ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 11, pp. 1640–1644. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © N.N. Smolyar, Yu.M. Yutilov, 2008, published in Zhurnal Organicheskoi Khimii, 2008, Vol. 44, No. 11, pp. 1663–1667.

Cyclotransformation in the Series of Monocyclic 3-Nitropyridin-2(1*H*)-ones

N. N. Smolyar and Yu. M. Yutilov†

Litvinenko Institute of Physical Organic and Coal Chemistry, Ukrainian National Academy of Sciences, Donetsk, 83114 Ukraine
e-mail: smolyar_nik@mail.ru

Received November 12, 2007

Abstract—The interaction of 3-nitropyridine-2(1*H*)-one and its N'-methyl derivative with hydrazine hydrate leads to the formation of the pyrazole and the carbodihydrazide. 4-Nitropyrazole and the carbodihydrazide are formed from 3,5-dinitropyridine-2(1*H*)-one and its N'-methyl derivative under similar conditions. The hydrazinolysis of 4-metyl- and 6-metyl-3-nitropyridine-2(1*H*)-ones provides the 3-methylpyrazole and the carbodihydrazide. A probable mechanism of the process of cyclotransformation of the 3-nitropyridine-2(1*H*)-ones under hydrazinolysis was suggested.

DOI: 10.1134/S1070428008110134

It was formerly established by an example of 5-nitropyridin-2(1*H*)-one that this compound heated with excess hydrazine hydrate was converted into a pyrazolyl-3-acetic acid hydrazide [1]. In the same way *N*-methyl-5-nitropyridin-2(1*H*)-one undervent cyclotransformation, but the hydrazide formation was accompanied with methylamine elimination.

It seemed significant to check whether this reaction would occur with 3-nitropyridin-2(1*H*)-one derivatives. It proved that on heating for 7 h 3-nitropyridin-2(1*H*)-one (**I**) with excess hydrazine hydrate a compound was isolated whose tests for amino and hydrazine groups were negative. Ammonia was found to liberate in the course of the reaction. The elemental analysis data corresponded to the formula $C_3H_4N_2$. The mass spectrometry showed that the molecular ion mass of the base was $[M]^+$ 68. In the IR spectrum of the compound obtained an absorption band of a C=N group was observed in the region 1630 cm^{-1}. The ^1H NMR spectrum of this base contained doublet signals of aromatic protons with the coupling constant of 2.4 Hz. The latter finding showed that the molecule of the compound obtained could not contain a pyridine ring for the coupling constants of the pyridine *ortho* protons equaled 6–7 Hz. Comparing the values of the coupling constants, chemical shifts in the ^1H NMR spectrum, the data of the IR spectrum and the elemental analysis we concluded that the base **II** obtained from compound **I** was nothing but unsubstituted pyrazole (**II**). Compound **II** was identified by the comparison with an authentic substance [2] by the lack of depression of the melting point of a mixed sample and by the identity of the IR and ^1H NMR spectra [3].

On the completion of the cyclotransformation of 3-nitropyridin-2(1*H*)-one (**I**) we isolated from the reaction mixture alongside pyrazole (**II**) a compound that based on the elemental analysis and mass spectrum was assigned a structure of carbodihydrazide (**III**). Compound **III** was identified by the comparison with an authentic substance [4] by the lack of depression of the melting point of a mixed sample.

On heating *N*-methyl-3-nitropyridin-2(1*H*)-one (**IV**) with hydrazine hydrate the cyclotransformation also occurred giving pyrazole (**II**) and equimolar quantity of carbodihydrazide (**III**). In the course of the reaction the methylamine evolution was observed (Scheme 1).

Consequently the cyclotransformation of 3-nitropyridin-2(1*H*)-ones **I** and **IV** occurring under relatively mild conditions in contrast to the cyclotransformation of 5-nitropyridin-2(1*H*)-ones involved the cleavage of two carbon–carbon bonds (C^2–C^3 and C^3–C^4) in the pyridine ring.

† Diceased.

The cyclotransformation of 3,5-dinitropyridin-2(1*H*)-one (**V**) and its N-methyl derivative **VI** attracted interest for in the molecules of these compounds were present both fragments of 5-nitro-, and 3-nitropyridin-2(1*H*)-ones. It should be established whether compounds **V** and **VI** would react with the hydrazine hydrate like 5-nitropyridin-2(1*H*)-one or like 3-nitropyridin-2(1*H*)-one.

At heating 3,5-dinitropyridin-2(1*H*)-one (**V**) with excess hydrazine hydrate under the conditions similar to the cyclotransformation of 3-nitropyridin-2(1*H*)-one (**I**) the color of the solution changed from yellow to dark red, and ammonia liberation was observed. On completion of the reaction a light-yellow base was extracted with hot benzene from the tarry residue. According to the elemental analysis the composition of the compound obtained corresponded to an empirical formula $C_3H_3N_3O_2$. As followed from its mass spectrum the mass of its molecular ion was $[M]^+$ 113. In the IR spectrum of this compound absorption bands were present in the region 1365 and 1515 cm^{-1} corresponding to the nitro group vibrations. In the ^1H NMR spectrum of this base a single peak appeared at 8.65 ppm characteristic of the methine protons of the aromatic ring. These findings permit a conclusion that the cyclotransformation also occurred here, and the product of this process was 4-nitropyrazole (**VI**). Alongside compound **VI** an equivalent quantity of carbodihydrazide (**III**) was isolated from the reaction mixture [3] (Scheme 2).

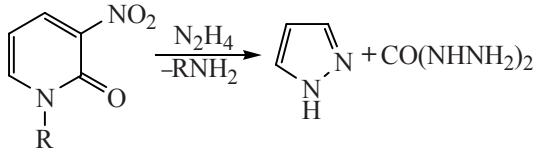
Likewise under similar conditions the heating of *N*-methyl-3,5-dinitropyridin-2(1*H*)-one (**VII**) with hydrazine hydrate resulted in the formation of 4-nitropyrazole (**VI**). In the course of the process an equimolar amount of carbodihydrazide (**III**) and methylamine was obtained. Compound **VI** was identified by the comparison with an authentic substance [5] by the lack of depression of the melting point of a mixed sample and by the identity of the IR and ^1H NMR spectra.

Thus 3,5-dinitropyridin-2(1*H*)-one (**V**) and its N-methyl derivative **VII** react with the hydrazine hydrate in the same way as the 3-nitropyridin-2(1*H*)-one converting into 4-nitropyrazole (**VI**).

Aiming at further investigation of the hydrazinolysis mechanism of 3-nitropyridin-2(1*H*)-one (**I**) derivatives it was necessary to establish the possible effect on the transformation process of the pyridine ring of methyl groups located in the positions *4* and *6* of the initial compounds. We selected as objects of the study 4-methyl-3-nitropyridin-2(1*H*)-one (**VIII**) and 6-methyl-3-nitropyridin-2(1*H*)-one (**IX**).

The reaction of 4-methyl-3-nitropyridin-2(1*H*)-one (**VIII**) with excess hydrazine hydrate led to the formation of a compound whose physicochemical characteristics corresponded to a 3-substituted pyrazole. In the IR spectrum of the obtained compound an absorption band appeared belonging to C=N group at 1630 cm^{-1}. In the ^1H NMR spectrum of this base two doublets of the aromatic protons were present with the chemical shifts 6.61 and 8.08 ppm and a coupling constant 2.4 Hz, and also a methyl group signal at 2.55 ppm. These data led us to conclusion that the compound obtained was 3-methylpyrazole (**X**). From the reaction mixture after the hydrazinolysis of compound **VIII** alongside pyrazole **X** a compound was isolated which based on the elemental analysis and the mass of the molecular ion in the mass spectrum the structure of carbodihydrazide (**III**) was assigned. The hydrazinolysis of 6-methyl-3-nitropyridin-2(1*H*)-one (**IX**) also yielded 3-methylpyrazole (**X**)

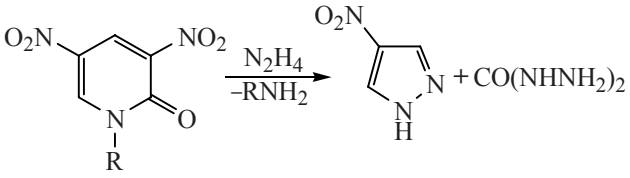
Scheme 1.



I, IV **II** **III**

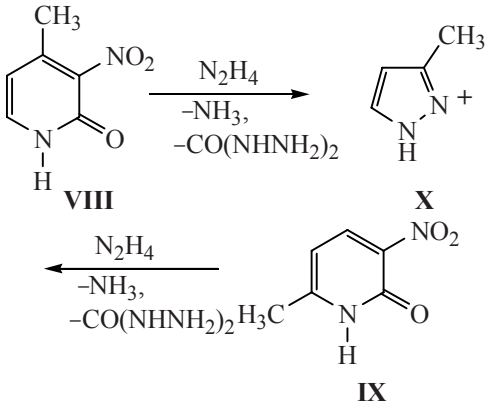
R = H (**I**), Me (**IV**).

Scheme 2.



V, VII **VI** **III**

Scheme 3.



VIII **X**

IX

and an equimolar quantity of carbodihydrazide (**III**) (Scheme 3).

The cyclotransformation of methylnitropyridones **VIII** and **IX** occurred similarly to the cyclotransformation of 3-nitropyridin-2(1*H*)-ones **I, IV, V**, and **VII** and involved the cleavage of two carbon–carbon bonds (C^2–C^3 and C^3–C^4) in the pyridine ring. The products of this cyclotransformation were 3-methylpyrazole (**X**) and carbodihydrazide (**III**). In this case the methyl group attached to the pyridine ring of initial nitropyridones **VIII** and **IX** did not affect the transformation of the rings.

In keeping with the experimental findings it was possible to suggest the most probable mechanism of the cyclotransformation process of monocyclic 3-nitropyridin-2(1*H*)-ones **I, IV, V, VII–IX** (Scheme 4).

The strong electronic effect of the nitro group on the carbonyl carbon atom in 3-nitropyridin-2(1*H*)-ones **I**, **IV, V**, and **VII** favors the nucleophilic attack of the hydrazine molecule on this atom followed by the opening of the pyridine ring.

In the formed hydrazide **XI** occurred further an addition of a hydrazine molecule to the nitroethylene fragment followed by the isomerization to enamine **XII** that underwent an intramolecular cyclization into structure **XIII**. The aromatization of the saturated pyrazole ring **XIII** requires not only the elimination of ammonia or methylamine, but also of nitroacetic acid hydrazide **XV**. We did not find compound **XV** among the reaction products, but we showed that this compound on heating with hydrazine hydrate was converted into carbodihydrazide (**III**). Therewith we failed to follow the fate of the methylene α-carbon of the nitroacetic acid as well as of the C^3 atom of nitropyridones **I, IV, V**, and **VII**. In both cases they remained in the intractable tarry reaction products.

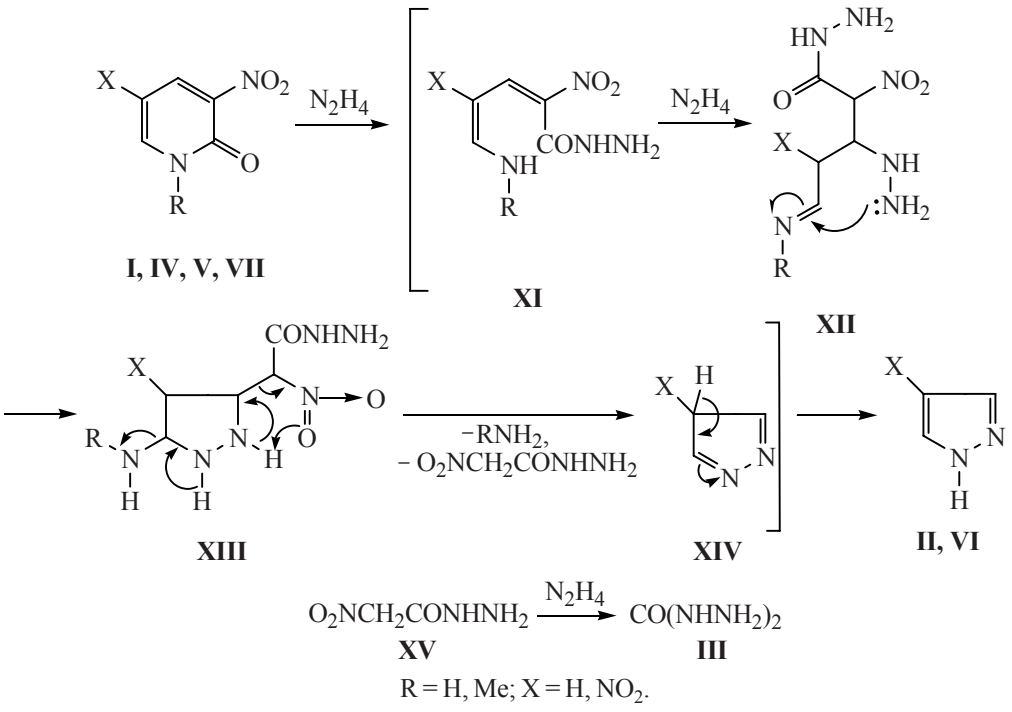
To confirm the involvement of the hypothetic structure **XI** in the suggested cyclotransformation mechanism we used as a model compound 4-(methylamino)-1,3-dinitro-1-ethoxycarbonylbuta-1,3-diene (**XVI**) whose synthesis was performed by Scheme 5.

The bromination of furfural **XVII** gave 2,3-dibromo-3-formylacrylic acid (**XVIII**) [6] that by treating with sodium nitrite was converted into the sodium nitromalonic aldehyde **XIX** [7]. The latter reacted with methylamine hydrochloride to give 3-(methylamino)-2-nitroacrolein (**XX**) [8] and the latter condensed with ethyl nitroacetate leading to the formation of compound **XVI** [9]. The heating of model compound **XVI** with hydrazine hydrate under the conditions analogous to the cyclotransformation of nitropyridones **I, IV, V, VII–IX** formed exclusively 4-nitropyrazole (**VI**) and carbodihydrazide (**III**).

EXPERIMENTAL

IR spectra of compounds synthesized were recorded on a spectrophotometer Perkin Elmer 180. ^{1}H NMR

Scheme 4.



R = H, Me; X = H, NO_2.

spectra were registered on a spectrometer Tesla BS-467 at operating frequency 80 MHz in CF_3COOH. The mass of molecular ions of compounds **II**, **III**, and **VI** was measured on a mass spectrometer Varian MAT-112 at ionizing electrons energy 70 eV at direct admission of the sample into the ion source. The purity and homogeneity of compounds obtained was checked by TLC on Silufol UV-254 plates (eluents ethanol, chloroform), development under UV irradiation or in iodine vapor. Compounds **I, IV, V, VII–IX** were obtained by procedures [10].

Pyrazole (II). *a*. A solution of 1.4 g (10 mmol) 3-nitropyridin-2(1*H*)-one (**I**) in 10 ml of hydrazine hydrate was heated for 7 h at 90–95°C. During the process the color of the solution changed from yellow to dark red. In the course of the reaction ammonia liberated that was passed through an alcoholic solution of hydrochloric acid and identified as ammonium chloride, mp 334–336°C (336°C [11]). On completion of the reaction the hydrazine hydrate was distilled off in a vacuum under an argon flow on a water bath. From the tarry residue pyrazole (**II**) was extracted into hot benzene. The solvent was distilled off to give compound **II** as colorless crystals, mp 69°C (69°C [2]). Yield 0.5 g (74%). IR spectrum, ν, cm^{-1}: 1630 (C=N). ^1H NMR spectrum, δ, ppm: 6.92 d (1H, H^4, *J* 2.4 Hz), 8.17 d (1H, H^3, *J* 2.4 Hz), 8.22 d (1H, H^5, *J* 2.4 Hz). Found, %: C 52.79; H 5.87; N 40.95. $[M]^+$ 68. $C_3H_4N_2$. Calculated, %: C 52.93; H 5.92; N 41.15.

After isolating pyrazole (**II**) carbodihydrazide (**III**) was extracted from the tarry residue with hot ethanol. Yield 0.68 g (75%), mp150–152°C (154°C [4]). Found, %: C 13.19; H 6.66; N 61.93. $[M]^+$ 90. CH_6N_4O. Calculated, %: C 13.33; H 6.71; N 62.19.

b. A mixture of 4.0 g (28.6 mmol) of 1-methyl-3-nitropyridin-2(1*H*)-one (**VII**) and 27.0 ml (578 mmol) of hydrazine hydrate was heated for 7 h at 95–100°C. In the course of the reaction the methylamine liberated that was passed through an alcoholic solution of hydrochloric acid and identified as methylamine hydrochloride, mp 224°C (226°C [11]). Reaction product **II** was isolated as described in method *a*. Yield 1.2 g (68%), mp 69°C.

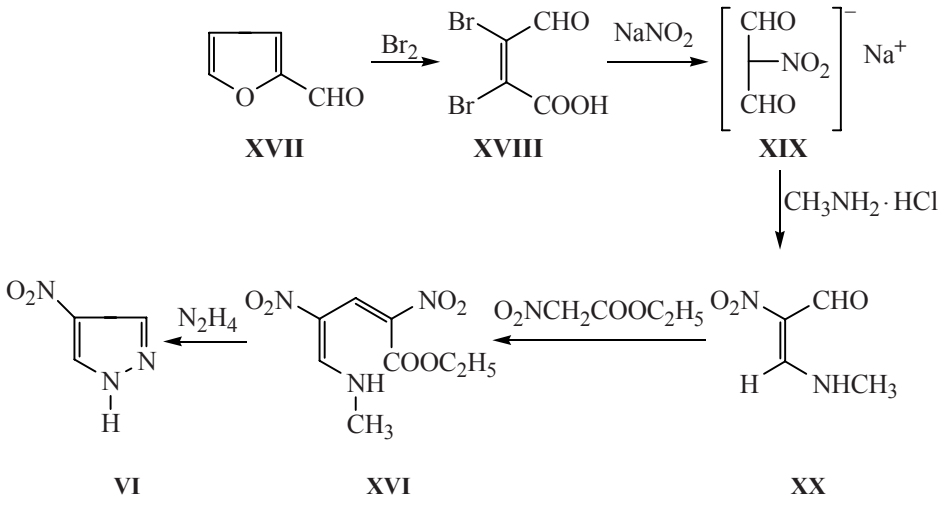
Alongside pyrazole (**II**) by extraction with hot ethanol from the reaction mixture an equivalent amount of carbodihydrazide (**III**) was isolated, mp 150–152°C. Yield 1.6 g (68%).

4-Nitropyrazole (VI). *a*. A solution of 1.85 g (10 mmol) of 3,5-dinitropyridin-2(1*H*)-one (**V**) in 10 ml (214 mmol) of hydrazine hydrate was heated for 7 h at 90–95°C. During the process the color of the solution changed from yellow to dark red and ammonia liberated that was identified as ammonium chloride as was done in the preparation of compound **II** by procedure *a*. On completion of the reaction the hydrazine hydrate was distilled off in an argon flow. The 4-nitropyrazole was extracted from the residue with hot benzene. Yield 1.0 g (87%), mp 160–162°C (from benzene) (162°C [5]). IR spectrum, ν, cm^{-1}: 1365 [$\nu_{symm}(NO_2)$], 1515 [$\nu_{asymm}(NO_2)$]. ^1H NMR spectrum, δ, ppm: 8.65 s (2H, H^3, H^5). Found, %: C 31.68; H 2.61; N 36.97. $[M]^+$ 113. $C_3H_3N_3O_2$. Calculated, %: C 31.87; H 2.67; N 37.16.

Alongside nitropyrazole **VI** by extraction with hot ethanol from the reaction mixture carbodihydrazide (**III**) was isolated, mp 150–152°C. Yield 0.8 g (87%).

b. A mixture of 4.2 g (28.6 mmol) of 1-methyl-3,5-dinitropyridin-2(1*H*)-one (**VII**) and 20 ml (400 mmol) of

Scheme 5.



hydrazine hydrate was heated under conditions similar to those at the preparation of compound **II** by procedure *b*. The subsequent workup was carried out along the procedure *b*. Yield 2.38 g (87%), mp 160–162°C (from benzene).

In the course of the reaction the liberated methylamine was passed through an ethanol solution of hydrochloric acid and identified as methylamine hydrochloride, mp 225°C (226°C [12]). By extraction with hot ethanol from the tarry residue carbodihydrazide (**III**) was isolated, mp 150–152°C. Yield 1.31 g (69%).

3-Methylpyrazole (X). *a*. A mixture of 1.55 g (10 mmol) of 4-methyl-3-nitropyridin-2(1*H*)-one (**VIII**) and 10 ml (200 mmol) of hydrazine hydrate was heated for 3–5 h at 110–120°C. During the process the color of the solution changed from yellow to dark red and ammonia liberated that was identified as ammonium chloride as was done in the preparation of compound **VI** by procedure *a*. On completion of the reaction the hydrazine hydrate was distilled off in an argon flow. The 3-methylpyrazole was extracted from the tarry residue with hot benzene and was identified as a picrate. Yield 0.55 g (67%), mp of picrate 140–142°C. IR spectrum, ν, cm^{-1}: 1630 (C=N). ^1H NMR spectrum, δ, ppm: 2.55 s (3H, CH_3), 6.61 (1H, H^4, *J* 2.4 Hz), 8.08 d (1H, H^5, *J* 2.4 Hz). Found, %: C 38.41; H 2.84; N 22.35. $C_4H_6N_2 \cdot C_6H_3N_3O_7$. Calculated, %: C 38.60; H 2.91; N 22.50.

By extraction with hot ethanol from the tarry residue carbodihydrazide (**III**) was isolated, mp 150–152°C. Yield 0.61 g (67%).

b. A mixture of 1.55 g (10 mmol) of 6-methyl-3-nitropyridin-2(1*H*)-one (**IX**) and 10 ml (200 mmol) of hydrazine hydrate was heated under conditions similar to those at the preparation of compound **X** by procedure *a*. The subsequent workup and identification of products was carried out along the procedure *a*. Yield of 3-methylpyrazole (**X**) 0.52 g (63%), mp of picrate 140–142°C. Carbodihydrazide (**III**) was isolated in amount of 0.57 g (63%), mp 150–152°C.

Reaction of nitroacetic acid hydrazide (XV) with hydrazine hydrate. A mixture of 3.0 g (20 mmol) hydrazine salt of nitroacetic acid hydrazide (**XV**) [12] and 20 ml (400 mmol) of hydrazine hydrate was heated for 10 h at 95–100°C. On completion of the reaction the hydrazine hydrate was distilled off in an argon flow in a vacuum. By extraction with hot ethanol from the tarry residue carbodihydrazide (**III**) was isolated. Yield 1.6 g (88%), mp 151–153°C (from ethanol).

Reaction of 4-(methylamino)-1,3-dinitro-1-ethoxycarbonylbuta-1,3-diene (XVI) with hydrazine hydrate. A solution of 1.3 g (5.3 mmol) of compound **XVI** in 5.0 ml (100 mmol) of hydrazine hydrate was heated for 7 h at 90–95°C. Ammonia liberated in the course of the reaction. On completion of the reaction the hydrazine hydrate was distilled off in an argon flow in a vacuum. By extraction with hot benzene from the tarry residue 4-nitropyrazole (**VI**) was isolated. Yield 0.5 g (83%), mp 160–162°C. Alongside 4-nitropyrazole (**VI**) by extraction with hot ethanol from the tarry residue carbodihydrazide (**III**) was obtained. Yield 0.4 g (88%), mp 150–152°C.

REFERENCES

1. Yutilov, Yu.M. and Smolyar, N.N., *Khim. Geterotsikl. Soedin.,* 1985, p. 1686; Rusinov, V.A. and Chupakhin, O.N., *Nitroaziny* (Nitroazines), Novosibirsk: Nauka, 1991, p. 350; Yutilov, Yu.M., *Adv. Heterocycl. Chem*., 2005, vol. 89, p. 161.
2. Pechman, H., *Ber.,* 1898, p. 2950.
3. Yutilov, Yu.M. and Smolyar, N.N., *Khim. Geterotsikl. Soedin*., 1986, p. 1136.
4. Staab, H.A. and Luking, M., *Chem. Ber*., 1962, vol. 95, p. 1275.
5. Chang, K.C., Grimmett, M.R., and Weawers, D.D., *Austral. J. Chem*., 1979, p. 1727.
6. *Sint. Org. Prep*., 1953, vol. 4, p. 157.
7. *Sint. Org. Prep*., 1953, vol. 4, p. 345.
8. Kvitko, S.M. and Perekalin, V.V., *Zh. Obshch. Khim.,* 1962, vol. 32, p. 144.
9. Kvitko, S.M., Perekalin, V.V. and Buival, N.V., *Zh. Org. Khim.,* 1966, vol. 2, p. 2253.
10. Burton, A.G., Halls, P.J. and Katritzky, A.R. *Tetrahedron, Lett*., 1971, vol. 24, 2211; Gruber, W., *Canad. J. Chem*., 1953, vol. 31, p. 1181; Fanta, P.E. and Stein, R.A. *J. Am. Chem. Soc*., 1955, vol. 77, p. 1045; Hertog, H.J. and Braun, F., *Rec. Trav. Chim.,* 1951, vol. 70, p. 182; Lappin, G.R. and Slezak, F.B. *J. Am. Chem. Soc*., 1950, vol. 72, p. 2806; Brown, E.V. and Burke, H.T., *J. Am. Chem. Soc*., 1955, vol. 77, p. 6053; Abramenko, P.I. and Zhiryakov, V.G., *Khim. Geterotsikl. Soedin*., 1972, p. 1541.
11. *Spravochnik khimika* (Handbook of Chemist), Leningrad: Khimiya, 1971, vol. 2, p. 28.
12. Ungande, H.E. and Kissinger, L.W., *J. Org. Chem*., 1957, vol. 22, p. 1662.