Organometallic synthesis in the furazan series
3.* Silyl derivatives of methylfurazans**

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The reactions of (lithiomethyl)furazans with chlorosilanes were investigated and a number of silyl derivatives of methylfurazans were prepared. The reactivity of these compounds was studied.

Key words: furazans, methylfurazans, organolithium synthesis, silylation, organosilicon compounds.

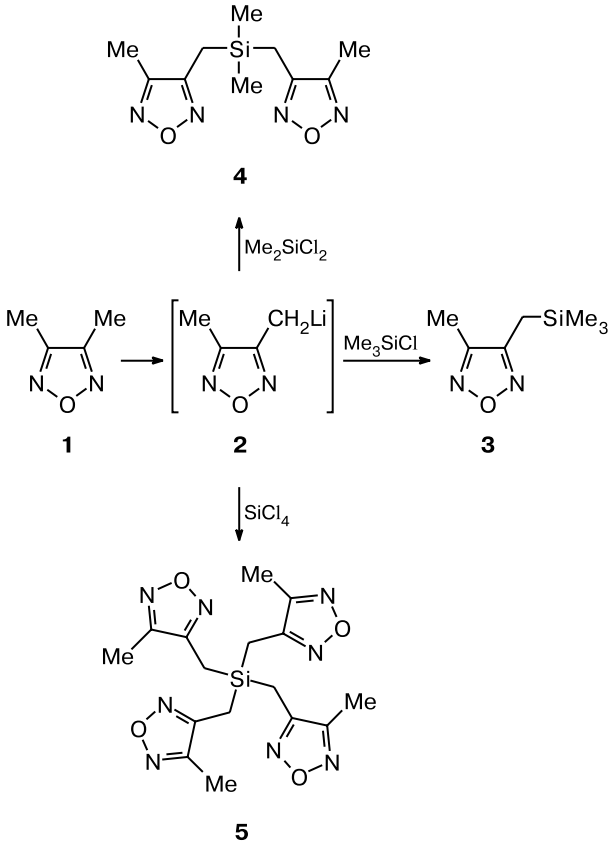
It is known that the electron-withdrawing character of the furazan ring promotes smooth lithiation of the methyl group attached to it. The resulting lithium derivative is carboxylated to give 4-methylfurazan-3-acetic acid in a high yield[3] and reacts with functionalized alkyl halides with easy replacement of the halogen, being converted into the corresponding derivatives.[1,4] This strategy is an efficient method for the preparation of modified alkylfurazans based on readily accessible 3,4-dimethylfurazan (**1**).

Now we studied the reactions of (lithiomethyl)furazans with electrophiles that contain a halogen atom bound to an element other than carbon and described the synthesis of organosilicon compounds.

We found that the addition of chlorotrimethylsilane, dichlorodimethylsilane, or tetrachlorosilane to a solution of Li derivative **2** in a pentane—THF mixture at −55 °C leads to the smooth formation of organosilicon compounds **3—5** (Scheme 1). Upon an increase in the number of furazan rings in the formed molecule, the yield decreases. Indeed, compound **3** is obtained in 95% yield, difurazan derivative **4** is separated in 56% yield, and the yield of tetrasubstituted silane **5** is only 37%. This result is, apparently, due to the loss during distillation; the viscosity of these compounds increases appreciably with an increase in the molecular weight.

In the case where a solution of compound **2** is added to a solution of $SiCl_4$ in THF, *i.e.*, with the opposite order of reactant mixing, GC/MS analysis showed stepwise replacement of the four Cl atoms in $SiCl_4$. However, the introduction of even one equivalent of compound **2** in the reaction medium gives rise to all of the possible substitution products.

Scheme 1



* For Part 2, see Ref. 1.

** The contents of this study was partly included in a report.[2]

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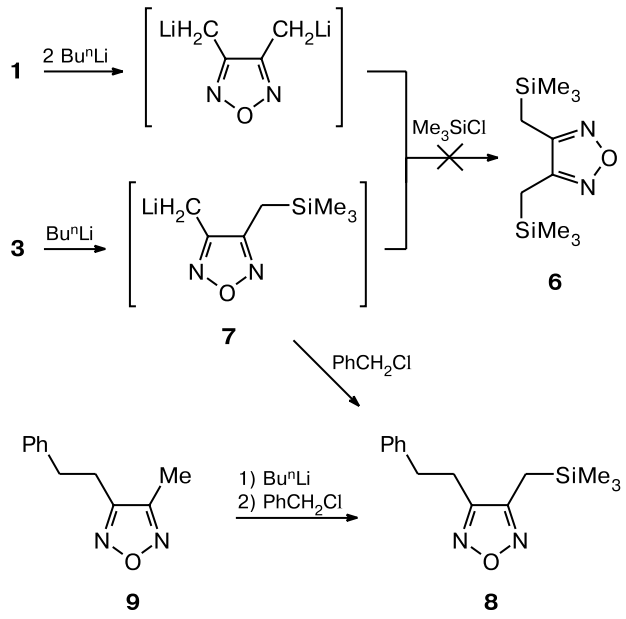
The attempts to prepare bis(trimethylsilyl) derivative **6** either by dilithiation of compound **1** or by lithiation of compound **3** followed by treatment of the intermediates with chlorotrimethylsilane failed (Scheme 2). Nevertheless, on treatment with benzyl chloride,[1] the lithiated silyl intermediate **7** gives the usual substitution product **8** in 76% yield. The same product, although in a lower yield, was formed upon lithiation and subsequent silylation of compound **9**.[1]

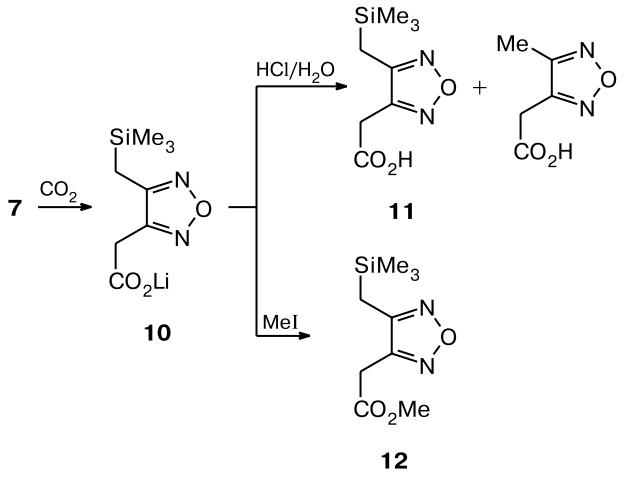
Scheme 2



Passing of dry carbon dioxide through a solution of intermediate **7** in a pentane—THF mixture results in a quantitative formation of the lithium salt of furazanacetic acid **10** (Scheme 3). Acidification of salt **10** with hydrochloric acid in order to prepare acid **11** gave a complex mixture of products. According to ^{1}H NMR data, the content of the target product **11** in this mixture was 55—65%, however, attempts to isolate compound **11** in a pure state failed. It is worth noting that 4-methylfurazan-3-acetic acid is formed as a major impurity (13—18% according to ^{1}H NMR data; monitoring based on an authentic sample[3]). The formation of this compound upon acidification of salt **10** implies that desilylation takes place in the acid medium. Treatment of salt **10** with methyl iodide results in ester **12**,[5] whose yield, however, does not exceed 30%. By using methyl bromide as the methylating agent, the yield of compound **12** was brought to 59%. The attempts to prepare the ethyl ester by using either ethyl chloride or diethyl sulfate failed.

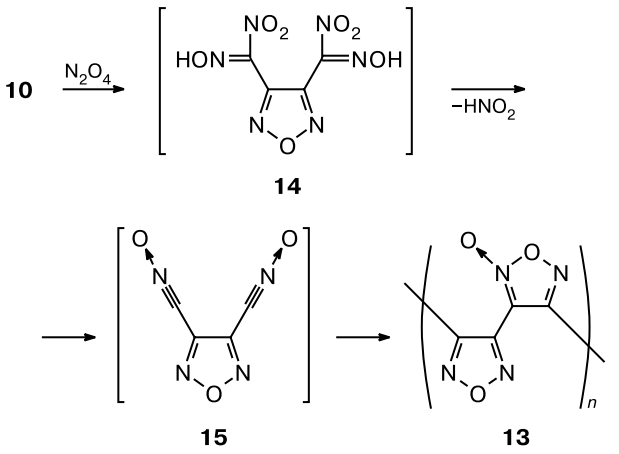
The peculiar behavior of Li salt **10** shows itself also when it reacts with nitrogen dioxide (Scheme 4). This

Scheme 3



affords an insoluble compound, which contains no H, Li, or Si atoms, according to elemental analysis, and is described by the formula $(C_4N_4O_3)_n$. Apparently, this is an oligomer corresponding to formula **13**. The transformation of α-substituted acetic acids on treatment with nitrogen oxides into furoxans is known to proceed through the intermediate formation of nitrolic acids.[6] Apparently, in the case of compound **10**, both methylene units behave similarly, the combination of nitrosation and nitration processes yielding bis(nitrolic) acid **14**. Elimination of nitrous acid from this product results in bifunctional derivative **15** with nitrile oxide groups. The intermolecular reaction of **15** analogous to the dimerization of nitrile oxides to furoxans leads to the formation of a chain of alternating furazan and furoxan rings.

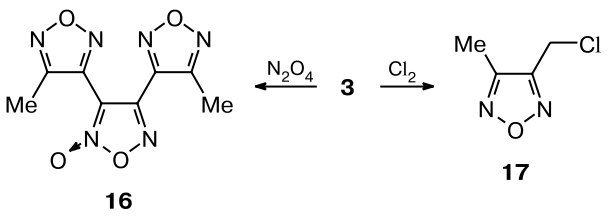
Scheme 4



Indeed, a similar treatment of trimethylsilyl derivative **3** with nitrogen oxides gives rise to furoxan **16** (Scheme 5).

Since the Me group at the furazan rings is inert to the action of nitrating reagents,[7] the methylene unit linked to the trimethylsilyl groups serves as the only reaction center in this reaction. Cleavage of the C—Si bond appears to be the primary step of this transformation, which is confirmed indirectly by the reaction of compound **3** with an electrophile such as chlorine. The product of the replacement of the trimethylsilyl group, 3-methyl-4-(chloromethyl)furazan **17**,[8] is inert with respect to excess chlorine and is formed in a high yield.

Scheme 5



The NMR signals were assigned relying on the previously identified pattern of influence of substituents in the furazan series on the spectral characteristics.[1,9,10]

The mass spectra of all the organosilicon compounds synthesized tend to exhibit intense molecular ion peaks. Its further fragmentation is determined by the simultaneous presence of two structural subunits. However, the major route of fragmentation is related to the presence of the Si—C bond, which produces intense $[M - Me]^+$ or $[M - Me(C_2N_2O)CH_2]^+$ peaks upon cleavage. The fragmentation route typical of furazans, due to loss of the NO molecule,[11] is of secondary importance for compounds **3—5**, **8**, and **9**; the corresponding low-intensity peaks were detected in all spectra.

Thus, we showed that the reactions of lithium derivatives of methylfurazans with chlorosilanes represent a facile route to organosilicon derivatives of the furazan series. It should be noted that the methyl group attached to the furazan ring containing a (trimethylsilyl)methyl fragment can be lithiated and further modified on treatment with C-electrophiles. It was found that silyl derivatives of methylfurazans can react with strong electrophilic reagents with cleavage of the C—Si bond.

Experimental

Melting points were determined on as Kofler hot stage and not corrected. ^1H and ^{13}C NMR spectra for natural isotope abundances were recorded on Bruker AM-300 (300.13 and 75.7 MHz, respectively) and Bruker DRX-500 (500.13 and 125.7 MHz) spectrometers. The NMR chemical shifts are given in the δ scale and referred to the solvent ($CDCl_3$) as the internal standard. Mass spectra were run on Finnigan MAT INCOS-50 and Varian MAT CH-111 instruments (EI, 70 eV). IR spectra were measured on a Specord IR-75 spectrometer (as KBr pellets for solids and in thin films for liquids). The course of the reaction was monitored and the purity of products was checked by GLC and TLC (on Silufol UV-254). GLC analysis was carried out on a Biochrom-1 (flame ionization detector, capillary column, helium as the carrier gas). 3,4-Dimethylfurazan (**1**) was prepared by a procedure we developed previously.[1]

3-Methyl-4-[(trimethylsilyl)methyl]furazan (3). A solution of Bu^nLi (2.05 g, 0.032 mol, 0.051 g mL^{-1}) in pentane was added dropwise with stirring at −55 °C under a static argon atmosphere into a 300-mL three-necked flask equipped with a thermometer and two dropping funnels with bypasses and containing 3,4-dimethylfurazan (**1**) (3.14 g, 0.032 mol) in 200 mL of anhydrous THF. The bright-yellow reaction mixture was stirred for 20 min at −55 °C, and a solution of Me_3SiCl (4.35 g, 0.04 mol) in 10 mL of anhydrous THF was quickly added. The mixture was stirred for 30 min at −55 °C. Then cooling was removed (the temperature of the mixture rose spontaneously to ~20 °C) and the mixture was stirred for an additional 1 h. The inorganic precipitate was filtered off and the solvent was evaporated. The remaining oil was distilled, the fraction with b.p. 39—40 °C (10 Torr) being collected to give 5.17 g (95%) of compound **3** as a colorless oil, $n_D^{20} = 1.454$. Found (%): C, 49.46; H, 8.41; N, 16.38; Si, 16.53. $C_7H_{14}N_2OSi$. Calculated (%): C, 49.37; H, 8.29; N, 16.45; Si, 16.49. MS, *m/z*: 170 $[M]^+$, 154 $[M - CH_4]^+$, 98 $[Me(C_2N_2O)Me]^{\bullet+}$. ^1H NMR, δ: −0.03 (s, 9 H, $SiMe_3$); 1.97 (s, 2 H, CH_2); 2.19 (s, 3 H, Me). ^{13}C NMR, δ: 153.2 (C—CH_2); 150.4 (C—Me); 12.2 (CH_2); 8.3 (Me); −1.7 (Si—Me). ^{29}Si NMR, δ: 3.8 ($SiMe_3$).

***Si*,*Si*-Dimethyl-*Si*,*Si*-bis[(4-methylfurazan-3-yl)methyl]silane (4).** The reaction between compound **1** (5.48 g, 0.056 mol) and Me_2SiCl_2 (3.6 g, 0.028 mol) was carried out by a similar procedure. The oil obtained after evaporation was distilled. The yield of compound **4** was 3.94 g (56%), colorless oil, b.p. 100—101 °C (10 Torr), $n_D^{20} = 1.516$. Found (%): C, 47.63; H, 6.42; N, 22.15; Si, 11.11. $C_{10}H_{16}N_4O_2Si$. Calculated (%): C, 47.60; H, 6.39; N, 22.20; Si, 11.13. MS, *m/z*: 252 $[M]^+$, 238 $[M - CH_4]^+$, 154 $[M - Me(C_2N_2O)CH_2 - H]^+$, 139 $[M - Me - Me(C_2N_2O)CH_2]^+$, 98 $[Me(C_2N_2O)Me]^{\bullet+}$. ^1H NMR, δ: 0.04 (s, 6 H, $SiMe_2$); 2.02 (s, 4 H, CH_2); 2.12 (s, 6 H, Me). ^{13}C NMR, δ: 152.2 (C—CH_2); 150.5 (C—Me); 9.4 (CH_2); 7.5 (Me); −3.6 (Si—Me). ^{29}Si NMR, δ: 5.2 ($SiMe_2$).

Tetrakis[(4-methylfurazan-3-yl)methyl]silane (5). The reaction between compound **1** (8.14 g, 0.083 mol) and $SiCl_4$ (3.4 g, 0.02 mol) was carried out by a similar procedure. The oil obtained after evaporation was distilled. The yield of compound **5** was 3.08 g (37%), thick oil, b.p. 118—119 °C (1 Torr). Found (%): C, 46.13; H, 4.85; N, 26.84; Si, 6.81. $C_{16}H_{20}N_8O_4Si$. Calculated (%): C, 46.14; H, 4.84; N, 26.91; Si, 6.74. MS, *m/z*: 416 $[M]^+$. ^1H NMR, δ: 2.08 (s, 8 H, CH_2); 2.21 (s, 12 H, Me). ^{13}C NMR, δ: 152.0 (C—CH_2); 150.5 (C—Me); 9.1 (CH_2); 7.4 (Me). ^{29}Si NMR, δ: 5.5 ($Si(CH_2)_4$).

4-(2-Phenylethyl)-3-(trimethylsilyl)methylfurazan (8). A solution of Bu^nLi (1.02 g, 0.016 mol, 0.047 g mL^{-1}) in pentane was added dropwise with stirring at −55 °C under argon to a solution of compound **9** [1] (2.72 g, 0.016 mol) in 150 mL of anhydrous THF. The bright-yellow reaction mixture was stirred for 20 min at −55 °C, and a solution of benzyl chloride (2.1 g, 0.0166 mol) in 20 mL of anhydrous THF was added. The mixture was stirred for 30 min at −55 °C. The cooling was removed,

the temperature of the reaction mixture was raised to ~20 °C, and the mixture was stirred for an additional 1 h, filtered through a short SiO_2 layer, and concentrated using a rotary evaporator. The product was purified by preparative chromatography (SiO_2 40/100, elution by a 1 : 3 CH_2Cl_2—pentane mixture) to give 3.17 g (76%) of an oily product **8**, b.p. 110—111 °C (13 Torr). Found (%): C, 64.61; H, 7.77; N, 10.71; Si, 10.70. $C_{14}H_{20}N_2OSi$. Calculated (%): C, 64.57; H, 7.74; N, 10.76; Si, 10.79. MS, *m/z*: 260 $[M]^+$, 244 $[M - CH_4]^+$, 230 $[M - NO]^+$. ^1H NMR, δ: −0.02 (s, 9 H, $SiMe_3$); 2.01 (s, 2 H, CH_2—Si); 2.87—3.04 (m, 4 H, CH_2—CH_2); 7.18 (d, 2 H, *m*-H arom.); 7.23—7.37 (m, 3 H, *o*-, *p*-H arom.). ^{13}C NMR, δ: 152.9 (C—CH_2Si); 150.6 (C—CH_2CH_2Ph); 139.8 (*i*-Ph); 128.6, 128.3, 128.6 (Ph); 33.5 (CH_2Ph); 24.7 (CH_2); 10.9 (C-CH_2Si); −1.2 (Si—Me).

Lithium 4-(trimethylsilyl)methylfurazan-3-acetate (10). A solution of Bu^nLi (3.047 g, 0.048 mol, 0.056 g mL^{-1}) in pentane was added dropwise with stirring at −55 °C under a static argon atmosphere to a solution of compound **3** (8.16 g, 0.048 mol) in 350 mL of anhydrous THF contained in a 500-mL three-necked flask equipped with a thermometer and two dropping funnels with bypasses. The mixture was stirred for 20 min at −55 °C. Dry carbon dioxide (threefold excess) was passed for 10—15 min through the resulting bright-yellow solution of intermediate **7**. The mixture was stirred for 30 min at −55 °C, allowed to warm-up spontaneously to ~20 °C, and concentrated to dryness under reduced pressure. The residue was recrystallized from Pr^iOH to give 10.1 g (96%) of product **10** as a white amorphous powder, m.p. >340 °C. Found (%): C, 43.66; H, 5.96; Li, 3.11; N, 12.65; Si, 12.78. $C_8H_{13}LiN_2O_3Si$. Calculated (%): C, 43.63; H, 5.95; Li, 3.15; N, 12.72; Si, 12.75. IR, ν/cm^{-1}: 2975, 2940, 1610, 1515, 1430, 1395, 1290, 1230, 1190, 1047, 910. ^1H NMR, δ: −0.02 (s, 9 H, $SiMe_3$); 2.12 (s, 2 H, CH_2); 3.40 (s, 2 H, CH_2CO_2Li). ^{13}C NMR, δ: 170.3 (CO_2Li); 153.0, 152.6 (ring C); 31.6 (CH_2CO_2Li); 10.9 (CH_2); −0.3 (Si—Me). ^{29}Si NMR, δ: 3.2 ($SiMe_3$).

Methyl 4-(trimethylsilyl)methylfurazan-3-acetate (12). ***A.*** A solution of MeI (1.7 g, 0.012 mol) in glyme (15 mL) was added dropwise with stirring to a solution of compound **10** (2.2 g, 0.01 mol) in anhydrous glyme (50 mL). The resulting mixture was stirred for 24 h at ~20 °C and concentrated under reduced pressure. The residue was dissolved in CCl_4, filtered through a short silica gel layer and concentrated to give 0.68 g (30%) of product **12** as a colorless oil, b.p. 91—92 °C (12 Torr). Found (%): C, 47.37; H, 7.09; N, 12.25; Si, 12.27. $C_9H_{16}N_2O_3Si$. Calculated (%): C, 47.34; H, 7.06; N, 12.27; Si, 12.30. MS, *m/z*: 228 $[M]^+$, 212 $[M - CH_4]^+$, 198 $[M - NO]^+$, 196 $[M - 2\,CH_4]^+$. IR, ν/cm^{-1}: 2950, 1730, 1620, 1530, 1280, 1215, 1170, 1020, 930. ^1H NMR, δ: −0.01 (s, 9 H, $SiMe_3$); 2.14 (s, 2 H, CH_2); 3.80 (s, 2 H, CH_2CO_2Me); 4.85 (s, 3 H, OMe).

B. The synthesis was carried out as described in procedure ***A*** but using MeBr to give 1.34 g (59%) of product **12**.

Poly(furazanylfuroxan) (13). A solution of N_2O_4 (3.68 g, 0.04 mol) in CH_2Cl_2 (25 mL) was added dropwise with stirring at 0—5 °C to a suspension of salt **10** (2.2 g, 0.01 mol) in CH_2Cl_2 (25 mL), and the mixture was stirred for 20 min. Then the reaction mixture was refluxed for 1.5 h and cooled. The filtered-off precipitate was washed with water, a 5% solution of $NaHCO_3$, once again with water, and with MeOH and dried in air to give 0.42 g (28%) of compound **13** as a light-cream-colored amorphous powder, decomp. at 170—176 °C. Found (%): C, 31.64; N, 36.80. $C_4N_4O_3$. Calculated (%): C, 31.59; N, 36.84. IR, ν/cm^{-1}: 1632, 1618, 1545, 1532, 1514, 1460, 1360, 1120, 1008, 928, 896.

3,4-Bis(4-methylfurazan-3-yl)furoxan (16). A solution of N_2O_4 (3.68 g, 0.04 mol) in CH_2Cl_2 (25 mL) was added dropwise with stirring at 0—5 °C to a solution of compound **3** (1.7 g, 0.01 mol) in CH_2Cl_2 (15 mL), and the mixture was stirred for 1 h. Then the reaction mixture was refluxed for 1.5 h, cooled, washed with a 5% solution of $NaHCO_3$ (2×30 mL) and water (2×30 mL), and dried over $MgSO_4$. The solution was filtered through a short silica gel layer and concentrated under reduced pressure. The residue was recrystallized from hexane to give 0.68 g (30%) of a colorless crystalline product **16**, m.p. 97—99 °C. Found (%): C, 38.44; H, 2.41; N, 33.53. $C_8H_6N_6O_4$. Calculated (%): C, 38.41; H, 2.42; N, 33.59. MS, *m/z*: 250 $[M]^+$, 234 $[M - O]^+$, 204 $[M - O - NO]^+$, 174 $[M - O - 2\,NO]^+$. IR, ν/cm^{-1}: 1622, 1612, 1536, 1518, 1506, 1448, 1360, 1176, 1020, 940. ^1H NMR, δ: 2.46, 2.51 (both s, each 3 H, Me). ^{13}C NMR, δ: 8.6, 8.8 (Me); 105.2 (CN→O); 136.2, 138.7, 142.8 (C=NO); 149.9, 151.1 (C—Me).

4-Chloromethyl-3-methylfurazan (17). A solution of chlorine (35.5 g, 0.5 mol) in CCl_4 (250 mL) was added to a solution of compound **3** (17 g, 0.1 mol) in CCl_4 (50 mL). The mixture was stirred for 36 h at ~20 °C and concentrated on a rotary evaporator and the residue was distilled to give 11.1 g (84%) of product **17** as a colorless liquid, b.p. 103—104 °C (17 Torr); *cf.* Ref. 8: b.p. 63 °C (8 Torr). ^1H NMR, δ: 2.38 (s, 3 H, Me); 4.63 (s, 2 H, CH_2). ^{13}C NMR, δ: 151.2 (C—CH_2); 150.7 (C—Me); 32.1 (CH_2); 7.8 (Me). Other characteristics were identical to the published values.[8]

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References

1. A. B. Sheremetev, E. A. Ivanova, A. Yu. Sizov, V. O. Kulagina, D. E. Dmitriev, and Yu. A. Strelenko, *Izv. Akad. Nauk, Ser. Khim.*, 2003, 651 [*Russ. Chem. Bull., Int. Ed.*, 2003, **52**, 679].
2. A. B. Sheremetev, E. A. Ivanova, and D. E. Dmitriev, *Mezhdunar. nauch. konf. "Organicheskii sintez i kombinatornaya khimiya"* [*Organic Synthesis and Combinatorial Chemistry*] (*Zvenigorod, March 4—7, 1999*), *Abstrs.*, Moscow, 1999, P-64 (in Russian).
3. R. G. Micetich, *Can. J. Chem.*, 1970, **48**, 2003.
4. A. Yu. Sizov and A. B. Sheremetev, *Izv. Akad. Nauk, Ser. Khim.*, 1992, 365 [*Bull. Russ. Acad. Sci., Div. Chem. Sci.*, 1992, **41**, 281 (Engl. Transl.)].
5. A. E. Vasil´vitskii, A. B. Sheremetev, T. S. Novikova, L. I. Khmel´nitskii, and O. M. Nefedov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 2876 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 2640 (Engl. Transl.)].

6. L. I. Khmel´nitskii, S. S. Novikov, and T. I. Godovikova, *Khimiya furoksanov. Stroenie i sintez* [*Chemistry of Furoxans. Structure and Synthesis*], Nauka, Moscow, 1996, 383 pp. (in Russian).
7. M. P. Zelenov, G. M. Frolova, S. F. Mel´nikova, and I. V. Tselinskii, *Khimiya Geterotsikl. Soedinen.*, 1982, 27 [*Chem. Heterocycl. Compd.*, 1982, **18** (Engl. Transl.)].
8. I. V. Vigalok, A. V. Ostrovskaya, N. V. Svetlakov, T. V. Zykova, and N. A. Zhikhareva, *Khimiya Geterotsikl. Soedinen.*, 1977, 30 [*Chem. Heterocycl. Compd.*, 1977, **13**, 25 (Engl. Transl.)].
9. Yu. A. Strelenko, A. B. Sheremetev, and L. I. Khmel´nitskii, *Khimiya Geterotsikl. Soedinen.*, 1992, 1101 [*Chem. Heterocycl. Compd.*, 1992, **28**, 927 (Engl. Transl.)].
10. D. E. Dmitriev, Yu. A. Strelenko, and A. B. Sheremetev, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 277 [*Russ. Chem. Bull., Int. Ed.*, 2002, **51**, 290].
11. R. M. Paton, in *Comprehensive Heterocyclic Chemistry II*, Eds. A. R. Katritzky, C. W. Rees, and E. F. V. Scriven, Pergamon, Oxford, 1996, **4**, 229.

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