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# Reactions of pentafluorobenzoylpyruvic ester and its copper(II) chelate with dinucleophiles

V.I. Saloutin*, S.G. Perevalov

*Institute of Organic Synthesis, Urals Division, Russian Academy of Sciences, 620219, GSP-147 Ekaterinburg, Russia*

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**Abstract**

Pentafluorobenzoylpyruvic ester reacts with dinucleophiles — hydrazine, phenylhydrazine, hydroxylamine hydrochloride, 1,2-ethylenediamine, 1,2-phenylenediamine, 2-aminophenol — to form heterocyclic compounds. Reactions between bis(ethyl pentafluorobenzoylpyruvate)copper (II) chelate and these amine hydrochlorides also produce heterocycles. The analytical data of these compounds — elemental analysis, IR-, $^{1}H$ and $^{19}F$ NMR spectral data — are reported. © 1999 Elsevier Science S.A. All rights reserved.

*Keywords:* Pentafluorobenzoylpyruvic ester; Copper(II) chelate; Diaminonucleophiles; Aminohydroxynucleophiles; Cyclocondensation; Heterocycles

## 1. Introduction

Tricarbonyl compounds — 4-aryl-2,4-dioxobutanoic (aroylpyruvic) acid [1,2] derivatives are valuable products in organic syntheses. These compounds are well studied in reactions with various nucleophiles. Reactions of nonfluorinated aroylpyruvic acids and their esters with various *N*,*N*- and *N*,*O*-dinucleophiles lead to formation of heterocyclic compounds [3–15].

Polyfluoroaromatic pentafluorobenzoylpyruvic ester (ethyl 4-pentafluorophenyl-2,4-dioxobutanoate, **1a**) [16] is a reactive compound that can be used to produce various substances containing fluorinated fragments and substituents.

As has been found recently, **1a** readily undergoes intramolecular cyclization due to substitution of a pentafluorophenyl *ortho*-fluorine atom effected by nucleophilic attack of the enol hydroxyl oxygen atom at C-2. This cyclization of **1a** leads to formation of reactive 5,6,7,8-tetrafluoro-2-ethoxycarbonyl-4H-chromen-4-one (**1c**) [16] which can react with amines [17].

Compound **1a** reacts with primary aliphatic monoamines producing derivatives of **1c** [16,17].

Reactions of **1a** and its copper(II) chelate **1b** with dinucleophiles have not been investigated previously.

## 2. Experimental details

Melting points were measured in open capillaries and are reported uncorrected. Infrared spectra were measured on a Specord 75 IR spectrometer and frequencies are reported in $cm^{-1}$.$^{1}H$ NMR spectra were recorded on a Tesla BS-567A instrument ($^{1}H$: 100 MHz) using TMS as internal standard.$^{19}F$ NMR spectra were recorded on a Tesla BS-587A instrument ($^{19}F$: 75 MHz) using $CFCl_3$ as internal standard. Chemical shifts are reported in ppm.

### 2.1. Materials

Compounds **1a** and **1b** were prepared from pentafluorochlorobenzene via described procedures [16,18]. 5,6,7,8-tetrafluoro-2-ethoxycarbonyl (**1c**) and -2-carboxy-4H-chromen-4-ones (**1d**) were prepared from **1a** or **1b** as described previously [16,19].

### 2.2. Synthesis of 5-pentafluorophenyl-3-ethoxycarbonylpyrazole (2)

#### 2.2.1. Method A

A mixture of compound **1a** (1.55 g; 5 mmol) and $N_2H_4 \cdot H_2O$ (0.26 g; 5.2 mmol) in 30 ml of MeOH was stirred at room temperature for 6 h. The solvent was removed at room temperature. The residue was washed with water (2 × 10 ml) and recrystallized from a chloroform–hexane mixture to give 1.03 g (67%) of **2** (m.p. 145–147°C). $^{1}H$ NMR ($CD_3COCD_3$)$\delta$: 1.38 (3H, t, $CH_3$, $J$= 7.1 Hz); 4.40

*Corresponding author. Fax: +7-3432-745954; e-mail: fc@ios.uran.ru


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(2H, q, $CH_2$, $J = 7.1$ Hz); 7.18 (1H, t, CH, $J_{H-F} = 1.6$ Hz); 13.53 (1H, w.s., NH) ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: − 166.81 (2F, m, *meta*-); −154.95 (1F, t, *para*-, $J_{3-4} = 20.7$ Hz); − 141.77 (2F, d-d, *ortho*-, $J_{2-3} = 20.5$; $J_{2-5} = 6.3$ Hz) ppm. IR ($cm^{-1}$): 3260, 3130, 3100 (NH); 1695 (C=O, ester); 1560, 1530 (C=C, NH); 980 (CF). Analysis: Found: C, 46.69; H, 2.19; F, 31.47; N, 9.30%. Calc. for $C_{12}H_7F_5N_2O_2$: C, 47.07; H, 2.30; F, 31.07; N, 9.15%.

#### 2.2.2. Method B

A mixture of compound **1b** (1.37 g, 2 mmol) and $N_2H_4 \cdot 2HCl$ (0.45 g, 4.3 mmol) in 50 ml of MeOH was stirred at room temperature for 4 h and then refluxed for 1 h. The reaction mixture was cooled, diluted with 200 ml of water. The precipitate was collected by filtration, recrystallized twice from a chloroform–hexane mixture to give 0.60 g (49%) of **2**. The physicochemical data were identical to those listed above.

#### 2.2.3. Method C

A powder of compound **1b** (1.37 g, 2 mmol) was added into a cold mixture of $N_2H_4 \cdot 2HCl$ (0.42 g, 4 mmol) and NaOH (0.16 g, 4 mmol) in 30 ml of EtOH. The reaction mixture was stirred at room temperature for 4 h and at 70°C for 1 h and then was cooled, diluted with 60 ml of water. The precipitate was collected, recrystallized twice from a chloroform–hexane mixture to give 0.58 g (47%) of **2**. The physicochemical data were identical to those listed in method A.

### 2.3. Synthesis of 1-phenyl-5-pentafluorophenyl-3-ethoxycarbonylpyrazole (3)

A mixture of compound **1a** (1.55 g, 5 mmol) and phenylhydrazine (0.65 g, 6.6 mmol) in 25 ml of MeOH was stirred at room temperature for 6 h, and then allowed to stand overnight. The solvent was removed almost to dryness. 40 ml of hexane was added to the residue, then this mixture was heated to a boiling. The solvent was removed to one-third of original volume. The residue was cooled and the precipitate was collected and recrystallized from hexane to give 0.29 g (15%) of **3** (m.p. 88–90°C). $^1H$ NMR ($CDCl_3$) $\delta$: 1.41 (3H, t, $CH_3$, $J = 7.2$ Hz); 4.45 (2H, q, $CH_2$, $J = 7.2$ Hz); 7.14 (1H, s, CH); 7.35 (5H, m, $C_6H_5$) ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: −161.53 (2F, m, *meta*-); −151.53 (1F, t-t, *para*-, $J_{3-4} = 20.7$; $J_{2-4} = 2.2$ Hz); −138.75 (2F, m, *ortho*-) ppm. IR ($cm^{-1}$): 1735 (C=O, ester); 1650, 1595, 1500 (C=N, C=C); 990 (CF). Analysis: Found: C, 56.49; H, 3.07; F, 25.05; N, 7.44%. Calc. for $C_{18}H_{11}F_5N_2O_2$ : C, 56.55; H, 2.90; F, 24.85; N, 7.33%.

### 2.4. Synthesis of 5-pentafluorophenyl-3-carboxyisoxazole (4)

#### 2.4.1. Method A

A mixture of compound **1a** (1.55 g, 5 mmol) and $NH_2OH \cdot HCl$ (0.42 g, 6 mmol) in 25 ml of MeOH was stirred at room temperature for 6 h, and then stored for 2 days. The solvent was removed and the residue was extracted with hot (70–80°C) hexane (4 × 10 ml). The extract was concentrated, and the residue was refluxed with a mixture of acetic acid (6 ml) and conc. HCl (3 ml). The solvent was removed to a 5 ml volume and the mixture was diluted with 50 ml of water. The resulting precipitate was collected by filtration, washed with water to give 0.35 g (25%) of **4** (m.p. 158–159.5°C). $^1H$ NMR ($CD_3COCD_3$) $\delta$: 7.28 (1H, t, CH, $J_{H-F} = 1.6$ Hz) ppm. $^{19}F$ NMR ($CD_3COCD_3$) $\delta$: −161.44 (2F, m, *meta*-); −150.66 (1F, t-t, *para*-, $J_{3-4} = 20.7$; $J_{2-4} = 3.7$ Hz); −138.03 (2F, m, *ortho*-) ppm. IR ($cm^{-1}$): 3470 (OH), 1715 (C=O, acid), 1655, 1580 (C=C), 1260 (COOH), 1000 (CF). Analysis: Found: C, 42.74; H, 0.62; F, 33.81; N, 4.92%. Calc. for $C_{10}H_2F_5NO_3$ : C, 43.07; H, 0.72; F, 34.03; N, 5.02%.

#### 2.4.2. Method B

A mixture of compound **1b** (1.37 g, 2 mmol) and $NH_2OH \cdot HCl$ (0.35 g, 5 mmol) in 20 ml of MeOH was refluxed for 8 h, cooled, and then 30 ml of aqueous HCl (5%) was added to the mixture, stirred at room temperature for 1 h. The resulting mixture was extracted with $CHCl_3$ (3 × 20 ml). The chloroform layer was evaporated to dryness. The residue was e×tracted with hot (70–80°C) heptane (4 × 10 ml). The heptane extract was evaporated to dryness and resulting residue was hydrolyzed as described above in method A to give 0.34 g (30.5%) of **4**. The physicochemical data were identical to those listed in method A.

### 2.5. Synthesis of 3-pentafluorobenzoylmethylenepiperazin-2-one (5)

A solution of 1,2-ethylenediamine (1.5 g, 25 mmol) in 10 ml of MeOH was added to a solution of compound **1a** (1.55 g, 5 mmol) in 10 ml of acetic acid under cooling. The mixture was stirred at room temperature for 6 h, and stored for 2 days. The precipitate was collected by filtration, washed with water (3 × 10 ml), dried. The dry precipitate was dissolved in 20 ml of conc. HCl. The solution was filtered rapidly, and filtrate was diluted with 40 ml of water. The resulting precipitate was collected by filtration, washed with water (4 × 10 ml), and dried at 110°C to give 0.66 g (43%) of **5** (m.p. > 270°C; subl. ~240°C). $^1H$ NMR (DMF-$D_7$) $\delta$: 3.64 (4H, w.s., 2 $CH_2$); 6.04 (1H, t, CH, $J_{H-F} = 1.6$ Hz); 8.59 (1H, w.s., NH,); 10.7 (1H, w.s., NH) ppm. $^{19}F$ NMR (DMF-$D_7$) $\delta$: −162.05 (2F, m, *meta*-); −154.56 (1F, t-t, *para*-, $J_{3-4} = 20.7$; $J_{2-4} = 1.7$ Hz); −143.00 (2F, m, *ortho*-) ppm. IR ($cm^{-1}$): 3360, 3290, 3200, 3120 (NH); 1690 (C=O, amide); 1600 (C=O, ketone); 1540, 1510 (C=C, NH); 1020, 980 (CF). Analysis: Found: C, 47.36; H, 2.23; F, 31.24; N, 9.04%. Calc. for $C_{12}H_7F_5N_2O_2$: C, 47.07; H, 2.30; F, 31.07; N, 9.15%.

Analogously, 0.40 g (26%) of **5** was obtained from 5 mmol of **1a** in a mixture with 10 ml of $MeCO_2H$ and 10 ml of MeCN at room temperatures for 3 weeks.

### 2.6. Synthesis of 3-(2-hydroxy-3,4,5,6-tetrafluoro)benzoylmethylenepiperazin-2-one (6)

A mixture of compound **1a** (1.55 g, 5 mmol) and 1,2-ethylenediamine (0.36 g, 6 mmol) in 30 ml of MeOH was stirred at room temperature for 1 h, then refluxed for 5 h, cooled. The precipitate was collected by filtration, then stirred in 20 ml of hot conc. HCl for 5 min, and collected again, washed with water (3 × 10 ml), dried at 120°C to give 0.27 g (18%) of yellow precipitate (m.p. > 270°C), IR-, NMR $^1$H and $^{19}$F spectra data were identical to those of previously described [17] authentic sample of compound **6**.

### 2.7. Synthesis of 3-pentafluorobenzoylmethylene-1,2,3,4-tetrahydroquinoxalin-2-one (7)

#### 2.7.1. Method A

A mixture of compound **1a** (3.10 g, 10 mmol) and 1,2-phenylenediamine (1.13 g, 10.5 mmol) in 50 ml of $CH_2Cl_2$ was stirred at room temperature for 6 h, stored for 3 days. The resulting precipitate was collected by filtration, washed with MeOH (3 × 10 ml) to give 2.65 g (75%) of **7** (m.p. 283°C (dec.)). $^1$H NMR (DMF-D7) $\delta$: 6.41 (1H, t, CH, $J_{H-F} = 1.8$ Hz); 7.30 (3H, m, $C_6H_4$); 7.69 (1H, m, $C_6H_4$); 12.1 (1H, w.s., NH); 13.2 (1H, w.s., NH) ppm. $^{19}$F NMR (DMF-$D_7$)$\delta$: −161.84 (2F, m, *meta*-); −153.45 (1F, t-t, *para*-, $J_{3-4} = 20.2$; $J_{2-4} = 2.5$ Hz); −142.36 (2F, m, *ortho*-) ppm. IR (cm$^{-1}$): 3225 (NH); 1680 (C=O, amide); 1640, 1590 (C=O, ketone; NH); 1550, 1510 (C=C, NH), 990 (CF). Analysis: Found: C, 54.30; H, 1.88; F, 26.67; N, 7.88%. Calc. for $C_{16}H_7F_5N_2O_2$: C, 54.25; H, 1.99; F, 26.82; N, 7.91%.

Analogously, 0.89 g (50%) of **7** was obtained from 5 mmol of **1a** in 25 ml of $CHCl_3$.

#### 2.7.2. Method B

A mixture of compound **1b** (1.71 g, 2.5 mmol) and 1,2-phenylenediamine dihydrochloride (1.00 g; 5.5 mmol) in 60 ml of MeOH was stirred at room temperature for 12 h, then stored for 2 days. The resulting precipitate was collected by filtration, stirred with 30 ml of cool conc. HCl for 5 min, and then collected again, washed with water (4 × 10 ml) and dried to give 1.04 g (59%) of **7**. The physicochemical data were identical to those listed in method A.

### 2.8. Synthesis of 3-pentafluorobenzoylmethylene-3,4-dihydro-2H-1,4-benzoxazin-2-one (8)

#### 2.8.1. Method A

A mixture of compound **1a** (1.55 g; 5 mmol) and 2-aminophenol (0.60 g; 5.5 mmol) in 25 ml of MeOH was stirred at room temperature for 6 h, then stored for 2 days. The precipitate was collected by filtration, washed with MeOH (3 × 5 ml) and dried to give 0.91 g (51%) of **8** (m.p. 210–212°C). $^1$H NMR ($CDCl_3$) $\delta$: 6.59 (1H, t, CH, $J_{H-F} = 1.9$ Hz); 7.25 (4H, m, $C_6H_4$); 12.82 (1H, w.s., NH) ppm. $^{19}$F NMR ($CDCl_3$) $\delta$: −161.56 (2F, m, *meta*-); −151.33 (1F, t-t, *para*-, $J_{3-4} = 20.8$; $J_{2-4} = 3.5$ Hz); −143.16 (2F, m, *ortho*-) ppm. IR: (cm$^{-1}$) 3450 (NH); 1760 (C=O, lactone); 1625 (C=O, ketone); 1600, 1570, 1520 (C=C, NH); 990(CF). Analysis: Found: C, 54.24; H, 1.80; F, 26.95; N, 4.01%. Calc. for $C_{16}H_6F_5NO_3$: C, 54.10; H, 1.70; F, 26.74; N, 3.94%.

Analogously, 0.85 g (48%) of **8** was obtained from 5 mmol of **1a** in 50 ml of 2-PrOH.

#### 2.8.2. Method B

A mixture of compound **1a** (1.55 g; 5 mmol) and 2-aminophenol (1.22 g; 11.25 mmol) in 25 ml of MeCN was refluxed for 45 min and then cooled. The precipitate was collected and recrystallized from MeCN to give 0.59 g (33%) of **8**. The physicochemical data were identical to those listed above in method A.

#### 2.8.3. Method C

A mixture of compound **1b** (1.37 g; 2 mmol) and 2-aminophenol hydrochloride (0.67 g; 4.6 mmol) in 15 ml of MeOH was refluxed for 30 min and then cooled. The precipitate was collected and stirred with 20 ml of cold aqueous HCl (10%), and the precipitate was collected again, washed with water (4 × 10 ml), recrystallized twice from MeCN and dried to give 0.46 g (33%) of **8**. The physicochemical data were identical to those listed in method A.

### 2.9. Synthesis of 3-(2-hydroxy-3,4,5,6-tetrafluoro)benzoylmethylene-3,4-dihydro-2H-1,4-benzoxazin-2-one (9)

#### 2.9.1. Method A

A mixture of compound **1d** (1.31 g; 5 mmol) and 2-aminophenol (1.20 g; 11 mmol) in 30 ml of MeOH was refluxed with intensive stirring for 90 min. The precipitate was collected by filtration and washed with hot MeOH (2 × 5 ml) to give 1.54 g (87%) of **9** (m.p. 276–278°C). $^1$H NMR (DMSO-$D_6$) $\delta$: 6.55 (1H, d, CH, $J_{H-F} = 0.7$ Hz); 7.26 (3H, m, $C_6H_4$); 7.73 (1H, m, $C_6H_4$); 12.29 (2H, w.s., NH, OH) ppm. $^{19}$F NMR (DMSO-$D_6$) $\delta$: −170.94 (1F, d-t, $F^5$, $J_{5-4} = 22.2$; $J_{5-6} = 24.8$; $J_{5-3} = 5.2$ Hz); −161.89 (1F, d-d-d, $F^3$, $J_{3-4} = 22.2$; $J_{3-6} = 9.3$ Hz); −154.03 (1F, d-t, $F^4$, $J_{4-6} = 4.0$ Hz); −143.06 (1F, d-d-d, $F^6$) ppm. IR (cm$^{-1}$): 3400, 3170, 2700–2200 (NH, OH); 1745 (C=O, lactone); 1620 (C=O, ketone); 1600, 1550, 1520 (C=C, NH); 995, 985 (CF). Analysis: Found: C, 54.65; H, 1.98; F, 21.70; N, 4.08%. Calc. for $C_{16}H_7F_4NO_4$: C, 54.41; H, 2.00; F, 21.51; N, 3.97%.

#### 2.9.2. Method B

A mixture of compound **1c** (0.54 g; 1.86 mmol) and 2-aminophenol (0.24 g; 2.23 mmol) in 20 ml of MeOH was refluxed for 18 h. The precipitate was collected by filtration and then twice treated with boiling MeCN (15 ml). Filtra-

tion of hot suspension gave 0.16 g (25%) of **9**. The IR- and NMR-spectral data of substance obtained were identical to those listed in method A.

### 2.10. Reaction of **1a** with 2-aminophenol

A mixture of compound **1a** (1.55 g; 5 mmol) and 2-aminophenol (0.63 g; 5.8 mmol) in 25 ml of MeOH was refluxed for 30 min, then cooled and stored at room temperatures for 4 h. The resulting precipitate was collected and dried with hot MeOH (3 × 3 ml) to give 0.94 g (53%) of **8**. The filtrate was stored at room temperature for 3 days. The precipitate was collected and then twice treated with boiling MeCN (15 ml). A hot suspension was filtered to give 0.32 g (18%) of **9**. The physicochemical data of obtained substances were identical to those listed in 2.8 and 2.9.

## 3. Results and discussion

In the present work, it has been found that interaction of diaminonucleophiles (phenylhydrazine, hydrazine hydrate, 1,2-ethylenediamine, 1,2-phenylenediamine) and aminohydroxynucleophiles (hydroxylamine hydrochloride, 2-aminophenol) with **1a** generally leads to formation of nucleophile cyclocondensation products in contrast with primary amines reactions with **1a** which give derivatives of **1c** [16,17].

These dinucleophiles cycloadd to different reaction centers of **1a**: either to $\beta$-ketoenolic (atoms C-2 and C-4, see Scheme 1) or to $\alpha$-hydroxyesteric fragments (atoms C-1 and C-2, see Schemes 2 and 3). The nucleophile cyclocondensation pathways and regioselectivity depend on the nucleophile and reaction conditions.

Analogously, these nucleophiles also add to nonfluorinated aroylpyruvic acids derivatives [3–15].

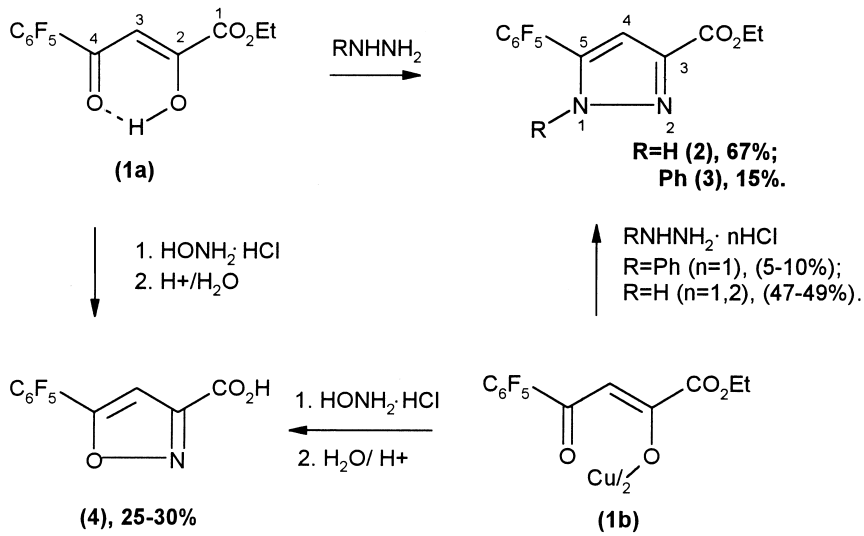
### 3.1. Reactions of ethyl pentafluorobenzoylpyruvate (**1a**) with hydrazines and of its copper (II) chelate (**1b**) with hydrazines hydrochlorides

Reactions of **1a** with hydrazines produced 5-pentafluorophenylpyrazole-3-carboxylic acid derivatives **2** and **3** under mild conditions in MeOH or in $CH_2Cl_2$ solutions at room temperature. These reactions usually did not possess a high selectivity, especially those of phenylhydrazine. Product **3** was isolated from a complicated mixture in low yield (15%). As a rule, reaction temperature increase caused a selectivity decrease. Only compounds **2** and **3** were isolated individually.

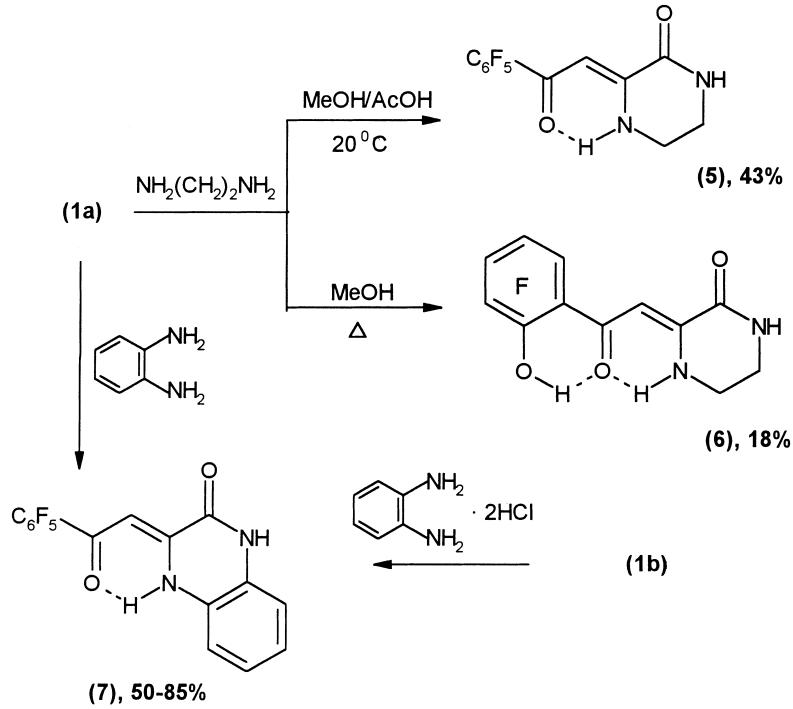
Furthermore, compounds **2** and **3** were prepared by reactions of copper (II) chelate **1b** with these hydrazine hydrochlorides. These reactions of **1b** proceeded at room temperature with subsequent heating at 60–70°C. The copper ions present in the reaction mixture made purification of pyrazoles **2** and **3** difficult because of their complexation. Yields of **3** from chelate **1b** were only 5–10%.

The position of the phenyl group in pyrazole ring of **3** at N-1 atom was confirmed spectroscopically by comparison of NMR $^1$H and $^{19}$F-spectra of pyrazoles **2** and **3**. The spin–spin coupling constant $J_{H-F} = 1.6$ Hz between pyrazole ring methylene H atom (at C-4) and *ortho*-fluorine atom of $C_6F_5$ group is observed in the NMR-spectra of **2**, but that is absent in the NMR-spectra of **3**. Probably, this fact results from deviation of the $C_6F_5$ ring from the pyrazole ring plane in the preferred conformation of pyrazole **3**. The data [3,5,6,16,19] also confirm much higher reactivity of carbonyl atom C-2 as compared with that of carbonyl atom C-4 of aroylpyruvates in reactions with N-nucleophiles.

The pyrazole structure formation is characteristic for nonfluorinated aroylpyruvic acids derivatives in their reactions with hydrazines [3–6].




Scheme 1.

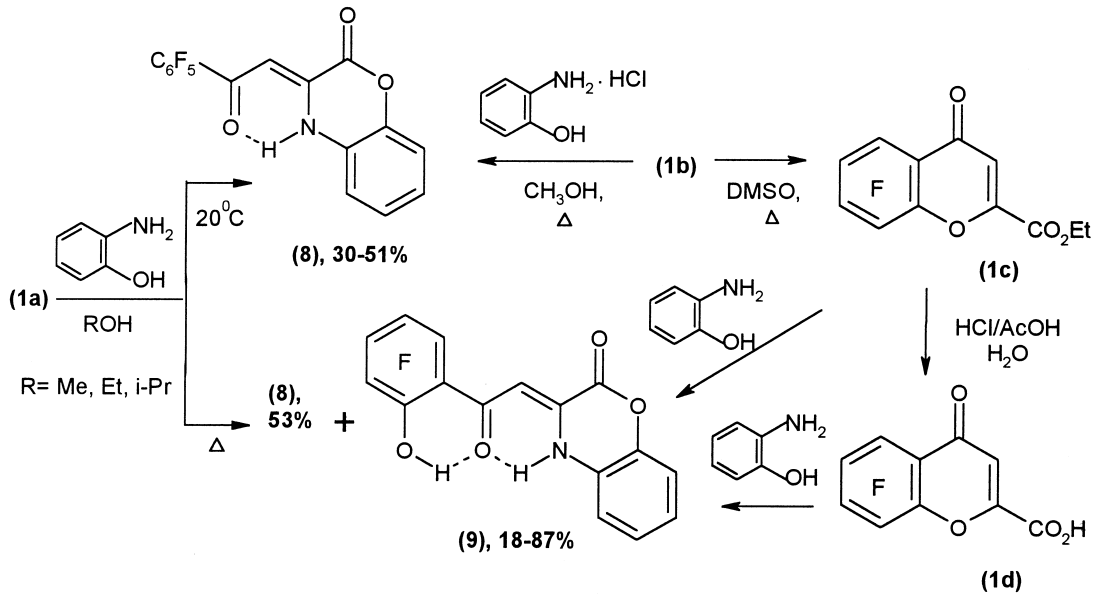



Scheme 2.

### 3.2. *Reactions of compounds* **1a** *and* **1b** *with hydroxylamine hydrochloride*

Only 5-pentafluorophenylisoxazole-3-carboxylic acid (**4**) was isolated from reactions of **1a** or **1b** with hydroxylamine hydrochloride followed by acidic hydrolysis of initial reactions products. The yields of **4** were low (25–30%). The products of initial reactions between **1a** or **1b** and hydroxylamine hydrochloride were difficulty separated mixtures. The mixtures of methyl- and ethyl-esters of acid **4** were isolated from these initial product mixtures in only 15–25% yields. These mixtures of esters gave colorless crystals with wide melting ranges.

The interaction of compound **1a** with 5 molar excess of free hydroxylamine at room temperature for 4 days gave a complicated unidentified mixture. Free hydroxylamine was




Scheme 3.

produced in situ from its hydrochloride and an equimolar amount of sodium methoxide in absolute MeOH. Probably, compound **1a** was decomposed under these conditions. No fluorine containing heterocycles were isolated from this reaction.

The nonfluorinated aroylpyruvic acid derivatives form 3-arylisoxazole-5-carboxylic acid derivatives in reactions with hydroxylamine hydrochloride [3,5].

The isoxazole ring substituent positions to structure **4** were assigned by experimental data for the interaction of compound **1a** with nucleophiles analogously to a structural assignment of pyrazole **3**. The spin–spin coupling constant $J_{H-F} = 1.6$ Hz between isoxazole ring methylene H (at C-4) and the *ortho*-fluorine atom of $C_6F_5$ is also observed in the NMR spectra of **4** confirming a structural analogy of C-3–C-4–C-5 fragments of pyrazole **2** and isoxazole **4**. A similar spin–spin coupling constant $J_{H-F} = 1.8$ Hz is observed in the NMR spectra of the ethyl- and methyl-esters of acid **4** mixture (84 : 16 molar).

The reaction equations of **1a** with 1,2-ethylenediamine, 1,2-phenylenediamine, 2-aminophenol producing products of their 1,2-cyclocondensation with $\alpha$-hydroxyester fragment of **1a**, and also those of **1b** are represented in Schemes 2 and 3.

### 3.3. *Interaction of compound* **1a** *with 1,2-ethylenediamine and of compound* **1b** *with 1,2-ethylenediamine hydrochloride*

The reactions between **1a** and 1,2-ethylenediamine were often not selective and led to formation of difficulty separated mixtures. The reactions of **1a** with a great excess (5–10 molar) of ethylenediamine in the presence of mixtures of MeOH–$MeCO_2H$ or MeCN–$MeCO_2H$ as solvents at room temperature produced 3-pentafluorobenzoylmethylenepiperazin-2-one (**5**) in 26–43% yields. The lower excess of ethylenediamine and heating the reaction mixture led to a decreasing yield of compound **5**.The heating under reflux of compound **1a** with equimolar or excess amounts of ethylenediamine in MeOH solution gave low yields (15–18%) of 3-(2-hydroxy-3,4,5,6-tetrafluoro)benzoylmethylenepiperazin-2-one (**6**) recently synthesized by ring opening of chromone **1c** by 1,2-ethylenediamine [17]. The reactions of **1a** with ethylenediamine under conditions different from those above gave complicated mixtures containing **5** and/or **6** as observed by TLC methods.

Nonfluorinated aroylpyruvic acids and their esters reacted with 1,2-ethylenediamine at 20–25°C producing polymeric substances formed by diamine bonding of aroylpyruvates with carbonyl groups of C-1 and C-2 atoms. Heating of these substances under reflux at 110°C in toluene led to their depolymerization to form 2-aroylmethylene-3,4,5,6-tetrahydropyrazin-3-ones which were produced directly from aroylpyruvates and 1,2-ethylenediamine under reflux in EtOH or toluene solutions [7].

Chelate **1b** reacted with 1,2-ethylenediamine dihydrochloride in alcohols and in mixtures of alcohols–water, alcohols–$MeCO_2H$ as solvents very slowly even with prolonged times of boiling. For example, 12 h of boiling of compound **1b** and 5 molar excess of ethylenediamine dihydrochloride led to a nearly quantitative recovery of starting **1b** containing some impurities plus compounds **5** and **6**. Addition of water or $MeCO_2H$ to reaction solvent did not change yields. Chelate **1b** and the diamine dihydrochloride did not react in the presence of $CF_3CO_2H$ or in solutions of $CHCl_3$ or $CCl_4$ on boiling. Complicated mixtures were produced in DMSO solutions at 80–90°C.

### 3.4. *Reaction of compound* **1a** *with 1,2-phenylenediamine and of compound* **1b** *with 1,2-phenylenediamine dihydrochloride*

Reaction of **1a** with 1,2-phenylenediamine in $CH_2Cl_2$ solution at room temperature gave 3-pentafluorobenzoylmethylene-1,2,3,4-tetrahydroquinoxalin-2-one (**7**) in 75% yield. The yield of **7** decreased in $CHCl_3$ to 50% and increased in MeOH to 80–85%, but **7** contained impurities in the latter case. Heating of reactants did not alter yield of **7** but caused contamination of **7** in all cases.

The product containing an *ortho*-hydroxyl group in the polyfluorophenyl ring analogous to **6** was not found in this reaction. This is, probably, explained by the lower basicity of 1,2-phenylenediamine as compared with that of 1,2-ethylenediamine that causes a more selective cyclocondensation reaction of 1,2-phenylenediamine with **1a** than that for 1,2-ethylenediamine.

The reactions of nonfluorinated aroylpyruvic acids or their sterically unhindered esters with 1,2-phenylenediamine under mild conditions led to formation of 3-aroylmethylene-1,2,3,4-tetrahydroquinoxalin-2-ones. The side formation of 4-arylbenzo[b]di-1,5-azepine-2-carboxylic acid derivatives was observed in reactions between the *t*-butyl ester of benzoylpyruvic acid or its arylamides and 1,2-phenylenediamine.These derivatives easily rearranged under heating to give the more stable aroylmethylenequinoxalones [8–13].

Compound **1b** reacted with 1,2-phenylenediamine dihydrochloride in cold MeOH to give only **7** in 59% yield.

### 3.5. *Reactions of compounds* **1a**, **1c** *and* **1d** *with 2-aminophenol and of compound* **1b** *with 2-aminophenol hydrochloride*

The reactions of **1a** with 2-aminophenol in alcoholic or MeCN solutions gave 3-polyfluorobenzoylmethylene-3,4-dihydro-2H-1,4-benzoxazin-2-ones (**8** and **9**). Only 3-pentafluorobenzoylmethylene-3,4-dihydro-2H-1,4-benzoxazin-2-one (**8**) was isolated from reactions in alcoholic or MeCN solutions at room temperature or at boiling. The yields of **8** from alcoholic solutions were 48–51% and these

were decreased to 30–33% from MeCN. Only **8** was isolated initially from reactions in boiling alcohols in 50–53% yields but also the side product, 3-(2-hydroxy-3,4,5,6-tetrafluorobenzoylmethylene)-3,4-dihydro-2H-1,4-benzoxazin-2-one (**9**), was isolated in 18% yield after storage of the reaction mixture for 3–4 days at room temperature.

Strong absorption bands at 1760 and at 1745 $cm^{-1}$ attributed to lactone carbonyl groups [13–15] are present in the IR spectra of **8** and **9**, respectively. The absorption of the amide carbonyl group of compound **7** and nonfluorinated aroylmethylenequinoxalones [13–15] near 1680 $cm^{-1}$ is absent in the IR spectra of **8** and **9**.

The alternative products of 2-aminophenol 1,2-cyclocondensation with the $\alpha$-hydroxyester fragment of **1a**, 2-polyfluorobenzoylmethylene-3,4-dihydro-2H-1,4-benzoxazin-3-ones, have not been observed.

The reactions of nonfluorinated aroylpyruvic acid esters with 2-aminophenol gave also 3-aroylmethylene-3,4-dihydro-2H-1,4-benzoxazin-2-ones which had **8** and **9** type structures [13–15].

We synthesized compound **9** also from tetrafluorochromones **1c** and **1d** as starting substances under conditions like that from **1a** for additional confirmation of structure **9**.

This reaction of **1a** proceeded slowly and unselectively in nonpolar solvents — $CHCl_3$ or $CH_2Cl_2$. This is, probably, explained by side cyclization of **1a** to chromone **1c** [16,19] with 2-aminophenol as base. Intermediate chromone reacted with 2-aminophenol slowly and unselectively and was isolated from reaction mixtures of **1a** in low yields (5–10%) in some cases under these conditions.

Compound **1b** produced **8** in 33% yield from reaction with 2-aminophenol hydrochloride in boiling MeOH. The difficulty separated and identified mixtures usually containing **8** (TLC data) were produced from **1b** under other examined reaction conditions similar those of **1a** with 2-aminophenol. These reactions of **1b** did not proceed completely at room temperature.

## 4. Conclusion

In the present work, it has been shown that polyfunctional fluoroaromatic compounds **1a** and **1b** reacted with some diamino- and hydroxyaminonucleophiles to form cyclocondensation products that were heterocyclic compounds of various types containing polyfluorophenyl substituents.

The formation of ring opening products of intermediate chromone **1c** effected by nucleophiles also has been observed in reactions between **1a** and 1,2-ethylenediamine or 2-aminophenol.

The cyclocondensation pathway was determined by the nucleophiles and reaction products nature and was generally consistent with that for nonfluorinated aroylpyruvates.

The copper(II) ion effect was proved to be considerable in some reactions of chelate **1b**. Compound **1b** was less reactive as compared with **1a**, so 1,2-ethylenediamine dihydrochloride did not react with **1b** completely. The ring opening products of chromone **1c** were not produced from **1b**, and yields of desirable products with a $C_6F_5$ group were slightly decreased.

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