RING–RING TAUTOMERISM

K. N. Zelenin and V. V. Alekseev

The superposition within a single molecule of competing ring–chain tautomeric pairs, the minimum structural requirement of which is the presence of one nucleophilic (OH, NH, SH, etc.) and two electrophilic (C=N, C=O, etc.) centers or the reverse, is a method of constructing ring–ring or ring–chain–ring tautomeric systems. On the basis of the structural characteristics of alkylidene derivatives of thiohydrazides, thiosemicarbazides, thiocarbonohydrazides and amidrazones, bis-hydrazones, bis-oximes, and oximohydrazones of 1,3-dioxo compounds, it has been possible to realize for the first time heterocyclic, tautomeric combinations of pyrazoline–isoxazoline, isoxazoline–1,3,4-thiadiazoline, pyrazoline–1,3,4-thiadiazoline, 1,3,4-thiadiazoline–1,2,4-triazolidene, 1,2,4-triazolidene–1,2,4,5-hexahydrotetrazine, 1,2,4,5-hexahydrotetrazine–tetrahydropyran, tetrahydropyran–1,3,4-thiadiazoline, etc.

Tautomerism is a fundamental property of heterocyclic derivatives that has attracted the constant attention of investigators [1]. In turn, ring–chain tautomerism (chain $\rightleftarrows$ ring, A $\rightleftarrows$ B) is essential to an understanding of the general questions of heterocyclic chemistry [2, 3]. Its study is particularly important in connection with problems of ring opening and recyclization [4]. These ring–chain transformations usually come about through a reversible intramolecular addition of OH, NH, SH, etc. groups by some sort of polar multiple bond. In this case, when there are more than two reacting portions in a single molecule, it is to be expected that the two ring–chain processes will compete and in so doing give rise to a three-membered equilibrium, ring (B)–chain (A)–ring (C), i.e., B $\rightleftarrows$ A $\rightleftarrows$ C. If the thermodynamic stability of chain A is small, such a superposition can lead to a new situation, to an equilibrium in which only the cyclic tautomers are observed, to the appearance of a ring–ring tautomerism (B $\rightleftarrows$ C).

A comparison of the simplest kinds of ring–ring of ring–chain–ring tautomerism, those with the simultaneous participation of three reaction centers (C=O and C=N multiple bonds on the one hand and OH, NH, and SH groups on the other, though the list can be extended considerably), shows (Table 1) that it is possible to realize a minimum of 21 combinations. Consider that the number of reaction centers can be more than three, include here variations in ring size, and add the variety of heterocycles that can be involved in the equilibrium, and one would expect this phenomenon to have been adequately described long ago. Meanwhile, up to the start of our investigations only one structural combination was known in the literature. This is the well-known mutarotation of carbohydrates with the participation of saturated furan and pyran rings, which comes about by the competing, intramolecular addition of two hydroxyl groups to one carbonyl group (2 nucleophiles + 1 electrophile, 2N + 1E*). Information about other combinations, including ring–ring tautomerism involving nitrogen heterocycles, was lacking prior to the start of our investigations. The present review also gives the results of a study of ring–ring and ring–chain–ring transformations obtained beginning in 1981 when ring–ring tautomerism was first observed in the thiobenzoylhydrazone of acetylacetone [5].

*These abbreviations for the classifications will be used in what follows.

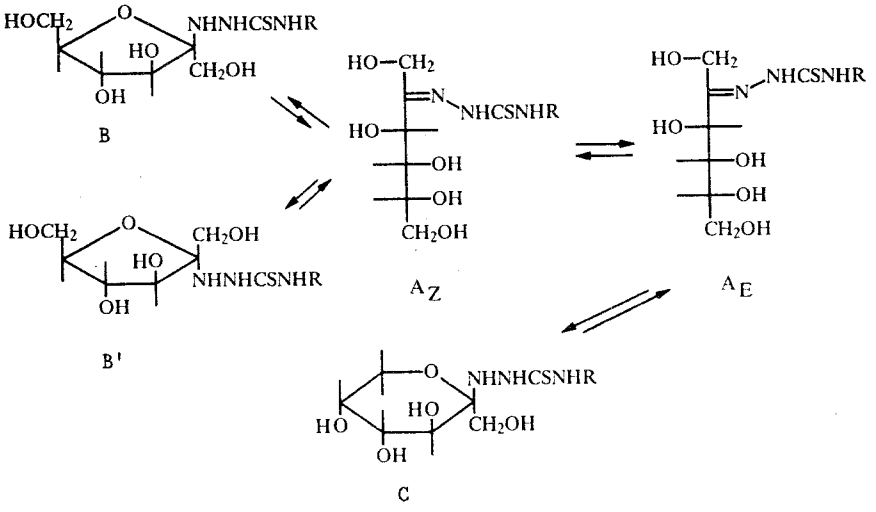
S. M. Kirov Military Medical Academy, Saint Petersburg 194175. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 851-860, June, 1992. Original article submitted April 22, 1992.

 0009-3122/92/2806-0708$12.50

TABLE 1. Simplest Combinations for Ring–Ring Tautomerism

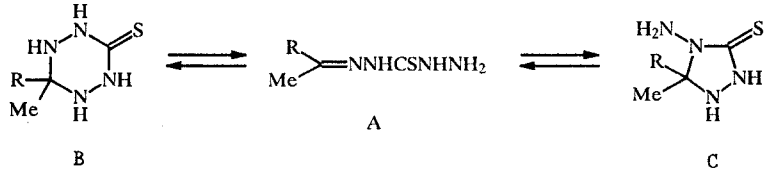
2 Nucleophiles + 1 Electrophile				Electrophiles + 1 Nucleophile			
C=O	2 OH	2 NH	2 SH	OH	2 C=O	2 C=N	C=O, C=N
	OH, NH	OH, SH	NH, SH	NH	2 C=O	2 C=N	C=O, C=N
C=N	2 OH	2 NH	2 SH				
	OH, NH	OH, SH	NH, SH	SH	2 C=O	2 C=N	C=O, C=N

1. 2 Nucleophiles and 1 Electrophile (2N + 1E). 2OH + C=N. Related to the mutarotation of carbohydrates is the behavior of fructose thiosemicarbazone and its 4-substituted homologs. It is known that a ring–chain equilibrium between the hydrazone and pyranose forms is inherent in aldose thiosemicarbazones [6]. In the case though of fructose derivatives Ia-c, there is a four-component equilibrium involving α- and β-furanose (B and B′, at 15%) forms and the β-pyranose form (C, 5%). They coexist with the linear tautomeric form, IA (60-65%), which predominates in this case and is present in comparable amounts of the geometric (A_Z and A_E) isomers [7].



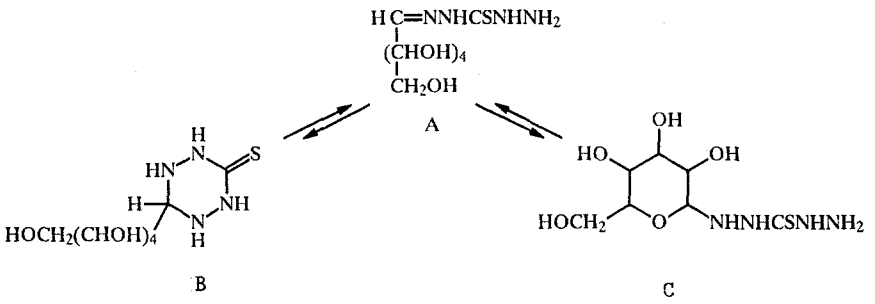
Ia R=H, b R=Me, c R=CH_2Ph

2NH + C=N. Thiocarbonohydrazone molecules have two NH groups that are potentially able to compete in a tautomeric process. However, until recently only the terminal amino group was thought to take part in the ring–chain equilibrium for these substances [8, 9], and only the thiocarbonohydrazone IA ⇄ 1,2,4,5-hexahydrotetrazine-3-thione IIB was established. At the same time, it is known [10-13] that the amino group in 1-alkylidenamidrazone molecules (equivalent to the NH(3) group in thiocarbonohydrazones) takes part in intramolecular addition at the C=N bond to establish an equilibrium with the cyclic, 1,2,4-triazoline form. On careful study of the structures of thiocarbonohydrazones II in DMSO solution, it was found [14] that in specific cases (R = alkyl) there is a ring–chain–ring equilibrium, IIB ⇄ IIA ⇄ IIC involving 1,2,4,5-hexahydrotetrazoline, 1,2,4-triazoline, and linear hydrazone forms. The content of 1,2,4-triazoline tautomer IIC in these derivatives does not exceed 25%, whereas thiocarbonohydrazone of acetaldehyde (II, R = H), for example, is pure 1,2,4,5-hexahydrotetrazine-3-thione IIB [8, 9].



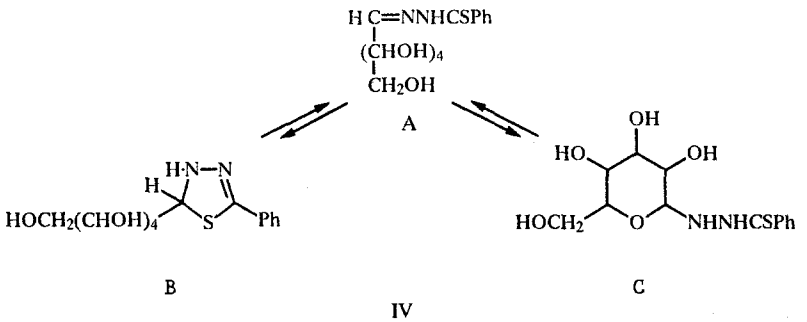
IIa R=Me, b R=Et, cR=C_4H_9, d R=CH_2Ph

OH, NH + C=N. It is not surprising that the ring–chain–ring equilibrium 1,2,4,5-hexahydrotetrazine-3-thione B ⇄ hydrazone A ⇄ tetrahydropyran C (in a ratio of 60:30:10 in DMSO) [6] appears in IIa, b, the thiocarbonohydrazones of glucose and galactose. At the same time, only ring–chain equilibrium IIA ⇄ IIIB is observed with mannose thiocarbonohydrazone, IIIc.



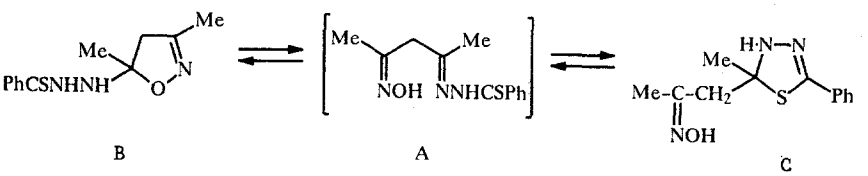
Carbohydrates III: a) glucose, b) galactose, c) mannose.

OH, SH + C=N. Ring–ring tautomerism was to be expected for aldose thiobenzoylhydrazones in view of the tendency of the thiobenzoylhydrazones of the simplest aldehydes and ketones to exist in the 1,3,4-thiadiazoline form; a tendency which they display to an even greater degree than do the thiocarbonohydrazones to occur in the 1,2,4,5-hexahydrotetrazone form, IIB. We found [19] that glucose thiobenzoylhydrazone, IV, in DMSO solution exists in the form of a ring–chain–ring tautomeric mixture of equal amounts of the 1,3,4-thiadiazoline-2, IVB, and pyranose, IVC, forms with a small (10%) amount of the hydrazone form, IVA.



IV

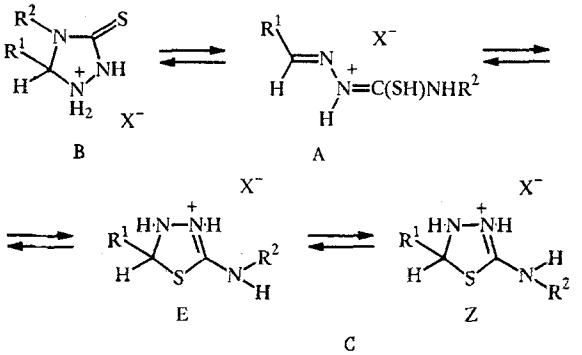
The behavior of the "oximothiobenzoylhydrazone" of acetylacetone, V, in solution is an example of this kind of ring–ring equilibrium. In any solution (DMSO, DMF, CH_3OH, $CHCl_3$, etc.), this substance exists in two cyclic forms, 5-thiobenzoyl-hydrazino-2-isoxazole, VB, and 5-(2-hydroxylimino)-1,3,4-thiadiazoline-2-one, VC (30% in DMSO) [20].



V

NH, SH + C=N. The possibility of ring–ring tautomerism is, a priori, obvious for thiosemicarbazones, in which there are two groups, NH and SH, that are similar in activity and that can be involved in the formation of a 1,2,4-triazoline or 1,3,4-thiadiazoline ring, respectively. It is even more likely that ketone 2,4-disubstituted thiosemicarbazones are characterized by the 1,2,4-triazoline structure [21-24], and that the thiosemicarbazones of almost any carbonyl compound in acidic solution have the 1,3,4-thiadiazoline structure [21-25]. It has been found [26] that such simple representatives of the thiosemicarbazones as aliphatic aldehyde derivatives VIa-g in saturated solutions of trifluoroacetic acid exist in the form of

ring–chain–ring tautomeric mixtures of the linear cation VIA and 1,2,4-triazoline VIB in an amount not exceeding 10%, and 1,3,4-thiadiazoline tautomer VIC (80-90%). The latter, in turn, is a mixture of the E and Z geometric isomers if R^2 = H [26].

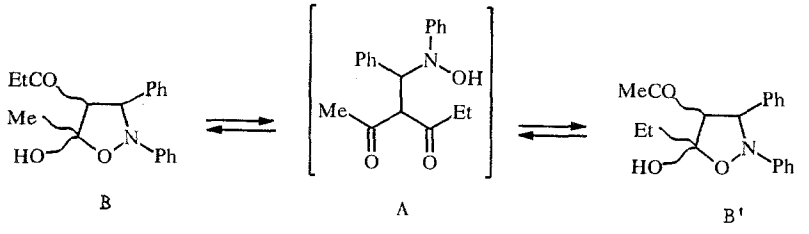


VI a R^1=CH_3, R^2=H; b R^1=R^2=CH_3; c R^1=CH_3, R^2=$CH_2C_6H_5$; d R^1=CH_3, R^2=C_6H_5; e R^1=C_2H_5, R^2=H; f R^1=C_2H_5, R^2=$CH_2C_6H_5$; g R^1=$CH(CH_3)_2$, R^2=H

2. 1 Nucleophile and 2 Electrophiles (1H + 2E).

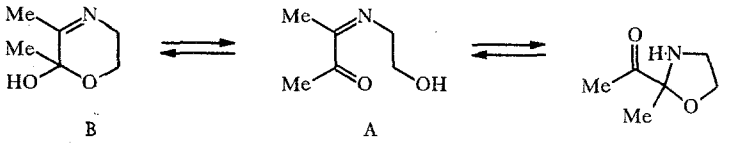
Less is known concerning ring–ring equilibria of this kind.

OH + 2 C=O. Knowing of the ring-chain tautomerism of β-N-hydroxylamino-aldehydes from the literature, we synthesized 4-acyl-5-hydroxyisoxazolidenes VII by the action of nitrones on 1,3-dioxo compounds and found that in this case, when the substituents are of similar bulk, it is possible to observe ring–ring equilibrium VIIB ⇄ $VIIB^1$ [29]. Tautomers VIIB and $VIIB^1$, in turn, occur as mixtures of diastereoisomers.



VII

OH + C=O, C=N. A report recently appeared [30] that the product of the condensation of ethanolamine with diacetyl VIII is involved in the triple ring–chain–ring equilibrium 2-hydroxy-5,6-dihydrooxazine VIIIB ⇄ α-iminoketone VIIA ⇄ 2-acetyl-oxazolidine VIIIC.



VIII

3. 2 Nucleophiles and 2 Electrophiles (2N + 2E). 2 NH + 2 C=N. When "bis-hydrazones" of 1,3-dioxo compounds, which in fact have 5-hydrazino-2-pyrazoline structure IXB [31-34], have an unsymmetric structure (R^1 = R^2, or R^3 = R^4), the tautomeric equilibrium of the two 5-hydrazino-2-pyrazoline forms, IXB ⇄ IXB^1 is observed [35, 36] (Table 2).

The fraction of tautomer IXB grows rapidly with the increasing bulk of the substituent in the 3 position (R^2); i.e., cyclization takes place at the sterically more accessible C=N bond. The nature of the solvent and the temperature have virtually no effect on the position of equilibrium IXB ⇄ IXB^1, which occurs when the volumes of the substituents in the 3 and 5 positions differ only insignificantly (see Table 2).

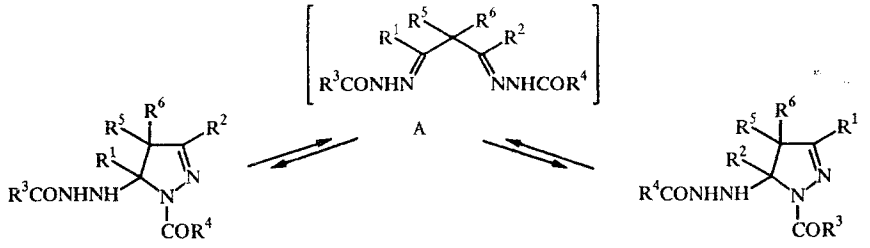
For these substances, IX, cis-trans isomerism is possible because of the different mutual arrangement of the alkyl groups in the 4 and 5 positions (if R^5 = R^6). This also occurs in derivative IXf (R^5 = H, R^6 = CH_3), which exists as a mixture of stereoisomers (cis:trans = 2:1).

TABLE 2. Tautomeric Composition of Compounds IX in Solutions

Compound	R^1	R^2	R^3	R^4	R^5	R^6	Solvent	B, %
a	CH_3	H	C_6H_5	C_6H_5	H	H	C_5D_5N	0
b	CH_3	C_2H_5	C_6H_5	C_6H_5	H	H	Acetone-D_6	60
c	CH_3	C_3H_7	C_6H_5	C_6H_5	H	H	$CDCl_3$	85
d	CH_3	i-C_4H_9	C_6H_5	C_6H_5	H	H	DMSO-D_6	100
e	CH_3	CH_3	C_6H_5	4-ClC_6H_4	CH_3	CH_3	DMSO-D_6	50

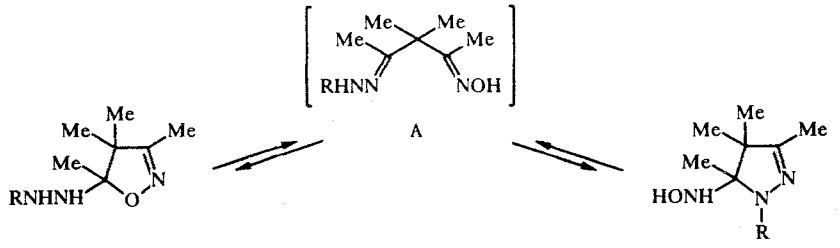
TABLE 3. Tautomeric Composition of Compounds X in Solutions

Compound	R	Solvent	Content, %		Solvent	Content, %	
			B	C		B	C
a	CH_3	C_6D_6	50	50	DMSO-D_6	95	5
b	C_2H_5	$CDCl_3$	15	85	C_5D_5N	55	45
c	$CH_2C_6H_5$	$CDCl_3$	7	93	DMSO-D_6	70	30
d	$CH(CH_3)_2$	$CDCl_3$	—	100	DMSO-D_6	5	95
e	C_6H_5	$CDCl_3$	—	100	DMSO-D_6	50	50



B IX B'

NH, OH + C=O, C=N. From the fact that β-monooximes tend to exist in the 5-hydroxy-2-isoxazoline [2, p. 104], and monohydrazones in the 5-hydroxy-2-pyrazoline form [37], competition between these rings was expected in the case of β-oximohydrazones. It is more common for these substances to have the 5-hydrazino-2-isoxazoline form, XB [38], but aldooximohydrazones of aroyl acetaldehydes occur as 5-hydroxylamino-2-pyrazones, XC [39]. Individual cases of "alkylhydronooximes" of 3,3-dimethyl-2,4-pentandione X (Table 3) form a ring–ring tautomeric mixture of 5-hydrazino-2-isoxazoline XB and 5-hydroxylamino-2-pyrazoline XC [40]



B X C

NH, SH + C=O, C=N. "Monothiobenzoylhydrazones" of acetylacetone, XIb exist in the crystalline state in the 5-hydroxy-2-pyrazoline form, XIB, which is usual for the acylhydrazones of 1,3-dioxo compounds. In any solvent, however, they demonstrate the capacity for 5-hydroxy-2-pyrazoline–1,3,4-thiadiazoline ring–ring tautomerism (XIB=XIC) [5, 41]. English investigators came to the same conclusion [42].

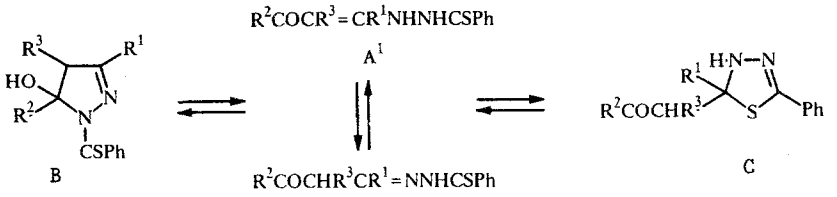
A systematic study of the effect of structural parameters and external factors on the position of tautomerism of this kind revealed that here there is, in principle, a four-component, ring–chain–ring equilibrium, B ⇄ A ⇄ A^1 ⇄ C (in DMSO solutions). In addition to the already mentioned, cyclic forms, XIB and XIC, linear tautomers, hydrazone XIA and enehydrazine

TABLE 4. Tautomeric Composition of Compounds XI in DMSO-D_6 Solutions

Compound	R^1	R^2	R^3	A^1	B	C
a	H	$C(CH_3)_3$	H	—	100	—
b	CH_3	CH_3	H	—	50	50
c	CH_3	$C(CH_3)_3$	H	15	85	—
d	CF_3	CH_3	H	—	100	—
e	C_2H_5	C_2H_5	H	—	35	65
f	C_2H_5	$C(CH_3)_3$	H	10	90	—
g	$CH(CH_3)_2$	$CH(CH_3)_2$	H	—	—	100
h	$CH(CH_3)_2$	$C(CH_3)_3$	H	5	95	—
i	$C(CH_3)_3$	$C(CH_3)_3$	H	*	55	30
j	CH_3	CH_3	CH_3	—	30	70
k	CH_3	CH_3	$CH(CH_3)_2$	—	25	75

*15% tautomer A.

XIA[1], can also be observed. This is reflected in Table 4 in the case of derivatives of aliphatic, β-dicarbonyl compounds. A similar situation is also characteristic of thiobenzoylhydrazones of aroylacetones ($R^1 = CH_3$, R^2 = aryl, R^3 = H) [43].



XI

Thus, the phenomenon of ring–ring, or in the more general case, ring–chain–ring tautomerism, which for a long time received no special attention, has proved to be quite widespread. Of 21 tautomeric combinations with three reaction centers (see Table 1), nine are so far known, and the total number of tautomeric variants realized comes to 12, with five of them being ring–ring equilibria.

Included among them are such tautomeric pairs as tetrahydropyran–1,2,4,5-hexahydrotetrazine, 1,3,4-thiadiazoline–tetrahydropyran, 1,3,4-thiadiazoline–1,2,4-triazoline, 1,3,4-thiadiazoline–isoxazoline, 1,2,4,5-hexahydrotetrazine –1,2,4-triazoline, etc. One can assume with confidence that the circle of new examples will expand. The property itself finds practical expression, as this occurs in mutarotation, where the competing stability of the α- and β-pyranose (furanose) forms determines the structure of the nucleotides obtainable from them.

In the course of investigation, new varieties of azolines were synthesized, 5-amino- and 5-hydrazino-2-isoxazolines [40, 44, 45], 5-hydroxylamino- [39], 5-hydrazino, and 5-methylene-2-pyrazolines [31-34, 46-48], among which were found compounds with valuable properties (antimicrobial [49-51] and antitumor [50-52] action, alcohol dehydrogenase inhibition [53, 54], etc.).

A basic improvement has been introduced, refining and supplementing ideas about the structure of thiosemicarbazones [22, 55, 56], thioacylhydrazones [15-18], thiocarbonohydrazones [14] , 1,3-bis-oximes [45, 57], 1,3-bis-hydrazones [31-36], 1,3-oximohydrazones [38-40], etc. [58].

It appears that the approach discussed should stimulate other ideas in the area of molecular design of tautomeric systems [59], a study, for example, of gradual, stepwise ring–chain tautomerism, a search for ring–chain equilibria with the participation of migrating groups besides the proton (including ring–chain acylotropy), etc.

LITERATURE CITED

1. J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, The Tautomerism of Heterocycles, Academic Press, New York (1976).
2. R. É. Valter, Ring–Chain Isomerism in Organic Chemistry [in Russian], Zinatne, Riga (1978).
3. R. E. Valters and W. Flitsch, Ring–Chain Tautomerism, Plenum, New York (1985).
4. H. Van der Plas, Ring Transformations of Heterocycles, Academic Press, New York (1973).
5. V. A. Khrustalev, V. V. Alekseev, and K. N. Zelenin, Zh. Org. Khim., **17**, 2451 (1981).
6. K. N. Zelenin, V. V. Alekseev, O. B. Kuznetsova, P. B. Terent'ev, V. V. Lashin, V. V. Ovcharenko, and L. A. Khorseeva, Zh. Org. Khim. (in press).
7. V. V. Alekseev and K. N. Zelenin, Khim. Geterotsikl. Soedin., No. 4, 565 (1992).
8. R. W. Lamon, J. Org. Chem., **34**, 756 (1969).
9. G. Rajendran and S. R. Jain, Org. Magnet. Resonance, **22**, 6 (1984).
10. V. A. Khrustalev, K. N. Zelenin, V. P. Sergutina, and V. V. Pinson, Khim. Geterotsikl. Soedin., No. 8, 1138 (1980).
11. V. A. Khrustalev, V. P. Sergutina, K. N. Zelenin, and V. V. Pinson, Khim. Geterotsikl. Soedin., No. 9, 1264 (1982).
12. V. V. Pinson, V. A. Khrustalev, K. N. Zelenin, and Z. M. Matveeva, Khim. Geterotsikl. Soedin., No. 10, 1415 (1984).
13. V. V. Pinson, "Syntheses in the amidrazone series by the reaction of S-methylthioamide iodides with hydrazine derivatives," Dissertation for the degree of Candidate of Chemical Sciences, VNIIINeftekhim. Leningrad (1986).
14. K. N. Zelenin, V. V. Alekseev (Alekseyev), T. Ye. Gabis, S. I. Yamimovich, and T. I(J). Pekhk (Pekh), Tetrahedron Lett., **31**, 3927 (1990).
15. K. N. Zelenin, V. A. Khrustalev, V. V. Pinson, and V. V. Alekseev, Zh. Org. Khim., **16**, 2237 (1980).
16. K. N. Zelenin, V. A. Khrustalev, V. V. Alekseev, P. A. Sharbatyan, and A. T. Lebedev, Khim. Geterotsikl. Soedin., No. 7, 904 (1982).
17. K. N. Zelenin, V. V. Alekseev, and V. A. Khrustalev, Zh. Org. Khim., **20**, 169 (1984).
18. V. V. Alekseev, "Synthesis and structure of thioacylhydrazones," Dissertation for the degree of Candidate of Chemical Science, VMedA, Leningrad (1983).
19. V. V. Alekseev and K. N. Zelenin, Khim. Geterotsikl. Soedin., No. 4, 571 (1992).
20. K. N. Zelenin, V. V. Alekseev, I. P. Bezhan, A. Yu. Ershov, V. A. Khrustalev, and S. I. Yakimovich, Khim. Geterotsikl. Soedin., No. 7, 1001 (1985).
21. M. Uda and S. Kubota, J. Heterocycl. Chem., **16**, 1275 (1979).
22. K. N. Zelenin, V. V. Alekseev, O. V. Solod, O. B. Kuznetsova, and V. N. Torocheshnikov, Dokl. Akad. Nauk SSSR, **296**, 1133 (1987).
23. K. Schulze, Ch. Richter, K. Klatt, and P. Ludwig, Z. Chem., **28**, 288 (1988).
24. K. N. Zelenin, O. B. Kuznetsova, V. V. Alekseev (Alekseyev), P. B. Terentyev, V. N. Torocheshnikov, and V. V. Ovcharenko, Tetrahedron (in press).
25. K. H. Mayer and D. Lauerer, Ann., **731**, 142 (1970).
26. K. N. Zelenin, V. V. Alekseev (Alekseyev), O. B. Kuznetsova, V. N. Torochesnikov, and L. A. Khorseyeva, Tetrahedron Lett. (in press).
27. K. N. Zelenin, I. P. Bezhan, L. A. Sviridova, G. A. Golubeva, and I. A. Motorina, Khim. Geterotsikl. Soedin., No. 8, 1137 (1985).
28. K. N. Zelenin, I. A. Motorina, L. A. Sviridova, I. P. Bezhan, A. Yu. Ershov, G. A. Golubeva, and Yu. G. Bundel', Khim. Geterotsikl. Soedin., No. 9, 1270 (1987).
29. K. N. Zelenin and I. P. Bezhan, Zh. Org. Khim., **25**, 876 (1989).
30. B. Alcaide, R. G. Rubio, J. Plumet, and I. M. Rodriguez-Campos, Tetrahedron Lett., **31**, 4211 (1990).
31. K. N. Zelenin, M. Yu. Malov, I. P. Bezhan, V. A. Khrustalev, and S. I. Yakimovich, Khim. Geterotsikl. Soedin., No. 6, 854 (1985).
32. K. N. Zelenin, M. Yu. Malov, I. V. Zerova, P. B. Terent'ev, and A. G. Kalandarishvili, Zh. Org. Khim., **24**, 1210 (1988).
33. K. N. Zelenin, M. Yu. Malov, S. I. Yakimovich, P. B. Terent'ev, and A. G. Kalandarishvili, Zh. Org. Khim., **24**, 426 (1988).

34. M. Yu. Malov, "5-Hydrazino-2-pyrazolines," Dissertation for the degree of Candidate of Chemical Sciences, VMedA, Leningrad (1988).
35. K. N. Zelenin, M. Yu. Malov, I. P. Bezhan, V. A. Khrustalev, and S. I. Yakimovich, Khim. Geterotsikl. Soedin., No. 7, 1000 (1985).
36. M. Yu. Malov, K. N. Zelenin, and S. I. Yakimovich, Khim. Geterotsikl. Soedin., No. 10, 1358 (1988).
37. N. A. Parpiev, V. G. Yusupov, S. I. Yakimovich, and Kh. T. Sharipov, Acylhydrazones and Their Complexes With Transition Metals, Fan, Tashkent (1988).
38. K. N. Zelenin, A. Yu. Ershov, I. P. Bezhan, V. A. Khrustalev, and S. I. Yakimovich, Khim. Geterotsikl. Soedin., No. 6, 855 (1989).
39. K. N. Zelenin, M. Yu. Malov, A. Yu. Ershov, A. G. Kalandarishvili, V. I. Kadantsev, and N. N. Kolotyrkina, Khim. Geterotsikl. Soedin., No. 7, 927 (1989).
40. K. N. Zelenin, A. Yu. Ershov, M. Yu. Malov, and S. I. Yakimovich, Dokl. Akad. Nauk SSSR, **289**, 1132 (1986).
41. K. N. Zelenin, V. V. Alekseev, V. A. Khrustalev, S. I. Yakimovich, V. N. Nikolaev, and N. V. Koshmina, Zh. Org. Khim., **20**, 180 (1984).
42. D. M. Evans, L. Hill, D. R. Taylor, and M. Myers, J. Chem. Soc. Perkin 1, No. 8, 1499 (1986).
43. S. I. Yakimovich, K. N. Zelenin, B. N. Nikolaev, N. V. Koshmina, V. V. Alekseev, and V. A. Khrustalev, Zh. Org. Khim., **19**, 1875 (1983).
44. K. N. Zelenin and A. Yu. Ershov, Khim. Geterotsikl. Soedin., No. 10, 1385 (1990).
45. A. Yu. Ershov, "Synthesis and structure of 5-functionally substituted isoxazolidenes and 2-isoxazolines," Dissertation for the degree of Candidate of Chemical Sciences, VMedA, Leningrad (1989).
46. M. Yu. Malov and A. Yu. Ershov, Abstracts of the Vth International IUPAC Conference on Organic Synthesis, Moscow (1986), p. 105.
47. M. Yu. Malov, K. N. Zelenin, and S. I. Yakimovich, Abstracts of the Vth All-Union Conference on the Chemistry of Dicarbonyl Compounds, Riga (1986), p. 136.
48. K. N. Zelenin, I. P. Bezhan, O. B. Kuznetsova, M. Yu. Malov, and V. V. Alekseev, Abstracts of the 2nd Regional Conference on the Chemistry of Eneamines, Perm (1991), p. 109.
49. K. N. Zelenin, L. A. Khorseeva, V. V. Alekseev, A. M. Korolyuk, E. P. Sivolodskii, G. A. Sofronov, and S. A. Kutsenko, Khim.-farm. Zh., No. 12, 40 (1990).
50. L. A. Khorseeva, V. V. Alekseev, and K. N. Zelenin, Abstracts of the XVth All-Union Chugaev Symposium on the Chemistry of Complex Compounds, Krasnoyarsk (1987), p. 301.
51. V. V. Alekseev, Abstracts of the VIIth All-Union Conference of the Chemistry of Dicarbonyl Compounds, Riga (1991), p. 5.
52. L. A. Khorseeva, V. V. Alekseev, K. N. Zelenin, M. T. Toshev, M. Yu. Lidak, and V. N. Verovskii, Koord. Khim., **17**, 396 (1991).
53. L. A. Kozhemyakin, K. N. Zelenin, Yu. Yu. Bonitenko, L. I. Ivanova, A. V. Zemlyanoi, and A. M. Korolyuk, Vopr. Med. Khim., No. 3, 43 (1990).
54. K. N. Zelenin, L. I. Ivanova, E. Yu. Bonitenko, A. Yu. Ershov, S. I. Yakimovich, and I. V. Zerova, Abstracts of the VIIth All-Union Conference of the Chemistry of Dicarbonyl Compounds, Riga (1991), p. 95.
55. K. N. Zelenin, O. V. Solod, A. B. Tomchin, and M. Yu. Malov, Khim. Geterotsikl. Soedin., No. 1, 128 (1986).
56. K. N. Zelenin, V. V. Alekseev, T. I. Pekhk, O. V. Solod, O. B. Kuznetsova, P. B. Terent'ev, and A. G. Kalandarishvili, Khim. Geterotsikl. Soedin., No. 9, 1260 (1990).
57. A. Yu. Ershov, S. I. Yakimovich, K. N. Zelenin, and I. V. Zerova, Zh. Org. Khim., **24**, 2287 (1988).
58. K. N. Zelenin, Abstracts of the VIIth All-Union Conference of the Chemistry of Dicarbonyl Compounds, Riga (1991), p. 12.
59. V. I. Minkin, L. P. Olekhnovich, and Yu. A. Zhdanov, Molecular Design of Tautomeric Systems [in Russian], Izd. Rost. Univ., Rostov-on-the-Don (1977).