# Structure and condensation reactions of 2,3-dihydrofuro[3,2-*c*]coumarin-3-one

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2,3-Dihydrofuro[3,2-*c*]coumarin-3-one was synthesized in quantitative yield from 3-(ω-bromoacetyl)-4-hydroxycoumarin in the presence of nucleophiles (including solvents). This compound undergoes keto-enol tautomerization and easily reacts with aromatic and heteroaromatic aldehydes to form crotonization products having a *Z* configuration and exhibiting strong fluorescence.

**Key words:** furocoumarinones, keto-enol tautomerism, dimerization, crotonization, X-ray diffraction study, fluorescence.

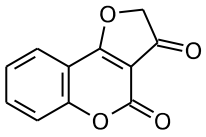
Many coumarin derivatives are characterized by strong photochemical activity and exhibit intense fluorescence. Due to such properties, these compounds are widely used as optical bleaching agents, luminescent labels, and laser dyes.[1,2] Furocoumarins are important coumarin derivatives, many of which not only exhibit photochemical activity but also have therapeutical properties and are used as efficient pharmaceuticals.[3,4]

Earlier, we have examined several new approaches to the synthesis of furocoumarins and their analogs. One of these approaches is based on the unusual Fries rearrangement of 7-hydroxy-4-methylcoumarin chloroacetate (**1**) giving 4-methyl-8*H*-furo[2,3-*h*]chromene-2,9-dione (**2**) followed by the reduction of **2** to alcohol **3** and the aromatization of the latter to form furo[2,3-*h*]coumarin derivative (**4**) (angelicin) (Scheme 1).[5,6]

The $^1$H NMR spectroscopic study showed that compound **2** exists exclusively in the keto form in solutions in $CDCl_3$, acetone-$d_6$, and DMSO-$d_6$. However, the keto-enol tautomerization of compound **2** was observed by electronic absorption spectroscopy (Scheme 2).[7]

It was shown that the transformations of the keto and enol forms of compound **2** provide a convenient route to the functionalization of furocoumarin **4** at the furan ring.[8,9]

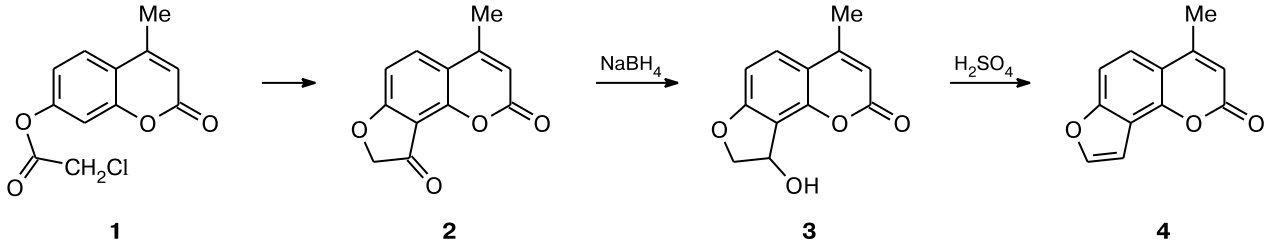
In the present study, we report a convenient procedure for the synthesis of the isomer of compound **2**, *viz.*, 2,3-dihydrofuro[3,2-*c*]coumarin-3(2*H*)-one (**5**), its tautomeric transformations, and some reactions at the furan ring.



**5**

Another field of our research on the reactions of β-di- and β,β-tricarbonyl compounds in the series of coumarin and its analogs[10,11] concerns the synthesis and transformations of ketone **5**.

**Scheme 1**




**1** **2** **3** **4**

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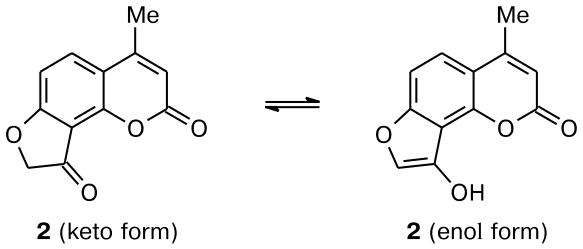
**Scheme 2**




**2** (keto form) **2** (enol form)

## Results and Discussion

Earlier,[12] ketone **5** has been synthesized by the reaction of 3-(ω–bromoacetyl)-4-hydroxycoumarins with triethylamine or a 1% sodium hydroxide solution in acetone. We found that ketone **5** can be easily synthesized by the bromination of 3-acetyl-4-hydroxycoumarin (**6**) followed by the treatment of bromo ketone **7** at room temperature for several minutes in DMSO in the presence of various nucleophilic and basic reagents, for example, of nitrite, nitrate, cyanide, or carbonate ions, amines (Scheme 3). We also found that the intramolecular cyclization giving ketone **5** competes with the bimolecular nucleophilic substitution of bromine. The substitution readily occurred with ammonium thiocyanate and sodium iodide in acetone at ~20 °C, whereas the reaction performed with heating gave ketone **5** as the only product. It should be noted that compounds **7a—c** also undergo cyclization to form ketone **5** in quantitative yield on heating in ethanol even in the absence of bases.

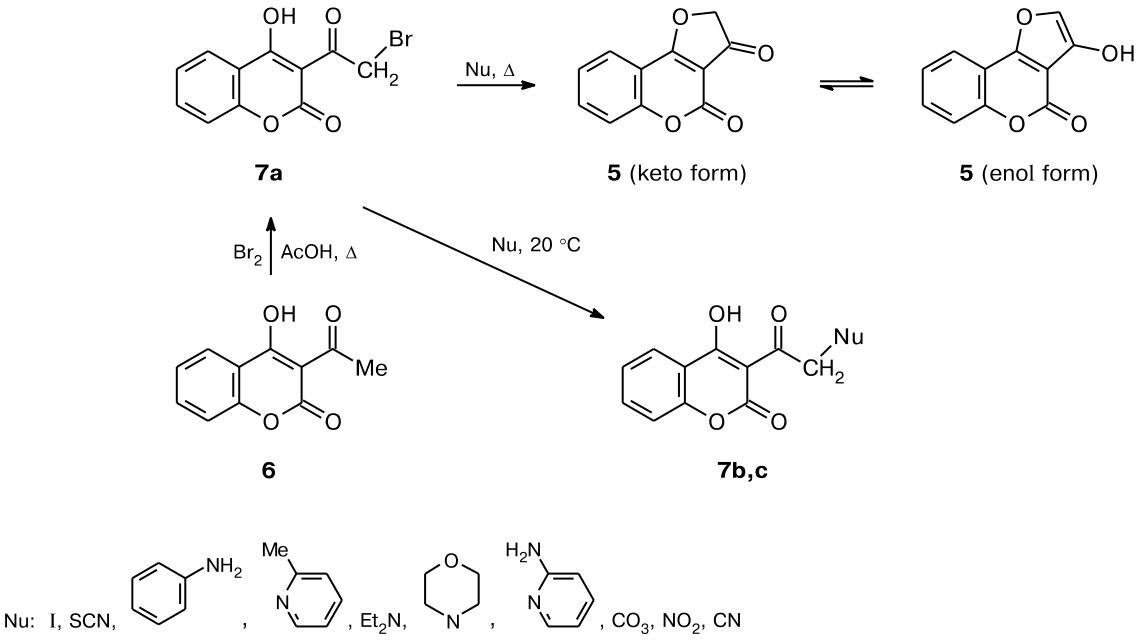
As can be seen from Scheme 3, ketone **5** can theoretically exist both in the keto and enol forms. Although the difference in the enthalpies of formation of two tautomers is very large (35.8 kcal $mol^{-1}$, see Table 1), we observed tautomeric transformations of ketone **5** when studying the solvatochromism by gradually changing the composition of the solvent from 100% $CCl_4$ to 100% MeOH. Thus, the corresponding spectral curves display an isosbestic point.

The electronic absorption spectra of ketone **5** in $CCl_4$—MeOH mixtures of variable composition are shown in Fig. 1.

To assign the observed spectral changes to the keto and enol forms, the electronic absorption spectra of both forms were calculated by the ZINDO/S method. Table 2 gives the calculated wavelengths and oscillator strengths.

Based on a comparison of the experimental data (see Fig. 1) with the results of the calculations (see Table 2), it can be concluded that the bathochromic shift of the long-wavelength absorption maximum of ketone **5** in methanol with respect to this maximum in carbon tetrachloride is, most likely, attributed to an increase in the contribution of the enol form to its structure. In a nonpolar solvent, the enol form can be stabilized by a hydrogen bond between the hydroxy group of the enol and the carbonyl oxygen atom of the lactone moiety. As shown earlier,[10] compound **6** undergoes similar tautomeric transformations.

**Scheme 3**




**7:** Nu = I (**b**), SCN (**c**)

**Table 1.** Enthalpies of formation and the relative energies (in parentheses) of two tautomeric forms of ketone **5** based on the results of quantum chemical calculations by the AM1, PM3, and MNDO methods (kcal mol$^{-1}$)

| Compound | AM1 | PM3 | MNDO |
|---|---|---|---|
| **5** (keto form) | −84.438 | −101.051 | −108.49 |
| | (0.00) | (0.00) | (0.00) |
| **5** (enol form) | −48.985 | −64.728 | −70.55 |
| | (−35.45) | (−36.32) | (−37.94) |

**Table 2.** Parameters of the electronic absortpion spectra of the keto and enol forms of ketone **5** calculated by the ZINDO/S method

| Compound | $\lambda_{max}$*/nm | Oscillator strength *f* |
|---|---|---|
| **5** (keto form) | 315 | 0.532 |
| | 276.5 | 0.251 |
| | 224.3 | 0.384 |
| | 221.7 | 0.254 |
| **5** (enol form) | 349 | 0.498 |
| | 249.9 | 0.08 |
| | 243.7 | 0.146 |
| | 230 | 0.542 |

* The position of the long-wavelength absorption maximum.

Being a β,β-tricarbonyl compound, ketone **6** easily acts as a CH-acid in the condensation reaction at the methyl group of the acetyl moiety only when it is involved in the complex with $BF_3$.[10,11] According to the X-ray diffraction data,[10] the acetyl group of 3-acetyl-4-hydroxycoumarin in the above-mentioned complex undergoes structural changes corresponding to its enolization, which apparently facilitates subsequent condensation reactions with aldehydes. When considering ketone **5** as a cyclic analog of compound **6**, we found that it can be subjected to condensation with aldehydes in the absence of complexation with boron compounds (Scheme 4).

The resulting α,β-unsaturated dicarbonyl compounds **8** and **9** were characterized by $^1$H NMR spectroscopy, mass spectrometry, and elemental analysis. In the $^1$H NMR spectra, the signal for the protons of the methylene group of the dihydrofuran ring is absent, but the spectra show a singlet at δ 7.0—7.5 characteristic of the methine proton.

According to the X-ray diffraction data for monohydrate of compound **8j**, there is one-half of the $C_{20}H_{15}NO$ molecule lying in a special position (on a plane of symmetry) and one-half of the disordered water molecule in the general position per asymmetric unit. The molecular structure of **8j** and the atomic numbering scheme are shown in Fig. 2. As can be seen from this figure, molecule **8j** has a *Z* configuration.

Ketone **5** is not involved in the crotonization with aliphatic aldehydes and ketones, as well as with aromatic ketones; however, it can react with heteroaromatic aldehydes. Some condensation reactions of ketone **5** afforded not the expected reaction products but dimer **10** (Scheme 5) as a result of the self-condensation of ketone **5**.

We examined in detail the reaction conditions, in which dimeric products are formed from **5**. Thus, the heating under reflux of compound **5** in acetic acid in the presence of catalytic amounts of concentrated hydrochloric (or sul-

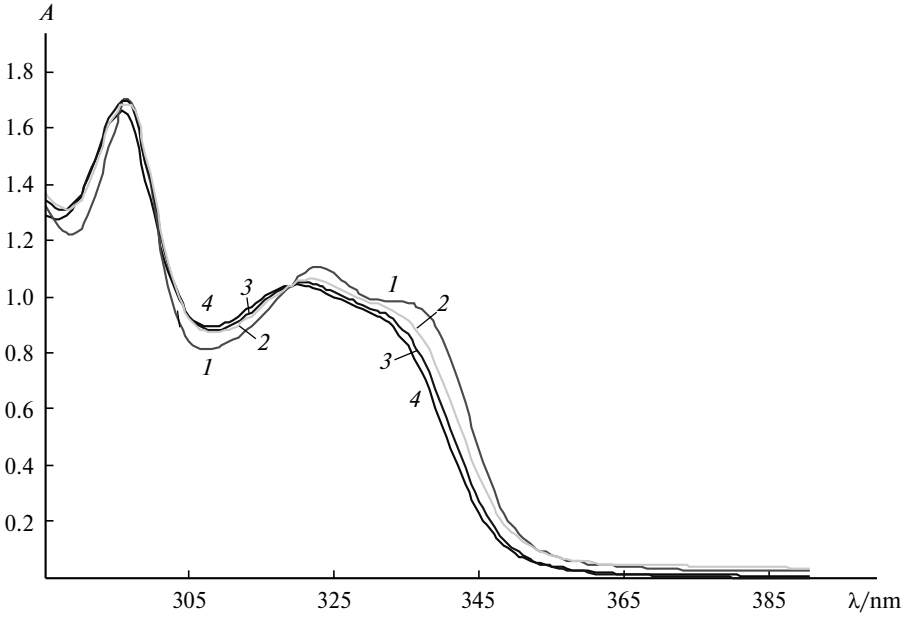
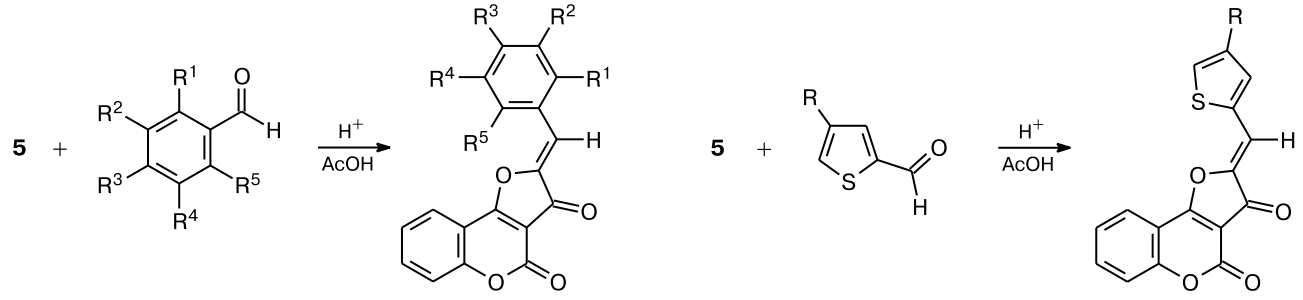



**Fig. 1.** Electronic absorption spectra of ketone **5** recorded at different $CCl_4$ to MeOH ratios: 100% $CCl_4$ (*1*), 60% $CCl_4$—30% MeOH (*2*), 30% $CCl_4$—60% MeOH (*3*), and 100% MeOH (*4*).

**Scheme 4**



**8a—l** **9a,b**

| **8** | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **a** | H | H | H | H | H |
| **b** | Cl | H | H | H | H |
| **c** | H | H | $NO_2$ | H | H |
| **d** | H | H | OMe | H | H |
| **e** | H | Br | OMe | H | H |
| **f** | H | OMe | OMe | OMe | H |

| **8** | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **g** | OH | OMe | H | H | H |
| **h** | OMe | H | OMe | H | Cl |
| **i** | OMe | H | H | Br | H |
| **j** | H | H | $NMe_2$ | H | H |
| **k** | H | Cl | H | H | H |
| **l** | OMe | H | OMe | H | H |

**9:** R = H (**a**), Br (**b**)

furic) acid led to the formation of 2,3′-bi(furo[3,2-*c*]-chromene)-3,4,4′-trione **10** in 45% yield.

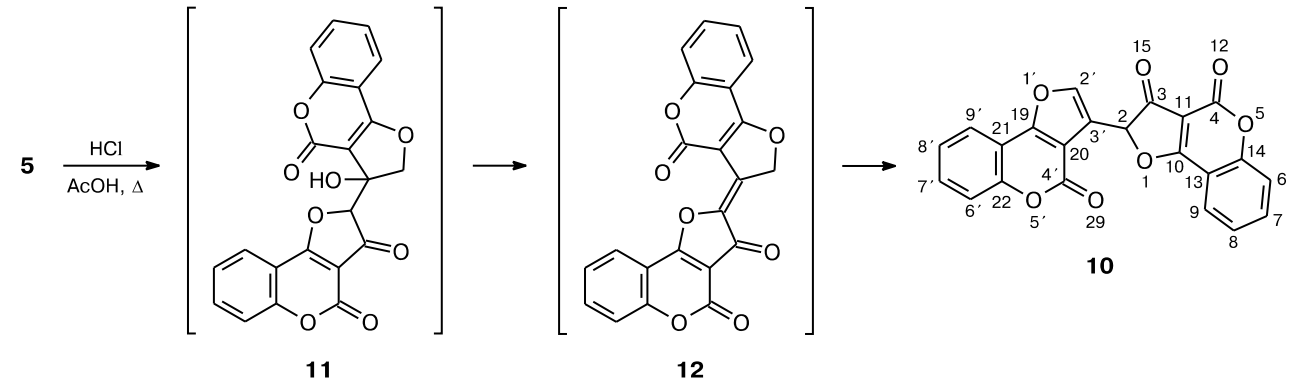
The $^1$H NMR spectrum is consistent with the structure of dimer **10**. Thus, the spectrum shows an intense doublet at δ 6.50 assigned to one proton at the C(2) atom of the dihydrofuranone ring and a singlet at δ 8.59 belonging to the proton at the C(2′) atom of the furan ring. In addition, there are peaks between the above-mentioned signals at δ 7.40—8.00 belonging to eight protons of the coumarin rings.

The mass spectrum of compound **10** has the most intense peak at $m/z$ = 387 corresponding to the molecular ion [M + 1].

We did not found products of aldol condensation (**11**) and crotonization (**12**) from the dimerization of compound **5**. Apparently, intermediate aldol **11** rapidly undergoes aromatization through dehydration to form the furan ring. Final dimer **10** appeared to be more stable than crotonization product **12**. As reported earlier,[13] the condensation of compound **2** proceeds in a similar way.

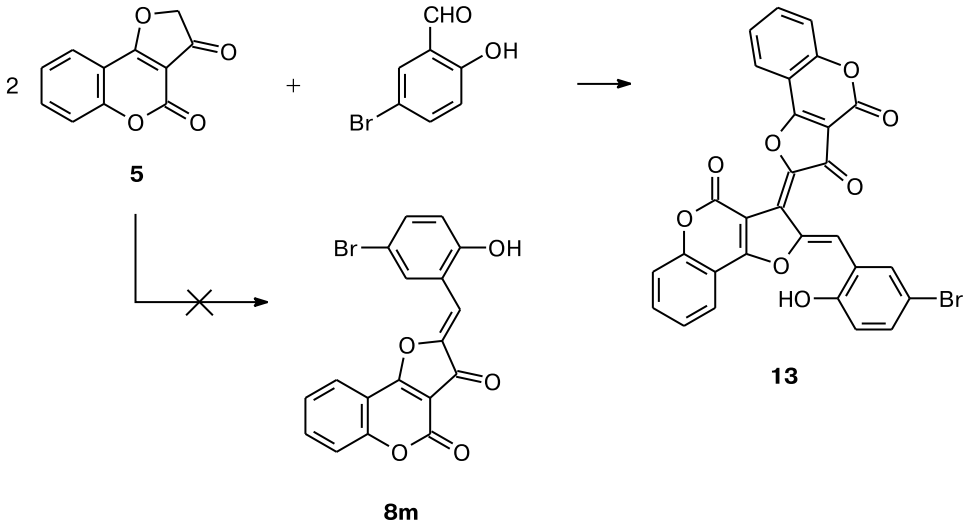
Apparently, ketone **5** can react with compounds **8** as well. The reaction of 5-bromo-2-hydroxybenzaldehyde with ketone **5** produced (2*E*,2′*Z*)-2′-(5-bromo-2-hydroxybenzylidene)-2′*H*,3*H*,4*H*,4′*H*-2,3′-bifuro[3,2-*c*]chromene-3,4,4′-trione **13** in 27% yield (Scheme 6). It should be noted that we did not detect the crotonization product, *viz.*, 2-(5′-bromo-2′-hydroxybenzylidene)-2*H*-furo[3,2-*c*]chromene-3,4-dione (**8m**), in the reaction mixture. It appeared that in the synthesis of compound **13**, the precipitation of the latter begins immediately after the addition of the mineral acid.

**Scheme 5**



**11** **12** **10**

**Scheme 6**




Most likely, the initially formed crotonization product rapidly reacts with the second molecule **5** that acts as a CH-acid. In this case, the initial formation of compound **10** is excluded, because this compound has a very low solubility and, if it were formed, it will immediately precipitate. This is why we failed to perform the corresponding condensation reactions with the use of compound **10**, including the use of 5-bromo-2-hydroxybenzaldehyde.

All condensation products of ketone **5** with aldehydes show intense absorption in the electronic absorption spectra (Table 3) and exhibit strong fluorescence (Table 4).

We estimated the solvent effect on the electronic absorption spectra of the resulting compounds. In particular, the absorption spectra of compound **8j** are solvent-dependent (Fig. 3). The solvent and the position of the long-wavelength absorption maximum (λ/nm) of this compound in the electronic absorption spectrum are as

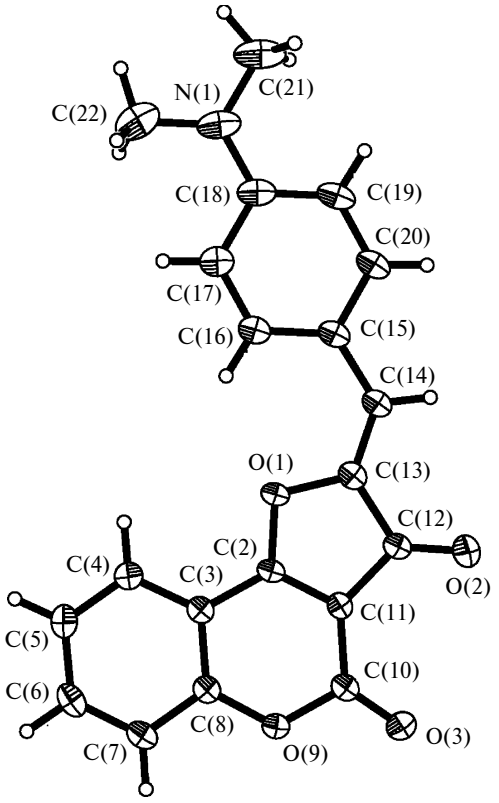



**Fig. 2.** Molecular structure of **8j**. Thermal ellipsoids are drawn at the 50% probability level.

**Table 3.** Experimental parameters of the electronic absorption spectra of compounds **8** and **9** and the corresponding parameters calculated by the ZINDO/S method

| Compound | Calculation, $\lambda_{max}$/nm (log$\varepsilon$) | Experiment, $\lambda_{max}$/nm ($f$) | |
|---|---|---|---|
| | | MeOH | $CCl_4$ |
| **8a** | 308.73 (0.705) | 352 (4.35) | 358 (4.25) |
| **8b** | | 351 (4.20) | 350 (4.23) |
| **8c** | 340.69 (1.022) | 354 (3.83) | 356 (3.88) |
| **8d** | 340.90 (0.875) | 394 (4.34) | 392 (4.35) |
| **8e** | | 384 (4.37) | 383 (4.35) |
| **8f** | 340.48 (0.841) | 396 (4.70) | 392 (4.74) |
| **8g** | 340.51 (0.872) | 355 (4.50) | 358 (4.51) |
| **8h** | | 411 (4.42) | 413 (4.41) |
| **8i** | | 392 (4.22) | 389 (4.19) |
| **8j** | 354.61 (0.864) | 494 (4.87) | 454 (4.82) |
| **8k** | | 348 (4.04) | 349 (4.56) |
| **8l** | 346.98 (0.874) | 422 (4.49) | 411 (4.47) |
| **9b** | | 381 (4.54) | 370 (4.55) |

**Table 4.** Fluorescence data for compounds **8** and **9***

| Compound | Solvent | Absorption band, λ/nm | Absorption, $\lambda^{abs}_{max}$/nm | Fluorescence, $\lambda^{fl}$/nm ($I_{rel}$) | Stokes shift, Δλ/nm |
|---|---|---|---|---|---|
| **8a** | Toluene | 389—399 | 389 | 410 (29.6) | 21 |
| **8b** | Toluene | 352—362 | 352 | — | — |
| **8c** | Toluene | 356—366 | 356 | — | — |
| **8d** | Toluene | 391—401 | 391 | 467 (9.2) | 76 |
| **8e** | Toluene | 381—391 | 381 | — | — |
| **8f** | Toluene | 363—373 | 363 | 515 (299.93) | 152 |
| | | 400—410 | 400 | 528 (476) | 128 |
| **8g** | Toluene | 360—370 | 360 | 472 (9.26) | 112 |
| **8h** | Toluene | 363—373 | 363 | 493 (173) | 130 |
| | | 417—427 | 417 | 493 (185) | 76 |
| **8i** | Toluene | 367—377 | 367 | — | — |
| | | 386—396 | 386 | — | — |
| **8j** | Toluene | 462—472 | 462 | 546 (364) | 84 |
| | $CCl_4$ | 454—464 | 454 | 510 (873) | 56 |
| | DMF | 484—494 | 484 | 636 (16) | 152 |
| **8k** | Toluene | 353—363 | 353 | — | — |
| **8l** | Toluene | 414—424 | 414 | 492 (169.5) | 78 |
| **9b** | Toluene | 377—387 | 377 | — | — |

* The spectra were recorded at concentrations of $1 \cdot 10^{-5}$ mol $L^{-1}$.

follows: $CCl_4$ (454), toluene (462), DMF (484), acetone (472), methanol (494), and aqueous acetone (499). It can be seen that the long-wavelength absorption maximum of compound **8j** undergoes a bathochromic shift in going from a nonpolar to polar solvent. This result is apparently associated with a substantial contribution of the bipolar resonance structure **B** (Scheme 7) to the electronic structure of compound **8j**.

Polar solvents provide better solvation of polarized molecules, thus increasing the contribution of the charge transfer to the long-wavelength absorption of compound **8j** in the electronic absorption spectrum.

This effect was particularly pronounced when we used aqueous acetone as the solvent. Thus, the absorption maximum of compound **8j** is bathochromically shifted almost to 500 nm, which is accompanied by an increase in the intensity of the absorption.

When analyzing the electronic absorption spectra of compound **8j**, the molecular parameters determined by X-ray diffraction should be considered in more detail. It is noteworthy that the N(1)—C(18), C(16)—C(17), and C(19)—C(20) bonds are substantially shortened, which is indicative of the electron-withdrawing properties of the dihydrofurocoumarinone moiety in accordance with the

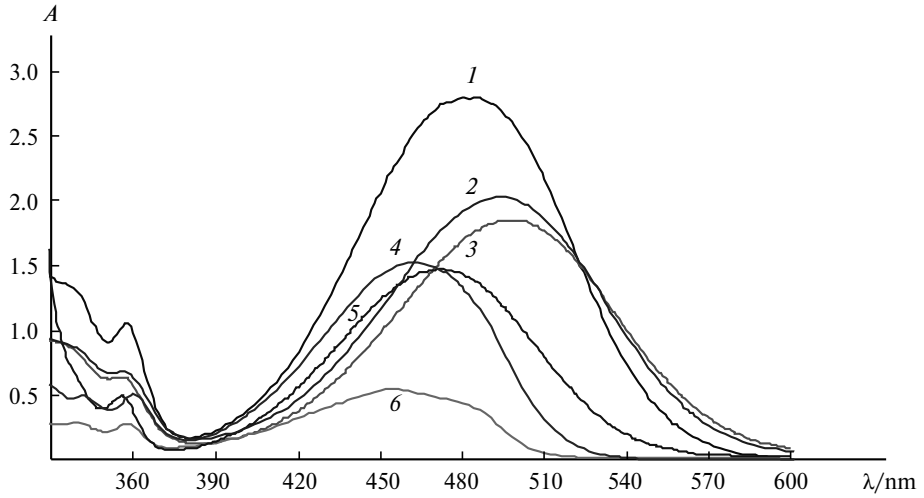
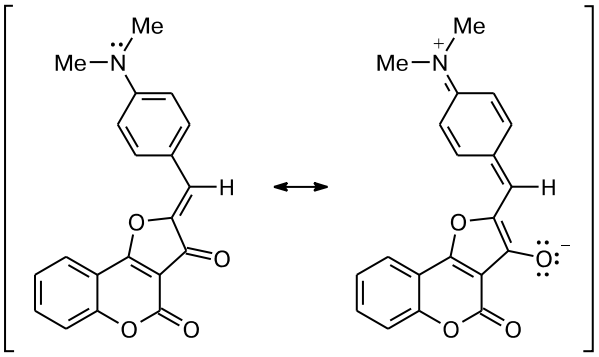



**Fig. 3.** Electronic absorption spectra of compound **8j** in different solvents: DMF (*1*), methanol (*2*), water—acetone, 2 : 3 (*3*), toluene (*4*), acetone (*5*), and $CCl_4$ (*6*).

**Scheme 7**



**8j (A)** **8j (B)**

contribution of the resonance structure **B** to the electronic structure of molecule **8j**.

It was of interest to compare our results with the corresponding data for *N*,*N*-dimethyl-4-nitroaniline. Studies by X-ray diffraction and computational methods showed[14] that there is a substantial direct polar conjugation between the dimethylamino group and the nitro group in *N*,*N*-dimethyl-4-nitroaniline, which is consistent with the quinoid resonance structure of this compound (Scheme 8).

A comparison of the structures displayed in Scheme 8 shows that the dihydrofurocoumarinone moiety in compound **8j** causes the rearrangement of the electronic structure of the benzene ring toward the resonance structure with quinoid character by analogy with the nitro group in *N*,*N*-dimethyl-4-nitroaniline. Earlier, similar effects have been found in other *N*,*N*-dimethylaniline derivatives containing the electron-withdrawing substituent in the *para* position.[15]

According to the X-ray diffraction data, molecules **8j** in the crystals are arranged in a head-to-tail fashion to form regular stacks running along the *b* axis (Fig. 4). The interplanar distance between the molecules in the stacks is 3.30 Å (Fig. 5). The disordered water molecules located between the stacks form intermolecular O(W)—H(1W)...O(2), O(W′)—H(1W)...O(2), O(W)—H(2W)...O(2),* and O(W′)—H(2W)—O(2)* hydrogen bonds with molecules **8j** (O...O, 2.824(2)—3.032(2) Å; O...H, 2.06—2.15 Å).

The resulting compounds exhibit fluorescence, which is particularly substantial in the case of compounds **8f**,**h**,**j**,**l** containing strong electron-releasing substituents. As can be seen from Table 4, the compounds containing halogen atoms or the nitro group at the phenyl ring do not have fluorescence. The exception is compound **8h**. Although the latter contains two strong electron-releasing groups in the *ortho* and *para* positions, it does not exhibit fluorescence.

The fluorescence spectra of compound **8j** were recorded in three solvents. An anomalously large Stokes shift was observed in DMF, the fluorescence intensity being decreased.

The reactions under study comprise one of the areas of our research on the transformations of β-di- and β,β-tricarbonyl compounds in the coumarin series.[10,11] Ketone **5** is a readily available compound and can be easily transformed at the furan ring to give new derivatives, which can be considered as promising fluorophores and biologically active compounds.

## Experimental

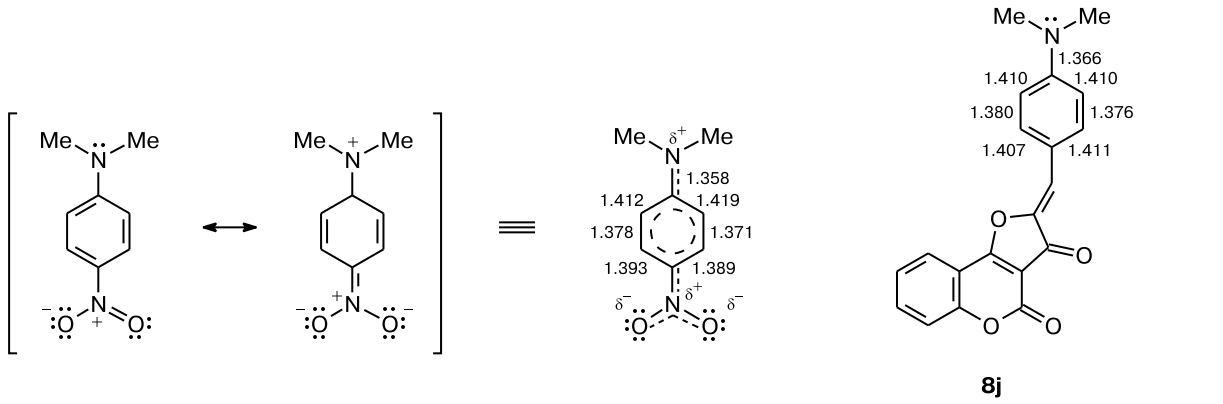
The $^1$H NMR spectra were recorded on a Bruker WP-200-SY spectrometer operating at 200 MHz in deuterated solvents (DMSO-$d_6$, $CDCl_3$, $CF_3COOD$) with $Me_4Si$ as the internal standard.

The mass spectra were obtained on a Finnigan MAT SSQ-710 mass spectrometer with 70 eV ionization energy.

The electronic absorption spectra were measured on an APEL PD-303UV spectrometer. The fluorescence spectra were recorded on a Shimadzu RF-50 spectrofluorometer with the use of a cell containing the solvent as the reference.

* The symmetry code: $2 - x$, $-y$, $1 - z$.

**Scheme 8**



**8j**

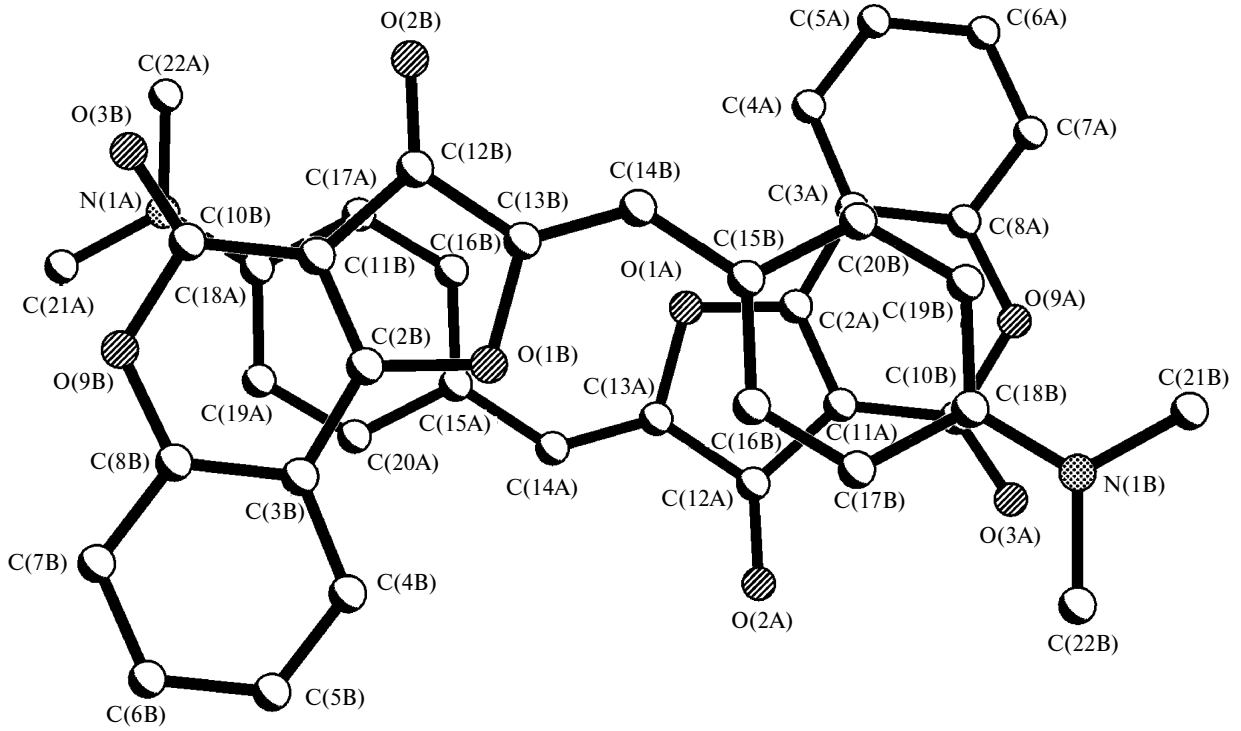



**Fig. 4.** Stacking of molecules **8j** in the crystal structure.

The course of the reactions was monitored and the purity of the reaction products was checked by TLC on Sillufol UV-254 plates using chloroform—acetone (16 : 1) (*A*), chloroform—acetone (5 : 1) (*B*), and hexane—acetone (2 : 1) (*C*) as solvent systems.

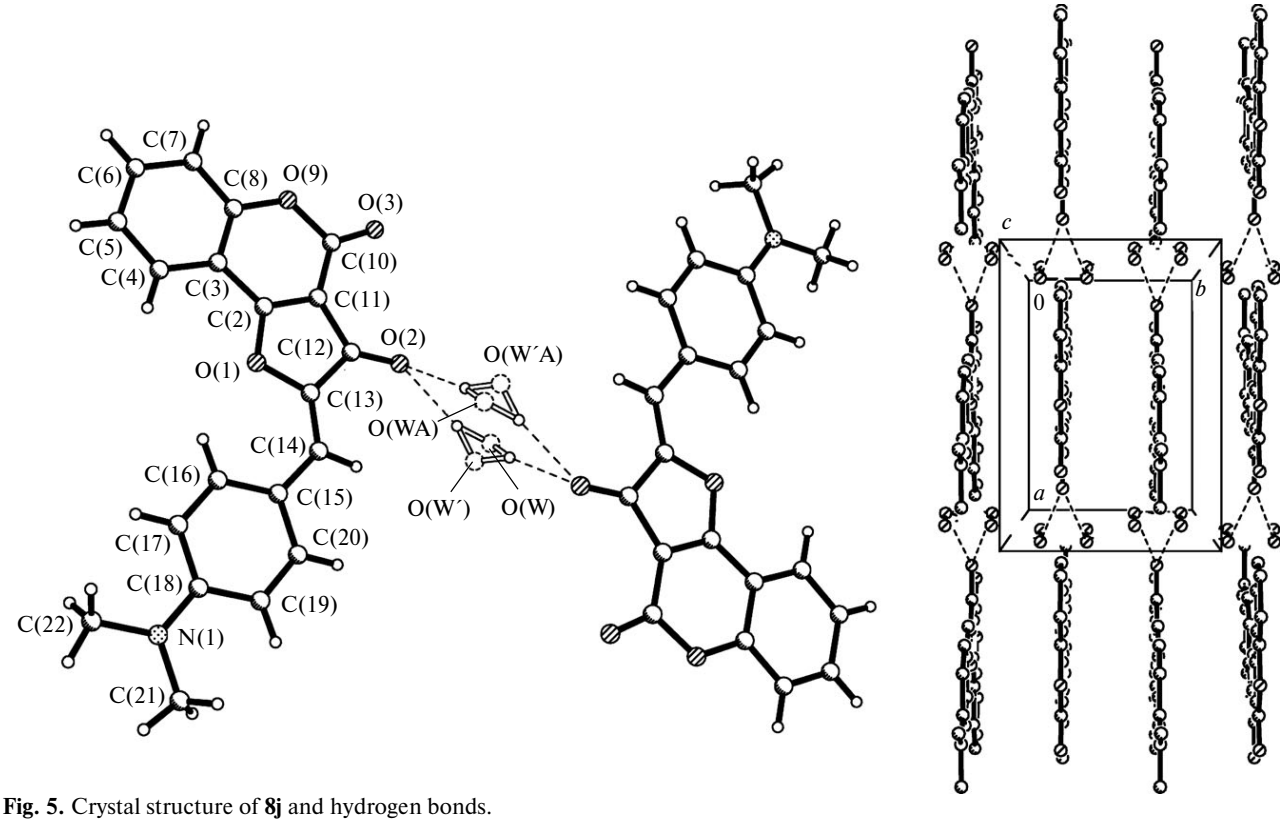



**Fig. 5.** Crystal structure of **8j** and hydrogen bonds.

Quantum chemical calculations by the ZINDO/S method were carried out using the Hyper Chem 6.0 program. The preliminary geometry optimization was performed by the MM+ molecular mechanics method.

Single crystals of compound **8j** were obtained by crystallization from acetic anhydride. The X-ray diffraction study was performed at 173(2) K on a Bruker SMART APEX2 CCD diffractometer (Mo-Kα radiation, $2\theta_{max} = 60.98°$). The crystal structure was solved by direct methods followed by calculations of Fourier maps with the use of the SHELXS-97 program package.[16] The structure was solved by the full-matrix least-squares method with anisotropic displacement parameters for all nonhydrogen atoms using the SHELXL-97 program package.[16] The hydrogen atoms (except for the H atoms of the water molecule) were located in the difference Fourier map and then positioned geometrically and refined isotropically by the least-squares method. In the crystal structure, the water molecule is disordered over two closely spaced positions, O(W) and O(W′), which are also disordered about the crystallographic plane, resulting in four positions with occupancies 0.25. One of the H atoms of the water molecule was found in difference Fourier map, and the second H atom was positioned geometrically on the direction of the only possible intermolecular hydrogen bond with molecule **8j**.

Principal crystallographic parameters and the X-ray data collection and refinement statistics for compound **8j** · $H_2O$ at 173 K:* $C_{20}H_{15}NO_4 \cdot H_2O$, $M$ = 351.35, orthorhombic system, space group *Pnma*, $a$ = 9.238(1) Å, $b$ = 6.597(1) Å, $c$ = 28.037(3) Å, $V$ = 1708.7(4) Å$^3$, $Z$ = 4, $d_{calc}$ = 1.37 g cm$^{-3}$, μ = 0.099 mm$^{-1}$, the total number of reflections is 10028, 2749 independent reflections, 189 refined parameters, $R$ = 0.055 based on 1813 reflections with $F_0 > 4\sigma(F_0)$, $wR(F^2)$ = 0.144, GOOF = 1.015, *hkl* ranges: $-11 \le h \le 13$, $-8 \le k \le 9$, $-40 \le l \le 34$; $\Delta\rho_{max}$ = = 0.417 e Å$^{-3}$, $\Delta\rho_{min}$ = −0.232 e Å$^{-3}$.

**3-(α-Bromoacetyl)-4-hydroxycoumarin (7a).** Bromine (18.9 g, 6.1 mL, 0.115 mol), which was dissolved in acetic acid (5 mL), was added dropwise with stirring (as the solution turned colorless) to a solution of 3-acetyl-4-hydroxycoumarin **2** (see Ref. 17) (20 g, 0.098 mol) in warm glacial acetic acid (70 mL). The reaction mixture was heated to 100 °C. After 10 min, the bromine color completely disappeared. The reaction mixture was allowed to cool. The precipitate that formed was filtered off and recrystallized from acetic acid. The yield was 22.9 g (82.6%), m.p. 145—146 °C (*cf.* lit. data:[12] m.p. 145—146 °C). $^1$H NMR ($CDCl_3$), δ: 4.83 (s, 2 H, $CH_2$); 7.26—7.43 (m, 2 H, H(6), H(8)); 7.70—7.80 (m, 1 H, H(7)); 8.08 (dd, 1 H, H(5), $^2J_{5,6}$ = 8 Hz, $^2J_{5,7}$ = 2 Hz); 16.45 (s, 1 H, OH).

**4-Hydroxy-3-(α-iodoacetyl)coumarin (7b).** A solution of sodium iodide (0.53 g, 3.5 mmol) in acetone (5 mL) was added to a solution of compound **7a** (1 g, 3.5 mmol) in acetone (20 mL) at ~20 °C. The precipitate of sodium bromide that formed was filtered off. The reaction mixture was poured onto ice. The precipitate that formed was filtered off and dissolved in acetone. The product was reprecipitated with water and washed with acetone. The yield was 0.52 g (45%), m.p. 134—136 °C. $^1$H NMR ($CDCl_3$), δ: 4.72 (s, 2 H, $CH_2$); 7.30—7.39 (m, 2 H, H(6), H(8)); 7.70—7.73 (m, 1 H, H(7)); 8.08 (dd, 1 H, H(5), $^2J_{5,6}$ = 8 Hz, $^2J_{5,7}$ = 2 Hz); 16.87 (s, 1 H, OH). MS, $m/z$ ($I_{rel}$ (%)): 331 [M + 1]$^+$ (100), 330 [M]$^+$ (80). Found (%): C, 40.23; H, 2.18; I, 38.29. $C_{11}H_7IO_4$. Calculated (%): C, 40.03; H, 2.14; I, 38.45.

**4-Hydroxy-3-(α-thiocyanatoacetyl)coumarin (7c).** A solution of ammonium thiocyanate (0.27 g, 3.5 mmol) in acetone (5 mL) was added to a solution of compound **7a** (1 g, 3.5 mmol) in acetone (30 mL) at ~20 °C. The precipitate that formed was filtered off, and the filtrate was poured into water. The resulting precipitate was filtered off and washed with acetone. The yield was 0.97 g (80.8%), m.p. 145—147 °C. $^1$H NMR ($CDCl_3$), δ: 4.59 (s, 2 H, $CH_2$); 7.30—7.45 (m, 2 H, H(6), H(8)); 7.75—7.83 (m, 1 H, H(7)); 8.11 (dd, 1 H, H(5), $^2J_{5,6}$ = 8 Hz, $^2J_{5,7}$ = 2 Hz); 15.91 (s, 1 H, OH). MS, $m/z$ ($I_{rel}$ (%)): 261 [M + 1]$^+$ (100). Found (%): C, 55.37; H, 2.72; N, 5.30; S, 12.40. $C_{12}H_7NO_4S$. Calculated (%): C, 55.17; H, 2.70; N, 5.36; S, 12.27.

**2,3-Dihydrofuro[3,2-*c*]coumarin-3-one (5).** An equimolar amount of sodium cyanide (potassium carbonate, sodium carbonate, aniline, or diethylamine; see Scheme 2) was added with stirring to a solution of compound **7a** (14 g, 0.05 mol) in DMSO (100 mL). After 10 min, the reaction mixture was poured onto ice. The precipitate that formed was filtered off and recrystallized from ethanol. The yield was 9 g (80%), m.p. 227—228 °C (*cf.* lit. data:[12] m.p. 227.5—228.5 °C). $^1$H NMR ($CDCl_3$), δ: 4.86 (s, 2 H, —$CH_2$—); 7.25—7.40 (m, 2 H, H(6), H(8)); 7.77—7.87 (m, 1 H, H(7)); 7.95 (dd, 1 H, H(5), $J_{5,6}$ = 8 Hz, $J_{5,7}$ = 1 Hz). MS, $m/z$ ($I_{rel}$ (%)): 203 [M + 1]$^{+\bullet}$ (100).

**Condensation of ketone 5 with aromatic aldehydes (general procedure).** Ketone **5** (0.3 g, 1.5 mmol) was dissolved with heating in glacial acetic acid. A solution of the corresponding aldehyde (0.002 mol) in acetic acid (3 mL) and concentrated sulfuric acid (0.1 mL) were added dropwise. The mixture was refluxed for 1 h and then cooled. The precipitate that formed was filtered off, washed with acetic acid, and recrystallized from acetic acid.

**(2*Z*)-2-Benzylidene-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8a).** The yield was 0.3 g (69%), m.p. 226—228 °C. $^1$H NMR ($CDCl_3$), δ: 7.09 (s, 1 H); 7.40—7.60 (m, 5 H, H(8), H(6), H(3′), H(5′), H(4′)); 7.75—7.95 (m, 3 H, H(7), H(2′), H(6′)); 8.07 (d, 1 H, H(9), $J_{9,8}$ = 8 Hz). MS, $m/z$ ($I_{rel}$ (%)): 291 [M + 1]$^+$ (100). Found (%): C, 74.97; H, 3.41. $C_{18}H_{10}O_4$. Calculated (%): C, 74.48; H, 3.47.

**(2*Z*)-2-(2′-Chlorobenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8b).** The yield was 0.31 g (63%), m.p. 231—233 °C. $^1$H NMR ($CDCl_3$), δ: 7.26—7.56 (m, 6 H, H(8), H(6), H(4′), H(5′), H(6′), CH); 7.79—7.84 (m, 1 H, H(7)); 8.05 (d, 1 H, H(9), $J_{9,8}$ = 8 Hz); 8.20 (m, 1 H, H(3′)). MS, $m/z$ ($I_{rel}$ (%)): 325 [M + 1]$^+$ (100), 326 [M + 2]$^+$ (90), 324 [M] (10), 327 [M + 3]$^+$ (13). Found (%): C, 66.59; H, 2.89; Cl, 11.04. $C_{18}H_9ClO_4$. Calculated (%): C, 66.58; H, 2.79; Cl, 10.92.

**(2*Z*)-2-(4′-Nitrobenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4-(2*H*)-dione (8c).** The yield was 0.23 g (45.5), m.p. >320 °C. $^1$H NMR (DMSO-$d_6$), δ: 7.24 (s, 1 H, CH); 7.60 (m, 2 H, H(8), H(6)); 7.97 (m, 1 H, H(7)); 8.33 (m, 5 H, H(9), H(2′), H(3′), H(5′), H(6′)). MS, $m/z$ ($I_{rel}$ (%)): 336 [M + 1]$^+$ (100), 337

* The single-crystal X-ray diffraction study of **8j** · $H_2O$ was performed also at room temperature. It was found that the crystal system and molecular geometry of compound **8j** remained unchanged. The low-temperature experiment allowed us to more precisely determine the disorder of the water molecule, the possible positions of its H atoms, and the intermolecular hydrogen bonds with the participation of these atoms. Principal crystallographic data for compound **8j** · $H_2O$ at 293 K: $C_{20}H_{15}NO_4 \cdot H_2O$, $M$ = 351.35, orthorhombic system, space group *Pnma*, $a$ = = 9.262(2) Å, $b$ = 6.666(1) Å, $c$ = 28.045(6) Å, $V$ = 1731.5(6) Å$^3$, $Z$ = 4.

$[M + 2]^+$ (17), 335 [M] (10). Found (%): C, 64.40; H, 2.51; N, 4.10. $C_{18}H_9NO_6$. Calculated (%): C, 64.48; H, 2.71; N, 4.18.

**(2*Z*)-2-(4´-Methoxybenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8d).** The yield was 0.32 g (66%), m.p. 227—228 °C. $^1$H NMR ($CDCl_3$), δ: 3.90 (s, 3 H, OMe); 7.00 (s, 1 H, CH); 7.04 (d, 2 H, H(2´), H(4´), $J_{4´,5´}$ = 1.5 Hz); 7.44—7.52 (m, 2 H, H(8), H(6)); 7.81—7.87 (m, 3 H, H(7), H(1´), H(5´)); 8.07 (d, 1 H, H(9), $J_{9,8}$ = 8 Hz). MS, *m/z* ($I_{rel}$ (%)): 321 $[M + 1]^+$ (100). Found (%): C, 71.10; H, 3.55. $C_{19}H_{12}O_5$. Calculated (%): C, 71.25; H, 3.78.

**(2*Z*)-2-(3´-Bromo-4´-methoxybenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8e).** The yield was 0.2 g (34.2%), m.p. 307—308 °C. $^1$H NMR (DMSO-$d_6$), δ: 3.97 (s, 3 H, OMe); 7.13 (s, 1 H, CH); 7.30 (d, 1 H, H(5´), $J_{5´,6´}$ = 8.79 Hz); 7.61 (m, 2 H, H(8), H(6)); 7.96 (m, 1 H, H(7)); 8.16—8.24 (m, 3 H, H(9), H(2´), H(6´)). MS, *m/z* ($I_{rel}$ (%)): 399 $[M + 1]^+$ (100), 401 [M + 2] (80), 400 $[M + 3]^+$ (25), 398 [M] (5). Found (%): C, 57.01; H, 2.69; Br, 19.42. $C_{19}H_{11}BrO_5$. Calculated (%): C, 57.17; H, 2.78; Br, 20.02.

**(2*Z*)-2-(3´,4´,5´-Trimethoxybenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8f).** The yield was 0.23 g (41%), m.p. >328 °C. $^1$H NMR ($CDCl_3$), δ: 3.95 (s, 3 H, OMe); 3.98 (s, 6 H, 2 OMe); 7.03 (s, 1 H, CH); 7.18 (s, 2 H, H(2´), H(6´)); 7.47—7.51 (m, 2 H, H(8), H(6)); 7.82 (m, 1 H, H(7)); 7.92 (d, 1 H, H(9), $J_{9,8}$ = 8 Hz). MS, *m/z* ($I_{rel}$ (%)): 381 $[M + 1]^+$ (100), 382 $[M + 2]^+$ (10), 380 [M] (7). Found (%): C, 66.23; H, 4.37. $C_{21}H_{16}O_7$. Calculated (%): C, 66.32; H, 4.24.

**(2*Z*)-2-(2´-Hydroxy-3´-methoxybenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8g).** The yield was 0.1 g (20.5%), m.p. 262—263 °C. $^1$H NMR (DMSO-$d_6$), δ: 3.85 (s, 3 H, OMe); 6.97 (m, 1 H, H(5´)); 7.11 (d, 1 H, H(3), $J_{4´,5´}$ = 8.33 Hz); 7.37 (s, 1 H, CH); 7.52—7.59 (m, 2 H, H(8), H(6)); 7.8 (d, 1 H, H(6´), $J_{6´,5´}$ = 7.86 Hz); 7.93 (m, 1 H, H(7)); 8.21 (d, 1 H, H(9), $J_{9,8}$ = 8 Hz); 9.76 (s, 1 H, OH). MS, *m/z* ($I_{rel}$ (%)): 337 $[M + 1]^+$ (100). Found (%): C, 67.39; H, 3.80. $C_{19}H_{12}O_6$. Calculated (%): C, 67.86; H, 3.60.

**(2*Z*)-2-(6´-Chloro-2´,4´-dimethoxybenzylidene)-4*H*-furo-[3,2-*c*]chromene-3,4(2*H*)-dione (8h).** The yield was 0.32 g (55.4%), m.p. 293—295 °C. $^1$H NMR (DMSO-$d_6$), δ: 3.89 (s, 3 H, OMe); 3.98 (s, 3 H, OMe); 7.17 (s, 1 H, CH); 7.25 (s, 1 H, H(3´)); 7.55—7.62 (m, 2 H, H(8), H(6)); 7.84 (s, 1 H, H(5´)); 7.80—8.20 (m, 2 H, H(9), H(7´)). MS, *m/z* ($I_{rel}$ (%)): 385 $[M + 1]^+$ (100), 386 $[M + 2]^+$ (20). Found (%): C, 61.85; H, 3.39. $C_{20}H_{13}ClO_6$. Calculated (%): C, 62.43; H, 3.41.

**(2*Z*)-2-(5´-Bromo-2´-methoxybenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8i).** The yield was 0.22 g (37%), m.p. >330 °C. $^1$H NMR ($CDCl_3$), δ: 3.70 (s, 3 H, OMe); 6.68 (d, 1 H, H(3´), $J_{3´,4´}$ = 8 Hz); 7.35—7.25 (m, 4 H, H(6), H(8), H(4´), CH); 7.62 (m, 1 H, H(7)); 7.81 (d, 1 H, H(9), $J_{9,8}$ = 8 Hz); 8.08 (d, 1 H, H(6´), *J* = 2 Hz). MS, *m/z* ($I_{rel}$ (%)): 399 [M] (100), 401 $[M + 2]^+$ (90), 402 $[M + 3]^+$ (24), 400 $[M + 1]^+$ (10). Found (%): C, 57.74; H, 2.50. $C_{19}H_{11}BrO_5$. Calculated (%): C, 57.17; H, 2.78.

**(2*Z*)-2-[4´-(Dimethylamino)benzylidene]-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8j).** The yield was 0.2 g (40%), m.p. 214—216 °C. $^1$H NMR (acetone-$d_6$), δ: 3.13 (s, 6 H, $NMe_2$); 6.80—7.00 (m, 3 H, H(2´), H(6´), CH); 7.46—7.62 (m, 2 H, H(8), H(6)); 7.69 (m, 3 H, H(7), H(3´), H(5´)); 8.25 (d, 1 H, H(9), $J_{9,8}$ = 8.54 Hz). MS, *m/z* ($I_{rel}$ (%)): 334 $[M + 1]^+$ (100), 335 $[M + 2]^+$ (10). Found (%): C, 71.59; H, 4.69; N, 3.9. $C_{20}H_{15}NO_4$. Calculated (%): C, 72.06; H, 4.54; N, 4.20.

**(2*Z*)-2-(3´-Chlorobenzylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (8k).** The yield was 0.09 g (19%), m.p. 242—244 °C. $^1$H NMR ($CDCl_3$), δ: 7.02 (s, 1 H, CH); 7.48—7.58 (m, 4 H, H(8), H(6), H(4´), H(6´)); 7.80—7.70 (m, 1 H, H(5´)); 7.86 (m, 1 H, H(7)); 7.94 (d, 1 H, H(2´), $^4J_{2´,4´}$ = 2.13 Hz); 8.07 (d, 1 H, H(9), $J_{9,8}$ = 8 Hz). MS, *m/z* ($I_{rel}$ (%)): 325 $[M + 1]^+$ (100), 327 $[M + 3]^+$ (25), 326 $[M + 2]^+$ (20). Found (%): C, 66.09; H, 2.58; Cl, 11.32. $C_{18}H_9ClO_4$. Calculated (%): C, 66.58; H, 2.79; Cl, 10.92.

**(2*Z*)-2-(2´,4´-Dimethoxybenzylidene)-4*H*-furo[3,2-*c*]-chromene-3,4(2*H*)-dione (8l).** The yield was 0.28 g (53%), m.p. 294—296 °C. $^1$H NMR ($CDCl_3$), δ: 3.88 (s, 3 H, OMe); 3.89 (s, 3 H, OMe); 6.48 (d, 1 H, H(3´), $^4J_{3´,5´}$ = 2.13 Hz); 6.66 (dd, 1 H, H(5´), $^4J_{5´,3´}$ = 2.13 Hz, $^3J_{5´,6´}$ = 8.86 Hz); 7.37—7.52 (m, 2 H, H(6), H(8)); 7.56 (s, 1 H, CH); 7.80 (m, 1 H, H(7)); 8.16 (d, 1 H, H(6´), $J_{6´,5´}$ = 8.85 Hz); 8.50 (d, 1 H, H(9), $J_{9,8}$ = = 7.94 Hz). MS, *m/z* ($I_{rel}$ (%)): 351 $[M + 1]^+$ (100). Found (%): C, 68.79; H, 3.96. $C_{20}H_{14}O_6$. Calculated (%): C, 68.57; H, 4.03.

**(2*Z*)-2-(2´-Thienylmethylidene)-4*H*-furo[3,2-*c*]chromene-3,4(2*H*)-dione (9a).** The yield was 0.16 g (36.6%), m.p. 254—256 °C. $^1$H NMR ($CDCl_3$), δ: 7.23 (t, 1 H, H(4´)); 7.38 (s, 1 H, CH); 7.46—7.56 (m, 2 H, H(6), H(8)); 7.65 (d, 1 H, H(5´), $J_{5,4}$ = 4.61 Hz); 7.78 (d, 1 H, H(3´), $J_{3,4}$ = 5.57 Hz); 7.86 (m, 1 H, H(7)); 8.12 (d, 1 H, H(9), $J_{9,8}$ = 7.7 Hz). MS, *m/z* ($I_{rel}$ (%)): 297 $[M + 1]^+$ (100), 298 $[M + 2]^+$ (18). Found (%): C, 64.86; H, 2.72; S, 10.82. $C_{16}H_8O_4S$. Calculated (%): C, 64.69; H, 2.78; S, 10.97.

**(2*Z*)-2-[(4´-Bromo-2´-thienyl)methylidene]-4*H*-furo[3,2-*c*]-chromene-3,4(2*H*)-dione (9b).** The yield was 0.26 g (46.7%), m.p. 276—278 °C. $^1$H NMR (DMSO-$d_6$), δ: 7.49 (s, 1 H, CH); 7.55—7.61 (m, 2 H, H(8), H(6)); 7.81 (d, 1 H, H(3´), $J_{3´,5´}$ = = 1.4 Hz); 7.96 (m, 1 H, H(7)); 8.06—8.16 (m, 2 H, H(5´), H(9´)). MS, *m/z* ($I_{rel}$ (%)): 377 $[M + 1]^+$ (100), 375 $[M - 1]^+$ (98), 376 [M] (23), 378 $[M + 2]^+$ (22). Found (%): C, 51.41; H, 1.89; Br, 21.32; S, 8.59. $C_{16}H_7BrO_4S$. Calculated (%): C, 51.22; H, 1.88; Br, 21.30; S, 8.55.

**(2*E*,2´*Z*)-2´-(5´-Bromo-2´-hydroxybenzylidene)-4*H*,4´*H*-2,3´-bifuro[3,2-*c*]chromenylidene-3,4,4´-trione (13).** Ketone **5** (0.3 g, 1.5 mmol) was dissolved with heating in glacial acetic acid, and a solution of the corresponding aldehyde (2 mmol) in acetic acid (3 mL) was added dropwise followed by the addition of concentrated sulfuric acid (0.1 mL), after which a precipitate immediately formed. The reaction mixture was refluxed for 1 h and then cooled. The precipitate that formed was filtered off, washed with acetic acid, and recrystallized from acetic acid. The yield was 0.16 g (27%), m.p. >315 °C. $^1$H NMR ($CF_3COOD$), δ: 7.66—7.85 (m, 5 H, H(8), H(8´), H(6´), H(6), H(3″)); 8.11—8.79 (m, 3 H, H(7´), H(7), H(4″)); 8.20—8.50 (m, 3 H, H(9), H(9´), H(6″)); 9.53 (s, 1 H, CH) (the absence of the signal of the OH group is associated with the effect of the solvent $CF_3COOD$). MS, *m/z* ($I_{rel}$ (%)): 567 $[M - 2]^+$ (100), 569 [M] (99), 568 $[M - 1]^-$ (25), 570 $[M + 1]^+$ (23). Found (%): C, 60.60; H, 2.10. $C_{29}H_{13}BrO_8$. Calculated (%): C, 61.18; H, 2.30.

**2,3´-Bi(furo[3,2-*c*]chromene)-3,4,4´-trione (10).** A mixture of ketone **5** (0.93 g, 4.6 mmol), glacial acetic acid (12 mL), and concentrated hydrochloric acid (6 mL) was refluxed for 3 h. The precipitate that formed was filtered off, washed with hot acetone, and recrystallized from DMSO. The yield was 0.71 g (80%), dark claret crystals, m.p. 310 °C (decomp.). $^1$H NMR (DMSO-$d_6$), δ: 6.50 (s, 1 H, H(2)); 7.30—7.60 (m, 4 H, H(8), H(6), H(8´), H(6´)); 7.70—8.20 (m, 4 H, H(9), H(7), H(9´), H(7´)); 8.52 (s, 1 H, H(2´)). MS, *m/z* ($I_{rel}$ (%)): 387 $[M + 1]^+$ (100).

Found (%): C, 67.77; H, 2.60. $C_{22}H_{10}O_7$. Calculated (%): C, 68.40; H, 2.61.

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