Chemistry of Heterocyclic Compounds, Vol. 49, No. 9, December, 2013 (Russian Original Vol. 49, No. 9, September, 2013)

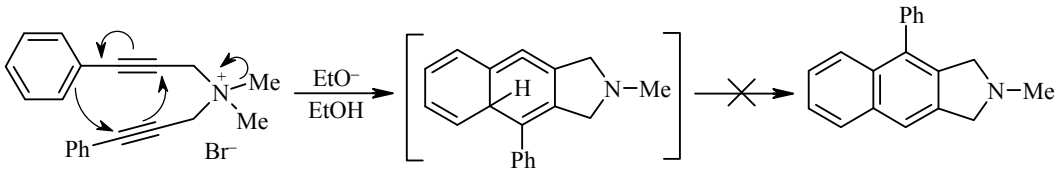
BASE-CATALYZED INTRAMOLECULAR DIELS–ALDER CYCLIZATION OF DIALKYL(3-ARYLPROP-2-YN-1-YL)-(3-PHENYLPROP-2-EN-1-YL)AMMONIUM BROMIDES IN AQUEOUS SOLUTION

E. O. Chukhajian[1], L. V. Ayrapetyan[1]*, El. O. Chukhajian[1], and H. A. Panosyan[1]

Dialkyl(3-arylprop-2-yn-1-yl)(3-phenylprop-2-en-1-yl)ammonium bromides, in contrast to their allyl analogs containing a 3-arylprop-2-en-1-yl group, undergo cyclization in aqueous solution in the presence of base upon prior heating to give potentially biologically active 2,2-dialkyl-6-chloro-4-phenyl-3a,4-dihydrobenzo[f]isoindolinium bromides in almost quantitative yield. Heat is released in the course of these reactions. We found that the introduction of a phenyl group at position 3 of the allyl fragment facilitates the cyclization. This is the first report of a base-catalyzed intramolecular cyclization of allyl analogs of dialkyl(3-arylprop-2-yn-1-yl)ammonium salts.

Keywords: dialkyl(3-arylprop-2-yn-1-yl)(3-phenylprop-2-en-1-yl)ammonium bromides, 2,2-dialkyl-6-chloro-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium bromides, base-catalyzed intramolecular cyclization.

In 1963, Iwai and Hiraoka [1] studied the reaction of dimethylbis(3-phenylprop-2-yn-1-yl)ammonium bromide with sodium ethylate in absolute ethanol as well as with aqueous sodium hydroxide. According to their report 2-methyl-4-phenylbenzo[*f*]isoindoline should have been formed according to a scheme below that would involve nucleophilic substitution of a methyl group and cyclization.



Despite these expectations, an amine product was not formed, suggesting to the authors that the second phenyl group at position 3 of the propargyl fragment creates steric hindrance in comparison to a hydrogen atom for the cyclization of this salt [1]. In our previous work [2], we showed that dialkyl-bis(3-phenylprop-2-yn-1-yl)ammonium bromides undergo cyclization upon heating in aqueous solution even in the absence of base.

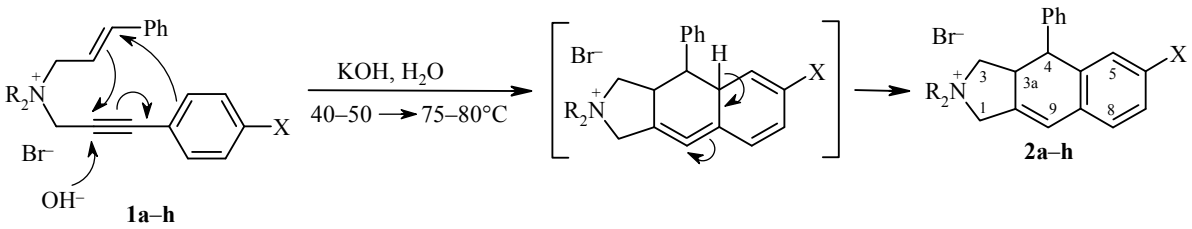
*To whom correspondence should be addressed, e-mail: shhl@mail.ru.

[1]Scientific and Technological Center of Organic and Pharmacological Chemistry of National Academy of Sciences of the Republic of Armenia, 26 Azatutyan Ave., Yerevan 0014, Armenia.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1367-1374, September, 2013. Original article submitted April 16, 2013.

 0009-3122/13/4909-1274©2013 Springer Science+Business Media New York

These findings indicate that a second phenyl group facilitates cyclization. Based on this, we suggested that a second phenyl group at position 3 of the allyl fragment in 3-phenylprop-2-yn-1-yl salts should also facilitate cyclization. In order to check this hypothesis, we studied the behavior of dialkyl(3-phenylprop-2-en-1-yl)-(3-phenylprop-2-yn-1-yl)ammonium bromides under base catalysis conditions. Contrary to our expectations, the cyclization of these salts required rather rigorous conditions [3] than for the cyclization of their allyl analogs [4-7]. Due to poor solubility of these salts in water, the cyclization was carried out in aqueous ethanol. It is not clear whether the reason for the usage of more rigorous conditions for this cyclization lies in use of aqueous ethanol as the solvent or is a consequence of the second phenyl group at position 3 of the allyl group. In order to solve this problem, we carried out the cyclization of dialkyl(3-phenylprop-2-en-1-yl)(3-phenyl-2-yn-1-yl)ammonium bromides **1a-e** and [3-(4-chlorophenyl)prop-2-yn-1-yl] analogs **1f-h** under conditions analogous to the cyclization of dimethylbis(3-phenylpropyn-2-yl)ammonium bromides [2], i.e., the mixture consisting of the salt, water, and 2 N aqueous KOH (the salt:alkali molar ratio was 5:1) was heated at 40-50°C for 5-6 min. Under these conditions, the starting salt completely dissolves and cyclization proceeds with a heat release. The temperature of the reaction mixture rises to 75-80°C. In the case of salts **1f**,**g** the temperature of the reaction mixture rises only to 55-60°C, and additional heating of the reaction mixture at 70-72°C for 15-20 min is required for complete conversion.



1a–h **2a–h**

a R = Me, **b**,**f** R = Et, **c** $R_2 = (CH_2)_4$, **d**,**g** $R_2 = (CH_2)_5$, **e**,**h** $R_2 = (CH_2)_2O(CH_2)_2$,
a–e X = H, **f–h** X = Cl

Final products **2a-h** are formed according to the mechanism, which we have already proposed for the cyclization of salts, containing an allyl or propargyl group along with the 3-alkenyl or 3-arylpropagyl fragments [8-10]. According to the proposed mechanism, the enyne fragment directly participates in the cyclization, while the base serves as the "driving force" of the process involving electron transfer through a six-membered cyclic mechanism.

Under these conditions, in contrast to cyclization in aqueous ethanol solution [3], we obtain only 2,2-dialkyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium bromides **2a-e** (83-92% yield) and their 6-chloro analogs **2f-h** (85-92% yield).

The formation of these compounds may be attributed to the very rapid rate of cyclization of salts **1a-h** in aqueous media under mild conditions and the inability of cyclic products **2a-h** to isomerize to give derivatives of 9-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium salts as observed in the case of bromides **1b**,**d** upon cyclization in aqueous ethanol solution in the presence of 0.5 equivalent of aqueous alkali upon heating for 5-6 h [3].

We should note that the ^{1}H and ^{13}C NMR spectra of 2,2-dialkyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium bromides and their 9-phenyl isomers [3] show characteristic differences. Thus, the methylene protons at position 1 in the ^{1}H NMR spectra of 4-phenyl derivatives **2a-h** appear at 4.6-5.0 ppm as an AB spin system with $^2J \sim 16.0$ Hz. The ^{13}C NMR spectra of these compounds have two signals for the 3a,4-CH groups at 40.2-41.9 and 48.3-48.6 ppm. The assignment of these signals to the 3a,4-CH groups was made using the results of DEPT and HMQC experiments. The ^{13}C NMR spectra of the 9-aryl derivatives have a signal for only one CH group at 35 ppm, while the other signals for sp^3-carbon atoms were assigned to CH_2 groups using the DEPT experimental data [3].

In order to establish the effect of the phenyl group at position 3 of the allyl fragment on the course of the cyclization, we carried out the reaction of dimethylallyl(3-phenylprop-2-yn-1-yl)ammonium bromide

lacking a phenyl group under the conditions for cyclization of the 3-phenyl analogs. We added 2 N aqueous KOH to a homogeneous solution consisting of 8 mmol salt and 1.8 ml water (the salt:alkali molar ratio was 5:1). No heat liberation was noted upon adding the alkali solution. The reaction course was followed by IR spectroscopy, occasionally taking probes of the reaction mixture. The probes were washed with ether to remove possible side products, and the spectra were recorded in a water-resistant calcium fluoride cell. We should note that we initially recorded the IR spectra of an aqueous solution of the starting salt without added alkali. The intensity of the absorption band at 2200-2220 cm^{-1} for the doubly-substituted acetylenic bond remained unchanged even upon prolonged standing at room temperature (probes were taken three times every 24 h). Then, KOH (0.1 g, 1.8 mmol) was added to the reaction mixture, which was then heated at 85-87°C for 2.5 h. A probe was taken for recording the IR spectrum. Under these conditions, the absorption characteristic for the doubly-substituted acetylenic bond had already disappeared. A precipitate of 2,2-dimethyl-3a,4-dihydrobenzo[*f*]isoindolinium bromide formed after maintenance of the reaction mixture for 20-25 min at room temperature. The melting point of the precipitate was 243-245°C. The melting point of a mixed sample of this precipitate and an authentic sample of the indicated salt was undepressed [4]. Thus, we conclude that the IR spectral data and the relative capacities of the allyl salts to undergo cyclization [4-7] suggest that the phenyl group at position 3 of the allyl fragment facilitates the cyclization analogously to 3-phenylpropargyl salts [2].

This result is the only case of a base-catalyzed cyclization of ammonium salts containing a 3-arylprop-2-yn-1-yl group along with an allyl group [4-7].

We should note that bromides **2a**,**e** obtained in aqueous ethanol [3] and aqueous solutions have the same structure as indicated by ^{1}H NMR spectroscopy but different melting points. Analogous studies by Laird and Ollis [11, 12] appeared after publication of our investigation of the cyclization of dialkyl(allyl)(3-arylpropargyl)ammonium bromides [4]. These authors also studied the base-catalyzed cyclization of dimethyl(3-phenylprop-2-en-1-yl)(3-phenylprop-2-yn-1-yl)ammonium bromide (**1a**) under conditions analogous to the conditions for the cyclization of dimethylbis(3-phenylprop-2-yn-1-yl)- [2] and dimethyl(propargyl)(3-phenylprop-2-yn-1-yl)ammonium bromides [13, 14]. Cyclization at room temperature gave 2,2-dimethyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium bromide (**2a**) in 56% yield. The structure of bromide **2a** was supported by ^{1}H NMR spectroscopy. The melting point of bromide salt **2a** given by these authors (158-160°C) does not correspond to the melting point of 2,2-dimethyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium bromide (**2a**), which we obtained in the cyclization of dimethyl(3-phenylprop-2-en-1-yl)(3-phenylprop-2-yn-1-yl)ammonium bromide both in aqueous ethanol solution [3] and in water. After neutralization of the mother liquor by adding 48% hydrobromic acid and evaporation, these authors isolated the remaining fraction of the salt (44% yield) but neither the melting point nor spectral data were given for the isolated salt.

Our studies have applied significance as well as importance for basic research; in contrast to the results of previous investigation [3], potentially biologically active 2,2-dialkyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium bromides **2a-e** and their 6-chloro analogs **2f-h** were isolated after 30 min in almost quantitative yield. These salts had been difficult to obtain by other methods.

2,2-Dialkyl-3a,4-dihydroisoindolinium and 2,2-dialkyl-3a,4-dihydrobenzo[*f*]isoindolinium bromides have pronounced hypertensive action and stimulate respiration. Their condensed analogs, synthesized in our previous work [15] have hypotensive and non-narcotic analgesic activity as well as anticoagulation activity, were protected by USSR Inventor's Certificates [16-24] and Republic of Armenia patents [25, 26].

The structures of the starting bromides (in particular, bromides **1f-h**, which are reported for the first time) and cyclic salts **2a-h** were demonstrated by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy data. Double resonance and two-dimensional COSY, NOESY, DEPT, and HMQC spectroscopy were used to confirm the structure of salts **2a-h**.

Thus, the cyclization of dialkyl(3-arylprop-2-yn-1-yl)(3-phenylprop-2-en-1-yl)ammonium bromide in aqueous solution upon brief heating in the presence of alkali gives potentially biologically active 2,2-dialkyl-4-phenyl-6-3a,4-dihydrobenzo[*f*]isoindolinium bromides in almost quantitative yield. These results differ from the data for previous attempts to cyclize analogous salts in aqueous ethanol solution, in which 9-phenyl isomers

were obtained under more rigorous conditions. It was also shown that the introduction of a phenyl group at position 3 of the allyl fragment facilitates cyclization.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75 IR spectrometer in chloroform. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 VX spectrometer (300 and 75 MHz, respectively) in DMSO-d_6–CCl_4 (1:3) with TMS as internal standard. The elemental analysis for C, H, and N was carried out on a compact Vario MICRO cube. The analysis for bromide anions was carried out by the method of Abramyan and Sargsyan [27]. The melting points were determined on an instrument manufactured by VEB Wägetechnik Rapido Radebeul Betrieb of the VEB Kombinat NAGEMA in the German Democratic Republic. The purity of the cyclic salts was monitored by thin-layer chromatography on Silufol UV-254 plates with 10:2:1:5 *n*-BuOH–EtOH–H_2O–AcOH as the eluent. Iodine vapor was used for visualization.

Starting dialkyl(3-phenylprop-2-yn-1-yl)- and dialkyl[3-(4-chlorophenyl)prop-2-yn-1-yl)amines were obtained according to our previous procedures [28, 29, 30]. Starting salts **1a-e** were prepared according to our reported procedure [3].

Synthesis of Bromides 1f-h (General Method). Phenylallyl bromide [31] (4.33 g, 22 mmol) was added to a solution of the corresponding *N*-[3-(4-chlorophenyl)prop-2-yn-1-yl]amine in ether (10 ml) and acetonitrile (4 ml), and the mixture was left at room temperature overnight to give a precipitate of salt **1f-h**.

Diethyl[3-(4-chlorophenyl)prop-2-yn-1-yl](3-phenylprop-2-en-1-yl)ammonium Bromide (1f). Yield 5.8 g (93%), white hygroscopic crystals, mp 85-87°C. IR spectrum, ν, cm^{-1}: 3050, 3010 (Ar), 2220 (C≡C), 1630 (–CH=CH–), 1600, 1580, 810 (Ar), 780, 720, 680 (Ph). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.61-7.54 (5H, m, H Ar); 7.39-7.25 (4H, m, H Ar), 7.09 (1H, d, *J* = 15.6, PhC<u>H</u>=); 6.53 (1H, dt, *J* = 15.6, *J* = 7.3, =C<u>H</u>CH_2); 4.77 (2H, s, C≡CCH_2); 4.37 (2H, d, *J* = 7.3, =CHC<u>H</u>$_2$); 3.63 (4H, q, *J* = 7.1, 2C<u>H</u>$_2$$CH_3$); 1.45 (6H, t, *J* = 7.1, 2CH_2C<u>H</u>$_3$). Found, %: C 63.54; H 6.18; Br 19.54; N 3.28. $C_{22}H_{25}BrClN$. Calculated, %: C 63.09; H 6.02; Br 19.08; N 3.34.

[3-(4-Chlorophenyl)prop-2-yn-1-yl](3-phenylprop-2-en-1-yl)piperidinium Bromide (1g). Yield 6.1 g (95%), shiny white crystals, mp 170-172°C. IR spectrum, ν, cm^{-1}: 3010 (Ar), 2240 (C≡C), 1630 (–CH=CH–), 1600, 1580, 840, 810 (Ar), 710, 700, 680 (Ph). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.60-7.56 (4H, m, H Ar); 7.40-7.25 (5H, m, H Ar); 7.08 (1H, d, *J* = 15.6, PhC<u>H</u>=); 6.54 (1H, dt, *J* = 15.6, *J* = 7.4, =C<u>H</u>CH_2); 4.86 (2H, s, C≡CCH_2); 4.51 (2H, d, *J* = 7.4, =CHC<u>H</u>$_2$); 3.79-3.72 (4H, m, 2,6-CH_2 piperidine); 2.08-1.92 (4H, m, 3,5-CH_2 piperidine); 1.80-1.70 (2H, m, 4-CH_2 piperidine). Found, %: C 64.58; H 6.01; Br 18.97; N 3.42. $C_{23}H_{25}BrClN$. Calculated, %: C 64.12; H 5.85; Br 18.55; N 3.25.

[3-(4-Chlorophenyl)prop-2-yn-1-yl](3-phenylprop-2-en-1-yl)morpholinium Bromide (1h). Yield 5.6 g (87%), white crystals, mp 153-155°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3060, 3010 (Ar), 2220 (C≡C), 1630 (–CH=CH–), 1600, 1580, 840, 810 (Ar), 720, 700, 680 (Ph). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.62-7.57 (4H, m, H Ar); 7.40-7.28 (5H, m, H Ar); 7.12 (1H, d, *J* = 15.7, PhC<u>H</u>=); 6.57 (1H, dt, *J* = 15.7, *J* = 7.5, =C<u>H</u>CH_2); 5.03 (2H, s, C≡CCH_2); 4.67 (2H, d, *J* = 7.5, =CHC<u>H</u>$_2$); 4.19-4.02 (4H, m, N(C<u>H</u>$_2$$CH_2$)$_2$O); 3.85-3.76 (4H, m, N($CH_2$C<u>H</u>$_2$)$_2$O). ^{13}C NMR spectrum, δ, ppm: 141.7; 135.0; 134.7 (=CH); 133.3; 128.3 (CH); 128.2 (2CH); 128.0 (2CH); 127.1 (2CH); 119.0 (2CH); 114.9 (CH); 89.7, 77.9 (C≡C); 61.2 (NCH_2); 59.6 (N(CH_2<u>C</u>H_2)$_2$O); 56.2 (N(<u>C</u>$H_2$$CH_2$)$_2$O); 50.1 ($CH_2$). Found, %: C 60.58; H 5.12; Br 18.93; N 3.45. $C_{22}H_{23}BrClNO$. Calculated, %: C 61.06; H 5.36; Br 18.46; N 3.24.

Intramolecular Cyclization of Bromides 1a-h (General Method). A mixture consisting of salt **1a-h** (2.8 mmol), water (1-2 ml), and 2 N aqueous KOH solution (0.28 ml) (the salt:KOH molar ratio was 5:1) was heated on a warm water bath for 5-6 min. The salt completely dissolved at 40-50°C. Heat generation rapidly ensued, and the temperature of the reaction mixture rose to 75-80°C. In the case of salts **1g**,**h**, the temperature rose only to 55-60°C and the mixture was heated at 70-72°C for 15-20 min to insure complete conversion. After

maintenance at room temperature for 1.0-1.5 h, the mixture was extracted with ether (2×15 ml) to remove possible side products. Filtration of the reaction mixture gave cyclic salts **2a-h**, which were then recrystallized from water or absolute ethanol.

2,2-Dimethyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium Bromide (2a). Yield 0.87 g (87%), shiny white crystals, mp 245-247°C (H_2O). IR spectrum, ν, cm^{-1}: 3060, 3020, 3000, 1940 (Ar), 1630 (C=CH), 1600, 1580, 770, 740, 700, 670 (Ar). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.46-7.31 (5H, m, H Ph); 7.21-7.13 (2H, m, H Ar); 7.04 (1H, td, *J* = 7.2, *J* = 2.2, H Ar); 6.73-6.70 (1H, m, H-9); 6.54 (1H, br. d, *J* = 7.6, H Ar); 4.78-4.64 (2H, m, 1-CH_2); 4.21 (1H, d, *J* = 14.0, 4-CH); 3.88-3.61 (3H, m, 3-CH_2, 3a-CH); 3.43 (3H, s, CH_3); 3.25 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 139.8; 137.2; 135.5; 133.5 (=C); 128.4; 128.4; 127.0; 126.8; 126.4; 126.3; 126.1; 121.2 (=CH); 68.0, 67.4 (1,3-CH_2); 51.9 (NCH_3); 51.4 (NCH_3); 48.6 (4-CH); 41.9 (3a-CH). Found, %: C 66.95; H 5.97; Br 22.91; N 4.14. $C_{20}H_{22}BrN$. Calculated, %: C 67.42; H 6.22; Br 22.43; N 3.93.

2,2-Diethyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium Bromide (2b). Yield 0.9 g (83%), shiny white crystals, mp 127-130°C (H_2O). IR spectrum, ν, cm^{-1}: 3060, 3020, 3000 (Ar), 1940 (Ph), 1640 (C=CH), 1610, 1570 (Ar), 770, 740, 710, 680 (Ph). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.45-7.30 (5H, m, H Ph); 7.21-7.12 (2H, m, H Ar); 7.02 (1H, td, *J* = 7.5, *J* = 2.0, H Ar); 6.71 (1H, q, *J* = 2.3, H-9); 6.50 (1H, br. d, *J* = 7.5, H Ar); 4.67 (2H, br. s, 1-CH_2); 4.23 (1H, d, *J* = 14.3, 4-CH); 3.82-3.37 (7H, m, 3-CH_2, 3a-CH, 2C$\underline{H_2}CH_3$); 1.33 (3H, t, *J* = 7.1, $CH_2C\underline{H_3}$); 1.26 (3H, t, *J* = 7.1, $CH_2C\underline{H_3}$). ^{13}C NMR spectrum, δ, ppm: 139.9; 137.4; 135.1; 133.5 (=C); 128.6 (2C); 127.1; 126.9; 126.5; 126.4; 126.2; 121.3 (=CH); 64.3, 64.2 (1,3-CH_2); 54.9 (N$\underline{C}H_2CH_3$); 53.4 (N$\underline{C}H_2CH_3$); 48.6 (4-CH); 41.3 (3a-CH); 8.5 ($NCH_2\underline{C}H_3$); 8.2 ($NCH_2\underline{C}H_3$). Found, %: C 69.22; Br 21.23; H 6.99; N 3.85. $C_{22}H_{26}BrN$. Calculated, %: C 68.75; H 6.82; Br 20.79; N 3.64.

4-Phenyl-2,2-tetramethylene-3a,4-dihydrobenzo[*f*]isoindolinium Bromide (2c). Yield 0.9 g (83%). The sample of salt **2c** obtained by the method described above did not give a depressed melting point in a mixed sample with an authentic sample [3].

2,2-Pentamethyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium Bromide (2d). Yield 1.0 g (90%), white crystals, mp 170-172°C (H_2O). IR spectrum, ν, cm^{-1}: 3060, 3030, 3010 (Ar), 1940 (Ph), 1630 (C=CH), 1610, 1580 (Ar), 780, 760, 720, 690 (Ph). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.46-7.32 (5H, m, H Ph); 7.23-7.11 (2H, m, H Ar); 7.03 (1H, ddd, *J* = 7.7, *J* = 6.9, *J* = 2.0, H Ar); 6.72 (1H, q, *J* = 2.0, H-9); 6.51 (1H, br. d, *J* = 7.7, H Ar); 4.81 (1H, br. d, *J* = 16.0, 1-CH_2); 4.69 (1H, br. d, *J* = 16.0, 1-CH_2); 4.21 (1H, dt, *J* = 14.3, *J* = 6.4, H-3a); 3.87-3.45 (7H, m, 3-CH_2, 4-CH, 2,6-CH_2 piperidine); 2.00-1.55 (6H, m, 3,4,5-CH_2 piperidine). ^{13}C NMR spectrum, δ, ppm: 139.8; 137.3; 134.9; 133.4 (=C); 128.5 (2C); 127.0; 126.9; 126.4; 126.3; 126.1; 121.4 (=CH); 65.1, 63.6 (1,3-CH_2); 60.5, 58.9 (2,6-CH_2 piperidine); 48.7 (4-CH); 40.8 (3a-CH); 20.9, 20.5, 20.4 (3,4,5-CH_2 piperidine). Found, %: C 70.16; H 6.78; Br 20.64; N 3.75. $C_{23}H_{26}BrN$. Calculated, %: C 69.70; H 6.61; Br 20.16; N 3.53.

4-Phenylspiro-3a,4-dihydrobenzo[*f*]isoindoline-2,4'-morpholinium Bromide (2e). Yield 1.0 g (92%), shiny crystals, mp 210-213°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3060, 3020, 3010 (Ar), 1940 (Ph), 1630 (C=CH), 1620, 1590 (Ar), 770, 760, 720, 680 (Ph). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.46-7.31 (5H, m, H Ph); 7.25-7.11 (2H, m, H Ar); 7.03 (1H, td, *J* = 7.5, *J* = 1.7, H Ar); 6.73 (1H, br. q, *J* = 2.3, H-9); 6.52 (1H, br. d, *J* = 7.5, H Ar); 5.04 (1H, dd, *J* = 16.0, *J* = 1.5) and 4.85 (1H, dt, *J* = 16.0, *J* = 2.1, 1-CH_2); 4.25 (1H, d, *J* = 14.4, 4-CH); 4.07-3.71 (9H, m) and 3.66-3.58 (2H, m, 3-CH_2, 3a-CH, N($C\underline{H_2}C\underline{H_2}$)$_2$O). ^{13}C NMR spectrum, δ, ppm: 139.5; 138.9; 135.2; 132.3; 132.1 (=C); 128.7; 127.4; 127.2 (3C, =CH); 126.4; 120.4 (3C); 66.2, 63.5 (1,3-CH_2); 61.4, 61.0 (N($CH_2\underline{C}H_2$)$_2$O); 59.4, 58.1 (N($\underline{C}H_2CH_2$)$_2$O); 48.3 (4-CH); 40.2 (3a-CH). Found, %: C 65.86; H 5.83; Br 20.55; N 3.73. $C_{22}H_{24}BrNO$. Calculated, %: C 66.34; H 6.07; Br 20.06; N 3.52.

6-Chloro-2,2-diethyl-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium Bromide (2f). Yield 1.0 g (86%), white crystals, mp 165-167°C (H_2O). IR spectrum, ν, cm^{-1}: 1940 (Ph), 1620 (C=CH), 1580 (Ar), 870 (Ph), 805 (Ar), 770, 730, 710, 690 (Ph). ^1H NMR spectrum , δ, ppm (*J*, Hz): 7.48-7.34 (5H, m, H Ph); 7.25-7.14 (2H, m, H Ar); 6.72 (1H, br. s, H-9); 6.41 (1H, br. s, H Ar); 4.72 (2H, s, 1-CH_2); 4.31 (1H, d, *J* = 14.3, 4-CH); 3.86-3.38 (7H, m, 3-CH_2, 3a-CH, N($C\underline{H_2}CH_3$)$_2$); 1.33 (3H, t, *J* = 7.1) and 1.27 (3H, t, *J* = 7.1, N($CH_2C\underline{H_3}$)$_2$). Found, %: C 63.56; H 6.17; Br 19.56; N 3.56. $C_{22}H_{25}BrClN$. Calculated, %: C 63.09; H 6.02; Br 19.08; N 3.34.

6-Chloro-2,2-pentamethylene-4-phenyl-3a,4-dihydrobenzo[*f*]isoindolinium Bromide (2g). Yield 1.0 g (85%), white crystals, mp 158-160°C (EtOH–H_2O). IR spectrum, ν, cm^{-1}: 1940, 1620 (C=CH), 1580, 3010 (Ar), 870 (Ph), 805, 820 (Ar), 690, 710, 730, 770. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.49-7.34 (5H, m, H Ph); 7.21 (1H, d, *J* = 8.1, H Ar); 7.15 (1H, ddd, *J* = 8.1, *J* = 2.0, *J* = 0.8, H Ar); 6.72 (1H, br. s, H-9); 6.42 (1H, br. s, H Ar); 4.84 (1H, br. d, *J* = 16.1) and 4.71 (1H, br. d, *J* = 16.1, 1-CH_2); 4.27 (1H, d, *J* = 13.4, 4-CH); 3.91-3.41 (7H, m, 3-CH_2, 3a-CH, 2,6-CH_2 piperidine); 2.00-1.54 (6H, m, 3,4,5-CH_2 piperidine). ^{13}C NMR spectrum, δ, ppm: 139.6; 138.9; 135.6; 132.2; 132.1 (=C); 128.7; 128.5 (br. s); 127.4; 127.2 (=CH); 126.3 (C-2,3,5,6 Ph); 126.2 (br. s); 120.3 (CH); 65.3, 63.6 (1,3-CH_2); 60.5, 58.7 (2,6-CH_2 piperidine); 48.3 (4-CH); 40.4 (3a-CH); 20.9, 20.4, 20.3 (3,4,5-CH_2 piperidine). Found, %: C 63.65; H 5.59; Br 18.29; N 3.46. $C_{23}H_{25}BrClN$. Calculated, %: C 64.12; H 5.85; Br 18.55; N 3.25.

6-Chloro-4-phenyl-3a,4-dihydrobenzo[*f*]isoindoline-2,4'-mopholinium Bromide (2h). Yield 1.1 g (92%), shiny white crystals, mp 170-172°C (H_2O). IR spectrum, ν, cm^{-1}: 1940 (Ph), 1640 (C=CH), 1600, 1590, 1520 (Ar), 870 (Ph), 810 (Ar), 780, 720, 700, 680 (Ph). ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 7.50-7.34 (5H, m, H Ph); 7.22 (1H, d, *J* = 8.1, H Ar); 7.16 (1H, dd, *J* = 8.1, *J* = 2.1, H Ar); 6.73 (1H, br. s, H-9); 6.41 (1H, d, *J* = 2.1, H Ar); 5.04 (1H, br. d, *J* = 16.0) and 4.85 (1H, br. d, *J* = 16.0, 1-CH_2); 4.28 (1H, d, *J* = 14.5, 4-CH); 4.07-3.71 (9H, m) and 3.66-3.57 (2H, m, 3-CH_2, 3a-CH, N($C\underline{H_2}C\underline{H_2}$)$_2$O). ^{13}C NMR spectrum, δ, ppm: 139.5 (=C); 138.9; 135.2; 132.3; 132.1 (=C); 128.7; 128.7 (br. s); 127.4; 127.2; 127.2 (br. s); 126.4 (=CH); 126.4; 66.2, 63.5 (1,3-CH_2); 61.4, 61.0 (N($CH_2\underline{C}H_2$)$_2$O); 59.4, 58.1 (N($\underline{C}H_2CH_2$)$_2$O); 48.3 (4-CH); 40.2 (3a-CH). Found, %: C 61.51; H 5.55; Br 18.98; N 3.46. $C_{22}H_{23}BrClNO$. Calculated, %: C 61.06; H 5.36; Br 18.46; N 3.24.

REFERENCES

1. I. Iwai and T. Hiraoka, *Pharm. Bull.*, **11**, 1564 (1963).
2. A. T. Babayan, E. O. Chukhajian, and El. O. Chukhajian, *Zh. Org. Khim*., **9**, 467 (1973).
3. E. O. Chukhajian, L. V. Ayrapetyan, and El. O. Chukhajian, *Khim. Geterotsikl. Soedin.*, 1410 (2012). [*Chem. Heterocycl. Compd.*, **48**, 1314 (2012)].
4. A. T. Babayan, E. O. Chukhajian, G. T. Babayan, El. O. Chukhajian, and F. S. Kinoyan, *Arm. Khim. Zh.*, **23**, 149 (1970).
5. El. O. Chukhajian, E. O. Chukhajian, and A. T. Babayan, *Zh. Org. Khim.*, **10**, 46 (1974).
6. A. T. Babayan, E. O. Chukhajian, and L. A. Manasyan, *Arm. Khim. Zh.*, **31**, 489 (1978).
7. E. O. Chukhajian, El. O. Chukhajian, K. G. Shakhatuni, and A. T. Babayan, *Khim. Geterotsikl. Soedin.*, 615 (1989). [*Chem. Heterocycl. Compd.*, **25**, 512 (1989)].
8. E. O. Chukhajian, M. K. Nalbandyan, and G. A. Panosyan, *Khim. Geterotsikl. Soedin.*, 528 (2007). [*Chem. Heterocycl. Compd.*, **43**, 430 (2007)].
9. E. O. Chukhajian, A. R. Gevorkyan, El. O. Chukhajian, and F. S. Kinoyan, *Zh. Org. Khim.*, **41**, 369 (2005).
10. E. O. Chukhajian, M. K. Nalbandyan, A. R. Gevorkyan, and F. S. Kinoyan, *Khim. Zh. Armenii*, **60**, 83 (2007).
11. T. Laird and W. D. Ollis, *J. Chem. Soc.*, *Chem. Commun.*, 557 (1972).
12. T. Laird, W. D. Ollis, and I. Sutherland, *J. Chem. Soc*., *Perkin Trans. 1*, 1477 (1980).
13. A. T. Babayan, E. O. Chukhajian, and G. T. Babayan, *Zh. Org. Khim.*, **6**, 1161 (1970).
14. E. O. Chukhajian, El. O. Chukhajian, K. G. Shakhatuni, and A. T. Babayan, *Khim. Geterotsikl. Soedin.*, 759 (1991). [*Chem. Heterocycl. Compd.*, **27**, 594 (1991)].
15. E. O. Chukhajian, *Khim. Geterotsikl. Soedin.*, 435 (1993). [*Chem. Heterocycl. Compd.*, **29**, 363 (1993)].
16. A. T. Babayan, V. P. Akopyan, E. O. Chukhajian, and K. G. Shakhatuni, *USSR Inventor's Certificate* 849744.

17. A. T. Babayan, E. O. Chukhajian, A. S. Saratikov, El. O. Chukhajian, K. G. Shakhatuni, N. S. Livshits, and L. V. Simak, *USSR Inventor's Certificate* 961310.
18. A. T. Babayan, V. P. Akopyan, S. A. Mirzoyan, E. O. Chukhajian, and K. G. Shakhatuni, *USSR Inventor's Certificate* 860455.
19. A. T. Babayan, E. O. Chukhajian, V. P. Akopyan, El. O. Chukhajian, and K. G. Shakhatuni, *USSR Inventor's Certificate* 1009059.
20. A. T. Babayan, E. O. Chukhajian, D. N. Lazareva, R. N. Abdulina, and F. S. Zarudii, *USSR Inventor's Certificate* 1045590.
21. A. T. Babayan, E. S. Gabrielyan, V. P. Akopyan, E. O. Chukhajian, L. A. Manasyan, and L. S. Balyan, *USSR Inventor's Certificate* 930881.
22. A. T. Babayan, E. S. Gabrielyan, V. P. Akopyan, E. O. Chukhajian, L. A. Manasyan, and L. S. Balyan, *USSR Inventor's Certificate* 959395.
23. A. T. Babayan, R. A. Aleksanyan, E. O. Chukhajian, G. L. Gabrielyan, and T. O. Asatryan, *USSR Inventor's Certificate* 728445; *Byul. Izobret.*, No. 8, 98 (1980).
24. A. T. Babayan, R. A. Aleksanyan, E. O. Chukhajian, El. O. Chukhajian, G. L. Gabrielyan, and T. O. Asatryan, *USSR Inventor's Certificate* 767096: *Byul. Izobret.*, No. 36, 117 (1980).
25. E. Chukhajian, K. Shakhatuni, El. Chukhajian, A. Babayan, V. Samvelyan, V. Akopyan, E. Janpoladyan, and E. Khoetyan, Republic of Armenia Pat. 573.
26. E. Chukhajian, K. Shakhatuni, El. Chukhajian, V. Akopyan, V Samvelyan, N. Gevorkyan, A. Akopyan, L. Balyan, and L. Edigarova, Republic of Armenia Pat. 574.
27. A. A. Abramyan, *Quantitative Microelemental Analysis of Organic Compounds* [in Armenian], Aipetrat, Yerevan (1963), p. 178.
28. E. O. Chukhajian, G. L. Gabrielyan, and A. T. Babayan, *Arm. Khim. Zh.*, **29**, 452 (1976).
29. A. R. Gevorkyan, E. O. Chukhajian, El. O. Chukhajian, and G. A. Panosyan, *Khim. Geterotsikl. Soedin.*, 212 (2004). [*Chem. Heterocycl. Compd.*, **40**, 177 (2004)].
30. E. O. Chukhajian, M. K. Nalbandyan, H. R. Gevorkyan, El. O. Chukhajian, H. A. Panosyan, A. G. Ayvazyan, and R. A. Tamazyan, *J. Heterocycl. Chem.*, **45**, 687 (2008).
31. R. A. Mitsch and N. H. Cromwell, *J. Org. Chem.*, **25**, 1719 (1960).