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Synthesis of 1,3,4-Oxadiazinium Bromides from 1,1-Dimethylhydrazine Derivatives and 1,3-Dibromopropyne

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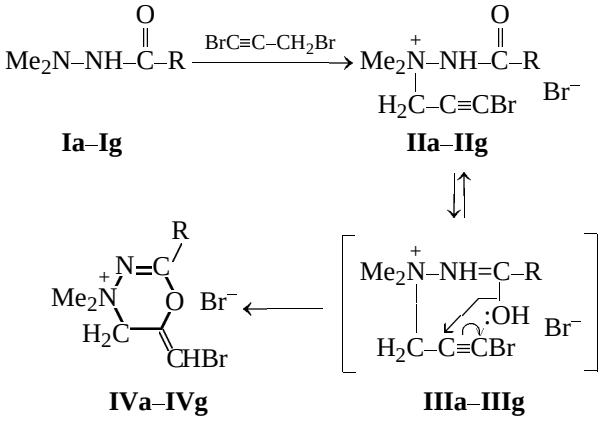
Abstract — 2-Aryl(heteryl, dimethylamino)-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromides were prepared in good yields by the reactions of 1-aroyl(heteroyl)-2,2-dimethylhydrazines and 1,1,4,4-tetramethylsemicarbazide with 1,3-dibromopropyne in MeOH or MeCN at 20–50°C.

Among diverse transformations of 1,1-dimethylhydrazine and its derivatives, their quaternization with haloalkynes has been studied relatively poorly. The reactions of 1,1-dimethylhydrazine with propargyl bromide [1] and propargyl chloride [2] yield 1,1-dimethyl-1-(propyn-2-yl)hydrazinium bromide and chloride, respectively. Aroylethynyl bromides react with 1,1-dimethylhydrazine in MeCN at 20°C to give 1-(1-bromo-2-aroylvinyl)-1,1-dimethylhydrazinium bromides [3]. The reactions of 1,1-dimethylhydrazines with propargyl bromide and 1,3-dibromopropyne in MeCN and benzene at 20°C gave in 30–72% yields the corresponding 1,1-dimethyl-1-(prop-2-ynyl)- and 1,1-dimethyl-1-(3-bromoprop-2-ynyl)hydrazinium bromides [4].

We found that the reactions of 1-benzoyl-, 1-(4-bromobenzoyl)-, 1-(2-chlorobenzoyl)-, 1-(4-toluyl)-, 1-(2-thenoyl), and 1-(2-furoyl)-2,2-dimethylhydrazines **Ia**–**If** and of 1,1,4,4-tetramethylsemicarbazide **Ig** with 1,3-dibromopropyne yield 2-aryl(heteryl, dimethylamino)-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromides **IVa**–**IVg**. In the first step, hydrazines **Ia**–**If** are alkylated with 1,3-dibromopropyne at the tertiary nitrogen atom to give 1-aroyl(heteroyl)-2-(3-bromoprop-2-ynyl)-2,2-dimethylhydrazinium bromides.



R = Ph (**a**), 4-BrC_6H_4 (**b**), 2-ClC_6H_4 (**c**), 4-MeC_6H_4 (**d**), 2-thienyl (**e**), 2-furyl (**f**), Me_2N (**g**).

Although formation of isomeric products, 1-aroyl(heteroyl)-2-(3-bromoprop-1-ynyl)-2,2-dimethylhydrazinium bromides, could also be expected, our previous studies [4] of the reactions of 1,1-dimethylhydrazones with 1,3-dibromopropyne and propargyl bromide showed that the tertiary nitrogen atom is alkylated exclusively with the CH_2Br fragment. The amide–imide tautomerism of bromides **IIa**–**IIf** in MeOH or

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MeCN solutions results in formation of intermediates **IIIa**–**IIIf**, which undergo intramolecular cyclization to give 1,3,4-oxadiazinium bromides **IVa**–**IVf**. The structure of the compounds was proved by elemental analysis and by ^{1}H, ^{13}C, and ^{15}N NMR and IR spectroscopy. The suggested mechanism is confirmed by isolation of 1-(4-bromobenzoyl)-2-(3-bromoprop-2-ynyl)-2,2-dimethylhydrazinium bromide **IIb** along with 1,3,4-oxadiazinium bromide **IVb** in the reaction of 1-(4-bromobenzoyl)-2,2-dimethylhydrazine **Ib** with 1,3-dibromopropyne.

1,1,4,4-Tetramethylsemicarbazide **Ig** reacts with 1,3-dibromopropyne similarly to give 2-dimethylamino-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide **IVg** in a good yield (76%). The starting 1,1,4,4-tetramethylsemicarbazide **Ig** was prepared by the reaction of *N*,*N*-dimethylcarbamoyl chloride with 1,1-dimethylhydrazine in benzene in the presence of triethylamine at 20°C in 65% yield by the procedure described in [5].

EXPERIMENTAL

The IR spectra were taken on a Specord IR-75 spectrophotometer (KBr pellets). The ^{1}H, ^{13}C, and ^{15}N NMR spectra were recorded at 20°C on a Bruker-400 spectrometer (400.13, 100.62, and 40.54 MHz, respectively) in DMSO-d_6. The internal references were HMDS and $MeNO_2$.

1-Aroyl(heteroyl)-2,2-dimethylhydrazines Ia–**If** were prepared as described in [6] from 1,1-dimethylhydrazine and benzoyl, 4-bromobenzoyl, 4-chlorobenzoyl, 4-toluyl, 2-thenoyl, and 2-furoyl chlorides in benzene at 20°C.

2-Phenyl-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide IVa. A solution of 1.8 g of 1,3-dibromopropyne in 20 ml of absolute MeOH was slowly added with stirring to a solution of 1.5 g of 1-benzoyl-2,2-dimethylhydrazine **Ia** in 30 ml of absolute MeOH. The mixture was heated to 50°C, stirred at this temperature for 5 h, and cooled to 0°C. The precipitate was filtered off, washed on the filter with cold ether, and dried in a vacuum. Yield of 1,3,4-oxadiazinium bromide **IVa** 3.0 g (91%); colorless crystalline substance, mp 148–149°C. IR spectrum, ν, cm^{-1}: 2950 (CH_2), 1610 (C=N), 1570 (C=C), 690 (CBr). ^{1}H NMR spectrum, δ, ppm: 3.53 d (6H, Me), 4.91 s (2H, CH_2), 6.80 s (1H, =CHBr), 7.61–7.98 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 55.7 (Me), 57.3 (CH_2), 94.8 (C=CHBr), 124.5–133.7 (Ph), 139.1 (CHBr), 157.2 (C=N). Found, %: C 39.64; H 3.85; Br 44.45; N 7.91. $C_{12}H_{14}Br_2N_2O$. Calculated, %: C 39.78; H 3.87; Br 44.20; N 7.93.

2-(4-Bromophenyl)-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide IVb and 1-(4-bromobenzoyl)-2-(3-bromoprop-2-ynyl)-2,2-dimethylhydrazinium bromide IIb. A solution of 1.78 g of 1,3-dibromopropyne in 10 ml of MeCN was added with stirring to a solution of 2.37 g of 1-(4-bromobenzoyl)-2,2-dimethylhydrazine **Ib** in 40 ml of MeCN. The mixture was stirred for 20 h at 20°C and then cooled to 0°C. The precipitate was filtered off, washed on the filtrate with cold MeCN, and vacuum-dried. Yield of **IVb** 1.2 g (28%), colorless crystals, mp 154–155°C (from acetone). IR spectrum, ν, cm^{-1}: 2920 (CH_2), 1625 (C=N), 1580 (C=C), 720 (CBr). ^{1}H NMR spectrum, δ, ppm: 3.56 s (6H, Me), 5.02 s (2H, CH_2), 6.84 s (1H, =CHBr), 7.68–7.86 m (4H, C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 56.3 (Me), 57.8 (CH_2), 95.7 (=CHBr), 126.7–132.7 (C_6H_4), 139.7 (*C*=CHBr), 157.4 (C=N). ^{15}N NMR spectrum (reference $MeNO_2$), δ_N, ppm: –117.6 (N=C), –289.0 (N^+Me_2). Found, %: C 32.23; H 2.84; Br 54.61; N 6.49. $C_{12}H_{13}Br_3N_2O$. Calculated, %: C 32.69; H 2.97; Br 54.36; N 6.35.

The filtrate after the separation of **IVb** was concentrated, cold diethyl ether was added with vigorous stirring, and the mixture was cooled to 0°C to precipitate **IIb**. Yield of **IIb** 1.37 g (32%), pink crystals, mp 156–157°C. IR spectrum, ν, cm^{-1}: 3420 (NH), 2930 (CH_2), 2240 (C≡C), 1640 (C=O), 680 (CBr). ^{1}H NMR spectrum, δ, ppm: 3.53 s (6H, Me), 4.91 s (2H, CH_2), 7.68–7.88 m (4H, C_6H_4), 10.68 s (1H, NH). Found, %: C 32.49; H 3.22; Br 53.65; N 6.56. $C_{12}H_{13}Br_3N_2O$. Calculated, %: C 32.69; H 2.97; Br 54.36; N 6.35.

2-(2-Chlorophenyl-5-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide IVc was prepared similarly to **IVa** from a mixture of 4.0 g of 1-(2-chlorobenzoyl)-2,2-dimethylhydrazine **Ic** and 3.96 g of 1,3-dibromopropyne in MeCN. Yield 3.26 g (41%), colorless crystals, mp 170–172°C (from MeCN). IR spectrum, ν, cm^{-1}: 2925 (CH_2), 1630 (C=N), 1590 (C=C), 740 (CCl). ^{1}H NMR spectrum, δ, ppm: 3.55 d (6H, Me), 5.08 d (2H, CH_2), 6.85 s (1H, =CHBr), 6.85–7.67 m (4H, C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 55.4 (Me), 57.2 (CH_2), 95.6 (=CHBr), 126.6–134.0 (C_6H_4), 139.2 (*C*=CHBr), 157.8 (C=N). Found, %: C 36.27; H 3.88; Br 40.44; Cl 9.32; N 7.08. $C_{12}H_{13}Br_2ClN_2O$. Calculated, %: C 36.26; H 3.55; Br 40.20; Cl 9.07; N 7.05.

2-(4-Toluyl)-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide IVd was prepared similarly to **IVa** from a mixture of 1.0 g of 1-(4-tolyl)-2,2-dimethylhydrazine **Id** and 1.1 g of 1,3-dibromopropyne (reaction time 7 h). Yield 1.5 g (71%), colorless crystals, mp 144–145°C (from MeCN). IR spectrum, ν, cm^{-1}: 2921 (CH_2), 1614 (C=N), 1568 (C=C),

683 (CBr). ^{1}H NMR spectrum, δ, ppm: 3.15 s (3H, C_6H_4Me), 3.50 s (6H, NMe_2), 4.88 d (2H, CH_2, *J* 6.0 Hz), 6.78 s (1H, =CHBr), 7.43–7.87 m (4H, C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 21.3 ($C_6H_4CH_3$), 55.9 (NMe), 57.5 (CH_2), 94.9 (=CHBr), 124.0–129.7 (C_6H_4), 144.6 (*C*=CHBr), 157.4 (C=N). Found, %: C 41.40; H 4.48; Br 42.82; N 7.20. $C_{12}H_{16}Br_2N_2O$. Calculated, %: C 41.49; H 4.25; Br 42.55; N 7.45.

2-(2-Thienyl)-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide IVe was prepared similarly to **IVa** from 1.7 g of 1-(2-thenoyl)-2,2-dimethylhydrazine **Ie** and 3.58 g of 1,3-dibromopropyne. Yield 3.59 g (68%), colorless crystals, mp 136–138°C. IR spectrum, ν, cm^{-1}: 2950 (CH_2), 1600 (C=N), 1565 (C=C), 730 (CBr), 690 (CS). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.50 s (6H, $2CH_3$), 4.89 s (2H, CH_2), 6.78 s (1H, =CHBr), 7.32 d.d (1H, H^3, ^3J 5.0, ^3J 3.4 Hz), 7.88 d (1H, H^4, ^3J 3.4 Hz), 8.09 d (1H, H^2, ^3J 5.0 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 56.0 (CH_3), 57.9 (CH_2), 95.05 (=CHBr), 128.66 (C^2), 128.80 (C^5), 133.32 (C^3), 135.04 (C^4), 139.26 (*C*=CHBr), 154.56 (C=N). Found, %: C 32.35; H 3.15; Br 43.65; N 7.82; S 8.73. $C_{10}H_{12}Br_2N_2OS$. Calculated, %: C 32.61; H 3.26; Br 43.48; N 7.61; S 8.70.

2-(2-Furyl)-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide IVf was prepared similarly to **IVa** from 1.54 g of 1-(2-furoyl)-2,2-dimethylhydrazine **If** and 3.58 g of 1,3-dibromopropyne. Yield 4.45 g (87%), colorless crystals, mp 141–142°C. IR spectrum, ν, cm^{-1}: 2920 (CH_2), 1610 (C=N), 1560 (C=C), 710 (CBr). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.44 s (6H, $2CH_3$), 4.84 s (2H, CH_2), 6.77 s (1H, CH), 6.84 d.d (1H, H^4, ^3J 3.7, ^3J 1.8 Hz), 7.41 d.d (1H, H^3, ^3J 3.7, ^4J 0.7 Hz), 8.14 d.d (1H, H^5, ^3J 1.8, ^4J 0.7 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 56.09 (CH_3), 58.08 (CH_2), 95.12 (CH), 113.13 (C^3), 118.84 (C^4), 139.00 (C^2), 140.53 (C=CHBr), 148.93 (C^5), 150.61 (C=N). Found, %: C 34.37; H 3.33; Br 45.65; N 8.02. $C_{10}H_{12}Br_2N_2O_2$. Calculated, %: C 34.09; H 3.41; Br 45.45; N 7.95.

2-Dimethylamino-6-bromomethylidene-4,4-dimethyl-5*H*-1,3,4-oxadiazinium bromide IVg was prepared similarly to **IVa** from 1.0 g of 1,1,4,4-tetramethylsemicarbazide **Ig** and 1.51 g of 1,3-dibromopropyne in MeCN at 80°C. Yield 2.0 g (76%), mp 180–182°C. IR spectrum, ν, cm^{-1}: 1590 (C=C), 1445 (C=N), 1280 (CN), 1070 (COC), 545 (CBr). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 6.54 s (1H, =CH), 4.61 s (2H, CH_2), 3.32 s (6H, N^+Me_2), 2.92 s (6H, NMe_2). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 153.61 (C=N), 140.05 (CH_2C=), 91.88 (CHBr), 57.99 (CH_2), 56.74 (N^+Me_2), 36.18 (NMe_2). ^{15}N NMR spectrum (DMSO-d_6), δ_N, ppm: –319.2 (NMe_2), –296.2 (N^+Me_2), –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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