Heteroatom Chemistry
Volume 17, Number 2, 2006

6-Polyfluoroacyl- and 6-Trichloroacetylnorkhellins: Synthesis and Reaction with Aromatic Amines

Vyacheslav Ya. Sosnovskikh and Roman A. Irgashev

Department of Chemistry, Ural State University, Lenina 51, Ekaterinburg 620083, Russian Federation

Received 20 July 2005; revised 13 September 2005

ABSTRACT: *Five new 6-polyhaloacylnorkhellins were synthesized in high yields from diethoxymethyl acetate and the condensation products of khellinone with R_FCO_2Et and CCl_3COCl. Reaction of 6-polyfluoroacylnorkhellins with primary aromatic amines yielded 6-(arylaminomethylene)-7-hydroxy-4,9-dimethoxy-7-(polyfluoroalkyl)furo[3,2-g]chroman-5-ones.* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:99–103, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20174

INTRODUCTION

The natural furochromone khellin (4,9-dimethoxy-7-methyl-5*H*-furo[3,2-*g*]chromen-5-one, **1a**), obtained from the fruits and seeds of *Ammi visnaga* L., possesses a high anti-atherosclerotic and lipid-altering activity [1] and is the active constituent of many modern medicines [2]. In view of the unique biological properties displayed by khellin **1a** on the one hand and by many fluorinated heterocyclic compounds [3] on the other hand, we have described recently [4–6] the synthesis of 7-polyfluoroalkyl- and 7-trichloromethylnorkhellins **1b,c** (Fig. 1), which are highly reactive building blocks for the preparation of new khellin derivatives with a potential biological activity [6].

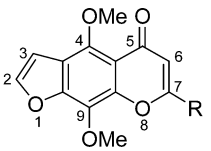
In continuation of our work on the synthesis of heterocyclic compounds derived from the naturally occurring furochromones, we speculated that an introduction of a polyfluoroacyl group onto the 6-position of norkhellin system **1d** could be an effective route to obtain a wide variety of partially fluorinated heterocycles with the biogenic moieties. The present work is devoted to the synthesis of 6-polyfluoroacylnorkhellins, which may be regarded as latent 1,3-dicarbonyl compounds, having at the 2-position a masked furosalicyloyl fragment.

RESULTS AND DISCUSSION

Recently [7], we have found that the reaction of 2-hydroxy-2-(polyfluoroalkyl)chroman-4-ones with diethoxymethyl acetate readily occurs at 140–150°C for 15 min to give 3-(polyfluoroacyl)chromones in good yields. A plausible pathway leading to the formation of these compounds is outlined in Scheme 1.

Now we have applied this reaction to the condensation products of khellinone (5-acetyl-6-hydroxy-4,7-dimethoxybenzo[*b*]furan) with R_FCO_2Et, which exist in a $CDCl_3$ solution as a mixture of ring-chain tautomers **2a–d** with the cyclic semiketal form predominating [6], and synthesized the new khellin derivatives, namely 6-polyfluoroacylnorkhellins **3a–d** in high yields (62–97%). In contrast to the 6-formylnorkhellin [8–10], these compounds were prone to the facile and reversible covalent hydrate

Correspondence to: Vyacheslav Ya. Sosnovskikh; e-mail: vyacheslav.sosnovskikh@usu.ru.

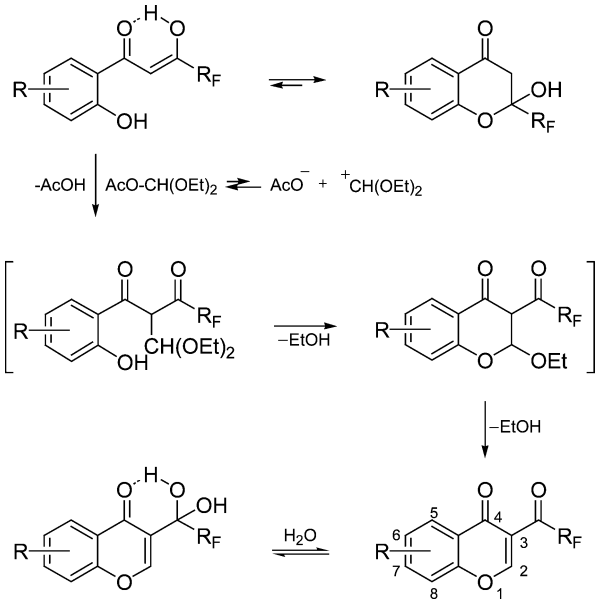


1a–d

R = Me (**a**), R_F (**b**), CCl_3 (**c**), H (**d**)

FIGURE 1 Khellin **1a** and its derivatives **1b–d**.

formation as observed from their ^1H and ^{19}F NMR spectra, which contained two sets of signals. The diagnostic signal for the proton H-7 in compounds **3a–d**, which appeared at δ 8.42–8.58 ppm, is shifted upfield to δ 8.33–8.34 ppm in hydrated forms **4a–d**. On the basis of the IR spectra (the absorption band of the OH group at around 3300 cm^{-1} is absent) and the elemental analysis, it is possible to assume that compounds **3a,c,d** in the solid state are pure substances and exist in equilibrium in solution between the nonhydrate **3** and hydrate **4** due to any water in the $CDCl_3$ or DMSO-d_6. The ratio of **3** and **4** depends on the number of fluorine atoms of the R_F group (~1% of **4** at $R_F = CF_2H$, ~6% at $R_F = (CF_2)_2H$, and ~15% at $R_F = C_2F_5$). At the same time, trifluoromethylated product is a mixture of **3b** and **4b** (~1:1) as evidenced by its IR spectrum in KBr (the band of the OH group at 3335 cm^{-1} is present) and the combustion analysis (molecular formula $C_{15}H_9F_3O_6 \cdot 0.5H_2O$). The ^1H and ^{19}F NMR spectra of this compound in a $CDCl_3$ solution contained two sets of signals, one of which belonged to chromone **3b** (56–58%) and another set was attributed to its hydrate **4b** (44–42%).



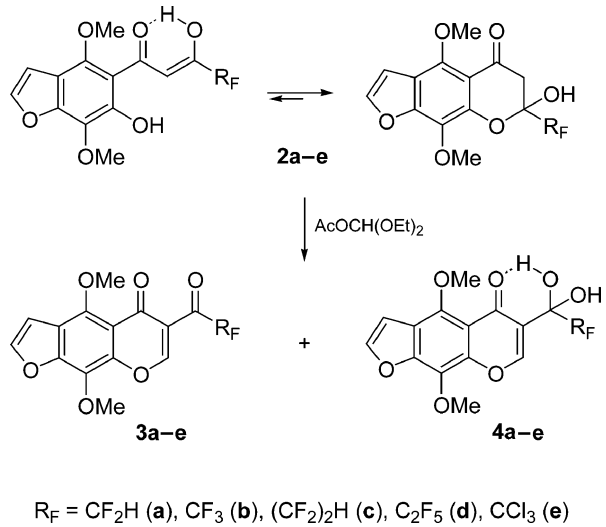
SCHEME 1

Note that the facile formation of covalent hydrates from the CF_3-containing β-dicarbonyl compounds is a well-known phenomenon [11–13]. The formation of hydrates **4** probably arises from the high hydrophilicity of compounds **3** due to the electrophilic character of the carbonyl carbon atom connected to a polyfluoroalkyl substituent and the formation of an intramolecular hydrogen bond between the OH and C=O groups.

It is important that trichloromethyl derivatives **2e** [5] also reacted with diethoxymethyl acetate under the same reaction conditions to give 6-trichloroacetylnorkhellin **3e** in 86% yield (**3e**:**4e** = 86:14 in a $CDCl_3$ solution). The structures of norkhellin derivatives **3a–e** compare well with the results of elemental analysis, ^1H, ^{19}F NMR, and IR spectroscopy (Scheme 2).

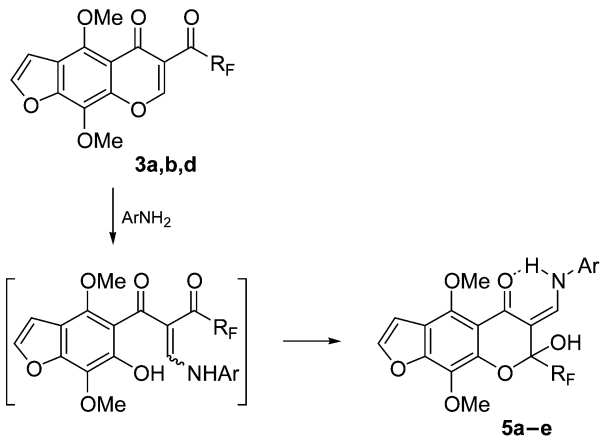
The presence of the electron-withdrawing COR_F group in furochromones **3** enhances the electrophilicity of the C-7 atom of the pyrone cycle, from the attack of which, as a rule, the interaction of chromones with nucleophilic agents begins [14,15]. Due to this fact, compounds **3** are promising substrates for synthesis of new benzofuran derivatives containing the polyfluoroalkyl group along with the natural fragment.

Indeed, we found that the reaction of 6-polyfluoroacylnorkhellins **3a,b,d** with primary aromatic amines (aniline, *p*-toluidine, *p*-anisidine) in methanol at room temperature or under reflux afforded 6-(arylaminomethylene)-7-hydroxy-7-(polyfluoroalkyl)furochroman-5-ones **5a–e** in 51–90% yields. The reaction includes the nucleophilic 1,4-addition of the amine with concomitant opening of the pyrone ring and subsequent intramolecular



R_F = CF_2H (**a**), CF_3 (**b**), $(CF_2)_2H$ (**c**), C_2F_5 (**d**), CCl_3 (**e**)

SCHEME 2



$R_F = CF_2H$, R = 4-$MeOC_6H_4$ (**5a**); $R_F = CF_3$, R = Ph (**5b**); $R_F = CF_3$, R = 4-MeC_6H_4 (**5c**); $R_F = CF_3$, R = 4-$MeOC_6H_4$ (**5d**); $R_F = C_2F_5$, R = 4-$MeOC_6H_4$ (**5e**)

SCHEME 3

cyclization of the intermediate at the COR_F group. The driving force for the process is the stabilization of the enamines **5** by a hydrogen bond between the pyranone carbonyl oxygen and the hydrogen of the NH group (Scheme 3). The reaction of **3a,c** with aliphatic primary amines (cyclohexylamine, benzylamine) gave only ill-defined mixtures of products under the same experimental conditions.

It should be noted that the reaction between equimolar quantities of 3-formylchromone and a primary aromatic amine leads to a mixture of the 3-(aryliminomethyl)chromone and 2-arylamino-3-(arylaminomethylene)chroman-4-one, making the isolation of pure compounds difficult [16]. 3-(Arylaminomethylene)-2-hydroxychroman-4-ones were prepared by acid-catalyzed reaction of 3-formylchromones with aromatic amino carboxylic acids in benzene or toluene [17]. Unlike the 6-polyhaloacylnorkhellins **3a–e**, 6-formylnorkhellin reacts with substituted anilines to give the corresponding anils [8]. This different behavior is not unexpected, considering that R_F group complicates a dehydration stage.

The structures of compounds **5a–e** are consistent with the IR, ^1H, and ^{19}F NMR spectra. The IR spectra of **5a–e** showed absorption bands in the two ranges 3460–3230 and 1650–1600 cm^{-1} due to the OH and NH groups and the aminoenone fragment. A characteristic feature of the ^1H NMR spectra is the appearance of one singlet at δ 8.34–9.14 ppm for the OH proton (doublet with $^4J_{H,F} = 4.2$ Hz in the case of **5e**), and two AX doublets ($J_{AX} = 12.7$–12.9 Hz) at δ 7.74–7.91 and 12.42–12.52 ppm for the =CH and NH protons, respectively. The addition of CD_3CO_2D to a solution of compound **5d** in DMSO-d_6 results to disappearance of signals due to OH and NH protons, whereas the doublet for the =CH proton turns into the singlet.

In summary, we have developed a simple and convenient method for the synthesis of 6-polyhaloacylnorkhellins, starting from readily obtainable 7-hydroxy-7-(polyhaloalkyl)-6,7-dihydronorkhellins and commercially available diethoxymethyl acetate. These compounds are of much interest as reactive precursors in the synthesis of other useful organic materials with polyfluoroalkyl groups and the natural fragment.

EXPERIMENTAL

^1H and ^{19}F NMR spectra were recorded on a Bruker DRX-400 spectrometer (^1H at 400.1 MHz and ^{19}F at 376.5 MHz) in $CDCl_3$ solution with TMS and C_6F_6 as internal standards, respectively. The digital resolution in the ^1H NMR spectra was 0.15 Hz per point. The percentage of the nonhydrated and hydrated forms **3** and **4** observed by ^1H and ^{19}F NMR spectra is indicated parenthetically. IR spectra were recorded on a "Perkin-Elmer spectrum BX-II" instrument as KBr disks. Elementary analyses were performed at the Microanalysis Services of the Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences. Melting points are uncorrected. The starting compounds **2a–e** were prepared by direct condensation of khellinone with R_FCO_2Et and CCl_3COCl according to the described procedures [5,6].

General Procedure for the Synthesis of 6-Polyhaloacylnorkhellins **3a–e**

A solution of compound **2** (1 mmol) in diethoxymethyl acetate (1.0 g, 6 mmol) was heated at 140–150°C for 15–20 min. After cooling, the resulting mixture was diluted with hexane (3 mL). The solid product obtained on standing was collected by filtration, washed with hexane, and dried to give **3** as colorless crystals.

6-(Difluoroacetyl)-4,9-dimethoxy-5H-furo[3,2-g]-chromen-5-one **3a**. Yield 97%, mp 127–128°C. IR (KBr): ν 3137, 1695, 1655, 1616, 1599, 1568, 1551, 1482 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.12 (s, 3H, MeO), 4.25 (s, 3H, MeO), 6.98 (t, 1H, CF_2H, $^2J_{H,F} = 53.5$ Hz), 7.08 (d, 1H, H-3, $J = 2.3$ Hz), 7.71 (d, 1H, H-2, $J = 2.3$ Hz), 8.58 (s, 1H, H-7). ^{19}F NMR (376 MHz, $CDCl_3$): δ **3a** (99%) 31.2 (d, HCF_2, $^2J_{F,H} = 53.5$ Hz); **4a** (1%) 28.6 (d, HCF_2, $^2J_{F,H} = 56.2$ Hz). Anal. Calcd for $C_{15}H_{10}F_2O_6$: C, 55.57; H, 3.11. Found: C, 55.60; H, 3.28.

4,9-Dimethoxy-6-(trifluoroacetyl)-5H-furo[3,2-g]-chromen-5-one **3b** *and 4,9-Dimethoxy-6-(2,2,2-trifluoro-1,1-dihydroxyethyl)-5H-furo[3,2-g]chromen-5-one* **4b**. Yield 83%, mp 144–145°C. IR (KBr): ν 3335, 1728, 1643, 1601, 1551, 1483 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ **3b** (56%) 4.10 (s, 3H, MeO), 4.25 (s, 3H, MeO), 7.08 (d, 1H, H-3, $J = 2.2$ Hz), 7.71 (d, 1H, H-2, $J = 2.2$ Hz), 8.52 (s, 1H, H-7); **4b** (44%) 4.09 (s, 3H, MeO), 4.24 (s, 3H, MeO), 6.28 (s, 2H, 2OH), 7.07 (d, 1H, H-3, $J = 2.2$ Hz), 7.70 (d, 1H, H-2, $J = 2.2$ Hz), 8.34 (s, 1H, H-7). ^{19}F NMR (376 MHz, $CDCl_3$): δ **3b** (58%) 87.3 (s, CF_3); **4b** (42%) 74.9 (s, CF_3). Anal. Calcd for $C_{15}H_9F_3O_6 \cdot 0.5H_2O$: C, 51.30; H, 2.87. Found: C, 51.25; H, 2.87.

4,9-Dimethoxy-6-(2,2,3,3-tetrafluoropropanoyl)-5H-furo[3,2-g]chromen-5-one **3c** *and 4,9-Dimethoxy-6-(2,2,3,3-tetrafluoro-1,1-dihydroxypropyl)-5H-furo[3,2-g]chromen-5-one* **4c**. Yield 88%, mp 139–140°C. IR (KBr): ν 3163, 1710, 1662, 1614, 1578, 1544, 1483 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ **3c** (95%) 4.10 (s, 3H, MeO), 4.25 (s, 3H, MeO), 6.88 (tt, 1H, CF_2CF_2H, $^2J_{H,F} = 53.4$ Hz, $^3J_{H,F} = 5.8$ Hz), 7.08 (d, 1H, H-3, $J = 2.3$ Hz), 7.72 (d, 1H, H-2, $J = 2.3$ Hz), 8.45 (s, 1H, H-7); **4c** (5%) 4.09 (s, 3H, MeO), 4.24 (s, 3H, MeO), 6.29 (tt, 1H, CF_2CF_2H, $^2J_{H,F} = 53.1$ Hz, $^3J_{H,F} = 6.2$ Hz), 6.35 (s, 2H, 2OH), 7.07 (d, 1H, H-3, $J = 2.3$ Hz), 7.70 (d, 1H, H-2, $J = 2.3$ Hz), 8.33 (s, 1H, H-7). ^{19}F NMR (376 MHz, $CDCl_3$): δ **3c** (93%) 24.2 (dt, HCF_2CF$_2$, $^2J_{H,F} = 53.4$ Hz, $^3J_{F,F} = 7.3$ Hz), 38.8 (td, HCF$_2CF_2$, $^3J_{F,F} = 7.3$ Hz, $^3J_{F,H} = 6.0$ Hz); **4c** (7%) 25.3 (dt, HCF_2CF$_2$, $^2J_{F,H} = 53.0$ Hz, $^3J_{F,F} = 7.9$ Hz), 30.7 (q, HCF$_2CF_2$, $^3J_{F,F} \sim {}^3J_{F,H} = 7.0$ Hz). Anal. Calcd for $C_{16}H_{10}F_4O_6$: C, 51.35; H, 2.69. Found: C, 51.25; H, 2.75.

4,9-Dimethoxy-6-(pentafluoropropanoyl)-5H-furo-[3,2-g]chromen-5-one **3d** *and 4,9-Dimethoxy-6-(2,2,3,3,3-pentafluoro-1,1-dihydroxypropyl)-5H-furo[3,2-g]chromen-5-one* **4d**. Yield 62%, mp 119–120°C. IR (KBr): ν 3133, 1701, 1661, 1605, 1569, 1481 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ **3d** (89%) 4.10 (s, 3H, MeO), 4.25 (s, 3H, MeO), 7.07 (d, 1H, H-3, $J = 2.3$ Hz), 7.71 (d, 1H, H-2, $J = 2.3$ Hz), 8.42 (s, 1H, H-7); **4d** (11%) 4.08 (s, 3H, MeO), 4.25 (s, 3H, MeO), 6.27 (s, 2H, 2OH), 7.07 (d, 1H, H-3, $J = 2.2$ Hz), 7.70 (d, 1H, H-2, $J = 2.2$ Hz), 8.33 (s, 1H, H-7). ^{19}F NMR (376 MHz, $CDCl_3$): δ **3d** (82%) 42.8 (q, CF_2, $J = 0.9$ Hz), 80.8 (t, CF_3, $J = 0.9$ Hz); **4d** (18%) 35.9 (s, CF_2), 83.4 (s, CF_3). Anal. Calcd for $C_{16}H_9F_5O_6$: C, 49.00; H, 2.31. Found: C, 48.86; H, 2.24.

4,9-Dimethoxy-6-(trichloroacetyl)-5H-furo[3,2-g]-chromen-5-one **3e** *and 4,9-Dimethoxy-6-(2,2,2-trichloro-1,1-dihydroxyethyl)-5H-furo[3,2-g]chromen-5-one* **4e**. Yield 86%, mp 134–135°C. IR (KBr): ν 3118, 1702, 1656, 1601, 1578, 1544, 1480 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ **3e** (86%) 4.09 (s, 3H, MeO), 4.25 (s, 3H, MeO), 7.06 (d, 1H, H-3, $J = 2.3$ Hz), 7.69 (d, 1H, H-2, $J = 2.3$ Hz), 8.45 (s, 1H, H-7); **4e** (14%) 4.07 (s, 3H, MeO), 4.26 (s, 3H, MeO), 6.85 (s, 2H, 2OH), 7.07 (d, 1H, H-3, $J = 2.3$ Hz), 7.70 (d, 1H, H-2, $J = 2.3$ Hz), 8.55 (s, 1H, H-7). Anal. Calcd for $C_{15}H_9Cl_3O_6$: C, 46.01; H, 2.32. Found: C, 45.90; H, 2.29.

General Procedure for the Synthesis of 6-(Arylaminomethylene)-7-hydroxy-7-(polyfluoroalkyl)-furochroman-5-ones **5a–e**

A solution of 6-polyfluoroacylnorkhellin **3b** or **3d** (0.3 mmol) and the aromatic amine (0.45 mmol) in methanol (5 mL) was allowed to stand at room temperature for 2 days. In the case of **3a**, solution was heated under reflux for 16 h. The crystalline product that precipitated was filtered off, washed with cold methanol (0.5–1 mL), and dried to give **5** as yellow crystals.

7-(Difluoromethyl)-7-hydroxy-4,9-dimethoxy-6-(4-anisidinomethylene)furo[3,2-g]-chroman-5-one **5a**. Yield 51%, mp 148–149°C. IR (KBr): ν 3445, 3226, 1649, 1617, 1556, 1516, 1480 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 3.76 (s, 3H, MeO), 3.93 (s, 3H, MeO), 3.97 (s, 3H, MeO), 6.12 (t, 1H, CF_2H, $^2J_{H,F} = 55.1$ Hz), 6.99 (d, 2H, H-2′, H-6′, $J = 9.0$ Hz), 7.12 (d, 1H, H-3, $J = 2.3$ Hz), 7.33 (d, 2H, H-3′, H-5′, $J = 9.0$ Hz), 7.74 (d, 1H, =CH, $J = 12.7$ Hz), 7.94 (d, 1H, H-2, $J = 2.3$ Hz), 8.34 (s, 1H, OH), 12.42 (d, 1H, NH, $J = 12.7$ Hz). Anal. Calcd for $C_{22}H_{19}F_2NO_7$: C, 59.06; H, 4.28; N, 3.13. Found: C, 58.77; H, 4.02; N, 3.32.

6-(Anilinomethylene)-7-hydroxy-4,9-dimethoxy-7-(trifluoromethyl)furo[3,2-g]chroman-5-one **5b**. Yield 79%, mp 210–211°C. IR (KBr): ν 3448, 3244, 1650, 1614, 1600, 1558, 1482 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 3.93 (s, 3H, MeO), 4.00 (s, 3H, MeO), 7.17 (d, 1H, H-3, $J = 2.3$ Hz), 7.18 (tt, 1H, H-4′, $J = 2.0$, 6.4 Hz), 7.39–7.45 (m, 4H, H-2′, H-3′, H-5′, H-6′), 7.91 (d, 1H, =CH, $J = 12.8$ Hz), 7.98 (d, 1H, H-2, $J = 2.3$ Hz), 9.14 (s, 1H, OH), 12.44 (d, 1H, NH, $J = 12.8$ Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ 79.2 (s, CF_3). Anal. Calcd for $C_{21}H_{16}F_3NO_6$: C, 57.94; H, 3.70; N, 3.22. Found: C, 57.66; H, 3.78; N, 2.96.

7-Hydroxy-4,9-dimethoxy-6-(4-toluidinomethylene)-7-(trifluoromethyl)furo[3,2-g]-chroman-5-one **5c**. Yield 85%, mp 204–205°C. IR (KBr): ν 3436, 3272,

1648, 1614, 1600, 1557, 1520, 1482 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 2.30 (s, 3H, Me), 3.93 (s, 3H, MeO), 3.98 (s, 3H, MeO), 7.16 (d, 1H, H-3, $J = 2.3$ Hz), 7.23 (d, 2H, H-2′, H-6′, $J = 8.5$ Hz), 7.29 (d, 2H, H-3′, H-5′, $J = 8.5$ Hz), 7.87 (d, 1H, =CH, $J = 12.8$ Hz), 7.98 (d, 1H, H-2, $J = 2.3$ Hz), 9.10 (s, 1H, OH), 12.44 (d, 1H, NH, $J = 12.8$ Hz). Anal. Calcd for $C_{22}H_{18}F_3NO_6$: C, 58.80; H, 4.04; N, 3.12. Found: C, 58.56; H, 3.92; N, 2.85.

7-Hydroxy-4,9-dimethoxy-6-(4-anisidinomethylene)-7-(trifluoromethyl)furo[3,2-g]-chroman-5-one **5d**. Yield 60%, mp 205–206°C. IR (KBr): ν 3463, 3250, 1649, 1618, 1556, 1516, 1480 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 3.77 (s, 3H, MeO), 3.93 (s, 3H, MeO), 3.98 (s, 3H, MeO), 7.00 (d, 2H, H-2′, H-6′, $J = 9.0$ Hz), 7.15 (d, 1H, H-3, $J = 2.3$ Hz), 7.35 (d, 2H, H-3′, H-5′, $J = 9.0$ Hz), 7.81 (d, 1H, =CH, $J = 12.9$ Hz), 7.97 (d, 1H, H-2, $J = 2.3$ Hz), 9.07 (s, 1H, OH), 12.48 (d, 1H, NH, $J = 12.8$ Hz); after addition of CD_3CO_2D: 3.77 (s, 3H, MeO), 3.93 (s, 3H, MeO), 3.98 (s, 3H, MeO), 7.00 (d, 2H, H-2′, H-6′, $J = 9.0$ Hz), 7.14 (d, 1H, H-3, $J = 2.3$ Hz), 7.35 (d, 2H, H-3′, H-5′, $J = 9.0$ Hz), 7.80 (s, 1H, =CH), 7.95 (d, 1H, H-2, $J = 2.3$ Hz). Anal. Calcd for $C_{22}H_{18}F_3NO_7$: C, 56.78; H, 3.90; N, 3.01. Found: C, 56.73; H, 3.80; N, 3.11.

7-Hydroxy-4,9-dimethoxy-6-(4-anisidinomethylene)-7-(pentafluoroethyl)furo[3,2-g]chroman-5-one **5e**. Yield 90%, mp 171–172°C. IR (KBr): ν 3467, 3244, 1649, 1616, 1560, 1516, 1482 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 3.77 (s, 3H, MeO), 3.94 (s, 3H, MeO), 3.97 (s, 3H, MeO), 7.00 (d, 2H, H-2′, H-6′, $J = 9.0$ Hz), 7.14 (d, 1H, H-3, $J = 2.3$ Hz), 7.35 (d, 2H, H-3′, H-5′, $J = 9.0$ Hz), 7.77 (d, 1H, =CH, $J = 12.9$ Hz), 7.97 (d, 1H, H-2, $J = 2.3$ Hz), 9.14 (d, 1H, OH, $^4J_{H,F} = 4.2$ Hz), 12.52 (d, 1H, NH, $J = 12.8$ Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ 38.7 (dd, C*F*F, $^2J_{F,F} = 276.1$ Hz, $^4J_{F,H} = 4.2$ Hz), 40.8 (d, CF*F*, $^2J_{F,F} = 276.1$ Hz), 85.0 (s, CF_3). Anal. Calcd for $C_{23}H_{18}F_5NO_7$: C, 53.60; H, 3.52; N, 2.72. Found: C, 53.33; H, 3.54; N, 2.60.

ACKNOWLEDGMENTS

The authors are grateful to Dr. B. I. Usachev for the synthesis of compounds **2a–e**.

REFERENCES

[1] Gammill, R. B.; Day, C. E.; Schurr, P. E. J Med Chem 1983, 26, 1672–1674.
[2] Mashkovskii, M. D. Lekarstvennye sredstva (Drugs); Gamta: Vilnyus, 1993; Vol. 1.
[3] Hiyama, T. Organofluorine Compounds. Chemistry and Application; Springer-Verlag: Berlin, 2000.
[4] Sosnovskikh, V. Ya.; Kutsenko, V. A. Mendeleev Commun 2000, 238–239.
[5] Sosnovskikh, V. Ya.; Usachev, B. I. Synthesis 2002, 42, 1007–1009.
[6] Sosnovskikh, V. Ya.; Usachev, B. I.; Vorontsov, I. I. Tetrahedron 2003, 59, 2549–2554.
[7] Sosnovskikh, V. Ya.; Irgashev, R. A. Synlett 2005, 1164–1166.
[8] Hishmat, O. H.; El-Diwani, H. I.; El-Naem, Sh. I.; Fawzi, N. M. Pol J Chem 1993, 67, 1987–1993.
[9] Fawzy, N. M.; Shalaby, A. M.; Zaki, M. E. A. Molec Online 1998, 2, 121–128.
[10] Hishmat, O. H.; Fawzy, N. M.; Farrag, D. S.; Abd El-All, A. S. Rev Roum Chim 1999, 44, 161–167.
[11] Morita, Y.; Kamakura, R.; Takeda, M.; Yamamoto, Y. J Chem Soc, Chem Commun 1997, 359–360.
[12] Sosnovskikh, V. Ya.; Usachev, B. I.; Sizov, A. Yu. Izv Acad Nauk, Ser Khim 2002, 1954–1960; Sosnovskikh, V. Ya.; Usachev, B. I.; Sizov, A. Yu. Russ Chem Bull, Int Ed 2002, 51, 2109–2115 (in English).
[13] Sosnovskikh, V. Ya.; Usachev, B. I.; Bogdanov, E. A. Izv Acad Nauk, Ser Khim 2001, 542–543; Sosnovskikh, V. Ya.; Usachev, B. I.; Bogdanov, E. A. Russ Chem Bull, Int Ed 2001, 50, 568–569 (in English).
[14] Sosnovskikh, V. Ya. Uspekhi Khimii 2003, 72, 550–578; Sosnovskikh, V. Ya. Russ Chem Rev 2003, 72, 489–516 (in English).
[15] Ellis, G. P. In The Chemistry of Heterocyclic Compounds; Wiley: New York, 1977; Vol. 31.
[16] Fitton, A. O.; Frost, J. R.; Houghton, P. G.; Suschitzky, H. J Chem Soc, Perkin Trans 1 1979, 1691–1694.
[17] Stankovicova, H.; Lacova, M.; Gaplovsky, A.; Chovancova, J.; Pronayova, N. Tetrahedron 2001, 57, 3455–3464.