Chemistry of Heterocyclic Compounds, Vol. 42, No. 3, 2006

SYNTHESIS OF HETEROCYCLES WITH POLYFLUOROALKYL SUBSTITUENTS FROM UNSATURATED COMPOUNDS CONTAINING POLYFLUOROALKYL GROUPS. (REVIEW)

G. G. Furin

Methods for the construction of heterocyclic systems containing polyfluoroalkyl substituents from derivatives of ethylene and acetylene are discussed. It is shown that various compounds with polyfluoroalkyl groups can be used as building blocks: α,β-unsaturated carbonyl compounds, their synthetic organosilicon equivalents (silyl-substituted alcohols, silyl ethers of enols), and also sulfones, nitriles, polyfluoroalkenes (in reactions at the double bond), acetylenecarboxylic acids, their esters, and polyfluoroalkynes.

Keywords: unsaturated compounds with a polyfluoralkyl group, polyfluoroalkyl-substituted heterocycles, dipolar cycloaddition, nucleophilic intramolecular cyclization, nucleophilic addition.

Over the last 20 years there have been many new developments in the use of the unique characteristics of fluorine-containing organic compounds [1-4].* Substitution of a hydrogen atom in a benzene ring or heterocycle by a polyfluoroalkyl group has a substantial effect on the physical characteristics and biological activity of the compound. Organofluorine compounds are used as pharmaceutical products, coolants, pesticides, and also in space technology [5-7]. The foregoing explains the considerable efforts put into the development of methods for the synthesis of heterocyclic compounds containing polyfluoroalkyl groups [8, 9] and the urgency of broad and comprehensive studies in this region.

The key methods for the production of these derivatives are based on two types of chemical transformations [10, 11]. The first includes processes that take place with the participation of the heterocyclic system into which the polyfluoroalkyl substituent is being introduced. The second type involves construction of the heterocyclic system itself from units containing polyfluoroalkyl groups.

The present review covers new data for the period 1981-2001 on the synthesis of heterocyclic compounds containing a polyfluoroalkyl substituent by the second method using various unsaturated compounds with polyfluoroalkyl groups as building blocks. Section 1 is devoted to the application of ethylene derivatives. The first part (1.1) covers many papers in which the heterocycles are constructed from α,β-unsaturated carbonyl compounds containing a polyfluoroalkyl group at the β-position: Acids (1.1.1), esters (1.1.2), aldehydes (1.1.3),

* See also R. D. Chambers, *Fluorine in Organic Chemistry*, Blackwell Publishing (2004), 406 pp. Editor's note.

N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk 630090; e-mail: furin@nioch.nsc.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 323-360, March, 2006. Original article submitted November 29, 2001; revision submitted August 27, 2005.

0009-3122/06/4203-0285

ketones (1.1.4). Saturated analogs of the indicated compounds that readily eliminate HHal and are converted into the necessary building blocks are also discussed. The next part of section 1 (1.2) is devoted to the use of synthetic equivalents of the α,β-unsaturated carbonyl compounds – silyl-substituted alcohols and silyl ethers of enols. Examples are then given (part 1.3) of the construction of heterocycles from other substituted ethylenes not containing C=O groups (β-polyfluoroalkylethylene halides, sulfones, nitriles) and also from imidoyl halides, in which the C=N bond takes part in the formation of the ring. The second part of the review concerns the use of acetylene compounds as building blocks.

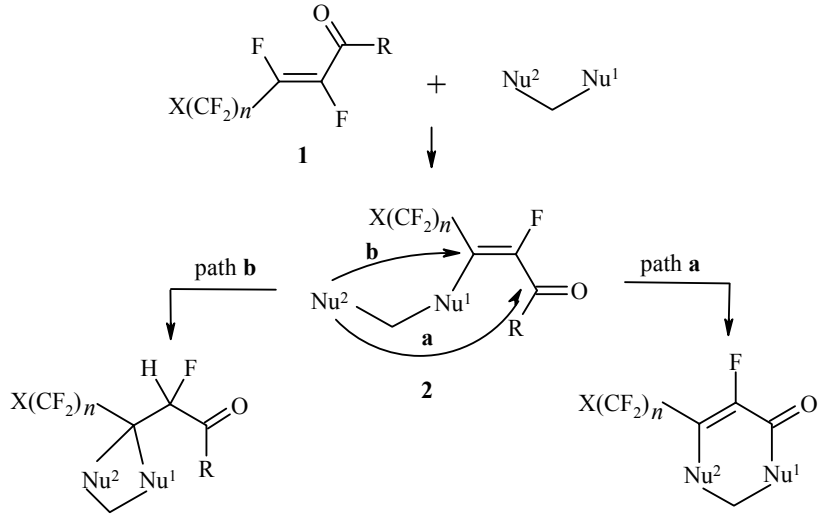
The review reflects the principal trends in the development of methods for the synthesis of polyfluoroalkyl-substituted heterocycles in order to discover new approaches to the formation of the heterocyclic system and to predict new promising methods for the construction of heterocycles. It provides a supplement to and an extension of the author's previous reviews [12-15].

1. ETHYLENE DERIVATIVES IN THE SYNTHESIS OF HETEROCYCLES

1.1. Carbonyl Compounds

Most of the publications over the period of the review were devoted to the synthesis of compounds containing polyfluoroalkyl groups by the reaction of polyfluorine-substituted carbonyl compounds (acids, esters, aldehydes, ketones) with nucleophilic reagents [8, 10]. As a rule, these compounds contain the $(CF_2)_nCXYCHZCO–$ fragment (X = F, Cl; Y = F, Cl, Br; Z = H, F) or the $–(CF_2)_nCX=CZCO–$ fragment that is formed from it as a result of the elimination of HY and also participates in the formation of the ring.

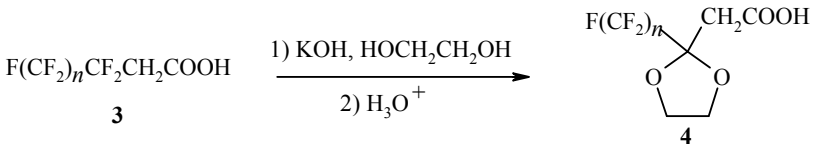
For compounds of type **1**, containing a system of conjugated bonds C=C–C=O, during the action of the binucleophilic reagent initial attack occurs at the β-carbon atom with the formation of a carbanion, stabilized by the elimination of a fluoride ion from the same atom.



R = H, OH, OAlk, Alk, Ar

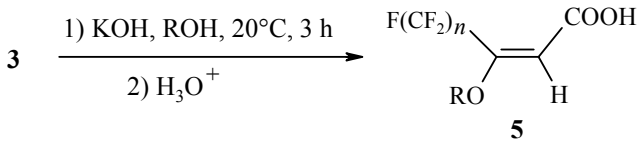
Intramolecular nucleophilic cyclization of the intermediate compound **2** can take place in two directions: The nucleophilic center attacks the carbon atom of the C=O group with elimination of the group R (path **a**); the carbon atom of the CF group attached to $(CF_2)_n$ is attacked with the generation of a carbanion, which then reacts with a proton from the reaction medium, leading to the formation of a heterocycle (path **b**) [15-19].

1.1.1. Acids. Few examples of the construction of heterocycles based on polyfluoroalkanoic acids have been described. Thus, with ethylene glycol in the presence of potassium hydroxide acids of type **3** (produced by the action of ethyl vinyl ether on the respective polyfluoroalkyl iodides in the presence of $Na_2S_2O_4$ followed by oxidation [20]) form the cyclic acetals **4** [21].



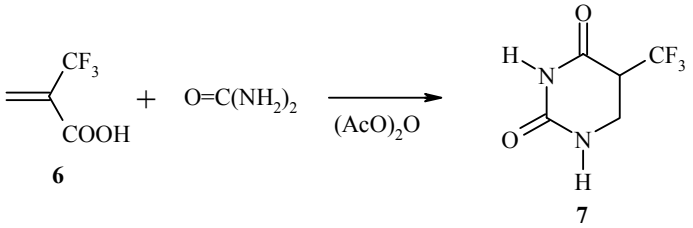
4, *n* (yield, %): 5 (77), 7 (86), 9 (84)

This reaction takes place through the intermediate formation of the unsaturated acids $F(CF_2)_nCF{=}CHCOOH$ under the action of the base, as was confirmed by the products **5** obtained in the reaction of the acids **3** with alcohols (mixtures of *Z*- and *E*-isomers) [21].

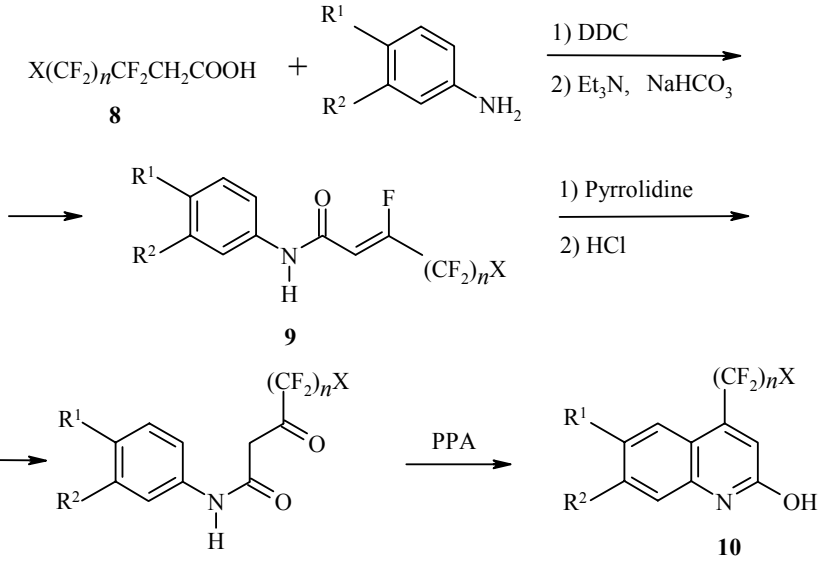


5 *n*, R (yield, %, *Z/E*): 5, Et (65, 95/5); 7, Et (86, 92/8);
9, Et (95, 100/0); 7, $C_2H_4OC_2H_4OH$ (98, 100/0)

It should be noted that α,β-unsaturated acids of type **1** (R = OH) themselves have not been used as starting compounds for the construction of heterocycles. Only the use of α-trifluoromethyl-substituted acrylic acid **6** for the synthesis of 5,6-dihydrouracils **7** is known [22].

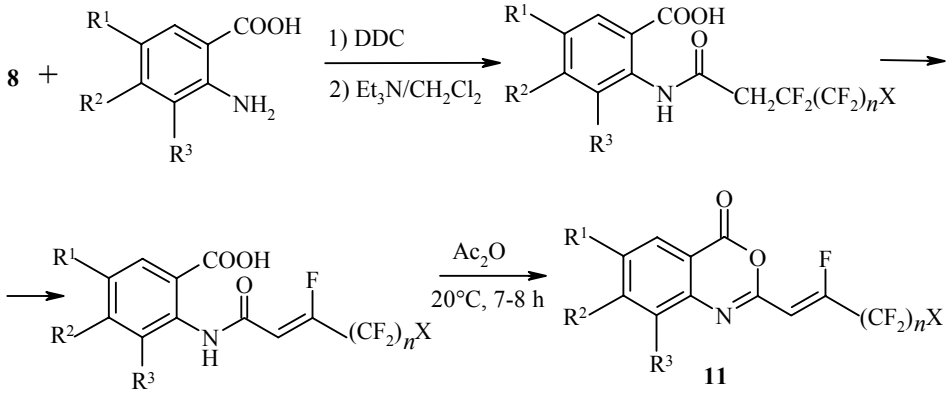


The reaction of acids of type **8** with anilines in the presence of N,N'-dicyclocarbodiimide (DCC) leads to the formation of the respective amides, which eliminate hydrogen fluoride under the action of Et_3N or $NaHCO_3$, giving high yields of the N-arylamides **9**. The further successive treatment of compounds **9** with pyrrolidine, HCl, and PPA gives 4-polyfluoroalkyl-2-quinolinols **10** [23, 24].



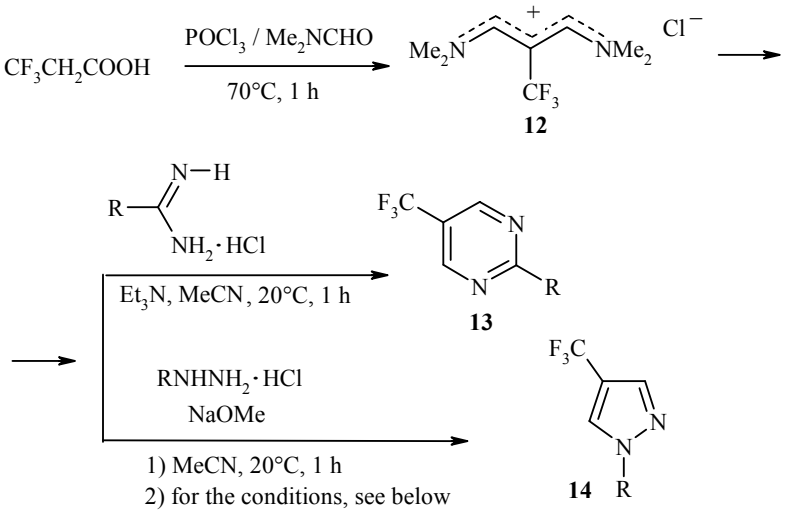
10 X, *n*, R^1, R^2 (yield, %): F, 1, Me, H (85), H, H (84), H, Me (82), H, Cl (80), Cl, 3, H, H (70), Br, H (59), H, Me (58), Cl, H (61), Me, H (62), F, 5, H, H (68), Br, H (56), Cl, H (65), H, Me (56), Me, H (66)

Substituted benzoxazinones **11** were synthesized similarly with high yields from the acids **8** and anthranilic acid or its derivatives [25, 26].



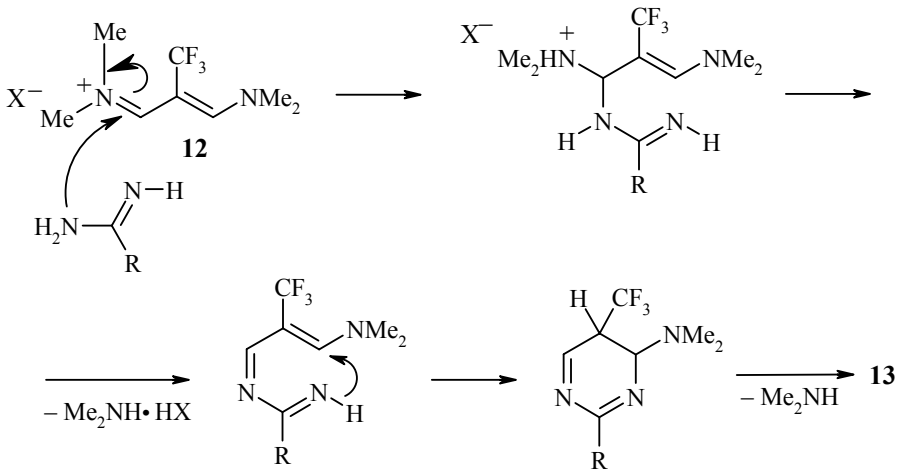
11 X, *n*, R^1, R^2, R^3 (yield, %): F, 5, H, Br, H (75), H, Cl, H (90), OMe, OMe, H (95); Cl, 3, H, Cl, H (88), H, H, Cl (93); Cl, 1, H, Cl, H (68), H, H, H (75), OMe, OMe, H (78); F, 3, H, Cl, H (88), OMe, OMe, H (95); Br, 1, H, H, H (75), OMe, OMe, H (78); F, 1, OMe, OMe, H (78), H, H, H (75)

An interesting method for the construction of heterocycles starting from γ,γ,γ-trifluoropropionic acid through the intermediate 1,5-diazapentadienium salt **12** was described in [27]. (See [28] for details of the method for the preparation of such salts.) Salts of type **12** have high reactivity and form five- and six-membered heterocycles in reaction with binucleophiles. Thus, the reactions of γ,γ,γ-trifluoropropionic acid with amidines or hydrazine derivatives in the presence of the $POCl_3/Me_2NCHO$ lead to the trifluoromethyl derivatives of pyrimidine **13** (yields 61-85%) or pyrazole **14** (yields 74-81%) respectively [27].



13 R = H, Me, Ph, NH_2, NHMe, OMe, SMe;
14 R (conditions of stage 2 of the reaction): H (AcOH or CF_3COOH, 70°C, 1 h); Me (AcOH, 20°C, 1 h); Ph (CF_3COOH, 70°C, 1 h)

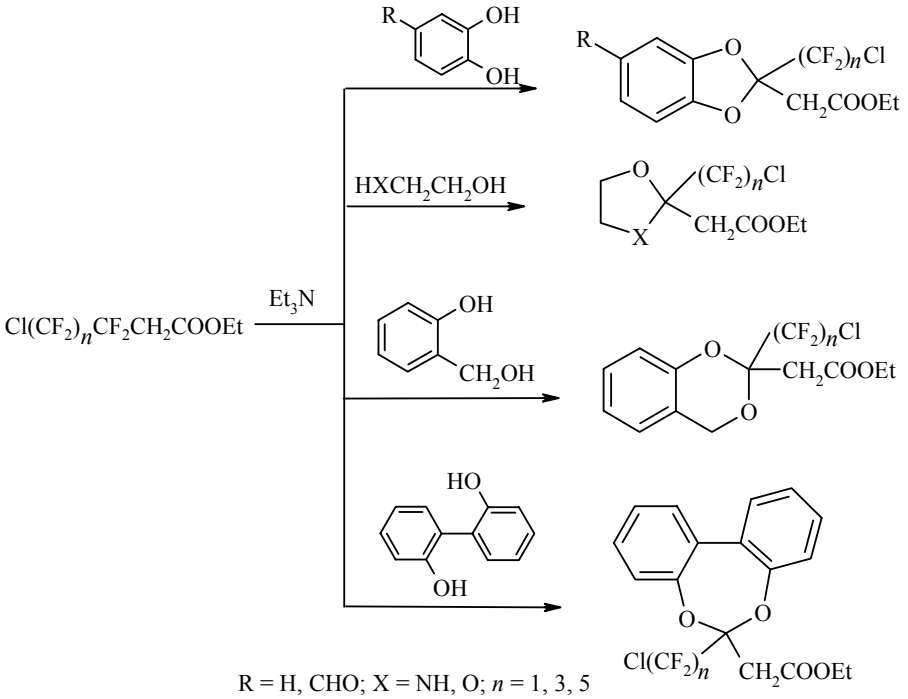
The reaction with amidines takes place according to the following scheme:



The NH_2 group of the amidine attacks the carbon of the salt **12** corresponding to the NMe_2 group. The intermediate imine undergoes cyclization with the formation of a dihydropyrimidine derivative, which is converted by elimination of the dialkylamine into the pyrimidine derivative **13**.

1.1.2. Esters. The reaction of the esters of polyfluoroalkanoic acids containing the $–CXYCH_2COOR$ fragment (see the beginning of section 1.1) with nucleophilic reagents in the presence of bases is widely used for the construction of heterocyclic systems. The action of the base initially leads to the elimination of HX and the formation of the corresponding unsaturated ester, the –CY=CHCOOR fragment of which takes part in further reaction with the nucleophile. The above-mentioned unsaturated esters have therefore also been used successfully in the synthesis of heterocycles.

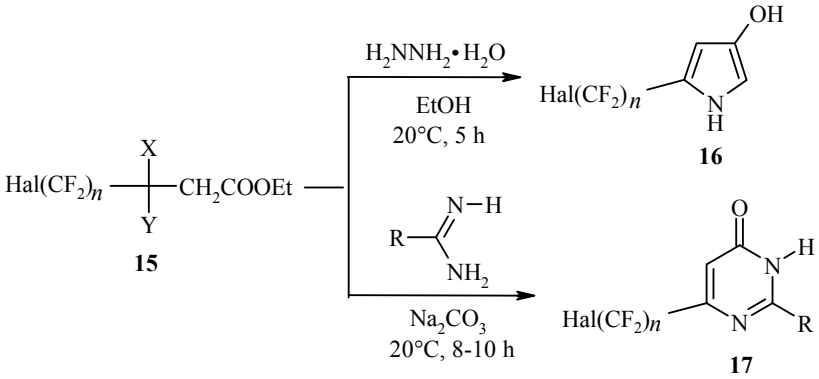
The carbon atom with the largest positive charge is the center of attack by the nucleophile. The formation of five-, six-, or seven-membered heterocycles, as shown in the examples given below, is possible depending on the structure of the nucleophile [29].



R = H, CHO; X = NH, O; *n* = 1, 3, 5

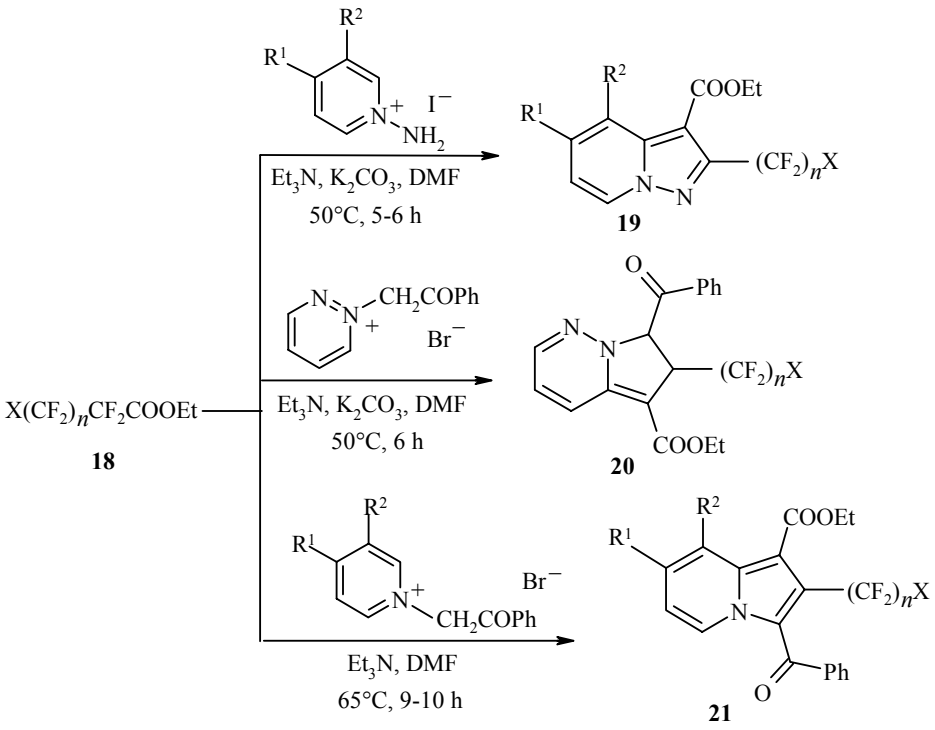
Convenient methods for the production of substituted pyrazoles **16** (72-90%) [30] and dihydropyrimidinones **17** (89-95%) [31] with high yields were developed on the basis of esters of type **15**.

Thus, reaction of the esters with hydrazine in alcohol leads to 3-hydroxy-5-polyfluoroalkylpyrazoles **16** (yields 89-95%). The solvents and the temperature, like the length of the polyfluoroalkyl chain, do not have a substantial effect on the reaction. The simple experimental procedure and the high yields of the products make such an approach very attractive. In the presence of sodium carbonate the esters **15** react with substituted amidines with the formation of 2-substituted 6-polyfluoroalkylpyrimidinones **17** (yields 72-90%), and the nature of the polyfluoroalkyl group has little effect on the reaction.



15, **16** Hal, *n*, X, Y: F, 1, F, F, F, Br, Cl, Cl; Cl, 1, 3, 5, 7, F, F;
17 R = Me, Ph; Hal, *n*, X, Y: F, 1, F, F, F, Br, Cl, Cl; Cl, 3, 5, F, F

The reaction of esters of type **18** with N-aminopyridinium, N-amino-γ-picolinium, and N-aminoisoquinolinium iodides and with N-phenacylpyridazinium, N-phenacylpyridinium, and N-phenacylisoquinolinium bromides in the presence of bases led to polyfluoroalkyl-substituted pyrazolopyridinium and pyrazoloisoquinolinium (**19**) and also to pyrrolopyridazinium (**20**), pyrrolopyridinium, and pyrroloisoquinolinium (**21**) compounds respectively [32].

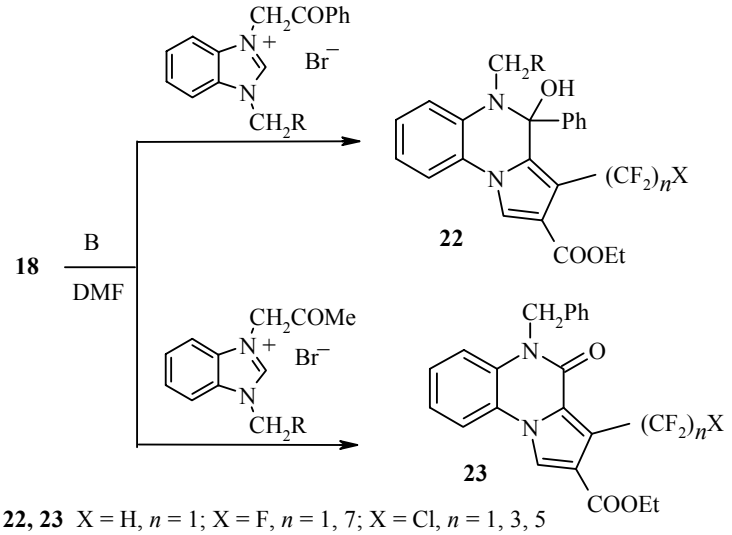


19 R^1, R^2 (or $R^1 + R^2$), X, *n* (yield, %): H, H, H, 1 (73), F, 7 (58), Cl, 3 (48), Cl 5 (74); Me, H, H, 1 (65), F, 1 (70), F, 7 (75), Cl, 3 (54); $(CH_2)_4$, H, 1 (77), F, 7 (77); Cl, 5 (65);

20 X, *n* (yield, %): H, 1 (80), F, 1 (70), F, 7 (95), Cl, 3 (80);

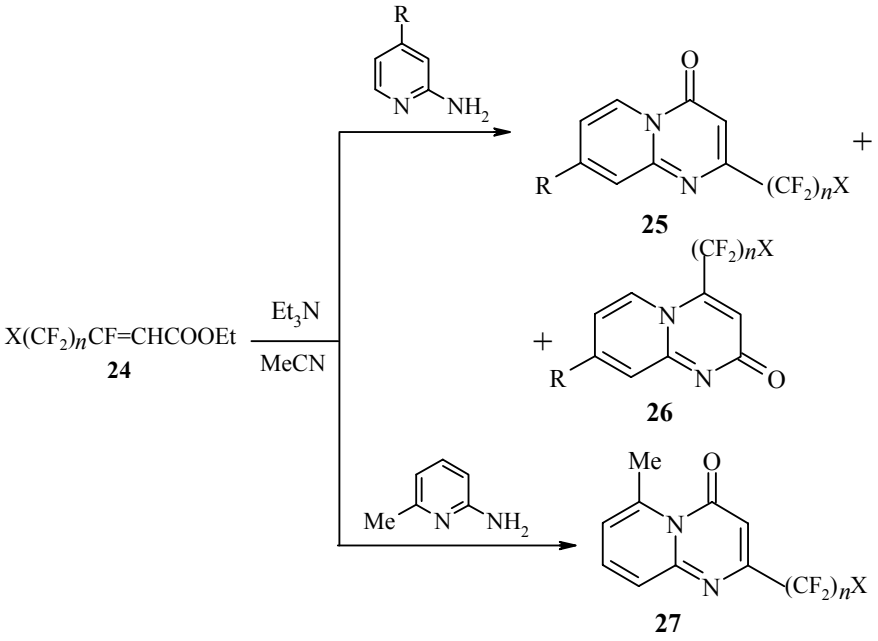
21 R^1, R^2 (or $R^1 + R^2$), X, *n* (yield, %): H, H, H, 1 (82), Cl, 3 (55), Cl, 5 (55); $(CH_2)_4$, H, 1 (55), Cl, 3 (58); Cl, 5 (47), F, 7 (40); H, CN, Cl, 5 (traces), F, 7 (traces)

In the case of substituted benzimidazolium bromides and its tetrahydro derivative tricyclic compounds **22** (yields 60-85%) and **23** (yields 75-78%) respectively, containing two nitrogen atoms, were obtained [33].



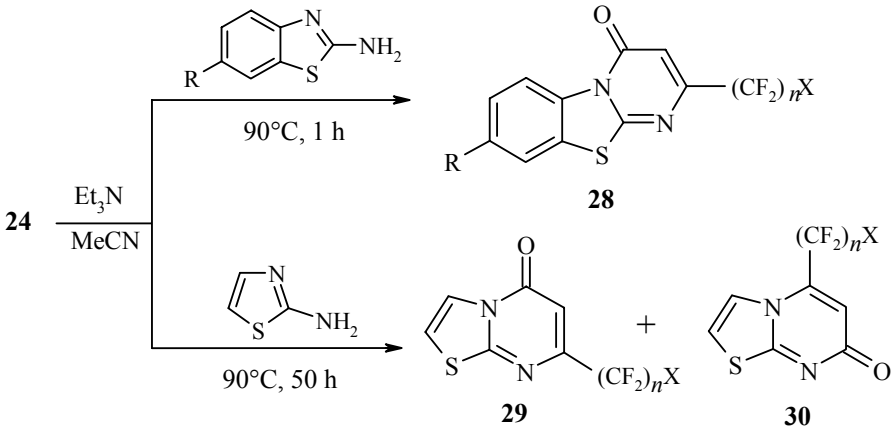
22, 23 X = H, *n* = 1; X = F, *n* = 1, 7; X = Cl, *n* = 1, 3, 5

Various compounds with two condensed heterocycles were obtained from unsaturated esters of type **24**. Thus, isomeric 4-polyfluoroalkyl-2H-pyrido[1,2-*a*]pyrimidin-2-ones **25** and **26** were obtained with yields of 33-59% in the reaction of the ester **24** and 4-R-aminopyridine in acetonitrile in the presence of triethylamine, while pyridopyrimidines **27** were obtained in the case of 2-amino-6-methylpyridine [34]. In these processes it is possible to use K_2CO_3 instead of Et_3N but under more rigorous conditions in acetonitrile.



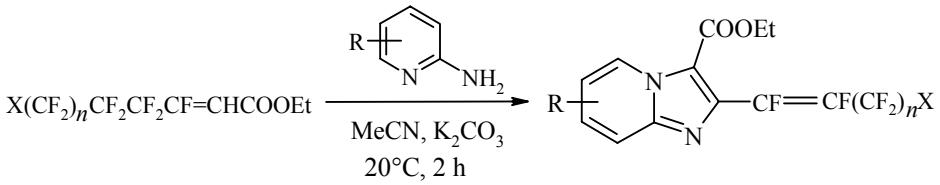
Product, R, X, *n* (yield, %): **25**, H, F, 3 (16), F, 5 (16), Cl, 3 (18), Cl, 5 (23); Me, F, 3 (18), Cl, 5 (25); **26**, H, F, 3 (54), F, 5 (43), Cl, 3 (50), Cl, 5 (42); Me, F, 3 (53), Cl, 5 (39); **27**, X, *n* (yield, %): Cl, 3 (42), Cl, 5 (47)

By using substituted 2-aminobenzothiazoles or 2-aminothiazole under similar conditions it was possible to obtain 2-polyfluoroalkyl-substituted 4H-pyrimido[2,1-*a*]benzothiazol-4-ones **28** or polyfluoroalkyl-5H-thiazolo[3,2-*a*]pyrimidin-5-one **29** and 7H-thiazolo[1,2-*a*]pyrimidin-7-ones **30** respectively [34].



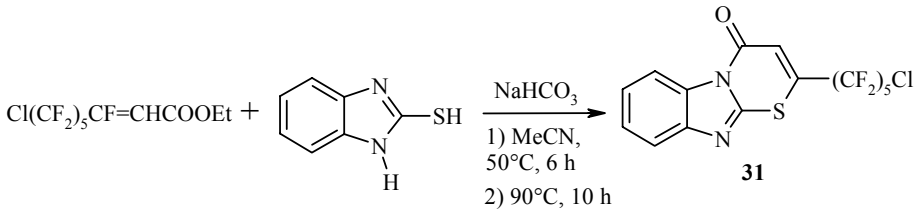
28 R, X, *n* (yield, %): H, Cl, 3 (67), F, 3 (70); F, 5 (70), Me, Cl, 3 (83), Cl, 5 (82); NO_2, Cl, 3 (71), F, 5 (73). Product, X, *n* (yield, %) : **29** Cl, 3 (22), F, 3 (13), Cl, 1 (15); **30** Cl, 3 (49), F, 3 (64), Cl, 1 (39)

In the same work polyfluoroalkenylimidazo[1,2-*a*]pyridines were synthesized from unsaturated esters of type **24** and substituted 2-aminopyridines [34].



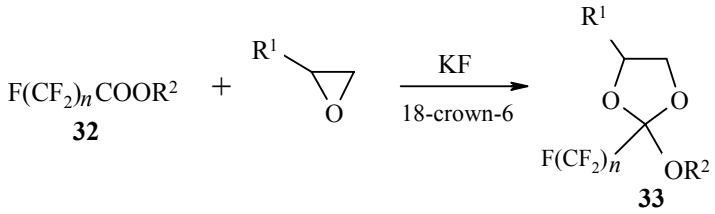
Reaction time (min), R in product, X, *n* (yield, %): 40, H, Cl, 1 (53);
60, H, F, 1 (59); 60, 7-Me, F, 1 (48); 70, 5-Me, Cl, 1 (46); 120, 6-Br, Cl, 3 (33)

In the case of 2-mercaptobenzimidazole 2-polyfluoroalkyl[1,3]thiazino[3,2-*a*]benzimidazol-4-one **31** was synthesized with a yield of 78% [34].



31

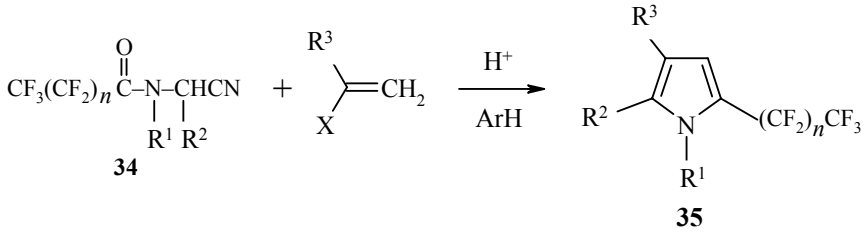
If the esters of polyfluoroalkanoic acids **32** not containing CH_2 groups are used, the heterocycles with polyfluoroalkyl substituents are formed under different conditions and by a different mechanism. The condensation of these esters with oxiranes in the presence of $Bu_4P^+Br^-$ (TBPB) or KBr/18-crown-6 as catalysts leads to the formation of 2,2,5-trisubstituted 1,3-dioxolanes **33** with yields of 50-85% [35].



33

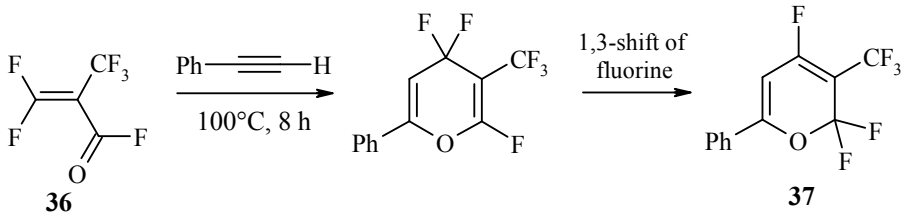
33 $R^1 = CH_2OMe, CH_2OPh$; R^2 = Me, Et, Pr-*i*, Bu; *n* = 1, 2

To conclude section 1.1.2 it should be mentioned that apart from the esters there are also examples where other derivatives of polyfluoroalkanoic and perfluoroalkenoic acids containing a carbonyl group have been used. (Derivatives not containing a CO group are discussed in section 1.1.3.) Thus, the pyrrole derivatives **35** were synthesized from the amides **34** [36].

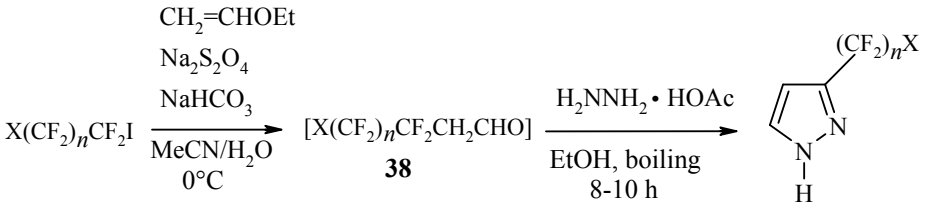


n = 0-7, R^1 = H, Alk, alkoxyalkyl, phenylalkyl; R^2 =Ar, furyl, thienyl;
R^3 = CN, NO_2, AlkOCO, RCO; X = H, Br, Cl

The substituted 2H-pyran **37** (yield 62%) was obtained from the acid fluoride **36**, acting as heterodiene in the Diels–Alder reaction with phenylacetylene [37].

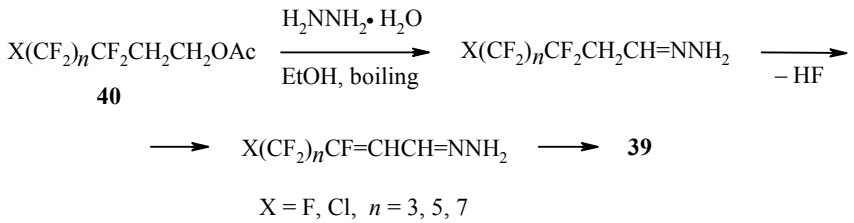


1.1.3. Aldehydes. Aldehydes with general formula **38**, mostly used for the construction of polyfluoroalkyl-substituted heterocycles, are obtained from fairly simple and accessible materials [38, 39] (see the scheme). The substituted pyrazoles **39** were synthesized with high yields (85-93%) as a result of the reaction of such aldehydes with hydrazine in alcohol [40, 41].



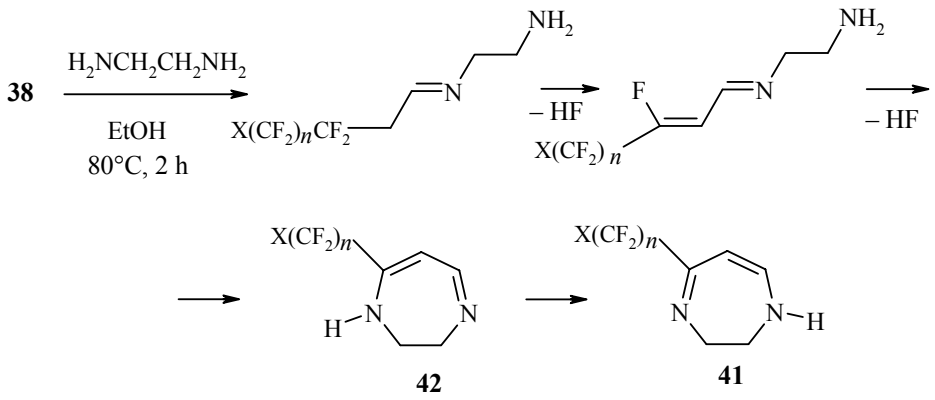
39 X = F, *n* = 2, 4, 6, 8; X = Cl, *n* = 4, 6, 8

Analogous products were obtained from the acetates **40**, which are the adducts of polyfluoroalkyl iodides and vinyl acetate formed under the conditions for the synthesis of the aldehydes **38** [38-41]. Compounds **40** react readily with hydrazine and are converted into pyrazoles of type **39** through the intermediate hydrazones [42].



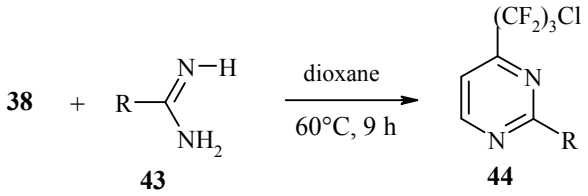
X = F, Cl, *n* = 3, 5, 7

The reaction of the aldehydes **38** with ethylenediamine leads to the substituted diazepines **41** (yields 86-94%). The structure of one of them (X = F, *n* = 0) was confirmed by X-ray crystallographic analysis [43, 44]. The reaction probably takes place through the intermediate formation of the enamine **42** [43].



n = 0, X = F, Cl, Br; *n* = 4, X = F, Cl

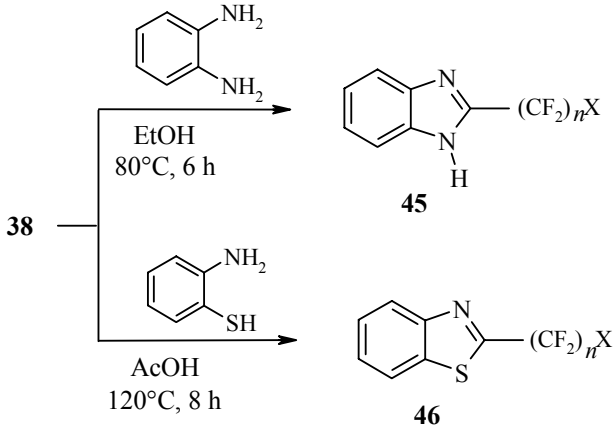
By using substituted amidines **43** (R = Me, Ph) and the aldehyde **38** (X = Cl, *n* = 3) it was possible to construct 2-methyl- and 2-phenyl-substituted pyrimidines **44** with yields of 77 and 82% respectively [31].



R = Me, Ph

Pyrimidines similar to compounds **44** were obtained in the reaction of the aldehydes **38** with ortho esters in the presence of ammonium carbonate [45] (see section 1.1.4).

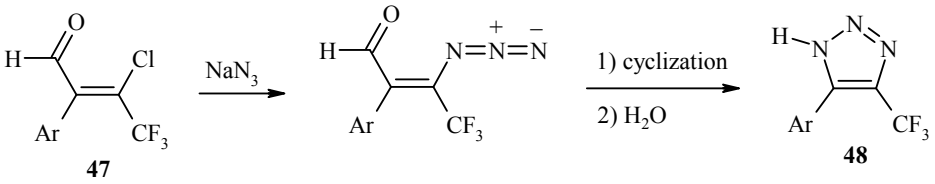
In the reactions of the aldehydes **38** with the aromatic binucleophiles *ortho*-phenylenediamine (in alcohol, dioxane, acetonitrile, THF) or *ortho*-aminothiophenol (in acetic acid) the substituted 1H-benzimidazoles **45** (yields 53-62%) or benzothiazoles **46** (yields 46-53%) respectively were obtained [46].



45, **46** *n* = 0, X = F, Cl, Br; *n* = 3, X = Cl; *n* = 4, X = F

The reaction of the aldehydes **38** with ortho esters in the presence of ammonium carbonate leads to substituted pyrimidines (see 1.1.4).

The use of α-aryl-β-chloro-β-trifluoromethylacroleins **47** for the construction of heterocycles is also known. In reaction with sodium azide they are transformed into the substituted triazoles **48** [47].

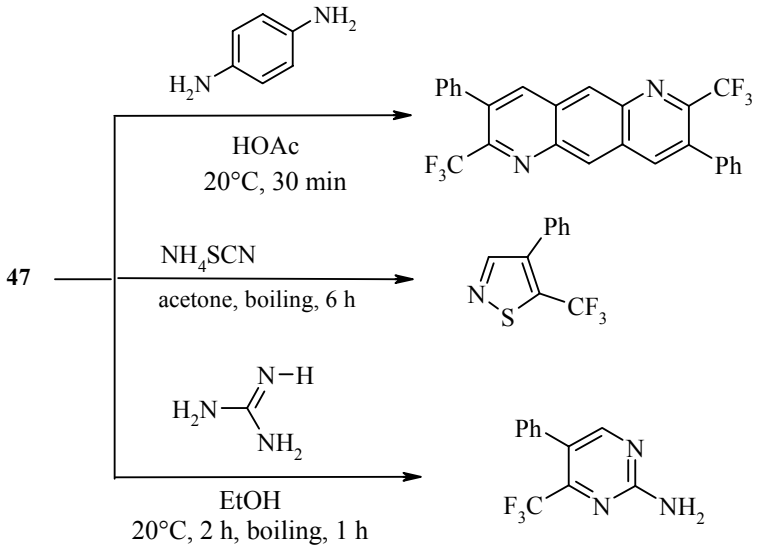


47 **48**

Ar (yield, %): Ph (68), C_6H_4Br-4 (79), $C_6H_4CF_3$-3 (32), $C_6H_4CF_3$-4 (54)

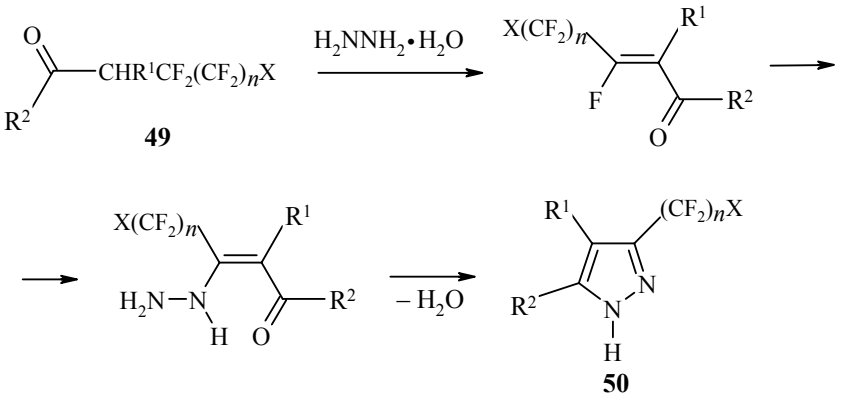
Nucleophilic substitution of the chlorine atom by the azide group takes place initially, and this is then followed by attack by the nucleophilic center of the azide group at the double bond and deformylation in the presence of water.

With acrolein **47** (Ar = Ph) other nucleophilic reagents, such as *para*-phenylenediamine, ammonium thiocyanate, and guanidine, form heterocyclic compounds containing a trifluoromethyl substituent (yields 68, 56, and 39% respectively) [47].

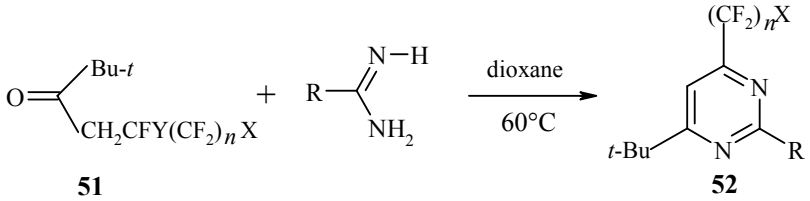


1.1.4. Ketones. The ketones used as building blocks in the synthesis of polyfluoroalkyl-substituted heterocycles represent a wide range of greatly varied structures. They included compounds of the aliphatic and cycloaliphatic series, chromones, etc.

The reaction of ketones of type **49** and hydrazine hydrate leads to the formation of 3-(polyfluoroalkyl)pyrazoles **50** probably according to the following scheme [24]:

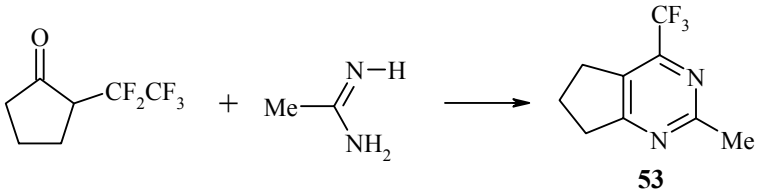


Substituted pyridazines **52** were obtained from ketones of type **51** [31].

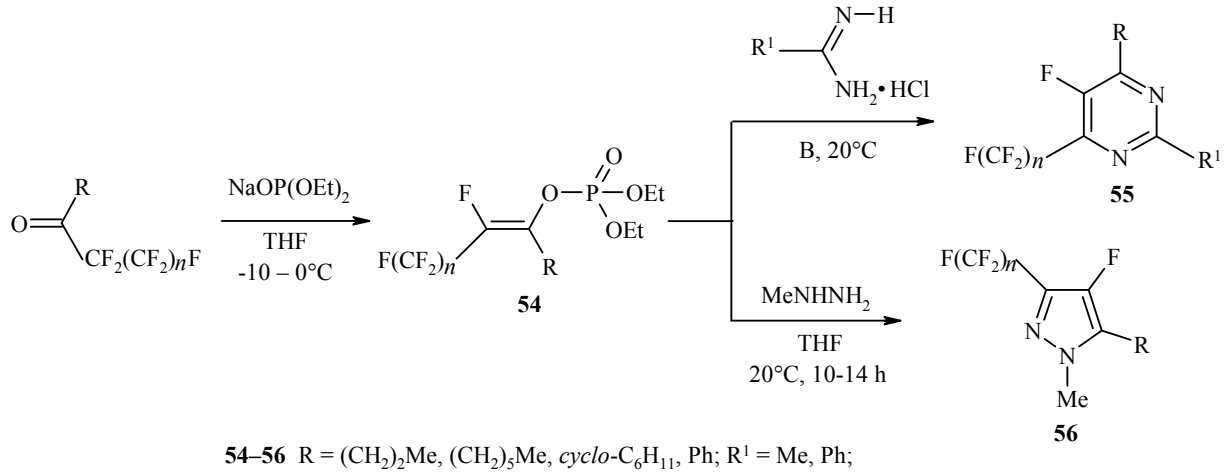


52 X, *n*, Y, R (yield, %): F, 1, Br, Me (80), Ph (89); Cl, 3, F, Me (78), Ph (85)

The bicyclic product **53** was obtained from 2-perfluoroethylcyclopentanone under the same conditions (yield 80%) [31].

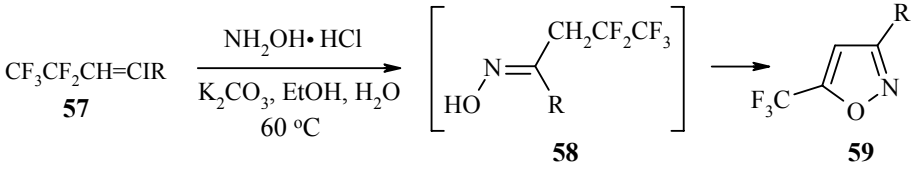


Ishihara and coauthors [48, 49] found that 1-substituted perfluoro-1-alkenyl phosphates **54**, obtained from polyfluoroalkyl alkyl ketones, can be used as precursors for the synthesis of various fluorine-containing pyrimidines and pyrazoles [48, 49]. Substituted pyrimidines **55** (yields 50-94%) are formed in their reaction with amidine hydrochlorides, while derivatives of pyrazole **56** (yields 82-91%) are formed with methylhydrazine [50].



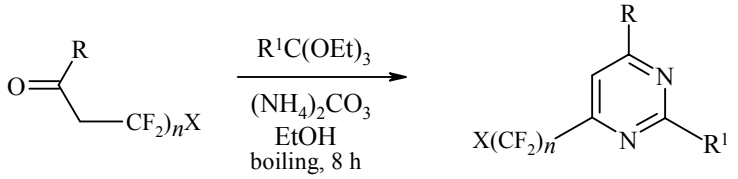
54–56 R = $(CH_2)_2Me$, $(CH_2)_5Me$, *cyclo*-C_6H_{11}, Ph; R^1 = Me, Ph;
n = 1, 5; B = NaH, MeONa, K_2CO_3, KOH

The 1:1 adducts **57** of pentafluoroethyl iodide with alkynes RC≡CH [51, 52] react smoothly with hydroxylamine, forming substituted 5-trifluoromethylisoxazoles **59** through the intermediate ketone derivatives **58**.

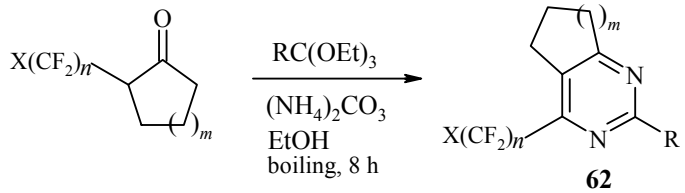


R = CH_2OH, CH(OH)Me, CH(OH)Ph, $CH_2CH(OH)Ph$, Ph

The ketones **60** and the structurally similar aldehydes **38** (R^1 = H, see section 1.1.3) enter into reaction with orthoesters in the presence of ammonium carbonate with the formation of polyfluoroalkylpyrimidines **61**, while in the case of cyclic ketones under the same conditions annelated pyrimidines **62** were obtained [45].

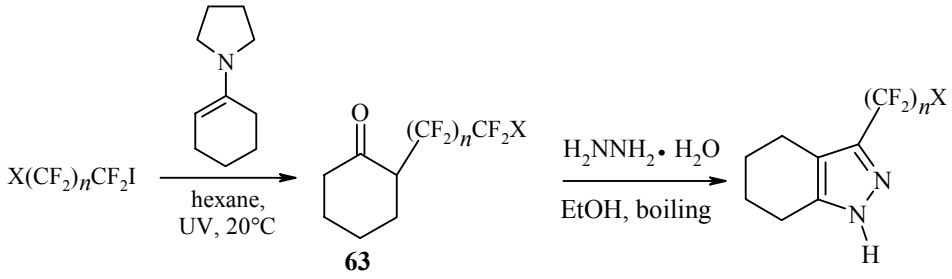


61 R^1 = Me, Et; X, *n*, R (yield, %): Cl, 4, Bu-*t* (90), Me (85), H (71);
Br, 2, H (70); F, 6, Bu-*t* (40)



62 R = Me, Et; X, *n*, *m*, (yield, %): F, 2, 1 (82);
Cl, 2, 2 (85); Cl, 4, 2 (85)

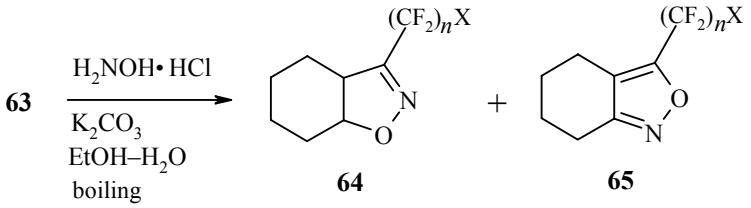
The reaction of 2-polyfluoroalkylcyclohexanones **63**, obtained from polyfluoroalkyl iodides and pyrrolidin-1-ylcyclohex-1-ene, with hydrazine hydrate leads to 3-polyfluoroalkyl-4,5,6,7-tetrahydroindazoles (yields 68-95%) [40, 41].



63

63 X = F, Cl; *n* = 2, 4, 6, 8

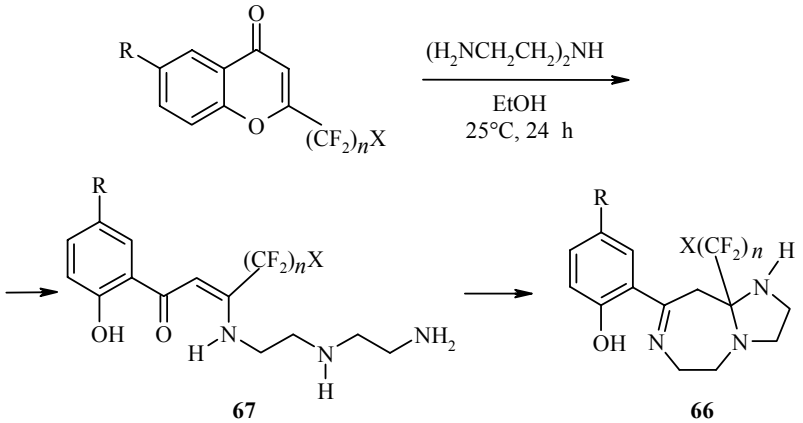
In the case of another binucleophile (hydroxylamine) mixtures of isomeric annelated isoxazoles **64** and **65** are formed, although the latter are obtained with very low yields [53].



64 **65**

64, **65** X, *n* (yield of **64**, %): F, 2 (90), 4 (80), 6 (79), 8 (75); Cl, 4 (82), 6 (81), 8 (85)

By using α,β-unsaturated cyclic ketones with polyfluoroalkyl substituents it was possible to synthesize complex bicyclic compounds; the triazabicyclodecenes **66** were obtained from polyfluoroalkylchromones and diethylenetriamine in alcohol at 25°C [54]

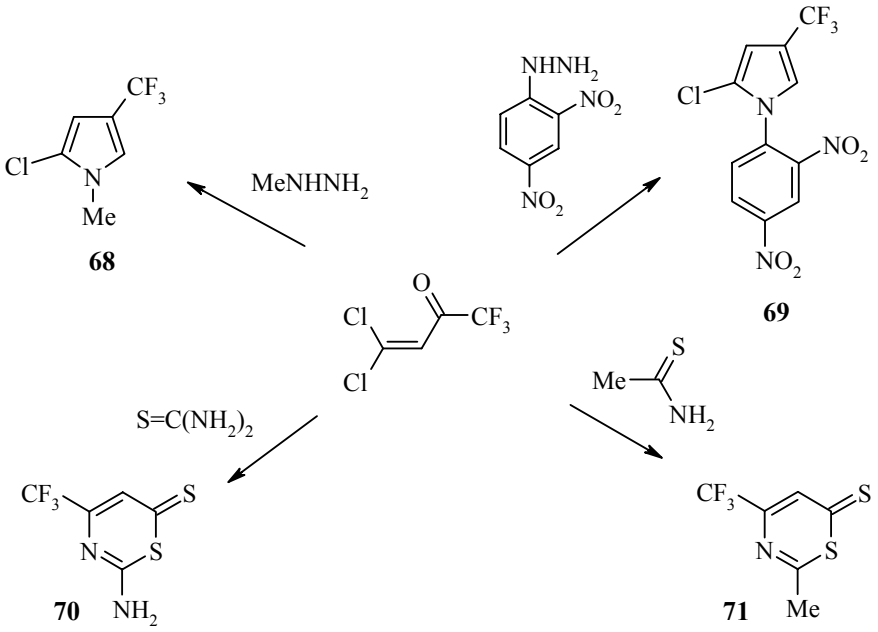


67 **66**

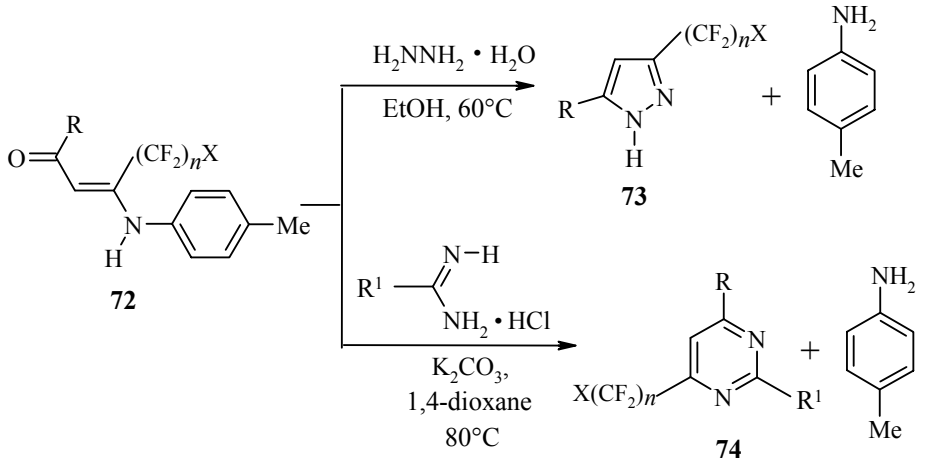
66 R, X, *n* (yield, %): H, H, 1 (54); H, H, 2 (54); H, F, 1 (80); Me, H, 2 (65); Me, F, 1 (87)

Nucleophilic attack by the primary amino group at the C(2) atom of the pyrone ring probably occurs at the first stage of the reaction. This is accompanied by opening of the ring and the formation of N-substituted aminoenones **67**, which then undergo cyclization with participation of the electrophilic centers and release of water to triazabicycles [54].

Trifluoromethyl 2,2-dichlorovinyl ketone was used successfully for the construction of variously substituted heterocycles having a CF_3 group among the substituents. Its reaction with N,N- and N,S-binucleophiles led to derivatives of pyrazole **68** (yield 56%) and **69** (yield 68%) and also thiazine **70** (51%) and **71** (56%) [55].

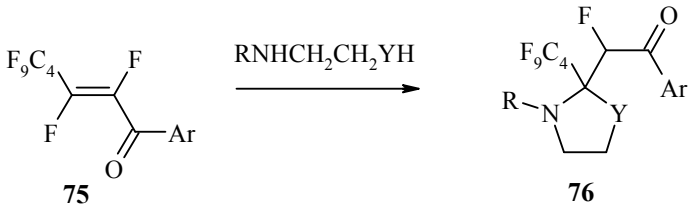


From β-polyfluoroalkyleneaminones **72** (the products from the reaction of N-arylpolyfluoroalkylimidoyl iodides and α-methyl ketones in the presence of sodium hydride) substituted pyrazoles **73** (yields 71-95%) were obtained in reactions with hydrazine, and substituted pyrimidines **74** (yields 70-96%) in reactions with amidines [56].



R^1 = Me, Ph. Product, R, X, *n* (yield, %): **73,** Me, Cl, 2 (72); Bu-*t*, Cl, 2 (71); Ph, F, 1 (90); Cl, 2 (93), Cl, 4 (86); 2-furyl, F, 1 (72), Cl, 2 (79), Cl, 4 (50); **74,** Me, F, 1 (70), Cl, 2 (96), Cl, 4 (94); Ph, F, 1 (70), Cl, 2 (90), Cl, 4 (93)

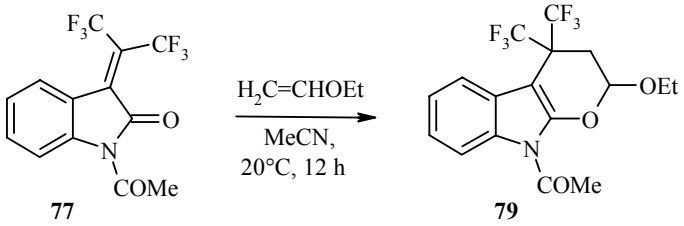
The reactions of compounds **75** with binucleophilic reagents take place by "Michael addition–elimination" and cyclization scheme with the formation of the five-membered heterocycles **76** [57].



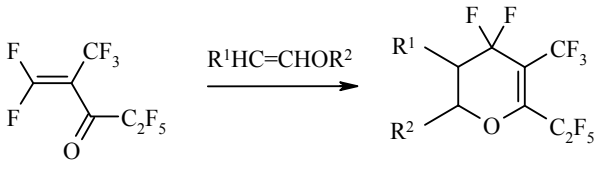
75 **76**

76 R = H, Y = NH; R = Me, Y = NH, O;
Ar = Ph, C_6H_4F-4, C_6H_4Cl-4, C_6H_4OMe-2

In reaction with ethyl vinyl ether or propylene the α,β-unsaturated ketones **77** and **78** act as dienes, leading to the formation of the Diels–Alder adducts **79** (yield 85%) or **80** (the conditions of synthesis were not given in the cited papers, yields indicated in the scheme) [37, 58, 59].



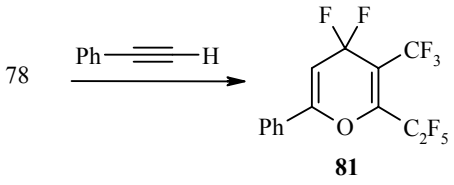
77 **79**



78 **80**

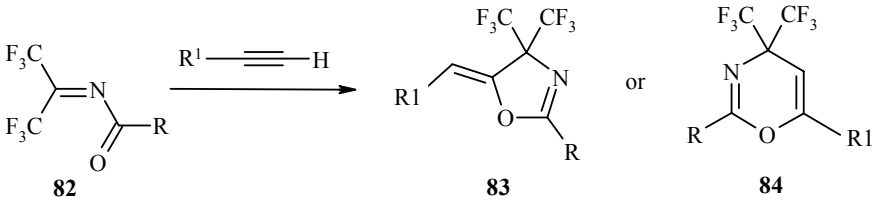
80 R^1, R^2 (yield, %) : H, Et (88); Me, Pr-*i* (80); H, Ac (62)

The vinyl ketone **78** reacts similarly with phenylacetylene, and the substituted 4H-pyran **81** is obtained (yield 8%) [59].



81

With substituted acetylenes the N-acylimines of hexafluoroacetone **82** form substituted azoxazolines **83** or 1,3-oxazines **84**, depending on the structure of the reagents and the reaction conditions [60].

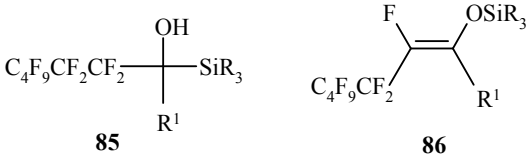


82 **83** **84**

Product, conditions of synthesis, R, R^1 (yield, %): **83**, dimethylaminopyridine, 0°C, Ph, COOEt (49), Ph, Ph (66), Bu-*t*, Ph (41), Bu-*t*, COOEt (34); 100°C, 48 h (80); toluene, 90°C, 50 h, Ph, Ac (11); boiling, 20 days, Ph, COOMe (36), C_6H_4Me-4, COOMe (30); C_6H_4Cl-4, C_6H_4Me-4 (29); **84**, boiling in xylene, 48 h, Ph, Ph (66), Ph, Bu-*t* (80)

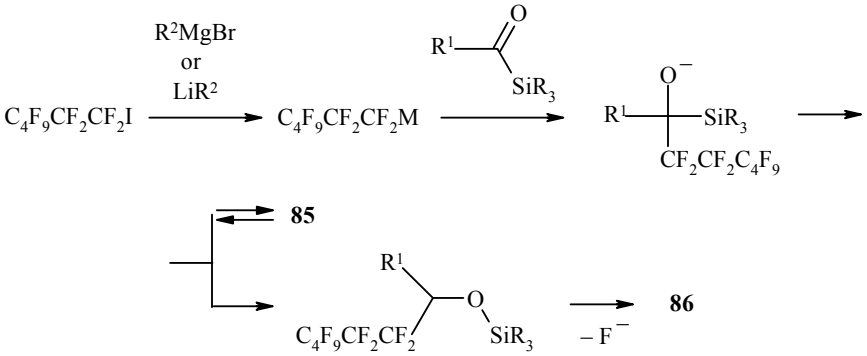
1.2. Synthetic Equivalents of Carbonyl Compounds

Synthetic equivalents of the carbonyl compounds examined above (silyl-substituted alcohols **85** [16] and silyl ethers of enols **86** [17, 18]) have been used successfully for the construction of various polyfluoroalkyl-substituted heterocycles.

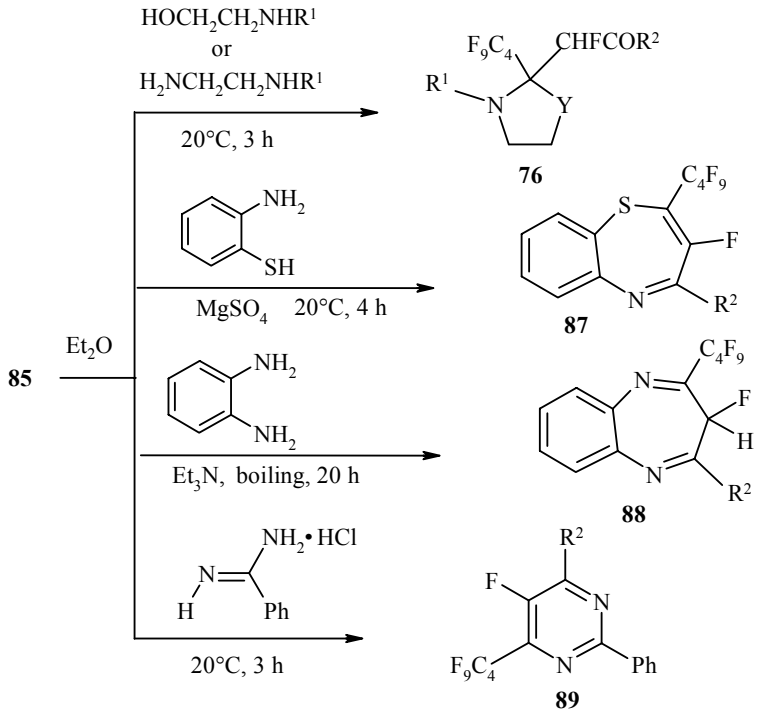


85 **86**

Compounds **85** and **86** were obtained according to the following scheme [19, 61-63]:

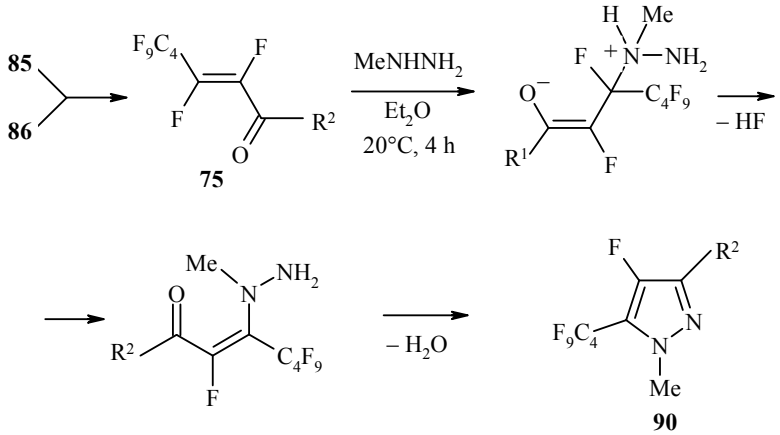


Products containing imidazoline **76** (Y = NH), oxazoline **76** (Y = O), thiazepine **87**, diazepine **88**, and pyrimidine **89** rings were obtained from compounds **85** and binucleophilic reagents under mild conditions with yields of 80-98% [57]. Some examples of such syntheses are presented below.



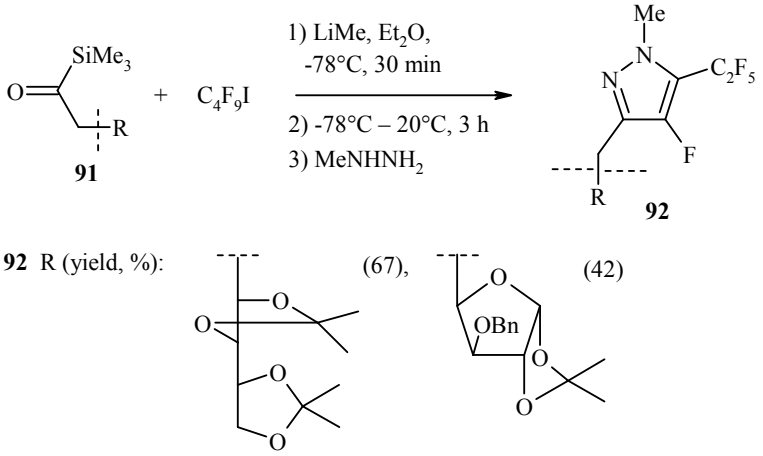
76 Y, R^1, R^2 (yield, %) : NH, H, Ph (88); NH, H, C_5H_{11} (94); NH, Me, Ph (88); O, H, Ph (91); O, Me, Ph (92); O, Me, C_5H_{11} (85). Product, R^2 (yield, %): **87,** Ph (87); **88,** Ph (92), C_6H_4F-4 (82), C_6H_4Cl-4 (98), C_6H_4OMe-4 (82); **89,** Ph (80)

The substituted pyrazoles **90** were synthesized from compounds **85** or **86** and methylhydrazine [19]. Initially an olefin of type **75** is formed, and its reaction with methylhydrazine leads to the product **90**.

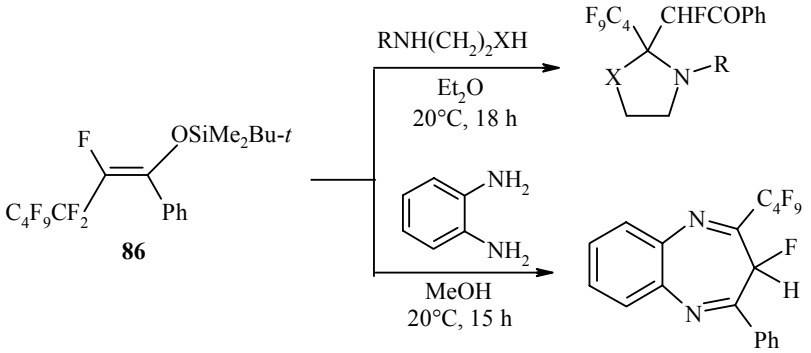


90 R^1 (yield, %): Ph (99), C_5H_{11} (57)

Starting from derivatives of natural sugars **91** and perfluorobutyl iodide, the sugars **92** modified with a pyrazole substituent were obtained similarly through an intermediate compound of type **85** or **86** and its reaction with methylhydrazine [19].



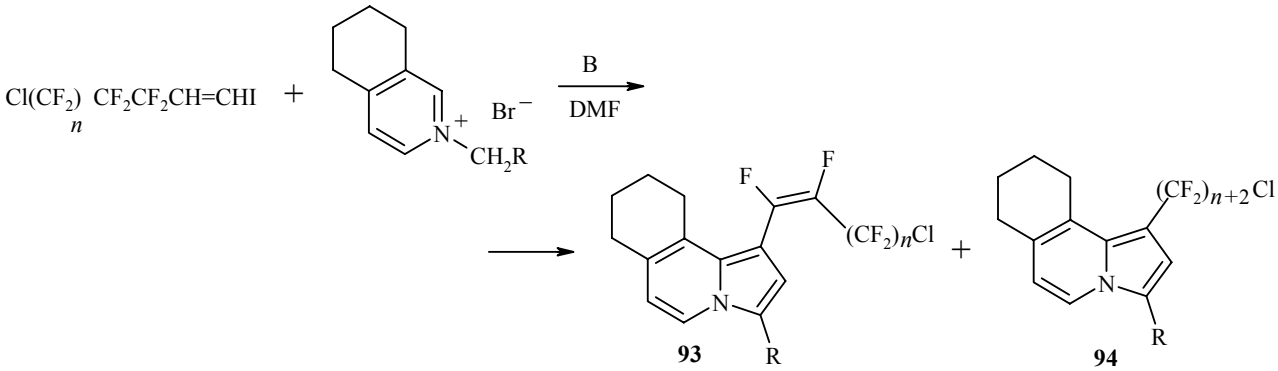
The synthesis of five- and seven-membered heterocycles with yields of 85-94% from compounds **86** and ethylenediamine, N-methylethanolamine, and *ortho*-phenylenediamine has been described [57].



R = H, Me; X = NH, O

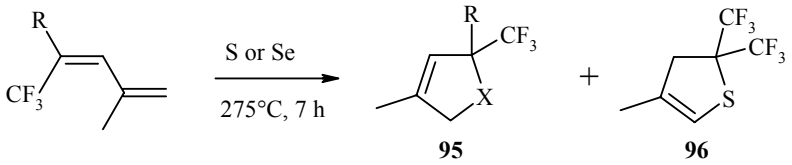
1.3. Other Compounds

In addition to the carbonyl compounds described above compounds not containing a C=O group have also been used successfully for the synthesis of polyfluoroalkyl-substituted heterocycles. The simplest of these are α-iodo-β-polyfluoroalkylethylenes, which react with N-cyanomethyltetrahydroisoquinolinium bromide in the presence of bases to form mixtures of tricyclic products **93** (yields 60-81%) and **94** (yields 35-55%) [21, 64].



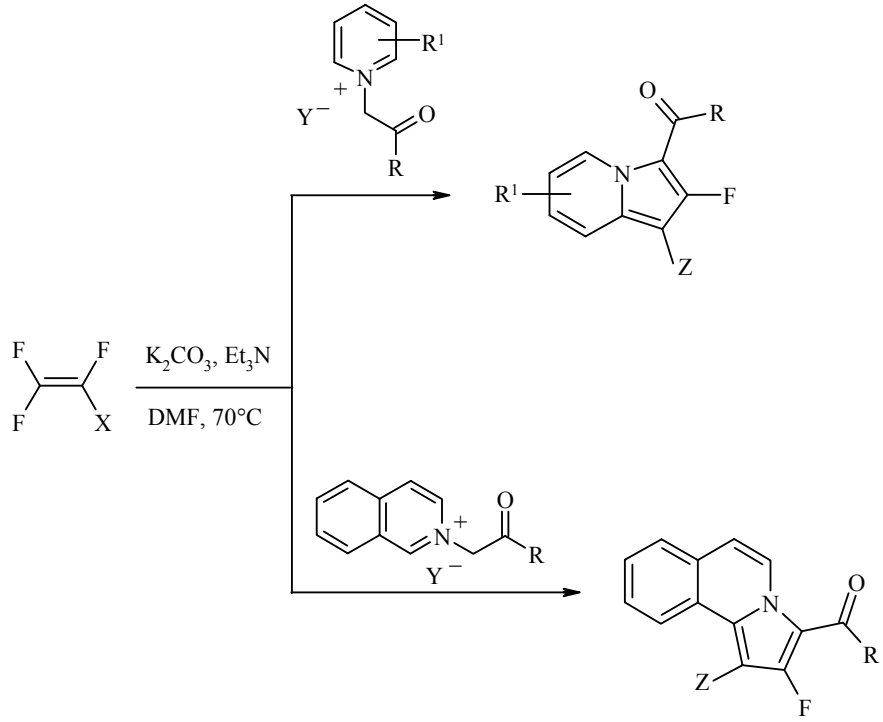
Product, *n*, R: **93,** 2, COPh, COOEt; **94,** 2, 4, COPh; 4, CN

Substituted 2,5-dihydrothiophenes **95** or 2,5-dihydroselenophenes were synthesized by heating 4-methyl-2-trifluoromethylpentadiene or 3-methyl-1,1-bis(trifluoromethyl)butadiene with sulfur or selenium respectively in an autoclave; with R = CF_3 a small yield of 2,3-dihydrothiophene **96** was also obtained [65].



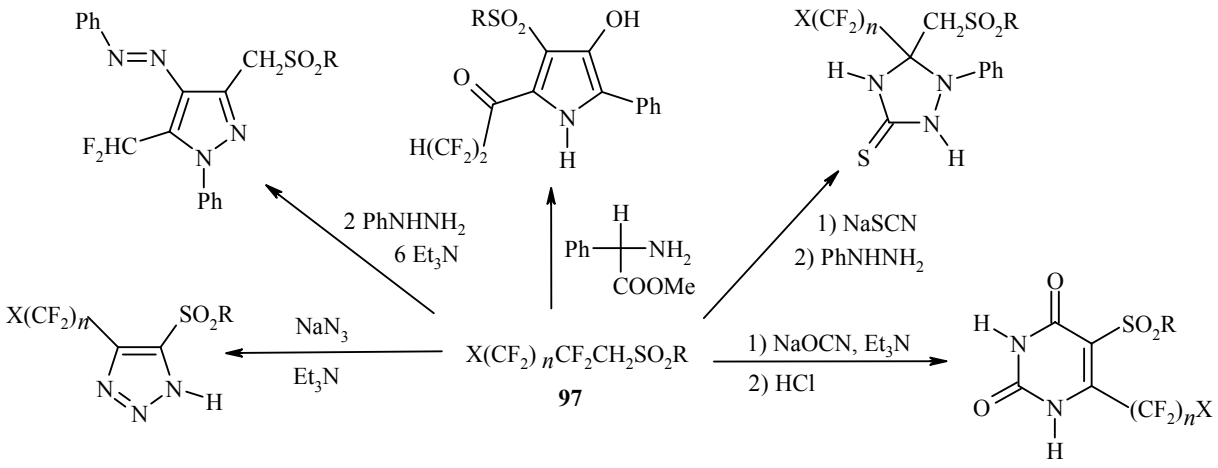
Product, R, X (yield, %): **95** CF_3, S (71); CF_3, Se (68); Me, S (91); Me, Se (not indicated); **96** (not indicated)

The reaction of certain fluorine-containing olefins with pyridinium or isoquinolinium salts (easily transformed into ylides) leads to the formation of indolizines and 4H-pyrrolo[1,2-*a*]benzimidazoles respectively [66].



X = Cl, Br, F, CF_3; R^1 = H, 4-Me, 3-Me; R = Ph, OEt; Y = Cl, Br; Z = F, CF_3

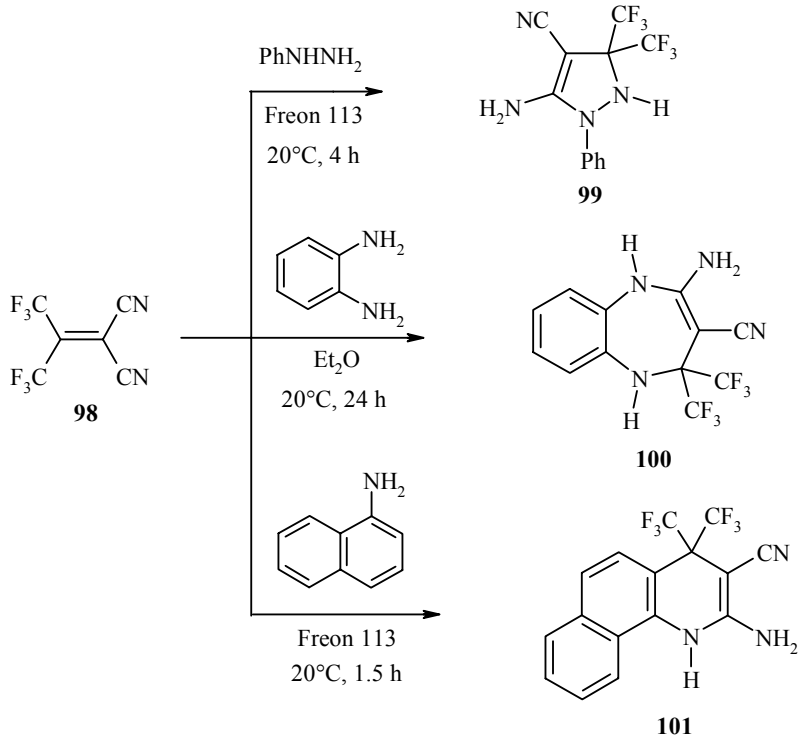
Like the carbonyl compounds (section 1), the sulfones **97** react with nucleophilic reagents, forming various heterocycles [66-68].



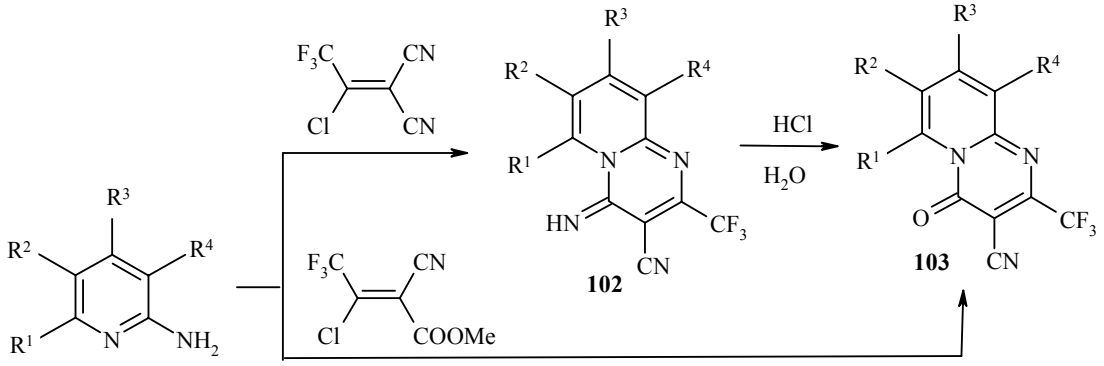
The first stage of the process is dehydrofluorination, leading to fluoroalkenyl sulfones. In the reaction with triethylamine in benzene, for example, dehydrofluorination is an equilibrium process [68].

$$X(CF_2)_nCF_2SO_2CH_2Ph + Et_3N \rightleftharpoons X(CF_2)_nCF{=}CHSO_2CH_2Ph + [Et_3N{\bullet}HF]$$

Derivatives of dicyanoethylene have been successfully used many times for the construction of heterocycles. Thus, the dihydropyrazole **99** was synthesized with a yield of 89% from the bis(trifluoromethyl)-substituted derivative **98** and phenylhydrazine, and its structure was confirmed by X-ray crystallographic analysis [69]. The dihydrobenzodiazepine **100** (yield 55%) was obtained from the olefin **98** and *ortho*-phenylenediamine [70], while the dihydrobenzoquinoline **101** (yield 91%) was obtained in the reaction with α-naphthylamine [71].



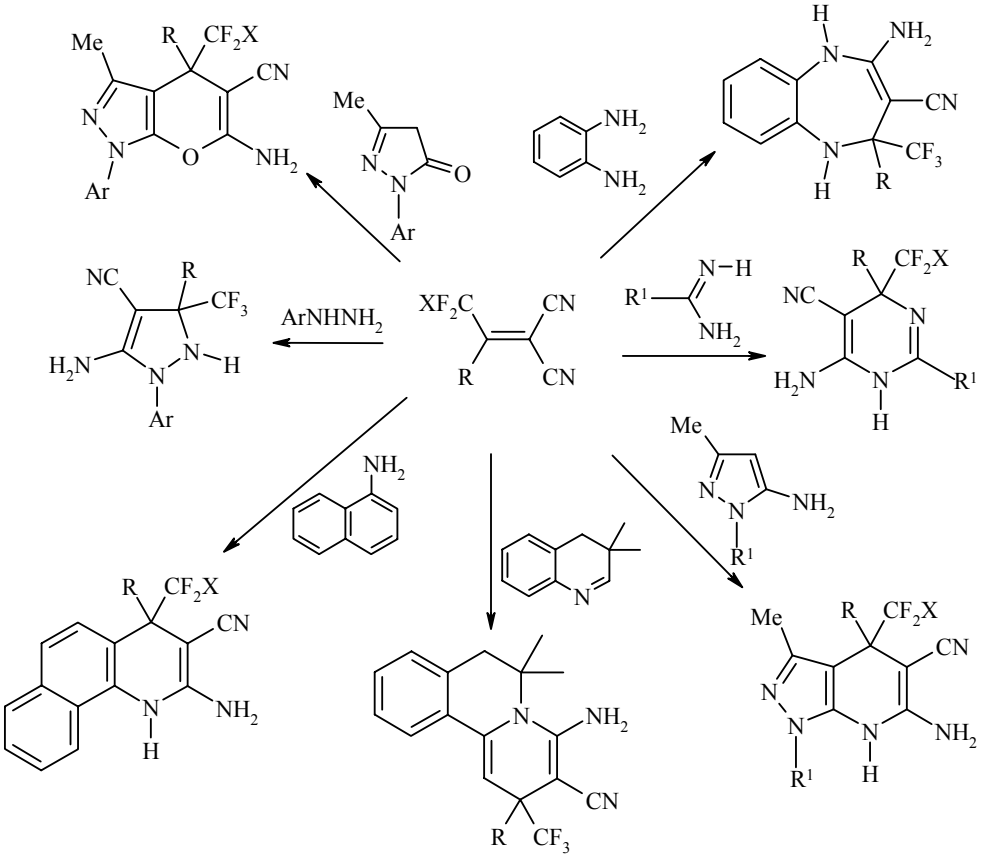
The reaction of 2-chloro-1,1-dicyano-2-trifluoromethylethylene with 2-aminopyridine and 2-aminopicolines at room temperature leads to high yields of pyrido[1,2-*a*]pyrimidines **102** [71]. The reaction probably takes place through alkenylation of the amino group by the 2-chloroethylene followed by intramolecular cyclization. The structure of 3-cyano-4-imino-7-methyl-2-trifluoromethyl-4H-pyrido[1,2-*a*]-pyrimidine (yield 56%) was confirmed by X-ray crystallographic analysis.



103 $R^1 = R^2 = R^3 = H$; R^1, R^2, R^3 or R^4 = Me, other R = H

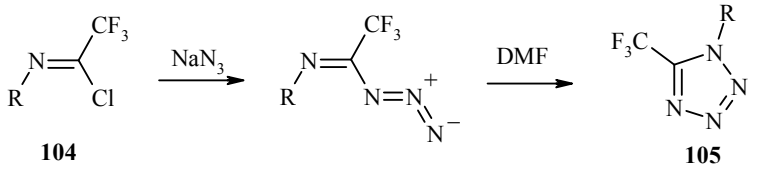
When 2-chloro-1-cyano-1-methoxycarbonyl-2-trifluoromethylethylene was used under similar conditions, substituted pyrido[1,2-*a*]pyrimidin-4-ones **103** were obtained (yields 23-53%) [71].

The reaction of 2-substituted 1,1-dicyano-2-trifluoromethylethylene and aromatic amines or diamines leads to various nitrogen-containing heterocyclic compounds [72, 73].



The examined examples show that the use of olefins with electron-withdrawing substituents, including polyfluoroalkyl, in reactions with nucleophiles can provide a general method for the synthesis of various heterocyclic compounds.

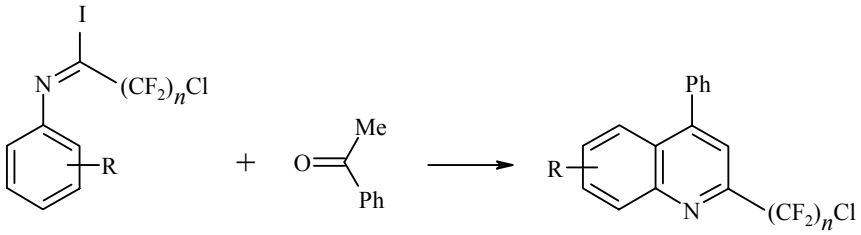
Other derivatives of polyfluoroalkanoic acids, i.e., imidoyl halides (which take part in the construction of the heterocycle through the C=N bond), have also found use as building blocks. Thus, substituted tetrazoles **105** were synthesized with yields of 53-91% from the imidoyl chlorides **104** and sodium azide [74-77].



104 **105**

105 R (yield, %): Ph (80), C_6H_4Me-4 (91), $C_6H_3Me_2$-3,4 (68), C_6H_4Cl-4 (53), $C_6H_3Cl_2$-3,4 (50), C_6H_4Br-4 (55), $C_6H_4NO_2$-2 (53), $C_6H_4NO_2$-4 (70), C_6H_4OMe-4 (94), $(CH_2)_3Ph$ (61)

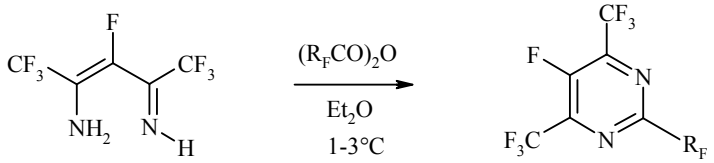
The reaction of imidoyl chlorides **106** with acetophenone led to the substituted quinolines **107** [78].



106 **107**

107 R = 4-Me, 2-Cl, 4-Cl, 4-I; n = 2, 4

2-Amino-4-iminoperfluoropent-2-ene, similar in structure to imidoylamidines, reacts with the anhydrides and chlorides of perfluoro carboxylic acids with the formation of 2,4,6-(perfluoroalkyl)-5-fluoropyrimidines [79].



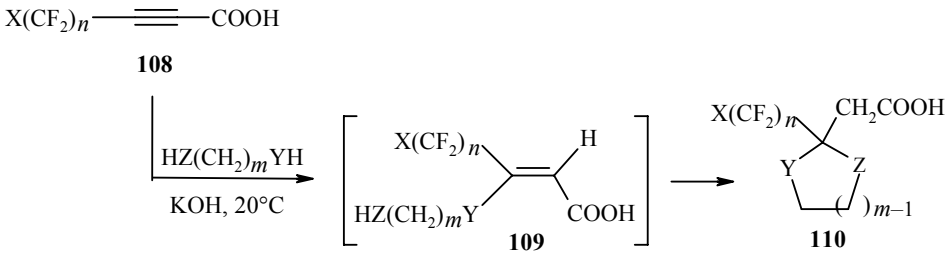
R_F (yield of pyrimidine, %): CF_3 (71), C_2F_5 (73), C_3F_7 (88)

2. METHODS FOR THE CONSTRUCTION OF HETEROCYCLES FROM ACETYLENE DERIVATIVES

Two main methods for the construction of heterocycles from acetylene derivatives are known: 1) reaction of these derivatives (mainly acetylenecarboxylic acids and esters) with binucleophiles; 2) cycloaddition of polyfluoroalkynes [mainly bis(trifluoromethyl)acetylene and trifluoromethylacetylene] with azides, diazomethanes, and other unsaturated compounds. Published data are discussed below in accordance with the indicated paths.

2.1. Nucleophilic Addition–Cyclization

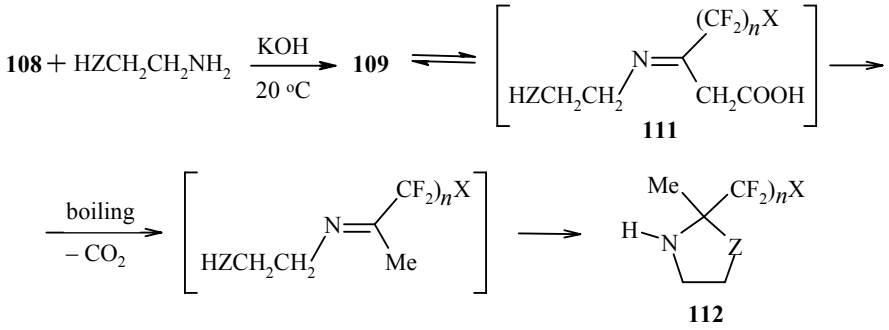
In the reaction of a binucleophilic reagent with acetylene derivatives with the general formula $X(CF_2)_nC{\equiv}CR$ (where R is a COOH, COOEt, or other group, see below) an intermediate addition product (an ethylene derivative) is formed as a result of reaction of one of the nucleophilic centers with the carbon atom attached to the $X(CF_2)_n$ group. In the addition product the second nucleophilic center attacks the same carbon atom or the carbon atom attached to the functional group R, leading to the formation of the heterocyclic compound. Thus, the heterocyclic compounds **110** were synthesized from acetylenecarboxylic acids of type **108** and ethanedithiol, propanedithiol, mercaptoethanol or ethylene glycol through the intermediate products **109** (mixtures of *cis* and *trans* isomers) [80, 81].



110 Y, Z, *m*, X, *n* (yield, %): S, S, 2, H, 1 (76), F, 1 (84); S, S, 3, H, 1 (74), H, 3 (26); S, O, 2, H, 1 (80), F, 1 (76); O, O, 2, H, 1 (64), F, 1 (63)

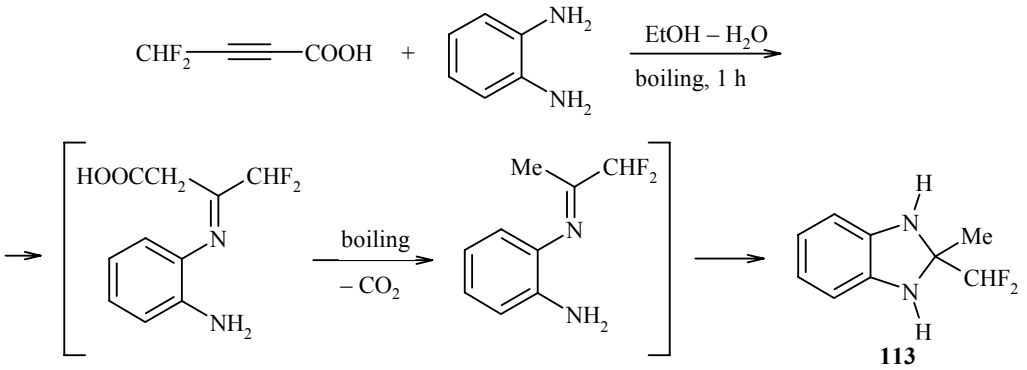
In the case of ethanedithiol (Y = Z = S) the diacids $\{CH_2SC[X(CF_2)_n]{=}CHCOOH\}_2$, which are the products from addition of two molecules of the acid **108** at the two nucleophilic centers, were also isolated in addition to compounds **110**. The products **109** were obtained from mercaptoethanol (Y = S, Z = O) with yields of >85%, and their cyclization at 60°C led to the products **110**.

During the reaction of the acids **108** with N-nucleophiles (Y = Z = NH, or Y = NH, Z = S) decarboxylation of the intermediate product (probably a mixture of the *cis* and *trans* isomers of the enamine **109** with the imine **111**) occurs, as a result of which the obtained heterocyclic compound **112** contains the Me substituent instead of the CH_2COOH group (see **110**) [82].

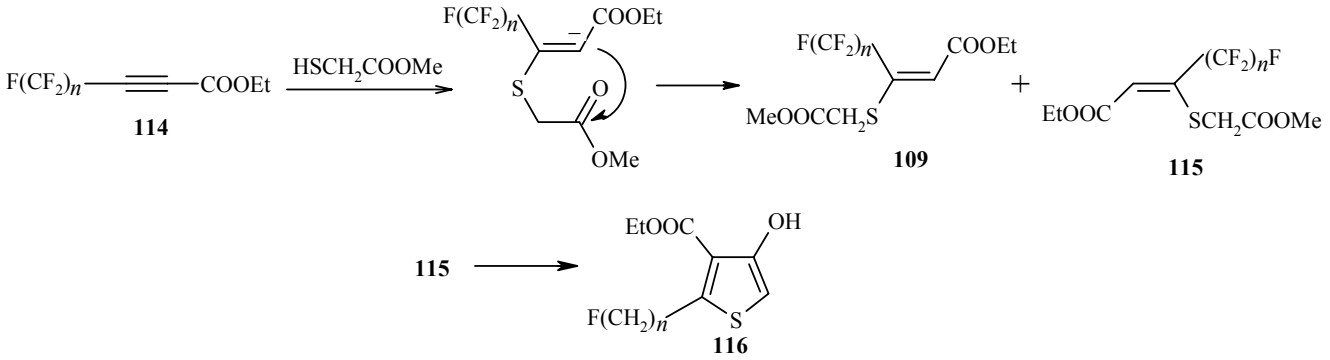


112 Z, X, *n* (yield, %): N, H, 1 (88), N, H, 3 (77), N, F, 1 (80), S, H, 1 (80)

Analogous transformations in the case of *ortho*-phenylenediamine led to the product **113** (yield 76%) [82].

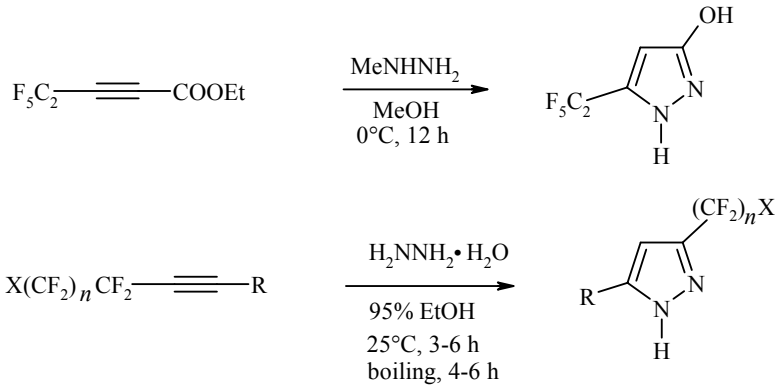


The *cis* and *trans* isomers of the products **109** and **115** from oxidation at the triple bond were obtained from esters of type **114**, as in the examples examined above. Under the reaction conditions the *Z*-isomer **115** undergoes cyclization to the substituted ester of thiophene-3-carboxylic acid **116** [83].



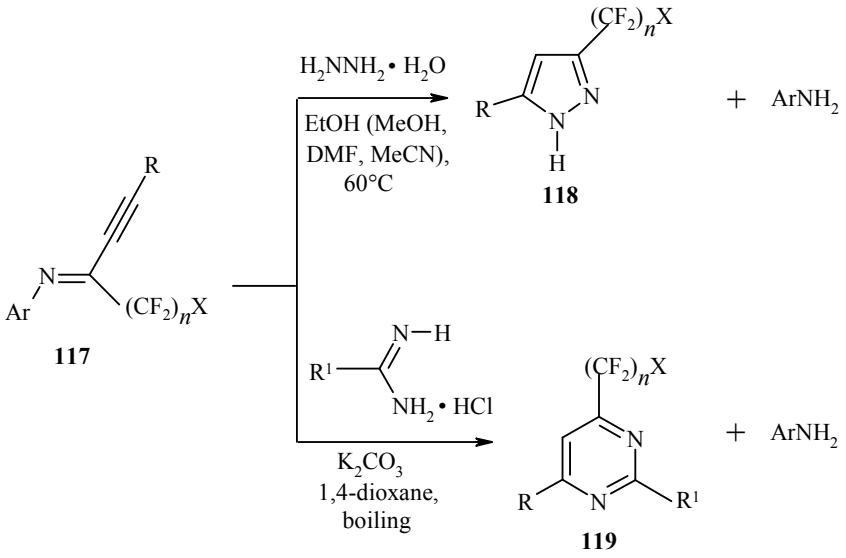
116 *n* (yield, %): 4 (63); 6 (56); 8 (53)

By using methylhydrazine and hydrazine hydrate as binucleophiles in reactions with acetylene derivatives containing a polyfluoroalkyl group it is possible to synthesize various substituted pyrazoles with yields of 52-98% [84, 85]. 3-Polyfluoroalkyl-substituted pyrazoles have high biological activity and can be used a herbicides, fungicides, and insecticides [85].



X, *n*, R: F, 1, Ph, CH_2OH, CH(OH)Me; F, 3, Ph; F, 5, Ph;
Cl, 3, Ph, CH_2OH, $C(OH)Me_2$; Cl, 5, CH_2OH

Substituted N-arylimines **117** (obtained from N-arylpolyfluoroalkylimidoyl iodide and acetylene derivatives in the presence of $Pd(PPh_3)_2Cl_2$/CuI in Et_3N/MeCN) under the influence of an excess of hydrazine hydrate or substituted amidine give pyrazole derivatives **118** (yields 94-99%) and pyrimidine derivatives **119** (yields 74-80%) respectively [86].

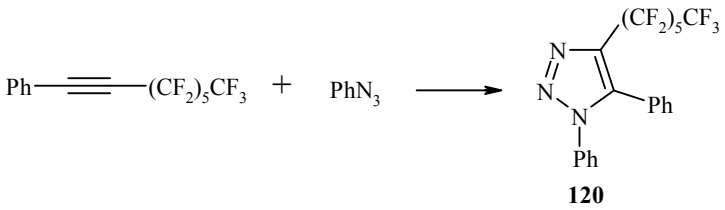


118, 119 R = Ph, $SiMe_3$, Bu, COMe; R^1 = Me, Ph; X = F, Cl; n = 2, 4

1.2. Dipolar Cycloaddition

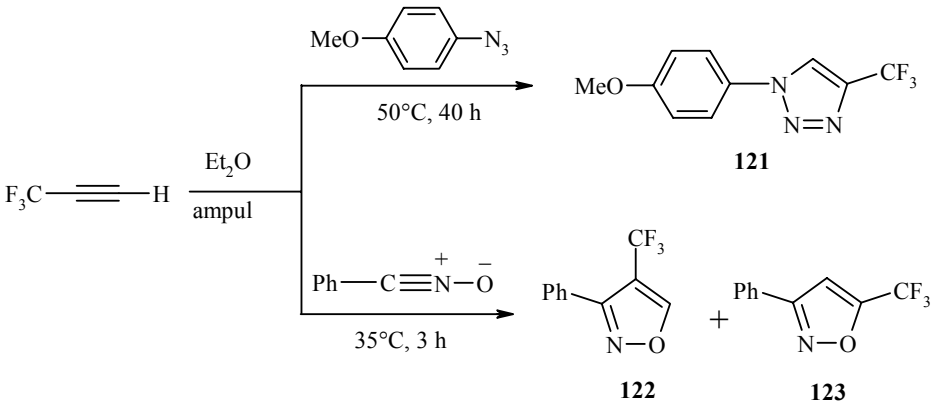
The ability of acetylene derivatives to form heterocycles through cycloaddition with unsaturated compounds also shows up in polyfluoroalkyl-substituted acetylenes, acting as dipolarophiles. Some examples of [3+2] and [4+2] cycloaddition are given below [87-92]

As a result of the reaction of phenyl azide with phenyl(perfluorohexyl)acetylene the triazole **120** was obtained with a 76% yield [87].

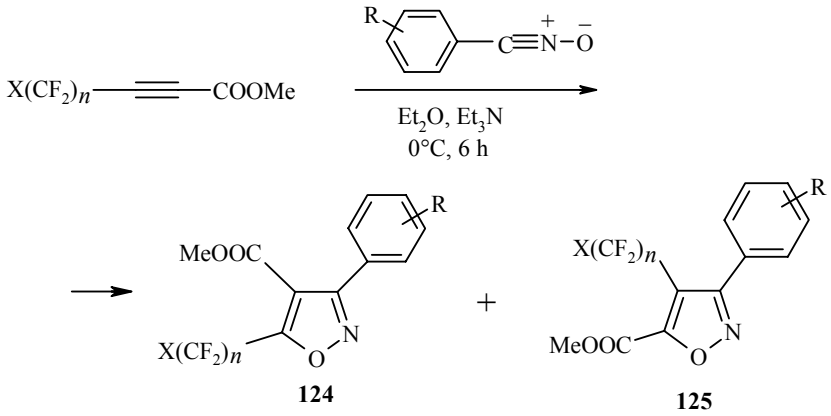


120

The high regioselectivity in the reactions of perfluoroalkylacetylene with 4-methoxyphenyl azide [88], benzonitrile oxide [89], or diazomethane [90], leading to the formation of five-membered heterocyclic compounds **121** (yield 65%), **122** (67%), and **123** (11%), has been demonstrated.

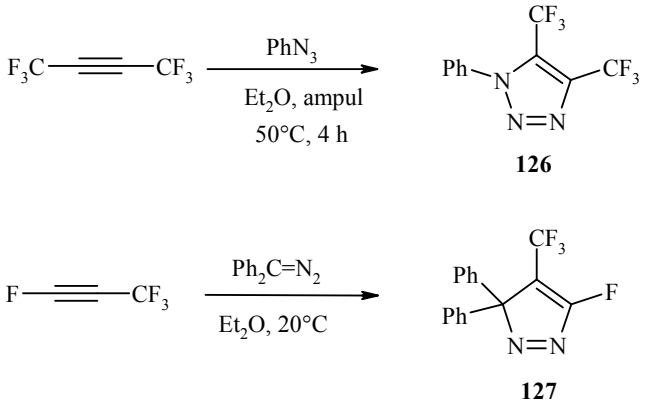


By the 1,3-bipolar cycloaddition of aromatic nitrile oxides and polyfluoroalkyl acetylene derivatives it is possible to synthesize polyfluoroalkylisoxazoles **124** and **125** [93]. The ratio of the isomers **124** and **125** amounts to ~90:10.

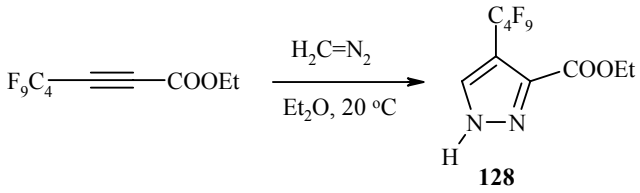


Mixture of **124** and **125**, R, *n*, X (total yield, %): H, 1, F (92); H, 2, F (94); H, 3, F (94); 2-Cl, 1, F (97), 2-Cl, 2, F (95), 2-Cl, 3, F (94), 4-Cl, 1, F (97); 4-Cl, 2, F (90); 4-Cl, 3, F (94)

Perfluoro-2-butyne reacts similarly with phenyl azide [88], and perfluoropropyne reacts with diphenyldiazomethane [94], giving respective products **126** (yield 80%) and **127** (35%).

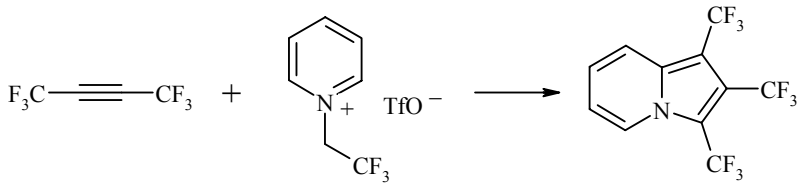


Regiospecific addition of diazomethane also occurs in the case of ethyl perfluorobutylacetylenecarboxylate and leads to the formation of compound **128** (yield 75%) [90].



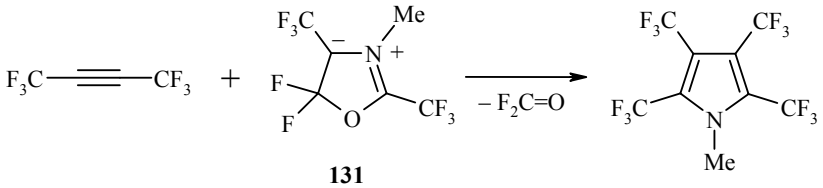
128

The pyridinium ylide formed from the salt **129** enters into reaction with perfluoro-2-butyne to form the indolizine **130** [95, 96].



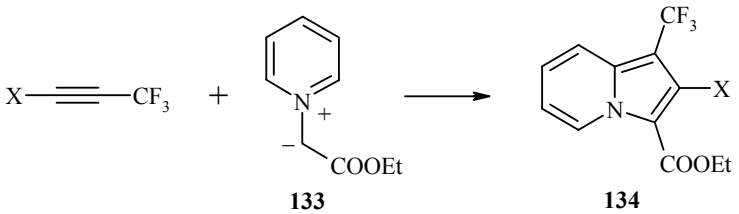
129 **130**

N-Methyl-N-(2-perfluoropropenyl)trifluoroacetamide can react with various dipolarophiles through the valence tautomer of cyclic azomethine ylide. Thus, [3+2] cycloaddition in the reaction with perfluoro-2-butyne leads to the trifluoromethyl derivative of pyrrole **132** [96].



131 **132**

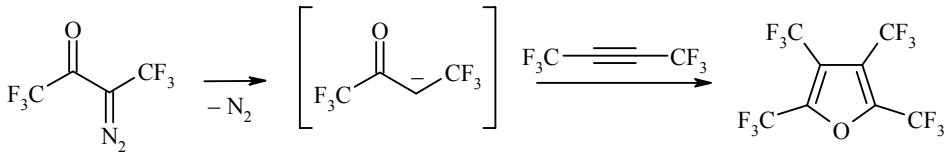
Perfluoro-2-butyne and other trifluoromethyl-substituted acetylenes also react with the pyridinium ylide **133**; [3+2] cycloaddition in the presence of sodium hydride results in the formation of substituted indolizines **134** [97-100].



133 **134**

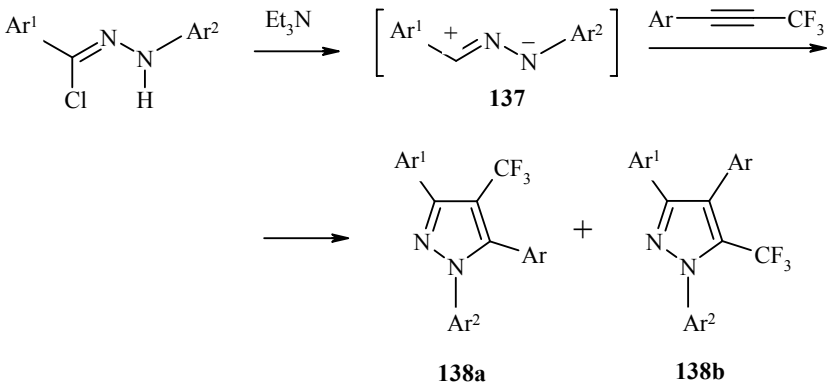
134 X (yield, %): F (13); CF_3 (24); H (22)

In photolytic reaction with perfluoro-2-butyne the hetero-1,3-diene **135** gives tetrakis(trifluoromethyl)furan **136** [98].



135 **136**

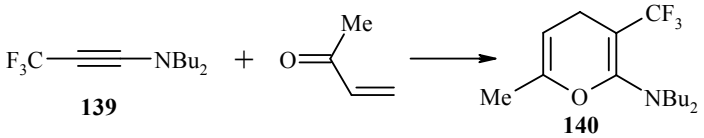
Being 1,3-dipoles, the nitrile imines **137** formed intermediately from ketone hydrazones enter into [3+2] cycloaddition with 1-aryl-3,3,3-trifluoro-1-propyne, giving the isomeric trifluoromethylpyrazoles **138a** and **138b** [101].



137 **138a** **138b**

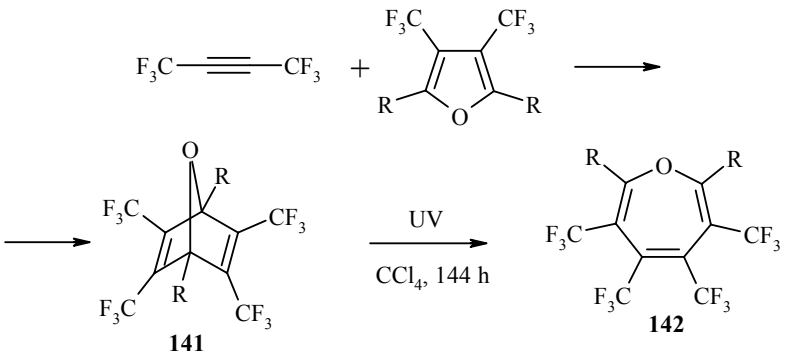
Ar, Ar^1, Ar^2 (yield of mixture of compounds **138a** and **138b**), **138a** : **138b** : C_6H_4Cl-2, Ph, C_6H_4Cl-4 (84), 97:3; C_6H_4OMe-4, C_6H_4Cl-4, Ph (87), 98:2; $C_6H_4NO_2$-4, C_6H_4Cl-2, Ph (80), 97:3; C_6H_4SMe-4, C_6H_4OMe-4, Ph (89), 96:4; $C_6H_4SO_2Me$-4, $C_6H_4NO_2$-4, Ph (73), 97:3; C_6H_4Cl-2, Ph, C_6H_4Cl-2 (87), 98:2; C_6H_4Cl-2, Ph, C_6H_4OMe-4 (85), 96:4); C_6H_4Cl-2, Ph, $C_6H_4NO_2$-4 (72), 97:3

A common feature of polyfluoroalkylacetylenes is their ability to enter into a Diels–Alder reaction with heterodienes, leading to heterocycles containing polyfluoroalkyl substituents. Thus, methyl vinyl ketone and substituted trifluoropropynylamine **139** form the adduct **140** (yield 97%) as a result of [4+2] cycloaddition [102].



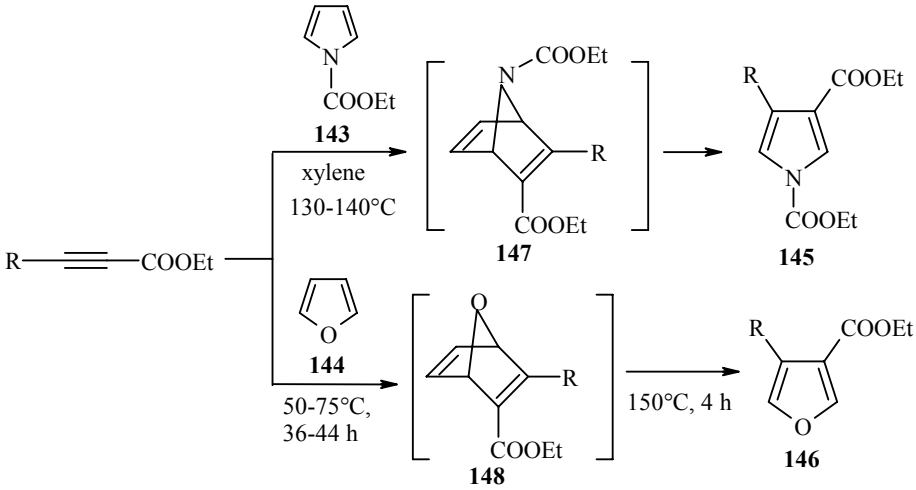
139 **140**

Perfluoroalkylacetylenes react with substituted furans, giving the Diels–Alder products **141**, the action of heat on which leads to the substituted oxepins **142** as a result of a thermal retro-Diels–Alder reaction [103-110].



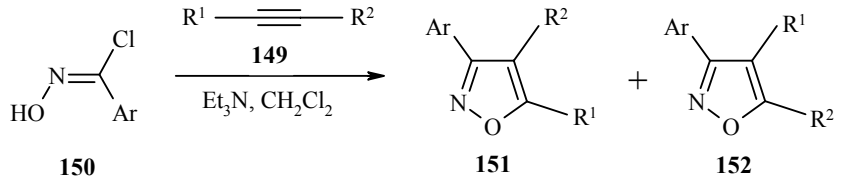
142 R (yield, %): Me (38), Et (35)

By the Diels–Alder reaction of ethyl polyfluoroalkylacetylenecarboxylates with the N-pyrrolecarboxylate ester **143** [103] or furan **144** [103, 104] it is possible to synthesize new derivatives of the above-mentioned heterocycles with polyfluoroalkyl substituents **145** and **146** through intermediate compounds **147** and **148**.



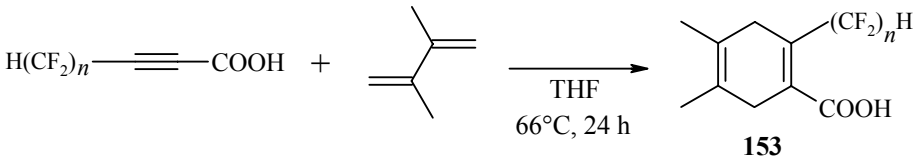
Compound, R (yield, %): **145**, CF_3 (44), C_5F_{11} (51), C_7F_{15} (65);
146, CF_3 (38), C_5F_{11} (55), C_7F_{15} (68); **148**, CF_3 (51), C_5F_{11} (81), C_7F_{15} (79)

In the reaction of acetylenes **149** with benzohydroxyimidoyl chloride **150** the presence of the base makes it possible to synthesize derivatives of 5-polyfluoroalkylisoxazole **151** and isomeric isoxazoles **152** [111].



Reaction temperature, °C, R^1, R^2, yield **151/152**, %, (**151 : 152**),
0, CF_3, COOMe, 49/3, (80:20); 0, C_2F_5, COOEt, 38/18 (79:21); 20, CF_2Cl, COOMe, 68/5 (87:13);
20, CHF_2, COOEt, 76/2 (85:15); 0, CF_3, H, 41/not indicated (ni) (77:23);
20, CF_3, 60/ ni (ni); 40, CF_3, Ph, ni/11 (ni)

The Diels–Alder reactions of polyfluoroalkylacetylenecarboxylic acids with 2,3-dimethyl-1,3-butadiene lead to the 1,4-addition products **153** [112].

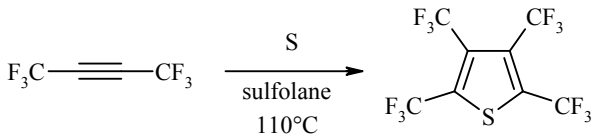


153

153 *n* (yield, %): 1 (94), 3 (86), 5 (91)

Analogous products were obtained in the case of 2-methyl-1,3-butadiene, furan, and 1,2,4,5-tetramethylbenzene [112].

To conclude section 2.2 it is necessary to mention the synthesis of tetrakis(trifluoromethyl)thiophene (yield 61%) from perfluoro-2-butyne and elemental sulfur [113]. The mechanism of the process is unknown.



In the present review an attempt has been made to draw the attention of chemists to an interesting and rapidly developing region of organic chemistry, concerning the synthesis of heterocyclic compounds with polyfluoroalkyl groups, and to acquaint specialists working on the creation of medicinal and agricultural products with the new methods of preparation. Data (mostly of the last decade) on methods for the construction of heterocyclic systems with polyfluoroalkyl substituents from certain unsaturated compounds containing polyfluoroalkyl groups have been classified and analyzed. The material examined in the review draws attention to the immense possibilities for the synthesis of various fluorine-containing products that are interesting prospective subjects for further research into their properties.

It can be seen that intramolecular nucleophilic cyclization involving an unsaturated polyfluoroalkyl-containing molecule has been used successfully in the construction of a heterocyclic system. At the same time the presence of the fluorine atoms in the starting materials provides the basis for the formation of new double bonds and their participation in the formation of the heterocycle and also motivates the search for new ways of introducing fluorine-containing functional groups.

Since advances in high selectivity have become a more and more important factor in chemical processes, it is clear that the new approaches to the construction of a heterocyclic system described in the review may find extensive use in the ordered synthesis of fluorine-containing substances.

The authors hope that the review will provide a give rise to a wider understanding of the unique characteristics of organofluorine compounds and extend their applications into other fields.

REFERENCES

1. G. A. Olah, R. D. Chambers, and G. K. S. Prakash (editors), *Synthetic Fluorine Chemistry*, John Wiley & Sons, New York, 1992.
2. N. Ishikawa (Ed.), *Fluorine Compounds, Modern Technology and Applications*, Mir, Moscow, 1984.
3. S. Scheithauer and R. Mayer, in: A. Senning (editor), *Topics in Sulfur Chemistry*, Georg Thieme Publ., Vol. 4, Stuttgart (1979).

4. J. Elguero, A. Fruchier, N. Jogerovic, and A. Werner, *Org. Prep. Proced. Int.*, **27**, 33 (1995).
5. R. Filler, Y. Kobayashi, and L. M. Yagupolskii (editors), *Studies in Organic Chemistry. 48. Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*, Elsevier Sci. Publ., Amsterdam (1993).
6. J. T. Welch and S. Eswarakrishnan, *Fluorine in Bioorganic Chemistry*, J. Wiley, New York (1991).
7. R. Filler and Y. Kobayashi, *Biomedical Aspects of Fluorine Chemistry*, Elsevier Biomedical Press, Kodansha, Tokyo, New York (1982).
8. K. Burger, U. Wucherpfenning, and E. Brunner, *Adv. Heterocycl. Chem.*, **60**, 1 (1994).
9. S. K. Ritter and C. Washington, *Chem. Eng. News*, **73**, 39 (1995).
10. R. D. Chambers and C. R. Sargent, *Adv. Heterocycl. Chem.*, **28**, 1 (1981).
11. G. G. Furin, *Zh. Org. Khim.*, **30**, 1704 (1994).
12. G. G. Furin, *Chemistry Rev.*, **2**0, Pt. 4, 1 (1996); OPA (Oversear Publishers Association), Amsterdam, Harwood Academic Publishers GmbH.
13. G. G. Furin, in: O. A. Attanasi and D. Spinelli (editors), *Targets in Heterocyclic Systems (Chemistry and Properties)*, Italian Society of Chemistry, Roma, **2**, 355 (1998).
14. G. G. Furin and E. L. Zhuzhgov, *Khim. Geterotsikl. Soedin.*, 147 (2002).
15. G. G. Furin, *Adv. Heterocycl. Chem.*, **87**, 273 (2004).
16. B. Dondy and C. Portella, *J. Org. Chem.*, **58**, 6671 (1993).
17. B. Dondy, P. Doussot, and C. Portella, *Tetrahedron Lett.*, **35**, 409 (1994).
18. B. Dondy, P. Doussot, B. Didier, R. Plantier-Rouon, J. P. Bouillon, and C. Portella, in: *Abstracts of 16th International Symposium on Fluorine Chemistry*, Durham, England (2000), 1P-114.
19. J.-P. Bouillon, B. Didier, B. Dondy, P. Doussot, R. Plantier-Royon, and C. Portella, *Eur. J. Org. Chem.*, No. 1, 187 (2001); *Chem. Abstr.*, **134**, 266239 (2001).
20. W.-Y. Huang, L. Lu, and Y. F. Zhang, *Chin. J. Chem.*, **8**, 281 (1990).
21. C. Zuczek, C. Gerardin-Charbonnier, S. Rocca, S. Thiebaut, and C. Selve, *J. Fluorine Chem.*, **99**, 41 (1999); *Chem. Abstr.*, **113**, 966994 (1990).
22. K. Kato, M. Takemitsu, H. Mizumoto, K. Tokoyada, and S. Arai, Ger. Offen DE 19835866 (1999); *Chem. Abstr.*, **130**, 168166 (1999).
23. J.-T. Liu and H.-J. Lu, *J. Fluorine Chem.*, **111**, 207 (2001).
24. W.-Y. Huang, Y.-S. Liu, and L. Lu, *Chin. Chem. Lett.*, **3**, 583 (1992); *Chem. Abstr.*, **118**, 22131 (1993).
25. J.-T. Liu and H.-J. Lu, in: *Abstracts of 13th European Symposium on Fluorine Chemistry*, Bordeaux, France (2001), 1-P16.
26. J.-T. Liu and H.-J. Lu, *J. Fluorine Chem.*, **111**, 213 (2001).
27. H. Yamanaka, T. Takekawa, K. Morita, and T. Ishihara, *Tetrahedron Lett.*, **37**, 1829 (1996).
28. H. Yamanaka and T. Ishihara, *J. Fluorine Chem.*, **105**, 295 (2000).
29. W.-Y. Huang, Y.-S. Liu, and L. Lu, *Chin. J. Chem.*, **12**, 79 (1994); *Chem. Abstr.*, **121**, 9182 (1994).
30. Q.-S. Hu, H.-P. Guan, and C.-M. Hu, *J. Fluorine Chem.*, **75**, 51 (1995).
31. H.-P. Guan, Q.-S. Hu, and C.-M. Hu, *Synthesis*, 997 (1996).
32. X.-C. Zhang and W.-Y. Huang, *J. Fluorine Chem.*, **87**, 57 (1998).
33. X.-C. Zhang and W.-Y. Huang, *Tetrahedron*, **54**, 12465 (1998).
34. Y.-S. Liu and W.-Y. Huang, *J. Chem. Soc, Perkin Trans. 1*, 981 (1997).
35. A. Kameyama, Y. Hatakeyama, and T. Nishikubo, *Tetrahedron Lett.*, **36**, 2781 (1995).
36. V. Kameswaran, Eur. Pat. Appl. EP 816337 (1998); *Chem. Abstr.*, **128**, 127929 (1998).
37. D. C. England, E. A. Donald, and F. J. Weigert, *J. Org. Chem.*, **46**, 144 (1981).
38. W.-Y. Huang and L. Lu, *Chin. J. Chem.*, **9**, 167 (1991); *Chem. Abstr.*, **115**, 136068 (1991).
39. S.-Z. Zhu, C.-Y. Qin, and B. Xu, *J. Fluorine Chem.*, **79**, 77 (1996).
40. X.-Q. Tang and C.-M. Hu, *J. Chem. Soc, Perkin Trans. 1*, 2161 (1994).
41. X.-Q. Tang and C.-M. Hu, *J. Chem. Soc., Perkin Trans. 1*, 1039 (1995).

42. X.-Q. Tang and C.-M. Hu, *Chin. Chem. Lett.*, **6**, 281 (1995); *Chem. Abstr.*, **123**, 83264 (1995).
43. Q.-F. Wang, Y.-Y. Mao, and C.-M. Hu, *J. Fluorine Chem.*, **94**, 79 (1999).
44. Q.-F. Wang, D. Hu, B.-H. Luo, and C.-M. Hu, *Tetrahedron Lett.*, **39**, 2377 (1998).
45. B.-H. Luo, H.-P. Guan, and C.-M. Hu, *Synlett*, 1261 (1997).
46. Q.-F. Wang, Y.-Y. Mao, S.-Z. Zhu, and C.-M. Hu, *J. Fluorine Chem.*, **95**, 141 (1999).
47. D. Greif, U. Eilitz, M. Pulst, D. Riedel, and M. Weeks, *J. Fluorine Chem.*, **94**, 91 (1999).
48. T. Ishihara, Jpn. Kokai Tokkyo Koho JP 01 22855 (1989); *Chem. Abstr.*, **111**, 134144 (1989).
49. T. Ishihara, Y. Okata, M. Kuroboshi, T. Shinozaki, and T. Ando, *Chem. Lett.*, 819 (1988); *Chem. Abstr.*, **109**, 210998 (1988).
50. R. D. Chambers, C. G. P. Jones, M. J. Silvester, and D. B. Speight, *J. Fluorine Chem.*, **25**, 47 (1984).
51. X.-Q. Tang and C.-M. Hu, *J. Fluorine Chem.*, **73**, 133 (1995).
52. X.-Q. Tang and C.-M. Hu, *J. Chem. Soc, Chem. Commun.*, 631 (1994).
53. X.-Q. Tang and C.-M. Hu, *J. Fluorine Chem.*, **74**, 9 (1995).
54. V. Ya. Sosnovskikh, Yu. G. Yatluk, and V. A. Kutsenko, *Izv. Akad. Nauk. Ser. Khim.*, 1825 (1999).
55. G. G. Levkovskaya, G. V. Bozhenkov, L. I. Larina, I. T. Evstaf'eva, and A. N. Mirskova, *Zh. Org. Khim.*, **37**, 684 (2001).
56. H.-B. Yu and W.-Y. Huang, *J. Fluorine Chem.*, **84**, 65 (1997).
57. B. Dondy, P. Doussot, M. Iznaden, M. Muzard, and C. Portella, *Tetrahedron Lett.*, **35**, 4357 (1994).
58. P. P. Righetti, A. Gamra, G. Tacconi, and G. Desimoni, *Tetrahedron*, **37**, 1779 (1981).
59. D. C. England, *J. Org. Chem.*, **46**, 147 (1981).
60. K. Burger, N. Sewald, E. Huber, and R. Ottlinger, *Z. Naturforsch.*, **44b**, 1298 (1989); *Chem. Abstr.*, **113**, 23805 (1990).
61. C Portella and B. Dondy, *Tetrahedron Lett.*, **32**, 83 (1991).
62. B. Dondy, P. Doussot, and C. Portella, *Synthesis*, 995 (1992).
63. P. Doussot and C. Portella, *J. Org. Chem.*, **58**, 6675 (1993).
64. X.-C. Zhang and W.-Y. Huang, *Synthesis*, **51** (1999).
65. H. Abele, A. Haas, M. Lieb, and M. Schelvis, *J. Fluorine Chem.*, **84**, 75 (1997).
66. H.-B. Yu, Q.-S. Zhang, and W.-Y. Huang, *Chin. J. Chem.*, **15**, 278 (1997); *Chem. Abstr.*, **127**, 248004 (1997).
67. Yu. Shermolovich and V. Timoshenko, *J. Fluorine Chem.*, **114**, 157 (2002).
68. V. M. Timoshenko, Ya. V. Nikolin, N. P. Kolesnik, and Yu. G. Shermolovich, *Zh. Org. Khim.*, **37**, 666 (2001).
69. K. V. Komarov, N. D. Chkanikov, S. V. Sereda, M. Yu. Antipin, Yu. T. Struchkov, A. F. Kolomiets, and A. V. Fokin, *Izv. Akad. Nauk SSSR. Ser. Khim.*, 2417 (1988); *Chem. Abstr.*, **110**, 192703 (1989).
70. K. V. Komarov, N. D. Chkanikov, S. V. Sereda, M. Yu. Antipin, Yu. T. Struchkov, A. F. Kolomiets, and A. V. Fokin, *Izv. Akad. Nauk SSSR. Ser. Khim.*, 1920 (1988).
71. A. F. Shidlovskii, A. Yu. Sizov, L. N. Luleshova, V. V. Nesterov, M. Yu. Antipin, A. S. Pereguzov, and N. D. Chkanikov, *Izv. Akad. Nauk. Ser. Khim.*, 1261 (2000).
72. A. V. Form and A. F. Kolomiyets, in: *Abstracts of the Seventh Regular Meeting of Japanese-Soviet Fluorine Chemists*, Fukuoka (1991), **2**, p. 4-1.
73. A. S. Golubev, P. V. Pasternak, A. F. Shidlowskii, L. N. Saveleva, B. B. Averkin, V. N. Nesterov, M. Yu. Antipin, A. S. Peregudov, and N. D. Chkanikov, *J. Fluorine Chem.*, **114**, 63 (2002).
74. W.-S. Huang, C.-Y. Yuan, and Z.-Q. Wang, *J. Fluorine Chem.*, **74**, 279 (1995).
75. W.-S. Huang and C.-Y. Yung, *Synthesis*, 511 (1996).
76. K. Uneyama, O. Morimoto, and F. Yamashita, *Tetrahedron Lett.*, **36**, 4821 (1986).
77. J.-B. Xiao, X.-M. Zhang, D.-I. Wang, and C.-G. Yuan, *J. Fluorine Chem.*, **99**, 83 (1999).
78. H.-B. Yu, Q.-S. Zhang, and W.-Y. Huang, *Chin. J. Chem.*, **15**, 278 (1997); *Chem. Abstr.*, **127**, 248004 (1997).

79. O. E. Petrova, M. A. Kurykin, and D. V. Gorlov, *Izv. Akad. Nauk. Ser. Khim.*, 2195 (1999).
80. H. Yamanaka, A. Murakami, M. Kuwabara, K. Fukunishi, and M. Norura, *Nippon Kagaku Kaishi*, 1864 (1989); *Chem. Abstr.*, **112**, 197575 (1990).
81. H. Yamanaka, K. Tamura, K. Funabiki, K. Fukunishi, and T. Ishihara, *J. Fluorine Chem.*, **57**, 177 (1992).
82. K. Funabiki, K. Tamura, T. Ishihara, and H. Yamanaka, *Bull. Chem. Soc. Jpn.*, **67**, 3021 (1994).
83. A. Chauvin, J. Greiner, R. Pastor, and A. Cambon, *Tetrahedron*, **42**, 663 (1986).
84. B. C. Hamper, M. L. Kurtzweil, and J. P. Beck, *J. Org. Chem.*, **57**, 5680 (1992).
85. X.-Q. Tang and C.-M. Hu, *J. Fluorine Chem.*, **73**, 129 (1995).
86. H.-B. Yu and W.-Y. Huang, *J. Fluorine Chem.*, **87**, 69 (1998).
87. R. J. De Pasquale, C. D. Padgett, and R. W. Rosser, *J. Org. Chem.*, **40**, 810 (1975).
88. N. P. Stepanova, N. A. Orlova, V. A. Galishev, E. S. Turbanova, and A. A. Petrov, *Zh. Org. Khim.*, **21**, 979 (1985).
89. E. S. Turbanova, N. P. Stepanova, V. A. Lebedev, V. A. Galishev, and A. A. Petrov, *Zh. Org. Khim.*, **19**, 221 (1983).
90. J. Froissard, J. Greiner, R. Pastor, and A. Cambon, *J. Fluorine Chem.*, **26**, 47 (1984).
91. N. Seewald and K. Burger, *Liebigs Ann. Chem.*, 947 (1992).
92. G. Meazza and G. Zanardi, *J. Fluorine Chem.*, **55**, 199 (1991).
93. Y.-C. Shen, J.-H. Zheng, and Y.-Z. Huang, *Synthesis*, 970 (1985).
94. G. B. Blackwell, R. N. Haszeldine, and D. R. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1 (1983).
95. R. E. Banks and S. N. Mohialdin, *J. Fluorine Chem.*, **38**, 289 (1988).
96. V. M. Koshelev, T. D. Taruskanova, A. N. Chekhlov, N. V. Vasil'ev, and A. F. Gontar', *Izv. Akad. Nauk SSSR. Ser. Khim.*, 1445 (1989).
97. R. E. Banks and S. N. Khaffaff, *J. Fluorine Chem.*, **51**, 407 (1991).
98. K. Burger and R. Ottlinger, *Chem.-Ztg.*, **101**, 402 (1977).
99. Z. V. Safronova, L. A. Simonyan, Yu. V. Zeifman, and N. P. Gambaryan, *Izv. Akad. Nauk SSSR. Ser. Khim.*, 1826 (1979).
100. K. Burger, U. Wassmuth, and S. Penninger, *J. Fluorine Chem.*, **20**, 813 (1983).
101. G. Meazza and G. Zanardi, *J. Fluorine Chem.*, **67**, 183 (1994).
102. T. Mantani, T. Konno, T. Ishihara, and H. Yamanaka, *Chem. Lett.*, 666 (2000); *Chem. Abstr.*, **133**, 176943 (2000).
103. A. Nezis, J. Fayn, and A. R. Cambon, *J. Fluorine Chem.*, **53**, 285 (1991).
104. A. Nezis, J. Fayn, and A. R. Cambon, *J. Fluorine Chem.*, **53**, 297 (1991).
105. R. D. Chambers, *Synth. Fluorine Chem.*, 359 (1992).
106. M. Nishida, Y. Hayakawa, M. Matsui, K. Shibata, and H. Muramatsu, *J. Heterocycl. Chem.*, **29**, 113 (1992).
107. A. B. Abubakar, B. L. Booth, N. N. Suliman, and A. E. Tipping, *J. Fluorine Chem.*, **56**, 359 (1992).
108. M. G. Barlow, N. N. Suliman, and A. E. Tipping, *J. Fluorine Chem.*, **70**, 59 (1995).
109. P. Muller and Z. Miao, *Helv. Chim. Acta.*, **77**, 1826 (1994).
110. R. N. Warrener, D. Margetic, E. R. Tiekink, and R. A. Russel, *Synlett*, 197 (1997).
111. B. C. Hamper and K. L. Leschinsky, *J. Heterocycl. Chem.*, **40**, 575 (2003).
112. M. Kawabara, K. Fukunishi, M. Nomura, and H. Yamanaka, *J. Fluorine Chem.*, **41**, 227 (1988).
113. R. D. Chambers, C. G. P. Jones, M. J. Silvester, and D. B. Speight, *J. Fluorine Chem.*, **26**, 47 (1984).