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LETTERS TO THE EDITOR

Synthesis of Heterocyclic 1,4-Diamino-2,3-dibromo-2-butenes

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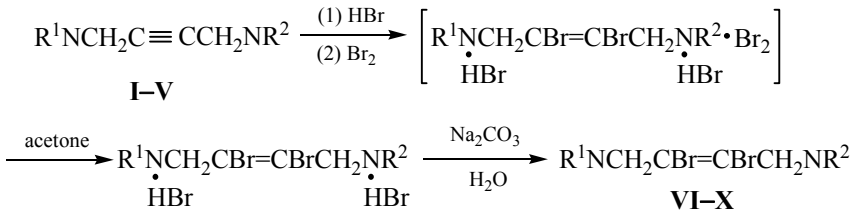
A practical importance of the unsaturated surfactant mono- and bisammonium salts is primarily caused by exhibiting a number of valuable properties like emulsifying ability and corrosion protection, antiviral and bactericidal activity. The pronounced antibacterial activity of unsaturated quaternary ammonium compounds determines the reason of their synthesis and the study of their properties, which will expand the scope of their practical application.

1,4-Diamines containing 2,3-dihaloalkenyl group can be used as intermediates in the synthesis of various classes of organic compounds which combine in the molecule the nitrogen and halogen atoms, in particular for obtaining bioactive compounds.

Previously, we have synthesized a series of 1,4-bisdialkylamino-2,3-dibromo-2-butenes, as well as their quaternized analogs. Antibacterial properties of these amines and basic cleavage of their quaternary analogs have been studied [1–3].

In continuation of these studies we have obtained some heterocyclic 1,4-diamino-2-butynes **I**–**V** and 1,4-diamino-2,3-dibromo-2-butenes **VI**–**X**. Morpholine and piperidine were used as heterocyclic amines. Amines **I**, **II** were prepared by reacting 1,4-dibromo-2-butyne with piperidine and morpholine, respectively. Amines **III**–**V** were synthesized by the Mannich reaction via aminomethylation of dimethylpropargylamine with piperidine and morpholine **III**, **IV** or of *N*-morpholinopropargylamine with piperidine **V**. Diamines **VI**–**X** were prepared from the corresponding 1,4-diamino-2-butynes **I**–**V** according to the following scheme.



$NR^1 = NR^2$ = *N*-piperidinyl (**I**, **VI**); $NR^1 = NR^2$ = *N*-morpholinyl (**II**, **VII**); NR^1 = *N*,*N*-dimethyl, NR^2 = *N*-piperidinyl (**III**, **VIII**); NR^1 = *N*,*N*-dimethyl, NR^2 = *N*-morpholinyl (**IV**, **IX**); NR^1 = *N*-piperidinyl, NR^2 = *N*-morpholinyl (**V**, **X**).

It is interesting to note that the previously synthesized 1,4-bisdialkylamino-2-butynes and their heterocyclic analogs are liquid substances, while 1,4-bismorpholino-2-butyne is a crystalline substance with a melting point of 85–86°C. Also all the synthesized heterocyclic 1,4-diamino-2,3-dibromo-2- butenes **VI**–**X** are crystalline substances, while among their dialkyl analogs only 1,4-bisdimethylamino-2,3-dibromo-2-butene is a crystalline material [1].

1,4-Di(piperidin-1-yl)but-2-yne (I). Yield 70%, bp 192–194°C (22 mm Hg), n_D^{20} 1.5060, R_f 0.51, *M*

220.11. ^{1}H NMR spectrum, δ, ppm: 1.38–1.48 m [4H, $N(CH_2)_2C\underline{H}_2$], 1.57–1.65 m [8H, $(NC\underline{H}_2(CH_2)_2]$, 2.45–2.52 m (8H, $NCH_2C\underline{H}_2$), 3.27 s (4H, $\equiv CCH_2$). ^{13}C NMR spectrum, δ_C, ppm: 24.0 (CH_2), 26.0 (CH_2), 48.1 ($\underline{C}H_2C\equiv$), 53.4 [$N(CH_2)_2$], 80.2 (C≡C).

1,4-Di(morpholin-4-yl)but-2-yne (II). Yield 75%, mp 85–86°C, R_f 0.58, M 223.2. ^{1}H NMR spectrum, δ, ppm: 2.43–2.47 m (8H, $NC\underline{H}_2CH_2$), 3.24 s (4H, $\equiv CCH_2$), 3.58–3.62 m (8H, OCH_2).

Dimethyl-(4-piperidin-1-ylbut-2-ynyl)amine (III). Yield 70%, bp 83–84°C (1 mm Hg), n_D^{20} 1.4840, R_f 0.39. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37–1.46 m [2H, $N(CH)_2C\underline{H}_2$], 1.56–1.65 m (4H, $NCH_2C\underline{H}_2$), 2.28 s (6H, NCH_3), 2.44–2.52 m (4H, $NC\underline{H}_2CH_2$), 3.24 t [2H, $(CH_2)_5NC\underline{H}_2$, *J* 2.0], 3.27 t [2H, $(CH_3)_2NC\underline{H}_2$, *J* 2.0).

Dimethyl-(4-morpholin-4-ylbut-2-ynyl)amine (IV). Yield 80%, bp 91–92°C (2 mm Hg), n_D^{20} 1.4850, R_f 0.37. ^{1}H NMR spectrum, δ, ppm.: 2.25 s (6H, NCH_3), 2.48–2.58 m (4H, $NC\underline{H}_2CH_2$), 3.21–3.28 m (4H, $NCH_2C\equiv$), 3.65–3.69 m (4H, OCH_2).

4-(4-Piperidin-1-ylbut-2-ynyl)morpholine (V). Yield 65%, bp 134–137°C (1 mm Hg), n_D^{20} 1.5060, R_f 0.38. ^{1}H NMR spectrum, δ, ppm: 1.36–1.45 m [2H, $N(CH_2)_2C\underline{H}_2$], 1.52–1.60 m (4H, $NCH_2C\underline{H}_2CH_2$), 2.38–2.43 m [4H, $NC\underline{H}_2(CH_2)_2$], 2.43–2.48 m (4H, $NC\underline{H}_2CH_2O$), 3.18–3.24 m (4H, $NCH_2C\equiv$), 3.58–3.62 m (4H, $NCH_2C\underline{H}_2O$).

General procedure of the synthesis of 1,4-bisamines (VI–X). To 0.05 mol of bisamine **I–V** was added dropwise 21 mL of 40% aqueous hydrobromic acid solution. To the formed hydrobromides, without isolating, at room temperature and with stirring was added dropwise 16 g of bromine. The complexes with bromine were filtered off. In the UV spectra of the complexes there are characteristic absorption bands at 220 and 270 nm (in the spectra of starting compounds, at 205 nm) [4]. Decomposition of the complexes with acetone (chemically pure) results in 1,4-diamino-2-butenes **VI–X** dihydrobromides. The treatment of dihydrobromides with aqueous Na_2CO_3 or K_2CO_3 solution followed by extraction with diethyl ether and removal of ether in a vacuum (40–50 mm Hg) gives bisamines **VI–X**.

1,4-Di(piperidin-1-yl)-2,3-dibromobut-2-ene (VI). Yield 65%, mp 82–83°C, R_f 0.68, M 385.1. ^{1}H NMR spectrum, ppm: 1.38–1.47 m [4H, $N(CH_2)_2C\underline{H}_2$], 1.52–1.61 m (8H, $NCH_2C\underline{H}_2CH_2$), 2.40–2.45 m [8H, $NC\underline{H}_2(CH_2)_2$], 3.44 s (4H, CH_2CBr). ^{13}C NMR spectrum, δ_C, ppm: 23.7 (CH_2), 25.3 (CH_2), 53.2 [$N(CH_2)_2$], 65.1 ($\underline{C}H_2CBr$), 121.5 (=CBr).

1,4-Di(morpholin-4-yl)-2,3-dibromobut-2-ene (VII). Yield 70%, mp 127–128°C, R_f 0.53, M 383.5. ^{1}H NMR spectrum, δ, ppm: 2.45–2.49 m (8H, $NC\underline{H}_2CH_2$), 3.51 s (4H, NCH_2CBr), 3.58–3.63 m (8H, OCH_2). ^{13}C NMR spectrum, δ_C, ppm: 52.3 (NCH_2), 64.8 ($\underline{C}H_2CBr$), 65.8 (OCH_2), 121.2 (=CBr).

Dimethyl-(4-piperidin-1-yl-2,3-dibromobut-2-enyl)amine (VIII). Yield 95%, mp 52–53°C, R_f 0.72, M 340.82. ^{1}H NMR spectrum, δ, ppm: 1.39–1.47 m [2H, $N(CH_2)_2C\underline{H}_2$], 1.52–1.61 m (4H, N $CH_2C\underline{H}_2CH_2$), 2.25 s [6H, $N(CH_3)_2$], 2.40–2.46 m (4H, $NC\underline{H}_2CH_2$), 3.43 s [2H, $(CH_3)_2NC\underline{H}_2C$=CBr], 3.45 s [2H, $(CH_2)_5$·$NC\underline{H}_2C$=CBr].

Dimethyl-(4-morpholin-1-yl-2,3-dibromobut-2-enyl)amine (IX). Yield 83%, mp 42°C, R_f 0.63, M 341.02. ^{1}H NMR spectrum, δ, ppm: 2.25 s [6H, $N(CH_3)_2$], 2.45–2.50 m (4H, $NC\underline{H}_2CH_2$), 3.43 s [2H, $O(CH_2)_4NC\underline{H}_2CBr$=], 3.51 s [2H, $(CH_3)_2NC\underline{H}_2CBr$=], 3.59–3.63 m (4H, OCH_2). ^{13}C NMR spectrum, δ_C, ppm: 44.2 (CH_3), 52.3 [$N(CH_2)_2$], 64.8 (NCH_2), 65.5 (NCH_2), 65.8 [$O(CH_2)_2$], 120.4 and 122.3 (C=C).

4-(4-Piperidin-1-yl-2,3-dibromobut-2-enyl)morpholine (X). Yield 80%, mp 88–89°C, R_f 0.75, M 380.2. ^{1}H NMR spectrum, δ, ppm: 1.38–1.47 m (2H, $NCH_2CH_2C\underline{H}_2$), 1.52–1.61 m (4H, $NCH_2C\underline{H}_2$), 2.40–2.44 m (4H, $NC\underline{H}_2CH_2$), 2.45–2.49 m (4H, $NC\underline{H}_2CH_2O$), 3.44 s [2H, $O(CH_2)_4NC\underline{H}_2CBr$=], 3.5 s [2H, $(CH_2)_5$·$NC\underline{H}_2CBr$=], 3.59–3.63 m (4H, $NCH_2C\underline{H}_2O$).

The NMR spectra were obtained on a Varian Mercury-300 spectrometer operating at 300.077 (^{1}H) and 75.453 MHz (^{13}C) in $(CD_3)_2SO$, internal reference TMS. The UV spectra were obtained on a Specord M-40 spectrometer in water (for salt) or acetonitrile (for complexes). TLC analysis was made on Silufol UV-254 plates eluting with a butanol–ethanol–water–acetic acid system, 10:7:6:4 (**I–VII**) or toluene–acetone mixture, 1:1 (**VIII–X**) and detecting with iodine vapors. Melting points were measured on a Boeitus instrument equipped with a supervisory device RNMK-0.5. GLC analysis was done on a LKhM-8MD instrument equipped with a detector for the thermal conductivity [oven temperature 170–220°C, 1500×3 mm, 10% Carbovax-20M on Inerton-AW-HMDS (0.2–0.25 mm), heating rate 16 deg min^{-1}, rate of the carrier gas (helium) 60 mL min^{-1}].

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