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N.S. Zefirov on His 70th Anniversary

## Reaction of Alkylsulfanylchloroacetylenes with 1,1-Dimethylhydrazine

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**Abstract**—Alkylsulfanylchloroacetylenes react with 1,1-dimethylhydrazine in diethyl ether at 20–22°C to give, depending on the reactant ratio, 3,6-bis(alkylsulfanylmethyl)-1,1,4,4-tetramethyl-1,4-dihydro-1,2,4,5-tetrazine-1,4-dium dichlorides (yield 67–80%) or 1-[2-(alkylsulfanyl)-1-(2,2-dimethylhydrazono)ethyl]-1,1-dimethylhydrazinium chlorides. The latter readily undergo dequaternization to the corresponding 2-alkylsulfanyl-*N*<sup>1</sup>,*N*<sup>2</sup>,*N*<sup>4</sup>-trimethylethanohydrazide hydrazones (yield up to 53%).

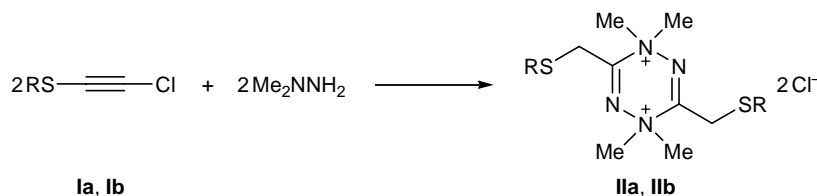
We previously showed that organylsulfanylchloroacetylenes **I** react with mono- and polyfunctional nucleophiles according to different pathways. Depending on the nucleophile nature and conditions, these reactions could produce not only normal nucleophilic substitution products but also sulfanyl-substituted heterocyclic compounds [1–7]. Reactions of compounds **I** with 1,1-dimethylhydrazine (which is a large-scale product of chemical industry) have not been studied so far. Taking into account the presence of two nucleophilic centers in the molecule of 1,1-dimethylhydrazine and of three electrophilic centers in the molecule of acetylene **I** (chlorine and two *sp*-carbon atoms), it was difficult to predict *a priori* the result of reaction between these compounds.

In the present work we were the first to examine reactions of ethylsulfanyl- and isopropylsulfanylchloroacetylenes **Ia** and **Ib** with 1,1-dimethylhydrazine

with the goal of extending the scope of synthetic applications of organylsulfanylchloroacetylenes, obtaining new data on nucleophilic substitution of halogen at an *sp*-hybridized carbon atom, and synthesizing new polyfunctional compounds. Prior to our studies, the available information on reactions of haloacetylenes with hydrazine and its derivatives was limited to a brief report on the reactions of perfluoroalkyl-(bromo)acetylenes with hydrazine, which afforded the corresponding 1,2,4,5-tetrazine derivatives [8]. Later, Elokhina *et al.* [9] showed that the reaction of aryl bromoethynyl ketones with 1,1-dimethylhydrazine gives no nitrogen-containing heterocycles but only products resulting from polymerization and hydrobromination of intermediate ethynylhydrazines.

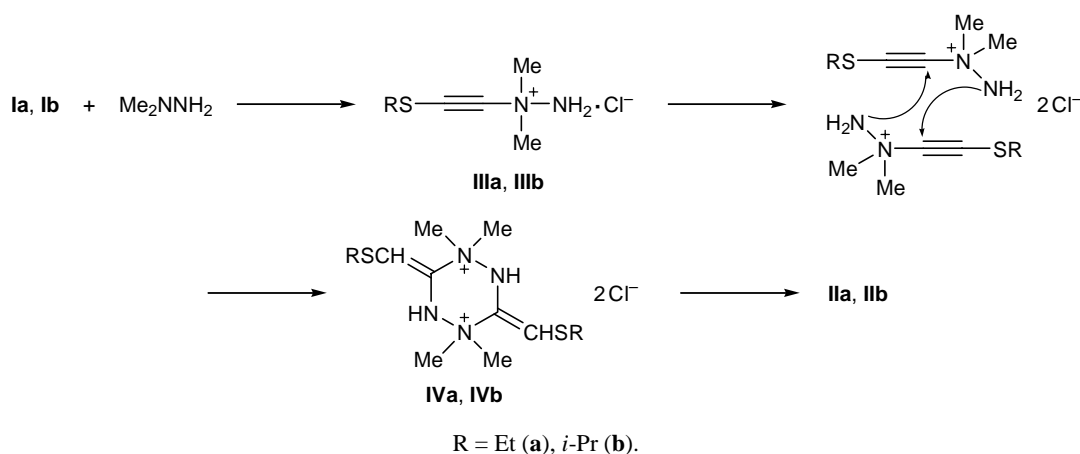
We have found that alkylsulfanylchloroacetylenes **Ia** and **Ib** readily react with an equimolar amount of 1,1-dimethylhydrazine in diethyl ether at 20–22°C to

Scheme 1.



R = Et (**a**), *i*-Pr (**b**).

Scheme 2.



give 3,6-bis(alkylsulfanylmethyl)-1,1,4,4-tetramethyl-1,4-dihydro-1,2,4,5-tetrazine-1,4-dium dichlorides **IIa** and **IIb**, respectively, in up to 80% yield (Scheme 1). Compounds **IIa** and **IIb** are colorless crystalline substances which are soluble in water, DMSO, and alcohols. The  $^{13}\text{C}$  NMR spectra of tetrazines **IIa** and **IIb** contain signals from carbon atoms in the alkylsulfanyl,  $\text{CH}_3\text{N}^+$ , and exocyclic methylene groups ( $\text{SCH}_2$ ), and a signal at  $\delta_{\text{C}}$  128 ppm which should be assigned to the two magnetically equivalent carbon atoms in the tetrazine ring [7, 10, 11]. In the  $^1\text{H}$  NMR spectra of **IIa** and **IIb** we observed signals from protons in the alkylsulfanyl group and two singlets at  $\delta \sim 2.7$  and 3.6 ppm, which correspond to the  $\text{SCH}_2$  and  $\text{CH}_3\text{N}$  groups, respectively. Stretching vibrations of the  $\text{C}=\text{N}$  bonds in the tetrazine ring appeared in the IR spectra of salts **IIa** and **IIb** at about  $1630\text{ cm}^{-1}$ . The structure of compounds **IIa** and **IIb** as onium salts was confirmed by mercurimetric titration which revealed 2 equiv of chloride ions per mole of compound **II**.

Scheme 2 illustrates possible mechanism of formation of tetrazinium salts **IIa** and **IIb**. It includes nucleophilic replacement of the chlorine atom at the triple bond in chloroacetylenes **Ia** and **Ib** by the tertiary nitrogen atom of 1,1-dimethylhydrazine to give ethynylammonium salts **IIIa** and **IIIb**. The latter undergo dimerization via nucleophilic attack by the amino group of one molecule on the  $sp$ -hybridized carbon atom of the other molecule. Prototropic isomerization of bis(alkylsulfanylmethylene)hexahydro-tetrazinium salts **IVa** and **IVb** thus formed leads to dihydro-tetrazine-1,4-dium dichlorides **IIa** and **IIb**.

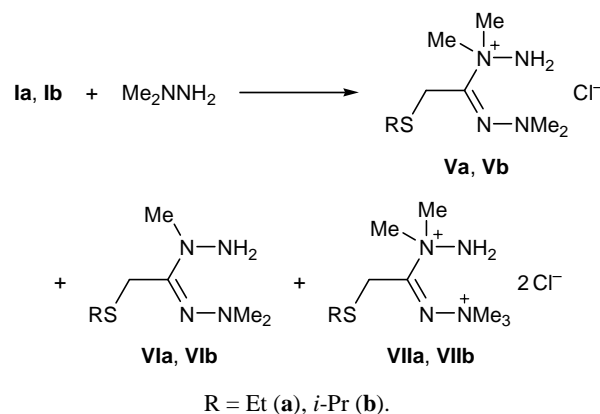
The proposed scheme is qualitatively consistent with the results of quantum-chemical calculations of electron density distribution in the molecules of alkyl-

sulfanylchloroacetylenes [7] and 1,1-dimethylhydrazine [12], according to which the  $sp$ -hybridized carbon atom linked to chlorine in acetylenes **I** possesses a positive charge and should undergo nucleophilic attack first. The alkylation of 1,1-dimethylhydrazine should involve the tertiary nitrogen atom which contributes most to the highest occupied molecular orbital.

We succeeded in detecting formation of ethynylammonium salts **III** by IR spectroscopy. The IR spectrum of the reaction mixture, apart from the absorption band belonging to the  $\text{C}=\text{N}$  bond in final product **II**, contained a strong band at  $2200\text{ cm}^{-1}$ , which is typical of stretching vibrations of the  $\text{C}\equiv\text{C}$  bond in alkylsulfanylethynyl(trialkyl)ammonium chlorides [2]. The corresponding absorption band of initial acetylenes **I** is located at lower frequencies,  $2150\text{--}2170\text{ cm}^{-1}$ . We failed to isolate intermediate hydrazinium chlorides **III** in the pure state, presumably due to high rate of intermolecular cyclization leading to tetrazines **IV**.

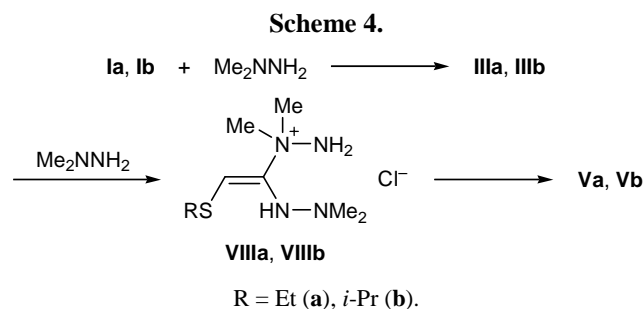
On the other hand, alkylsulfanylchloroacetylenes **I** reacted with excess 1,1-dimethylhydrazine (5 equiv)

Scheme 3.



under comparable conditions (diethyl ether, room temperature) in a different way, and the products were 1,1-dimethyl-1-[2-(alkylsulfanyl)-1-(2,2-dimethylhydrazono)ethyl]hydrazinium chlorides **Va** and **Vb** together with compounds **VIa**, **VIIa** and **VIIb**, **VIIIb** which were formed as a result of further transformations of **Va** and **Vb** (Scheme 3).

The formation of salts **Va** and **Vb** may be illustrated by Scheme 4 which includes nucleophilic replacement of the halogen atom at the *sp*-hybridized carbon atom in chloroacetylene **I** by the tertiary nitrogen atom of 1,1-dimethylhydrazine, followed by regio- and stereoselective addition of the second 1,1-dimethylhydrazine molecule to intermediate ethynylammonium salt **III** and prototropic isomerization of intermediate **VIII**.



Compounds **Va** and **Vb** are unstable, and they readily undergo disproportionation to produce equilibrium mixtures of compounds **V**, **VI**, and **VII** (Scheme 5). The  $^1\text{H}$  NMR spectra of compounds **Va** and **Vb**, recorded in 40–50 h after dissolution, contain several singlets from the  $\text{NCH}_3$  protons, and signals from protons in the alkylsulfanyl groups are transformed into unresolved multiplets. In the  $^{13}\text{C}$  NMR spectra of mixtures **V–VII** we observed three signals corresponding to  $\text{C}=\text{N}$  moiety. Signals from carbon atoms in the  $\text{RS}$  group are also tripled. In addition, two  $\text{Me}_2\text{N}^+$  signals from structures **V** and **VII**, one signal from the  $\text{Me}_3\text{N}^+$  group in structure **VII**, and three signals from methyl carbon atoms at an uncharged nitrogen atom were present in the  $^{13}\text{C}$  NMR spectrum.

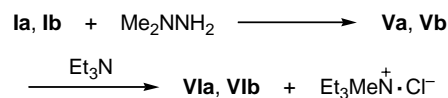
**Scheme 5.**



In order to isolate individual products, mixtures **V–VII** were treated with triethylamine. We thus obtained 2-alkylsulfanyl- $\text{N}^1, \text{N}^4, \text{N}^4$ -trimethylethanolhydrazide hydrazones **VIa** and **VIb** in up to 53% yield (Scheme 6). Compounds **VIa** and **VIb** are stable liquids which can

readily be distilled under reduced pressure. Their structure was proved by the  $^1\text{H}$  and  $^{13}\text{C}$  NMR and IR spectra and elemental analyses. The  $^{13}\text{C}$  NMR spectra of **VIa** and **VIb** contained signals from carbon atoms in the  $\text{RS}$ ,  $\text{CH}_3\text{N}^+$ , and  $\text{SCH}_2$  groups, as well as from the  $\text{C}=\text{N}$  carbon atom (the most downfield signal,  $\delta_{\text{C}}$  162 ppm; cf. [13, 14]). Compounds **VIa** and **VIb** showed in the  $^1\text{H}$  NMR spectra signals from protons in the alkylsulfanyl group and three singlets at  $\delta$  ~2.4, 2.9, and 3.8 ppm, which belong to protons in the  $\text{Me}_2\text{N}$ ,  $\text{Me}_3\text{N}$ , and  $\text{SCH}_2$  groups, respectively. Stretching vibrations of the  $\text{C}=\text{N}$  bond gave rise to IR absorption at about  $1600 \text{ cm}^{-1}$ .

**Scheme 6.**



Thus the results of the reaction of alkylsulfanylchloroacetylenes with 1,1-dimethylhydrazine extend the available information on the reactivity of haloacetylenes with respect to difunctional nucleophiles. The examined reaction opens a new synthetic route to functionally substituted hydrazidines and tetrazines which attract interest as potential complexing agents, photochromic compounds, and biologically active substances.

## EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer from samples prepared as KBr pellets or thin films. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured on a Bruker DPX-400 instrument at 400 and 100 MHz, respectively, using  $\text{DMSO}-d_6$  as solvent and tetramethylsilane as internal reference. The purity of the products was checked by GLC on a Tsvet-500 chromatograph equipped with a thermal conductivity detector and glass columns (3 m  $\times$  4 mm) packed with 10% of PSM-1000 on Inerton Super (0.125–0.150 mm); carrier gas helium. Mercurimetric titration of salts was performed with a 0.01 N solution of  $\text{Hg}(\text{NO}_3)_2$  in aqueous isopropyl alcohol using 1,5-diphenylcarbazone as indicator.

**3,6-Bis(ethylsulfanylmethyl)-1,1,4,4-tetramethyl-1,4-dihydro-1,2,4,5-tetrazine-1,4-dium dichloride (IIa).** A solution of 5.06 g (42.0 mmol) of acetylene **Ia** in 20 ml of anhydrous diethyl ether was added dropwise under stirring over a period of 30 min

to a solution of 2.52 g (42.0 mmol) of 1,1-dimethylhydrazine in 100 ml of anhydrous diethyl ether. The reaction was accompanied by heat evolution, and the temperature was maintained at 20–22°C by external cooling. The mixture was then stirred for 8 h at 20–22°C, and the precipitate was filtered off, washed with anhydrous diethyl ether (3×10 ml), and dried under reduced pressure. Yield 5.10 g (67%), colorless crystals, mp 80–81°C. IR spectrum (KBr),  $\nu$ ,  $\text{cm}^{-1}$ : 3056, 2988, 2924 (C–H); 2800–2600 (ammonium band); 1626 (C=N).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.25 t (6H,  $\text{CH}_3$ ), 2.74 s (4H,  $\text{SCH}_2$ ), 2.96 q (4H,  $\text{CH}_3\text{CH}_2\text{S}$ ), 3.59 s (12H,  $\text{CH}_3\text{N}^+$ ).  $^{13}\text{C}$  NMR spectrum,  $\delta_{\text{C}}$ , ppm: 16.15 ( $\text{CH}_3$ ), 27.16 ( $\text{CH}_3\text{CH}_2\text{S}$ ), 39.50 ( $\text{SCH}_2$ ), 59.95 ( $\text{CH}_3\text{N}^+$ ), 128.66 (C=N). Found, %: C 39.57; H 7.28; Cl 19.81; N 15.16; S 17.53.  $\text{C}_{12}\text{H}_{26}\text{Cl}_2\text{N}_4\text{S}_2$ . Calculated, %: C 39.88; H 7.20; Cl 19.67; N 15.51; S 17.73.

**3,6-Bis(isopropylsulfanylmethyl)-1,1,4,4-tetramethyl-1,4-dihydro-1,2,4,5-tetrazine-1,4-diiium dichloride (IIb)** was synthesized in a similar way from 2.04 g (34.0 mmol) of 1,1-dimethylhydrazine and 4.58 g (34.0 mmol) of acetylene **Ib**. Yield 5.30 g (80%), mp 77–79°C. IR spectrum, KBr,  $\nu$ ,  $\text{cm}^{-1}$ : 3076, 2988, 2920 (C–H); 2800–2600 (ammonium band); 1632 (C=N).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.36 d (12H,  $\text{CH}_3$ ), 2.74 s (4H,  $\text{CH}_2\text{S}$ ), 3.54 q (2H, CH), 3.60 s (12H,  $\text{CH}_3\text{N}^+$ ).  $^{13}\text{C}$  NMR spectrum,  $\delta_{\text{C}}$ , ppm: 23.65 ( $\text{CH}_2\text{S}$ ), 23.82 ( $\text{CH}_3$ ), 37.74 (CH), 57.38 ( $\text{CH}_3\text{N}^+$ ), 127.23 (C=N). Found, %: C 43.32; H 7.52; Cl 18.39; N 14.60; S 16.53.  $\text{C}_{14}\text{H}_{30}\text{Cl}_2\text{N}_4\text{S}_2$ . Calculated, %: C 43.18; H 7.71; Cl 18.25; N 14.39; S 16.45.

**Reaction of ethylsulfanylchloroacetylene (Ia) with 1,1-dimethylhydrazine at a ratio of 1:5.** A solution of 2.77 g (23 mmol) of acetylene **Ia** in 20 ml of anhydrous diethyl ether was added dropwise under stirring over a period of 30 min to a solution of 6.9 g (115 mmol) of 1,1-dimethylhydrazine in 100 ml of anhydrous diethyl ether. The reaction was accompanied by heat evolution, and the temperature was maintained at 20–22°C by external cooling. The mixture was then stirred for 12 h at 20–22°C, and the solvent was removed under reduced pressure. The residue, 4.53 g, was an oily material. IR spectrum (film),  $\nu$ ,  $\text{cm}^{-1}$ : 3400, 3212 (N–H); 2970, 2876, 2750 (C–H); 2448, 2360, 2336 (ammonium band); 1672, 1643, 1636, 1624 (C=N); 1284, 1172, 1098, 1012, 938, 896, 856, 748, 536 ( $\delta\text{C–H}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.13–1.17 m ( $\text{CH}_3$ ), 2.36–2.47 m ( $\text{CH}_2\text{S}$ ), 2.58 s [ $\text{N}(\text{CH}_3)_2$  in **Va** and **VIa**], 2.90 s [ $\text{N}(\text{CH}_3)$  in **VIa**], 3.34 s [ $(\text{CH}_3)_2\text{N}^+$  in **Va** and **VIIa**], 3.52 s [ $(\text{CH}_3)_3\text{N}^+$  in **VIIa**], 6.75

(NH).  $^{13}\text{C}$  NMR spectrum,  $\delta_{\text{C}}$ , ppm: 14.59, 14.75, 15.00 ( $\text{CH}_3$ ); 25.68, 25.87, 25.99 ( $\text{CH}_3\text{CH}_2\text{S}$ ); 24.08, 33.82 ( $\text{SCH}_2$ ); 45.74 ( $\text{NCH}_3$  in **VIa**); 47.09, 48.05 [ $(\text{CH}_3)_2\text{N}$  in **Va** and **VIa**]; 56.83, 59.31 [ $(\text{CH}_3)_2\text{N}^+$  in **Va** and **VIIa**]; 64.77 [ $(\text{CH}_3)_3\text{N}^+$  in **VIIa**]; 162.75, 162.96, 165.32 (C=N).

**2-Ethylsulfanyl- $N^1, N^4, N^4$ -trimethylethano-hydrazide hydrazone (VIa).** A solution of 5.30 g (44 mmol) of acetylene **Ia** in 20 ml of anhydrous diethyl ether was added dropwise under stirring over a period of 30 min to a solution of 13.20 g (220 mmol) of 1,1-dimethylhydrazine in 100 ml of anhydrous diethyl ether. The reaction was accompanied by heat evolution, and the temperature was maintained at 20–22°C by external cooling. The mixture was then stirred for 12 h at 20–22°C, and a solution of 11.5 g (114 mmol) of triethylamine in 30 ml of anhydrous diethyl ether was added dropwise under stirring. The precipitate was filtered off and washed with anhydrous diethyl ether (3×10 ml), and the filtrate was distilled under reduced pressure. Yield 4.45 g (53%), bp 98°C (5 mm),  $n_{\text{D}}^{20} = 1.5060$ . IR spectrum (film),  $\nu$ ,  $\text{cm}^{-1}$ : 3300 (N–H); 2978, 2932, 2918, 2848, 2806, 2776 (C–H); 1584 (C=N).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.23 t (3H,  $\text{CH}_3$ ), 2.27 s [6H,  $(\text{CH}_3)_2\text{N}$ ], 2.52 q (2H,  $\text{CH}_3\text{CH}_2\text{S}$ ), 2.80 s (3H,  $\text{CH}_3\text{N}$ ), 3.70 s (2H,  $\text{SCH}_2$ ).  $^{13}\text{C}$  NMR spectrum,  $\delta_{\text{C}}$ , ppm: 14.73 ( $\text{CH}_3$ ), 23.28 ( $\text{CH}_3\text{CH}_2\text{S}$ ), 25.77 ( $\text{SCH}_2$ ), 37.59 ( $\text{CH}_3\text{N}$ ), 48.87 [ $(\text{CH}_3)_2\text{N}$ ], 161.88 (C=N). Found, %: C 44.35; H 9.69; N 29.38; S 16.92.  $\text{C}_7\text{H}_{18}\text{N}_4\text{S}$ . Calculated, %: C 44.21; H 9.47; N 29.47; S 16.84.

**2-Isopropylsulfanyl- $N^1, N^4, N^4$ -trimethylethano-hydrazide hydrazone (VIb)** was synthesized in a similar way from 15.61 g (26 mmol) of 1,1-dimethylhydrazine and 7 g (52 mmol) of acetylene **Ib**. Yield 3.8 g (36%), bp 95°C (2 mm),  $n_{\text{D}}^{20} = 1.4920$ . IR spectrum (film),  $\nu$ ,  $\text{cm}^{-1}$ : 3300 (N–H); 2939, 2846, 2807, 2759 (C–H); 1578 (C=N).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.24 d (6H,  $\text{CH}_3$ ), 2.29 s [6H,  $(\text{CH}_3)_2\text{N}$ ], 2.81 s (3H,  $\text{CH}_3\text{N}$ ), 2.93 (1H, CH), 3.74 s (2H,  $\text{SCH}_2$ ).  $^{13}\text{C}$  NMR spectrum,  $\delta_{\text{C}}$ , ppm: 22.98 ( $\text{CH}_3$ ), 23.40 (CH), 35.78 ( $\text{SCH}_2$ ), 37.84 ( $\text{CH}_3\text{N}$ ), 48.65 [ $(\text{CH}_3)_2\text{N}$ ], 162.64 (C=N). Found, %: C 46.93; H 9.87; N 27.70; S 15.55.  $\text{C}_8\text{H}_{20}\text{N}_4\text{S}$ . Calculated, %: C 47.06; H 9.80; N 27.45; S 15.69.

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