Chemistry of Heterocyclic Compounds, Vol. 37, No. 11, 2001

SYNTHESIS OF 3-N,N-DIALKYLAMINO-5-(3,5,6-TRICHLORO-1,4-BENZOQUINON-2-YL)THIAZOLINE-2-THIONES*

J. Gulbis and R. Valters

N,N-Dialkylhydrazides of S-(4,6,7-trichloro-2,5-dihydroxy-2,3-dihydrobenzo[b]-3-furanyl)dithiocarbonic acids have been obtained by the reaction of 3,4,6,7-tetrachloro-2,5-dihydroxy-2,3-dihydrobenzo[b]furan with N,N-dialkylhydrazinium salts of N,N-dialkylhydrazides of dithiocarbonic acids. Recyclization in boiling ethanol in the presence of conc. HCl with subsequent oxidation leads to the formation of 3-N,N-dialkylamino-5-(3,5,6-trichloro-1,4-benzoquinon-2-yl)thiazoline-2-thiones. An attempt at recyclization in boiling trifluoroacetic acid led to the formation of 3-N,N-dialkylamino-5,6,8-trichloro-7-hydroxy-2,3,3a,8b-tetrahydrothiazolo[4,5-b]benzo[d]furane-2-thiones.

Keywords: 3-N,N-dialkylamino-5-(3,5,6-trichloro-1,4-benzoquinon-2-yl)thiazoline-2-thiones, N,N-dialkylhydrazides of S-(4,6,7-trichloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]-2-furanyl)dithiocarbonic acid, N,N-dialkyl hydrazinium salts of N,N-dialkylhydrazides of dithiocarbonic acid, intramolecular charge transfer, oxidation, recyclization.

The present work is a continuation of investigations [1-5] on the synthesis of heteryl-substituted trichloro-1,4-benzoquinones by the recyclization reaction of 3,4,6,7-tetrachloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]furan (**1**) derivatives. In molecules of heteryl-substituted trichloro-1,4-benzoquinones an intramolecular charge transfer is observed between the electron-donating heterocycle and the electron-withdrawing benzoquinone fragment, which is reflected in their electronic spectra. To study this phenomenon it seemed of interest to introduce heterocyclic systems possessing stronger electron-donating properties, such as thiazolines, thiazolinethiones, and tetrathiafulvalenes. For this purpose we studied previously the reaction of benzofuran **1** with the anions of N-methyl- and N-phenyldithiocarbamates [3], N,N-diethyldithiocarbamate [4], butyl dithiocarbonate, and tert-butyl trithionate [5], and carried out a recyclization reaction of the products obtained by nucleophilic substitution of the chlorine atom in position 3 of benzofuran **1**.

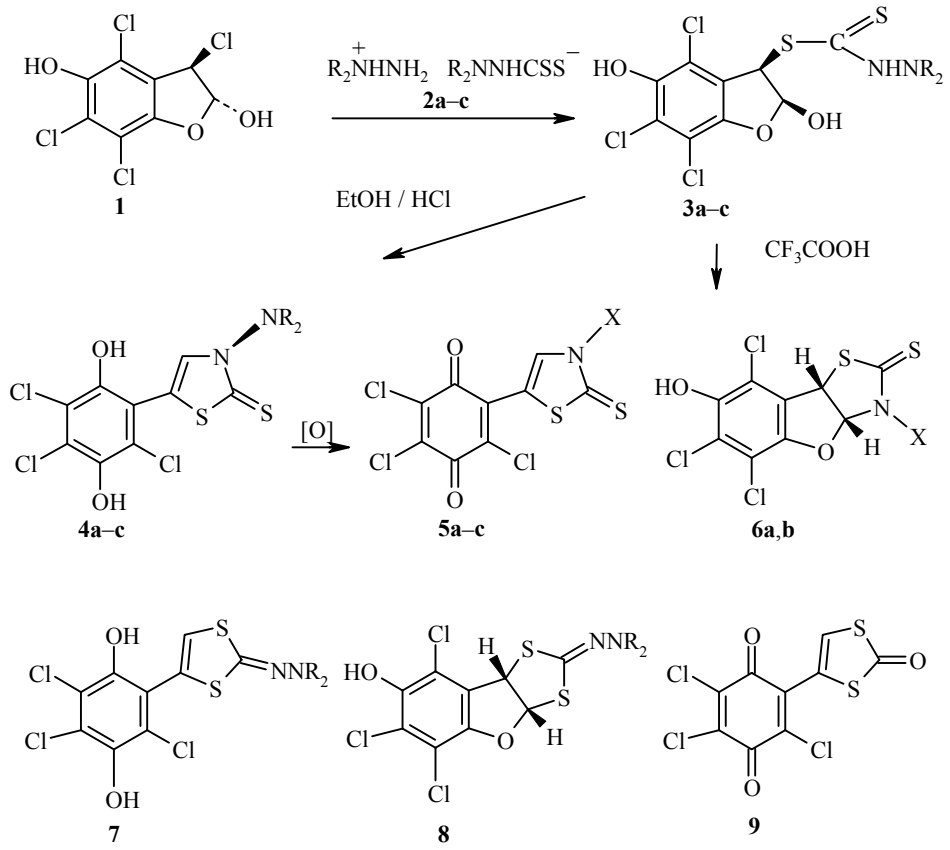
The aim of the present work was the synthesis of N,N-dialkylhydrazides of S-(4,6,7-trichloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]-2-furanyl)dithiocarbonic acids **3a-c** by the interaction of benzofuran **1** with the N,N-dialkylhydrazinium salts of N,N-dialkylhydrazides of dithiocarbonic acid **2a-c**, the study of their recyclization reactions, and the oxidation of the recyclization products. Freshly prepared salts **2a-c** were used, obtained by the reaction of carbon disulfide with N,N-dimethyl-, N,N-diethyl-, and

* Dedicated to Professor E. Lukevics on his 65th birthday.

Riga Technical University, Riga LV-1048, Latvia; e-mail: rvalters@latnet.lv. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1556-1561, November, 2001. Original article submitted March 28, 2001.

 0009-3122/01/3711-1424$25.00

N,N-pentamethylenehydrazines. Based on previous investigations [3-5] the formation of four isomeric products may be proposed from the recyclization or cyclization, *viz*. derivatives of thiazolinethione **4**, dithiole **7**, and tricyclic compounds **6** and **8**.



2–**4** **a** R = Me, **b** R = Et, **c** R_2 = –$(CH_2)_5$–;

5, **6** **a** X = NMe_2, **b** X = NEt_2, **c** X = $N(CH_2)_5$, **d** X = Me

The nucleophilic substitution reaction proceeds readily in ethanolic solution (yields of compounds **3a-c** were 54-95%). The coupling constant ^3J of about 3 Hz observed in the ^{1}H NMR spectra of compounds **3a-c** between the protons in positions 2 and 3 of the 2,3-dihydrobenzo[b]furan ring confirms the *cis* configuration of the 2,3 substituents (see [6]).

The recyclization of compounds **3a-c** was carried out under various conditions. Prolonged boiling in anhydrous toluene led to the formation of a difficultly separable mixture. The most successful proved to be recyclization in boiling ethanol in the presence of conc. hydrochloric acid, leading to the formation of the hydrochlorides of 3-N,N-dialkylamino-5-(3,4,6-trichloro-2,5-dihydroxyphenyl)thiazoline-2-thiones **4a-c·HCl**. Compounds **4a-c·HCl** were soluble in water with difficulty, practically insoluble in nonpolar organic solvents, and soluble in ethanol, DMF, and DMSO. Drying hydrochlorides **4a-c·HCl** at 80°C in vacuum for 3 h leads to loss of hydrogen chloride and the formation of bases **4a-c**. In the ^{1}H NMR spectra of compounds **4a-c** a singlet was observed for the 4-H proton at7.65-7.98 ppm which excludes the structure of tricyclic compounds **6** or **8**. In the spectra of the latter two doublets must be displayed in the range 6.2-7.5 ppm with ^3J about 7 Hz (see [4,5]). Oxidation of compounds **4a-c** with 1,4-benzoquinone in aqueous methanol solution leads to the formation of 3-N,N-dialkylamino-5-(3,5,6-trichloro-1,4-benzoquinon-2-yl)thiazoline-2-thiones **5a-c**. In the ^{1}H NMR spectra of compounds **5a-c** a singlet was observed for the 4-H proton at 8.18-8.42 ppm ($CDCl_3$). Two absorption bands

TABLE 1. Chemical Shifts of the 4-H Proton and λ_{max} (log ε) for the Charge Transfer Band of Compounds **5a-c** and of Model Compounds **5d** and **9**

Compound	^{1}H NMR spectrum, 4-H, δ, ppm ($CDCl_3$)	UV spectrum, λ_{max} (log ε) (EtOH)	Literature
5a	8.38	574 (3.62)	
5b	8.18	571 (3.68)	
5c	8.42	579 (3.72)	
5d	8.27	578 (3.50)	[3]
9	7.16	465 (3.06)	[5]

were present in the electronic spectra of benzoquinones **5a-c**, an intense band at 334 nm, which was assigned to the $\pi\rightarrow\pi^*$ transition in the 1,4-benzoquinone system, and a band in the visible portion of the spectrum at 571-579 nm, caused by an intramolecular charge transfer between the thiazoline and the benzoquinonoid portions of the molecule. The chemical shifts of the 4-H protons and the λ_{max} (log ε) of the charge transfer band of compounds **5a-c** and of the model compounds **5d** and **9** synthesized previously are given in Table 1. It is easy to be convinced that these data confirm the structure of compounds **5**, consequently structure **4** for the recyclization product is confirmed and structure **7** is disproved.

On attempting to recyclize compounds **3a,b** in boiling trifluoroacetic acid solution, the cyclization products **6a,b** were obtained, *viz*. 3-N,N-dialkylamino-5,6,8-trichloro-7-hydroxy-2,3,3a,8b-tetrahydrothiazolo-[4,5-*b*]benzo[*d*]furan-2-thiones. Two doublets were observed in their ^{1}H NMR spectra at 5.7-5.8 and 6.8-6.9 ppm (^3J = 8 Hz), which confirms the *cis* configuration of the 3a-H and 8b-H protons and is in agreement with the data of the ^{1}H NMR spectrum of the previously synthesized [3] 3-methyl derivative **6d** [two doublets at 5.81 (8b-H) and 6.93 ppm (3a-H), ^3J = 7 Hz, in DMSO-d_6). An attempt to effect the cyclization of **4a,b**$\rightarrow$**6a,b** in boiling trifluoro-acetic acid was unsuccessful. After boiling for 3 h the initial **4a,b** were isolated from the reaction mixture.

EXPERIMENTAL

The IR spectra were recorded on a Specord M 80 instrument for suspensions in nujol and in hexachlorobutadiene. The electronic spectra were obtained on a Specord M 40 instrument for solutions in ethanol ($c = 5\cdot10^{-5}$ M). The ^{1}H NMR spectra were obtained on a Bruker WH 90/DS (90 MHz) instrument, solvents were $CDCl_3$ or DMSO-D_6, internal standard was TMS. The homogeneity of compounds was checked by TLC on plates with a bound layer of Silufol UV 254 silica gel, eluent was chloroform or toluene, visualization was with UV light. 3,4,6,7-Tetrachloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]furan (**1**) was obtained by the procedure of [6].

N,N-Dialkylhydrazinium Salts of N,N-Dialkylhydrazides of Dithiocarbonic Acid (2a-c). A solution of the N,N-dialkylhydrazine (0.2 mol) in ether (15 ml) was slowly added dropwise with stirring and cooling (0-10°C) to a solution of carbon disulfide (6 ml, 0.1 mol) in ether (100 ml). The cooling bath was removed and the mixture stirred for 1 h at room temperature. The precipitated solid was removed, washed with ether, and dried. The salt was dissolved in anhydrous dichloromethane (100 ml), the solution filtered, ether was added to the filtrate until slight turbidity, then it was left at 0°C for 24 h. The colorless hygroscopic crystals were separated. Yields were almost quantitative. The salts were soluble in alcohols, chloroform, and dichloromethane, and insoluble in benzene, toluene, and ether.

General Procedure for Obtaining N,N-Dialkylhydrazides of S-(4,6,7-Trichloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]furan-2-yl)dithiocarbonic Acid (3a-c). A solution of freshly prepared dialkylhydrazinium salt **2a-c** (6 mmol) in ethanol (30 ml) was added dropwise during 15-30 min with stirring and cooling (0-5°C) to

a solution of benzofuran **1** (1.45 g, 5 mmol) in ethanol (30 ml). The reaction mixture was stirred at <10°C for a further 1 h, then poured into 1% aqueous acetic acid solution (200 ml), and extracted with ether (2 × 80 ml). The ether extracts were combined and dried over magnesium sulfate. The solution was evaporated to dryness, the residue dissolved in chloroform (20 ml) and kept in the refrigerator for 24 h. The crystals of compound **3a-c** were separated, washed on the filter with a small quantity of chloroform, and dried in a vacuum desiccator.

N,N-Dimethylhydrazide of S-(4,6,7-Trichloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]-3-furanyl)-dithiocarbonic Acid (3a). Yield 95%; mp 173-175°C (decomp.). IR spectrum (thin film), ν, cm^{-1}: 3470 and 3380 (OH), 2965, 2870, 1602, 1510. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 3.01 [6H, s, $N(CH_3)_2$]; 5.22 (1H, d, ^3J = 3.4, 3-H); 5.69 (1H, d d, ^3J = 3.4, ^3J = 8, 2-H); 7.52 (1H, d, ^3J = 8, 2-OH); 10.01 (1H, s, NH); 10.11 (1H, s, OH). Found, %: C 34.23; H 2.70; Cl 27.89; N 7.18. $C_{11}H_{11}Cl_3N_2O_3S_2$. Calculated, %: C 33.90; H 2.85; Cl 27.29; N 7.19.

N,N-Diethylhydrazide of S-(4,6,7-Trichloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]-3-furanyl)-dithiocarbonic Acid (3b). Yield 57%; mp 139-141°C (decomp.). IR spectrum (thin film), ν, cm^{-1}: 3459 and 3115 (OH), 2975, 2839, 1606, 1510. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 1.09 (6H, t, CH_3); 3.33 (br signal overlapping signal of H_2O, NCH_2); 5.38 (1H, d, ^3J = 3, 3-H); 5.78 (1H, dd, ^3J = 3, ^3J = 8, 2-H); 7.38 (1H, d, ^3J = 8, 2-OH); 10.0 (1H, s, NH); 10.18 (1H, s, OH). Found, %: C 37.36; H 3.45; Cl 26.31; N 6.77. $C_{13}H_{15}Cl_3N_2O_3S_2$. Calculated, %: C 37.38; H 3.62; Cl 25.46; N 6.71.

N,N-Pentamethylenehydrazide of S-(4,6,7-Trichloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]-3-furanyl)dithiocarbonic Acid (3c). Yield 54%; mp 154-156°C (decomp.). IR spectrum (thin film), ν, cm^{-1}: 3307 (OH), 3039, 2947, 2855, 1576. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 1.53 [6H, br. signal, $–(CH_2)_3–$]; 3.42 (br signal overlapping signal of H_2O, NCH_2); 5.23 (1H, d, ^3J = 3.4, 3-H); 5.74 (1H, dd, ^3J = 3.4, ^3J = 8, 2-H); 7.47 (1H, d, ^3J = 8, 2-OH); 9.96 (1H, s, NH); 10.11 (1H, s, OH). Found, %: C 38.45; H 3.09; Cl 25.32; N 5.72. $C_{14}H_{15}Cl_3N_3O_3S_2$. Calculated, %: C 39.13; H 3.52; Cl 24.75; N 6.52.

General Procedure for Obtaining 3-N.N-Dialkylamino-5-(3,4,6-trichloro-2,5-dihydroxyphenyl)thiazoline-2-thiones (4a-c). Conc. HCl (3 ml) was added to a solution of compound **3a-c** (2 mmol) in ethanol (15 ml) and the mixture was boiled for 4 h. After cooling, the solution was poured into water (100 ml), the precipitated solid was separated, washed with water, dried at 40°C, and the hydrochlorides **4a-c·HCl** were obtained. After drying in vacuum at 80°C for 3 h the bases **4a-c** were obtained.

3-N,N-Dimethylamino-5-(3,4,6-trichloro-2,5-dihydroxyphenyl)thiazoline-2-thione (4a). Yield 85%; mp 247-250°C (decomp.). IR spectrum (thin film), ν, cm^{-1}: 3372 (OH), 2964, 1642, 1558. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.87 (6H, s, NCH_3); 7.98 (1H, s, 4-H); 9.98 (2H, br. signal, OH).

Hydrochloride 4a·HCl. Found, %: Cl 33.92. $C_{11}H_9Cl_3N_2O_2S_3$·HCl. Calculated, %: Cl 34.76. After drying at 80°C in vacuum for 3 h the mp is unchanged. Found, %: C 35.67; H 2.42; Cl 28.30; N 7.46. $C_{11}H_9Cl_3N_2O_2S_2$. Calculated, %: C 35.55; H 2.44; Cl 28.62; N 7.54.

3-N,N-Diethylamino-5-(3,4,6-trichloro-2,5-dihydroxyphenyl)thiazoline-2-thione (4b). Yield 83%; mp 188-192°C (decomp.). IR spectrum (thin film), ν, cm^{-1}: 3381 (OH), 2972, 2840, 1621, 1540. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.96 (6H, t, CH_3); 3.36 (br signal overlapping signal of H_2O, NCH_2); 7.65 (1H, s, 4-H); 9.94 (2H, br. signal, OH).

Hydrochloride 4b·HCl. Found, %: Cl 32.05. $C_{13}H_{13}Cl_3N_2O_2S_2$·HCl. Calculated, %: Cl 32.51. After drying in vacuum at 80°C for 3 h the mp is unchanged. Found, %: C 39.95; H 3.30; Cl 26.31; N 6.67. $C_{13}H_{13}Cl_3N_2O_2S_2$. Calculated, %: C 39.06; N 3.28; Cl 26.61; N 7.01.

5-(3,4,6-Trichloro-2,5-dihydroxyphenyl)-3-piperidinothiazoline-2-thione (4c). Yield 82%; mp 225-228°C (decomp.). IR spectrum (thin film), ν, cm^{-1}: 3324 (OH), 2960, 2873, 1631, 1522. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.65 [6H, br. signal, $(CH_2)_3$]; 3.11 (br signal overlapping signal of H_2O, NCH_2); 7.98 (1H, s, 4-H); 10.0 (2H, br. signal, OH).

Hydrochloride 4c·HCl. Found, %: Cl 30.83. $C_{14}H_{13}Cl_3N_2O_2S_2$·HCl. Calculated, %: 31.62. After drying at 80°C in vacuum for 3 h the mp is unchanged. Found, %: C 40.32; H 3.14; Cl 24.65; N 6.68. $C_{14}H_{13}Cl_3N_2O_2S_2$. Calculated, %: C 40.84; H 3.18; Cl 25.83; N 6.80.

General Procedure for Obtaining 3-N,N-Dialkylamino-5-(3,5,6-trichloro-1,4-benzoquinon-2-yl)thiazoline-2-thiones (5a-c). A solution of 1,4-benzoquinone (0.25 g) in methanol (10 ml) was added to a solution of hydroquinone **4a-c** (1 mmol) in methanol (10 ml) and the mixture stirred for 30 min. Distilled water (5 ml) was added, the mixture was stirred for a further 30 min, the precipitate was separated, washed on the filter with 70% aqueous methanol, and dried.

3-N,N-Dimethylamino-5-(3,5,6-trichloro-1,4-benzoquinon-2-yl)thiazoline-2-thione (5a). Yield 71%; mp 190-192°C. UV spectrum (EtOH), λ_{max} (log ε): 334 (4.21), 574 (3.62). IR spectrum (thin film), ν, cm^{-1}: 2967, 1668 (C=O), 1602, 1542, 1524. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.12 (6H, s, NCH_3); 8.38 (1H, s, 4-H). Found, %: Cl 28.07. $C_{11}H_7Cl_3N_2O_2S_2$. Calculated, %: Cl 28.77.

3-N,N-Diethylamino-5-(3,5,6-trichloro-1.4-benzoquinon-2-yl)thiazoline-2-thione (5b). Yield 76%; mp 173-175°C. UV spectrum (EtOH), λ_{max} (log ε): 334 (4.25), 571 (3.68). IR spectrum (thin film), ν, cm^{-1}: 2971, 2840, 1676 and 1664 (C=O), 1562. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.07 (6H, t, CH_3); 3.02 (2H, br. signal, NCH_2); 3.85 (2H, br. signal, NCH_2); 8.18 (1H, s, 4-H). Found, %: C 39.39; H 2.56; Cl 26.07; N 6.86. $C_{13}H_{11}Cl_3N_2O_2S_2$. Calculated, %: C 39.25; H 2.79; Cl 26.74; N 7.04.

5-(3,5,6-Trichloro-1,4-benzoquinon-2-yl)-3-piperidinothiazoline-2-thione (5c). Yield 71%; mp 183-185°C. UV spectrum (EtOH), λ_{max} (log ε): 334 (4.26), 579 (3.72). IR spectrum (thin film), ν, cm^{-1}: 2940, 2852, 1670 (C=O), 1606, 1548, 1528. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.73 [6H, br. signal, $(CH_2)_3$]; 3.36 (4H, br. signal, NCH_2); 8.42 (1H, s, 4-H). Found, %: C 40.84; H 2.59; Cl 25.20; N 6.77. $C_{14}H_{11}Cl_3N_2O_2S_2$. Calculated, %: C 41.04; H 2.71; Cl 25.96; N 6.84.

5,6,8-Trichloro-3-N,N-dimethylamino-7-hydroxy-2,3,3a,8b-tetrahydrothiazolo[4,5-*b*]benzo[*d*]furan-2-thione (6a). A solution of compound **3a** (1 mmol) in trifluoroacetic acid (15 ml) was boiled for 4 h. The cooled solution was poured into cold water (100 ml), the precipitated solid was separated, washed with distilled water, dried, and recrystallized from toluene. Yield 86%; mp 260-262°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, J (Hz): 2.91 (6H, s, CH_3); 5.69 (1H, d, J = 8, 8b-H); 6.93 (1H, d, ^3J = 8, 3a-H); 10.29 (1H, br. signal, OH). Found, %: C 35.30; H 2.20; Cl 28.37; N 7.28. $C_{11}H_9Cl_3N_2O_2S_2$. Calculated, %: C 35.55; H 2.44; Cl 28.62; N 7.54.

5,6,8-Trichloro-3-N,N-diethylamino-7-hydroxy-2,3,3a,8b-tetrahydrothiazolo[4,5-*b*]benzo[*d*]furan-2-thione (6b) was obtained from compound **3b** analogously to the previous method. Yield 94%; mp 161-163°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, J (Hz): 1.0 (6H, t, CH_3); 3.42 (br. signal, overlapping signal of H_2O, NCH_2); 5.80 (1H, d, J = 8, 8b-H); 6.78 (1H, d, ^3J = 8, 3a-H); 10.26 (1H, br. signal, OH). Found, %: C 38.54; H 2.91; Cl 26.64; N 6.74. $C_{13}H_{13}Cl_3N_2O_2S_2$. Calculated, %: C 39.06; H 3.28; Cl 26.61; N 7.01.

REFERENCES

1. R. E. Valter, G. A. Karlivan, M. F. Utinan, and Yu. V. Gulbis, *Sib. Khim. Zh.*, No. 4, 39 (1992).
2. R. Valters, G. Karlivans, J. Gulbis, M. Utinans, and A. Bace, *Phosph., Sulfur, and Silicon*, **95 & 96**, 457 (1994).
3. Yu. V. Gulbis, R. E. Valter, G. A. Karlivan, and M. F. Utinan, *Khim. Geterotsikl. Soedin.*, 111 (1994).
4. G. A. Karlivan, R. E. Valter, A. E. Batse, and Yu. V. Gulbis, *Khim. Geterotsikl. Soedin.*, 463 (1996).
5. G. A. Karlivan, R. E. Valter, and Yu. V. Gulbis, *Khim. Geterotsikl. Soedin.*, 1055 (1998).
6. R. E. Valter, E. E. Liepin'sh, G. A. Karlivan, V. R. Zin'kovska, and M. F. Utinan, *Zh. Org. Khim.*, **21**, 436 (1985).