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Synthesis of 6-Bromo-3a,4-dihydrobenzo[*f*]isoindolinium Bromides and Their Aqueous-Alkaline Cleavage

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Abstract—Cyclization of allyl[3-(4-bromophenyl)prop-2-ynyl]ammonium bromides under basic catalysis conditions, unlike their propargyl analogs, occurs under heating of the reaction mixture at 90–92°C. Cyclization, which is the main reaction route, is accompanied by rearrangement–cleavage to form 1-allyl-*p*-bromocinnamaldehyde. A favorable effect of the substituents on the nitrogen atom and the presence of the bromine atom in the *4* position of the aromatic ring on the cyclization and rearrangement–cleavage reactions is established.

Keywords: 1-allyl-*p*-bromocinnamaldehyde, allyl[3-(4-bromophenyl)prop-2-ynyl]ammonium bromides, 6-bromo-3a,4-dyhydrobenzo[*f*]isoindolinium bromides, base-catalyzed intramolecular cyclization, isomeric 2-dialkylaminomethyl-7-bromo-3-methylnaphthalenes, 3-dialkylaminomethyl-7-bromo- 2-methylnaphthalenes, rearrangement–cleavage, aqueous-alkaline cleavage.

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We earlier showed that propagyl[3-(4-bromophenyl)prop-2-ynyl]ammonium bromides, except for their dimethyl analog, in the presence of alkali (0.2 mol per mole salt) at room temperature undergo cyclization accompanied by self-heating and form 6-bromobenzo[*f*]isoindolinium bromides in high yields [1, 2].

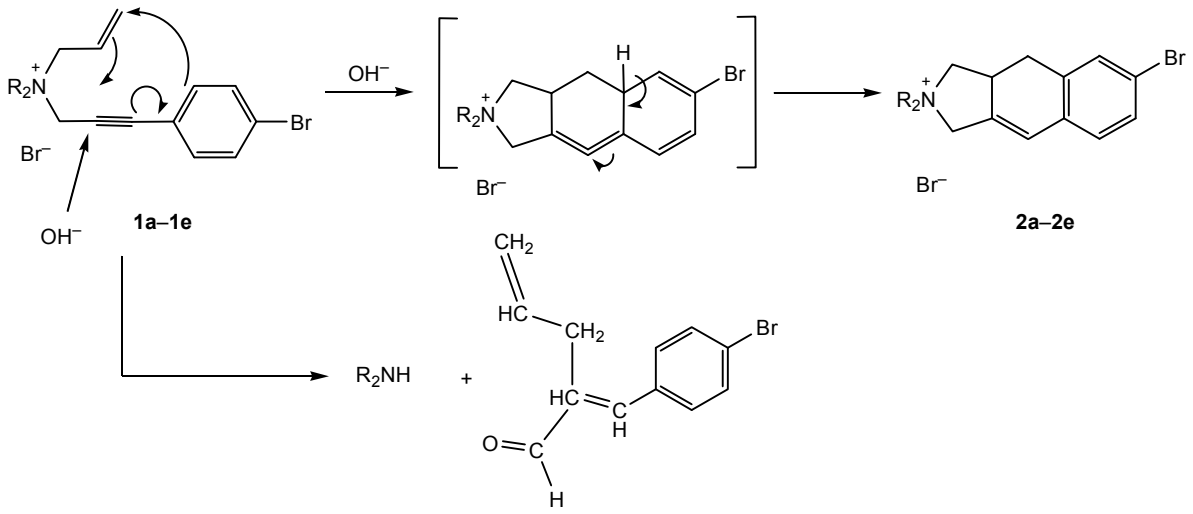
As known, the cyclization of ammonium salts containing an allylic-type group along with various 3-arylprop-2-ynyl fragments in the presence of alkali (0.2 mol per mole salt) occurs under heating at 90–92°C for 2 h [3–5]; along with cyclization, which is the main reaction route, take place also rearrangement–cleavage reaction. It should be noted that with [3-(naphthalene-1-yl)prop-2-ynyl] analogs take place only cyclization under the above conditions [6]. In our recent works [7, 8] we found that (3-phenylprop-2-enyl)(3-arylprop-2-ynyl)ammonium bromides, unlike the above salts [6], undergo base-catalyzed cyclization under heating at 40–45°C for 6–15 min. Under these conditions, the heterogeneous system undergo homogenization followed by cyclization with self-heating. The yields of cyclic products are high.

The obtained results give grounds to say that the phenyl group in the *3* position of the allylic system favors cyclization, like this is the case with bis-(3-phenylprop-2-ynyl) salts [9]. This phenomenon is the only precedent of the base-catalyzed intramolecular cyclization of ammonium salts containing an allylic group along with 3-arylprop-2-ynyl [3–6].

These results provide evidence for the cyclization mechanism proposed in [10, 11], as well as are consistent with published data, according to which diene synthesis involves nucleophilic addition of diene to dienophile. Since the phenyl group in the *3* position of the allylic system in comparison with hydrogen atom increases the positive charge of the dienophile, thereby facilitating nucleophilic addition.

Aimed at developing and extending the scope of the base-catalyzed intramolecular cyclization, in the present work we planned to study cyclization of allyl [3-(4-bromophenyl)prop-2-ynyl]ammonium bromides. If positive results were obtained, we could prepare potentially biologically active 6-bromo-3a,4-dihydrobenzo[*f*]isoindolinium bromides hardly accessible by other synthetic routes. We also expected to reveal the effect of substituents at the nitrogen atom and in the

Scheme 1.



1, **2** R = Me (**a**), R = Et (**b**), R_2 = –$(CH_2)_4$– (**c**), R_2 = –$(CH_2)_5$– (**d**), R_2 = –$(CH_2)_2O(CH_2)_2$– (**e**).

aromatic ring on cyclization and rearrangement–cleavage and to obtain further evidence for the proposed cyclization mechanism. To achieve the above goals, we performed by alkylation of dimethyl-, diethylamines and pyrrolidine, piperidine and morpholine with allyl bromide in acetonitrile medium were synthesized test salts: bromides of dimethyl- (**1a**) and diethyl(allyl)[3-(4-bromophenyl)prop-2-ynyl]ammonium (**1b**), as well as allyl[3-(4-bromophenyl)prop-2-ynyl]-pyrrolidinium (**1c**), -piperidinium (**1d**), and –morpholinium bromides (**1e**). Cyclization of salts **1a–1e** occurred according to the mechanism proposed in [10, 11]. Actually, the IR spectral study undertaken to establish the cyclization mechanism showed that the enyne moiety was directly involved in intramolecular cyclization as a π^4-fragment [10], and alkali was a driving force of this process [11].

The yields of cyclic products **2a–2e** were 70, 85, 80, 72, and 71%, respectively.

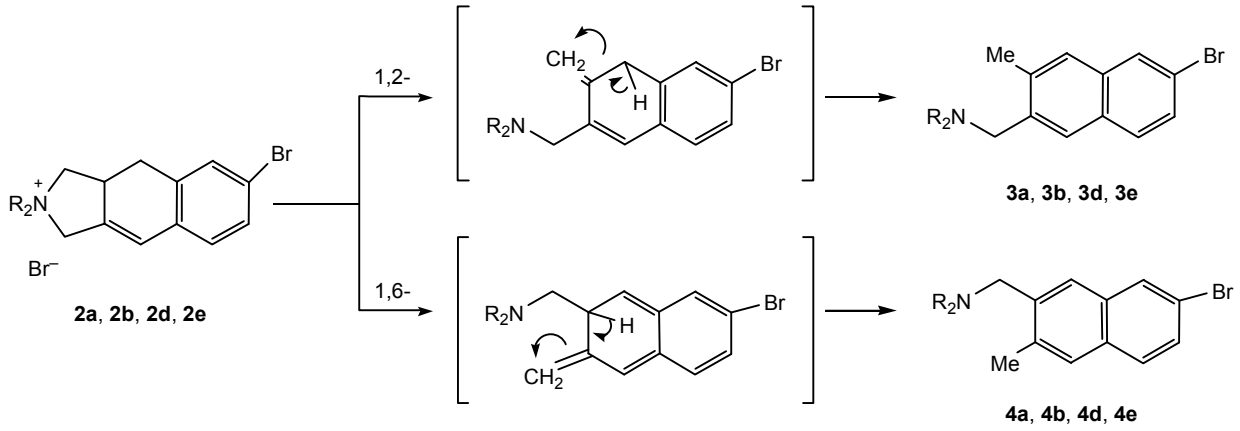
Along with cyclization, we also observed rearrangement–cleavage to form 1-allyl-*p*-bromocynnamaldehyde in yields of 15, 20, 18, and 20% from salts **1a**, **1c**, **1d**, and **1e**, respectively. In the case of salt **1b**, the yield of the rearrangement–cleavage product is as low as 6%. The fact that the yields of cyclization product from salt **1b** is 85%, whereas the yield of the rearrangement–cleavage product is 6% can be considered as evidence showing that the ethyl substituents on the nitrogen atom favor cyclization. These data are consistent with the mechanism proposed in [10, 11], as well as with the results of the kinetic study in [12], which showed that the rate of cyclization of salt **1b** is much higher compared to the other salts. It should be noted that the reaction with piperidinium salt **1d** was performed by stepwise adding 0.3 mol of alkali per 1 mol of the starting salt, because alkali is consumed for rearrangement–cleavage and, therefore, part of the starting salt does not have time to undergo cyclization. Judging from the yields of cyclic products, we can suggest that alkyl substituents on the nitrogen atom favor cyclization [11] (Scheme 1). The fairly low yields of cyclic products from piperidinium **1d** and morpholinium **1e** salts can be explained by that the bromine substituent favors rearrangement–cleavage.

Our study allowed to develop a practical method of synthesis of potentially biologically active 2,2-dialkyl-6-bromo-3a,4-dihydrobenzo[*f*]isoindolinium, 6-bromo-3a,4-dihydrobenzo[*f*]-pyrrolidinium and -piperidinium, and 6-bromo-3a,4-dihydro[spirobenzo[*f*]isoindolin]-2,4'-morpholinium bromides.

Salts **2a**, **2b**, **2d**, and **2e** underwent smooth 1,2- and 1,6-cleavage in aqueous alkali to form a mixture of isomeric 3-dialkylaminomethyl-2-methyl- and 2-dialkylaminomethyl-3-methyl-7-bromonaphthalenes in total yields of 57–60% (Scheme 2).

According to ^{1}H and ^{13}C NMR, the estimated ratios of the isomeric amines in the mixtures were as follows: **3a** : **4a** = 5.5 : 4.5; **3b** : **4b** = 4.4 : 5.6; **3d** : **4d** = 6 : 4; and **3e** : **4e** = 6 : 4. Hydrochlorides of analogous dialkylaminomethylnaphthalenes are known to show anti-

Scheme 2.



3, **4**, R = Me (**a**), R = Et (**b**), R_2 = –$(CH_2)_5$– (**d**), R_2= –$(CH_2)_2O(CH_2)_2$– (**e**).

acetylcholine, antihistamine, as well as papaverine- and atropine-like activities [13]. It is not excluded that the synthesized dialkylaminomethylnaphthalenes **3a**, **3b**, **3d**, **3e** and **4a**, **4b**, **4d**, **4e** may, too, exhibit such activities.

The structures of [3-(4-bromophenylprop-2-ynyl)]-pyrrolidine, initial salts **1a**–**1e**, cyclization products **2a**–**2e**, 1-allyl-*p*-bromocinnamaldehyde, and isomeric amines **3a**, **3b**, **3d**, **3e** and **4a**, **4b**, **4d**, **4e** were established by IR and ^{1}H and ^{13}C NMR spectroscopy, using 2D NMR techniques (DEPT, HMQC, NOESY) for signals assignment.

Thus, dialkyl(allyl)[3-(4-bromophenyl)prop-2-ynyl] ammonium, as well as allyl[3-(4-bromophenyl)prop-2-ynyl]-pyrrolidinium, -piperidinium, and -morpholinium bromides undergo base-catalyzed cyclization to form in high yields 6-bromo-3a,4-dihydrobenzo[*f*]-isoindolinium bromides hardly accessible by other synthetic routes. Alongside with cyclization, which is the preferential reaction direction, take rearrangement–cleavage reaction. The synthesized cyclic salts undergo smooth 1,2- and 1,6-cleavage in an aqueous alkaline medium.

EXPERIMENTAL

The IR spectra were registered on a Specord 75 IR spectrophotometer in $CHCl_3$. The ^{1}H and ^{13}C NMR spectra were obtained on a Varian Mercury 300 VX spectrometer (300 and 75 MHz, respectively) in a 1 : 3 DMSO-d_6–CCl_4 mixture, internal reference TMS. Analysis for C, H, and N was performed on a Vario Micro cube analyzer, and analysis for Br^-, by the Abramyan and Sargsyan method [14]. The melting points were measured on a Wägetechnik Rapido melting point apparatus. The purity of cyclic salts was checked by TLC on Silufol UV-254 plates; eluent *p*-BuOH–EtOH–H_2O–AcOH, 10 : 2 : 1 : 5; visualization by exposure to iodine vapor.

The starting dialkyl[3-(4-bromophenyl)prop-2-ynyl]amines were synthesized according to [2].

The previously unknown **1-[3-(4-bromophenyl-prop-2-ynyl)]pyrrolidine** was prepared by the reaction of 2.8 g (4 mmol) of pyrrolidin-1-amine, 1.2 g (4 mmol) of Paraform, and 7 g (4 mmol) of *p*-bromophenylacetylene in 70 mL of dioxane in the presence of 0.15 g of copper diacetate and 0.2 g of iron(III) chloride. The reaction mixture was heated for 70 h at 90–95°C and then made acidic with 25% HCl. The solvent was removed at reduced pressure, and the residue was treated with ether (2 × 60 mL) to separate unreacted (*p*-bromophenyl)acetylene, after which it was made alkaline and treated with ether (3 × 70 mL). The ethereal extract was dried over $MgSO_4$, the solvent was distilled off, and the product was isolated by vacuum distillation. Yield 5 g (47%), bp 139–140°C (3–4 mm Hg), mp 172°C (picrate; from EtOH). IR spectrum, ν, cm^{-1}: 2230 (disubstituted C≡C bond), 840–810 (para-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 1.70–1.84 m (4H, β,β'-CH_2), 2.52–2.64 m (4H, α,α'-CH_2), 3.55 s (2H, CH_2–C≡C), 7.25–7.30 m ($2H_{arom}$), 7.42–7.46 m ($2H_{arom}$). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 23.3 (β-CH_2), 42.7 ($\underline{C}H_2$–C≡C), 51.5 (α-CH_2), 82.7 and 86.5 (C≡C), 121.2, 121.8, 130.9 (2-CH), 132.5 (2-CH). Found, %:

C 59.39; H 5.44; N 5.15; Br 30.46. $C_{13}H_{14}NBr$. Calculated, %: C 59.11; H 5.34; N 5.30; Br 30.25.

Synthesis of 2,2-dialkyl(allyl)[3-(4-bromophenyl)-prop-2-ynyl]ammonium and allyl[3-(4-bromophenyl)prop-2-ynyl]pyrrolidinium, -piperidinium, and -morpholinium bromides (*general procedure*). To a solution of 8 mmol of corresponding dialkyl[3-(4-bromophenyl)prop-2-ynyl]amine in 5 mL of MeCN and 10 mL of absolute ether (in the case of pyrrolidinium **1c** and morpholinium **1e** salts, in MeCN exclusively) was added 1.45 g (12 mmol) 3-bromo-1-phenylprop-1-ene [15], the mixture was left to stand for 2–3 h at room temperature, and the white crystals of salts **1a–1e** were filtered off.

Allyl(dimethyl)[3-(4-bromophenyl)-prop-2-ynyl]-ammonium bromide (1a). Yield 2.9 g (98%), white crystals, mp 185–187°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3020, 3010, 1580 (aromatic ring), 2230 (disubstituted C≡C bond), 1640, 995, 925 (unconjugated C=C bond), 840–810 (*p*-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 3.31 s [6H, $N(CH_3)_2$], 4.34 d (2H, $C\underline{H}_2$–CH=CH_2, *J* 7.4), 4.81 s (2H, CH_2–C≡C), 5.70 d.d (1H, =CH_2, *J* 10.0, 1.7), 5.79 d.d (1H, =CH_2, *J* 16.8, 1.6), 6.16 d.d.t (1H, =CH, *J* 16.8, 10.0, 7.4), 7.50–7.58 m ($4H_{arom}$). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 49.1 (CH_3), 53.6 (CH_2), 64.8 (CH_2), 78.4 and 89.2 (C≡C), 119.4 (C_6H_4), 123.1 (C_6H_4), 125.3 (=CH_2), 127.8 (=CH), 131.2 (2-CH, C_6H_4), 133.3 (2-CH, C_6H_4). Found, %: C 47.04; H 4.89; Br 44.72; N 3.74. $C_{14}H_{17}Br_2N$. Calculated, %: C 46.83; H 4.77; Br 44.5; N 3.9.

Allyl(diethyl)[3-(4-bromophenyl)-prop-2-ynyl]-ammonium bromide (1b). Yield 2.7 g (89%), white crystals, mp 155–157°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3010, 1600 (aromatic ring), 2230 (disubstituted C≡C bond), 1640, 995, 920 (unconjugated C=C bond), 845–825 (*p*-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 1.42 t (6H, CH_3, *J* 7.2), 3.57 q (4H, $C\underline{H}_2$–CH_3, *J* 7.2), 4.21 br.d (2H, CH_{2allyl}, *J* 7.2), 4.69 s (2H, CH_2–C≡C), 5.67 d.d (1H, =CH_2, *J* 10.1, 1.6), 5.81 d.d (1H, =CH_2, *J* 16.8, 1.6), 6.15 d.d.t (1H, =CH, *J* 16.8, 10.1, 7.2), 7.49–7.58 m ($4H_{arom}$). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 7.3 (CH_3), 48.8 (CH_{2allyl}), 53.7 ($\underline{C}H_2$–CH_3), 60.2 ($\underline{C}H_2$–C≡C), 78.3 ($\underline{C}$≡C), 88.9 (C≡$\underline{C}$), 119.4 (CBr), 123.1 (C_{ipso}), 125.1 (=CH_{allyl}), 127.1 (=CH_{2allyl}), 131.2 (2-CH), 133.3 (2-CH). Found, %: C 49.86; H 5.61; Br 41.48; N 3.51. $C_{16}H_{21}Br_2N$. Calculated, %: C 49.64; H 5.47; Br 41.28; N 3.62.

Allyl-[3-(4-bromophenyl)prop-2-ynyl]pyrrolidinium bromide (1c). Yield 2.5 g (80%), white crystals, mp 145–146°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3020, 1580 (aromatic ring), 2230 (disubstituted C≡C bond), 1640, 990, 925 (unconjugated C=C bond), 845–820 (*p*-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 2.19–2.32 m (4H, β-CH_2), 3.76–3.89 m (4H, α-CH_2), 4.29–4.40 m (2H, CH_{2allyl}), 4.74 s (2H, CH_2–C≡C), 5.67 d.d (1H, =CH_2, *J* 10.1, 1.7), 5.81 d.d.t (1H, =CH_2, *J* 16.8, 1.7, 1.0), 6.18 d.d.t (1H, =CH, *J* 16.8, 10.1, 7.2), 7.50–7.57 m ($4H_{arom}$). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 21.7 (β-CH_2), 50.9 (CH_{2allyl}), 61.0 (α-CH_2), 62.5 ($\underline{C}H_2$–C≡C), 79.1 ($\underline{C}$≡C), 88.3 (C≡$\underline{C}$), 119.4, 123.1, 126.0 (=CH), 127.1 (=CH_2), 131.2 (2-CH_{arom}), 133.3 (2-CH_{arom}). Found, %: C 49.85; H 5.58; Br 41.49; N 3.51. $C_{16}H_{21}Br_2N$. Calculated, %: C 49.64; H 5.47; Br 41.28; N 3.62.

Allyl-[3-(4-bromophenyl)prop-2-ynyl]piperidinium bromide (1d). Yield 2.7 g (85%), white crystals, mp 135–136°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3010, 1610 (aromatic ring), 2230 (disubstituted C≡C bond), 1630, 995, 925 (unconjugated C=C bond), 840, 825 (*p*-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 1.69–1.80 m (2H, CH_2), 1.90–2.06 m (4H, α-CH_2), 3.65–3.79 m [2H, $N(CH_2)_2$], 4.35 br.d (2H, $\underline{C}H_2$–CH=CH_2, *J* 7.3), 4.79 s (2H, $\underline{C}H_2$–C≡C), 5.68 br.d.d (1H, =CH_2, *J* 10.0, 1.7), 5.82 br.d.d (1H, =CH_2, *J* 16.8, 1.7), 6.15 d.d.t (1H, =CH, *J* 16.8, 10.0, 7.3), 7.53 s ($4H_{arom}$). ^{13}C NMR spectrum (75.48 MHz, DMSO-d_6 + CCl_4), δ, ppm: 19.1 (2-CH_2), 20.3 (CH_2), 49.6 (NCH_2), 57.4 [$N(CH_2)_2$], 60.8 (NCH_2), 78.1 ($\underline{C}$≡C), 89.3 (C≡$\underline{C}$), 119.5 (CBr), 123.1, 124.7 (=CH), 127.6 (=CH_2), 131.2 (2-CH), 133.3 (2-CH). Found, %: C 51.36; H 5.42; Br 40.24; N 3.43. $C_{17}H_{21}Br_2N$. Calculated, %: C 51.15; H 5.3; Br 40.03; N 3.51.

Allyl-[3-(4-bromophenyl)prop-2-ynyl]morpholinium bromide (1e). Yield 2.6 g (82%), white crystals, mp 185–186°C (abs. EtOH). IR spec-trum, ν, cm^{-1}: 3020, 1580 (aromatic ring), 2230 (di-substituted C≡C bond), 1630, 990, 925 (unconjugated C=C bond), 840, 820 (*p*-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 3.69–3.83 m [4H, $O(CH_2)_2$], 4.00–4.15 m [4H, $N(CH_2)_2$], 4.51 d (2H, $\underline{C}H_2$–CH=CH_2, *J* 7.3), 4.95 s (2H, $\underline{C}H_2$–C≡C), 5.71 br.d.d (1H, =CH_2, *J* 9.9, 1.7), 5.86 br.d.d

(1H, =CH_2, *J* 16.9, 1.7), 6.18 d.d.t (1H, =CH, *J* 16.9, 9.9, 7.3), 7.51–7.59 m (4H_{arom}). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 50.1 (CH_2), 56.3 [N(CH_2)$_2$], 59.5 [O(CH_2)$_2$], 61.1 (CH_2), 77.8 (C≡C), 89.7 (C≡C), 119.4 (CBr), 123.1, 124.4 (=CH), 128.1 (=CH_2), 131.2 (2-CH), 133.4 (2-CH). Found, %: C 48.12; H 4.89; Br 40.01; N 3.38. $C_{16}H_{19}Br_2NO$. Calculated, %: C 47.91; H 4.77; Br 39.84; N 3.49.

Intramolecular cyclization of salts 1a–1e (*general procedure*). To a solution of 6 mmol of salt **1a–1e** in 3.5 mL of water, 0.4 mL of 3 N KOH (salt : alkali molar ratio 5 : 1) was added. No self-heating was observed. The reaction mixture was heated at 75–80°C for 2.5 h and then treated with ether (2 × 35 mL) to remove by-products. Cyclic salts **2a–2e** were isolated from the reaction mixture by filtration. Titration revealed 10–20% of secondary amines in the ethereal extract. The ethereal extract was made acidic with HCl. The HCl solution was made basic and extracted to isolate secondary amines: dimethylamine, dimethylpyrro-lidine, dimethylpiperidine, and dimethylmorpholine; their picrates melted at 154–155, 130, 145, and 140°C, respectively, and gave no melting point depression with the authentic samples. Diethylamine hydro-chloride melted at 223–224°C and gave no melting point depression with the authentic sample. The ethereal extract that contained a nonamine product was washed with water and dried over $CaCl_2$. The ether was distilled off, and the residue was distilled in a vacuum to isolate 1-allyl-*p*-bromocinnamaldehyde. The yields of the latter from salts **2a–2e** were 15, 6, 20, 18, and 20%, respectively.

1-Allyl-*p*-bromocinnamaldehyde, bp 88–94°C (2–3 mmHg), mp 193–195°C (hydrazone). IR spectrum, ν, cm^{-1}: 3090, 1590 (aromatic ring), 1700 (carbonyl group conjugated with the double bond), 1630, 840, 800 (terminal vinyl bond), 880, 840, 800 (*p*-substituted benzene ring). According ^{1}H and ^{13}C NMR, two stereoisomers were isolated in a 95 : 5 ratio. ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 3.21 d.t (2H, CH_2, *J* 5.6, 1.8), 5.01 d.t.d (1H, =CH_2, *J* 17.2, 1.8, 1.6), 5.05 d.t.d (1H, =CH_2, *J* 10.3, 1.8, 1.6), 5.87 d.t.d (1H, =CH_{allyl}, *J* 17.2, 10.3, 5.6), 7.45 br.s (1H, =CH), 7.43–7.48 m (2H_{arom}); 7.55–7.60 m (2H_{arom}), 9.56 s (1H, CHO). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 28.0 (CH_2), 115.4 (=CH_2), 123.2, 130.9 (2-CH, C_6H_4), 131.3 (2-CH, C_6H_4), 133.1, 133.5 (=CH), 139.4, 148.5 (=CH), 193.2 (CHO). Found, %: C 57.61; H 4.61; Br 32.03; O 6.54. $C_{12}H_{11}BrO$. Calculated, %: C 57.4; H 4.42; Br 31.82; O 6.37.

6-Bromo-2,2-dimethyl-3a,4-dihydrobenzo[*f*]isoindolinium bromide (2a). Yield 1.5 g (70%), white crystals, mp 247–250°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 1610, 1580 (aromatic ring), 880–875, 825–805 (1,2,4-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 2.68 t (1H, CH_2, *J* 15.6, 15.2), 3.01 d.d (1H, CH_2, *J* 15.2, 6.3), 3.17 s (3H, CH_3), 3.21–3.44 m (1H, CH), 3.30 s (3H, CH_3), 3.58 d.d (1H, NCH_2CH, *J* 11.3, 10.5), 4.01 d.d (1H, NCH_2CH, *J* 11.3, 8.0), 4.37 d.t (1H, NCH_2=CH, *J* 16.2, 2.3), 4.46 br.d (1H, NCH_2=CH, *J* 16.2), 6.63 q (1H, =CH, *J* 2.4), 7.13 d (1H, C_6H_3, *J* 8.0), 7.40 d.d (1H, C_6H_3, *J* 8.0, 1.9), 7.44 br.s (1H, C_6H_3). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 30.5 (CH_2), 35.5 (CH), 51.8 (CH_3), 52.4 (CH_3), 67.1 (NCH_2), 68.8 (NCH_2), 119.9, 120.3 (=CH), 128.0 (CH_{arom}), 129.7 (CH_{arom}), 130.5 (CH_{arom}), 132.6, 136.1, 137.1. Found, %: C 47.17; H 4.72; Br 44.84; N 3.79. $C_{14}H_{16}Br_2N$. Calculated, %: C 46.96; H 4.5; Br 44.63; N 3.91.

6-Bromo-2,2-diethyl-3a,4-dihydrobenzo[*f*]isoindolinium bromide (2b). Yield 2.0 g (85%), white crystals, mp 218–220°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3030, 1590 (aromatic ring), 820–805, 885–875 (1,2,4-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 1.35 t (3H, CH_3, *J* 7.3), 1.38 t (3H, CH_3, *J* 7.3), 2.83 d.d (1H, CH_2, *J* 15.2, 15.0), 2.98 d.d (1H, CH_2, *J* 15.2, 6.5), 3.26–3.42 m (1H, CH), 3.44–3.58 m (2H, C$H_2$$CH_3$), 3.66 q (2H, C$H_2$$CH_3$, *J* 7.3), 3.73 d.d (1H, NCH_2, *J* 11.6, 10.0), 4.21 d.d (1H, NCH_2, *J* 11.6, 8.4), 4.57 d.t (1H, NCH_2, *J* 16.5, 2.2), 4.60 d.t (1H, NCH_2, *J* 16.5, 2.0), 6.61 br.s (1H, =CH), 7.06 d (1H, C_6H_3, *J* 8.0), 7.30 d.d (1H, C_6H_3, *J* 8.0, 1.8), 7.34 br.s (1H, C_6H_3). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 8.2 and 8.4 (2-CH_3), 31.0 (CH_2), 34.9 (CH), 53.4 (NCH_2), 54.8 (NCH_2), 63.9 (NCH_2), 64.8 (NCH_2), 120.0, 120.4 (CH), 127.5 (CH), 129.3 (CH), 130.3 (CH), 132.2, 135.7, 136.1. Found, %: C 49.97; H 5.33; Br 41.59; N 3.41. $C_{16}H_{20}Br_2N$. Calculated, %: C 49.77; H 5.22; Br 41.38; N 3.63.

6-Bromo-2,2-tetramethylene-3a,4-dihydrobenzo-[*f*]isoindolinium bromide (2c). Yield 1.8 g (80%), white crystals, mp 235–237°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3010, 1600 (aromatic ring), 885–875, 825–805 (1,2,4-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 2.15–2.31 m (4H, β,β'-CH_2), 2.79 br.t (1H, CH_2, *J* 15.3), 3.00 d.d (1H, CH_2, *J* 15.3, 6.4), 3.22–3.38 m (1H, CH), 3.63–3.75 m (2H, α-CH_2),

3.79–3.93 m (3H, α'-CH_2 and NCH_2), 4.24 d.d (1H, NCH_2, *J* 11.2, 7.9), 6.59 d.t (1H, =CH, *J* 2.5, 2.2), 7.06 d (1H, C_6H_3, *J* 8.0), 7.30 d.d.d (1H, C_6H_3, *J* 8.0, 2.0, 0.8), 7.34 br.d (1H, C_6H_3, *J* 2.0). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 21.3 (β-CH_2), 21.5 (β'-CH_2), 30.7, 35.8, 62.4, 62.9, 64.3, 65.8, 119.9, 120.1, 127.5, 129.3, 130.3, 132.3, 135.6, 136.5. Found, %: C 50.25; H 4.93; Br 41.83; N 3.53. $C_{16}H_{18}Br_2N$. Calculated, %: C 50.03; H 4.72; Br 41.6; N 3.65.

6-Bromo-2,2-pentamethylene-3a,4-dihydrobenzo-[*f*]isoindolinium bromide (2d). Yield 1.7 g (72%), white crystals, mp 235–236°C (abs. EtOH). IR spectrum, ν, cm^{-1}: 3040, 1600 (aromatic ring), 885–870, 825–805 (1,2,4-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 1.54–1.66 m (2H, γ-CH_2), 1.77–1.90 m (4H, β,β'-CH_2), 2.67 t (1H, CH_2, *J* 15.2), 3.00 d.d (1H, CH_2, *J* 15.2, 6.4), 3.22–3.37 m (1H, CH), 3.43 br.t (2H, CH_2, *J* 5.7), 3.51 d.d (1H, CH_2, *J* 11.5, 10.5), 3.54 br.t (2H, CH_2, *J* 5.7), 4.14 br.d.d (1H, CH_2, *J* 11.5, 8.0), 4.36 br.d.t (1H, N^+CH_2, *J* 16.4, 2.2), 4.57 br.d (1H, N^+CH_2, *J* 16.4), 6.60 br.q (1H, =CH, *J* 2.3), 7.14 d (1H, C_6H_3, *J* 8.0), 7.40 d.d.d (1H, C_6H_3, *J* 8.0, 2.0, 0.7), 7.46 br.s (1H, C_6H_3). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 20.4 (γ-CH_2), 20.6 (β-CH_2), 21.0 (β'-CH_2), 30.6 (CH_2), 34.4 (CH), 59.3 (CH_2), 61.3 (CH_2), 63.7 (CH_2), 66.3 (CH_2), 120.0, 120.1 (=CH), 128.0 (=CH), 129.7 (=CH), 130.5 (=CH), 132.6, 136.0, 136.6. Found, %: C 51.49; H 5.15; Br 40.37; N 3.39. $C_{17}H_{20}Br_2N$. Calculated, %: C 51.28; H 5.06; Br 40.14; N 3.52.

Spiro[6-bromo-3a,4-dihydrobenzo[*f*]isoindolin-2,4']morpholinium bromide (2e). Yield 1.7 g (71%), white crystals, mp 275–276°**C** (abs. EtOH). IR spectrum, ν, cm^{-1}: 3040, 1580 (aromatic ring), 885–870, 825–805 (1,2,4-substituted benzene ring). ^{1}H NMR spectrum (300.09 MHz, DMSO-d_6 + CCl_4), δ, ppm (*J*, Hz): 2.69 t (1H, CH_2, *J* 15.3), 3.01 d.d (1H, CH_2, *J* 15.3, 6.5), 3.23–3.39 m (1H, CH), 3.51–3.56 m (2H, NCH_2), 3.59–3.67 m (3H, CH_2), 3.86–4.01 m [4H, $O(CH_2)_2$], 4.27 d.d (1H, CH_2, *J* 11.5, 8.1), 4.47 d.t (1H, CH_2, *J* 16.4, 2.3), 4.74 br.d (1H, CH_2, *J* 16.4), 6.62 br.q (1H, =CH, *J* 2.3), 7.15 d (1H, C_6H_3, *J* 8.1), 7.40 d.d.d (1H, C_6H_3, *J* 8.1, 2.0, 0.8), 7.46 br.s (1H, C_6H_3). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 30.4 (CH_2), 34.3 (CH), 58.3 (CH_2), 59.8 (CH_2), 61.0 (OCH_2), 61.5 (OCH_2), 63.6 (CH_2), 66.8 (CH_2), 120.0, 120.3 (=CH), 128.0 (=CH), 129.7 (=CH), 130.5 (=CH), 132.5, 135.9, 136.0. Found, %: C 48.25; H 4.73; Br 40.16; N 3.38. $C_{16}H_{18}Br_2NO$. Calculated, %: C 48.03; H 4.53; Br 39.94; N 3.50.

Aquoeus-alkaline cleavage of salts 2a, 2b, 2d, and 2e (*general procedure*). Potassium hydroxide, 0.3 g, was added to a solution of 2 mmol of salt **2a**, **2b**, **2d**, or **2e** in 2–3 mL of water, and the mixture was heated at 110–120°C with simultaneous distillation of water (10–15 mL of water was intermittently added to the reaction mixture. To complete the cleavage, the reaction mixture was heated at 140–145°C for 5–7 min. The total reaction time was 1.5 h. Then the reaction mixture and the distillate were treated with Et_2O (3 × 50 mL). The extract was washed with water and dried over $MgSO_4$. The ether was removed, and the residue was distilled in a vacuum to obtain a mixture of isomeric amines **3a**, **3b**, **3d**, **3e** and **4a**, **4b**, **4d**, **4e**.

7-Bromo-3-(dimethylaminomethyl)-2-methylnaphthalene (3a) and 7-bromo-2-(dimethylaminomethyl)-3-methylnaphthalene (4a) (isomer mixture, **3a/4a** 5.5 : 4.5). Yield 0.3 g (60%), bp 110–120°C (2–3 mmHg), n_D^{20} 1.5970. IR spectrum, ν, cm^{-1}: 3040, 1600, 1570 (aromatic ring), 885–870, 825–805 (1,2,4- and 1,2,4,5-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 2.23 s [6H, $(CH_3)_2$], 2.50 d (1.65H, CH_3, *J* 0.9), 2.52 d (1.35H, CH_3, *J* 0.9), 3.47 br.s (0.9H, CH_2), 3.48 br.s (1.1H, CH_2), 7.43 d.d (0.45H, =CH, *J* 8.7, 2.0) and 7.44 d.d (0.55H_{arom}, =CH, *J* 8.7, 2.0), 7.50 br.s (0.45H, =CH), 7.56 br.s (0.55H, =CH), 7.58–7.67 m (2H_{arom}), 7.88 d (0.45H_{arom}, *J* 2.0) and 7.91 d (0.55H_{arom}, *J* 2.0). Found, %: C 60.69; H 5.91; N 5.15; Br 28.91. $C_{14}H_{16}NBr$. Calculated, %: C 60.45; H 5.8; N 5.03; Br 28.72.

7-Bromo-3-(dimethylaminomethyl)-2-ethylnaphthalene (3b) and 7-bromo-2-(dimethylaminomethyl)-3-ethylnaphthalene (4b) (isomer mixture, **3b/4b** 4.4 : 5.6). Yield 0.35 g (57%), bp 142–143°C (2–3 mmHg), n_D^{20} 1.5670. IR spectrum, ν, cm^{-1}: 3020, 1610, 1580 (aromatic ring), 880–875, 825–805 (1,2,4- and 1,2,4,5-substituted benzene ring). ^{1}H NMR spectrum, δ, ppm: 1.04 t (6H, 2-CH_3, *J* 7.1), 2.50 and 2.52 s (3H, CH_3), 2.53 q [4H, $N(CH_2)_2$, *J* 7.1], 3.62 and 3.63 s (2H, NCH_2), 7.42 d.d (0.44H, C_6H_3, *J* 8.7, 1.8), 7.4 d.d (0.56H, C_6H_3, *J* 8.7, 1.8), 7.48 br.s (0.44H, =CH), 7.54 br.s (0.56H, =CH), 7.61 d (0.56H, CH_3, *J* 8.7), 7.65 d (0.44H, CH_3, *J* 8.7), 7.65 br.s (0.56H, =CH), 7.69 br.s (0.44H, =CH), 7.87 d (0.44H, C_6H_3, *J* 1.8), 7.91 d.d (0.56H, C_6H_3, *J* 1.8). ^{13}C NMR spectrum (75.47 MHz, DMSO-d_6 + CCl_4), δ, ppm: 11.4 (2-CH_3),

18.95 and 18.99 (CH_3), 46.2 [$N(\underline{C}H_2CH_3)_2$], 55.89 and 55.96 ($NCH_2$), 117.84, 118.37, 126.30, 126.52, 127.16, 127.37, 127.48, 127.87, 128.04, 128.08, 128.60, 128.68, 129.71, 130.51, 132.46, 133.28, 135.56, 136.32, 136.83, 137.50. Found, %: C 62.96; H 6.79; N 4.43; Br 26.31. $C_{16}H_{20}NBr$. Calculated, %: C 62.75; H 6.58; N 4.57; Br 26.09.

7-Bromo-2-methyl-3-(piperidinomethyl)naphthalene (3d) and 7-bromo-3-methyl-2-(piperidinomethyl)naphthalene (4d) (isomer mixture, **3d/4d** 4 : 6). Yield 0.4 g (59%), honey-like substance. IR spectrum, ν, cm^{-1}: 3040, 1620, 1580 (aromatic ring), 885–875, 820–805 (1,2,4- and 1,2,4,5-substituted benzene ring). ^1H NMR spectrum, δ, ppm: 1.41–1.59 m (6H, 3-CH_3), 2.37–2.43 m (4H, α,α'-CH_2), 2.50 s (1.7H, CH_3), 2.52 s (1.3H, CH_3), 3.49 s (0.8H, CH_2), 3.50 s (1.2H, CH_2), 7.42 d.d (0.4H, C_6H_3, *J* 8.7, 2.0), 7.43 d.d (0.6H, C_6H_3, *J* 8.7, 2.0), 7.49 br.s (0.4H, =CH, C_6H_2), 7.54 br.s (0.6H, =CH, C_6H_2), 7.57 br.s (0.6H, =CH, C_6H_2), 7.62 br.s (0.4H, =CH, C_6H_2), 7.61 d (0.4H, C_6H_3, *J* 8.7), 7.64 d (0.4H, C_6H_3, *J* 8.7), 7.86 d (0.4H, C_6H_3, *J* 2.0), 7.91 d (0.6H, C_6H_3, *J* 2.0). Found, %: C 64.38; H 6.45; N 4.28; Br 25.32. $C_{17}H_{20}NBr$. Calculated, %: C 64.16; H 6.33; N 4.4; Br 25.1.

7-Bromo-2-methyl-3-(morpholinomethyl)naphthalene (3e) and 7-bromo-3-methyl-2-(morpholinomethyl)naphthalene (4e) (isomer mixture, **3e/4e** 4 : 6). Yield 0.4 g (58%), honey-like substance. IR spectrum, ν, cm^{-1}: 3060 (CH_{arom}), 1640, 1580 (aromatic ring), 885–870, 825–805 (1,2,4- and 1,2,4,5-substituted benzene ring). ^1H NMR spectrum, δ, ppm: 2.41–2.46 m (4H, NCH_{2morph}), 2.52 d (1.8H, CH_3, *J* 0.8), 2.54 d (1.2H, CH_3, *J* 0.8), 3.56 s (0.8H, CH_2), 3.57 s (1.2H, CH_2), 3.57–3.61 m (4H, OCH_{2morph}), 7.43 d.d (0.4H, C_6H_3, *J* 8.7, 2.0), 7.45 d.d (0.6H, C_6H_3, *J* 8.7, 2.0), 7.51 br.s (0.4H, =CH, C_6H_2), 7.57 br.s (0.6H, =CH, C_6H_2), 7.60 br.s (0.6H, =CH, C_6H_2), 7.63 br.s (0.4H, =CH, C_6H_2), 7.62 d (0.6H, C_6H_3, *J* 8.7), 7.65 d (0.4H, C_6H_3, *J* 8.7), 7.88 d (0.4H, C_6H_3, *J* 2.0), 7.92 d (0.6H, C_6H_3, *J* 2.0). Found, %: C 60.23; H 5.88; N 4.26; Br 25.16. $C_{16}H_{18}NOBr$. Calculated, %: C 60.01; H 5.67; N 4.37; Br 24.95.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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