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Review

Chemically oxidative fluorination with fluoride ions

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Dedicated to Professor Véronique Gouverneur on the occasion of her receipt of the ACS Award for Creative Work in Fluorine Chemistry 2015.

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ABSTRACT

Although the chemical oxidation of fluoride ions is generally challenging due to the high electronegativity of fluorine, in the past four years, a number of oxidative fluorination reactions via the reactivity umpolung of substrates or fluorides have been developed. These reactions can introduce fluorine into nucleophilic or electron-neutral systems. This short review provides a summary on the recent developments of oxidative fluorination of arenes, alkanes, and alkenes with fluorides promoted by various oxidants. These newly developed reactions are of high selectivity and efficiency, and provide a pathway for the more efficient use of the abundant, yet less nucleophilic fluorides.

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1. Introduction

Fluorine, as an element with a small van der Waals radius (147 pm) and the highest electronegativity (3.98) in the periodic table, is usually considered as "a small atom with big ego" due to its important application in life sciences- and materials-related researches [1]. Introduction of fluorine atom or fluorinated moiety often imparts beneficial properties, such as metabolic stability, binding affinity, unique biological properties, and corrosion resistance to the target molecule, and a variety of fluorine-containing pharmaceuticals, agrochemicals, and materials have been developed [2]. Recently, increasing attention has been paid to the development of practical and selective fluorination reagents and exploitation of conceptually new methods for the formation of carbon–fluorine bonds [3].

Conventionally, fluorine atoms can be introduced in several manners: (1) electrochemical fluorination of C–H bonds with HF (the Simons process) or a fluoride salt; (2) radical fluorination of hydrocarbons with fluorine gas or CoF_3; (3) nucleophilic fluorination of pre-functionalized substrates bearing a leaving group; (4)

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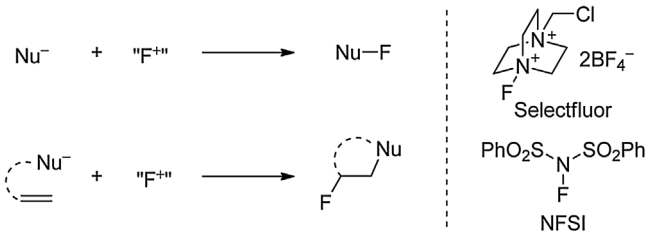
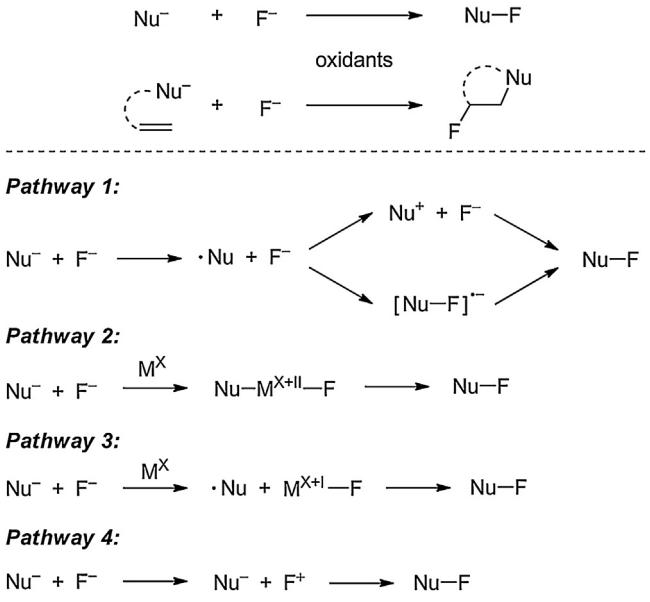


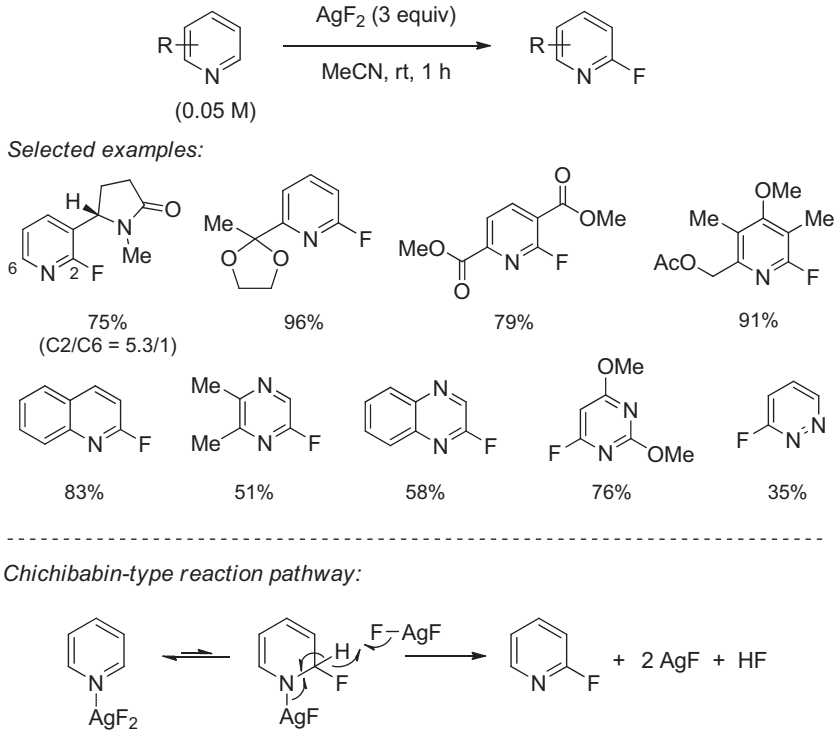
Scheme 1. Electrophilic fluorination with Selectfluor and NFSI.



Scheme 2. Oxidative fluorination with fluoride ion.

fluoride-addition across a double or triple carbon–carbon bond [2]. Recently, electrophilic fluorination of anionic carbon centers, C–H bonds, and unsaturated compounds such as alkenes has become a common method for selective introduction of fluorine atoms due to the mildness of the reaction conditions (Scheme 1) [3a–c]. However, the electrophilic fluorination reagents represented by Selectfluor and NFSI are obtained from elemental fluorine [4], a very strong oxidant usually prepared by electrolysis of anhydrous HF. Considering that the fluoride ion is stable and abundant in nature [5], the direct oxidative fluorination of substrates with a fluoride ion is an ideal alternative method for the current electrophilic fluorination reactions (Scheme 2). Particularly, in recent years, the development of ^{18}F radiolabeling for positron emission tomography (PET) imaging also calls for the development of oxidative fluorination with [^{18}F]fluorides, not only because [^{18}F]fluorides are much easier to access and handle than [^{18}F]fluorine gas, but also because the fluorination with [^{18}F]fluorides can be conducted without added ^{19}F carrier, which produces the ^{18}F labeled probes in higher specific radioactivity [3d–e].

Mechanistically, the oxidative fluorination with fluoride ions can proceed in four ways (Scheme 2): (1) oxidation of the substrate to form an electrophilic carbon center (carbocation, radical cation, or high-valency metal fluorides) followed by nucleophilic fluorination (Pathway 1); (2) oxidation of the substrate to form a high-valent metal fluorides followed by reductive elimination (Pathway 2); (3) oxidation of the substrate to form a carbon-centered radical or radical cation species followed by fluorination with the fluorine radical or its equivalents (high-valency metal fluorides) (Pathway 3); (4) oxidation of fluoride to fluoronium ion followed by electrophilic fluorination (Pathway 4). The fourth pathway is less possible to occur because even the oxidation of fluoride to fluorine radical is not a trivial transformation due to the high electronegativity of fluorine [6]. Historically, the elemental fluorine was prepared via electrolysis of anhydrous HF [7]. It was not until 1986 that Christe reported the first truly chemical



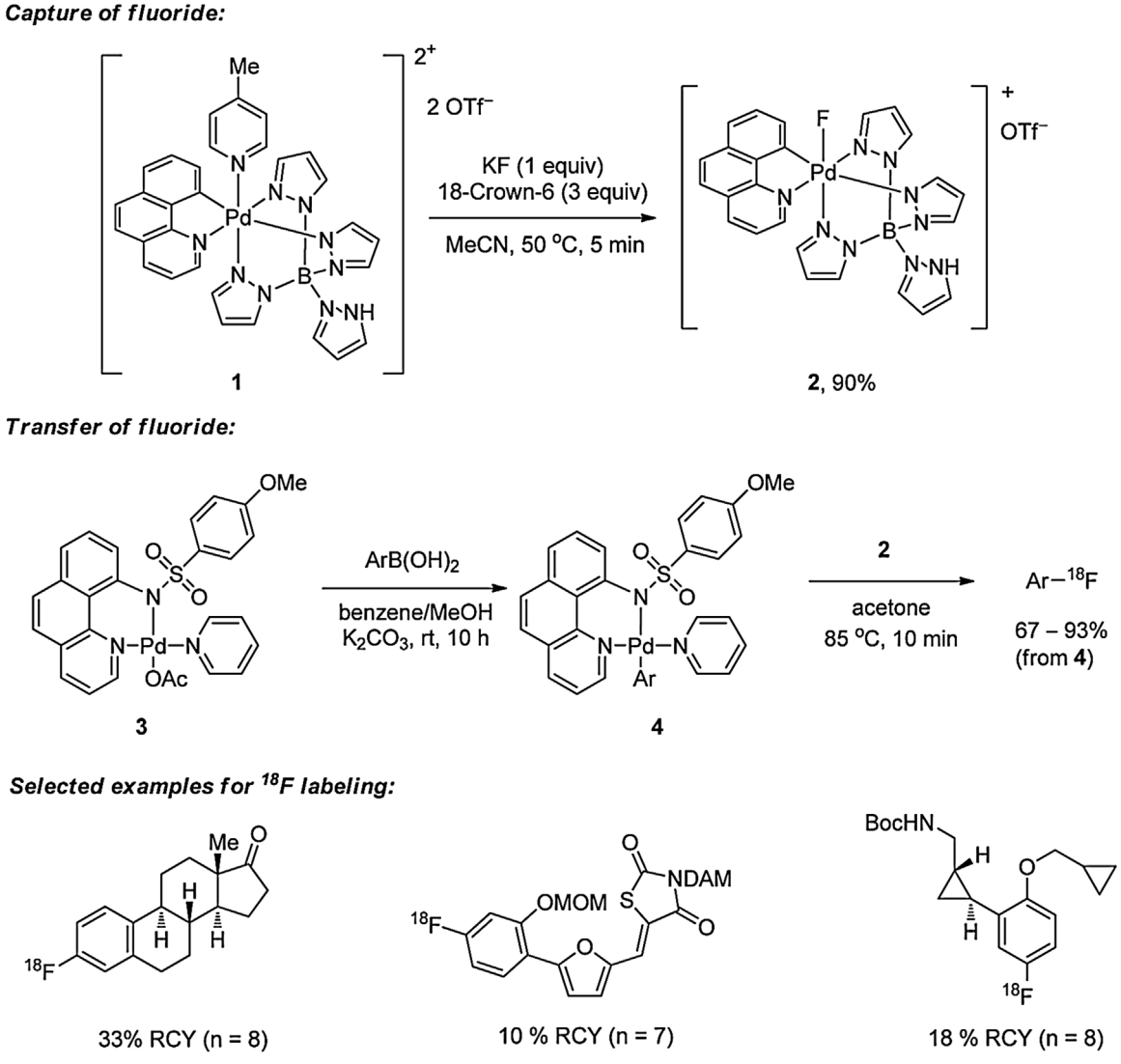
Scheme 3. AgF_2-mediated C–H fluorination of pyridines and diazines.

generation of fluorine gas via the displacement reaction between K_2MnF_6 and super Lewis acid SbF_5 followed by a spontaneous decomposition, in which a fluoride is oxidized by high-valent transition-metal Mn^{IV} [8]. Although Christe's oxidation of fluoride is not practical for the synthesis of organofluorine compounds, it implies that chemically oxidative fluorination with fluorides via radical pathway (the third pathway) is possible and some recently developed Mn-catalyzed fluorination reactions have been proposed to proceed in such a way [9]. As for the first pathway, electrochemical fluorination reactions have verified its feasibility, albeit usually with poor selectivity (due to over fluorination) [10]. Recent employment of mild chemical oxidants has improved the selectivity and expanded the substrate scope. Finally, according to the recently developed reductive elimination of C–F bond from high-valent palladium complexes [11], the second pathway is also viable and has been demonstrated in palladium-, nickel-, and copper-promoted oxidative fluorination reactions.

Based on the discussions made above, this review aims to provide a brief summary on the recent developments of oxidative fluorination of arenes, alkanes, alkenes, as well as their derivatives with various nucleophilic fluorides as the sole fluorine source by chemical means, while the electrochemical processes with fluorides and chemical processes with fluorine gas and some reagents derived from fluorine gas (such as Selectfluor and NFSI) have been excluded. Note that the chemically oxidative fluorination described in this review refers to the fluorination process using a chemical oxidant, which distinguishes from the electrochemically oxidative fluorination (electrofluorination).

2. Oxidative fluorination of arenes

Before 2013, there had been many examples on the oxidative fluorination of arenes with high-valent metal fluorides such as CoF_3, MnF_3, AgF_2, and CeF_4, which serve as both oxidants and fluorination reagents; however, these reactions usually led to over-fluorination products [12]. Serendipitously, in 2013, Hartwig and Fier found that *N*-heteroarenes can be selectively C–H fluorinated with AgF_2 under very mild conditions (Scheme 3) [13]. The reactions of pyridines, quinolines, and various diazines afford the monofluorination products in good yields with exclusive *ortho*-position selectivity. This is a useful synthetic approach for the late-stage modification of complex molecules containing heterocycles such as pyridines. As for the mechanism of this reaction, the authors proposed a Chichibabin reaction-type pathway [13]. It could also be possible that the reaction involves a stepwise one-electron oxidation process, in which the fluoride react with a heteroarene radical cation followed by deprotonation. Anyhow,



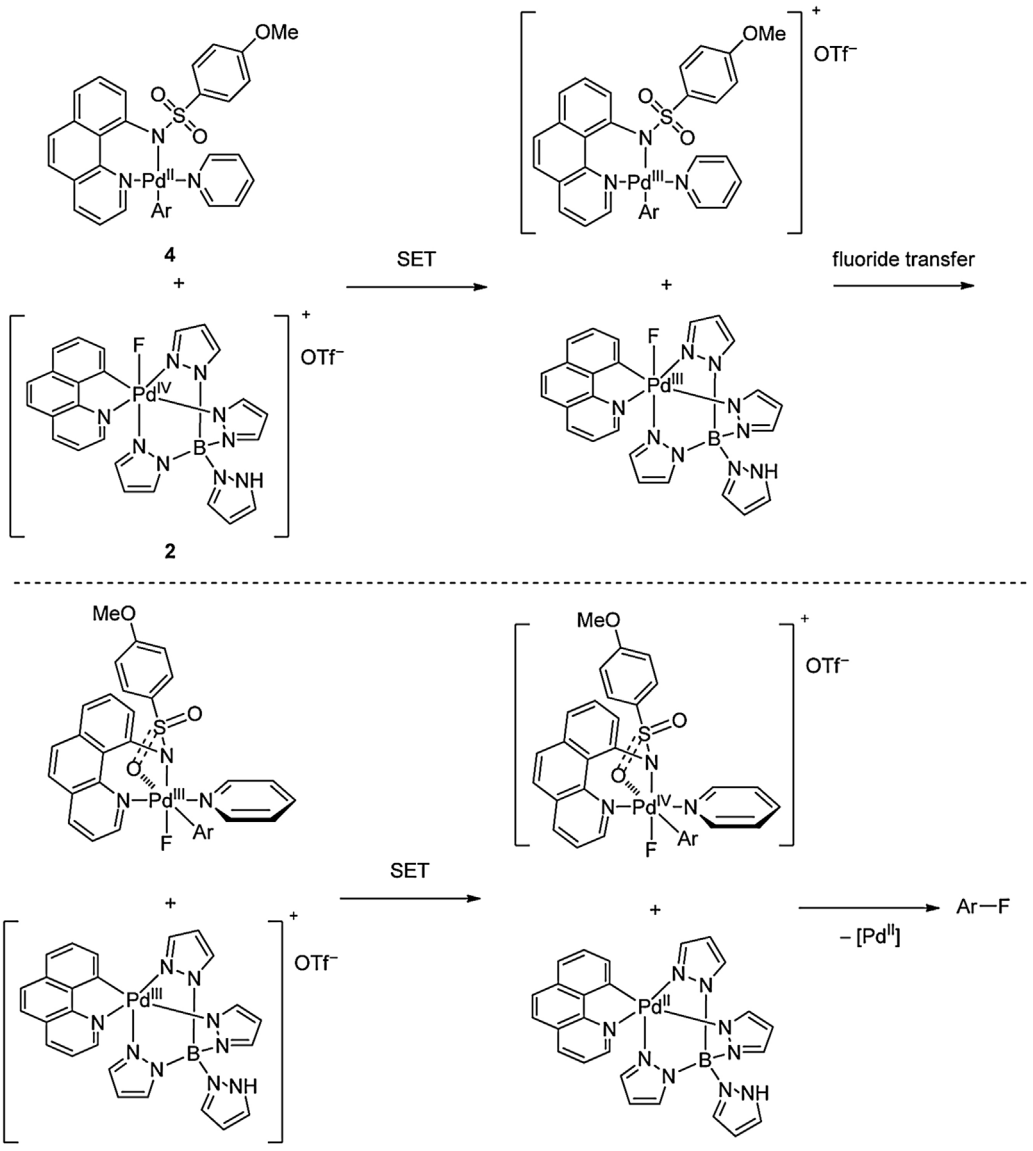
Scheme 4. Palladium-mediated oxidative fluorination (RCY = radiochemical yield).

the nitrogen atom on the heterocycle plays an important role on the orientation of this reaction.

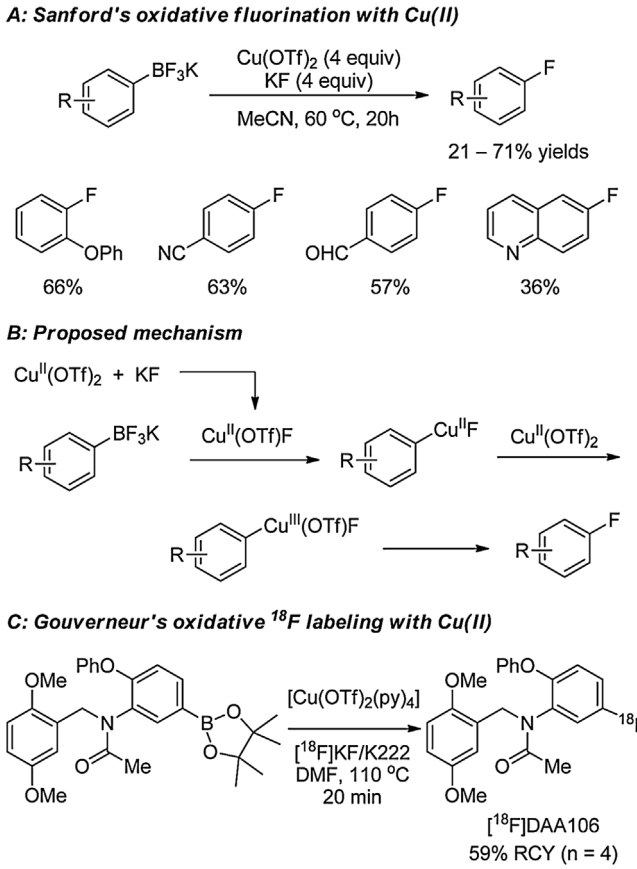
In addition to the direct use of commercially available high-valent metal fluorides, the combination of salts or oxides of high-valent metals and additional fluorides is a more convenient way. Historically, several combined oxidative fluorination systems including $Tl(OCOCF_3)_3/KF/BF_3$ [14], $Pb(OAc)_4/BF_3{\cdot}Et_2O$ [15], and PbO_2/HF or HF-pyridine [12c,16] had been used for the fluorination of arenes (including phenols), aryltrimethylsilanes, and triarylboroxines; however, drawbacks such as requirement for stoichiometric amounts of toxic metals, limited substrate scopes, as well as low yields, preclude the current application of these methods.

In 2011, Ritter and co-workers developed an effective electrophilic fluoride transfer reaction by using a Pd^{IV} complex as both the fluorine carrier and oxidant (Scheme 4) [17]. Treatment of the ionic Pd^{IV} complex **1** with nucleophilic fluoride (KF) affords a new ionic Pd^{IV}–F complex **2** in 5 min, which could further react with arylpalladium(II) complex **4**, generated via transmetalation between aryl boronic acids and a Pd^{II} complex **3**, to give the corresponding aryl fluorides in 10 min. Based on the regioselectivity for amino-fluorination of an asymmetric stilbene (Scheme 21, *vide infra*), a single-electron-transfer (SET) process involving fluoride transfer was proposed for this oxidative fluorination (Scheme 5) [18]. Despite the high cost of the palladium complexes, this method can be readily used in the synthesis of ^{18}F-labeled aryl fluorides. However, the use of Ar–Pd^{II} complex is not applicable for the fluorination of *ortho*-substituted substrates. Ritter et al. later found that the employment of arylsilver(I) compounds is a useful supplement, which is suitable for the preparation of sterically hindered aryl fluorides [18].

In late 2013, Sanford and co-workers showed that the combination of a copper(II) salt as oxidant and a fluoride salt enables the direct fluorination of aryl boron derivatives (Scheme 6A) [19]. Thus, the $Cu(OTf)_2$-mediated fluorination of aryltrifluoroborates with KF proceeds under mild conditions (at 60 °C, over 20 h) with a broad substrate scope and functional group tolerance. Functional groups such as ketones, esters, and aldehydes are compatible with this method. Pyridine derivatives can also undergo fluorination, albeit in low yields. However, substrates containing chloride, bromide and iodide on the aromatic ring are susceptible to undergo competing halodeboronation under the reaction conditions. A possible pathway for this transformation is the reductive elimination of aryl fluoride from the Ar–Cu^{III}–F complex that is formed via oxidation of a Ar–Cu^{II}–F complex by



Scheme 5. Proposed mechanism of fluoride transfer from Pd(IV) to arenes.

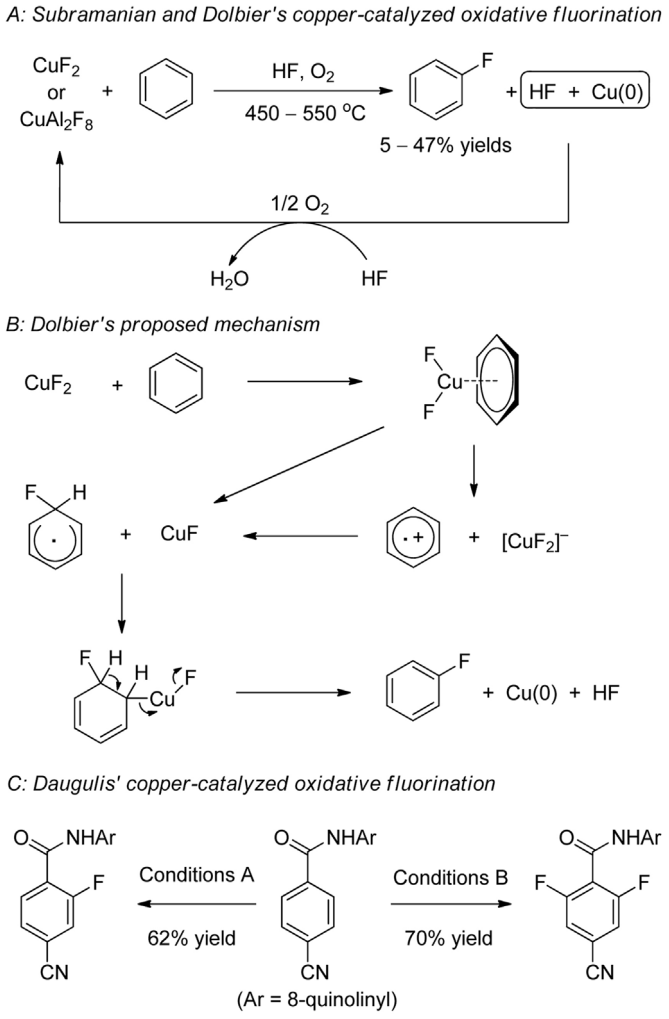


Scheme 6. Copper-mediated oxidative fluorination of aryltrifluoroborates and aryl boronic esters (RCY = radiochemical yield).

$Cu(OTf)_2$ (Scheme 6B). Gouverneur and co-workers have adapted this protocol in the radiosynthesis of an array of ^{18}F arenes, such as TSPO PET ligand [^{18}F]DAA106 (Scheme 7C), from readily accessible aryl boronic esters upon treatment with [^{18}F]KF/K222 and commercially available $[Cu(OTf)_2(py)_4]$ (py = pyridine) [20].

In addition to high-valency transition-metals, other oxidants such as hypervalent iodine compounds, *N*-oxides, even oxygen can also be used for oxidative fluorination under proper conditions.

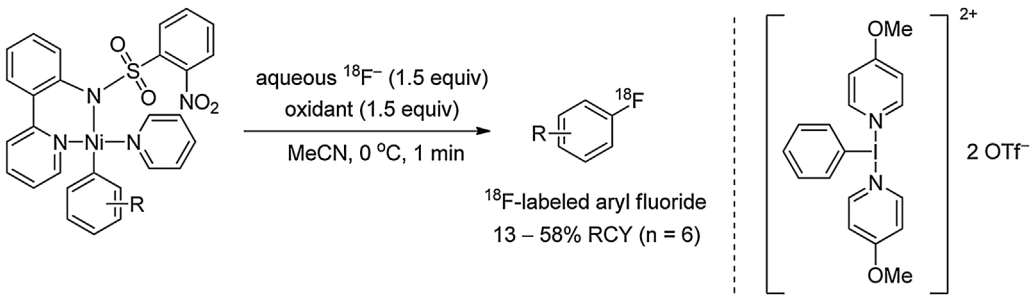
In 2014, following their discovery of Pd^{IV}-promoted fluorination reaction, Ritter and coworkers reported the fluorination of well-defined Ni^{II} complexes with aqueous fluoride and a hypervalent iodine compound (Scheme 7), which enables a more practical ^{18}F fluorination due to the combination of the fluoride capture process and the fluorine transfer process in a single step and avoidance of extensive drying procedures [21]. The fluorination reaction proceeds in less than 1 min and is not only successful for the synthesis of both electron-rich and -poor, highly



Scheme 8. Copper-catalyzed oxidative fluorination of arenes.

functionalized aryl fluorides, but also is applicable to synthesize alkenyl fluorides.

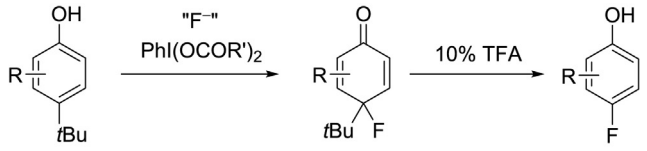
Since 2002, Subramanian and Dolbier have independently reported the monofluorination of benzene with anhydrous HF and O_2 under the catalysis of a copper(II) salt at very high temperatures (450–550 °C) (Scheme 8A) [22,23]. Copper(II) difluoride that may be regenerated via oxidation of copper(0), is proposed to be the active fluorination reagent (Scheme 8B) [23]. In the middle of 2013,



Scheme 7. Nickel-mediated oxidative fluorination for PET imaging (RCY = radiochemical yield).

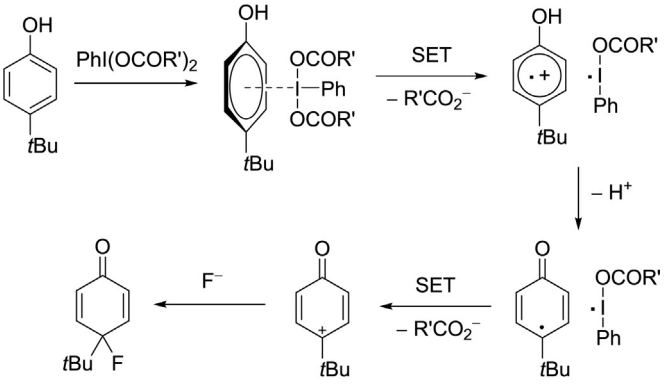
Daugulis and coworkers developed a copper-catalyzed selective fluorination of aromatic C–H bonds under mild conditions, which relies on the assistance of an amide directing group and employs *N*-methylmorpholine-*N*-oxide (NMO) as oxidant and AgF as fluorine source (Scheme 8C) [24]. A simple change of reaction conditions can result in selective mono- or difluorination of benzoic acid and benzylamine derivatives with excellent functional group tolerance. Although no detailed information is available, it has been proposed that this transformation proceeds via an Ar–Cu^{III}–F intermediate.

A: Langlois' oxidative para-fluorination of phenols

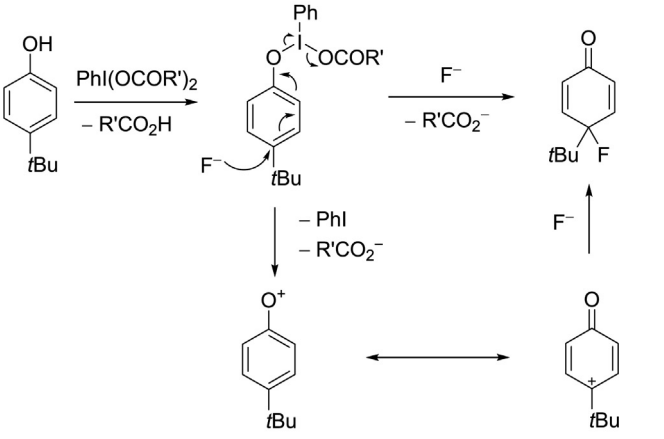


B: Possible reaction pathways for C-F bond formation

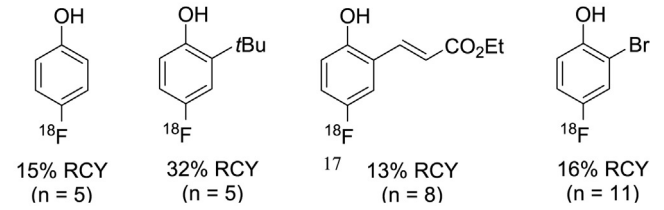
1) One-electron oxidation



2) Two-electron oxidation



C: Examples for oxidative ^{18}F labeling (Gouverneur)

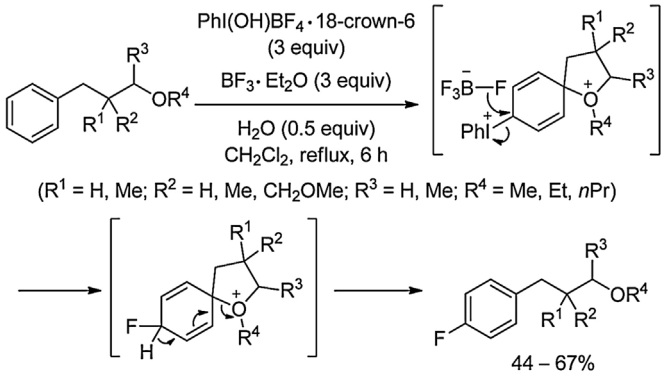


Scheme 9. Hypervalent iodine compound-mediated oxidative fluorination of phenols (RCY = radiochemical yield).

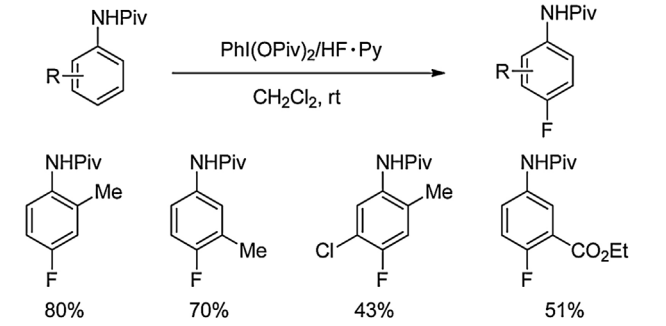
The oxidative fluorination can also be performed under metal-free conditions by using hypervalent iodine compounds. As early as 2002, Langlois and coworker reported the dearomative fluorination of 4-*tert*-butylphenols and 4-*tert*-butylacetanilide using the combination of $PhI(OCOCF_3)_2$ and $Et_3N{\cdot}3HF$ [25]. The fluorinated enone and enimine intermediates readily aromatized to *para*-fluorinated phenols and amine products after acid-catalyzed debutylation, which constitutes a formal oxidative fluorination of the aromatic C–H bonds of phenols (Scheme 9A). It is proposed that the C–F bond is formed via nucleophilic fluorination of a phenoxylenium cation or a phenoxyiodine(III) complex (Scheme 9B). Gouverneur and coworkers have synthesized ^{18}F fluorinated phenols from 4-*tert*-butylphenols using tetra-*n*-butylammonium [^{18}F]fluoride as the fluoride source after a modification of Langlois' reaction conditions (Scheme 9C) [26].

However, the use of *tert*-butyl group as a traceless directing group has a limitation on the substrate scopes. In 2011, Miyamoto and coworkers reported the *para*-selective aromatic C–H fluorination of 3-phenylpropyl ethers by reaction with an activated iodosylbenzene monomer/18-crown-6 complex [$PhI(OH)BF_4{\cdot}$18-C-6] in the presence of $BF_3{\cdot}Et_2O$ and water (Scheme 10A) [27]. The distal alkoxy group, which may react with the phenyl ring at the ipso-position to stabilize the arenium ion that is generated form electrophilic iodination of the phenyl ring at the *para*-position, plays an important role in facilitating the fluorination. In 2014, Meng and Li developed a *para*-selective, aromatic C–H fluorination of readily available anilides using PhI $(OPiv)_2$ and pyridine/hydrogen fluoride (Scheme 10B) [28]. In contrast to phenols, which readily undergo difluorination at the *para* position to give difluorodienones [16,25], the fluorination of anilides under similar conditions only affords the *para*-monofluorinated aromatic products. Besides, this reaction tolerates functionalities such as alkyl, halogen, and ester groups at *ortho*- or/and *meta*-positions.

A: Hypervalent iodine mediated C-H fluorination of 3-phenylpropyl ethers



B: Hypervalent iodine mediated C-H fluorination of anilides

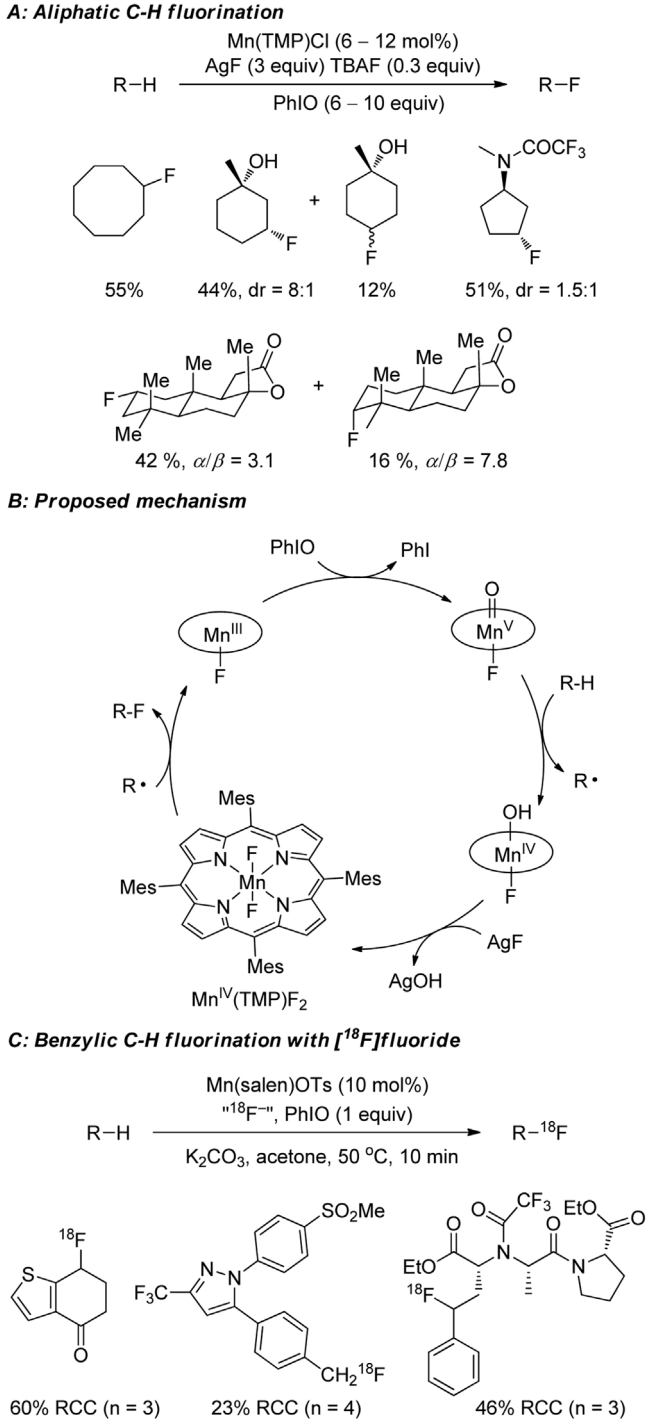


Scheme 10. Hypervalent iodine compound-mediated oxidative fluorination of 3-phenylpropyl ethers and anilides.

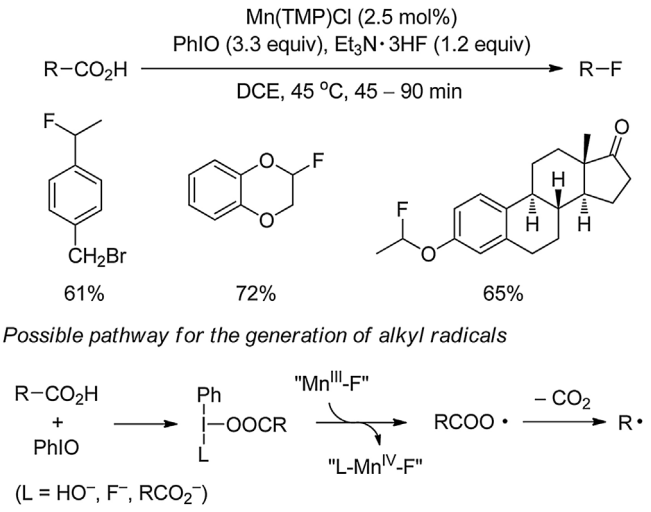
3. Oxidative fluorination of alkanes

The conventional direct fluorination of alkanes with high valent-metal fluorides such as CoF_3 not only leads to over-fluorination, but also tends to give skeletal rearrangement products [29]. Early research by Feiring showed that toluene derivatives bearing electron-withdrawing substituents are fluorinated on the methyl group when treated with PbO_2, NiO_2, CoF_3, $Co(OAc)_3$, AgF_2, or AgO in liquid hydrogen fluoride [12c]. For instance, the reaction of 4-methylbenzonitrile with PbO_2/HF gives benzylic monofluorination product. However, similar to aromatic fluorination, the harsh reaction conditions and narrow substrate scope put limitations on the practical application of this method.

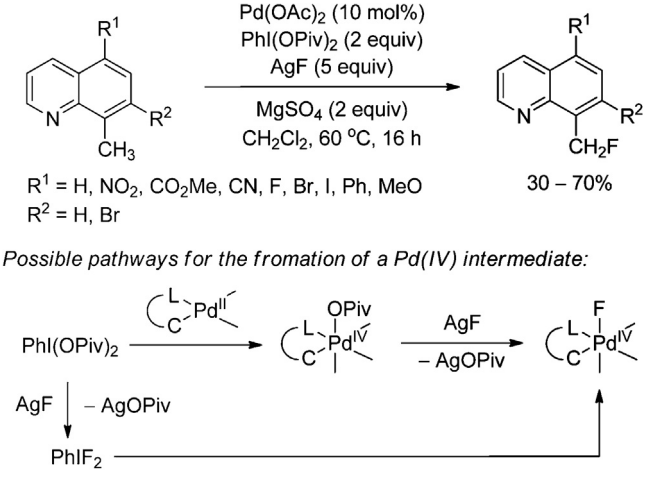
In 2012, Groves and coworkers developed a manganese-porphyrin-catalyzed oxidative C(sp^3)–H monofluorination with PhIO and fluoride ions (Scheme 11A) [9]. Simple alkanes and functionalized alkanes such as terpenoids are selectively fluorinated at sites that are otherwise difficult to access. Mechanism studies suggested that the bulky pre-catalyst $Mn^{III}Cl$ first reacts with AgF to form the active catalytic species $Mn^{III}F$, which is oxidized by PhIO to give the highly reactive Mn^{V}–oxo species. Then hydrogen atom abstraction from C–H by Mn^{V}–oxo species gives a carbon-centered radical and a $Mn^{IV}(OH)F$ species. Finally, the $Mn^{IV}(OH)F$ species undergoes a ligand-exchange to form a $Mn^{IV}F_2$ species, which serves as a fluorine radical source and reacts with the carbon radical to give the fluorination product. (Scheme 11B) In fact, a well-defined $Mn^{IV}(TMP)F_2$ complex has been isolated and established to be the key intermediate for radical transfer of fluorine. Similarly, the selective benzylic C–H fluorination has been achieved by switching the ligand on manganese from porphyrin to salen (Scheme 11C) [30]. Notably, the high affinity of Mn^{III} for fluoride enables a convenient late-stage ^{18}F labeling of aliphatic C–H bonds with the in-situ generated [^{18}F]fluorides, avoiding the conventional and laborious dry-down step prior to reaction [31].



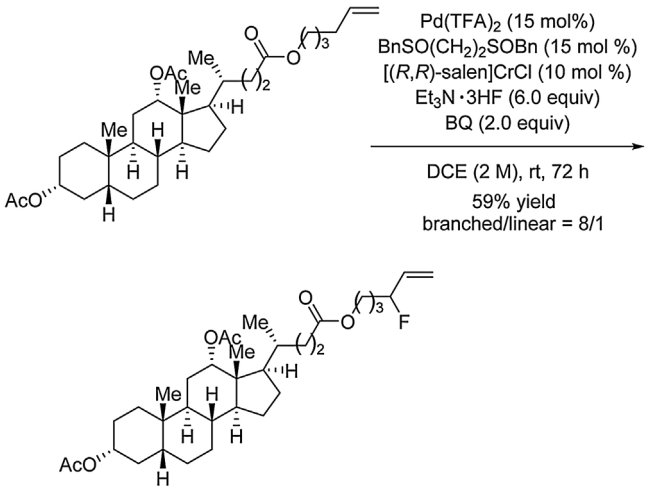
Scheme 11. Manganese-catalyzed oxidative C–H monofluorination (RCC = radiochemical conversion).



Scheme 12. Manganese-catalyzed oxidative fluorodecarboxylation.



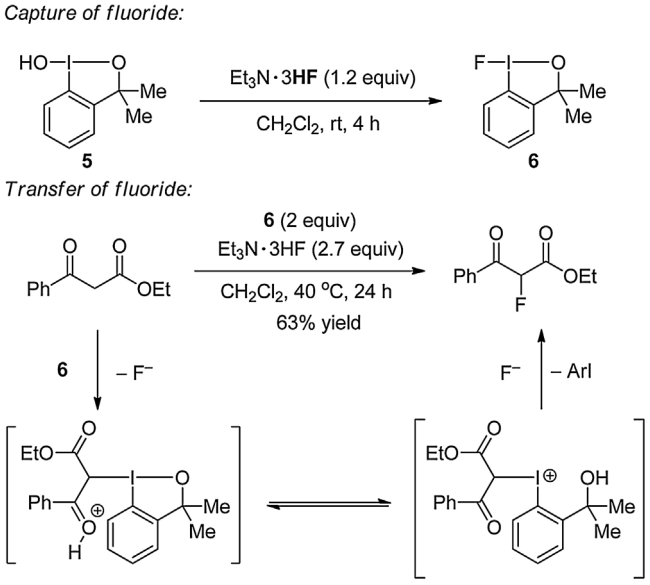
Scheme 13. Palladium-catalyzed oxidative benzylic C–H fluorination.



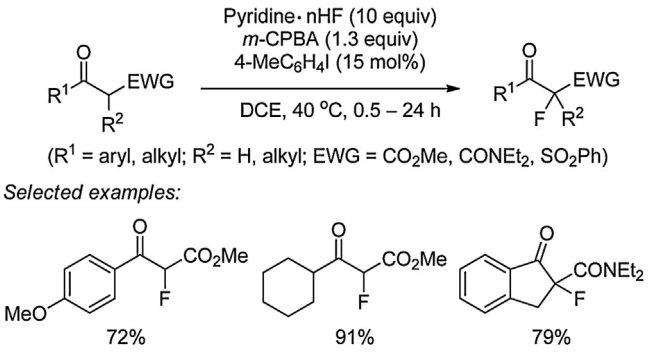
Scheme 14. Palladium-catalyzed oxidative allylic C–H fluorination.

This manganese-catalytic system is also applicable for oxidative fluorination of carboxylic acids. Very recently, Groves and coworkers developed the first catalytic decarboxylative fluorination reaction based on the nucleophilic fluoride ions by using a manganese-porphyrin catalysis system (Scheme 12) [32]. The catalyzed reaction of fluorinated benzylic and aryloxy carboxylic acids with KF or $Et_3N{\cdot}3HF$ in the presence of PhIO affords the corresponding fluorides in moderate yields, probably proceeding through the interaction of the Mn^{III} catalyst with iodine(III) carboxylates formed in situ from PhIO and the carboxylic acid substrates.

In addition to the manganese catalytic systems, the palladium catalytic systems are also promising for oxidative fluorination, which has been used for fluorination of benzylic and allylic C–H bonds with fluorides. In 2012, Sanford and coworkers presented a Pd-catalyzed benzylic C–H fluorination with AgF as the fluoride source and the hypervalent iodine reagent as the oxidant (Scheme 13) [33]. The reactions of 8-methylquinoline derivatives afford the 8-fluoromethylquinolines in moderate yields accompanying some C–H oxygenation byproducts. A possible pathway for C–F bond formation is the reductive elimination of a Pd^{IV}-alkyl fluoride



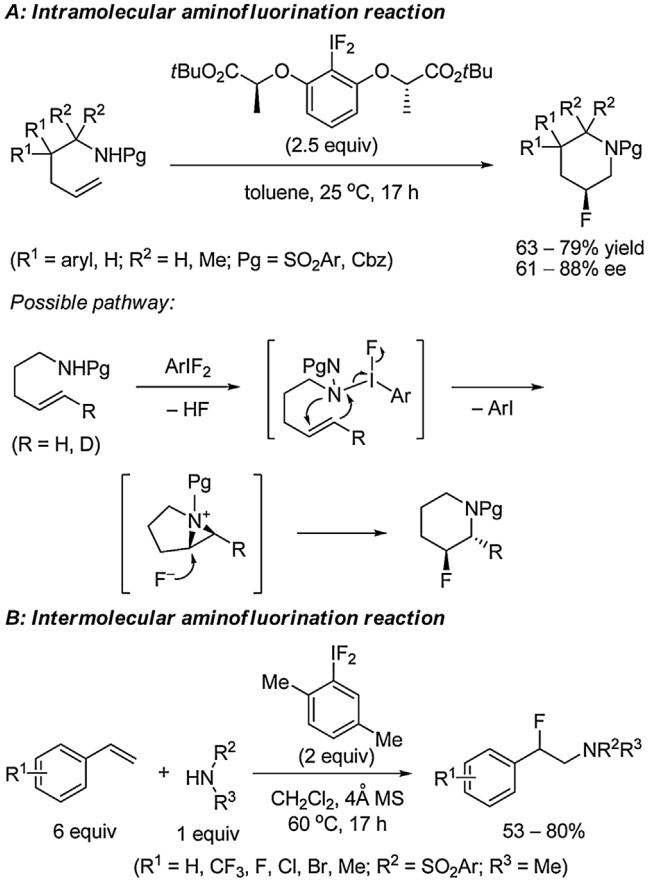
Scheme 15. Hypervalent iodine compound-mediated oxidative C–H fluorination.



Scheme 16. Aryl iodide-catalyzed oxidative C–H fluorination.

complex that arises from the oxidation of a cyclometalated Pd^{II}-alkyl complex by $PhI(OPiv)_2$ followed by ligand exchange of pivalate for fluoride at the resultant Pd^{IV} intermediate. Inspired by the allylic C–H functionalization with a Pd^{II}–sulfoxide catalyst system developed by White and coworkers, Braun and Doyle reported a Pd-catalyzed allylic C–H fluorination with $Et_3N{\cdot}3HF$ and benzoquinone (BQ) (Scheme 14) [34]. However, the employment of a Cr^{I}-complex as the co-catalyst is necessary to improve the conversion of the alkenes. A series of alkyl-substituted terminal alkenes are subject to the reaction to give the branched allylic fluorination products in moderate yields.

Hypervalent iodine reagents such as (difluoroiodo)arenes have been used as electrophilic fluorination reagents [35–37]. In 2013, Stuart and coworkers reported an electrophilic fluorination of $C(sp^3)$–H bonds using a well-defined hypervalent iodine reagent (Scheme 15) [35]. The air and moisture stable fluoroiodane **6**,



Scheme 17. (difluoroiodo)arenes-mediated oxidative aminofluorination of alkenes under metal-free conditions.

readily prepared by nucleophilic fluorination of the hydroxyiodane **5** with $Et_3N{\cdot}3HF$, was used as an electrophilic fluorinating agent to monofluorinate 1,3-ketoesters and difluorinate 1,3-diketones in good yields. In 2014, Kita, Shibata and coworkers developed a catalyzed fluorination of β-carbonyl compounds using a hypervalent iodine compound $ArIF_2$ in-situ generated from pyridine-hydrogen fluoride, *m*-CPBA, and a catalytic amount of iodoarene (Scheme 16) [36]. The reactions of an array of secondary and tertiary β-ketoesters, β-ketoamides, and β-ketosulfones provide the monofluorination products in good to excellent yields.

4. Oxidative fluorination of alkenes

Historically, the oxidative fluorination of alkenes had been conducted with high valent metal fluorides such as CoF_3 and $Pb(OAc)_2F_2$ [38]. Recently, more attention has been paid on oxidative fluorination of alkenes with mild and selective oxidants such as hypervalent iodine compounds [36,39–47].

(Difluoroiodo)arenes, which are readily available from (dichloroiodo)arenes and hydrogen fluorides, have been exploited for the fluoro-functionalization of a series of alkens and alkynes, and several reviews on hypervalent iodine compounds have covered this topic [39]. In 2013, Nevado and coworkers reported the first asymmetric fluorination of alkenes with chiral (difluoroiodo)arenes as the fluorination reagents (Scheme 17A) [40]. Regio- and enantioselective aminofluorination of pentenamines and hexenamines was achieved by using a di-*tert*-butyl lactate based hypervalent iodine compound. A reaction mechanism involving oxidation of sulfonamide rather than alkene was proposed. The intermolecular aminofluorination of styrene derivatives with (difluoroiodo)(*p*-xylene) and sulfonamides affords 2-fluoro-2-arylethanamines in good yields (Scheme 17B). Kita and Shibata demonstrated that the intramolecular reaction can be performed catalytically, by generating the chiral $ArIF_2$ reagent in situ in the presence of (*R*)-binaphthyl diiodide, *m*CPBA, and aqueous HF [36].

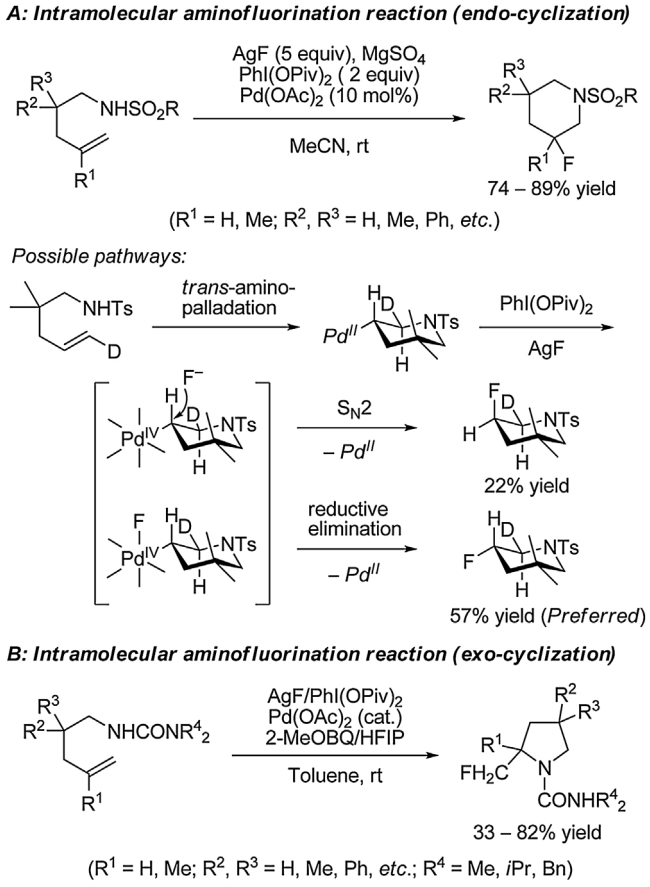
The combination of a nonfluorinated hypervalent iodine compound and a nucleophilic fluoride source is more convenient than the direct use of (fluoroiodo)arenes.

In 2009, Liu and coworkers reported a palladium-catalyzed intramolecular aminofluorination of enamines using the combination of PhI $(OPiv)_2$ and AgF (Scheme 18A) [41]. The reaction is believed to proceed through amino-palladation of alkenes followed by oxidative fluorination involving a Pd^{IV}–F complex. Interestingly, the regioselectivity of the aminofluorination can be controlled by the protecting group: pentenamines with a sulfonyl group prefers *endo*-cyclization [41] while the ones with a urea protecting group undergoes *exo*-cyclization (Scheme 18B) [42]. Intermolecular aminofluorination of styrene derivatives have been achieved in a similar way [43].

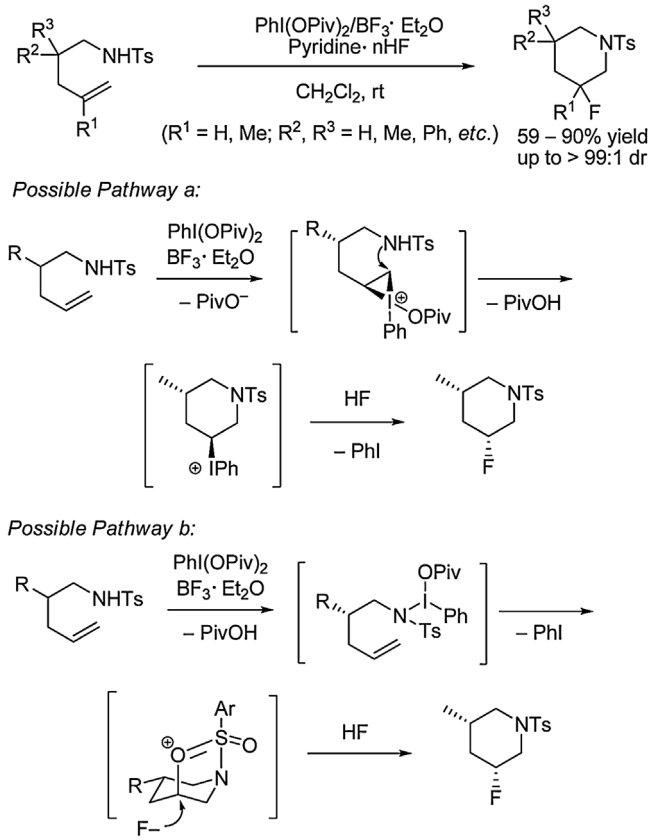
Several other research groups have shown that the enamines can also undergo fluorocyclizations under metal-free conditions (Scheme 19) [44–46]. In the presence of a hypervalent iodine compound and $BF_3{\cdot}Et_2O$, the reactions of sulfonyl-protected pentenamines and butenamines afford the *endo*-cyclization prodcuts in high yields.

Oxidants other than hypervalent iodine compounds have also been developed for fluorination of alkene systems.

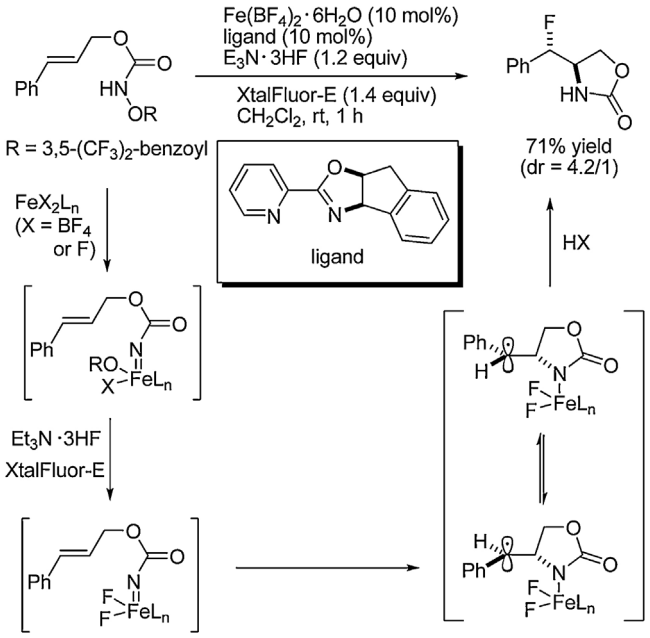
Xu and coworkers showed that iron(II)-catalyzed aminofluorination of allyl alcohol-derived acyloxyl carbamates with $Et_3N{\cdot}3HF$ as fluoride source affords the *exo*-cyclization products in high regioselectivity (Scheme 20) [48]. In this reaction, the functionalized hydroxylamine serves as the oxidant and an iron–nitrenoid is a possible intermediate.



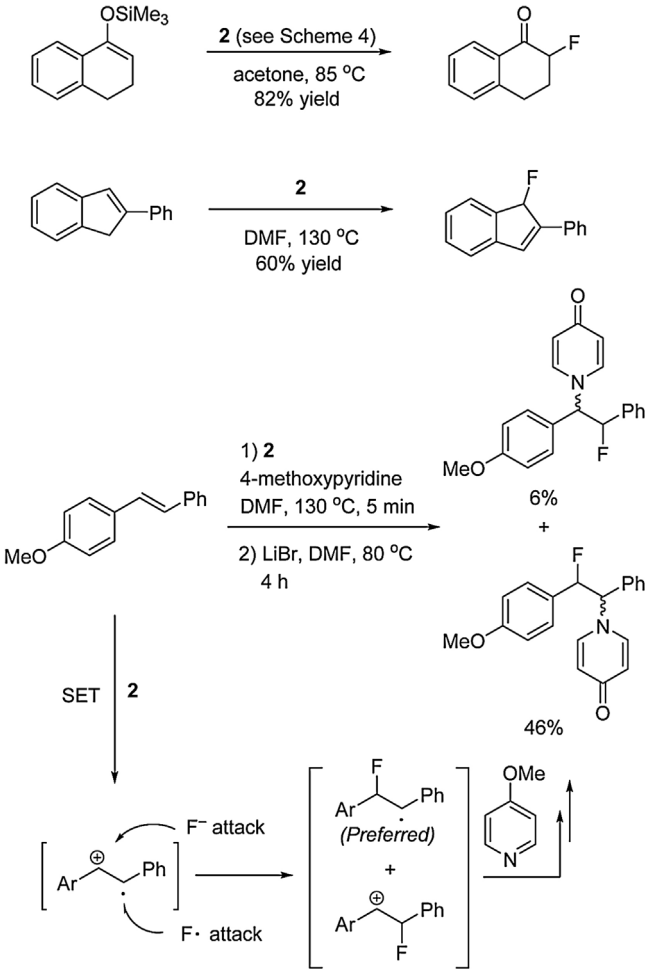
Scheme 18. Hypervalent iodine compound-mediated intramolecular olefin aminofluorination under palladium catalysis.



Scheme 19. Hypervalent iodine compound/$BF_3{\cdot}Et_2O$-mediated intramolecular olefin aminofluorination under metal-free conditions.



Scheme 20. Iron-catalyzed intramolecular olefin aminofluorination.



Scheme 21. Palladium-mediated oxidative fluorination of olefins.

In addition, as described previously, a well-defined Pd^{IV}–F complex prepared from a fluoride salt has been recognized as an efficient electrophilic fluorination reagent [18]. Ritter and coworkers showed that this Pd^{IV}–F complex is not only applicable for the fluorination of alkene derivatives such as enol ethers and 2-phenylindene to afford α-fluoroketones and allyl fluorides, respectively, but also can difunctionalize alkenes such as stilbenes to afford aminofluorination products (Scheme 21).

5. Conclusions

In summary, over the past four years, a number of oxidative fluorination reactions using the combination of nucleophilic fluorides and additional oxidants have been developed for introducing fluoride into the nucleophilic or electron-neutral systems. These newly developed reactions are of high selectivity and efficiency, and provide a pathway for the more efficient use of the abundant, yet less nucleophilic fluorides. However, compared with the wide substrate scope of fluorination with nitrogen-based electrophilic fluorination reagents, the oxidative fluorination with fluorides is still in its infancy. It is expected that in the future, more attention will be paid on these conceptually novel transformations to extend their synthetic applications.

Acknowledgements

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