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Reactions of 6,6-Dialkyl-5,7-dioxo-4,8-dioxaspiro[2.5]octane-1,1,2,2-tetracarbonitriles with O-Centered Nucleophiles

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Abstract—The reactions of 6,6-dialkyl-5,7-dioxo-4,8-dioxaspiro[2.5]octane-1,1,2,2-tetracarbonitriles with primary aliphatic alcohols lead to the formation of alkyl 2,2,3,3-tetracyanocyclopropanecarboxylates; the reactions of the same compounds with ketone oximes give 2-amino-4,4-bis(alkylideneaminooxy)-6-(alkylideneaminooxycarbonyl)-3-azabicyclo[3.1.0]hex-2-ene-1,5-dicarbonitriles, while with aldehyde oximes 2-amino-2-oxo-1,5-dicyano-3-azabicyclo[3.1.0]hex-2-ene-6-carboxylic acid is formed.

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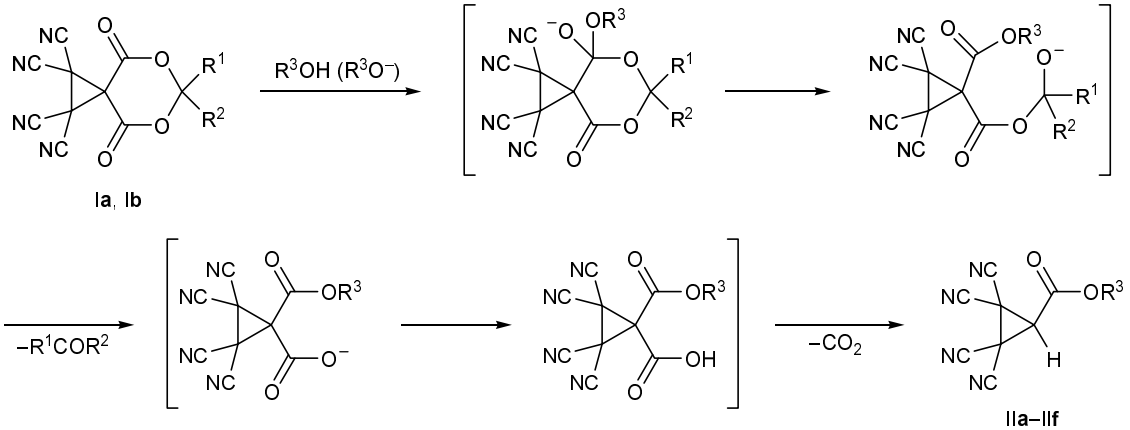
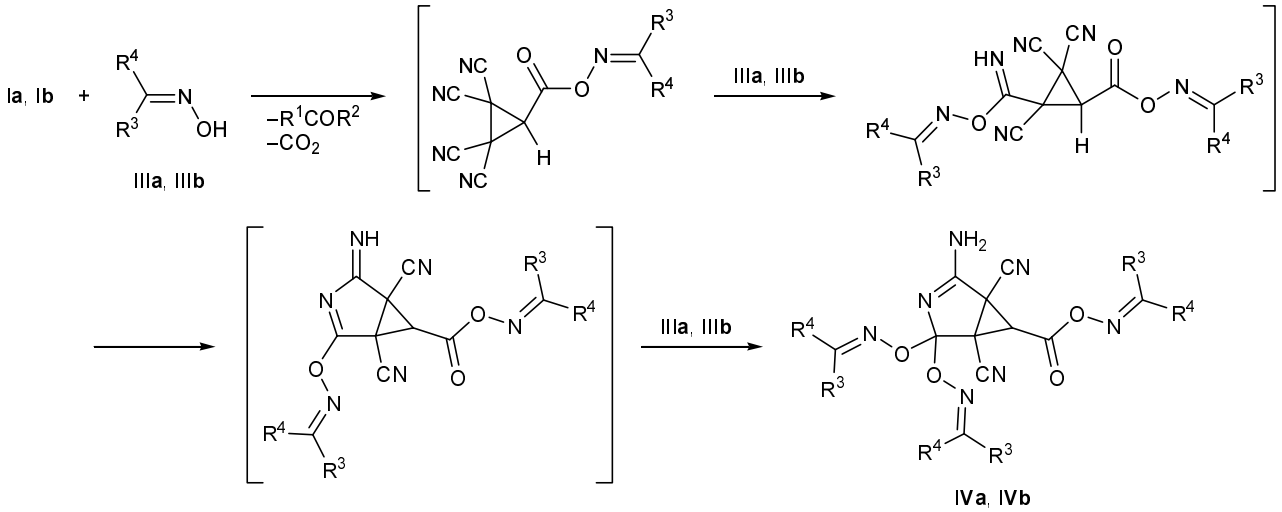
Reactions of electron-deficient cyclopropanes having six electron-acceptor substituents with O-centered nucleophiles lead to formation of heterocyclic compounds with various structures and functional substitution patterns. Hexacyanocyclopropane is known to react with alcohols and oximes to afford, depending on the conditions and reactant ratio, derivatives of diazatricyclo[3.3.1.0]nonadiene [1, 2] or azabicyclo[3.1.0]-hexene [2]. Transformations of hexacyanocyclopropane analogs in which one or two cyano groups are replaced by carbonyl or ester groups are even more diverse. The reaction direction and structure of products formed from these compounds strongly depend on the activity of the carbonyl group, nucleophile nature, and catalyst. The most typical representatives are diacetyltetracyanocyclopropane [3] and phthaloyltetracyanocyclopropane [4]. The first of these reacts with alcohols in the presence of the corresponding alkoxide as catalyst to give 3-oxabicyclo[3.1.0]hexene derivatives [3], its reactions with oximes lead to 3,8-dioxatricyclo[4.3.0.0^{1,5}]nonanes [5], and dihydrofuran derivatives are formed in reactions with alkoxides and oximates [3]. On the other hand, phthaloyltetracyanocyclopropane does not react with alcohols in the presence of a catalytic amount of alkoxide, its reactions with alkoxides and oximates give dihydrofurans [4],

Scheme 1.



I, $R^1 = R^2$ = Me (**a**), $R^1R^2 = (CH_2)_5$ (**b**); **II**, R^3 = Me (**a**), Et (**b**), Pr (**c**), Bu (**d**), $HOCH_2CH_2$ (**e**), $PhCH_2$ (**f**).

Scheme 2.



I, $R^1 = R^2 =$ Me (**a**), $R^1R^2 = (CH_2)_5$ (**b**); **III**, **IV**, $R^3 = R^4 =$ Me (**a**), $R^3 =$ Me, $R^4 =$ Et (**b**).

and, unlike diacetyltetracyanocyclopropane, it is converted into 3-azabicyclo[3.1.0]hex-2-enes via reaction with oximes at the cyano groups without opening of the three-membered ring [5]. Reactions of pentacyanocyclopropanecarboxylic acid derivatives with O-centered nucleophiles also give rise to various products [6]. Derivatives having an inactivated carbonyl group (amide or imide) react only at the cyano groups with formation of fused aminodihydropyrroles [7, 8].

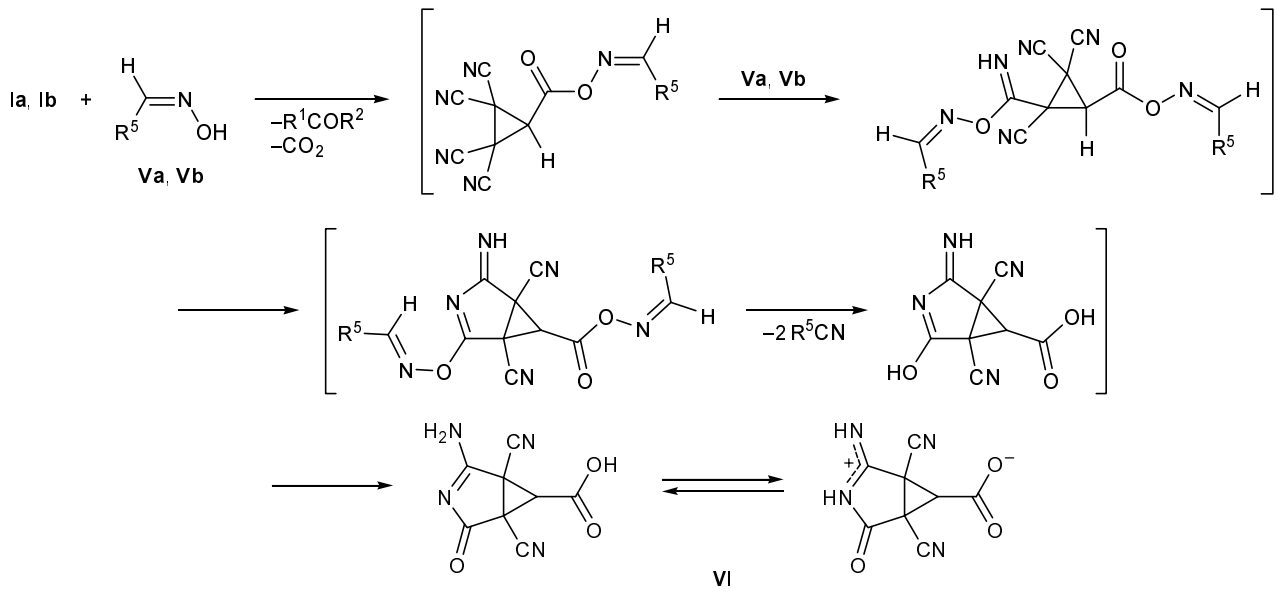
We recently reported on the synthesis of new hexacyanocyclopropane analogs, spirocyclic compounds **I**, in which two geminal cyano groups are replaced by Meldrum's acid residue [9]. In the present article we describe reactions of these compounds with some O-centered nucleophiles, namely primary aliphatic alcohols and oximes. We found that compounds **Ia** and **Ib** react with primary aliphatic alcohols in the presence of the corresponding alkoxides or triethylamine as catalyst to afford alkyl 2,2,3,3-tetracyanocyclopropanecarboxylates **IIa**–**IIf** (Scheme 1).

Unlike alcohols, reactions of spiro compounds **Ia** and **Ib** with ketone oximes **IIIa** and **IIIb** in acetonitrile required no catalyst, and the corresponding 2-amino-4,4-bis(alkylideneaminooxy)-6-(alkylideneaminooxycarbonyl)-3-azabicyclo[3.1.0]hex-2-ene-1,5-dicarbonitriles **IVa** and **IVb** were thus obtained in 50–55% yield (Scheme 2). In reactions with aldehyde oximes **Va** and **Vb**, cyclopropanes **Ia** and **Ib** were converted into the same compound, 2-amino-1,5-dicyano-4-oxo-3-azabicyclo[3.1.0]hex-2-ene-6-carboxylic acid (**VI**), regardless of the aldehyde nature or substituent in the acetal fragment of spiro cyclopropane **I** (Scheme 3). Product **VI** is very readily soluble in water but is almost insoluble in acetonitrile, dioxane, and alcohol; presumably, it exists as inner salt.

We propose the following mechanism of these reactions. In all cases, initial attack by nucleophile is likely to be directed at the carbonyl group of **I**, leading to cleavage of the acetal–ester fragment, which is accompanied by liberation of carbon dioxide and the corresponding ketone. In the reactions with aliphatic alcohols, the transformation is terminated at that stage, and the resulting ester crystallizes from the reaction mixtures. Oxime are stronger O-nucleophiles than alcohols due to α-effect [10], and they add at the cyano groups to give finally compounds **IVa** and **IVb**. We previously reported [2] on unusual reaction of aldehyde oximes with hexacyanocyclopropane, which involved elimination of the corresponding nitrile from the primary adduct; the final product may formally be regarded as that resulting from addition of water. Presumably, analogous mechanism is operative in the formation of acid **VI** (Scheme 3).

The structure of the products was assumed on the basis of their IR, NMR, and mass spectra and elemental compositions. The IR spectra of all compounds **II**, **IV**, and **VI** contained absorption bands typical of stretching vibrations of nonconjugated cyano groups (2250–2270 cm^{-1}), cyclopropane C–H bonds (3040–3060 cm^{-1}), and ester carbonyl (1710–1730 cm^{-1}). In the ^1H NMR spectra of **IIa**–**IIf**, the singlet at δ 4.62–4.85 ppm was assigned to the cyclopropane ring

Scheme 3.



R^5 = Me (**a**), Ph (**b**).

proton. Somewhat reduced intensity of that signal must be noted, which is likely to be caused by exchange processes. In addition, the spectrum of **IIe** revealed appreciable broadening of the hydroxy proton signal. Compounds **IVa** and **IVb** showed in the spectra a singlet at δ 3.00–3.1 ppm from the cyclopropane ring proton, while protons of the amino group in the aminoimine fragment appeared as a singlet at δ 7.5–7.6 ppm. The spectrum of **IVb** was characterized by doubling of signals from the methyl and methylene protons, presumably due to the presence of isomers relative to the double carbon–nitrogen bonds in the oxime fragments.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Bruker AM-500 spectrometer at 500.13 MHz using DMSO-d_6 as solvent. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT Incos 50 instrument. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates; spots were visualized by UV irradiation, treatment with iodine vapor, or heating).

Methyl 2,2,3,3-tetracyanocyclopropane-1-carboxylate (IIa). *a*. Metallic sodium, 0.01 g (0.0005 mol), was dissolved in 2 ml of methanol, and a solution of 0.27 g (0.001 mol) of compound **Ia** in 5 ml of acetonitrile was added in one portion under stirring. During the reaction, the solution turned yellow, and gas evolution was observed. When the reaction was complete (TLC), the solvent and excess alcohol were distilled off until a solid began to separate, the mixture was cooled, and the colorless precipitate was filtered off, washed with cold diethyl ether, and dried in air. Yield 0.136 g (68%), mp 131–133°C (decomp.). IR spectrum, ν, cm^{-1}: 3060 (CH, cyclopropane), 2260 (C≡N), 1720 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.87 s (3H, CH_3), 4.68 s (1H, CH). Found, %: C 54.29; H 2.12; N 27.52. $C_9H_4N_4O_2$. Calculated, %: C 54.01; H 2.01; N 27.99.

b. The procedure was the same as in *a*, but 0.31 g (0.001 mol) of compound **Ib** was used instead of **Ia**. Yield 0.123 g (54%).

Compounds **IIb**–**IIe** were synthesized as described above for compound **IIa** according to method *a* using the corresponding alcohol.

Ethyl 2,2,3,3-tetracyanocyclopropane-1-carboxylate (IIb). Yield 0.154 g (72%), mp 135–139°C (decomp.). IR spectrum, ν, cm^{-1}: 3060, 3065 (CH, cyclopropane); 2260 (C≡N); 1725 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.38 t (3H, CH_3), 4.33 q (2H, CH_2), 4.63 s (1H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 199 (3) $[M - 15]^+$, 185 (4), 169 (75), 157 (8), 142 (100), 130 (20), 115 (15), 105 (40), 88 (20), 77 (43), 65 (35), 51 (23), 45 (50), 38 (20). Found, %: C 56.21; H 2.87;

N 26.11. $C_{10}H_6N_4O_2$. Calculated, %: C 56.08; H 2.82; N 26.16.

Propyl 2,2,3,3-tetracyanocyclopropane-1-carboxylate (IIc). Yield 0.160 g (70%), mp 140–145°C (decomp.). IR spectrum, ν, cm^{-1}: 3060 (CH, cyclopropane), 2240 (C≡N), 1725 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.95 t (3H, CH_3), 1.67 m (2H, $CH_2C\mathbf{H}_2CH_3$), 4.18 t (2H, $C\mathbf{H}_2CH_2CH_3$), 4.73 s (1H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 213 (1) $[M - 15]^+$, 169 (10), 141 (10), 115 (1), 105 (15), 88 (5), 77 (20), 65 (15), 51 (10), 42 (100). Found, %: C 57.91; H 3.59; N 24.01. $C_{11}H_8N_4O_2$. Calculated, %: C 57.89; H 3.53; N 24.55.

Butyl 2,2,3,3-tetracyanocyclopropane-1-carboxylate (IId). Yield 0.182 g (75%), mp 150–155°C (decomp.). IR spectrum, ν, cm^{-1}: 3055 (CH, cyclopropane), 2260 (C≡N), 1730 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.98 t (3H, CH_3), 1.47 m (2H, $CH_2CH_2C\mathbf{H}_2CH_3$), 1.72 m (2H, $CH_2C\mathbf{H}_2CH_2CH_3$), 4.25 t (2H, $C\mathbf{H}_2CH_2CH_2CH_3$), 4.62 s (1H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 213 (3) $[M - 29]^+$, 187 (4), 149 (9), 141 (13), 115 (3), 105 (10), 84 (5), 77 (13), 56 (100), 41 (50). Found, %: C 59.61; H 4.68; N 23.01. $C_{12}H_{10}N_4O_2$. Calculated, %: C 59.50; H 4.16; N 23.13.

2-Hydroxyethyl 2,2,3,3-tetracyanocyclopropane-1-carboxylate (IIe). Yield 0.180 g (78%), mp 172–175°C (decomp.) IR spectrum, ν, cm^{-1}: 3550 (OH), 3060 (CH, cyclopropane), 2260 (C≡N), 1715 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.67 t (2H, $OC\mathbf{H}_2CH_2OH$), 4.27 m (2H, $OCH_2C\mathbf{H}_2OH$), 4.76 s (1H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 200 (20) $[M - 30]^+$, 187 (5), 170 (20), 142 (100), 115 (10), 105 (30), 88 (10), 77 (23), 65 (11), 51 (10), 45 (13). Found, %: C 52.24; H 2.68; N 24.28. $C_{10}H_6N_4O_3$. Calculated, %: C 52.18; H 2.63; N 24.34.

Benzyl 2,2,3,3-tetracyanocyclopropane-1-carboxylate (IIf). Yield 0.2 g (75%), mp 155–157°C (decomp.). IR spectrum, ν, cm^{-1}: 3055 (CH, cyclopropane), 2250–2270 (C≡N), 1725 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.38–7.51 m (5H, C_6H_5), 5.29 s (2H, $OC\mathbf{H}_2C_6H_5$), 4.85 s (1H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 276 (25) $[M]^+$, 194 (6), 155 (30), 147 (35), 120 (5), 107 (20), 91 (100), 77 (23), 65 (25), 51 (13). Found, %: C 65.13; H 2.93; N 20.21. $C_{15}H_8N_4O_2$. Calculated, %: C 65.21; H 2.89; N 20.29.

2-Amino-4,4-bis(1-methylethylideneaminooxy)-6-(1-methylethylideneaminooxycarbonyl)-3-azabicyclo[3.1.0]hex-2-ene-1,5-dicarbonitrile (IVa). Compound **Ia**, 0.001 mol (0.27 g), was dispersed in 3 ml of acetonitrile, and 0.29 g (0.004 mol) of acetone oxime was added in one portion. After stirring for 5 min, the mixture became homogeneous and turned red. The solution was left to stand for 24 h at room temperature in a closed vessel. The pink precipitate was filtered off, washed with cold propan-2-ol, recrystallized from 1,4-dioxane, and dried in air. Yield 0.194 g (50%), colorless needles, mp 190–194°C (decomp.). IR spectrum, ν, cm^{-1}: 3380 (NH_2), 2260 (CN), 1740 (C=O), 1660 (C=N). ^{1}H NMR spectrum, δ, ppm: 7.5 s (2H, NH_2), 3.08 s (1H, CH), 2.01 s [6H, $C(O)ON{=}C(CH_3)_2$], 1.852 s (6H, CH_3), 1.85 s (6H, CH_3). Found, %: C 52.76; H 5.44; N 25.36. Calculated, %: C 52.71; H 5.46; N 25.31.

2-Amino-4,4-bis(1-methylpropylideneaminooxy)-6-(1-methylpropylideneaminooxycarbonyl)-3-azabicyclo[3.1.0]hex-2-ene-1,5-dicarbonitrile (IVb) was synthesized in a similar way. Yield 0.236 g (55%), mp 168–172°C (decomp.). IR spectrum, ν, cm^{-1}: 3385 (NH_2), 2270 (CN), 1735 (C=O), 1670 (C=N). ^{1}H NMR spectrum, δ, ppm: 7.5 s (2H, NH_2), 3.05 s (1H, CH), 2.35 q [2H, $C(O)ON{=}CC\mathbf{H}_2CH_3$], 2.20 m (4H, $C\mathbf{H}_2CH_3$), 2.00 s [3H, $C(O)ON{=}CCH_3$], 1.85 s (6H, $CON{=}CCH_3$), 1.05 m (6H, $CH_2C\mathbf{H}_3$). Found, %: C 55.97; H 6.31; N 22.89. Calculated, %: C 55.93; H 6.34; N 22.83.

2-Amino-4-oxo-1,5-dicyano-3-azabicyclo[3.1.0]-hex-2-ene-6-carboxylic acid (VI). *a.* Compound **Ia**, 0.001 mol (0.27 g), was dispersed in 5 ml of acetonitrile, and 0.2 ml of acetaldehyde oxime was added in one portion. While stirring, the mixture became homogeneous, and gas evolution was observed. The solution was left to stand for 24 h at room temperature in a closed vessel, the precipitate was filtered off, washed with acetonitrile, and dried in air. Yield 0.116 g (57%), mp 176–180°C (decomp.). IR spectrum, ν, cm^{-1}: 3380, 3320 (NH, NH_2); 3050 (CH, cyclopropane); 2260, 2270 (CN); 1710, 1680 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.96 s (1H, NH), 7.45 s (2H, NH_2), 3.17 s (1H, CH). Found, %: C 47.10; H 1.93; N 27.49. Calculated, %: C 47.07; H 1.97; N 27.45.

b. Compound **VI** was synthesized in a similar way from 0.31 g (0.001 mol) of spirocyclopropane **Ib**. Yield 0.05 g (52%).

c. Compound **Ia**, 0.27 g (0.001 mol), and benzaldehyde oxime, 0.24 g (0.002 mol), were mixed with 3 ml of acetonitrile. The mixture became homogeneous while stirring, and, after 10 min, a flaky material separated and then dissolved. The mixture was left to stand

for 3 days at room temperature, and the precipitate was filtered off, washed with acetonitrile, and dried in air. Yield 0.065 g (32%).

REFERENCES

1. Nasakin, O.E., Lukin, P.M., Vershinin, E.V., Lindeman, S.V., and Struchkov, Y.T., *Mendeleev Commun.*, 1994, no. 5, p. 185.
2. Nasakin, O.E., Lukin, P.M., Vershinin, E.V., Yashkanova, O.V., Lyshchikov, A.N., Urman, Ya.G., Lindeman, S.V., Struchkov, Yu.T., and Bulai, A.Kh., *Russ. J. Org. Chem.*, 1995, vol. 31, p. 333.
3. Yashkanova, O.V., Nasakin, O.E., Urman, Ya.G., Khrustalev, V.N., Nesterov, V.N., Antipin, M.Yu., Lukin, P.M., and Vershinin, E.V., *Russ. J. Org. Chem.*, 1997, vol. 33, p. 484.
4. Yashkanova, O.V., Nasakin, O.E., Urman, Ya.G., Khrustalev, V.N., Nesterov, V.N., Antipin, M.Yu., and Lukin, P.M., *Russ. J. Org. Chem.*, 1997, vol. 33, p. 475.
5. Lukin, P.M., Manzenkov, A.V., Urman, Ya.G., Khrustalev, V.N., Nesterov, V.N., and Antipin, M.Yu., *Russ. J. Org. Chem.*, 2000, vol. 36, p. 226.
6. Siaka, S., *Cand. Sci. (Chem.) Dissertation*, Moscow, 1998.
7. Yashkanova, O.V., Lukin, P.M., Nasakin, O.E., Urman, Ya.G., Khrustalev, V.N., Nesterov, V.N., and Antipin, M.Yu., *Russ. J. Org. Chem.*, 1997, vol. 33, p. 877.
8. Siaka, S., Lukin, P.M., Nasakin, O.E., Antipin, M.Yu., and Khrustalev, V.N., *Russ. J. Org. Chem.*, 1999, vol. 35, p. 269.
9. Kayukova, O.V., Kayukov, Ya.S., Nikolaev, A.N., and Nasakin, O.E., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 1382.
10. March, J., *Advanced Organic Chemistry. Reactions, Mechanisms, and Structure*, New York: Wiley, 1985. Translated under the title *Organicheskaya khimiya*, Moscow: Mir, 1987, vol. 2, p. 79.