Chemistry of Heterocyclic Compounds, Vol. 46, No. 2, 2010

BASE CATALYZED INTRAMOLECULAR CYCLOADDITION OF DIALKYL(4-HYDROXYBUTYN-2-YL)[3-(*p*-TOLYL)PROPYN-2-YL]AMMONIUM CHLORIDES AND INTRAMOLECULAR RECYCLIZATION OF THE PRODUCTS OBTAINED

E. O. Chukhajian[1]*, L. V. Ayrapetyan[1], El. O. Chukhajian[1], and H. A. Panosyan[2]

Dialkyl(4-hydroxybutyn-2-yl)[3-(p-tolyl)propyn-2-yl]ammonium chlorides undergo a diene synthesis type intramolecular cyclization in aqueous base medium to give 2,2-dialkyl-4-hydroxymethyl-6-methyl-benzo[f]isoindolinium chlorides. Under conditions of aqueous base fission intramolecular cyclization of the latter gives 4-dialkylaminomethyl-8-methyl-1,3-dihydronaphtho[1,2-c]furans.

Keywords: 4-dialkylaminomethyl-8-methyl-1,3-dihydronaphtho[1,2-*c*]furans, dialkyl(4-hydroxybutyn-2-yl)[3-(*p*-tolyl)propyn-2-yl]ammonium chlorides, 2,2-dialkyl-4-hydroxymethyl-6-methylbenzo[f]isoindolinium chlorides, intramolecular cyclization, base catalysis, recyclization.

We have found that $CH_2C{\equiv}CCH_2OH$ groups can take part in intramolecular cyclization [1-5] and that the cyclization products can recyclize intramolecularly in conditions of aqueous base fission [2-6].

Opening of the ring occurs with intramolecular nucleophilic attack by an alkoxy anion formed in basic medium, the recyclization not involving ring expansion or contraction but the formation of a dihydrofuran ring in place of the pyrrole fragment. Based on this reaction we have developed an original synthetic route for amines with a hydrogenated furan ring pharmacophore [2-6]. It should be noted that only one example is known of a recyclization of a purely intramolecular nature, i.e. the thermal reaction of iminobenzylfurandiones to 4-allylpyrrole-2,3-diones [7].

Many examples have been reported in the literature of the recyclization of carbo- and, particularly, heterocyclic compounds, some of which are collected in review articles [8-12]. In all cases the action of various

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

[1]Institute of Organic Chemistry, Scientific Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, Yerevan 0091, Armenia.

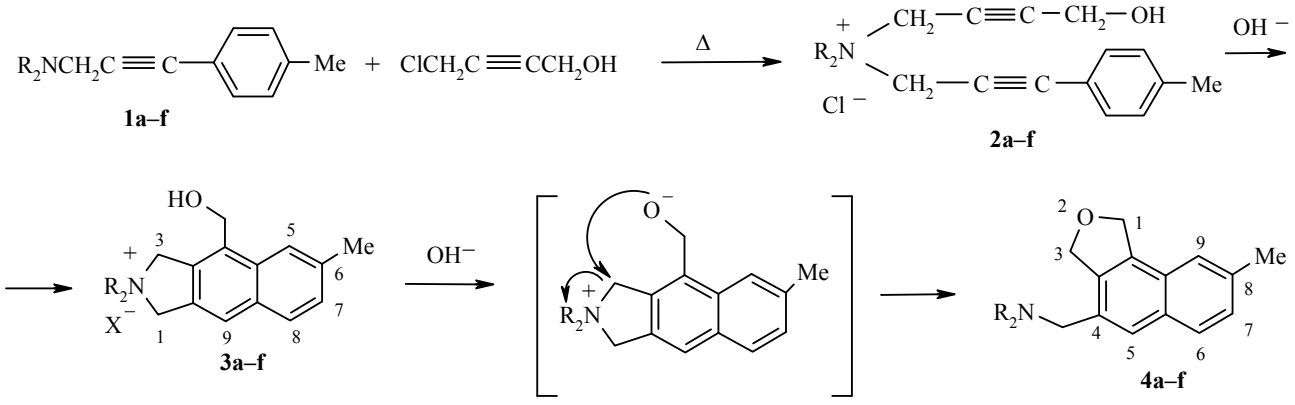
[2]Molecular Structure Research Center, National Academy of Sciences of Armenia, Yerevan 0014, Armenia; e-mail: henry@msrc.am.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 187-194, February, 2010. Original article submitted January 16, 2009; revision submitted May 28, 2009.

nucleophilic, electrophilic, or dipolar reagents leads to ring opening followed by a closure. The process is often accompanied by ring expansion or contraction with the introduction of a heteroatom into it or with exchange of an existing heteroatom for another.

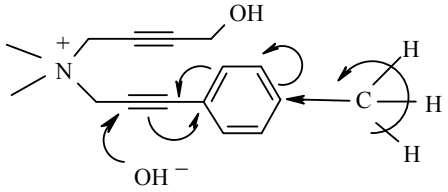
In continuation of our study of the above reaction this report concerns alkylation of the amines **1a-f**, the dialkyl(4-hydroxybutyn-2-yl)[3-(p-tolyl)propyn-2-yl]ammonium chlorides **2a-f**, and a study of the recyclization of the synthesized 2,2-dialkyl-4-hydroxymethyl-6-methylbenzo[f]isoquinolinium salts **3a-f**. In addition to resolving preparative questions it was also interesting to determine the effect of a methyl substituent in the *para* position of the benzene ring on the cyclization of salt **2**.

It was found that cyclization of salts **2a-e** occurs in the presence of aqueous KOH at a molar ratio of salt **2** to KOH of about 1:1, i.e. more forcing conditions when compared with their 3-R^1-substituted analogs (R^1 = phenyl, *p*-chlorophenyl, alkenyl) in which this ratio was 5: 1 [1-4].



1–4 a R = Me, **b** R = Et, **c** R = Pr, **d** R + R = $(CH_2)_4$,
e R + R = $(CH_2)_5$, **f** R + R = $(CH_2)_2O(CH_2)_2$; **3a–d, f** X = Cl, **e** X = Br

The lower reactivity of compounds **2a-e** is in line with the scheme proposed before for the cyclization of their analogs (**3**, R^1 = phenyl, alkenyl), according to which the $CH_2C{\equiv}CR^1$ takes part directly in the cyclization and base is the driving force for the process which includes electron transfer *via* a six-membered cyclic mechanism [13-15]. Evidently the methyl substituent in the *para* position of the benzene ring in salts **2a-f** unfavourably affects their cyclization because the shift of electrons caused by the positive inductive and hyperconjugative effects of a CH_3 group opposes the electron transfer in the six-membered cyclic mechanism.



Previously, a kinetic investigation of the cyclization of dimethyl(propargyl)[3-(*p*-tolyl)propyn-2-yl]-ammonium bromide has also shown that the presence of a methyl group in the *para* position of the benzene ring decreases the reaction rate [16]. It should be noted that, in contrast to the ammonium, pyrrolidinium, and piperidinium salts discussed **2a-e**, the cyclization of the morpholinium substituted salt **2f** occurs with a vigorous exotherm, even with a molar ratio of salt **2f** to KOH of 5:1. The observed effect can be explained by the marked inductive effect of a morpholine fragment associated with the presence of the unshared electron pair of the oxygen atom.

It was also found that only the salts **2e,f** gave the corresponding products **3e,f** in a crystallizable state while after cyclization of salt **2e** the reaction product was acidified with hydrobromic acid to give the hydrobromide salt **3e**. Salts **3a-d** could not be separated and characterized because of their hygroscopic properties and the salts form a glassy mass. All of the salts **3a-f** undergo recyclization without their separation from the reaction mixture following cyclization of compounds **2a-f**. The recyclizations were performed in the presence of an equimolar or two fold amount (in the case of salt **3f**) of KOH at 80-85ºC and with an overall yield of 62-70% for amines **4b-f** while the yield of amine **4a** was only 32% due to strong tarring. It should be noted that the products **4a-f** are formed in 8-15% yield *via* the above reported cyclization of salts **2a-f** with a five fold excess of salt **2** with respect to KOH.

The composition and structure of the novel compounds **1c,d,f, 2a-f, 3e-f, 4a-f** were confirmed from elemental analytical data and also from their IR spectra and NMR spectra of compounds **2e,f, 3e,f** and **4a-f**. Assignment of the signals in the ^{1}H NMR and ^{13}C NMR spectra of salts **3e,f** and amines **4a-f** were carried out from their 2D COSY, NOESY, and HMQC spectra.

The IR spectra of salts **3a,f** show the absence of the absorption bands in the region 2220-2240 (disubstituted acetylene bond) and 810-840 cm^{-1} (*para*-substituted benzene ring) which are characteristic of the salts **2a-f** but there are present bands at 820 and 870 cm^{-1} for the 1,2,4- and *penta*-ubstituted benzene rings respectively. Salts **2, 3** show absorptions at 1040, 1080, and 3200-3500 (OH groups), 1580, 1600, and 3130-3150 cm^{-1} (aromatic ring). The spectra of amines **4a-f** show absorption bands at 720-800 and 870 cm^{-1} (1,2,4- and *penta*-substituted benzene rings respectively) as well as bands at 1010, 1050, 1060-1110 cm^{-1} (ring C–O-C) and at 1500, 1580, 1600 and 3030-3040 cm^{-1} (aromatic ring).

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer for KBr tablets or in vaseline oil. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury VX 300 instrument (300 and 75 MHz respectively) at 300 K for solutions in DMSO-d_6–CCl_4 (1:3) and were referred to the residual non-deuterated solvent signal.

The starting amines **1a,b,e** were synthesized *via* a Mannich reaction as reported in [17] and 4-chloro-2-butynol was obtained using a reported method [18].

Synthesis of the Starting Amines (1c,d,f) (General Method). A mixture of *p*-tolylacetylene (120 mmol), paraformaldehyde (118 mmol), the corresponding secondary amine (120 mmol), ferric chloride (0.6 g), copper diacetate (0.4 g), and dioxane (80 ml) was held for 62 h at 90-92ºC, acidified with 20% aqueous HCl, and solvent was distilled off under reduced pressure. After removal of organic admixtures by extracting with ether (2×50 ml), the residue was basified with 20% aqueous NaOH solution and extracted with ether (3×50 ml). Drying over $MgSO_4$, evaporation of the extract, and vacuum distillation of the residue gave the target amine **1**.

Dipropyl[3-(*p*-tolyl)propyn-2-yl]amine (1c). Yield 16.90 g (62%); bp 135-136ºC (1-2 mm Hg), n_D^{20} 1.5212, mp of picrate 98-102ºC (EtOH). IR spectrum, ν, cm^{-1}: 810, 840, 1560, 1580, 2230, 3020. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.23 and 7.07 (2H, m and 2H, m, C_6H_4); 3.51 (2H, s, C$\underline{H_2}$C≡CAr); 2.44 (4H, m, N(CH_2)$_2$); 2.34 (3H, s, Ar-CH_3); 1.47 (4H, sext., *J* = 7.3, C$\underline{H_2}$CH$_3$); 0.92 (6H, t, *J* = 7.3, CH$_2$C$\underline{H_3}$). Found, %: C 84.18; H 10.32; N 6.26. $C_{16}H_{23}N$. Calculated, %: C 83.79; H 10.11; N 6.11.

N-[3-(*p*-Tolyl)propyn-2-yl]pyrrolidine (1d). Yield 10.20 g (43%); bp 157-158ºC (1 mm Hg), n_D^{20} 1.5570, mp of picrate 138-140ºC (EtOH). IR spectrum, ν, cm^{-1}: 810-840, 1560, 1600, 2220, 3030. ^{1}H NMR spectrum, δ, ppm: 7.24 and 7.07 (2H, m and 2H, m, C_6H_4); 3.54 (2H, s, C$\underline{H_2}$C≡CAr); 2.61 (4H, m, N(CH_2)$_2$); 2.35 (3H, s, Ar-CH_3); 1.78 (4H, m, N(CH$_2$C$\underline{H_2}$)$_2$) . Found, %: C 84.78; H 8.76; N 7.19. $C_{14}H_{17}N$. Calculated, %: C 84.37; H 8.54; N 7.03.

N-[3-(*p*-Tolyl)propyn-2-yl]morpholine (1f). Yield 12.05 g (46.7%); bp 151-153ºC (3-4 mm Hg), n_D^{20} 1.5632, mp picrate 157-158ºC (EtOH). IR spectrum, ν, cm^{-1}: 810-840, 1560, 1600, 2230, 3030. ^1H NMR spectrum, δ, ppm: 7.26 and 7.09 (2H, m and 2H, m, C_6H_4); 3.63 (4H, m, $O(CH_2)_2$); 3.43 (2H, s, $C\underline{H_2}C{\equiv}CAr$); 2.53 (4H, m, $N(CH_2)_2$); 2.35 (3H, s, Ar-CH_3). Found, %: C 78.54; H 8.19; N 6.71. $C_{14}H_{17}NO$. Calculated, %: C 78.14; H 7.96; N 6.51.

Alkylation of Amines 1a-f by 4-Chloro-2-butynol to Give Salts 2a-f (General Method). Chromatographically pure 4-chloro-2-butynol (30 mmol) was added to a solution of the amine **1a-f** (15 mmol) in acetonitrile (10 ml). The reaction mixture was held at 90-92ºC for 2-3 h and then for salts **2a-e** the solvent was removed under reduced pressure. The salts **2a-e** were washed with absolute ether (3 x 20 ml) and dried over P_2O_5. Salt **2f** crystallized upon cooling the reaction mixture and was filtered off and recrystallized from absolute alcohol. Salts **2a-e** are hygroscopic and it was not possible to determine their melting points.

(4-Hydroxybutyn-2-yl)[3-(*p*-tolyl)propyn-2-yl]dimethylammonium chloride (2a). Yield 4.10 g (98%). IR spectrum, ν, cm^{-1}: 810-840, 1560, 1600, 2230, 3030, 3100-3500. Found, %: C 69.57; H 7.46; Cl 13.01; N 5.21. $C_{16}H_{20}ClNO$. Calculated, %: C 69.18; H 7.26; Cl 12.76; N 5.04.

(4-Hydroxybutyn-2-yl)[3-(*p*-tolyl)propyn-2-yl]diethylammonium chloride (2b). Yield 3.76 g (82%). IR spectrum, ν, cm^{-1}: 810-850; 1560, 1600, 2220, 3020, 3100-3500. Found, %: C 71.08; H 8.12; Cl 11.86, N 4.76. $C_{18}H_{24}ClNO$. Calculated, %: C 70.69; H 7.91; Cl 11.59; N 4.58.

(4-Hydroxybutyn-2-yl)[3-(*p*-tolyl)propyn-2-yl]dipropylammonium chloride (2c). Yield 4.40 g (88%). IR spectrum, ν, cm^{-1}: 810-840, 1540, 1600, 2220, 3030, 3200-3500. Found, %: C 72.34; H 8.66; Cl 10.94; N 4.36. $C_{20}H_{28}ClNO$. Calculated, %: C 71.94; H 8.45; Cl 10.62; N 4.19.

N-(4-Hydroxybutyn-2-yl)-N-[3-(*p*-tolyl)propyn-2-yl]pyrrolidinium chloride (2d). Yield 3.91 g (86%). IR spectrum, ν, cm^{-1}: 810-840, 1540, 1600, 2220, 3030, 3200-3500. Found, %: C 71.56; H 7.46; Cl 11.99; N 4.76. $C_{18}H_{22}ClNO$. Calculated, %: C 71.16; H 7.25; Cl 11.67; N 4.61.

N-(4-Hydroxybutyn-2-yl)-N-[3-(*p*-tolyl)propyn-2-yl]piperidinium chloride (2e). Yield 4.41 g (93%). IR spectrum, ν, cm^{-1}: 810-840, 1550, 1600, 2220, 3020, 3200-3500. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.46 and 7.17 (2H, m and 2H, m, C_6H_4); 5.60 (1H, br. s, OH); 4.96 (2H, s, $C\underline{H_2}C{\equiv}CAr$); 4.72 (2H, t, *J* = 1.9, $NC\underline{H_2}C{\equiv}CCH_2$); 4.18 (2H, t, *J* = 1.9, $C\underline{H_2}OH$); 3.82 (4H, m, $N(CH_2)_2$); 2.38 (3H, s, Ar-CH_3); 1.96 (4H, m, $N(CH_2C\underline{H_2})_2$); 1.73 (2H, m, $N(CH_2CH_2)_2C\underline{H_2}$). Found, %: C 72.21; H 7.83; Cl 11.47; N 4.45. $C_{19}H_{24}ClNO$. Calculated, %: C 71.81; H 7.61; Cl 11.15; N 4.41.

N-(4-Hydroxybutyn-2-yl)-N-[3-(*p*-tolyl)propyn-2-yl]morpholinium chloride (2f). Yield 4.00 g (83%); mp 198-200ºC (abs. EtOH). IR spectrum, ν, cm^{-1}: 810-840, 1600, 2220, 3020, 3200-3500. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.48 and 7.18 (2H, m and 2H, m, C_6H_4); 5.57 (1H, br. s, OH); 5.13 (2H, s, $C\underline{H_2}C{\equiv}CAr$); 4.87 (2H, t, *J* = 2.0, $N(C\underline{H_2}C{\equiv}CCH_2$); 4.18 (2H, t, *J* = 2.0, $C\underline{H_2}OH$); 4.05 (4H, m, $N(CH_2)_2$); 3.84 (4H, m, $O(CH_2)_2$); 2.39 (3H, s, Ar-CH_3). Found, %: C 68.01; H 7.11; Cl 11.33; N 4.61. $C_{18}H_{22}ClNO_2$. Calculated, %: C 67.61; H 6.89; Cl 11.08; N 4.38.

Cyclization of Salts 2a-f to Salts 3a-f (General Method). An aqueous solution of KOH (3N, 0.7 ml) was added to a solution of salt **2a-f** (10 mmol) in water (4 ml) (5:1 molar ratio of salt to KOH). The mixture was heated to 50ºC. For salt **2f**, the temperature was raised to 100ºC and in the remaining cases to 85ºC. After cooling to room temperature, the reaction mixture was extracted with ether and dichloromethane (2:1, 3×30 ml). Titration of the extract with 0.1N H_2SO_4 showed that the extract contained 8-15% of amine **4a-f**, the picrate of which did not depress the melting point of the picrate of amine **4a-f** prepared by recyclization of salts **3a-f** (see below). After extraction, the aqueous solution was acidified with 20% aqueous HCl (or HBr in the case of salt **2e**). The cyclization products **3e,f** were separated in the crystalline state, filtered, washed on the filter with water, and dried. For separation of the products **3a-d** the acidified mass was evaporated to dryness and the residue was extracted with absolute ethanol. Addition of ether to the alcohol extract gave the glassy salts **3a-d**. They could not be prepared and characterized in the crystalline state.

4-Hydroxymethyl-6-methyl-2,2-pentamethylenebenzo[*f*]isoindolinium Bromide (3e). Yield 2.50 g (69%); mp 263-264ºC. IR spectrum, ν, cm^{-1}: 720, 870, 1030, 1050, 1080, 1580, 3040, 3200-3500. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 9.33 (1H, br. s, OH); 8.04 (1H, s, H-9); 7.93 (1H, d, *J* = 8.4, H-8); 7.52 (1H, d, *J* = 1.8, H-5); 7.45 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-7); 5.44 and 5.34 (2H, t, *J* = 2.9 and 2H, dd, J_1 = 3.2, J_2 = 2.5, H-1 and H-3); 4.34 (2H, d, *J* = 5.3, C$\underline{H_2}$OH); 3.40 and 3.02 (2H, m and 2H, m, α-H piperidino); 2.50 (3H, s, CH_3); 1.86-1.59 and 1.38 (5H, m and 1H, m, β,γ-H piperidino). ^{13}C NMR spectrum, δ, ppm: 137.45, 136.89, 134.77, 131.19, 130.62, 128.58, 128.42, 127.32, 122.91 and 120.76 (C arom.); 73.50 and 73.06 (C-1 and C-3); 56.98 (OCH_2); 52.03 (C-α piperidino); 22.38 (C-β piperidino); 21.37 (C-γ piperidino) and 21.17 (CH_3). Found, %: C 63.21; H 7.04; Br 22.38; N 4.05. $C_{19}H_{24}BrNO$. Calculated, %: C 62.99; H 6.68; Br 22.05; N 3.87.

4-Hydroxymethyl-6-methylspirobenzo[*f*]isoindoline-2,4'-morpholinium chloride (3f). Yield 2.30 g (73%), mp 158-159ºC. IR spectrum, ν, cm^{-1}: 720; 870, 1020, 1050, 1070, 1110, 1580, 1600, 3030, 3200-3400. 1H NMR spectrum, δ, ppm (*J*, Hz): 7.88 (1H, s, H-9); 7.75 (1H, d, *J* = 8.4, H-8); 7.75 (1H, d, *J* = 1.6, H-5); 7.31 (1H, dd, J_1 = 8.4, J_2 = 1.6, H-7); 5.88 (1H, br. s, OH); 5.53 and 5.21 (2H, s and 2H, s H-1, H-3); 4.97 (2H, s, C$\underline{H_2}$OH); 4.14 and 4.01 (2H, dt, J_1 = 13.8, J_2 = 5.0, and 2H dt, J_1 = 13.8, J_2 = 4.6, NCH_2 morpholino); 3.77 (4H, t, *J* = 4.8, OCH_2 morpholino); 2.54 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 135.32, 132.96, 131.29, 131.04, 129.27, 128.63, 127.88, 127.82, 122.88 and 121.26 (C arom.); 66.1 and 65.8 (C-1 and C-3); 61.39 (OC morpholino); 58.36 (NC morpholino); 58.09 (4-CH_2); 56.98 (4-CH_2) and 21.48 (CH_3). Found, %: C 68.02; H 7.16; Cl 11.33; N 4.61. $C_{18}H_{22}ClNO_2$. Calculated, %: C 67.61; H 6.93; Cl 11.08; N 4.38.

Recyclization of Salts 3a-f to Amines 4a-f (General Method). Salts **3a-f** were prepared by cyclization of compounds **2a-f** (10 mmol) in water (3 ml) and underwent cyclization without separation from the reaction mixture after extraction of the latter with a mixture of ether and dichloromethane (3:1, 2×25 ml). The product obtained contained the salts **3a-e** and was treated with a solution of KOH (10 mmol) in water (2 ml) (in the case of salt **3f** a solution of KOH (20 mmol) in water (4 ml)) and the mixture was held for 3-3.5 h at 80-85°C. Tarring occurred with salt **3a**. The cooled product was extracted with a mixture of ether and dichloromethane (3:1, 3×25 ml) and the extract was washed with water. In all cases, titration of the extract with 0.1N H_2SO_4 indicated the presence of 5.4-5.5 mmol (54-55%) of amine **4b-f**. The ether extract was dried over $MgSO_4$. Evaporation of solvent gave amines **4c,f** in the crystalline state and were recrystallized from a mixture of ether and dichloromethane (2:1). Amines **4a,b,d,e** were separated from the residue by distillation. After distillation, amines **4b,e** crystallized and were recrystallized from a mixture of ether and dichloromethane.

4-Dimethylaminomethyl-8-methyl-1,3-dihydronaphtho[1,2-*c*]furan (4a). Yield 0.77 g (32%); bp 128-130ºC (1-2 mm Hg). IR spectrum, ν, cm^{-1}: 730, 790, 870, 1060, 1100, 1580, 1600, 3030. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.71 (1H, d, *J* = 8.4, H-6); 7.53 (1H, s, H-5); 7.31 (1H, d, *J* = 1.9, H-9); 7.25 (1H, dd, J_1 = 8.4, J_2 = 1.9, H-7); 5.35 (2H, t, *J* = 3.2, H-3); 5.20 (2H, t, *J* = 3.2, H-1); 3.45 (2H, s, 4-CH_2); 2.51 (3H, s, 8-CH_3); 2.21 (6H, s, NCH_3). ^{13}C NMR spectrum, δ, ppm: 136.04, 134.92, 133.72, 130.82, 130.12, 127.57. 127.16, 126.51, 126.37, and 122.30 (C arom); 73.42 and 72.32 (C-1 and C-3); 62.31 (4-CH_2); 44.88 (NCH_3); 21.23 (8-CH_3). Found, %: C 80.02; H 8.14; N 6.03. $C_{16}H_{19}NO$. Calculated, %: C 79.63; H 7.94; N 5.81.

4-Diethylaminomethyl-8-methyl-1,3-dihydronaphtho[1,2-*c*]furan (4b). Yield 1.70 g (62%); bp 135-137ºC (3-4 mm Hg), mp 123-125 (ether–dichloromethane), mp picrate 187-190ºC (EtOH). IR spectrum, ν, cm^{-1}: 720, 760, 870, 1050, 1100, 1600, 3030. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.70 (1H, d, *J* = 8.4, H-6); 7.53 (1H, s, H-5); 7.31 (1H, d, *J* = 1.8, H-9); 7.25 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-7); 5.34 (2H, t, *J* = 3.1, H-3); 5.22 (2H, t, *J* = 3.1, H-1); 3.60 (2H, s, 4-CH_2); 2.51 (3H, s, 8-CH_3); 2.50 (4H, q, *J* = 7.1, C$\underline{H_2}$$CH_3$); 1.04 (6H, t, *J* = 7.1, CH_2C$\underline{H_3}$). Found, %; C 80.65; H 8.83; N 5.45. $C_{18}H_{23}NO$. Calculated, %; C 80.26; H 8.61; N 5.21.

4-Dipropylaminomethyl-8-methyl-1,3-dihydronaphtho[1,2-*c*]furan (4c). Yield 1.90 g (64.1%); mp 97-98ºC (ether–dichloromethane), mp picrate 184-185ºC (EtOH). IR spectrum, ν, cm^{-1}: 770, 800, 870, 1050, 1110, 1580, 3040. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.70 (1H, d, *J* = 8.3, H-6); 7.53 (1H, s, H-5); 7.31 (1H, d, *J* = 1.8, H-9); 7.25 (1H, dd, J_1 = 8.3, J_2 = 1.8, H-7); 5.34 (2H, t, *J* = 3.0, H-3); 5.22 (2H, t, *J* = 3.0, H-1); 3.58 (2H, s, 4-CH_2); 2.51 (3H, s, 8-CH_3); 2.36 (4H, t, *J* = 7.3, NCH_2); 1.48 (4H, sext., *J* = 7.3, C$\underline{H_2}$$CH_3$); 0.85 (6H, t,

J = 7.3, $CH_2C\underline{H}_3$). ^{13}C NMR spectrum, δ, ppm: 135.82, 134.67, 133.60, 130.87, 130.77, 127.41, 127.01, 126.38, 126.21 and 122.22 (C arom.); 73.47 and 72.23 (C-1 and C-3); 57.62 (4-CH_2); 55.36 (C-α propyl); 21.19 (8-CH_3); 19.50 (C-β propyl); 11.47 (C-γ propyl). Found, %: C 81.16; H 9.38; N 4.86. $C_{20}H_{27}NO$. Calculated, %: C 80.76; H 9.15; N 4.71.

N-(8-Methyl-1,3-dihydronaphtho[1,2-*c*]furan-4-yl)methylpyrrolidine (4d). Yield 1.80 g (66%); bp 200-201ºC (1-2 mm Hg); mp picrate 189-192ºC (EtOH). IR spectrum, ν, cm^{-1}: 780, 805, 870, 1130, 1500, 1600, 3040. ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.71 (1H, d, J = 8.3, H-6); 7.55 (1H, s, H-5); 7.31 (1H, d, J = 1.8, H-9); 7.25 (1H, dd, J_1 = 8.3, J_2 = 1.8, H-7); 5.35 (2H, t, J = 3.1, H-3); 5.21 (2H, t, J = 3.1, H-1); 3.66 (2H, s, 4-CH_2); 2.51 (3H, s, 8-CH_3); 2.48 (4H, m, α-CH_2 pyrrolidine); 1.77 (4H, m, β-CH_2 pyrrolidine). Found, %: C 81.27; H 8.14; N 5.39. $C_{18}H_{21}NO$. Calculated, %: C 80.86; H 7.92; N 5.24.

N-(8-Methyl-1,3-dihydronaphtho[1,2-*c*]furan-4-yl)methylpiperidine (4e). Yield 1.91 g (68%); bp 209-210ºC (1-2 mm Hg); mp 65-66ºC (ether–dichloromethane), mp picrate 194-195ºC (EtOH), mp hydrochloride 244-245ºC (abs. EtOH). IR spectrum, ν, cm^{-1}: 720, 770, 790, 870, 1010, 1030, 1130, 1580, 3030. ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.69 (1H, d, J = 8.4, H-6); 7.50 (1H, s, H-5); 7.30 (1H, d, J = 1.8, H-9); 7.24 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-7); 5.34 (2H, t, J = 3.1, H-3); 5.22 (2H, t, J = 3.1, H-1); 3.49 (2H, s, 4-CH_2); 2.51 (3H, s, 8-CH_3); 2.36 (4H, m, α-CH_2 piperidine); 1.55 (4H, m, β-CH_2 piperidine); 1.44 (2H, m, CH_2 γ-piperidine). ^{13}C NMR spectrum, δ, ppm: 136.00, 134.71, 133.66, 130.84, 130.71, 129.93, 127.41, 127.02, 126.25 and 122.17 (C arom.), 73.46 and 72.23 (C-1 and C-3); 61.84 (4-CH_2); 53.92 (C-α piperidine); 25.51 (C-β piperidine); 23.90 (C-γ piperidine); 21.20 (8-CH_3). Found, %: C 81.53; H 8.47; N 5.22. $C_{19}H_{23}NO$. Calculated, %: C 81.14; H 8.24; N 4.98.

N-(8-Methyl-1,3-dihydronaphtho[1,2-*c*]furan-4-yl)methylmorpholine (4f). Yield 1.98 g (70%); mp 117-118ºC (ether–dichloromethane), mp picrate 107-108ºC (EtOH), mp hydrochloride 175-176ºC (abs. EtOH). IR spectrum, ν, cm^{-1}: 730, 760, 870, 1010, 1060, 1570, 1600, 3030. ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.71 (1H, d, J = 8.3, H-6); 7.53 (1H, s, H-5); 7.32 (1H, d, J = 1.9, H-9); 7.26 (1H, dd, J_1 = 8.3, J_2 = 1.9, H-7); 5.35 (2H, t, J = 3.0, H-3); 5.24 (2H, t, J = 3.0, H-1); 3.60 (4H, m, OCH_2 morpholine); 3.55 (2H, s, 4-CH_2); 2.52 (3H, d, 8-CH_3); 2.40 (4H, m, NCH_2 morpholine). ^{13}C NMR spectrum, δ, ppm: 135.91, 134.98, 133.84, 130.66, 128.84, 127.44, 127.15, 126.62, 126.49 and 122.19 (C arom.), 73.42 and 72.26 (C-1 and C-3); 66.01 (OCH_2 morpholino); 61.41 (4-CH_2); 53.03 (NCH_2 morpholine); 21.19 (8-CH_3). Found, %: C 76.72; H 7.69; N 5.19. $C_{18}H_{21}NO_2$. Calculated, %: C 76.33; H 7.47; N 4.94.

REFERENCES

1. E. O. Chukhadzhyan, A. R. Gevorkyan, El. O. Chukhadzhyan, K. G. Shakhatuni, F. S. Kinoyan, and G. A. Panosyan, *Khim. Geterotsikl. Soedin.*, 34 (2004). [*Chem. Heterocycl. Comp.*, **40**, 29 (2004)].
2. E. O. Chukhajian, A. A. Khachatryan, A. R. Gevorkyan, and G. A. Panosyan, *Khim. Geterotsikl. Soedin.*, 834 (2007). [*Chem. Heterocycl. Comp.*, **43**, 701 (2007)].
3. A. R. Gevorkyan, E. O. Chukhadzhyan, El. O. Chukhadzhyan, and G. A. Panosyan, *Khim. Geterotsikl. Soedin.*, 212 (2004). [*Chem. Heterocycl. Comp.*, **40**, 177 (2004)].
4. E. O. Chukhajian, M. K. Nalbandyan, and G. A. Panosyan, *Khim. Geterotsikl. Soedin.*, 528 (2007). [*Chem. Heterocycl. Comp.*, **43**, 430 (2007)].
5. E. O. Chukhajian, H. R. Gevorkyan, A. A. Khachatryan, El. O. Chukhajiyan, and H. A. Panosyan, *Khim. Geterotsikl. Soedin.*, 1329 (2006). [*Chem. Heterocycl. Comp.*, **42**, 1151 (2006)].
6. E. O. Chukhajian, H. R. Gevorkyan, El. O. Chukhajian, K. G. Shakhatuni, H. A. Panosyan, and R. A. Tamazyan, *J. Heterocycl. Chem.*, **40**, 1059 (2003).
7. W. M. F. Fabian and G. Kollenz in: H. S. Rzepa and C. O. Kappe (editors), *Proceedings of the ECHET, The Electronic Conference on Heterocyclic Chemistry 98* (1998).

8. D. T. Brown, *Mechanisms of Molecular Migrations*, Vol. 1, Wiley, New York (1968), p. 209.
9. M. Wahrem, *Z. Chem.*, **9**, 241 (1969).
10. V. P. Litvinov, *Usp. Khim.*, 45 (1999).
11. S. P. Gromov and A. N. Kost, *Heterocycles*, **38**, 1127 (1994).
12. G. G. Danagulyan, *Khim. Geterotsikl. Soedin.*, 1445 (2005). [*Chem. Heterocycl. Comp.*, **41**, 1205 (2005)].
13. E. O. Chukhadzhyan, A. R. Gevorkyan, El. O. Chukhadzhyan, and F. S. Kinoyan, *Zh. Org. Khim.*, **41**, 369 (2005).
14. E. O. Chukhajian, M. K. Nalbandyan, H. R. Gevorkyan, El. O. Chukhajian, and H. A. Panosyan, *J. Heterocycl. Chem.*, **45**, 687 (2008).
15. E. O. Chukhadzhyan, M. K. Nalbandyan, A. R. Gevorkyan, and F. S. Kinoyan, *Arm. Khim. Zh.*, **60**, 83 (2007).
16. I. A. Abramyan-Babayan and A. T. Babayan, *Arm. Khim. Zh.*, **25**, 19 (1972).
17. El. O. Chukhadzhyan, E. O. Chukhadzhyan, and A. T. Babayan, *Zh. Org. Khim,* **10**, 46 (1974).
18. G. Dupont, R. Dulou, and G. Lefebvre, *Bull. Soc. Chim. Fr.*, 816 (1954).