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Three-Component Condensation of 2-Naphthylamine with Aromatic Aldehydes and 5-(2-Furyl)-1,3-cyclohexanedione

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Abstract—Three-component condensation of 5-(2-furyl)-1,3-cyclohexanedione with 2-naphthylamine and aromatic or heteroaromatic aldehydes afforded 12-aryl(hetaryl)-9-(2-furyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]-acridin-11-ones possessing two asymmetric carbon atoms (C^9 and C^{12}). The products were found to be formed as mixtures of diastereoisomers.

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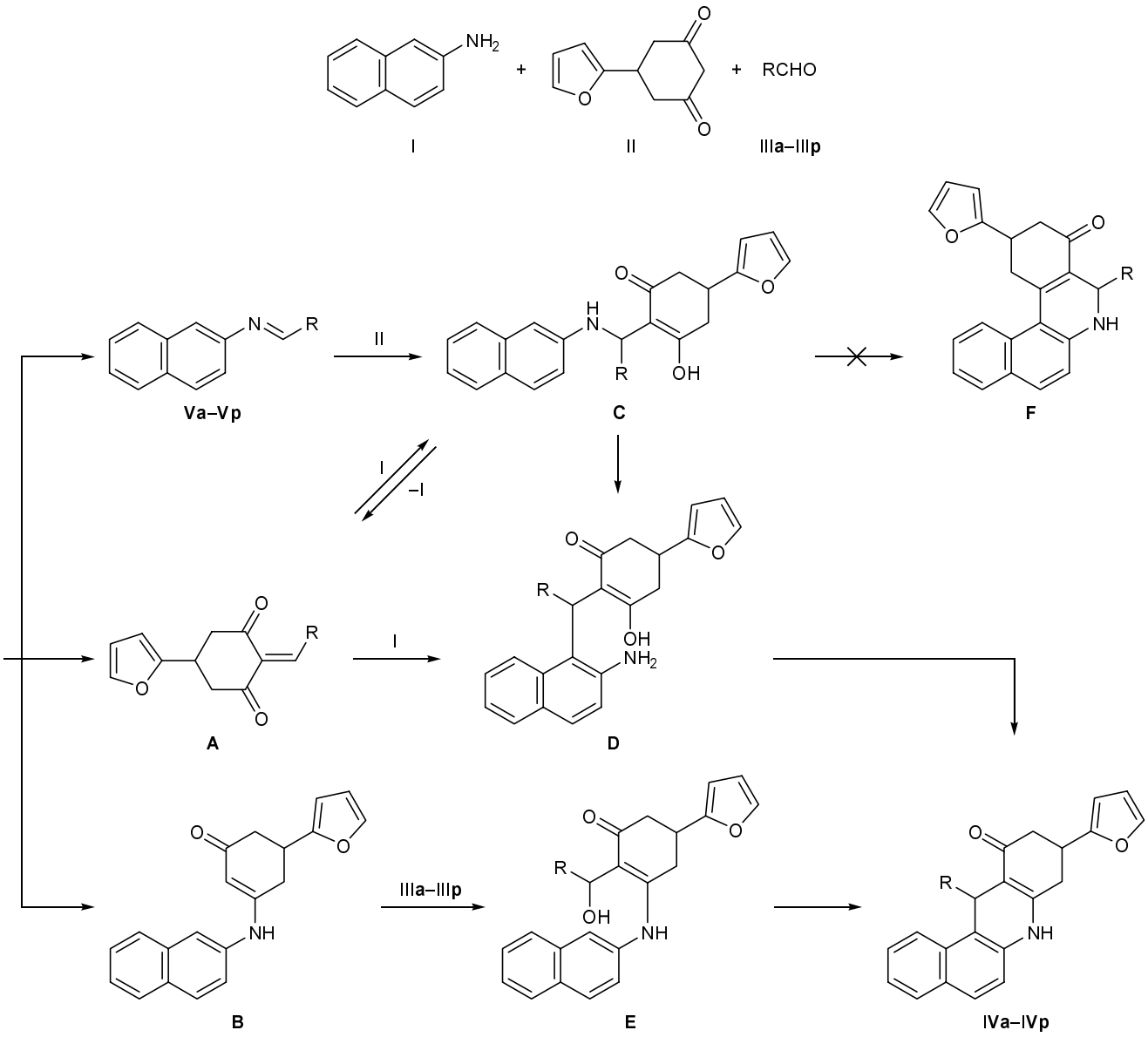
Reactions of 2-naphthylamine with carbonyl compounds are widely used in the synthesis of benzo[*f*]-quinoline derivatives. Among these, Doebner, Doebner–Miller, Conrad–Limpach, and Knorr syntheses are well known [1]. We previously showed [2] that 2-naphthylamine reacts with aromatic aldehydes and cyclohexanone in the presence of acid catalyst to give tetrahydrobenzo[*a*]phenanthridine derivatives (i.e., compounds containing fused benzoquinoline and cyclohexane fragments). Reactions of 2-naphthylamine with aromatic aldehydes and 3- or 4-methylcyclohexanone lead to formation of two types of products, methyl-substituted tetrahydrobenzo[*a*]phenanthridines and tetrahydrobenzo[*a*]acridines [3]. Both these include a benzo[*f*]quinoline fragment and attract interest as structural analogs of alkaloids [4, 5], enzyme inhibitors [6], bactericides [7], and antibiotics [8]. Blache *et al.* [4] reported that modified acridine derivatives, in particular tetrahydroacridines having a carbonyl group (floxacrine analogs), exhibit a stronger antibacterial activity than the corresponding compounds having no carbonyl group.

The present work was aimed at synthesizing new partially hydrogenated oxo derivatives of acridine containing a benzo[*f*]quinoline fragment. For this purpose, we examined three-component condensation of 2-naphthylamine (**I**) with 5-(2-furyl)-1,3-cyclohexanedione (**II**) and aromatic or heteroaromatic aldehydes **IIIa**–**IIIp**. The use of cyclic β-diketone in this reaction allowed us to introduce a carbonyl group into a fused heteroring simultaneously with building of azaphenanthrene skeleton. Moreover, insofar as 5-(2-furyl)-1,3-cyclohexanedione is an unsymmetrical ketone, the resulting molecule will contain both pharmacophoric furan ring and an asymmetric center which is an important attribute of biologically active compounds whose effect strongly depends on the steric structure.

As aldehyde components in the condensation with amine **I** and diketone **II** we used substituted benzaldehydes **IIIa**–**IIIm**, 3- and 4-pyridinecarbaldehydes **IIIn** and **IIIo**, and 2-furaldehyde **IIIp**. The reactions were carried out by heating equimolar amounts of the reactants in boiling ethanol. Due to high reactivity of β-diketone **II**, its condensation with amine **I** and aldehydes **III** in alcoholic medium required no acid catalyst; presumably, the enol form of **II** played the role of such a catalyst. As a result, the corresponding 12-aryl(hetaryl)-9-(2-furyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-ones **IVa**–**IVp** were obtained in 27–79% yield.

The formation of benzo[*a*]acridine systems may be accomplished along three pathways since each reactant in a three-component system is capable of reacting first with any of the two other components. Therefore, the first reaction stage could produce three intermediates: *N*-aryl(hetaryl)methylidene-2-naphthylamine (**V**), 2-aryl(heteryl)methylidene-5-(2-furyl)-1,3-cyclohexanedione **A**, and 5-(2-furyl)-3-(2-naphthylamino)-2-cyclohexenone **B** (Scheme 1). The next stage is reaction of intermediate **V**, **A**, or **B** with the third component, and it can include a sequence of transformations. For instance, Schiff base **V** takes up diketone **II**

Scheme 1.



R = 2-FC_6H_4 (**a**), 4-FC_6H_4 (**b**), 3-HOC_6H_4 (**c**), 4-HOC_6H_4 (**d**), 3,4-$(HO)_2C_6H_3$ (**e**), 3,4-$(MeO)_2C_6H_3$ (**f**), 3,4-$CH_2O_2C_6H_3$ (**g**), 4-HO-3-$MeOC_6H_3$ (**h**), 3-EtO-4-HOC_6H_3 (**i**), 3-EtO-4-EtC(O)OC_6H_3 (**j**), 4-$PrOC_6H_4$ (**k**), 4-$Me_2NC_6H_4$ (**l**), 4-$Et_2NC_6H_4$ (**m**), 3-pyridyl (**n**), 4-pyridyl (**o**), 2-furyl (**p**).

molecule to give 2-[aryl(2-naphthylamino)methylidene]-5-(2-furyl)-1,3-cyclohexanedione **C** which undergoes hydramine fission into 2-naphthylamine (**I**) and 2-arylmethylidene-1,3-cyclohexanedione **A**. The latter adds to 2-naphthylamine (**I**) at the carbon atom possessing the largest electron density (in the α-position with respect to the amino group) with formation of enamino hydroxy ketone **D** whose dehydration is accompanied by ring closure to give benzo[*a*]acridinone system **IV**. It should be noted that the formation of enamino hydroxy ketone **D** may be regarded as resulting from rearrangement of intermediate **C** via migration of the arylmethylidenecyclohexandione fragment to the naphthalene α-carbon atom, as in the transformation of alkyl-, dialkyl-, and trialkyl(phenyl)ammonium halides known as the Hofmann–Martius rearrangement [9].

Cyclohexanedione **A** is capable of reacting with the third component, naphthylamine **I**, by adding at the amino group or α-carbon atom in the naphthalene ring, yielding amino diketone **C** or enamino hydroxy ketone **D**. The above noted transformation of intermediate **C**

into **D**, followed by cyclocondensation to benzo[*a*]-acridinone **IV**, makes the addition of **A** at the α-carbon atom preferred to the addition at the amino group.

Cyclohexenone **B** takes up aldehyde **III** at the endocyclic double bond, leading to intermediate **E**. The latter may be regarded as a substituted benzyl alcohol which is capable of undergoing condensation with aromatic compounds, as in acid-catalyzed reactions of arenes with aldehydes [10]. The condensation involves electron-rich α-carbon atom of the naphthalene fragment to give final benzo[*a*]acridinone **IV**.

Of the three possible primary intermediates (**V**, **A**, and **B**), we succeeded in isolating only Schiff bases **V**. Insofar as isolated Schiff bases **V** smoothly reacted with furylcyclohexanediones **II** to produce benzo[*a*]-acridinones **IV**, the pathway involving initial reaction of amine **I** with aldehydes **IIIa**–**IIIk**, despite its apparent complexity, seems to be the most probable. On the other hand, the two other pathways cannot be ruled out, for the rate of subsequent transformations of intermediate cyclohexanedione **A** and cyclohexenone **B** may be much higher than the rate of their formation.

The yield of target products **IV** depends on the substituent R in initial aldehydes **III**. The reactions with benzaldehydes **IIIf**–**IIIi** and **IIIk**–**IIIm** having electron-donor alkoxy or alkylamino groups in the benzene ring, as well with 3-pyridinecarbaldehyde (**IIIn**), are characterized by high yields of the corresponding benzoacridinones **IV**. The yields of compounds **IIIa** and **IIIp** from *o*-fluorobenzaldehyde and 2-furaldehyde, respectively, are lower, presumably due to negative inductive effect of the fluorine and oxygen atoms; in addition, the condensations with **IIIa** and **IIIp** were accompanied by formation of unidentified by-products.

It should be noted that reactions of some amines **V** with cyclohexanedione **II** have already been reported [11]. However, on the basis of only IR spectral data, the products were assigned the structure of 5-aryl-2-furyl-1,2,3,4-tetrahydrobenzo[*a*]phenanthridin-4-ones **F** which are isomeric to benzoacridinones **IV**. Structure **F** could be formed as a result of intramolecular ring closure in intermediate amino ketones **C**. Using IR and ^{1}H NMR spectroscopy and mass spectrometry in combination with published data [3, 12] obtained with the aid of two-dimensional NMR techniques (COSY, NOESY, HSQC, and HMBC), we found that, like the products of three-component condensation of amine **I** with aromatic (heteroaromatic) aldehydes and furylcyclohexanedione **II**, the compounds described in [11] have the structure of 12-R-9-(2-furyl)-7,8,9,10,-11,12-hexahydrobenzo[*a*]acrydin-11-ones **IV**, regardless of the substituent R.

The IR spectra of **IVa**–**IVp** contained strong absorption bands at 1590 and 1525 cm^{-1} which should be assigned to the enaminocarbonyl fragment (1580, 1520 cm^{-1}) [13]. Strong bands at 3320–3270 and 1640–1630 cm^{-1} belong, respectively, to stretching and bending vibrations of the secondary amino group. Stretching vibrations of the alkyl and cycloalkyl C–H bonds appear at 2955–2875 cm^{-1}, and those of aromatic and heteroaromatic C–H bonds, at 3070–3030 cm^{-1}. Vibrations of the furan C–O–C fragment give rise to a strong absorption band at 1255–1230 cm^{-1}. Alkoxy-substituted compounds **IVf**–**IVk** show in the spectra an additional C–O–C band in the same region. The ester carbonyl group in benzoacridinone **IVj** is characterized by absorption at 1720 cm^{-1}.

The mass spectra of **IVa**–**IVp** contained the molecular ion peaks with a relative intensity of 13 to 34%. The most abundant ion (100%) is $[M - R]^+$ (*m*/*z* 314). Also, $[M - R + H]^+$ ion peak was present (*m*/*z* 315, I_{rel} 15–18%). Compound **IVl** showed in the spectrum a peak from the $[R + H]^+$ ion with *m*/*z* 121 (I_{rel} 32%), indicating relative stability of *N*,*N*-dimethylaniline ion to electron impact. In the mass spectra of all acridinones **IV** we observed an ion peak with *m*/*z* 192 (I_{rel} 8–25%), resulting from elimination of the $C_4H_3OCHCH_2CO$ fragment from the $[M - R]^+$ ion, and ion peak with *m*/*z* 191 $[192 - H]^+$ (I_{rel} 7–20%).

The ^{1}H NMR spectra of **IVa**–**IVp** were similar to those described previously for structurally related benzoacridinones [3]. Signals from the furan ring protons appeared as doublets at δ 5.75–6.39 and 7.94–8.08 ppm. Analysis of the aliphatic region of the spectrum showed that the isolated products are mixtures of two stereoisomers with pseudoequatorial and pseudoaxial orientation of the furyl substituent on C^9 at a ratio of 2:1. The 9-H proton gives two multiplets at δ 3.27–3.57 ppm. On the basis of their positions and half-widths, the upfield multiplet was assigned to the axial 9-H proton, and the downfield, to equatorial. The half-width of the 9-H$_{ax}$ signal is larger than that of 9-H$_{eq}$, for coupling constant *ax*–*ax*′ (~9 Hz) is much greater than *ax*–*eq*′ or *eq*–*eq*′ (~6 Hz).

We also observed separate signals from the NH and 12-H protons (singlets) in each stereoisomer. Their intensity ratio was consistent with the intensity ratio of 9-H. In the isomer with axial furyl substituent on C^9, the NH and 12-H protons suffer from shielding effect of the furan ring, and their signals are located in

a stronger field, as compared to the isomer with equatorial 9-(2-furyl) group. Correspondingly, the 4'-H proton in the furan ring gives two signals belonging to different diastereoisomers. We succeeded in separating some compounds **IV** into particular isomers by fractional crystallization from DMF (**IVb**, **IVe**, **IVh**, **IVi**) or ethanol–benzene (1:3) (**IVd**).

EXPERIMENTAL

The IR spectra were recorded in KBr on a Nicolet Protege-460 Fourier spectrometer. The NMR spectra were measured on Bruker AC-500 (500 MHz) and Tesla BS-567 (100 MHz) instruments from solutions in DMSO-d_6 using tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were run on a Finnigan MAT Incos-50 mass spectrometer and on a Hewlett–Packard HP 5890/5972 GC–MS system (HP-5MS column, 30 m×0.25 mm×0.25 μm, 5% of phenylmethylsilicone; injector temperature 250°C). The melting points were determined on a Kofler apparatus.

5-(2-Furyl)-1,3-cyclohexanedione (**II**) was synthesized from diethyl malonate and furfurylideneacetone with intermediate isolation of 6-(2-furyl)-2,4-dioxocyclohexanecarboxylic acid [11], mp 150–151°C. *N*-Aryl(hetaryl)methylidene-2-naphthylamines **Va**–**Vb** were prepared as described in [2].

12-Aryl(hetaryl)-9-(2-furyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-ones IVa–IVp (*general procedure*). *a.* A solution of 5 mmol of 2-naphthylamine (**I**), 5 mmol of 5-(2-furyl)-1,3-cyclohexanedione (**II**), and 5 mmol of aldehyde **IIIa**–**IIIp** in 20 ml of ethanol was heated for 3–4 h under reflux. The precipitate was filtered off and washed with diethyl ether.

b. A solution of 5 mmol of diketone **II** and 5 mmol of Schiff base **IIIa**–**IIIp** in 20 ml of 1-butanol was heated for 2.5–3 h under reflux. The products were isolated as described above in *a*. Yield 32–78%.

12-(2-Fluorophenyl)-9-(2-furyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVa). Yield 29%, mp 311–312°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.50 m (2H, 8-H); 2.92 m (2H, 10-H); 3.36 m and 3.54 m (1H, 9-H); 5.90 d.d and 6.39 d.d (1H, 4'-H, ^3J = 3.3, ^4J = 1.4); 5.95 s and 6.01 s (1H, 12-H); 6.22 d (1H, 3'-H, ^3J = 7.3); 6.87–7.15 m (4H, H_{arom}); 7.30 m, 7.58 m, and 7.79 m (6H, 1-H–6-H); 8.01 d (1H, 5'-H, ^3J = 1.4); 9.81 s and 9.90 s (1H, NH). Found, %: N 3.34. $C_{27}H_{20}FNO_2$. Calculated, %: N 3.42.

12-(4-Fluorophenyl)-9-(2-furyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVb). Yield 48%.

Isomer 9-*ax*. mp 238–239°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.53 m (2H, 8-H), 2.90 m (2H, 10-H), 3.42 m (1H, 9-H), 5.75 d.d (1H, 4'-H, ^3J = 3.5, ^4J = 1.5), 5.81 s (1H, 12-H), 6.12 d (1H, 3'-H, ^3J = 3.5), 6.80 t and 7.16 d (4H, H_{arom}, ^3J = 8.8), 7.20–7.50 m and 7.60–7.74 m (6H, 1-H–6-H), 7.90 d (1H, 5'-H, ^3J = 1.2), 9.70 s (1H, NH). Found, %: N 3.17. $C_{27}H_{20}FNO_2$. Calculated, %: N 3.42.

Isomer 9-*eq*. mp 303–304°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.53 m (2H, 8-H), 2.90 m (2H, 10-H), 3.35 m (1H, 9-H), 6.32 d.d (1H, 4'-H, ^3J = 3.5, ^4J = 1.5), 5.90 s (1H, 12-H), 6.12 d (1H, 3'-H, ^3J = 3.5), 6.80 t and 7.16 d (4H, H_{arom}, ^3J = 8.8), 7.20–7.50 m and 7.60–7.74 m (6H, 1-H–6-H), 7.90 d (1H, 5'-H, ^3J = 1.2), 9.78 s (1H, NH). Found, %: N 3.23. $C_{27}H_{20}FNO_2$. Calculated, %: N 3.42.

9-(2-Furyl)-12-(3-hydroxyphenyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVc). Yield 43%, mp 317–318°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.58 m (2H, 8-H); 2.89 m (2H, 10-H); 3.46 m and 3.57 m (1H, 9-H); 5.71 s and 5.79 s (1H, 12-H); 5.90 d.d and 6.40 d.d (1H, 4'-H, ^3J = 3.4, ^4J = 1.3); 6.20 d (1H, 3'-H, ^3J = 3.4); 6.41 m, 6.63 m, and 6.88 m (4H, H_{arom}); 7.30–7.42 m and 7.60–7.80 m (6H, 1-H–6-H); 7.92 d (1H, 5'-H, ^3J = 1.4); 8.96 s and 9.04 s (1H, OH); 9.72 s and 9.80 s (1H, NH). Found, %: C 79.43; H 5.04; N 3.27. $C_{27}H_{21}NO_3$. Calculated, %: C 79.61; H 5.16; N 3.44.

9-(2-Furyl)-12-(4-hydroxyphenyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVd). Yield 36%.

Isomer 9-*ax*. mp 272–273°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.60 m (2H, 8-H), 2.95 m (2H, 10-H), 3.46 m (1H, 9-H), 5.72 s (1H, 12-H), 5.90 d.d (1H, 4'-H, ^3J = 3.6, ^4J = 1.5), 6.12 d (1H, 3'-H, ^3J = 3.6), 6.48 d and 7.00 d (4H, H_{arom}, ^3J = 7.8), 7.18–7.54 m and 7.61–7.80 m (6H, 1-H–6-H), 7.90 d (1H, 5'-H, ^3J = 1.7), 9.00 br.s (1H, OH), 9.69 s (1H, NH). Found, %: C 79.53; H 4.91; N 3.29. $C_{27}H_{21}NO_3$. Calculated, %: C 79.61; H 5.16; N 3.44.

Isomer 9-*eq*. mp 301–302°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.60 m (2H, 8-H), 2.95 m (2H, 10-H), 3.32 m (1H, 9-H), 5.78 s (1H, 12-H), 6.33 d.d (1H, 4'-H, ^3J = 3.6, ^4J = 1.5), 6.12 d (1H, 3'-H, ^3J = 3.6), 6.48 d and 7.00 d (4H, H_{arom}, ^3J = 7.8), 7.18–7.54 m and 7.61–7.80 m (6H, 1-H–6-H), 7.90 d (1H, 5'-H, ^3J = 1.7), 9.00 br.s (1H, OH), 9.78 s (1H, NH). Found, %: C 79.37; H 4.88; N 3.31. $C_{27}H_{21}NO_3$. Calculated, %: C 79.61; H 5.16; N 3.44.

12-(3,4-Dihydroxyphenyl)-9-(2-furyl)-7,8,-9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVe). Yield 35%.

Isomer 9-*ax*. mp 275–276°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.50 m (2H, 8-H), 2.89 m (2H, 10-H), 3.50 m (1H, 9-H), 5.65 s (1H, 12-H), 5.90 d.d (1H, 4'-H, ^3J = 3.7, ^4J = 1.8), 6.12 d (1H, 3'-H, ^3J = 3.7), 6.44 m and 6.60 s (3H, H_{arom}), 7.14–7.42 m and 7.57–7.78 m (6H, 1-H–6-H), 7.96 d (1H, 5'-H, ^3J = 1.6), 9.52 s (1H, NH). Found, %: C 76.48, H 4.72, N 3.11. $C_{27}H_{21}NO_4$. Calculated, %: C 76.60; H 4.96; N 3.31.

Isomer 9-*eq*. mp 301–302°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.50 m (2H, 8-H), 2.89 m (2H, 10-H), 3.36 m (1H, 9-H), 5.70 s (1H, 12-H), 6.30 d.d (1H, 4'-H, ^3J = 3.7, ^4J = 1.8), 6.12 d (1H, 3'-H, ^3J = 3.7), 6.44 m and 6.60 s (3H, H_{arom}), 7.14–7.42 m and 7.57–7.78 m (6H, 1-H–6-H), 7.96 d (1H, 5'-H, ^3J = 1.6), 9.63 s (1H, NH). Found, %: C 76.44; H 4.89; N 2.97. $C_{27}H_{21}NO_4$. Calculated, %: C 76.60; H 4.96; N 3.31.

12-(3,4-Dimethoxyphenyl)-9-(2-furyl)-7,8,9,10,-11,12-hexahydrobenzo[*a*]acridin-11-one (IVf). Yield 71%, mp 253–254°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.53 m (2H, 8-H), 2.90 m (2H, 10-H), 3.36 m and 3.50 m (1H, 9-H), 3.65 s (3H, OMe), 3.70 s (3H, OMe), 5.71 s and 5.80 s (1H, 12-H), 5.87 d.d and 6.30 d.d (1H, 4'-H, ^3J = 3.5, ^4J = 1.6), 6.12 d (1H, 3'-H, ^3J = 3.5), 6.51 m and 6.91 d (3H, H_{arom}, ^3J = 7.9), 7.22–7.41 m and 7.64–7.73 m (6H, 1-H–6-H), 7.93 t (1H, 5'-H, ^3J = 1.3), 9.40 s and 9.50 s (1H, NH). Found, %: C 77.07; H 5.39; N 3.18. $C_{29}H_{25}NO_4$. Calculated, %: C 77.16; H 5.54; N 3.10.

9-(2-Furyl)-12-(3,4-methylenedioxyphenyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVg). Yield 79%, mp 292–293°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.50 m (2H, 8-H), 2.91 m (2H, 10-H), 3.38 m and 3.51 m (1H, 9-H), 5.80 m (3H, 12-H, OCH_2O), 5.89 d.d and 6.30 d.d (1H, 4'-H, ^3J = 3.3, ^4J = 1.5), 6.13 d (1H, 3'-H, ^3J = 3.3), 6.48–6.63 m (3H, H_{arom}), 7.23–7.41 m and 7.62–7.75 m (6H, 1-H–6-H), 7.91 t (1H, 5'-H, ^3J = 1.4), 9.42 s and 9.51 s (1H, NH). Found, %: C 77.09; H 4.76; N 3.05. $C_{28}H_{21}NO_4$. Calculated, %: C 77.24; H 4.83; N 3.22.

9-(2-Furyl)-12-(4-hydroxy-3-methoxyphenyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVh). Yield 56%.

Isomer 9-*ax*. mp 320–321°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.52 m (2H, 8-H); 2.88 m (2H, 10-H); 3.47 m (1H, 9-H); 3.65 s (3H, OMe); 5.70 s (1H, 12-H); 5.85 d.d (1H, 4'-H, ^3J = 3.4, ^4J = 1.5); 6.12 d (1H, 3'-H, ^3J = 3.4); 6.40 m, 6.82 s, and 6.90 s (3H, H_{arom}); 7.18–7.48 m and 7.58–7.78 m (6H, 1-H–6-H); 7.95 d (1H, 5'-H, ^3J = 1.6); 9.50 s (1H, NH). Found, %: C 76.66; H 5.13; N 3.10. $C_{28}H_{23}NO_4$. Calculated, %: C 76.89; H 5.26; N 3.20.

Isomer 9-*eq*. mp 325–326°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.52 m (2H, 8-H); 2.88 m (2H, 10-H); 3.38 m (1H, 9-H); 3.72 s (3H, OMe); 5.76 s (1H, 12-H); 6.30 d.d (1H, 4'-H, ^3J = 3.4, ^4J = 1.5); 6.12 d (1H, 3'-H, ^3J = 3.4); 6.40 m, 6.82 s, and 6.90 s (3H, H_{arom}); 7.18–7.48 m and 7.58–7.78 m (6H, 1-H–6-H); 7.95 d (1H, 5'-H, ^3J = 1.6); 9.60 s (1H, NH). Found, %: C 76.73; H 5.19; N 3.23. $C_{28}H_{23}NO_4$. Calculated, %: C 76.89; H 5.26; N 3.20.

12-(3-Ethoxy-4-hydroxyphenyl)-9-(2-furyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVi). Yield 39%.

Isomer 9-*ax*. mp 280–281°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 t and 3.98 q (5H, OEt); 2.50 m (2H, 8-H); 2.90 m (2H, 10-H); 3.41 m (1H, 9-H); 5.62 s (1H, 12-H); 5.81 d.d (1H, 4'-H, ^3J = 3.7, ^4J = 1.7); 6.15 d (1H, 3'-H, ^3J = 3.7); 6.40 m, 6.80 s, and 6.88 s (3H, H_{arom}); 7.17–7.48 m and 7.59–7.80 m (6H, 1-H–6-H); 7.90 d (1H, 5'-H, ^3J = 1.6); 9.53 s (1H, NH). Found, %: C 77.08; H 5.39; N 2.97. $C_{29}H_{25}NO_4$. Calculated, %: C 77.16; H 5.54; N 3.10.

Isomer 9-*eq*. mp 285–286°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 t and 3.98 q (5H, OEt); 2.50 m (2H, 8-H); 2.90 m (2H, 10-H); 3.30 m (1H, 9-H); 5.70 s (1H, 12-H); 6.31 d.d (1H, 4'-H, ^3J = 3.7, ^4J = 1.7); 6.15 d (1H, 3'-H, ^3J = 3.7); 6.40 m, 6.80 s, and 6.88 s (3H, H_{arom}); 7.17–7.48 m and 7.59–7.80 m (6H, 1-H–6-H); 7.90 d (1H, 5'-H, ^3J = 1.6); 9.62 s (1H, NH). Found, %: C 76.92; H 5.45; N 3.16. $C_{29}H_{25}NO_4$. Calculated, %: C 77.16; H 5.54; N 3.10.

2-Ethoxy-4-[9-(2-furyl)-11-oxo-7,8,9,10,12-hexahydrobenzo[*a*]acridin-12-yl]phenyl propanoate (IVj). Yield 37%, mp 215–216°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.12 t, 1.30 t, and 3.78–4.00 m (10H, OEt, OCOEt); 2.51 m (2H, 8-H); 2.92 m (2H, 10-H); 3.27 m and 3.48 m (1H, 9-H); 5.70 d.d and 6.30 d.d (1H, 4'-H, ^3J = 3.5, ^4J = 1.5); 5.86 s and 5.94 s (1H, 12-H); 6.18 d (1H, 3'-H, ^3J = 3.5); 6.40–6.72 m and 7.00 d (3H, H_{arom}, ^3J = 7.9); 7.16–7.47 m and 7.58–7.80 m (6H, 1-H–6-H); 7.93 d (1H, 5'-H, ^3J = 1.5); 9.65 s and 9.75 s (1H, NH). Found, %: C 75.55; H 5.61; N 2.56. $C_{32}H_{29}NO_5$. Calculated, %: C 75.74; H 5.72, N 2.76.

9-(2-Furyl)-12-(4-propoxyphenyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVk). Yield 56%,

mp 261–262°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00 m, 1.71 m, and 3.80 m (7H, OPr); 2.50 m (2H, 8-H); 2.90 m (2H, 10-H); 3.33 m and 3.50 m (1H, 9-H); 5.79 s and 5.82 s (1H, 12-H); 5.85 d.d and 6.30 d.d (1H, 4'-H, ^3J = 3.4, ^4J = 1.4); 6.12 d (1H, 3'-H, ^3J = 3.4); 6.58 d and 7.06 d (4H, H_{arom}, ^3J = 7.3); 7.23–7.40 m and 7.62–7.75 m (6H, 1-H–6-H); 7.92 d (1H, 5'-H, ^3J = 1.5); 9.39 s and 9.48 s (1H, NH). Found, %: C 79.93; H 5.86; N 3.02. $C_{30}H_{27}NO_3$. Calculated, %: C 80.18; H 6.01; N 3.12.

12-(4-Dimethylaminophenyl)-9-(2-furyl)-7,8,9,-10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVl). Yield 54%, mp 313–314°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.50 m (2H, 8-H), 2.88 m (2H, 10-H), 3.29 s (6H, Me), 3.33 m and 3.52 m (1H, 9-H), 5.68 s and 5.73 s (1H, 12-H), 5.91 d.d and 6.32 d.d (1H, 4'-H, ^3J = 3.5, ^4J = 1.5), 6.21 d (1H, 3'-H, ^3J = 3.5), 6.48 d and 6.96 d (4H, H_{arom}, ^3J = 7.5), 7.28–7.45 m and 7.58–7.75 m (6H, 1-H–6-H), 7.96 d (1H, 5'-H, ^3J = 1.5), 9.65 s and 9.72 s (1H, NH). Found, %: C 79.91; H 5.54; N 6.32. $C_{29}H_{26}N_2O_2$. Calculated, %: C 80.18; H 5.99; N 6.45.

12-(4-Diethylaminophenyl)-9-(2-furyl)-7,8,9,10,-11,12-hexahydrobenzo[*a*]acridin-11-one (IVm). Yield 69%, mp 300–301°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.08 t and 3.22 q (10H, Et), 2.47 m (2H, 8-H), 2.85 m (2H, 10-H), 3.39 m and 3.50 m (1H, 9-H), 5.70 s and 5.76 s (1H, 12-H), 5.85 d.d and 6.30 d.d (1H, 4'-H, ^3J = 3.4, ^4J = 1.6), 6.14 d (1H, 3'-H, ^3J = 3.4), 6.48 d and 6.96 d (4H, H_{arom}, ^3J = 7.6), 7.20–7.40 m and 7.60–7.71 m (6H, 1-H–6-H), 7.95 d (1H, 5'-H, ^3J = 1.6), 9.70 s and 9.80 s (1H, NH). Found, %: C 80.37; H 6.26; N 5.82. $C_{31}H_{30}N_2O_2$. Calculated, %: C 80.52; H 6.49; N 6.06.

9-(2-Furyl)-12-(3-pyridyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVn). Yield 58%, mp 312–313°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.59 m (2H, 8-H); 2.95 m (2H, 10-H); 3.38 m and 3.56 m (1H, 9-H); 5.82 s and 5.89 s (1H, 12-H); 5.85 d.d and 6.39 d.d (1H, 4'-H, ^3J = 3.6, ^4J = 1.4); 6.19 d (1H, 3'-H, ^3J = 3.6); 7.12 d, 7.55 s, 8.20 d, and 8.50 d (4H, C_5H_4N, ^3J = 7.7); 7.28–7.48 m and 7.68–7.81 m (6H, 1-H–6-H); 7.94 d (1H, 5'-H, ^3J = 1.4); 9.89 s and 9.96 s (1H, NH). Found, %: C 79.41; H 5.04; N 6.97. $C_{26}H_{20}N_2O_2$. Calculated, %: C 79.59; H 5.10; N 7.14.

9-(2-Furyl)-12-(4-pyridyl)-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-11-one (IVo). Yield 38%, mp 289–290°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.52 m (2H, 8-H), 2.96 m (2H, 10-H), 3.33 m and 3.49 m (1H, 9-H), 5.80 s and 5.87 s (1H, 12-H), 5.90 d.d and 6.33 d.d (1H, 4'-H, ^3J = 3.5, ^4J = 1.5), 6.20 d (1H, 3'-H, ^3J = 3.6), 7.00–8.50 m (11H, 1-H–6-H, 5'-H, C_5H_4N), 9.50 s and 9.60 s (1H, NH). Found, %: C 79.36; H 4.93; N 7.01. $C_{26}H_{20}N_2O_2$. Calculated, %: C 79.59; H 5.10; N 7.14.

9,12-Di(2-furyl)-7,8,9,10,11,12-hexahydrobenzo-[*a*]acridin-11-one (IVp). Yield 27%, mp 299–300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.49 m (2H, 8-H), 2.99 m (2H, 10-H), 3.29 m and 3.50 m (1H, 9-H), 5.61 s and 5.70 s (1H, 12-H), 5.85–6.32 m (4H, 3'-H, 4'-H, furyl), 7.00–7.75 m (7H, 1-H–6-H, C_4H_3O), 8.03 d (1H, 5'-H, ^3J = 1.7), 9.58 s and 9.67 s (1H, NH). Found, %: C 78.61; H 5.05; N 3.42. $C_{25}H_{19}NO_3$. Calculated, %: C 78.74; H 4.99; N 3.67.

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