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Synthesis of 1-Aryl-2-[2-(dimethylamino)ethyl]-1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones and Their Analogs

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Abstract—Methyl *o*-hydroxybenzoylpyruvate heated with *N,N*-dimethylethylenediamine and aromatic aldehydes affords in a high yield 5-aryl-3-hydroxy-4-(2-hydroxyphenyl)-1-[2-(dimethylamino)ethyl]-1,5-dihydro-2*H*-pyrrol-2-ones, which easily split off water at boiling in acetic acid and are converted into 1-aryl-2-[(2-dimethylamino)ethyl]-1,2-dihydrochromeno[2,3-*c*]pyrrol-3,9-diones. The developed route of synthesis provides a wide range of derivatives of 1-aryl-2-[ω-(dialkylamino)alkyl]-1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones.

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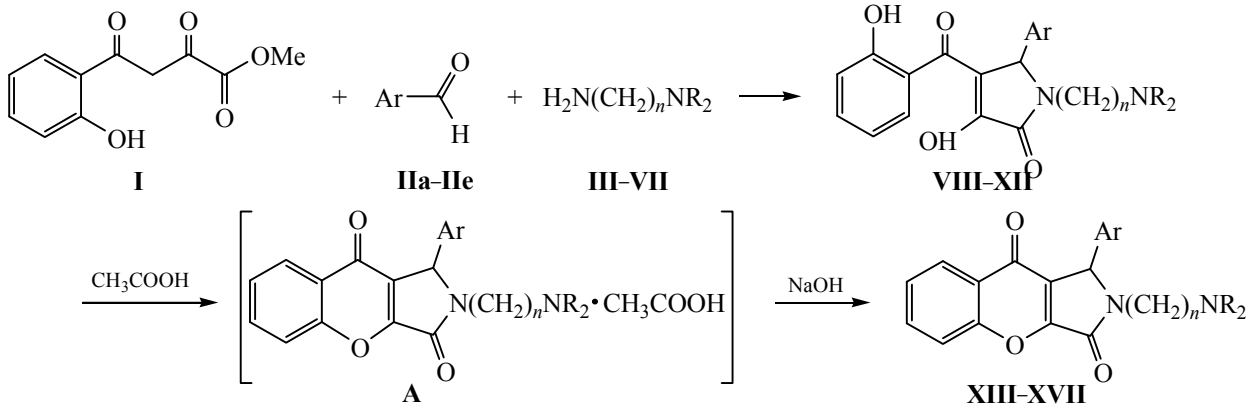
It was shown previously that a reaction of methyl *o*-hydroxybenzoylpyruvate with a mixture of aromatic aldehyde and heterylamine [1] or with a Schiff base [2] leds to 1-aryl-2-heteryl- or 1,2-diaryl-1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones, respectively. It is also known that the reactions of acylpyruvate esters with a mixture of aromatic aldehyde and *N,N*-dimethylethylenediamine [3] or *N,N*-diethylethylenediamine [4] leads to 5-aryl-4-acyl-3-hydroxy-1-(*N,N*-dialkylaminoethyl)-1,5-dihydro-2*H*-pyrrol-2-ones. Such pyrrole derivatives are pharmacologically active compounds with various type of activity [3–6]. The activity of 2-aryl(hetero)-1,2-dihydrochromeno[2,3-*c*]-pyrrol-3 ,9-diones without substituents in position 1 was studied [7], and it was stated that 2-(3-morpholin-4-yl-propyl)-1-phenyl-1,2-dihydrochromeno[2,3-*c*]-pyrrole-3 ,9-dione exhibited antitumor activity, being an inhibitor of Hsp90 [8]. Taking into account that some of the drugs used in medical practice contain ω-dialkylaminoalkyl group [9], we found it interesting to



I **IIa–IIe** **III–VII** **VIII–XII** **A** **XIII–XVII**

Ar = C_6H_5 (**a**), 4-ClC_6H_4 (**b**), 4-$O_2NC_6H_4$ (**c**), 4-$CH_3OC_6H_4$ (**d**), 3,4-$(CH_3O)_2C_6H_3$ (**e**); R_2N = $(CH_3)_2N$ (**III, VI, VIIIa–VIIIe, XIa–XIe, XIIIa–XIIIe, XVIa–XVIe**), $(C_2H_5)_2N$ (**IV, IXa, IXd, XIVa, XIVd**), $O(CH_2CH_2)_2N$ (**V, VII, Xa, Xb, Xe, XIIa, XIId, XIIe, XVa, XVb, XVe, XVIIa, XVIId, XVIIe**); *n* = 2 (**III–V, VIII–X, XIII–XV**), 3 (**VI, VII, XI, XII, XVI, XVII**).

search for an approach to the synthesis of 2-(ω-dialkylaminoalkyl)-1,2-dihydrochromeno[2,3-*c*]-pyrrole-3,9-diones. In order to obtain such functionally substituted fused heterocyclic compounds we studied the transformation of methyl *o*-hydroxybenzoyl-pyruvate into substituted pyrrolones and cyclization of the latter into 1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones (see the scheme).

At heating equimolar amounts of ester **I**, aromatic aldehyde **II**, and substituted aliphatic amine **III**–**VII** in methanol formed pyrrolones **VIII**–**XII** in a good yield. Their structure is doubtless, because such compounds are described in the literature [3, 4]. Their composition is confirmed by elemental analysis, and structure, by IR and ^{1}H NMR spectroscopy. The obtained compound **VIII**–**XII** are lemon-yellow crystalline substances, sparingly soluble in alcohol, dioxane and ethyl acetate, but readily soluble in acetic acid and aqueous solutions of acids and bases. When heated in acetic acid, hydroxypyrrolones **VIII**–**XII** undergo dehydration with the formation of 1,2-dihydrochromeno[2,3-*c*]pyrrol-3,9-diones, which exist in solution in the form of acetates (**A**). By treating them with a solution of sodium hydroxide we obtained substituted chromone free bases **XIII**–**XVII**. This method of formation of pyran ring is often used in the synthesis of heteropyrones [10, 11] and the chromone fused derivatives [12]. It was unnecessary to isolate the substituted pyrroles **VIII**–**XII** in an individual state. To methanolic suspension of a compound **VIII**–**XII** was added acetic acid and the reaction mixture was refluxed for 1 h. This approach can be used as a convenient one-pot method of synthesis. Its disadvantage is the large amount of impurities in the final product, which makes its purification slightly more difficult. Substituents at the nucleus of the aromatic aldehyde affect the yield of products **XIII**–**XVII:** The electron-acceptors increase the yield of chromenopyrroles, while electron-donors reduce it.

The structure of the synthesized compounds was confirmed by IR and ^{1}H NMR spectroscopy (Table 1), and their composition, by the data of elemental analysis (Table 2). The IR spectra of 1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones, taken from the tablets with KBr, contain in the region of 1590–1720 cm^{-1} three characteristic absorption bands: 1600–1620 cm^{-1} (moderate intensity band of C=C stretching vibrations), 1640–1665 cm^{-1} (strong band of stretching vibrations of the C^9=O), and 1695–1720 cm^{-1} (strong band of C^3=O stretching vibrations). The relative

Table 1. Spectral characteristics of compounds **VIII–XVII**

Comp. no.	IR spectrum (KBr), ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm
VIIIa[a]	1606 (C=C); 1616 (C=O ketone); 1687 (C^2=O); 3429 (OH)	2.72–2.86 m [7H, H$_C$ NCH$_2$, N(CH$_3$)$_2$], 2.97 m (1H, H$_B$ CH$_2$NMe$_2$), 3.24 m (1H, H$_A$ CH$_2$NMe$_2$), 3.83 m (1H, H$_A$ NCH$_2$), 5.42 s (1H, C^5-H), 6.64 d (1H, $^3J_{HH}$ 8.4 Hz, C$^{3'}$-H), 6.74 d.d (1H, $^3J_{HH}$ 7.8, $^3J_{HH}$ 8.1 Hz, C$^{5'}$-H), 7.16–7.31 m (6H, C$^{4'}$-H, 5H arom.), 8.61 d (1H, $^3J_{HH}$ 7.8 Hz, C$^{6'}$-H), 13.35 s (1H, OH)
VIIIb	1605 (C=C); 1618 (C=O ketone); 1691 (C^2=O); 3430 (OH)	2.75–2.91 m [7H, H$_C$ NCH$_2$, N(CH$_3$)$_2$], 3.00 m (1H, H$_B$ CH$_2$NMe$_2$), 3.27 m (1H, H$_A$ CH$_2$NMe$_2$), 3.83 m (1H, H$_A$ NCH$_2$), 5.47 s (1H, C^5-H), 6.64 d (1H, C$^{3'}$-H), 6.74 d.d (1H, C$^{5'}$-H), 7.14–7.33 m (5H, C$^{4'}$-H, 4H arom.), 8.62 d (1H, C$^{6'}$-H), 13.37 s (1H, OH)
VIIIc[a]	1607 (C=C); 1619 (C=O ketone); 1699 (C^2=O); 3427 (OH)	2.69–2.84 m [7H, H$_C$ NCH$_2$, N(CH$_3$)$_2$], 3.02 m (1H, H$_B$ CH$_2$NMe$_2$), 3.38 m (1H, H$_A$ CH$_2$NMe$_2$), 3.94 m (1H, H$_A$ NCH$_2$), 5.54 s (1H, C^5-H), 6.64 d (1H, $^3J_{HH}$ 8.4 Hz, C$^{3'}$-H), 6.74 d.d (1H, $^3J_{HH}$ 7.8, $^3J_{HH}$ 8.1 Hz, C$^{5'}$-H), 7.22 d.d (1H, $^3J_{HH}$ 8.1, $^3J_{HH}$ 8.4 Hz, C$^{4'}$-H), 7.57 d (2H arom.), 8.11 d (2H arom.), 8.61 d (1H, $^3J_{HH}$ 7.8 Hz, C$^{6'}$-H), 9.55 s (1H, OH), 13.67 s (1H, OH)
VIIId	1605 (C=C); 1610 (C=O ketone); 1689 (C^2=O); 3432 (OH)	2.70–2.86 m [7H, H$_C$ NCH$_2$, N(CH$_3$)$_2$], 2.97 m (1H, H$_B$ CH$_2$NMe$_2$), 3.27 m (1H, H$_A$ CH$_2$NMe$_2$), 3.67–3.87 m (4H, H$_A$ NCH$_2$, CH$_3$O), 5.36 s (1H, C^5-H), 6.63 d (1H, C$^{3'}$-H), 6.70–6.79 m (3H, C$^{5'}$-H, 2H arom.), 7.16–7.28 m (3H, C$^{4'}$-H, 2H arom.), 8.58 d (1H, C$^{6'}$-H)
VIIIe	1600 (C=C); 1618 (C=O ketone); 1698 (C^2=O); 3428 (OH)	2.70–2.85 m [7H, H$_C$ NCH$_2$, N(CH$_3$)$_2$], 2.96 m (1H, H$_B$ CH$_2$NMe$_2$), 3.27 m (1H, H$_A$ CH$_2$NMe$_2$), 3.67–3.84 m (7H, H$_A$ NCH$_2$, 2 CH$_3$O), 5.36 s (1H, C^5-H), 6.63–6.89 m (5H, C$^{3'}$-H, C$^{5'}$-H, 3H arom.), 7.22 d.d (1H, C$^{4'}$-H), 8.61 d (1H, C$^{6'}$-H)
IXa	1605 (C=C); 1617 (C=O ketone); 1688 (C^2=O); 3430 (OH)	1.12 т (6H, 2CH$_3$), 2.88 m (1H, H$_C$ NCH$_2$), 2.97–3.18 m (6H, 3 NCH$_2$), 3.78 m (1H, H$_A$ NCH$_2$), 5.39 s (1H, C^5-H), 6.64 d (1H, C$^{3'}$-H), 6.77 d.d (1H, C$^{5'}$-H), 7.16–7.31 m (6H, C$^{4'}$-H, 5H arom.), 8.62 d (1H, C$^{6'}$-H), 13.44 s (1H, OH)

Table 1. (Contd.)

Comp. no.	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum, δ, ppm
IXd	1605 (C=C); 1614 (C=O ketone); 1689 (C^2=O); 3432 (OH)	1.12 т (6H, $2CH_3$), 2.89 m (1H, H_C NCH_2), 2.96–3.18 m (6H, 3 NCH_2), 3.69 s (3H, CH_3O), 3.79 m (1H, H_A NCH_2), 5.37 s (1H, C^5-H), 6.63 d (1H, $C^{3'}$-H), 6.69–6.79 m (3H, $C^{5'}$-H, 2H arom.), 7.15–7.29 m (3H, $C^{4'}$-H, 2H arom.), 8.59 d (1H, $C^{6'}$-H)
Xa	1606 (C=C); 1615 (C=O ketone); 1682 (C^2=O); 3429 (OH)	2.42–2.52 m (6H, $3NCH_2$), 2.79 m (1H, H_C NCH_2), 3.52–3.62 m (4H, $2OCH_2$), 3.78 m (1H, H_A NCH_2), 5.43 s (1H, C^5-H), 6.64 d (1H, $C^{3'}$-H), 6.75 d.d (1H, $C^{5'}$-H), 7.16–7.32 m (6H, $C^{4'}$-H, 5H arom.), 8.61 d (1H, $C^{6'}$-H)
Xb	1605 (C=C); 1614 (C=O ketone); 1683 (C^2=O); 3432 (OH)	2.42–2.52 m (6H, $3NCH_2$), 2.79 m (1H, H_C NCH_2), 3.52–3.62 m (4H, $2OCH_2$), 3.79 m (1H, H_A NCH_2), 5.45 s (1H, C^5-H),), 6.63 d (1H, $C^{3'}$-H), 6.74 d.d (1H, $C^{5'}$-H), 7.13–7.33 m (5H, $C^{4'}$-H, 4H arom.), 8.63 d (1H, $C^{6'}$-H)
Xe	1605 (C=C); 1617 (C=O ketone); 1688 (C^2=O); 3430 (OH)	2.41–2.52 m (6H, $3NCH_2$), 2.79 m (1H, H_C NCH_2), 3.55–3.62 m (4H, $2OCH_2$), 3.68–3.81 m (7H, H_A NCH_2, 2 CH_3O), 5.46 s (1H, C^5-H), 6.63–6.89 m (5H, $C^{3'}$-H, $C^{5'}$-H, 3H arom.), 7.22 d.d (1H, $C^{4'}$-H), 8.61 d (1H, $C^{6'}$-H)
XIa	1604 (C=C); 1617 (C=O ketone); 1687 (C^2=O); 3430 (OH)	1.68–1.82 m (2H, CH_2), 2.61–2.82 m [7H, H_C NCH_2, $N(CH_3)_2$], 2.83–2.93 m (2H, CH_2NMe_2), 3.49 m (1H, H_A NCH_2), 5.31 s (1H, C^5-H), 6.64 d (1H, $C^{3'}$-H), 6.71 d.d (1H, $C^{5'}$-H), 7.15–7.34 m (6H, $C^{4'}$-H, 5H arom.),8.68 d (1H, $C^{6'}$-H)
XIb	1605 (C=C); 1619 (C=O ketone); 1684 (C^2=O); 3430 (OH)	1.74–1.86 m (2H, CH_2), 2.59–2.76 m [7H, H_C NCH_2, $N(CH_3)_2$], 2.88–2.97 m (2H, CH_2NMe_2), 3.52 m (1H, H_A NCH_2), 5.33 s (1H, C^5-H), 6.65 d (1H, $C^{3'}$-H), 6.71 d.d (1H, $C^{5'}$-H), 7.17–7.33 m (5H, $C^{4'}$-H, 4H arom.), 8.68 d (1H, $C^{6'}$-H)
XIc	1605 (C=C); 1617 (C=O ketone); 1685 (C^2=O); 3428 (OH)	1.74–1.86 m (2H, CH_2), 2.59–2.76 m [7H, H_C NCH_2, $N(CH_3)_2$], 2.88–2.97 m (2H, CH_2NMe_2), 3.52 m (1H, H_A NCH_2), 5.52 s (1H, C^5-H), 6.64 d (1H, $C^{3'}$-H), 6.74 d.d (1H, $C^{5'}$-H), 7.22 d.d (1H, $C^{4'}$-H), 7.57 d (2H arom.), 8.11 d (2H arom.), 8.61 d (1H, $C^{6'}$-H)
XId	1600 (C=C); 1611 (C=O ketone); 1689 (C^2=O); 3422 (OH)	1.69–1.82 m (2H, CH_2), 2.62–2.82 m [7H, H_C NCH_2, $N(CH_3)_2$], 2.84–2.95 m (2H, CH_2NMe_2), 3.49 m (1H, H_A NCH_2), 3.69 s (3H, CH_3O), 5.29 s (1H, C^5-H), 6.30–6.86 m (4H, $C^{3'}$-H, $C^{5'}$-H, 2H arom.), 7.15–7.28 m (3H, $C^{4'}$-H, 2H arom.), 8.68 d (1H, $C^{6'}$-H), 10.37 s (1H, OH), 13.77 s (1H, OH)
XIe	1604 (C=C); 1616 (C=O ketone); 1683 (C^2=O); 3426 (OH)	1.69–1.82 m (2H, CH_2), 2.62–2.81 m [7H, H_C NCH_2, $N(CH_3)_2$], 2.83–2.95 m (2H, CH_2NMe_2), 3.49 m (1H, H_A NCH_2), 3.69 s (3H, CH_3O), 3.76 s (3H, CH_3O), 5.31 s (1H, C^5-H), 6.63–6.89 m (5H, $C^{3'}$-H, $C^{5'}$-H, 3H arom.), 7.22 d.d (1H, $C^{4'}$-H), 8.61 d (1H, $C^{6'}$-H)
XIIa	1604 (C=C); 1616 (C=O ketone); 1689 (C^2=O); 3435 (OH)	1.67–1.91 m (2H, CH_2), 2.64 m (1H, H_C NCH_2), 2.74–3.05 m (6H, $3NCH_2$), 3.49 m (1H, H_A NCH_2), 3.75–3.87 m (4H, $2OCH_2$), 5.36 s (1H, C^5-H), 6.66–6.76 m (2H, $C^{3'}$-H, $C^{5'}$-H), 7.17–7.33 m (6H, $C^{4'}$-H, 5H arom.), 8.37 d (1H, $C^{6'}$-H)
XIId	1603 (C=C); 1614 (C=O ketone); 1679 (C^2=O); 3440 (OH)	1.66–1.92 m (2H, CH_2), 2.61 m (1H, H_C NCH_2), 2.74–3.05 m (6H, $3NCH_2$), 3.52 m (1H, H_A NCH_2), 3.69 s (3H, CH_3O), 3.75–3.87 m (4H, $2OCH_2$), 5.36 s (1H, C^5-H), 6.62–6.81 m (4H, $C^{3'}$-H, $C^{5'}$-H, 2H arom), 7.16–7.29 m (3H, $C^{4'}$-H, 2H arom.), 8.37 d (1H, $C^{6'}$-H)
XIIe	1604 (C=C); 1616 (C=O ketone); 1690 (C^2=O); 3435 (OH)	1.66–1.92 m (2H, CH_2), 2.61 m (1H, H_C NCH_2), 2.74–3.05 m (6H, $3NCH_2$), 3.52 m (1H, H_A NCH_2), 3.64–3.87 m (10H, $2OCH_2$, $2CH_3O$), 5.37 s (1H, C^5-H), 6.63–6.89 m (5H, $C^{3'}$-H, $C^{5'}$-H, 3H arom.), 7.22 d.d (1H, $C^{4'}$-H), 8.61 d (1H, $C^{6'}$-H)
XIIIa[b]	1610 (C=C); 1660 (C^9=O); 1718 (C^3=O)	2.14 s [6H, $N(CH_3)_2$], 2.34–2.40 m (2H, CH_2NMe_2), 2.71 m (1H, H_C NCH_2), 3.84 m (1H, H_A NCH_2), 5.74 s (1H, C^1-H), 7.31–7.40 m (5H arom.), 7.52 d.d (1H, $^3J_{HH}$ 7.8, $^3J_{HH}$ 8.1 Hz, C^7-H), 7.78–7.89 m (2H, C^5-H, C^6-H), 8.03 d (1H, $^3J_{HH}$ 7.8 Hz, C^8-H)
XIIIb	1609 (C=C); 1653 (C^9=O); 1718 (C^3=O)	2.16 s [6H, $N(CH_3)_2$], 2.36–2.45 m (2H, CH_2NMe_2), 2.78 m (1H, H_C NCH_2), 3.86 m (1H, H_A NCH_2), 5.78 s (1H, C^1-H), 7.35–7.42 m (4H arom.), 7.52 d.d (1H, C^7-H), 7.78–7.90 m (2H, C^5-H, C^6-H), 8.03 d (1H, C^8-H)

Table 1. (Contd.)

Comp. no.	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum, δ, ppm
XIIIc	1609 (C=C); 1652 (C^9=O); 1711 (C^3=O)	2.17 s [6H, $N(CH_3)_2$], 2.36–2.48 m (2H, CH_2NMe_2), 2.80 m (1H, H_C NCH_2), 3.91 m (1H, H_A NCH_2), 5.98 s (1H, C^1-H), 7.53 d.d (1H, C^7-H), 7.68–7.76 m (2H arom.) 7.79–7.91 m (2H, C^5-H, C^6-H), 8.02 d (1H, C^8-H), 8.18–8.25 m (2H arom.)
XIIId	1609 (C=C); 1652 (C^9=O); 1714 (C^3=O)	2.16 s [6H, $N(CH_3)_2$], 2.34–2.42 m (2H, CH_2NMe_2), 2.79 m (1H, H_C NCH_2), 3.76 s (3H, CH_3O), 3.84 m (1H, H_A NCH_2), 5.68 s (1H, C^1-H), 6.85–6.93 m (2H arom.), 7.21–7.30 m (2H arom.) 7.52 d.d (1H, C^7-H), 7.76–7.89 m (2H, C^5-H, C^6-H), 8.03 d (1H, C^8-H)
XIIIe	1609 (C=C); 1653 (C^9=O); 1716 (C^3=O)	2.17 s [6H, $N(CH_3)_2$], 2.35–2.44 m (2H, CH_2NMe_2), 2.82 m (1H, H_C NCH_2), 3.72 s (3H, CH_3O), 3.76 s (3H, CH_3O), 3.85 m (1H, H_A NCH_2), 5.78 s (1H, C^1-H), 6.83–6.92 m (3H arom.), 7.52 d.d (1H, C^7-H), 7.78–7.90 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)
XIVa	1609 (C=C); 1653 (C^9=O); 1711 (C^3=O)	0.85–1.01 m (6H, $2CH_3$), 2.32–2.65 m (6H, $3NCH_2$), 2.83 m (1H, H_C NCH_2), 3.83 m (1H, H_A NCH_2), 5.76 s (1H, C^1-H), 7.29–7.41 m (5H arom.), 7.52 d.d (1H, C^7-H), 7.79–7.90 m (2H, C^5-H, C^6-H), 8.03 d (1H, C^8-H)
XIVd	1610 (C=C); 1653 (C^9=O); 1710 (C^3=O)	0.85–0.98 m (6H, $2CH_3$), 2.34–2.64 m (6H, $3NCH_2$), 2.82 m (1H, H_C NCH_2), 3.64–3.78 m (4H, H_A NCH_2, CH_3O), 5.70 s (1H, C^1-H), 6.86–6.95 m (2H arom.), 7.21–7.29 m (2H arom.) 7.53 d.d (1H, C^7-H), 7.80–7.91 m (2H, C^5-H, C^6-H), 8.03 d (1H, C^8-H)
XVa	1610 (C=C); 1661 (C^9=O); 1700 (C^3=O)	2.27–2.47 m (6H, $3NCH_2$), 2.86 m (1H, H_C NCH_2), 3.49–3.60 m (4H, $2OCH_2$), 3.85 m (1H, H_A NCH_2), 5.78 s (1H, C^1-H), 7.32–7.39 m (5H arom.), 7.52 d.d (1H, C^7-H), 7.78–7.89 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)
XVb	1610 (C=C); 1664 (C^9=O); 1701 (C^3=O)	2.25–2.48 m (6H, $3NCH_2$), 2.85 m (1H, H_C NCH_2), 3.48–3.62 m (4H, $2OCH_2$), 3.86 m (1H, H_A NCH_2), 5.81 s (1H, C^1-H), 7.35–7.43 m (4H arom.), 7.52 d.d (1H, C^7-H), 7.78–7.89 m (2H, C^5-H, C^6-H), 8.03 d (1H, C^8-H)
XVe	1609 (C=C); 1653 (C^9=O); 1714 (C^3=O)	2.28–2.46 m (6H, $3NCH_2$), 2.87 m (1H, H_C NCH_2), 3.51–3.58 m (4H, $2OCH_2$), 3.72 s (3H, CH_3O), 3.76 s (3H, CH_3O), 3.83 m (1H, H_A NCH_2),), 5.69 s (1H, C^1-H), 6.83–6.92 m (3H arom.), 7.52 d.d (1H, C^7-H), 7.79–7.89 m (2H, C^5-H, C^6-H), 8.03 d (1H, C^8-H)
XVIa	1610 (C=C); 1654 (C^9=O); 1708 (C^3=O)	1.46–1.73 m (2H, CH_2), 2.08 s [6H, $N(CH_3)_2$], 2.13–2.23 m (2H, CH_2NMe_2), 2.86 m (1H, H_C NCH_2), 3.65 m (1H, H_A NCH_2), 5.69 s (1H, C^1-H), 7.31–7.39 m (5H arom.), 7.52 d.d (1H, C^7-H), 7.79–7.90 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)
XVIb	1611 (C=C); 1663 (C^9=O); 1695 (C^3=O)	1.49–1.74 m (2H, CH_2), 2.11 s [6H, $N(CH_3)_2$], 2.15–2.26 m (2H, CH_2NMe_2), 2.85 m (1H, H_C NCH_2), 3.67 m (1H, H_A NCH_2), 5.74 s (1H, C^1-H), 7.35–7.42 m (4H arom.), 7.52 d.d (1H, C^7-H), 7.79–7.90 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)
XVIc	1609 (C=C); 1652 (C^9=O); 1711 (C^3=O)	1.53–1.77 m (2H, CH_2), 2.12 s [6H, $N(CH_3)_2$], 2.19–2.30 m (2H, CH_2NMe_2), 2.85 m (1H, H_C NCH_2), 3.71 m (1H, H_A NCH_2), 5.94 s (1H, C^1-H), 7.53 d.d (1H, C^7-H), 7.68–7.75 m (2H arom.) 7.80–7.91 m (2H, C^5-H, C^6-H), 8.03 d (1H, C^8-H), 8.14–8.24 m (2H arom.)
XVId	1610 (C=C); 1654 (C^9=O); 1708 (C^3=O)	1.48–1.74 m (2H, CH_2), 2.11 s [6H, $N(CH_3)_2$], 2.15–2.26 m (2H, CH_2NMe_2), 2.85 m (1H, H_C NCH_2), 3.63 m (1H, H_A NCH_2), 3.76 s (3H, CH_3O), 5.63 s (1H, C^1-H), 6.85–6.92 m (2H arom.), 7.21–7.28 m (2H arom.) 7.52 d.d (1H, C^7-H), 7.78–7.90 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)
XVIe	1610 (C=C); 1653 (C^9=O); 1707 (C^3=O)	1.48–1.74 m (2H, CH_2), 2.10 s [6H, $N(CH_3)_2$], 2.13–2.25 m (2H, CH_2NMe_2), 2.90 m (1H, H_C NCH_2), 3.64 m (1H, H_A NCH_2), 3.72 s (3H, CH_3O), 3.76 s (3H, CH_3O), 5.61 s (1H, C^1-H), 6.86–6.92 m (3H arom.), 7.52 d.d (1H, C^7-H), 7.77–7.89 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)
XVIIa	1610 (C=C); 1663 (C^9=O); 1719 (C^3=O)	1.50–1.79 m (2H, CH_2), 2.13–2.26 m (6H, $3NCH_2$), 2.87 m (1H, H_C NCH_2), 3.43–3.56 m (4H, $2OCH_2$), 3.68 m (1H, H_A NCH_2), 5.70 s (1H, C^1-H), 7.31–7.40 m (5H arom.), 7.52 d.d (1H, C^7-H), 7.79–7.91 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)

Table 1. (Contd.)

Comp. no.	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum, δ, ppm
XVIId	1609 (C=C); 1653 (C^9=O); 1718 (C^3=O)	1.50–1.79 m (2H, CH_2), 2.14–2.39 m (6H, $3NCH_2$), 2.87 m (1H, H_C NCH_2), 3.47–3.55 m (4H, $2OCH_2$), 3.65 m (1H, H_A NCH_2), 3.76 s (3H, CH_3O), 5.63 s (1H, C^1-H),), 6.84–6.92 m (2H arom.), 7.21–7.29 m (2H arom.) 7.52 d.d (1H, C^7-H), 7.78–7.90 m (2H, C^5-H, C^6-H), 8.04 d (1H, C^8-H)
XVIIe	1608 (C=C); 1660 (C^9=O); 1711 (C^3=O)	1.48–1.79 m (2H, CH_2), 2.14–2.39 m (6H, $3NCH_2$), 2.87 m (1H, H_C NCH_2), 3.47–3.68 m (5H, H_A NCH_2, $2OCH_2$), 3.72 s (3H, CH_3O), 3.76 s (3H, CH_3O), 5.63 s (1H, C^1-H), 6.84–6.94 m (3H arom.), 7.53 d.d (1H, C^7-H), 7.77–7.89 m (2H, C^5-H, C^6-H), 8.05 d (1H, C^8-H)

[a] Spin–spin coupling constants in the *o*-hydroxybenzoyl fragment of compounds **VIIIa** and **VIIIc**. The same values in all compounds **VIII–XII**. [b] Spin–spin coupling constants C^7–H and C^8–H. The same values in all compounds **XIII–XVII**.

intensity and position of these bands depend on the nature of the substituents, but the overall picture is similar for all compounds. In the region of 3200–3600 cm^{-1} there are no absorption bands, which confirms the involvement of OH groups into the cyclocondensation. In the ^1H NMR spectra of compounds **XIII–XVII** (Table 1) in the region of 5.30–5.80 ppm there is a singlet, which corresponds to the signal of the hydrogen atom C^1–H. The signals of C^5–H and C^6–H appear as a multiplet in the region of 7.75–7.95 ppm, C^7–H gives rise to a doublet of doublets in the region of 7.50–7.60 ppm, C^8–H appears as a doublet at 8.00–8.10 ppm. The hydrogen atoms of methylene groups in position *2* of the heterocycle are enantiotopic, and appear as two multiplets in the spectra of all studied compounds.

The compounds **XIII–XVII** are colorless crystalline substances, readily soluble in most organic solvents.

The developed route of the synthesis is convenient, simple for processing and provides a wide range of derivatives of 1-aryl-2-[ω-(dialkylamino)alkyl]-1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones of interest for searching for the biologically active substances. A scope of application of this approach to the synthesis of fused chromone derivatives will be considered in the future.

EXPERIMENTAL

The IR spectra of the substances were recorded on a Spectrum One (Perkin Elmer) spectrometer with resolution 1 cm^{-1} (12 scans) from the tablets with KBr. The ^1H NMR spectra were obtained on a Varian VXR-300 spectrometer from the solutions in DMSO-d_6, internal reference HMDS.

3-Hydroxy-4-(2-hydroxybenzoyl)-1-[2-(dimethylamino)ethyl]-5-phenyl-1,5-dihydro-2*H*-pyrrol-2-one (VIIIa). To a solution of 0.01 mol of benzaldehyde in 15 ml of anhydrous methanol was added 0.01 mol of 2-(dimethylamino)ethylamine, and the mixture was heated to 50°C and left standing for 20 min. To the mixture heated to 30–35°C was added 0.01 mol of methyl *o*-hydroxybenzoylpyruvate, the reaction mixture was heated to boiling, kept for 30 minutes at a temperature of 35–40°C, then cooled, the precipitate was filtered off, washed with methanol and ethyl acetate, and then the compound **VIIIa** without additional purification was used for further transformations. For analysis, a sample of compound **VIIIa** was purified by crystallization and dried at 85°C for 7 days.

Similarly were prepared compounds **VIIIb–VIIIe**, **IXa**, **IXe**, **Xa**, **Xb**, **Xe**, **XIa–XIe**, **XIIa**, **XIId**, **XIIe**. Melting points, yields and data of elemental analysis of compounds **VIII–XII** are given in Table 2.

2-[2-(Dimethylamino)ethyl]-1-phenyl-1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-dione (XIIIa). *a*. A solution of 0.005 mol of 3-hydroxy-4-(2-hydroxybenzoyl)-1-[2-(dimethylamino)ethyl]-5-phenyl-1,5-dihydro-2*H*-pyrrol-2-one (**VIIIa**) in 10 ml of glacial acetic acid was refluxed for 1 h, then cooled, poured into 100 ml of a mixture of ice and water and alkalinized with 10% solution of sodium hydroxide to a pH 8.5–9. The precipitate was filtered off, washed on the filter with ice water until neutral washings, dried, and the compound **XIIIa** was purified by crystallization.

Similarly were prepared compounds **XIIIb–XIIe**, **XIVa**, **XIVe**, **XVa**, **XVb**, **XVe**, **XVIa–XVIe**, **XVIIa**, **XVIId**, **XVIIe**. Melting points, yields and data of

Table 2. Yields, melting points, and elemental analysis data for compounds **VIII–XVII**

Comp. no.	Yield, %	mp, °C (solvent for crystallization)	Found, %			Formula	Calculated, %		
			C	H	N(Cl)		C	H	N(Cl)
VIIIa	85	213–215 (ethyl acetate)	68.71	6.11	7.54	$C_{21}H_{22}N_2O_4$	68.84	6.05	7.65
VIIIb	87	219–221 (ethyl acetate)	62.70	5.37	(8.72)	$C_{21}H_{21}ClN_2O_4$	62.92	5.28	(8.84)
VIIIc	86	224–225 (dioxane)	61.45	5.08	9.96	$C_{21}H_{21}N_3O_6$	61.31	5.14	10.21
VIIId	76	247–248 (ethyl acetate)	66.70	6.17	6.97	$C_{22}H_{24}N_2O_5$	66.65	6.10	7.07
VIIIe	82	224–226 (ethyl acetate)	64.69	6.23	6.45	$C_{23}H_{26}N_2O_6$	64.78	6.15	6.57
IXa	69	214–216 (ethyl acetate)	69.87	6.52	7.14	$C_{23}H_{26}N_2O_4$	70.03	6.64	7.10
IXd	74	195–197 (ethyl acetate)	68.05	6.73	6.44	$C_{24}H_{28}N_2O_5$	67.91	6.65	6.60
Xa	89	232–234 (ethyl acetate)	67.45	6.03	6.71	$C_{23}H_{24}N_2O_5$	67.63	5.92	6.86
Xb	92	229–233 (dioxane)	62.42	5.19	(8.15)	$C_{23}H_{23}ClN_2O_5$	62.37	5.23	(8.00)
Xe	76	212–214 (acetonitrile)	63.91	5.95	5.80	$C_{25}H_{28}N_2O_7$	64.09	6.02	5.98
XIa	88	194–198 (ethyl acetate)	69.25	6.31	7.52	$C_{22}H_{24}N_2O_4$	69.46	6.36	7.36
XIb	94	198–201 (dioxane)	63.85	5.70	(8.39)	$C_{22}H_{23}ClN_2O_4$	63.69	5.59	(8.55)
XIc	90	213–215 (dioxane)	62.36	5.40	10.03	$C_{22}H_{23}N_3O_6$	62.11	5.45	9.88
XId	87	241–242 (ethanol)	67.54	6.32	6.58	$C_{23}H_{26}N_2O_5$	67.30	6.38	6.82
XIe	79	242–243 (ethyl acetate)	65.23	6.56	6.64	$C_{24}H_{28}N_2O_6$	65.44	6.41	6.36
XIIa	92	175–184 (dioxane)	68.41	6.07	6.89	$C_{24}H_{26}N_2O_5$	68.23	6.20	6.63
XIId	86	184–187 (ethyl acetate)	66.24	6.35	6.33	$C_{25}H_{28}N_2O_6$	66.36	6.24	6.19
XIIe	75	245–246 (ethyl acetate)	64.57	6.42	6.00	$C_{26}H_{30}N_2O_7$	64.72	6.27	5.81
XIIIa	71	203–204 (ethanol–water, 1:1)	72.46	5.84	8.31	$C_{21}H_{20}N_2O_3$	72.40	5.79	8.04
XIIIb	78	201–202 (ethanol)	66.03	5.19	(9.13)	$C_{21}H_{19}ClN_2O_3$	65.88	5.00	(9.26)
XIIIc	82	229–230 (DMF–ethanol, 1:3)	64.07	4.77	10.84	$C_{21}H_{19}N_3O_5$	64.12	4.87	10.68
XIIId	61	171–172 (2-propanol)	69.98	5.73	7.29	$C_{22}H_{22}N_2O_4$	69.83	5.86	7.40
XIIIe	63	184–185 (ethanol)	67.96	5.87	6.58	$C_{23}H_{24}N_2O_5$	67.63	5.92	6.86
XIVa	77	175–176 (ethanol–water, 1:1)	73.07	6.11	7.48	$C_{23}H_{24}N_2O_3$	73.38	6.43	7.44
XIVd	68	131–132 (2-propanol)	71.23	6.30	7.17	$C_{24}H_{26}N_2O_4$	70.92	6.45	6.89
XVa	78	194–195 (DMF–ethanol, 1:4)	71.04	5.62	6.95	$C_{23}H_{22}N_2O_4$	70.75	5.68	7.17
XVb	82	179–180 (DMF–ethanol, 1:4)	64.72	4.83	(8.56)	$C_{23}H_{21}ClN_2O_4$	65.02	4.98	(8.34)
XVe	71	193–194 (ethanol)	66.97	5.96	6.50	$C_{25}H_{26}N_2O_6$	66.66	5.82	6.22
XVIa	63	186–187 (ethanol–water, 3:1)	72.78	6.36	7.41	$C_{22}H_{22}N_2O_3$	72.91	6.12	7.73
XVIb	75	192–194 (ethanol)	66.43	5.60	(8.57)	$C_{22}H_{21}ClN_2O_3$	66.58	5.33	(8.93)
XVIc	71	168–169 (acetonitrile)	65.03	5.27	10.09	$C_{22}H_{21}N_3O_5$	64.86	5.20	10.31
XVId	57	172–173 (ethanol–water, 3:1)	70.24	5.94	7.39	$C_{23}H_{24}N_2O_4$	70.39	6.16	7.14
XVIe	61	174–175 (ethanol)	67.95	6.44	6.80	$C_{24}H_{26}N_2O_5$	68.23	6.20	6.63
XVIIa	68	200–201 (acetonitrile)	71.03	6.23	6.68	$C_{24}H_{24}N_2O_4$	71.27	5.98	6.93
XVIId	49	211–212 (DMF–ethanol, 1:5)	69.35	6.24	6.19	$C_{25}H_{26}N_2O_5$	69.11	6.03	6.45
XVIIe	57	172–173 (ethanol)	66.98	6.10	6.32	$C_{26}H_{28}N_2O_6$	67.23	6.08	6.03

elemental analysis of compounds **XIII–XVII** are shown in Table 2.

b. To a solution of 0.005 mol of benzaldehyde in 10 ml of anhydrous methanol was added 0.005 mol of 2-(dimethylamino)ethylamine, the mixture was heated to 50°C and left standing for 20 min. To the mixture heated to 30–35°C was added 0.005 mol of methyl *o*-hydroxytbenzoylpyruvate, the reaction mixture was heated to boiling, kept for 30 minutes at a temperature of 35–40°C, cooled, and to the formed suspension was added 10 ml of glacial acetic acid, the mixture was refluxed for 1 h, cooled, poured into 100 ml of a mixture of ice and water and alkalinized with 10% solution of sodium hydroxide to pH 8.5–9. The oil was separated by decanting, washed with ice-cold water, the residue was ground with water–2-propanol, the precipitate was filtered off, washed with water–2-propanol, and compound **XIIIa** was purified by crystallization from ethanol. Yield 62%.

Similarly were prepared compound **XVe** with the yield 54% and compound **XVIIa** with the yield 50%.

The mixed samples of each compound **XIIIa**, **XVe**, and **XVIIa** obtained by methods a and b, did not show the melting point depression. Their IR and ^{1}H NMR spectra are identical.

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