ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 6, pp. 1184–1188. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © V.V. Shchepin, Yu.G. Stepanyan, S.V. Romashev, P.S. Silaichev, 2008, published in Zhurnal Obshchei Khimii, 2008, Vol. 78, No. 6, pp. 956–960.

Reaction of Organozinc Reagents Formed from α,α-Dibromocarbonyl Compounds and Zinc with (3-Phenylprop-2-enylidene)malonodinitriles and Primary Amides of 2-Cyano-5-phenylpenta-2,4-dienoic Acid

V. V. Shchepin†, Yu. G. Stepanyan, S. V. Romashev, and P. S. Silaichev

Perm State University,
ul. Bukireva 15, Perm, 614990 Russia

Received October 1, 2007

Abstract—Organozinc compounds formed from 1-aryl-2,2-dibromoalkanes, α,α-dibromopinacoline, and dialkyl dibromomalonates and zinc react with (3-phenylprop-2-enylidene)malonodinitriles and primary amides of 2-cyano-5-phenylpenta-2,4-dienoic acid to form 2-alkyl-2-aroyl-3-(phenylvinyl)cyclopropan-1,1-dicarboxylic acid dinitriles, N-substituted amides of 3-(phenylvinyl)-2-(2,2-dimethylpropanoyl)-1-cyanocyclopropan-1-carboxylic acids, and alkyl 3-R-6-(phenylvinyl)-2,4-dioxo-5-cyano-3-azabicyclo[3.1.0]-hexan-1-carboxylates as a single stereoisomer.

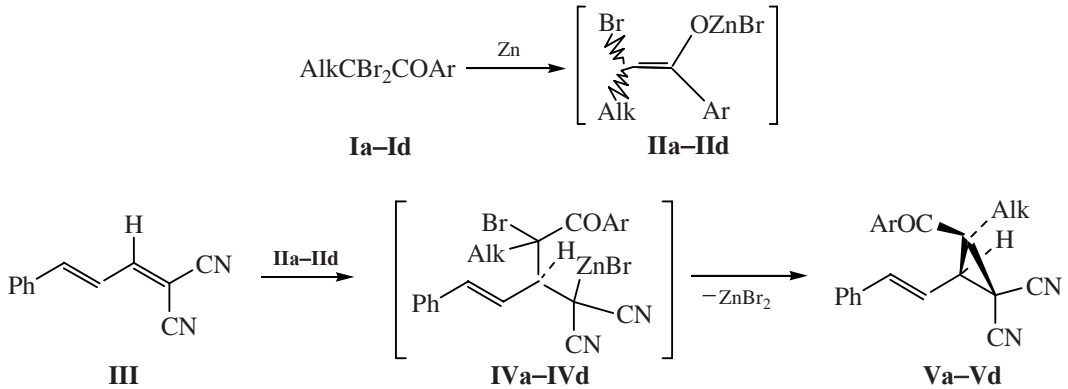
DOI: 10.1134/S1070363208060145

Organozinc reagents formed from 1-aryl-2,2-dibromoalkanones, α,α-dibromopinacoline, dialkyl dibromomalonates and zinc were used previously for cyclopropanation of 2-arylmethylenemalonodinitriles [1] and primary amides of 2-cyano-5-phenylpenta-2,4-dienoic acid [2, 3].

With the purpose to investigate cyclopropanation of compounds containing two conjugated double bonds, we focused in the present work on reaction of zinc enolates formed from 1-aryl-2,2-dibromoalkanones and zinc with (3-phenylprop-2-enylidene) malonodinitriles. The reaction was found to occur according to Scheme 1.

In going to (3-phenylprop-2-enylidene)malonodinitrile having two conjugated double bonds, the reaction direction does not alter, and substrate **III**

Scheme 1.



I, II, IV, V, Alk = CH_3, Ar = 4-ClC_6H_4 (**a**), 4-FC_6H_4 (**b**), 4-$CH_3C_6H_4$ (**c**), Alk = C_2H_5, Ar = C_6H_5 (**d**).

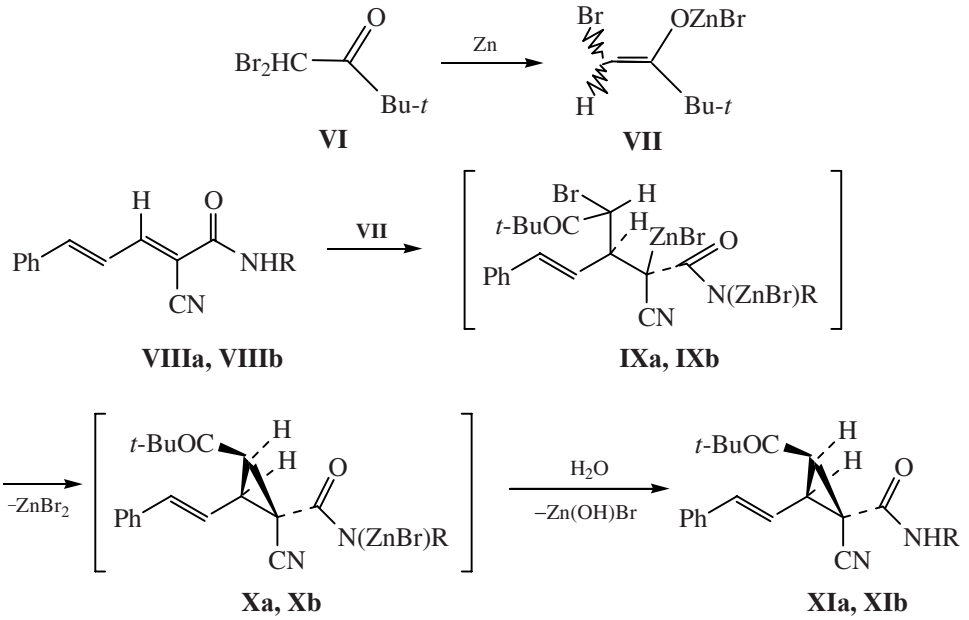
† Deceased.

reacts with zinc enolates **IIa–IId** by the C^3 atom exclusively. Probably, the first step involves intermediates **IVa–IVd** which then undergo cyclization to give 2-alkyl-2-aroyl-3-(phenylvinyl)cyclopropane-1,1-dicarbodinitriles **Va–Vd**.

The composition and structure of compounds **Va–Vd** were established by elemental analysis and IR and ^{1}H NMR spectroscopy. The IR spectra contain characteristic absorption bands (ν, cm^{-1}) of the aroyl carbonyl (1680–1690) and cyano groups (2210–2220). The ^{1}H NMR spectra contain signals at 3.24–3.34, 5.83–5.93, and 6.87–6.90 ppm, belonging to the cyclopropane and double-bond protons, respectively. The $^3J_{HH}$ value of the double-bond protons is about 15.5 Hz, what tells about their *trans* location. The presence of a single set of proton signals shows that the reaction products are formed as a single geometric isomer. Comparison of the chemical shifts of the methine protons in **Va–Vd** (3.24–3.34 ppm) with those in previously studied 2-alkyl-3-aryl-2-aroylcyclopropane-1,1-dicarbodinitriles [1] suggests that the alkyl group and the cyclopropane proton are located *cis* to one another.

Primary amides of 2-cyano-5-phenylpenta-2,4-dienoic acid **VIIIa** and **VIIIb**, when reacted with zinc enolate prepared from α,α-bromopinacoline and zinc form corresponding substituted cyclopropanes **XIa** and **XIb** according to probable Scheme 2.

Scheme 2.



VIII–XI, R = Bz (**a**), C_6H_{11} (**b**).

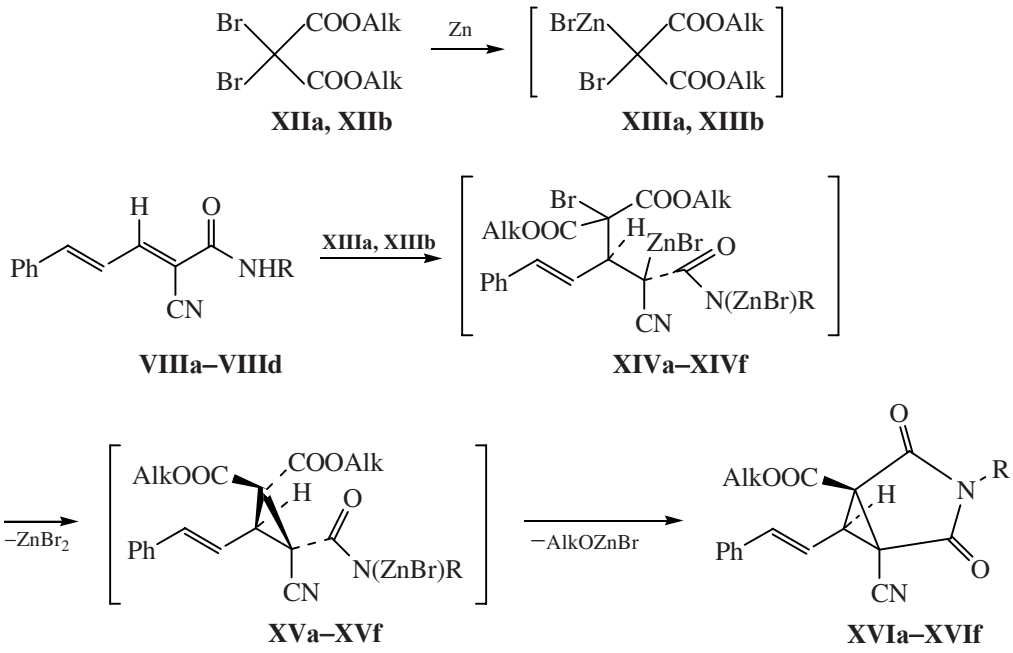
Zinc enolate **VII** adds evidently to the C^3 atom of electrophilic substrates **VIIIa** and **VIIIb** to give intermediates **XIa** and **XIb**. The latter undergo spontaneous cyclization to form intermediates **XIa** and **XIb** whose subsequent hydrolysis leads to target N-substituted amides of 2-(2,2-dimethylpropanoyl)-3-(2-phenylvinyl)-1-cyanocyclopropane-1-carboxylic acids **XIa** and **XIb**.

The structure of compounds **XIa** and **XIb** was established by IR and ^{1}H NMR spectroscopy. The IR spectra contain characteristic bands (ν, cm^{-1}) of the carbonyl (1660–1680) and cyano groups (2230–2240), and N–H bond (3335–3338). The ^{1}H NMR spectra contain characteristic signals (δ, ppm) of the *tert*-butyl (1.08–1.14), cyclopropane (3.12–3.17, 3.37), and double-bond protons (6.25, 6.61). The presence of only one set of signals shows that the products are formed as a single geometric isomer. The $^3J_{HH}$ value of the methine protons in the ^{1}H NMR spectra of compounds **XIa** and **XIb** is 9.3 Hz. Consequently, the pivaloyl radical and methyl proton are located on different sides of the cyclopropane ring plane.

Primary amides of 2-cyano-5-phenylpenta-2,4-dienoic acid **VIIIa–VIIId**, when reacted with organozinc compounds **XIIIa** and **XIIIb** prepared

from alkyl dibromomalonates and zinc, give alkyl 3-R-5-cyano-2,4-dioxo-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]-hexane-1-carboxylates **XVIa–XVIf**. The reaction is likely to proceed according to Scheme 3.

Scheme 3.



XII, XIII, Alk = CH_3 (**a**), C_2H_5 (**b**); **VIII**, R = CH_3 (**a**), Ph (**b**), Bz (**c**), C_6H_{11} (**d**); **XIV–XVI**, Alk = CH_3, R = CH_3 (**a**), Ph (**b**), Bz (**c**), Alk = C_2H_5, R = CH_3 (**d**), Bz (**e**), C_6H_{11} (**f**).

Organozinc compounds **XIIIa** and **XIIIb** in an ether–THF–HMPA medium evidently regiospecifically react with electrophilic substrates **VIIIa–VIIId** to form intermediates **XIVa–XIVf**. The latter undergo cyclization into corresponding cyclopropanation products **XVa–XVf**. These products contain an amido group activated by ZnBr substitution for hydrogen and an ester group located on the same side of the cyclopropane structural fragment, which favors further heterocyclization. Experiments showed that the amido group attacks the ester one to form final reaction products **XVIa–XVIf**.

The structure of the compounds obtained was established by IR and ^{1}H NMR spectroscopy. The IR spectra show characteristic absorption bands (ν, cm^{-1}) of the ester (1720–1725), imido (1700–1705, 1780–1795), and cyano groups (2240–2245). The ^{1}H NMR spectra contain characteristic signals (δ, ppm) in the range 2.95–3.30, assignable to the cyclopropane proton (CH), signals at 6.18–6.23, related to the double-bond protons, signals of the methoxy (3.66–3.67) or ethoxy group [1.03–1.08 (CH_3) and 4.10–4.13 (CH_2O)].

EXPERIMENTAL

The IR spectra were registered on a Specord IR-75 spectrometer in mineral oil. The ^{1}H NMR spectra were taken on a Tesla BS-567A (100 MHz) spectrometer for solutions of compounds **Va–Vd; XIa, XIb**; and **XVIa–XVIf** in $CDCl_3$ against internal HMDS.

2-Alkyl-2-aroyl-3-(phenylvinyl)cyclopropane-1,1-dicarbodinitriles Va–Vd. A mixture of 2 g of fine zinc turnings, 5 ml of ether, and 5 ml of ethyl acetate was treated with 0.065 mol of dibromoalkanone **Ia–Id**. Spontaneous reaction took place. After the reaction was complete, the mixture was refluxed for 15–20 min, cooled, decanted from zinc to another flask, treated with 0.05 mol of substrate **III** in 2 ml of ethyl acetate, refluxed for 30–40 min, cooled, hydrolyzed with 5% acetic acid, and extracted with benzene. The solvent was removed, and the residue was crystallized from a methanol–acetone mixture.

2-(4-Chlorobenzoyl)-2-methyl-3-(2-phenylvinyl)-cyclopropane-1,1-dicarbodinitrile (Va). Yield 48%, mp 144–146°C. IR spectrum, ν, cm^{-1}: 1690, 2220. ^{1}H

NMR spectrum, δ, ppm: 1.75 s (3H, CH_3), 3.34 d (1H, CH), 5.83 d.d, 6.87 d (2H, CH=CH, *J* 15.5 Hz), 7.15–7.80 m (9H, arom). Found, %: C 72.66; H 4.33; N 8.04. $C_{21}H_{15}ClN_2O$. Calculated, %: C 72.73; H 4.36; N 8.08.

2-(4-Fluorobenzoyl)-2-methyl-3-(2-phenylvinyl)-cyclopropane-1,1-dicarbodinitrile (Vb). Yield 47%, mp 147–149°C. IR spectrum , ν, cm^{-1}: 1690, 2220. ^1H NMR spectrum, δ, ppm: 1.76 s (3H, CH_3), 3.34 d (1H, CH), 5.89 d.d, 6.88 d (2H, CH=CH, *J* 15.5 Hz), 7.06–7.93 m (9H, arom). Found, %: C 76.30; H 4.55; N 8.46. $C_{24}H_{15}FN_2O$. Calculated, %: C 76.30; H 4.58; N 8.48.

2-Methyl-2-(4-methylbenzoyl)-3-(2-phenylvinyl)-cyclopropane-1,1-dicarbodinitrile (Vc). Yield 45%, mp 151–153°C. IR spectrum, ν, cm^{-1}: 1680, 2210. ^1H NMR spectrum, δ, ppm: 1.75 s (3H, CH_3), 2.42 s (3H, 4-CH_3C$_6$H$_4$), 3.24 d (1H, CH), 5.84 d.d, 6.87 d (2H, CH=CH, *J* 15.5 Hz), 7.21–7.76 m (9H, arom). Found, %: C 80.90; H 5.54; N 8.55. $C_{22}H_{18}N_2O$. Calculated, %: C 80.96; H 5.56; N 8.58.

2-Benzoyl-2-ethyl-3-(2-phenylvinyl)cyclopropane-1,1-dicarbodinitrile (Vd). Yield 43%, mp 158–160°C. IR spectrum, ν, cm^{-1}: 1680, 2210. ^1H NMR spectrum, δ, ppm: 0.95 t (3H, CH_3-ethyl, *J* 7.5), ~2.04 m (1H, CH_2-ethyl), ~2.34 m (1H, CH_2-ethyl), 3.34 d (1H, CH), 5.93 d.d, 6.90 d (2H, CH=CH), 7.13–7.87 m (10H, arom). Found, %: C 80.92; H 5.53; N 8.54. $C_{22}H_{18}N_2O$. Calculated, %: C 80.96, H 5.56, N 8.58.

N-Substituted 1-cyano-2-(2,2-dimethylpropanoyl)-3-(2-phenylvinyl)cyclopropane-1-carboxamides XIa and XIb. A mixture of 4 g of fine zinc turnings, 7 ml of ether, and 10 ml of ethyl acetate was treated with 0.025 mol of α,α-dibromopinacoline and heated until reaction began, after which it occurred spontaneously. After the reaction was complete, the mixture was refluxed for 15 min, cooled, decanted to another flask, treated with 0.01 mol of compound **VIIIa** and **VIIIb**, refluxed for 30–40 min, cooled, and hydrolyzed with 5% acetic acid. The reaction product was extracted with benzene, the solvent was removed, and the residue was crystallized from ethyl acetate or methanol.

***N*-Benzyl-2-cyano-3-(2,2-dimethylpropanoyl)-4-(2-phenylvinyl)cyclopropane-1-carboxamide (XIa)**. Yield 68%, mp 118–120°C. IR spectrum, ν, cm^{-1}: 1680, 2240, 3338. ^1H NMR spectrum, δ, ppm: 1.17 s (9H, 3CH_3), 3.12 d.d, 3.37 d (2H, 2CH), 4.46 d (2H, CH_2Ph), 6.25 d.d, 6.61 d (2H, CH=CH, *J* 15.5 Hz), 6.85–7.31 m (10H, C_6H_5), 9.5 t (1H, NH). Found, %: C 77.64; H 6.74; N 7.21. $C_{25}H_{26}N_2O_2$. Calculated, %: C 77.69; H 6.78; N 7.25.

***N*-(Cyclohexyl)-2-cyano-3-(2,2-dimethylpropanoyl)-4-(2-phenylvinyl)cyclopropane-1-carboxamide (XIb)**. Yield 49%, mp 172–174°C. IR spectrum, ν, cm^{-1}: 1660, 2230, 3335. ^1H NMR spectrum, δ, ppm: 1.18 s (9H, 3CH_3), 1.25–2.00 m (10H, C_6H_{11}), 3.17 d.d, 3.37 d (2H, 2CH), 3.75 m (1H, C_6H_{11}), 6.25 d.d, 6.61 d (2H, CH=CH, *J* 15.5), 7.1–7.40 m (5H, C_6H_5), 9.7 d (1H, NH). Found, %: C 76.12; H 7.97; N 7.35. $C_{24}H_{30}N_2O_2$. Calculated, %: C 76.16; H 7.99; N 7.40.

Alkyl 3-R-5-cyano-2,4-dioxo-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]hexane-1-carboxylates (XVIa–XVIe). A mixture of 2 g of zinc fine turnings, 7 ml of ether, and 10 ml of THF was treated with 0.024 g of dialkyl dibromomalonate. The reaction mixture was heated until reaction began, and then it occurred spontaneously. After the reaction was complete, the mixture was refluxed for 5 min, cooled, decanted to another flask containing 0.01 mol of N-substituted 3-aryl-2-cyanopropanamide and 1.5 ml of HMPA, refluxed for 30–40 min, and hydrolyzed with 5% acetic acid. The reaction product was extracted with benzene, the solvent was removed, and the residue was crystallized from methanol.

Methyl 5-cyano-2,4-dioxo-3-methyl-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate (XVIa). Yield 71%, mp 144–145°C. IR spectrum, ν, cm^{-1}: 1705, 1725, 1800, 2240. ^1H NMR spectrum, δ, ppm: 2.31 s (3H, CH_3), 3.66 s (3H, $COOCH_3$), 3.30 d.d (1H, CH), 6.18 d.d, 6.51 d (CH=CH, *J* 15.5 Hz), 7.05-7.15 m (5H, C_6H_5). Found, %: C 65.76; H 4.51; N 9.01. $C_{17}H_{14}N_2O_4$. Calculated, %: C 65.80; H 4.55; N 9.03.

Methyl 5-cyano-2,4-dioxo-3-phenyl-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate (XVIb). Yield 66%, mp 181–183°C. IR spectrum, ν, cm^{-1}: 1705, 1720, 1780, 2240. ^1H NMR spectrum, δ, ppm: 3.25 d.d (1H, CH), 3.67 (3H, CH_3), 6.23 d.d, 6.61 d (2H, CH=CH, *J* 15.5 Hz), 7.25–7.34 m (10H, 2C_6H_5). Found, %: C 70.91; H 4.30; N 7.48. $C_{22}H_{16}N_2O_4$. Calculated, %: C 70.96; H 4.33; N 7.52.

Methyl 5-cyano-3-benzyl-2,4-dioxo-3-phenyl-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate (XVIc). Yield 66%, mp 146-148°C. IR spectrum, ν, cm^{-1}: 1705, 1720, 1780, 2240. ^1H NMR spectrum, δ, ppm: 2.95 d.d (1H, CH), 3.67 s (3H, CH_3), 4.58 s (2H, CH_2Ph), 6.23 d.d, 6.61 d (2H, CH=CH, *J* 15.5), 7.25–7.34 m (10H, 2C_6H_5). Found,

%: C 71.42; H 4.67; N 7.25. $C_{23}H_{18}N_2O_4$. Calculated, %: C 71.49; H 4.70; N 7.25.

Ethyl 5-cyano-2,4-dioxo-3-methyl-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate (XVId). Yield 68%, mp 113–115°C. IR spectrum, ν, cm^{-1}: 1700, 1725, 1795, 2240. ^1H NMR spectrum, δ, ppm: 1.03 t (3H, CH_3-ethyl), 2.30 s (3H, CH_3), 3.33 d.d (1H, CH), 4.13 q (2H, CH_2OOC), 6.20 d.d, 6.58 d (2H, CH=CH, *J* 15.5 Hz), 7.10–7.20 (5H, C_6H_5). Found, %: C 66.60; H 4.95; N 8.61. $C_{18}H_{16}N_2O_4$. Calculated, %: C 66.66; H 4.97; N 8.64.

Ethyl 5-cyano-3-benzyl-2,4-dioxo-3-phenyl-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate (XVIe). Yield 61%, mp 154–156°C. IR spectrum, ν, cm^{-1}: 1705, 1725, 1785, 2245. ^1H NMR spectrum, δ, ppm: 1.06 t (3H, CH_3-ethyl), 3.27 d.d (1H, CH), 4.11 q (2H, CH_2OOC), 4.58 s (2H, CH_2Ph), 6.20 d.d, 6.63 d (2H, CH=CH, *J* 15.5), 7.20–7.40 m (10H, $2C_6H_5$). Found, %: C 71.94; H 4.99; N 6.94. $C_{24}H_{20}N_2O_4$. Calculated, %: C 71.99; H 5.03; N 7.00.

Ethyl 3-(cyclohexyl)-5-cyano-2,4-dioxo-3-phenyl-6-(2-phenylvinyl)-3-azabicyclo[3.1.0]hexane-1-carboxylate (XVIe). Yield 78%, mp 125–128°C. IR spectrum, ν, cm^{-1}: 1705, 1720, 1780, 2240. ^1H NMR spectrum: 1.08 t (3H, CH_3), 1.10–2.19 m (10H, C_6H_{11}), 3.15 d.d (1H, CH), 3.79 m (1H, C_6H_{11}), 4.10 q (2H, CH_2), 6.23 d.d, 6.61 d (2H, CH=CH, *J* 15.5), 7.11–7.25 m (5H, C_6H_5). Found, %: C 70.35; H 6.13; N 7.10. $C_{23}H_{24}N_2O_4$. Calculated, %: C 70.39; H 6.16; N 7.14.

REFERENCES

1. Shchepin, V.V., Stepanyan, Yu.G., Silaichev, P.S., and Vakhrin, M.I., *Zh. Obshch. Khim*., 2006, vol. 76, no. 10, p. 1674.
2. Shchepin, V.V., Silaichev, P.S., Stepanyan, Yu.G., Lebedev, K.P., and Vakhrin, M.I., *Zh. Obshch. Khim*., 2006, vol. 76, no. 5, p. 780.
3. Shchepin, V.V., Silaichev, P.S., Stepanyan, Yu.G., Vakhrin, M.I., Ezhikova, M.A., and Kodess, M.I., *Zh. Org. Khim*., 2006, vol. 42, no. 11, p. 1639.