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SYNTHESIS OF FUNCTIONALLY-SUBSTITUTED 2-PHENYL(2-FURYL)-1,3,4-OXADIAZINE HYDROBROMIDES FROM BENZOYL(2-FUROYL)HYDRAZINES AND 1,3-DIBROMOPROPYNE

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The reaction of benzoyl(2-furoyl)hydrazines with 1,3-dibromopropyne on heating in acetonitrile in 1:1 or 1:2 ratio of the reagents gave exclusively substituted 2-phenyl(2-furyl)-1,3,4-oxadiazine hydrobromides.

Keywords: benzoylhydrazine, 1,3-dibromopropyne, substituted 1,3,4-oxadiazine hydrobromide, 2-furoylhydrazine, heterocyclization.

Benzoylhydrazine reacts with methyl iodide in benzene in the presence of sodium to give 1-benzoyl-1-methylhydrazine [1]. Interaction of 1,1-dimethylhydrazine with propargyl bromide and 1,3-dibromopropyne in absolute acetonitrile at 20°C is accompanied by quaternization of the tertiary nitrogen atom and the formation of 1,1-dimethyl-1-(propyn-1-yl)hydrazine hydrazinium bromide and 1,1-dimethyl-1-(3-bromo-2-propyn-1-yl) hydrazinium bromide respectively [2, 3]. Reaction of 1,1-dimethylhydrazine with 1-aroyl-2-bromoacetylenes at 20°C in MeCN gave 1-(2-aroyl-1-bromovinyl)-1,1-dimethylhydrazinium bromides [4].

We have observed that the reaction of benzoylhydrazine (**1a**) and 2-furoylhydrazine (**1b**) with 1,3-dibromopropyne **2** in acetonitrile on heating (80°C) gave 6-bromomethylidene-4-(3-bromo-2-propyn-1-yl)-2-phenyl(furyl-2)-5H-1,3,4-oxadiazine hydrobromides **3a,b** as the sole reaction products in 45 and 66% yields with equimolar ratios of the reagents and 68 and 80% yields with a two-fold excess of the acetylene **2**.

A molecule of hydrogen bromide is lost in the first stage of the reaction to give the 1,2-disubstituted hydrazines **A**, which could not be isolated. As a result of amidimide tautomerism in the MeCN solution compounds **A** form the acetylene intermediates **B** which readily cyclize on heating in the conditions of the reaction to give the substituted 1,3,4-oxadiazines **C**. Subsequently they react with a second molecule of 1,3-dibromopropyne **2** to give the 6-bromomethylidene-4-(3-bromo-2-propyn-1-yl)-2-phenyl(2-furyl)-5H-1,3,4-oxadiazine hydrobromides **3a,b**.

The structures of compounds **3a,b** were confirmed by elemental analysis, IR and ^{1}H and ^{13}C NMR spectra.

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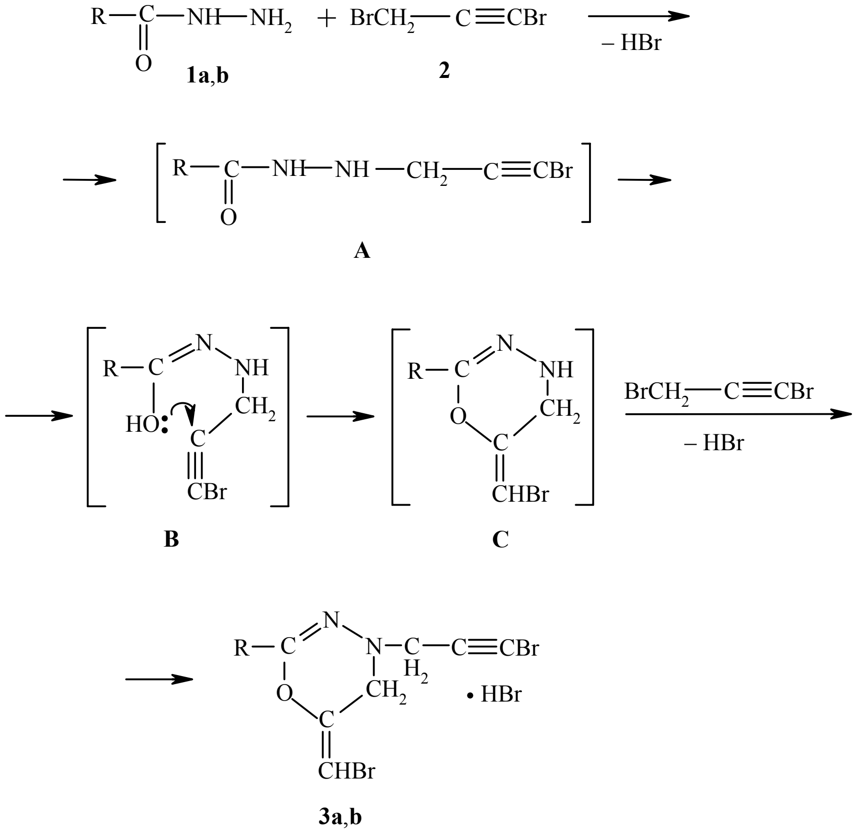

a R = Ph, **b** R = 2-furyl

EXPERIMENTAL

IR spectra of KBr discs were recorded with a Bruker-25 spectrometer. ^1H, ^{13}C, and ^{15}N NMR spectra of DMSO-d_6 solution with HMDS (δ 0.05 ppm) and nitromethane (for ^{15}N) as internal standards were recorded on Bruker DRX-400 spectrometer (400, 100, and 40 MHz respectively).

6-Bromomethylidene-4-(3-bromo-2-propyn-1-yl)-2-phenyl-5H-1,3,4-oxadiazine Hydrobromide (3a). 1,3-Dibromopropyne **2** (3.96 g, 0.02 mol) in dry acetonitrile (10 ml) was added dropwise with stirring to a solution of benzoylhydrazine **1a** (1.36 g, 0.01 mol) in dry acetonitrile (40 ml). The reaction mixture was then slowly heated to 80°C and stirred at this temperature for 5 h. The acetonitrile was partially evaporated, dry chloroform (40 ml) was added, and the mixture cooled to 0°C. The viscous precipitate was recrystalized from dry methanol. The crystalline precipitate was filtered off, washed on the filter with cold methanol, and dried in vacuum to give white crystals of compound **3a** (3.07 g, 68%); mp 159-160°C .

When an equimolar ratios of the reagents were used [compound **1a** (1.36 g, 0.01 mol), 1,3-dibromopropyne **2** (1.98 g, 0.01 mol) 1.04 g of compound **3a** was obtained (56% based on 1,3-dibromopropyne). IR spectrum, ν, cm^{-1}: 3015, 3250 (CH_2), 2210 (C≡C), 1640 (C=N), 1545 (C=C), 1295 (C–O–C), 745 (C–Br). ^1H NMR spectrum, δ, ppm: 3.88 (2H, s, CH_2–C≡); 3.94 (2H, s, CH_2 in the ring); 7.37 (1H, s, =CHBr); 7.46-7.74 (5H, m, C_6H_5); 9.74 (1H, br. s, HBr). ^{13}C NMR spectrum, δ, ppm: 46.18 (CH_2–C≡), 46.31 (≡CBr); 62.22 (CH_2 in the ring); 75.75 ($CH_2\text{–}\underline{C}\equiv$); 110.74 (=CHBr); 127.43, 128.44, 131.61, 133.52 (C_6H_5); 128.92 ($\underline{C}$=CHBr), 165.70 (C=N). ^{15}N NMR spectrum, δ, ppm: -229.6 (C=N), -299.7 (N–CH_2). Found, %: C 34.65; H 2.40; Br 53.15; N 6.08. $C_{13}H_{11}Br_3N_2O$. Calculated, %: C 34.59; H 2.44; Br 53.22; N 6.21.

6-Bromomethylidene-4-(3-bromo-2-propyn-1-yl)-2-(2-furyl-5H-1,3,4-oxadiazine Hydrobromide (3b) was obtained analogously to compound **3a** from 2-furoylhydrazine **1b** (1.26 g, 0.01 mol) and 1,3-dibromopropyne **2** (3.96 g, 0.02 mol) in dry acetonitrile (40 ml) at 80°C as white crystals (3.52 g, 80%); mp 140-142°C. IR spectrum, ν, cm^{-1}: 3010, 3220 (CH_2), 2190 (C≡C), 1630 (C=N), 1570 (C=C), 1290 (C–O–C), 720 (C–Br). ^{1}H NMR spectrum, δ, ppm: 3.89 (2H, s, CH_2–C≡); 3.96 (2H, s, CH_2 in the ring); 7.36 (1H, s, =CHBr); 6.61-7.84 (3H, m, furyl); 9.81 (1H, br. s, HBr). ^{13}C NMR spectrum, δ, ppm: 46.18 ($\underline{CH_2}$–C≡); 46.72 (≡CBr); 62.46 (CH_2 in the ring); 75.59 (CH_2–$\underline{C}$≡); 110.51 (=CBr); 128.72 ($\underline{C}$=CHBr); 111.86, 114.31, 145.45, 146.43 (furyl); 157.14 (C=N). ^{15}N NMR spectrum, δ, ppm: -235.6 (C=N), -304.7 (N–CH_2). Found, %: C 29.66; H 1.94; Br 54.62; N 6.37. $C_{11}H_9Br_3N_2O_2$. Calculated, %: C 29.93; H 2.04; Br 54.42; N 6.35.

Compound **3b** (1.19 g) was obtained from equimolar ratios of the reagents [compound **1b** (1.26 g, 0.01 mol), 1,3-dibromopropyne **2** (1.98 g, 0.01 mol)] in 66% yield based on 1,3-dibromopropyne.

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