5	C_2H_5	T	150—151	$C_9H_{14}N_2O_4S$	43.90	5.73	11.38	13.00	43.80	5.74	11.33	12.92
19	*i*-C_3H_7	CH_3	α+β[d)]	147—150	$C_9H_{14}N_2O_4S$	43.90	5.73	11.38	13.00	43.73	5.71	11.54	12.99

a) Calcd: Cl, 10.79. Found: Cl, 10.69. b) Calcd: Cl, 11.27. Found: Cl, 11.12. c) Calcd: Br, 21.41. Found: Br, 21.49.
d) A stereoisomeric mixture of *cis* and *trans* isomers.

TABLE 2. NMR DATA OF *N*-CARBAMOYL-2-IMINO-4-ALKOXYCARBONYL-5-SUBSTITUTED 1,3-OXATHIOLANES (ppm from TMS) IN CD_3SOCD_3 SOLUTIONS

Compound	Configuration		H_A	Δ_c^t [a)]	H_B	Δ_c^t [a)]	J_{AB}(Hz)	COOR′			Δ_c^t [a)]	NH_2	
								CH_3	Δ_c^t [a)]	CH_2			
6	C[b)]	(α)	4.83	−0.14	5.98	0.11	6.2±0.1	3.25	0.48			7.04	7.32
	T[c)]	(β)	4.69		6.09		3.9±0.1	3.73				7.05	7.30
7	C	(α)	4.83	−0.17	5.98	0.07	6.2±0.1	0.72	0.46	3.70	0.46	7.03	7.30
	T	(β)	4.66		6.05		3.9±0.1	1.18		1.18		7.03	7.30
8	C	(α)	4.76	−0.18	5.95	0.01	6.4±0.1	0.99	0.42			7.00	7.30
	T	(β)	4.58		5.96		5.6±0.1	1.41				7.00	7.30
9	C		4.76		5.88		6.2±0.1	3.28				not located	
	T												
10	C		4.76		5.89		6.2±0.1	0.78		3.75		not located	
	T												
11	C	(α)	4.79	−0.10	6.00	0.22	6.1±0.1	0.72	0.53	3.70	0.55	not located	
	T	(β)	4.69		6.22		3.8±0.1	1.25		4.25		not located	
12	C												
	T		4.74		6.13		4.5±0.1	1.23		4.23		7.10	7.35
13	C	(α)	4.79	−0.20	6.00	0.20	6.1±0.1	0.70	0.52	3.65	0.55	not located	
	T	(β)	4.59		6.20		3.8±0.1	1.22		4.20		not located	
14	C												
	T		4.71		6.09		4.4±0.1	1.23		4.21		7.05	7.33
15	C	(α)	4.97	−0.21	6.10	0.14	6.4±0.1	0.76	0.47	3.76	0.46	7.12	7.38
	T	(β)	4.76		6.24		3.8±0.1	1.23		4.22		7.12	7.38
16	C	(α)	4.50	−0.12	4.88	0.23	6.2±0.1	3.72	0.00			6.90	7.14
	T	(β)	4.38		5.11		3.9±0.1	3.72				6.90	7.14
17	C												
	T		4.43		4.94		3.6±0.1	3.74				6.91	7.16
18	C												
	T		4.45		4.95		3.9±0.1	1.22		4.21		6.95	7.20
19	C		4.90	−0.49	4.30	0.47	6.2±0.1	3.71	0.03			6.91	7.15
	T		4.41		4.77		3.9±0.1	3.74				6.91	7.15

a) A differential shift between *trans* and *cis* isomers. b) *Cis* isomer. c) *Trans* isomer.

trans isomers of the oxathiolanes are summarized in Table 2. Assignments of two doublets responsible for the 4- and 5-protons were made by double irradiation technique. Of the doublets of the AB spin system the lines of the doublet at lower field are somewhat broader than those at higher field (Figs. 2 and 3). Irradiation of the benzene protons causes narrowing of the proton α (designated as H_B) to the irradiated group. Such coupling between aromatic and benzylic protons have been observed before in other classes of compounds.[7] The NH_2 signals of the carbamoyl group always appear at two positions, near 7.00 ppm and near 7.30 ppm, which might be due to the presence of *syn* and *anti* isomers.[4]

It can be seen from the Table that there is no clear relation between the electronegativities of the substituent on the benzene ring and the chemical shifts and vicinal coupling constants of the oxathiolane ring protons. The observed coupling constants (J_{AB}) are in the range 6.0—6.4 Hz for the α-forms and 3.6—4.5 Hz for the β-forms, except for the *t*-butyl ester. It is a common assumption that in five-membered rings which cannot deviate appreciably from planarity, J_{cis} is always larger than J_{trans}[8] as expected from the Karplus rule.[9] However, several reports showed that in the absence of other information such conclusion were doubtful.[10] The Dreiding model indicates that the 1,3-oxathiolane ring should exist predominantly as a very slightly distorted envelope conformation with the oxygen as the "flap" atom. Recently X-ray diffraction studies[11] showed that in the crystal structure of cholest-4-one-3-spiro(2,5-oxathiolane) the oxathiolane ring exists in a slightly distorted envelope conformation with the methylene carbon adjacent to oxygen lying 0.5 Å out of the plane defined by the other four atoms and with a torsional angle of 34.3° between the two carbon atoms. Pasto and coworkers[12] and Bovey and coworkers[13] indicated from analysis of coupling constants for a series of 2-substituted 1,3-oxathiolanes that there is one highly preferred envelope conformation, but the latter concluded that rapid pseudorotation takes place. However, it was shown from an X-ray diffraction study of the structure of ethylene carbonate which is the oxygen analog of 2-imino-1,3-oxathiolane that the molecule has the half-chair C_2 conformation,[14] though 1,3-dioxolane which is the oxygen analog of 1,3-oxathiolane, possesses a slightly distorted envelope conformation.[15] Accordingly, it seems to be difficult to infer from available data the conformation of 2-carbamoylimino-1,3-oxathiolanes. Hence, in the present case the relative values of the coupling constants cannot be considered a reliable indication of the configuration of substituents.

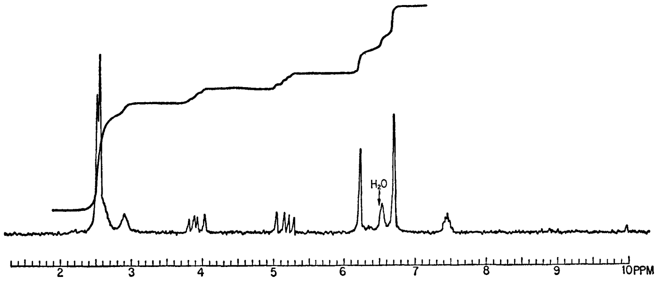

Fig. 1. NMR spectrum of a stereoisomeric mixture of *cis*- and *trans* isomers of *N*-carbamoyl-2-imino-4-methoxycarbonyl-5-phenyl-1,3-oxathiolane (**6**) (60 MHz).

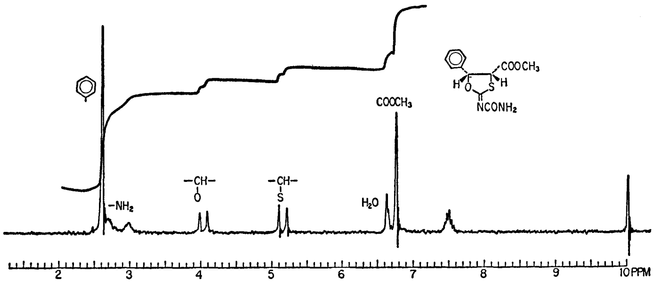

Fig. 2. NMR spectrum of *cis* isomer (**6α**) (60 MHz).

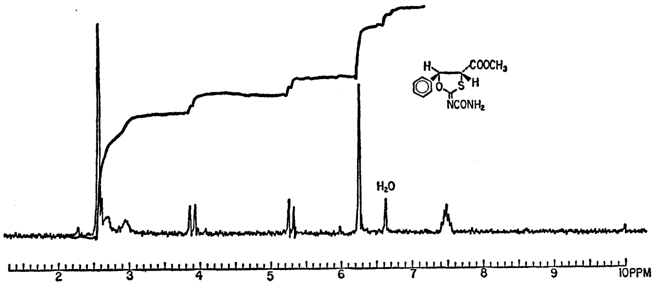

Fig. 3. NMR spectrum of *trans* isomer (**6β**) (60 MHz).

It is interesting to note that with the 5-aryl derivatives the signals of the alkoxycarbonyl groups for the α-forms always appear at a higher field by *ca.* 0.5 ppm than those for the β-forms, while the signals for the β-forms are in almost the same positions as those for the derivatives not having the aryl group (near 3.72 ppm for the methyl and near 1.22 and 4.15 ppm for the ethyl signals). This means that[8] the alkoxycarbonyl protons of the α-forms may experience the long-range shielding of the benzene ring. It should be noted that the H_A proton of the β-form resonates at higher field than that of the α-form, whereas the H_B proton of the former is located at lower field than

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7) a) G. P. Newsoroff and S. Sternhell, *Aust. J. Chem.*, **21**, 747 (1968); b) H. Rottendorf and S. Sternhell, *ibid.*, **17**, 1315 (1964); c) G. Ceccarelli, G. Berti, G. Lippi, and B. Macchia, *Organic Magnetic Resonance*, **2**, 379 (1970).

8) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd Ed., Pergamon Press, New York, N. Y. (1969), p. 288.

9) M. Karplus, *J. Amer. Chem. Soc.*, **85**, 2870 (1963).

10) a) F. A. L. Anet and J. M. Muchowski, *Chem. Ind.* (London), **1963**, 81; b) L. H. Zalkow and M. Ghosal, *Chem. Commun.*, **1967**, 922.

11) A. Cooper and D. A. Norton, *J. Org. Chem.*, **33**, 3535 (1968).

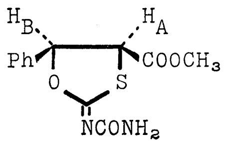
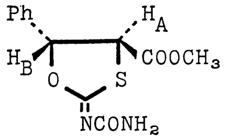
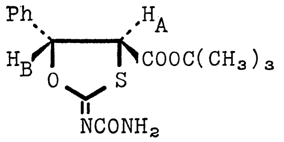
12) D. J. Pasto, F. M. Klein, and T. W. Doyle, *J. Amer. Chem. Soc.*, **89**, 4368 (1967).

13) G. E. Wilson, Jr., M. G. Huang, and F. A. Bovey, *ibid.*, **92**, 5907 (1970).

14) C. J. Brown, *Acta Crystallogr.*, **7**, 92 (1954).

15) S. Furberg and O. Hassel, *Acta Chem. Scand.*, **4**, 1584 (1950).

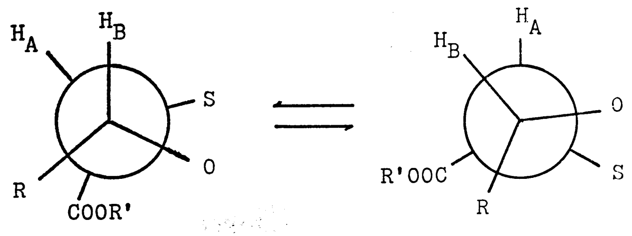
TABLE 3. OBSERVED NOE AND INTERNUCLEAR DISTANCE FOR H-H INTERACTION

No.	Steucture	Proton irradiated	Proton observed	NOE (%)	Internuclear distance (Å)
6α		H_B	H_A	28	2.3—2.5
		H_A	H_B	19	
6β		H_B	H_A	7	2.7—3.1
		H_A	H_B	8	
8β		H_B	H_A	14	2.7—3.1
		H_A	H_B	11	

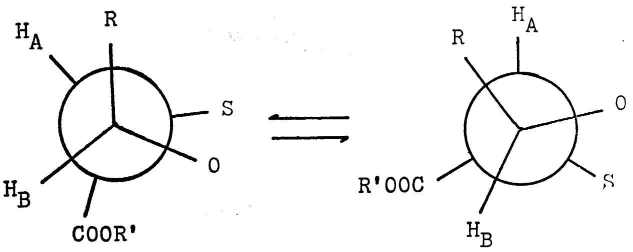
that of the latter. These differential shifts of the ring protons can be attributed to the long-range shielding of the benzene and alkoxycarbonyl groups.[16] The above facts suggest that the higher-melting α-forms possess the *cis* configuration, the lower-melting β-forms the *trans* arrangement.[17,18]

Conclusive evidence supporting these stereochemical assignments can be provided through studies of the nuclear Overhauser effect (NOE). The NOE results obtained when irradiating and observing protons are shown in Table 3, along with the internuclear distance as measured from Dreiding models on the assumptions of the slightly distorted envelope conformation in which rapid pseudorotation occurs. Recetly, Bell and Saunders[19] have shown that there is a linear relationship between the intramolecular nuclear Overhauser effect and the sixth power of the internuclear distance. Table 3 shows that the internuclear distance between the 4- and 5-protons is much shorter for the *cis* form than for the *trans*. Thus, a larger NOE would be expected for the α-form than for the β-form. The results are in good agreement with expectations.

On the assumptions of pseudorotation, one would expect that the molecule would assume the two limiting conformations **2α** and **2α'** for the *cis* isomer and **2β** and **2β'** for the *trans* one, whether in an envelope conformation or in a half-chair C_2 one. In the *cis* forms, the difference in energy between the two conformations should not be large, because there is no 1 ; 3 diaxial interaction. However, in the *trans* forms, electrostatic repulsion between the two substituents may be larger in **2β'** than in **2β**. Since there is no 1 ; 3 diaxial interaction, conformation **2β** may be preferred to conformation **2β'**. This argument could explain the fact that J_{AB} is larger for the *cis* than for the *trans* isomer. However, since the introduction of the bulkier substituent into the 4- or 5-position should lead to an increase in population of **2β**, the *trans* isomer of *t*-butyl ester (**8β**) might be more heavily populated in **2β** than those of methyl and ethyl esters. This speculation leads to a contradiction to the fact that **8β** has an unusually larger J_{AB}, as compared with **6β** and **7β**. A plausible explanation for this is that the C=NCONH$_2$ group on the 2-position exerts some



2α 2α'



2β 2β'

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[16] Similar arguments have been made before in the case of cinnamic ester derivatives,[16a] 4,5-diphenyl-1,3-dioxolan-2-one,[16b] and 4,5-diphenyl-1,3-dithiolane-2-thione.[16b]; a) T. Hayashi, *J. Org. Chem.*, **31**, 3253 (1966); b) C. G. Overberger and A. Drucker, *ibid.*, **29**, 360 (1964).

[17] Form C has *cis* configuration, form T, *trans*.

[18] In the case of 1,3-dioxolanes[16b),18)] and 1,3-dithiolane-2-thiones, the *cis* isomers always have melting points higher than the *trans*; F. A. L. Anet, *J. Amer. Chem. Soc.*, **84**, 747 (1962).

[19] R. A. Bell and J. K. Saunders, *Can. J. Chem.*, **48**, 1114 (1970).

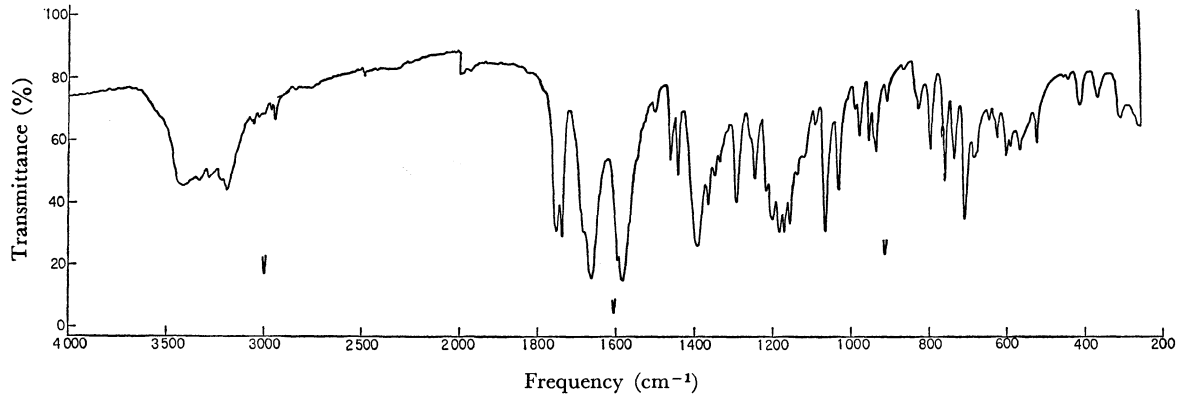

Fig. 4. IR spectrum of *cis*-*N*-carbamoyl-2-imino-4-methoxycarbonyl-5-phenyl-1,3-oxathiolane (**6α**).

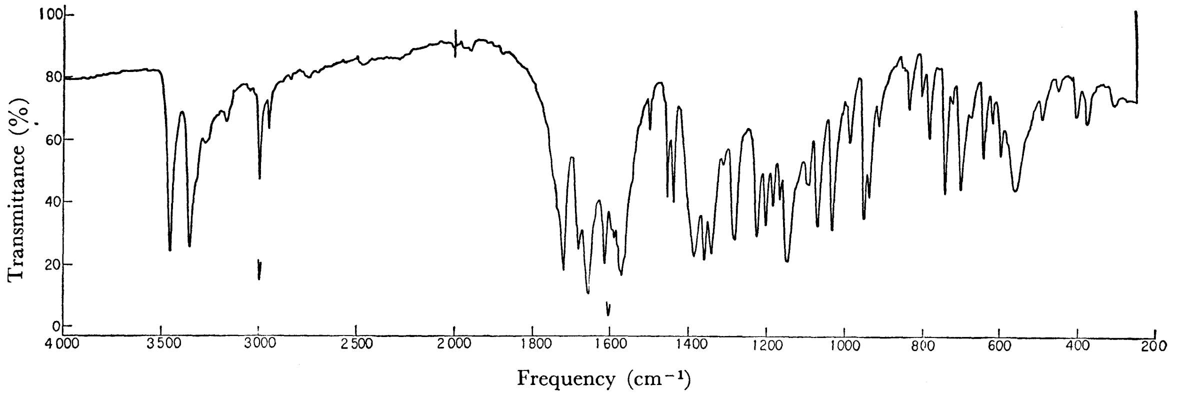

Fig. 5. IR spectrum of *trans*-*N*-carbamoyl-2-imino-4-methoxycarbonyl-5-phenyl-1,3-oxathiolane (**6β**).

TABLE 4. IR DATA OF *N*-CARBAMOYL-2-IMINO-4-ALKOXYCARBONYL-5-SUBSTITUTED 1,3-OXATHIOLANES[a]

Compound	NH_2 stretching		Ester C=O stretching	Carbamoyl C=O stretching	NH_2 deformation	C=N stretching
6α	3300 br	3190 br	1753 s 1740 s	1680 s		1580 s
6β	3454 s	3354 s	1722 s	1658 s	1612 m	1570 s
7α	3300 br	3180 br	1743 s	1680 s		1576 s
7β	3454 s	3354 s	1718 s	1687 s	1610 m	1569 s
8α	3275 s	3212 br	1728 s	1682 s		1560 s
8β	3455 s	3350 m	1714 s	1660 m	1612 m	1575 s
9C	3420 m	3310 br	1744 s	1682 s	1615 m	1580 s
10C	3350 br 3290 m	3240 br 3200 br	1741 s	1687 s	1620 m	1585 s
11α	3360 br	3160 m	1740 s	1695 s		1566 s
11β	3360 br	3160 m	1740 s	1684 s	1605 m	1566 s
12T	3450 s	3352 s	1722 s	1660 s	1615 s	1575 s
13C	3290 br	3180 br	1758 s	1695 s	1625 s	1588 s
14T	3450 s	3350 s	1725 s	1660 s	1618 m	1575 s
15α+β[b]	3488 br 3335 m	3270 br 3200 m	1735 s 1727 s	1674 s	1610 m	1588 s
16α+β[b]	3300 br	3180 br	1750 s 1745 s	1685 s	1620 m	1582 s
17T	3360 br 3290 m	3240 br 3200 m	1738 s 1731 s	1678 s		1573 s
18T	3470 s	3200 s	1730 s	1673 s	1620 m	1580 s
19α+β[b]	3400 br 3330 m	3295 br 3230 m	1740 s	1665 s		1570 s

a) IR spectra were measured in KBr pellets (cm^{-1}). b) A stereoisomeric mixture of *cis* and *trans* isomers.

steric interaction on the 4- or 5-position, which shifts an equilibrium to the **2**β' side to that extent.

Although a stereoisomeric mixture of 5-alkyl substituted derivatives could not be separated, configurational assignments for the measurements of *cis* : *trans* ratios were made on the basis of the relative values of the coupling constants.[20]

The IR spectra are also useful for diagnostic purposes. The ester C=O stretching band for the *cis* isomers always appears at a higher frequency region than that of the *trans* one. The ester C=O band of **6α** exceptionally splits into a doublet (Fig. 4). It was also observed that the NH$_2$ stretching bands of the carbamoyl group are rather sharp doublet in the *trans* isomers, whereas the *cis* isomers showed broad absorption in the region between 3500 and 3000 cm^{-1} (Figs. 4 and 5).

The isomeric compositions of fourteen oxathiolanes, as evaluated from the integration of the area under the appropriate NMR signals, are given in Table 5. The reaction of **1** with benzaldehyde in the presence of potassium fluoride led to the predominant formation of the *cis* isomer. When potassium carbonate was used as a catalyst, the yield of the *trans* isomer inincreased. The reaction with *p*-anisaldehyde produced exclusively the *cis* isomer, whereas *o*-anisaldehyde afforded predominantly the *trans* isomer. On the contrary, the reaction with *p*-chloro- and *p*-bromobenzaldehydes provided exclusively the *trans* isomer, whereas *o*-chlorobenzaldehyde resulted predominantly in the *cis* isomer. Furthermore, the reaction of acetaldehyde led to an almost equimolar mixture of the *cis* and *trans* isomers, while propionaldehyde and *n*-butyraldehyde predominantly produced the *trans* isomers. From the results it is difficult to observe any relationship between the electronegativities and steric requirement of the 5-substituent and the stereoisomeric compositions of the products. It was found that the *cis*(α) isomers are always produced more rapidly than the *trans*(β) forms. It was thought at first that the *cis* isomers are the kinetically-favored products and are thermodynamically unstable relative to the more slowly formed *trans* isomers. However, it was shown that under the conditions employed in the reactions the *cis* isomers did not isomerize into the *trans* ones. Under the more drastic conditions the *cis* isomer was converted into a higher-melting product, whose structure still remains undetermined.

TABLE 5. STEREOISOMERIC COMPOSITION OF PRODUCTS **2**

Compound	Catalyst	*Cis* %[c]	*Trans* %[c]
6	C[a]	55	45
	F[b]	75	25
7	C	55	45
	F	75	25
8	C	25	75
9	C	100	0
	F	100	0
10	C	100	0
	F	100	0
11	F	21	79
12	C	0	100
	F	0	100
13	F	73	27
14	F	0	100
15	F	24	76
16	C	53	47
	F	53	47
17	C	0	100
	F	0	100
18	C	0	100
	F	0	100
19	F	25	75

a) Potassium carbonate b) Potassium fluoride
c) Figures represent the average of at least three experiments.

Experimental

All melting points were uncorrected. NMR spectra were obtained with Varian HA-100D and JEOL C-60 spectrometers in deuterodimethyl sulfoxide solution using tetramethylsilane as an internal standard. The nuclear Overhauser effects (NOE) were measured as % area increase using the electric integrator of the instrument. The spectra were run as filtered (fine sintered glass) and carefully degassed CD$_3$SOCD$_3$ solutions, the concentration varying between 5 and 10%. A small amount of TMS was added as an internal lock.

IR spectra were determined in the KBr pellet using a Perkin-Elmer 521 spectrophotometer. Mass spectra were taken with a JMS-01S instrument operating at 75 eV.

*Reactions of Thiocyanoacetic Esters (**1**) with Aldehydes.* *General Procedure*: A solution containing thiocyanoacetic ester (**1**) (0.03 mol) and an aldehyde (0.03 mol) in 20 m*l* of moist ether was stirred mechanically in the presence of potassium carbonate or fluoride (5.0 g) at room temperature. The reaction required 3—4 hr, when the benzaldehydes having an electron-attractive substituent were used, and 7—8 hr, when the benzaldehydes having an electron-donating substituent were used. After the catalyst was removed by filtration and washed with 20 m*l* of ether, the filtrate and washings were combined and allowed to stand overnight in an open vessel. The precipitated crystals were collected on a filter and washed with ether, until the crystals became colorless. A small fraction of the crystals was subjected to NMR analysis for the measurement of isomeric ratios. The rest of the crystals were recrystallized from an appropriate alcohol, until the lower-melting isomer was removed (α-form).

The filtrate, from which the crude α-isomer was removed, was allowed to stand for several more days, until the formation of crystals ceased. The precipitate was washed repeatedly with ether and then a small fraction was subjected to NMR analysis. The rest of the precipitate was recrystallized from appropriate alcohol, until a pure lower-melting isomer was obtained.

cis *and* trans *5-Phenyl-4-methoxycarbonyl-2-carbamoylimino-1,3-oxathiolanes (**6α** and **6β**).* A mixture of methyl thiocyanoacetate (3.5 g) and benzaldehyde (3.5 g) in 20 m*l* of moist ether was stirred in the presence of potassium carbonate (5.0 g) for 6 hr. After the catalyst was removed by filtration, the filtrate was allowed to stand overnight at room

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[20] Since a stereoisomeric mixture of 5-alkyl derivatives could not be separated, the NOE of the 5-methyl derivatives (**16**) was measured in a solution containing the *cis* and *trans* isomers (*ca.* 1 : 1). In this case the 5-methyl protons of the *cis* and *trans* isomers appeared at the same position. When the methyl protons were irradiated, the % area increase in the H$_A$ proton signal was 7% for the *trans* isomer, and 0% for the *cis* isomer.

temperature. The resulting precipitate was collected on a filter and washed with ether, until the reddish yellow color was removed. After the crystals were weighed, a small fraction was subjected to NMR analysis. The rest of the precipitate was recrystallized from methanol. The crude product contained 80% *cis*-**6**.

The filtrate was allowed to stand for another three days and then the resulting precipitate was washed with ether repeatedly. After the precipitate was weighed, a small fraction was subjected to NMR analysis. The rest of it was recrystallized from ethanol. The crude product contained 40% *trans*-**6**. The *cis* isomer (yield 2.4 g) has mp 190—191°C, molecular ion peak at *m/e* 280. The *trans* isomer has mp 138—139°C, molecular ion peak at *m/e* 280.

cis *and* trans *5-Phenyl-4-ethoxycarbonyl-2-carbamoylimino-1,3-oxathiolanes (**7α** and **7β**).* A solution of ethyl thiocyanoacetate (3.5 g) and benzaldehyde (3.5 g) in 20 m*l* of ether was stirred in the presence of potassium carbonate (5.0 g) for 6 hr. The first precipitate was recrystallized from ethanol, giving 2.5 g of **7α**, mp 190—191°C, molecular ion peak at *m/e* 294. The second precipitate was recrystallized from methanol, giving 0.2 g of **7β**, mp 159—160°C, molecular ion peak at *m/e* 294.

*Attempted Epimerization of **7α** with Potassium Carbonate in Ethanol.* To 2.0 m*l* of ethanol were added 0.5 g of **7α** and 0.2 g of potassium carbonate and the mixture was refluxed for an hour and then allowed to stand for two days at room temperature. The solvent was removed in a vacuum. The resulting crystals proved to be the starting material by IR and NMR analyses.

*Attempted Epimerization of **6α** with Sodium Methoxide in Methanol.* In 30 m*l* of methanol was dissolved 0.05 g of sodium and then 0.2 g of **6α**. After the solution was allowed to stand at 50°C for 6 hr, the solvent was removed in a vacuum. The resulting solid product was recrystallized from ethanol. The crystals remained unmelted at 250°C.

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