4-Formylsydnonimine derivatives

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The procedure for the synthesis of 4-formylsydnonimine derivatives based on the reaction of 4-lithiosydnonimines with (methoxymethylidene)dimethylammonium methyl sulfate was proposed.

Key words: sydnonimines, 1,2,3-oxadiazolium-5-amidines, metallation, (methoxymethylidene)dimethylammonium methyl sulfate.

Sydnonimines (1,2,3-oxadiazolium-5-amidines) are one of the most examined representatives of mesoionic heterocyclic compounds.[1,2] Studies on the synthesis and properties study of sydnonimines are of great interest mainly due to the wide spectrum of their pharmacological activities.[2] Currently it was shown that sydnonimines are effective exogenous donors of nitric oxide (NO), which is an unique intracellular metabolism regulator.[3—5]

At present, there exists virtually one procedure for the synthesis of sydnonimines, *viz.*, cyclization of properly substituted *N*-nitrosoaminoacetonitrile derivatives. This considerably limits the range of the representatives of this promising class of heterocyclic compounds for subsequent studies.

The aim of the present work is the development of the procedure for the synthesis of hitherto unknown 4-formylsydnonimine derivatives. The presence of such a highly reactive fragment as the formyl group in a mesoionic compound opens wide possibilities for the synthesis of various, previously unavailable sydnonimine derivatives.

N(6)-Acyl, -sulfonyl, and other *N*(6) derivatives of sydnonimines unsubstituted at the C(4) atom of the mesoionic ring undergo fairly smooth electrophilic substitution. They are brominated under the action of molecular bromine in the absence of a catalyst[6] and mercurated under the action of mercury salts.[7] However, no data on the direct formylation of sydnonimines under the action of the Vilsmeier reagent are available. Our attempt to carry out the direct formylation of *N*(6)-benzoyl-3-isopropylsydnonimine under the action of the Vilsmeier reagent prepared from dimethylformamide and oxalyl chloride to produce the desired product, *i.e.*, the corresponding 4-formylderivative, failed. This reaction resulted in a mixture of salt-like products that were difficult to identify.

We explain this result firstly by the fact that the electrophilic reagent attacks the exocyclic nitrogen atom of the sydnonimine fragment bearing a considerable negative charge. It was confirmed indirectly by the facts that *N*(6)-derivatives of sydnonimine form salts with strong acids and quaternary ammonium salts at the exocyclic nitrogen atom under the action of strong electrophiles (for example, methyl iodide).[9] The coordination of an electrophile to the N(6) atom results in a decrease in the electron density of the aromatic ring of the mesoionic compound and prevents electrophilic substitution reaction. An additional argument is that sydnonimines do not undergo nitration and sulfonation in acidic medium unlike their oxygen analogs, sydnones.[10,11]

Earlier,[12] we have shown that *N*(6)-derivatives of sydnonimines unsubstituted on C(4) atom **1** smoothly undergo metallation under the action of BuLi to produce the corresponding 4-lithio derivatives. Unfortunately, this kind of lithio derivatives possess low nucleophilicity and are thermally unstable. Our attempt to introduce 4-lithio derivatives of sydnonimines into the reaction with dimethylformamide has lead only to decomposition products of mesoionic compound. This problem could be solved by using (methoxymethylidene)dimethylammonium methyl sulfate (**2**) as the electrophilic agent, which is applied in the cases of organometallic compounds with low reactivity.[13—15]

The choice of this reagent is caused by its high electrophilicity. It should also be noted that in its reaction with sydnonimine organolithium derivative intermediate **3** should form, which is stable against the secondary attack by the organometallic reagent; hydrolysis of **3** affords the target 4-formyl derivative **4** (Scheme 1).

Sydnonimines containing various substituents in both the position N(3) of the mesoionic ring and the exocyclic atom N(6) were introduced into this reaction. The results obtained are presented in Table 1.

As follows from these data, the method is of rather general character and can be applied to both *N*(6)-acetyl, *N*(6)-benzoyl, and *N*(6)-arylsulfonyl derivatives of sydnon-

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2395—2398, December, 2009.

1066-5285/09/5812-2474

Scheme 1

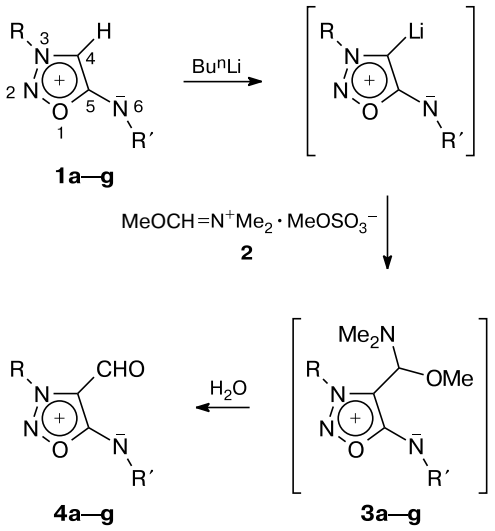

Table 1. Synthesis of 4-formylsydnonimine derivatives

1	R	R′	Yield **4** (%)
a	Me	COPh	61
b	CH_2Me	COPh	64
c	CH_2Me	COMe	45
d	$CHMe_2$	COMe	64
e	$CHMe_2$	COPh	91
f	$CHMe_2$	$SO_2C_6H_4Me$	83
g	$(CH_2)_2OMe$	COPh	38
h	$(CH_2)_2OMe$	$SO_2C_6H_4Me$	10
i	NMe_2	COMe	41
j	NMe_2	$SO_2C_6H_4Me$	64
k	$CHMe_2$	$COCF_3$	62

imines. *N*(6)-Trifluoroacetyl group also does not prevent the normal course of the reaction and aldehyde **4k** is produced in satisfactory yield. The method is applicable for the synthesis of 4-formylsydnonimines containing both alkyl and dialkylamino groups at the atom N(3). It should be particularly noted that the presence of the 2-methoxyethyl group at the atom N(3) of the sydnonimine ring (**1g**, **1h**) reduces considerably the yields of aldehydes; the reaction mixtures contain great amount of decomposition products of sydnonimine organolithium derivative. We explain this fact by the possibility of the intramolecular chelation in such 4-lithioorganic derivatives of sydnonimines.

This type of chelation should considerably decrease the reactivity of sydnonimine organolithium derivative and lead to the prevalence of sydnonimine ring decomposition over the reaction with an electrophile.

However, the yields in the reaction under study are satisfactory, and it can be considered as a general procedure for the synthesis of 4-formylsydnonimine derivatives.

Experimental

All reactions with organometallic compounds were carried out under dry argon in anhydrous solvents. All commercially available reagents (Aldrich, Acros) were used without additional purification. Column chromatography was carried out using Merck Silica gel (40—60 μm). ^{1}H NMR spectra were recorded on a Bruker WM-400 spectrometer with an operating frequency of 400 MHz.

The starting reagents and sydnonimines were prepared according to the known procedures: **1c**,[16] **1d**,[16] **1i**,[16] **1e**,[17] 3-methylsydnonimine and 3-ethylsydnonimine hydrochlorides[18], 3-isopropylsydnonimine and 3-dimethylaminosydnonimine hydrochlorides[16], (2-methoxyethylamino)acetonitrile[19], (methoxymethylidene)dimethylammonium methyl sulfate[13].

***N*(6)-Benzoyl-3-methylsydnonimine (1a).** 3-Methylsydnonimine hydrochloride (5 g, 0.037 mol) was added to a solution of benzoyl chloride (5.1 mL, 0.044 mol) in dichloromethane (70 mL) and then triethylamine (11.8 mL, 0.085 mol) was added over 15 min at −20 °C. The mixture was kept for 16 h, then water (50 mL) was added, the aqueous layer was extracted with dichloromethane (3×50 mL). The combined extract was dried with sodium sulfate, filtered through a layer of Al_2O_3 (2×3 cm) using dichloromethane as the eluent. The solvent was evaporated *in vacuo*, the residue was recrystallized from isopropyl alcohol. Compound **1a** was obtained in a yield of 4.6 g (61%), m.p. 224—225 °C. Found (%): C, 59.07; H, 4.51; N, 20.61. $C_{10}H_9N_3O_2$. Calculated (%): C, 59.11; H, 4.46; N, 20.68. ^{1}H NMR ($CDCl_3$), δ: 4.20 (s, 3 H, Me); 7.38—7.51 (m, 3 H, *m*,*p*-H, Ph); 8.19 (s, 1 H, H(4)); 8.26—8.30 (m, 2 H, *o*-H, Ph).

***N*(6)-Benzoyl-3-ethylsydnonimine (1b)** was prepared analogously to **1a** from benzoyl chloride (12 mL, 0.10 mol), 3-ethylsydnonimine hydrochloride (12.7 g, 0.085 mol) and triethylamine (27 mL, 0.20 mol) in dichloromethane (150 mL). Compound **1b** was obtained in a yield of 9.3 g (50.4%), m.p. 175—176 °C. Found (%): C, 60.95; H, 5.42; N, 19.29. $C_{11}H_{11}N_3O_2$. Calculated (%): C, 60.82; H, 5.10; N, 19.34. ^{1}H NMR ($CDCl_3$), δ: 1.69 (t, 3 H, Me, J = 7.4 Hz); 4.49 (q, 2 H, C$\underline{H}_2$, J = 7.4 Hz); 7.37—7.5 (m, 3 H, *m*,*p*-H, Ph); 8.16 (s, 1 H, H(4)); 8.22—8.30 (m, 2 H, *o*-H, Ph).

3-Isopropyl-*N*(6)-tosylsydnonimine (1f). A solution of triethylamine (19.2 mL, 138 mmol) in dichloromethane (50 mL) was added with vigorous stirring over 1 h to a mixture of 3-isopropylsydnonimine hydrochloride (15 g, 92 mmol) and *p*-toluenesulfonyl chloride (19.3 g, 101 mmol) in dichloromethane (150 mL) at −20 °C. The mixture was stirred at room temperature for 30 min and kept for 16 h. The precipitate was filtered off and washed with dichloromethane. The solution obtained was washed with water (50 mL) and 5% solution of K_2CO_3, dried with sodium sulfate, concentrated *in vacuo*, filtered through the a layer of Al_2O_3 (2×3 cm) using chloroform as the eluent. The solution obtained was concentrated *in vacuo*, the residue was recrystallized from a mixture of isopropyl alcohol and petroleum ether (1 : 1.2). Compound **1f** was obtained in a yield of 18.5 g (72%), m.p. 106—108 °C. Found (%): C, 51.56; H, 5.61; N, 14.82. $C_{12}H_{15}N_3O_3S$. Calculated (%): C, 51.23; H, 5.37; N, 14.94. ^{1}H NMR ($CDCl_3$), δ: 1.7 (d, 6 H, CH(C$\underline{H}_3$)$_2$, J = 6.8 Hz); 2.40 (s, 3 H, $C_6H_4C\underline{H}_3$); 4.80—4.90 (m, 1 H, C$\underline{H}$Me$_2$); 7.27 (d, 2 H, *m*-H, C_6H_4, J = 8.0 Hz); 7.52 (s, 1 H, H(4)); 7.87 (d, 2 H, *o*-H, C_6H_4, J = 8.0 Hz).

3-(2-Methoxyethyl)sydnonimine hydrochloride. A solution of sodium nitrite (23 g, 0.33 mol) in water (100 mL) was added over 30 min with stirring and cooling to −5 °C to a solution of *N*-(2-methoxyethyl)aminoacetonitrile (36 g, 0.32 mol) and 11 *M* HCl (29 mL, 0.32 mol) in water (100 mL). After 30 min, diethyl ether (100 mL) was added to the reaction mixture, the aqueous layer was extracted with diethyl ether (3×70 mL). The organic phase was dried with potassium carbonate, filtered through the a layer of Al_2O_3. Hydrogen chloride (12.8 g, 0.35 mol) was passed through the obtained solution at −20 °C with stirring. The mixture was stirred for 2 h at 0 °C, the precipitate was filtered off and recrystallized from isopropyl alcohol. 3-(2-Methoxyethyl)sydnonimine hydrochloride was obtained in a yield of 45.4 g (79%), m.p. 137—139 °C. Found (%): C, 33.47; H, 5.63; N, 23.38. $C_5H_{10}ClN_3O_2$. Calculated (%): C, 33.44; H, 5.61; N, 23.40. ^{1}H NMR (DMSO-d_6), δ: 3.28 (s, 3 H, MeO); 3.87 (t, 2 H, CH_2N, J = 4.8 Hz); 4.87 (t, 2 H, MeOC$\underline{H}_2$, J = 4.8 Hz); 8.10 (s, 1 H, H(4)); 10.01 (br.s, 2 H, N$\underline{H}_2$).

***N*(6)-Benzoyl-3-(2-methoxyethyl)sydnonimine (1g)** was prepared analogously to **1a** from benzoyl chloride (3.9 mL, 0.034 mol), 3-(2-methoxyethyl)sydnonimine hydrochloride (5 g, 0.028 mol), and triethylamine (8.9 mL, 0.064 mol) in methylene chloride (50 mL). Compound **1g** was obtained in a yield of 4.5 g (65%), m.p. 86—87 °C. Found (%): C, 58.35; H, 5.48; N, 16.86. $C_{12}H_{13}N_3O_3$. Calculated (%): C, 58.29; H, 5.30; N, 16.99. ^{1}H NMR ($CDCl_3$), δ: 3.44 (s, 3 H, CH_3); 3.89 (t, 2 H, CH_2N, J = 4.8 Hz); 4.62 (t, 2 H, MeOC$\underline{H}_2$, J = 4.8 Hz); 7.43—7.54 (m, 3 H, *m*,*p*-H, Ph); 8.29 (s, 1 H, H(4)); 8.28—8.31 (m, 2 H, *o*-H, Ph).

3-(2-Methoxyethyl)-*N*(6)-tosylsydnonimine (1h) was prepared analogously to **1f** from 3-(2-methoxyethyl)sydnonimine hydrochloride (5 g, 0.028 mol), *p*-toluenesulfonyl chloride (5.9 g, 0.031 mol), and triethylamine (5.8 mL, 0.042 mol) in dichloromethane (50 mL). Compound **1h** was obtained in a yield of 2.8 g (34%), m.p. 104—106 °C. Found (%): C, 48.75; H, 5.37; N, 14.25. $C_{12}H_{15}N_3O_4S$. Calculated (%): C, 48.48; H, 5.08; N, 14.13. ^{1}H NMR ($CDCl_3$), δ: 2.4 (s, 3 H, C$\underline{H}_3$Ph); 3.38 (s, 3 H, C$\underline{H}_3$O); 3.84 (t, 2 H, C$\underline{H}_2$N, J = 4.8 Hz); 4.59 (t, 2 H, MeOC$\underline{H}_2$, J = 4.8 Hz); 7.27 (d, 2 H, *m*-H, C_6H_4, J = 8.5 Hz); 7.61 (s, 1 H, H(4)); 7.83 (d, 2 H, *o*-H, C_6H_4, J = 8.5 Hz).

3-Dimethylamino-*N*(6)-tosylsydnonimine (1j) was prepared analogously to **1f** from 3-*N*,*N*-dimethylaminosydnonimine hydrochloride (2 g, 0.012 mol), *p*-toluenesulfonyl chloride (2.7 g, 0.013 mol), and triethylamine (2.5 mL, 0.018 mol) in dichloromethane (50 mL). Compound **1j** was obtained in a yield of 2.5 g (72%), m.p. 81—82 °C. Found (%): C, 46.97; H, 5.29; N, 19.68. $C_{11}H_{14}N_4O_3S$. Calculated (%): C, 46.80; H, 5.00; N, 19.85. ^{1}H NMR ($CDCl_3$), δ: 2.37 (s, 3 H, C$\underline{H}_3C_6H_4$); 3.20 (s, 6 H, NMe_2); 7.22 (d, 2 H, *m*-H, C_6H_4, J = 8.5 Hz); 7.44 (s, 1 H, H(4)); 7.83 (m, 2 H, *o*-H, C_6H_4, J = 8.5 Hz).

3-Isopropyl-*N*(6)-trifluoroacetylsydnonimine (1k). Trifluoroacetic anhydride (10.4 mL, 0.074 mol) was added with stirring to a solution of 3-isopropylsydnonimine hydrochloride (10 g, 0.062 mol) in dichloromethane (200 mL). Then triethylamine (20.5 mL, 0.15 mol) was added with stirring at −20 °C over 30 min. The reaction mixture was kept for 16 h. Water (150 mL) was added, the solution was saturated with potassium carbonate, the layers were separated, the aqueous layer was extracted with dichloromethane (3×30 mL). The combined extract was dried with sodium sulfate, filtered through a layer of silica gel and concentrated *in vacuo*. The residue was recrystallized from a mixture of isopropyl alcohol and petroleum ether (1 : 2). Compound **1k** was obtained in a yield of 12.1 g (88%) **1k**, m.p. 103—104 °C. Found (%): C, 37.71; H, 3.69; N, 18.71. $C_7H_8F_3N_3O_2$. Calculated (%): C, 37.68; H, 3.61; N, 18.83. ^{1}H NMR ($CDCl_3$), δ: 1.77 (d, 6 H, CH(C$\underline{H}_3$)$_2$, J = 6.8 Hz); 4.99—5.10 (m, 1 H, C$\underline{H}$Me$_2$); 7.28 (s, 1 H, H(4)).

***N*(6)-Benzoyl-4-formyl-3-methylsydnonimine (4a).** *N*(6)-Benzoyl-3-methylsydnonimine (**1a**) (0.5 g, 2.46 mmol) and THF (50 mL) were placed in a three-neck flask (100 mL). The solution was cooled to −90 °C and 2.5 *M* solution of BuLi in hexane (1.1 mL, 2.71 mmol) was added. The mixture was stirred for 40 min at −90 °C, then (methoxymethylidene)-dimethylammonium methyl sulfate (**2**) (0.61 g, 2.96 mmol) was added. The reaction mixture was warmed to room temperature and a saturated solution of sodium hydrogencarbonate (1 mL) was added. The mixture obtained was dried with sodium sulfate, filtered through a layer of Al_2O_3 (2×3 cm) using a mixture of chloroform and ethyl acetate (5 : 1) as the eluent, the solvent was evaporated *in vacuo*. The residue was chromatographed on a column with SiO_2 (30×2 cm, eluent, chloroform—ethyl acetate, 5 : 1) and recrystallized from a mixture of isopropyl alcohol and petroleun ether (1 : 10). Compound **4a** was obtained in a yield of 0.35 g (61%), m.p. 171—172 °C. Found (%): C, 57.06; H, 3.88; N, 18.09. $C_{11}H_9N_3O_3$. Calculated (%): C, 57.14; H, 3.92; N, 18.17. ^{1}H NMR ($CDCl_3$), δ: 4.48 (s, 3 H, Me); 7.35—7.60 (m, 3 H, *m*,*p*-H, Ph); 8.22—8.30 (m, 2 H, *o*-H, Ph); 10.28 (s, 1 H, CHO).

***N*(6)-Benzoyl-3-ethyl-4-formylsydnonimine (4b)** was prepared analogously to **4a** from *N*(6)-benzoyl-3-ethylsydnonimine (**1b**) (0.5 g, 2.30 mmol), 2.5 *M* solution of BuLi in hexane (1.0 mL, 2.53 mmol), and (methoxymethylidene)dimethylammonium methyl sulfate (**2**) (0.57 g, 2.76 mmol). Compound **4b** was obtained in a yield of 0.36 g (64%), m.p. 131—132 °C. Found (%): C, 59.02; H, 4.51; N, 17.28. $C_{12}H_{11}N_3O_3$. Calculated (%): C, 58.77; H, 4.52; N, 17.13. ^{1}H NMR ($CDCl_3$), δ: 1.67 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.4 Hz); 4.88 (q, 2 H, C$\underline{H}_2$Me, J = 7.4 Hz); 7.39—7.58 (m, 3 H, *m*,*p*-H, Ph); 8.21—8.29 (m, 2 H, *o*-H, Ph); 10.2 (s, 1 H, CHO).

***N*(6)-Acetyl-3-ethyl-4-formylsydnonimine (4c)** was prepared analogously to **4a** from *N*(6)-acetyl-3-ethylsydnonimine (**1c**) (0.5 g, 3.23 mmol), 2.5 *M* solution of BuLi in hexane (1.4 mL, 3.55 mmol), and compound **2** (0.79 g, 3.87 mmol). Compound **4c** (yellow oil) was obtained in a yield of 0.27 g (45%). Found (%): C, 45.82; H, 50.5; N, 21.74. $C_7H_9N_3O_3$. Calculated (%): C, 45.90; H, 4.95; N, 22.94. ^{1}H NMR ($CDCl_3$), δ: 1.60 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.4 Hz); 2.21 (s, 3 H, COMe); 4.85 (q, 2 H, C$\underline{H}_2$Me, J = 7.4 Hz); 10.0 (s, 1 H, CHO).

***N*(6)-Acetyl-4-formyl-3-isopropylsydnonimine (4d)** was prepared analogously to **4a** from *N*(6)-acetyl-3-isopropylsydnonimine (**1d**) (0.5 g, 2.96 mmol), 2.5 *M* solution of BuLi in hexane (1.3 mL, 3.26 mmol), and compound **2** (0.73 g, 3.55 mmol). Compound **4d** was obtained in a yield of 0.37 g (64%), m.p. 31—32 °C. Found (%): C, 48.82; H, 5.52; N, 21.52. $C_8H_{11}N_3O_3$. Calculated (%): C, 48.73; H, 5.62; N, 21.31. ^{1}H NMR ($CDCl_3$), δ: 1.69 (d, 6 H, CH(C$\underline{H}_3$)$_2$, J = 6.8 Hz); 2.27 (s, 3 H, COMe); 5.60 (m, 1 H, C$\underline{H}$Me$_2$); 9.98 (s, 1 H, CHO).

***N*(6)-Benzoyl-4-formyl-3-isopropylsydnonimine (4e)** was prepared analogously to **4a** from *N*(6)-benzoyl-3-isopropylsydnonimine (**1e**) (0.5 g, 2.16 mmol), 2.5 *M* solution of BuLi in hexane (0.95 mL, 2.38 mmol), and compound **2** (0.53 g,

2.60 mmol). Compound **4e** was obtained in a yield of 0.51 g (91%), m.p. 112—113 °C. Found (%): C, 60.33; H, 4.94; N, 16.34. $C_{13}H_{13}N_3O_3$. Calculated (%): C, 60.23; H, 5.05; N, 16.21. ^{1}H NMR ($CDCl_3$), δ: 1.69 (d, 6 H, $CH(C\underline{H}_3)_2$, J = 6.8 Hz); 5.74 (m, 1 H, $C\underline{H}Me_2$); 7.41—7.51 (m, *m*,*p*-H, Ph); 8.24—8.26 (m, 2 H, *o*-H, Ph); 10.12 (s, 1 H, CHO).

4-Formyl-3-isopropyl-*N*(6)-tosylsydnonimine (4f) was prepared analogously to **4a** from 3-isopropyl-*N*(6)-tosylsydnonimine (**1f**) (0.5 g, 1.78 mmol), 2.5 *M* solution of BuLi in hexane (0.78 mL, 1.96 mmol), and compound **2** (0.44 mL, 2.14 mmol). Compound **4f** was obtained in a yield of 0.46 g (83%), m.p. 139—140 °C. Found (%): C, 50.58; H, 4.91; N, 13.65. $C_{13}H_{15}N_3O_4S$. Calculated (%): C, 50.48; H, 4.89; N, 13.58. ^{1}H NMR ($CDCl_3$), δ: 1.67 (d, 6 H, $CH(C\underline{H}_3)_2$, J = 6.8 Hz); 2.44 (s, 3 H $C\underline{H}_3C_6H_4$); 5.67 (m, 1 H, $C\underline{H}Me_2$); 7.33 (d, 2 H, *m*-H, C_6H_4, J = 8.5 Hz); 7.97 (d, 2 H, *o*-H, C_6H_4, J = 8.5 Hz); 9.68 (s, 1 H, CHO).

***N*(6)-Benzoyl-4-formyl-3-(2-methoxyethyl)sydnonimine (4g)** was prepared analogously to **4a** from *N*(6)-benzoyl-3-(2-methoxyethyl)sydnonimine (**1g**) (0.3 g, 1.22 mmol), 2.5 *M* solution of BuLi in hexane (0.54 mL, 1.34 mmol), and compound **2** (0.30 g, 1.46 mmol). Compound **4g** was obtained in a yield of 0.13 g (38%), m.p. 76—77 °C. Found (%): C, 56.31; H, 4.82; N, 15.33. $C_{13}H_{13}N_3O_4$. Calculated (%): C, 56.72; H, 4.76; N, 15.27. ^{1}H NMR ($CDCl_3$), δ: 3.35 (s, 3 H, OMe); 3.85 (t, 2 H, NCH_2, J = 4.5 Hz); 5.0 (t, 2 H, CH_2O, J = 4.5 Hz); 7.37—7.56 (m, 3 H, 2 *m*,*p*-H, Ph); 8.19—8.29 (m, 2 H, *o*-H, Ph); 10.2 (s, 1 H, CHO).

4-Formyl-3-(2-methoxyethyl)-*N*(6)-tosylsydnonimine (4h) was prepared analogously to **4a** from 3-(2-methoxyethyl)-*N*(6)-tosylsydnonimine (**1h**) (0.5 g, 1.68 mmol), 2.5 *M* solution of BuLi in hexane (0.74 mL, 1.85 mmol), and compound **2** (0.42 g, 2.02 mmol). Compound **4h** (yellow oil) was obtained in a yield of 0.057 g (10%). Found (%): C, 47.85; H, 4.71; N, 12.84. $C_{13}H_{15}N_3O_5S$. Calculated (%): C, 47.99; H, 4.65; N, 12.92. ^{1}H NMR ($CDCl_3$), δ: 1.2 (s, 3 H, $C_6H_4C\underline{H}_3$); 3.30 (s, 3 H, $OC\underline{H}_3$); 3.82 (t, 2 H, NCH_2, J = 4.5 Hz); 4.94 (t, 2 H, CH_2O, J = 4.5 Hz); 7.27 (d, 2 H, *m*-H, C_6H_4, J = 8.5 Hz); 7.97 (d, 2 H, *o*-H, C_6H_4, J = 8.5 Hz); 9.70 (s, 1 H, CHO).

***N*(6)-Acetyl-3-dimethylamino-4-formylsydnonimine (4i)** was prepared analogously to **4a** from *N*(6)-acetyl-3-dimethylaminosydnonimine (**1i**) (0.5 g, 2.94 mmol), 2.5 *M* solution of BuLi in hexane (1.3 mL, 3.24 mmol), and compound **2** (0.72 g, 3.53 mmol). Compound **4i** was obtained in a yield of 0.24 g (41%), m.p. 60—61 °C. Found (%): C, 42.44; H, 5.14; N, 28.36. $C_7H_{10}N_4O_3$. Calculated (%): C, 42.42; H, 5.09; N, 28.27. ^{1}H NMR ($CDCl_3$), δ: 2.23 (s, 3 H, COMe); 3.23 (s, 6 H, NMe_2); 9.80 (s, 1 H, CHO).

3-Dimethylamino-4-formyl-*N*(6)-tosylsydnonimine (4j) was prepared analogously to **4a** from 3-dimethylamino-*N*(6)-tosylsydnonimine (**1j**) (0.4 g, 1.42 mmol), 2.5 *M* solution of BuLi in hexane (0.62 mL, 1.56 mmol), and compound **2** (0.35 mL, 1.70 mmol). Compound **4j** was obtained in a yield of 0.30 g (64%), m.p. 135—136 °C. Found (%): C, 46.42; H, 4.52; N, 18.06. $C_{12}H_{14}N_4O_4S$. Calculated (%): C, 46.45; H, 4.55; N, 18.05. ^{1}H NMR ($CDCl_3$), δ: 2.40 (s, 3 H, $C_6H_4C\underline{H}_3$); 3.22 (s, 6 H, NMe_2); 7.39 (d, 2 H, *m*-H, C_6H_4, J = 8.5 Hz); 7.96 (d, 2 H, *o*-H, C_6H_4, J = 8.5 Hz); 9.60 (s, 1 H, CHO).

4-Formyl-3-isopropyl-*N*(6)-trifluoroacetylsydnonimine (4k) was prepared analogously to **4a** from *N*(6)-trifluoroacetyl-3-isopropylsydnonimine (**1k**) (0.5 g, 2.24 mmol), 2.5 *M* solution of BuLi in hexane (0.99 mL, 2.47 mmol), and compound **2** (0.55 g, 2.69 mmol). Compound **4k** was obtained in a yield of 0.35 g (62%), m.p. 78—79 °C. Found (%): C, 38.09; H, 3.08; N, 16.71. $C_8H_8F_3N_3O_3$. Calculated (%): C, 38.26; H, 3.21; N, 16.73. ^{1}H NMR ($CDCl_3$), δ: 1.75 (d, 6 H, $CH(C\underline{H}_3)_2$, J = 6.8 Hz); 5.73—5.86 (m, 1 H, $C\underline{H}Me_2$); 10.14 (s, 1 H, CHO).

References

1. C. G. Newton, C. A. Ramsden, *Tetrahedron*, 1982, **38**, 2967.
2. V. G. Yashunskii, L. E. Kholodov, *Usp. Khim.*, 1980, **49**, 54 [*Russ. Chem. Rev.* (*Engl. Transl.*), 1980, **49**].
3. K. Schonafinger, *II Farmaco*, 1999, **54**, 316.
4. V. G. Granik, N. B. Grigor´ev, *Oksid azota (NO). Novyi put´ k poisku lekarstv* [*Nitric oxide (NO). New way to the search of medicines]*, Vuzovskaya kniga, Moscow, 2004, 360 (in Russian).
5. E. Yu. Khmel´nitskaya, V. I. Levina, L. A. Truhacheva, N. B. Grigor´ev, V. N. Kalinin, I. A. Cherepanov, S. N. Lebedev, V. G. Granik, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 2725 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 2840].
6. V. S. Fedorovich, *Zh. Ob. Khim.*, 1964, **34**, 3075 [*J. Gen. Chem.* (*Engl. Transl.*), 1964, **34**].
7. H. Kato, M. Hashimoto, M. Ohta, *Nippon Kagaku Zasshi.*, 1957, **78**, 707.
8. V. G. Yashunskii, L. E. Holodov, O. I. Samoilova, *Chem. Communs.*, 1965, **30**, 4257.
9. V. G. Yashunskii, O. I. Samoilova, L. E. Kholodov, *Zh. Obshch. Khim.,* 1964, **34**, 2050 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1964, **34**].
10. E. E. Nifant´ev, V. S. Blagoveshchensky, A. M. Sokurenko, L. S. Sklyarsky, *Zh. Obshch. Khim.*, 1974, **44**, 108 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1974, **44**].
11. V. G. Yashunskii, V. F. Vasil´eva, Yu. N. Sheinker, *Zh. Obshch. Khim.*, 1959, **29**, 2712 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1959, **29**].
12. I. A. Cherepanov, N. V. Egorova, K. B. Martinovich, V. N. Kalinin, *Dokl. AN*, 2000, **374**, 64 [*Dokl. Chem.* (*Engl. Transl.*), 2000, **374**, 175].
13. R. Knorr, P. Loew, P. Hassel, H. Bronberger, *J. Org. Chem.*, 1984, **49**, 1288.
14. S. Y. Cho, J. Y. Baek, S. S. Han, S. K. Kang, J. D. Ha, J. H. Ahn, J. D. Lee, K. R. Kim, H. G. Cheon, S. D. Rhee, S. D. Yang, G. H. Yon, C. S. Pak, J.-K. Choi, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 499.
15. H. H. Wasserman, J. L. Ives, *J. Org. Chem.*, 1985, **50**, 3573.
16. M. Goetz, K. Grozinger, *J. Heterocycl. Chem.*, 1970, 123.
17. V. G. Yashunskii, V. G. Ermolaeva, *Zh. Obshch. Khim.*, 1962, **32**, 182 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1962, **32**].
18. J. H. Boyer, J. Kooi, *J. Am. Chem. Soc.*, 1976, **98**, 1099.
19. J. H. Short, T. D. Darby, *J. Med. Chem.*, 1968, **11**, 848.

Received March 12, 2009