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# New Fluoroaryl-containing β,β'-Dioxoesters in the Synthesis of Fluorobenzopyran-2(4)-ones*

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**Abstract**—For the first time were obtained ethyl 2-(2-methoxy-3,4,5,6-tetrafluorobenzoyl)-3-oxobutanoate and ethyl 2-pentafluorobenzoyl-3-oxobutanoate and their copper chelates. The compounds were prepared by acylation of ethyl acetoacetate with 2-methoxy-3,4,5,6-tetrafluoro- and pentafluorobenzoyl chlorides. Cyclization of these β,β'-dioxoesters afforded substituted chromones. 2-Methyl-5-methoxy-6,7,8-trifluoro-3-ethoxycarbonylchromone hydrolyzes depending on reaction conditions either to 5-hydroxy-2-methyl-6,7,8-trifluorochromone or to 5-hydroxy-2-methyl-6,7,8-trifluorochromone-3-carboxylic acid. Reaction with morpholine provided 7-substituted product, and with aqueous ammonia as a result of rearrangement forms 3-acetimidoyl-4-hydroxy-5-methoxy-6,7,8-trifluorocoumarin. Hydrolysis of the latter yields 3-acetyl-4-hydroxy-5-methoxy-6,7,8-trifluorocoumarin.

The coumarin and chromone fragments are known to be found both in natural and synthetic biologically active compounds. Therefore creation of new representatives of this class compounds is promising. One of the preparation methods for fluoro-containing benzopyran-2(4)-ones consists in acylation of various β-oxoesters with pentafluorobenzoyl chloride [1, 2]. We developed a method for modification of the fluoroaryl component by selective ortho-methoxylation of pentaflurobenzoic acid that afforded depending on the reaction conditions 2-methoxy-3,4,5,6-tetrafluoro- or 2,6-dimethoxy-3,4,5-trifluorobenzoic acids in good yields [3]. We recently demonstrated that the acylation of ethyl acetoacetate with 2,6-dimethoxy-3,4,5-trifluorobenzoyl chloride gave rise to the corresponding β,β'-dioxoester that on prolonged heating i hydrobromic acid cyclized into 5-hydroxy-2-methyl-6,7,8-trifluorochromone [4].

In extension of these studies in the present paper is reported on acylation of ethyl acetoacetate with 2-methoxy-3,4,5,6-tetrafluorobenzoyl chloride. 2-Methoxy-3,4,5,6-tetrafluorobenzoic acid (**Ia**) was previously obtained by us [3] as crude uncharacterized substance (~90% of the main compound combined with hard-to-separate impurities). An analytically pure sample of **Ia** was obtained on hydrolysis of its chloride **IIa**. Hydrolysis of acyl chloride IIa occurs rapidly and quantitatively in water solution of sodium hydrogen carbonate, but in water the compound does not appreciably change for a week. The preparation of 2-methoxy-3,4,5,6-tetrafluorobenzoyl chloride (**IIa**) did not require additional purification of crude acid **Ia**, and it was obtained by heating the crude acid with excess phosphorus pentachloride.

The acylation of ethyl acetoacetate with benzoyl chloride **IIa** in the presence of magnesium ethylate affords the corresponding β,β'-dioxoester **IIIa** as occurs with the use as acylation agent of 2,6-dimethoxy-3,4,5-trifluorobenzoyl chloride [4]. Note that similar reaction with pentafluorobenzoyl chloride (**IIb**) results in 2-methyl-5,6,7,8-tetrafluoro-3-ethoxycarbonylchromone [1]. Treating β,β'-dioxoester **IIIa** with a water solution of copper(II) acetate afforded copper chelate **IVa** (Scheme 1). The same chelate can be obtained directly from ethyl acetoacetate and benzoyl chloride **IIa** without intermediate isolation of β,β'-dioxoester **IIIa** by treating the reaction mixture with copper(II) acetate. Treatment of copper chelate **IVa** with hydrochloric acid furnishes free compound **IIIa** in quantitative yield. Unlike the previously obtained ethyl 3-(2,6-dimethoxy-3,4,5-trifluorobenzoyl)-2-oxobutanoate ββ'-dioxoester **IIIa** cyclizes into 2-methyl-5-methoxy-6,7,8-trifluoro-3-ethoxycarbonylchromone (**Va**) at distilling in a vacuum at 220°C or at heating in DMSO to 100°C (Scheme 1). Chromone **Va** can be obtained from chelate **IVa** but in a notably lower yield due to strong tarring.

It turned out that the use of chelating in acylation of ethyl acetoacetate with pentafluorobenzoyl chloride (**IIb**) afforded copper chelate of ethyl 2-pentafluoro-

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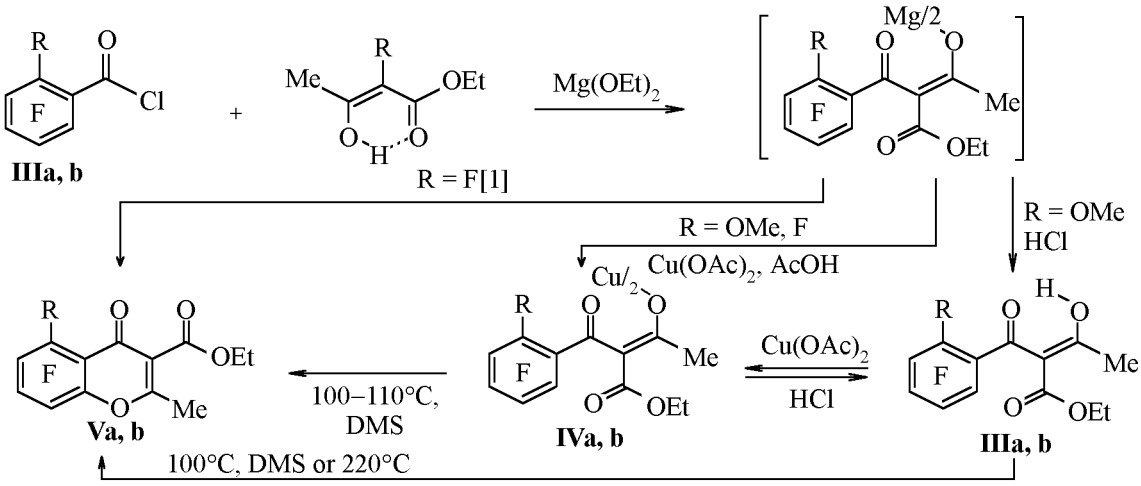
**Scheme 1.**




R = OMe (**a**), F (**b**).

benzoyl-3-oxobutanoate (**IVb**) (Scheme 1). The treatment of the latter with hydrogen chloride provided β,β'-dioxoester **IIIb**, although formerly had been assumed [1] that it was impossible to isolate this compound due its instability and cyclization into 2-methyl-3-ethoxycarbonyl-5,6,7,8-tetrafluorochromone (**Vb**) resulting from elimination of the *ortho*-fluorine. β,β'-Dioxoester **IIIb** easily undergoes cyclization at heating to 100–110°C in DMSO solution or without solvents. Unlike its monomethoxy-substituted analog **IVa** chelate **IVb** at heating in DMSO undergoes cyclization into chromone **Vb**.

β,β'-Dioxoesters **IIIa, b** may undergo the keto-enol tautomerism, therefore presumably they may exist in four tautomeric forms.

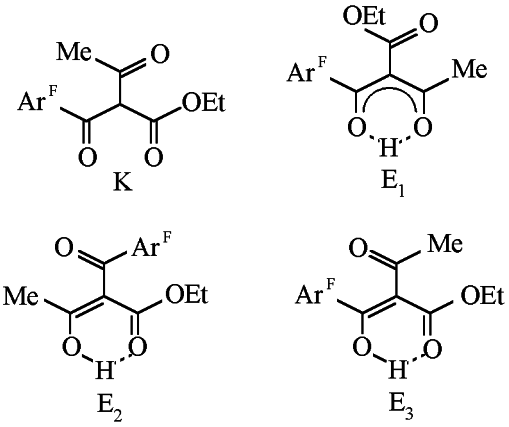



**Table 1.** Elemental analyses of compounds synthesized

| Compd. no. | Found, % | | | Formula | Calculated, % | | |
|---|---|---|---|---|---|---|---|
| | C | H | F | | C | H | F |
| Ia | 42.87 | 1.80 | 33.75 | $C_8H_4F_4O_3$ | 42.91 | 1.94 | 33.91 |
| IIa | 39.81 | 1.34 | 30.70 | $C_8H_3ClF_4O_2$ | 39.76 | 1.25 | 31.45 |
| IIIa | 50.16 | 3.86 | 22.71 | $C_{14}H_{12}F_4O_5$ | 50.01 | 3.60 | 22.60 |
| IIIb | 47.93 | 2.73 | 29.15 | $C_{13}H_9F_5O_4$ | 48.16 | 2.80 | 29.30 |
| IVa | 46.06 | 3.15 | 20.56 | $C_{28}H_{22}CuF_8O_{10}$ | 45.81 | 3.02 | 20.71 |
| IVb | 43.89 | 2.22 | 26.70 | $C_{26}H_{16}CuF_{10}O_8$ | 43.99 | 2.27 | 26.76 |
| Va | 53.11 | 3.49 | 17.99 | $C_{14}H_{11}F_3O_5$ | 53.17 | 3.51 | 18.02 |
| VI[a] | 56.41 | 5.15 | 9.83 | $C_{18}H_{19}F_2NO_6$ | 56.40 | 5.00 | 9.91 |
| VII[b] | 50.22 | 2.72 | 19.85 | $C_{12}H_8F_3NO_4$ | 50.19 | 2.81 | 19.85 |
| VIII | 50.23 | 2.54 | 19.56 | $C_{12}H_7F_3O_5$ | 50.01 | 2.45 | 19.78 |
| X | 48.23 | 1.85 | 20.52 | $C_{11}H_5F_3O_5$ | 48.19 | 1.84 | 20.79 |

[a] % N: [a] Found 3.64, calculated 3.65; [b] Found 4.93, calculated 4.88.

**Table 2.** Yields, physical constants, and spectral characteristics of compounds synthesized

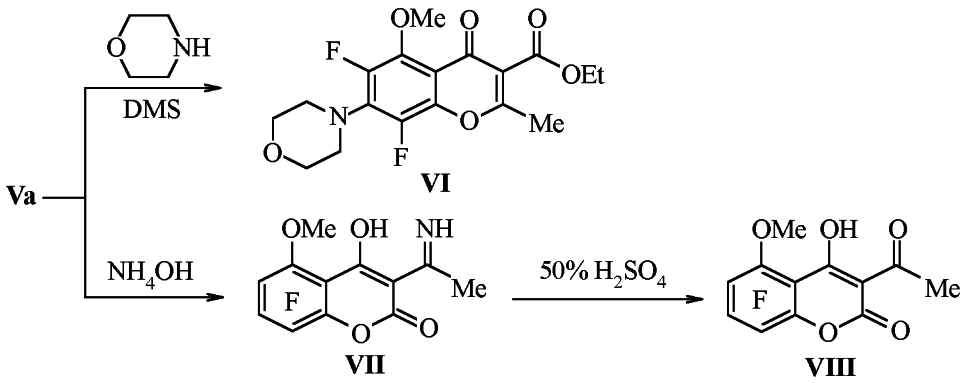
| Compd. no. | Yield, % | mp, °C (bp, °C) *p*, mm Hg) | IR spectrum, ν, $cm^{-1}$ | NMR spectra (in $CDCl_3$), δ, ppm, *J*, Hz | |
|---|---|---|---|---|---|
| | | | | $^1H$ | $^{19}F$ |
| **Ia** | 98 | 87–88 | 3080 (OH), 1725 ($CO_2H$), 1645, 1520, 1490 (C=C arom), 1030 (C–F) | 9.07 br.s (1H, $CO_2H$), 4.05 d [3H, $OCH_3$, $J(CH_3–F^3)$ 1.9] | –140.11 d.d.d ($F^6$), –151.14 d.t ($F^4$), –155.88 d.d.q ($F^3$), –162.68 d.d ($F^5$) $J_{5,6}= J_{6,5}= 22.5$, $J_{5,4}= J_{4,5}= J_{4,3}= J_{4,3}= 20.5$, $J_{6,3}= J_{3,6}= 9.3$, $J_{6,4}= J_{4,6}= 4.4$, $J_{5,3}= J_{3,5}= 0$, $J(F^3–CH_3)$ 1.9 |
| **IIa** | 88 | 70–90/3 | 1770 (COCl), 1630, 1510, 1490 (C=C arom), 1020 (C–F) | 4.13 d [3H, $OCH_3$, $J(CH_3–F^3)$ 2.4] | –141.40 d.d.d ($F^6$), –149.63 d.t ($F^4$), –154.01 d.d.q ($F^3$), –162.75 d.d ($F^5$) $J_{6,5}= J_{5,6}= 22.0$, $J_{6,3}= J_{3,6}=$ 9.3, $J_{6,4}= J_{4,6}= 4.9$, $J_{4,5}=$ $J_{5,4}= J_{4,3}= J_{3,4}= 20.0$, $J_{3,5}= 0$ $J(F^3–CH_3)$ 2.4 |
| **IIIa** | 79[a], 95[b] | Oily substance | 2970, 2930 (OH), 1715 (C=O), 1640, 1570 (C=O, C=C), 1510, 1485 (C=C arom), 1020 (C–F) | $E_1:E_2$ = 7:1 $E_1$: 17.55 s (1H, OH), 4.05 q [2H, $O\underline{C}\underline{H}_2CH_3$, $J(CH_2–CH_3)$ 7.1], 3.94 d [3H, $OCH_3$, $J(CH_3–F^3)$ 2.0], 2.54 s (3H, $CH_3$), 1.05 t [3H, $OCH_2\underline{C}\underline{H}_3$, $J(CH_3–CH_2)$ 7.1] $E_2$: 14.61 s (1H, OH), 4.10 q [2H, $O\underline{C}\underline{H}_2CH_3$, $J(CH_2–CH_3)$ 7.1], 3.89 br.s (3H, $OCH_3$), 2.46 s (3H, $CH_3$), 1.10 t [3H, $OCH_2\underline{C}\underline{H}_3$, $J(CH_3–CH_2)$ 7.1] | $E_1:E_2$ = 7:1 $E_1$: –144.18 d.d.d ($F^6$), –155.13 t.d ($F^4$), –157.23 d.d.q ($F^3$), –164.42 d.d.d ($F^5$) $E_2$: –145.82 d.d.d ($F^6$), –156.22 t.d ($F^4$), –157.23 d.d.q ($F^3$), –164.42 d.d.d ($F^5$) $J_{6,5}= J_{5,6}= 23.0$, $J_{6,3}= J_{3,6}=$ = 8.8, $J_{6,4}= J_{4,6}= 2.0$, $J_{4,5}= J_{5,4}=$ $J_{4,3}= J_{3,4}= 20.0$, $J_{3,5}= J_{5,3}= 0$ |
| **IIIb** | 99 | Oily substance | 2930 (OH), 1710 (C=O), 1650, 1570 (C=O, C=C), 1520, 1500 (C=C arom), 985 (C–F) | $E_1:E_2$ = 4:1 $E_1$: 17.44 s (1H, OH), 4.10 q [2H, $O\underline{C}\underline{H}_2CH_3$, $J(CH_2–CH_3)$ 7.1], 1.12 t [3H, $OCH_2\underline{C}\underline{H}_3$, $J(CH_3–CH_2)$ 7.1], 2.57 s (3H, $CH_3$) $E_2$: 14.65 s (1H, OH), 4.40 q [2H, $O\underline{C}\underline{H}_2CH_3$, $J(CH_2–CH_3)$ 7.1], 1.39 t [3H, $OCH_2\underline{C}\underline{H}_3$, $J(CH_3–CH2$ 7.1], 2.47 s (3H, $CH_3$) | $E_1:E_2$ = 4:1 $E_1$: –142.79 m (2F), –153.05 m (1F), –161.89 m (2F) $E_2$: –144.58 m (2F), –153.96 m (1F), –165.93 m (2F) |

**Table 2.** (Contd.)

| Compd. no. | Yield, % | mp, °C (bp, °C) *p*, mm Hg) | IR spectrum, ν, $cm^{-1}$ | NMR spectra (in $CDCl_3$), δ, ppm, *J*, Hz | |
|---|---|---|---|---|---|
| | | | | $^1H$ | $^{19}F$ |
| **VIa** | 78[a], 89[b] | 135–139 | 1700 (C=O), 1615, 1590 (C=O, C=C), 1490, 1450, 1400 (C=C arom), 1025 (C–F) | – | – |
| **VIb** | 29 | 162–164 | 1680 (C=O), 1630, 1580 (C=O, C=C), 1495, 1450, 1430 (C=C), 980 (C–F) | – | – |
| **Va**[c] | 39 | 66–68 | 1735 ($CO_2Et$), 1660 (C=O), 1630 (C=C), 1485, 1115 (C=C arom), 1020 (C–F) | 4.35 q [2H, $OC\underline{H}_2CH_3$, $J(CH_2\text{-}CH_3)$ 7.1], 3.96 d [3H, $OCH_3$, $J(CH_3\text{–}F^6)$ 0.8], 2.47 c (3H, $CH_3$), 1.35 t [3H, $OCH_2C\underline{H}_3$, $J(CH_3\text{-}CH_2)$ 7.1] | –150.49 d.d ($F^7$), –156.36 d ($F^6$), –159.58 d ($F^8$) $J_{7,6}= J_{6,7}= 21.0$, $J_{7,8}= J_{8,7}= 20.0$, $J_{6,8} = J_{8,6} = 0$ |
| **VI** | 68 | 90–92 | 1700 ($CO_2Et$), 1650 (C=O), 1600, 1550 (C=C), 1010 (C–F) | 4.32 q [2H, $OC\underline{H}_2CH_3$, $J(CH_2\text{-}CH_3)$ 7.1], 3.87 s (3H, $OCH_3$), 3.84–3.79 m (4H, $2CH_2$), 3.44–3.38 m (4H, $2CH_2$), 2.42 s (3H, $CH_3$), 1.35 t [3H, $OCH_2C\underline{H}_3$, $J(CH_3\text{-}CH_2)$ 7.1] | –143.08 d ($F^6$), –148.17 m ($F^8$) $J_{6,8} = J_{8,6} = 4.1$ |
| **VII**[c] | 83 | 217–222 | 3160, 2940 (NH, OH), 1650 (C=O), 1610, 1515, 1480 (C=C), 1040 (CF) | 12.81 br.s (1H, OH), 6.70 br.s (1H, NH), 4.0 d [3H, $OCH_3$, $J(CH_3\text{–}F)$ 1.2], 2.71 s (3H, $CH_3$) | –150.31 t ($F^7$), –159.04 d ($F^8$), –160.04 d ($F^6$) $J_{6,7}= J_{7,6}= J_{7,8}= J_{8,7}= 21$, $J_{6,8}= J_{8,6} = 0$ |
| **VIII** | 50 | 101–103 | 3430 (OH), 1750 (C=O), 1640 (C=O), 1580, 1520 (C=C), 1040 (CF) | 18.65 br.s (1H,OH), 4.04 d [3H, $OCH_3$, $J(CH_3\text{–}F^6)$ 1.5], 2.78 s (3H, $CH_3$) | –145.70 t ($F^7$), –156.92 d.d ($F^6$), –159.18 d ($F^8$) $J_{7,6}= J_{6,7}= 21.5$, $J_{7,8}= J_{8,7}= 21.1$, $J_{6,8} = J_{8,6} = 0$, $J(F^6\text{–}CH_3)$ 1.5 |
| **X** | 77[a], 49[b] | 158–160 | 3100, 2720 (OH), 1750 ($CO_2H$), 1665 (C=O), 1575, 1510 (C=C arom), 1010 (CF) | 12.88 br.s (1H, $CO_2H$), 11.29 s (1H, OH), 3.1 s (3H, $CH_3$) | –142.95 t ($F^7$), –159.82 d.d ($F^6$), –165.92 d.d ($F^8$) $J_{7,6}= J_{6,7}= J_{7,8}= J_{8,7}= 20.7$, $J_{6,8}= J_{8,6} = 3.0$ |

[a] Yields by method *a*. [b] Yields by method *b*. [c] NMR spectra in $CD_3COCD_3$.

**Scheme 2.**




The structure of compounds **IIIa, b** was established from the data of NMR spectroscopy, published values of chemical shifts and rules of their changes in the series of β-di and β,β'-tricarbonyl compounds. This information was supplemented with the spectral characteristics of ethyl 2-(2,6-dimethoxy-3,4,5-trifluorobenzoyl)-2-oxobutanoate (**IIIc**) that were published by us in [4]. In the $^{1}H$ and $^{19}F$ NMR spectra of dioxoesters **IIIa–c** appear two sets of signals. Virtually total lack in the $^{1}H$ NMR spectra of methine proton signals corresponding to oxo form, and the presence of two enol proton peaks evidence that the β,β'-dioxoethers **IIIa–c** exist as two enol tautomers. The signals of enol protons appear in the downfield region of the $^{1}H$ NMR spectra with characteristic chemical shifts.

The resonance at ~17 ppm can be assigned to enol form $E_1$ with nonbonded ester group for similar chemical shifts have signals from enol form of β-diketone type from a series of methyl 2-acetylbenzoylacetates [5] and 2-acetylbenzoylmethanes [6]. On the other hand, enol proton peak of the cis-enol form of unsubstituted fluoroaryl(alkyl)-containing β-diketones in located in the ~14 ppm region [7]; however an electron-withdrawing substituent in *2*-position of the β-dicarbonyl compound (here an ester group) should cause a downfield shift of the enol proton as is actually observed.

The second enol form $E_2$ was selected from presumable tautomers $E_2$ and $E_3$ that should have close values of chemical shifts (~14 ppm) on the grounds of alteration of the positions of enol proton peak depending on the electronic characteristics of substituent in the aromatic ring. The downfield signal of enol proton shifts upfield in the case of electron-withdrawing substituent in the aryl ring in the ring-substituted benzoylacetones [8] and benzoylacetates [9]. β,β'-Dioxoesters **IIIa–c** are distinguished by the structure of the aromatic substituent, and the electron-withdrawing qualities of the substituent increase with increasing number of fluorine atoms and decreasing number of methoxy groups in the series **IIIc** < **IIIa** < **IIIb**. In this series of substituents the signal of ~14 ppm region shifts downfield, i.e. in the opposite direction to that observed in the series ring-substituted benzoylacetates and benzoylacetones. The observed direction of shift is characteristic at variation of electronic properties of a substituent located in the α-position of a β-dicarbonyl compound.

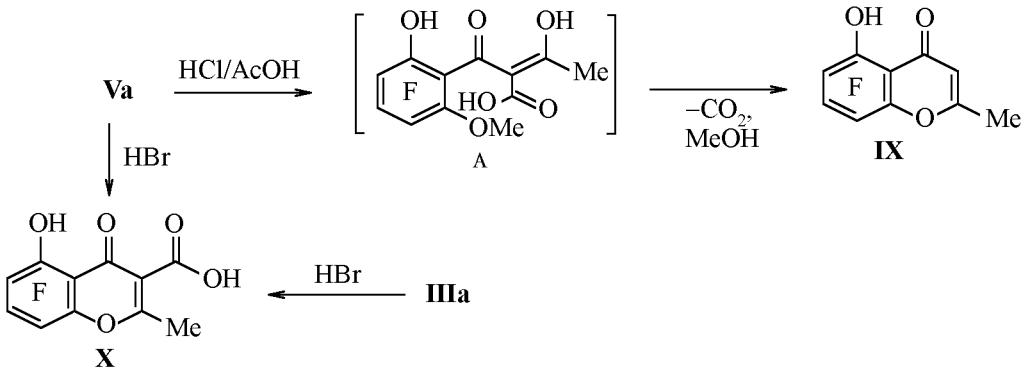
This relationship is also valid for enol proton signals from $E_1$ tautomer of compounds **IIIa–c**. Here as expected the hydroxy proton peak shifts upfield in the series **IIIc** – **IIIa** – **IIIb**.

A trend should be noted of increasing content of enol form $E_1$ with nonchelated ester group in the series of β,β'-dioxoesters **IIIb** – **IIIa** – **IIIc**, i.e., with decreasing electron-withdrawing properties of the aromatic substituent.

The study of chemical properties of chromone **Va** revealed its similarity in reactivity to the previously studied chromone **Vb** [10, 11]. For instance, compound **Va** with morpholine in DMSO affords 7-substituted compound **VI**. The substitution in *7* position was deduced from analysis of its $^{19}F$ NMR spectrum where appeared two doublet signals from two fluorine atoms with the coupling constant of 4.1 Hz indicating *meta*-position of fluorine atoms in the molecule of chromone **VI**. Thus the appearance of a substituent in *5* position of the chromone ring does not change the direction of its reaction with the secondary amines [10].

At boiling in aqueous ammonia chromone **Va** suffers acyl-lactone rearrangement yielding 3-acetimidoyl-4-hydroxy-5-methoxy-6,7,8-trifluorocoumarin (**VII**) (Scheme 2) analogously to reaction

**Scheme 3.**




of chromone **Vb** [11]. 3-Acetimidoylcoumarin (**VII**) on heating in the aqueous sulfuric acid affords 3-acetylcoumarin (**VIII**), and the methoxy group is not hydrolyzed under these conditions.

Chromone **Vb** was previously shown [11] to hydrolyze in acidic medium at the ester group, and with partial rearrangement formed 3-acetyl-5,6,7,8-tetrafluorocoumarin. 5-Methoxy-substituted chromone **Va** does not undergo hydrolysis under these conditions, and its heating to boiling resulted in decarboxylation and hydrolysis of the methyl ether to afford 5-hydroxy-2-methyl-6.7.8-trifluorochromone (**IX**). This chromone was previously obtained by heating β,β'-dioxoester **IIIb** in concn. HBr [4]. Since the cleavage of a phenol ether requires more rigid conditions (boiling in concn. HBr), the formation of 5-hydroxychromone under these mild conditions may result from cyclization of an intermediate product of pyran ring opening by methanol elimination accompanied by decarboxylation (Scheme 3).

On boiling in concn. HBr chromone Va affords chromone-3-carboxylic acid (X). The same product can be prepared from β,β'-dioxoester **IIIa**. Under similar conditions dioxoester **IIIc** yields chromone (**IX**) [4]. The possibility to obtain acid (**X**) from β,β'-dioxoester **IIIa** may be due to its rapid cyclization into chromone stable against decarboxylation under the reaction conditions.

Thus in the study were obtained for the first time fluoroaryl-containing β,β'-dioxoesters, and was demonstrated the possibility of their application to the synthesis of fluoroheterocycles of benzopyran series.

## EXPERIMENTAL

IR spectra were registered on spectrometer Specord 75IR from mulls in mineral oil (KBr pellet for compound **Ia**). NMR spectra were recorded on spectrometer BS-587A Tesla ($^1$H at 80 MHz, internal reference TMS; $^{19}$F at 75 MHz, internal reference $CFCl_3$). Elemental analyses were carried out on Carlo Erba CHNS-O EA 1108 analyzer.

**2-Methoxy-3,4,5,6-tetrafluorobenzoic acid (Ia).** To acyl chloride **IIa** (0.33 g, 1.36 mmol) was added 10% water solution of sodium hydrogen carbonate (50 ml), and the mixture was stirred for 1 h at 20°C. Then to the reaction mixture was added 10% HCl solution till pH ~3. The separated precipitate was filtered off. Yield 0.3 g.

**2-Methoxy-3,4,5,6-tetrafluorobenzoyl chloride (IIa).** To acid **Ia** (27.36 g, 0.12 mol) prepared by procedure [3] was added phosphorus pentachloride (30 g, 0.15 mol), and the mixture in a flask equipped with a reflux condenser was shaken till the end of vigorous reaction. Then the reaction mixture was refluxed for 1 h and left standing at 20°C for 12 h. The vacuum distillation of the reaction mixture afforded 26 g of acyl chloride **IIa**.

**Ethyl 2-(2-methoxy-3,4,5,6-tetrafluorobenzoyl)-3-oxobutanoate (IIIa).** (a) To a solution of $Mg(OEt)_2$ freshly prepared from magnesium turnings (9.36 g, 39 mmol) was added dropwise ethyl acetoacetate (4.7 g, 36 mmol), and the mixture was stirred for 1 h at 59°C. Then was added a solution of acyl chloride **IIa** (7.8 g, 31 mmol) in benzene (10 ml). The mixture was stirred for 1 h at 20°C and 15 min at 50°C. On cooling to the reaction mixture was added concn. HCl (7.8 ml) and water (12 ml). The benzene layer was separated, and water layer was extracted with benzene. The combined benzene solutions were dried on magnesium sulfate and filtered. We obtained 8.5 g of β,β'-dioxoester **IIIa**.

(b) To a solution of chelate **IVa** (19 g, 52 mmol) in ethyl ether (100 ml) was added concn. HCl (7 ml) and water (15 ml). The mixture was stirred for 15 min

at 20°C. The ether layer was separated, the water layer was extracted with ether (2 × 15 ml). The combined ether extracts were dried with magnesium sulfate, filtered, and ether was distilled off at reduced pressure. Yield 16.55 g.

**Ethyl 2-pentafluorobenzoyl-3-oxobutanoate (IIIb).** Through a solution of chelate **IVb** (0.3 g, 0.845 mmol) in anhydrous ethyl ether (50 ml) was passed a flow of dry hydrogen chloride till the reaction mixture turned brown. The separated precipitate was filtered off. The ether was distilled off at 3 mm Hg on a water bath at 5°C. Yield 0.27 g.

**Bis[ethyl 2-(2-methoxy-3,4,5,6-tetrafluorobenzoyl)-3-hydroxy-2-butanoato]copper(II) (IVa).** (a) To a solution of compound **IIIa** (0.27 g, 0.8 mmol) in methanol (5 ml was added a solution of copper acetate (0.3 g, 1.6 mmol) in water (10 ml). The separated bright blue precipitate was filtered off and dried at 100°C. Yield 0.23 g.

(b) To a solution of $Mg(OEt)_2$ freshly prepared from magnesium turnings (3.65 g, 0.15 mol) was added dropwise ethyl acetoacetate (16.9 g, 0.18 mol). The mixture was stirred for 1 h at 50°C, then was added a solution of acyl chloride **IIa** (25 g, 0.1 mol) in benzene (45 ml). The mixture was stirred for 1 h at 20°C and 15 min at 50°C. On cooling to the reaction mixture was added a solution of copper acetate (12.95 g) and acetic acid (5.9 g) in water (40 ml). The organic layer was separated, the water layer was extracted with ether (3 × 30 ml). The ether extracts were combined with the organic layer and dried with magnesium sulfate. The solution was evaporated at 20°C. The residue was reprecipitated from methanol with water, and dried. Yield 33.5 g.

**Bis(ethyl 2-pentafluorobenzoyl-3-hydroxy-2-butanoato)copper(II) (IVb)** was obtained along procedure *b* from pentaflyorobenzoyl chloride (**IIb**) (18.4 g, 0.08 mol) and ethyl acetoacetate (11.7 g, 0.09 mol). Yield of the dark-green chelate **IVb** 8.3 g.

**2-Methyl-5-methoxy-6,7,8-trifluoro-3-ethoxycarbonyl-4*H*-1,4-dihydrobenzopyran-4-one (Va).** (a) β,β'-Dioxoester IIIa (16.5 g, 49 mmol) was distilled at 225–226°C and 8 mm Hg. The compound distilled crystallized on cooling (mp 50–60°C) and was recrystallized from hexane. We obtained 6 g of chromone Va as colorless powder.

(b) A solution of chelate IVa (4.1 g, 11.1 mmol) in DMSO (15 ml) was heated to 80°C for 3 h. After cooling to the reaction mixture was added a mixture of concn. HCl (15 ml) and water (30 ml). The separated tarry precipitate was recrystallized from hexane. Yield 0.6 g (18%).

**2-Methyl-5,6,7,8-tetrafluoro-3-ethoxycarbonyl-4*H*-1,4-dihydrobenzopyran-4-one (Vb).** (a) β,β'-Dioxoester (**IIIb**) (6.48 g, 0.02 mol) was heated to 100–110°C for 1 h. The solid precipitate was recrystallized from a mixture $CCl_4$–hexane, 1 : 2. We obtained 5.6 g (92%) of chromone **Vb** as yellow powder, mp 91–92°C [1]. Physical constants are consistent with published in [1].

(b) A solution of chelate **IVb** (0.5 g, 1.41 mmol) in DMSO (12 ml) was heated for 3 h to 80°C and kept for 24 h at 20°C. Then was added a mixture of HCl concn. (12 ml) and water (12 ml). The reaction mixture was extracted with ether, the extract was washed with water and dried. The solution was evaporated, the residue was recrystallized from a mixture $CCl_4$–hexane, 1 : 2. We obtained 0.2 g (47%) of chromone **Vb**, mp 91–92°C [1].

**6,8-Difluoro-2-methyl-5-methoxy-7-morpholino-3-ethoxycarbonyl-4*H*-1,4-dihydrobenzopyran-4-one (VI).** A mixture of chromone **Va** (0.3 g, 0.95 mmol) and morpholine (0.33 g, 3.79 mmol) in DMSO (3 ml) was kept for 24 h at 20°C. To the reaction mixture was added concn. HCl (5 ml) and water (5 ml). The precipitated tarry substance was separated, washed with boiling hexane (10 ml), and dried. We obtained 0.25 g of chromone **VI** as yellow powder.

**3-Acetimidoyl-4-hydroxy-5-methoxy-6,7,8-trifluo-2*H*-1,2-dihydrobenzopyran-2-one (VII).** A mixture of chromone **Va** (0.3 g, 0.95 mmol) and 25% aqueous ammonia (6 ml) was heated at stirring for 15 min. The separated precipitate was filtered off, washed with water (10 ml), and dried at 80°C. Yield 0.225 g.

**3-Acetyl-4-hydroxy-5-methoxy-6,7,8-trifluoro-2*H*-1,2-dihydrobenzopyran-2-one (VIII).** A mixture of chromone **VII** (0.4 g, 1.39 mmol), $H_2SO_4$ (2 ml), and water (2 ml) was heated to 80°C for 2 h. The separated precipitate was filtered off, dissolved in boiling benzene (20 ml), filtered from insoluble impurities, and the solution was evaporated. Yield of colorless powder 0.19 g.

**5-Hydroxy-2-methyl-6,7,8-trifluoro-4*H*-1,4-dihydrobenzopyran-4-one (IX).** A mixture of chromone **VIII** (0.3 g, ).95 mmol), concn. HCl (0.4 ml), and glacial acetic acid (1.5 ml) was boiled for 48 h, and then poured into water (10 ml). The separated precipitate was filtered off, washed with

water, and dried. Yield 0.18 g (71%), mp 128–129°C [4]. Physical constants are consistent with those published in [4].

**5-Hydroxy-2-methyl-3-carboxy-6,7,8-trifluoro-4*H*-1,4-dihydrobenzopyran-4-one (X).** (a) A mixture of chromone **Va** (0.3 g, 0.95 mmol) and concn. HBr (0.8 ml) was heated to 130°C for 3 h removing the volatile products. The reaction mixture was cooled, the crystallized substance was washed with water (10 ml), and hexane (10 ml). We obtained 0.2 g of acid **X** as yellow crystals.

(b) Similarly from β,β'-dioxoester **IIIa** (0.3 g, 0.89 mmol) in 8 h was obtained 0.12 g of acid **X**.

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