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Reactions of 1,1,4,4-Tetramethylsemicarbazide with Prop-2-ynyl Bromide, Allyl Bromide, and 1,3-Dibromoprop-1-yne

V. N. Elokhina, A. S. Nakhmanovich, E. V. Abramova, and L. I. Larina

Favorskii Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences,
ul. Favorskogo 1, Irkutsk, 664033 Russia
e-mail: k301@irioch.irk.ru

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Abstract—1,1,4,4-Tetramethylsemicarbazide readily undergoes alkylation with prop-2-ynyl bromide and allyl bromide at the tertiary nitrogen atom of the hydrazine fragment to give 1-(prop-2-yn-1-yl)- and 1-(prop-2-en-1-yl)-1,1-dimethyl-2-(dimethylaminocarbonyl)hydrazinium bromides, respectively. A new procedure was proposed for the synthesis of 6-bromomethylidene-2-dimethylamino-4,4-dimethyl-5,6-dihydro-4*H*-1,3,4-oxadiazin-4-ium bromide by reaction of 1,1,4,4-tetramethylsemicarbazide with 1,3-dibromoprop-1-yne in acetonitrile.

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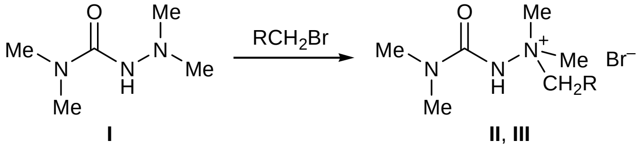
Alkylation of 1,1-dimethylhydrazine has attracted attention of many researchers. There are extensive published data on reactions of 1,1-dimethylhydrazine with various haloalkanes [1–4]. However, quaternization of 1,1-dimethylhydrazine and its derivatives with alkynyl and alkenyl halides has been studied relatively poorly. We previously synthesized 1,1-dimethyl-1-(prop-2-yn-1-yl)- and 1,1-dimethyl-1-(3-bromoprop-2-yn-1-yl)-2-alkylidene(or arylmethylidene)hydrazinium bromides in 30–72% yield by reactions of the corresponding dimethylhydrazones with prop-2-yn-1-yl bromide and 1,3-dibromoprop-1-yne, respectively [5]. Treatment of 1-aroyl-2,2-dimethylhydrazines with prop-2-yn-1-yl bromide and allyl bromide gave 1,1-dimethyl-1-(prop-2-yn-1-yl)- and 1,1-dimethyl-1-(prop-2-en-1-yl)-2-aroylhydrazinium bromides [6], while their reaction with 1,3-dibromoprop-1-yne in methanol or acetonitrile at 20–50°C led to the formation of 2-aroyl-6-bromomethylidene-4,4-dimethyl-5,6-dihydro-4*H*-1,3,4-oxadiazin-4-ium bromides [7].

In continuation of our studies on the alkylation of 1,1-dimethylhydrazine derivatives, in the present work we examined reactions of 1,1,4,4-tetramethylsemicarbazide (**I**) with prop-2-yn-1-yl bromide, allyl bromide, and 1,3-dibromoprop-1-yne. Initial 1,1,4,4-tetramethylsemicarbazide (**I**) was synthesized in 38% yield by reaction of dimethylcarbamoyl chloride with 1,1-dimethylhydrazine in benzene at 20°C in the presence of triethylamine.

We found that prop-2-yn-1-yl bromide and allyl bromide react with 1,1,4,4-tetramethylsemicarbazide (**I**) in anhydrous methanol or propan-2-ol on heating to 60–80°C with formation of 1-(prop-2-yn-1-yl)- and 1-(prop-2-en-1-yl)-1,1-dimethyl-2-(dimethylaminocarbonyl)hydrazinium bromides **II** and **III**, respectively (Scheme 1).

Scheme 1.

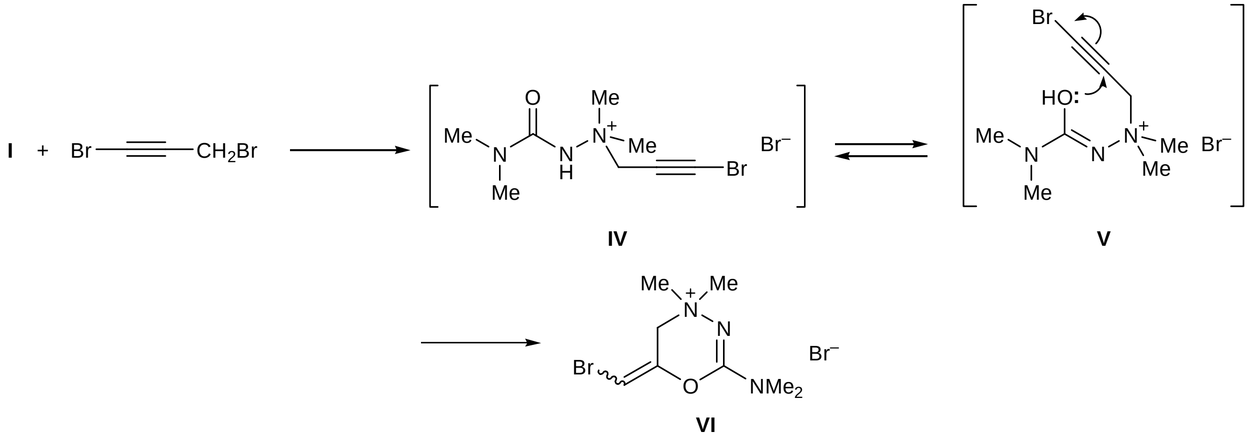


II, R = HC≡C; **III**, R = H_2C=CH.

The 1,1,4,4-tetramethylsemicarbazide molecule possesses two tertiary nitrogen atoms. The basicity of the nitrogen atom in the amide fragment is reduced due to displacement of electron density toward the carbonyl group; therefore, the alkylation occurs exclusively at the tertiary nitrogen atom in the hydrazine fragment.

By reaction of 1,1,4,4-tetramethylsemicarbazide (**I**) with 1,3-dibromoprop-1-yne in acetonitrile we obtained 6-bromomethylidene-2-dimethylamino-4,4-dimethyl-5,6-dihydro-4*H*-1,3,4-oxadiazin-4-ium bromide (**VI**) (Scheme 2). In the first stage, alkylation of semicarbazide **I** with 1,3-dibromopropyne at the tertiary nitrogen atom of the hydrazine fragment gives

Scheme 2.



intermediate bromide **IV**. Here, the formation of isomeric *N*-(3-bromoprop-1-yn-1-yl) is hardly probable: as we showed previously while studying the reaction of 1,1-dimethyl-2-(2-cyanoethyl)hydrazine with 1,3-dibromoprop-1-yne, only the CH_2Br group of the latter participates in the alkylation of the tertiary nitrogen atom [8]. Tautomeric amide–imide transformation of bromide **IV** gives rise to intermediate **V** which undergoes intramolecular cyclization with formation of 1,3,4-oxadiazinium bromide **VI**. The structure of compound **VI** was proved by the IR and ^{1}H, ^{13}C, and ^{15}N NMR spectra.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Specord IR-75 spectrometer. The ^{1}H, ^{13}C, and ^{15}N NMR spectra were measured at 20°C on a Bruker DPX-400 instrument at 400.13, 100.62, and 40.54 MHz, respectively, using DMSO-d_6 as solvent; the chemical shifts were determined relative to HMDS (^{1}H, ^{13}C) or $MeNO_2$ (^{15}N) as internal reference.

2-(Dimethylaminocarbonyl)-1,1-dimethyl-1-(prop-2-yn-1-yl)hydrazinium bromide (II). Prop-2-yn-1-yl bromide, 1.33 g (0.011 mol), was slowly added under stirring to a solution of 1.31 g (0.01 mol) of 1,1,4,4-tetramethylsemicarbazide in 15 ml of anhydrous methanol. The mixture was heated to 60°C and stirred for 1 h at that temperature. It was then cooled, the solvent was partially distilled off under reduced pressure, and the product was precipitated with cold anhydrous acetone. The precipitate was filtered off and dried under reduced pressure. Yield 1.68 g (67%), colorless crystals, mp 129–131°C. IR spectrum, ν, cm^{-1}: 3445 (NH), 2120 (C≡C), 1680 (C=O), 1380 (C–N). ^{1}H NMR spectrum, δ, ppm: 9.74 br.s (1H, NH), 5.04 s (2H, CH_2), 4.05 s (1H, HC≡), 3.64 s (6H, Me_2N^+), 2.93 s (6H, Me_2N). ^{13}C NMR spectrum, δ_C, ppm: 154.57 (C=O), 83.10 (HC≡), 72.03 (≡**C**CH_2), 57.02 (CH_2N^+), 54.27 (Me_2N^+), 36.10 (Me_2N). ^{15}N NMR spectrum, δ_N, ppm: –306.2 (NMe_2), –291.4 (NH), –239.6 (Me_2N^+). Found, %: C 38.65; H 6.08; Br 32.22; N 16.49. $C_8H_{16}BrN_3O$. Calculated, %: C 38.40; H 6.40; Br 32.00; N 16.80.

2-(Dimethylaminocarbonyl)-1,1-dimethyl-1-(prop-2-en-1-yl)hydrazinium bromide (III) was synthesized in a similar way from 1.31 g (0.01 mol) of compound **I** and 1.21 g (0.01 mol) of allyl bromide in propan-2-ol at 80°C. Yield 2.16 g (86%), colorless crystals, mp 145–147°C. IR spectrum, ν, cm^{-1}: 3420 (NH), 1685 (C=O), 1545 (C=C), 1275 (C–N). ^{1}H NMR spectrum, δ, ppm: 9.51 br.s (1H, NH), 6.00 t (1H, CH, ^3J = 17.0, 10.0, 7.3 Hz), 5.61 d (1H, =CH_2-*cis*, ^3J = 10.0 Hz), 5.58 d (1H, =CH_2-*trans*, ^3J = 17.0 Hz), 4.61 d (2H, NCH_2, ^3J = 7.3 Hz), 3.54 s (6H, Me_2N^+), 2.86 s (6H, Me_2N). ^{13}C NMR spectrum, δ_C, ppm: 154.79 (C=O), 127.52 (CH), 125.95 (=CH_2), 68.39 (NCH_2), 54.11 (Me_2N^+), 36.22 (Me_2N). ^{15}N NMR spectrum, δ_N, ppm: –306.1 (NMe_2), –291.7 (NH), –240.2 (Me_2N^+). Found, %: C 37.90; H 6.96; Br 31.68; N 16.70. $C_8H_{18}BrN_3O$. Calculated, %: C 38.10; H 7.14; Br 31.75; N 16.67.

6-Bromomethylidene-2-dimethylamino-4,4-dimethyl-5,6-dihydro-4*H*-1,3,4-oxadiazin-4-ium bromide (VI). 1,3-Dibromoprop-1-yne, 1.51 g (8 mmol), was slowly added under stirring to a solution of 1.0 g (8 mmol) of semicarbazide **I** in 15 ml of anhydrous acetonitrile. The mixture was heated to 80°C and stirred for 5 h at that temperature. The solution was cooled, the solvent was removed under reduced pressure, the residue was ground with cold anhydrous acetone, and the precipitate was filtered off and dried under reduced pressure. Yield 2.0 g (76%), colorless crystals, mp 180–182°C. IR spectrum, ν, cm^{-1}: 1590 (C=C), 1445 (C=N), 1280 (C–N), 1070 (C–O–C), 545 (C–Br). ^{1}H NMR spectrum, δ, ppm: 6.54 s (1H, =CH), 4.61 s (2H, CH_2), 3.32 s (6H, Me_2N^+), 2.92 s (6H, Me_2N). ^{13}C NMR spectrum, δ_C, ppm: 153.61 (C=N), 140.05 (CH_2**C**=), 91.88 (CHBr), 57.99 (CH_2), 56.74 (Me_2N^+), 36.18 (Me_2N). ^{15}N NMR spectrum, δ_N, ppm: –319.2 (Me_2N), –296.2 (Me_2N^+), –171.1 (C=N). Found, %: C 28.95; H 4.42; Br 48.48; N 12.56. $C_8H_{15}Br_2N_3O$. Calculated, %: C 29.18; H 4.56; Br 48.63; N 12.77.

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