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Synthesis of 12-Hetaryl-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-ones

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Abstract—Three-component condensation of naphthalen-2-amine with 5-arylfuran(thiophene, *N*-methylpyrrole)-2-carbaldehyde and 5,5-dimethylcyclohexane-1,3-dione, as well as condensation of *N*-[(5-arylfuran-(thiophen)-2-ylmethylidene]naphthalen-2-amine with 5,5-dimethylcyclohexane-1,3-dione gave the corresponding 12-[5-arylfuran(thiophen, *N*-methylpyrrol)-2-yl]-7,8,9,10-tetradrobenzo[*a*]acridin-11(12*H*)-ones.

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Organic compounds possessing an acridine fragment exhibit high biological activity. There are published data [1–3] on the synthesis of acridine-based labeled conjugates with drugs, peptides, proteins, and nucleic acids and antitumor and DNA-binding agents. Blache et al. [4] reported that modified acridine derivatives having a carbonyl group (alkaloid floxacrine analogs) show a higher antibacterial activity than those lacking carbonyl group.

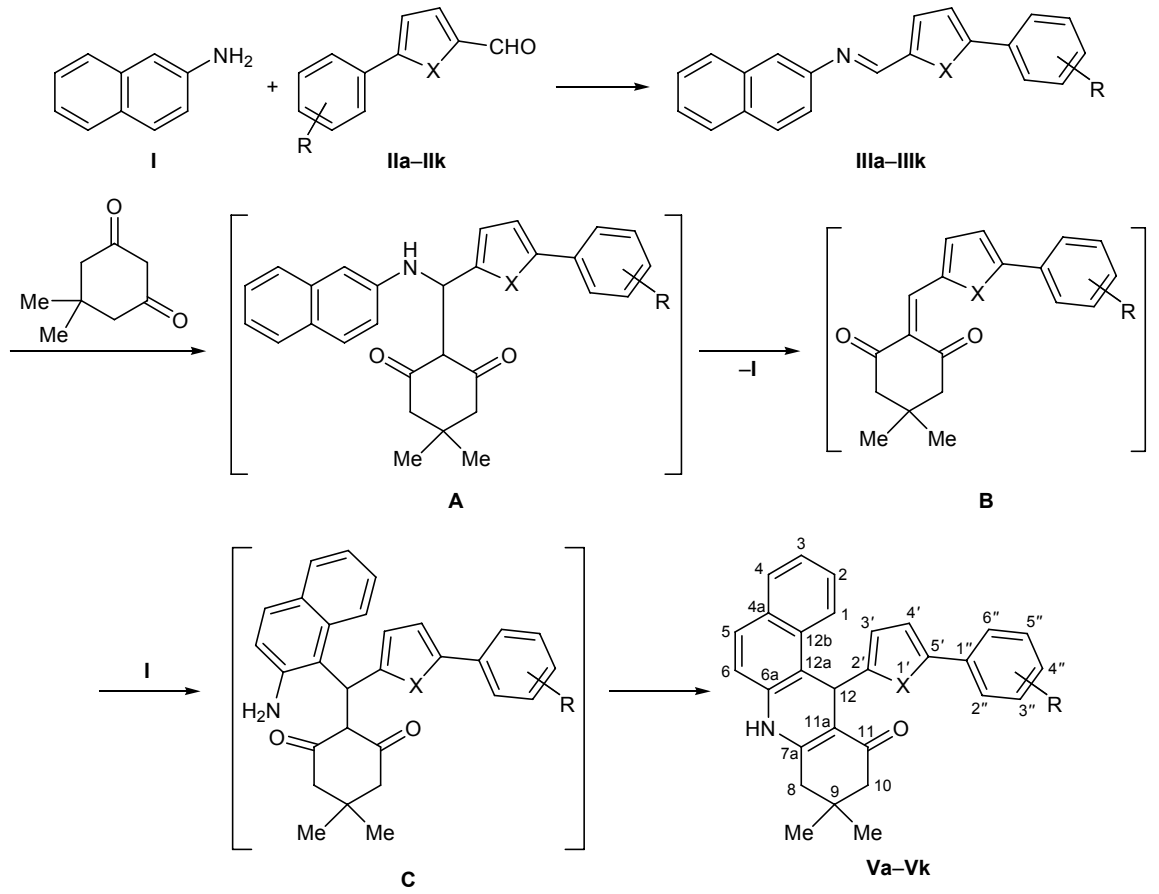
Dihydroacridine derivatives are complex polynuclear aza heterocyclic systems; therefore, development of simple and efficient methods for the synthesis of such compounds is an important problem of pharmaceutics. The most interesting are those reactions which ensure preparation of maximally functionalized heterocyclic compounds in a minimum number of steps. Three-component reaction of aromatic amines with aldehydes and CH acids provides a convenient one-step procedure for the synthesis of polyfunctionalized polynuclear heterocyclic systems. Following this approach, we previously synthesized benzo[*a*]- and benzo[*c*]-acridinone derivatives [5, 6].

In the present article we report on a selective synthesis of 12-[5-arylfuran(thiophene, *N*-methylpyrrol)-2-yl]-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-ones **Va**–**Vk** in two ways: (1) by heating an equimolar mixture of Schiff base **IIIa**–**IIIh** and 5,5-dimethylcyclohexane-1,3-dione (dimedone) in boiling ethanol for 50–60 min and (2) by heating an equimolar mixture of naphthalen-2-amine (**I**), heterocyclic aldehyde **IIa**–**IIk**, and dimedone in boiling ethanol for 2–4 h. As a rule, crystalline products were isolated (Scheme 1).

Schiff bases **IIIa**–**IIIh** were prepared by reaction of naphthalen-2-amine (**I**) with 5-arylfuran(or thiophene)-2-carbaldehydes **IIa**–**IIh** in alcoholic solution on heating for 30–50 min. Compounds **IIIa**–**IIIh** were isolated as individual substances, so that we were able to use them in the above transformation. No individual Schiff bases were isolated in the reactions with 5-aryl-1-methyl-1*H*-pyrrole-2-carbaldehydes **IIi**–**IIk**, and the corresponding benzo[*a*]acridine derivatives **Vi**–**Vk** were obtained only by three-component condensation of amine **I** with aldehydes **IIi**–**IIk**, and dimedone (**IV**).

Previously unknown compounds **Va**–**Vk** were formed in 40–85% yield. Due to high reactivity of the β-dicarbonyl component, no addition of acid catalyst was necessary. The cyclic structure of diketone **IV** makes it possible to introduce a carbonyl group into the fused heterocyclic structure simultaneously with generation of partly hydrogenated benzo[*a*]acridine fragment.

Scheme 1.



X = O, R = 4-O_2N (**a**), 4-Br (**b**), 2-F_3C (**c**), 4-H_2NSO_2 (**d**), 2-O_2N-4-MeO (**e**), 2-Br-4-Me (**f**); X = S, R = 4-O_2N (**g**), 3-O_2N (**h**); X = NMe, R = 4-Br (**i**), 2-Br (**j**), 2-Cl (**k**).

In keeping with the proposed reaction scheme (Scheme 1), Schiff base **III** takes up dimedone molecule to form unstable intermediate **A** which then decomposes into arylmethylidene diketone **B** and initial naphthalen-2-amine (**I**). Addition of the latter (through the α-carbon atom with respect to the amino group, which is characterized by the highest electron density) to the exocyclic double bond of **B** leads to intermediate **C** which undergoes heterocyclization with elimination of water to afford final product **V**.

The yield of the final products depends on the nature of the heterocyclic aldehyde component. The best yields of benzo[*a*]acridinones (51–85%) were obtained in the reactions of naphthalen-2-amine (**I**) with dimedone and furan and thiophene derivatives **IIa**–**IIh**, while the yields of pyrrole-containing analogs **Vi**–**Vk** were lower (40–50%).

The structure of compounds **IIIa**–**IIIh** and **Va**–**Vk** was confirmed by their elemental compositions and ^1H and ^{13}C NMR, IR, and mass spectra. Signals in the NMR spectra of **IIIb**, **Va**, **Vg**, and **Vi** were assigned with the aid of two-dimensional shift correlation techniques (COSY-45, NOESY, HSQC, HMBC). All experimental data were processed using XWIN-NMR 3.5 software package.

The two-dimensional NMR spectra of **Va**, **Vg**, and **Vi** were analyzed with a view of determining the position of the carbonyl group, which is crucial for the elucidation of the reaction mechanism. The presence of cross-peaks between the NH proton and C^8H_2 group in the HMBC and NOESY spectra convincingly proves the position of the oxo group on C^{11}. The observed couplings with quaternary carbon atoms in the HMBC spectrum were fully consistent with the proposed structure. The C^{11} nucleus (δ_C 193 ppm) displayed couplings with protons on C^{12} and C^{10}; the C^{7a} carbon atom (whose signal was expectedly located at δ_C 150–152 ppm) showed cross-peaks with protons on C^8 and C^{12}; and the C^{11a} nucleus (δ_C 102–106 ppm) was coupled both with protons on C^8 and C^{12} and with

the pseudoequatorial proton on the C^{10} atom and NH proton.

The ^{1}H NMR spectra of Schiff bases **IIIa**–**IIIh** and tetrahydrobenzoacridinones **Va**–**Vk** are superpositions of signals from different molecular fragments. The ^{1}H NMR spectra of **IIIa**–**IIIh** may be divided into three parts: (1) seven-spin aromatic proton system of the naphthalene ring, *AB* system of the five-membered heteroaromatic ring, and either *AA′BB′* or *ABCD* system (depending on the substitution pattern in the benzene ring). Apart from these parts, the ^{1}H NMR spectra of **Va**–**Vk** contain two *AB* systems from protons in the cyclohexane fragment and a singlet from 12-H.

According to the two-dimensional NMR correlation spectra, Schiff bases **IIIa**–**IIIh** were formed exclusively as *E* isomers. In the NOESY spectrum of **IIIb** the CH=N proton displayed couplings with 1-H, 3-H, and 3′-H. Obviously, if the CH=N bond in **IIIb** had *Z* configuration, no couplings with 1-H and 3-H would be observed because of remoteness of the CH=N proton from the naphthalene ring. There was no cross-peak between 1-H and 3′-H in the NOESY spectrum of **IIIb**, which also counts in favor of the *E* configuration; the corresponding cross peak should be observed for the *Z* isomer.

In the IR spectra of **IIIa**–**IIIk** stretching vibrations of the N=CH group give rise to absorption in the region 1634–1604 cm^{-1}. The IR spectra of **IIIa**, **IIIe**, **IIIg**, and **IIIh** contain strong absorption bands at 1356–1343 cm^{-1} due to stretching vibrations of the nitro group. Stretching vibrations of the C–F bonds in **IIIc** appear at 1151 cm^{-1}. Compounds **IIIb** and **IIIf** are characterized by a medium-intensity band at 489 and 486 cm^{-1}, respectively, which belongs to stretching vibrations of the C–Br bond. An intense band at 1148 cm^{-1} in the IR spectrum of **IIId** was assigned to symmetric stretching vibrations of the sulfonyl group.

In the IR spectra of tetrahydrobenzoacridinones **Va**–**Vk** we observed absorption bands corresponding to stretching vibrations of free (3440–3400 cm^{-1}) and associated NH group (3275–3257 cm^{-1}), which is typical of incomplete association of amines. It is known that the larger the low-frequency shift of the latter band and the higher its intensity, the higher the degree of association [7]. It may be concluded that tetrahydrobenzoacridinones **Va**, **Vc**, **Vd**, and **Vi**–**Vk** are associated to a greater extent and that compounds **Vb** and **Vf**–**Vh** are almost unassociated. Stretching vibrations of the C=O bond conjugated with the enamine fragment appeared in the region 1602–1579 cm^{-1}.

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Protege-460 spectrometer with Fourier transform from samples prepared as thin films or KBr pellets. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker Avance-500 spectrometer at 500 and 125 MHz, respectively, from 2–5% solutions in DMSO-d_6; the chemical shifts were determined relative to tetramethylsilane as internal standard. The elemental analyses were obtained on a Vario MICRO Superuser CHNS analyzer, except for halogen-containing compounds whose elemental composition was determined by classical microanalysis.

5-Arylfuran-2-carbaldehydes IIa–IIf were synthesized according to a procedure analogous to that described in [8]. A cold (0–5°C) solution of arenediazonium chloride prepared by diazotization of 0.1 mol of the corresponding aromatic amine was added dropwise under stirring to a solution of 0.1 mol (9.6 g) of furfural and 1 g of $CuCl_2 \cdot 2H_2O$ in 40 mL of acetone. During the addition, the temperature was maintained in the range from 20 to 30°C to ensure nitrogen evolution at a rate of 2–3 bubbles per second. The mixture was stirred until nitrogen no longer evolved and diluted with 200 mL of water, and the product was filtered off or isolated by vacuum distillation (aldehyde **IIc**) and recrystallized.

5-(4-Nitrophenyl)furan-2-carbaldehyde (IIa). Yield 60%, mp 203–204°C; published data: mp 212–213 [9], 199–200°C [10].

5-(4-Bromophenyl)furan-2-carbaldehyde (IIb). Yield 44%, mp 151–152°C. Found, %: C 52.43; H 3.10. $C_{11}H_7BrO_2$. Calculated, %: C 52.62; H 2.81.

5-(2-Trifluoromethylphenyl)furan-2-carbaldehyde (IIc). Yield 42%, mp 41–42°C. Found, %: C 59.81; H 2.69. $C_{12}H_7F_3O_2$. Calculated, %: C 60.01; H 2.94.

4-(5-Formylfuran-2-yl)benzenesulfonamide (IId). Yield 40%, mp 201–202°C. Found, %: C 52.76; H 3.70; N 5.45. $C_{11}H_9NO_4S$. Calculated, %: C 52.58; H 3.61; N 5.57.

5-(4-Methoxy-2-nitrophenyl)furan-2-carbaldehyde (IIe). Yield 35%, mp 103–104°C. Found, %: C 58.46; H 3.23; N 5.46. $C_{12}H_9NO_5$. Calculated, %: C 58.30; H 3.67; N 5.67.

5-(2-Bromo-4-methylphenyl)furan-2-carbaldehyde (IIf). Yield 36%, mp 80–81°C. Found, %: C 54.16; H 3.13. $C_{12}H_9BrO_2$. Calculated, %: C 54.37; H 3.42.

5-Arylthiophene-2-carbaldehydes IIg and IIh (*general procedure*). The corresponding aromatic amine, 0.1 mol, was dissolved (if necessary, on heating) in 60 mL of 20% aqueous HCl. The solution was cooled to 0–5°C, and a solution of 7 g of sodium nitrite in 25 mL of water was added dropwise under stirring. When the reaction was complete, the resulting solution of arenediazonium salt was filtered and added dropwise under stirring to a mixture of 15 mL (12.25 g, 0.11 mol) of thiophene-2-carbaldehyde, 40 mL of DMSO, and 1.5 g (8.7 mmol) of $CuCl_2 \cdot 2H_2O$. The mixture was stirred at 15–25°C to ensure nitrogen evolution at a moderate rate. When nitrogen no longer evolved, the mixture was diluted with 150 mL of water, and the precipitate was filtered off and recrystallized from ethanol–DMF.

5-(4-Nitrophenyl)thiofene-2-carbaldehyde (IIg). Yield 50%, mp 175–176°C. Found, %: C 56.32; H 2.96; N 6.12. $C_{11}H_7NO_3S$. Calculated, %: C 56.64; H 3.03; N 6.01.

5-(3-Nitrophenyl)thiophene-2-carbaldehyde (IIh). Yield 28%, mp 144–145°C [11].

5-Aryl-1-methyl-1*H*-pyrrole-2-carbaldehydes IIi–IIk (*general procedure*). A solution of arenediazonium chloride prepared by diazotization of 0.1 mol of the corresponding aromatic amine was neutralized, cooled to 0–5°C, and added dropwise under stirring to a mixture of 0.1 mol (10.9 g) of 1-methyl-1*H*-pyrrole-2-carbaldehyde, 1 g of $CuCl_2 \cdot 2H_2O$, and 4.0 g of magnesium oxide in 40 mL of acetone. The mixture was stirred at 20–30°C until nitrogen no longer evolved, 200 mL of water was added, and the product was isolated by vacuum distillation. Aldehyde **IIi** was recrystallized from hexane.

5-(4-Bromophenyl)-1-methyl-1*H*-pyrrole-2-carbaldehyde (IIi). Yield 40%, mp 91–92°C. Found, %: C 54.34; H 3.69; N 5.52. $C_{12}H_{10}BrNO$. Calculated, %: C 54.57; H 3.82; N 5.30.

5-(2-Bromophenyl)-1-methyl-1*H*-pyrrole-2-carbaldehyde (IIj). Yield 54%, bp 173–175°C (4 mm). Found, %: C 54.69; H 4.01; N 5.13. $C_{12}H_{10}BrNO$. Calculated, %: C 54.57; H 3.82; N 5.30.

5-(2-Chlorophenyl)-1-methyl-1*H*-pyrrole-2-carbaldehyde (IIk). Yield 50%, bp 165–170°C (2 mm), n_D^{20} = 1.6350. Found, %: C 65.75; H 4.26; N 6.17. $C_{12}H_{10}ClNO$. Calculated, %: C 65.61; H 4.59; N 6.38.

(*E*)-*N*-[5-Arylfuran(thiophen)-2-ylmethylidene]-naphthaalen-2-amines IIIa–IIIh (*general procedure*). A solution of 1.43 g (0.01 mol) of naphthalen-2-amine (**I**) and 0.01 mol of aldehyde **IIa–IIh** in 20 mL of alcohol was heated for 40–60 min under reflux. After cooling, the precipitate was filtered off and recrystallized from alcohol.

(*E*)-*N*-[5-(4-Nitrophenyl)furan-2-ylmethylidene]-naphthaalen-2-amine (IIIa). Yield 75%, yellow crystals, mp 180°C. IR spectrum, ν, cm^{-1}: 3440, 3117, 2924, 2847, 1685, 1666, 1599, 1514, 1473, 1343, 1329, 1291, 1261, 1105, 1040, 965, 852, 809, 751. ^1H NMR spectrum, δ, ppm: 7.25 d (1H, 4′-H), 7.29 d (1H, 3′-H), 7.35 t (1H, 6-H), 7.49 t (1H, 7-H), 7.51 d.d (1H, 3-H), 7.62 d (2H, 3″-H, 5″-H), 7.74 d (1H, 1-H), 7.80 d (2H, 2″-H, 6″-H), 7.90–7.93 m (2H, H_{arom}), 7.98 d (1H, 4-H), 8.72 s (1H, CH=N). Found, %: C 73.73; H 4.16; N 8.11. $C_{21}H_{14}N_2O_3$. Calculated, %: C 73.68; H 4.12; N 8.18.

(*E*)-*N*-[5-(4-Bromophenyl)furan-2-ylmethylidene]naphthalen-2-amine (IIIb). Yield 83%, yellow crystals, mp 144–145°C. IR spectrum, ν, cm^{-1}: 3436, 3085, 3051, 2922, 1630, 1612, 1584, 1472, 1457, 1406, 1375, 1272, 1201, 1163, 1071, 964, 862, 827, 797, 744, 489, 472. ^1H NMR spectrum, δ, ppm: 7.31 d (1H, 4′-H), 7.32 d (1H, 3′-H), 7.47 t (1H, 6-H), 7.52 t (1H, 7-H), 7.56 d.d (1H, 3-H), 7.70 d (2H, 3″-H, 5″-H), 7.77 d (1H, 1-H), 7.82 d (2H, 2″-H, 6″-H), 7.92 d (1H, 5-H), 7.93 d (1H, 8-H), 7.96 d (1H, 4-H), 8.62 s (1H, CH=N). ^{13}C NMR spectrum, δ_C, ppm: 154.80 ($C^{5'}$), 151.81 ($C^{2'}$), 148.67 (C^2), 148.11 (CH=N), 133.70 (C^{8a}), 132.07 ($C^{3''}$), 131.61 (C^{4a}), 128.92 (C^4), 128.50 ($C^{1''}$), 127.88 (C^8), 127.58 (C^5), 126.48 (C^7), 126.22 ($C^{2''}$), 125.50 (C^6), 121.81 ($C^{4''}$), 120.93 (C^3), 119.75 ($C^{3'}$), 118.33 (C^1), 109.41 ($C^{4'}$). Found, %: C 67.10; H 3.70; Br 21.18; N 3.76. $C_{21}H_{14}BrNO$. Calculated, %: C 67.04; H 3.75; Br 21.24; N 3.72.

(*E*)-*N*-[5-(2-Trifluoromethylphenyl)furan-2-ylmethylidene]naphthalen-2-amine (IIIc). Yield 65%, yellow crystals, mp 80–82°C. IR spectrum, ν, cm^{-1}: 3430, 3078, 3042, 2918, 1634, 1598, 1523, 1470, 1445, 1413, 1362, 1343, 1267, 1200, 1126, 1150, 1063, 961, 867, 732. ^1H NMR spectrum, δ, ppm: 6.79–6.83 m (2H, 3′-H, 4′-H), 7.30–7.33 m (3H, H_{arom}), 7.52–7.58 m (2H, 7-H, 6-H), 7.79–7.81 m (3H, H_{arom}), 7.89–7.92 m (3H, H_{arom}), 8.64 s (1H, CH=N). Found, %: N 3.79. $C_{22}H_{14}F_3NO$. Calculated, %: N 3.83.

4-{5-[(*E*)-(Naphthalen-2-ylimino)methyl]furan-2-yl}benzenesulfonamide (IIId). Yield 92%, brown crystals, mp 195–196°C. IR spectrum, ν, cm^{-1}: 3416, 3340, 3240, 3058, 2923, 2853, 1629, 1611, 1600, 1578, 1423, 1324, 1288, 1148, 1094, 1030, 829, 785, 750, 538, 479. ^1H NMR spectrum, δ, ppm: 7.50 s (2H, NH_2), 7.18–7.22 m (2H, 3′-H, 4′-H), 7.39–7.43 m (3H,

H_{arom}), 7.60–7.64 m (2H, 7-H, 6-H), 7.80–7.83 m (3H, H_{arom}), 7.90–7.95 m (3H, H_{arom}), 8.63 s (1H, CH=N). Found, %: C 66.93; H 4.28; N 7.42; S 8.43. $C_{21}H_{16}N_2O_3S$. Calculated, %: C 67.00; H 4.28; N 7.44; S 8.52.

(*E*)-*N*-[5-(4-Methoxy-2-nitrophenyl)furan-2-ylmethylidene]naphthalen-2-amine (IIIe). Yield 41%, brown crystals, mp 70–71°C. IR spectrum, ν, cm^{-1}: 3431, 3054, 2963, 2932, 2853, 1611, 1587, 1529, 1479, 1437, 1381, 1356, 1297, 1267, 1226, 1206, 1052, 1025, 796, 755. ^{1}H NMR spectrum, δ, ppm: 3.11 s (3H, OCH_3), 6.94 d (1H, 4′-H), 7.29 d (1H, 3′-H), 7.34–7.36 d.d (1H, 5-H), 7.43–7.50 m (3H, H_{arom}), 7.57 d (1H, 4-H), 7.72 s (1H, 1-H), 7.82 d (1H, 8-H), 7.88–7.93 m (3H, H_{arom}), 8.54 s (1H, CH=N). Found, %: C 71.00; H 4.38; N 7.49. $C_{22}H_{16}N_2O_4$. Calculated, %: C 70.96; H 4.33; N 7.52.

(*E*)-*N*-[5-(2-Bromo-4-methylphenyl)furan-2-ylmethylidene]naphthalen-2-amine (IIIf). Yield 80%, brown crystals, mp 128–129°C. IR spectrum, ν, cm^{-1}: 3051, 2920, 2854, 1628, 1607, 1584, 1503, 1475, 1461, 1372, 1337, 1270, 1243, 1202, 1163, 1022, 991, 955, 887, 863, 809, 790, 753. ^{1}H NMR spectrum, δ, ppm: 2.21 s (3H, CH_3), 6.90 d (1H, 4′-H), 7.20 d (1H, 3′-H), 7.37–7.39 d.d (1H, 5-H), 7.51–7.53 m (3H, H_{arom}), 7.60 d (1H, 4-H), 7.84 s (1H, 1-H), 7.86 d (1H, 8-H), 7.92–7.96 m (3H, H_{arom}), 8.62 s (1H, CH=N). Found, %: C 67.80; H 4.09; Br 20.42; N 3.62. $C_{22}H_{16}BrNO$. Calculated, %: C 67.71; H 4.13; Br 20.47; N 3.59.

(*E*)-*N*-[5-(4-Nitrophenyl)thiophen-2-ylmethylidene]naphthalen-2-amine (IIIg). Yield 76%, yellow crystals, mp 195–196°C. IR spectrum, ν, cm^{-1}: 3440, 3051, 2928, 1610, 1587, 1530, 1464, 1350, 1230, 1200, 1169, 884, 831, 800, 739, 673, 482. ^{1}H NMR spectrum, δ, ppm: 7.45–7.52 m (3H, 3′-H, 4′-H, 3-H), 7.75 m (2H, 7-H, 6-H), 7.88–7.92 m (4H, H_{arom}), 8.01–8.24 m (4H, H_{arom}), 8.93 s (1H, CH=N). Found, %: C 70.40; H 4.00; N 7.78; S 9.02. $C_{21}H_{14}N_2O_2S$. Calculated, %: C 70.37; H 3.94; N 7.82; S 8.95.

(*E*)-*N*-[5-(3-Nitrophenyl)thiophen-2-ylmethylidene]naphthalen-2-amine (IIIh). Yield 69%, yellow crystals, mp 131–132°C. IR spectrum, ν, cm^{-1}: 3443, 3053, 2923, 2854, 1604, 1585, 1526, 1453, 1345, 1288, 1232, 1202, 1165, 890, 863, 825, 802, 744, 732, 678, 476. ^{1}H NMR spectrum, δ, ppm: 7.38–7.47 m (3H, 3-H, 3′-H, 4′-H), 7.69–7.73 m (2H, 6-H, 7-H), 7.81–7.87 m (4H, H_{arom}), 8.00–8.19 m (4H, H_{arom}), 8.81 s (1H, HC=N). Found, %: C 70.39; H 3.89; N 7.86; S 9.01. $C_{21}H_{14}N_2O_2S$. Calculated, %: C 70.37; H 3.94; N 7.82; S 8.95.

Compounds Va–Vk (*general procedure*). *a*. 5,5-Dimethylcyclohexane-1,3-dione, 1.40 g (0.01 mol), was added to solution of 0.01 mol of Schiff base **IIIa–IIIh** in 30 mL of ethanol, and the mixture was heated for 2–3 h under reflux. After cooling, the precipitate was filtered off, washed with diethyl ether, and recrystallized from ethanol–benzene (1 : 2) or washed with the same solvent mixture.

b. A solution of 1.43 g (0.01 mol) of naphthalen-2-amine (**I**), 0.01 mol of aldehyde **IIa–IIk**, and 1.40 g (0.01 mol) of 5,5-dimethylcyclohexane-1,3-dione in 30 mL of ethanol was heated for 3–4 h under reflux. After cooling, the product was isolated as described above in *a*.

9,9-Dimethyl-12-[5-(4-nitrophenyl)furan-2-yl]-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Va). Yield 70%, yellow crystals, mp 310–312°C. IR spectrum, ν, cm^{-1}: 3263, 3192, 3090, 2965, 2939, 2869, 1602, 1582, 1519, 1510, 1491, 1469, 1428, 1390, 1334, 1295, 1260, 1236, 1206, 1144, 1109, 847, 825, 815, 784, 750, 591. ^{1}H NMR spectrum, δ, ppm: 1.00 s and 1.05 s (3H each, CH_3), 2.12 d and 2.26 d (1H each, 10-H), 2.48 d and 2.58 d (1H, 8-H), 5.97 s (1H, 12-H), 6.12 d (1H, 3′-H), 6.99 d (1H, 4′-H), 7.25 d (1H, 6-H), 7.34 t (1H, 3-H), 7.55 t (1H, 2-H), 7.64 d (2H, 2″-H, 6″-H), 7.75 d (1H, 5-H), 7.79 d (1H, 4-H), 8.16 d (2H, 3″-H, 5″-H), 8.24 d (1H, 1-H), 9.84 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 193.11 (CO), 160.57 ($C^{2'}$), 152.34 (C^{7a}), 148.88 ($C^{5'}$), 145.40 ($C^{5''}$), 136.11 ($C^{1''}$), 134.29 (C^{6a}), 131.32 (C^{12b}), 130.28 (C^{4a}), 128.43 (C^4), 128.33 (C^5), 126.92 (C^2), 124.44 ($C^{3''}$), 123.87 (C^3), 123.11 ($C^{2''}$), 122.55 (C^1), 117.10 (C^6), 113.48 (C^{12a}), 111.34 ($C^{4'}$), 108.29 ($C^{3'}$), 102.81 (C^{11a}), 50.26 (C^{10}), 40.18 (C^8), 32.23 (C^9), 29.80 (C^{12}), 29.20 and 26.46 (CH_3). Found, %: C 75.00; H 5.26; N 5.97. $C_{29}H_{24}N_2O_4$. Calculated, %: C 74.98; H 5.21; N 6.03.

12-[5-(4-Bromophenyl)furan-2-yl]-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vb). Yield 85%, colorless crystals, mp 296°C. IR spectrum, ν, cm^{-1}: 3427, 3264, 3181, 3090, 2949, 2925, 1593, 1579, 1520, 1499, 1468, 1429, 1400, 1266, 1240, 1151, 1072, 823, 781, 746, 593. ^{1}H NMR spectrum, δ, ppm: 1.02 s and 1.07 s (3H each, CH_3), 2.12 d and 2.28 d (1H each, 10-H), 2.51 d and 2.60 d (1H each, 8-H), 5.94 s (1H, 12-H), 6.02 d (1H, 4′-H), 6.72 d (1H, 3′-H), 7.26 d (1H, H_{arom}), 7.37–7.40 m (3H, H_{arom}), 7.52 d (2H, H_{arom}), 7.57 t (1H, H_{arom}), 7.77 d (1H, H_{arom}), 7.82 d (1H, H_{arom}), 8.26 d (1H, H_{arom}), 9.85 s (1H, NH). Found, %: C 70.02; H 4.90; Br 16.09; N 2.78. $C_{29}H_{24}BrNO_2$. Calculated, %: C 69.88; H 4.85; Br 16.03; N 2.81.

9,9-Dimethyl-12-[5-(2-trifluoromethylphenyl)-furan-2-yl]-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vc). Yield 69%, yellow crystals, mp 272–273°C. IR spectrum, ν, cm^{-1}: 3427, 3264, 3181, 3090, 2949, 2925, 1593, 1579, 1520, 1499, 1468, 1429, 1400, 1266, 1240, 1151, 1072, 823, 781, 746, 593. ^{1}H NMR spectrum, δ, ppm: 0.95 s and 1.02 s (3H each, CH_3), 2.09 d and 2.22 d (1H each, 10-H), 2.45 d and 2.52 d (1H each, 8-H), 5.94 s (1H, 12-H), 6.14 d (1H, H_{arom}), 6.56 d (1H, H_{arom}), 7.24 d (2H, H_{arom}), 7.32 t (1H, H_{arom}), 7.39 t (1H, H_{arom}), 7.48 d (1H, H_{arom}), 7.53–7.58 m (1H, H_{arom}), 7.67 d (1H, H_{arom}), 7.73 d (1H, H_{arom}), 7.78 d (1H, H_{arom}), 8.15 d (1H, H_{arom}), 9.84 s (1H, NH). Found, %: N 2.91. $C_{30}H_{24}F_3NO_2$. Calculated, %: N 2.87.

4-[5-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)furan-2-yl]benzenesulfonamide (Vd). Yield 73%, brown crystals, mp 279–280°C. IR spectrum, ν, cm^{-1}: 3331, 2954, 2928, 1600, 1581, 1521, 1499, 1467, 1433, 1402, 1328, 1267, 1240, 1153, 1095, 1056, 1021, 832, 815, 800, 745, 618, 544. ^{1}H NMR spectrum, δ, ppm: 1.00 s and 1.04 s (3H each, CH_3), 2.12 d and 2.27 d (1H each, 10-H), 2.50 d and 2.56 d (1H each, 8-H), 5.94 s (1H, 12-H), 6.04 d (1H, 4′-H), 6.82 d (1H, 3′-H), 7.25 d (1H, H_{arom}), 7.30 s (2H, NH_2), 7.35 t (1H, H_{arom}), 7.55 d (1H, H_{arom}), 7.58 d (2H, H_{arom}), 7.60 t (1H, H_{arom}), 7.72–7.76 m (2H, H_{arom}), 7.73 d (1H, H_{arom}), 8.26 d (1H, H_{arom}), 9.84 s (1H, NH). Found, %: C 69.91; H 5.22; N 5.58; S 6.70. $C_{29}H_{26}N_2O_4S$. Calculated, %: C 69.86; H 5.26; N 2.87; S 6.43.

12-[5-(4-Methoxy-2-nitrophenyl)furan-2-yl]-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Ve). Yield 62%, yellow crystals, mp 288–290°C. IR spectrum, ν, cm^{-1}: 3262, 3186, 3082, 2951, 2928, 2868, 1599, 1582, 1536, 1500, 1466, 1386, 1310, 1279, 1262, 1237, 1206, 1147, 1024, 822, 800, 788, 750. ^{1}H NMR spectrum, δ, ppm: 1.00 s and 1.02 s (3H each, CH_3), 2.13 d and 2.19 d (1H each, 10-H), 2.52 d and 2.55 d (1H each, 8-H), 3.76 s (3H, OCH_3), 5.87 s (1H, 12-H), 6.09 d (1H, 4′-H), 6.44 d (1H, 3′-H), 7.12 d (1H, H_{arom}), 7.24 d (1H, H_{arom}), 7.30–7.32 m (2H, H_{arom}), 7.45–7.52 m (2H, H_{arom}), 7.78 d (1H, H_{arom}), 8.11 d (1H, H_{arom}), 9.79 s (1H, NH). Found, %: C 80.21; H 6.00; N 3.16. $C_{30}H_{27}NO_3$. Calculated, %: C 80.15; H 6.05; N 3.12.

12-[5-(2-Bromo-4-methylphenyl)furan-2-yl]-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vf). Yield 67%, colorless crystals, mp 310–312°C. IR spectrum, ν, cm^{-1}: 3435, 3257, 3183, 2926, 1599, 1584, 1522, 1501, 1467, 1398, 1382, 1309, 1261, 1239, 1180, 1146, 1124, 1074, 1020, 983, 819, 750, 594. ^{1}H NMR spectrum, δ, ppm: 0.99 s and 1.03 s (3H each, CH_3), 2.13 d (1H, 10-H), 2.20 s (3H, 4″-CH_3), 2.22 d (1H, 10-H), 2.46 d and 2.53 d (1H each, 8-H), 5.91 s (1H, 12-H), 6.03 d (1H, 4′-H), 6.81 d (1H, 3′-H), 7.15 d (1H, H_{arom}), 7.24 d (1H, H_{arom}), 7.41–7.48 m (2H, H_{arom}), 7.54–7.59 m (2H, H_{arom}), 7.74 d (1H, H_{arom}), 7.78 d (1H, H_{arom}), 8.22 d (1H, H_{arom}), 9.81 s (1H, NH). Found, %: C 70.24; H 5.07; Br 15.66; N 2.69. $C_{30}H_{26}BrNO_2$. Calculated, %: C 70.32; H 5.11; Br 15.59; N 2.73.

9,9-Dimethyl-12-[5-(4-nitrophenyl)thiophen-2-yl]-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vg). Yield 60%, brown crystals, mp 279–280°C. IR spectrum, ν, cm^{-1}: 3331, 2954, 2928, 1600, 1581, 1521, 1499, 1467, 1433, 1402, 1328, 1267, 1240, 1153, 1095, 1056, 1021, 832, 815, 800, 745, 618, 544. ^{1}H NMR spectrum, δ, ppm: 0.98 s and 1.03 s (3H each, CH_3), 2.19 d and 2.24 d (1H each, 10-H), 2.43 d and 2.51 d (1H each, 8-H), 6.11 s (1H, 12-H), 6.70 d (1H, 4′-H), 7.25 d (1H, 3′-H), 7.31 d (1H, H_{arom}) 7.35 t (1H, H_{arom}), 7.49 t (1H, H_{arom}), 7.52 t (1H, H_{arom}), 7.79 d (1H, H_{arom}), 7.88 m (2H, H_{arom}), 8.02 d (1H, H_{arom}), 8.05 d (1H, H_{arom}), 8.21 (1H, H_{arom}), 9.93 s (1H, NH). Found, %: C 72.52; H 5.07; N 5.78; S 6.70. $C_{29}H_{24}N_2O_3S$. Calculated, %: C 72.48; H 5.03; N 5.83; S 6.67.

9,9-Dimethyl-12-[5-(3-nitrophenyl)thiophen-2-yl]-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vh). Yield 51%, yellow crystals, mp 210–212°C. IR spectrum, ν, cm^{-1}: 3410, 3251, 3192, 2952, 2929, 1600, 1519, 1508, 1494, 1463, 1430, 1390, 1340, 1265, 1247, 1144, 1109, 1031, 852, 813, 761, 695. ^{1}H NMR spectrum, δ, ppm: 0.96 s and 1.05 s (3H each, CH_3), 2.15 d and 2.28 d (1H each, 10-H), 2.47 d and 2.56 d (1H each, 8-H), 6.15 s (1H, 12-H), 6.66 d (1H, 3′-H), 7.33 d (1H, 6-H), 7.34 d (1H, 4′-H), 7.35 t (1H, 3-H), 7.49 t (1H, 2-H), 7.57 t (1H, 5″-H), 7.84 d (1H, 4-H), 7.84 d (1H, 5-H), 7.86 d (2H, 6″-H), 8.00 d (1H, 4″-H), 8.01 d (1H, 1-H), 8.15 (1H, 2″-H), 10.01 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 193.11 (CO), 152.33 ($C^{2'}$), 151.35 (C^{7a}), 148.29 ($C^{3''}$), 138.17 ($C^{5'}$), 135.49 ($C^{1''}$), 134.31 (C^{6a}), 131.21 (C^{12b}), 130.99 ($C^{6''}$), 130.52 ($C^{5''}$), 130.36 (C^{4a}), 128.53 (C^{4}), 128.46 (C^{5}), 127.10 (C^{2}), 125.19 ($C^{3'}$), 124.88 ($C^{4'}$), 123.85 (C^{3}), 122.26 (C^{1}), 121.40 ($C^{4''}$), 118.70 ($C^{2''}$), 117.10 (C^{6}), 115.07 (C^{12a}), 105.95 (C^{11a}), 50.20 (C^{10}), 40.03 (C^{8}), 32.21 (C^{9}), 31.08 (C^{12}), 29.13 and 26.61 (CH_3). Found, %: C 72.42; H 5.00; N 5.81; S 6.71. $C_{29}H_{24}N_2O_3S$. Calculated, %: C 72.48; H 5.03; N 5.83; S 6.67.

12-[5-(4-Bromophenyl)-1-methyl-1*H*-pyrrol-2-yl]-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vi). Yield 50%, gray crystals, mp >320°C. IR spectrum, ν, cm^{-1}: 3430, 3269, 3192, 3077, 2951, 2929, 1600, 1519, 1508, 1494, 1463, 1430, 1390, 1340, 1265, 1247, 1144, 1109, 1031, 852, 813, 761, 695. ^{1}H NMR spectrum, δ, ppm: 0.97 s and 1.05 s (3H each, CH_3), 2.13 d and 2.25 d (1H each, 10-H), 2.47 d and 2.57 d (1H each, 8-H), 4.01 s (3H, NCH_3), 5.59 d (1H, 3′-H), 5.79 s (1H, 12-H), 5.91 d (1H, 4′-H), 7.24 d (1H, 2″-H, 6″-H), 7.35 d (1H, 6-H), 7.35 t (1H, 3-H), 7.52 t (1H, 2-H), 7.52 d (1H, 3″-H, 5″-H), 7.77 d (1H, 5-H), 7.82 d (1H, 4-H), 7.94 d (1H, 1-H), 9.91 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 193.49 (CO), 150.77 (C^{7a}), 141.85 ($C^{2'}$), 133.86 (C^{6a}), 132.51 ($C^{1''}$), 131.26 ($C^{3''}$), 131.17 (C^{12b}), 130.61 ($C^{5'}$), 130.35 (C^{4a}), 129.75 ($C^{2''}$), 128.46 (C^4), 127.66 (C^5), 126.86 (C^2), 123.55 (C^3), 122.00 (C^1), 119.07 ($C^{4''}$), 117.22 (C^6), 116.53 (C^{12a}), 108.55 ($C^{4'}$), 107.39 ($C^{3'}$), 106.83 (C^{11a}), 50.33 (C^{10}), 40.30 (C^8), 32.30 (NCH_3), 32.25 (C^9), 28.92 (CH_3), 28.10 (C^{12}), 26.69 (CH_3). Found, %: C 70.20; H 5.37; Br 15.58; N 5.42. $C_{30}H_{27}BrN_2O$. Calculated, %: C 70.15; H 5.32; Br 15.62; N 5.48.

12-[5-(2-Bromophenyl)-1-methyl-1*H*-pyrrol-2-yl]-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vj). Yield 44%, gray crystals, mp 283°C. IR spectrum, ν, cm^{-1}: 3440, 3276, 3191, 3089, 2959, 2925, 2889, 1600, 1582, 1519, 1493, 1451, 1427, 1397, 1381, 1257, 1235, 1144, 1113, 822, 759, 746, 684, 580. ^{1}H NMR spectrum, δ, ppm: 0.90 s and 0.99 s (3H each, CH_3), 2.07 d and 2.20 d (1H each, 10-H), 2.45 d and 2.54 d (1H each, 8-H), 3.72 s (3H, NCH_3), 5.45 s (1H, 12-H), 5.70 d (1H, 4′-H), 7.21–7.41 m (7H, H_{arom}), 7.62 d (1H, H_{arom}), 7.73 d (1H, H_{arom}), 7.88 d (1H, H_{arom}), 10.07 s (1H, NH). Found, %: C 70.11; H 5.36; Br 15.65; N 5.51. $C_{30}H_{27}BrN_2O$. Calculated, %: C 70.15; H 5.32; Br 15.62; N 5.48.

12-[5-(2-Chlorophenyl)-1-methyl-1*H*-pyrrol-2-yl]-9,9-dimethyl-7,8,9,10-tetrahydrobenzo[*a*]acridin-11(12*H*)-one (Vk). Yield 40%, light brown crystals, mp 289–290°C. IR spectrum, ν, cm^{-1}: 3462, 3275, 3191, 3090, 3063, 2961, 2929, 2872, 1594, 1581, 1520, 1493, 1468, 1450, 1428, 1396, 1383, 1258, 1236, 1146, 1036, 812, 744, 694, 581. ^{1}H NMR spectrum, δ, ppm: 0.89 s and 0.99 s (3H each, CH_3), 2.07 d and 2.21 d (1H each, 10-H), 2.39 d and 2.52 d (1H each, 8-H), 3.69 s (3H, NCH_3), 5.47 s (1H, 12-H), 5.69 d (1H, 4′-H), 7.24 d (1H, 3′-H), 7.27–7.31 m (4H, H_{arom}), 7.41–7.45 m (3H, H_{arom}), 7.72 d (1H, H_{arom}), 7.76 t (1H, H_{arom}), 7.87 t (1H, H_{arom}), 9.86 s (1H, NH). Found, %: C 77.21; H 5.40; Cl 7.52; N 5.92. $C_{30}H_{27}ClN_2O$. Calculated, %: C 77.16; H 5.83; Cl 7.59; N 6.00.

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