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Synthesis and Spectral Characteristics of 4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxy(ethoxy)phenyl Carboxylates

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Abstract—By reaction of vanillin and ethyl vanillin with 1-naphthylamine in ethanol previously unknown azomethines (Schiff's bases) were obtained as individual *E*-isomers which in heterocyclizatoion with dimedone provided in 33–77% yield individual 4-(10,10-dimethyl -8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxy(ethoxy)phenyl carboxylates formed as a result of recombination of the adduct of azomethine and dimedone occurring by the type of Hofmann–Martius rearrangement. The structure of compounds obtained was confirmed by elemental analyses, UV, IR, and ^{1}H NMR spectra.

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Introduction of fragments from the naturally occurring substances, like esters of plant phenols, into molecules of benzoacridines is a promising way to new bioactive compounds. In a number of publications [1–3] an information appeared on the synthesis based on acridines of labaled conjugates with drugs, peptides, proteins, or nucleic acids, of preparations with antitumor activity and DNA-bonding properties. In [4] data are cited that modified acridine molecules, in particular, tetrahydro derivatives having a carbonyl group (analogs of floxacrin alkaloid) exhibit higher antibacterial activity than the decarbonylated compounds of this series.

Unlike benzo[*a*]acridone derivatives obtained proceeding from 2-naphthylamine compounds of this class based on 1-naphthylamine, benzo[*c*]-acridones, are less known. In this study we investigated a reaction of condensation products of esters **Ia–Io** with 1-naphthylamine (**II**), 2-methoxy-(ethoxy)-4-(1-naphthyliminoethyl)phenyl esters **IIIa–IIIo,** with 5,5-dimethyl -1,3-cyclohexanedione (dimedone) (**IV**). The reaction was carried out by boiling equimolar amounts of reagents in ethanol (in the synthesis of compounds **Va–Vd**, **Vf–Vo**) or in the 2-propanol–butanol mixture, 1:1 (in the synthesis of compound **Ve**). Thanks to the high reactivity of the β-dicarbonyl compound the reaction occurred without acid catalyst. The absence of acid favors the retention of the labile ester group. The use of a cyclic β-diketone in this reaction makes it possible to introduce a carbonyl group into the structure of fused heterocycle simultaneously with the building up of a partially hydrogenated benzo[*h*]quinoline fragment As a result formed in 33–77% yield previously unknown 4-(10,10-dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]-acridin-7-yl)-2-methoxy(ethoxy)phenyl esters **Va–Vo**.

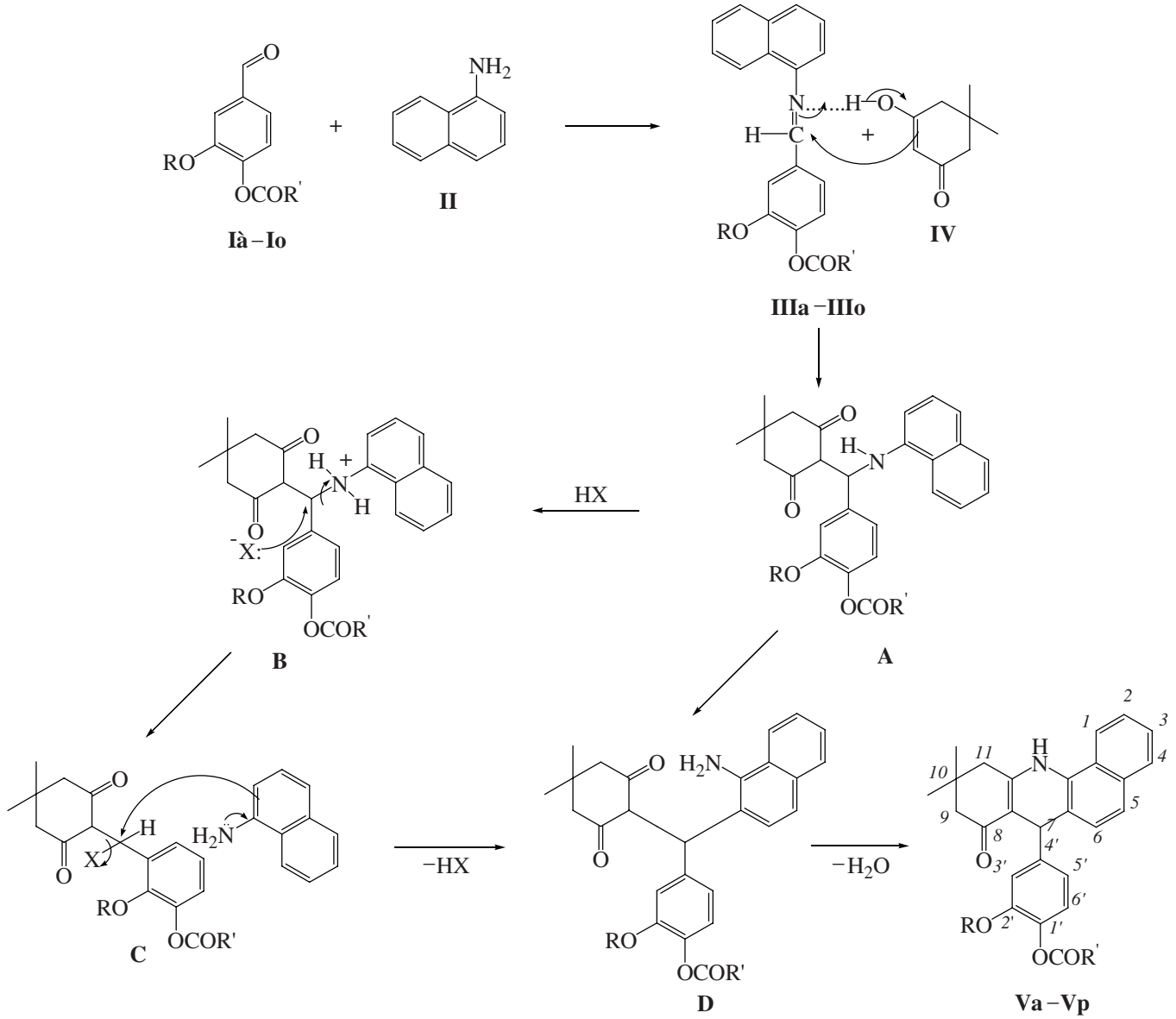
In the first stage 4-formyl-2-methoxy(ethoxy)-phenyl ester **Ia–Io** reacted with 1-naphthylamine (**II**), yielding azomethine **IIIa–IIIo** that in its turn added a dimedone (**IV**) molecule forming 4-[(4,4-dimethyl-2,6-dioxocyclohexyl)-(1-naphthylamino)methyl]-2-methoxy(ethoxy)-phenyl ester **A**. Then intermediate **A** underwent protonation by reaction with a solvent molecule HX converting into cation **B**. In the next stage an alkoxy anion X^- formed in the previous stage attacked cation **B** at the asymmetric carbon leading to the hydramine cleavage of this structure into 1-naphthylamine (**II**) and 3-[(4,4-dimethyl-2,6-dioxocyclohexyl)alkoxymethyl]-2-methoxy(ethoxy)phenyl ester **C**. The latter in reaction with 1-naphthylamine (**II**) may add both to the amino group and to the carbon atom possessing the highest electron density and located in the β-position of the naphthalene framework giving respectively 4-[(04,4-dimethyl-2,6-dioxocyclohexyl)(1-naphthylamino)-

methyl]-2-methoxy(ethoxy)phenyl ester **A** or 4-[(1-amino-2-naphthyl)(4,4-dimethyl-2,6-dioxocyclohexyl)-methyl]-2-methoxy(ethoxy)phenyl ester **D**. We guess that the latter alternative is preferable for the benzo[*c*]acridinone derivatives **Va–Vo** formed in the final stage can be obtained only by the dehydrocyclization of intermediate **D**. In keeping with the data of [5] it is presumable that the water molecules liberated during dehydrocyclization are involved into the protonation of intermediate **A** alongside the alcohol molecules.

The formation of ester **D** can be regarded as a result of a rearrangement of cation **B** proceeding by the migration of arylmethylencyclohexanedione fragment into the β-position of the naphthalene framework analogously to the process occurring at the transformtion of alkyl-, dialkylanilines halides and trialkylammomium salts known as Hofmann–Martius rearrangement [6].

The described mechanism is analogous to that suggested for the synthesis of 7-(*o*- and *p*-R-phenyl)-10,10-dimethyl-8,9,10,11-tetrahydrobenzo[*c*]acridin-8-ones [5] and besides it is in agreement with the mechanism of synthesis of benzo[*c*]acridines from 2-(naphthylaminomethylene)cyclohexanones [7].

Azomethines **IIIa–IIIo** prepared from 4-formyl-2-methoxy(ethoxy)phenyl esters of acids **Ia–Io** and 1-naph-



R = Me, R' = Me (**a**), Et (**b**), *i*-Pr (**c**), C_9H_{19} (**d**), C(Me)=CH_2 (**e**), Bn (**f**), $CH_2CH(Me)Ph$ (**g**), Ph (**h**), *p*-MePh (**i**), *p*-ClPh (**j**), *p*-NO_2Ph (**k**), *m*-NO_2Ph (**l**); R = Et, R' = Me (**m**), Ph (**n**), *p*-MePh (**o**).

thylamine (**II**) in ethanol were isolated in the form of individual *E*-isomers [8] although this had failed before [5]. Therefore it was possible to use the compounds in the above discussed reaction.

A similar reaction of dimedone, 1-naphthylamine and some aromatic aldehydes in ethanol was studied in [9]. Lielbriedis et al. presumed that the reaction products were isomeric to hexahydrobenzo[*c*]acridinones hexahydrobenzo[*c*]phenanthridines arising from cyclocondensation of the product of dimedone reaction with Schiff's bases. However applying to the structure estimation the combination of below cited spectral methods and taking into consideration the results of previous research [5, 10, 11] at the use of combined analysis of a number 2D NMR methods (COSY, NOESY, HSQC, and HMBC) and X-ray diffraction study we established that the only products of reaction between esters **IIIa–IIIo** and dimedone (**IV**), independent of the structure of the acid residue in the ester group were 4-(10,10-dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxy(ethoxy)phenyl carboxylates **Va–Vo**. The structure of compounds synthesized is in agreement with UV, IR, and ^{1}H NMR spectra.

For the electron absorption spectra of esters **Va–Vo** observed in the UV range the presence is characteristic of absorption maxima in four regions: at 215–227, 239–269, 279–286, and 368–378 nm. The complex spectral pattern is due to the presence in the structure of compounds synthesized of several chromophore fragments: naphthalene framework, benzene rings, and also carbonyl and ester groups. The substituents in the phenyl ring of the acid residue of the ester group virtually do not affect the position and intensity of the spectral bands, and only electron-acceptor nitro group in the *para*-position to the ester one brings about the smoothing of the vibronic structure of the spectrum and disappearance of a band in the region 279–286 nm.

It is known that at incomplete amines association in the IR spectra alongside the absorption bands of the associated amino groups appear absorption bands of the free NH group [12]. In the spectra of compounds we synthesized **Va–Vo** the absorption band of the stretching vibrations of the free secondary amine group was observed at 3448–3425 cm^{-1}, and of associated, at 3342–3283 cm^{-1}. It is also known that the stronger the absorption band of the associated amino group is shifted to lower frequencies and the greater its intensity, the higher is the association degree [12]. As to esters **Va–Vo**, note that stronger associated are compounds **Va** and **Vc**, and compounds **Vd, Vg**, and **Vj** are virtually non-associated. In the IR spectra of phenyl carboxylates **Va–Vd, Vf, Vg**, and **Vm** the strong band $\nu_{C=O}$ appears in the region 1767–1758 cm^{-1}. The conjugation of the carbonyl group with multiple bond decreases the frequency of $\nu_{C=O}$ vibration for all types of carbonyl compounds approximately by 20 cm^{-1} [12]. Therefore in the IR spectra of compounds **Ve, Vh–Vl, Vn**, and **Vo** the strong band corresponding to the carbonyl of the ester group is shifted to the region 1747–1732 cm^{-1}. The absorption band of the vinilog amide fragment is observed at 1602–1578 cm^{-1}. The intensity of this band is higher than that of the ester carbonyl. These data are in agreement with the results published in [5, 13]. The very strong band in the region 1502–1490 cm^{-1} should be assigned to the skeleton vibrations of aromatic carbon-carbon bonds. The most strong bands in the region 1129–1013 cm^{-1} should be assigned to the vibrations of the fragment C–O–C of ether and ester groups. Out-of-plane bending vibrations of the C–H bonds of aromatic and heteroaromatic rings appear as one or several strong bands at 797–694 cm^{-1}. IR spectrum of compound **Ve** contains a strong band at 939 cm^{-1} corresponding to out-of-plane bending vibrations of =C–H bond of the terminal methylene group–C(Me)=CH$_2$. In the IR spectra of compounds **Vk** and **Vl** a very strong band is present in the region 1533–1529 cm^{-1} belonging to the antisymmetrical stretching vibrations of the nitro group.

In the ^{1}H NMR spectra of esters **Va–Vo** a singlet is observed in the region 9.14–9.28 ppm corresponding to the proton of the secondary amino group. The singlet at 4.94–5.30 ppm should be assigned to the methine proton H^7 of the dihydropyridine ring. The downfield shift of this proton signal compared to the common position of the methine proton signals in the cyclic compounds is caused by an anisotropic effect of the contiguous aromatic rings. The protons of methyl groups attached to C^{10} gave rise to two singlets at 1.02–1.10 and 1.11–1.17 ppm. The proton signal of the methyl group located in a pseudo-equatorial position appeared in a weaker field. The singlet from the protons of methoxy group in compounds **Va–Vl** is seen in the region 3.70–3.78 ppm. The ethoxy group protons in esters **Vm–Vo** are observed as two signals, a triplet and broadened quartet. The triplet overlapps with two singlets of protons from methyl groups linked to C^{10} and appears at 0.87–1.39 ppm, and the quartet with the coupling constant of 5.5–6.2 Hz is located in the region 3.83–3.88 ppm. The protons of methylene groups at C^9 and C^{11} give rise each to two broadened doublets at

2.16–2.22 (^2J 16.4–17.2 Hz) and 2.65–2.73 ppm (^2J 16.2–16.9 Hz) respectively. The signal of protons H^9 appears upfield with respect to proton signal from H^{11} due to the shielding effect of the neighboring carbonyl group. The naphthalene protons show up as two doublets and a multiplet. A diffuse doublet at 8.40–8.48 ppm with a coupling constant 7.0–7.8 Hz should be assigned to proton H^1. This is consistent with data of [15]. The multiplet in the region 7.16–7.67 ppm, and also a broadened doublet at 7.76–7.84 ppm with a coupling constant 7.8–8.4 Hz belongs to the other five protons H^{2-6}. The protons H^3, H^5 and H^6 of vanillin and ethyl vanillin structures appear as a singlet and two doublets respectively (singlet of proton H^3 in the region 6.90–7.15 ppm, and doublets of protons H^6 and H^5, in the region 6.57–6.73 and 6.74–6.98 ppm with a coupling constant 7.0–7.8 Hz). A small upfield shift of H^3 proton in compounds **Vm–Vo** as compared with this signal in compounds **Va–Vl** may originate from the influence of a stronger +*M*-effect of ethoxy group than +*M*-effect of methoxy group. Besides the upfield shift of signals from protons H^3, H^5, and H^6 may be caused by the shielding effect of the bulky R' substituent [C_9H_{19}, $CH_2CH(Me)Ph$]. The protons of phenyl substituent R' are observed as one or several multiplets (depending on the nature of the substituent in question) in the region 7.06–8.67 ppm. The broadened singlet at 8.78 ppm in the spectrum of compound **Vl** should be assigned to the proton of the substituent *m*-NO_2Ph situated in the region of shielding from two acceptor groups (ester and nitro groups).

EXPERIMENTAL

IR spectra were recorded on an IR Fourier spectrophotometer Nicolet Protégé-460 from samples pelletized with KBr. UV spectra were taken on a spectrophotometer Specord UV Vis for (4–7)×10^{-5} M solutions in ethanol. ^{1}H NMR spectra were registered on spectrometers Tesla BS-567 (100 MHz) (**Va–Vd, Vh–Vk, Vm–Vo**) and Tesla BS-587 (80 MHz) (**Ve–Vg**, and **Vl**) from 5% solutions in DMSO-d_6, internal reference TMS. Melting points of compounds were measured on Koeffler heating block.

2-Methoxy(ethoxy)-4-(1-naphthyliminomethyl)-phenyl esters IIIa, IIId–IIIo were prepared by procedure [8].

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxy(ethoxy)-phenyl carboxylates Va–Vo. *a*. A solution of 2 mmol of dimedone (**IV**) and 2 mmol of azomethine **IIIa–IIId**, **IIIf–IIIo** in 30 ml of ethanol was boiled for 3–10 h. The resinous substance obtained after evaporation of the solvent was recrystallized from a mixture of acetone and 1,4-dioxane, 1:1, washed with hexane, and dried. Yield of esters **Va–Vd, Vf–Vo** 33–77%.

b. A solution of 2 mmol of dimedone (**IV**) and 2 mmol of azomethine **IIIe** in 30 ml of a mixture of 2-propanol and 1-butanol, 1:1, was boiled for 8 h. The separated precipitate was filtered off, recrystallized from a mixyure of acetone with methanol, 1:1, washed with ethyl ether, and dried. Yield of ester **Ve** 35%.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*C*]acridin-7-yl)-2-methoxyphenyl acetate (Va). Yield 48%, mp 276°C. UV spectrum, λ_{max}, nm (log ε): 218 (4.71), 258 (4.42), 281 (4.19), 368 (4.17). IR spectrum, cm^{-1}: 3438 v.w [ν(N–C_{free})], 3289 c [ν(N–H_{bound})], 3062 m, 3044 w [ν(C–H_{arom})], 2961 v.s, 2934 s, 2875 m [ν(C–H_{aliph})], 1759 s [ν(C=O_{ester})], 1591 v.s (O=C–C=C–N–H), 1496 v.s (Ar), 1420 m, 1386 v.s, 1372 s, 1344 w [δ(C–H_{aliph})], 1119 w, 1034 w (C–O–C), 791 w, 766 v.w, 742 w [δ(C–H_{arom})]. ^{1}H NMR spectru, δ, ppm (*J*, Hz): 1.08 s, 1.15 s (6H, 2Me, H^{10}), 1.96–2.35 (2 br.d + s) (2H, H^9 + 3H, OCOMe), 2.68 (2 br.d) (2H, H^{11}, ^2J 16.9), 3.73 s (3H, OMe), 5.22 s (1H, H^7), 6.64 d, 6.77 d (2H, H^5, H^6, ^3J 7.5), 7.02 s (1H, H^3), 7.19–7.62 m, 7.76 br.d (5H, H^{2-6}, ^3J 7.9), 8.42 br.d (1H, H^1, ^3J 7.6), 9.14 s (1H, NH). Found, %: C 76.32; H 6.51; N 3.42. $C_{28}H_{27}NO_4$. Calculated, %: C 76.17; H 6.16; N 3.17.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*C*]acridin-7-yl)-2-methoxyphenyl propionate (Vb). Yield 43%, mp 246°C. UV spectrum, λ_{max}, nm (log ε): 218 (4.41), 259 (4.09), 282 (3.75), 368 (3.83). IR spectrum, cm^{-1}: 3440 m [ν(N–C_{free})], 3283 s [ν(N–H_{bound})], 3062 m, 3042 w [ν(C–H_{arom})], 2961 s, 2933 v.s, 2872 m [ν(C–H_{aliph})], 1761 s [ν(C=O_{ester})], 1591 v.s (O=C–C=C–N–H), 1497 v.s (Ar), 1417 m, 1384 v.s, 1373 c, 1343 m [δ(C–H_{aliph})], 1122 C, 1032 C (C–O–C), 792 C, 764 v.s, 740 C [δ(C–H_{arom})]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00–1.27 (2 s + t) (6H, 2Me, H^{10} + 3H, $OCOCH_2\underline{Me}$), 2.16 (2 br.d) (2H, H^9, ^2J 16.5), 2.50 q (2H, $OCO\underline{CH_2}Me$, ^3J 6.4), 2.68 (2 br.d) (2H, H^{11}, ^2J 16.2), 3.73 s (3H, OMe), 5.23 s (1H, H^7), 6.66 d, 6.79 d (2H, H^5, H^6, ^3J 7.4), 7.03 s (1H, H^3), 7.20–7.64 m, 7.78 br.d (5H, H^{2-6}, ^3J 8.0), 8.45 d (1H, H^1, ^3J 7.4), 9.18 C (1H, NH). Found, %: C 76.74; H 6.86; N 3.51. $C_{29}H_{29}NO_4$. Calculated, %: C 76.46; H 6.42; N 3.07.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl

isobutyrate (Vc). Yield 40%, mp 253°C. UV spectrum, λ_{max}, nm (log ε): 217 (4.66), 258 (4.34), 281 (4.05), 368 (4.09). IR spectrum, cm^{-1}: 3448 v.w [ν(N–Ç$_{free}$)], 3300 s [ν(N–H$_{bound}$)], 3058 m, 3032 v.w [ν(C–H$_{arom}$)], 2957 s, 2932 v.s, 2874 m [ν(C–H$_{aliph.}$)], 1764 v.s [ν(C=O$_{ester}$)], 1588 v.s (O=C–C=C–N–H), 1495 v.s (Ar), 1417 m, 1385 s, 1366 m, 1341 w [δ(C–H$_{aliph.}$)], 1124 v.s, 1096 s, 1032 s (C–O–C), 797 s, 770 v.s, 751 s [δ(C–H $_{arom}$)]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.07 s, 1.14 s (6H, 2Me, H^{10}), 1.22 d (6H, OCOCH<u>Me</u>$_2$, ^3J 6.5), 2.16 (2 br.d) (2H, H^9, ^2J 16.4), 2.58–2.91 (m + 2 br.d) (2H, OCO<u>CH</u>(Me)$_2$ + 2H, H^{11}), 3.73 s (3H, OMe), 5.24 s (1H, H^7), 6.64 d, 6.78 d (2H, H^5, H^6, ^3J 7.1), 7.02 s (1H, H^3), 7.20–7.67 m, 7.79 br.d (5H, H$^{2-6}$, ^3J 8.1), 8.44 d (1H, H^1, ^3J 7.5), 9.17 s (1H, NH). Found, %: C 76.90; H 7.00; N 2.68. $C_{30}H_{31}NO_4$. Calculated, %: C 76.73; H 6.65; N 2.98.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl decanoate (Vd). Yield 60%, mp 248–250°C. UV spectrum, λ_{max}, nm (log ε): 218 (4.60), 269 (4.26), 280 (4.19), 377 (3.82). IR spectrum, cm^{-1}: 3327 m [ν(N–H$_{bound}$)], 3056 m [ν(C–H$_{arom}$)], 2954 s, 2926 v.s, 2854 m [ν(C–H$_{aliph}$)], 1762 s [ν(C=O$_{ester}$)], 1600 v.s (O=C–C=C–N–H), 1495 v.s (Ar), 1418 s, 1385 v.s, 1369 v.s, 1345 m [δ(C–H $_{aliph.}$)], 1122 v.s, 1034 s (C–O–C), 766 v.s [δ(C–H$_{arom}$)]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.92 t [3H, OCO(CH$_2$)$_8$<u>Me</u>, ^3J 4.1], 1.10 s, 1.15 s (6H, 2Me, H^{10}), 1.20–1.49 m [12H, OCO(CH$_2$)$_2$(<u>CH</u>$_2$)$_6$Me], 1.64 m [2H, OCOCH$_2$<u>CH</u>$_2$(CH$_2$)$_6$Me], 2.17 (2 br.d) (2H, H^9, ^2J 16.6), 2.39–2.58 br.t [2H, OCO<u>CH</u>$_2$(CH$_2$)$_7$Me], 2.65 (2 br.d) (2H, H^{11}, ^2J 16.3), 3.70 br.s (3H, OMe), 4.95 C (1H, H^7), 6.60 br.d, 6.75 br.d (2H, H^5, H^6, ^3J 7.1), 6.92 br.s (1H, H^3), 7.22–7.64 m, 7.80 br.d (5H, H$^{2-6}$, ^3J 8.0), 8.40 br.d (1H, H^1, ^3J 7.6), 9.28 br.s (1H, NH). Found, %: C 78.39; H 8.27; N 2.43. $C_{36}H_{43}NO_4$. Calculated, %: C 78.09; H 7.83; N 2.53.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl methacrylate (Ve). Yield 35%, mp 226–230°C. UV spectrum, λ_{max}, nm (log ε): 217 (4.69), 258 (4.33), 279 (4.11), 370 (4.04). IR spectrum, cm^{-1}: 3432 m [ν(N–Ç$_{free}$)], 3291 s [ν(N–H$_{bound}$)], 3056 m, 3041 w [ν(C–H$_{arom}$)], 2957 v.s, 2929 s, 2871 m [ν(C–H$_{aliph.}$)], 1739 s [ν(C=O$_{ester}$)], 1591 v.s (O=C–C=C–N–H), 1497 v.s (Ar), 1418 m, 1385 v.s, 1376 s, 1343 w, 1321 m [δ(C–H$_{aliph.}$)], 1129 v.s, 1036 s (C–O–C), 939 s [δ(=CH$_2$)], 791 s, 766 v.s, 737 s [δ(C–H$_{arom}$)]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.09 s, 1.15 s (6H, 2Me, H^{10}), 1.97 s (3H, OCOC<u>Me</u>=CH$_2$), 2.19 (2 br.d) (2H, H^9), 2.72 (2 br.d) (2H, H^{11}), 3.75 s (3H, OMe), 5.27 s (1H, H^7), 5.80 br.s, 6.21 br.s (2H, OCOCMe=<u>CH</u>$_2$), 6.69 d, 6.88 d (2H, H^5, H^6, ^3J 7.2), 7.10 s (1H, H^3), 7.16–7.65 m, 7.83 br.d (5H, H$^{2-6}$, ^3J 8.0), 8.48 d (1H, H^1, ^3J 7.2), 9.22 s (1H, NH). Found, %: C 77.32; H 6.51; N 3.40. $C_{30}H_{29}NO_4$. Calculated, %: C 77.06; H 6.25; N 3.00.

4-(10,10-Dimethyl -8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenylphenylacetate (Vf). Yield 38%, mp 272–274°C. UV spectrum, λ_{max}, nm (log ε): 215 (4.71), 263 (4.39), 279 (4.24), 373 (3.94). IR spectrum, cm^{-1}: 3304 s [ν(N–H$_{bound}$)], 3064 m, 3029 m [ν(C–H$_{arom}$)], 2957 s, 2925 v.s, 2871 m [ν(C–H$_{aliph.}$)], 1764 c [ν(C=O$_{ester}$)], 1599 v.s (O=C–C=C–N–H), 1490 v.s (Ar), 1418 m, 1401 v.s, 1373 v.s, 1344 C [δ(C–H$_{aliph.}$)], 1121 v.s, 1031 s (C–O–C), 748 v.s, 729 C, 694 C [δ(C–H$_{arom}$)]. ^{1}H, δ, ppm (*J*, Hz): 1.02 C, 1.11 C (6H, 2Me, H^{10}), 2.20 (2 br.d) (2H, H^9), 2.69 (2 br.d) (2H, H^{11}), 3.58 C (2H, OCO<u>CH</u>$_2$Ph), 3.78 br.s (3H, OMe), 5.01 C (1H, H^7), 6.62 br.d, 6.74 br.d (2H, H^5, H^6, ^3J 7.4), 6.99 C (1H, H^3), 7.15–7.56 m, 7.84 br.d (10H, H$^{2-6}$, H$_{arom}$, ^3J 8.3), 8.41 br.d (1H, H^1, ^3J 7.2), 9.14 C (1H, NH). Found, %: C 78.99; H 6.37; N 2.86. $C_{34}H_{31}NO_4$. Calculated, %: C 78.89; H 6.04; N 2.71.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl 3-phenylbutyrate (Vg). Yield 77%, mp 228–230°C. UV spectrum, λ_{max}, nm (log ε): 218 (4.47), 265 (4.05), 284 (3.87), 377 (3.69). IR spectrum, cm^{-1}: 3329 m [ν(N–H$_{bound}$)], 3058 m, 3027 m [ν(C–H$_{arom}$)], 2957 s, 2926 s, 2867 m [ν(C–H$_{aliph.}$)], 1758 s [ν(C=O$_{ester}$)], 1602 v.s (O=C–C=C–N–H), 1494 v.s (Ar), 1417 c, 1384 v.s, 1371 v.s, 1342 m [δ(C–H$_{aliph.}$)], 1123 v.s, 1033 s (C–O–C), 764 s, 700 s [δ(C–H$_{arom}$)]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.04 s, 1.12 s (6H, 2Me, H^{10}), 1.32 d (3H, OCOCH$_2$CH<u>Me</u>Ph, ^3J 6.5), 2.16 (2 br.d) (2H, H^9), 2.57–2.97 m (4H, OCO<u>CH</u>$_2$CHMePh, H^{11}), 3.07–3.95 (m + s) (1H, OCOCH$_2$<u>CH</u>MePh + 3H, OMe), 5.21 s (1H, H^7), 6.57 br.d, 6.80 br.d (2H, H^5, H^6, ^3J 7.4), 7.02 s (1H, H^3), 7.06–7.67 m, 7.80 br.d (10H, H$^{2-6}$, H$_{arom}$, ^3J 8.4), 8.44 d (1H, H^1, ^3J 7.0), 9.21 s (1H, NH). Found, %: C 79.59; H 6.92; N 3.05. $C_{36}H_{35}NO_4$. Calculated, %: C 79.24; H 6.46; N 2.57.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl benzoate (Vh). Yield 49%, mp 258–262°C. UV spectrum, λ_{max}, nm (log ε): 223 (4.73), 258 (4.42), 281

(4.25), 372 (4.07). IR spectrum, cm^{-1}: 3299 s [ν(N–H_{bound})], 3060 m, 3037 w [ν(C–H_{arom})], 2954 s, 2929 s, 2869 m [ν(C–H_{aliph})], 1741 s [ν(C=O_{ester})], 1589 v.s (O=C–C=C–N–H), 1494 v.s (Ar), 1417 m, 1384 s, 1373 s, 1344 w, 1315 w [δ(C–H_{aliph})], 1122 s, 1079 s, 1061 s, 1024 s (C–O–C), 710 v.s [δ (C–H_{arom})]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.08 s, 1.13 s (6H, 2Me, H*10*), 2.19 (2 br.d) (2H, H*9*, ^{2}*J* 17.1), 2.70 (2 br.d) (2H, H*11*, ^{2}*J* 16.8), 3.72 s (3H, OMe), 5.28 s (1H, H*7*), 6.73 br.d, 6.82 br.d (2H, H*5*, H*6*, ^{3}*J* 7.0), 7.10 br.s (1H, H*3*), 7.23–7.71 m, 7.80 br.d, 7.95–8.21 m (10H, H*2-6*, H_{arom}, ^{3}*J* 7.8), 8.46 d (1H, H*1*, ^{3}*J* 7.4), 9.21 s (1H, NH). Found, %: C 78.92; H 6.22; N 2.48. $C_{33}H_{29}NO_4$. Calculated, %: C 78.71; H 5.80; N 2.78.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl *p*-methyl benzoate (Vi). Yield 42%, mp 140–146°C. UV spectrum, λ_{max}, nm (log ε): 218 (4.48), 242 (4.49), 281 (4.13), 369 (3.92). IR spectrum, cm^{-1}: 3329 s [ν(N–H_{bound})], 3060 m, 3037 w [ν(C–H_{arom})], 2953 s, 2924 v.s, 2867 m [ν(C–$H_{aliph.}$)], 1742 s [ν(C=O_{ester})], 1589 v.s (O=C–C=C–N–H), 1502 v.s (Ar), 1418 m, 1391 s, 1384 s, 1340 w, 1319 w [δ(C–H_{aliph})], 1123 s, 1066 s, 1018 s (C–O–C), 748 v.s [δ(C–H_{arom})]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.06 s, 1.12 s (6H, 2Me, H*10*), 2.17 (2 br.d) (2H, H*9*, ^{2}*J* 16.9), 2.42 s [3H, OCO(*p*-Me)Ph], 2.69 (2 br.d) (2H, H*11*, ^{2}*J* 16.6), 3.71 s (3H, OMe), 5.24 s (1H, H*7*), 6.70 d, 6.87 d (2H, H*5*, H*6*, ^{3}*J* 7.8), 7.07 br.s (1H, H*3*), 7.20–7.65 m, 7.70–8.06 m (9H, H*2–6*, H_{arom}), 8.44 br.d (1H, H*1*, ^{3}*J* 7.1), 9.17 s (1H, NH). Found, %: C 78.93; H 6.49; N 3.20. $C_{34}H_{31}NO_4$. Calculated, %: C 78.89; H 6.04; N 2.71.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl *p*-chlorobenzoate (Vj). Yield 74%, mp 194–198°C. UV spectrum, λ_{max}, nm (log ε): 219 (4.49), 242 (4.52), 283 (3.92), 372 (3.73). IR spectrum, cm^{-1}: 3427 m [ν(N–H_{free})], 3342 m [ν(N–H_{bound})], 3066 m [ν(C–H_{arom})], 2955 s, 2925 v.s, 2868 m [ν(C–H_{aliph})], 1747 s [ν(C=O_{ester})], 1590 v.s (O=C–C=C–N–H), 1495 v.s (Ar), 1418 m, 1398 s, 1384 s, 1376 s, 1344 w, 1310 w [δ(C–H_{aliph})], 1123 s, 1091 s, 1067 s, 1013 s (C–O–C), 753 v.s [δ(C–H_{arom})]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.08 s, 1.13 s (6H, 2Me, H*10*), 2.17 (2 br.d) (2H, H*9*, ^{2}*J* 17.1), 2.70 (2 br.d) (2H, H*11*, ^{2}*J* 16.8), 3.72 s (3H, OMe), 5.25 s (1H, H*7*), 6.70 d, 6.91 d (2H, H*5*, H*6*, ^{3}*J* 7.8), 7.09 s (1H, H*3*), 7.21–7.67 m, 7.78 br.d, 7.93–8.16 m (9H, H*2-6*, H_{arom}, ^{3}*J* 8.5), 8.43 br.d (1H, H*1*, ^{3}*J* 7.1), 9.18 s (1H, NH). Found, %: C 74.04; H 5.68; N 3.01. $C_{33}H_{28}ClNO_4$. Calculated, %: C 73.67; H 5.24; N 2.60.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl *p*-nitrobenzoate (Vk). Yield 34%, mp 264–266°C. UV spectrum, λ_{max}, nm (log ε): 217 (4.26), 260 (4.27), 370 (3.80). IR spectrum, cm^{-1}: 3431 m [ν(N–H_{free})], 3324 s [ν(N–H_{bound})], 3053 m [ν(C–H_{arom})], 2962 s, 2922 v.s, 2866 m [ν(C–H_{aliph})], 1732 s [ν(C=O_{ester})], 1596 v.s (O=C–C=C–N–H), 1529 v.s [ν(NO_2)], 1502 v.s (Ar), 1419 m, 1408 s, 1390 v.s, 1385 v.s [δ(C–H_{aliph})], 1121 v.s, 1074 s, 1035 s, 1014 s (C–O–C), 714 v.s [δ(C–H_{arom})]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 s, 1.14 s (6H, 2Me, H*10*), 2.18 (2 br.d) (2H, H*9*, ^{2}*J* 16.8), 2.68 (2 br.d) (2H, H*11*, ^{2}*J* 16.5), 3.73 s (3H, OMe), 5.26 s (1H, H*7*), 6.72 d, 6.96 d (2H, H*5*, H*6*, ^{3}*J* 7.7), 7.12 s (1H, H*3*), 7.20–7.60 m, 7.77 br.d (5H, H*2–6*, ^{3}*J* 8.0), 8.19–8.53 m (5H, H_{arom}, H*1*), 9.21 s (1H, NH). Found, %: C 72.48; H 5.56; N 5.45. $C_{33}H_{28}N_2O_6$. Calculated, %: C 72.25; H 5.14; N 5.11.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-methoxyphenyl *m*-nitrobenzoate (Vl). Yield 48%, mp 280–284°C. UV spectrum, λ_{max}, nm (log å): 219 (4.62), 258 (4.26), 283 (3.95), 373 (3.74). IR spectrum, cm^{-1}: 3425 m [ν(N–H_{free})], 3301 s [ν(N–H_{bound})], 3067 m, 3040 w [ν(C–H_{arom})], 2956 v.s, 2929 c, 2868 m [ν(C–H_{aliph})], 1746 s [ν(C=O_{ester})], 1589 v.s (O=C–C=C–N–H), 1533 v.s [ν(NO_2)], 1497 v.s (Ar), 1419 m, 1391 s, 1385 s [δ(C–H_{aliph})], 1125 s, 1060 s, 1032 s (C–O–C), 753 s, 718 v.s [δ(C–H_{arom})]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.10 s, 1.17 s (6H, 2Me, H*10*), 2.22 (2 br.d) (2H, H*9*), 2.73 (2 br.d) (2H, H*11*), 3.76 br.s (3H, OMe), 5.30 s (1H, H*7*), 6.73 d, 6.98 d (2H, H*5*, H*6*, ^{3}*J* 7.0), 7.15 s (1H, H*3*), 7.29–7.62 m, 7.70–8.03 m (6H, H*2–6*, H_{arom}), 8.31–8.67 m (3H, H*1*, H_{arom}), 8.78 br.s (1H, H_{arom}), 9.20 s (1H, NH). Found, %: C 72.33; H 5.45; N 4.98. $C_{33}H_{28}N_2O_6$. Calculated, %: C 72.25; H 5.14; N 5.11.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-ethoxyphenyl acetate (Vm). Yield 37%, mp 292–296°C. UV spectrum, λ_{max}, nm (log ε): 223 (4.34), 264 (4.12), 282 (3.92), 378 (3.74). IR spectrum, cm^{-1}: 3311 s [ν(N–H_{bound})], 3073 m, 3038 v.w [ν(C–H_{arom})], 2956 s, 2928 v.s, 2872 m [ν(C–$H_{aliph.}$)], 1767 s [ν(C=O_{ester})], 1578 v.s (O=C–C=C–N–H), 1493 v.s (Ar), 1423 m, 1386 v.s, 1371 v.s, 1346 m [δ(C–H_{aliph})], 1120 s, 1041 s (C–O–C), 755 s [δ(C–H_{arom})]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.92–

1.39 (2 s + t) (6H, 2Me, H^{10} + 3H, OCH$_2$Me), 2.18 (2 br.d) (2H, H^9, ^2J 17.2), 2.24 s (3H, OCOMe), 2.70 (2 br.d) (2H, H^{11}, ^2J 16.9), 3.83 br.q (2H, OCH$_2$Me, ^3J 5.8), 4.94 s (1H, H^7), 6.57 br.d, 6.75 br.d (2H, H^5, H^6, ^3J 7.7), 6.90 br.s (1H, H^3), 7.19–7.62 m, 7.83 br.d (5H, H$^{2-6}$, ^3J 8.1), 8.40 br.d (1H, H^1, ^3J 7.7), 9.16 s (1H, NH). Found, %: C 76.77; H 6.90; N 3.51. $C_{29}H_{29}NO_4$. Calculated, %: C 76.46; H 6.42; N 3.07.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*c*]acridin-7-yl)-2-ethoxyphenyl benzoate (Vn). Yield 33%, mp 302–306°C. UV spectrum, λ_{max}, nm (log ε): 227 (4.66), 265 (4.36), 286 (4.15), 376 (3.94). IR spectrum, cm^{-1}: 3426 m [ν(N–H$_{free}$)], 3297 s [ν(N–H$_{bound}$)], 3070 m, 3037 w [ν(C–H$_{arom}$)], 2955 s, 2929 v.s, 2871 m [ν(C–H$_{aliph}$)], 1740 s [ν(C=O$_{ester}$)], 1581 v.s (O=C–C=C–N–H), 1495 v.s (Ar), 1422 w, 1401 s, 1373 v.s, 1344 m, 1313 m [δ(C–H$_{aliph}$)], 1120 s, 1079 s, 1061 s, 1024 s (C–O–C), 706 v.s [δ(C–H$_{arom}$)]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.90–1.32 (2 s + t) (6H, 2Me, H^{10} + 3H, OCH$_2$Me), 2.17 (2 br.d) (2H, H^9, ^2J 16.9), 2.72 (2 br.d) (2H, H^{11}, ^2J 16.6), 3.88 br.q (2H, OCH$_2$Me, ^3J 6.2), 5.01 s (1H, H^7), 6.67 d, 6.79 d (2H, H^5, H^6, ^3J 7.1), 6.97 br.s (1H, H^3), 7.30–7.73 m, 7.84 br.d, 7.94–8.18 m (10H, H$^{2-6}$, H$_{arom}$, ^3J 7.7), 8.42 d (1H, H^1, ^3J 7.8), 9.19 s (1H, NH). Found, %: C 79.25; H 6.44; N 3.19. $C_{34}H_{31}NO_4$. Calculated, %: C 78.89; H 6.04; N 2.71.

4-(10,10-Dimethyl-8-oxo-7,8,9,10,11,12-hexahydrobenzo[*C*]acridin-7-yl)-2-ethoxyphenyl *p*-methylbenzoate (Vo). Yield 40%, mp 294–296°C. UV spectrum, λ_{max}, nm (log å): 221 (4.62), 239 (4.68), 283 (4.22), 378 (3.87). IR spectrum, cm^{-1}: 3307 s [ν(N–H$_{bound}$)], 3068 m, 3038 w [ν(C–H$_{arom}$)], 2955 s, 2927 v.s, 2871 m [ν(C–H$_{aliph}$)], 1739 s [ν(C=O$_{ester}$)], 1579 v.s (O=C–C=C–N–H), 1495 v.s (Ar), 1425 w, 1401 s, 1385 s, 1373 v.s, 1345 m, 1314 m [δ(C–H$_{aliph.}$)], 1122 s 1069 s, 1019 s (C–O–C), 747 v.s [δ(C–H$_{arom}$)]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.87–1.32 (2 s + t) (6H, 2Me, H^{10} + 3H, OCH$_2$Me), 2.17 (2 br.d) (2H, H^9, ^2J 17.0), 2.45 s [3H, OCO(*p*-Me)Ph], 2.71 (2 br.d) (2H, H^{11}, ^2J 16.7), 3.88 br.q (2H, OCH$_2$Me, ^3J 5.5), 5.02 s (1H, H^7), 6.72 br.d, 6.87 br.d (2H, H^5, H^6, ^3J 7.8), 6.98 br.s (1H, H^3), 7.20–7.59 m, 7.76–8.08 m (9H, H$^{2-6}$, H$_{arom}$), 8.42 br.d (1H, H^1, ^3J 7.6), 9.17 s (1H, NH). Found, %: C 79.20; H 6.51; N 2.25. $C_{35}H_{33}NO_4$. Calculated, %: C 79.07; H 6.26; N 2.63.

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