

REACTIONS OF POLYFLUOROAROMATIC ORGANOZINC COMPOUNDS WITH ACYL CHLORIDES AND DMFAndrei S. VINOGRADOV¹, Vyacheslav I. KRASNOV² and Vyacheslav E. PLATONOV^{3,*}

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Dedicated to Professor Oldřich Paleta on the occasion of his 70th birthday and in recognition of his contribution to organic fluorine chemistry.

N,N-Dimethylbis(polyfluoroaryl)methanamines and polyfluoroarenes were obtained from polyfluoroaromatic organozinc compounds in DMF in the presence of acyl chlorides.

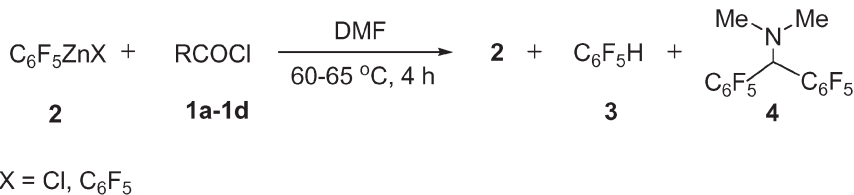
Keywords: Polyfluoroaromatic organozinc compounds; DMF; Acyl chlorides; *N,N*-Dimethylbis(polyfluoroaryl)methanamines.

The preparation of polyfluoroaromatic organozinc compounds from chloropolyfluoroarenes and Zn as well as from perfluoroarenes and Zn/SnCl₂ in DMF was recently reported¹⁻⁴. Chemical properties of these organozinc compounds were studied. As a result, hydro- and bromopolyfluoroarenes, perfluorobiaryls¹⁻³ and allylpolyfluoroarenes⁴ have been obtained. Another important aspect of the chemistry of polyfluoroaromatic organozinc compounds is the reactions of the compounds with acyl chlorides in DMF for the purpose of obtaining polyfluoroaromatic ketones. Acetyl (**1a**), propionyl (**1b**), pivaloyl (**1c**) and benzoyl chlorides (**1d**) were used to investigate the reactions with C₆F₅ZnX (X = Cl, C₆F₅) (**2**) in some detail; it turned out that pentafluorobenzene (**3**) and *N,N*-dimethyl-1,1-bis-(perfluorophenyl)methanamine (**4**) were formed instead of the expected polyfluoroaromatic ketones. The reactions of other polyfluoroaromatic organozinc compounds with acyl chloride **1d** were performed to synthesize *N,N*-dimethylbis(polyfluoroaryl)methanamines.

RESULTS AND DISCUSSION

Heating compound **2** with acyl chlorides **1a**, **1b** resulted in the formation of compound **3** whereas with acyl chloride **1c** the reaction mixture contained amine **4** along with **3** (Scheme 1; Table I, runs 1–3).

Formation of amine **4** was observed when acyl chloride **1d** was used (Scheme 1). When an equimolar ratio of acyl chloride **1d** or **1c** and **2** was used in the reaction, a considerable amount of **2** was not consumed (Table I, runs 3, 4). When increasing the amount of acyl chloride **1d** (Table I, run 5), the reaction of compound **2** occurred completely, leading to a mixture of compounds **3** and **4**.

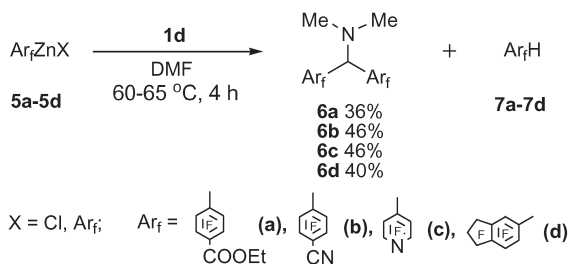


SCHEME 1

TABLE I
Reactions of compound **2** with acyl chlorides

Run No.	R	Reactants molar ratio 2 /(1a-1d)	Ratio of 2 : 3 : 4 (by ¹⁹ F NMR)
1	Me (1a)	1:2	3
2	Et (1b)	1:2.2	3
3	Me ₃ C (1c)	1:1.1	~5.1:1:1.3
4	Ph (1d)	1:1.1	~2.9:1:3
5	Ph (1d)	1:2.5	~0:1:1.5

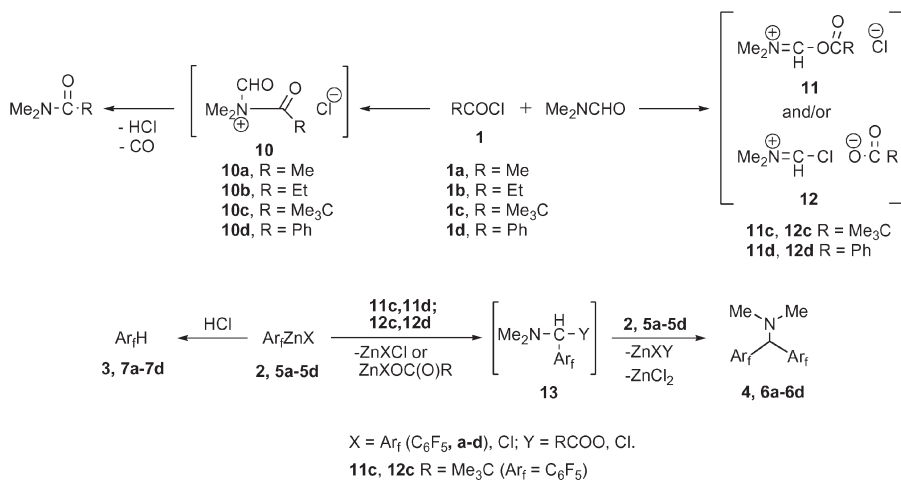
We also performed the reactions of other organozinc reagents with acyl chloride **1d** in DMF to synthesize analogues of amine **4**. Thus, from organozinc reagents (**5a-5d**), obtained from ethyl pentafluorobenzoate, pentafluorobenzonitrile, pentafluoropyridine and decafluoroindane under the action of Zn/SnCl₂ in DMF^{2,4}, the corresponding *N,N*-dimethylbis-(polyfluoroaryl)methanamines (**6a-6d**) along with polyfluoroarenes (**7a-7d**) were synthesized (Scheme 2).



SCHEME 2

In the reaction of compound **5a** with acyl chloride **1d**, amine **6a** and compound **7a** are formed along with a small amount of ethyl 4-benzoyl-2,3,5,6-tetrafluorobenzoate (**8**) and diethyl 2,2',3,3',5,5',6,6'-octafluorobiphenyl-4,4'-dicarboxylate (**9**) according to GC-MS and ^{19}F NMR.

Formation of compound **3** from reagent **2** and acyl chlorides **1a-1d** as well as of polyfluoroarenes **7a-7d** from reagents **5a-5d** and benzoyl chloride (**1d**) in DMF could occur as a result of transamidation. For example, this process can include intermediate formation of ammonium salts (**10a-10d**) and their conversion to amides and unstable formyl chloride, decomposing to CO and HCl^{5,6}. The reaction of HCl with reagents **2**, **5a-5d** gives compounds **3**, **7a-7d** (Scheme 3). It was shown^{5,6} that transamidation occurred under severe reaction conditions. Probably, the presence of ZnCl_2 and the other zinc compounds as Lewis acids in the studied reactions promoted transamidation under milder conditions.



SCHEME 3

Another direction of the reaction of acyl chlorides **1c** and **1d** with DMF is the interaction of electrophilic centres of **1c** and **1d** with oxygen of DMF with the formation of Vilsmeier reactants^{7,8} **11c**, **11d** and/or **12c**, **12d** (Scheme 3). Formation of amine **4** can be rationalized by the participation of the present reactants, and also intermediate compound **13**. The latter reaction with **2** probably gives amine **4** (Scheme 3). In a similar manner, formation of amines **6a–6d** in the reactions of reagents **5a–5d** with acyl chloride **1d** could be explained.

The presence of $(\text{PhCO})_2\text{O}$ in the reaction products of **2** and **5a** with acyl chloride **1d** is consistent with the participation of salt **12d** in the discussed process of the formation of amines **4** and **6a**. Formation of $(\text{PhCO})_2\text{O}$ is assumed to proceed by the reaction of **1d** with **12d** or $\text{ZnX}(\text{OCOR})$ ($\text{R} = \text{Ph}$; $\text{X} = \text{Cl}, \text{C}_6\text{F}_5; \text{Cl}, 4\text{-EtOCOC}_6\text{F}_4$). The participation of DMF in the formation of amines **4** and **6a–6d** is consistent with the data on the synthesis of a similar compound $(\text{Me}_2\text{NCH}(\text{CF}=\text{CFCF}_3)_2)$ from organocadmium reagents $(\text{CF}_3\text{CF}=\text{CFCdX})$ and acyl chloride **1d** in DMF⁹.

Preliminarily, organozinc reagents **5a–5d** were treated with CaCl_2 to decrease the formation of inactive PhCOF . As shown by a separate experiment, a mixture of reagent **2** and PhCOF in DMF at 70 °C (4 h) does not appreciably change. PhCOF can be prepared from acyl chloride **1d** under the action of ZnF_2 ¹⁰; this salt may arise in the formation of organozinc reagents **5a–5d**.

The formation of compound **8** is assumed to proceed by the reaction of **5a** with acyl chloride **1d**; product **9** could be formed as a result of air oxidation of compound **5a** to ethyl 2,3,5,6-tetrafluorophenyl-4-carboxylate radical with subsequent coupling.

CONCLUSION

In the investigation of the reactions of polyfluoroaromatic organozinc compounds with acyl chlorides and DMF, the method of synthesis of as yet undescribed *N,N*-dimethylbis(polyfluoroaryl)methanamines has been developed. In these reactions, the formation of polyfluoroarenes also took place. As regards the mechanism of formation of *N,N*-dimethylbis(polyfluoroaryl)methanamines and polyfluoroarenes, the participation of Vilsmeier reactants and transamidation in the reactions of acyl chlorides with DMF have been suggested. Further investigation of the processes of this type will shed more light on these problems and will also lead to a better understanding of the synthetic aspects of similar reactions.

EXPERIMENTAL

NMR spectra were recorded on a spectrometer Bruker AC-200 (188.3 MHz for ^{19}F and 200 MHz for ^1H) for the reaction mixtures containing organozinc compounds in DMF or CCl_4 solution. C_6F_6 (-162.9 ppm from CCl_3F) and $(\text{Me}_3\text{Si})_2\text{O}$ (0.04 ppm from TMS) were used as internal standards. Chemical shifts (δ) are given in ppm relative to CCl_3F and TMS. Coupling constants (J) are given in Hz. IR spectra were recorded on a Bruker Vector 22 IR spectrophotometer. UV spectra were measured on a Hewlett-Packard 8453 UV spectrophotometer. Molecular weights and molecular formulae were determined mass-spectrometrically on a Finnigan MAT 8200 high-resolution instrument (nominal ionizing electron energy 70 eV). GC-MS analyses were performed with a Hewlett-Packard G1800A apparatus (30 m capillary column, HP-5). GLC analyses were carried out on a Hewlett-Packard HP 5980 instrument (30 m capillary column, HP-5). Melting points were determined in a Kofler block.

Organozinc compounds **2**, **5a–5d** were obtained by the methods described in refs^{2,4}. To solutions of organozinc compounds **5a–5d**, equimolar quantity of CaCl_2 (heated at 250–300 °C for 3 h) was added, and the resulting mixtures were stirred at room temperature for 3 h. The solutions of the organozinc compounds were then decanted; these solutions contained Ar_fZnCl and $(\text{Ar}_f)_2\text{Zn}$ along with Ar_fH ($\text{Ar}_f = \text{C}_6\text{F}_5$, **a–d**, Scheme 2) (^{19}F NMR).

Assignments of signals in the ^{19}F NMR spectrum of amine **6b** were made on the basis of calculation (additive scheme) using the chemical shifts of the *ortho* and *meta* fluorine atoms of amine **4** and $\text{C}_6\text{F}_5\text{CN}$ ¹¹. ^{19}F NMR spectrum of 5-allylnonafluoroindane⁴ was used in assigning fluorine signals of amine **6d**.

Reactions of Compounds **2** with Acyl Chlorides **1a–1d**

To a solution of **2** (7.28 g, 10.2 mmol, purity 91%, with 9% of **3**) acyl chloride **1a** (1.57 g, 20.0 mmol) was added, the mixture was heated at 60–65 °C for 4 h and then allowed to cool to room temperature. The reaction mixture contained only **3** (^{19}F NMR). A similar result was obtained in the reaction of **2** (22.64 g, 31.7 mmol) with acyl chloride **1b** (6.51 g, 70.4 mmol).

To a solution of **2** (7.87 g, 9.3 mmol, purity 96%, with 4% of **3**) acyl chloride **1c** (1.21 g, 10.0 mmol) was added, the mixture was heated at 60–65 °C for 4 h and then allowed to cool to room temperature. The reaction mixture contained 64% of the initial compound **2**, 14% of compound **3** and 18% of amine **4** (^{19}F NMR).

To a solution of **2** (3.94 g, 4.6 mmol, purity 96%, with 4% of **3**) acyl chloride **1d** (0.7 g, 5.0 mmol) was added, the mixture was heated at 60–65 °C for 4 h and then allowed to cool to room temperature. The reaction mixture contained 40% of the starting compound **2**, 14% of **3** and 42% of amine **4** (^{19}F NMR).

Reactions of Compounds **2** with Benzoyl Fluoride

To a solution of **2** (2.36 g, 2.8 mmol, purity 96%, with 4% of **3**) benzoyl fluoride (0.37 g, 3.0 mmol) was added, the mixture was heated at 70 °C for 4 h and then allowed to cool to room temperature. According to the ^{19}F NMR spectrum, only the signals of the starting compounds were observed.

N,N-Dimethylbis(polyfluoroaryl)methanamines. General Procedure

To a solution of a polyfluoroaromatic organozinc compound (**2**, **5a–5d**), acyl chloride **1d** (3.52 g, 25.0 mmol) was added, the mixture was heated at 60–65 °C for 4 h and then allowed to cool to room temperature. According to ^{19}F NMR, the reaction mixture contained 43–73% of amines (**4**, **6a–6d**), 7–42% of polyfluoroarenes (**3**, **7a–7d**) and unidentified impurities; in the reactions of **5b–5d** with acyl chloride **1d**, the formation of PhCOF was observed (^{19}F NMR, $\delta \sim 18^{10}$). To the reaction mixture, 50 ml of water were added, and the organic products were extracted with CHCl_3 (3 \times 5 ml). Each combined extract was washed with 50 ml of 10% aqueous Na_2CO_3 and 50 ml of water, dried over K_2CO_3 , and CHCl_3 was distilled off. In the reactions with compounds **2**, the CHCl_3 distilled contained compound **3** (^{19}F NMR). To each residue obtained in the reactions with reagents **5b–5d** (in other cases the residues were distilled in vacuo, ~ 3 Torr) and each distillation fraction, 10 ml of diethyl ether were added and HCl was then passed through the solution to obtain the hydrochlorides. The solid was filtered off and washed with 5–10 ml of diethyl ether. For the preparation of amines **4**, **6a–6d**, 50 ml of 10% aqueous Na_2CO_3 were added to the solid, and the mixture was heated at 90–100 °C (10 min), then allowed to cool to room temperature. After cooling, the amine was filtered off and washed with 50 ml of water.

N,N-Dimethyl-1,1-bis(perfluorophenyl)methanamine (**4**). From the reaction of organozinc compound **2** (7.14 g, 10 mmol, purity 91%, with 9% of **3**), the fraction (1.32 g) with b.p. 117–127 °C containing (GLC) amine **4** (90%) and the fraction (0.88 g) with b.p. 172–173 °C containing amine **4** (8%), PhCOOH (4%), $(\text{PhCO})_2\text{O}$ (84%) were obtained. The ^{19}F NMR spectrum of the residue (0.21 g) did not give F signals. From the fractions, hydrochloride of amine **4** (1.01 g) and then amine **4** (0.86 g, 44%) were isolated. Amine **4**, m.p. 53–54 °C. IR (CCl_4): 2995, 2961, 2874, 2828, 2779, 1651, 1522, 1505, 1124, 1006, 804. UV (EtOH (log ϵ)): 204 (4.14), 210 (4.14), 263 (3.25). ^1H NMR (200 MHz, CCl_4): 2.27 s, 6 H (Me); 5.12 s, 1 H (CH). ^{19}F NMR (188 MHz, CCl_4): -162.3 m, 4 F (F-3 and F-5); -154.8 t, 2 F, $^3J_{\text{FF}} = 21$ (F-4); -140.5 m, 4 F (F-2 and F-6). MS, m/z (%): 391 (47) $[\text{M}^+]$, 347 (62) $[\text{M}^+ - \text{NMe}_2]$, 278 (25), 224 (100) $[\text{M}^+ - \text{C}_6\text{F}_5]$, 42 (17), 28 (12). HRMS: found 391.03999, $\text{C}_{15}\text{H}_7\text{F}_{10}\text{N}$ [M] requires 391.04187. For $\text{C}_{15}\text{H}_7\text{F}_{10}\text{N}$ (391.2) calculated: 46.05% C, 1.80% H, 48.56% F, 3.58% N; found: 46.16% C, 1.66% H, 48.03% F, 3.59% N.

Diethyl 4,4'-[(dimethylamino)methylene]bis(2,3,5,6-tetrafluorobenzoate) (**6a**). From the reaction of **5a** (9.01 g, 10 mmol, purity 95%, with 5% of ethyl 2,3,5,6-tetrafluorobenzoate (**7a**)), the fraction (1.41 g) with b.p. 80–170 °C containing (GC-MS) *N,N*-dimethylbenzamide, $(\text{PhCO})_2\text{O}$, compounds **7a**, **8**, **9** and amine **6a** were obtained. GC-MS, m/z (%): compound **8**: 326 $[\text{M}]^+$, 281 $[\text{C}_6\text{H}_5\text{COC}_6\text{F}_4\text{CO}]^+$, 221 $[\text{C}_6\text{F}_4\text{CO}_2\text{Et}]^+$, 148 $[\text{C}_6\text{F}_4]^+$, 105 $[\text{C}_6\text{H}_5\text{CO}]^+$, 77 $[\text{C}_6\text{H}_5]^+$, 51; compound **9**: 442 $[\text{M}]^+$, 397 $[\text{EtO}_2\text{CC}_6\text{F}_4\text{C}_6\text{F}_4\text{CO}]^+$, 386, 369 $[\text{EtO}_2\text{CC}_6\text{F}_4\text{C}_6\text{F}_4]^+$, 342, 324 $[\text{C}_6\text{F}_4\text{C}_6\text{F}_4\text{CO}]^+$, 296 $[\text{C}_6\text{F}_4\text{C}_6\text{F}_4]^+$, 176 $[\text{C}_6\text{F}_4\text{CO}]^+$, 148 $[\text{C}_6\text{F}_4]^+$, 45. ^{19}F NMR spectrum of this fraction contained signals (-141.2 , -139.5), which were assigned to ketone **8** by comparison with the ^{19}F NMR spectrum of the pure ketone. According to ^{19}F NMR spectrum, this fraction contained amine **6a** (47%), compound **7a** (22%), ketone **8** (27%) and compound **9** (4%). The residue (0.45 g) contained mainly **6a**; the hydrochloride (0.36 g) and amine **6a** (0.3 g, 12%) were isolated. Similarly, the fraction gave amine **6a** (0.6 g, 24%). Amine **6a**, m.p. 78–79 °C. IR (CCl_4): 2987, 2874, 2828, 2779, 1745, 1652, 1490, 1308, 1221, 1017, 985. UV (EtOH (log ϵ)): 204 (4.34), 230 (4.30), 279 (3.59). ^1H NMR (200 MHz, CCl_4): 1.38 t, 6 H, $^3J_{\text{HH}} = 7.1$ (CH_2CH_3); 2.31 s, 6 H (Me); 4.38 q, 4 H, $^3J_{\text{HH}} = 7.1$ (CH_2CH_3); 5.23 s, 1 H (CH). ^{19}F NMR (188 MHz, CCl_4): -140.4 m, 4 F; -139.9 m, 4 F. MS, m/z (%): 499 (25) $[\text{M}]^+$, 455

(12) $[M^+ - NMe_2]$, 278 (100) $[M^+ - EtO_2CC_6F_4]$, 250 (18). HRMS: found 499.10228, $C_{21}H_{17}F_8NO_4$ [M] requires 499.10297. For $C_{21}H_{17}F_8NO_4$ (499.4) calculated: 50.51% C, 3.43% H, 30.44% F, 2.80% N; found: 50.20% C, 3.41% H, 30.41% F, 2.73% N.

4,4'-[(Dimethylamino)methylene]bis(2,3,5,6-tetrafluorobenzonitrile) (**6b**). From the reaction of **5b** (8.93 g, 10 mmol, purity 91%, with 9% of 2,3,5,6-tetrafluorobenzonitrile (**7b**)), the corresponding hydrochloride (1.05 g) and then amine **6b** (0.93 g, 46%) were isolated. Amine **6b**, m.p. 112–114 °C. IR (CCl_4): 3003, 2963, 2882, 2832, 2783, 2245, 1647, 1496, 1304, 995. UV (EtOH (log ϵ)): 204 (4.32), 223 (4.30), 241 (4.42), 294 (3.71). 1H NMR (200 MHz, CCl_4): 2.32 s, 6 H (Me); 5.32 s, 1 H (CH). ^{19}F NMR (188 MHz, CCl_4): -137.9 m, 4 F (F-2 and F-6); -132.6 m, 4 F (F-3 and F-5). MS, m/z (%): 405 (52) $[M]^+$, 361 (23) $[M^+ - NMe_2]$, 292 (12), 231 (100) $[M^+ - NCC_6F_4]^+$, 42 (19). HRMS: found 405.05121, $C_{17}H_7F_8N_3$ [M] requires 405.05168. For $C_{17}H_7F_8N_3$ (405.3) calculated: 50.38% C, 1.74% H, 37.51% F, 10.37% N; found: 50.37% C, 1.70% H, 37.19% F, 10.34% N.

N,N-Dimethyl-1,1-bis(perfluoropyridin-4-yl)methanamine (**6c**). From the reaction of **5c** (8.85 g, 10 mmol, purity 93%, with 7% of 2,3,5,6-tetrafluoropyridine (**7c**)), the corresponding hydrochloride (1.04 g) and then amine **6c** (0.83 g, 46%) were isolated. Amine **6c**, m.p. 86–87 °C. IR (CCl_4): 2994, 2964, 2907, 2877, 2833, 2784, 1643, 1477, 1262, 998. UV (EtOH (log ϵ)): 202 (4.07), 273 (3.82). 1H NMR (200 MHz, CCl_4): 2.35 s, 6 H (Me); 5.35 s, 1 H (CH). ^{19}F NMR (188 MHz, CCl_4): -142.1 m, 4 F (F-2 and F-6); 90.0 widened m, 4 F (F-3 and F-5). MS, m/z (%): 357 (25) $[M]^+$, 313 (7) $[M^+ - NMe_2]$, 207 (100) $[M^+ - NC_5F_4]$, 42 (22), 28 (23). HRMS: found 357.05194, $C_{13}H_7F_8N_3$ [M] requires 357.05121. For $C_{13}H_7F_8N_3$ (357.2) calculated: 43.71% C, 1.98% H, 42.55% F, 11.76% N; found: 43.82% C, 1.96% H, 42.91% F, 11.66% N.

N,N-Dimethyl-1,1-bis(perfluoro-2,3-dihydro-1H-inden-5-yl)methanamine (**6d**). From the reaction of **5d** (12.50 g, 10 mmol, purity 90%, with 10% of nonafluorindane (**7d**)), the corresponding hydrochloride (1.42 g) and then amine **6d** (1.23 g, 40%) were isolated. Amine **6d**, m.p. 117–118.5 °C. IR (CCl_4): 2994, 2964, 2877, 2832, 2783, 1650, 1503, 1327, 1254, 1205, 1162, 950. UV (EtOH (log ϵ)): 205 (4.47), 277 (3.59). 1H NMR (200 MHz, CCl_4): 2.34 s, 6 H (Me); 5.35 s, 1 H (CH). ^{19}F NMR (188 MHz, CCl_4): -140.6 m, 2 F (F-7); -131.2 quin, 4 F, $^3J_{FF} = 4.5$ (F-2); -122.0 m, 2 F (F-6); -115.5 m, 2 F (F-4); -109.0 and -108.2 both m, 8 F (F-1 and F-3). MS, m/z (%): 616 (2) $[M]^+$, 572 (13) $[M^+ - NMe_2]$, 336 (100) $[M^+ - C_9F_9]$, 42 (10). HRMS: found 615.02898, $C_{21}H_7F_{18}N$ [M] requires 615.02909. For $C_{21}H_7F_{18}N$ (615.3) calculated: 40.99% C, 1.15% H, 55.58% F, 2.28% N; found: 41.25% C, 1.31% H, 55.34% F, 2.06% N.

REFERENCES

1. Krasnov V. I., Platonov V. E.: *Zh. Org. Khim.* **2000**, *36*, 1524; *Russ. J. Org. Chem.* **2000**, *36*, 1488.
2. Miller A. O., Krasnov V. I., Peters D., Platonov V. E., Miethchen R.: *Tetrahedron Lett.* **2000**, *41*, 3817.
3. Krasnov V. I., Vinogradov A. S., Platonov V. E.: *Mendeleev Commun.* **2006**, *3*, 168.
4. Vinogradov A. S., Krasnov V. I., Platonov V. E.: *Zh. Org. Khim.* **2008**, *44*, 101; *Russ. J. Org. Chem.* **2008**, *44*, 95.
5. Coppinger G. M.: *J. Am. Chem. Soc.* **1954**, *76*, 1372.
6. Knunyants I. L., Cheburkov Yu. A., Aronov Yu. E.: *Izv. Akad. Nauk SSSR, Ser. Khim.* **1966**, 1038; *Chem. Abstr.* **1966**, *65*, 10491.

7. Barton D. H. R., Ollis W. D. (Eds): *Comprehensive Organic Chemistry. The Synthesis and Reactions of Organic Compounds*, Vol. 1 (J. F. Stoddart, Ed.), p. 1118. Pergamon Press, Oxford 1979.
8. Majid T. N., Knochel P.: *Tetrahedron Lett.* **1990**, 31, 4413.
9. Burton D. J., Yang Z.-Yu., Morken P. A.: *Tetrahedron* **1994**, 50, 2993.
10. Sekiya A., Ishikawa N.: *Bull. Chem. Soc. Jpn.* **1978**, 51, 1267.
11. Pushkina L. N., Stepanov A. P., Zhukov V. S., Naumov A. D.: *Zh. Org. Khim.* **1972**, 8, 586; *J. Org. Chem. U.S.S.R.* **1972**, 8, 592.