Journal contents

POLYFLUOROARENES AND Zn: HYDROGENOLYSIS REACTIONS, SYNTHESIS AND CHEMICAL PROPERTIES OF POLYFLUOROAROMATIC ORGANOZINC COMPOUNDS

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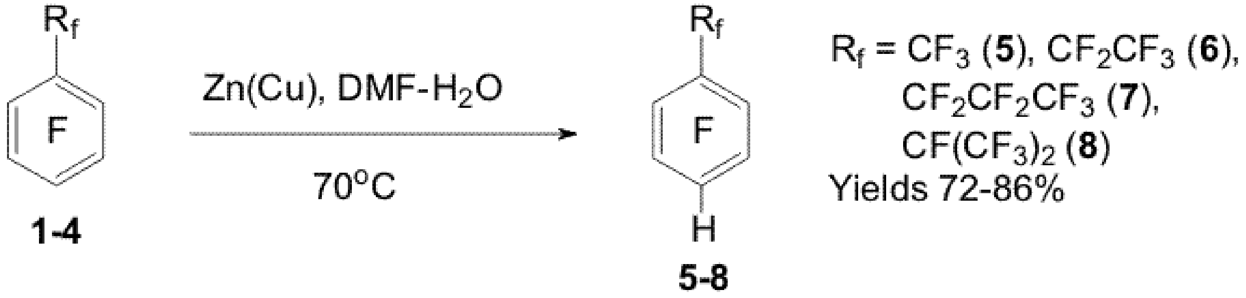
Among chemical properties of polyfluorinated aromatic compounds the reactions with nucleophilic, electrophilic, radical reagents and carbenes have been studied in sufficient details. The processes initiated by electron transfer have not been studied adequately yet. The reactions of hydrodehalogenation of polyfluoroarenes under the action of metals and the reactions of formation of polyfluoroaryl metallo-organic compounds may be ascribed to these processes. We found a convenient reducing system Zn(Cu) in aqueous dimethylformamide (**DMF**) to study regularities of the reactions of polyfluoroarenes hydrodehalogenation as well as conditions for obtaining polyfluoroaryl organozinc compounds from polyfluoroarenes and zinc.

Systematic investigation of influence of the chemical structure of polyfluoroarenes on the rate and regioselectivity of their hydrodehalogenation as well as formation of polyfluoroaryl organozinc compounds is important for the study of these processes regularities running with probable participation of anion radicals. From the synthetic point of view the investigation urgency lies in modification of perfluoroalkyl substituents, inert to the action of many reagents, by means of the hydrodefluorination reactions as well as in development of an approach to obtain partially fluorinated arenes by hydrogenolysis of C-F bonds of the aromatic ring of perfluoroarenes and hydrogenolysis of C-Cl bonds of polychloroarenes. Polyfluoroaryl organozinc compounds may be used to obtain various functional derivatives of polyfluoroarenes.

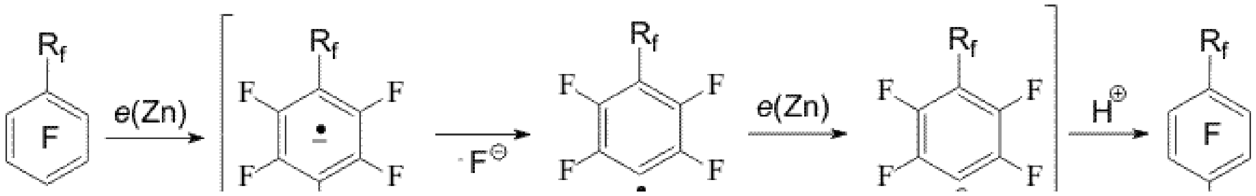
1.Perfluoroarenes hydrodefluorination and perfluorochloroarenes hydrodechlorination under the action of Zn(Cu) in aqueous DMF

Perfluoroalkylbenzene series containing CF_3 (**1**), CF_2CF_3 (**2**), $CF_2CF_2CF_3$ (**3**), $CF(CF_3)_2$ (**4**) were found to exhibit high regioselectivity of hydrodefluorination under the action of Zn(Cu) in aqueous DMF [1-3]. The reaction takes place in the para position of the aromatic ring while the rest bonds, including C-F bonds, are in the benzyl position. Addition of electrolytes (NaCl, $CaCl_2$ etc.) accelerates the hydrodefluorination (Scheme 1).



Scheme 1

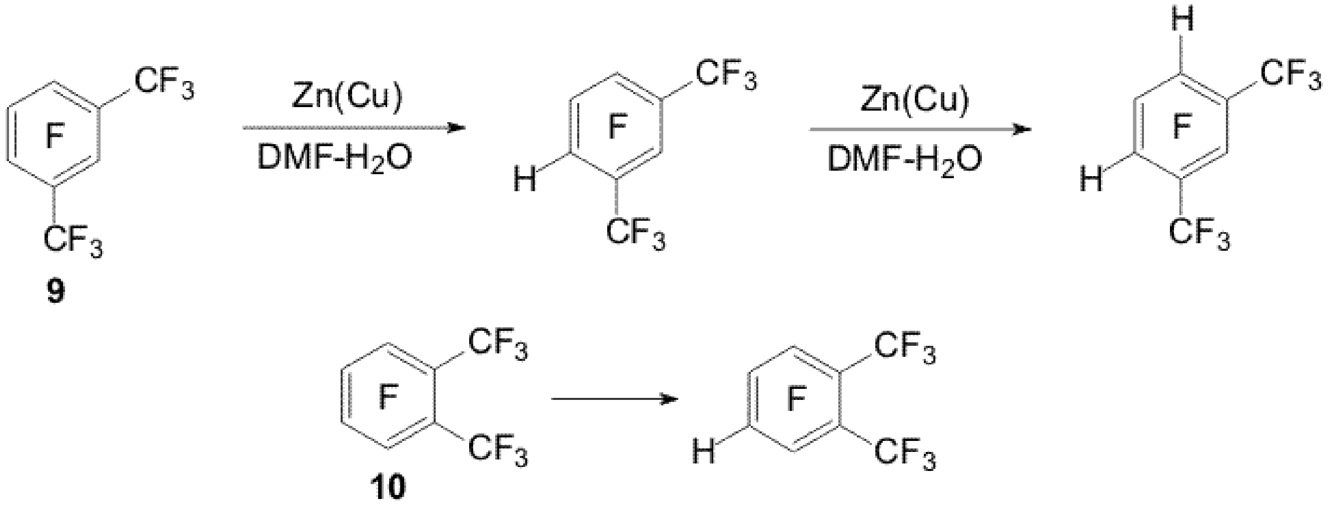
It was proposed that the hydrodefluorination mechanisms included the formation of the anion-radical of polyfluoroarene and detachment of fluoride ion from it [2].The forming radical possesses high electron affinity [4] and is reduced to a carbanion resulting in a hydro derivative in a protonic media [2,5] (Scheme 2).



Scheme 2

The presence of the perfluoroalkyl group of a great volume (perfluoro-*tert*-butyl group) may favour replacement of the *ortho* fluorine atom by hydrogen. At that regioselectivity of perfluoro-*tert*-butylbenzene hydrodefluorination depends on the ratio of DMF and water. The prevailing formation of the *ortho*-hydro derivative (64%) was observed at 46 % (mole) of water, whereas at 83 % (mole) of water prevailed the formation of the *para*-hydro derivative (99%) [3].

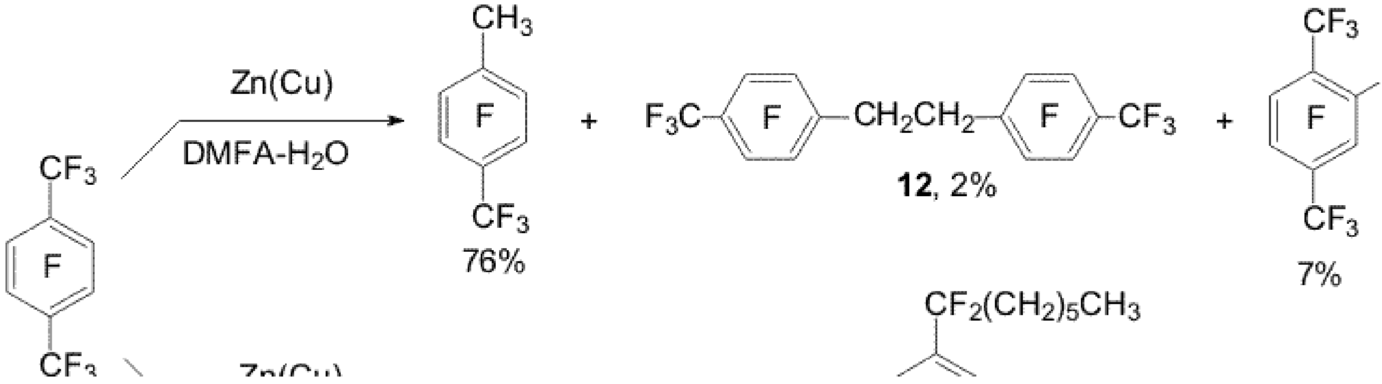
In perfluorinated m- and o-xylenes **9**, **10** under the action of Zn(Cu) the fluorine atoms of the aromatic ring in the para-position towards to the CF_3-group are replaced by hydrogen [6] (Scheme 3).

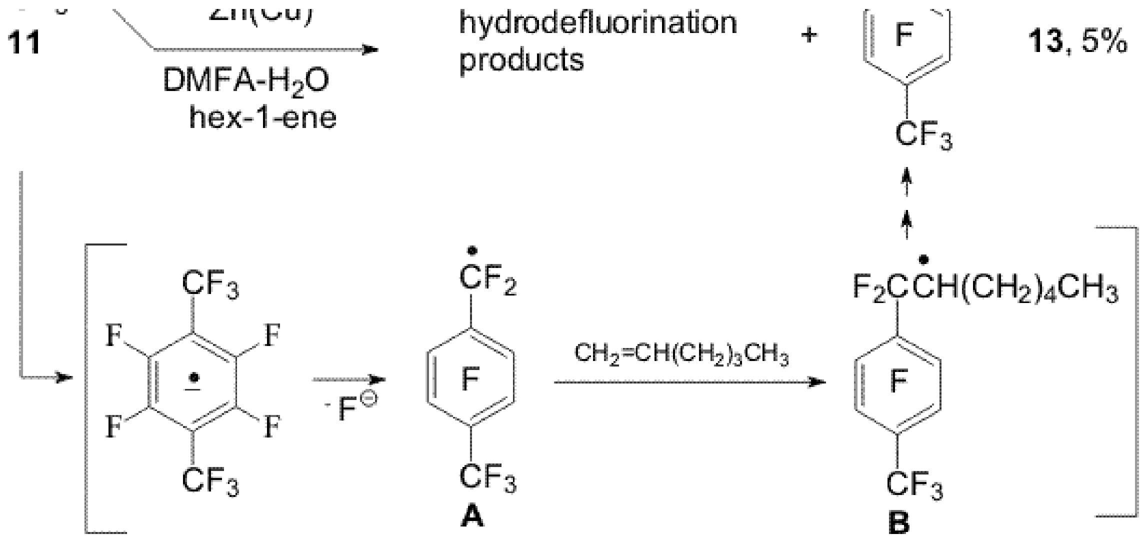


Scheme 3

The hydrogenolysis mechanism of the aryl C-F bonds in the present perfluoroxylenes is similar to the mentioned above for perfluoroalkylbenzenes.

The main direction of the reaction of perfluoro-*p*-xylene (**11**) with Zn(Cu)-DMF-H_2O is conversion of the trifluoromethyl group into methyl one as well as formation of 1,2-bis(4-trifluoromethyl-2,3,5-tetrafluorophenyl)ethane (**12**); the hydrogenolysis of the C-F bond of the aromatic ring takes place to a lesser degree in comparison with the hydrogenolysis of the C-F bond of the CF_3-group [6]. Compound **12** is not formed in the presence of hexane-1. Whereas compound **13** has been found probably forming as a result of addition of benzyl type radical (**A**) to the double bond of hexene-1 followed by reduction of new radical (**B**) into the corresponding carbanion (Scheme 4).

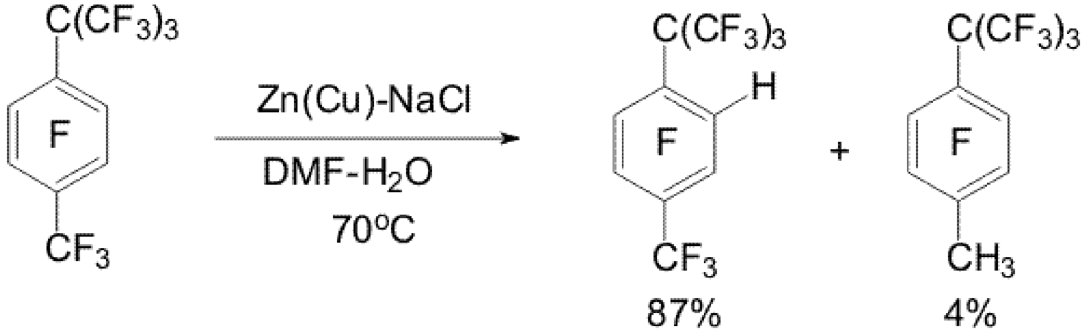




Scheme 4

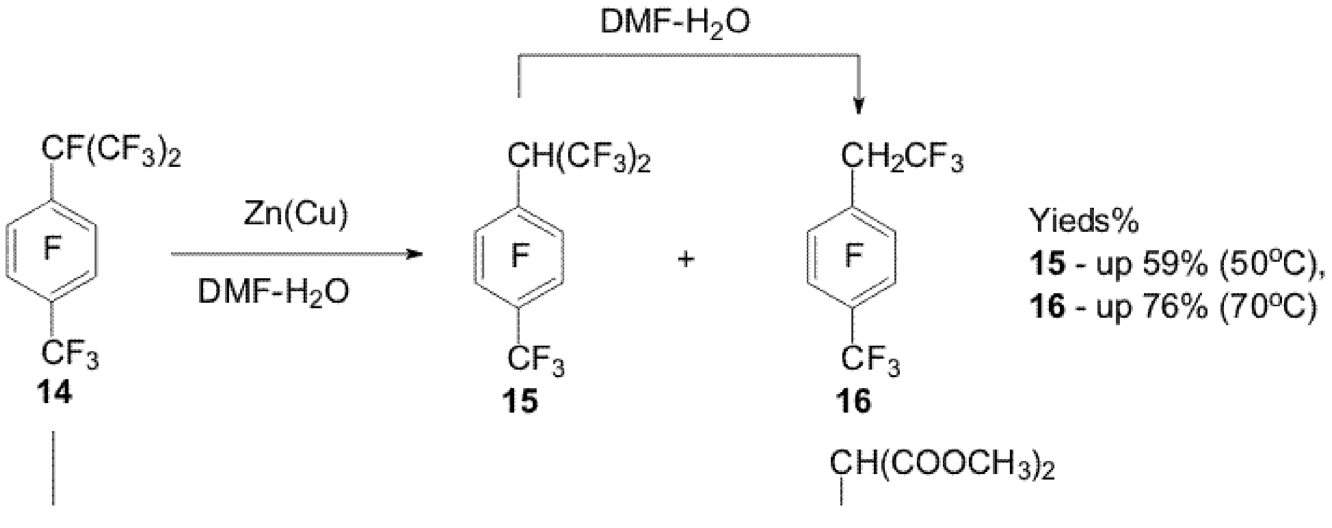
The estimation of prospective fragmentation direction of anion radicals of perfluoroxylenes based on consideration of the structure and energies of molecular orbitals of the ground Π- and excited Σ- states is in agreement with the regularities of perfluoroxylenes behaviour under the action of Zn(Cu) [6].

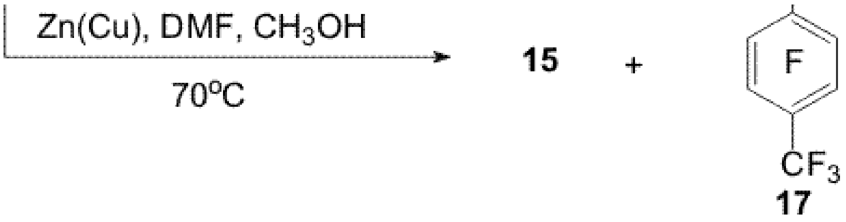
The hydrofluorination of perfluoro-4-*tert*-butyltoluene under the action of Zn(Cu) takes place predominantly in the *ortho* position towards the perfluoro-*tert*-butyl group, the trifluoromethyl group is less affected by the process [3,7,8] (Scheme 5).



Scheme 5

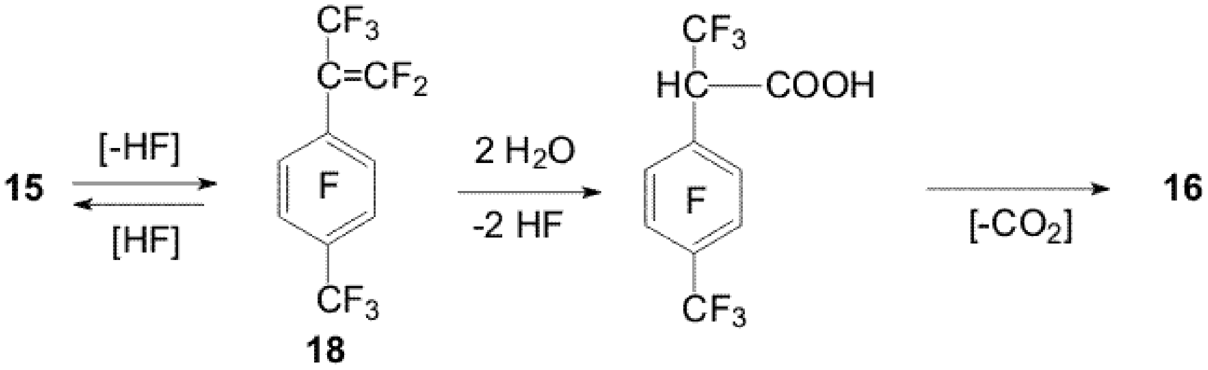
Only the heptafluoroisopropyl group in perfluoro-p-cymene (**14**) undergoes transformation [6]. It was managed to obtain hexafluoroisopropyl derivative **15** along with trifluoroethyl derivative **16** at 50^{o}C under the action of Zn(Cu) in DMF-H$_2$O. The latter is obtained in a good yield at 70-90^{o}C. Compound **16** is formed from derivative **15** at heating in aqueous DMF. Trifluoroethyl derivative **16** was not found under the action of Zn(Cu) on cymene **14** in a DMF-methanol mixture and first forming cymene **15** yields a derivative of malonic acid **17** [5,7,8] (Scheme 6).





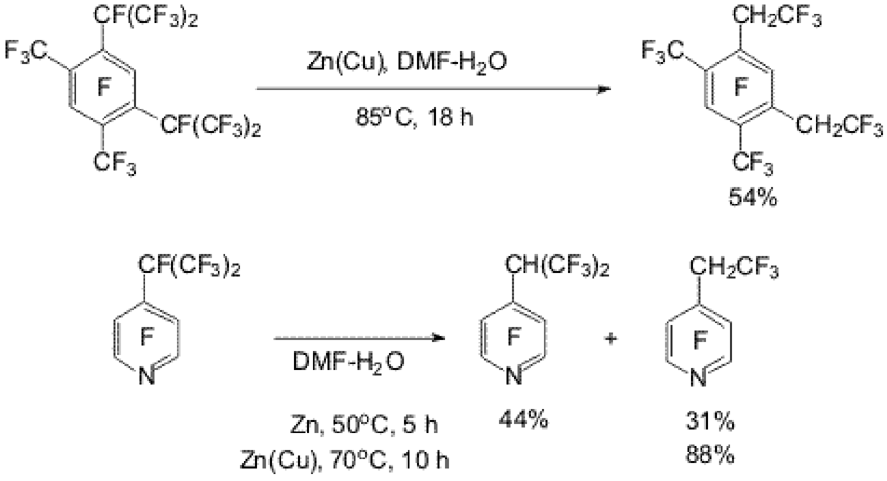
Scheme 6

These data along with transformation of perfluoro-α,4-dimethylstyrene (**18**) in aqueous DMF (including in the presence of Zn(Cu)) into products **15** and **16** makes possible to suggest a scheme of formation of the trifluoroethyl group via intermediate styrene **18** (Scheme 7).



Scheme 7

Transformations with formation of $CH(CF_3)_2$ and(or) CH_2CF_3 derivatives of perfluoroarenes occurs in the reactions of compounds containing $CF(CF_3)_2$ group in the *para* position towards trifluoromethyl, nitrile groups or heteroatom [8-10] (Scheme 8).



Scheme 8

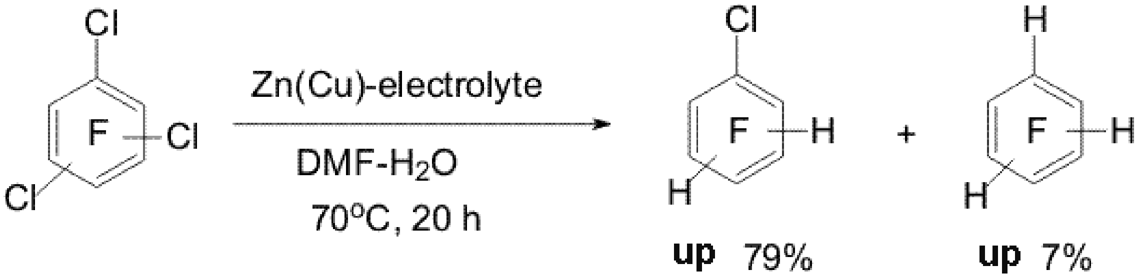
2,3,5,6-Tetrafluoropyridine was obtained from pentafluoropyridine (**19**) under the action of Zn(Cu)-DMF-H_2O at 70°C. Octafluoronaphthalene (**20**) under similar conditions yields a mixture of α- and β-hydroderivatives. Decafluorodiphenyl (**21**) enters the hydrodefluorination reaction in the presence of NH_4Cl to substitute the fluorine atom in position 4 [7].

Reactions of some perfluoroarenes under the action of Zn(Cu) may be carried out in water in the absence of organic solvent. In this case the direction of hydrodefluorination of compounds 1, 9, 11, 14, 19-21 is the same as in aqueous DMF. Using electrolytes is necessary to carry the reactions with the mentioned substrates (except pyridine **19**) [5,11].

The reactions of selective hydrodechlorination of polyfluorochloroarenes under the action of Zn or Zn(Cu) are of a synthetic interest for obtaining partially fluorinated arenes taken into account that polyfluorochloroarenes are readily obtained by replacement of chlorine by fluorine in perchloroarenes.

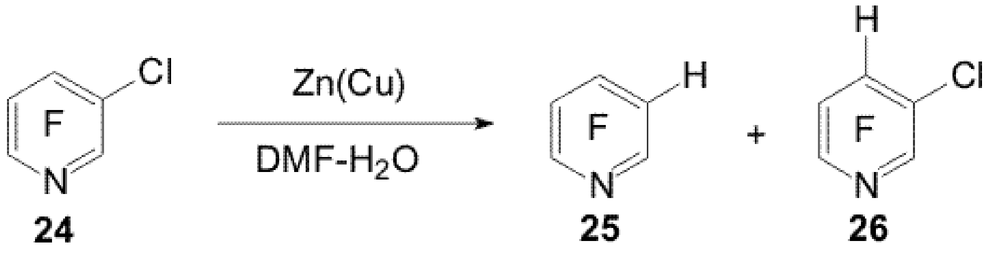
Easiness of hydrodehalogenation in series of C_6F_5-Hal compounds varies as C_6F_5-Br > C_6F_5-Cl > C_6F_5-F. The conversion of chloropentafluorobenzene (**22**) into pentafluorobenzene (**23**) already does not require using Zn(Cu) and can be executed by means of Zn. Partial hydrodechlorination of a mixture of *o*-, *m*-, *p*-dichlorotetrafluorobenzenes to form chlorotetrafluorobenzenes occurs when dichlorotetrafluorobenzenes are treated with Zn in aqueous DMF at 20°C or in boiling with Zn in aqueous NaCl solution. Complete hydrodechlorination into tetrafluorobenzenes takes place under the action of Zn(Cu) in DMF-H^2O at 70°C, in this case addition of electrolytes (NaCl, Na_2SO_4, NH_4Cl) promotes the reaction [7, 12].

The action of Zn (Cu) on a mixture of 1,2,3-, 1,2,4- and 1,3,5-trifluorotrichlorobenzenes in aqueous DMF at 70°C both in the absence and presence of salts brings predominantly to obtaining chlorotrifluorobenzenes [7,12] (Scheme 9). Isomeric mixtures of dichlorotetrafluoro- and trifluorotrichlorobenzenes were obtained in the reaction of hexachlorobenzene with KF [13].



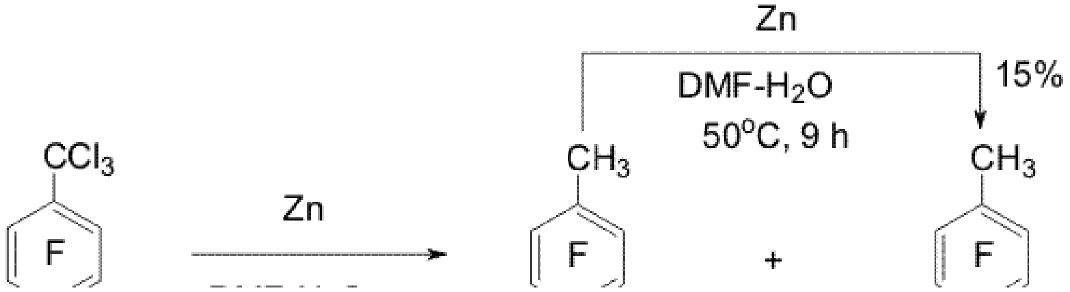
Scheme 9

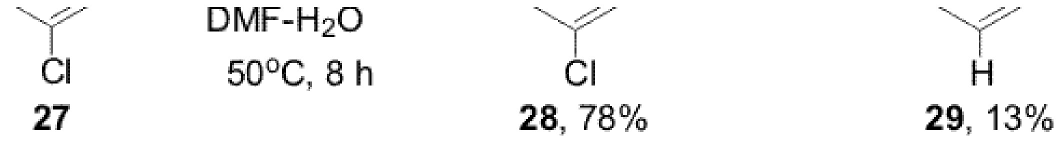
In contrast to chloropolyfluorobenzenes, under the action of Zn(Cu) in aqueous DMF 3-chlorotetrafluoropyridine (2**4**) affords hydrogenolysis products with both C-Cl(**25**) and C-F bonds (**26**) (Scheme 10). An increase in water quantity results in increasing compound **26** share. In water the ratio of compounds **25** and **26** is 1 : 2 [12].



Scheme 10

Benzyl C-Cl bonds in 1-trichloromethyl-2,3,5,6-tetrafluoro-4-chlorobenzene (27) more easy undergo hydrodechlorination under the action of Zn-DMF-H_2O than the C-Cl bond of the aromatic ring [12] (Scheme 11).

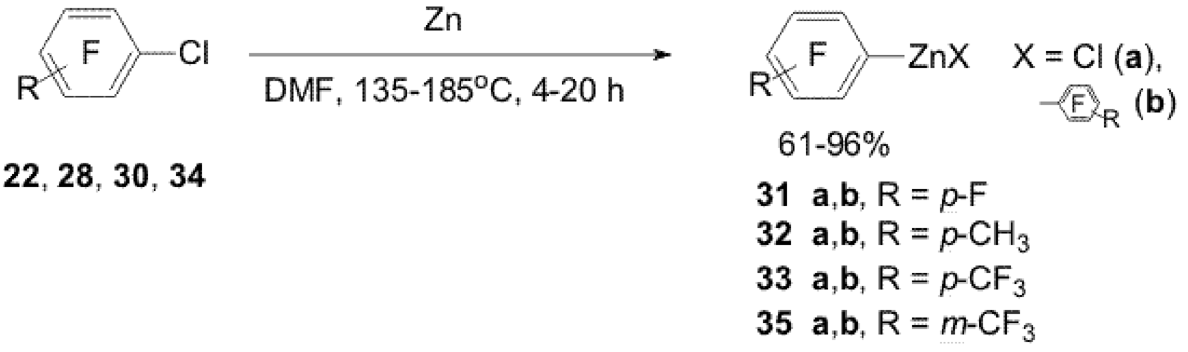




Scheme 11

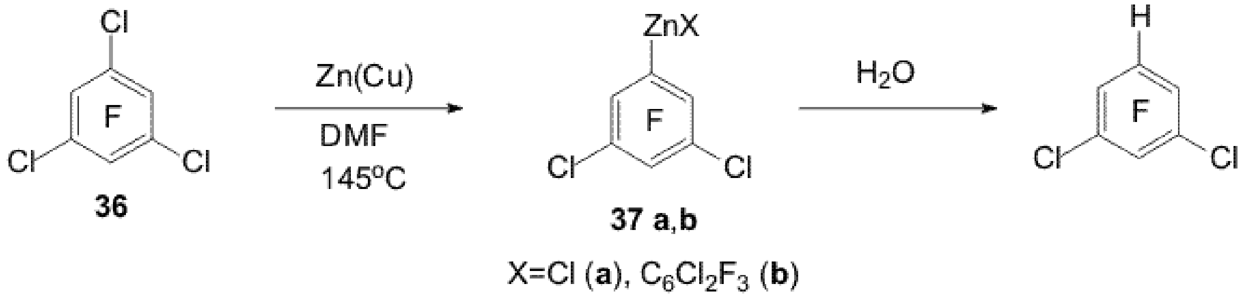
2. Obtaining polyfluoroaromatic organozinc compounds

From compounds **22**, 4-chloro-2,3,5,6,-tetrafluorotoluene (**28**), 4-chloroheptafluorotoluene (**30**) and Zn in DMF were obtained organozinc compounds with participation of the C-Cl bond (**31a,b**-**33a,b**) [44] (Scheme 12).



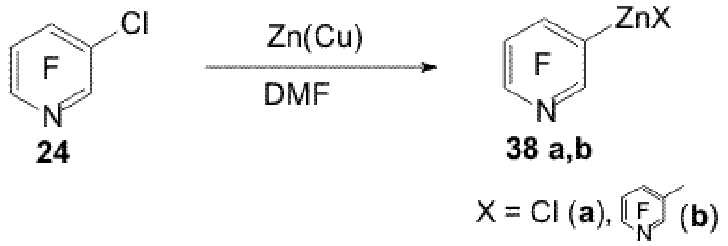
Scheme 12

Compounds **22** and **30** practically entirely are converted into organozinc reagents at 135°C (4 h) in contrast to chlorofluorotoluene **28** that does not react with Zn under similar conditions. The formation of organozinc reagents **32a,b** from compound 28 requires a prolong heating with zinc powder at elevated temperatures and is followed by the formation of a noticeable amount of 2,3,5,6-tetrafluorotoluene (**29**). Organozinc compounds **35a,b** are formed from 3-chloroheptafluorotoluene (**34**) and Zn (Scheme 12).
Organozinc compounds 37a,b are formed at heating 1,3,5-trifluorotrichlorobenzene (**36**) with Zn in dry DMF. Their subsequent treatment with water can be used to obtain a product of replacement of one chlorine atom in compound **3**6 by hydrogen [12] (Scheme 13).



Scheme 13

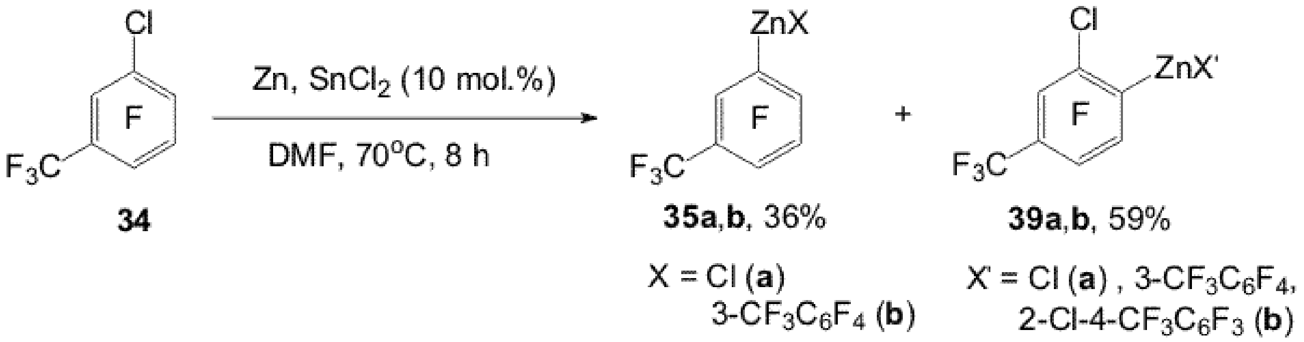
Organozinc compounds with participation of the C-Cl bond (**38a,b**) are obtained from chlorofluoropyridine **24** in the reaction with Zn(Cu) in DMF [1,12](Scheme 14).



Scheme 14

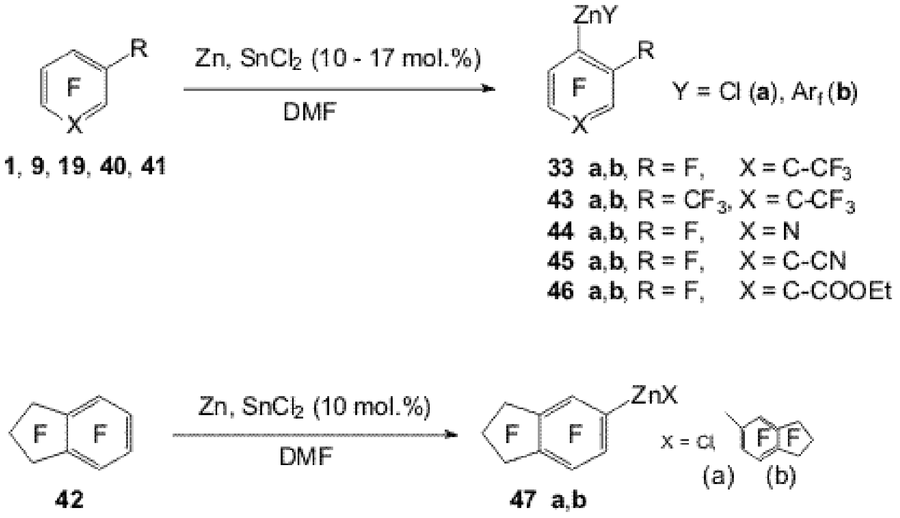
An addition of 10 mole % $SnCl_2$ to Zn in the reaction with chlorofluoroarene **34** changes the process direction and organozinc compounds **39a,b** are obtained with participation of the C-F bond in the *para*-

position towards the CF_3-group as main products along with smaller quantity of organozinc compounds **35a,b** forming by insertion of Zn by the C-Cl bond [15](Scheme 15).



Scheme 15

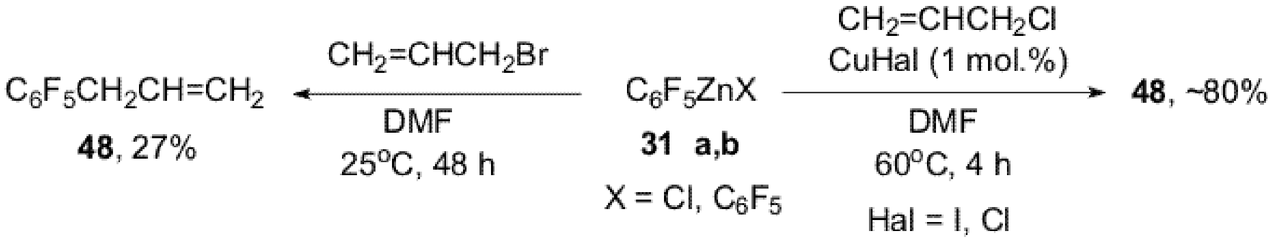
When perfluoroarenes **1,9,19,** pentafluorobenzonitrile (**40**), ethyl pentafluorobenzoate(**41**) and decafluoroindane (**42**) are used in the reactions with Zn to obtain organozinc compounds **33(a,b)**, **43 (a,b)-47(a,b)** there is used $SnCl_2$ as a catalyst [14,16] (Scheme 16).



Scheme 16

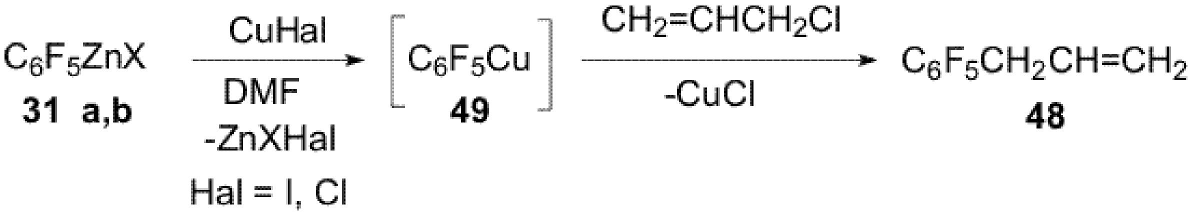
3. Reactions of polyfluoroaryl organozinc compounds with allylhalides

The reaction of organozinc compounds **31a,b** with allyl bromide takes place at room temperature to afford allylpentafluorobenzene (**48**)[14]. This process may be considered as nucleophilic replacement of the bromine atom in allylbromide with the pentafluorophenyl group. In contrast to allylbromide the reaction with allylchloride almost does not occur. It has been shown that salts of univalent copper (CuCl, CuI) accelerate the process with allylchloride and compound **48** is obtained in a ~80% yield (Scheme 17).



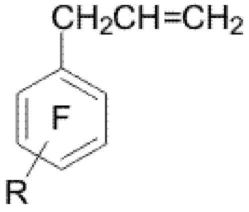
Scheme 17

The catalytic role of the salts is likely comes to their interaction with C_6F_5ZnX via intermediate formation of an organocopper compound **49**. The latter reacts with allylchloride and apparently yields derivative **48** (Scheme 18).

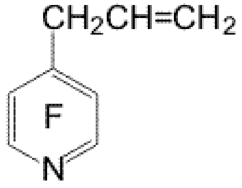


Scheme 18

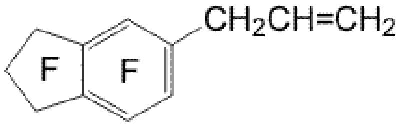
Copper chloride was also used as a catalyst for obtaining 1-allyl-4-methyl-2,3,5,6-tetrafluorobenzene (**50**), 1-allyl-4-trifluoromethyl-2,3,5,6-tetrafluorobenzene (**51**) , 1-allyl-5-trifluoromethyl-2,3,4,6-tetrafluorobenzene (**52**) , 4-allyl-2,3,5,6-tetrafluorobenzonitrile (**53**) , 4-allyl-2,3,5,6-tetrafluoroethylbenzoate (**54**), 4-allyl-2,3,5,6-tetrafluoropyridine (**55**) and 5-allylnonafluoroindane (**56**) in good yields from allylchloride and organozinc compounds **32 (a,b)**, **33(a,b)**, **35(a,b)**, **44(a,b) - 47(a,b).**



50, R = 4-CH_3 (64%)
51, R = 4-CF_3 (86%)
52, R = 5-CF_3 (66%)
53, R = 1-CN (74%)
54, R = 1-COOEt (87%)



55, 75%

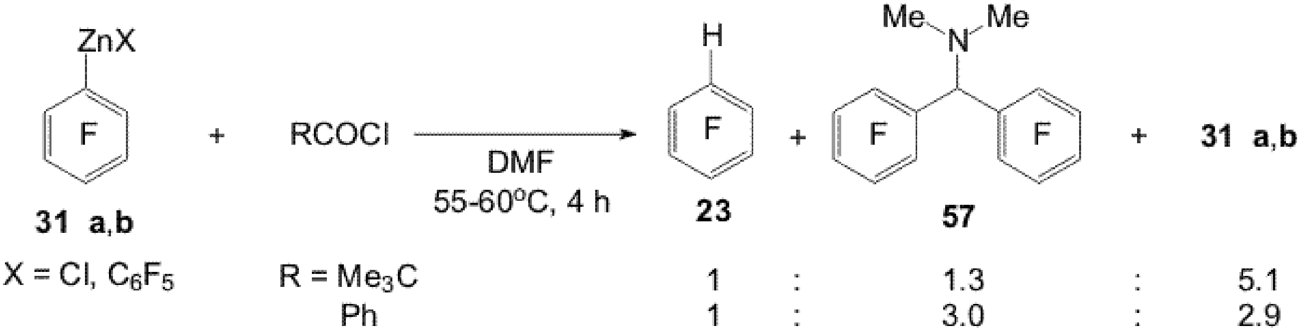


56, 71%

4. Reactions of polyfluoroaryl organozinc compounds with acylchlorides

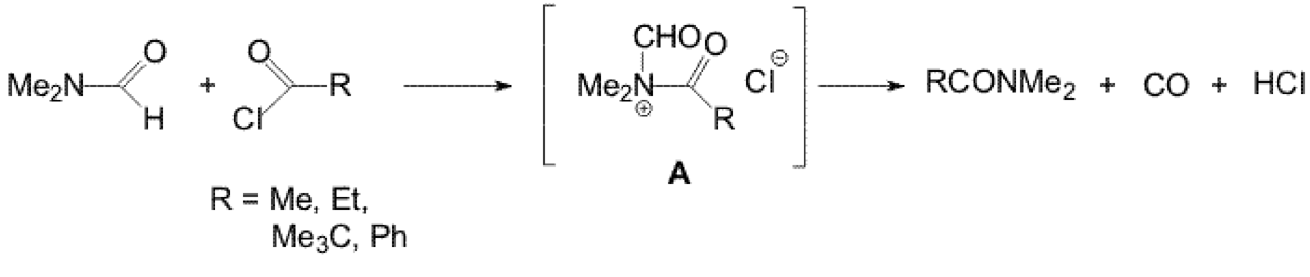
The interaction of compounds **31a,b** with chloroanhydrides of acetic and propionic acids result in hydroderivative **23**[17].

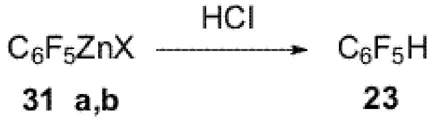
In the reaction of compounds **31a,b** with pivaloyl- and benzoyl chlorides along with product **23** there is formed N,N-dimethyl-1,1-bis(pentafluorophenyl)methaneamine (**57**) (Scheme 19).



Scheme 19

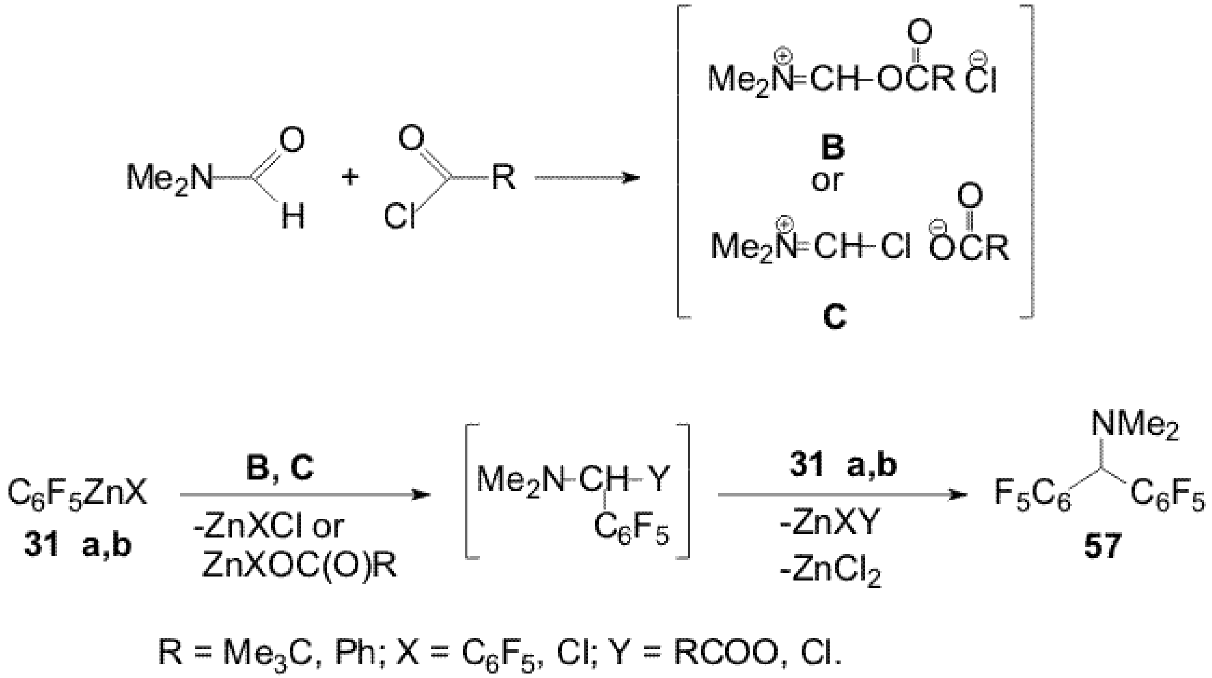
Compound **23** is possibly obtained at the expense of the reamidation reaction with intermediate formation of ammonium cations (**A**) and their conversion into amides and unstable formyl chloride dissociating to CO and HCl. The latter reacts with organozinc reagent to afford **23** (Scheme 20).





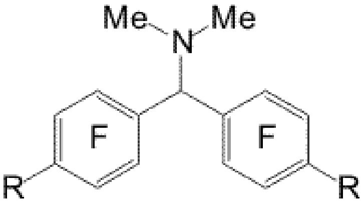
Scheme 20

Another direction of the reaction of pivaloyl- and banzoyl chlorides with DMF is apparently the interaction of electrophilic centers of these chloroanhydrides with the oxygen atom of DMF with intermediate formation of Vilsmeier reagents (B or C). Amine **57** is probably obtained with participation of these reagents that is shown in Scheme 21:

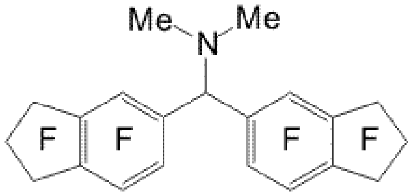


Scheme 21

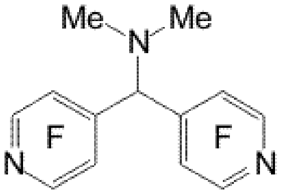
Polyfluoroaromatic organozinc compounds **33a,b** , **44 (a,b) - 47(a,b)** react with the benzoylchloride excess in DMF also with formation of appropriate N,N-dimethyl-bis(polyfluoroaryl)methaneamines **58-62** [17,18].



58, R = CF_3 (45%)
59, R = CN (46%)
60, R = COOEt (36%)

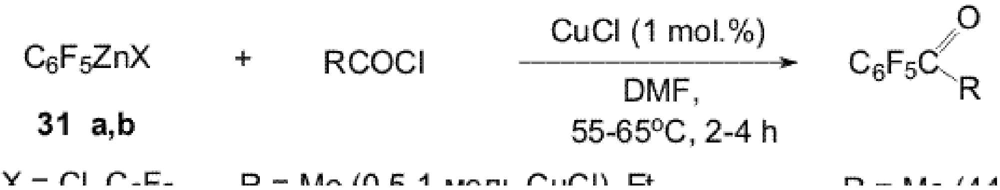


61, 40%



62, 46%

Carrying out the reactions of compounds **31a,b** with acylchlorides in the presence mainly of CuCl in small quantities already changes the main conversion direction and polyfluoroaromatic ketones are formed instead of amine **57**.

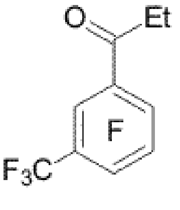


Scheme 22

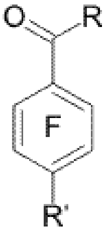
The reaction of propionylchloride with organozinc compounds **33a,b** and **35a,b** in the presence of CuCl (1 mole %) results in 4-propionyl- (63) and 3-propionylheptafluorotoluene (**64**) accordingly [19]. 4-Benzoylheptafluorotoluene (**65**) was synthesized from reagent 33a,b and benzoylchloride.

The reaction of organozinc compounds **45a,b** with propionyl- and benzoyl chlorides in the presence of CuCl afford 4-propionyl- (**66**) and benzoyl-2,3,5,6-tetrafluorobenzonitrile (**67**) accordingly, and ethyl 4-propionyl- (**68**) and ethyl 4-benzoyl-2,3,5,6-tetrafluorobenzoate (**69**) are obtained from organozinc compounds **46a,b**.
4-Propionyl-(**70**) and 4-benzoyl-2,3,5,6-tetrafluoropyridine (**71**) were synthesized from organozinc compounds **44a,b** in the reactions with propionyl- and benzoylchlorides.

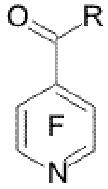
In a similar way from compounds **47a,b** with propionyl- and benzoylchlorides there were produced 5-propionyl-(**72**) and 5-benzoyl-1,1,2,2,3,3,4,6,7-nonafluoroindane (**73**)[19].



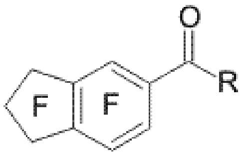
64, 45%



63, R' = CF$_3$, R = Et (58%)
65, R' = CF$_3$, R = Ph (72%)
66, R' = CN, R = Et (43%)
67, R' = CN, R = Ph (75%)
68, R' = COOEt, R = Et (43%)
69, R' = COOEt, R = Ph (64%)

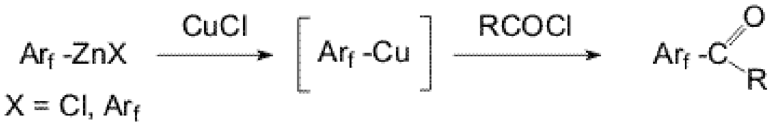


70, R = Et (68%)
71, R = Ph (76%)



72, R = Et (50%)
73, R = Ph (41%)

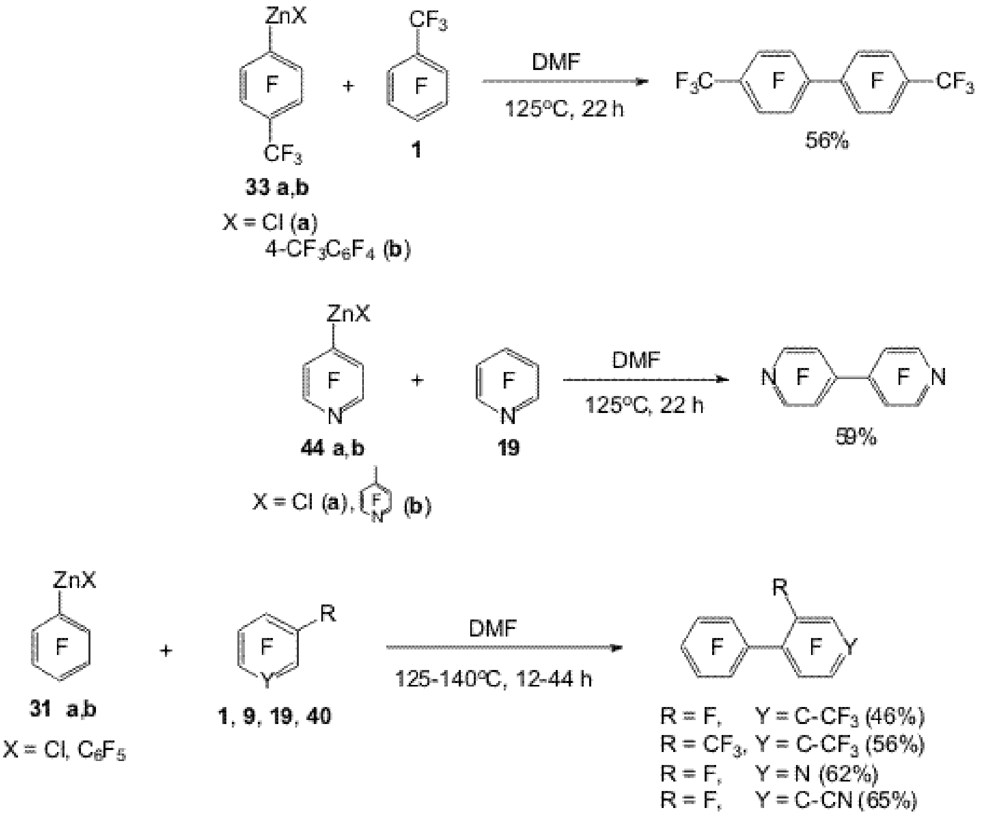
The change in the main direction of the reaction of polyfluoroaryl organozinc compounds with acylchlorides in DMF in the presence of CuCl can be explained by means of the remetallation process and intermediate formation of polyfluoroaryl organocopper compounds participating in obtaining polyfluoroaromatic ketones (Scheme 23).



Scheme 23

5. Reactions of polyfluoroaryl organozinc compounds with perfluoroarenes

Polyfluoroaryl organozinc compounds at heating with polyfluoroarenes in DMF form symmetrical and asymmetrical polyfluorodiaryls [20].The orientation of the entering polyfluoroaryl group corresponds to that observed in the nucleophilic reactions of these perfluoroarenes [21] (Scheme 24).



Scheme 24

Organozinc compounds 31a,b and pentafluoronitrobenzene give 4-(pentafluorophenyl)-2,3,5,6-tetrafluoronitrobenzene with a touch of 2-(pentafluorophenyl)-3,4,5,6-tetrafluoronitrobenzene.

Thus, the hydrodehalogenation reaction of perfluoro- and polyfluorochloroarenes under the action of Zn(Cu) in aqueous DMF makes possible to obtain partially fluorinated aromatic compounds. By means of the reactions of polyfluoroaryl organozinc compounds with electrophilic reagents the following compounds can be produced: allylpolyfluoroarenes, N,N-dimethyl-bis(polyfluoroaryl)methaneamines, polyfluoroaromatic ketones as well as symmetrical and asymmetrical polyfluorodiaryls.

References

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