Received: September, 2013

The reactions of alkylation, arylation, alkenylation, and alkynylation of polyfluoroarenes and -hetarenes by their aromatic rings

T.D.Petrova, V.E.Platonov

N.N.Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch, Russian Academy of Sciences, pr. Akademika Lavrent,eva 9, Novosibirsk, 630090 Russia

e-mail: petrova@nioch.nsc.ru (mailto:petrova@nioch.nsc.ru), platonov@nioch.nsc.ru (mailto:platonov@nioch.nsc.ru)

Abstract: Review considers the reactions of alkylation, arylation, alkenylation, and alkynylation of polyfluoroarenes and вЂ“hetarenes occurring in the aromatic ring and leading to the formation of C_{Ar}-C bond. Review contains information on the traditional methods of conducting such transformations which include, for example, reactions of polyfluoroarenes with electrophilic, nucleophilic, radical reagents. Along with these methods, reactions using of metal complex catalysis are considered. The application of metal complex catalysis expands the area the substrates used. This method includes cross-coupling reactions between metal or metal compounds and aryl halides catalyzed by transition metal complexes with various organic ligands. Kumada, Negishi, Suzuki, Stille, Hiyama, Heck, and Sonogashira reactions are presented. For polyfluoroarenes and вЂ“hetarenes C_{Ar}-Hal bond transformations involves also C_{Ar}-F bond.

Keywords: polyfluoroarenes and вЂ“hetarenes, alkylation, arylation, alkenylation, alkynylation, metal complex catalysis, palladium catalysts, cross-coupling reactions.

ADDENDUM

The major text of the review references the studies published before the middle of 2010. The Addendum covers the studies published in the second half of 2010, in 2011 and 2012. The material is submitted in relation to the chapters of the review major text (See Fluorine Notes 1(92) (/public/2014/1_2014/index.html) and 2(93) (/public/2014/2_2014/index.html).

II. Transformations involving C_{Ar}-H bond

1. Direct introduction of alkyl-, aryl- (hetaryl-) and unsaturated groups

1.1. Reactions in the presence of acid catalysts

Mono- and di-isopropylation of tri- and tetrafluorobenzenes under the action of isopropylchloride in the presence of $AlCl_3$ see [1]. Tert-butylation of 3,5-difluorophenol at position 4 occurs in the presence of $ZrCl_4$ under the action of di-tert- butyl ether [2]. 1,3-Difluorobenzene is benzylated at position 4 by the Friedel-Crafts reaction with yield 62% in the presence of boron trifluoride etherate, while p-chlorobenzylhydroxamate provides the source of benzyl cations [3]. The pentafluorophenylation of perfluoro-(1,2-diethylbenzocyclobutene) under the action of SbF_5 is shown in [4]. The hetarylation of 1,3,5-trifluorobenzene occurs at its interaction with 2-amino-1,3-thiazol in the presence of $AlCl_3$ [5]. The intramolecular reaction of polyfluorinated quinolines formation from polyfluorinated anilides by the Friedel-Crafts transformation described in the major text [12,13,24] was applied in studies [6,7]. In addition to the Skraup reactions shown in scheme 6, the transformation of 3,5-difluoro-4-R-aniline (R=CH_2COOH, Br) to a quinoline derivative was realized under the action of H_2SO_4 and $FeSO_4$ [8]. The rearrangement of aza-Cope 2,4-difluoro-N-(3-phenylprop-2-ene-1-yl)aniline in the presence of boron trifluoride etherate results in the formation of 2,4-difluoro-6-(3-phenylprop-2-ene-1-yl)aniline [9].

1.2 Thermal and photochemical transformationsВ

1,3-Difluoro- and 1,2,3-trifluoro-5-methyl-benzo[CЃ]phenanthrenes, as precursors of polyfluorinated fullerenes, were synthesized with the yield of 65%; their synthesis involved the step of intramolecular arylation in the course of photocyclization of the corresponding 1,3-di- or 1,2,3-trifluoro-6-(1-(naphtalene-2-yl)prop-1-ene-2-yl)naphtalenes in the presence of iodine and propylenoxide/water mixture [10].

1.3 Reactions in the presence of bases

The alkylation of 2,6-difluoronitrobenzene with ethylchloropropionate in the presence of potassium tert-butylate occurs according to that shown in scheme 16 (yield 99%) [11]. When 4,6,7- or 4,5,7-trifluoroquinoline interacts with CH_3I and sodium amide in liquid ammonia the methylation occurs at C_{Ar}-H bond between fluorines. The bond is deprotonated under the action of 1 eq. of sodium amide resulting in the formation of quinoliny anions that react as nucleophiles with CH_3I resulting in methyl derivatives of trifluoroquinolines [12]. The new pathway to the functionalisation of C_{Ar}-H bond without use of metals by the cross-coupling of APiP’Pi(I) with APiC-H in the presence of organic catalysts and bases was applied to the arylation of 1,4-difluorobenzene at position 2 under the action of p-methoxybromo- or вЂ“iodobenzene in the presence of potassium tert-butylate and 1,10-phenantroline used for catalyst (with bromide the yield was 81% [13]) or quinoline-1-amino-2-carbonic acid (yield 64% [14]).

1.4 Metal-complex catalysis

1.4.1 Use of palladium catalystsB

In addition to scheme 18 at similar conditions the interaction beB tween pentafluorobenzene or 2,3,5,6-tetrafluoroanisole and 5-bromo-11-phenyltetracene in order to produce polyfluoroaryltetracenes [15], that between pentafluorobenzene and 9-bromo-10-phenylanthracene in order to produce 9-pentafluorophenyl-10-phenylanthracene [16], and the reactions of pentafluorobenzene with various arylsulfonates or aryltriflates [17] were studied. 3-Bromo-2вЂ™,6вЂ™-difluorobiphenyl with aza-group at position 2 is prepared from 1,3-difluorobenzene and 2-substituted 1,3-dibromobenzene [18], while 2,3,4,5,6-pentafluoro-4$^{\text{вЂ™}}$-methylbiphenyl is produced from pentafluorobenzene and p-chlorotoluene [19].

In the synthesis of polyfluorinated biaryls or terphenyls the reactions of pentafluorobenzene with bromobenzene, its corresponding derivatives or 1,3-dibromobenzene were used, while some novel trifluoroacetate palladium complexes with hetero-bis(carbene) ligands were used for catalysts, but the finish product yields were not very high [20]. The arylation of pentafluorobenzene or 1,4-difluorobenzene to corresponding biphenyl derivatives by the action of aryliodides with Ag_2CO_3 or $AgNO_3$ added to palladium catalyst was described [21-23]. Another variant of the same reaction, not with pentafluorobenzene only, but with isomeric tetra- or trifluorobenzenes, is conducted if $Pd(OAc)_2$ is doped not only with Ag_2CO_3, but also with sulfides, e.g., with methylethylsulfide to promote the reaction [24]. Polyfluorinated biphenyls are produced from pentafluorobenzene or isomeric tetrafluorobenzenes through the interaction with simple aryls, such as benzene, toluene or anisole in the presence of $Pd(OAc)_2$ without oxidizers or additives, if the reaction is conducted in imidazole ionic liquids (ILs) {[$bmimPF_6$] and [$bmimBF_4$]}, that are further regenerated. The reaction is catalysed with AcOH [25]. An easy process for direct arylation under the action of bromoarenes, that requires only catalytic amounts of $Pd(OAc)_2$, without ligands, substoichiometric amounts of Ag_2CO_3, without bases, was realised when 1,3,5-trifluorobenzene was reacted with 2-bromoethylbenzoate resulting in a biphenyl derivative with yield of 89% [26]. Ag_2CO_3 was applied as well in the cross-coupling of polyfluoroarenes (pentafluorobenzene, isomeric tetrafluorobenzenes, 1,3,5-trifluorobenzene, 1,3-difluorobenzene, 2,3,5,6-tetrafluoroanisole, 2,3,5,6-tetrafluorotoluene) with aromatic or heterocyclic carboxylic acids. When so doing, decarboxylation is combined with C_{Ar}-H bond breaking to result in the formation of polyfluorinated biaryls. In this reaction $Pd(TFA)_2/PCy_3$ was used as catalyst. Silver salts promote decarboxylative cross-coupling [27]. Oxidative arylation of pentafluorobenzene or 1,2,4,5-tetrafluorobenzene occurs at its interaction with benzene derivatives containing 2-pyridylsulfonyl group, in the presence of $Pd(OAC)_2$, Ag_2CO_3 and benzoquinone [28]. As to the non-fluorinated substance, its C_{Ar} -H bond at ortho-position to 2-pyridylsulfonyl group, activated by this group, participates in the reaction. The formation of two new bisaryl C_{Ar}-C_{Ar} bonds occurs by the way of oxidative coupling between 1,2-difluorobenzene and phenylcarbamates, two ortho-positions to carbamate group being activated in those molecules. The reaction uses $Pd(OAc)_2$, $Na_2S_2O_8$ as oxidizers, and occurs only in the presence of CF_3COOH resulting in the formation of tetrafluoroterphenyl (yield 78%) [29]. Oxidative coupling with N-aryloxazolidinones under similar conditions occurs both at ortho-, and at para-position to fluorine, with the participation of C_{Ar}-H bond of the aryl fragment at ortho-position to C_{Ar}-N bond [30]. Pentafluorobenzene, 3-substituted 1,2,4,5-tetrafluorobenzenes, isomeric trifluorobenzenes, and polyfluorobiphenyls undergo arylation to corresponding biphenyls or terphenyls via their cross-coupling with arenes in the presence of $Pd(OAc)_2$, pivalic acid and copper bis-acetate [31]. The study on polyfluoroarenes hetarylation by their cross-coupling with various heterocyclic halogenated or non-halogenated systems was continued. For the findings on reactions of pentafluorobenzene or substituted 2,3,5,6-tetrafluorobenzene with bromothiophenes see [32, 33], m-difluorobenzene with 3-bromothiophene see [34], 1,2,4,5-tetrafluorobenzene with various heterocyclic bromoderivatives see [35]. The hetarylation of pentafluorobenzene and 1,2,4,5-tetrafluorobenzene by quinoline-2-yl tosylate or quinoline-2,4-diyl bis(tosylate) is described in [36]. For the oxidative hetarylation of pentafluorobenzene, tetrafluoro-substituted benzenes and biphenyls, isomeric difluorobenzenes in the presence of silver compounds, pivalic acid and oxygen used as the oxidizer through their cross-coupling with thiophene and its derivatives, benzothiophene, indole and its derivatives, or coumarins, see [37-40].

The direct alkenylation of pentafluorobenzene, 1,2,4,5-tetrafluorobenzene, isomeric trifluoro- and difluorobenzenes was conducted by direct coupling of polyfluoroarenes with allyl ethers, styrene or other olefins under the conditions of palladium-catalysed oxidative arylation of alkenes by the FujiwaraвЂ“Moritani reaction [41-48]. In the FujiwaraвЂ“Moritani reaction C_{Ar}-H bond is activated due to its palladation through the interaction with Pd(II) formed from Pd(0) under the action of some oxidizer at the process conditions. The palladium compound is further added to the olefin double bond, and the reaction result depends on the OI-H elimination in the olefin. A similar alkenylation product results from the reaction of 1,2,4,5-tetrafluorobenzene with iodoallyl ether at similar conditions [49]. During the interaction of pentafluorobenzene, monosubstituted 2,3,5,6-tetrafluoro- or 2,4,5-trifluorobenzenes with O±,O±-dibromostyrenes containing N-pyrrol- or N-indole-moieties at their ortho-positions, in the presence of $Pd(OAc)_2$ and Ru-Phos, intermolecular alkenylation of fluoroarene C-H bond occurs with further intramolecular alkenylation of C-H bond in pyrrole or indole, thus providing a convenient pathway to the production of, e.g., 4-polyfluoroaryl-pyrrole[1,2-a]quinolines [50]. Intramolecular oxidative olefination of 3-(2',4'-difluorophenyl-methylamino)cyclohex-2-enone under the action of $Pd(OAc)_2$ in oxygen medium results in the formation of N-alkyl-difluorocarbazolone [51]. The direct arylation of m-difluorobenzene with 1-[2-(2,6-dibromophenyl)diazene-1-yl]pyrrolidine in the system of n-BuLi, $ZnCl_2$ and $Pd(PPh_3)_4$ follows the Negishi reaction. Both bromines participate in the transformation [52].

1.4.2 Use of rhodium-based, nickel-based and other metal-based catalystsB

Many complexes of transition metals are applicable as catalysts in the cross-coupling reactions. Thus in oxygen medium, under the catalytic action of nickel, manganese, cobalt or iron chlorides in the presence of РўРњPMgClLiCl, $(TMP)_2Zn_2MgCl_22LiCl$ system the dimerisation of m-difluorobenzene, 3,5-difluorobenzonitril, substituted 2,4-difluorobenzene, 1,2,4-trifluorobenzene and 1,2,4,5-tetrafluorobenzene occurs with abstraction of hydrogen between two fluorines. This results in the formation of biphenyls, necessarily containing 4 fluorines at positions 2, 6, 2', 6' [53]. The arylation of phenyl rings in 2-(3вЂ™,4вЂ™,5вЂ™-trifluorophenyl)pyridine under the action of p-methoxychlorobenzene [54] or that in 2-($2^{\text{вЂ™}}$,$4^{\text{вЂ™}}$-difluorophenoxy)pyridine under the action of p-methoxybromobenzene [55] at position 2' or $6^{\text{вЂ™}}$ of their rings is catalised with ruthenium catalyst $[Ru(p\text{-cymene})(MesCO_2)_2]$ through the activation of C-H bond and with further rate-determining oxidative addition of arylhalogenide. p-Difluorobenzene is arylated by p-bromanisole with the help of a molybdenum diacetate complex [56].

$CoBr_2$ complexes with variable ligands are used in the addition of polyfluorinated aromatic imines to alkenes or alkynes, resulting in corresponding alkyl- or alkenyl- derivatives of those imines. The reaction involves the activation of C-H bond in the fluorinated ring at ortho-position to fluorine and вЂ“C=N- fragment. (p-Methoxyphenyl)imine of 3,5-difluoroacetophenone reacts with ethylPµne trimethylsilyl derivative, making use of 1,10-phenanthroline ligand, and resulting in ethylsilyl derivative [57], while the reaction with 1,2-diphenylethyne, phosphine ligand and various additives results in the olefination of the imine fluorinated phenyl ring [58]. Olefination of pentafluorobenzene and isomeric tetrafluorobenzenes by the action of 1,2-diethylethyne occurs with complex nickel catalyst and with the participation of one or two C_{Ar}-H bonds, while C_{Ar}-F bond remains non-activated. In so doing the ligand nature performs as the governing factor because each substance enters the reaction only in the presence of the given ligand [59]. Unlike this, in [60] it was shown that the combination of $Ni(cod)_2$ and $PCyp_3$ performs as an efficient catalyst in the alkenylation of wide range of polyfluorobenzenes with 2 to 5 fluorines on their rings, under the action of alkynes, and resulting in polyfluorophenylethenes. Like in the earlier study [59], the preferential activation of C_{Ar}-H bond as to compare with C_{Ar}-F bond has place. Those findings and considerations on the reaction mechanism add the data described in [57] cited in the present chapter of the major text. In dioxane medium $[Rh(cod)(OH)]_2$ catalytic system with dpp-benzene ligand efficiently promotes the direct alkenylation of polyfluorobenzenes with butyl ester of ethylenecarbonic acid, while in partially aquatic medium hydroarylation of olefin takes place [61]. The direct arylation of 1,4-difluorobenzene or 1,3,5-trifluorobenzene was carried out through the oxidative coupling with para-substituted phenylboronic acid, using iron-based catalyst $Fe(OTf)_3$ with 4,7-bis[4-(trifluoromethyl)phenyl]-1,10-phenanthroline ligand and di-tert-butylperoxide as the oxidizer [62]. The reaction follows the pathway of homolytic aromatic substitution and results in the formation of aryl radical from arylboronic acid and peroxide.

2. Reactions with pre-activation of C_{Ar}-H bond by metalationB

2.1 Formation of lithium derivatives and their reactions.

For the methylation of 2,3,4,5-tetrafluorobenzoic acid by n-BuLi and CH_3I (yield 56%) see [1]. The examples of hydroxyalkylation reactions shown in scheme 39 may be amended with that of pentafluorobenzene and 3-alkyl-2-formylthiophene with n-BuLi in THF [63].

2.2 Formation and transformation of polyfluorinated organocopper compounds.

A general method for copper-catalyzed (CuCl, 1,10-phenanthroline) dimerisation by cross-coupling of two aromatic compounds (arenes, hetarenes) is proposed using iodine as oxidizer. The iodination of one arene occurs followed by subsequent arylation of the most acidic C-H bond in the other. The method advantage is the small excess of the second arene. The arylation and hetarylation of pentafluorobenzene, tetra- and trifluorobenzenes, and substituted p-H-tetrafluorobenzenes is hence CЃarried out [64]. The examples shown in scheme 42 are added to the reactions between pentafluorobenzene and pyridine 2-acetylene derivative or fluorobenzene 4-acetylene derivative, both conducted in the presence of oxygen used for the oxidizer, $CuCl_2$, 1,10-phenanthroline and substituted benzoquinone [65]. The novel pathway to 2-(polyfluoroaryl)benzofuran (yield exceeds 90%) is a tandem reaction of 1-(2,2-dibromovinyl)-2-naphthol or Ps-dibromovinylphenol with pentafluorobenzene or p-H-derivative of 2,3,5,6-tetrafluorobenzene, catalised by monovalent copper (CuI, 1,10-phenanthroline), in the course of the process C_{Ar}-H bond is activated and intramolecular C-Pћ bond is formed [66]. Direct benzylation of 1,2,4,5-tetrafluorobenzene occurs under the action of acetophenone N-tosylhydrazone in the presence of CuI and t-BuOLi resulting in the formation of 1,2,4,5-tetrafluoro-3-(1-phenylethyl)benzene [67]. The assumed transformation mechanism involves the migrational introduction of Cu-carbene formed from Cu-Ar_F, and carbene from tosylate. It was proposed to conduct the allylation of C_{Ar}-H bond in pentafluorobenzene and substituted 2,3,5,6-tetrafluorobenzenes by the action of allylphosphates in the presence of copper acetylacetonate and 1,10-phenanthroline [68]. A copper-based catalytic system (CuCl, 1,10-phenanthroline) was used for the direct coupling of polyfluoroarenes, particularly, pentafluorobenzene with propargylphosphates resulting in the formation of (polyfluorophenyl)allenes [69].

2.3 Formation and transformation of polyfluoroarylorganoboron compounds

In 2010-2012 polyfluorophenylboronic acids were being actively applied in arylation or hetarylation by the Suzuki reaction through their cross-coupling with iodo-, bromo- Pё chloro- arenes or hetarenes. When so doing the arylation involved both the participation of halogenated arenes, and the transformation of halogenaryl fragments belonging to some complicated substance, e.g., heterocyclic. In order to simplify and cheapen the process and to increase its yield they varied the catalyst metal component, its state in use (e.g., supported or non), the catalyst amount, the organic ligand nature, the applied base, media and other reaction conditions, including the use of microwave irradiation. Further in Chapters 2.3.1вЂ“2.3.3 we cite the studies within this avenue of inquiry, but the list is not exhaustive.

2.3.1 Difluorophenylboronic acids.

For Suzuki reactions of 2,4-difluorophenylboronic acid 1 with bromoarenes and palladium-based catalytic systems, resulting in biphenyl derivatives, see [70-74]. Diarylmethane derivatives result from coupling with benzylbromide [75]. The arylation of heterocycle by bromophenyl fragment [76, 77], or its hetarylation in addition to scheme 46 were carried out [78-83]. The arylation of acid 1 to biphenyl derivatives was also realized through its cross-coupling with iodobenzene [84] or p-iodophenol [85]. In the first case a specially prepared catalyst was used, that was nano-palladium supported on a silicon sphere with mezoporous walls. The iodine atom participates also in the coupling reaction of acid 1 with 3-bromo-4-iodobenzonitril [86]. Hetarylation of acid 1 or its ester with the participation of iodine atom in the heterocycle is described in [87]. Heterocyclic chlorides are also active in the reactions with acid 1 [88-92]. Hetarylation with the participation of 5-chloro- [93] or 3-cyanoderivatives of acid 1 [94] are described as well.

In similar directions they also applied 3,5-difluorophenylboronic acid 3 or its ester, or substituted acids and esters. The Suzuki reaction was realized with palladium-based catalytic systems and bromo- [95-97], iodo- [96] phenyl derivatives or bromonaphtyl derivatives [98], and with halogenated aryl substituent in heterocyclic compounds [99], all resulting in the formation of biphenyl- or branched polyphenylen- systems. Further to the data presented in scheme 47 the hetarylation of acid 3 or its ester was realized through the coupling of bromo- [100-108], chloro- [109-115], iodo-[116, 117] or triflate-[118, 119] heterocyclic derivatives with those substituents on the heterocyclic ring. Acid 3 undergoes alkenylation during its cross-coupling with methyl-4-bromopent-4-enoate in the presence of palladium-based catalyst [120], or during cross-coupling by the Libeskind-Srogl reaction with gPµm-dithioacetale of O±-oxoketene [121], similar to the reaction with gPµm-dihalogenated olefins. The reaction is catalised with Pd(0) compounds and promoted with Cu(I) compounds, particularly, Pd(PPh_3)$_4$ doped with thiophene-2-carboxylate Cu(I). Homo-coupling of acid 3 to corresponding biphenyl occurs without bases or ligands in the presence of cheap and stable $CuSO_4$ in DMF with molecular sieves (yield 67%) [122] or in water using Cu(II) OI-cyclodextrin complex as nanocatalyst [123]. Finally, the first example is described of direct C-H arylation by the Suzuki reaction of non-halogenated hetarene under the action of arylboronic acid and catalised with iron salts. Therefore, acid 3 reacts with pyrrole in the presence of oxalate Fe(II)\pyclen dihydrate system, resulting in 52% yield of pyrrole substituted at position 2 with difluorophenyl moiety [124].

For other isomeric difluorophenylboronic acids: 3,4-difluorophenyl- 2, 2,5-difluorophenyl- 4 , 2,6-difluorophenyl- 6 they mostly investigated the Suzuki reaction. For cross-coupling with heterocyclic halogenated derivatives of acid 2 see [105,125-129], for that of acid 4 see [105, 130, 131], for substituted acid 4 see [132], for its ester see [133], for acid 6 see [134-138], for substituted acids 6 see [139], for its ester see [140]. The Suzuki reaction, i.e. arylation of acid 2, 4 or 6 to corresponding biphenyl systems and acid 2 with bromoderivative of 2,3,4,9-tetrahydro-1H-fluorene are described in [99, 141-151], including that of substituted ester of acid 6 [152]. Besides of that, from the acid 6 ester and bromobiphenyl using a catalyst doped with CuCl difluoroterphenyl was produced [153], and the reaction of acid 6 with a triflate derivative of substituted naphthalene resulted in the introduction of naphtalene fragment on its difluorophenyl ring [154]. Acid 2 similarly to its isomer 3, under similar conditions undergoes olefination under the action of dithioacetals of O±-oxoketene [121]. The use of a bimetal catalytic system Pd/Cu [Cu(OAc)$_2$, CuCl, Pd(OAc)$_2$] made it possible to conduct the hetarylation of acid 2 via its cross-coupling with various non-substituted heterocyclic substances due to direct arylation of the heterocycle C-H bond [155].

2.3.2 Trifluorophenylboronic acids.

The formation of biphenyl derivatives from 3,4,5-trifluorophenylboronic acid 7 and halogenPsarenes (I, Br, Cl) or triflate derivatives of arenes by the Suzuki reaction was investigated in [145, 156-161], that from 2,3,4-trifluorophenylboronic acid in [162,163], and that from 2,4,5-trifluorophenylboronic acid in [164]. The Suzuki arylation of acid 7 by its cross-coupling with substituted 3,3вЂ™-dibromobiphenyl results in hexafluoroquaterphenyl [165]. Suzuki heteroarylation occurs during the interaction of acid 7 with 2-bromopyridine [166] and bromoderivative of benzoselenophene [167], 2,3,4-trifluorophenylboronic acid with substituted bromobenzene and 4-bromo-1,2-diazol [162], 2,4,5-trifluorophenylboronic acid with bromoxazol derivative [168] and 2,3,5-trifluorophenylboronic acid with 5-bromoderivative of N-alkyl-6-methylpyridine-2-on [169]. The alkenylation of acid 7 in the oxidative variant of Heck reaction occurs at its coupling with 3-(p-nitrophenylsulfonyl)-4-vinyloxazolidine-2-on, where Pd(PћACЃ)$_2$-sulphoxide is used as catalyst, and the reaction is conducted in the presence of benzoquinone [170]. The production of 2-(3,4,5-trifluorophenyl)-2H-chromene from acid 7 in the presence of nickel catalyst, based on the activation of Csp^3-O bond by nickel catalyst and its transformation to Csp^3-C bond, was proposed in [171]. With Ni-bis(cyclooctadiene), PPh_3 catalyst without use of a base 2-arylated 2-H-chromene was produced with yield 94%.

Tetrafluorophenylboronic acids

The Suzuki reaction between 2,3,4,5-tetrafluorophenylboronic acid and 2-bromopyridine results in 2-(2',3',4',5'-tetrafluorophenyl)pyridine with yield 40% [172].

2.3.3 Pentafluorophenylboronic acid and polyfluorophenylborates

In addition to Suzuki reactions of pentafluorophenylboronic acid with 4РЃC_6H_4Р’r вЂ“type arenes as mentioned in the major text, the spectrum of substituents РЃ [160] was widened and new results were obtained on the acid interaction with amine-substituted bromocyclophane [173]. The Suzuki reactions of potassium salts of isomeric difluorophenylborates with substituted bromobenzenes result in the corresponding biphenyls [70a], while the reaction of 2,6-difluorophenylborate potassium salt with p-bromoiodobenzene results in a halogenated derivative of biphenyl due to the participation of iodine in this reaction [174]. The Suzuki cross-coupling of potassium 2,4-difluorophenylborate with substituted thiophenediazonium tetrafluoroborate results in 3-difluorophenyl derivative of thiophene [175], while that with substituted benzenediazonium tetrafluoroborate results in the corresponding difluorobiphenyl [176]. Finally, in the presence of palladium catalyst, potassium 3,5-difluorophenylborate undergoes alkenylation through the cross-coupling with tetrasubstituted benzene derivative, containing a bromovinyl group as one of substituents [177].

III. Transformations by C_{Ar}-Hal bonds (Br, Cl, I)

1. Reactions with Na- or Mg-organic derivatives

The chief addendum to this chapter concern the reactions between Mg-organic derivatives, produced from polyfluorinated bromo- or chlorobenzenes, and various types of halogenated compounds, resulting in arylation (hetarylation), alkenylation or alkynylation of original halogenated polyfluoroarenes. Among those palladium- or nickel- catalysed reactions is the heteroarylation of 3,5-difluorophenyl magnesium bromide under the action of methyl ester of 2,4-dichloropyridine-6-carbonic acid in the presence of $ZnCl_2$ and $Pd(PPh_3)_4$, that proceeds with the participation of chlorine atom at the 2-position in pyridine [178], hetarylation of 3,4,5-trifluorophenyl magnesium bromide by its cross-coupling with 2-phenyl-4-chloroquinoline using only catalytic amount of $NiCl_2$, without ligands, at room temperature, resulting in 2,4-diphenylquinoline with three fluorines on the same phenyl ring [179]. For the hydroxyalkylation of pentafluorophenyl magnesium bromide through the reaction with 3-formylderivative of N-tris[(isopropyl)silyl]indole see [180]. The interaction between 3,4-difluorophenyl magnesium bromide and tert-butyl ester of bromoacetic acid in the presence of $Fe(acac)_3$ results in tert-butyl ester of (3,4-difluorophenyl)acetic acid [181]. The reductive variant of Heck reaction is realized during the cross-coupling in the presence of $Fe(acac)_3$ of 3,4-difluorophenyl magnesium bromide with allyl ether that performs as an allyl electrophile, resulting in the formation of 3,4-difluorophenyl allyl derivative exemplifying the allylation process during cross-coupling of arylmagnesium halogenides with allyl systems containing different leaving groups (acetate, tosylate, etc.) [182]. For the allylation of 2,4,5-trifluorophenyl magnesium bromide with bromoallyl see [183]. The reaction between pentafluorophenyl magnesium bromide and aromatic or heterocyclic nitrovinyl derivatives in the presence of $Si(CH_3)_3Cl$ in ether or ether/THF mixture occurs through the nucleophilic addition of pentafluorophenyl anion to the double bond and the formation of a hydropentafluorophenylation product [184]. The interaction of this magnesium bromide with 1,2-diiodoethyne results in 1,2-dipentafluorophenylethyne [185]. 8,9-Difluorofenantridine-6(5H)-on is produced through the intramolecular hetarylation of N-phenyl- 2-bromo-4,5-difluorobenzamide under the action of t-BuOK and catalytic amount of 1,10-phenanthroline or AIBN [186].

2. Reactions with Р’-organic compounds (Suzuki reaction).

The active investigations on the Suzuki reaction applications in the synthesis of polyfluorinated biphenyl derivatives are being continued. In addition to scheme 68 it was shown that tetra-Ps-substituted biphenyl is successfully produced by the Suzuki reaction starting with chloropentafluorobenzene and 2,6-dimethylphenylboronic acid and using triarylphosphines for the ligands of palladium-based catalysts [187]. In the synthesis of tri-Ps-substituted biphenyl from 2-methylphenylboronic acid and chloropentafluorobenzene carbazolylphosphine ligands proved to be highly efficient [188], while acenaphtoimidazolidene palladium complex was found to be the most efficient catalyst in the reaction with non-substituted phenylboronic acid [189]. The Suzuki reaction between bromopentafluorobenzene and phenylboronic acid was catalised by specially prepared palladium-nanoparticle-loaded monoliths [190]. Using $PdCl_2(dppf)$ for catalyst a diphenyl derivative is prepared from bromopentafluorobenzene and an ester of phenylboronic acid, containing 2-

benzothiazol moiety at position 3 and hydroxybenzyl substituent at position 4 [191]. Finally, the Suzuki reaction between iodopentafluorobenzene and phenylboronic acid is catalysed with a novel variant of catalyst, which is palladium impregnated on magnetite: $Pd(OH)_2/Fe_3O_4$ [192]. For the Suzuki reactions of polyfluorinated biphenyls formation from 2,3,5,6-tetrafluoro-4-bromomethylcarboxylate see [193], for the transformations of 1-bromo-2,4,5-trifluorobenzene catalysed with Pd-catalyst, which was pre-prepared by treatment of highly monodisperced cross-linked microcapsules of polystyrene containing phosphine ligands with a solution of $Pd_2(dba)_3/CH_2Cl_2$, see [194], the data on the reactions of various isomeric bromodifluorobenzenes and their substituted analogues are summarized in [195-198]. For 1-bromo-2,4-difluorobenzene the вЂњflowвЂќ variant of Suzuki reaction with Рї-methoxybromobenzene was implemented through its transformation according to Br-Li-B scheme followed with its ultrasound-stimulated cross-coupling catalysed with palladium-based catalyst $C_{45}H_{58}ClNPPd$ and resulting in biphenyl [199]. For the Suzuki reaction between isomeric difluorodibromobenzenes and arylboronic acids, with the participation of one or two bromines, see [200-202]. The Suzuki reaction of 1-chloro-2,6-difluorobenzene resulting in 2,6-difluorobiphenyl using small amount of palladium-based catalyst stable in the air, is described in [203]. Difluoro-Рѕ-terphenyls are produced through the Suzuki cross-coupling of 2-bromo-3,5-difluoro-2',4'-dimethoxybiphenyl with phenylboronic or 4-chlorophenylboronic acid [204], while for the synthesis of polyfluorinated teraryls a two-step process is proposed, that starts with polyfluoroarylhalogenide and hetarylhalogenide, and conducted as a one-pot borylation with the help of bis-boronic acid and the Suzuki cross-coupling, thus simplifying the total process in experiment. The reaction was realized with 1-chloro-2,6-difluorobenzene and N-(4-chlorophenyl)pyrrole with $B_2(OH)_4$ and xPos-Pd-G_2, 2-(2,4,6вЂ”i-$Pr_3C_6H_2)C_6H_4PCy_2$ used for the catalyst [205]. A compound with three fluorinated rings, with Рћ-CF_2-group between two of them, and with terminal CF_3 group produced by the Suzuki cross-coupling of 5-[(4-bromo-2,6-difluorophenyl)difluoromethoxy]-1,3-difluoro-2-trifluoromethylbenzene with 4-(4-ethylcyclohexyl)-2-fluorophenylboronic acid [206]. For the hetarylation through the Suzuki cross-coupling of 3-bromo-5,6-difluorophenol see [207], for that of 6-bromo-5,7-difluoro-2,2-dimethyl-2,3-dihydroquinoline-4(1H)-on see [208], for that of 1-chloro-3,4-difluorobenzene see [19]. 4-Bromo-3,5-difluorobenzene sulphamide is methylated at position 4 by the action of methylboronic acid, with $Pd(PPh_3)_4$ catalyst [209], and the alkenylation of halogenated benzene with participation of iodine atom is conducted through the cross-coupling between 1-iodo-2,4-difluoro-3,5-dichlorobenzene and О±-trifluoromethyl-vinylboronic acid [210]. In similar manner they carry out the reaction of 1-iodo-2,3,4-trifluoro-5-carboxybenzene with potassium salt of vinyltrifluoroborate [211].

3. Reactions with Cu-organic compounds and copper catalysis.

The solventless Ulmann homo-coupling of 2-iodo-4,5,6-trifluoroanisole in the presence of copper results in 2,2вЂ™-bis-methoxyhexafluorobiphenyl. The homo-coupling of substituted 1-iodo-2,4-difluorobenzene occurs similarly [212], and the heating of iodopentafluorobenzene with 1-iodo-8-(p-methoxyphenyl)naphtalene in the presence of copper in DMF results in low yield (18%) of a naphthalene derivative with C_6F_5-group at position 1 [213].

4. Obtaining and transformation of Zn-organic derivatives

The benzylation of 2,6-difluoro-3-iodomethylbenzoate follows the Negishi reaction through the cross-coupling with 2-fluorine-3-chlorobenzylbromide in the presence of Zn/THF, $Si(CH_3)_3Cl$, $Pd(PPh_3)_4$ system [214]. 2-Hydroxy-5-bromoderivative of methylbenzoate at the conditions of Negishi reaction (Zn/THF, palladium catalyst) with 1-bromo-2,4-difluorobenzene performs as the arylating agent resulting in the formation of a biphenyl derivative [215]. Biphenyls with 2-aminogroups or other nitrogen-containing groups at position 2 (e.g., azomethine) are produced through the coupling of corresponding benzene N-derivatives, containing chlorine or bromine at Рѕ-position, with 3,4,5-trifluorophenyl magnesium bromide in the presence of $ZnCl_2$ and palladium catalyst PEPSI or $Pd(dba)_2$,P(t-Bu$)_3$, HBF_4 [216]. For the hetarylation of 1-bromo-3,5-difluoro-4-trifluoromethyl benzene at the conditions of the Negishi reaction ($ZnBr_2$, $Pd(PPh_3)_4$, THF) see [217], 1-bromo-3,5-difluorobenzene ($ZnCl_2$, $Pd(PPH_3)_4$, THF) see [178, 218]. The alkylation of 1-bromo-3,5-difluorobenzene under the action of ethyl-4-bromobutanoate, zinc, I_2 and nickel catalyst $Ni(PPh_3)_2Cl_2$ is also disclosed [219]. A method for the obtaining of ArZnРґ from ArX (X= Br, Cl, I) with cobalt-based catalyst Co-Xantphos and LiCl in РўHF was developed, the resulting reagents easily undergo iron-catalysed ($FeCl_3$) cross-coupling with halogenated derivatives, with the substitution of ZnX group. That is how 1-bromo-3,4-difluorobenzene with cycloheptylbromide are converted to 1,2-difluoro-4-cycloheptylbenzene [220]. As the development of ideas on the iron-based catalysis of Negishi reaction a number of iron complexes [FeX(dpbz)$_2$] (here X=4-tolyl, Cl, Br) were synthesised and characterized, and their importance for the reactions with Zn-derivatives of aromatic compounds was exemplified by the reaction of bis-(3,4-difluorophenyl)zinc with cycloheptyl bromide [221]. In [222] it was shown that in Zn/THF system with cobalt catalyst Co-PГantphos, the reaction between 1-bromo-3,4-difluorobenzene and internal alkyn 1,2-bis(butyl)ethyne results in the arene alkenylation and the formation of 1-(3,4-difluorophenyl)-1,2-bis(butyl)ethene through the interaction of thus formed arylzinc reagent with the alkyn-catalyst complex, the formation of ortho-alkenyl-arylzinc intermediate and further formation of the final product.

5. Reactions with Sn-organic derivatives (the Stille reaction).

1-Bromo-2,4-difluorobenzene and its isomers are hetarylated by the Stille cross-coupling with pyridine-2-tributyl tin in the presence of Pd(PPh$_3$)$_4$ resulting in 2-(difluorophenyl)pyridines [223]. Cross-coupling between 1,4-dibromo-2,3,5,6-tetrafluorobenze and pyridine-4-trimethyl tin with PdCl$_2$(PPh$_3$)$_2$ and LiCl results in 4-(4-bromo-2,3,5,6-tetrafluorophenyl)pyridin with yield 40% [224], the interaction of 1-bromo-2,4-difluoro-5-nitrobenzene with tributylvinyl tin results in the introduction of vinyl group instead of bromine [225]. Replacing bromine with vinyl occurs in the case of 6-bromo-5,7-difluoroquinoline [226]. By the way of cross-coupling between 1-iodo-2,4,6-trifluoro-3,5-dichlorobenzene and tributyl(2-phenylethinyl)tin (palladium-based catalyst) the alkynylation of difluoroarene occurs with the participation of iodine atom [227].

7. Reactions of Li-organic compounds.

This chapter may summarise some studies [228, 229] where polyfluorohalogenPsarene does not react directly with organolithium compounds, but a method is disclosed for the transformation of C_{Ar}-Br bond in bromo-2,4-, 2,6-difluorobenzenes or bromo-3,4,5-trifluorobenzene to C_{Ar}-Csp^3 bond through the interaction of the above compounds with methyl- or t-butylisobutyrates in the presence of Pd$_2$(dba)$_3$/davephos, resulting in the corresponding OI-di- or trifluorophenyl derivatives of the original isobutyrates. Here lithium dicyclohexylamide (Cy)$_2$NLi was applied to convert the butyrate to an enole, which further interacts with Pd-catalyst to form Pd-enolate, and after that the oxidative addition of bromoarene to this system takes place followed by the elimination of the OI-arylation product. It is important that under given conditions the OI-arylation of ethers takes place though the modification of Pd-catalyst or ligand results in O±-arylation. In [230] the first example of palladium-catalysed selective mono- O±-arylation of acetone by arylhalogenides or tosylates is reported. The reaction easiness and selectivity are due to the use of P,N-ligands. By the reaction of 1-bromo-3,5-difluorobenzene with acetone, used both for reagent and solvent, in the presence of [Pd(eta; 3-cinnamyl)(Cl)]$_2$, $C_{24}H_{26}NOP$, 1-(3,5-difluorophenyl)propane-2-on was produced.

8. Reactions of alkenylation.

In recent 2 years a number of studies were conducted on the transformation of C_{Ar}-HP°l (Br, Cl, I) bond, related to the alkenylation according to the Heck reaction or its modifications. Those are the reactions of 1-bromo-2,4-difluoro- and 1-bromo-3,4-difluorobenzene with butyl acrylate using Pd-based catalyst [231, 232]. For example, Pd$_2$-(GO) catalyst applied in [231] constitutes Pd-nanoparticles supported on graphite oxide. The product of Heck reaction between 2,3,4-trifluoro-6-bromoaniline and allylic alcohol, without separation, in a one-pot process by the Larock reaction was converted to a quinoline polyfluorinated derivative [233]. Trifluorostilbenes are produced by the Heck reaction from 1-bromo-3,4,5-trifluorobenzene and styrene [234] or 4-hydroxystyrene [235], when so doing, in the first case, the mechanochemical process activation due to solids grinding with the help of a high-speed mill makes it possible to conduct the reaction without any solvent. The stilbene fragment results from the Heck cross-coupling between 1-bromo-3,5-difluoro-4-formylbenzene and triarylamine, one of aryl substituents of which is a p-vinylphenyl group [236]. The Heck reaction between 2-bromo-4,5-difluorobenzylacetate and methyl 2-{[(benzyloxy)carbonyl]amino}prop-2-enoate allows introducing of substituted olefin group into difluoroarene instead of bromine atom [237]. The nickel-catalysed coupling between 1-bromo-3,4-difluorobenzene and diphenylethyne results in triarylethylene due to the hydroarylation of alkyn [238].

9. Reactions of alkynylation

The alkynylation of polyfluoroarylhalogenide derivatives by various alkyns under variable conditions was being studied intensively in recent years. One may mark a set of studies using alkyn trialkylsilyl derivatives that contribute to the suppression of non-desired by-process that is actually alkyn transformation under the reaction conditions. It comprises the alkynylation of 1-bromo-2,3,4-trifluorobenzene with trimethylsilylethyne under standard conditions of the Sonogashira reaction (CuI, Pd-based catalyst) [239], that of bromo- or iodo-pentafluorobenzenes [240] with the formation of trimethylsilylethyne derivative and bis-alkynylation of 1,2-dibromo-4,5-difluorobenzene with trimethylsilylethyne [241], with further the Hiyama transformation of thus formed polyfluoroaryltrimethylsilyl derivatives to internal diarylalkyns through their interaction with arylhalogenides present in the same system. The reactions with trimethylsilylethyne, 1-bromo-2,4-difluorobenzene [242] and 4-bromo-2,6-difluorobenzylidene-N,N-dimethylamine [243] were conducted, incidentally, under microwave irradiation. For the alkynylation of 1-bromo-2,3,5,6-tetrafluorobenze by tri(isopropyl)silylethyne see [244]. Finally, 1-iodo-2,5-difluorobenzene is alkynylated by cross-coupling with 2-tert-butyl-6-[2-(trimethylsilyl)ethynyl]-[1,2,4]triazolo[1,5-a]pyrimidine [245]. Under standard conditions of the Sonogashira reaction bromopentafluorobenzene is coupled with but-3-yn-1-ol [246] and 9-(prop-2-ynyl)-9H-fluorene [247]. The alkynylation of 4-bromo-2,3,5,6-tetrafluoroaniline with 3-ethylhept-1-ine is described in [248], while that of 4-bromo-2,3,5,6-tetrafluorobenzonitril with (4-aminophenyl)ethyne in [249]. The Sonogashira reaction between various bromodifluorobenzenes or complex molecules comprising bromodifluorophenyl fragments with aromatic or aliphatic terminal alkyns is studied in [209, 250-252]. In the case of reaction of isomeric dibromodifluorobenzenes either one or both bromines participate, resulting in either mono- or dialkynyl derivatives, or in a mixture thereof [253-255]. For the series of polyfluoroaryliodo derivatives there are new findings on the Sonogashira reactions. Partially fluorinated p-substituted tolanes are formed under standard conditions via the coupling between iodopentafluorobenzene with p-phenylsubstituted ethynes [240], or with (2-p-tolylethynyl)silver using AuI/dppe for catalyst. The reaction occurs only with at least very small additive of Pd(0) co-catalyst (0.1 mol%) [256]. For the reactions of iodopentafluorobenzene with pent-1-yne see [253], for those with 2-ethynyl azulene see [257], for those with heterocyclic alkyn see [258]. A number of polyfluorinated Ps-alkynyl anilines (tetra-, tri-, or difluoroderivatives), those being promising units for the production of polyfluorinated benzoazaheterocycles, were synthesised by the Sonogashira reaction of polyfluorinated Ps-iodoanilines with terminal alkyns [259]. The reaction of 1,4-diiodo-2,3,5,6-tetrafluorobenzene with phenylethyne at standard conditions leading to a tolane derivative with the participation of one iodine atom was studied in [260]. Isomeric 1,2-diiodotetrafluorobenzene undergoes Sonogashira alkynylation reaction under the action of terminal alkynes with the formation of mono- or di-derivatives [253]. The coupling of isomeric iododifluorobenzenes with phenylethyne [261] or (3-chlorophenyl)ethyne [262] results in the formation of tolanes, while their Sonogashira reaction with ethylpropiolate [263] or propiolic acid [264] results in the corresponding alkynyl derivatives. Similarly, the reaction between 2-iodo-4,6-difluoroaniline and prop-1-yne results in the formation of an alkynyl derivative [265].

IV. Transformation by C_{Ar}-F bond

The interaction between perfluoro[2,2]-para-cyclophane and ethylacetoacetate in the presence of NaH occurs with the participation of aromatic fluorine and the formation, at last, of the product of ethylacetoacetate enolate addition [266]. At heating of fluorinated anilides with t-BuOK in DMF at 80^0C intramolecular hetarylation occurs due to the intramolecular cyclisation resulting in the formation of fluorinated oxindoles. This transformation is described in [267] for N-methyl-N-(2,4,6-trifluorophenyl)anilide of 2-phenylbutane acid. 4-Tri(isopropylsilyl)alkynyl derivative of 2,2вЂ™-dibromooctafluorobiphenyl is produced through the nucleophilic substitution of fluorine at position 4 of the said biphenyl via the reaction with tri(isopropylsilyl)ethyne and n-BuLi, while a compound with two internal alkyn fragments and thiophene fragments is formed through the interaction between a 4-(pentafluorophenylethynyl) derivative of this dibromooctafluorobiphenyl and 2-ethynyl-5-(5-hexylthiophene-2-yl)thiophene in the presence of n-BuLi [268]. The reaction between bis(pentafluorophenyl)ethyne with 1-(ethynylphenyl)-4-(ethynyl)benzene and n-BuLi due to the nucleophilic substitution of fluorine in one of its pentafluorophenyl rings results in the corresponding internal polyfluorinated polyethynylated polyphenylene [240]. Within the framework of a study on the synthesis of O±-bound mixed thiophene-pyrrole hexamers with either one or two terminal pentafluorophenyl groups the interaction between hexafluorobenzene and N-alkyl-2,5-bis-(5-iodothiophene-2-yl)-pyrrole was studied in the presence of n-BuLi, which under the research conditions resulted in the formation of a product of iodine replacing with C_6F_5-group [269]. During the reaction between bromobenzenes with pentafluorophenoxy- or pentafluorothiophenoxy- group in ortho-position and n-BuLi bromine is replaced with lithium, and consequential intramolecular nucleophilic substitution of fluorine is followed by the cyclisation to result in the corresponding tetrafluoro-dibenzofuran or вЂ“dibenzothiophene with simultaneous replacing fluorine at position 3 of the heterocycle with a butyl group [270]. Having in mind the design of a novel triphenylphosphine ligand containing pentafluorophenyl group, for the needs of metalPscomplex catalysis of olefin polymerisation, pentafluorophenyl group was introduced at the only one available (within its three phenyl rings) free ortho-position to C_{Ar}вЂ“P bond of the original alkoxysubstituted triphenylphosphine, through the interaction of the original phosphine with hexafluorobenzene and n-BuLi [271]. The intermolecular cyclisation to polyfluorinated benzo[f]quinolines according to the Skraup reaction occurs through the interaction of polyfluorinated 2-naphtylamines with glycerin in H_2SO_4 or CF_3SO_3H at high temperature (150-160^{o}C). It is assumed that vicarious electrophilic substitution of fluorine occurs at O±-position of the naphtalene ring. This is a rare case of fluorine ipso-substitution at obviously electrophilic conditions, attributable to the electrophilic ipso-attack at O±-position at the first step of the transformation followed by the aromatisation of thus formed intermediate cationic Пѓ-complex due to the elimination of HF [272]. In [273] as an outgrowth of reactions shown in scheme 115, air-stable complexes of Ni(II) and Pd(II) with bis(diimidazolidene) N-heterocyclic ligands $(diNHC)_2NiBr_2$ and $PdCl_2(diNHC)$ were synthesised and characterised, to be used in the Suzuki reaction between octafluorotoluene and phenylboronic acid. The nickel complex contributes to the phenylation of octafluorotoluene at para-position to CF_3-group, while palladium complex does not activate C_{Ar}-F bond in the Suzuki reaction. The use of $Ni(cod)_2$, PPh_3 as catalyst made it possible to carry out the Suzuki arylation of arylimine (N-2,4,5-trifluorobenzylydene)-N-benzylamine under the action of p-methoxyphenylboronic acid. In this case p-methoxyphenyl group replaces fluorine at ortho-position to imine group [274]. The data on ortho-methylation of polyfluorinated arylimines with the help of platinum-based catalyst $[Pt_2Me_4(SMe_2)_{2]}$ [275, 276] add those shown in scheme 120. The monoarylation of hexafluorobenzene, pentafluorobenzene, 1,2,3,4-tetrafluorobenzene, and 1,3,5-trifluorobenzene under the action of p-methoxyphenyl magnesium bromide, $ZnCl_2$ TMEDA and nickel catalyst $Ni(acac)_2$ with new alkoxydiphosphine ligand PPћP ($C_{37}H_{30}$PћP$_2$) occurs through the cross-coupling between polyfluoroarenes and the formed Zn-organic compound resulting in the product of one fluorine substitution, whereas in the case of F,H-arenes the reaction involves ortho-position to C_{Ar}-H bond. This monoarylation stems from the high rate of the product elimination from its complex with catalyst [277]. The arylation at ortho-position to nitro-groupPµ of polyfluorinated nitrobenzenes with 2Г·5 fluorines follows the Suzuki reaction with phenylboronic acid ester, $Pd(PPh_3)_4$, under microwave irradiation and with aluminium-supported KF [278]. Palladium-based catalyst $PdCl_2$ dppf .$(CH_3CN)_2$ activates C_{Ar}-F bond in polyfluorinated phenyl ring of 2-polyfluoro (penta, 2,3,5,6-tetra- and 2,3,6-trifluoro)phenyloxazoline, at ortho-position to oxazoline substituent, making it possible to conduct arylation or hetarylation at this position by the Suzuki reaction with very wide spectrum of arylboronic acids and 3-thiopheneboronic acid. At similar conditions the reaction between prop-1-enylboronic acid and 2-pentafluorophenyl derivative of oxazolidyne occurs via the alkenylation of the latter at the same position [279]. Finally, the Sonogashira alkynylation of hexafluorobenzene with trimethylsilylethyne was carried out resulting in trimethylsilyl-pentafluorophenylethyne [280].

V. Transformation of other substituents in polyfluoroarene

Most of the emerged studies on the introduction of alkyl-, aryl- (hetaryl)- or unsaturated groups into polyfluoroarene by the way of the available, non-halogen, substituent transformation refer to the transformation of compounds with carbonyl C=Pћ fragment involved in various functionalities. One example is the Knoevenagel condensation of aromatic aldehydes resulting in the formation of some alkenyl derivatives. Thus, when 2,3,5,6-tetrafluoroterephtalic aldehyde is heated with malononitrile in the presence of $ZnCl_2$ its formyl groups are transformed to 1,1-dicyanovinyl groups [281]. The Knoevenagel condensation of 2,4,6- or 2,4,5-trifluorobenzaldehyde with 2-(4-methoxy-3-nitrobenzylsulfonyl)acetic acid results in a substituted trifluorostyrylbenzylsulfone [282]. The ethyl ester of 3-(2,4,5-trifluorophenyl)propenoic acid is produced from 2,4,5-trifluorobenzaldehyde under the action of the Wittig reagent $Ph_3P=CHCOOEt$ [283], while 2,6-difluorobenzaldehyde at the conditions of Hommer-Wadsworth-Emmons reaction converts to 3-(2,6-difluorophenyl)prop-2-ene-1-ol [284]. Another pathway to the formation of polyfluorinated alkenyl derivatives is decarboxylative Mizoroki-Heck coupling reaction of polyfluorinated benzoic acids with non-saturated ethers in the presence of palladium-based catalysts. Therefore, the reaction between 2,4,6-trifluoro- or 2,6-difluorobenzoic acid and methylacrylate was conducted in the presence of $Pd(OAc)_2$ with carbene ligands in oxygen medium used as oxidizer [285], while the transformation of pentafluorobenzoic acid, 2,4,6-trifluoro- or 2,6-difluorobenzoic acid with allylacetate is catalysed by $Pd(OAc)_2$ with addition of Cu_2O and Ag_2CO_3 [286]. The decarboxylative olefination of 2,6-difluoro-4-methoxybenzoic acid by reaction with propylacrylate or N,Ndimethylacrylamide is Rh-catalysed using 4R,5R-DIOP[Rh(OH)(cod)$_2$] catalytic system [287]. As further development of scheme 123 the decarboxylative hetarylation of 2,6-difluorobenzoic acid, 2,4,6- or 2,3,6-trifluorobenzoic acids with N-(t-butylcarboxy)-indole (catalyst Pd(TFA)$_2$, Ag_2CO_3) [288] or 2-chlorothiophene (catalyst Pd(TFA)$_2$, PCy_3, Ag_2CO_3) was conducted [289], while that of pentafluoro- or 2,6-difluorobenzoic acid was carried out under the action of some other heterocyclic systems (4,5-dimethyl-1,3-thiazole or benzothiazole) in the presence of $PdCl_2$, PPh_3, Ag_2CO_3 [290]. Scheme 124 was complemented with the decarboxylative arylation and hetarylation with the coupling of Рљ-salts of pentafluorobenzoic acid, 4-substituted 2,3,5,6-tetrafluorobenzoic acid, 2,3,5-trifluoro-, 2,6- and 1,3-difluorobenzoic acid with a wide set of substituted bromo- and chlorobenzenes, 1-bromonaphtalene, 2- and 3-chlorothiophene, 2-bromopyridine. The reactions were conducted in diglyme in the presence of Pd(OAc)$_2$, PCy_3 [291]. For the reduction of difluorobenzoic acids or esters to alcohols, i.e. the transformation of C=Рћ to CH_2 group see [292, 293]. The interesting palladium-catalysed C_{Ar}вЂ“N to C_{Ar}вЂ“C bond transformation was revealed in the reaction between arylhydrazines and olefines [294]. In particular, the interaction of 2,5-difluorophenylhydrazine with tert-butylacrylate (catalyst Pd(OAc)$_2$, ligand 4,7-diphenyl-2,9-dimethyl-1,10-phenanthroline) results in (2,5-difluorophenyl)tert-butylacrylate. An intermediate arylpalladium complex is assumed to be generated in the course of the reaction, and to participate actively in the formation of C-C bond during the interaction with olefin. The Grignard reagent addition-removal to О±-hydroxyacrylonitriles occurs with the formation of alkenenitrils, realised e.g., in the reaction between 2-[(3,4-difluorophenyl)(hydroxymethyl)]acrylonitrile and n-BuMgHal resulting in 2-(3,4-difluorobenzylidene)heptanonitril [295]. As an amendment to Scheme 129, by the Meerwein reaction by the radical pathway via diazonium salts starting with 2,4- or 2,6-difluoroaniline in the presence of $CuCl_2$ under the action of thiophene-2-carbonic acid hetarylation occurs at position 5 [296], while in the presence of $TiCl_3$ starting with 3,4,5-trifluoroaniline diazonium salt is arylated under the action of 4-chloroaniline [297] or 4-(2-aminoethyl)phenol [298], while so doing the aryl group holds ortho-position regarding to amino- or hydroxy- group correspondingly. 2,3,5,6-Tetrafluoro-4-aminobenzoic acid reacts with toluene when treated with $NaNO_2$, KI or p-toluenesulfonic acid resulting in 2,3,5,6-tetrafluoro-4-benzyl-benzoic acid [299]. And finally, ruthenium-based carboxylate complex [Ru(O_2CMes)$_2$ (p-cymen)] catalyzes the transformation of phenolic C_{Ar}вЂ“O bond to C_{Ar}вЂ“C bond. That is how 3,4,5-trifluoro- or 2,5-difluorophenol by the reaction with 1-(2-methoxyphenyl)-1H-pyrazole, in the presence of that catalyst and p-toluenesulfonylchloride, arylate the methoxyphenyl ring of the said pyrazole at position 4, resulting in 1-(2-methoxy-4-tri- or 4-difluorophenyl)1H-pyrazole, correspondingly [300].

List of Abbreviations (/public/2014/1_2014/images/abbrev_en.pdf)

References (images/references_en.pdf)

В

Recommended for publication by prof. V.E. Platonov

В