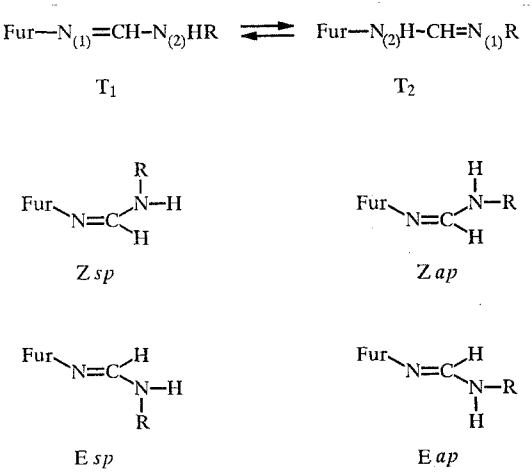
SYNTHESIS OF HETEROCYCLES BASED ON THE PRODUCTS OF THE ADDITION OF POLYHALOGENOALKANES TO UNSATURATED SYSTEMS. 3.* STRUCTURE AND STEREOCHEMISTRY OF SUBSTITUTED N-FURYLFORMAMIDINES

D. M. Antonov, L. I. Belen'kii, V. S. Bogdanov, A. A. Dudinov, M. M. Krayushin, V. N. Nesterov, Yu. T. Struchkov, and B. I. Ugrak

It was established with the aid of the ^1H, ^{13}C, and ^{15}N NMR spectra as well as the x-ray structural analysis that the substituted furylformamidines, which are key compounds in the synthesis of furo[2,3-d]pyrimidines, are E-isomers of $N_{(1)}$-furyl-$N_{(2)}$-R-formamidines (R = H, Alk, Ar), independently of the nature of the substituent at the second N atom, and occur mainly in the form of the antiplanar rotamers.

A preliminary communication [2] described the synthesis of substituted furo[2,3-d]pyrimidines based on the available 3,5,5,5-tetrachloropentan-2-one — a product of the radical addition of CCl_4 to methyl vinyl ketone. Key intermediate compounds in this synthesis are the corresponding substituted N-furylformamidines, which proved to be stable compounds most frequently, whereby many of them existed in the form of two isomers each judging from the ^1H and ^{13}C NMR spectra. This induced us to investigate their structure and stereochemistry in more detail. Such an investigation also presented independent interest in connection with the known data on the physiological activity of amidines [3, 4].

The $N_{(1)}$, $N_{(2)}$-disubstituted formamidines [$N_{(1)}$ and $N_{(2)}$ are sp^2- and sp^3-hybridized atoms of nitrogen correspondingly] under consideration may occur in two tautomeric forms (T_1 and T_2) for each of which the E- and Z-isomers are possible; the last may thereby be presented as two rotamers — the synplanar (sp) and antiplanar (ap). For the monosubstituted formamidines (R = H), the situation is simplified since such rotamers are identical.



*For Communication 2, see [1].

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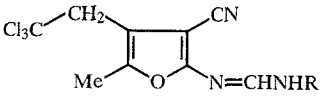
TABLE 1. ^{1}H NMR Spectra of the Substituted Amidines (I)-(X)

Compound	Solvent	Content of the	$J_{CH,NH}$	δ, ppm				Other signals (SSCC, Hz)
				=CH	NH	5-Me	CH_2	
I	DMSO-D_6	100	—	7,75 b	8,10 b	2,25 s	3,53 s	—
II	acetone-D_6	90	4,4	8,31 d	7,40 b	2,30 s	3,86 s	NMe 2,97 q (4,9; 0,8) 3,09 d (4,9)
		10	—					
	$CDCl_3$	90	4,3	8,29 d	5,50 b	2,29 s	3,75 s	NMe 3,04 d(4,8) 3,09 br. s
		10	11,4	8,12 d	6,45 b			
	DMSO-D_6	90	4,4	8,17 d	8,23 b	2,26 s	3,85 s	NMe 2,82 (4,9) 2,92 (4,9)
		10	—					
III	DMSO-D_6	60	12,8	8,21 d	8,81 d	2,26 s	3,83 s	*t*-Bu 1,24 s
		40	4,9	7,90 d	8,05 d	2,25 s		1,38 s
	CD_3OD	60	—	8,27 s	—	2,24 s	3,75 s	*t*-Bu 1,30 s
		40	—	7,91 s	—	2,22 s		1,40 s
	$CDCl_3$	90	13,1	8,29 d	6,32 d	2,30 s	3,74 s	*t*-Bu 1,38 s
		10	4,9	8,04 d	5,18 b	2,28 s		1,48 s
	acetone-D_6	60	13,2	8,34 d	7,58 b	2,30 s	3,84 s	*t*-Bu 1,40 s
		40	5,0	8,06 d	7,10 b	2,31 s	3,86 s	1,48 s
IV*	DMSO-D_6	70	12,0	8,80 d	10,94 d	2,34 s	3,91 s	Ph 7,10 m, 7,32 m; 7,84 m
		30	4,8	8,26 d	10,36 d			
	CD_3OD	60	—	8,75 s	—	2,29 s	3,79 s	Ph 7,05 m, 7,14 m, 7,30 m, 7,78 m
		40	—	8,22 s				
	$CDCl_3$	60	—	8,74 s	7,78 b	2,35 s	3,78 s	Ph 7,10 m 7,14 m 7,38 m; 7,78 m
		40	—	8,04 s	8,37 b			
V	DMSO-D_6	70	12,0	8,80 d	10,98 d	2,33 s	3,91 s	*p*-ClC_6H_4 7,30 m; 7,38 m, 7,85 m
		30	4,3	8,27 d	10,44 d			
VI	DMSO-D_6	80	12,0	8,90 d	11,18 d	2,32 s	3,90 s	*p*-AcC_6H_4 7,36 m 7,92 m
		20	—	8,27 d	10,64 b			
VII	DMSO-D_6	60	11,5	8,58 d	10,68 d	2,30 s	3,89 s	*p*-$Et_2NC_6H_4$ 1,05 (Me); 3,30 (CH_2); 6,64 m 7,07 m; 7,62 m(Ar)
		40	4,9	8,13 d	10,10 b			
VIII	DMSO-D_6	100	—	8,00 d	8,38 b	—	—	4-Ph, 5-Ph 7,0...7,7 m
	acetone-D_6	100	14,2 and 4,4	8,55 dd	Overlapped by the Ph signal	—	—	4-Ph, 5-Ph 7,1...7,7 m
	acetone-D_6 (4 : 1)	100	14,2 and 4,4	8,45 dd	7,86 br. s 8,27 b d(14Hz)	—	—	4-Ph, 5-Ph 7,1...7,7 m
IX	DMSO-D_6	100	—	8,27 s	—	2,28 s	3,86 s	OCH_2 3,64 m NCH_2 3,54 m
X	DMSO-D_6	100	—	7,75 s	—	—	—	OCH_2 3,62 m NCH_2 3,46 m C_6H_4 6,95 m 7,25
	$CDCl_3$	100	—	7,45 s	—	—	—	OCH_2 3,71 NCH_2 2,89 C_6H_4 6,84m; 7,17
	C_6D_6	100	—	6,99 s	—	—	—	OCH_2 3,53 NCH_2 2,53 C_6H_4 6,92m; 7,27

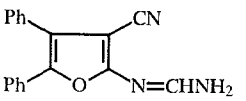
*The ^{1}H NMR spectrum of the amidine (IV) enriched at the nitrogen of the $NH_{(2)}Ph$ fragment with the isotope ^{15}N by 95% (the solution in DMSO-D_6) is as follows: the major isomer has =CH 8.80 ppm, d.d, $^3J_{CH,^{15}NH}$ 11.9 Hz, $^2J_{^{15}N,CH}$ 5.5 Hz, ^{15}NH 10.92 ppm, d.d, $^1J_{^{15}N,H}$ 89.9 Hz, $^3J_{^{15}N,CH}$ 11.9 Hz, and the minor isomer has the =CH 8.26 ppm, d.d, $^3J_{CH,^{15}NH}$ 4.9 Hz, $^2J_{^{15}N,CH}$ 8.0 Hz, ^{15}NH 10.40 ppm, d.d, $^3J_{CH,^{15}NH}$ 4.9 Hz, $^1J_{^{15}N,H}$ 91.7 Hz.

The given paper presents the results of the ^{1}H, ^{13}C, and ^{15}N NMR study of the structure, configuration, and rotational isomerism of the amidines with the Fur = 5-methyl-4-(2,2,2-trichloroethyl)-3-cyanofuryl-2 and R = H (I), Me (II), *t*-Bu (III), Ph (IV), p-ClC_6H_4 (V), p-$MeCOC_6H_4$ (VI), and p-$Et_2NC_6H_4$ (VII), as well as N-(4,5-diphenyl-3-cyano-2-furyl)formamidine

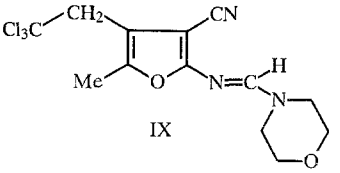
(VIII). Moreover, data on the x-ray structural analysis are presented for the amidine (IV). Model compounds studied were "fixed" amidines incapable of tautomeric conversions — morpholino[5-methyl-4-(2,2,2-trichloroethyl)-3-cyanofuryl-2-imino]methane (IX) [2] and morpholino(p-chlorophenylimino)methane (X) [5].



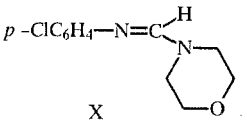
I-VII



VIII



IX



X

It was noted in the preliminary communication [2] that some of the amidines (II)-(VII) under consideration are mixtures of two isomers, but it was only possible to come to an unambiguous conclusion concerning the character of the isomerism after additional investigation. It is more convenient to begin the examination of this question with the simpler monosubstituted formamidines (I) and (VIII).

The PMR spectrum of the compounds (VIII) obtained with the 4:1 mixture of acetone-D_6–DMSO-D_6 as the solvent (see Table 1) contains, besides the signals of the protons of two phenyl groups, a doublet of doublets of the =CH proton at 8.45 ppm with the $^3J_{NH,CH}$ 14 Hz and 4 Hz, a doublet with broad components of the NH proton at 8.27 ppm with the $^3J_{NH,CH}$ 14 Hz, and a broad signal of the other NH proton with the unresolved cis-constant. These data do not allow an exclusion of the possibility that two protons occur at different atoms of nitrogen ($N_{(1)}$ and $N_{(2)}$) of the structure (Ib). However, the chemical shifts of the nitrogen atom $N_{(1)}$ and $N_{(2)}$ obtained from the ^{15}N spectrum (Table 2), as well as the multiplicity and value of the $^1J_{NH}$ (93.3 Hz, triplet), indicate that both protons are bound to one nitrogen atom, namely to $N_{(2)}$, in the tautomeric form T_1, and the signal of $N_{(1)}$ is a doublet in consequence of the splitting at the =CH proton with the ^2J 6.2 Hz.

In the ^1H spectrum of the amidine (I), the protons of the NH_2 group (~20°C) are described by one broad signal; they are only weakly nonequivalent at 40°C (Table 1). In the ^{15}N spectrum (Table 2), the signal of the amino group has the triplet structure with the $^1J_{NH}$ 94 Hz; this corresponds with the tautomeric form T_1 as in the case of the compound (VIII).

In the amidine (II), the NH proton occurs at the same atom of nitrogen $N_{(2)}$ as does the methyl group, since the PMR spectrum shows the doublet splitting of the N–CH_3 signal with the J 4.9 Hz in consequence of the spin–spin interaction of the methyl protons with the proton of the NH group. Therefore, the amidine (II) also exists in the tautomeric form T_1. The analogous structure may also be proposed for the amidine (III), which also has an alkyl substituent at the $N_{(2)}$ atom, since the conjugation of the amidine fragment with the furan ring may only be realized in the form T_1.

In contrast to $N_{(2)}$-unsubstituted (I), (VIII), and alkyl-substituted furylformamidines (II), (III), the amidine fragment may be conjugated with one of the aromatic systems in both tautomeric forms in the case of the amidines (IV)-(VII). We will note that the tautomeric equilibria of the type considered with the simultaneous presence of the tautomers T_1 and T_2 in the mixture were tangibly observed precisely for the $N_{(1)}$, $N_{(2)}$-diarylamidines (see [2]). The choice between the tautomeric structures for the aryl-substituted amidines (IV)-(VII) was based on the analysis of the ^1H spectrum of the compound (IV) containing the NHPh group, in which the nitrogen was enriched by 95% with the isotope ^{15}N (Table 1). The signals of both NH protons for the two different isomers are split into doublets with the constants of 89.9 and 91.7 Hz due to the spin–spin interaction with the ^{15}N nuclei across one chemical bond. These signals are also split by the =CH proton (11.9 and 4.9 Hz). Therefore, as in the case of amidines containing the NH_2 and NHAlk groups, it is possible to choose in favor of the tautomeric form T_1 for the amidines with the NHAr group.

We will note that the aryl groups are bound to nitrogen atoms having different hybridization in the tautomers T_1 and T_2. This should be reflected in the ^{13}C CSs of the aryl atoms of carbon, including the α-atoms $C_{(1)}$. In fact, in the spectrum of the amidine (IV), the $\delta C_{(1)}$ is equal for the two isomers at 139.03 and 138.69 ppm; the values for the amidine (V) are 138.14 and 137.69 ppm (the tautomers T_1), and the $\delta C_{(1)}$ is 150.50 ppm in the spectrum of the synthesized model compound (X) (Table 3). The CSs thereby show weak dependence on the substituents at the "amine" $N_{(2)}$ atom [3]. This also testifies in favor of the form T_1 for the amidines (IV) and (V). In the ^{13}C spectra of the amidines (VI) and (VII), the signal of the $C_{(1)}$ atom is shifted

TABLE 2. ^{15}N NMR Spectra of the Substituted Formamidines (I)-(IV) and (VIII)-(X) in DMSO-D_6* (the CSs of ^{15}N in ppm from $MeNO_2$ [external], the $J_{^{15}N^1H}$ in Hz)

Compound	$N_{(1)}$		$N_{(2)}$		
	δ	$^2J_{NH}$	δ	$^1J_{NH}$	$^2J_{NH}$
I	—	—	-276,2 t	93,3	—
II	-187,9 d	5,1	-211,3 d	88,0	—
III**	-184,6 d	5,8	-241,3 d	90,4	—
	-189,6 d	2,7	-245,2 d	87,8	12,2
IV**	—	—	-251,1	89,9	—
			-253,6	91,7	—
VIII	-186,3 d	6,2	-273,3 t	93,0	—
IX	-188,1 d	2,4	-268,5 m	—	—
X	-155,5	4,2	-283,4 m	—	—

*The concentrations and temperatures are as follows: (I) 0.17 g/ml, 45°C; (II) 0.26 g/ml, 25°C; (III) 0.41 g/ml, 19°C; (IV) 0.05 g/ml, 26°C; (VIII) 0.13 g/ml, 35°C; (IX) 0.20 g/ml, 33°C; (X) 0.35 g/ml, 24°C.

**The mixture of isomers is as follows: (III) 60 and 40%; (IV) 70 and 30%. The data for the major isomer are presented in the upper line.

in relation to its position in the spectrum of the amidine (IV) for the influence of the electron-acceptor and electron-donor p-substituents ($COCH_3$ and NEt_2) correspondingly, i.e., to low or high field. It can be seen by a comparison of the ^{13}C spectra of the amidines studied (the E-isomers in the tautomeric form T_1) with the spectrum of the model amidine (IX) that the CSs of the atoms of the furan ring which are closest to the $N_{(1)}$ atom show little difference.

Analysis of the NMR spectra of the amidines (I)-(VII) also allows the resolution of problems associated with the geometrical and rotational isomerism of these compounds. The ^{13}C spectra of the amidines (I) and (VIII) only contain, in each case, one doublet of the carbon in $N_{(1)}$=CH (Table 3). This indicates that the compounds only exist in one configuration. The character of this configuration (E or Z) may be explained on the basis of the existing literature data and the results of the x-ray structural analysis of the amidine (IV) communicated in the present paper. To begin with, only a few formamidines, for which the z-configuration is found, are known. However, they are thermodynamically unstable, and are converted to the E-isomers [5]. It is also known [6] that, in the case of the spin–spin interaction of the ^{15}N and ^1H nuclei across two bonds separated by a carbon atom with the trigonal hybridization ion, the $^2J_{NH}$ reaches a high negative value (up to −20 Hz) when the =CH proton occurs in the cis orientation to the unshared electron pair of the nitrogen atom. For formamidines, aldimines, and oximes, such a configuration in relation to the $N_{(1)}$=CH bond is accomplished in the Z-isomers. The values of the $^2J_{NH}$ for them equal −9.8 to −10.4 Hz in the spectra of aldimines [7, 8], −13.8 to −18.8 Hz for aldoximes [9, 10], and −12.9 to −13.5 Hz for heterocycles [10], whereas, in the case of the trans orientation of the proton and the unshared pair of electrons (E-isomerism), these constants have the values of 2-4, 2-3, and 3-4 Hz correspondingly [7-10]. The data of the $^2J_{NH}$ for the formamidines are encountered very rarely. We only know the value of 2.4 Hz [11, 12] for the formamidine $PhN{=}CHNMe_2$, which probably pertains to the E-configuration and is close to the values for the E-isomers in the series of compounds considered above.

Taking the above information into account, it can be assumed that the compounds (I)-(VIII) (Table 2) are E-isomers. In particular, the $^1J_{CH}$ constants for the amidine carbon in the ^{13}C spectra of the isomers of the amidine (III) hardly differ. This provides additional rejection of the presence of E- and Z-isomers in the given case. For example, when such isomerism occurs in imines, aldoximes, and hydrazones, the values of the $^1J_{CH}$ for the Z-isomer are 12-17 Hz higher than those for the E-isomer; the differences, as in the case of the $^2J_{NH}$, are determined by the mutual orientation of the unshared pair of electrons of the nitrogen atom and the =CH proton [13, 14].

Data on the temperature dependence of the spectra may serve as additional confirmation of the E-configuration of the amidines (II)-(VII). For example, the heating of the solution of the amidine (II) in DMSO-D_6 to 95°C and the subsequent cooling to room temperature do not lead to any changes in the ^1H spectrum. An analogous picture is also observed in the case of the amidines (III)-(VI). It should only be kept in mind that, in contrast to the compounds (I) and (VIII), two subspectra are observed

TABLE 3. ^{13}C NMR Spectra of the Amidines (I)-(X) in DMSO-D_6[*1] (chemical shifts, δ, ppm)

Compound	5-Me[*2]	CH_2[*3]	CCl_3[*4]	CH[*5]	CN(c)	$C_{(2)}$[*6]	$C_{(3)}$[*7]	$C_{(4)}$[*8]	$C_{(5)}$[*9]	NR or Ph substituent in the furan ring[*10]
I	11,98	48,71	99,69	154,06	115,29	163,32	79,30	111,89	144,67	—
II	12,33	48,81	99,93	153,01; 152,89	115,88	163,66	79,22	112,10	144,40	Me 27,17 27,02
III	12,36; 12,27	48,82	99,89	152,43; 150,80	115,82; 115,70	163,50; 163,30	78,70; 79,24	111,98	144,35	Me 29,68 C_{quat} 51,33
IV	12,37	48,59; 48,57	99,85	150,60; 148,81	115,20	161,77; 162,02	82,09; 81,98	112,59	146,16	$C_{(1)}$ 139,03 138,69 *o*-C 116,77 119,96 *m*-C 129,47 128,81 *p*-C 123,55 123,94
V	12,45	48,61	99,84	150,38; 148,78	115,12	161,47; 161,73	82,71	112,70	146,38	$C_{(1)}$ 138,14 137,69 *o*-C 118,26 121,53 *m*-C 129,30 128,78 *p*-C 127,33 127,65
VI	12,44	48,52	99,76	150,10; 148,90	114,93	161,04; 161,42	83,39	112,80	146,77	Me 26,36 CO 96,27 $C_{(1)}$ 143,27 143,00 *o*-C 115,90 119,24 *m*-C 129,95 129,50 *p*-C 131,80
VII	12,30	48,67	99,89	147,54; 150,35	115,60	162,38; 162,75	80,45	112,35	145,31	Me 12,35 CH_2 43,71 $C_{(1)}$ 144,67 144,61 *o*-C 115,60 121,51 *m*-C 112,58 111,61 *p*-C 127,5 127,42
VIII	—	—	—	155,30; 155,98	115,23; 115,39	164,08; 165,02	80,97	121,93	140,27	$C'_{(1)}$ and $C''_{(1)}$ 129,37, 131,11; *o*-C 125,00, 128,79; *m*-C 128,91, 129,03; *p*-C 127,43, 128,27
IX	12,36	48,66	99,89	153,16	115,57	162,48	79,97	112,22	144,83	NCH_2 42,73, 49,10; OCH_2 65,39, 66,42
X	—	—	—	152,69	—	—	—	—	—	NCH_2 42,70, 48,20; OCH_2 66,00; $C_{(1)}$ 150,50; *o*-C 122,32; *m*-C 128,60; *p*-C 125,90

[*1] For the amidines (II)-(VIII), the upper line presents the chemical shifts of the signals of the major isomer; the lower line presents those of the minor isomer.

[*2] q, J 129-130 Hz.

[*3] t, J 134-137 Hz.

[*4] t, J 6 Hz.

[*5] d, J 174-182 Hz.

[*6] d, J 7-9 Hz.

[*7] t, J 5 Hz.

[*8] t.q., J_t 6 Hz, J_q 3.5 Hz or m.

[*9] t.q., J_t 5.6 Hz, J_q 6.9-7.3 Hz.

[*10] The signals of the atoms of the substituents have the following characteristics. Me q, J 138 Hz (II), 127 Hz (VI), and 134 Hz (VII). CH_2 t, J 134 Hz (VII), 140 Hz (NCH_2) (IX), and 145 Hz (OCH_2) (IX). Broad signals in (X).

TABLE 4. Bond Angles ω (deg) in the Molecule of the Crystallosolvate of the Amidine (IV) with Dimethylsulfoxide

Angle	ω	Angle	ω
$C_{(2)}O_{(1)}C_{(5)}$	107,8 (3)	$Cl_{(2)}C_{(8)}C_{(7)}$	112,1 (3)
$O_{(1)}C_{(2)}C_{(3)}$	108,9 (3)	$Cl_{(3)}C_{(8)}C_{(7)}$	111,7 (3)
$O_{(1)}C_{(2)}N_{(1)}$	122,5 (3)	$C_{(3)}C_{(9)}N_{(3)}$	178,9 (4)
$C_{(3)}C_{(2)}N_{(1)}$	128,5 (3)	$N_{(1)}C_{(10)}N_{(2)}$	119,4 (4)
$C_{(2)}C_{(3)}C_{(4)}$	107,1 (3)	$C_{(12)}C_{(11)}C_{(16)}$	120,2 (3)
$C_{(2)}C_{(3)}C_{(9)}$	124,8 (3)	$C_{(12)}C_{(11)}N_{(2)}$	123,4 (3)
$C_{(4)}C_{(3)}C_{(9)}$	128,0 (3)	$C_{(16)}C_{(11)}N_{(2)}$	116,5 (4)
$C_{(3)}C_{(4)}C_{(5)}$	106,1 (3)	$C_{(11)}C_{(12)}C_{(13)}$	119,5 (4)
$C_{(3)}C_{(4)}C_{(7)}$	124,9 (4)	$C_{(12)}C_{(13)}C_{(14)}$	120,8 (4)
$C_{(5)}C_{(4)}C_{(7)}$	128,6 (4)	$C_{(13)}C_{(14)}C_{(15)}$	119,6 (4)
$O_{(1)}C_{(5)}C_{(4)}$	110,2 (3)	$C_{(14)}C_{(15)}C_{(16)}$	120,5 (4)
$O_{(1)}C_{(5)}C_{(6)}$	114,5 (4)	$C_{(11)}C_{(16)}C_{(15)}$	119,4 (4)
$C_{(4)}C_{(5)}C_{(6)}$	135,3 (4)	$C_{(2)}N_{(1)}C_{(10)}$	119,6 (4)
$C_{(4)}C_{(7)}C_{(8)}$	116,5 (3)	$C_{(10)}N_{(2)}C_{(11)}$	126,6 (4)
$Cl_{(1)}C_{(8)}Cl_{(2)}$	108,3 (2)	$O_{(2)}S_{(1)}C_{(17)}$	104,6 (2)
$Cl_{(1)}C_{(8)}Cl_{(3)}$	107,9 (2)	$O_{(2)}S_{(1)}C_{(18)}$	105,8 (3)
$Cl_{(2)}C_{(8)}Cl_{(3)}$	108,2 (2)	$C_{(17)}S_{(1)}C_{(18)}$	98,1 (3)
$Cl_{(1)}C_{(8)}C_{(7)}$	108,7 (3)		

in each case for the protons of the amidine fragment with the different intensity of the signals of the corresponding atoms (Table 1). In particular, the heating of the solution of the amidine (III) in DMSO-D_6 up to 95°C for 1 h demonstrates the usual picture of dynamic NMR: the broadening of the signals of the =CH, NH, and $C(CH_3)_3$ and the coalescence of the last. When the sample is cooled, the initial spectrum is restored, whereby the 2:3 ratio of the minor and major components is unchanged. A similar temperature dependence is also observed for the amidine (IV), having a phenyl substituent at the $N_{(2)}$ atom. The heating of the compound (IV) leads to broadening and coalescence of the doublets of the protons of both the =CH and the NH at 95°C, as well as the shift of the average NH signal to high field. This process is reversible and the initial proportion of the isomers is preserved on cooling the system. As in the case of the amidine (III), the rate of the interconversion of the isomers at 23°C is low in the NMR time scale.

The data presented indicate the E-configuration of both isomers in the case of the amidines (II)-(VII). Taking into account the information above on their occurrence in a single tautomeric form (T_1), they permit the conclusion that the observed subspectra should refer to the rotational isomers, and their temperature dependence should refer to the inhibited rotation around the $=C-N_{(2)}$ bond, slowed in the NMR time scale at room temperature, which was observed in different amidine systems [15, 16].

It is interesting to note that, for the aryl-substituted amidines (IV)-(VII) with the E_{sp} (minor) isomers, the signal of the ring o-protons in the ^1H spectra is shifted to low field by 0.5-0.6 ppm relative to the signals of the o-protons in the E_{ap} isomers. In the E_{sp} configuration, the protons appear in the proximity of the $C=N_{(1)}$ fragment, and the shift of the protons to low field to 7.8-7.9 ppm is probably associated with the influence of the anisotropy of this bond. The significant difference in the CSs of the o-protons in the spectra of the isomeric $N_{(1)}$-aryl-$N_{(2)}$-arylacetamidines (by 0.77 ppm) was also previously observed [2], but, in contrast to the results presented above, it pertained to the o-protons in two tautomeric forms of the type T_1 and T_2.

The values of the $\Delta G_C^{\#}$, which were equal to 78.3 and 77.0 kJ/mole for the major and minor isomers correspondingly, were determined for the observed dynamic process in the compound (III) for the coalescence of the signals of the protons of the tert-butyl groups (the case of the unequal doublet [17], $\delta\nu_0$ = 29.7 Hz, T_C = 363 K). The values obtained lie in the region of the values for the energy of activation of the rotation around the $=C-N_{(2)}$ bond for formamidines having different nitrogen-containing hetaryls at the $N_{(1)}$ atom and, at the $N_{(2)}$ atom, having two methyl groups (76.6-85.8 kJ/mole [15]). The equilibrium is thereby shifted in favor of the antiplanar isomer with the transoid disposition of the =Ch and NH protons. The analogous situation also occurs for other amidines (Table 1). In spite of the fact that the position of the equilibrium for the rotational isomers depends on the solvent, the antiplanar conformation is predominant for all the amidines (III)-(VII) in all the solvents utilized. The influence of the solvent was studied in the greatest detail for the formamidines (III) and (IV). The ratios of the ap-

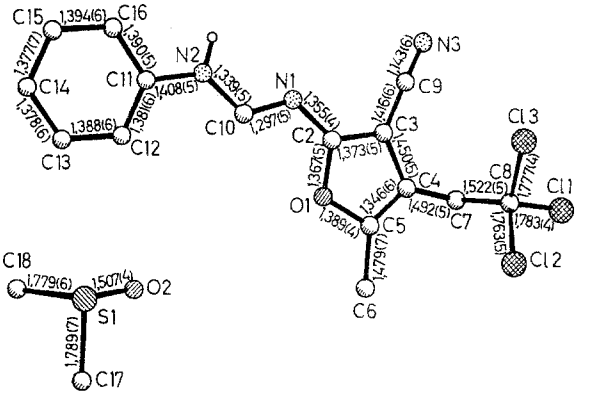
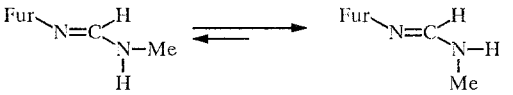


Fig. 1. General view of the independent part of the cell of the crystallosolvate of the amidine (IV) with dimethylsulfoxide. Bond lengths are presented.

and sp-isomers in DMSO-D_6, CD_3OD, and $CDCl_3$ for (III) were found to be 60:40, 60:40, and 90:10; the corresponding ratios for (IV) were 70:30, 60:40, and 60:40.

In the case of the N-methyl-substituted amidine (II), the synplanar conformation is found to be the more thermodynamically favorable conformation. We also observed a similar phenomenon for the analog having two phenyl groups in the furan ring [4]. It can be assumed that the small methyl substituent interacts comparatively weakly with the unshared electron pair of the $N_{(1)}$ atom, and the vicinal interaction of the hydrogen atom at the amidine carbon with the substituent at the $N_{(2)}$, which is less in the synplanar conformation, becomes decisive for the shift of the equilibrium.



The data presented above on the structure and stereochemistry of substituted formamidines in solution are in agreement with the results of the x-ray structural investigation which was performed for the formamidine (IV). Figure 1 shows the general form of the independent part of the elementary cell containing the molecule of the amidine (IV) and the crystallosolvate molecule of dimethylsulfoxide and indicates the bond lengths; the bond angles are presented in Table 4. Of the two isomers existing in the solution, only one antiplanar isomer is realized in the crystalline state.

The molecule of the amidine (IV) is the E-isomer in relation to the $N_{(1)}=C_{(10)}$ double bond: The $C_{(2)}N_{(1)}C_{(10)}N_{(2)}$ torsion angle equals 179.0°. Three plane fragments can be isolated in the molecule (IV): the furan ring (plane 1), the benzene ring (plane 2), and the amidine fragment with the adjoining atoms $C_{(2)}N_{(1)}C_{(10)}N_{(2)}C_{(11)}$ (plane 3). The dihedral angles between the plane 3 and the planes 1 and 2 comprise 7.4° and 10.4° correspondingly; this should not prevent the conjugation of the amidine fragment with the π-system of the furan ring or with the benzene ring if the amidine should exist in the form of the tautomer T_2. It can be seen from the data of the x-ray structure analysis that the amidine (IV) has the structure of the type T_1, in which the amidine fragment is conjugated with the furan ring. In fact, the lengths of the double bonds $C_{(2)}C_{(3)}$ and $N_{(1)}C_{(10)}$ of 1.373(5) Å and 1.297(5) Å correspondingly are somewhat increased by comparison with the standard values of the lengths of the double bonds C=C (1.341 Å in the unsubstituted furan) and N=C (1.279 Å) [18]. The lengths of the single bond and double bond in the amidine fragment are close to the average values for different amidines presented in the work [19], as well as to the values for the corresponding bonds in a few studied formamidines: 1.334(5) Å and 1.302(6) Å in $N_{(1)}$, $N_{(1)}$-hexamethylene-$N_{(2)}$-p-nitrophenylformamidine [20] and 1,334 Å and 1.288 Å in $N_{(2)}$-hydroxyformamidine (formamidoxime) [21].

The contacts between the molecules of (IV) in the crystal are comparable with the sums of the van der Waals radii of the corresponding atoms: $Cl_{(2)}...N_{(3)}$ (1 + x, y, z) 3.153(4) Å and $C_{(10)}...C_{(14)}$ (−x − 1, −y − 1, −z − 1) 3.386 Å (the corresponding values of the sums are 3.30 Å for the N−Cl pair and 3.40 Å for the C−C pair [22]). The intermolecular hydrogen bond observed in the crystal $N_{(2)}-H_{(2)}...O_{(2)}$ (−x, −y, −z) [$N_{(2)}...O_{(2)}$ 2.839(5) Å, $H_{(2)}...O_{(2)}$ 1.94(6) Å, $N_{(2)}-H_{(2)}$ 0.90(6) Å, the $N_{(2)}-H_{(2)}...O_{(2)}$ angle 175(2)°] combines the molecules of the amidine and dimethylsulfoxide.

TABLE 5. Atomic Coordinates ($\times 10^5$; $\times 10^3$ for the hydrogen atoms) in the Structure of the Crystallosolvate of the Amidine (IV) with Dimethylsulfoxide

Atom	x	y	z	Atom	x	y	z
Cl(1)	2492(1)	4885(1)	-55(1)	C(15)	-8116(6)	-5728(5)	-6359(3)
Cl(2)	3252(1)	2583(1)	-1239(1)	C(16)	-7554(5)	-4622(5)	-5542(3)
Cl(3)	1026(1)	1831(1)	-41(1)	C(17)*	8648(7)	1548(7)	1784(4)
S(1)*	7192(2)	1312(1)	2497(1)	C(18)*	5636(7)	1994(8)	1530(5)
O(1)	-1597(3)	489(3)	-3880(2)	H(2)	-637(6)	-243(5)	-426(4)
O(2)*	7802(4)	2497(5)	3388(3)	H(61)	142(7)	293(6)	-371(4)
N(1)	-3992(4)	-675(4)	-3541(2)	H(62)	140(8)	109(7)	-381(5)
N(2)	-5711(4)	-2499(4)	-4668(2)	H(63)	23(8)	231(7)	-461(5)
N(3)	-3396(4)	1624(5)	-961(3)	H(71)	-33(5)	395(5)	-146(3)
C(2)	-2611(4)	303(4)	-3262(3)	H(72)	80(4)	407(4)	-216(3)
C(3)	-2023(4)	1293(4)	-2396(3)	H(10)	-365(5)	-154(5)	-483(4)
C(4)	-572(4)	2167(4)	-2505(3)	H(12)	-453(6)	-285(6)	-631(4)
C(5)	-370(4)	1644(4)	-3409(3)	H(13)	-553(10)	-479(9)	-767(6)
C(6)	791(6)	2042(7)	-4017(4)	H(14)	-776(5)	-650(5)	-770(4)
C(7)	352(5)	3492(4)	-1804(3)	H(15)	-904(6)	-643(6)	-641(4)
C(8)	1700(4)	3195(4)	-850(3)	H(16)	-814(9)	-447(8)	-489(6)
C(9)	-2791(4)	1464(4)	-1605(3)	H(171)*	974(7)	119(6)	226(4)
C(10)	-4333(4)	-1550(4)	-4386(3)	H(172)*	823(7)	101(7)	125(5)
C(11)	-6215(4)	-3585(4)	-5514(3)	H(173)*	847(6)	279(6)	192(4)
C(12)	-5467(5)	-3639(5)	-6300(3)	H(181)*	489(7)	192(7)	173(5)
C(13)	-6042(5)	-4754(5)	-7105(3)	H(182)*	597(7)	285(7)	138(5)
C(14)	-7362(6)	-5794(5)	-7136(3)	H(183)*	534(7)	137(6)	87(5)

*The atoms of the solvate molecule of dimethylsulfoxide.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on the Bruker WM-250 spectrometer. The ^{13}C NMR spectra were recorded on the Bruker AM-300 spectrometer with the working frequency of 75.47 MHz. The ^{13}C CSs were measured with the accuracy exceeding 0.1 ppm in relation to the signal of the solvent from the spectra obtained with the ^{13}C–^{1}H regime with the complete suppression of the spin–spin interaction with protons, and were presented in relation to TMS. The ^{13}C–^{1}H SSCCs were measured from the high-resolution ^{13}C spectra obtained with the regime of "gated decoupling" with the accuracy of ± 1 Hz for ^{1}J and ± 0.3 Hz for ^{2}J and ^{3}J. The assignment of the signals was performed on the basis of the values of the CSs, the SSCCs, and the concentrations of the isomers determined from the ^{1}H NMR spectra. The narrowing of the resonance signals was utilized for the treatment of the spectra (the Lorentz–Gauss transformation).

The ^{15}N spectra were obtained on a Bruker AM-300 spectrometer with the working frequency of 30.42 MHz. Methods both of nonselective transfer of the ^{1}H → ^{15}N polarization (INERT) [2] and of the selective transfer of the polarization from one of the protons (SPT) [24], which allowed a sharp decrease in the time of the experiment, were utilized for the plotting of the spectra. The ^{15}N CSs (± 0.05 ppm) were presented relative to $CH_3{}^{15}NO_3$ as an external standard. The high-field CSs are presented with the minus sign. The accuracy of the measurement of the ^{15}N–^{1}H SSCC comprises ± 0.4 Hz. The ^{13}C and ^{15}N spectra of the compounds studied were taken in ampuls with the external diameter of 10 mm; the ampul with the diameter of 5 mm was utilized for the amidine (IV) labeled with the isotope ^{15}N.

The cell parameters and the intensities of the 3517 independent reflections with the $I \geq 3\sigma$ were measured on a 4-circle Siemens P3/PC automatic diffractometer ($LMoK_\alpha$, a graphite monochromator, the $\theta/2\theta$-scanning, and the $\theta_{max} = 30°C$). The crystals of the 1:1 crystallosolvate of the amidine (IV) with dimethylsulfoxide were triclinic: $a = 8.888(2)$ Å, b = 9.071(3) Å, c = 13.113(4) Å, $\alpha = 90.04(2)°$, $\beta = 106.63(2)°$, $\gamma = 98.85(2)°$, V = 999.8(1.0) Å^3, $d_{calc} = 1.291$ g/cm^3, and Z = 2; the space group is P1. The structure was deciphered by the direct method using the SHELTXTL programs and was specified by the full-matrix method of least squares with the anisotropic approximation for the nonhydrogen atoms. The hydrogen atoms were developed objectively by the difference synthesis and were included in the specification in the isotropic approximation with the

fixed B_{iso}. The final values of the divergence factors were R = 0.061 and R_W = 0.061. All calculations were performed using the SHELTXTL PLUS programs (PC version). The atomic coordinates are given in Table 5; the isotropic equivalent thermal parameters may be obtained from the authors.

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