The crystals of (V) were rhombic, with (at 20°C) $a = 16.216(2)$, $b = 7.9542(9)$, $c = 23.965(3)$ Å, space group Pbca. The elementary cell parameters and the intensities of 647 independent reflections, 552 of which had $I \geq 2\sigma$, used in the subsequent calculations, were obtained on a Hilger-Watts automatic four-circle diffracometer (λ_{MoK_α}, graphite monochromator, $\theta/2\theta$ scanning, $\theta \leq 24°$). The structure was calculated directly using the MULTAN program, and refined by least squares in isotropic approximation for all the nonhydrogen atoms. All the hydrogen atoms save two, located from the difference series, were placed in the calculated positions with $B_{iso} = 6$ Å^2, and were not refined. The final values of the divergence factors were $R = 0.081$ and $R_w = 0.065$. All calculations were carried out on an Eclipse/200 computer using the INEXTL programs [12].

LITERATURE CITED

1. O. Diels and K. Alder, Ber. Chem. Ges., 60, 716 (1927).
2. G. N. Dorofeenko, E. I. Sadekova, and V. M. Goncharova, Khim. Geterotsikl. Soedin., No. 10, 1038 (1970).
3. V. I. Dulenko and N. N. Alekseev, Doklady. Akad. Nauk SSSR, 206, 351 (1972).
4. V. I. Dulenko, S. V. Tolkunov, and N. N. Alekseev, Khim. Geterotsikl. Soedin., No. 10, 1351 (1981).
5. V. I. Dulenko, S. V. Tolkunov, and N. N. Alekseev, Khim. Geterotsikl. Soedin., No. 1, 37 (1983).
6. A. T. Balaban, G. N. Dorofeenko, A. Dinculescu, J. Fischer, V. V. Mezheritzky, and A. V. Koblik, Adv. Heterocycl. Chem. (A. R. Katritzky, editor) Acad. Press, New York (1982), Suppl. 2, p. 128.
7. E. G. Popova and L. A. Chetkina, Zh. Skh. Khim., 20, 665 (1979).
8. E. G. Popova, L. A. Chetkina, and B. V. Kotov, Zh. Skh. Khim., 21, 116 (1981).
9. N. S. Zefirov and V. A. Palyulin, Dokl. Akad. Nauk SSSR, 252, 111 (1980).
10. I. V. Komissarov, N. S. Semenov, V. I. Luk'yanenko, V. F. Donets, A. T. Dolzhenko, L. V. Dulenko, and V. I. Dulekno, Khim.-farm. Zh., No. 5, 93 (1977).
11. G. N. Dorofeenko and L. V. Dulenko, Khim. Geterotsikl. Soedin., No. 3, 417 (1969).
12. R. G. Gerr, A. I. Yanovskii, and Yu. T. Struchkov, Kristallografiya, 28, 1029 (1981).

INVESTIGATION OF AZOLES AND AZINES.

75.* STRUCTURE OF 2-ARYL-1,3-OXAZINE-4,6-DIONES IN THE GAS PHASE

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and B. A. Ivin

UDC 547.867.2:541.623:543.51'

The mass-spectrometric fragmentation of a number of potentially tautomeric 2-aryl-1,3-oxazine-4,6-diones and model substances that fix the possible tautomeric forms was studied. The characteristic fragmentation pathways that are peculiar to one or another tautomer and the characteristic ions that make it possible to identify them in tautomeric mixtures were ascertained. It is shown that in the gas phase 2-aryl-1,3-oxazine-4,6-diones exist in mixtures of 4-hydroxy, 6-oxo, dipolar-ionic, and dicarbonyl forms; the amounts of the latter two forms increase with intensification of the electron-acceptor properties of the substituent in the para position of the benzene ring.

Inasmuch as they are trans-fixed β-dicarbonyl compounds, 2-aryl-1,3-oxazine-4,6-diones I can exist in four tautomeric forms:

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*See [1] for Communication 74.

Leningrad Institute of Pharmaceutical Chemistry, Leningrad 197022. All-Union Scientific-Research Technological Institute of Antibiotics and Enzymes for Medical Use, Leningrad 198020.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 552-556, April, 1990. Original article submitted December 16, 1987; revision submitted May 3, 1989.

0009-3122/90/2604-0472$12.50

TABLE 1. Mass Spectra of 2-Aryl-1,3-oxazine-4,6-diones Ia-g and Model Substances II-VI

Compound	Peaks of the characteristic ions and their intensities (% relative to the maximum)										
	M^+	$F_1(F_3)$	F_2	F_4	F_5	F_6	F_7	F_9	F_{10}	F_{11}	F_{12}
Ia	189 (37)	161 (21)	105 (100)	104 (17)	69 (9)	42 (5)	103 (4)	112 (3)	41 (6)	148 (7)	—
Ib	246 (59)	218 (6)	148 (100)	147 (19)	83 (6)	56 (1)	146 (6)	—	55 (2)	191 (13)	—
Ic	233 (38)	205 (11)	135 (100)	134 (21)	83 (10)	56 (2)	133 (3)	126 (1)	55 (2)	178 (14)	—
Id	217* (44)	189* (14)	119* (100)	118* (41)	83* (9)	56 (8)	117 (2)	126 (1)	55 (3)	162* (19)	—
Ie	203 (80)	175 (26)	105 (100)	104 (47)	83 (11)	56 (13)	103 (3)	126 (3)	55 (10)	148 (28)	—
If**	237 (50)	209 (23)	139 (100)	138 (52)	83 (24)	56 (25)	137 (3)	126 (3)	55 (8)	182 (24)	—
Ig	248 (99)	220 (76)	150 (86)	149 (60)	83 (100)	56 (37)	148 (0)	126 (7)	55 (14)	193 (46)	—
IIa	203* (42)	175* (47)	105* (100)	118 (1)	69 (8)	42 (1)	103 (2)	126* (10)	41 (3)	162 (1)	—
IIb	217 (61)	189 (87)	105 (100)	118 (6)	83 (5)	56 (1)	103 (2)	140 (7)	55 (6)	162 (0)	—
III	217* (10)	189* (67)	105* (77)	118* (100)	83* (25)	56 (5)	103 (3)	—	55 (2)	—	—
IV**	251 (1)	—	139 (7)	—	—	70 (100)	137 (1)	—	—	—	—
V	203 (8)	175 (34)	105 (13)	118 (1)	69 (100)	42 (8)	103 (79)	—	41 (12)	—	—
VIa	261 (29)	191 (29)	135 (100)	134 (13)	69 (3)	42 (3)	133 (4)	—	—	178 (5)	219 (67)
VIb	231 (20)	161 (59)	105 (64)	104 (27)	69 (4)	—	103 (6)	—	—	148 (6)	189 (100)
VIc**	265 (29)	195 (54)	139 (64)	138 (26)	69 (5)	—	137 (4)	—	—	182 (8)	223 (100)
VId	276 (16)	206 (67)	150 (33)	149 (28)	69 (9)	—	—	—	—	193 (6)	234 (100)

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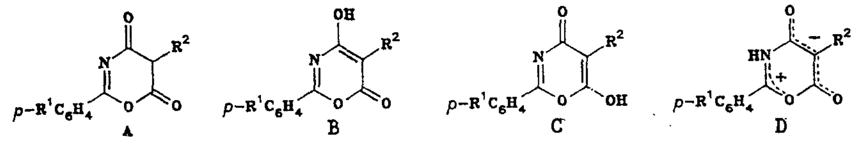
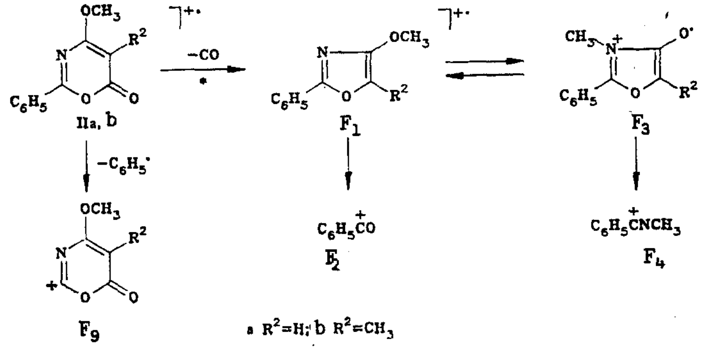
*The elementary compositions of the ions were confirmed by high-resolution mass spectra.

**The peaks of the ions that contain the ^{35}Cl isotope are presented.



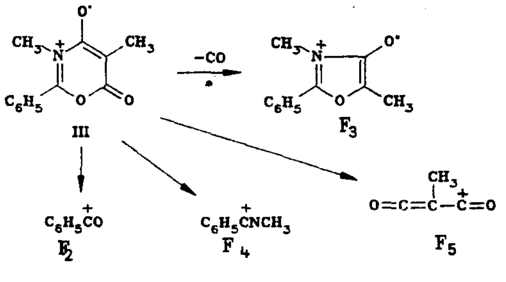
I a $R^1=R^2=H$; b $R^1=(CH_3)_2N$, $R^2=CH_3$; c $R^1=CH_3O$, $R^2=CH_3$; d $R^1=R^2=CH_3$; e $R^1=H$, $R^2=CH_3$; f $R^1=Cl$, $R^2=CH_3$; g $R^1=NO_2$, $R^2=CH_3$

We have previously shown [2] that these compounds in solutions in DMSO and THF exist primarily in enol form B with a hydroxy group attached to the $C_{(4)}$ atom. A study of the structures of these potentially tautomeric systems in the gas phase seemed of considerable interest, since the solvation and associative effects that occur in solutions are excluded in this case. An informative method in this respect is mass spectrometry, examples of the use of which for the investigation of tautomeric transformations are known [3, 4].



To ascertain the characteristic fragmentation pathways that are peculiar to one or another tautomeric form we studied the mass spectra of methylated analogs II-V and 4-O-acetyl derivatives VI, which model the possible tautomeric forms. An analysis of the data presented in Table 1 shows that the mass spectra of 2-phenyl-4-methoxy-6H-1,3-oxazin-6-ones IIa, b, which model the B form, are characterized by high intensities of the peaks of the molecular ion (M^+) and the $[M - CO]^+$ (F_1) and benzoyl (F_2, 100%) ions. The absence of ion peaks at 98* and 112 ($[M - C_6H_5CO]^+$) makes it possible to assume for these compounds the successive fragmentation of M^+ with the ejection of CO and splitting out of the benzoyl cation from the resulting 2-phenyl-4-methoxyoxazolium ion (F_1). The peak of a rearranged ion at 118 (F_4), which is characteristic for the mass spectra of the analogous 2-phenyl-4-methoxy-6H-1,3-thiazin-6-ones [5], is a low-intensity peak in the spectra of IIa, b.

The fragmentation of 3,5-dimethyl-2-phenyl-6-oxo-1,3-oxazinium-4-olate (III), which models dipolar-ionic form D, is realized via several pathways, among which the most likely is the formation of an ion at 118 (F_4): its peak has the maximum intensity in the spectrum. The other pathways include the elimination of a molecular of CO from M^+ and/or the formation of a benzoyl cation. The formation of a carbonyl ketene ion (F_5) and decreased (as compared with models of the B form) stability of M^+ are also characteristic for the mass-spectrometric fragmentation of betaine III.



A peculiarity of the fragmentation of a model of dicarbonyl form A — 2-(p-chlorophenyl)-5,5-dimethyl-5,6-dihydro-4H-1,3-oxazine-4,6-dione (IV) — is the formation of a high-intensity peak of a dimethyl ketene ion (F_6) and low stability of M^+. A pathway with the formation of a benzoyl cation from M^+ and, evidently, from the $[M - (CH_3)_2C{=}C{=}O]^+$ ion is realized to a small extent. A similar fragmentation pathway is also observed for 2-phenyl-5,5-dimethyl-5,6-dihydro-4H-1,3-thiazine-4,6-dione [5].

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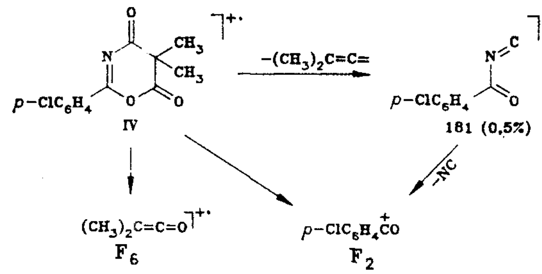
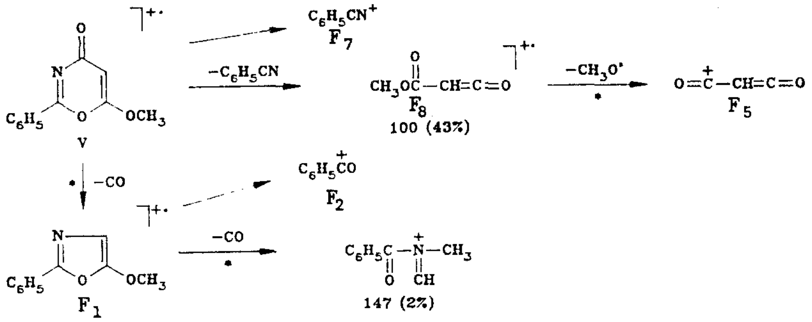
*In the text and in the schemes the numbers that characterize the ions are the m/z values.



As in the case of a number of other 4H-1,3-oxazin-4-ones [6, 7], the principal pathway of the fragmentation of 2-phenyl-6-methoxy-4H-1,3-oxazin-4-one (V), which models the C form, is retrodiene cleavage with the formation of benzonitrile (F_7) and methoxycarbonyl ketene (F_8) ions. A methoxy radical is then split out from F_8, which leads to a carbonyl ketene ion (F_5), the peak of which has the maximum intensity in the spectrum. The other pathways of fragmentation of V include the successive elimination of a molecule of CO and a benzoyl cation or two molecules of CO from M^+.

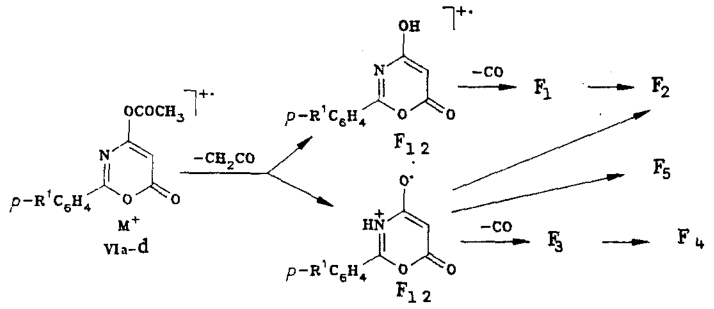
Thus the mass-spectrometric behavior of the model substances, while having common features, has characteristic peculiarities that make it possible to form a judgment regarding the presence of one or another tautomeric form in a mixture. Thus the high intensities of the peaks of the benzoyl (100%) and $[M - CO]^+$ ions and the high stability of M^+ serve as a sign of 4-hydroxy-6-oxo form B. Intense peaks of $ArCNH^+$ (F_4) ions and carbonyl ketene (F_5) ions characterize betaine structure D. Dicarbonyl form A is identified from the intense peak of the ketene ion (F_6) and from the low stability of M^+. Finally, 6-hydroxy-4-oxo form C is determined from the presence in the mass spectrum of the peak of a benzonitrile ion (F_7). One evidently cannot use the peak of the carbonyl ketene ion (F_5) for this purpose, since the F_8 ion, which contains a hydrogen atom instead of a methyl group, should undergo fragmentation via a different pathway (splitting out of CO_2).



By examining the intensities of the peaks of the characteristic ions in the mass spectrum of 2-phenyl-1,3-oxazine-4,6-dione (Ia) from these points of view one can conclude that all possible tautomers are present in the gas phase. The presence of intense peaks of benzoyl (100%) and M^+ (37%) ions constitutes evidence that the 4-hydroxy-6-oxo form predominates in the tautomeric mixture. The percentage of the 6-hydroxy tautomer is insignificant, which follows from the low intensity of the peak of the benzonitrile ion (4%), especially since low-intensity peaks of this ion are also present in the spectra of models of the other forms. The presence of peaks of F_4 (17%) and F_5 (7%) ions is evidently associated with the presence of a dipolar-ionic form, while the peak of a ketene ion (5%) indicates the small contribution of structure A.

In comparing the mass spectra of 2-aryl-5-methyl-1,3-oxazine-4,6-diones Ib-g one should first of all note that fragmentation of M^+ with ejection of the substituent from the benzene ring is not characteristic for any of the compounds of this series. On the other hand, the nature of the substituent in the para position of the benzene ring has a substantial effect on the distribution of the intensities of the peaks of the characteristic ions. Common features in the mass spectra of all of these compounds are the high intensities of the M^+ peaks and the peaks of the benzoyl cation; the peak of the latter, with the exception of the spectrum of 2-(p-nitrophenyl)oxazine Ig, has the maximum intensity. Consequently, in these cases the fragmentation of aryloxazines Ib-g is determined primarily by the fragmentation of the 4-hydroxy-6-oxo tautomer. At the same time, intensification of the electron-acceptor properties of the substituent in the benzene ring leads to an increase in the intensities of the peaks of the methyl ketene (F_6) and $ArCNH^+$ (F_4) ions, which correspond to fragmentation of, respectively, the dicarbonyl and dipolar-ionic forms. The simultaneous increase in the intensity of the peak of carbonyl ketene ion F_5 (which in the case of oxazine Ig becomes the maximally intense peak), by virtue of the information stated above, evidently corresponds to an increase in the percentage in the tautomeric mixture of form D rather than form C, especially since the peak of the benzonitrile ion (F_7) in this case vanishes almost completely.

The fragmentation of aryloxazines Ia-g may be accompanied to a small extent by elimination of an aryl substituent with the formation of the F_9 ion (at 126 or 112). Similar fragmentation is observed only in the spectra of models of the 4-hydroxy-6-oxo form (IIa, b). The certain increase in the intensity of the peak of this ion on passing from the p-methoxy to the p-nitro compound is evidently due to weakening of the bond of the benzene and oxazine rings in M^+ of the 4-hydroxy tautomer as a consequence of a decrease in the degree of delocalization of the positive charge.



a $R^1=CH_3O$; b $R^1=H$; c $R^1=Cl$; d $R^1=NO_2$

In addition to the examined fragmentation pathways, the fragmentation of the M^+ ions of Ia-g may occur with splitting out of an $R^2C{=}C{=}O$ fragment. The resulting F_{11} ion gives a rather intense peak in the mass spectra of 2-aryl-1,3-oxazine-4,6-diones. It should be noted that this sort of fragmentation pathway is not characteristic for any of II-V, which model tautomeric forms A-D.

4-O-Acetylated derivatives of oxazines I (VIa-d), which, like 4-methoxyoxazines IIa, b, model structure B, in contrast to the latter, undergo fragmentation of the "ketene" type with the formation of an $[M - CH_2{=}C{=}O]^+$ (F_{12}) ion, which corresponds to the molecular ion for similarly substituted oxazines I. The F_{12} ion in turn undergoes fragmentation via the scheme that is characteristic for a mixture of tautomers B and D. An exception is VId, in the mass spectrum of which one observes a low-intensity (6%) peak of an $[M - CO]^+$ ion (248).

In summarizing the material set forth above one may conclude that in the gas phase, according to mass-spectrometric data, 2-aryl-1,3-oxazine-4,6-diones exist in mixtures of three possible tautomeric forms A, B, and D with preponderance of the 4-hydroxy tautomer in most cases. The percentages of the dipolar-ionic and dicarbonyl forms increase with intensification of the electron-acceptor properties of the substituent in the para position of the benzene ring.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of Id and IV were recorded with an IKS-29 spectrometer. The PMR spectra were obtained with a Varian EM-360 spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The mass spectra of Ia-g and II-V were recorded with a LKB-2091 spectrometer (Sweden), while the mass spectra of VI were recorded with an MKh-1310 spectrometer at an ionizing voltage of 70 eV and an ion-source temperature of 200°C under direct-introduction conditions; the temperature of the input system was 80-180°C. The high-resolution mass spectra of Id, IIa, and III were obtained with an MKh-1310 spectrometer with processing of the data with an SM-1403 minicomputer.

Compounds I-V were obtained by the methods described in [2], while IV was obtained in analogy with [8]. The synthesis of VI and their characteristics will be presented in a separate publication.

2-(p-Tolyl)-5-methyl-5,6-dihydro-4H-1,3-oxazine-4,6-dione (Id, $C_{12}H_{11}NO_3$). This compound was obtained in 70% yield and had mp 179-182°C (dec.) and R_f 0.58 (ethyl acetate). IR spectrum: 3400-3100 (OH), 1700 (C=O); 1630 (C=C); 1550 (C=N); 1610 sh, 1580, 1510 cm^{-1} (C$\overset{\cdots}{-}$C). PMR spectrum (d_6-DMSO): 12.4 (1H, broad s, OH), 8.07 (2H, d, 9 Hz), 7.47 (2H, d, 9 Hz, C_6H_4), 2.38 (3H, s, CH_3), 1.80 ppm (3H, s, 5-CH_3).

2-(p-Chlorophenyl)-5,5-dimethyl-5,6-dihydro-4H-1,3-oxazine-4,6-dione (IV, $C_{12}H_{10}NO_3$). This compound was obtained in quantitative yield and had mp 154-156°C and R_f 0.67 (ethyl acetate). IR spectrum: 1795, 1723 (C=O); 1610 (C=N); 1590, 1565 cm^{-1} (C$\cdots$C). PMR spectrum (d_6-DMSO): 8.22 (2H, d, 9 Hz), 7.70 (2H, d, 9 Hz, C_6H_4), 1.40 ppm (6H, s, 5-CH_3).

LITERATURE CITED

1. I. P. Yakovlev, M. B. Ganina, V. N. Kuklin, E. P. Studentsov, and B. A. Ivin, Zh. Org. Khim., 26, 716 (1990).
2. V. É. Zakhs, I. P. Yakovlev, N. A. Smorygo, V. A. Gindin, and B. A. Ivin, Khim. Geterotsikl. Soedin., No. 3, 386 (1987).
3. Yu. N. Sheinker, Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk, No. 2, 37 (1980).
4. N. A. Klyuev, V. G. Zhil'nikov, G. G. Aleksandrov, I. I. Grandberg, and G. N. Lipunova, Zh. Org. Khim., 19, 2615 (1983).
5. A. I. Krylov, V. N. Kuklin, and B. A. Ivin, Khim. Geterotsikl. Soedin., No. 10, 1409 (1987).
6. T. H. Koch, R. H. Higgins, and H. F. Schuster, Tetrahedron Lett., No. 5, 431 (1977).
7. T. Kinoshita, T. Onoue, M. Watanabe, and S. Furukawa, Chem. Pharm. Bull., 28, 795 (1980).
8. J. C. Martin, K. C. Brannock, and R. H. Meen, J. Org. Chem., 31, 2966 (1966).

SYNTHESIS OF 5-(5-R-2-FURYL)THIAZOLE DERIVATIVES BY THE REACTION OF 2-(5-R-FURFURYL)THIURONIUM SALTS WITH ACETIC ANHYDRIDE

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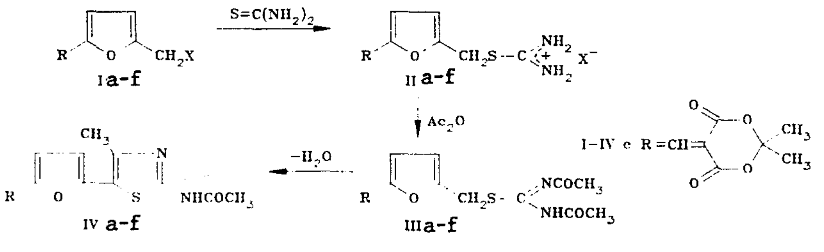
UDC 547.722:543.422.25.4.6

2-Acetamide-4-methyl-5-(5-R-2-furyl)thiazoles were obtained by the reaction of 2-(5-R-furfuryl)thiuronium salts with acetic anhydride. The reaction intermediates – 2-(5-R-furfuryl)-1,3-diacetylthioureas – were isolated and characterized.

It has been previously shown [1, 2] that 2-(5-nitrofurfuryl)thiuronium bromide reacts with carboxylic acid anhydrides to give 5-(5-nitro-2-furyl)thiazole derivatives. The aim of the present research was an experimental study of this new reaction for the formation of a thiazole ring.

Thiuronium salts II were obtained by the reaction of equimolar amounts of halomethylfurans I with thiourea.



I—IV a R=$COOC_2H_5$; b R=CN; c R=CHO; d R=NO_2; e R=CH=CHNO$_2$; I a–c, II a-c X=Cl; Id–f, IId -f X=Br

The IR spectra of salts II contain the characteristic (for thiuronium salts) intense absorption band at 1640-1660 cm^{-1} – an overtone of stretching vibrations of the NH bond (Table 1) [3]. A characteristic singlet of protons of the CH_2S group at 4.4-4.6 ppm is present in the PMR spectra of salts II.

Krasnodar Polytechnical Institute, Krasnodar 350670. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 557-562, April, 1990. Original article submitted July 14, 1988; revision submitted February 14, 1989.

0009-3122/90/2604-0477$12.50