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Vanillin Esters of Aromatic Carboxylic Acids in the Synthesis of Benzo[*a*]acridine and Benzo[*b*][4,7]phenanthroline Derivatives

N.G. Kozlov, A.B. Tereshko, and K.N. Gusak

Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, Minsk, 220072 Belarus
e-mail: loc@ifoch.bas-net.by

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Abstract—By condensation of vanillin esters of substituted benzoic acids with 2-naphthylamine and 6-quinolylamines and also with cyclic β-diketones (1,3-cyclohexanedione and dimedone) 2-methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)- and 2-methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]-phenanthrolin-12-yl)phenyl benzoates were prepared.

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The introduction of vegetable phenols fragments into the molecules of fused nitrogen-containing heterocycles, in particular, into acridine and 4,7-phenanthroline derivatives, analogs of natural alkaloids, antitumor drugs, and reagents for the medical biochemical analysis [1–3], is a promising way to preparation of biologically active compounds with a wide range of action.

We formerly demonstrated [4, 5] that reaction of vanillin alkanoates with 2-naphthylamine and 6-quinolylamines and with cyclic 1,3-diketones afforded benzo[*a*]-acridine and benzo[*b*][4,7]-phenanthroline derivatives containing ester moieties in the molecules which supply the compounds with sufficient solubility in fats and water-alcoholic media important for biologic testing of the compounds and for preparation of drugs preforms.

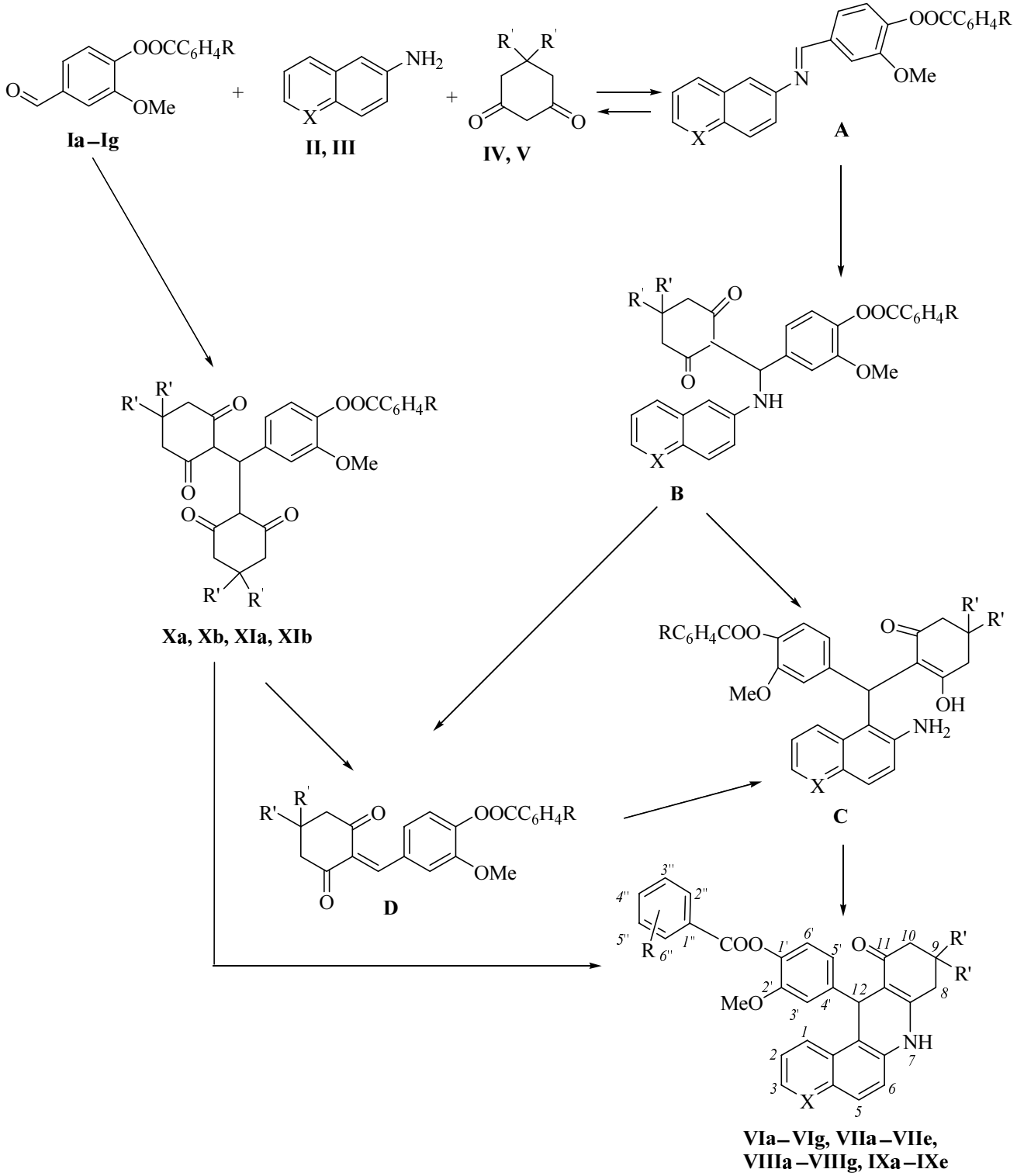
In the present study in order to obtain new representatives of the above compound classes by reaction with 2-naphthylamine and 6-quinolylamines and also with cyclic 1,3-diketones (1,3-cyclohexanedione and dimedone) we investigated for the first time vanillin esters of aromatic carboxylic acids (benzoic, alkyl-, halo-, and nitrobenzoic acids), (3-methoxy-4-formylphenyl) arenecarboxylates **Ia–Ig**,

The condensation of esters **Ia–Ig** with 2-naphthylamine (**II**), 6-quinolylamine (**III**), 1,3-cyclohexanedione (**IV**), and dimedone (**V**) occurred at boiling equivalent amounts of the reagents in 1-butanol. Due to the high lability of the protons of the methylene group in the position *2* in the 1,3-diketones **IV** and **V** the reaction proceeded with no catalysts providing a possibility even at the high temperature of the process to prevent the hydrolysis and decarboxylation of the ester group in formyl benzoates **Ia–Ig** involved into the condensation through the aldehyde group. As a result individual 2-methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo-[*a*]acridin-12-yl)- and 2-methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*]-[4,7]phenanthrolin-12-yl)pnenyl esters of benzoic acids **VIa–VIg** and **VIIa–VIIe** and their 9-dimethyl derivatives **VIIIa–VIIIg** and **IXa–IXe** were obtained in 65–89% yields.

The order of reagents mixing when first to the heated solution of amine **II** or **III** in 1-butanol is added the aldehyde component, vanillin ester **I**, suggests the initial formation of azomethine **A**, whose condensation with the third component, 1,3-diketone **IV** or **V**, occurs analogously to the data of [6] through a rearrangement of the intermediate aminodiketone **B** by migration of 2-(aroyloxyphenyl)-methylene-1,3-cyclohexanedione fragment into the position *1* of naphthalene or the position *5* of quinoline skeleton affording enaminohydroxyketone **C** that undergoes cyclization into benzo-[*a*]acridine and benzo-[*b*][4,7]phenanthroline system respectively. Note that in the course of the reaction of azomethine **A** with 1,3-diketone **IV** or **V** intermediate **C** may also result from the hydramine cleavage of aminodiketone **B** into 2-naphthylamine, 6-quinolylamine and 2-arylmethylene-1,3-cyclohexanedione **D** that further adds to amine **II** or **III** at the carbon atom (in the position *1* of naphthalene or the position *5* of quinoline skeleton).

Inasmuch as azomethines formation is reversible the reaction mixture may contain simultaneously all the three components: aldehyde (vanillin ester **I**), amines **II** or **III**,

Scheme.



X = CH (**II, VIa–VIg, VIIIa–VIIIg**), N (**III, VIIa–VIIe, IXa–IXe**); R = H (**Ia, VIa–XIa**), 2-Cl (**Ib, VIb–XIb**), 4-Cl (**Ic, VIc–IXc**), 4-Br (**Id, VId–IXd**), 4-NO_2 (**Ie, VIe–IXe**), 4-Me (**If, VIf, VIIIf**), 2,4-Cl_2 (**Ig, VIg, VIIIg**); R' = H (**III, VIa-VIg, VIIa–VIIe, Xa, Xb**), Me (**IV, VIIIa–VIIIg, IXa–IXe, XIa, XIb**).

and β-diketones **IV** or **V**. Therewith 2-arylmethylene-1,3-cyclohexanedione **D** may form directly from the ester and 1,3-diketone and further react with amine along the above described mechanism. To test this assumption we carried out a reaction of vanillin esters **Ia** and **Ib** with 1,3-diketones **IV**and **V** under the conditions of the three-component condensation. However although the reaction was performed with equimolar amounts of the reagents instead of the presumed 2-arylmethylene-1,3-cyclohexanediones **D** we obtained 4-[bis(2,6-dioxocyclohexyl)methyl]- 2-methoxyphenyl benzoates **Xa, Xb** and **XIa, XIb**. Yet the formation of the latter was not unexpected for the 1,3-cyclohexanedione and dimedone are known [7, 8] to be applied for quantitative determination and identification of aldehydes just as bisdiketones. At boiling in ethanol of a double excess of diones **IV** and **V** with esters **Ia** and **Ib** benzoates **Xa, Xb** and **XIa, XIb** were obtained in 68–80%, yields, and the heating of the benzoates with 2-naphthylamine or 6-quinolylamine in butanol gave rise to target esters **VIa, VIb, VIIIa, VIIIb** and **VIIa, VIIb, IXa, IXb** apparently because of hydrolytic cleavage of the tetraones **Xa, Xb** and **XIa, XIb** into diketones **IV** and **V** and 2-aryl-methylene-1,3-cyclohexanediones **D** and the reaction of the latter *in situ* with amines **II** and **III** in the described fashion.

The structure of compounds **VIa–VIg**, **VIIa–VIIe**, **VIIIa–VIIIg**, **IXa–IXe** was established from IR, NMR, and mass spectra. Their IR spectra contain characteristic absorption bands of the stretching and bending vibrations of the N–H bond at 3320–3290 and 1660–1645 cm^{-1} respectively. The stretching vibrations of the keto group conjugated to the enamine moiety appear at 1620–1610 cm^{-1}. The carbonyl of the ester group gives rise to a strong band in the region 1635–1630 cm^{-1}. The displacement of the band to lower frequencies is apparently caused by the formation of intermolecular hydrogen bonds involving the ester, amino, and enolized ketone carbonyl groups. The C–O–C fragments present in the molecules of compounds **VIa–VIg**, **VIIa–VIIe**, **VIIIa–VIIIg**, **IXa–IXe** give absorption bands in the region 1235–1210 cm^{-1}. The stretching vibrations of cycloaliphatic bonds appear as bands at 2955–2830 cm^{-1}, the vibrations of the bonds in the aromatic rings, at 3140–3030 cm^{-1}. In the spectra of compounds **VIe–IXe** strong bands at) 1545–1530 and 1360–1355 cm^{-1} correspond to the stretching vibrations of the nitro groups.

The ^1H NMR spectra of compounds **VIa–VIg**, **VIIa–VIIe**, **VIIIa–VIIIg**, **IXa–IXe** with respect to position and multiplicity of the proton signals originating from the benzoacridine and benzophenanthroline skeletons, and also the proton signals of methoxy group and aromatic protons of the vanillin fragment are identical to the previously published spectra of the vanillin alkanoates [4, 5]. The location of the aromatic protons of the R substituent is governed by the anisotropic effect of the substituents in the phenyl ring. In the spectra of dimedone derivatives **VIIIa–VIIIg** and **IXa–IXe** the methyl groups protons give rise to signals at 0.97–1.16 ppm. In the spectra of esters **VIa** and **VIIIa** a singlet from a methyl group protons is observed at 2.40–2.48 ppm.

In the mass spectra of esters **VIa–VIg**, **VIIa–VIIe**, **VIIIa–VIIIg**, **IXa–IXe** appear the peaks of molecular ions $[M]^+$ (I_{rel} 16–24%). The most abundant (100%) is the ion $[M - MeO - RCOOC_6H_3]^+$ (m/z 248 for compounds **VIa–VIg**, 249 for esters **VIIa–VIIe**, 276 and 277 for dimedone derivatives **VIIIa–VIIIg** and **IXa–IXe** respectively). In the spectra of esters **VIa–VIg** and **VIIIa–VIIIg** a peak of ion is present with *m/z* 192 (I_{rel} 13–36%), in the spectra of esters **VIIa–VIIe** and **IXa–IXe**, with m/z 193 (I_{rel} 18–39%), corresponding to the loss of ion $[M - MeO - RCOOC_6H_3]^+$ of a fragment CH_2CH_2CO for compounds **VIa–VIg**, **VIIa–VIIe** and $(CH_3)_2CHCH_2CO$ for derivatives **VIIIa–VIIIg**, **IXa–IXe**.

EXPERIMENTAL

Mass spectra were measured on a mass spectrometer Finnigan MAT INCOS-50 with ionizing electrons energy 70 eV and on a GC-MS instrument Hewlett-Packard HP 5890/5972 in electron impact mode at the energy 70 eV, column HP-5MS [length 30 m, internal diameter 0.25 mm, stationary phase film 0.25 μm thick (5% PLMe Silicone)], vaporizer temperature 250°C. IR spectra were recorded on a Fourier spectrometer Nicolet Protege-460. ^1H NMR spectra were registered on spectrometers Bruker-AC 500 (500 MHz) and Tesla BS-567 (100 MHz) in DMSO-d_6, internal reference TMS.

The melting points were measured on a Koeffler heating block.

3-Methoxy-4-formylphenyl benzoates **Ia–Ik** were prepared by procedure [4].

2-Methoxy-4-(11-oxo-[and 9,9-dimethyl-11-oxo]-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-, 2-methoxy-4-(11-oxo-[and 9,9-dimethyl-11-oxo]-7,8,-9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)phenyl benzoates VIa–VIg, VIIa–VIIe, VIIIa–VIIIg, IXa–IXe. A solution of 10 mmol of ester **Ia–Ik**

in 20 ml of 1-butanol was added to a solution heated to 60–80°C of 10 mmol of 2-naphthylamine (**II**) (for compounds **VIa–VIg** and **VIIIa–VIIIg**) or 6-quinolylamine (**III**) (for phenanthrolines **VIIa–VIIe** and **IXa–IXe**) in 20 ml of 1-butanol. The reaction mixture was heated at reflux for 15–20 min, then thereto was added 10 mmol of 1,3-cyclohexanedione (**IV**) (for compounds **VIa–VIg**, **VIIa–VIIe**) or dimedone (**V**) (for dimethyl derivatives **VIIIa–VIIIg**, **IXa–IXe**), and the mixture was boiled for 3–4 h (10–15 min for acridines **VIc** and **VIf**). On cooling the separated crystalline precipitate of the reaction product (for compounds **VIIIa** and **VIIIe** after evaporating the solution to a half of the volume) was filtered off, compounds **VIa–VIg** and **VIIIb–VIIIg** were boiled with benzene, ester **VIIIa** was recrystallized from toluene, phenanthroline derivatives **VIIa–VIIe** and **IXa–IXe** were washed with ethyl ether and recrystallized ftom a mixture ethanol–benzene, 1:1 v/v.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)phenyl benzoate (VIa). Yield 85%, mp 317–318°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.87– 2.10 m (2H, H^{9}), 2.20–2.32 m (2H, H^{10}), 2.55–2.68 m (2H, H^{8}), 3.78 s (3H, OMe), 5.93 s (1H, H^{12}), 6.57 d (1H, H$^{5'}$, ^3J 7.4), 6.78 d (1H, H$^{6'}$, ^3J 7.4), 7.16 s (1H, H$^{3'}$), 7.30 m, 7.39 m, 7.70 d, 7,77 d, 7.95 d (6H, H$^{1-6}$, ^3J 7.9), 7.50 d (2H, H$^{3'', 5''}$, ^3J 7.8), 7.67 t, (1H, H$^{4''}$, ^3J 7.8), 8.05 d (2H, H$^{2'', 6''}$, ^3J 7.8), 9.52 s (1H, NH). Found, %: C 78.17; H 5.18; N 2.74. $C_{31}H_{25}NO_4$. Calculated, %: C 78.30; H 5.30; N 2.95.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)phenyl 2-chlorobenzoate (VIb). Yield 83%, mp 291–292°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.90–2.12 m (2H, H^{9}), 2.24–2.35 m (2H, H^{10}), 2.56–2.70 m (2H, H^{8}), 3.76 s (3H, OMε), 5.94 s (1H, H^{12}), 6.59 d (1H, H$^{5'}$, ^3J 7.7), 6.82 d (1H, H$^{6'}$, ^3J 7.7), 7.19 s (1H, H$^{3'}$), 7.30 m, 7.40 m, 7.52 m, 7.71 d, 7,76 d, 7.95 m (10H, H$^{1-6, 3''-6''}$, ^3J 7.8), 9.51 s (1H, NH). Found, %: C 72.87; H 4.53; Cl 6.64; N 2.56. $C_{31}H_{24}ClNO_4$. Calculated, %: C 73.01; H 4.74; Cl 6.9; N 2.75.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)phenyl 4-chlorobenzoate (VIc). Yield 88%, mp 259–260°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.01 m (2H, H^{9}), 2.24–2.43 m (2H, H^{10}), 2.53–2.73 m (2H, H^{8}), 3.75 s (3H, OMe), 5.97 s (H^{12}), 6.60 d (1H, H$^{5'}$, ^3J 7.3), 6.79 d (1H, H$^{6'}$, ^3J 7.3), 7.20 s (1H, H$^{3'}$), 7.29 m, 7.40 m, 7.69 d, 7,72 d, 7.92 d (6H, H$^{1-6}$, ^3J 7.6), 7.50 d, 8.04 d (4H, H$^{2'', 3'', 5'',6''}$, ^3J 8.0), 9.48 s (1H, NH). Found, %: C 72.91; H 4.61; Cl 6.70; N 2.62. $C_{31}H_{24}ClNO_4$. Calculated, %: C 73.01; H 4.74; Cl 6.95; N 2.75.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)phenyl 4-bromobenzoate (VId). Yield 83%, mp 301–302°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.98 m (2H, H^{9}), 2.22–2.38 m (2H, H^{10}), 2.55–2.72 m (2H, H^{8}), 3.72 s (3H, OMe), 5.96 s (H^{12}), 6.57 d (1H, H$^{5'}$, ^3J 7.1), 6.78 d (1H, H$^{6'}$, ^3J 7.1), 7.20 s (1H, H$^{3'}$), 7.30 m, 7.39 m, 7.69 d, 7,74 d , 7.94 d (6H, H$^{1-6}$, ^3J 7.7), 7.65 d, 7.98 d (4H, H$^{2'', 3'', 5'',6''}$, ^3J 8.1), 9.47 s (1H, NH). Found, %: C 67.01; H 4.23; Br 14.24; N 2.39. $C_{31}H_{24}BrNO_4$. Calculated, %: C 67.16; H 4.36; Br 14.41; N 2.53.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)phenyl 4-nitrobenzoate (VIe). Yield 85%, mp 293–294°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.01 m (2H, H^{9}), 2.31 m (2H, H^{10}), 2.66 m (2H, H^{8}), 3.72 s (3H, OMe), 5.97 s (1H, H^{12}), 6.61 d (1H, H$^{5'}$, ^3J 7.7), 6.84 d (1H, H$^{6'}$, ^3J 7.7), 7.23 s (1H, H$^{3'}$), 7.31 m, 7.40 m, 7.71 d, 7.77 d , 7.95 d (6H, H$^{1-6}$, ^3J 7.9), 8.29 d, 8.37 d (4H, H$^{2'', 3'', 5'',6''}$, ^3J 8.2), 9.52 s (1H, NH). Found, %: C 71.37; H 4.47; N 5.15. $C_{31}H_{24}N_2O_6$. Calculated, %: C 71.53; H 4.65; N 5.38.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)phenyl 4-methylbenzoate (VIf). Yield 89%, mp 301–302°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.98 m (2H, H^{9}), 2.28–2.48 m (5H, 2H^{10}, ArMe), 2.59–2.72 m (2H, H^{8}), 3.68 s (3H, OMe), 5.90 s (H^{12}), 6.60 d (1H, H$^{5'}$, ^3J 7.4), 6.90 d (1H, H$^{6'}$, ^3J 7.4), 7.19 s (1H, H$^{3'}$), 7.30– 7.58 m, 7.72–8.08 m (10H, H$^{1-6, 3''-6''}$), 9.72 s (1H, NH). Found, %: C 78.37; H 5.38; Cl 2.64. $C_{32}H_{27}NO_4$. Calculated, %: C 78.51; H 5.56; N 2.86.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)phenyl 2,4-dichlorobenzoate (VIg). Yield 72%, mp 276–277°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.95– 2.08 m (2H, H^{9}), 2.22–2.40 m (2H, H^{10}), 2.55–2.72 m (2H, H^{8}), 3.79 s (3H, OMe), 5.95 s (1H, H^{12}), 6.57 d (1H, H$^{5'}$, ^3J 7.5), 6.81 d (1H, H$^{6'}$, ^3J 7.5), 7.21 s (1H, H$^{3'}$), 7.29 m, 7.39 m, 7.46 d, 7.55 s, 7.69 d, 7.74 d, 7.93 d, 7.99 d (10H, H$^{1-6, 3'', 5'',6''}$, ^3J 7.9), 9.48 s (1H, NH). Found, %: C 68.27; H 4.13; Cl 12.74; N 2.39. $C_{31}H_{23}Cl_2NO_4$. Calculated, %: C 68.39; H 4.26; Cl 13.06; N 2.57.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)phenyl benzoate (VIIa). Yield 81%, mp 316–317°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.88 – 2.07 m (2H, H^{9}), 2.23–2.40 m (2H, H^{10}), 2.47–2.73 m (2H, H^{8}), 3.74 s (3H, OMe),

5.93 s (1H, H^{12}), 6.58 d (1H, H$^{5'}$, ^3J 7.4), 6.82 d (1H, H$^{6'}$, ^3J 7.5), 7.19 s (1H, H$^{3'}$), 7.35 d.d (1H, H^2, ^3J 7.8, ^4J 4.3), 7.47–7.57 m (3H, H$^{6,\ 3'',\ 5''}$), 7.62 t (1H, H$^{4''}$, ^3J 8.4), 7.86 d (1H, H^5, ^3J 8.8), 8.05 d (2H, H $^{2'',\ 6''}$, ^3J 8.4), 8.32 d (1H, H^1, ^3J 7.8), 8.66 d (1H, H^3,^3J 4.3), 9.66 s (1H, NH). Found, %: C 75.50; H 4.97; N 5.71. $C_{30}H_{24}N_2O_4$. Calculated, %: C 75.61; H 5.08; N 5.88.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)phenyl 2-chlorobenzoate (VIIb). Yield 72%, mp 292–293^{O}C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.90– 2.07 m (2H, H^9), 2.22–2.41 m (2H, H^{10}), 2.48–2.72 m (2H, H^8), 3.73 s (3H, OMe), 5.93 s (H^{12}), 6.58 d (1H, H$^{5'}$, ^3J 7.5), 6.81 d (1H, H$^{6'}$, ^3J 7.4), 7.19 s (1H, H$^{3'}$), 7.33 d.d (1H, H^2, ^3J 8.0, ^2J 4.0), 7.47–7.56 m (3H, H$^{6,\ 3'',\ 5''}$), 7.86 d (1H, H^5, ^3J 8.9), 8.03 d (2H, H$^{2'',\ 6''}$), 8.33 d (1H, H^1, ^3J 7.7), 8.64 d (1H, H^3, ^3J 3.8), 9.64 s (1H, NH). Found, %: C 70.36; H 4.46; Cl 6.71; N 5.37. $C_{30}H_{23}ClN_2O_4$. Calculated, %: C 70.52; H 4.54; Cl 6.94; N 5.48.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)phenyl 4-chlorobenzoate (VIIc). Yield 68%, mp 315–316°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.95 m, 2.03 m (2H, H^9), 2.28 m, 2.36 d. t (2H, H^{10}, ^2J 16.0), 2.58 m, 2.69 d.t (2H, H^8, ^2J 16.0), 3.74 s (3H, OMe), 5.93 s (1H, H^{12}), 6.58 d (1H, H$^{5'}$, ^3J 7.8), 6.81 d (1H, H$^{6'}$, ^3J 7.8), 7.18 s (1H, H$^{3'}$), 7.37 d.d (1H, H^2, ^3J 8.1, ^2J 4.0), 7.46–7.55 m (3H, H$^{6,\ 3'',\ 5''}$), 7.86 d (1H, H^5, ^3J 8.9), 8.03 d (2H, H$^{2'',\ 6''}$, ^3J 9.0), 8.33 d (1H, H^1, ^3J 7.5), 8.64 d (1H, H^3, ^3J 3.8), 9.58 s (NH). Found, %: C 70.34; H 4.42; Cl 6.76; N 5.35. $C_{30}H_{23}ClN_2O_4$. Calculated, %: C 70.52; H 4.54; Cl 6.94; N 5.48.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)phenyl 4-bromobenzoate (VIId). Yield 71%, mp 310–311°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.98 m (2H, H^9), 2.35 m (2H, H^{10}), 2.65 m (2H, H^8), 3.76 s (3H, OMe), 5.92 s (1H, H^{12}), 6.61 d (1H, H$^{5'}$, ^3J 7.2), 6.80 d (1H, H$^{6'}$, ^3J 7.2), 7.19 s (1H, H$^{3'}$), 7.37 d.d (1H, H^2, ^3J 8.0, ^2J 4.4), 7.53 d (1H, H^6, ^3J 8.8), 7.65 d (2H, H$^{3'',\ 5''}$, ^3J 7.9), 7.86 d (1H, H^5, ^3J 8.8), 7.92 d (2H, H$^{2'',\ 6''}$, ^3J 7.9), 8.30 d (1H, H^1, ^3J 8.0), 8.62 d (1H, H^3, ^3J 4.6), 9.68 s (1H, NH). Found, %: C 64.71; H 3.96; Br 14.18; N 4.98. $C_{30}H_{23}BrN_2O_4$. Calculated, %: C 64.86; H 4.14; Br 14.41; N 5.05.

2-Methoxy-4-(11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)phenyl 4-nitrobenzoate (VIIe). Yield 79%, mp 288–289^{O}C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.99 m (2H, H^9), 2.32 m (2H, H^{10}), 2.64 m (2H, H^8), 3.77 s (3H, OMe), 5.95 s (1H, H^{12}), 6.59 d (1H, H$^{5'}$, ^3J 7.5), 6.85 d (1H, H$^{6'}$, ^3J 7.5), 7.21 s (1H, H$^{3'}$), 7.32 d.d (H^2, ^3J 7.7, ^2J 4.4), 7.52 d, 7.88 d (2H, H^{5,6}, ^3J 9.0), 8.31 m (5H, H$^{1,\ 2'',\ 3'',\ 5'',\ 6''}$), 8.63 d (1H, H^3, ^3J 4.1), 9.60 s (1H, NH). Found, %: C 60.04; H 4.37; N 7.88. $C_{30}H_{23}N_3O_6$. Calculated, %: C 69.10; H 4.41; N 8.06.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-2-methoxyphenyl benzoate (VIIIa). Yield 80%, mp 275–276°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 s (3H, Me), 1.12 s (3H, Me), 2.18 d. d (2H, H^{10}, ^2J 16.0), 2.48 m (2H, H^8), 3.73 s (3H, OMe), 5.92 s (1H, H^{12}), 6.62 d (1H, H$^{5'}$, ^3J 7.6), 6.81 d (1H, H$^{6'}$, ^3J 7.6), 7.17 s (1H, H$^{3'}$), 7.30 m, 7.41 m, 7.70 d, 7,76 d, 7.97 d (6H, H$^{1-6}$, ^3J 7.8), 7.48 d (2H, H$^{3'',\ 5''}$, ^3J 8.0), 7.66 t, (1H, H$^{4''}$, ^3J 8.0), 8.04 d (2H, H $^{2'',\ 6''}$, ^3J 8.0), 9.43 s (1H, NH). Found, %: C 78.57; H 5.63; N 2.62. $C_{33}H_{29}NO_4$. Calculated, %: C 78.71; H 5.80; N 2.78.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-2-methoxyphenyl 2-chlorobenzoate (VIIIb). Yield 79%, mp 294–295°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 s (3H, Me), 1.11 s (3H, Me), 2.17 d.d (2H, H^{10}, ^2J 16.0), 2.50 m (2H, H^8), 3.77 s (3H, OMe), 5.91 s (H^{12}), 6.62 d (H$^{5'}$, ^3J 7.6), 6.82 d (H$^{6'}$, ^3J 7.6), 7.20 s (H$^{3'}$), 7.30 m, 7.42 m, 7.53 m, 7.70 d, 7.77 d, 7.97 m (10H, H$^{1-6,\ 3''-\ 6''}$, ^3J 7.9), 9.43 s (1H, NH). Found, %: C 73.51; H 5.03; Cl 6.38; N 2.41. $C_{33}H_{28}ClNO_4$. Calculated, %: C 73.67; H 5.25; Cl 6.59; N 2.60.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-2-methoxyphenyl 4-chlorobenzoate (VIIIc). Yield 81%, mp 285–286°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.97 s (3H, Me), 1.12 s (3H, Me), 2.15 m (2H, H^{10}), 2.47 m (2H, H^8), 3.72 s (3H, OMe), 5.92 s (1H, H^{12}), 6.60 d (1H, H$^{5'}$, ^3J 7.3), 6.79 d (1H, H$^{6'}$, ^3J 7.3), 7.20 s (1H, H$^{3'}$), 7.29 m, 7.41 m, 7.70 d, 7.74 d, 7.96 d (6H, H$^{1-6}$, ^3J 7.7), 7.49 d, 8.02 d (4H, H $^{2'',\ 3'',\ 5'',6''}$, ^3J 7.9), 9.40 s (1H, NH). Found, %: C 73.55; H 5.11; Cl 6.36; N 2.39. $C_{33}H_{28}ClNO_4$. Calculated, %: C 73.67; H 5.25; Cl 6.59; N 2.60.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-2-methoxyphenyl 4-bromobenzoate (VIIId). Yield 76%, mp 297–298°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 s (3H, Me), 1.11 s (3H, Me), 2.18 d.d (2H, H^{10}, ^2J 16.3), 2.48 d (2H, H^8), 3.71 s (3H, OMe), 5.90 s (1H, H^{12}), 6.58 d (1H, H$^{5'}$, ^3J 7.5), 6.77 d (1H, H$^{6'}$, ^3J 7.5), 7.18 s (1H, H$^{3'}$), 7.27 m, 7.39 m, 7.68 d, 7.73 d, 7.95 d (6H, H$^{1-6}$, ^3J 7.8), 7.62 d, 7.99 d (4H, H $^{2'',\ 3'',\ 5'',6''}$, ^3J 8.1), 9.36 s (1H, NH). Found,

%: C 67.87; H 4.63; Br 13.51; N 2.19. $C_{33}H_{28}BrNO_4$. Calculated, %: C 68.05; H 4.85; Br 13.72; N 2.40.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-2-methoxyphenyl 4-nitrobenzoate (VIIIe). Yield 70%, mp 281–282°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.97 s (3H, Me), 1.12 s (3H, Me), 2.18 d.d (2H^{10}, ^2J 16.3), 2.49 m (2H^8), 3.73 s (3H, OMe), 5.92 s (1H, H^{12}), 6.62 d (1H, H$^{5'}$, ^3J 7.5), 6.84 d (1H, H$^{6'}$, ^3J 7.5), 7.22 s (1H, H$^{3'}$), 7.31 m, 7.41 m, 7.70 d, 7.76 d, 7.99 d (6H, H$^{1-6}$, ^3J 7.9), 8.28 d, 8.34 d (4H, H$^{2'', 3'', 5'', 6''}$, ^3J 8.3), 9.34 s (1H, NH). Found, %: C 72.06; H 5.08; N 4.88. $C_{33}H_{28}N_2O_6$. Calculated, %: C 72.25; H 5.14; N 5.11.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-2-methoxyphenyl 4-methylbenzoate (VIIIf). Yield 83%, mp 265–266°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 s (3H, Me), 1.11 s (3H, Me), 2.16 d.d (2H, H^{10}, ^2J 16.3), 2.45 m (5H, 2H^8, ArMe), 3.73 s (3H, OMe), 5.91 s (1H, H^{12}), 6.59 d (1H, H$^{5'}$, ^3J 7.6), 6.78 d (1H, H$^{6'}$, ^3J 7.6), 7.18 s (1H, H$^{3'}$), 7.28 m, 7.40 m, 7.68 d, 7.72 d, 7.99 d (6H, H$^{1-6}$, ^3J 7.8), 7.26 d, 7.92 d (4H, H $^{2'', 3'', 5'',6''}$, ^3J 8.1), 9.37 s (1H, NH). Found, %: C 78.73; H 5.83; N 2.58. $C_{34}H_{31}NO_4$. Calculated, %: C 78.89; H 6.04; N 2.71.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*a*]acridin-12-yl)-2-methoxyphenyl 2,4-dichlorobenzoate (VIIIg). Yield 86%, mp 269–270°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00 s (3H, Me), 1.14 s (3H, Me), 2.19 d.d (2H, H^{10}, ^2J 16.2), 2.48 m (2H, H^8), 3.78 s (3H, OMe), 5.92 s (H^{12}), 6.60 d (H$^{5'}$) (^3J 7.7), 6.81 d (H$^{6'}$, ^3J 7.7), 7.20 s (H$^{3'}$), 7.29 m, 7.42 m, 7.54 s, 7.70 d, 7.75 d, 7.95 d, 8.00 d (10H, H$^{1-6, 3'', 5'',6''}$, ^3J 8.0), 9.40 s (1H, NH). Found, %: C 69.07; H 4.53; Cl 12.02; N 2.28. $C_{33}H_{27}Cl_2NO_4$. Calculated, %: C 69.23; H 4.75; Cl 12.39; N 2.45.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)-2-methoxyphenyl benzoate (IXa). Yield 75%, mp 263–264°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 s (3H, Me), 1.13 s (3H, Me), 2.18 d.d (2H, H^{10}, ^2J 16.2), 2.49 m (2H, H^8), 3.74 s (3H, OMe), 5.89 s (1H, H^{12}), 6.61 d (1H, H$^{5'}$, ^3J 7.4), 6.82 d (1H, H$^{6'}$, ^3J 7.4), 7.19 s (1H, H$^{3'}$), 7.37 d.d (1H, H^2, ^3J 7.6, ^2J 4.1), 7.47–7.57 m (3H, H$^{6, 3'', 5''}$), 7.63 t (1H, H$^{4''}$), 7.87 d (1H, H^5, ^3J 8.8), 8.05 d (2H, H$^{2'', 6''}$, ^3J 8.0), 8.37 d (1H, H^1, ^3J 7.9), 8.65 d (1H, H^3, ^3J 4.4), 9.56 s (1H, NH). Found, %: C 76.02; H 5.47; N 5.43. $C_{32}H_{28}N_2O_4$. Calculated, %: C 76.17; H 5.59; N 5.55.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)-2-methoxyphenyl 2-chlorobenzoate (IXb). Yield 65%, mp 244–245°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.97 s (3H, Me), 1.12 s (3H, Me), 2.17 d.d (2H, H^{10}, ^2J 16.1), 2.48 m (2H, H^8), 3.73 s (3H, OMe), 5.93 s (H^{12}), 6.58 d (H$^{5'}$, ^3J 7.5), 6.81 d (H$^{6'}$, ^3J 7.4), 7.19 s (H$^{3'}$), 7.33 d.d (H^2, ^3J 8.0, ^2J 4.0), 7.47–7.56 m (3H, H$^{6, 3'', 5''}$), 7.86 d (1H, H^5, ^3J 8.9), 8.03 d (2H, H$^{2'', 6''}$, ^3J 8.9), 8.33 d (1H, H^1, ^3J 7.7), 8.63 d (1H, H^3, ^3J 3.9), 9.51 s (1H, NH). Found, %: C 71.18; H 4.92; Cl 6.43; N 5.03. $C_{32}H_{27}ClN_2O_4$. Calculated, %: C 71.30; H 5.05; Cl 6.58; N 5.20.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)-2-methoxyphenyl 4-chlorobenzoate (IXc). Yield 75%, mp 263–264°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 s (3H, Me), 1.13 s (3H, Me), 2.18 d.d (2H, H^{10}), 2.49 m (2H, H^8), 3.74 s (3H, OMe), 5.89 s (1H, H^{12}), 6.61 d (1H, H$^{5'}$, ^3J 7.4), 6.82 d (1H, H$^{6'}$, ^3J 7.4), 7.19 s (1H, H$^{3'}$), 7.37 d.d (1H, H^2, ^3J 8.0 ^2J 3.9), 7.48– 7.55 m (3H, H$^{6, 3'', 5''}$), 7.87 d (1H, H^5, ^3J 8.9), 8.03 d (2H, H$^{2'', 6''}$, ^3J 9.0), 8.33 d (1H, H^1, ^3J 7.4), 8.63 d (1H, H^3, ^3J 3.8), 9.51 s (1H, NH). Found, %: C 71.18; H 4.96; Cl 6.37; N 5.02. $C_{32}H_{27}ClN_2O_4$. Calculated, %: C 71.30; H 5.05; Cl 6.58; N 5.20.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)-2-methoxyphenyl 4-bromobenzoate (IXd). Yield 72%, mp 284–285°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00 s (3H, Mε), 1.16 s (3H, Me), 2.17 d.d (2H^{10}, ^2J 16.0), 2.48 m (2H^8), 3.75 s (3H, OMe), 5.90 s (1H, H^{12}), 6.60 d (1H, H$^{5'}$, ^3J 7.4), 6.82 d (1H, H$^{6'}$, ^3J 7.4), 7.18 s (1H, H$^{3'}$), 7.34 d.d (1H, H^2, ^3J 7.8, ^2J 4.3), 7.50 d (H^6, ^3J 9.0), 7.65 d (2H, H$^{3'', 5''}$, ^3J 8.0), 7.85 d (1H, H^5, ^3J 9.0), 7.95 d (2H, H$^{2'', 6''}$, ^3J 8.0), 8.35 d (1H, H^1, ^3J 7.8), 8.63 d (1H, H^3, ^3J 4.2), 9.50 s (1H, NH). Found, %: C 65.63; H 4.42; Br 13.67; N 4.59. $C_{32}H_{27}BrN_2O_4$. Calculated, %: C 65.87; H 4.63; Br 13.67; N 4.80.

4-(9,9-Dimethyl-11-oxo-7,8,9,10,11,12-hexahydrobenzo[*b*][4,7]phenanthrolin-12-yl)-2-methoxyphenyl 4-nitrobenzoate (IXe). Yield 80%, mp 277–278°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 s (3H, Mε), 1.14 s (3H, Mε), 2.19 d.d (2H^{10}, ^2J 16.1), 2.50 m (2H^8), 3.77 s (3H, OMe), 5.93 s (1H, H^{12}), 6.61 d (1H, H$^{5'}$, ^3J 7.3), 6.80 d (1H, H$^{6'}$, ^3J 7.3), 7.20 s (1H, H$^{3'}$), 7.32 d.d (1H, H^2, ^3J 7.1, ^2J 4.0), 7.51 d, 7.85 d (2H, H^{5,6}, ^3J 8.9), 8.32 m (5H, H$^{1, 2'', 3'', 5'', 6''}$), 8.60 d (1H, H^3, ^3J 4.3), 9.62 s (1H, NH). Found, %: C 69.67; H 4.83; N 7.49. $C_{32}H_{27}N_3O_6$. Calculated, %: C 69.95; H 4.92; N 7.65.

4-[Bis(2,6-dioxocyclohexyl)methyl]-2-methoxyphenyl and 4-[bis(4,4-dimethyl-2,6-

dioxocyclohexyl)methyl]-2-methoxyphenyl benzoates (Xa, Xb, XIa, XIb). A solution of 10 mmol of ester **Ia** or **Ib**, 20 mmol of 1,3-cyclohexandione (**IV**) (for compounds **Xa, Xb**) or dimedone (**V**) (for ketones **XIa, XIb**) in 30 ml of ethanol was boiled for 3 h. The precipitate of reaction product **Xa, Xb**, and **XIa** was filtered off and recrystallized from benzene, bisdiketone **XIb** was recrystallized from 1-butanol and washed with ethyl ether.

4-[Bis(2,6-dioxocyclohexyl)methyl]-2-methoxyphenyl benzoate (Xa). Yield 80%, mp 277–278°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.00 m, 2.34 m, 2.68 m (14H, CH_2, $CH_{cycloaliph.}$), 3.75 s (3H, OMe), 4.65 s [1H, ROCO(OMe)C_6H_3CH] 6.76 d, 7.01 m (3H, H $^{3",\ 5",\ 6"}$, ^3J 8.1), 7.57 t, 7.71 t, 8.07 d (5H, Ph, ^3J 7.8). Found, %: C 69.97; H 5.53. $C_{27}H_{26}O_7$. Calculated, %: C 70.12; H 5.67.

4-[Bis(2,6-dioxocyclohexyl)methyl]-2-methoxyphenyl 2-chlorobenzoate (Xb). Yield 68%, mp 207–208°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.04 m, 2.35 m, 2.65 m (14H, CH_2, $CH_{cycloaliph.}$), 3.84 s (3H, OMe), 4.67 s [1H, ROCO–(OMe)C_6H_3CH], 6.74 d, 6.97 d, 7.05 C (3H, H $^{3",\ 5",\ 6"}$, ^3J 8.0), 7.45 t, 7.62 m, 8.02 d (4H, H_{arom}, ^3J 7.7). Found, %: C 65.16; H 4.93; Cl 6.94. $C_{27}H_{25}ClO_7$. Calculated, %: C 65.27; H 5.07; Cl 7.13.

4-[Bis(4,4-dimethyl-2,6-dioxocyclohexyl)-methyl]-2-methoxyphenyl benzoate (XIa). Yield 71%, mp 217–218°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 s (6H, Me), 1.10 s (6H, Me), 2.20 d.d, 2.52 m (10H, CH_2, $CH_{cycloaliph.}$, ^2J 16.1), 3.75 s (3H, OMe), 4.64 s [1H, ROCO(OMe)C_6H_3CH] 6.77 d, 7.00 m (3H, H $^{3",\ 5",\ 6"}$, ^3J 7.9), 7.55 t, 7.70 t, 8.06 d (5H, Ph, ^3J 7.6). Found, %: C 71.68, H 6.48. $C_{31}H_{34}O_7$. Calculated, %: C 71.80; H 6.61.

4-[Bis(4,4-dimethyl-2,6-dioxocyclohexyl)-methyl]-2-methoxyphenyl 2-chlorobenzoate (XIb). Yield 71%, mp 187–188°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 s (6H, Me), 1.13 s (6H, Me), 2.24 d.d, 2.49 m (10H, CH_2, $CH_{cycloaliph.}$, ^2J 16.0), 3.80 s (3H, OMe), 4.79 s [1H, ROCO(OMe)–C_6H_3CH], 6.76 d, 6.92 s, 7.04 d (3H, H $^{3",\ 5",\ 6"}$, ^3J 7.7), 7.48 m, 8.00 d (4H, H_{arom}, ^3J 7.9). Found, %: C 67.17; H 5.83; Cl 6.24. $C_{31}H_{33}ClO_7$. Calculated, %: C 67.32; H 6.01; Cl 6.41.

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