

2-Phenacyl-3-quinoxalone (III). A solution of 0.01 mole of o-phenylenediamine in 50 ml of dry benzene was added to 0.01 mole of 5-phenylfuran-2,3-dione in 200 ml of dry benzene, after which the mixture was allowed to stand for several hours. The resulting precipitate was removed by filtration to give 1.9 g (75%) of a yellow crystalline substance with mp 267-268° (from ethanol). Found: N 10.50%.  $C_{16}H_{12}N_2O_2$ . Calculated: N 10.60%.

No melting-point depression was observed for a mixture of the above product with 2-phenacyl-3-quinoxalone obtained from o-phenylenediamine and methyl benzoylpyruvate.

Benzoylpyruvic Acid Phenylamide (IV). A solution of 0.011 mole of aniline in 15 ml of dry benzene was added to a solution of 0.011 mole of 5-phenylfuran-2,3-dione in 150 ml of dry benzene, after which the solvent was removed to give 2.9 g (94.7%) of a product with mp 118° (from toluene). Found: N 5.41%.  $C_{16}H_{13}NO_3$ . Calculated: N 5.24%. No melting-point depression was observed for a mixture of the above product with benzoylpyruvic acid phenylamide obtained from methyl phenyloxamate and acetophenone in the presence of sodium methoxide.

3,6-Diphenyl-3,4-dihydro-1,3-oxazine-2,4-dione (V). A 0.044-mole sample of phenyl isocyanate was added to a solution of 0.011 mole of 5-phenylfuran-2,3-dione in 150 ml of dry benzene, after which the mixture was heated at 80° for 2 h. The resulting precipitate was removed by filtration to give 2.18 g (72%) of a product with mp 237-238° (from ethanol). Found: N 5.41%.  $C_{18}H_{11}NO_3$ . Calculated: N 5.27%.

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#### RESEARCH ON VINYL ESTERS OF THE FURAN SERIES

#### XII\*. REACTION OF VINYL ESTERS OF FURAN CARBOXYLIC ACIDS

#### WITH AMINES AND AZOLES

Yu. A. Mansurov, G. G. Skvortsova,  
and V. K. Voronov

UDC 547.725'77:542.951.1

The reaction of vinyl esters of furan-2-carboxylic, 5-bromofuran-2-carboxylic, and trans- $\beta$ -(2-furyl)acrylic acids with aliphatic, aromatic, and heterocyclic amines was investigated. It was established that azoles add to the double bond of the vinyloxy group of the ester in conformity with the Markownikoff rule.  $\alpha$ -(1-Azoly)ethyl esters of the furan-2-carboxylic and  $\beta$ -(2-furyl)acrylic acids were synthesized. Acylation of the amines takes place during the reaction of vinyl esters of the furan series with diethylamine, aniline, p-vinyloxyaniline, morpholine, and piperidine.

The synthesis of esters containing an azole ring or another cyclic amine fragment in addition to a furan ring seems of interest for the preparation of substances with biological activity and complexing properties. The reactions of vinyl esters of acids of the furan series with amines have not been studied.

\*See [1] for communication XI.

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TABLE 1.  $\alpha$ -(1-Azoly)ether Esters of Acids of the Furan Series

Com- pound	mp, °C (crystal- lization solvent)	Empirical formula	Found, %			Calc., %			Yield, %
			C	H	N	C	H	N	
XX	81 (heptane)	C <sub>10</sub> H <sub>10</sub> N <sub>2</sub> O <sub>3</sub>	58,3	5,0	13,7	58,2	4,9	13,6	85
XXI	91 (petroleum ether)	C <sub>14</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub>	65,6	4,6	11,0	65,6	4,7	10,9	92
XXII	75 (hexane)	C <sub>13</sub> H <sub>11</sub> N <sub>2</sub> O <sub>3</sub>	60,9	4,2	16,3	60,7	4,3	16,3	98
XXIII	89 (hexane- acetone)	C <sub>12</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub>	62,1	5,3	12,1	62,1	5,2	12,1	90
XXIV	100 (hexane)	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub>	68,2	5,0	9,9	68,1	5,0	9,9	97
XXV*	160	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>3</sub>	49,9	4,6	11,6	49,8	4,6	11,5	99
XXVI†	131	C <sub>14</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>3</sub>	57,5	4,4	9,7	57,4	4,5	9,6	99

\* Found: Cl 14.6%. Calculated: Cl 14.7%.

† Found: Cl 12.3%. Calculated: Cl 12.1%.

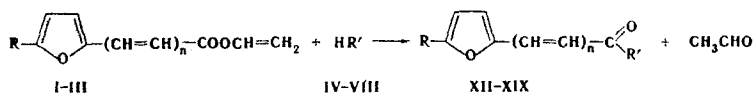
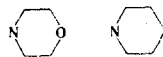
TABLE 2. Amides of Acids of the Furan Series

Com- pound	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
			C	H	N	C	H	N	
XII*	—	C <sub>9</sub> H <sub>13</sub> NO <sub>2</sub>	64,7	7,9	8,3	64,7	7,8	8,4	73
XIII	59 (isooctane)	C <sub>9</sub> H <sub>11</sub> NO <sub>3</sub>	59,7	6,0	7,8	59,7	6,1	7,7	88
XIV	66 (octane)	C <sub>10</sub> H <sub>13</sub> NO <sub>2</sub>	67,3	7,4	7,9	67,0	7,3	7,8	94
XV	108 (octane)	C <sub>11</sub> H <sub>13</sub> NO <sub>3</sub>	63,8	6,4	6,8	63,8	6,3	6,8	86
XVI	122 (heptane)	C <sub>12</sub> H <sub>15</sub> NO <sub>2</sub>	69,9	7,3	7,0	70,2	7,4	6,8	91
XVII†	123 (alcohol)	C <sub>11</sub> H <sub>9</sub> NO <sub>2</sub>	70,7	4,8	7,5	70,6	4,9	7,5	32
XVIII	87 (pet. ether)	C <sub>13</sub> H <sub>11</sub> NO <sub>3</sub>	68,1	4,9	6,1	68,1	4,8	6,1	37
XIX	106 (benzene)	C <sub>13</sub> H <sub>10</sub> BrNO <sub>3</sub>	50,8	3,5	4,4	50,7	3,3	4,5	36

\* This compound had bp 108° (3 mm) and  $n_D^{20}$  1.5040; according to [9], bp 108-109° (3 mm),  $n_D^{20}$  1.5040, and  $d_4^{20}$  1.0638.

† According to [10], this compound has mp 123.5°.

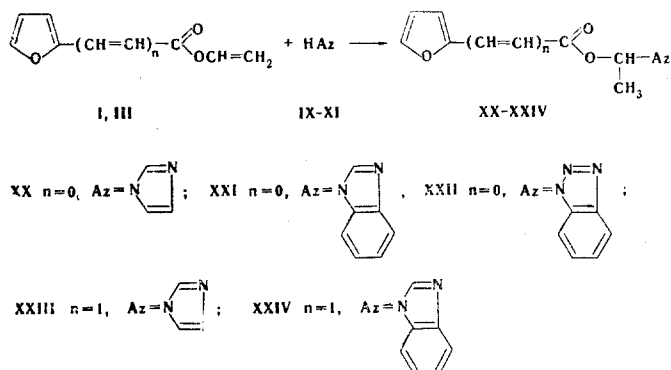
We have investigated the reaction of vinyl esters of furan-2-carboxylic (I), 5-bromofuran-2-carboxylic (II), and trans- $\beta$ -(2-furyl)acrylic (III) acids with diethylamine (IV), aniline (V), p-vinyloxyaniline (VI), morpholine (VII), piperidine (VIII), imidazole (IX), benzimidazole (X), and benzotriazole (XI). The investigation was made at various temperatures and reagent ratios, with UV irradiation, in the presence of sodium metal, the sodium salts of the amines, and potassium hydroxide, and also without a catalyst. Acid amides are formed in all cases in the reaction of I-III with aliphatic, heterocyclic, and aromatic amines (IV-VIII), and the vinyloxy group is split out in the form of acetaldehyde:

I-III, XII-XIX R = H, Br; n = 0, 1; IV-VIII, XII-XIX R' = N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>, NHC<sub>6</sub>H<sub>5</sub>, NHC<sub>6</sub>H<sub>4</sub>OCH=CH<sub>2</sub>-p,

This sort of reaction was also observed in the acylation of amines with vinyl acetate by Kost and Yurkevich [2]. They showed that the case of the acylation of amines with complex vinyl esters increases as the nucleophilic properties of the amines increase. The same dependence is observed in the reaction of vinyl esters of the furan series with amines [3]. The reaction of esters I-III with secondary amines IV, VII, and VIII proceeds readily at room temperature and even in the absence of a catalyst to give amides XII-XVI in high yields [4]. Primary amines V and VI react with greater difficulty. Thus furoylaniline (XVII) is obtained in 31.6% yield at 20°, whereas N-(2-furoyl)- and N-(5-bromo-2-furoyl)-p-vinyloxyanilides (XVIII, XIX) are obtained in yields of this sort only on heating to 70°. Compounds XVIII and XIX were obtained by alternative synthesis [5] by reaction of furan-2- and 5-bromofuran-2-carboxylic acid chlorides with p-vinyloxyaniline. The  $\beta$ -(2-furyl)acrylic acid N-morpholyamide structure was confirmed by the PMR spectrum.

The reaction of I and III with azoles proceeds in another direction. According to quantum-chemical calculations [6], the maximum positive charge is concentrated on the pyrrole nitrogen atom of IX-XI. Owing to the nonuniform distribution of the  $\pi$ -electron density, azoles display both basic and acidic properties. The combination of strong basic properties due to the p electrons of the nitrogen atom in the 3

position and the acid properties of the proton attached to the nitrogen atom in the 1 position is evidently responsible for the possibility of the addition of azoles to the double bond of the vinyloxy groups of esters I and III. In fact, in contrast to the amines IV-VIII, azoles IX-XI react with I and III to give  $\alpha$ -(1-azolyl)-ethyl esters of furan-2-carboxylic and trans- $\beta$ -(2-furyl)acrylic acids (XX-XXIV):



Compounds XX-XXIV are obtained by mixing equimolecular amounts of the starting components without the addition of a catalyst and a solvent in 53-61% yields after 3 h. The yields of the desired products increase when the reaction temperature is raised to 40-50° and also in aqueous media [7].

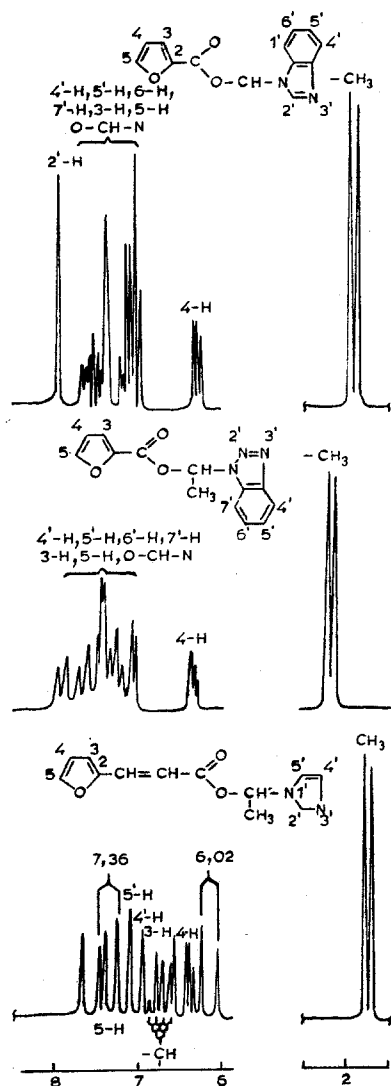


Fig. 1. PMR spectra of  $\alpha$ -(1-benzimidazolyl)- and  $\alpha$ -(1-benzotriazolyl)-ethyl furan-2-carboxylates and  $\alpha$ -(1-imidazolyl)ethyl  $\beta$ -(2-furyl)acrylate.

The reaction of I and III with azoles (reagent ratio 1:1) in acetone in the presence of solid potassium hydroxide at  $-20$  to  $+50^\circ$  was investigated. The optimum temperature was  $-20$  to  $-30^\circ$ ; the yields of the desired products in this case reach 85-98%. The presence in the acyl residue of III of a greater donor furylvinyl substituent as compared with the furyl substituent in I increases the polarization of the double bond of the vinyloxy group and facilitates addition of the azoles. The double bond of the acrylic fragment of ester III is less active in this reaction. The azoles are arranged in order  $\text{IX} < \text{X} < \text{XI}$  with respect to their capacity to react with I and III. This order corresponds to the increase in the acidic properties from IX to XI. The structures of the synthesized azolyethyl esters of the furan series (XX-XXII) are confirmed by data from the IR spectra, in which the absorption bands at  $1650$  and  $3300\text{--}3400\text{ cm}^{-1}$  ( $\text{--C=C--}$  stretching vibrations in I and N-H vibrations in IX-X) vanish, and absorption bands at  $2945\text{--}2990$  and  $1340\text{ cm}^{-1}$  corresponding to the vibrations of C-H and  $\text{CH}_3$  groups [8] appear. The IR spectra of  $\alpha$ -(1-imidazolyl)- and  $\alpha$ -(1-benzimidazolyl)-ethyl  $\beta$ -(2-furyl)acrylates (XXIII, XXIV) contain a band at  $1635\text{--}1540\text{ cm}^{-1}$  affiliated with the  $\text{--C=C--}$  vibrations of the acrylic fragment of the acid. The absorption bands at  $1490\text{--}1499$  and  $3108\text{ cm}^{-1}$  correspond to the  $\text{--C=C--}$  and  $\text{--C=N--}$  vibrations of the azole rings. The frequencies of the vibrations of the furan ring, the carbonyl group, and the ester grouping in XX-XXIV are retained.

The structures of the products of the addition of azoles to the double bond of the vinyloxy group unambiguously confirm the PMR spectra (Fig. 1). The doublet at strong field ( $\delta = 1.89, 2.16$ , and  $1.71$  ppm, respectively) in the PMR spectra of XXI-XXIII is affiliated with the protons of the  $\text{CH}_3$  group, which couple with the methyldyne protons, the signal of which (quartet) appears at weak field ( $\delta = 6.75\text{--}8.03$  ppm) and is superimposed in the signals of the protons of the furan and azole rings. If products of addition of the azoles to the vinyl esters had been formed, signals of two methylene protons would have been present at 3-4 ppm.

Thus the reaction of vinyl esters of acids of the furan series with amines and azoles proceeds in different directions. A method was worked out for the preparation of new amides of acids of the furan series on the basis of vinyl esters and amines. A method is proposed for the synthesis of azolyethyl esters of the furan series containing several active reaction centers with complexing properties.

We obtained the corresponding hydrochlorides (XXV and XXVI), which are quite soluble in water, by reaction of XX and XXI with dry hydrogen chloride in either solution at room temperature. Compounds XX and XXI are probable protonated at the nitrogen atom in the 3 position. The synthesized azolyethyl esters of acids of the furan series may be of interest as pharmacological preparations. The properties of XX-XXVI are presented in Table 1.

## EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of  $\text{CCl}_4$  solutions of the compounds were recorded at room temperature with a BS 4873V spectrometer with hexa-methyldisiloxane as the internal standard.

General Method for the Preparation of Amides of Furan-2-carboxylic and  $\beta$ -(2-furyl)acrylic Acids (XII-XIX). Equimolecular amounts of the vinyl ester of furan-2-carboxylic acid or trans- $\beta$ -(2-furyl)acrylic acid (I-III) with the appropriate amine (IV-VIII) were stirred at  $20^\circ$  for 2-6 h. The reaction mixture crystallized. The crystals were separated, washed, dried, and recrystallized. Amides XVIII and XIX were synthesized at  $70^\circ$  (Table 2).

The PMR spectrum of amide XV contains a singlet at strong field ( $\delta = 3.54$  ppm) that is affiliated with the protons of the four methylene groups of the morpholine ring. The protons of the  $\text{--CH=CH--}$  group gives two doublets owing to spin-spin coupling between them ( $\delta = 6.60$  and  $7.30$  ppm;  $J = 14.6$  Hz). The remaining signals are due to the protons of the furan ring. Their multiplicity is also a consequence of spin-spin coupling between them ( $\delta_4 6.34$ ,  $\delta_3 6.45$ ,  $\delta_5 7.32$  ppm;  $J_{4,3} = 3.3$ , and  $J_{4,5} = 1.8$  Hz). The  $J_{3,5}$  constant is not resolved, although it does appear in the spectrum. The 5-H signal is therefore represented as a broad singlet.

N-(2-furoyl)-p-vinyloxyanilide (XVIII). A 3.39-g (0.026 mole) sample of furan-2-carboxylic acid chloride was added slowly dropwise at  $-10$  to  $+5^\circ$  to a mixture of 3.38 g (0.025 mole) of VI and 3.63 g (0.026 mole) of triethylamine in 10 ml of acetone, after which the mixture was stirred for 1 h at the indicated temperature and for 1 h at  $20^\circ$ . It was then poured into cold water, and the resulting oil began to crystallize. The solid material was removed by filtration, washed with water, and dried to give 5.7 g ( $\sim 100\%$ ) of XVIII with mp  $87^\circ$  [from petroleum ether-benzene (4:1)].

Anilide XIX was similarly obtained in 95% yield from XVIII.

$\alpha$ -(1-Imidazolyl)ethyl Furan-2-carboxylate (XX). A) A 13.8-g (0.1 mole) sample of I was added dropwise at 20–30° to a mixture of 6.8 g (0.1 mole) of IX and 0.83 g of pulverized potassium hydroxide in 50 ml of acetone, after which the mixture was stirred for 1 h and worked up to give 13.8 g (85.2%) of XX with mp 80–81° (heptane).

B) A mixture of 6.8 g (0.1 mole) of IX and 13.8 g (0.1 mole) of I was stirred at 20° for 3 h, after which it was allowed to stand overnight. Workup gave 11.1 g (53.3%) of XX with mp 80–81°. Esters XXI–XXIV were similarly obtained (see Table 1).

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#### RING - CHAIN TRANSFORMATIONS WITH PARTICIPATION OF THE C = N GROUP

#### IV.\* QUANTITATIVE STUDY OF THE TAUTOMERISM OF 3-(m- or p-X-ARYLAMINO)-3-PHENYLPHthalIDES

R. É. Valter and V. P. Tsiekure

UDC 547.588.21:543.422.6

The ring-chain tautomeric equilibrium constants ( $K$ ) of aryl-ring-substituted 3-aryl-amino-3-phenylphthalides in dioxane were measured by UV spectroscopy. A satisfactory linear correlation between  $\log K/K_0$  and the  $\sigma^+$  constants of the substituents in the aryl ring was found.

It has been shown [2] that the tautomeric equilibrium  $I \rightleftharpoons II$  is observed in solutions of 3-arylamino-3-phenylphthalides (II).

\*See [1] for communication III.

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