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Synthesis of Potentially Bioactive 6-Bromobenzo[*f*]isoindolinium Bromides by Base-Catalyzed Intramolecular [4+2]-Cycloaddition

E. O. Chukhadzhian[a], H. R. Gevorgyan[a,c], L. V. Ayrapetyan[a], El. O. Chukhadzhian[a], K. G. Shahkhatuni[a], A. S. Mkrtchyan[a], and G. A. Panosyan[b]*

[a] *Institute of Organic Chemistry of Scientific Technological Center of Organic and Pharmaceutical Chemistry of National Academy of Sciences of Armenia, pr. Azatutyan 26, Yerevan, 0014 Armenia*
**e-mail: hasulik4@mail.ru*

[b] *Molecular Structure Research Center of Scientific Technological Center of Organic and Pharmaceutical Chemistry of National Academy of Sciences of Armenia, Yerevan, 0014 Armenia*

[c] *National Polytechnical University of Armenia, Yerevan, 0009 Armenia*

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Abstract—Intramolecular cyclization of bromides of diethyl-, dipropyl-, and penthamethylenepropargyl[3-(4-bromophenyl)prop-2-ynyl]ammonium into 6-bromobenzo[f]isoindolinium bromides catalyzed with bases occurs with moderate self-heating. The morpholine analog even in more diluted solutions reacts with vigorous self-heating. Cyclization of dimethyl analog takes place only at heating at 80–85°C during 1 h.

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Research on the synthesis of nitrogen- and oxygen-containing heterocyclic compounds is one of important tasks of organic chemistry. Besides an obvious theoretical interest they possess a practical value: they are present in the composition of antibiotics, alkaloids, proteins, cordial glycosides, etc. There is only scarse information on compounds of isoindolinium series and their condensed analogs that may be due to the difficulty of their preparation methods.

Base-catalyzed intramolecular [4+2]-cycloaddition of ammonium salts, containing π^2-group along with different π^4-fragments, is a new direction in organic chemistry and provides great possibilities for the synthesis of biologically active di-, tri-, polycyclic isoindolinium and tetrahydro-1*H*-isoindolium salts [1–3].

As known, dialkylpropargyl[3-(4-chlorophenyl)-prop-2-ynyl]ammonium bromides [4] as compared to 3-phenylprop-2-ynyl analogs [5] undergo [4+2]-cycloaddition in milder conditions (molar ratio salt–alkali 10 : 1), forming biologically active 6-chlorobenzo[*f*]isoindolinium bromides.

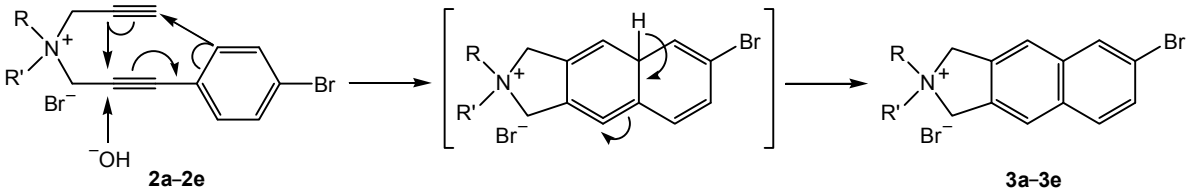
Extending and developing the area of base-catalyzed intramolecular cyclization we brought in the reaction in this study quaternary ammonium salts, containing propargyl group along with 3-(4-bromophenyl)prop-2-ynyl.

This study along with the practical has a theoretical issue: the data, obtained in the course of investigation, may confirm the mechanism we previously have suggested for the base-catalyzed intramolecular cyclization reaction [3, 6].

To this end we synthesized dialkyl [3-(4-bromophenyl)prop-2-ynyl]amines **1a–1e**, alkylation of which with propargyl bromide in acetonitrile or diethyl ether provided dialkylpropargyl[3-(4-bromophenyl)prop-2-ynyl]ammonium bromides **2a–2e** in almost quantitative yields.

As a result of cyclization of salts **2a–2e** 2,2-dialkyl-6-brombenzo[*f*]isoindolinium bromides **3a–3e** are formed in 85–98% yields (see the scheme). The structure of the initial amines **1a–1e**, salts **2a–2e**, and products of their cyclization **3a–3e** was established by IR and ^{1}H, ^{13}C NMR spectroscopy.

Salts **2a–2e** undergo cyclization along the cyclization mechanism that we have previously suggested basing on the data of IR spectroscopy [6, 7], and experimental data from [3, 8, 9], according to which the enyne fragment is directly involved into intramolecular cyclization as π^4-fragment, and alkali is the driving force of the cyclization that includes an electron transfer by six-membered cyclic mechanism of counter clockwise direction [3].



R = R' = Me (**a**), Et (**b**), Pr (**c**); R,R' = $(CH_2)_5$ (**d**), $(CH_2)_2O(CH_2)_2$ (**e**).

The effect on the cyclization of substituents at the nitrogen atom and at the aromatic ring was discovered. So, the cyclization of [3-(4-bromophenylprop-2-ynyl)]-dimethylpropargylammonium bromide **2a** in the presence of 0.2 mol of alkali per 1 mol of initial salt occurs at heating of reaction mixture at 80–85°C during 1 h. Meanwhile, the cyclization of 3-(4-chlorophenyl)prop-2-ynyl analog proceeds at room temperature [4]. The cyclization of salts **2b–2d** in the same conditions occurs with self-heating. Because of the poor solubility of salt **2e** in water the cyclization was performed in diluted solution in the presence of ethanol. Even in these conditions the cyclization of salt **2e** occurs with self-heating.

The obtained experimental data agree well with the results of the kinetic study previously performed by Babayan et al. [10, 11] for establishing the cyclization mechanism, and also with the cyclization mechanism that we suggested [3, 6].

Hence at increasing volume of alkyl substituent or the presence of piperidinium cycle the positive charge of nitrogen atom is mostly neutralized, providing easier electron transfer in the cyclization (see the scheme) [3, 6]. At the cyclization of salt **2e** because of the lone electron pair of oxygen atom of morpholinium fragment the positive charge of nitrogen atom is to a large extent neutralized, therefore self-heating occurs even in dilute solution.

In favor of the above said contribute also the data of kinetic investigations, according to which the rate of cyclization of propargyl(3-phenylpropargyl)morpholinium bromide significantly exceeds the rate of cyclization of other analogs [11].

The cyclization of salts **2b–2d** occurs with moderate self-heating at the application of even 0.2 mol of alkali per 1 mol of initial salt, compared to 3-(4-chlorophenyl)prop-2-ynyl analogs, cyclization of which, excluding dimethyl analog, occurs with active self-heating already in the presence of 0.1 mol of alkali per 1 mol of initial salt [4]. This can be explained by less electro-negativity of bromine atom compared to chlorine atom, which hampers the cyclization by six-membered cyclic mechanism.

EXPERIMENTAL

IR spectra of amines **1a–1e** (thin layer) and salts **2a–2e** (films from chloroform), **3a–3e** (mineral oil) were registered on a spectrophotometer Specord 75 IR. ^1H and ^{13}C NMR spectra were recorded on a spectrometer Mercury-300VX Varian (300 and 75 MHz respectively) in DMSO-d_6–CCl_4. Chemical shifts were measured from internal reference TMS. Elemental analysis was carried out on an analyzer vario MICRO cube. Melting points of salts were established on an instrument VEB Wägetechnik Rapido Radebeul Betriebdes. Purity of cyclic salts was monitored by TLC on Silufol UV-254 plates, eluent 1-BuOH–EtOH–H_2O–AcOH, 10 : 2 : 1 : 5, development with iodine vapor.

Amines **1a–1e** were obtained by methods [4, 12].

Dimethyl[3-(4-bromophenyl)prop-2-ynyl]amine (1a). Into a metal cylinder was placed 2.1 g (70 mmol) of paraformaldehyde, 30 mL of dioxane was added, and then was charged 12.7 g (70 mmol) of 4-bromophenylacetylene [13] in 25 mL of dioxane, 3.15 g (70 mmol) of dimethylamine, dissolved in 30 mL of dioxane, 0.3 g of iron chloride, and 0.3 g of copper diacetate. The reaction mixture was heated for 60–65 h at 90–95°C, then acidified with 25% solution of HCl to acid reaction. At low pressure the solvent was distilled off. The reaction mixture and the distillate were treated with diethyl ether to remove unreacted 4-bromophenylacetylene, and the reaction mixture was alkalinized with 20% solution of NaOH. The reaction product was extracted with ether (3 × 70 mL), the ether extract was dried with $MgSO_4$. After distilling off the ether amine **1a** was isolated by vacuum distillation. Yield 6.66 g (40%), bp 122°C (3 mmHg), n_D^{20} 1.5820, mp of picrate 142°C (from anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3050, 3020, 1580 (aromatic ring), 720, 820 (*p*-substituted benzene ring). ^1H NMR

spectrum, δ, ppm: 2.28 s (6H, CH_3), 3.40 s (2H, CH_2), 7.27–7.31 m (2H) and 7.43–7.47 m (2H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 43.4 ($2CH_3$), 47.7 (CH_2), 83.6, 85.7 (C≡C), 121.3, 121.7, 130.9 (2CH), 132.6 (2CH). Found, %: C 55.21; H 5.19; Br 33.83; N 5.75. $C_{11}H_{12}BrN$. Calculated, %: C 55.46; H 5.04; Br 33.61; N 5.88.

Compounds (1b–1e). General method. A mixture of 1.65 g (55 mmol) of paraformaldehyde, 10 g (55 mmol) of 4-bromophenylacetylene, 55 mmol of the corresponding secondary amine dissolved in 100 mL of dioxane, 0.3 g of iron chloride, 0.2 g of copper diacetate were heated at reflux for 60–65 h at 90–95°C, then worked up similarly to the synthesis of amine **1a**.

[3-(4-Bromophenyl)prop-2-ynyl]diethylamine (1b). Yield 6.6 g (45%), bp 145°C (2 mmHg), n_D^{20} 1.5631, mp of picrate 185–188°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3030, 1500 (aromatic ring), 800 (*p*-substituted benzene ring). ^1H NMR spectrum, δ, ppm: 1.06 t (6H, CH_3, *J* 7.2 Hz), 2.53 q (4H, $C\underline{H}_2CH_3$, *J* 7.2 Hz), 3.54 s (2H, $CH_2C{\equiv}C$), 7.24–7.29 m (2H) and 7.42–7.46 m (2H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 12.2 ($2CH_3$), 40.6 (CH_2), 46.5 ($2CH_2$), 83.2, 85.7 (C≡C), 121.2, 121.8, 130.8 (2CH), 132.6 (2CH). Found, %: C 58.42; H 6.16; Br 30.33; N 5.14. $C_{13}H_{16}BrN$. Calculated, %: C 58.65; H 6.01; Br 30.08; N 5.26.

[3-(4-Bromophenyl)prop-2-ynyl]dipropylamine (1c). Yield 7.76 g (48%), bp 150–152°C (3–4 mmHg), n_D^{20} 1.5525, mp of picrate 132–134°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3030, 1480 (aromatic ring), 800 (*p*-substituted benzene ring). ^1H NMR spectrum, δ, ppm: 0.91 t (6H, CH_3, *J* 7.4 Hz), 1.40–1.53 m (4H, $C\underline{H}_2CH_3$), 2.40–2.45 m [4H, $N(CH_2)_2$], 3.52 s (2H, $CH_2C{\equiv}C$), 7.24–7.28 m (2H) and 7.41–7.46 m (2H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 11.4 ($2CH_3$), 20.1 ($2CH_2$), 41.8 (NCH_2), 55.0 [$N(CH_2)_2$], 83.2, 86.0 (C≡C), 121.2, 121.9, 130.9 (2CH), 132.6 (2CH). Found, %: C 60.96; H 6.94; Br 27.51; N 4.63. $C_{15}H_{20}BrN$. Calculated, %: C 61.22; H 6.80; Br 27.21; N 4.76.

[3-(4-Bromophenyl)prop-2-ynyl]piperidine (1d). Yield 6.27 g (41%), bp 175–177°C (4–5 mmHg), n_D^{20} 1.5876, mp 38–40°C (crystallizes at room temperature), mp of picrate 197°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3060, 1590 (aromatic ring), 850, 810 (*p*-substituted benzene ring). ^1H NMR spectrum, δ, ppm: 1.38–1.46 m (2H, CH_2), 1.55–1.62 m (4H, $2CH_2$), 2.45–2.51 m [4H, $N(CH_2)_2$], 3.39 s (2H, $CH_2C{\equiv}C$), 7.26–7.31 m (2H) and 7.42–7.47 m (2H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 23.4 (CH_2), 25.2 ($2CH_2$), 47.6 (NCH_2), 52.5 [$N(CH_2)_2$], 83.3, 86.3 (C≡C), 121.2, 121.8, 130.9 (2CH), 132.6 (2CH). Found, %: C 60.21; H 5.35; Br 29.08; N 5.16. $C_{14}H_{16}BrN$. Calculated, %: C 60.43; H 5.50; Br 28.78; N 5.03.

[3-(4-Bromophenyl)prop-2-ynyl]morpholine (1e). Yield 7.85 g (51%), bp 172–174°C (4–5 mmHg), n_D^{20} 1.5898, mp 43–44°C (crystallizes at room temperature), mp of picrate 180–183°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3030, 1580 (aromatic ring), 800 (*p*-substituted benzene ring). ^1H NMR spectrum, δ, ppm: 2.51–2.55 m [4H, $N(CH_2)_2$], 3.44 s (2H, $CH_2C{\equiv}C$), 3.61–3.65 m [4H, $O(CH_2)_2$], 7.28–7.32 m (2H) and 7.43–7.48 m (2H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 47.2 (NCH_2), 51.6 [$N(CH_2)_2$], 65.8 [$O(CH_2)_2$], 83.7, 85.5 (C≡C), 121.4, 121.6, 131.0 (2CH), 132.6 (2CH). Found, %: C 55.41; H 5.14; Br 28.86; N 4.88. $C_{13}H_{14}BrNO$. Calculated, %: C 55.71; H 5.00; Br 28.57; N 5.00.

In all reactions also the initial 4-bromophenylacetylene was isolated in 5–10% yield.

Salts 2a–2e were obtained in almost quantitative yields by reaction of 5 mmol of amines **1a–1e** with 10 mmol of propargyl bromide in 4–5 mL of acetonitrile (**2b–2e**) or in 10 mL of anhydrous ethyl ether (**2a**). At room temperature white crystalline salts **2a**, **2b**, and **2d–2e** precipitated, at the preparation of salt **2c** acetonitrile was distilled off at low pressure, the salt was washed with anhydrous ether.

[3-(4-Bromophenyl)prop-2-ynyl]dimethylpropargylammonium bromide (2a). Yield 1.77 g (99%), white crystals, mp 183–185°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3020, 3010, 1800 (aromatic ring), 2220 (disubstituted acetylene bond), 2130 (monosubstituted acetylene bond), 840–810 (*p*-substituted benzene ring). ^1H NMR spectrum, δ, ppm: 3.41 s (6H, CH_3), 3.80 t (1H, ≡CH, *J* 2.5 Hz), 4.78 d (2H, $C\underline{H}_2C{\equiv}CH$, *J* 2.5 Hz), 4.92 s (2H, $C\underline{H}_2C{\equiv}C$), 7.55 s (4H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 49.2 ($2CH_3$), 53.1 (NCH_2), 53.7 (NCH_2), 71.5 (≡C), 77.9 (≡C), 82.8 (≡CH), 89.6 (≡C), 119.4, 123.2, 131.2 (2CH), 133.4 (2CH). Found, %: C 47.35; H 4.05; Br 44.57; N 4.05. $C_{14}H_{15}Br_2N$. Calculated, %: C 47.06 H 4.20; Br 44.82; N 3.92.

[3-(4-Bromophenyl)prop-2-ynyl]propargyldiethylammonium bromide (2b). Yield 1.83 g (95%), white crystals, mp 152–154°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3120, 1600 (aromatic ring), 2220

(disubstituted acetylene bond), 2100 (monosubstituted acetylene bond), 810 (*p*-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 1.44 t (6H, CH_3, *J* 7.1 Hz), 3.68 q (4H, $C\underline{H}_2CH_3$, *J* 7.1 Hz), 3.81 t (1H, ≡CH, *J* 2.5 Hz), 4.64 d (2H, $C\underline{H}_2C{\equiv}CH$, *J* 2.5 Hz), 4.77 s (2H, $C\underline{H}_2C{\equiv}C$), 7.54 s (4H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 7.9 (2C, CH_3), 48.5 (NCH_2), 49.1 (NCH_2), 54.6 (2C, $C\underline{H}_2CH_3$), 71.2 (≡C), 77.7 (≡C), 82.6 (≡CH), 89.2 (≡C), 119.3, 123.1, 131.2 (2CH), 133.4 (2CH). Found, %: C 50.16; H 5.09; Br 41.26; N 3.52. $C_{16}H_{19}Br_2N$. Calculated, %: C 49.87; H 4.93; Br 41.56; N 3.64.

[3-(4-Bromophenyl)prop-2-ynyl]propargyldipropylammonium bromide (2c). Yield 1.96 g (95%), white crystals, mp 142°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 2220 (disubstituted acetylene bond), 2100 (monosubstituted acetylene bond), 1600, 1580 (aromatic ring), 810 (*p*-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 1.04 t (6H, CH_3, *J* 7.2 Hz), 1.81–1.95 m (4H, $C\underline{H}_2CH_3$), 3.50–3.58 m [4H, $N(CH_2)_2$], 3.80 t (1H, ≡CH, *J* 2.3 Hz), 4.68 d (2H, $C\underline{H}_2C{\equiv}CH$, *J* 2.3 Hz), 7.54 s (4H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 10.4 ($2CH_3$), 15.5 ($2CH_2$), 49.7 (NCH_2), 50.2 (NCH_2), 60.9 [$N(CH_2)_2$], 71.3 (≡C), 77.8 (≡C), 82.6 (≡CH), 89.4 (≡C), 119.3, 123.1, 131.2 (2CH), 133.3 (2CH). Found, %: C 52.62; H 5.73; Br 38.38; N 3.11. $C_{18}H_{23}Br_2N$. Calculated, %: C 52.30; H 5.57; Br 38.74; N 3.39.

[3-(4-Bromophenyl)prop-2-ynyl]propargylpiperidinium bromide (2d). Yield 1.94 g (98%), white crystals, mp 153–155°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3050, 1580 (aromatic ring), 2240 (disubstituted acetylene bond), 2100 (monosubstituted acetylene bond), 840 (*p*-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 1.65–1.77 m (2H, CH_2), 1.94–2.03 m (4H, $2CH_2$), 3.78–3.83 m [5H, ≡CH, $N(CH_2)_2$], 4.77 d (2H, $C\underline{H}_2C{\equiv}CH$, *J* 2.5 Hz), 4.89 s (2H, $C\underline{H}_2C{\equiv}C$), 7.55 s (4H, C_6H_4). ^{13}C NMR spectrum, δ, ppm: 19.1 ($2CH_2$), 20.1 (CH_2), 49.4 (NCH_2), 50.4 (NCH_2), 57.4 [$N(CH_2)_2$], 71.0 (≡C), 77.4 (≡C), 82.9 (≡CH), 89.5 (≡C), 119.4, 123.1, 131.1 (2CH), 133.4 (2CH). Found, %: C 51.68; H 4.95; Br 40.04; N 3.40. $C_{17}H_{19}Br_2N$. Calculated, %: C 51.38; H 4.79; Br 40.30; N 3.53.

[3-(4-Bromophenyl)prop-2-ynyl]propargylmorpholinium bromide (2e). Yield 1.91 g (96%), white crystals, mp 128–130°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3030, 1580 (aromatic ring), 2220 (disubstituted acetylene bond), 2100 (monosubstituted acetylene bond), 860, 820 (*p*-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 3.78–3.85 m [4H, $O(CH_2)_2$], 3.87 t (1H, ≡CH, *J* 2.4 Hz), 4.04–4.10 m [4H, $N(C\underline{H}_2CH_2)_2O$], 4.92 d (2H, $C\underline{H}_2C{\equiv}CH$, *J* 2.4 Hz), 5.04 s (2H, $C\underline{H}_2C{\equiv}C$), 7.52–7.61 m (4H, C_6H_4). Found, %: C 47.87; H 4.11; Br 40.40; N 3.71. $C_{16}H_{17}Br_2NO$. Calculated, %: C 48.12; H 4.26; Br 40.10; N 3.51.

2,2-Dimethyl-6-bromobenzo[*f*]isoindolinium bromide (3a). To a solution of 3 mmol of salt **2a** in 2.8 mL of water was added 0.2 mL of 3 N solution of KOH (molar ratio salt–base 5 : 1) and the mixture was heated for 1 h at 80–85°C. After cooling the mixture was extracted with diethyl ether to remove possible admixtures, then the precipitate was filtered off. Yield 0.9 g (85%), white crystals, mp 255°C (H_2O). IR spectrum, ν, cm^{-1}: 3030, 1580 (aromatic ring), 890, 825 (1,2,4- and penta-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 3.50 s (6H, CH_3), 5.16 br.s (2H, NCH_2), 5.18 br.s (2H, NCH_2), 7.59 dd (1H, =CH, C_6H_3, *J* 8.7, 2.0 Hz), 7.86 d (1H, =CH, C_6H_3, *J* 8.7 Hz), 7.94 s (1H, =CH, C_6H_2), 7.99 s (1H, =CH, C_6H_2), 8.12 d (1H, =CH, C_6H_3, *J* 2.0 Hz). ^{13}C NMR spectrum, δ, ppm: 51.2 (2C, CH_3), 68.8 [2C, $N(CH_2)_2$], 119.8 (CH), 121.5 (CH), 122.4 (CH), 129.3 (CH), 129.5 (CH), 129.7 (CH), 131.2, 132.2, 132.9, 133.9. Found, %: C 47.41; H 4.02; Br 44.45; N 4.11. $C_{14}H_{15}Br_2N$. Calculated, %: C 47.06; H 4.20; Br 44.82; N 3.92.

Compounds 3b–3d. General method. To a solution of 3 mmol of salt **2b–2d** in 2 mL of water was added 0.2 mL of 3 N solution of KOH (molar ratio salt–base 5 : 1). After 3–4 min the temperature of reaction mixture raised from 25°C to 65–70°C. Cyclic salt **3d** was isolated from reaction mixture by filtration. At the preparation of salts **3b** and **3c** after cooling the reaction mixture was treated with ethyl ether to remove possible admixtures and acidified with aqueous solution of HBr. The solvent was distilled off till dryness at low pressure. From the residue the organic salt was extracted by anhydrous ethanol. From alcohol solution cyclic salts **3b** and **3c** were precipitated by adding ethyl ether.

2,2-Diethyl-6-bromobenzo[*f*]isoindolinium bromide (3b). Yield 1.0 g (87%), white crystals, mp 203–205°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3030, 1580 (aromatic ring), 870, 805 (1,2,4- and penta-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 1.35 t (6H, CH_3, *J* 7.1 Hz), 3.73 q (4H, $C\underline{H}_2CH_3$, *J* 7.1 Hz), 5.17 br.s (2H, NCH_2), 5.20 br.s (2H, NCH_2), 7.57 d.d (1H, =CH, C_6H_3, *J* 8.7, 1.8 Hz), 7.86 d (1H, =CH, C_6H_3, *J* 8.7 Hz), 7.89 s (1H, =CH, C_6H_2), 7.94 s

(1H, =CH, C_6H_2), 8.12 d (1H, =CH C_6H_3, *J* 1.8 Hz). ^{13}C NMR spectrum, δ, ppm: 8.7 (2C, CH_3), 55.6 (2C, $\underline{C}H_2CH_3$), 65.4 [2C, $N(CH_2)_2$], 119.7, 120.8 (CH), 121.7 (CH), 129.2 (CH), 129.5 (CH), 129.6 (CH), 131.3, 132.3, 133.0, 133.9. Found, %: C 50.21; H 4.75; Br 41.22; N 3.84. $C_{16}H_{19}Br_2N$. Calculated, %: C 49.87; H 4.93; Br 41.56; N 3.64.

2,2-Dipropyl-6-bromobenzo[*f*]isoindolinium bromide (3c). Yield 1.08 g (87%), white crystals, mp 175°C (anhydrous EtOH). IR spectrum, ν, cm^{-1}: 3050, 1600 (aromatic ring), 880, 805 (1,2,4- and penta-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 0.97 t (6H, CH_3, *J* 7.2 Hz), 1.67–1.80 m (4H, $C\underline{H}_2CH_3$), 3.57–3.65 m (4H, $C\underline{H}_2CH_2CH_3$), 5.20 s (2H, NCH_2), 5.22 s (2H, NCH_2), 7.57 d.d (1H, =CH, C_6H_3, *J* 8.6, 2.0 Hz), 7.86 d (1H, =CH, C_6H_3, *J* 8.6 Hz), 7.88 s (1H, =CH, C_6H_2), 7.93 s (1H, =CH C_6H_2), 8.12 d (1H, =CH, C_6H_3, *J* 2.0 Hz). ^{13}C NMR spectrum, δ, ppm: 10.3 (2C, CH_3), 16.5 (2C, $\underline{C}H_2CH_3$), 62.6 (2C, $\underline{C}H_2CH_2CH_3$), 66.2 (2C, NCH_2), 119.7, 120.6 (CH), 121.5 (CH), 129.1 (CH), 129.5 (2CH), 131.3, 132.4, 133.1, 133.9. Found, %: C 51.95; H 5.74; Br 39.11; N 3.21. $C_{18}H_{23}Br_2N$. Calculated, %: C 52.30; H 5.57; Br 38.74; N 3.39.

2,2-Pentamethylene-6-bromobenzo[*f*]isoindolinium bromide (3d). Yield 1.14 g (96%), white crystals, mp 240°C (EtOH). IR spectrum, ν, cm^{-1}: 3080, 1580 (aromatic ring), 890, 805 (1,2,4- and penta-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 1.74–1.83 m (2H, CH_2), 1.95–2.03 m (4H, $2CH_2$), 3.74 –3.79 m [4H, $N(CH_2)_2$], 5.19 s (2H, NCH_2), 5.21 s (2H, NCH_2), 7.58 d.d (1H, =CH, C_6H_3, *J* 8.7, 2.0 Hz), 7.87 d (1H, =CH, C_6H_3, *J* 8.7 Hz), 7.93 s (1H, =CH, C_6H_2), 7.97 s (1H, =CH, C_6H_2), 8.13 d (1H, =CH, C_6H_3, *J* 2.0 Hz). ^{13}C NMR spectrum, δ, ppm: 20.4 (CH_2), 20.8 ($2CH_2$), 59.2 [$N(CH_2)_2$], 65.7 [$N(CH_2)_2$], 119.8, 121.5 (CH), 122.5 (CH), 129.2 (CH), 129.5 (2CH), 131.2, 131.6, 132.3, 133.9. Found, %: C 51.72; H 4.64; Br 39.99; N 3.73. $C_{17}H_{19}Br_2N$. Calculated, %: C 51.38; H 4.79; Br 40.30; N 3.53.

6-bromo-1,3-dihydrospiro(benzo[*f*]isoindol-2,4'-morpholin)-2-ium bromide (3e). A mixture of 3 mmol of salt **2e**, 3.5 mL of water, and 2 mL of ethanol was stirred for 3–5 min at 65°C till it was homogeneous, cooled to 40°C, and 0.2 mL of 3 N solution of KOH was added (molar ratio salt–basis 5 : 1). During 2–3 min the temperature of the reaction mixture raised to 75–80°C. The precipitate formed after 10–15 min was filtered off. Yield 1.17 g (97%), white crystals, mp 258–259°C (EtOH). IR spectrum, ν, cm^{-1}: 3030, 1590 (aromatic ring), 880, 810 (1,2,4- and penta-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 3.82–3.87 m [4H, $O(CH_2)_2$], 4.06–4.11 m [4H, $(C\underline{H}_2CH_2)_2O$], 5.38 br.s (2H, NCH_2), 5.40 br.s (2H, NCH_2), 7.58 d.d (1H, =CH, C_6H_3, *J* 8.7, 2.0 Hz), 7.87 d (1H, =CH, C_6H_3, *J* 8.7 Hz), 7.94 s (1H, =CH, C_6H_2), 7.99 s (1H, =CH, C_6H_2), 8.13 d (1H, =CH, C_6H_3, *J* 2.0 Hz). ^{13}C NMR spectrum, δ, ppm: 58.2 [$N(\underline{C}H_2CH_2)_2O$], 61.3 [$O(CH_2)_2$], 65.9 [$N(CH_2)_2$], 119.8, 121.6 (CH), 122.6 (CH), 129.2 (CH), 129.5 (2CH), 131.2, 131.3, 131.9, 133.9. Found, %: C 48.51; H 4.11; Br 39.65; N 3.35. $C_{16}H_{17}Br_2NO$. Calculated, %: C 48.12; H 4.26; Br 40.10; N 3.51.

REFERENCES

1. Chukhadzhyan, É.O., *Chem. Heterocycl. Compd*., 1993, vol. 29, p. 363. doi 10.1007/BF00529871
2. Chukhajian, E.O., Shahkhatuni, K.G., and Chukhajian, El.O., *Chem. Sustainable Develop*., 2013, vol. 21, p. 263.
3. Chukhajian, E.O., Nalbandyan, M.K., Gevorkyan, H.R., Chukhajian, El.O., Panosyan, H.A., Ayvazyan, A.G., and Tamazyan, R.A., *J. Heterocycl. Chem*., 2008, p. 687.
4. Babayan, A.T., Chukhadzhyan, E.O., and Manazyan, L.A., *Arm. Khim. Zh*., 1978, vol. 31, p. 489.
5. Babayan, A.T., Chukhadzhyan, E.O., and Babayan, G.T., *Zh. Org. Khim*., 1970, vol. 6, p. 1161.
6. Chukhadzhyan, E.O., Gevorkyan, A.R., Chukhadzhyan, El.O., and Kinoyan, F.S., *Russ. J. Org. Chem*., 2005, vol. 41, p. 358. doi 10.1007/s11178-005-0170-6
7. Chukhadzhyan. E.O., Nalbandyan, M.K., Gevorkyan, A.R., and Kinoyan, F.S., *Arm. Khim. Zh*., 2007, vol. 60, p. 83.
8. Chukhadzhyan, E.O., Gevorkyan, A.R., Khachatryan, A.A., Chukhadzhyan, El.O., and Panosyan, G.A., *Chem. Heterocycl. Compd*., 2006, vol. 42, p. 1151. doi 10.1007/s10593-006-0219-7
9. Chukhajian, E.O., Nalbandyan, M.K., Gevorkyan, A.R., Shakhatuni, K.G., and Panosyan, G.A., *Chem. Heterocycl. Compd*., 2008, vol. 44, p. 671. doi 10.1007/s10593-008-0090-9
10. Abramyan-Babayan, I.A. and Babayan, A.T., *Arm. Khim. Zh*., 1972, vol. 25, p. 19.
11. Babayan, A.T., Atomyan, A.V., Abramyan, I.A., Kislina, I.S., and Vinnik, M.I., *Arm. Khim. Zh*., 1975, vol. 28, p. 965.
12. Chukhajian, E.O., Khachatryan, A.A., Gevorkyan, A.R., and Panosyan, G.A., *Chem. Heterocycl. Compd*., 2007, vol. 43, p. 701. doi 10.1007/s10593-007-0114-x
13. Dufraisse, C. and Dequesnes, A., *Bull. Soc. Chim. Fr*., 1931, vol. 49, p. 1880.