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Electrochemical Fluorination of Alkenes by Hypervalent λ^3-Iodane Mediator

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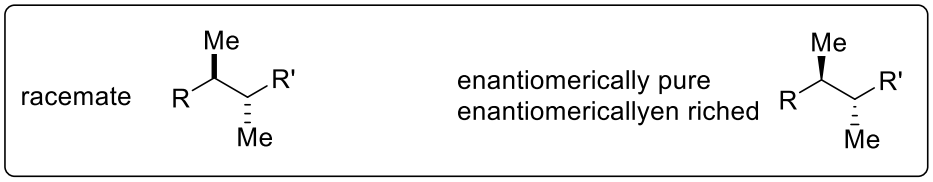
In this thesis, the relative configuration of racemates is represented by straight lines (bold or hashed). The absolute configuration of enantiomerically pure or enriched compounds is represented by wedge-shaped lines (bold or hashed).



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Although the road is endless and faraway,

I still want to pursue the truth in the world.

---Yuan Qu

Abstract

As alkenes are one of the most important functional groups, their functionalization has developed into a powerful tool for generating highly functionalized skeletons in organic synthesis, finding a widely applicable alkene fluorination protocol is of great importance for the preparation of fluorinated compounds. In recent years, hypervalent iodane compounds have attracted much interest due to their reactivity, ease of synthesis and their mild reaction conditions, and they have been successfully employed in numerous fluorination reactions. Herein, we developed a new protocol to synthesize the hypervalent λ^3-iodanes by electrochemical method and applied it in different fluorination reactions.

We first established a general ex-cell and in-cell electrochemical protocol for the 1,1-difluorination of a variety of electronically substituted diverse styrenes. For electron-rich and oxidation sensitive styrenes, we employed 4-*tert*-butyliodobenzene as the mediator, amine·HF as the electrolyte and fluorine source in an undivided cell for the ex-cell electrochemical 1,1-difluorination. For electron-poor styrenes, we used 4-iodotoluene as the mediator, Py·HF as the electrolyte and fluoro source, dry degassed DCM as the solvent under Argon atmosphere in an undivided cell for the in-cell electrochemical 1,1-difluorination. The desired product can be obtained in a wide substrate scope with moderate to good yields.

Then, we developed a method to prepare 5-fluoromethyl-2-oxazolines through electrochemical iodoarene-catalyzed fluorocyclization of *N*-allylcarboxamides. We found that the product could be obtained best yield under 8 mA constant current in 4.0 h electrolysis by utilizing Py·HF as the electrolyte and fluorine source, 20% of 4-*tert*-butyliodobenzene as the catalyst, DCM as the solvent under Air atmosphere. The reaction proceeds under mild reaction conditions with high efficiency, and broad substrate scope, including natural-product-derived and polyfunctionalized molecules.

Last, we present an electrochemical iodoarene-catalyzed aminofluorination of alkenes as a general, efficient, and mild approach for the synthesis of 3-fluoropiperidine compounds. We found the best yield was obtained under 8 mA constant current in the presence of 20% of 4-iodobenzotrifluoride as the catalyst, $BF_3 \cdot Et_2O$ as the fluorine source, and $n Bu_4NBF_4$ as the electrolyte and in DCM at room temperature after 4 h electrolysis. The reaction proceeds smoothly to afford the desired product with moderate to good yields at room temperature under air in an undivided cell.

Table of Contents

I. Theoretical Background

1. Introduction

In recent decades, with the growing concept of green chemistry,[1] hypervalent iodine compounds have received more and more attention in organic synthetic chemistry.[2] Due to their similar properties as transition metals, hypervalent iodanes play a great role in the functionalization of organic compounds, solve the problems of harsh conditions and pollution of many heavy metal-catalyzed reactions, and providing new methods for the functionalization reactions of organic compounds.

In 1886, the chemist Willgerodt synthesized the first hypervalent λ^3-iodane compound $PhICl_2$ (**1**),[3] (Figure 1) which subsequently attracted the attention of many chemists and further research into hypervalent iodine compounds. In 1892, Willgerodt also reported the synthesis of iodosobenzene (**2a**) and $PhI(OAc)_2$ (**3**).[4] Later, Hartmann and Meyer synthesized 2-iodoxybenzoic acid in 1893[5] and diaryl iodonium salts in 1894.[6] Subsequently, research on hypervalent iodine compounds suffered a long period of depression. In the 1980s, with the discovery of several new hypervalent iodanes and the development of modern organic synthesis techniques, hypervalent iodine chemistry became one of the hot spots again in organic chemistry research. In recent years, the use of hypervalent iodine for various functionalization reactions under metal-free and mild conditions has driven the development of hypervalent iodine chemistry.

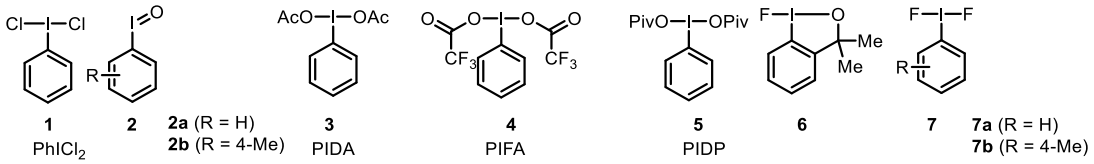


Figure 1. Important representatives of the hypervalent iodanes.

For hypervalent iodanes there are two major classes: the tri- and the pentavalent iodanes, or according to IUPAC λ^3- and λ^5-iodanes. However, λ^5-iodanes are used almost exclusively as oxidizing agents, but the corresponding λ^3-iodanes are also frequently used in atom transfer reactions. The iodine atom in λ^3-iodane (RIX_2) has 10 valence electrons and exhibits a distorted, trigonal T-shaped geometry. The two electronegative heteroatomic ligands X occupy the top position, while the less electronegative carbon ligand R and the two electron lone pairs are located at the equatorial position (Figure 2a). This three-center-four-electron (3c-4e) bond is called a hypervalent bond. Both I-X bonds are strongly polarized and thus longer and weaker than a normal covalent bond, which explains the electrophilicity of the hypervalent iodane atom.[7] In a study of ligand effects on hypervalent iodine compounds, the *trans* effect exhibited by the substituents X, as observed in transition metal complexes, significantly influences the stability and thus the reactivity of hypervalent iodane molecules.[8] In linear λ^3-iodanes $ArIX_2$, the interaction of the filled 5p

orbital of the central iodine atom and the half-filled orbitals of the two ligands L trans to each other leads to formation of three molecular orbitals: bonding, nonbonding and antibonding (Figure 2b).

For the classification of hypervalent iodane molecules, Martin and Arduengo have introduced a nomenclature known as the Martin-Arduengo nomenclature.[9] The basic structure of this designation is [N-X-L], where X is the central atom, N is the number of valence electrons at the central atom and L the number of ligands. The following are the two main types of hypervalent iodanes: 10-I-3 and 12-I-5. Since λ^5-iodanes are commonly used as an oxidizing agent, here we focus on the more widely used and valuable λ^3-iodanes.

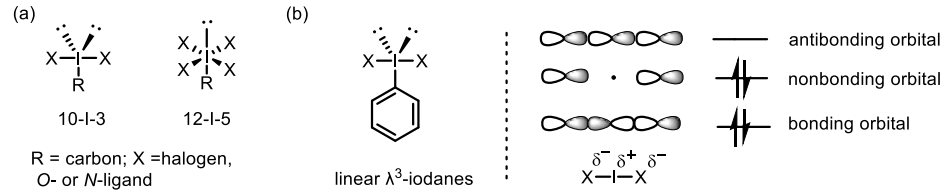


Figure 2. (a) Typical structural types of λ^3-iodanes and λ^5-iodanes (b) linear λ^3-iodanes structures and molecular orbitals of the hypervalent X-I-X bond.

Due to similar oxidation properties with some transition metals such as Hg (II), Pb (IV), Cr (VI) and Os (VIII), λ^3-iodanes are often used as oxidizing agents that are easy to prepare, mild and environmentally friendly. Probably the best known and most used λ^3-iodanes for oxidation are (bisacetoxyiodo)benzene (**3**, PIDA) and [bis(trifluoroacetoxy)iodo]benzene (**4**, PIFA). They are also used in many total syntheses of biologically important natural products, [10,11] such as erysotramidine [12] and isoprekinamycin.[13] In addition, hypervalent iodanes have shown promising applications in organic electrochemistry,[14-16] photochemistry[17,18] and asymmetric synthesis.[19,20] However, (dichloroiodo)benzene **1** and (difluoroiodo)arene **7a** and **7b** are also often used as effective electrophilic halogenation reagents.[21-23] In particular, (difluoroiodo)arenes **7** play a very important role in the fluorination reactions because of their unique properties.[22]

In 1901, Weinland and Stille reported the first synthesis of difluoroiodotoluene (**7b**),[24] by treating iodosotoluene (**2b**) with aqueous HF. Until now, many other synthetic methods have been reported.[25] In principle, two general strategies are applicable to obtain difluoro λ^3-iodanes **7**, the first method involves ligand exchange on an existing λ^3-iodanes compound **8** with nucleophilic fluorides (Figure 3a, top). This one-step ligand exchange can be performed using different organic and inorganic fluorine sources, such as TBAF, AgF or KF, but in most cases HF with ligand trapping additives, such as HgO, is required.[26-29] Another strategy relies on the oxidative fluorination of an iodoarene **9** using electrophilic reagents like F_2 gas, XeF_2, and ClF (Figure 3a, below).[30-33] In 2005, a significant advancement to more practicable and general applicable synthetic methods has been reported by Shreeve and co-workers using selectfluor (**10**)

(Figure 3b), which plays a dual role: as oxidant and F-delivering agent.[34] In 2017, Gilmour and co-workers developed an operationally simple route to synthesis of difluoroiodotoluene (**7b**) by using CsF to replace the traditional hazardous HF reagents.[35] However, (difluoroiodo)arenes **7** are difficult to handle because of the highly hygroscopic properties. Their isolation and purification as well as the in storage are difficult. As a result, they are usually prepared *in situ* and used directly without any isolation. To address these issues, in 2012, Legault and co-workers reported the crystal structure of the firs cyclic fluoroiodane **6** (Figure 1), which has since attracted considerable attention from the fluorination community as it represents an air- and moisture-stabilized fluorinated iodane.[36] In the five-membered ring structure, the presentation of oxygen ligand makes **6** a bench-stable electrophilic fluorination reagent. As **6** is purely an "electrophilic" fluorinating agent, it has also been extensively investigated in different fluorination reactions, such as, α-fluorinations of carbonyl compounds,[37-39] *gem*-difluorination of styrenes,[40,41] fluorocyclization of alkenes.[39, 42-48] However, the reaction often requires stoichiometric amounts of this fluorinated reagent and requires metal-based Lewis acid to activate the reagent, which greatly limits its wide application in organic synthesis. Despite the low stability of linear difluoro λ^3-iodanes **7**, especially difluoroiodotoluene (**7b**), have been established as more powerful and selective fluorination reagents in organic synthesis.[49-64] In recent years, several groups have applied aryl iodides as catalysts together with selectfluor (**10**)[35,65-73] or *m*CPBA[74-78] as the oxidant and the amine·HF as the fluorine source, using this mixture to generate hypervalent iodine compounds $ArIF_2$ *in situ* for the various fluorination reactions.

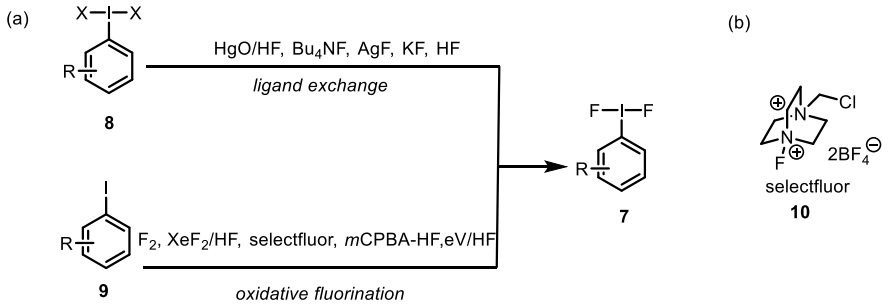
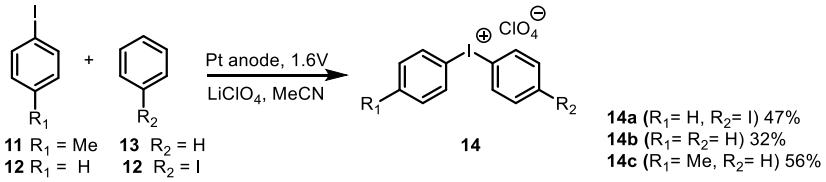


Figure 3. (a) Methods for the preparation of difluoro λ^3-iodanes (b) The structure of selectfluor (**10**)

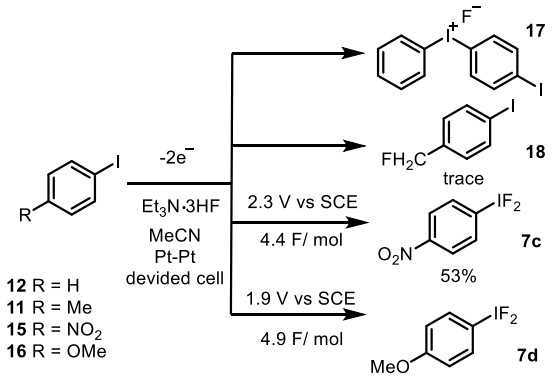
Nevertheless, their preparation typically requires the use of an excess of expensive or hazardous oxidants such as *m*CPBA, peractic acid, oxone, hydrogen peroxide, and selectfluor (**10**), which makes the whole process cumbersome. Organic electrosynthesis, which employs electrons as reagents, has been demonstrated to be a versatile and environmentally friendly synthetic tool and attracted renewed interests.[79-85] Electrochemical methods for the generation of hypervalent iodanes has not been reported recently.[86-90] Rather, the potential of this strategy was discovered a long time ago. The first report on the electrogeneration of diaryliodonium salts **14a**-**14c** dates to 1967, wherein Miller and Hoffmann described the anodic oxidation of aryl iodides coupling with benzene derivatives using a platinum anode in

combination with an $LiClO_4/CH_3CN$ electrolyte and a divided cell under potentiostatic conditions (Scheme 1).[91]



Scheme 1. First electrochemical synthesis of diaryliodonium salts.

Since then, several hypervalent iodanes have been synthesized using electrochemical methods. In contrast, the electrochemical generation of hypervalent λ^3-F-iodanes is considerably more difficult. Until 1994, the Fuchigami group achieved this transformation by constant potential electrolysis of several 4-substituted iodobenzenes **9** in a divided cell using an electrolyte consisting of $Et_3N{\cdot}3HF$ in acetonitrile and platinum electrodes (Scheme 2).[92] In this way, the electrolysis of iodobenzene (**12**) showed only the formation of the diaryliodonium salt (**17**), whereas 4-iodotoluene (**11**) leads to benzyl fluorination under same conditions, producing fluorinated product 1-(fluoromethyl)-4-iodobenzene (**18**) and some other by-products. In the case of the 1-iodo-4-nitrobenzene (**15**), the desired product (difluoroiodo)arene (**7c**) was obtained in 53% yield (2.3 V vs. SCE). The electron-rich 4-iodoanisol (**16**) was oxidized at lower positive potential (1.9 V vs. SCE), but the desired product (difluoroiodo)arene (**7d**) was much less stable and could not be isolated.



Scheme 2. Direct anodic oxidation of iodobenzene derivatives.

This electrochemical protocol can serve as a complementary method for the diverse synthesis of fluorinated compounds and provides a new method to prepare fluorinated compounds of interest in medicinal chemistry and chemical biology. However, the preparation of fluorinated compounds with this method has been rarely reported. The group of Prof. Dr. Tanja Gulder investigates fluorination reactions with the electrochemical method for some challenging transformations. The presented work focuses on electrochemical strategies to achieve some fluorination reactions.

2. State of Knowledge

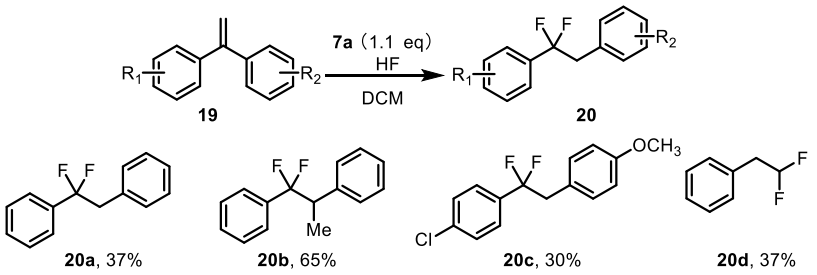
2.1. Linear Hypervalent λ^3-Iodane Mediated Fluorinations of Alkenes

Fluorine-containing compounds have shown wide applications due to their distinct chemical, physical, and biological properties. These unique properties make organofluorine compounds are frequently utilized in pharmaceutical, agrochemical, and materials sciences.[93-96] For these reasons, methods to synthesizing such molecules have been actively investigated for many years. Hypervalent iodanes are also widely used in carbon-fluorine bond building reactions due to their similar properties as transition metals.[97,98] Importantly, fluorination reactions mediated by hypervalent iodine compounds generally have milder reaction conditions and their own characteristics in terms of substrate scope and regioselectivity. (Difluoroiodo)arenes **7** is one of the more widely used λ^3-iodane compounds for carbon-fluorine bond construction, which has good nucleophilicity and can provide a fluorine source. This part presents a short summary of some of the reactions for the construction of carbon-fluorine bonds mediated by hypervalent iodanes.

2.1.1 Stoichiometric *gem*-Difluorination of Alkenes

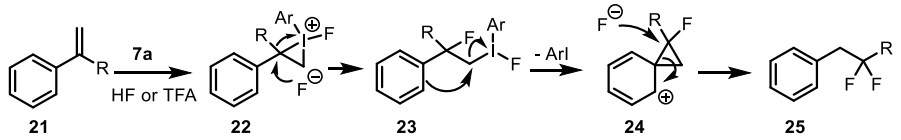
The geminal difluoro group, or 1,1-difluoro group, is of particular importance in medicinal chemistry due to its specific steric and electronic properties.[99,100] The *gem*-difluoro group can serve as carbonyl and sulfonyl mimetics, as well as replace oxygen atoms in phosphates, sulfates, and aryl ethers. More specifically, the difluoromethyl (CF_2H) moiety can be used as a biofacilitator for alcohols and thiols because of the nature of its highly polarized C-H bond. Although great progress has been achieved in synthesis of CF_2-containing compounds, these approaches generally use pre-installed CF_2 groups such as $BrCF_2R$ to generate CF_2-containing small molecules.[101-103] Among the methods developed, direct difluorination of alkenes mediated by hypervalent iodanes is one of the most attractive strategies for the synthesis of *gem*-difluorinated compounds.

The use of styrene derivatives **19** as the starting materials to generate *gem*-difluorinated products **20** mediated by hypervalent iodane has been known for a long time.[104-107] Especially 1,1-diphenylethene (**19a**) has been a popular substrate to explore electrophilic fluorinations with a range of modified linear λ^3-difluoroaryliodines. In this process, the role of HF did not exceed that of an acidic additive, which activated **7a** for the nucleophilic attack at the λ^3-iodane atom via hydrogen bonding. Similar yields were obtained When HF was replaced by a different acid such as TFA. Although the substrate scope of this transformation was rather limited, the method allowed, in general, the conversion of tri- and monosubstituted alkenes **19b** and **19d** as well as starting materials with differently equipped aryl portions, such as **19c**, to the desired products in 30%−65% yields (Scheme 3).



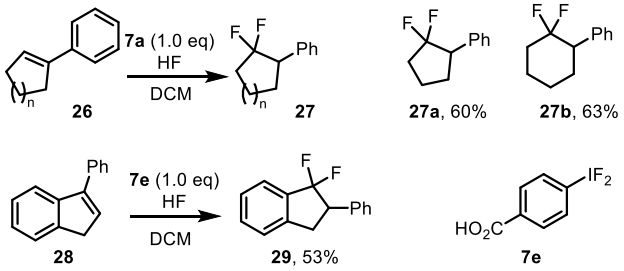
Scheme 3. Fluorination of diphenylethene **19** with $PhIF_2$ and examples thereof.

Mechanistic studies showed that, the activated iodane **7a** attacks the alkene in **21** to form a three-membered cyclic iodiranium **22**, which would be opened by the nucleophilic attack of the fluoride ion leading to the alkyl iodonium adduct **23**. Then, due to the good leaving group ability of the iodoarene moiety in **23**, an intramolecular 1,2-phenyl shift produced the spirocyclic phenonium ion **24**, which is then attacked by a second fluoride at the fluorinated carbon to produce the geminal difluorinated product **25** (Scheme 4).



Scheme 4. Proposed mechanism of the *gem*-difluorination of styrene **21** involving a 1,2-aryl shift.

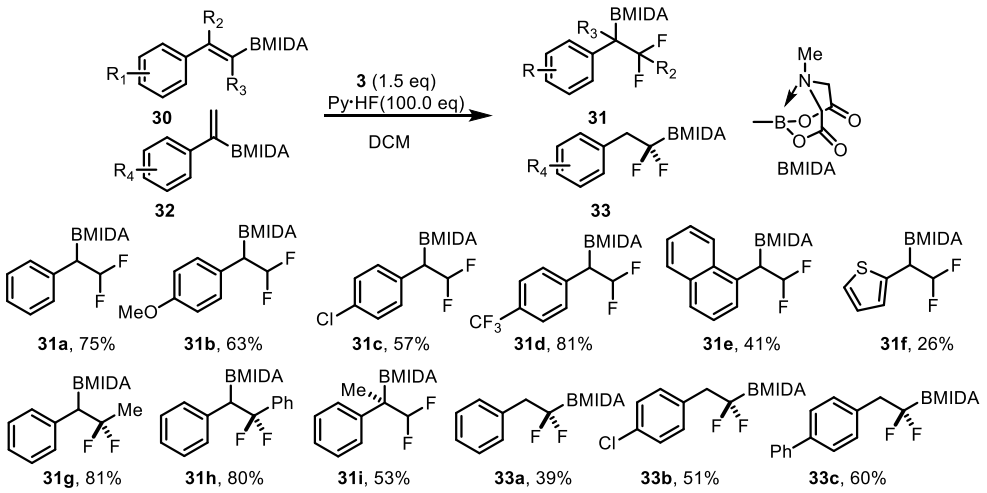
Internal olefins **26** in conjugation to an aromatic ring have also been studied in such transformations, where they undergo fluorinative rearrangements to give *gem*-difluorinated products.[106,107] Examples of these transformations from Zupan and Patrick include the conversion of 1-phenylcyclopentene (**26a**), phenylcyclohexene (**26b**), and phenylindene (**28**) to the corresponding *gem*-difluorinated products **27a**, **27b** and **29** in 53%−63% yields (Scheme 5).



Scheme 5. Fluorinative rearrangement of cyclic alkenes **26** and **28** with (difluoroiodo)arenes.

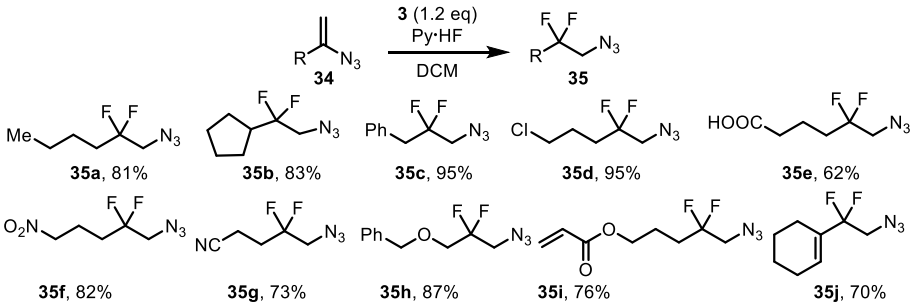
In 2018, Wang and co-workers developed a regioselective migratory *gem*-difluorination of aryl-substituted alkenyl *N*-methyl-iminodiacetyl (MIDA) boronates with Py·HF in the presence of stoichiometric amounts

of the oxidant PIDA (**3**).[108] Depending on the substitution pattern of the substrates, the protocol enabled the efficient construction of α- and β-difluorinated alkylboron compounds (Scheme 6). A number of commonly encountered functional groups such as ether **30b**, chloro **30c**, and trifluoromethyl **30d** were well tolerated, giving the corresponding products **31b**-**31d** in moderate to good yields. Other aryl-substituted alkenyl MIDAboronates, such as naphthyl- **30e** and thienyl-substituted **30f** substrates were also compatible with the reaction conditions, albeit in lower yields. Substrates substituted with an additional methyl or aryl group at α-position provided the difluoroethyl product **31g** or difluorobenzyl product **31h** in 81% and 80% yield. By installing a substituent at the position α to boron, the difluoromethylated tertiary alkylboronate can be obtained **31i** in 53% yield. Interestingly, the employment of 1,1-disubstituted alkenyl MIDA boronates **32a**-**32c** resulted in the chemoselective formation of α-difluorinated alkylboronates **33a**-**33c**, with no formation of β-difluorinated alkylboronates observed.



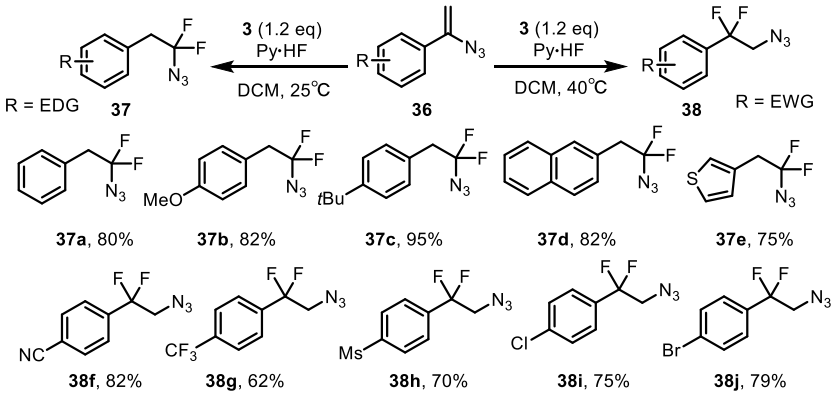
Scheme 6. Stoichiometric *gem*-difluorination of substituted styrenes **30** and **32**.

In 2020, the Bi group reported a novel *gem*-difluorination including an1,2-azide migration. Starting from the readily available α-vinyl azides **34** *in situ* generated $PhIF_2 \cdot HF$ enabled the synthesis of a range of β-difluorinated alkyl azides (Scheme 7).[109] Vinyl azides **34** bearing alkyl and benzyl groups were smoothly converted to products **35a**-**35c** in 81%−95% yield. α-Alkyl vinyl azides **34d**-**34h** featuring a variety of functionalities on the terminal carbon of the alkyl chain, (e.g., chloro, carboxylic acid, nitro, cyano, and ether groups) also proved to be suitable substrates, giving products **35d**-**35h** in 62%−95% yield. Substrates with α-substituents such as acrylic ester **34i**, cyclohexenyl **34j** moieties also selectively delivered the desired *gem*-difluorinated products **35i** and **35j** in 76% and 70% yields, without detrimental fluorination of the other unsaturated functionality of the α-substituents.



Scheme 7. Stoichiometric *gem*-difluorination of vinyl azides **34**.

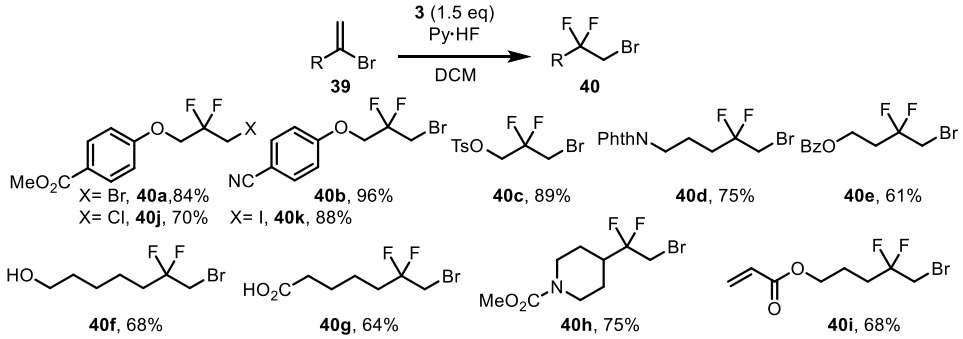
Interestingly, α-aryl vinyl azides **36** featuring alkyl and alkoxy groups (EDGs) at any position on the aryl ring were efficiently transformed into the corresponding 1,2-aryl migration products **37a**-**37e** in 75%−95% yield, and no 1,2-azide migration products were observed (Scheme 8). Azides with strong electron-withdrawing groups (EWGs) on the aryl moiety **36f**-**36j** underwent the expected *gem*-difluorination and 1,2-azide migration to afford the corresponding products **38f**-**38j** in 62%−82% yields.



Scheme 8. Stoichiometric *gem*-difluorination of α-aryl vinyl azides **36**.

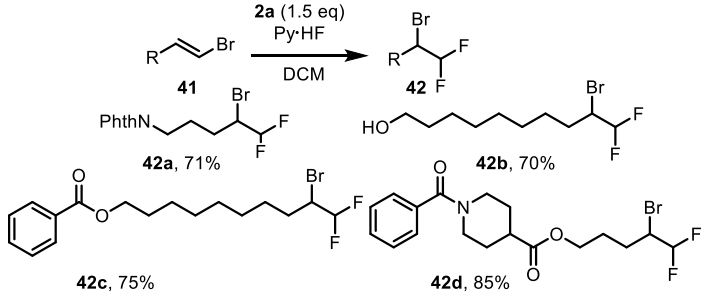
In 2021, Liu and co-workers developed a *gem*-difluorination following a 1,2-halo migration of vinyl halides **39** with *in situ* generated $PhIF_2$·HF (Scheme 9).[110] Substrates such as **39a** and **39b**, are compatible for the reaction, giving the corresponding products **40a** and **40b** in 84% and 96% yields, respectively. A series of commonly encountered functional groups were well tolerated, such as tosyloxy **39c**, imide **39d**, ester **39e**, hydroxyl **39f**, carboxyl **39g** moieties on the terminal carbon of the alkyl chain also underwent the reaction smoothly, providing the corresponding products **40c**-**40g** in moderate to excellent yields. In the case of the substrate with an *N*-protected piperidine moiety, the reaction proceeded smoothly as well and furnished the desired product **40h** in 75% yield. It is worth noting that the other unsaturated functionality in **39** such as **39i** remained intact during the reaction, leading to 68% yield of the desired product. Moreover, the reaction

was not restricted to vinyl bromides. Vinyl chloride **39j** and vinyl iodide **39k** were also competent substrates in this reaction system, yielding the corresponding products **40j** and **40k** in good yields.



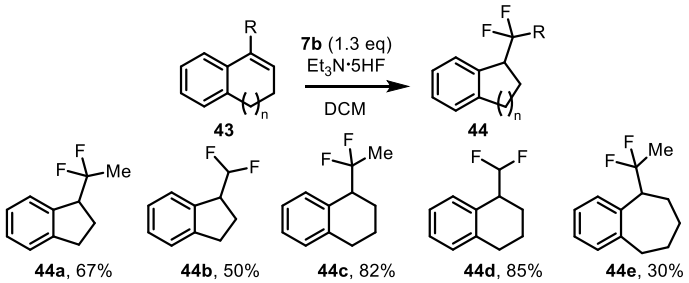
Scheme 9. Stoichiometric *gem*-difluorination of vinyl halides **39**.

For the β-substituted vinyl bromides **41**, they used a combination of PhIO (**2a**) and Py·HF in DCM to provide the secondary difluoromethyl substituted bromides in 70%−85% yield at room temperature (Scheme 10). A good functional group tolerance was found as expected (**42a**-**42d**).



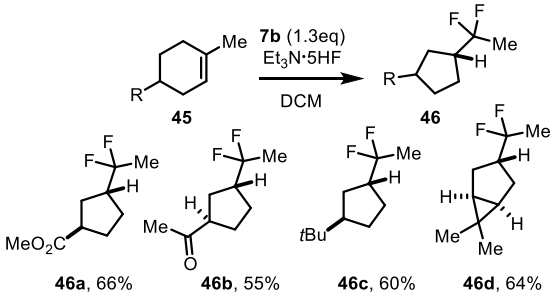
Scheme 10. Stoichiometric *gem*-difluorination of vinyl bromides **41**.

In addition, **7b** was also used for ring-contraction and ring-expansion reactions of alkenes. In 1998, Hara and Yoneda reported *gem*-difluorination of cycloalkenes under ring-contraction.[111] In this case, the addition of $Et_3N{\cdot}5HF$ was crucial for activating **7b** and served as the electrophilic fluorination reagents in order to obtain good yields of products **44**. For cyclohexenes **43a** and **43b**, heptenes **43c** and **43d**, and octenes **43e**, the reaction gave the desired product **44a**-**44e** in 30%−85% yield (Scheme 11).



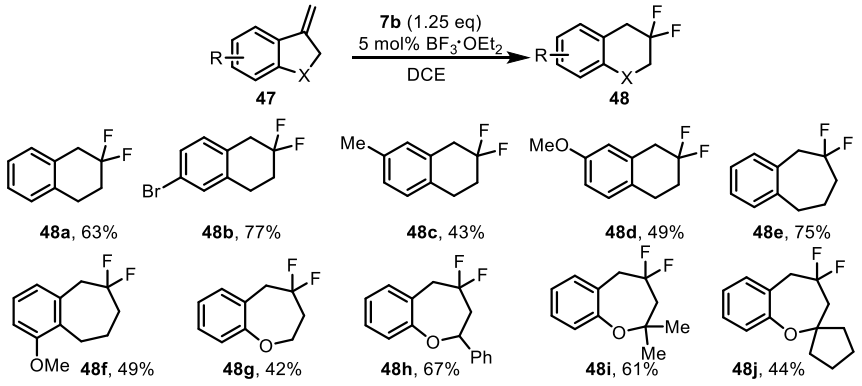
Scheme 11. Fluorine-triggered ring contractions of aryl annulated cycloalkenes **43**.

Interestingly, these ring contraction reactions are not limited to benzylic alkenes. Unexpectedly, the methylated cyclohexene **45a** underwent the fluorinative ring contraction to give the difluoroethyl cyclopentane **46a** in 66% yield. This outcome was also observed in the case of 4-acetyl **45b** and 4-*tert*-butylcyclohexene **45c** derivatives as well as carene (**45d**), giving the corresponding products **46b**-**46d** in 55%−64% yields (Scheme 12).



Scheme 12. Fluorinative ring contraction of cyclic alkenes **45** bearing trisubstituted alkene moieties.

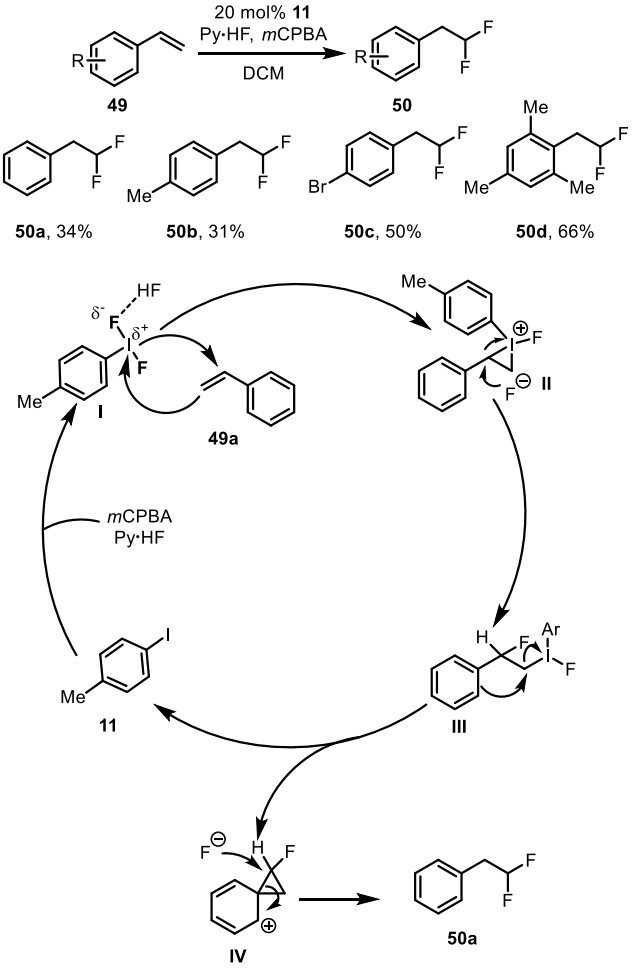
In 2019, Murphy and co-workers developed a fluorinative ring-expansion of alkenes **47** mediated by **7b**, which provided β, β-difluoroalkyl arenes **48** in moderate to good yields (Scheme 13).[112] Substrates with different substituents, such as bromo **47b**, methyl **47c** and methoxy **47d** were compatible with the transformation to afford the desired products **48b**-**48d** in 33%−79% yield. Tetralin derivatives **47e** and **47f** were also tolerated, giving the desired products **48e** and **48f** in 75% and 49% yields, respectively. Alkene substrates derived from the chromane skeleton **47g**-**47j** were also investigated, and the desired product **48g**-**48j** was obtained in 42%−67% yield. This mild and operationally simple reaction constitutes a novel strategy for synthesizing fluorinated motifs not readily accessible via other direct fluorination methods.



Scheme 13. Fluorinative ring-expansion of alkenes **47** mediated by **7b**.

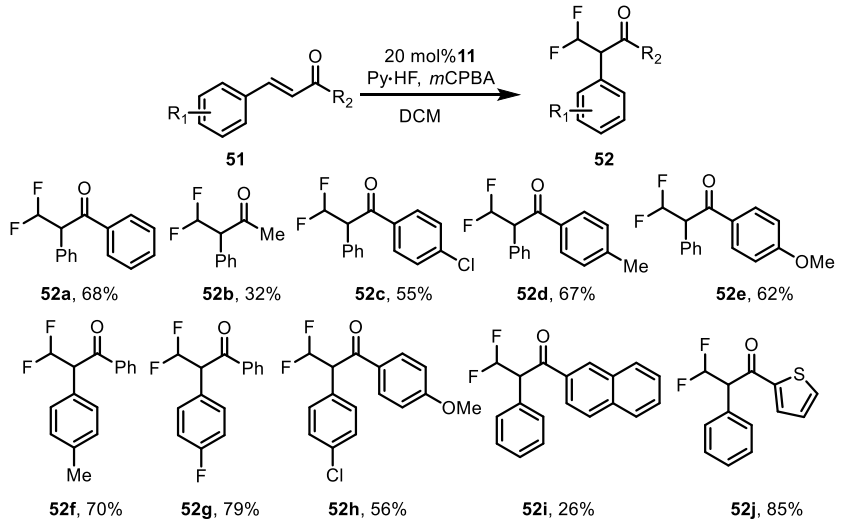
2.1.2 Catalytic *gem*-Difluorination of Alkenes

Despite importance of hypervalent iodane in fluorination reactions, the catalytic 1,1-difluorination of alkenes remains a challenge. As a result, stoichiometric strategies that are employed, where efficiency is frequently compromised by the loss of configurational integrity. Reagent cost, tempered nucleophilicity, and solubility issues must also be considered. In 2015, Kitamura and co-workers reported *gem*-difluorination of styrenes **49** under hypervalent iodane catalysis.[113] When styrenes **49** were reacted with 20 mol% 4-iodotoluene (**11**) as catalyst, *m*CPBA as the oxidant, and an excess Py·HF as the fluorine source, they were converted to the *gem*-difluoride products **50a**-**50d** in 34%−66% yield (Scheme 14). Although the catalytic efficiency in the fluorination of styrenes is not high, the present results indicated that the fluorination of styrene can, in principle, proceed moderately under the catalytic conditions.



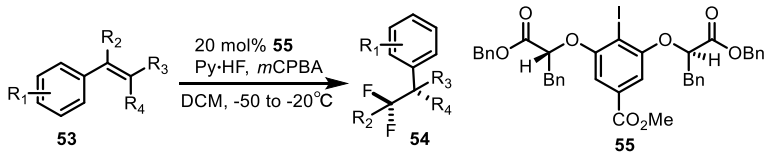
Scheme 14. Catalytic *gem*-difluorination of styrenes **49** and proposed mechanism**.**

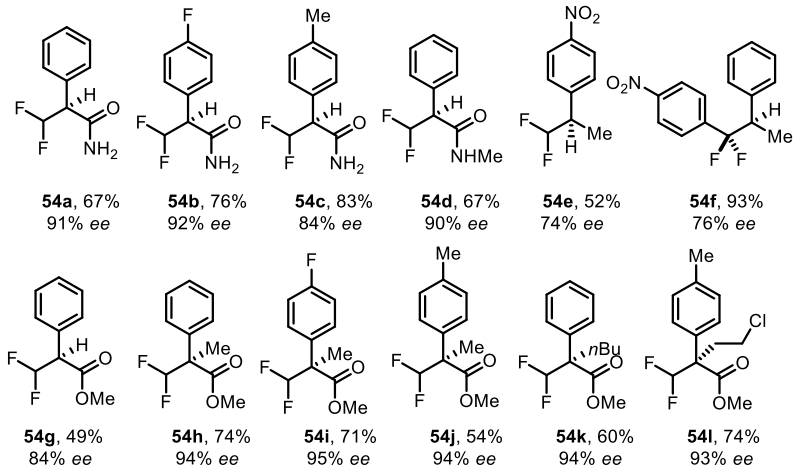
In 2018, the Kitamura group expanded the substrate scope of a catalytic *gem*-difluorination to α-aryl-α, β-unsaturated ketones **51**.[114] The fluorination reaction of α, β-unsaturated ketones **51** bearing alkyl groups such as methyl **51b**, electron-donating, electron-withdrawing, electron-donating, naphthyl **51i**, and thienyl **52j** groups gave the corresponding fluorinated products **52b**-**52j** in 26%−85% yield (Scheme 15).



Scheme 15. Catalytic *gem*-difluorination of α, β-unsaturated ketones **51**.

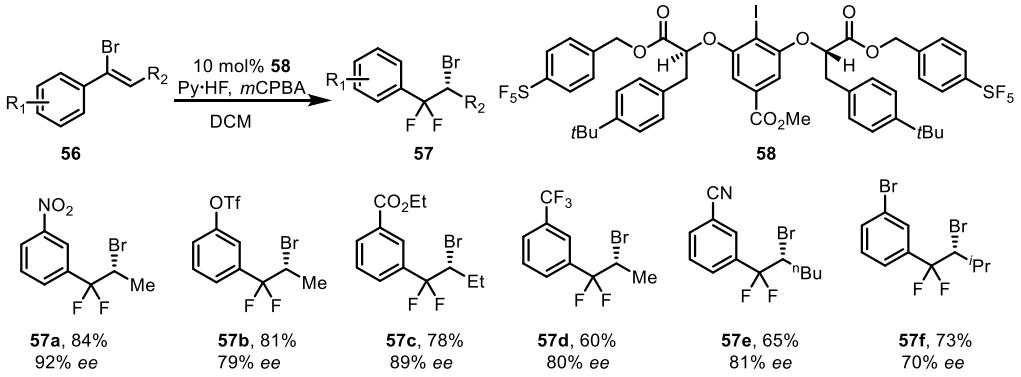
This general strategy for *gem*-difluorinations was further advanced by Jacobsen and co-workers in 2016, who developed a catalytic, asymmetric synthesis of difluoromethylated stereocenters from cinnamic acid-derived precursors **53** (Scheme 16).[115] Using this method, cinnamate acid amides **53a**-**53d** and cinnamate acid esters **53g**-**53l** with differently substituted aromatic rings as well as styrenyl derivatives **53e** and **53f**, have been converted to the corresponding 1,1-difluorinated compounds **54** in mostly good yields (49%−93%) and excellent enantioselectivities (82%−96% *ee*), even on a gram scale. Even simple styrene derivatives **53e** without any conjugation to carbonyl groups rearranged to the *gem*-difluorinated compounds, albeit with slightly deteriorated enantioselectivities (74% *ee*). For substrates with two electronically different aromatic ring substituents, migration of the more electron-rich aromatic was observed **54f**. Cinnamic acid esters **53h**-**53l** with a trisubstituted double bond are also suitable for the *gem*-difluorination. This method also allowed for variations of the β-alkyl substituent to longer aliphatic residues **54k** without loss any of selectivity.

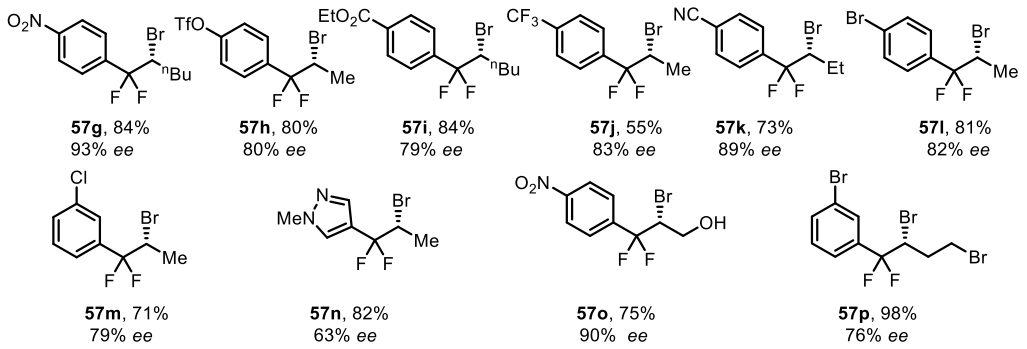




Scheme 16. Catalytic enantioselective *gem*-difluorination of cinnamate acid amides and esters **53**.

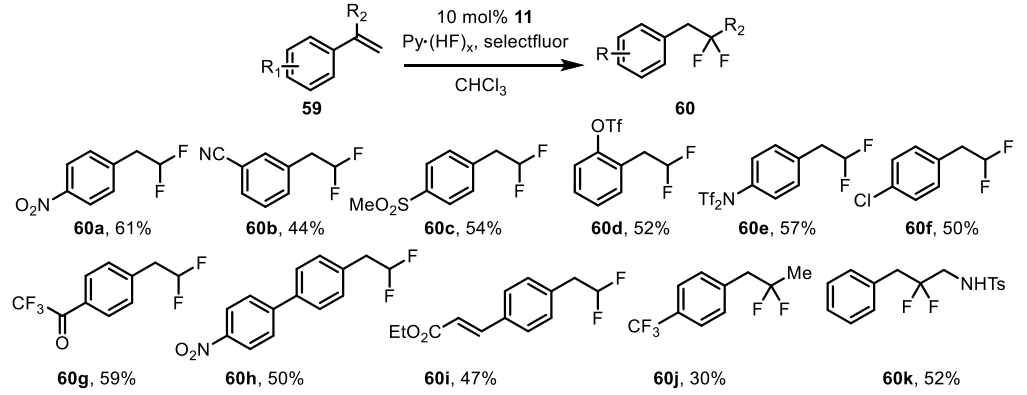
In 2020, Jacobsen and co-workers used similar conditions to develop the catalytic, enantioselective synthesis of *gem*-difluorinated bromides **57** by the oxidative rearrangement of α-bromostyrenes **56** (Scheme 17). [116] Styrenyl bromides **56** bearing electron-withdrawing *m*- and *p*-substituents such as such as nitro **56a**, **56g**, tosyloxy **56b**, **56h**, ester **56c**, **56i**, trifluoromethyl **56d**, **56j**, cyano **56e**, **56k**, bromo **56f**, **56l** groups were effective substrates, affording products **57a**-**57q** in 52%−84% yield and 70%−93% *ee*. Substrates bearing a free alcohol functionality **56o** or primary aliphatic bromide **56p** substituents also reacted smoothly, affording the desired products with 90% *ee* and 76% *ee*, respectively. In this reaction, they found that the formation of catalyst decomposition product results from attack of a carbonyl group of catalyst on the bromonium ion intermediate, catalysts bearing electron-withdrawing substituents on the benzyl ester were prepared and evaluated with the goal of attenuating the nucleophilicity of the ester carbonyl and thereby limiting the decomposition pathway. And after examining several candidates, the *p*-SF_5 derivative **58** was identified as optimal for both conversion and enantioselectivity.





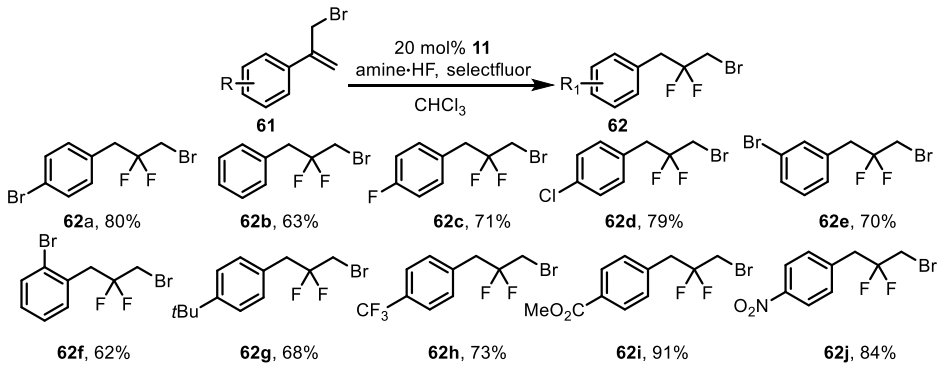
Scheme 17. Catalytic enantioselective *gem*-difluorination of α-bromostyrenes **56**.

In parallal to Jacobsen, the Gilmour group developed a new protocol for catalytic *gem*-difluorinations of styrenes **59** by using selectfluor as an oxidant instead of *m*CPBA. This method is compatible with a range of electronically and substitutionally diverse styrenes, which can be converted to the corresponding 1,1-difluorinated compounds **60** in moderate yields (Scheme 18). [117] Styrenes bearing electron-withdrawing substituents such as nitro **59a**, cyano **59b**, sulfonyl **59c**, tosyloxy **59d**, chloro **59f**, α, β-unsaturated ester **59i**, trifluoromethyl **59j** functionalities were effective substrates, affording products **60a**-**60k** in 44%−61% yield.



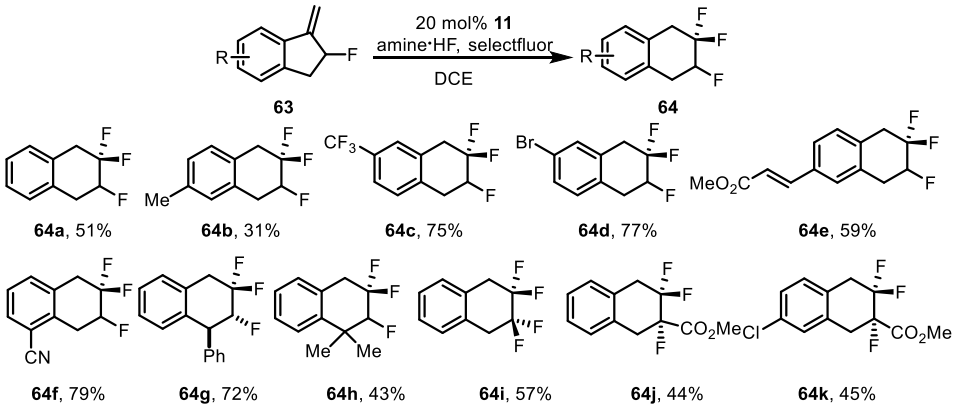
Scheme 18. Catalytic *gem*-difluorination of styrenes **59**.

With this protocol, Gilmour et al. have also accomplished *gem*-difluorinations of styrenes having an allylic bromide moiety. In 2021, they reported the difluorinative rearrangement of various substituted α-(bromomethyl)styrenes **61** to corresponding 1,1-difluorinated compounds **62** in good to excellent yields (Scheme 19).[118] To explore the scope of this geminal difluorination, the scope of α-(bromomethyl)styrenes **61** with different electronic properties and substitution patterns of the aryl ring was investigated. Substrates bearing either electron-donating (e.g., *tert*-butyl) or electron-withdrawing groups (e.g., fluoro, chloro, bromo, trifluoromethyl, nitro, ester) at the different position of the phenyl rings were compatible with the transformation to afford the desired products **62a**-**62j** in 63%−91% yield.



Scheme 19. Catalytic *gem*-difluorination of α-(bromomethyl)styrenes **61**.

In the same year, they also reported the difluorinative ring expansion of fluorinated methyleneindanes **63** to generate trifluorinated tetralins **64** compounds. [119] A range of diverse substituents are tolerated under standard catalytic conditions with moderate to good yields (Scheme 20). In this transformation, electron-deficient substrates proved to be better precursors as exemplified by the trifluoromethyl **63c**, bromo **63d** and cyano **63f** species compared to the methyl compound **63b**. Substrate **63e** with an α, β-unsaturated ester moiety produced the desired product in 59% yield. The addition of substituents on the saturated ring system was tolerated (see **63g** and **63h**), and catalysis enabled the formation of the tetrafluorinated compound **64i**. Interestingly, despite the addition of an additional electron-withdrawing group, catalysis was observed under the standard conditions reported (**64j** and **64k**, 44% and 57% yields, respectively.)



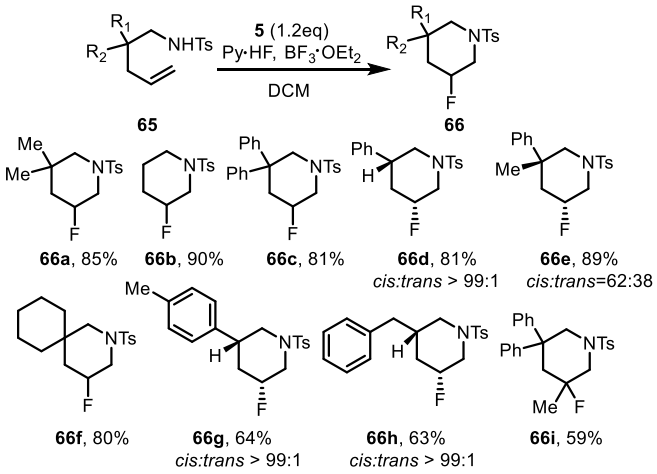
Scheme 20. Catalytic *gem*-difluorination of fluorinated methyleneindanes **63**.

2.1.3 Stoichiometric Fluorocyclizations of Alkenes

Fluorocyclizations are a powerful transformation for the synthesis of fluorinated carbo- and heterocycles, as these reactions can provide complex products in a one-pot process.[120] Fluorocyclizations have been developed using both electrophilic and nucleophilic fluorine sources,[121] and the methodology has already

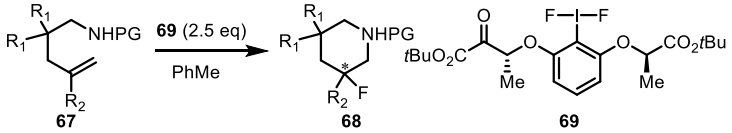
enabled the preparation of carbocycles as well as oxygen-, nitrogen-, and sulfur-containing heterocycles, including of biologically relevant targets such as Sofosbuvir. Despite these advances, fundamental key problems need to be addressed. At present, many of the methodologies suffer from a lack of generality, which, for the case of electrophilic fluorination, stems from the low reactivity of the fluorinating reagents towards commonly used feedstock alkenes. In recent years, hypervalent λ^3-iodanes have been widely used to solve these problems, and a short summary of hypervalent λ^3-iodane mediated fluorocyclization reactions for the synthesis of *N*-heterocyclic compounds is presented here.

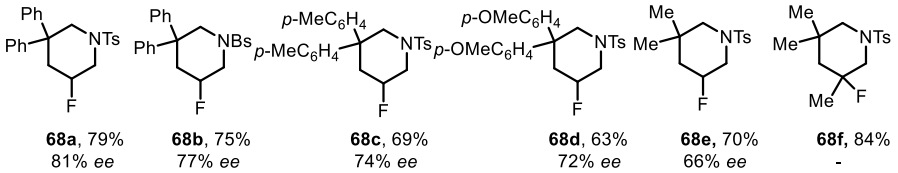
In 2012, the groups of Meng and Zhong developed a regioselective metal-free method for the intramolecular oxidative aminofluorination of unactivated terminal alkenes **65** employing a $PhI(OPiv)_2$/Py·HF system in the presence of $BF_3{\cdot}Et_2O$ (Scheme 21).[122] A number of tosyl-protected pent-4-en-1-amines **65** were readily converted to form 3-fluoro-piperidines **66** in good yields and with high diastereoselectivity. Substrates bearing different groups at the β-carbon afforded desired products **66a**-**66i** in 59%−90% yield.



Scheme 21. Aminofluorination of alkenes **65** using stoichiometric amounts of in-situ generated F-iodanes.

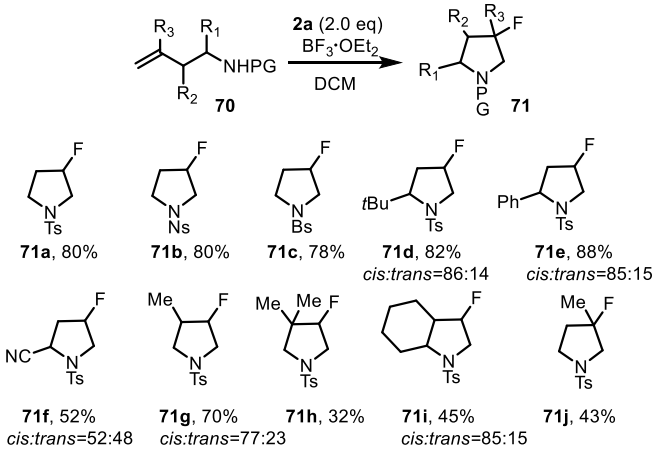
In 2013, Nevado and coworkers reported an elegant method for the intramolecular enantioselective aminofluorination of alkenes **67** by using stoichiometric amounts of chiral electrophilic $ArIF_2$ **69** (Scheme 22).[123] In this process, β-fluoropiperidines **68** could be obtained in 63%−84% yields and 66%−81% *ee*. with different *N*-protecting groups **67a**, **67b** and *gem*-diaryl **67c**, **67d** or alkyl **67e**, **67f** groups at the carbon chains.





Scheme 22. Stoichiometric intramolecular enantioselective aminofluorination of alkenes **66**.

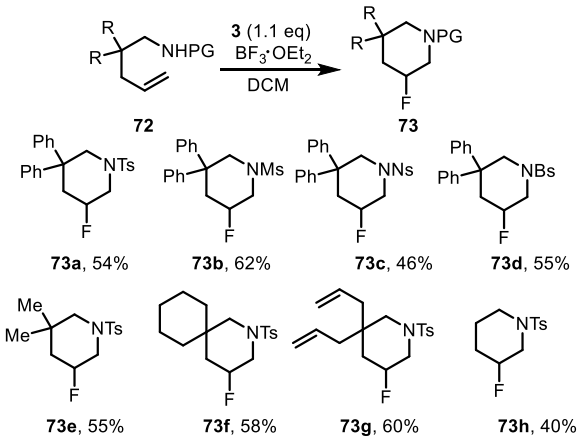
In 2014, Zhang and co-workers developed a mild and efficient intramolecular aminofluorination reaction of homoallylic amines **70** to provide 3-fluoropyrrolidines **71**, in which a commonly used Lewis acid $BF_3 \cdot Et_2O$ was utilized as the fluorine source together with **2a** as the oxidant (Scheme 23).[124] The different *N*-protecting group of the alkenes **70** were run smoothly to give the corresponding 3-fluoropyrrolidine products **71a**-**71c** in 78%−80% yields. When *tert*-butyl **70d**, phenyl **70e**, or cyano **70f** groups were attached to the α-carbon of the amino group, the desired products **71d**-**71f** could be obtained in 52%−88% yield, while the diastereomeric ratio (*cis/trans*) varied from 52:48 to 86:14. When a methyl or two methyl groups at the allylic position, the desired aminofluorinated products **71g** and **71h** were achieved in 70% and 32% yields, respectively. The reaction of aminoalkene **70i**, in which the C-C double bond and the amino group were attached to a six-membered ring afforded bicyclic product **71i** in 45% yield with a diastereomeric ratio (*cis/trans*) of 85:15. For a 1,1-disubstituted alkene **70j**, the aminofluorination reaction proceeded smoothly to produce **71j** in 43% yield.



Scheme 23. Aminofluorination of alkenes **70** using stoichiometric amounts of in-situ generated F-iodanes.

In the same year, Li and coworkers reported the PIDA (**3**)-mediated intramolecular aminofluorination of alkenes **71** by using $BF_3 \cdot Et_2O$ as the fluorine source (Scheme 24). [125] In this protocol, β-fluoropiperidines could be obtained in 46%−62% yields with different protecting groups at the nitrogen atom. Besides, substrates with *gem*-disubstitutents on carbon chains bearing methyl (**72e**), cyclohexyl (**72f**), and allyl (**72g**)

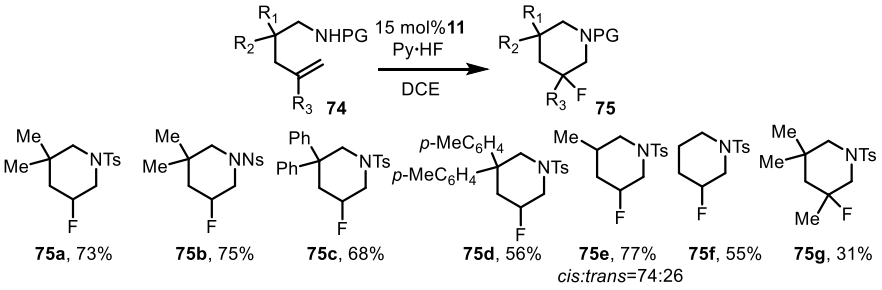
groups were suitable for the reaction to afford the corresponding products **73e**-**73g** in 55%−60% yields. Notably, the linear substrate **72h** gave the desired product **73h** in 40% yield.



Scheme 24. Aminofluorination of alkenes **72** using stoichiometric amounts of in-situ generated F-iodanes.

2.1.4 Catalytic Fluorocyclizations of Alkenes

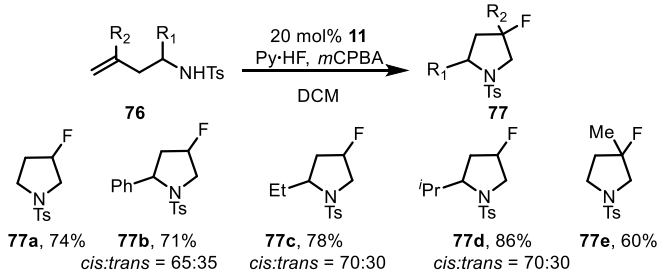
In 2014, the Kita and Shibata groups accomplished the aminofluorination of alkenes **73** with the *in situ* formation of hypervalent iodine compound **7b** as the key for their reaction (Scheme 25). [126] The desired products **75** were obtained in good yields, of up to 75% yield under the reaction conditions consisting of *p*-TolI (**11**)/ Py·HF /*m*CPBA system. Substrates with different protecting groups and different *gem*-disubstitutents at the carbon chains were suitable for the reaction to afford the corresponding products **75** in moderate yields. Moreover, the linear substrate **74f** and 1,1-disubstituted alkene **74g** gave the desired products **75f** and **75g** in 55% and 31% yields, respectively.



Scheme 25. Catalytic intramolecular aminofluorination of alkenes **74**.

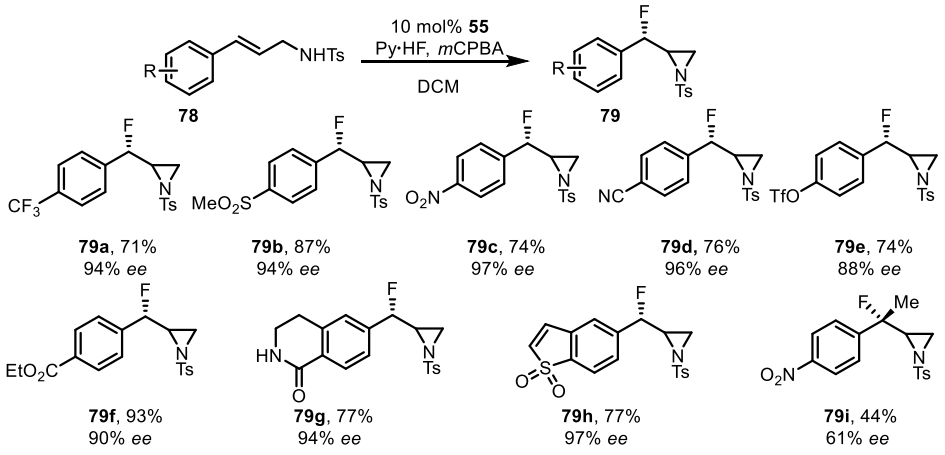
In 2017, Kitamura and co-workers developed the intramolecular aminofluorination of alkenes **76** by using *p*-iodotoluene (**11**) as the catalyst, Py·HF as the fluorine source, and *m*CPBA as the terminal oxidant (Scheme 26).[127] The substrates employed in this catalytic aminofluorination afforded products **77** in good to high yields. Substrates with phenyl **76b**, ethyl **76c** or isopropyl **76d** group was attached to the α-carbon

of the amino group, the desired products **77b**-**77d** could be obtained in 71%−86% yield, while the diastereomeric ratio (*cis/trans*) varied from 65:35 to 70:30. For a 1,1-disubstituted alkene **76e**, the aminofluorination reaction proceeded smoothly to produce **77e** in 43% yield.



Scheme 26. Catalytic intramolecular aminofluorination of alkenes **76**.

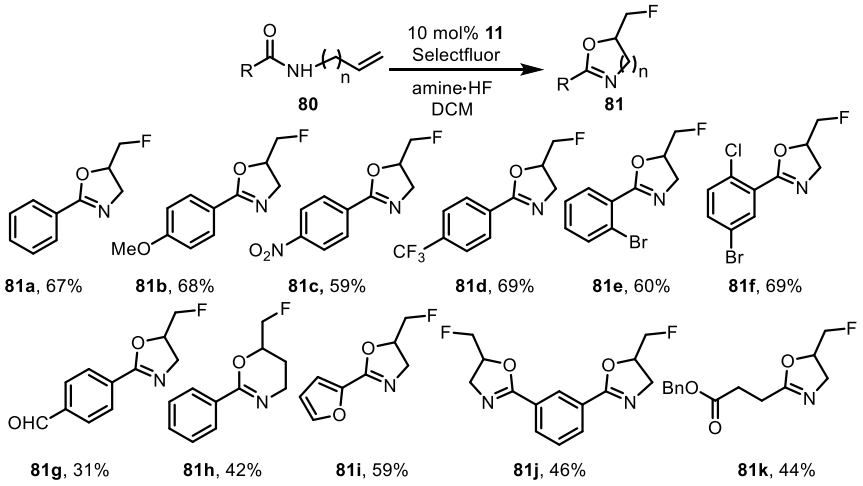
In 2018, Jacobsen reported the stereoselective synthesis of *syn*-β-fluoroaziridine via chiral aryl iodide-catalyzed fluorination of allylic amines **78** (Scheme 27).[128] The method emploied Py·HF as the nucleophilic fluoride source together with *m*CPBA as the stoichiometric oxidant, afforded access to arylethylamine derivatives **79** featuring fluorine-containing stereocenters. A variety of electron-deficient cinnamyl tosylamides **78** were found to undergo clean conversion to the corresponding β-fluoroaziridine products **79a**-**79h** as single diastereoisomers and with high enantioselectivity (up to 93% yield, 97% *ee*). The reaction of a trisubstituted γ-methyl-*N*-tosylcinnamylamine **78i** gave the corresponding product **79i** with a dramatically decreased yield and enantioselectivity under the same conditions (44% yield, 61% *ee*).



Scheme 27. Enantioselective oxidative fluoroaziridination of cinnamylamine derivatives **78**.

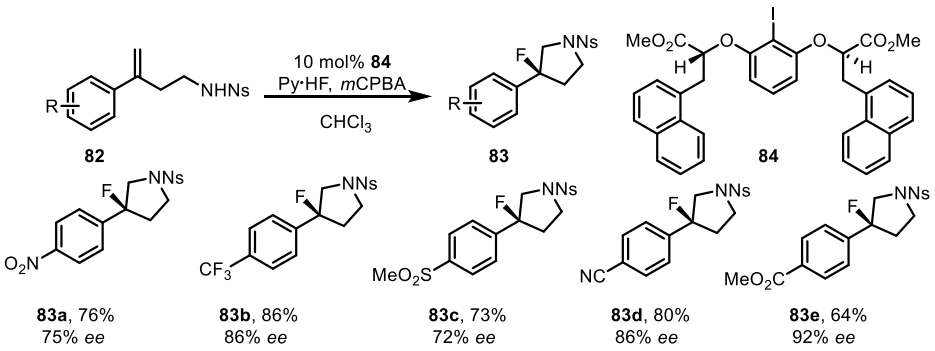
In 2018, Gilmour developed a simple route to 5-fluoromethyl-2-oxazolines **81** by fluorocyclization of *N*-allylcarboxamides **80** via I(I)/I(III) catalysis (Scheme 28).[129] This metal-free fluorocyclization employs 10 mol% *p*-iodotoluene (**11**) catalyst, amine/HF as fluorine source and selectfluor as oxidant. *N*-

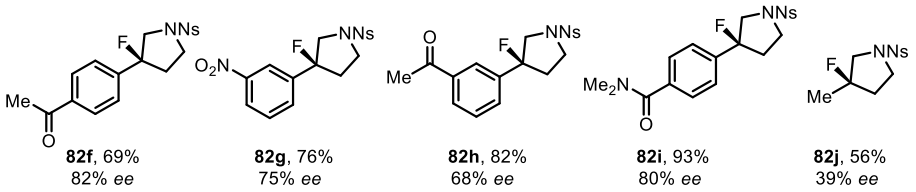
allylcarboxamides **80** bearing either electron-donating such as methoxyl **80b** or electron-withdrawing groups such as nitro **80c**, trifluoromethyl **80d**, bromo **80e** at the position of the phenyl rings were compatible with the transformation to yield the 2-oxazolines **81b**-**81f** in 59%−69% yields. Notably, the aldehyde derivative **80g** was also tolerated, generating the desired product **81g** in an acceptable 31% yield. *N*-(but-3-en-1-yl)benzamide **80h** was also tolerated, producing with 42% yield. Starting from furanyl derivative, oxazolines **81i** was obtained in 59% yield. The reaction conditions were suitable for substrate **80j** and **80k**, affording the desired product **81j** and **81k** in 46% and 44% yields, respectively.



Scheme 28. Catalytic fluorocyclization of *N*-allylcarboxamides **80**.

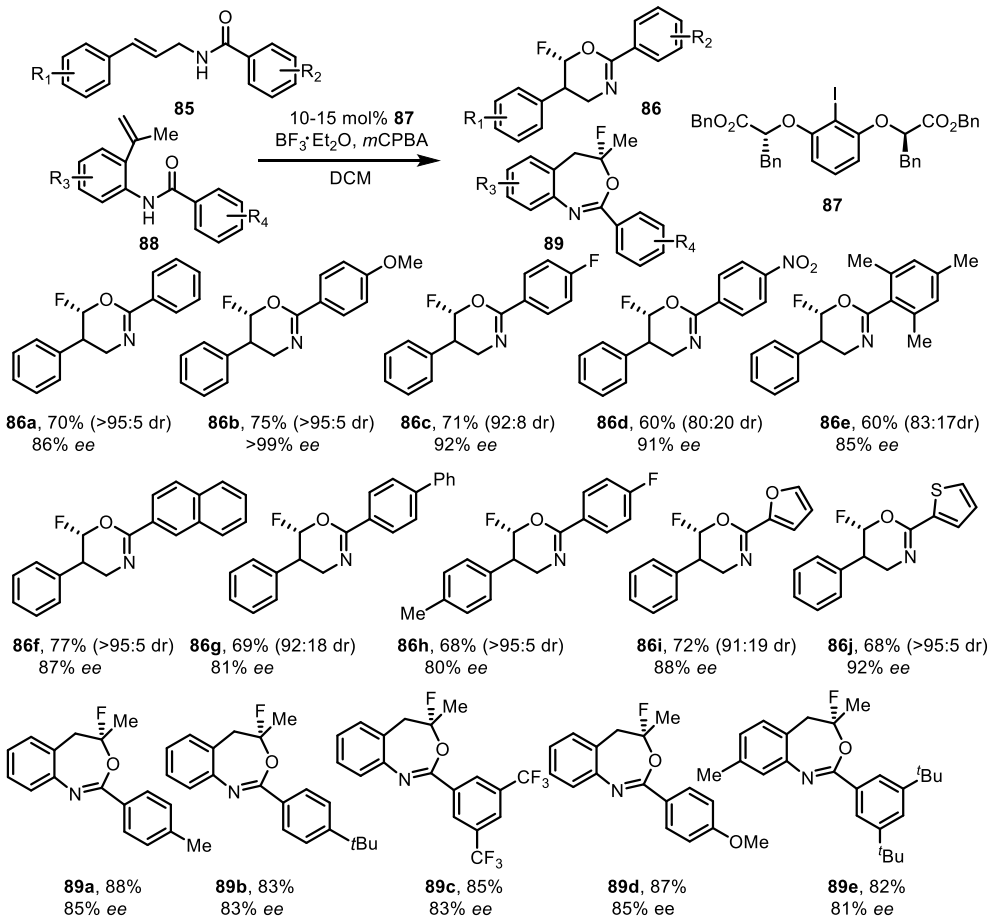
In 2020, Szabo and co-workers developed a new method for the synthesis of chiral pyrrolidines with endocyclic tertiary C-F stereocenters (Scheme 29).[130] The fluorocyclization reactions of various 1,1-disubstituted styrene derivatives **82** were catalyzed by *in situ* generated hypervalent iodanes. Substrates bearing electron-withdrawing substituents such as such as nitro **82a**, **82g**, trifluoromethyl **82b**, methyl sulfonyl **82c**, cyano **82d**, ester **82e**, methyl carbonyl **82f**, **82h** and dimethylamide **82i** were tolerated, affording the desired products **83a**-**83i** in 64%−93% yield and 68%−92% *ee*. Alkyl-substituted alkene derivative **82j** also underwent fluorocyclization reaction affording **83j** in 56% yield and 39% *ee*.





Scheme 29. Catalytic enantioselective intramolecular aminofluorination of alkenes **82**.

In 2021, Jiang group reported the catalytic asymmetric nucleophilic fluorination using $BF_3{\cdot}Et_2O$ as the fluorine reagent and dual-activating reagent in the presence of chiral iodine catalyst (Scheme 30).[131] Various chiral fluorinated oxazine products **86a-86j** were obtained in 60%−77% yields with good to excellent enantioselectivities (up to >99% *ee*) and diastereoselectivities (up to >20:1 dr). To further understanding of the scope of this catalytic system, substrates **88a-88e** were employed to undergo the fluorination process. Various substituted *N*-(2-(prop-1-en-2-yl)phenyl)benzamides **88** including either electrondonating substituents or steric hindrance substituents could be tolerated, afforded the corresponding fluorinated products **89a-89e** with 80%−88% yield and 80%−85% *ee* (Scheme 31).



Scheme 30. Catalytic asymmetric aminofluorination of *N*-cinnamylbenzamides **85** and **88**.

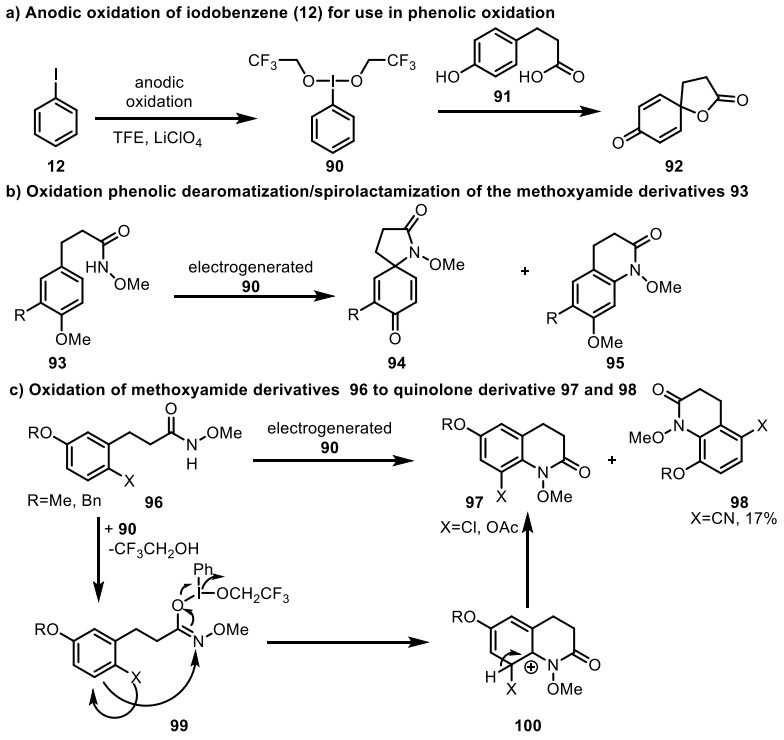
2.2 Electrochemically Generated λ³-Iodane in Organic Synthesis

Hypervalent iodanes represent a well-studied and frequently used class of reagents in organic synthesis. Their use, whether as stoichiometric regent or generated *in situ* from aryl iodide precursors via oxidation, and the associated waste and separation problems constitute the main challenges leading to sustainable and scalable processes. In this context, the anodic oxidation of aryl iodides demonstrates an important alternative method for the synthesis of hypervalent iodanes, which avoids the use of expensive or often dangerous chemical oxidation reagents. In recent years, the electrochemically generated hypervalent iodanes have been successfully used as in-cell or ex-cell mediators for different valuable chemical transformations, such as oxidations and atom transfer reactions, such as fluorination.

2.2.1 Electrochemically Generated λ³-Iodanes in Oxidations

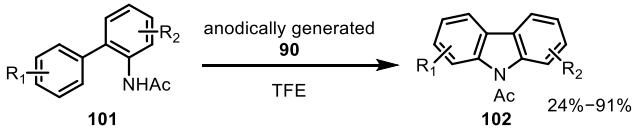
In 2006, the Nishiyama group developed an electrochemical method for the generation of [bis(trifluoroethoxy)iodo]benzene **90** (Scheme 31a), where the reactivity of **90** was superior to commercially available λ³-iodanes, such as (diacetoxy)iodo)benzene(**3**, PIDA) in oxidative dearomatizations. Electrolysis was performed in an undivided glassy carbon cell, which also served as anode and was equipped with a platinum wire as cathode, using a constant current density of 0.3 mA/cm^2, TFE as the solvent and $LiClO_4$ (0.05 M) as the electrolyte. Although the generated λ³-iodanes are only stable in solution, their scope of applications has been impressively demonstrated in various oxidation reactions. These include the *in situ* oxidation of 4-hydroxyphenylpropionic acid (**91**), which was added to the reaction mixture after the electrolysis from **91** to produce **92** (Scheme 31a). [132] In most cases, the dearomatization product **92** was obtained in good yields (79%–97%). The hypervalent iodane **90** generated from the anodic oxidation proved to be the most powerful oxidant in this series, leading to the formation of **92** in 97% yield, even better than the 84% yield with [bis(trifluoroacetoxy)iodo]benzene (**4**, PIFA). Similarly, the phenolic dearomatization/spirolactamization of the methoxyamide derivatives **93** was achieved in high yields using the electrochemically generated **90** (Scheme 31b).[133] The spirocyclic products **94** were obtained exclusively when the substituent R is hydrogen or halogen, while in the case of strong electron-donating substituents (R=OMe) the reaction was unselective and gave a mixture of **94** and **95** in an approximately 50:50 ratio.

The same anodically generated λ³-iodane **90** was also used to synthesize quinoline derivatives **97** and **98** from amide substrates **96** (Scheme 31c). [134] Different chemoselectivities were observed depending on the aryl substituent. While the substrates **96** with chloro or acetoxy substituents exhibited a complex mechanism via intermediates **99** and **100** including the migration of the substituent X, the cyano derivative **96** exhibited the ortho-cyclized product **98** to a minor extent (17%).



Scheme 31. Anodic oxidation of iodobenzene (**12**) and use of electrogenerated **90**.

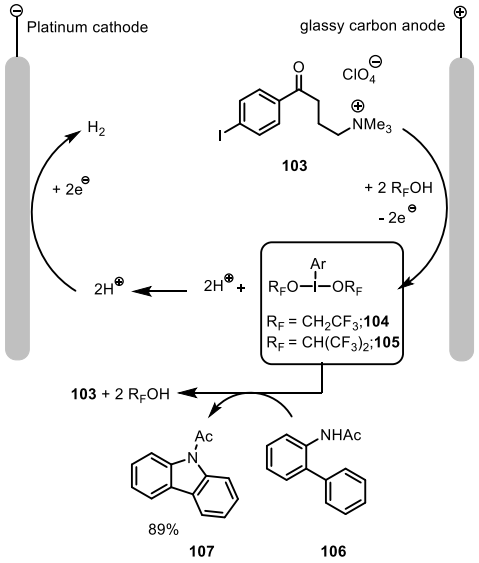
In 2010, Nishiyama and co-workers applied this anodically generated λ^3-iodane **90** for the synthesis of carbazoles **102** by oxidative cyclization of phenyl acetanilide derivatives **101** (Scheme 32).[135] The reaction shows good functional group tolerance and the carbazole products **102** were generally obtained in 24%−91% yields.



Scheme 32. Intramolecular synthesis of carbazoles using anodically generated iodane **90**.

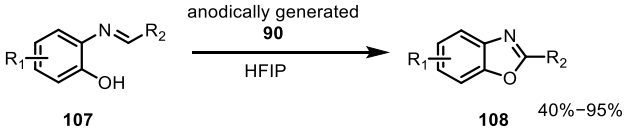
In 2016, Francke and co-workers developed a novel recyclable iodine(I)/(III) redox mediator system for electrosynthesis. [136] Within the iodine(I) precursor **103**, a conductive dimethylammonium group was installed, which obviates the need for an external electrolyte and facilitates reusability. The supporting electrolyte was merged with the mediator by tethering the redox-active iodophenyl moiety to an alkylammonium group, allowing for straightforward recovery and reuse of both components. The ionically tagged aryl iodide **103** is anodically oxidized in fluorinated alcohols such as trifluoroethanol (TFE) and 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) to the corresponding hypervalent iodanes **104** and **105**, respectively (Scheme 33). Notably, both intramolecular and intermolecular dehydrogenative C-N bond

formation could be achieved with amides and simple arenes in this protocol. Ultimately, a method was established in which **103** could be used as an external mediator, making a wide range of C-N coupling reactions accessible as shown, for example, by the conversion of **106** to **107**.



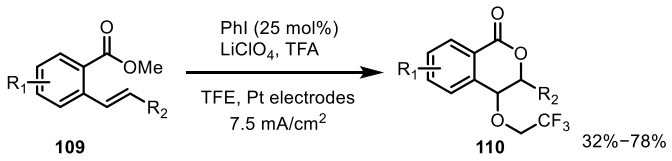
Scheme 33. Electrochemical generation of hypervalent iodanes **104** and **105** for C-N bond formation.

In 2017, the Francke group used this hypervalent iodane **90** as an ex-cell mediator for the synthesis of benzoxazoles **108** through the oxidative cyclization of 2-(benzylideneamino)phenol substrate **107** (Scheme 34). [137] The reaction proceeded smoothly, showing broad functional group tolerance, and benzoxazole derivatives **108** were usually obtained in 40%−95% yields.



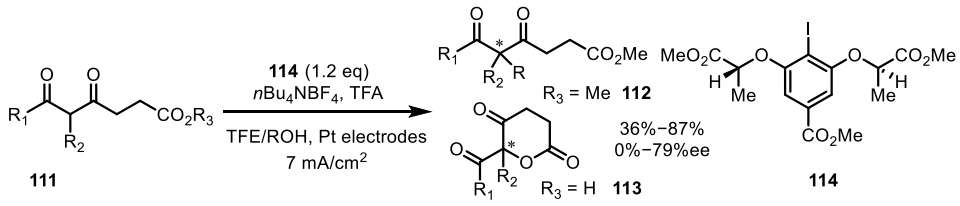
Scheme 34. Intramolecular C-O bond formation via electrochemical generated hypervalent iodane **90**.

In 2018, Hilt and co-workers developed an electrochemical trifluoroethoxylactonization of vinyl benzoic esters **109** for the synthesis of trifluoroethoxysubstituted isochromanones **110** with iodobenzene (**12**) as mediator via an in-cell method (scheme 35). [138] The electrolysis was conducted in an H-type cell under constant current density (7.5 mA/cm^2) at room temperature. This reaction was the first example with two chemical bonds formed simultaneously, especially for the incorporation of weak trifluoroethoxylate nucleophile. Under optimized conditions, 12 derivatives of **110** were synthesized in 32%−78% isolated yield.



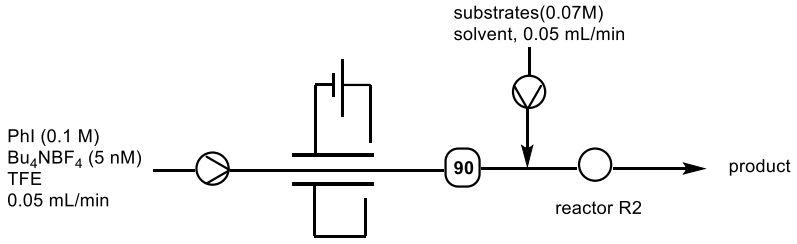
Scheme 35. Electrochemical trifluoroethoxylactonization of vinyl benzoic esters **109** mediated by hypervalent iodane.

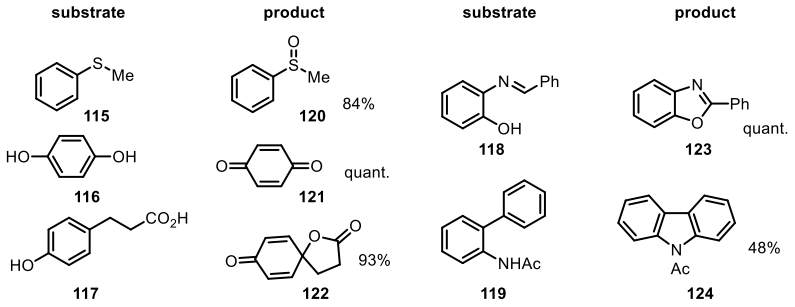
In 2018, Wirth and co-workers reported an enantioselective lactonization of diketo acid derivatives **111** employing electrochemistry (scheme 36).[139] With chiral iodoarene **114** as redox mediator, a variety of α-lactonizations and α-alkoxylations of diketo acid derivatives **111** were afforded desired products **112** and **113** in 36%−87% yields and 0%−79% *ee*. The reaction can be carried out via an in-cell process since the oxidative potential of chiral iodoarene **114** (1.83 V, vs Ag/AgCl) was lower than that of diketo acid derivatives **111**(2.07 V, vs Ag/AgCl). Furthermore, the solution can be electrolyzed in an electrochemical flow microreactor where a concentration of the supporting electrolyte (5 mM) could be employed to conduct the enantioselective electrochemical process.



Scheme 36. Electrochemical enantioselective lactonization of diketo acid derivatives **111**.

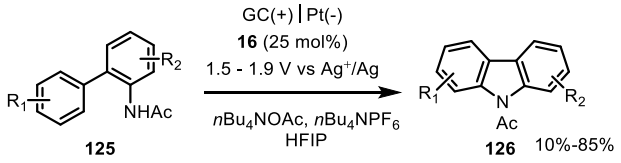
In 2019, Wirth and co-workers described a method for the continuous-flow electrochemical generation of hypervalent iodane **90** and its synthetic application.[140] The anodic oxidation of iodoarenes under flow conditions was carried out smoothly in fluorinated alcohols using a glassy carbon anode and a platinum cathode. As this hypervalent iodane **90** is not bench-stable and decompose immediately upon removal of the solvent, its generation and immediate use in flow is highly advantageous.





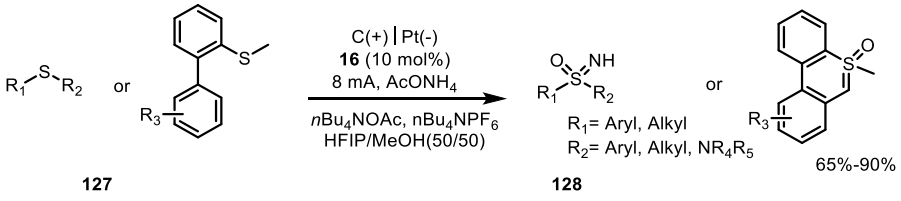
Scheme 37. Synthetic applications of the electrogenerated hypervalent iodane **90**.

In 2020, Powers and co-workers reported an electrocatalytic C-N coupling via an in-situ anodically generated hypervalent iodane (Scheme 38).[141] A series of *N*-acetylcarbazole **126** were obtained with yields of up to 85% in an undivided cell with a glassy carbon anode and platinum cathode electrodes, under a potential of 1.5 V (CPE) to 1.9 V vs. Ag+/Ag reference electrode at room temperature using HFIP as solvent. The developed method was applied to intra- and intermolecular C-N bond formation reactions.



Scheme 38. Electrochemical generation of hypervalent iodanes for C-N bond formation.

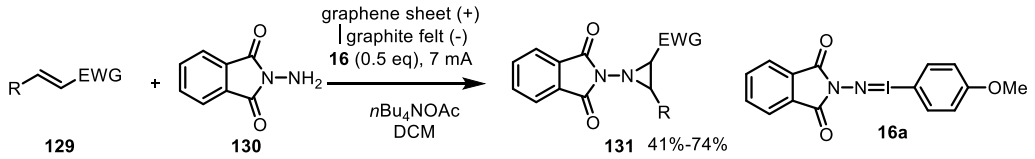
In 2021, the Wang and Xu groups developed the method for the preparation of NH-sulfoximines, NH-sulfonimidamides, and dibenzothiazines **128** by the generation in situ of an active hypervalent iodane using electricity as the oxidant, which avoids the need for an excess of a hypervalent iodine reagent relative to conventional approaches (Scheme 39).[142] Moreover, this protocol features broad substrate scope and wide functional group tolerance, delivering the desired compounds **128** with 65%−90%yields (Scheme 39).



Scheme 39. Electrochemical oxidative syntheses of NH-sulfoximines, NH-sulfonimidamides and dibenzothiazines **128** via anodically generated hypervalent iodane.

In 2021, the Dai and Cheng groups reported an electrochemical aziridination of electron-deficient alkenes **129** mediated by hypervalent iodane (Scheme 38).[143] Hypervalent-iodane-stabilized nitrene

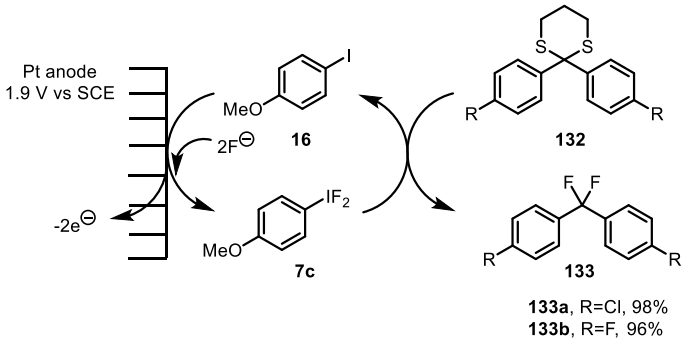
hydroxyhydrazine **16a** was suggested as the *in situ* generated nitrogen source for the stepwise aziridination. This protocol can be employed to the azirdination of α, β-unsaturated esters, amides, nitrile and ketones derivatives **129** to give a series *N*-containing products **131** in 41%−74% yields.



Scheme 40. Electrochemical aziridination of electron-deficient alkenes **129**.

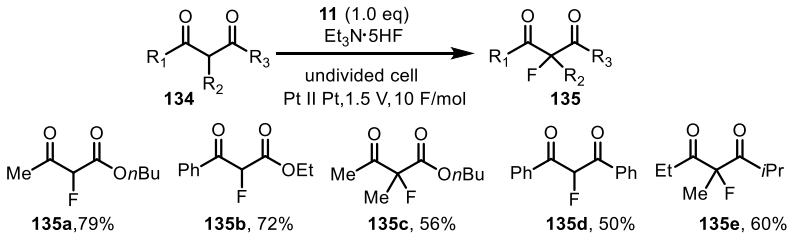
2.2.2 Electrochemically Generated λ³-Iodanes in Fluorination Reactions

In 1994, electrochemically generated hypervalent fluoro-iodanes **7c** was successfully used as mediator for the indirect anodic *gem*-difluorination of dithioketals **132** by the Fuchigami group (Scheme 41).[92] The reaction was successfully carried out applying the ex-cell method, where the dithioketal substrates **132** were added to the mixture after the electrolysis. In addition, the reaction was also carried out in an in-cell method, where the dithioketal substrates **132** were present already during the electrolysis. The in-cell mediated difluorination reaction enabled the use of aryl iodides in catalytic amounts, where 5 mol% of **16** was sufficient to give the *gem*-difluorinated products **133a** and **133b** in 98% and 96% yield.



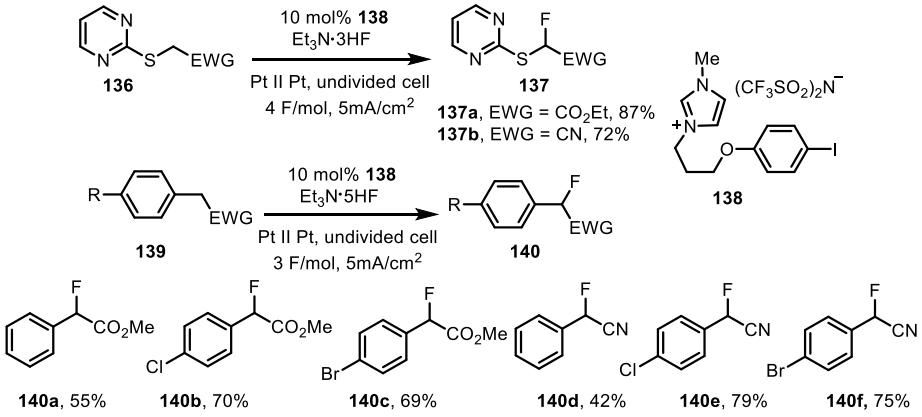
Scheme 41. Indirect anodic *gem*-difluorination of dithioketals **132**.

In 1998, Hara and co-workers electrochemically synthesized the valuable fluorinating agent, $TolIF_2$ (**7b**), by changing the electrolyte from $Et_3N{\cdot}3HF$ to $Et_3N{\cdot}5HF$. The electrochemically generated **7b** was successfully used as an in-cell mediator for the indirect anodic fluorination of β-dicarbonyl compounds **134** (Scheme 42).[144] Thus, the α-fluoro-β-dicarbonyl products **135** were obtained in good yields through constant potential electrolysis (1.5 V vs. Ag/Ag^+) of a 50:50 mixture of **11** and β-dicarbonyl substrates **134** in $Et_3N{\cdot}5HF$ in a Teflon PFA undivided cell. The fluorination of unsubstituted β-dicarbonyl substrates **134** proceeded selectively providing the monofluorinated compounds **135** as main products in 50%−79% yields.



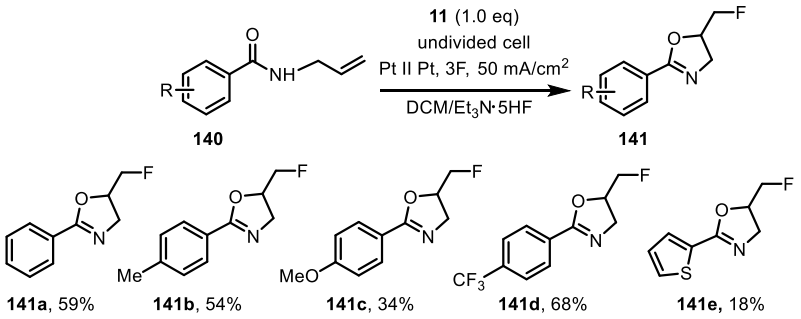
Scheme 42. Indirect anodic fluorinations of β-dicarbonyl compounds **134**.

In 2010, the Fuchigami group reported a novel indirect electrochemical fluorination system by employing a task-specific ionic liquid (TSIL) combined with an iodoarene moiety **138** as the mediator in a HF-based ionic liquid (Scheme 43).[145] The system was successfully tested for the monofluorination of **136** and **139**, whereby the electrolysis was carried out in the constant current mode using 0.1 equivalent of the mediator **138** in an undivided cell. The desired products **137** and **140** could be obtained in 42%−87% yields.



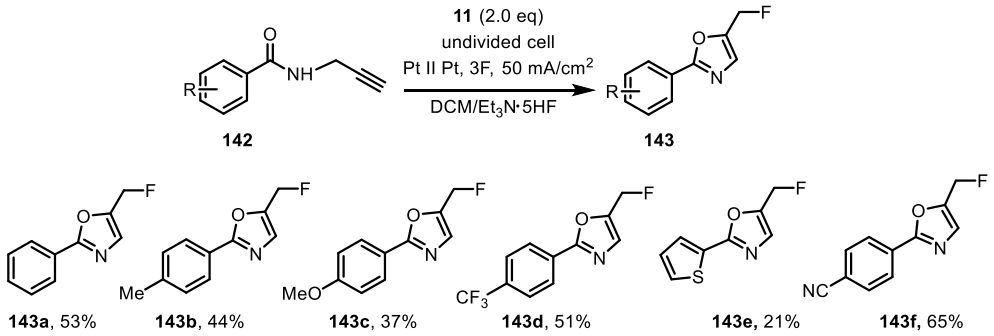
Scheme 43. Indirect anodic fluorinations of **136** and **139**.

In 2019, the Waldvogel group established a sustainable synthesis of 5-fluoromethyl-2-oxazolines **141** via hypervalent λ^3-iodane mediated fluorocyclization using electric current as the oxidant (Scheme 44).[146] The electrolysis was performed under constant current conditions in an undivided cell equipped with two platinum electrodes in a mixture of DCM/Et_3N·5HF (50:50). *N*-allylcarboxamides **140** bearing either electron-donating, such as methoxyl **140c,** or electron-withdrawing groups, such as trifluoromethyl **140d**, at the phenyl rings were compatible with the transformation to yield the 2-oxazolines **141c** and **141d** with 34% and 68% yields, respectively. Starting from furanyl derivative **140e**, oxazoline **141e** was obtained only in 18% yield.



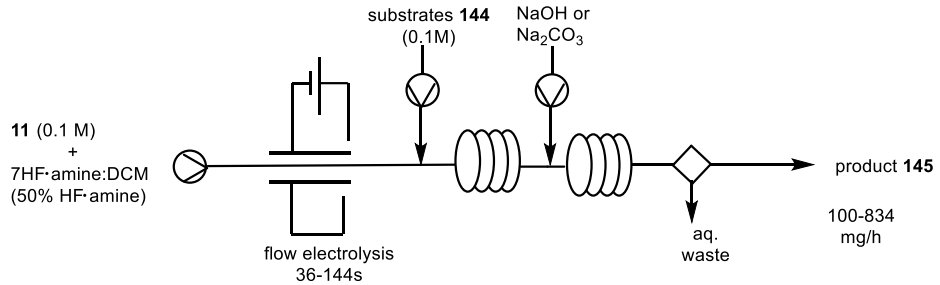
Scheme 44. Electrochemical fluorocyclization of *N*-allylcarboxamides **140** by a hypervalent iodane mediator.

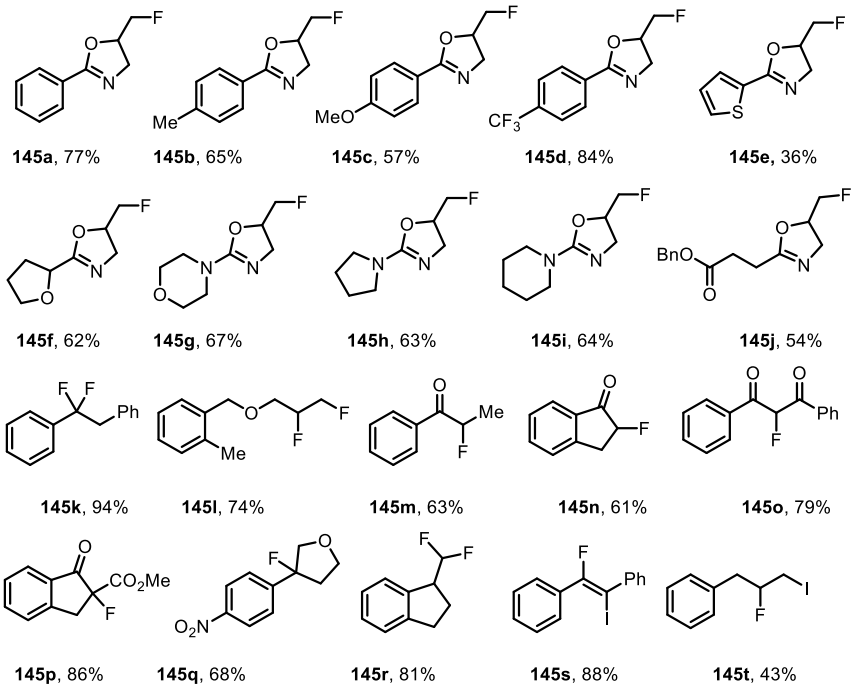
In the same year, the group of Waldvogel also achieved the synthesis of 5-fluoromethyl-2-oxazoles **143** by hypervalent λ^3-iodane mediated fluorocyclization of *N*-propargylamides **142** with electric current as green oxidant (Scheme 45). [147] The electrochemical protocol was applicable to a wide range of substrates **142** and provided oxazoles **143** bearing an exocyclic fluoromethyl group with yields up to 65% yield.



Scheme 45. Electrochemical fluorocyclization of *N*-propargylamides **142** by hypervalent iodane mediator.

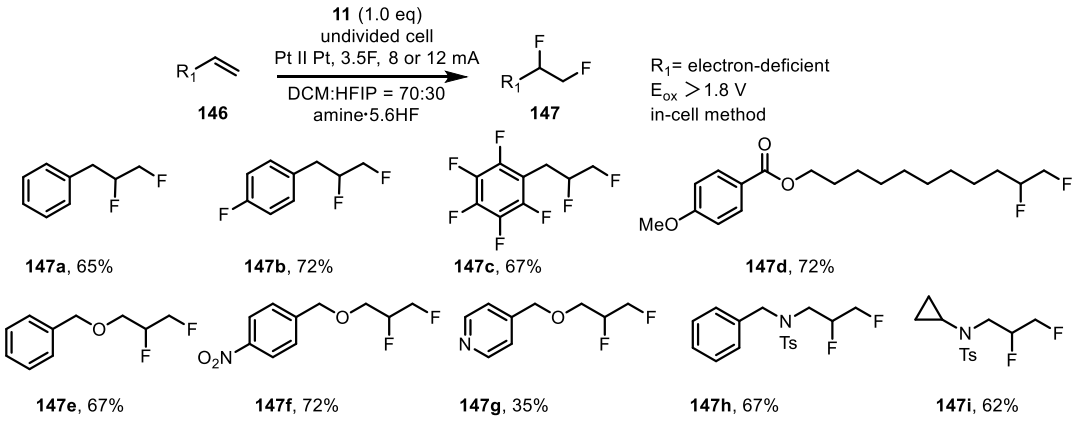
In 2021, Wirth and coworkers reported a scalable, versatile, and safe electrochemical fluorination protocol in a flow system for various types of substrates. The strategy proceeded through a transient (difluoroiodo)arene (**7b**), generated by anodic oxidation of the iodoarene mediator **11** (Scheme 46).[148] For substrates **144**, such as **144a-144j** reacted smoothly to deliver the desired products **145a-145j** in 36%−84% yield. Other substrates **144**, **144k-144t** also reacted successfully to afford the desired products **145k-145t** in 43%−94% yield.

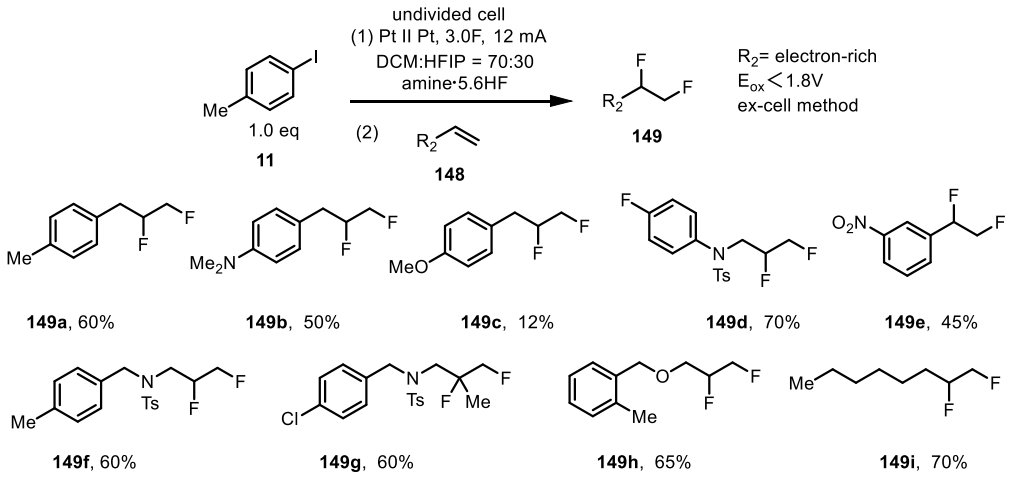




Scheme 46. Electrochemical fluorinations of **144** by hypervalent iodane mediator

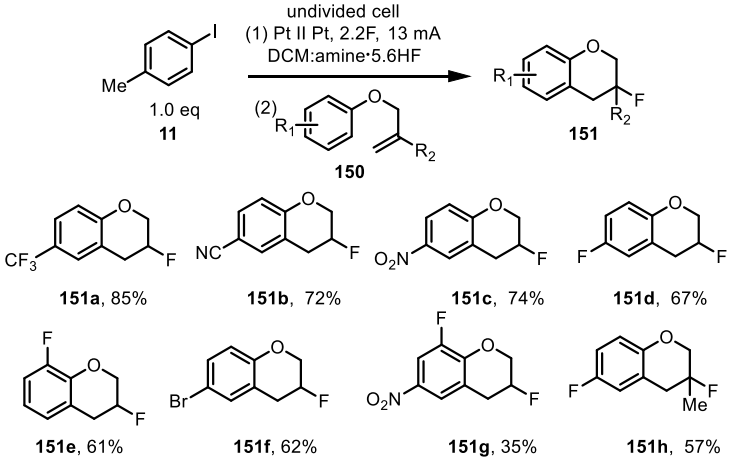
In 2020, the Lennox group reported the anodic vicinal difluorination reaction of nonactivated alkenes **146**, representing an important landmark (Scheme 47). [149a] Electrolysis was conducted in an undivided cell at 8-12 mA/cm^2 using 1.0 equivalent of the 4-iodotoluene (**11**), the mediator being converted at the anode to the difluoroiodotoluene (**7b**). The fluorination of electron-deficient nonactivated alkenes **146** can be carried out using the in-cell approach, whereas electron-rich substrates **148** have to be added to the cell after completing the formation of **7b**. The desired products **147** and **149** could be obtained in 35%−72% yields.





Scheme 47. Electrochemical vicinal difluorination of alkenes **146** and 1**48** by hypervalent iodane mediator

In 2021, the same group accomplished a method for the synthesis of 3-fluorinated chromanes **151** from allylic phenol ethers (Scheme 48). [149b] The external oxidant-free approach utilizes the electrochemically generated hypervalent iodine species, difluoroiodotoluene (**7b**), which mediated the fluoroarylation of alkenes **150**. The utilization of an ex-cell method was key to the success of the process. Good yields (35%−87%) and selectivity for this transformation were achieved for electron poor substrates **150**.

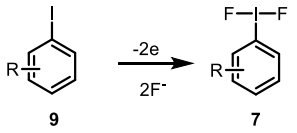


Scheme 48. Electrochemical fluorocyclization of aryl allyl ethers **150** by hypervalent iodane mediator

3. Motivation and Goals

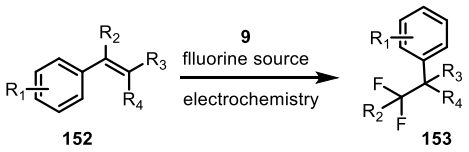
In the past decades, a combination of increasing importance of fluorine-containing molecules and the successful development of bench stable, commercially available fluorine sources have brought the expansion of fluorine chemistry into the mainstream organic synthesis community. However, in many cases, methods for the synthesis of fluorinated compounds in general are often difficult, mainly due to the specific nature of fluorine atoms and the fact that often the introduction of fluorine-containing groups at specific positions in a molecule is the only way to improve its physiological activity. It is necessary to develop diverse and effective methodologies for the synthesis of desired fluorinated target molecules. Based on the experience of hypervalent iodane mediated fluorination methods of the Gulder group [42,43] and preliminary studies by Christoph Brunner, [150] a former member of the Gulder group, we envisioned an electrochemical hypervalent iodane-mediated approach for selective fluorination reactions.

Electrochemical oxidation offers an attractive alternative to traditional chemical reagents for large-scale applications, mainly due to the generation of less toxic waste than that generated by current chemical processes. In addition, electrochemical conditions are compatible with a wide range of functional groups, thus providing a new approach to small molecule synthesis. Generation of the hypervalent F-iodane species *in situ* by electrochemical methods would provide a highly rewarding tool to fluorination chemistry (Scheme 49). Therefore, the development of new methods for the synthesize of hypervalent iodane reagents by electrochemical methods possesses unparalleled promise.



Scheme 49. Proposed electrochemical oxidation process.

In 2018, our group started the research on the topic of electrochemical hypervalent iodane-mediated fluorination reactions. Based on the preliminary results obtained in Christoph's thesis on the 1,1-difluorination, we continued to optimize the reaction conditions using styrene as the substrate. Therefore, substrates **152** (Scheme 50) should be used to further optimize the reaction conditions with the aim of establishing a widely applicable and easy to carry out reaction providing high yields for products **153**. Once optimal reaction conditions are established the substrate scope should be evaluated for a broad range of electronically diverse styrenes bearing electron-rich and electron-deficient functional groups, the latter providing a challenge due to the low activity.



Scheme 50. The conception of *gem*-difluorination of styrenes with electrochemically generated **7**.

To ensure that hypervalent iodanes is generated by electrochemical oxidation, various reaction parameters need to be tested. Reaction parameters must be tested: including current, charge, solvent, and fluorine source. In addition to the commonly used $Et_3N{\cdot}3HF$, other fluorine sources such as Py·HF, fluorinated salts (KF, Bu_4NF, etc.), $BF_3{\cdot}Et_2O$ can be tested. Finally, the *in situ* generation of hypervalent iodanes will then be used with different substrates to synthesize different fluorinated products.

The main goals are therefore:

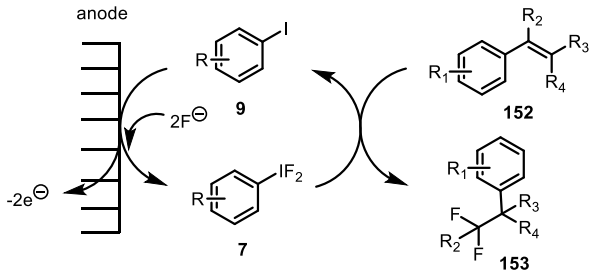
- Evaluation of anodic generation of hypervalent λ^3-iodanes mediated fluorination reaction conditions.
- Optimization of reaction parameters for the *in situ* use of the prepared F-iodanes as electrophilic fluorination reagents with a focus on broad applicability with different substrates.
- Prepare and evaluate cyclic voltammograms to determine suitable substrates for catalytic electrochemical fluorination.
- Investigate the substrates scope

II. Results and Discussion

1. 1, 1- versus 1, 2-Difluorinations of Styrenes – A Guide towards Electrochemical Hypervalent λ^3-Iodane Mediated Fluorinations

Fluorine-containing organic compounds are widely used in pharmaceutical, agrochemical, and materials industries. The geminal difluoro functional group is of particular interest due to its unique pharmacological properties as a bioisostere and modulator of lipophilicity and oxidative stability. [93-96] As such, substantial research efforts have been devoted to their syntheses. Among the methods developed, *gem*-difluorinations of styrene derivatives are one of the most attractive strategies for the synthesis of 1,1-difluorinated products because of the good functional group compatibility and the procedures are mostly efficient from an economical point of view. The common approach was to use (difluoroiodo)arenes **7** directly or to generate (difluoroiodo)arenes **7** *in situ* by ligand exchange with nucleophilic fluorides on an existing λ^3-iodane. In recent years, selectfluor (**10**) and *m*CPBA have been found suitable for the challenging task of selective oxidation of aryl iodides, leading to the formation of reactive hypervalent F-iodane species *in situ*. [35,65-78]

Organic electrosynthesis has been recognized as an atom economical and eco-friendly benign synthetic strategy in synthesis, where the redox process relies on electrons, not the conventional chemical oxidants and reductants. Therefore, electrochemical *in situ* generation of hypervalent iodine species directly used in organic synthesis is more sustainable. In this part, we developed an electrochemical method for *gem*-difluorinations of styrenes **152** as a general, efficient, and mild approach for the synthesis of 1,1-difluorinated compounds **153** (Scheme 51).

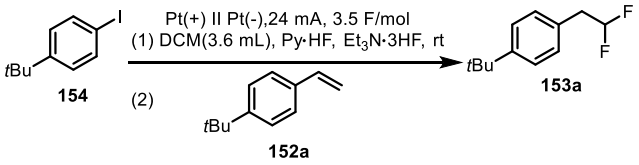


Scheme 51. Electochemical 1,1-difluorinations of styrenes mediated by hypervalent iodanes **9**.

Based on our design, 4-*tert*-butylstyrene (**152a**) was chosen as the model substrate for the optimization of reaction conditions. We employed 4-*tert*-butyliodobenzene (**154**) as the mediator, amine·HF as the electrolyte and fluorine source in an undivided cell equipped with platinum electrodes for the envisioned ex-cell electrochemical 1,1-difluorination. After the electrolysis, 4-*tert*-butylstyrene (**152a**) was added to the cell for the subsequent reaction. We first explored the effect of amine·HF ratio to the reaction (Table 1,

entries 1-5). Unfortunately, when we used $Et_3N{\cdot}3HF$ as the fluorine source, the reaction failed completely (Table 1, entry 1). [92,144] In this case, the poor conductivity of $Et_3N{\cdot}3HF$ may lead to a higher potential of the system, and various by-products may be generated. Gratifyingly, the desired product **153a** was obtained in a very promising 25% yield when we used Py·HF as the fluorine source (Table 1, entry 5). Then we tried the effect of different ratios of mixed Py·HF and $Et_3N{\cdot}3HF$ on this reaction. Whether 25:75 or 75:25 for Py·HF and $Et_3N{\cdot}3HF$, the desired product was obtained in 50% or 41% yields, respectively (Table 1, entries 2 and 5). We found that the best 74% yield was obtained for Py·HF and $Et_3N{\cdot}3HF$ in a 50:50 ratio (entry 3).

Table 1. Amine/HF ratio screening for the reaction.



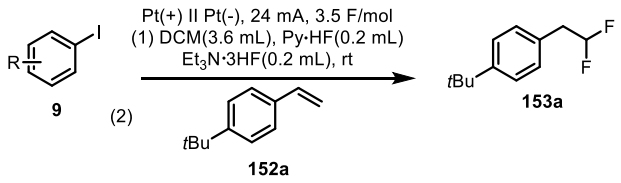
Entry	Py·HF (mL)	$Et_3N{\cdot}3HF$ (mL)	Yield[a] (%)
1	0	0.4	< 5
2	0.1	0.3	50
3	**0.2**	**0.2**	**74**
4	0.3	0.1	41
5	0.4	0	25

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard.

We also attempted to improve the yield by using other iodobenzenes. Therefore, we equipped the iodobenzene core with different substituents. Although a slightly better yield was obtained with 4-iodotoluene (**11**), we still used 4-*tert*-butyliodobenzene (**154**) as the mediator because the by-product of methyl oxidation could not be separated from the desired product due to their similar polarity (Table 2, entry 1). When iodobenzene (**12**) was used as the mediator, the desired product was obtained in 56% yield (Table 2, entry 2). When electron-deficient 4-iodonitrobenzene (**15**) was used as the mediator, a yield of 23% was obtained, which may be due to the high oxidation potential of the substance not being easily oxidized (Table 2, entry 3). When the electron-rich 4-iodoanisole (**16**) was used as the mediator, the reaction failed completely, probably due to the low oxidation potential of the substance leading to its decomposition at the anode (Table 2, entry 4). Other mediators, such as 2,4,6-Me-**9**, were also used to optimize the reaction to obtain a 37% yield (Table 2, entry 5). Furthermore, different equivalents of **154** were tested. With 20 mol% **154**, the yield significant decreased to 9% (Table 2, entry 7). Using 1.0

equivalents of reagent **154** the yield of **153a** was slightly decreased to 64% (Table 2, entry 8). While increasing the equivalents to 1.2 equivalents or 1.5 equivalents of 4-*tert*-butyliodobenzene (**154**) resulted in a slightly decreased 70% yield (Table 2, entries 9-10).

Table 2. Iodobenzene screening for the reaction.

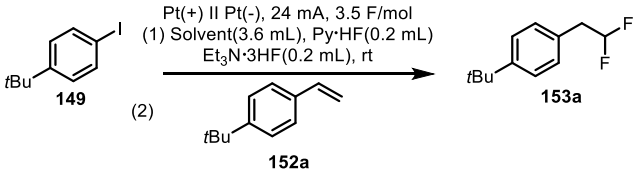


Entry	R	Eq.of **9**	Yield[a] (%)
1	4-Me	1.2	76[b]
2	4-H	1.2	56
3	4-NO_2	1.2	23
4	4-OMe	1.2	< 5
5	2,4,6-Me	1.2	37
6	**4-*t*Bu**	**1.2**	**74**
7	4-*t*Bu	0.2	9
8	4-*t*Bu	1.0	64
9	4-*t*Bu	1.5	70
10	4-*t*Bu	2.0	70

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard. [b]Mediator oxidation product(s) could not be separated from desired product.

The evaluation of solvents was subsequently carried out. As shown in Table 3, the corresponding product **153a** could be obtained in 74% yield in DCM (Table 3, entry 1). When DCE was used as the solvent, a slightly decreased yield of 65% was observed (Table 3, entry 2). Fluorinated solvents are known to stabilize hypervalent iodanes by the anodic oxidation of iodoarenes, so we chose fluorinated alcohols as solvents to optimize the reaction. [139] However, to our surprise, no products were formed when we used TFE or HFIP as solvents (Table 3, entries 3-4). Other solvents, such as $CHCl_3$ or MeCN, were used as solvents, no products were produced (Table 3, entries 5-6).

Table 3. Solvent screening for the reaction.

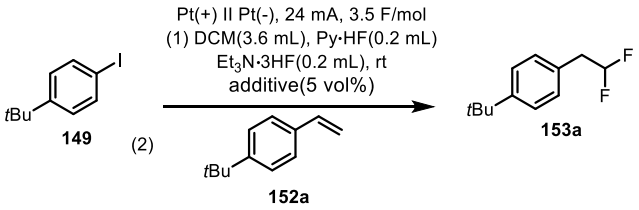


Entry	Solvent	Yield[a] (%)
1	**DCM**	**74**
2	DCE	65
3	TFE	-
4	HFIP	-
5	$CHCl_3$	-
6	MeCN	-

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard.

Although the strategy of enhancing the yield with fluorinated solvents failed, we wondered if we could use some additives to stabilize the hypervalent iodane, so we tried different additives to optimize the reaction. With the optimized solvent in hand, we then investigated the effect of different additives. Unfortunately, the additive HFIP reduced the reaction yield to 45% (Table 4, entry 2). When PEG 200 was used as the additive, the desired product **153a** could not be obtained. 1,2-dimethoxyethane was also utilized as the additive in this system, however, no conversion of the 4-*tert*-butylstyrene (**152a**) occurred either. The ethylene glycol additive resulted in trace yields for the same reaction as PEG 200 (Table 4, entry 5).

Table 4. Additives screening for the reaction.



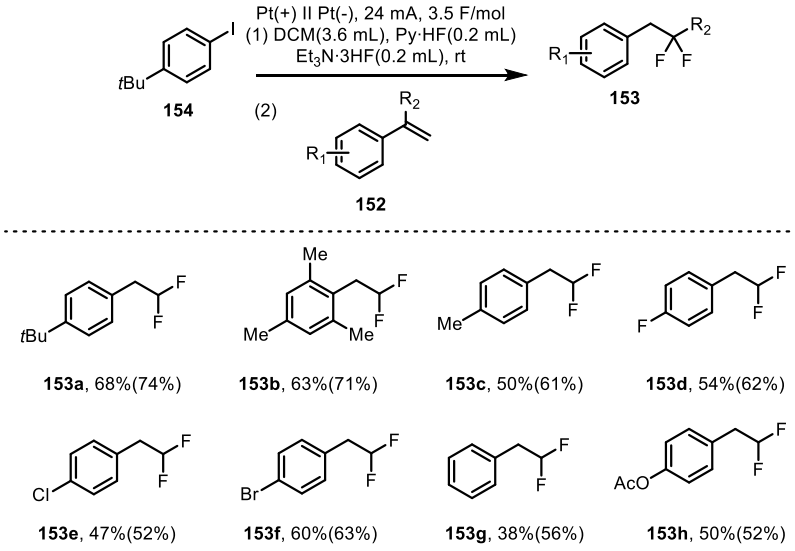
Entry	Additive (5 vol%)	Yield[a] (%)
1	-	**74**
2	HFIP	45
3	PEG 200	< 5
4	1,2-dimethoxyethane	< 5
5	ethylene glycol	< 5

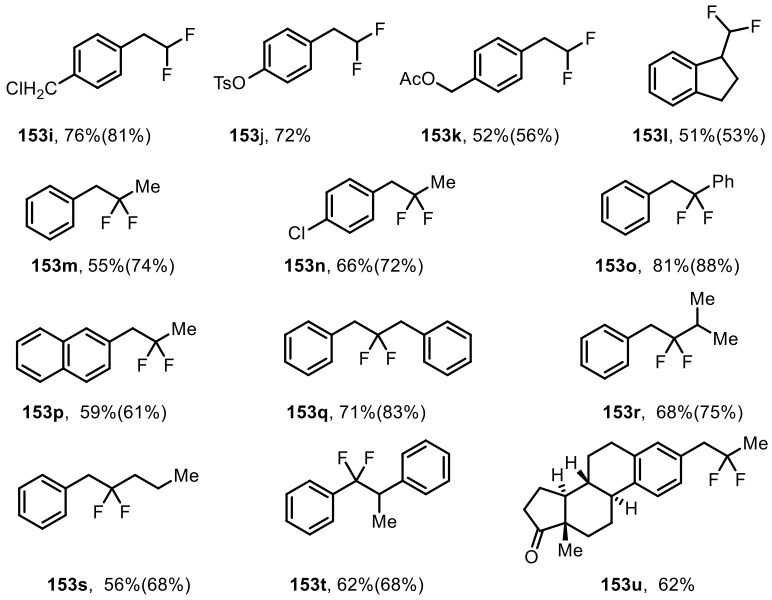
[a]Determined by NMR spectroscopy from the crude mixture

with ethyl fluoroacetate as the internal standard.

With the optimized reaction conditions in hand, we explored the generality of the protocol with various electron-rich or oxidation sensitive styrenes (Scheme 52). It was found that a wide range of styrenes **152** with different substituents could be reacted smoothly in moderate to good yields (38%−88%). For instance, reactions with 4-Me and sterically hindered 2,4,6-Me substituted substrates proceed successfully and afforded the corresponding products **153c** and **153b** in 50% and 63% yields, respectively. Styrene substituted with halogens including 4-F **152d**, 4-Cl **152e**, 4-Br **152f**, yielded **153d-153f** of the desired product in 47%−60% yields. For styrene (**152g**), an isolated yield of 38% was obtained due to the low boiling point of the product and its volatility. Additionally, 4-OAc, 4-CH_2Cl, 4-OTs, 4-CH_2OAc substituted styrenes were tolerated, gave the desired product **153h-153k** in 50%−76% yields. For the cyclic substrate 1,2-dihydronaphthalene (**152l**), the ring-contracted product **153l** was obtained in 51% yield.

Next, we turned our attention to the applicability of our developed procedure. Gratifyingly, α-substituted styrenes **152m-152s** were well tolerated and gave good yields of the desired products **153m-153s**. For example, the use of α-methyl styrene **152m** gave the corresponding product **153m** with a yield of 55%. The 4-Cl-substituted α-methyl styrene **152n** was also suitable for this system, which afforded **153n** in 70% yield. The 1,1-diphenylethylene substrate (**152o**) was compatible and the difluorinated product **153o** was obtained smoothly in 81% yield. In addition, α-naphtyl substituted substrate **152p** was also studied, and the corresponding product **153p** was generated in 59% yield. Other α-alkyl substituted substrates, such as benzyl **152q**, isopropyl **152r** and propyl **152s**, were also well tolerated and gave the target products **153q-153s** in 56−71% yields. To our surprise, α, β-disubstituted styrene **152t**, a challenging substrate, was also tolerated, produced product **153t** in 62% yield. Moreover, estrone derivative **152u** could be smoothly converted to the corresponding geminal difluorinated product **153u** in good 62% yield.



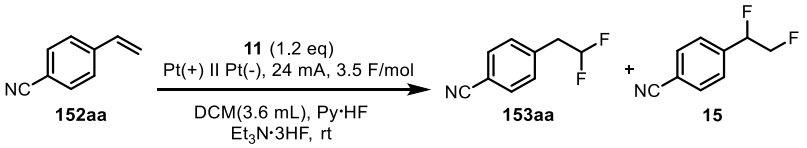


Scheme 52. Substrate scope for the ex-cell conversion of styrenes **152**.

However, when electron-deficient substrate 4-cyanostyrene (**152aa**) was submitted to the ex-cell reaction conditions, the desired product **153aa** was afforded in a trace yield only, but giving a moderated yield of 1,2-difluorinated product **155**. Therefore, we have to change our strategy for the 1,1-difluorination of electron-deficient styrenes. As CV studies revealed that electron-deficient styrene has a higher oxidation potential than electron-donating styrene, then we tried to focus on in-cell electrochemical 1,1-difluorination of electron-deficient styrenes. Based on previous literature, [67,117] electron deficient substrates tend to give the 1,2-product as the phenonium ion intermediate cannot be formed and thus no 1,2-aryl migration takes place. Increasing the ratio of amine to HF would lead to the easy formation of 1,1-difluorinated products, and only in highly acidic HF, such as Py·HF, the intermediate is stabilized, resulting in the formation of 1,1-difluorinated products.

First, we conducted a preliminary screening of the reaction conditions. We tried to increase the yield of 1,1-difluorinated product **153aa** by decreasing the current, and the 1,2-difluorinated products **155** were still obtained in 19%-32% yield at either 24 or 12 and 6 mA (Table 5, entries 1-3). Then we attempted to use 0.4 mL Py·HF as the fluorine source, since it contains more content of HF, and to our delight, we obtained 18% of the target product **153aa**, despite 31% of the 1,2-difluorinated product **155** (Table 5, entry 4).

Table 5. Initial screening of reaction conditions.

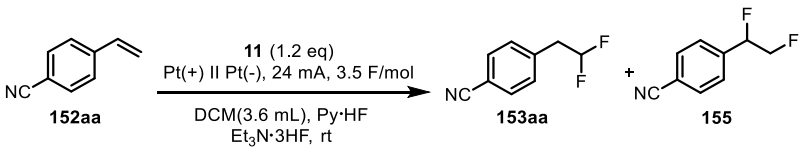


Entry	Py·HF (mL)	$Et_3N·3HF$ (mL)	Current (mA)	Yield **153aa**, **155**[a] (%)
1	0.2	0.2	24	trace, 21
2	0.2	0.2	12	trace, 32
3	0.2	0.2	6	trace, 19
4	**0.4**	**0**	**12**	**18, 31**

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard.

We continued to optimize the solvent and gas atmosphere to verify if this will have a positive effect on the reaction. When we used an argon atmosphere, the desired product **152aa** did not increase, but the 1,2-difluorinated **155** product decreased slightly. By using dried and degassed DCM on air, the yield of both fluorinated products slightly increased (Table 6, entry 3). We then conducted the reaction using dry degassed DCM in argon under the same conditions, to our surprise, 47% of the desired yield **152aa** and 45% of the 1,2-difluorinated product **155** were obtained (Table 6, entry 4).

Table 6. Solvent and atmosphere screening.



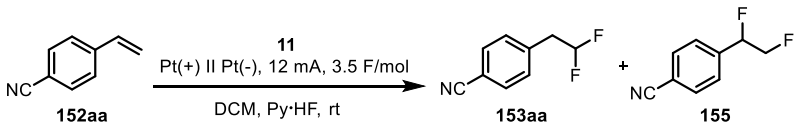
Entry	DCM	atmosphere	Yield **153aa**, **155**[a] (%)
1	distilled	air	18, 31
2	distilled	argon	18, 26
3	dry+degassed	air	27, 28
4	**dry+degassed**	**argon**	**47, 45**

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard.

We next attempted to increase the yield by increasing the amount of mediator, and unexpectedly we got a reduced yield (Table 7, entries 2 and 3). When we increased the amount of Py·HF, the reaction using 2.0 mL of Py·HF gave the best 56% yield (Table 7, entries 4 and 5). While reducing the mediator to catalytic amounts resulted in decrease yield (Table 7, entries 6 and 7). When the reaction was carried out without 4-

iodotoluene (**11**), no desired product was obtained at all, but 67% of the 1,2-difluorinated product **155** was obtained instead (Table 7, entry 8).

Table 7. Iodobenzene and Py·HF screening for the reaction.

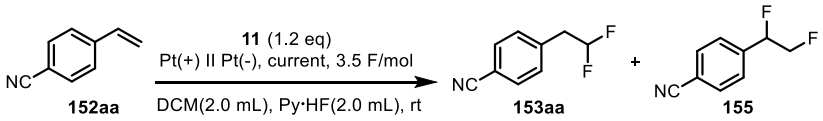


Entry	4-TolI (eq)	DCM (mL)	Py·HF (mL)	Yield **153aa**, **155**[a] (%)
1	1.2	3.6	0.4	47, 45
2	1.5	3.6	0.4	43, 30
3	2.0	3.6	0.4	37, 13
4	1.2	2.4	1.6	55, 8
5	**1.2**	**2.0**	**2.0**	**56, 1**
6	0.6	2.0	2.0	46, 38
7	0.2	2.0	2.0	11, 55
8	-	2.0	2.0	-, 67

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard.

We then attempted to increase the yield by reducing the current, lowering the current to 10 mA gave a slight increase in the desired product **153aa**, and further lowering to 8 mA gave no increase in **153aa** yield (Table 8, entries 2 and 3).

Table 8. Current screening for the reaction.

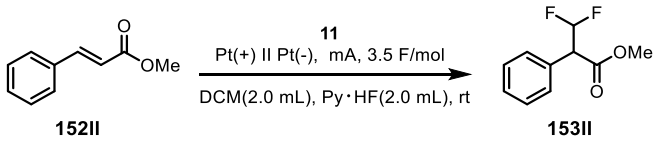


Entry	Current (mA)	Yield **153aa**, **155**[a] (%)
1	12	56, 1
2	**10**	**60, 2**
3	8	56, 3

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard.

Furthermore, we would like to achieve catalytic reactions with some substrates, so we chose **152ll** as the substrate and performed a simple optimization of it, and to our excitement, with 0.2 equivalents of catalyst, the reaction yielded the target product **153ll** smoothly with a very good 80% yield (Table 9, entry 2), and reducing the amount of catalyst to 0.1 equivalents, the yield decreased to 67% (Table 9, entry 3), and without catalyst, the reaction could not proceed (Table 9, entry 4), which demonstrated the importance of catalyst for this reaction.

Table 9. Optimization for catalytic reaction conditions for the difluorination of methyl cinnamate (**152ll**).



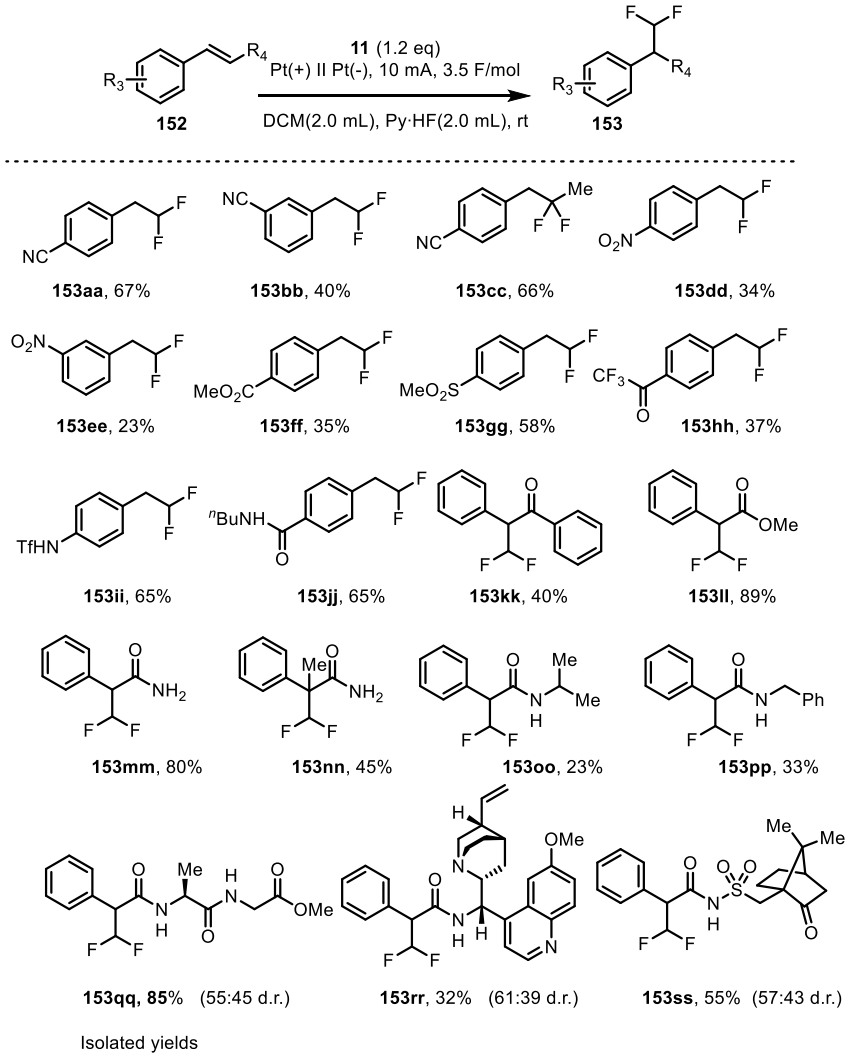
152ll **153ll**

Entry	4-TolI (**11**, eq)	Current (mA)	Yield **153ll** [a] (%)
1	1.2	10	90
2	**0.2**	**8**	**80**
3	0.1	8	67
4	-	8	-

[a]Determined by NMR spectroscopy from the crude mixture with ethyl fluoroacetate as the internal standard.

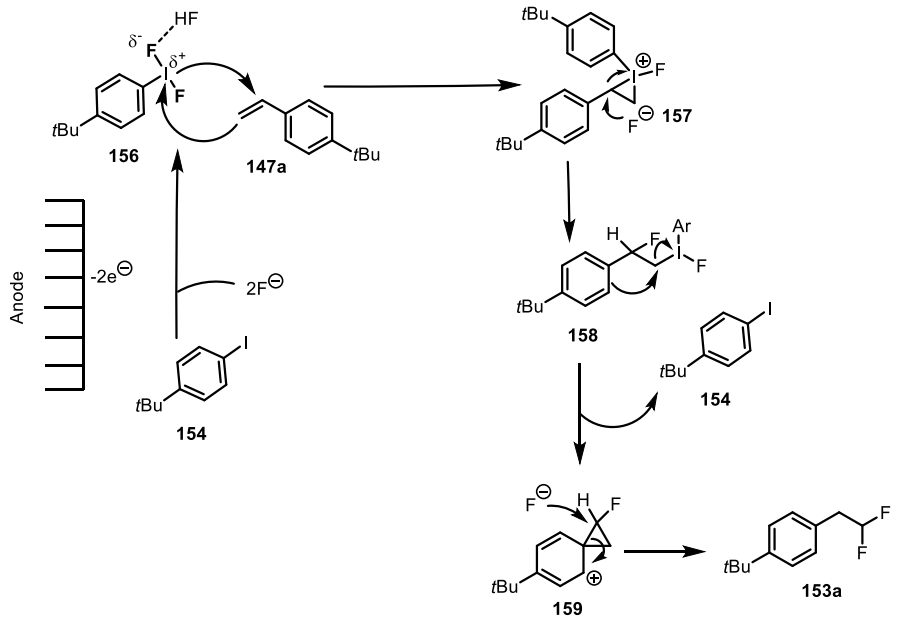
After extensive re-optimization, we found that the desired 1,1-difluorinated product **152aa** could be obtained in 67% isolated yield under 10 mA constant current by utilizing Py·HF as the electrolyte and fluorine source, 1.2 equivalents of 4-iodotoluene (**11**) as the mediator, degassed DCM as the solvent under Argon atmosphere. With the new in-cell optimized reaction conditions in hand, the scope of electron-deficient substituted styrenes **152** were examined (Scheme 53). Styrenes bearing various functional groups such as strongly electron-withdrawing were compatible with the reaction conditions to afford the desired 1,1-difluorinated products **152aa**-**152hh** in moderate to good yields. For example, reactions with *meta*-, *para*-CN and NO_2 **152aa**-**152ee** substituted styrenes proceed successfully, gave the corresponding products **153aa**-**153ee** in 23%−67% yields. Other electron-withdrawing groups substituted with styrene were also compatible, such as CO_2Me, SO_2Me, $COCF_3$ **152ff**-**152hh**, were subjected to the reaction conditions, to obtain the target products **153ff**-**153hh** in 35%−58% yields. Substrates **152ii** and **152jj** underwent the reaction easily to produce the product **153ii** and **153jj** in good yields. We also tested commercially available ElectraSyn 2.0 set-up and found that the yield obtained with **153aa** was comparable to our set-up. To further demonstrate the synthetic utility of the electrosynthesis, the 1,1-difluorination reaction of **152aa** was

performed on a gram scale. Gratifyingly, the reaction generated the desired product **153aa** in 48% yield. Furthermore, we also investigated the scope of β-substituted styrenes. Specifically, chalcone **152kk** and methyl cinnamate **152ll** were tolerated, thus delivered the expected products **153kk** and **153ll** in 40% and 89% yields, respectively. In addition, we also achieved catalytic 1,1-difluorination of methyl cinnamate**152ll**. Various cinnamides such as **152mm**-**152pp** were also tolerated in the reaction, affording the desired product **153mm**-**153pp** in moderate to good yields. It is noteworthy that for dipeptide substrate **152qq**, the product **153qq** was obtained in a high yield. In addition, this protocol is also compatible with complex cinnamides scaffolds, such as quinine derivative **152rr**, camphor derivative **152ss**, successfully gave the corresponding products **153rr** and **153ss** in 32% and 55% yields, respectively.



Scheme 53. Substrate scope of electron-deficient and β-substituted styrenes **152**.

To gain deeper insight into the mechanism, mechanistic investigations were performed. Based on the geminal difluorintion of styrenes reported previously, the mechanism of the reaction can be verified as shown in Figure 4 and Figure 5. Then, the mechanism of the reaction can be explained as shown in Scheme 54. First, 4-*tert*-butyliodobenzene (**154**) loses two electrons and generates *t*BuC$_6$H$_4$IF$_2$ (**156**) under electric current and anion. Then 4-*tert*-butylstyrene (**152a**) would attack by the activated iodane **156** to form a three-membered cyclic iodiranium **157**, which would be opened by the nucleophilic attack of the fluoride ion leading to the alkyl iodonium adduct **158**. Then, due to the good leaving group ability of the iodoarene moiety in **158**, an intramolecular 1,2-phenyl shift produced the spirocyclic phenonium ion **159**, which is then attacked by a second fluoride at the fluorinated carbon to produce the geminal difluorinated product **153a**.



Scheme 54. Proposed Mechanism of 1,1-Difluorinations of Styrenes.

To gain more insight into this reaction, cyclic voltammetry (CV) experiments were carried out. As shown in the Figure 6 and 7, the oxidation peak of mediator **154** was observed at 2.76 V, while the oxidation peak of model substrate **152a** was found at 3.01 V. These results show that **154** and **152a** were more easily oxidized simultaneously under standard conditions, so the ex cell approach could be better understood for this type of substrate. For electron-deficient olefins such as **152aa**, we found that such substrate has a higher oxidation peak at 3.79 V than that of mediator **11** at 2.56 V, which means that we could use the in cell method for such substrates (shown in the Figure 8 and 9).

2. Electrochemical Iodoarene-Catalyzed Synthesis of Fluorinated 2-Oxazolines

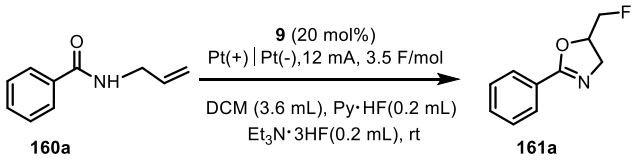
N-Heterocyclic compounds are very important as pharmaceuticals, agrochemicals, and ligands for organometallic chemistry.[151-153] Of the various heterocyclic compounds, the oxazolines are important structural motifs in many biologically natural compounds.[154-156] Furthermore, chiral oxazolines have been widely used as auxiliaries and ligands in asymmetric synthesis.[157] Although numerous methods have been reported for the synthesis of 2-oxazolines **161** from carboxylic acids,[158-160] esters,[161,162] nitriles,[163-165] aldehydes,[166-168] amides,[169-171] and alkenes.[172-174] However, most of them suffer from disadvantages, including long reaction times, high reaction temperatures, the use of complex and expensive reagents and toxic solvents, the requirement of a large amount of catalyst and low product yields. Therefore, the development of a new efficient, simple, and practical method for the synthesis of 2-oxazolines **161** is still highly in demand. Moreover, the modification of the oxazolines motif by introduction of a fluorine atom is of great importance both for biology and organic synthesis research, but the methods to access monofluoromethyl-substituted oxazolines through alkene cyclization are rare. As a result, the efficient synthesis of these fluorinated heterocycles **161** has attracted much attention.

Among the methods developed, cyclization of *N*-allylcarboxamides **160** is one of the most attractive strategies for the synthesis of oxazolines **161** because of the rapid structural assembly, good functional group compatibility, and economical procedure.[175-179] In recent years, hypervalent iodine reagents have been used in the synthesis of fluorine-containing heterocyclic compounds.[129,146,148] Unfortunately, most of these reactions require stoichiometric iodobenzene or a huge excess of amine·HF. In 2019, Waldvogel group established a method for synthesizing 5-fluoromethyl-2-oxazolines **161** by hypervalent iodoarene-mediated fluorocyclization using electric current as the sole oxidant. [146] Inspired by our previous results and our long-standing interest in hypervalent iodane-mediated reactions, we have recently discovered an efficient I(I)/I(III)-catalyzed fluorocyclization of *N*-allylcarboxamides **160** to 5-fluoromethyl-2-oxazolines **161** using electric current as the oxidant. Herein, we presented our research results in detail.

Initially, we started our investigation using *N*-allylbenzamide **160a** as the model substrate (Table 10). The reaction was performed in an undivided cell using platinum plate as anode and cathode, 4-iodotoluene (**11**) as catalyst, Py·HF (0.2 mL) and $Et_3N{\cdot}3HF$ (0.2 mL) as electrolyte and fluorine source, 12 mA constant current as the oxidant in DCM at room temperature. Pleasingly, the desired product 2-oxazolines **161a** was obtained with 49% yield (Table 10, entry 1). Then, we investigated different iodobenzenes, as shown in entries 2-6 of Table 8. When the electron-rich 4-iodoanisole (**16**) was used as the mediator, the reaction gave a low 18% yield. When 2-CO_2Me-**9** was used as the mediator, the desired product was obtained in 49%

yield (Table 2, entry 2). When 4-*tert*-butyliodobenzene (**154**) was used as the mediator, the desired product was obtained in 77% yield (Table 10, entry 4). Other mediators, such as 4-Br-2,6-Me-**9** and 2,4,6-Me-**9**, were also used to optimize the reaction to obtain 72% and 45% yield, respectively (Table 10, entries 5 and 6).

Table 10. Iodobenzene screening for the reaction.

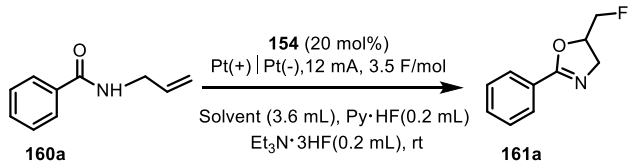


Entry	R	Yield[a] (%)
1	4-Me	49
2	4-OMe	18
3	2-CO_2Me	49
4	**4-*t*Bu**	**77**
5	4-Br-2,6-Me	72
6	2,4,6-Me	45

[a] Determined by 1H NMR with an internal standard.

Next, various solvents were carefully screened. As shown in Table 11, the corresponding product **161a** could be obtained in 77% yield in DCM (Table 11, entry 1). When DCE was used as the solvent, the yield decreased dramatically to 29% (Table 11, entry 2). Using other solvents such as MeCN or $CHCl_3$ as solvents, the desired product **161a** was obtained in 20% and 21% yields, respectively (Table 11, entries 3-4).

Table 11. Solvent screening for the reaction.

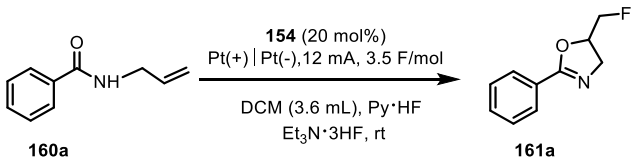


Entry	Solvent	Yield[a] (%)
1	**DCM**	**77**
2	DCE	29
3	MeCN	20
4	$CHCl_3$	21

[a]Determined by ^{1}H NMR with an internal standard.

We next explored the effect of the amine/HF ratio (Table 12). Unfortunately, when we used 0.4 mL $Et_3N{\cdot}3HF$ as the fluorine source, the reaction failed completely (Table 11, entry 1). Pleasingly, the desired product **161a** was obtained in a 36% yield when we used 0.1 mL Py·HF and 0.3 mL $Et_3N{\cdot}3HF$ as the fluorine source (Table 11, entry 2). This means that Py·HF as the fluorine source would be important for this reaction, so we continued to increase the amount of Py·HF to improve the yield. When 0.2 mL and 0.2 mL or 0.3 mL and 0.1 mL of Py·HF and $Et_3N{\cdot}3HF$ were used, the desired products were obtained in good yields of 77% or 95%, respectively (Table 12, entries 3 and 4). Finally, we found that the best yield was obtained for 0.4 mL Py·HF (Table 12, entry 5).

Table 12. Amine/HF ratio screening for the reaction.

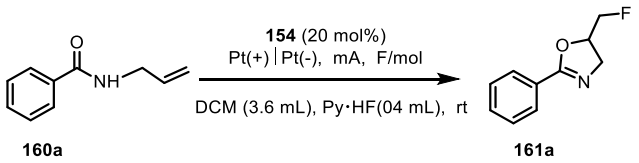


Entry	Py·HF (mL)	$Et_3N{\cdot}3HF$ (mL)	Yield[a] (%)
1	0	0.4	trace
2	0.1	0.3	36
3	0.2	0.2	77
4	0.3	0.1	95
5	**0.4**	**0**	**＞95**

[a]Determined by ^1H NMR with an internal standard.

Last, the current and applied charge were then examined (Table 13). When we lowered the current to 10 mA, there was no decrease in the reaction yield (Table 13, entry 2). Therefore, we continued to lower the current to 8mA and reduced the charge to 2.4 F, and the yield remained unchanged (Table 13, entry 3).

Table 13. Current and charge screening for the reaction.



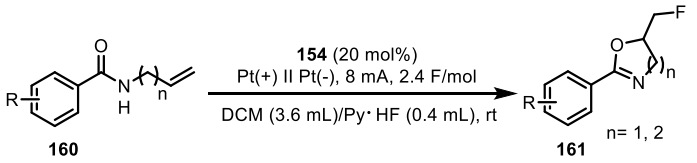
Entry	Charge (F)	Current (mA)	Yield[a] (%)
1	3.5	12	＞95
2	3.5	10	＞95

3	**2.4**	**8**	**>95**

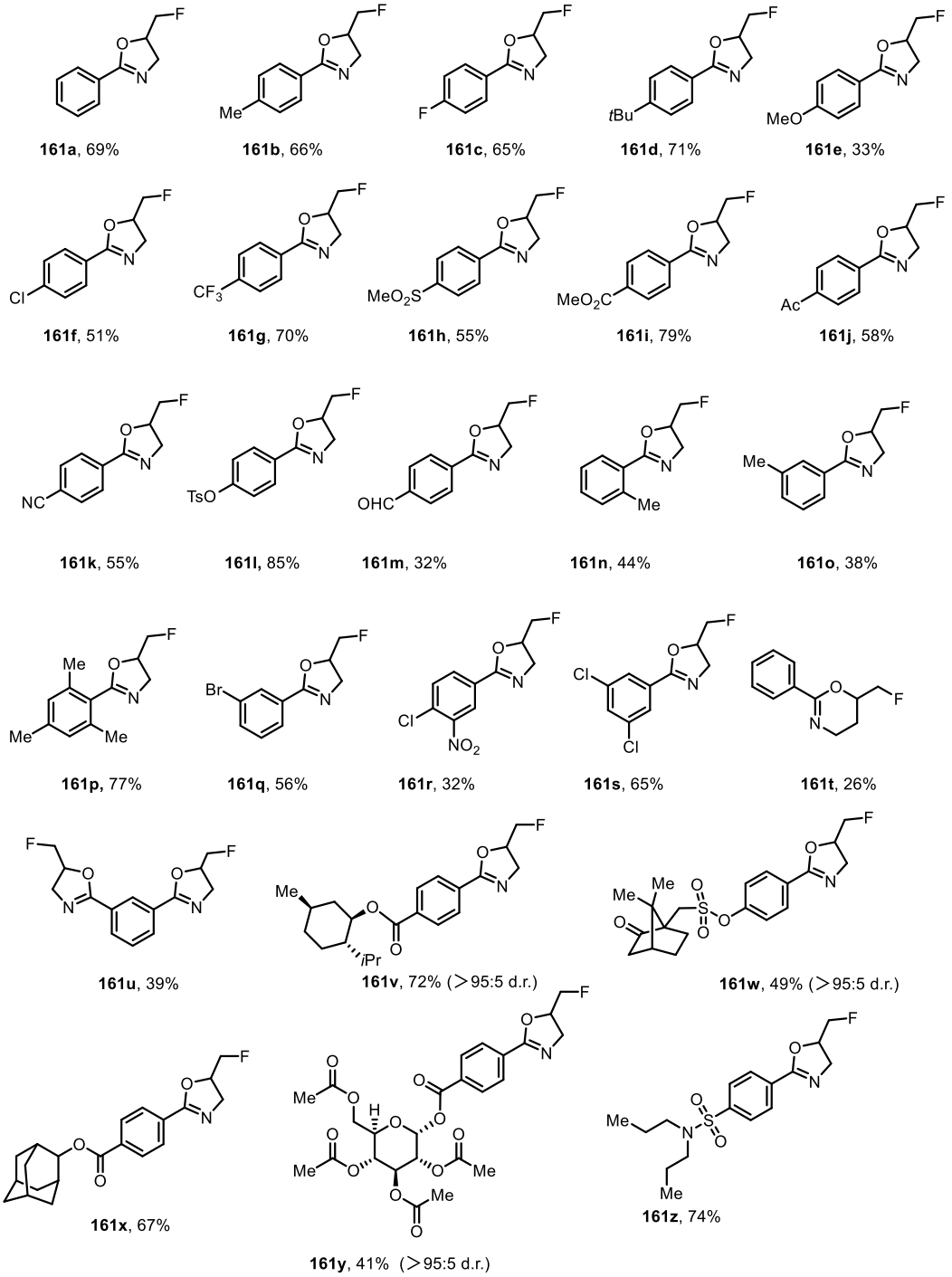
[a]Determined by ^{1}H NMR with an internal standard.

With the optimal reaction conditions in hand, the scope of *N*-allylcarboxamides **160** with different electronic properties and substitution patterns of the aryl ring was investigated (Scheme 55). As previously reported, hydrolysis during column chromatography results in reduced isolated yield. Therefore, under the standard conditions, the model substrate **160a** gave the 2-oxazoline **161a** only in 69% isolated yield. *N*-allylcarboxamides **160** bearing either electron-donating or electron-withdrawing groups were compatible with the transformation to afford the 2-oxazolines **161b**-**161l** in 33%−85% yields. For instance, reactions with *ortho*-**160n**, *meta*-**160o**, *para*-methyl **160b**-substituted, and sterically hindered **160p** *N*-allylcarboxamides **160** proceed successfully, afforded the corresponding products **161n**-**161p** and **161b** in 38%−77% yields. Electron-donating groups such as *tert*-butyl **160d** and methoxy-substituted **160e** substrates proceeded well. The target products **161d** and **161e** were obtained in 71% and 33% yields, respectively. *N*-allylcarboxamides **160** substituted with halogens including 4-F **160c**, 4-Cl **160f**, 3-Br **160q**, gave the corresponding products in moderate yields (**161c**, 65%; **161f**, 51%; **161q**, 56%). Electron-withdrawing groups substituted substrates, such as CF_3 **160g**, SO_2Me **160h**, CO_2Me **160i**, Ac **160j**, CN **160k**, OTs **160l**, at the *para*-position of the phenyl rings gave the desired products **161g**-**161j** in moderate to good yield (55%−85%). Notably, CHO-substituted *N*-allylcarboxamide **160m** was tolerated, even though it is well-known to be easily oxidized, generating the desired product **161m** in 32% yield. Disubstituted substrates such as **160r** and **160s** were also tolerated, gave the desired products **161r** and **161s** in 32% and 65% yields, respectively. Furthermore, *N*-(but-3-en-1-yl)benzamide **160t**, a challenging substrate for cyclization reaction, was also tolerated, although produced the corresponding product **161t** only with 26% yield. We then observed that the optimal reaction conditions were suitable for substrate **160u**, afforded the bisoxazoline **161u** in 39% yield.

In addition, a particularly noteworthy aspect of this protocol is its amenability to late-stage synthetic applications. This procedure is also compatible with complex natural products and pharmaceuticals derivatives, such as L-menthol **160v**, camphor **160w**, and 2-adamantanol **160x** derivatives, successfully gave the corresponding products **161v**-**161x** in 49%−72% yields. Furthermore, glycoside **160y**, probenecid **160z**, and dihydrocholesterol **160aa** derivatives, were submitted to the reaction conditions, thus provided desired products **161y**-**161z** and **161aa** in 41%−74%.



160 **161**



161a, 69% **161b**, 66% **161c**, 65% **161d**, 71% **161e**, 33%

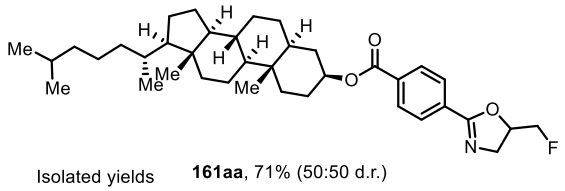
161f, 51% **161g**, 70% **161h**, 55% **161i**, 79% **161j**, 58%

161k, 55% **161l,** 85% **161m**, 32% **161n**, 44% **161o**, 38%

161p, 77% **161q**, 56% **161r**, 32% **161s**, 65% **161t**, 26%

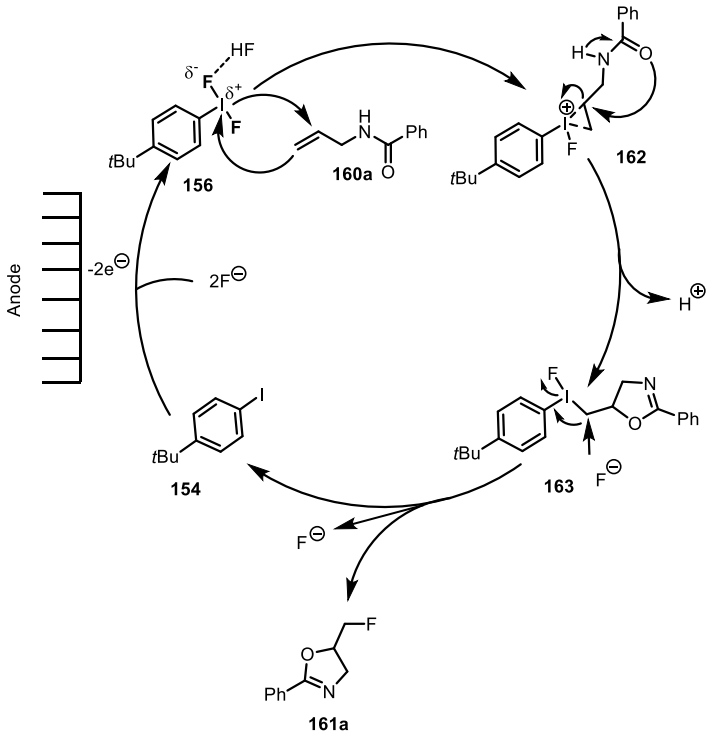
161u, 39% **161v**, 72% (>95:5 d.r.) **161w**, 49% (>95:5 d.r.)

161x, 67% **161y**, 41% (>95:5 d.r.) **161z**, 74%



Scheme 55. Substrate scope of *N*-allylcarboxamides **160**.

Based on previous literature,[146] a plausible mechanism was proposed. As shown in Scheme 56, first, 4-*tert*-butyliodobenzene (**154**) loses two electrons and generates (4-(*tert*-butyl)phenyl)difluoro-λ^3-iodane (**156**) under electric current and fluoride anion. Then **156** was attacked by the nucleophilic double bond in **160a** to form the iodonium species **162**. Intramolecular ring opening of the three-membered heterocycle by the carbonyl forms the 5-(λ^3-iodanyl)methyloxazoline **163**, which is converted into product **161a** and 4-*tert*-butyliodobenzene (**154**) after an S_N2-type substitution with fluoride acting as the nucleophile.



Scheme 56. Proposed Mechanism of Fluorocyclization of *N*-allylcarboxamides **160**.

To gain more insight into this reaction, cyclic voltammetry (CV) experiments were carried out. As shown in the Figure 6 and 10, the oxidation peak of mediator **154** was observed at 2.76 V, while no obvious oxidation peak of **160a** was observed at 0−4.5 V. These results indicate that **160a** was not easily oxidized under standard conditions, and therefore, for this reaction, a catalytic amount of **154** was possible.

3. Electrochemical Iodoarene-Catalyzed Intramolecular Aminofluorination of Alkenes

Azaheterocyclic compounds such as piperidines are also important structural motifs in a variety of biologically interesting compounds and can be used as useful building blocks for the synthesis of complex natural products.[180-183] The 3-fluoropiperidines **165** are particularly important in medicinal chemistry due to their specific steric and electronic properties.[184-186] Therefore, developing effective and rapid fluorination methods to access such molecules is important and highly desired. The alkene difunctionalization would represent a general and effective route as alkene functionalization has proved to be a powerful approach to access azaheterocycles.[187-190] Although great progress has been achieved, [122,123,125,126] few effective approaches are available for the synthesis of these fluorinated molecules. Among the methods developed, intramolecular aminofluorination of alkenes is one of the most attractive strategies for the synthesis of β-fluoropiperidines because of the rapid structural assembly, good functional group compatibility, and economical procedure.

In recent years, direct aminofluorination of alkenes **164** mediated by hypervalent iodanes has become one of the most attractive strategies to synthesize amino-fluoro-compounds without using a noble metal catalyst.[122-127] In this part, electrochemistry has been explored as an efficient, versatile, and sustainable approach for the intramolecular aminofluorination of alkenes. Meanwhile, our goal is to use a readily available, cheap, and easily handled fluorine source, so we choose $BF_3 \cdot Et_2O$ to replace the traditional toxic HF to achieve this transformation. Herein, we first disclosed an electrochemical iodoarene-catalyzed intramolecular aminofluorination of alkenes to provide 3-fluoropiperidines with $BF_3 \cdot Et_2O$ as the fluorine source.

Based on our design, we employed alkene tosylamide **164a** as the model substrate and probed various reaction conditions in an undivided cell equipped with platinum electrodes for the envisioned electrochemical aminofluorination. At first, we employed one equivalent 4-*tert*-butyliodobenzene (**154**) as the mediator. To our delight, the aminofluorination product **165a** was obtained in 52% yield (Table 14, entry 1). While reducing the mediator to the catalytic 0.2 equivalents resulted in a significant decrease in 13% yield (Table 14, entry 4). We also attempted to improve the yield by using other iodobenzenes. When iodobenzene (**12**) was used as the mediator, the desired product was obtained in 17% yield (Table 14, entry 3). When electron-deficient 4-iodonitrobenzene (**15**) was used as the mediator, a yield of 37% was obtained (Table 14, entry 4). When the electron-rich 4-iodoanisole (**16**) was used as the mediator, the reaction gave only 6% yield (Table 14, entry 5). Other mediators, such as 4-CN-**9**, 4-CO_2Me-**9** were also used to optimize the reaction to obtain 37% and 66% yields (Table 14, entries 6 and 7). When we used 4-F-**9** as the mediator,

the yield of target product **165a** increased to 75% (Table 14, entry 8). We achieved the best yield when using 4-iodobenzotrifluoride (**166**) as the mediator, obtaining the expected product in 77% yield (Table 14, entry 9). We then tried using a catalytic amount of **166**, to our great surprise, the yield did not decrease (Table14, entry 10).

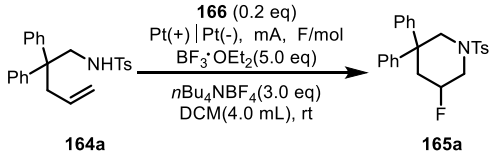
Table 14. Iodobenzene screening for the reaction.

Entry	R	Eq. of 9	Yield[a] (%)
1	4-*t*Bu	1.0	52
2	4-*t*Bu	0.2	13
3	4-H	1.0	17
4	4-NO_2	1.0	37
5	4-OMe	1.0	6
6	4-CN	1.0	37
7	4-CO_2Me	1.0	66
8	4-F	1.0	75
9	4-CF_3	1.0	77
10	**4-CF_3**	**0.2**	**77**

[a] Determined by NMR spectroscopy from the crude mixture with 1,3,5-trimethoxybenzene as the internal standard.

Then, the current and applied charge were examined next. Increasing the current to 12 mA, or lowering to 4 mA gave a slight decrease in yield (Table 15, entries 1 and 3). By reducing the charge to 2.4 F, the yield was also slightly reduced (Table15, entry 4).

Table 15. Current and charge screening for the reaction.



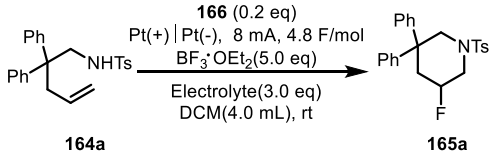
Entry	Charge (F)	Current (mA)	Yield[a] (%)

1	4.8	12	67
2	**4.8**	**8**	**77**
3	4.8	4	75
4	2.4	8	67

[a] Determined by NMR spectroscopy from the crude mixture with 1,3,5-trimethoxybenzene as the internal standard.

Next, different electrolytes were screened, the yield decreased substantially to 16% when $nBu_4NPF_6$was used as the electrolyte (Table 16, entry 2). When nBu$_4$NHSO$_4$ or nBu$_4$NOAc were used as the electrolyte, no product was formed (Table 16, entries 3 and 4).

Table 16. Electrolyte screening for the reaction.



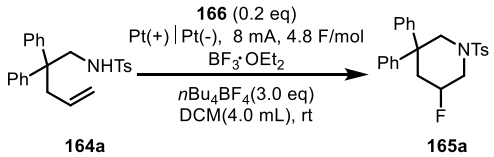
164a **165a**

Entry	Electrolyte	Yield[a] (%)
1	***n*Bu$_4$NBF$_4$**	**77**
2	nBu$_4$NPF$_6$	16
3	nBu$_4$NHSO$_4$	-
4	nBu$_4$NOAc	-

[a] Determined by NMR spectroscopy from the crude mixture with 1,3,5-trimethoxybenzene as the internal standard.

Finally, we optimized the amount of fluorine source. When the amount of $BF_3{\cdot}Et_2O$ was increased to 7.0 equivalents, the yield did not increase (Table 17, entry 1). When the amount of $BF_3{\cdot}Et_2O$ is reduced to 3.0 equivalents, resulting in a slight decrease in 73% yield (Table 17, entry 3). However, when the amount of $BF_3{\cdot}Et_2O$ is reduced to 1.0 equivalent, the yield dropped significantly to 20% (Table 17, entry 4). Without $BF_3{\cdot}Et_2O$, there was no product formed (Table 17, entry 5).

Table 17. $BF_3{\cdot}Et_2O$ screening for the reaction.



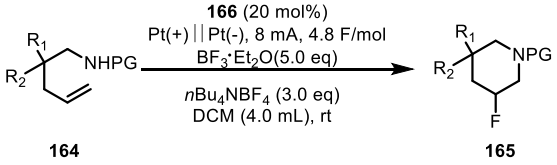
164a **165a**

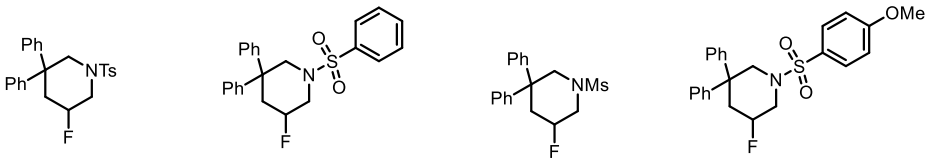
Entry	$BF_3{\cdot}Et_2O$(eq)	Yield[a] (%)

1	8	77
2	**5**	**77**
3	3	73
4	1	20
5	-	-

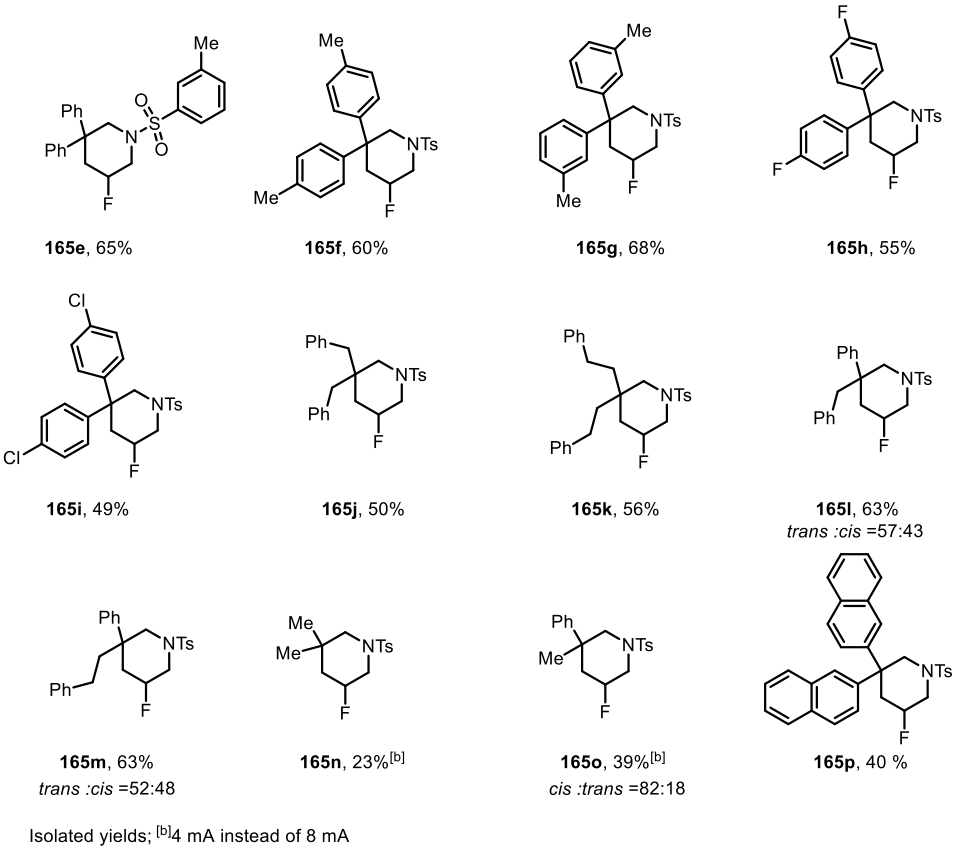
[a] Determined by NMR spectroscopy from the crude mixture with 1,3,5-trimethoxybenzene as the internal standard.

With the optimized reaction conditions in hand, we explored the generality of the protocol with various substrates (Scheme 57). Substrates **164** with different protecting groups on the nitrogen atom were firstly investigated, and all these substrates were suitable for the reaction, such as methylsulfonyl **164b** and different arylsulfonyl **164c**-**164e** groups, gave the corresponding products **165b**-**165e** in 47%–65% yields. Then we turned our attention to investigating various *gem*-disubstituted substrates. To our delight, reactions with substrates bearing different *gem*-diaryl groups, such as **164f**-**164i**, afforded the desired products **165f**-**165i** in 49%–60% yields. Substrates bearing different alkyl groups, such as **164j** and **164k**, were suitable for the reaction to provide the products **165j** and **165k** in 50% and 56% yields, respectively. Moreover, substrate with one phenyl group and one alkyl group substitute **164l** and **164m** also reacted smoothly to deliver the isomeric products **165l** and **165m** in 63% and 63% yields. However, for substrates **164n** with *gem*-methyl groups, with only 23% of desired product **165n** being obtained. Substrate **164o** with one phenyl group and one methyl group substitute afforded product **165h** in 39% yield with a 82 : 18 (*cis : trans*) isomer ratio. Notably, the substrate with *gem*-naphthyl groups **164p** was also suitable for the reaction to produce the product **165p** in 40% yield.





165a, 71% **165b**, 64% **165c**, 42% **165d**, 60%



165e, 65% **165f**, 60% **165g**, 68% **165h**, 55%

165i, 49% **165j**, 50% **165k**, 56% **165l**, 63%
trans :cis =57:43

165m, 63%
trans :cis =52:48

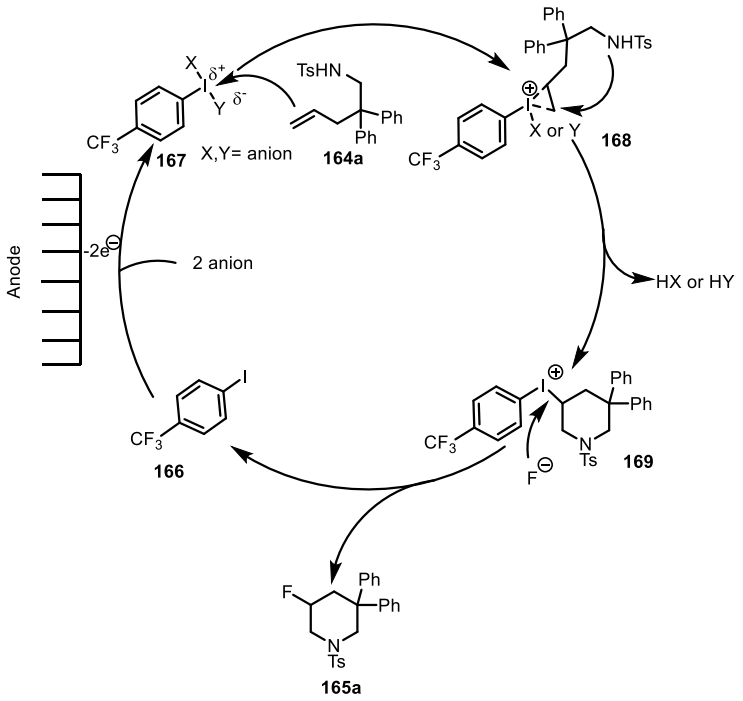
165n, 23%[b] **165o**, 39%[b]
cis :trans =82:18

165p, 40 %

Isolated yields; [b]4 mA instead of 8 mA

Scheme 57. Substrate scope.

Based on previous literature, [122,123,125,126] a plausible mechanism was proposed. As shown in Scheme 58, first, 4-iodobenzotrifluoride (**166**) loses two electrons and generates λ^3-iodane **167** under electric current and anion. Then intermediate **167** is attacked by the nucleophilic double bond in **164a** to form the iodonium species **168**. This intermediate is intramolecularly attacked by the sulfonamide nitrogen to form the kinetically preferred intermediate **169**, which rapidly reacts with a fluoride ion to form the product **165a** and 4-iodobenzotrifluoride (**166**) through an S_N2 reaction.



Scheme 58. Proposed Mechanism of Aminofluorination of Alkenes.

To gain more insight into this reaction, cyclic voltammetry (CV) experiments were carried out. As shown in the Figure 11 and 12, the oxidation peak of mediator **166** was observed at 3.01 V and the oxidation peak of Me in **164a** was observed at 2.71 V, while no obvious oxidation peak of the C-C double bond in **164a** was observed at 0−4.5 V. These results indicate that **164a** was not easily oxidized under standard conditions, and therefore, for this reaction, a catalytic amount of **166** was possible.

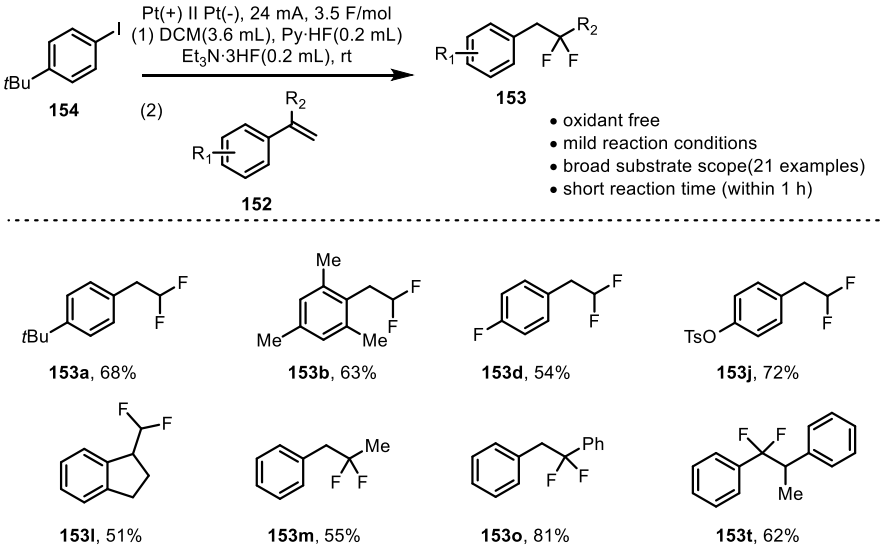
4. Summary and Perspectives

Organofluorine compounds have shown wide applications due to their distinct chemical, physical, and biological properties. These unique properties make fluorinated compounds are frequently utilized in pharmaceutical, agrochemical, and materials sciences. [93-96] The tremendous benefit of fluorinated organic scaffolds has certainly raised a huge demand for effective, generally applicable, and selective strategies to install fluorine atoms at specific position in a carbon skeleton. Although numerous methods have been reported for the synthesis of organofluorine compounds, the most challenging transformation remains the formation of the parent C-F bond, primarily because of the high hydration energy of fluoride, strong metal-fluorine bonds, and highly polarized bonds to fluorine. Besides the development of new concepts for the construction of C-F bonds in general, the introduction of mild, selective, environmentally benign, cost and atom economic methods is still highly desirable.

In recent years, hypervalent λ^3-fluoroiodanes as electrophilic fluorinating agents have shown unprecedented and novel reactivity and selectivity in the synthesis of fluorine-containing compounds. Their broad application, in particular on larger scale, however, has been hampered by the chemical instability of hypervalent λ^3-fluoro iodanes associated with their poor atom economy. Selectfluor[35,65-73] and *m*CPBA[74-78] have been found to be best suited to fulfill the challenging task of selectively oxidizing the iodoarene and thus forming in situ the reactive F-iodane species. Although selectfluor and *m*CPBA are comparable cheap and easy-to-handle reagents, their role here is just that of an electron acceptor. Given the comparable high molecular weights of these oxidants and the thus associated waste generated during turn-over, their application cannot be rendered as economic and sustainable. Replacing these organic oxidants by a more environmentally benign alternative is among the biggest challenges in hypervalent λ^3-fluoro iodane mediated transformations today. Electrochemistry offers a mild and efficient alternative to conventional chemical approaches for redox transformations, which employs electrons as reagents, has been demonstrated to be a versatile and environmentally friendly synthetic tool and attracted renewed interests. The goal of this doctoral thesis was to develop new, effective, and mild methods for the synthesis of hypervalent λ^3-fluoro iodanes by electrochemical method and apply them in different fluorination reactions. The results of this thesis are summarized below.

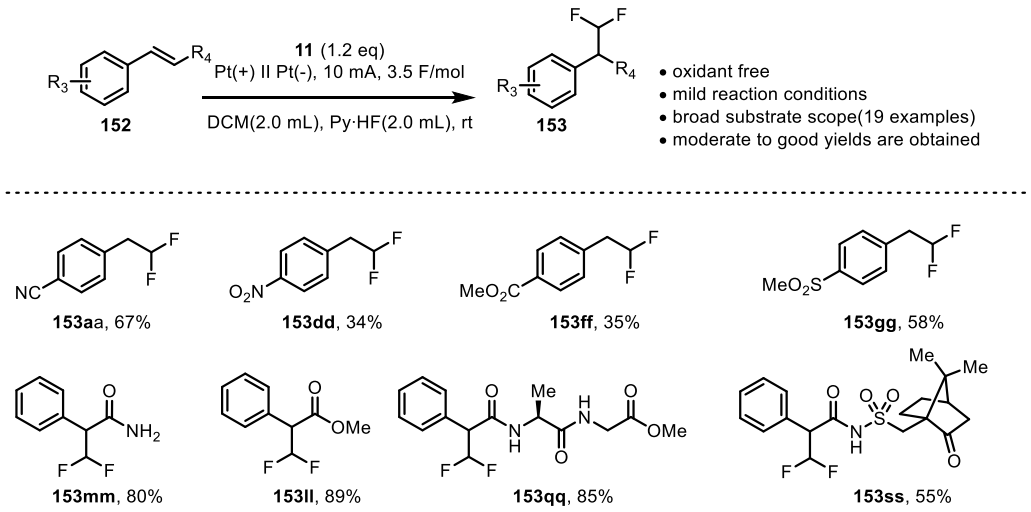
Starting with styrene as model substrate extensive reaction optimizations were performed in the first stage of this PhD thesis to achieve the electrochemical *gem*-difluorination. Due to the low oxidation potential of styrene substrates especially for electron donating substitution substrates **152**, we use an ex-cell method to avoid oxidative decomposition of the substrate. Using 4-*tert*-butyliodobenzene (**154**) as the mediator together with mixture 0.2 mL Py·HF and 0.2 mL $Et_3N{\cdot}3HF$ as the electrolyte and fluorine source, under 24

mA constant current, we established an efficient method allowing to access *gem*-difluorinated products **153** in moderate to good yields. Various electron-rich or oxidation sensitive styrenes and α-substituted styrenes were well tolerated, giving moderate to good yields of the desired products **153**.



Scheme 59. Substrate scope of styrenes.

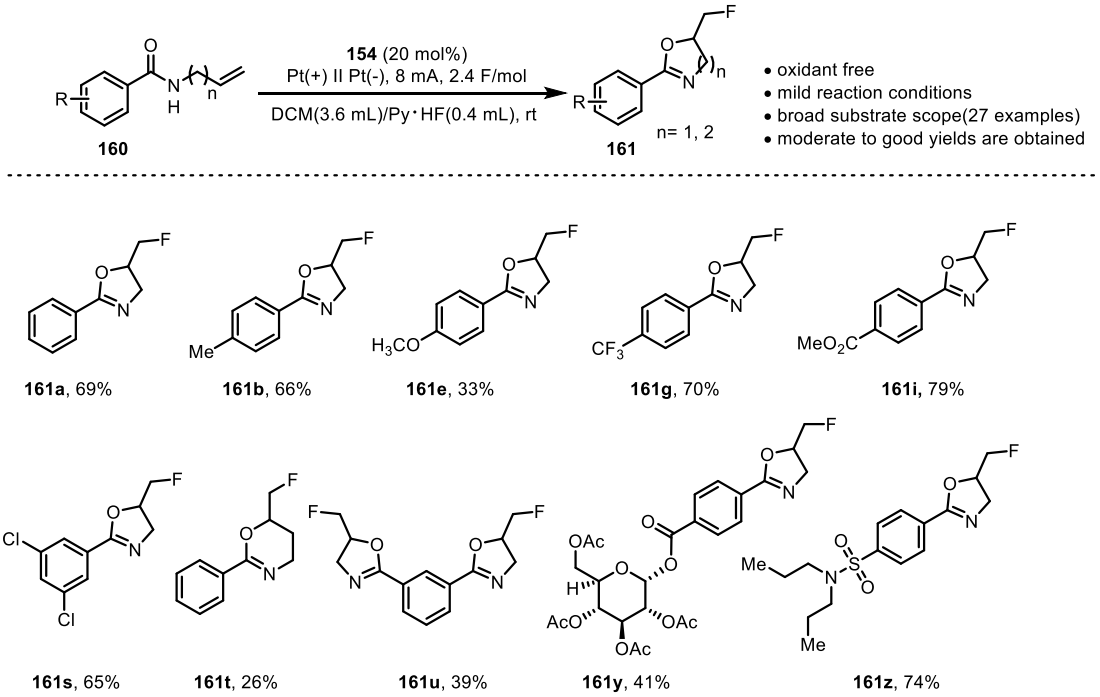
For electron-poor styrenes and β-substituted styrenes **152**, we used the in-cell electrochemical method to achieve the 1,1-difluorination reaction. Various electron-withdrawing groups substituted styrenes and β-substituted styrenes **152** were compatible with the reaction conditions to afford the desired 1,1-difluorinated products **153** in moderate to good yields. Notably, we have also achieved catalytic 1,1-difluorination of methyl cinnamate **152ll**.



Scheme 60. Substrate scope of electron-poor and α-substituted styrenes **152**.

In this part, a general ex-cell and in-cell electrochemical protocol for the 1,1-difluorination of a variety of electronically and substitutionally diverse styrenes **152** was established. Moderate to good yields of desired products were obtained in a wide substrate scope. This electrochemical protocol can serve as a supplement for diversified synthesis of fluorinated compounds, and provides a new method to prepare 1,1-difluorinated compounds.

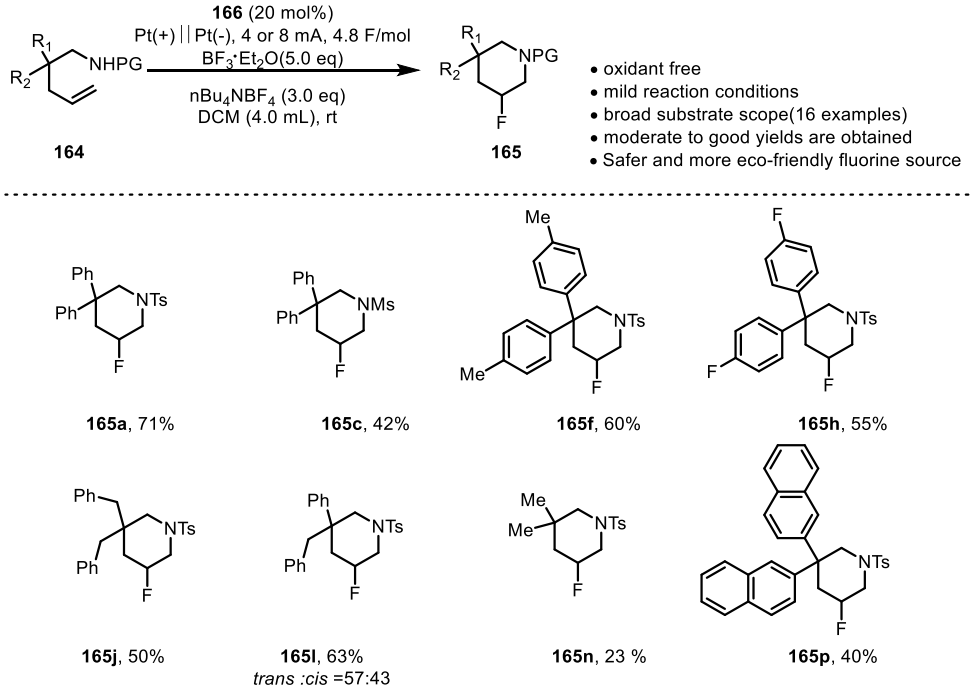
In the second part of this thesis, we established a method a method for the preparation of 5-fluoromethyl-2-oxazolines **161** by electrochemical iodoarene-catalyzed fluorocyclization of *N*-allylcarboxamides **160**. With the optimal reaction conditions in hand, the scope of *N*-allylcarboxamides **160** with different electronic properties and substitution patterns of the aryl ring were investigated. *N*-allylcarboxamides **160** bearing either electron-donating or electron-withdrawing groups at the position of the phenyl rings were compatible with the transformation to afford the 2-oxazolines **161** in 59%−69% yields. This procedure was also compatible with complex natural products and pharmaceuticals derivatives, such as glycoside **160y**, probenecid **160z**, successfully afforded the corresponding products **161y** and **161z** in 41% and 74% yields.



Scheme 61. Substrate scope of *N*-allylcarboxamides **160**.

In this part, we have developed a method to prepare 5-fluoromethyl-2-oxazolines **161** through electrochemical iodoarene-catalyzed fluorocyclization of *N*-allylcarboxamides **160**. The reaction proceeds in an undivided cell under mild reaction conditions with high efficiency, and broad substrate scope. Its mild conditions make it suitable for late-stage functionalization of complex natural products and drugs.

In the third part of this thesis, we developed an electrochemical iodoarene-catalyzed aminofluorination of alkenes **164** as a general, efficient, and mild approach for the synthesis of 3-fluoropiperidine compounds**165**. Substrates with different protecting groups on the nitrogen atom were investigated, gave the corresponding products **165** in 47%–65%yields. Moreover, reactions of substrates bearing different *gem*-diaryl groups, afforded desired products in moderate to good yields. Substrates bearing different alkyl groups or with one phenyl group and one alkyl group were suitable for the reaction to provide the products in moderate to good yields. However, for substrates with *gem*-methyl groups, with only 23% of product being obtained.



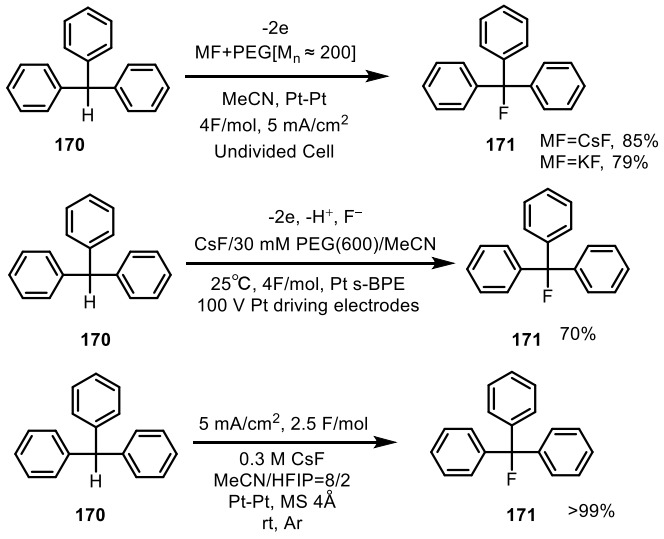
Scheme 62. Substrate scope of alkenes.

In this part, a general electrochemical protocol for the electrochemical iodoarene-catalyzed intramolecular aminofluorination of alkenes **164** was established. The reaction proceeded under mild conditions and displayed broad functional group compatibility. The electrochemical protocol was used for the diversified synthetic conversion of fluorinated products, which further confirms the potential applicability of the method in organic synthesis and pharmaceutically relevant research.

However, to establish ecologically and environmentally sustainable approaches, additional optimizations should be made and new strategies for the introduction of fluorine into organic molecules should be developed. For future projects, special attention should be paid to the application of non-toxic and eco-friendly fluoride sources. Although the electrochemical method is known to be a safer method compared to the corresponding chemical method using dangerous fluorinating reagents, HF and its salts are intrinsically

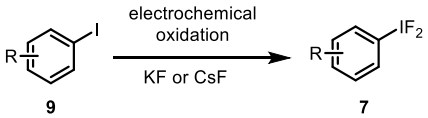
hazardous and corrosive. To avoid using such hazardous supporting electrolytes and fluorine sources, alternative methods have been proposed.

Inorganic fluoride salts such as alkali-metal fluorides (MFs) are stable, easy to handle, and inexpensive. Therefore, alkali-metal fluorides (MFs) are strong candidates for reagents in nucleophilic fluorination as well as supporting electrolytes in chemical and electrochemical fluorination. The challenge to overcome problems such as poor solubility and low nucleophilicity of MF in organic solvents is important. Fuchigami and coworkers utilized KF or CsF as the supporting electrolyte and fluorine source in MeCN solution dissolved with the help of a poly(ethylene glycol) (PEG) additive.[191] Shida and Iangi group reported fundamental properties of metal fluorides (KF or CsF) in fluorinated alcohols (HFIP or TFE) and demonstrated their application to electrochemical fluorination of triphenylmethane (**170**) (Scheme 63). [192,193]



Scheme 63. Anodic fluorination of **170**.

Depending on these developments, this concept may be transferred to hypervalent λ^3-iodanes mediated fluorination reactions. By introducing iodoarenes into this system, even alkali-metal fluorides might be a suitable fluorine source for the generation of λ^3-F-iodanes. Therefore, the establishment of new and catalytic methods should be possible by anodic oxidation (Scheme 64).



Scheme 64. Proposed electrochemical oxidation **9** for the synthesis **7** with alkali-metal fluorides.

Although methods to introduce fluorine into small organic molecules have been actively investigated for many years, however, due to the specific nature of fluorine atoms and the fact that often the introduction of fluorine-containing groups at specific positions in the molecule is the only way to improve its physiological activity, so it is necessary to develop diverse and effective methodologies for the synthesis of our desired fluorinated target molecules. This work, therefore, made a valuable contribution to the selective introduction of fluorine atoms into organic molecules.

III. Experimental Section

1. General Information

1.1 Solvents and Reagents

Solvents used in reactions were p.A. grade. Solvents for chromatography were technical grade and distilled prior to use. 1,1,1,3,3,3-Hexafluoroisopropanol (HFIP) was purchased from Fluorochem with a purity > 99% and was distilled prior to use. Reagents were purchased at the highest commercial quality and used without further purification. Reactions of air- or moisture-sensitive reagents were carried out in flame dried glassware and under argon atmosphere using dry solvents. Solvents used in reactions were p.A. grade. Anhydrous DCM, diethyl ether and THF were obtained from a MBraun MB-SPS 800 solvent purification system and were dried under argon atmosphere using the following columns:

Dichloromethane: 2× MB-KOL-A (aluminium oxide)

Diethyl ether: 1× MB-KOL-A (aluminium oxide), 1 × MB-KOL-M type 2 (molecular sieves 3Å)

Tetrahydrofuran: 2× MB-KOL-M type 2 (molecular sieves 3 Å)

Other dry solvents were obtained from Acros in the highest purity available and used without further purification. HPLC-grade solvents (acetonitrile, n-hexane, isopropanol) were purchased from Fisher Scientific.

1.2 Analytical Methods and Equipment

Thin Layer Chromatography

Reactions were monitored by thin layer chromatography (TLC) carried out on Merck silica gel aluminium plates with F-254 indicator using UV light as the visualizing agent and the following staining solutions combined with heat as developing agents:

Blue Stain (CAM): $Ce(SO_4)_2$ (2.00 g), $(NH_4)_6Mo_7O_{24}$ (5.00 g), conc. H_2SO_4 (12.0 mL) in H_2O (188 mL)

Potassium permanganate solution ($KMnO_4$): $KMnO_4$ (8.00 g), $NaHCO_3$ (4.00 g) in H_2O (200 mL)

Molybdic acid solution (MoO_3): $12MoO_3 \cdot H_3PO4$ (10.0 g) in 95% EtOH (200 mL)

Ninhydrin solution: Ninhydrin (1.00 g), AcOH (6.00 mL) in EtOH (194 mL)

Silica Gel Column Chromatography

Column chromatography (flash chromatography) was performed using Silica Gel 60 (230 - 400 mesh, particle size 40 - 60 μm) purchased from Acros. The solvents for purification via column chromatography were purchased with the label technical grade and were distilled prior to use. Solvent mixtures are understood as volume/volume.

Mass Spectrometry

Mass spectra were conducted on a Thermo Scientific LTQ-FT Ultra (ESI HRMS), a ThermoFisher Scientific LTQ Orbitrap XL spectrometer (ESI HRMS), a Finnigan MAT 8230 spectrometer (EI HRMS) or a Bruker Daltonics MicrOTOF spectrometer (ESI HRMS).

Infared Spectroscopy

IR spectra were recorded on a JASCO FT-IR-4100 (ATR, KBr and Film) and are reported in terms of wave numbers (cm^{-1}).

Nuclear Magnetic Resonance Spectroscopy

NMR spectra were recorded on Bruker AV300, Bruker AV400, Bruker AV500, Bruker AV500-cryo, Varian MERCURYplus 300 and Varian MERCURYplus 400 spectrometers. The spectra were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$ @ 7.26 ppm, $CDCl_3$ @ 77.00 ppm ^{13}C NMR). The following abbreviations (or combinations thereof) were used to explain the multiplicities: s =singlet, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplets, q = quartet, p = pentet, quint = quintet (with 1:2:3:2:1 intensity), hept = heptet, m = multiplet, b = broad.

Electrochemical equipments

Potentiostatic electrolysis was carried out with an ElectraSyn 2.0 pro package from IKA against an Ag/AgCl reference electrode, while the following setup was used for galvanostatic electrolysis:

Potentiostat HMP4040 from Rohde & Schwarz.

Electrolysis cells made of Teflon based on the model of Waldvogel et al [146]

IKA Plate (RCT Digital) magnetic stirrer from IKA

MLS WS 200/1 safety test leads red and black (2 m each) from SKS Hirschmann

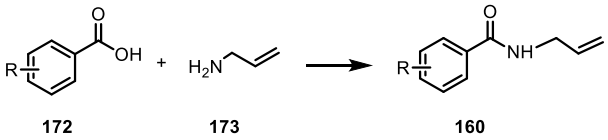
AK 10 alligator clips red and black from SKS Hirschmann

Platinum foils (8 cm ×1 cm × 0.1 mm) from Alfa Aesar as anode and cathode

2. Synthetic Procedures & Analytical Data

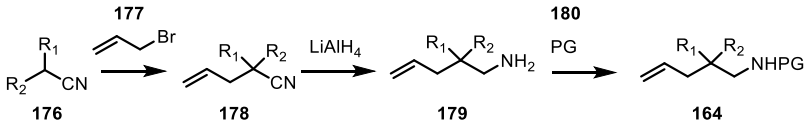
2.1. General Procedures

GP1: General Procedure for the Synthesis of *N*-Allylcarboxamides **160**



To a stirred solution of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimid hydrochloride (**174**, 1.15 g, 6.00 mmol, 1.2 equiv) and 4-(dimethylamino)-pyridine (**175**, 855 mg, 7.00 mmol, 1.4 equiv) in CH_2Cl_2 (12 mL) was added triethylamine (0.90 mL, 6.50 mmol, 1.3 equiv), allylamine (**173**, 0.45 mL, 6.00 mmol, 1.2 equiv) and carboxylic acid derivative (**172**, 5.00 mmol, 1.0 equiv) at 0 °C. After slowly warming the reaction mixture to ambient temperature it was stirred for further 23 h. After completion the suspension was filtered through celite and water (15 mL) was added to the filtrate and the aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, concentrated under reduce pressure and purified by flash chromatography.

GP2: General Procedure for the Synthesis of Unactivated Alkenes **164**

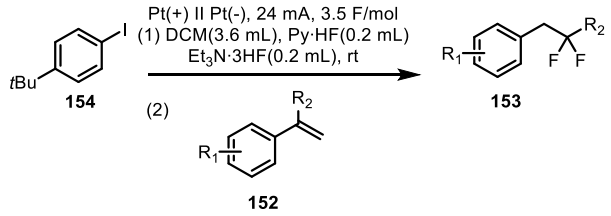


A solution of LDA (2.5 equiv) in THF was cooled to -78 °C, and nitrile **176** (5.00 mmol, 1.0 equiv) was added dropwise. After stirring the reaction mixture for 2h at -78°C, a solution of allyl bromide **177** (1.0 equiv) in THF was added. The mixture was monitored by TLC. After completion, the reaction was quenched by a saturated aqueous solution of NH_4Cl (20 mL). The mixture was extracted with ether (3 x 20 mL). The combined organic phases were dried over Na_2SO_4 and filtered. The filtrate was concentrated under vacuum to give the crude residue **178**, which was used directly for the next step.

To a suspended solution of $LiAlH_4$ (2.0 equiv) in abs. Et_2O, a solution of **178** in dry Et_2O was added dropwise at 0°C under Argon atmosphere. The reaction mixture was stirred for 2 h at room temperature. The reaction was quenched by sequentially adding dropwise at 0°C wet THF, 15% aqueous NaOH and water (v/v/v=20:20:60). The reaction mixture was stirred at room temperature for 15 min, and the solid was filtered off. The filtrate was concentrated under vacuum to give the product **179** which was used in the next step without further purification.

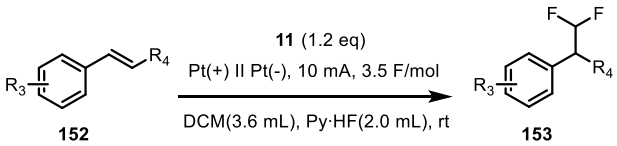
To a solution of **179** and triethylamine (2.0 equiv) in CH_2Cl_2, TsCl (**180a**, 1.5 equiv) was added at 0 °C. The reaction mixture was stirred at room temperature for 12 h. The mixture was washed with 10% $NaHCO_3$ (20 mL), brine, and dried with Na_2SO_4. The solvent was evaporated, and the residue was purified by flash column chromatography on silica gel to give the desired product **164**.

GP3: General Procedure for the *gem*-Difluorination of Oxidation Sensitive Styrenes **152**



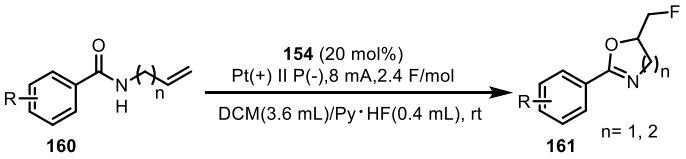
An undivided Teflon® cell equipped with a platinum anode (1×1.2 cm^2) and a platinum cathode (1×1.2 cm^2) was charged with DCM (3.6 mL). Py·HF (0.2 mL) and $Et_3N·3HF$ (0.2 mL) were added followed by 4-*tert*-butyl-iodobenzene (**154**, 0.30 mmol, 1.2 eq). The electrolysis was carried out on air at room temperature under constant current (24 mA) until 3.5 F/mol of electricity have passed. The corresponding substrate **152** (0.25 mmol, 1.0 eq) was added to the cell and the resulting mixture was stirred until consumption of starting material (TLC) at room temperature. The reaction mixture was poured into a sat. $NaHCO_3$ solution (50 mL) and extracted with DCM (3×10 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO4 and the solvent was removed under reduced pressure. The products were purified via column chromatography on silica gel.

GP4: General Procedure for the *gem*-Difluorination of Electron-poor or β-Substituted Styrenes **152**



An undivided Teflon® cell equipped with a platinum anode (1×1.2 cm^2) and a platinum cathode (1×1.2 cm^2) was charged with dry and degassed DCM (2.0 mL) followed by addition of 4-iodotoluene (**11**, 0.30 mmol, 1.2 eq) and the corresponding substrate **152** (0.25 mmol, 1.0 eq). Py·HF (2.0 mL) was added, the lid was sealed, and the electrolysis was carried out at room temperature under constant current (10 mA) until 3.5 F/mol of electricity have passed. The reaction mixture was poured into a sat. $NaHCO_3$ solution (50 mL) and extracted with DCM (3×10 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The products were purified via column chromatography on silica gel.

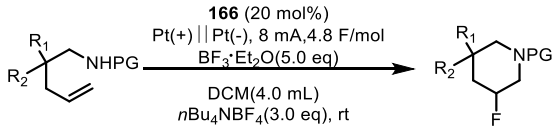
GP5: General Procedure for the Fluorocyclization of *N*-Allylcarboxamides **160**



160 161

A Teflon® undivided cell equipped with a platinum anode (1×1.2 cm^2) and a platinum cathode (1×1.2 cm^2) was charged with DCM (3.6 mL) followed by addition of 4-*tert*-butyliodobenzene (**154**, 0.1 mol, 20 mol%) and the corresponding substrate **160** (0.5 mmol, 1.0 eq) added followed by Py·HF (0.4 mL). The electrolysis was carried out at room temperature under constant current (8 mA) until 3.5 F/mol of electricity have passed. The reaction mixture was poured into sat. $NaHCO_3$ solution (10 mL) and extracted with DCM (3×15 mL). The combined organic layer was washed with brine (15 mL), dried over Na_2SO_4, and the solvent was removed under reduced pressure. The products were purified via column chromatography on silica gel.

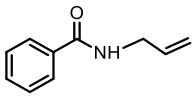
GP6: General Procedure for the aminofluorination of alkenes **164**



164 165

A Teflon® undivided cell equipped with a platinum anode (1×1.2 cm^2) and a platinum cathode (1×1.2 cm^2) was charged with DCM (4.0 mL), 4-iodobenzotrifluoride (**166**, 0.05 mmol, 0.2 eq) and the corresponding substrate **164** (0.25 mmol, 1.0 eq) added followed by $BF_3{\cdot}OEt_2$ (1.25 mmol, 5.0 eq). *n*Bu_4NBF_4(249.0 mg, 3.0 eq). The electrolysis was carried out at room temperature under constant current (8 mA) until 4.8/mol of electricity have passed. The reaction mixture was poured into sat. $NaHCO_3$ solution (10 mL) and extracted with DCM (3×10 mL). The combined organic layer was washed with brine (15 mL), dried over Na_2SO_4, and the solvent was removed under reduced pressure. The products were purified via column chromatography on silica gel.

2.2 Analytical Data for the *N*-allylcarboxamides and Unactivated Alkenes

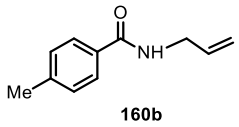


160a

***N*-allylbenzamide (160a)**, prepared from benzoic acid (**172a**) (611 mg, 5.00 mmol) following the general procedure GP1; slightly yellow oil (781 mg, 97%); **TLC:** R_f = 0.62 (silica gel, 50:50 hexane:EtOAc) [UV];

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 – 7.74 (m, 2H), 7.52 – 7.43 (m, 1H), 7.43 – 7.35 (m, 2H), 6.57 (s, 1H), 5.91 (ddt, *J* = 17.2 Hz, 10.2 Hz, 5.7 Hz, 1H), 5.23 (dq, *J* = 17.1 Hz, 1.5 Hz, 1.5 Hz, 1H), 5.15 (dq, *J* = 10.2 Hz, 1.5 Hz, 1H), 4.05 (tt, *J* = 5.7 Hz, 1.5 Hz, 2H) ppm.

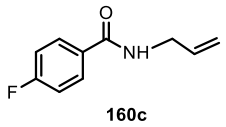
The analytical data are in accordance to those reported in the literature.[146]



160b

***N*-allyl-4-methylbenzamide (160b)**, prepared from **172b** (5.00 mmol) following the general procedure GP1; white solid (806 mg, 92%); **m.p.** = 76 °C; **TLC:** R_f = 0.62 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 – 7.67 (m, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 6.28 (s, 1H), 5.93 (ddt, *J* = 17.2, 10.2, 5.7 Hz, 1H), 5.27 – 5.15 (m, 2H), 4.07 (tt, *J* = 5.7, 1.6 Hz, 2H), 2.39 (s, 3H).

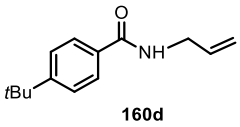
The analytical data are in accordance to those reported in the literature.[146]



160c

***N*-allyl-4-fluorobenzamide (160c)**, prepared from **172c**(5.00 mmol) following the general procedure GP1; white solid (806 mg, 90%); **m.p.** = 68 °C; **TLC:** R_f = 0.62 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82 – 7.77 (m, 2H), 7.12 – 7.07 (m, 2H), 6.27 (s, 1H), 5.98– 5.87 (m, 1H), 5.28– 5.16 (m, 2H), 4.09– 4.04 (m, 2H).

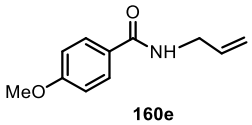
The analytical data are in accordance to those reported in the literature.[146]



160d

***N*-allyl-4-(*tert*-butyl)benzamide (160d)**, prepared from **172d** (5.00 mmol) following the general procedure GP1; white solid (1032 mg, 95%); **m.p.** = 61 °C; **TLC:** R_f = 0.62 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.75 – 7.70 (m, 2H), 7.46 – 7.42 (m, 2H), 6.24 (s, 1H), 5.93 (ddt, *J* = 17.1, 10.2, 5.6 Hz, 1H), 5.39 – 5.15 (m, 2H), 4.08 (tt, *J* = 5.7, 1.6 Hz, 2H), 1.33 (s, 9H).

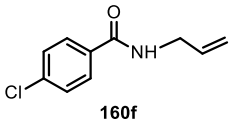
The analytical data are in accordance to those reported in the literature.[146]



160e

***N*-allyl-4-methoxybenzamide (160e)**, prepared from **172e** (5.00 mmol) following the general procedure GP1; white solid (899 mg, 94%); **m.p.** = 45 °C; **TLC:** R_f = 0.60 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.78 – 7.73(m, 2H), 6.93 – 6.88 (m, 2H), 6.23 (s, 1H), 5.99– 5.86 (m, 1H), 5.28 – 5.14 (m, 2H), 4.06 (tt, *J* = 5.7, 1.5 Hz, 2H), 3.83 (s, 3H).

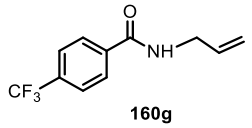
The analytical data are in accordance to those reported in the literature.[146]



160f

***N*-allyl-4-chlorobenzamide (160f)**, prepared from **172f** (5.00 mmol) following the general procedure GP1; white solid (890 mg, 92%); **m.p.** = 74 °C; **TLC:** R_f = 0.64 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 – 7.70 (m, 2H), 7.40 – 7.36 (m, 2H), 6.40 (s, 1H), 5.91 (ddt, *J* = 17.1, 10.1, 5.7 Hz, 1H), 5.20 – 5.15 (m, 2H), 4.05 (tt, *J* = 5.7, 1.5 Hz, 2H).

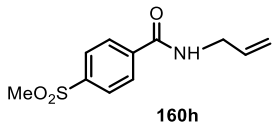
The analytical data are in accordance to those reported in the literature.[194]



160g

***N*-allyl-4-(trifluoromethyl)benzamide (160g)**, prepared from **172g** (5.00 mmol) following the general procedure GP1; white solid (1111 mg, 97%); **m.p.** = 103 °C; **TLC:** R_f = 0.66 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.7 Hz, 2H), 6.41 (s, 1H), 5.93 (ddt, *J* = 16.5, 9.5, 5.6 Hz, 1H), 5.29 – 5.18 (m, 2H), 4.11 – 4.07 (m, 2H).

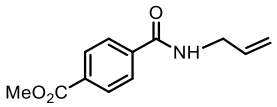
The analytical data are in accordance to those reported in the literature.[146]



160h

***N*-allyl-4-(methylsulfonyl)benzamide (160h)**, prepared from **172h** (5.00 mmol) following the general procedure GP1; white solid (1076 mg, 90%); **m.p.** = 134 °C; **TLC:** R_f = 0.63 (silica gel, 50:50

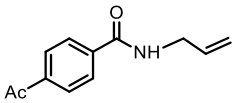
hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (s, 4H), 6.60 (s, 1H), 5.93 (ddt, *J* = 17.1, 10.2, 5.7 Hz, 1H), 5.29 – 5.18 (m, 2H), 4.09 (tt, *J* = 5.8, 1.5 Hz, 2H), 3.06 (s, 3H).



160i

methyl 4-(allylcarbamoyl)benzoate (160i), prepared from **172i** (5.00 mmol) following the general procedure GP1; white solid (996 mg, 91%); **m.p.** = 109 °C; **TLC:** R_f = 0.63 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 – 8.04 (m, 2H), 7.84 – 7.82(m, 2H), 6.50 (s, 1H), 5.97 – 5.87 (m, 1H), 5.28 – 5.16 (m, 2H), 4.10 – 4.05 (m, 2H), 3.92 (s, 3H).

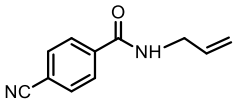
The analytical data are in accordance to those reported in the literature.[194]



160j

4-acetyl-*N*-allylbenzamide (160j), prepared from **172j** (5.00 mmol) following the general procedure GP1; white solid (934 mg, 92%); **m.p.** = 117 °C; **TLC:** R_f = 0.42 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 – 7.93 (m, 2H), 7.87 – 7.84 (m, 2H), 6.66 (s, 1H), 5.97 – 5.86 (m, 1H), 5.29 – 5.14 (m, 2H), 4.10 – 4.05 (m, 2H), 2.60 (s, 3H).

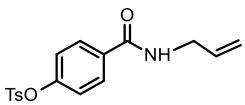
The analytical data are in accordance to those reported in the literature.[194]



160k

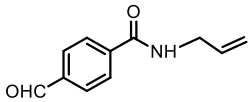
***N*-allyl-4-cyanobenzamide (160k)**, prepared from **172k** (5.00 mmol) following the general procedure GP1; white solid (781 mg, 97%); **m.p.** = 98 °C; **TLC:** R_f = 0.44 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.90 – 7.87 (m, 2H), 7.73 – 7.71 (m, 2H), 5.91 (ddt, *J* = 17.1, 10.2, 5.7 Hz, 1H), 5.28 – 5.18 (m, 2H), 4.08 (tt, *J* = 5.7, 1.5 Hz, 2H).

The analytical data are in accordance to those reported in the literature.[194]



160l

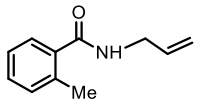
4-(allylcarbamoyl)phenyl 4-methylbenzenesulfonate (160l), prepared from **172l** (5.00 mmol) following the general procedure GP1; white solid (1523 mg, 92%); **m.p.** = 142 °C; **TLC:** R_f = 0.50 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 – 7.67 (m, 4H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.06 – 7.02 (m, 2H), 6.28 (s, 1H), 5.95 – 5.85 (m, 1H), 5.27 – 5.16 (m, 2H), 4.07 – 4.03 (m, 2H), 2.44 (s, 3H).



160m

***N*-allyl-4-formylbenzamide (160m)**, prepared from **172m** (5.00 mmol) following the general procedure GP1; white solid (803 mg, 85%); **m.p.** = 81 °C; **TLC:** R_f = 0.48 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.03 (s, 1H), 7.94 – 7.88 (m, 4H), 6.73 (s, 1H), 5.98 – 5.85 (m, 1H), 5.30 – 5.15 (m, 2H), 4.12 – 4.04 (m, 2H).

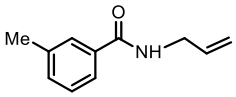
The analytical data are in accordance to those reported in the literature.[129]



160n

***N*-allyl-2-methylbenzamide (160n)**, prepared from **172n** (5.00 mmol) following the general procedure GP1; white solid (831 mg, 95%); **m.p.** = 65 °C; **TLC:** R_f = 0.62 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.36 – 7.27 (m, 2H), 7.21 – 7.16 (m, 2H), 5.97 – 5.87 (m, 2H), 5.28 – 5.16 (m, 2H), 4.06 – 4.02 (m, 2H), 2.43 (s, 3H).

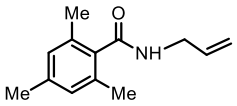
The analytical data are in accordance to those reported in the literature.[195]



160o

***N*-allyl-3-methylbenzamide (160o)**, prepared from **172o** (5.00 mmol) following the general procedure GP1; colorless oil (831 mg, 95%); **TLC:** R_f = 0.62 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.58 – 7.53 (m, 1H), 7.32 – 7.28 (m, 2H), 6.34 (s, 1H), 5.97 – 5.88 (m, 1H), 5.27 – 5.15 (m, 2H), 4.09 – 4.05 (m, 2H), 2.38 (s, 3H).

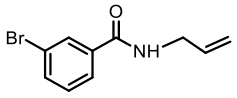
The analytical data are in accordance to those reported in the literature.[195]



160p

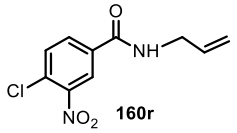
***N*-allyl-2,4,6-trimethylbenzamide (160p)**, prepared from **172p** (5.00 mmol) following the general procedure GP1; white solid (893 mg, 88%); **m.p.** = 112 °C; **TLC:** R_f = 0.60 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.83 (s, 2H), 5.92 (ddt, *J* = 17.3, 10.3, 5.8 Hz, 1H), 5.74 (s, 1H), 5.28 – 5.15 (m, 2H), 4.07 (tt, *J* = 5.8, 1.4 Hz, 2H), 2.28 (s, 6H), 2.26 (s, 3H).

The analytical data are in accordance to those reported in the literature.[146]



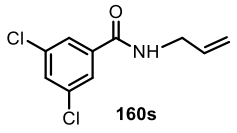
160q

***N*-allyl-3-methylbenzamide (160q)**, prepared from **172q** (5.00 mmol) following the general procedure GP1; white solid (1076 mg, 90%); **m.p.** = 66 °C; **TLC:** R_f = 0.63 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (t, *J* = 1.9 Hz, 1H), 7.70 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.62 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.32 (s, 1H), 5.92 (ddt, *J* = 17.1, 10.2, 5.7 Hz, 1H), 5.28– 5.17 (m, 2H), 4.07 (tt, *J* = 5.8, 1.6 Hz, 2H).



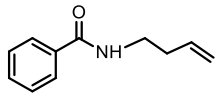
160r

***N*-allyl-4-chloro-3-nitrobenzamide (160r)**, prepared from **172r** (5.00 mmol) following the general procedure GP1; yellow solid (984 mg, 82%); **m.p.** = 59 °C; **TLC:** R_f = 0.49 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 2.0 Hz, 1H), 7.96 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.65 – 7.61 (m, 1H), 6.67 (s, 1H), 5.97 – 5.86 (m, 1H), 5.30 – 5.18 (m, 2H), 4.10 – 4.06 (m, 2H).



160s

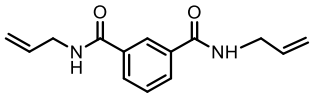
***N*-allyl-3,5-dichlorobenzamide (160s)**, prepared from **172s** (5.00 mmol) following the general procedure GP1; white solid (1031 mg, 90%); **m.p.** = 99 °C; **TLC:** R_f = 0.63 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 – 7.63 (m, 2H), 7.48 – 7.45 (m, 1H), 6.28 (s, 1H), 5.96 – 5.84 (m, 1H), 5.29 – 5.17 (m, 2H), 4.08 – 4.04 (m, 2H).



160t

***N*-(but-3-en-1-yl)benzamide (160t)**, prepared from **172t** (5.00 mmol) following the general procedure GP1; colorless oil (814 mg, 93%); **TLC:** R_f = 0.60 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 – 7.73 (m, 2H), 7.50 – 7.44 (m, 1H), 7.43 – 7.37 (m, 2H), 6.33 (s, 1H), 5.88 – 5.76 (m, 1H), 5.17 – 5.08 (m, 2H), 3.55 – 3.49 (m, 2H), 2.40 – 2.34 (m, 2H).

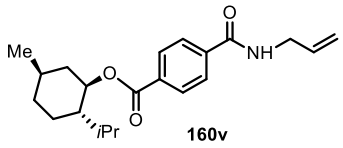
The analytical data are in accordance to those reported in the literature.[129]



160u

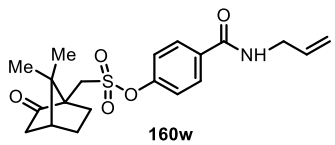
***N*^{1},*N*^{3}-diallylisophthalamide (160u)**, prepared from **172u** (5.00 mmol) following the general procedure GP1; white solid (1037 mg, 85%); **m.p.** = 119 °C; **TLC:** R_f = 0.48 (silica gel, 20:80 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.24 – 8.22 (m, 1H), 7.93 – 7.90 (m, 2H), 7.49 – 7.41 (m, 1H), 6.87 (s, 1H), 5.94 – 5.80 (m, 2H), 5.25 – 5.11 (m, 4H), 4.05 – 3.99 (m, 4H).

The analytical data are in accordance to those reported in the literature.[129]



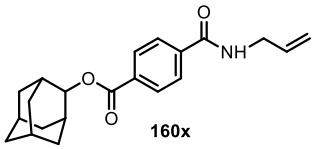
160v

(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-(allylcarbamoyl)benzoate (160v), prepared from **172v** (1.00 mmol) following the general procedure GP1; white solid (312 mg, 91%); **m.p.** = 81 °C; **TLC:** R_f = 0.52 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 – 8.06 (m, 2H), 7.85 – 7.83 (m, 2H), 6.39 (s, 1H), 5.99 – 5.88 (m, 1H), 5.30 – 5.17 (m, 2H), 4.98 – 4.90 (m, 1H), 4.12 – 4.07 (m, 2H), 2.14 – 2.10 (m, 1H), 1.97 – 1.89 (m, 1H), 1.76 – 1.70 (m, 2H), 1.59 – 1.52 (m, 2H), 1.18 – 1.06 (m, 2H), 0.94 – 0.90 (m, 7H), 0.80 – 0.77 (m, 3H).



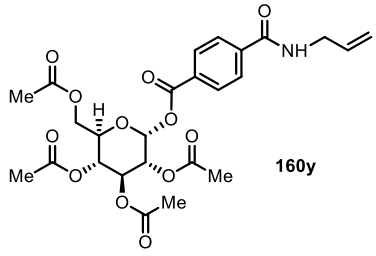
160w

4-(allylcarbamoyl)phenyl ((1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonate (160w), prepared from **172w** (1.00 mmol) following the general procedure GP1; colorless oil (340 mg, 87%); **TLC:** R_f = 0.60 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 – 7.74 (m, 2H), 7.36 – 7.33 (m, 2H), 6.27 (s, 1H), 5.98 – 5.88 (m, 1H), 5.28 – 5.16 (m, 2H), 4.09 – 4.06 (m, 2H), 3.35 (dd, *J* = 15.3, 1.3 Hz, 1H), 2.92 (d, *J* = 15.3 Hz, 1H), 2.47 – 2.40 (m, 1H), 2.15 – 2.59 (m, 5H), 1.51 – 1.44 (m, 1H), 0.96 (s, 3H), 0.83 (s, 3H).



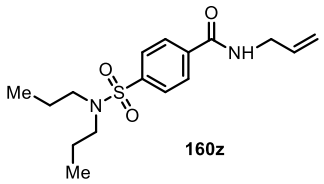
160x

***N*-allyl-4-(*N*,*N*-dipropylsulfamoyl)benzamide (160x)**, prepared from **172x** (1.00 mmol) following the general procedure GP1; white solid (312 mg, 92%); **m.p.** = 117 °C; **TLC:** R_f = 0.49 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.14 – 8.11 (m, 2H), 7.86 – 7.84 (m, 2H), 6.38 (s, 1H), 6.00 – 5.89 (m, 1H), 5.30 – 5.24 (m, 1H), 5.22 – 5.18 (m, 2H), 4.12 – 4.08 (m, 2H), 2.16 – 2.13 (m, 4H), 1.93 – 1.78 (m, 8H), 1.65 (d, *J* = 12.4 Hz, 2H).



160y

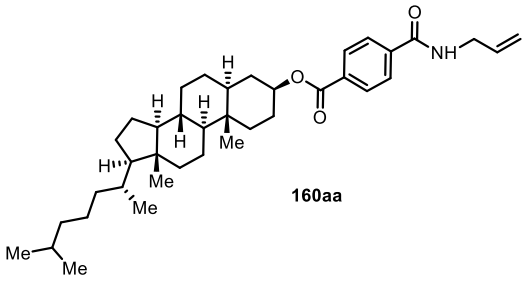
(2R,3R,4S,5R,6R)-2-(acetoxymethyl)-6-((4-(allylcarbamoyl)benzoyl)oxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate (160y), prepared from **172y** (1.00 mmol) following the general procedure GP1; white solid (428 mg, 80%); **m.p.** = 101 °C; **TLC:** R_f = 0.34 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.10 – 8.07 (m, 2H), 7.86 – 7.83 (m, 2H), 6.35 (s, 1H), 5.99 – 5.88 (m, 1H), 5.35 – 5.29 (m, 2H), 5.24 – 5.17 (m, 4H), 4.35 – 4.19 (m, 2H), 4.13 – 4.06 (m, 2H), 3.94 (ddd, *J* = 10.0, 4.4, 2.2 Hz, 1H), 2.08 – 1.97 (m, 12H).



160z

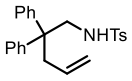
***N*-allyl-4-(*N*,*N*-dipropylsulfamoyl)benzamide (160z)**, prepared from **172z** (5.00 mmol) following the general procedure GP1; white solid (1523 mg, 94%); **m.p.** = 76 °C; **TLC:** R_f = 0.64 (silica gel, 50:50

hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89 – 7.87 (m, 2H), 7.84 – 7.77 (m, 2H), 6.45 (s, 1H), 5.98 – 5.88 (m, 1H), 5.30 – 5.16 (m, 2H), 4.11 – 4.06 (m, 2H), 3.09 – 3.04 (m, 4H), 1.58 – 1.49 (m, 4H), 0.88 – 0.82 (m, 6H).



160aa

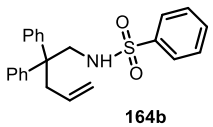
(3S,5S,8R,9S,10S,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-(allylcarbamoyl)benzoate (160aa), prepared from **172aa** (1.00 mmol) following the general procedure GP1; white solid (460 mg, 80%); **m.p.** = 188 °C; **TLC:** R_f = 0.88 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.09 – 8.06 (m, 2H), 7.84 – 7.81 (m, 2H), 6.30 (s, 1H), 5.99 – 5.89 (m, 1H), 5.30 – 5.18 (m, 2H), 4.99 – 4.91 (m, 1H), 4.10 (tt, *J* = 5.8, 1.6 Hz, 2H), 2.00 – 1.92 (m, 2H), 1.83 – 1.63 (m, 5H), 1.58 – 1.47 (m, 4H), 1.37 – 1.22 (m, 10H), 1.17 – 0.98 (m, 10H), 0.91– 0.89 (m, 3H), 0.87 – 0.85 (m, 9H), 0.66 (s, 3H).



164a

***N*-(2,2-diphenylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164a)**, prepared from **176a** (5.00 mmol) and **180a** (5.00 mmol) following the general procedure GP2; white solid (1271 mg, 65%); **m.p.** = 136 °C; **TLC:** R_f = 0.25 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.66 – 7.58 (m, 2H), 7.45 – 7.29 (m, 1H), 7.31 (s, 1H), 7.32 – 7.26 (m, 2H), 7.29 – 7.23 (m, 2H), 7.26 – 7.22 (m, 1H), 7.22 (d, *J* = 7.3 Hz, 1H), 7.11 – 7.04 (m, 4H), 5.29 (ddt, *J* = 18.3, 9.5, 7.1 Hz, 1H), 5.01 – 4.91 (m, 2H), 3.85 (t, *J* = 6.4 Hz, 1H), 3.55 (d, J = 6.4 Hz, 2H), 2.92 (dt, *J* = 7.3, 1.2 Hz, 2H), 2.45 (s, 3H) ppm.

The analytical data are in accordance to those reported in the literature.[119]

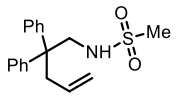


164b

***N*-(2,2-diphenylpent-4-en-1-yl)benzenesulfonamide (164b)**, prepared from **176a** (5.00 mmol) and **180b** (5.00 mmol) following the general procedure GP2; white solid (1206 mg, 64%); **m.p.** = 157 °C; **TLC:** R_f

= 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 – 7.70 (m, 2H), 7.59 – 7.46 (m, 3H), 7.28 – 7.19 (m, 6H), 7.06 – 7.04 (m, 4H), 5.31 – 5.21 (m, 1H), 4.94 – 4.90 (m, 2H), 3.87 (t, *J* = 6.4 Hz, 1H), 3.54 (d, *J* = 6.4 Hz, 2H), 2.89 (d, *J* = 7.1 Hz, 2H).

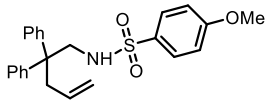
The analytical data are in accordance to those reported in the literature.[123]



164c

***N*-(2,2-diphenylpent-4-en-1-yl)methanesulfonamide (164c)**, prepared from **176a** (5.00 mmol) and **180c** (5.00 mmol) following the general procedure GP2; white solid (977 mg, 62%); **m.p.** = 108 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 4H), 7.25 – 7.22 (m, 2H), 7.18 – 7.15 (m, 4H), 5.41– 5.30 (m, 1H), 5.13 – 5.01 (m, 2H), 3.78 (s, 3H), 2.97 – 2.94 (m, 2H), 2.68 (s, 3H).

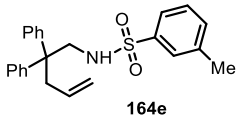
The analytical data are in accordance to those reported in the literature.[123]



164d

***N*-(2,2-di-*p*-tolylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164d)**, prepared from **176a** (5.00 mmol) and **180d** (5.00 mmol) following the general procedure GP2; white solid (1302 mg, 64%); **m.p.** = 123 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.65 (m, 2H), 7.30 – 7.21 (m, 6H), 7.09 – 7.06 (m, 4H), 6.98 – 6.94 (m, 2H), 5.34 – 5.24 (m, 1H), 4.99 – 4.94 (m, 2H), 3.89 (s, 3H), 3.83 (t, *J* = 6.5 Hz, 1H), 3.53 (d, *J* = 6.5 Hz, 2H), 2.93 – 2.91 (m, 2H).

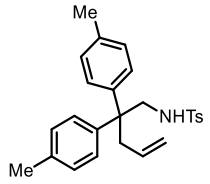
The analytical data are in accordance to those reported in the literature.[123]



164e

***N*-(2,2-diphenylpent-4-en-1-yl)-3-methylbenzenesulfonamide (164e)**, prepared from **176a** (5.00 mmol) and **180e** (5.00 mmol) following the general procedure GP2; white solid (1173 mg, 60%); **m.p.** = 106 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 – 7.50 (m, 2H), 7.40 – 7.33 (m, 2H), 7.30 – 7.19 (m, 6H), 7.07 – 7.04 (m, 4H), 5.32 – 5.14 (m, 1H), 4.96 – 4.91 (m, 2H), 3.85 (t, *J* = 6.4 Hz, 1H), 3.54 (d, *J* = 6.3 Hz, 2H), 2.90 (d, *J* = 7.1 Hz, 2H), 2.40 (s, 3H).

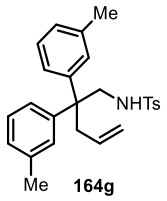
The analytical data are in accordance to those reported in the literature.[123]



164f

***N*-(2,2-di-*p*-tolylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164f)**, prepared from **176f** (2.00 mmol) and **180a** (5.00 mmol) following the general procedure GP2; white solid (570 mg, 68%); **m.p.** = 144 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.8 Hz, 2H), 7.28 – 7.26 (m, 2H), 7.05 (d, *J* = 7.8 Hz, 4H), 6.93 (d, *J* = 7.8 Hz, 4H), 5.32 – 5.22 (m, 1H), 4.95 – 4.91 (m, 2H), 3.83 (t, *J* = 6.4 Hz, 1H), 3.47 (d, *J* = 6.4 Hz, 2H), 2.85 (d, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 2.31 (s, 6H).

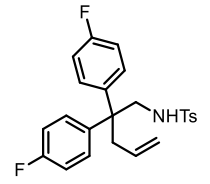
The analytical data are in accordance to those reported in the literature.[123]



164g

***N*-(2,2-di-*m*-tolylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164g)**, prepared from **176g** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (436 mg, 52%); **m.p.** = 125 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.60 – 7.56 (m, 2H), 7.28 – 7.25 (m, 2H), 7.16 – 7.10 (m, 2H), 7.03 – 6.99 (m, 2H), 6.84 – 6.81 (m, 4H), 5.31 – 5.17 (m, 1H), 4.96 – 4.89 (m, 2H), 3.82 (t, *J* = 6.3 Hz, 1H), 3.49 (d, *J* = 6.2 Hz, 2H), 2.87– 2.84 (m, 2H), 2.42 (s, 3H), 2.27 (s, 6H).

The analytical data are in accordance to those reported in the literature.[123]

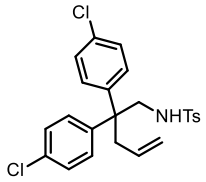


164h

***N*-(2,2-bis(4-fluorophenyl)pent-4-en-1-yl)-4-methylbenzenesulfonamide (164h)**, prepared from **176h** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (555 mg, 65%); **m.p.**

= 130 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 – 7.60 (m, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.02 – 6.98 (m, 4H), 6.96 – 6.91 (m, 4H), 5.30– 5.20 (m, 1H), 4.96 – 4.91 (m, 2H), 4.00 – 3.94 (m, 1H), 3.47 (d, *J* = 6.6 Hz, 2H), 2.84 – 2.82 (m, 2H), 2.43 (s, 3H).

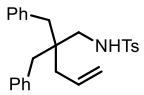
The analytical data are in accordance to those reported in the literature.[196]



164i

***N*-(2,2-bis(4-chlorophenyl)pent-4-en-1-yl)-4-methylbenzenesulfonamide (164i)**, prepared from **176i** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (588 mg, 64%); **m.p.** = 139 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 – 7.57 (m, 2H), 7.28 – 7.21 (dd, *J* = 22.0, 8.2 Hz, 7H), 6.96 (d, *J* = 8.2 Hz, 4H), 5.30 – 5.18 (m, 1H), 4.97 – 4.92 (m, 2H), 3.85 (s, 1H), 3.47 (d, *J* = 6.8 Hz, 2H), 2.82 (d, *J* = 7.2 Hz, 2H), 2.43 (s, 3H).

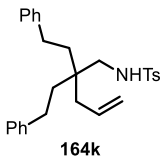
The analytical data are in accordance to those reported in the literature.[196]



164j

***N*-(2,2-dibenzylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164j)**, prepared from **176j** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (561 mg, 67%); **m.p.** = 137 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.30 – 7.22 (m, 8H), 7.11– 7.09 (m, 4H), 5.97 – 5.87 (m, 1H), 5.17 – 5.07 (m, 2H), 4.11 (t, *J* = 6.7 Hz, 1H), 2.73 (d, *J* = 6.9 Hz, 2H), 2.69 – 2.61 (m, 4H), 2.44 (s, 3H), 2.04 (d, *J* = 7.1 Hz, 2H).

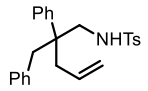
The analytical data are in accordance to those reported in the literature.[196]



164k

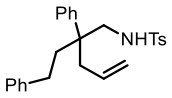
***N*-(2,2-diphenethylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164k)**, prepared from **176k** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (536 mg, 60%); **m.p.** = 137°C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J*

= 7.9 Hz, 2H), 7.29 – 7.24 (m, 6H), 7.21 – 7.16 (m, 6H), 5.85 – 5.74 (m, 1H), 5.18 – 5.10 (m, 2H), 4.95 (t, *J* = 7.0 Hz, 1H), 2.82 (d, *J* = 6.8 Hz, 2H), 2.55 (dd, *J* = 10.8, 6.3 Hz, 4H), 2.41 (s, 3H), 2.14 (d, *J* = 7.4 Hz, 2H), 1.67 – 1.55 (m, 4H).



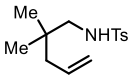
164l

***N*-(2-benzyl-2-phenylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164l)**, prepared from **176l** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (535 mg, 66%); **m.p.** = 155 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.64 (m, 2H), 7.32 – 7.23 (m, 5H), 7.14 – 7.06 (m, 5H), 6.81– 6.78 (m, 2H), 5.70 – 5.60 (m, 1H), 5.11 – 5.04 (m, 2H), 4.10 (t, *J* = 6.4 Hz, 1H), 3.14 (dd, *J* = 6.4, 2.8 Hz, 2H), 3.00 – 2.91 (m, 2H), 2.53 – 2.47 (m, 1H), 2.45 (s, 3H), 2.40 – 2.34 (m, 1H).



164m

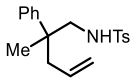
4-methyl-*N*-(2-phenethyl-2-phenylpent-4-en-1-yl)benzenesulfonamide (164m), prepared from **176m** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (545 mg, 65%); **m.p.** = 117 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.37 – 7.21 (m, 9H), 7.19 – 7.13 (m, 1H), 7.06 – 7.04 (m, 2H), 5.70 – 5.59 (m, 1H), 5.18 – 5.08 (m, 2H), 4.03 – 3.98 (m, 1H), 3.24– 3.07 (m, 2H), 2.68 – 2.50 (m, 2H), 2.47 – 2.40 (m, 4H), 2.29 – 2.22 (m, 1H), 2.01 – 1.85 (m, 2H).



164n

***N*-(2,2-dimethylpent-4-en-1-yl)-4-methylbenzenesulfonamide (164n)**, prepared from **176n** (5.00 mmol) and **180a** (5.00 mmol) following the general procedure GP2; white solid (694 mg, 52%); **m.p.** = 70 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 – 7.71 (m, 2H), 7.32 – 7.29 (m, 2H), 5.78 – 5.67 (m, 1H), 5.04 – 4.97 (m, 2H), 4.50 – 4.46 (m, 1H), 2.68 (d, *J* = 6.9 Hz, 2H), 2.43 (s, 3H), 1.96 (d, *J* = 7.5 Hz, 1H), 0.86 (s, 6H).

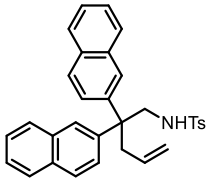
The analytical data are in accordance to those reported in the literature.[197]



164o

4-methyl-*N*-(2-methyl-2-phenylpent-4-en-1-yl)benzenesulfonamide (164o), prepared from **176o** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (441 mg, 67%); **m.p.** = 73 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.62 (m, 2H), 7.32 – 7.27 (m, 4H), 7.24 – 7.17 (m, 3H), 5.54 – 5.43 (m, 1H), 5.01 – 4.95 (m, 2H), 4.04 (t, *J* = 6.5 Hz, 1H), 3.14 – 3.01 (m, 2H), 2.49 – 2.44 (m, 1H), 2.43 (s, 3H), 2.32 – 2.27 (m, 1H), 1.31 (s, 3H).

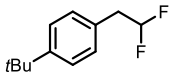
The analytical data are in accordance to those reported in the literature.[198]



164p

***N*-(2,2-di(naphthalen-2-yl)pent-4-en-1-yl)-4-methylbenzenesulfonamide (164p)**, prepared from **176p** (2.00 mmol) and **180a** (2.00 mmol) following the general procedure GP2; white solid (540 mg, 55%); **m.p.** = 195 °C; **TLC:** R_f = 0.24 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 4H), 7.71 (d, *J* = 2.0 Hz, 2H), 7.64 (d, *J* = 8.7 Hz, 2H), 7.57 – 7.54 (m, 2H), 7.52 – 7.47 (m, 4H), 7.18 – 7.16 (m, 2H), 6.99 (dd, *J* = 8.7, 1.9 Hz, 2H), 5.36 – 5.26 (m, 1H), 5.04 – 4.93 (m, 2H), 3.94 (t, *J* = 6.3 Hz, 1H), 3.77 (d, *J* = 6.3 Hz, 2H), 3.13 – 3.11 (m, 2H), 2.39 (s, 3H).

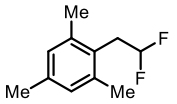
2.3 Analytical Data for the *gem*-Difluorination of Styrenes



153a

1-(*tert*-butyl)-4-(2,2-difluoroethyl)benzene (153a), prepared from **152a** (40.1 mg, 0.25 mmol) following the general procedure GP3; yellow oil (33.7 mg, 68%); **TLC:** R_f = 0.38 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.94 (tt, *J* = 56.7, 4.6 Hz, 1H), 3.14 (td, *J* = 17.4, 4.6 Hz, 2H), 1.36 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.5, 129.6, 125.8, 116.9 (t, *J* = 241.3 Hz), 40.56 (t, *J* = 21.8 Hz), 34.63, 31.46 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.64 (dt, *J* = 56.8, 17.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 198 (22) $[M]^+$, 183 (100) $[M\text{-}Me]^+$, 155 (38), 91 (9) $[PhCH_2]^+$.

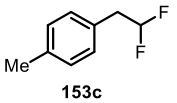
The analytical data are in accordance to those reported in the literature.[113]



153b

2-(2,2-difluoroethyl)-1,3,5-trimethylbenzene (153b), prepared from **152b** (36.6 mg, 0.25 mmol) following the general procedure GP3; yellow oil (29.0 mg, 63%); **TLC:** R_f = 0.38 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.91 (s, 2H), 5.91 (tt, *J* = 56.8, 4.8 Hz, 1H), 3.23 (td, *J* = 16.7, 4.8 Hz, 2H), 2.34 (s, 6H), 2.29 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.6, 137.1, 129.4, 126. 7 (t, *J* = 5.7 Hz), 116.8 (t, *J* = 242.1 Hz), 34.43 (t, *J* = 22.1 Hz), 20.98, 20.42 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.28 (dt, *J* = 56.7, 16.9 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 184 (32) $[M]^+$, 133 (100) $[M\text{-}CHF_2]^+$, 91 (9) $[PhCH_2]^+$, 77 (4) $[Ph]^+$.

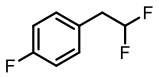
The analytical data are in accordance to those reported in the literature.[113]



153c

1-(2,2-difluoroethyl)-4-methylbenzene (153c), prepared from **152c** (29.4 mg, 0.25 mmol) following the general procedure GP3; yellow oil (19.5 mg, 50%); **TLC:** R_f = 0.38 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15 (s, 4H), 5.90 (tt, *J* = 56.7, 4.6 Hz, 1H), 3.10 (td, *J* = 17.3, 4.6 Hz, 2H), 2.35 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.3, 129.8, 129.5, 117.0 (t, *J* = 241.3 Hz), 40.66 (t, *J* = 21.8 Hz), 21.21 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.86 (dt, *J* = 56.7, 17.2 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 156 (35) $[M]^+$, 105 (100) $[M\text{-}CHF_2]^+$, 91 (4) $[M\text{-}CH_2CHF_2]^+$, 77 (12) $[Ph]^+$.

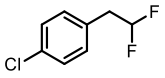
The analytical data are in accordance to those reported in the literature.[113]



153d

1-(2,2-difluoroethyl)-4-fluorobenzene (153d), prepared from **152d** (30.5 mg, 0.25 mmol) following the general procedure GP3; colorless oil (21.6 mg, 54%); **TLC:** R_f = 0.50 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.07 – 7.00 (m, 2H), 5.90 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.11 (td, *J* = 17.4, 4.5 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4 (d, *J* = 245.9 Hz), 131.5 (d, *J* = 8.1 Hz), 116.5, 115.7 (d, J = 21.4 Hz), 40.22 (t, *J* = 22.1 Hz), 31.26 (d, *J* = 7.5 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.14 – -115.23 (m), -115.26 (dt, *J* = 56.9, 18.3 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 160 (34) $[M]^+$, 141 (3) $[M\text{-}F]^+$, 109 (100) $[M\text{-}CHF_2]^+$.

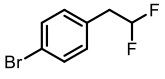
The analytical data are in accordance to those reported in the literature.[113]



153e

1-chloro-4-(2,2-difluoroethyl)benzene (153e), prepared from **152e** (34.6 mg, 0.25 mmol) following the general procedure GP3; yellow oil (20.7 mg, 47%); **TLC:** R_f = 0.30 (silica gel, pentane) [UV]. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 5.93 (tt, *J* = 56.4, 4.5 Hz, 1H), 3.14 (td, *J* = 17.3, 4.5 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.7, 131.3, 130.9 (t, *J* = 5.8 Hz), 129.0, 128.5, 116.3 (t, *J* = 241.6 Hz), 40.36 (t, *J* = 22.1 Hz), 31.20 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.17 (dt, *J* = 56.5, 17.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 178/176 (13/38) $[M]^+$, 127/125 (37/100) $[M\text{-}CHF_2]^+$.

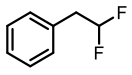
The analytical data are in accordance to those reported in the literature.[117]



153f

1-bromo-4-(2,2-difluoroethyl)benzene (153f), prepared from **152f** (45.8 mg, 0.25 mmol) following the general procedure GP3; colorless oil (33.2 mg, 60%); **TLC:** R_f = 0.30 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.37 (m, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 5.91 (tt, *J* = 56.4, 4.5 Hz, 1H), 3.10 (td, *J* = 17.3, 4.5 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 132.0, 131.7, 131.4 (t, *J* = 5.8 Hz), 121.8, 116.2 (t, *J* = 241.5 Hz), 40.39 (t, *J* = 22.1 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.13 (dtd, *J* = 56.3, 17.5, 3.1 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 222/220 (46/47) $[M]^+$, 171/169 (98/100) $[M\text{-}CHF_2]^+$, 90 (34) $[M\text{-}Br\text{-}CHF_2]^+$.

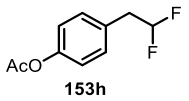
The analytical data are in accordance to those reported in the literature.[113]



153g

(2,2-difluoroethyl)benzene (153g), prepared from **152g** (26.0 mg, 0.25 mmol) following the general procedure GP3; colorless oil (13.5 mg, 38%); **TLC:** R_f = 0.50 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 – 7.23 (m, 5H), 5.93 (tt, *J* = 56.6, 4.6 Hz, 1H), 3.15 (td, *J* = 17.3, 4.6 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 132.6 (t, *J* = 5.9 Hz), 129.9, 128.8, 127.6, 116.8 (t, *J* = 241.4 Hz), 41.08 (t, *J* = 21.9 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.81 (dt, *J* = 56.6, 17.3 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 142 (33) $[M]^+$, 91 (100) $[M\text{-}CHF_2]^+$.

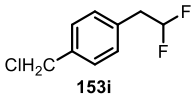
The analytical data are in accordance to those reported in the literature.[113]



153h

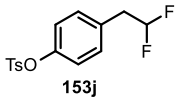
4-(2,2-difluoroethyl)phenyl acetate (153h), prepared from **152h** (40.5 mg, 0.25 mmol) following the general procedure GP3; colorless oil (25.0 mg, 50%); **TLC:** R_f = 0.20 (silica gel, 95:5 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.09 (m, 2H), 7.07 – 6.91 (m, 2H), 5.85 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.07 (td, *J* = 17.3, 4.5 Hz, 2H), 2.24 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.5, 150.2, 130.9, 130.1 (t, *J* = 6.0 Hz), 121.9, 116.5 (t, *J* = 241.4 Hz), 40.33 (t, *J* = 22.1 Hz), 21.16 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.95 (dt, *J* = 56.5, 17.5 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 200 (9) $[M]^+$, 158 (64) [M-Ac], 107 (100) [M-Ac-CHF_2], 77 (16) $[Ph]^+$.

The analytical data are in accordance to those reported in the literature.[113]



153i

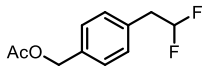
1-(chloromethyl)-4-(2,2-difluoroethyl)benzene (153i), prepared from **152i** (38.2 mg, 0.25 mmol) following the general procedure GP3; colorless oil (36.2 mg, 76%); **TLC:** R_f = 0.45 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 5.91 (ttd, *J* = 56.5, 4.5, 0.9 Hz, 1H), 4.57 (s, 2H), 3.14 (td, *J* = 17.3, 4.5 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.9, 132.8 (t, *J* = 5.8 Hz), 130.3, 129.0, 116.5 (t, *J* = 241.5 Hz), 45.93, 40.66 (t, *J* = 22.1 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.88 (dtd, *J* = 56.5, 17.4, 2.7 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 1392, 1267, 1108, 1030, 1020, 663cm^{-1}; **MS** (EI, positive 70 eV): *m/z* (%) =192/190 (9/25) $[M]^+$, 155 (100) $[M\text{-}Cl]^+$, 104 (12) [M-Cl-CH_2CF_2]$^+$; **HRMS** (EI) calcd. for $C_9H_9ClF_2^+$ $[M]^+$ 190.0355, found 190.0353.



153j

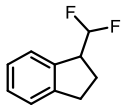
4-(2,2-difluoroethyl)phenyl 4-methylbenzenesulfonate (153j), prepared from **152j** (68.6 mg, 0.25 mmol) following the general procedure GP3; yellow solid (56.2 mg, 72%); **m.p.** = 50 °C ($CHCl_3$); **TLC:** R_f = 0.30 (silica gel, 95:5 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.6 Hz, 2H), 5.88 (tt, *J* = 56.4, 4.5 Hz, 1H), 3.10 (td, *J* = 17.3, 4.4 Hz, 2H), 2.45 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.1, 145.6, 132.5, 131.5 (t, *J* = 5.9 Hz), 131.2, 129.9, 128.6, 122.7, 116.2 (t, *J* = 241.5 Hz), 40.26 (t, *J* = 22.3 Hz), 21.81 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.14 (dt, *J* = 56.4, 17.3 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 1367, 1151, 1020, 862, 795, 675;

MS (EI, positive 70 eV): *m/z* (%) = 312 (34) $[M]^+$, 155 (78) $[Tos]^+$, 91 (100) $[PhCH_2]^+$; **HRMS** (EI) calcd. for $C_{15}H_{14}F_2O_3S^+$ $[M]^+$ 312.0626, found 312.0618.



153k

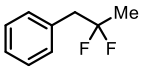
4-(2,2-difluoroethyl)benzyl acetate (153k), prepared from **152k** (44.1 mg, 0.25 mmol) following the general procedure GP3; colorless oil (28.3 mg, 52%); **TLC:** R_f = 0.30 (silica gel, 90:10 pentane:EtOAc) [CAN]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 5.90 (tt, *J* = 56.5, 4.6 Hz, 1H), 5.08 (s, 2H), 3.12 (td, *J* = 17.3, 4.5 Hz, 2H), 2.08 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.9, 135.4, 132.6 (t, *J* = 5.8 Hz), 130.1, 128.7, 116.6 (t, *J* = 241.4 Hz), 65.98, 40.67 (t, *J* = 22.0 Hz), 21.05 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.91 (dt, *J* = 56.5, 17.2 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 1758, 1510, 1370, 1190, 911; **MS** (EI, positive 70 eV): *m/z* (%) = 214 (39) $[M]^+$, 172 (100) $[M\text{-}Ac]^+$, 155 (64) $[M\text{-}OAc]^+$, 107 (86) $[M\text{-}Ac\text{-}CH_2CHF_2]^+$, 91 (15) $[PhCH_2]^+$, 77 (18) $[Ph]^+$; **HRMS** (ESI+) calcd. for $C_{11}H_{13}F_2O_2^+$ $[M+H]^+$ 215.0878, found 215.0877.



153l

1-(difluoromethyl)-2,3-dihydro-*1H*-indene (153l), prepared from **152l** (32.5 mg, 0.25 mmol) following the general procedure GP3; colorless oil (21.4 mg, 51%); **TLC:** R_f = 0.50 (silica gel, pentane) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 1H), 7.30 – 7.26 (m, 1H), 7.25 – 7.17 (m, 2H), 5.80 (td, *J* = 56.9, 5.5 Hz, 1H), 3.61 (tdt, *J* = 14.3, 8.8, 5.7 Hz, 1H), 3.10 – 2.88 (m, 2H), 2.31 (dtd, *J* = 13.4, 8.8, 6.1 Hz, 1H), 2.18 – 2.04 (m, 1H, CH_2) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.0, 139.0 – 138.8 (m), 128.0, 126.7, 125.5 (d, *J* = 1.6 Hz), 124.9, 118.3 (t, *J* = 242.6 Hz), 49.17 (t, *J* = 20.6 Hz), 31.52, 25.66 – 25.41 (m) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.78 (ddd, *J* = 57.0, 38.8, 14.2 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 168 (34) $[M]^+$, 117 (100) $[M\text{-}CHF_2]^+$, 91 (11) $[PhCH_2]^+$.

The analytical data are in accordance to those reported in the literature.[113]

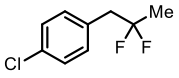


153m

(2,2-difluoropropyl)benzene (153m), prepared from **152m** (29.5 mg, 0.25 mmol) following the general procedure GP3; colorless oil (21.5 mg, 55%); **TLC:** R_f = 0.57 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.19 (m, 5H), 3.15 (t, *J* = 15.5 Hz, 2H), 1.54 (t, *J* = 18.4 Hz, 3H) ppm; **^{13}C NMR**

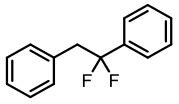
(101 MHz, $CDCl_3$) δ 133.9 (t, *J* = 5.1 Hz), 130.4, 128.6, 127.45, 123.6 (t, *J* = 239.5 Hz), 44.58 (t, *J* = 26.3 Hz), 22.96 (t, *J* = 27.5 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -88.97 (dtd, *J* = 33.7, 18.3, 15.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 156 (45) $[M]^+$, 91 (100) $[M\text{-}CF_2Me]^+$, 65 (22) $[CF_2Me]^+$.

The analytical data are in accordance to those reported in the literature.[113]



153n

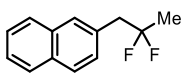
1-chloro-4-(2,2-difluoropropyl)benzene (153n), prepared from **152n** (38.2 mg, 0.25 mmol) following the general procedure GP3; yellow oil (31.5 mg, 66%); **TLC:** R_f = 0.40 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.26 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 3.11 (t, *J* = 15.5 Hz, 2H), 1.54 (t, *J* = 18.3 Hz, 3H, CH_3) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.5, 132.3 (t, *J* = 4.9 Hz), 131.7, 128.8, 123.2 (t, *J* = 239.6 Hz), 43.87 (t, *J* = 26.6 Hz), 23.00 (t, *J* = 27.5 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -89.41 (dtd, *J* = 33.8, 18.3, 15.5 Hz, 2F) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 1494, 1391, 1091, 931, 775 cm^{-1}; **MS** (EI, positive 70 eV): *m/z* (%) = 192/190 (11/33) $[M]^+$, 127/125 (42/100) $[M\text{-}CH_2CHF_2]^+$; **HRMS** (EI) calcd. for $C_9H_9ClF_2^+$ $[M]^+$ 190.0355, found 190.0360.



153o

(1,1-difluoroethane-1,2-diyl)dibenzene (153o), prepared from **152o** (45.1 mg, 0.25 mmol) following the general procedure GP3; colorless solid (44.2 mg, 81%); **TLC:** R_f = 0.50 (silica gel, pentane) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 5H), 7.26 – 7.19 (m, 3H), 7.13 – 7.05 (m, 2H), 3.39 (t, *J* = 15.8 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.0 (t, *J* = 26.4 Hz), 132.8 (t, *J* = 4.1 Hz), 130.8, 129.8 (t, *J* = 2.0 Hz), 128.3 (d, *J* = 1.9 Hz), 127.4, 125.3 (t, *J* = 6.2 Hz), 122.1 (t, *J* = 244.1 Hz), 46.02 (t, *J* = 28.6 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -94.86 (zt, *J* = 15.8 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 218 (29) $[M]^+$, 127 (100) $[M\text{-}PhCH_2]^+$, 91 (30) $[PhCH_2]^+$.

The analytical data are in accordance to those reported in the literature.[113]

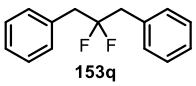


153p

2-(2,2-difluoropropyl)naphthalene (153p), prepared from **152p** 42.1 mg, 0.25 mmol) following the general procedure GP3; colorless oil (30.5 mg, 59%); **TLC:** R_f = 0.52 (silica gel, 90:10 pentane:DCM) [$KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 3H), 7.74 (s, 1H), 7.55 – 7.46 (m, 2H), 7.42 (d,

J = 8.3 Hz, 1H), 3.33 (t, *J* = 15.4 Hz, 2H), 1.58 (t, *J* = 18.4 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.5, 132.7, 131.4, 129.3, 128.3, 128.2, 127.9, 127.8, 126.2 (d, *J* = 25.5 Hz), 123.8 (t, *J* = 239.7 Hz), 44.70 (t, *J* = 26.4 Hz), 23.04 (t, *J* = 27.5 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -88.49 (dt, *J* = 18.7, 15.5 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 206 $[M]^+$, 141 $[M\text{-}CF_2CH_3]^+$, 115 $[M\text{-}C_6H_4\text{-}CH_3]^+$.

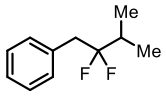
The analytical data are in accordance to those reported in the literature.[40]



153q

(2,2-difluoropropane-1,3-diyl)dibenzene (153q), prepared from **152q** (48.6 mg, 0.25 mmol) following the general procedure GP3; colorless oil (41.2 mg, 71%); **TLC:** R_f = 0.35 (silica gel, pentane) [CAM]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 6H), 7.31 – 7.26 (m, 4H), 3.13 (td, *J* = 16.4, 2.2 Hz, 4H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.3 (t, *J* = 4.2 Hz), 130.6, 128.5, 127.5, 123.2 (t, *J* = 243.7 Hz), 42.55 (t, *J* = 25.6 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -94.71 (p, *J* = 16.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 232 (60) $[M]^+$, 212 (12) $[M\text{-}HF]^+$, 141 (20) $[M\text{-}PhCH_2]^+$, 91 (100) $[PhCH_2]^+$.

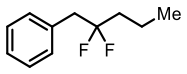
The analytical data are in accordance to those reported in the literature.[41]



153r

(2,2-difluoro-3-methylbutyl)benzene (153r), prepared from **152r** (36.6 mg, 0.25 mmol) following the general procedure GP3; colorless oil (31.1 mg, 68%); **TLC:** R_f = 0.60 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 3.24 – 3.07 (m, 2H), 2.02 (tpd, *J* = 13.9, 7.0, 1.8 Hz, 1H), 1.08 (dd, *J* = 6.8, 1.6 Hz, 6H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.7 (t, *J* = 4.2 Hz), 130.5, 128.5, 127.3, 125.6 (t, *J* = 244.6 Hz), 40.59 (t, *J* = 26.3 Hz), 33.79 (t, *J* = 24.4 Hz), 15.96 (t, *J* = 5.0 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.04 (q, *J* = 16.7 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 184 (38) $[M]^+$, 149 (3) $[M\text{-}HF\text{-}CH_3]^+$, 91 (100) $[PhCH_2]^+$, 77 (5) $[Ph]^+$.

The analytical data are in accordance to those reported in the literature.[41]

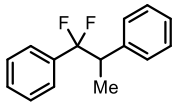


153s

(2,2-difluoropentyl)benzene (153s), prepared from **152s** (40.1 mg, 0.25 mmol) following the general procedure GP3; colorless solid (25.8 mg, 56%); **TLC:** R_f = 0.60 (silica gel, pentane) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 3.15 (t, *J* = 16.1 Hz, 2H), 1.83 – 1.67 (m, 2H), 1.65 – 1.51 (m, 2H),

0.95 (t, *J* = 7.4 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.8 (t, *J* = 4.9 Hz), 130.4, 128.5, 127.4, 124.4 (t, *J* = 242.0 Hz), 43.14 (t, *J* = 26.3 Hz), 37.94 (t, *J* = 24.8 Hz), 15.73 (t, *J* = 4.8 Hz), 14.01 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.48 (p, *J* = 16.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 184 (36) $[M]^+$, 169 (5) $[M\text{-}CH_3]^+$, 91 (100) $[PhCH_2]^+$, 77 (4) $[Ph]^+$.

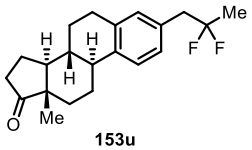
The analytical data are in accordance to those reported in the literature.[41]



153t

(1,1-difluoropropane-1,2-diyl)dibenzene (153t), prepared from **152t** (48.6 mg, 0.25 mmol) following the general procedure GP3; colorless oil (36.0 mg, 62%); **TLC:** R_f = 0.55 (silica gel, 95:5 hexanes:EtOAc) [CAN]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 1H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.26 – 7.22 (m, 5H), 7.16 – 7.11 (m, 2H), 3.51 – 3.39 (m, 1H), 1.45 (d, *J* = 7.2 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) 138.8 (dd, *J* = 3.7, 2.4 Hz), 136.4 (t, *J* = 26.9 Hz), 129.5, 129.3, 128.1, 128.0, 127.4, 125.8 (t, *J* = 6.3 Hz), 123.4 (t, *J* = 247.4 Hz), 48.52 (t, *J* = 26.8 Hz), 14.81 (t, *J* = 4.2 Hz) ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -100.07 (dd, *J* = 241.2, 13.2 Hz), -101.91 (dd, *J* = 241.3, 15.6 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 232 (14) $[M]^+$, 127 (16), $[M\text{-}PhCH_2CH_3]^+$, 105 (100) $[PhCH_2CH_3]^+$, 77 (14) $[Ph]^+$.

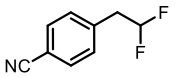
The analytical data are in accordance to those reported in the literature.[199]



153u

(8R,9S,13S,14S)-3-(2,2-difluoropropyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (153u), prepared from **152u** (73.6 mg, 0.25 mmol) following the general procedure GP3; colorless solid (51.5 mg, 62%); **TLC:** R_f = 0.40 (silica gel, 90:10 pentane:EtOAc) [CAN]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 7.00 (s, 1H), 3.08 (t, *J* = 15.7 Hz, 2H), 2.92 (dd, *J* = 9.0, 4.2 Hz, 2H), 2.51 (dd, *J* = 18.7, 8.6 Hz, 1H), 2.46 – 2.39 (m, 1H), 2.30 (td, *J* = 10.7, 4.2 Hz, 1H), 2.20 – 2.12 (m, 1H), 2.12 – 1.93 (m, 3H), 1.71 – 1.38 (m, 8H), 1.35 – 1.24 (m, 1H), 0.92 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 220.9, 138.9, 136.7, 131.2 (t, *J* = 4.9 Hz), 131.0, 127.7, 125.5, 123.6 (t, *J* = 239.3 Hz), 50.66, 48.10, 44.43, 44.02 (t, *J* = 26.2 Hz), 38.25, 35.97, 31.73, 29.44, 26.61, 25.80, 23.04 (t, *J* = 27.5 Hz), 21.71, 13.97 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -89.00 (dtd, *J* = 34.1, 18.3, 15.6 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 2930, 1390, 1236, 1133, 1084, 735 cm^{-1}; **MS** (EI, positive 70 eV): *m/z*

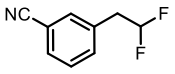
(%) = 332 (100) $[M]^+$, 253 (33) $[M\text{-}CH_2CF_2CH_3]^+$; **HRMS** (EI) calcd. for $C_{21}H_{26}F_2O^+$ $[M]^+$ 332.1946, found 332.1939.



153aa

4-(2,2-difluoroethyl)benzonitrile (153aa), prepared from **152aa** (32.3 mg, 0.25 mmol); following the general procedure GP4; yellowish solid(28.0 mg, 67%); **TLC:** R_f = 0.24 (silica gel, 95:5 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 5.98 (tt, *J* = 56.1, 4.3 Hz, 1H), 3.23 (td, *J* = 17.3, 4.3 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.8 (t, *J* = 5.4 Hz), 132.5, 130.8, 118.6, 115.6 (t, *J* = 241.9 Hz), 111.8, 40.88 (t, *J* = 22.3 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.23 (dt, *J* = 56.2, 17.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 167 (31) $[M]^+$, 116 (100) $[M\text{-}CHF_2]^+$.

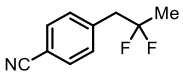
The analytical data are in accordance to those reported in the literature.[117]



153bb

3-(2,2-difluoroethyl)benzonitrile (153bb), prepared from **152bb** (32.3 mg, 0.25 mmol) following the general procedure GP4; colorless oil (17.5 mg, 40%); **TLC:** R_f = 0.24 (silica gel, 95:5 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (dt, *J* = 7.3, 1.6 Hz, 1H), 7.56 (s, 1H), 7.54 – 7.44 (m, 2H), 5.95 (tt, *J* = 56.1, 4.3 Hz, 1H), 3.19 (td, *J* = 17.4, 4.2 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 134.55, 133.90 (t, *J* = 5.4 Hz), 133.6, 131.4, 129.7, 118.6, 115.7 (t, *J* = 241.9 Hz), 113.1, 40.42 (t, *J* = 22.3 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.49 (dt, *J* = 56.0, 17.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 167 (30) $[M]^+$, 116 (100) $[M\text{-}CHF_2]^+$.

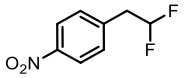
The analytical data are in accordance to those reported in the literature.[117]



153cc

4-(2,2-difluoropropyl)benzonitrile (153cc), prepared from **152cc** (35.8 mg, 0.25 mmol) following the general procedure GP4; colorless oil containing 5% of an impurity that could not be removed (corrected: 29.9 mg, 66%); **TLC:** R_f = 0.50 (silica gel, 95:5 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 7.9 Hz, 2H), 3.20 (t, *J* = 15.5 Hz, 2H), 1.57 (t, *J* = 18.3 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.0 (t, *J* = 4.4 Hz), 132.3, 131.2, 122.7 (t, *J* = 240.2 Hz), 118.8, 111.6, 44.49

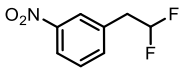
(t, *J* = 26.5 Hz), 23.27 (t, *J* = 27.3 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -89.45 (dtd, *J* = 33.9, 18.5, 15.6 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 2230, 1612, 1393, 1232, 1338 882, 789 cm^{-1}; **MS** (EI, positive 70 eV): *m/z* (%) = 181 (49) $[M]^+$, 116 (100) $[M\text{-}CHF_2]^+$, 102 (1) $[M\text{-}CH_2CHF_2]^+$. **HRMS** (ESI+) calcd. for $C_{10}H_{10}F_2N^+$ $[M]^+$ 182.0776, found 182.0773.



153dd

1-(2,2-difluoroethyl)-4-nitrobenzene (153dd), prepared from **152dd** (37.3 mg, 0.25 mmol) following the general procedure GP4; colorless oil (15.9 mg, 34%); **TLC:** R_f = 0.67 (silica gel, 85:15 pentane:EtOAc) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 – 8.17 (m, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 5.99 (tt, *J* = 56.1, 4.3 Hz, 1H), 3.27 (td, *J* = 17.3, 4.3 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.7, 139.7 (d, *J* = 5.4 Hz), 131.0, 124.0, 119.4 – 110.8 (m), 40.67 (t, *J* = 22.3 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.22 (dt, *J* = 55.9, 17.3 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 187 (100) $[M]^+$, 141 (30) $[M\text{-}NO_2]^+$, 136 (33) $[M\text{-}CHF_2]^+$, 101 (98) $[M\text{-}NO_2\text{-}2HF]^+$.

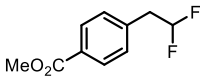
The analytical data are in accordance to those reported in the literature.[117]



153ee

1-(2,2-difluoroethyl)-3-nitrobenzene (153ee), prepared from **152ee** (37.3 mg, 0.25 mmol) following the general procedure GP4; yellow oil (10.8 mg, 23%); **TLC:** R_f = 0.40 (silica gel, 95:5 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.22 – 8.12 (m, 2H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 6.00 (tt, *J* = 56.1, 4.2 Hz, 1H), 3.27 (td, *J* = 17.3, 4.3 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.2, 129.8, 125.0, 122.9, 115.6 (t, *J* = 241.9 Hz), 40.48 (t, *J* = 22.4 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.56 (dt, *J* = 56.2, 17.3 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 187 (93) $[M]^+$, 136 (62) $[M\text{-}CHF_2]^+$, 101 (100) $[M\text{-}CH_2CHF_2]^+$.

The analytical data are in accordance to those reported in the literature.[117]

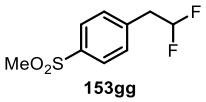


153ff

methyl 4-(2,2-difluoroethyl)benzoate (153ff), prepared from **152ff** (40.5 mg, 0.25 mmol) following the general procedure GP4; colorless oil (17.7 mg, 35%); **TLC:** R_f = 0.69 (silica gel, 90:10 pentane:EtOAc) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 5.95 (tt, *J* = 56.3,

4.5 Hz, 1H), 3.92 (s, 3H), 3.20 (td, *J* = 17.2, 4.5 Hz, 2H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.9, 137.7 (d, *J* = 5.6 Hz), 130.1, 130.0, 129.6, 116.2 (t, *J* = 241.8 Hz), 52.32, 40.95 (t, *J* = 22.2 Hz) ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -114.87 (dt, *J* = 56.3, 17.4 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 200 (30) $[M]^+$, 169 (100) $[M\text{-}OCH_3]^+$, 149 (9) $[M\text{-}OCH_3\text{-}HF]^+$, 141 (11) $[M\text{-}CO_2CH_3]^+$.

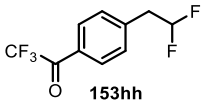
The analytical data are in accordance to those reported in the literature.[40]



153gg

1-(2,2-difluoroethyl)-4-(methylsulfonyl)benzene (153gg), prepared from **152gg** (45.6 mg, 0.25 mmol) following the general procedure GP4; colorless solid (31.9 mg, 58%); **TLC:** R_f = 0.17 (silica gel, 85:15 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 – 7.78 (m, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 5.97 (tt, *J* = 56.1, 4.3 Hz, 1H), 3.24 (td, *J* = 17.4, 4.3 Hz, 2H), 3.05 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.0, 138.7 (t, *J* = 5.4 Hz), 131.1, 127.9, 115.7 (t, *J* = 241.9 Hz), 44.60, 40.70 (t, *J* = 22.3 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.23 (dt, *J* = 56.0, 17.2 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 220 (64) $[M]^+$, 205 (66) $[M\text{-}CH_3]^+$, 141 (100) $[M\text{-}SO_2CH_3]^+$, 101 (76) $[M\text{-}SO_2CH_3\text{-}2HF]^+$.

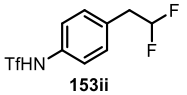
The analytical data are in accordance to those reported in the literature.[117]



153hh

1-(4-(2,2-difluoroethyl)phenyl)-2,2,2-trifluoroethan-1-one (153h), prepared from **152hh** (43.0 mg, 0.25 mmol) following the general procedure GP4; colorless oil (19.4 mg, 37%); **TLC:** R_f = 0.17 (silica gel, 95:5 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 8.01 (m, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 5.99 (tt, *J* = 56.0, 4.3 Hz, 1H), 3.26 (td, *J* = 17.3, 4.3 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.2 (q, *J* = 35.2 Hz), 140.7 (t, *J* = 5.4 Hz), 130.8, 130.6 (d, *J* = 2.2 Hz), 129.4, 116.8 (q, *J* = 291.2 Hz), 115.7 (t, *J* = 242.0 Hz), 41.02 (t, *J* = 22.3 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -71.52, -115.01 (dt, *J* = 56.3, 17.3 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 238 (4) $[M]^+$, 169 (100) $[M\text{-}CF_3]^+$, 141 (14) $[M\text{-}COCF_3]^+$.

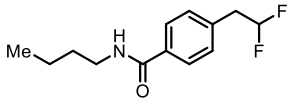
The analytical data are in accordance to those reported in the literature.[117]



153ii

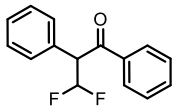
***N*-(4-(2,2-difluoroethyl)phenyl)-1,1,1-trifluoromethanesulfonamide (153ii)**, prepared from **152ii** (95.2 mg, 0.25 mmol) following the general procedure GP4; colorless oil (47.2 mg, 65%); **TLC:** R_f = 0.40 (silica

gel, 85:15 pentane:EtOAc) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 7.26 – 7.22 (m, 2H), 5.91 (tt, *J* = 56.4, 4.4 Hz, 1H), 3.13 (td, *J* = 17.4, 4.5 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.2, 132.1 (t, *J* = 5.7 Hz), 131.3, 124.0, 121.5, 119.9 (q, *J* = 322.6 Hz), 116.2 (t, *J* = 241.5 Hz), 40.32 (t, *J* = 22.1 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -75.36, -115.18 (dt, *J* = 56.6, 17.6 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3288, 1515, 1414, 1199, 1137, 1113, 1056, 1022, 941 cm^{-1}; **MS** (EI, positive 70 eV): *m/z* (%) = 289 (36) $[M]^+$, 238 (14) $[M\text{-}CHF_2]^+$, 156 (100) $[M\text{-}Tf]^+$. **HRMS** (ESI-) calcd. for $C_9H_7F_5NO_2S^-$ $[M\text{-}H]^-$ 288.0123, found 288.0121.



153jj

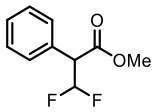
***N*-butyl-4-(2,2-difluoroethyl)benzamide (153jj)**, prepared from **152jj** (50.8 mg, 0.25 mmol) following the general procedure GP4; colorless solid (39.3 mg, 65%); **m.p.** = 67 °C (EtOAc); **TLC:** R_f = 0.18 (silica gel, 85:15 pentane:EtOAc) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 – 7.71 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.29 (br s, 1H), 5.92 (tt, *J* = 56.4, 4.5 Hz, 1H), 3.43 (td, *J* = 7.2, 5.7 Hz, 2H), 3.16 (td, *J* = 17.3, 4.4 Hz, 2H), 1.62 – 1.54 (m, 2H), 1.46 – 1.34 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.2, 135.8 (t, *J* = 5.7 Hz), 134.3, 130.1, 127.4, 116.2 (t, *J* = 241.6 Hz), 40.74 (t, *J* = 22.1 Hz), 39.94, 31.83, 20.26, 13.87 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.98 (dt, *J* = 56.5, 17.2 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3313, 2934, 1632, 1540, 1107, 1016, 842, 684 cm^{-1}; **MS** (EI, positive 70 eV): *m/z* (%) = 241 (9) $[M]^+$, 198 (20) $[M\text{-}CH_2CH_2CH_3]^+$, 169 (100) $[M\text{-}n\text{BuNH}]^+$, 101 (15) $[M\text{-}CONHn\text{Bu-}2HF]^+$; **HRMS** (ESI+) calcd. for $C_{13}H_{18}F_2NO^+$ $[M+H]^+$ 242.1351, found 242.1352.



153kk

3,3-difluoro-1,2-diphenylpropan-1-one (153kk), prepared from **152kk** (52.1 mg, 0.25 mmol) following the general procedure GP4; colorless oil (18.5 mg, 40%); **TLC:** R_f = 0.56 (silica gel, 65:35 pentane:DCM) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 – 7.86 (m, 2H), 7.57 – 7.48 (m, 1H), 7.47 – 7.28 (m, 8H), 6.45 (ddd, *J* = 56.3, 55.0, 6.9 Hz, 1H), 4.97 (td, *J* = 10.2, 6.9 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.2 (d, *J* = 8.1 Hz), 135.7 (d, *J* = 2.5 Hz), 133.9, 131.7 (d, *J* = 8.1 Hz), 129.5, 129.2, 129.0, 128.9, 128.8, 116.8 (dd, *J* = 243.7, 241.5 Hz), 60.69 – 54.63 (m) ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -115.97 (ddd, *J* = 280.8, 55.0, 10.1 Hz), -126.45 (ddd, *J* = 280.8, 56.2, 10.2 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 246 (1) $[M]^+$, 225 (4) $[M\text{-}HF]^+$, 105 (100) $[Bz]^+$, 77 (38) $[Ph]^+$.

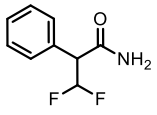
The analytical data are in accordance to those reported in the literature.[114]



153ll

methyl 3,3-difluoro-2-phenylpropanoate (153ll), prepared from **152ll** (40.5 mg, 0.25 mmol) following the general procedure GP4; colorless oil (44.5 mg, 89%); **TLC:** R_f = 0.65 (silica gel, 90:10 pentane:Et_2O) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 – 7.32 (m, 6H), 6.25 (td, *J* = 55.5, 6.8 Hz, 1H), 4.03 (ddd, *J* = 11.9, 10.2, 6.8 Hz, 1H), 3.75 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.3 (dd, *J* = 11.5, 1.9 Hz), 131.2 (d, *J* = 7.6 Hz), 129.2, 128.9, 128.9, 120.3 – 111.6 (m), 55.95 (t, *J* = 23.8 Hz), 52.77 ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -117.26 (ddd, *J* = 282.6, 55.3, 10.5 Hz), -123.85 (ddd, *J* = 282.6, 55.7, 11.9 Hz) ppm; **MS** (EI, positive 70 eV): *m/z* (%) = 200 (86) $[M]^+$, 141 (87) $[M\text{-}CO_2Me]^+$, 122 (63) $[M\text{-}CO_2Me\text{ -}F]^+$, 91 (100) $[M\text{-}CHF_2\text{-}CO_2Me]^+$.

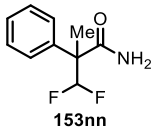
The analytical data are in accordance to those reported in the literature.[115]



153mm

3,3-difluoro-2-phenylpropanamide (153mm), prepared from **152mm** (36.8 mg, 0.25 mmol) following the general procedure GP4; colorless solid (37.1 mg, 80%); **TLC:** R_f = 0.38 (silica gel, 80:20 DCM:Et_2O) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 2.6 Hz, 5H), 6.34 (td, *J* = 55.6, 5.4 Hz, 1H), 6.12 – 5.99 (m, 1H), 5.69 (br s, 1H), 3.88 (ddd, *J* = 15.7, 10.4, 5.4 Hz, 1H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.1, 129.4, 129.3, 129.0, 115.8 (t, *J* = 242.9 Hz), 57.12 – 55.74 (m), 29.86 ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -118.89 (ddd, *J* = 281.0, 55.3, 10.3 Hz), -123.92 (ddd, *J* = 281.0, 55.9, 15.9 Hz) ppm; **MS** (ESI+) = 186 $[M+H]^+$.

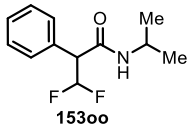
The analytical data are in accordance to those reported in the literature.[115]



153nn

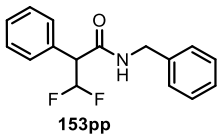
3,3-difluoro-2-methyl-2-phenylpropanamide (153nn), prepared from **152nn** (40.3 mg, 0.25 mmol) following the general procedure GP4; colorless solid (22.4 mg, 45%); **TLC:** R_f = 0.51 (silica gel, 50:50 pentane:EtOAc) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.47 – 7.44 (m, 2H), 7.43 – 7.38 (m, 2H), 7.38 – 7.34 (m, 1H), 6.33 (t, *J* = 55.8 Hz, 1H), 5.45 (br d, *J* = 26.2 Hz, 2H), 1.74 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.5, 136.3, 129.0, 128.6, 127.8, 117.4 (t, *J* = 246.7 Hz), 54.56 (t, *J* = 20.5 Hz), 18.10

ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -126.57 (d, *J* = 53.9 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3395, 1658, 1618, 1113, 700, 665 cm^{-1}; **MS** (ESI+) = 200 $[M+H]^+$; **HRMS** (ESI+) calcd. for $C_{10}H_{12}F_2NO^+$ $[M+H]^+$ 200.0881, found 200.0882.



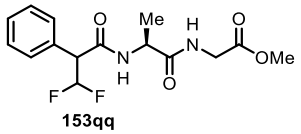
153oo

***N*-benzyl-3,3-difluoro-2-phenylpropanamide (153oo)**, prepared from **152oo** (47.3 mg, 0.25 mmol) following the general procedure GP4; orange solid (13.1 mg, 23%); **m.p.** = 69 °C (EtOAc); **TLC:** R_f = 0.70 (silica gel, 75:25 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.34 (m, 5H), 6.35 (td, *J* = 55.8, 5.6 Hz, 1H), 5.37 (br s, 1H), 4.08 (dp, *J* = 8.0, 6.5 Hz, 1H), 3.75 (ddd, *J* = 15.6, 10.0, 5.6 Hz, 1H), 1.13 (d, *J* = 6.6 Hz, 3H), 1.06 (d, *J* = 6.6 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.3 (dd, *J* = 7.6, 3.5 Hz), 132.3 (d, *J* = 6.3 Hz), 129.3, 129.2, 128.7, 116.3 (t, *J* = 242.9 Hz), 57.15 (t, *J* = 22.5 Hz), 41.94, 29.85, 22.64, 22.49 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.40 (ddd, *J* = 279.8, 55.8, 10.1 Hz), -124.08 (ddd, *J* = 279.7, 56.2, 15.5 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3274, 1640, 1555, 1118, 1051, 750, 698 cm^{-1}; **MS** (ESI+) = 228 $[M+H]^+$; **HRMS** (ESI+) calcd. for $C_{12}H_{16}F_2NO^+$ $[M+H]^+$ 228.1194, found 228.1194**.**



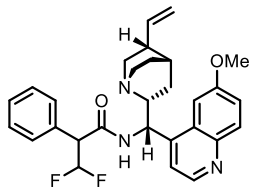
153pp

***N*-benzyl-3,3-difluoro-2-phenylpropanamide (153pp)**, prepared from **152pp** (59.3 mg, 0.25 mmol) following the general procedure GP4; yellow oil (22.7 mg, 33%); **TLC:** R_f = 0.20 (silica gel, 75:25 pentane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.35 (m, 5H), 7.33 – 7.15 (m, 4H), 7.15 – 6.94 (m, 1H), 6.40 (td, *J* = 55.8, 5.5 Hz, 1H), 5.93 (br s, 1H), 4.41 (pd, *J* = 14.6, 5.9 Hz, 2H), 3.85 (ddd, *J* = 15.5, 10.0, 5.6 Hz, 1H) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.31 (dddd, *J* = 280.3, 55.1, 9.9, 2.8 Hz), -123.84 (dddd, *J* = 280.6, 56.3, 23.1, 15.6 Hz); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.1 (dd, *J* = 7.6, 3.7 Hz), 137.6, 129.5 – 129.2 (m, 2C), 128.9, 127.8, 127.7, 116.2 (t, *J* = 243.1 Hz), 115.8, 115.6, 57.12 (t, *J* = 22.7 Hz), 43.79 ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3299, 1648, 1430, 1060, 731, 696 cm^{-1}; **MS** (ESI+) = 276 $[M+H]^+$; **HRMS** (ESI+) calcd. for $C_{16}H_{16}F_2NO^+$ $[M+H]^+$ 276.1194, found 276.1195.



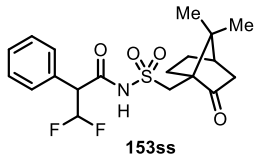
153qq

methyl (3,3-difluoro-2-phenylpropanoyl)-L-alanylglycinate (153qq), prepared from **152qq** (72.6 mg, 0.25 mmol) following the general procedure GP4; produced as an 55:45 mixture of inseperable diastereomers; colorless solid (69.7 mg, 85%); **m.p.** = 113 °C (MeOH); **TLC:** R_f = 0.69 (silica gel, 90:10 DCM:MeOH) [UV]; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.43 (dt, *J* = 7.9, 2.0 Hz, 2H), 7.40 – 7.27 (m, 3H), 6.48 – 6.09 (m, 1H), 4.43 (dq, *J* = 21.4, 7.1 Hz, 1H), 4.06 (tt, *J* = 10.9, 6.6 Hz, 1H), 4.01 – 3.74 (m, 2H), 3.68 (d, *J* = 21.9 Hz, 3H), 1.37 (d, *J* = 7.1 Hz, 3H, CH_3 *major*), 1.26 (d, *J* = 7.1 Hz, 3H, CH_3 *minor*) ppm; **^{13}C NMR** (101 MHz, CD_3OD) δ 174.8, 171.4, 170.3 (d, *J* = 10.4 Hz), 134.1 (d, *J* = 8.7 Hz), 129.9, 129.8, 129.3, 118.0 (t, *J* = 241.7 Hz), 57.11 (t, *J* = 23.4 Hz), 52.55, 50.08, 41.74, 18.23 ppm; *major diastereomer*: **^{19}F NMR** (376 MHz, CD_3OD) δ -119.15 (ddd, *J* = 125.5, 55.4, 10.5 Hz), -125.51 (ddd, *J* = 124.0, 56.2, 11.5 Hz) ppm; **^{13}C NMR** (101 MHz, CD_3OD) δ 175.05, 171.58, 170.54 (d, *J* = 9.8 Hz), 134.19 (d, *J* = 8.4 Hz), 129.88, 129.80, 129.35, 117.82 (t, *J* = 241.6 Hz), 57.11 (t, *J* = 23.4 Hz), 52.60, 50.17, 41.84, 17.94 ppm; *minor diastereomer*: **^{19}F NMR** (376 MHz, CD_3OD) δ -118.40 (ddd, *J* = 125.6, 55.4, 10.6 Hz), -126.26 (ddd, *J* = 124.1, 56.2, 11.5 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3300, 1646, 1212, 1063, 700 cm^{-1}; **MS** (ESI+) = 329 $[M+H]^+$, **HRMS** (ESI+) calcd. for $C_{15}H_{19}F_2N_2O_4^+$ $[M+H]^+$ 329.1307, found 329.1307.



153rr

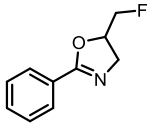
3,3-difluoro-*N*-((S)-(6-methoxyquinolin-4-yl)((1S,2R,4S,5R)-5-vinylquinuclidin-2-yl)methyl)-2-phenylpropanamide (153rr), prepared from **152rr** (113.4 mg, 0.25 mmol) following the general procedure GP4; colorless solid (39.3 mg, 32%); **m.p.** = 71 °C (EtOAc); **TLC:** R_f = 0.27 (silica gel, 49:49:2 EtOAc:MeOH:Et_3N) [UV]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.6 Hz, 1H), 8.03 (d, *J* = 9.2 Hz, 1H), 7.54 (s, 1H), 7.45 – 7.35 (m, 6H), 7.31 (d, *J* = 4.6 Hz, 1H), 6.23 (td, *J* = 55.7, 5.6 Hz, 1H), 5.66 (dt, *J* = 17.4, 9.7 Hz, 1H), 5.02 – 4.87 (m, 2H), 4.01 – 3.83 (m, 3H), 3.87 (ddd, *J* = 15.7, 10.2, 5.6 Hz, 1H), 3.12 (dd, *J* = 13.9, 10.1 Hz, 1H), 3.06 – 2.74 (m, 1H), 2.63 – 2.46 (m, 2H), 2.25 (s, 1H), 1.97 – 1.88 (m, 1H), 1.73 – 1.63 (m, 1H), 1.62 – 1.51 (m, 2H), 1.46 – 1.37 (m, 1H), 1.34 (ddt, *J* = 14.2, 12.4, 3.8 Hz, 1H), 1.20 – 1.04 (m, 1H), 0.96 (dd, *J* = 13.8, 6.7 Hz, 1H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.3, 158.4 – 157.6 (m), 156.8, 147.7, 144.9, 141.2, 132.06, 129.5, 129.0, 128.7, 121.7, 116.0 (t, *J* = 243.2 Hz), 114.9, 101.8, 56.73 (t, *J* = 22.2 Hz), 55.80, 55.73, 49.32, 40.74, 39.56, 34.09, 27.88, 27.33, 25.74, 25.09 ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -118.43 (dd, *J* = 281.5, 56.8 Hz), -123.42 (ddd, *J* = 280.7, 55.6, 15.4 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 2932, 1665, 1509, 1242, 1229, 1063, 731 cm^{-1}; **MS** (ESI+) = 492 $[M+H]^+$; **HRMS** (ESI+) calcd. for $C_{29}H_{32}F_2N_3O_2^+$ $[M+H]^+$ 492.2457, found 492.2454.



153ss

***N*-(((7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methyl)sulfonyl)-3,3-difluoro-2-phenylpropanamide (153ss)**, prepared from **152ss** (90.4 mg, 0.25 mmol) following the general procedure GP4; produced as an 57:43 mixture of inseperable diastereomers; colorless oil (54.9 mg, 55%); **TLC:** R_f = 0.22 (silica gel, 50:50 hexane:EtOAc) [CAM]; **^{1}H NMR** (500 MHz, $CDCl_3$, *mixture of diastereomers*) δ 7.43 – 7.32 (m, 5H), 6.33 (tdd, *J* = 55.3, 8.5, 5.7 Hz, 1H), 2.41 – 2.30 (m, 1H), 2.27 – 2.13 (m, 1H), 2.11 (q, *J* = 4.5 Hz, 1H), 2.07 – 1.96 (m, 1H), 1.90 (d, *J* = 18.7 Hz, 1H), 1.76 (ddd, *J* = 14.0, 9.4, 4.6 Hz, 1H), 1.41 (ddt, *J* = 13.1, 9.4, 3.9 Hz, 1H), 1.01 (d, *J* = 19.1 Hz, 3H), 0.84 (d, *J* = 24.1 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, *mixture of diastereomers*) δ 216.2, 215.5, 167.8 (dd, *J* = 8.5, 3.1 Hz), 167.5 (dd, *J* = 9.0, 3.4 Hz), 148.7, 137.3, 130.0 (t, *J* = 7.5 Hz), 129.5, 129.5, 129.4, 124.3, 115.1 (t, *J* = 244.2 Hz), 115.1 (t, *J* = 243.9 Hz) 59.02, 58.96, 57.12 (t, *J* = 23.7 Hz), 56.90 (t, *J* = 23.3 Hz) 51.71, 51.59, 49.08, 48.74, 42.84, 42.83, 27.11, 27.07, 26.10, 19.86, 19.62, 19.53 ppm; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -117.59 (ddd, *J* = 283.5, 54.9, 10.3 Hz), -117.75 (ddd, *J* = 283.7, 54.8, 9.6 Hz), -124.30 (ddd, *J* = 55.4, 48.6, 13.2 Hz), -124.30 (ddd, *J* = 615.7, 55.6, 13.2 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 2963, 1717, 1456, 1351, 1230, 700 cm^{-1}; **MS** (ESI+) = 400 $[M+H]^+$; **HRMS** (ESI+) calcd. for $C_{19}H_{24}F_2NO_4S^+$ $[M+H]^+$ 400.1389, found 400.1389.

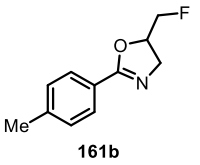
2.4 Analytical Data for the Fluorocyclization of *N*-allylcarboxamides



161a

5-(Fluoromethyl)-2-phenyl-oxazoline (161a), prepared from **160a** (80.5 mg, 0.5 mmol) following the general procedure GP5; yellow oil (61.8 mg, 69%); **TLC:** R_f = 0.28 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.94 (m, 2H), 7.50 – 7.46 (m, 1H), 7.43 – 7.38 (m, 2H), 4.97 – 4.85 (m, 1H), 4.66 – 4.54 (m, 1H), 4.53 – 4.41 (m, 1H), 4.14 (ddd, *J* = 14.9 Hz, 10.2 Hz, 1.5 Hz, 1H), 3.86 (dd, *J* = 14.9 Hz, 7.5 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.0, 131.4, 128.3, 128.2, 127.3, 83.4 (d, *J* = 175.2 Hz), 77.5 (d, *J* = 19.5 Hz), 55.8 (d, *J* = 6.0 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -228.97 (td, *J* = 47.1, 19.3 Hz) ppm;

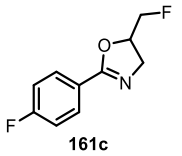
The analytical data are in accordance to those reported in the literature.[129]



161b

5-(Fluoromethyl)-2-(*p*-tolyl)-oxazoline (161b), prepared from **160b** (87.6 mg, 0.5 mmol) following the general procedure GP5; white solid (63.7 mg, 66%); **m.p.** = 42 °C; **TLC:** R_f = 0.28 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 4.94 – 4.82 (m, 1H), 4.63 – 4.52 (m, 1H), 4.51 – 4.39 (m, 1H), 4.11 (ddd, *J* = 14.8, 10.2, 1.5 Hz, 1H), 3.82 (dd, *J* = 14.8, 7.5 Hz, 1H), 2.37 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.0, 141.8, 129.0, 128.1, 124.5, 83.3 (d, *J* = 175.0 Hz), 77.4 (d, *J* = 16.4 Hz), 55.6 (d, *J* = 6.0 Hz), 21.4 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -228.71 (td, *J* = 47.5, 19.5 Hz) ppm;

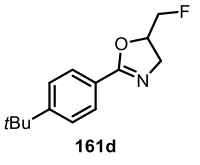
The analytical data are in accordance to those reported in the literature.[146]



161c

5-(Fluoromethyl)-2-(4-fluorophenyl)-oxazoline (161c), prepared from **160c** (89.5 mg, 0.5 mmol) following the general procedure GP5; white solid (64.0 mg, 65%); **m.p.** = 65 °C; **TLC:** R_f = 0.28 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.92 (m, 2H), 7.10 – 7.05 (m, 2H), 4.96 – 4.84 (m, 1H), 4.65 – 4.53 (m, 1H), 4.53 – 4.40 (m, 1H), 4.12 (ddd, *J* = 15.0, 10.2, 1.4Hz, 1H), 3.84 (dd, *J* = 14.8, 7.5 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.5 (*J* = 291.5 Hz), 130.5 (d, *J* = 8.9 Hz), 123.6 (d, *J* = 3.1 Hz), 115.4 (d, *J* = 22.0 Hz), 83.3 (d, *J* = 175.4 Hz), 77.7 (d, *J* = 19.5 Hz), 55.7 (d, *J* = 5.9 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -107.93 (hept, *J* = 4.6 Hz), -229.21 (td, *J* = 47.2, 19.8 Hz) ppm;

The analytical data are in accordance to those reported in the literature.[146]

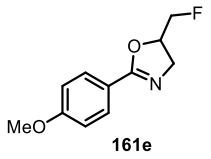


161d

5-(Fluoromethyl)-2-(4-(1,1-dimethylethyl)phenyl)-oxazoline (161d), prepared from **160d** (108.6 mg, 0.5 mmol) following the general procedure GP5; beige solid (83.5 mg, 71%); **m.p.** = 47°C; **TLC:** R_f = 0.28 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.5 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 1H), 4.94 – 4.83 (m, 1H), 4.63 – 4.51 (m, 1H), 4.50 – 4.38 (m, 1H), 4.12 (ddd, *J* = 14.9, 10.2, 1.5

Hz, 1H), 3.84 (dd, *J* = 14.8, 7.4 Hz, 1H), 1.32 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.0, 154.9, 128.0, 125.2, 124.4, 83.4 (d, *J* = 175.1 Hz), 77.3 (d, *J* = 19.7 Hz), 55.7 (d, *J* = 5.8 Hz), 34.9, 31.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -228.84 (td, *J* = 47.4, 19.5 Hz) ppm;

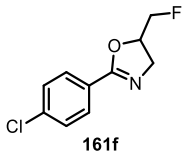
The analytical data are in accordance to those reported in the literature.[146]



161e

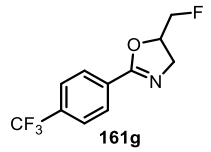
5-(Fluoromethyl)-2-(4-methoxyphenyl)-oxazoline (161e), prepared from **160e** (95.6 mg, 0.5 mmol) following the general procedure GP5; yellow oil (34.5 mg, 33%); **TLC:** R_f = 0.25 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 – 7.88 (m, 1H), 6.93 – 6.89 (m, 1H), 4.96 – 4.84 (m, 1H), 4.65 – 4.53 (m, 1H), 4.52 – 4.41 (m, 1H), 4.12 (ddd, *J* = 14.7, 10.2, 1.5 Hz, 1H), 3.86 – 3.80(m, 4H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.8, 162.2, 130.0, 119.9, 113.7, 83.5 (d, *J* = 175.1 Hz), 77.4 (d, *J* = 19.5 Hz), 55.7 (d, *J* = 5.8 Hz), 55.3 ppm; ^{19}F NMR (376 MHz, acetone-d_6) δ -234.32 (td, *J* = 47.1, 19.4 Hz).

The analytical data are in accordance to those reported in the literature.[129]



161f

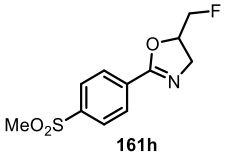
2-(4-Chlorophenyl)-5-(fluoromethyl)-oxazoline (161f), prepared from **160f** (97.5 mg, 0.5 mmol) following the general procedure GP5; white solid (54.3 mg, 51%); **m.p.** = 53 °C; **TLC:** R_f = 0.29 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.6 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 4.96 – 4.84 (m, 1 H), 4.65 – 4.53 (m, 1 H), 4.53 – 4.39 (m, 1 H), 4.12 (ddd, *J* = 14.9, 10.2, 1.5 Hz, 1H), 3.85 (dd, *J* = 14.9, 7.6 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.1, 137.6, 129.5, 128.6, 125.8, 83.2 (d, *J* = 175.4 Hz), 77.7 (d, *J* = 19.5 Hz), 55.7 (d, *J* = 6.0 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.28 (td, *J* = 47.3, 19.9 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3429, 2966, 1655, 1265, 1092, 838, 668 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{10}H_{10}ClFNOS^+$ $[M+H]^+$ 214.0429, found 214.0429.



161g

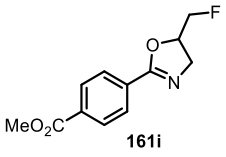
5-(Fluoromethyl)-2-(4-(trifluoromethyl)phenyl)-oxazoline (161g), prepared from **160g** (114.5 mg, 0.5 mmol) following the general procedure GP5; colourless oil (86.5 mg, 70%); **TLC:** R_f = 0.32 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 5.03 – 4.92 (m, 1H), 4.71 – 4.58 (m, 1H), 4.57 – 4.44 (m, 1H), 4.20 (dd, *J* = 15.1 Hz, 10.2 Hz, 1H), 3.93 (dd, *J* = 15.1 Hz,7.6 Hz, 1H) ppm ; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.9, 133.1 (q, *J* = 32.6 Hz), 130.7, 128.6, 125.4 (q, *J* = 3.8 Hz), 123.7(q, *J* = 272.5Hz), 83.2 (d, *J* = 175.6 Hz), 78.0 (d, *J* = 19.6 Hz), 55.9 (d, *J* = 6.0 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ 63.0(s), -228.97 (td, *J* = 47.0, 20.2 Hz) ppm;

The analytical data are in accordance to those reported in the literature.[129]



161h

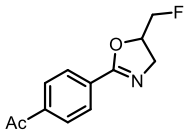
5-(fluoromethyl)-2-(4-(methylsulfonyl)phenyl)-oxazoline (161h), prepared from **160h** (119.5 mg, 0.5 mmol) following the general procedure GP5; white solid (70.7 mg, 55%); **m.p.** = 98 °C; **TLC:** R_f = 0.29 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.3 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 5.01 – 4.90 (m, 1H), 4.72 – 4.56 (m, 1H), 4.53 – 4.38 (m, 1H), 4.18 (dd, *J* = 14.9, 10.6 Hz, 1H), 3.92 (dd, *J* = 15.3, 7.6 Hz, 1H), 3.05 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.37, 142.80, 132.29, 129.10, 127.36, 83.09 (d, *J* = 175.6 Hz), 78.14 (d, *J* = 19.4 Hz), 55.80 (d, *J* = 6.1 Hz), 44.30 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -230.37 (td, *J* = 47.2, 21.0 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3423, 2931, 1725, 1650, 1403, 1293, 1149, 782, 561, 529 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{11}H_{13}FNO_3S^+$ $[M+H]^+$ 258.0595, found 258.0616.



161i

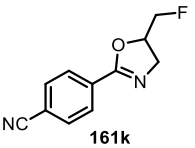
Methyl 4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzoate (161i), prepared from **160i** (109.5 mg, 0.5 mmol) following the general procedure GP5; white solid (93.6 mg, 79%); **m.p.** = 86 °C; **TLC:** R_f = 0.29 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 4H), 5.00 – 4.94 (m, 1H), 4.70 – 4.58 (m, 1H), 4.56 – 4.43 (m, 1H), 4.19 (dd, *J* = 14.7, 10.4 Hz, 1H), 3.95 – 3.89 (m, 4H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 163.6, 132.8, 130.9, 129.6, 128.3, 83.1 (d, *J* = 175.6 Hz), 78.1 (d, *J* = 19.5 Hz), 55.5 (d, *J* = 5.9 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3628, 2957, 1612, 1410, 1117, 708 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.81 (td, *J* = 47.1, 20.2 Hz) ppm; **HRMS** (ESI+) calcd. for $C_{12}H_{13}FNO_3^+$ $[M+H]^+$ 238.0874, found 238.0885.



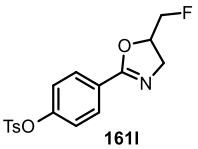
161j

1-(4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)phenyl)ethenone (161j), prepared from **160j** (101.6 mg, 0.5 mmol) following the general procedure GP5; white solid (64.1 mg, 58%); **m.p.** = 128 °C; **TLC:** R_f = 0.18 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.04 – 7.94 (m, 4H), 5.02 – 4.86 (m, 1H), 4.70 – 4.56 (m, 1H), 4.55 – 4.38 (m, 1H), 4.16 (dd, *J* = 15.1, 10.3 Hz, 1H), 3.89 (dd, *J* = 15.2, 7.7 Hz, 1H), 2.60 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.4, 163.2, 139.1, 131.2, 128.4, 128.2, 83.2 (d, *J* = 175.5 Hz), 77.93 (d, *J* = 19.5 Hz), 55.70 (d, *J* = 5.9 Hz), 26.7 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.73 (td, *J* = 47.2, 20.2 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3586, 2876, 1683, 1261, 990, 857 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{12}H_{13}FNO_2^+$ $[M+H]^+$ 222.0925, found 222.0934.



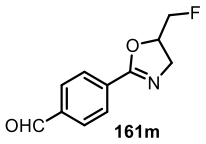
161k

4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzonitrile (161k), prepared from **160k** (93.4 mg, 0.5 mmol) following the general procedure GP5; white solid (56.1 mg, 55%); **m.p.** = 95 °C; **TLC:** R_f = 0.20 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 5.05 – 4.90 (m, 1H), 4.73 – 4.58 (m, 1H), 4.57 – 4.40 (m, 1H), 4.20 (dd, *J* = 14.8, 9.9 Hz, 1H), 3.93 (dd, *J* = 15.3, 7.7 Hz, 1H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.6, 132.1, 131.2, 128.8, 118.1, 115.0, 83.0 (d, *J* = 175.9 Hz), 78.3 (d, *J* = 19.5 Hz), 55.6 (d, *J* = 6.1 Hz) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -230.39 (td, *J* = 47.2, 20.9 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3408, 2955, 2229, 1652, 1265, 1072, 854, 669 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{11}H_{10}FN_2O^+$ $[M+H]^+$ 205.0772, found 205.0781.



161l

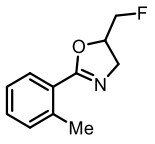
4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)phenyl 4-methylbenzenesulfonate (161l), prepared from **160l** (148.4 mg, 0.5 mmol) following the general procedure GP5; white solid (148.4 mg, 85%); **m.p.** = 88 °C; **TLC:** R_f = 0.23 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 4.94 – 4.83 (m, 1H), 4.64 – 4.50 (m, 1H), 4.50 – 4.36 (m, 1H), 4.13 – 4.07 (m, 1H), 3.83 (dd, *J* = 15.0, 7.6 Hz, 1H), 2.40 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.8, 151.7, 145.6, 131.9, 129.8, 129.7, 128.4, 126.1, 122.3, 83.1 (d, *J* = 175.3 Hz), 77.9 (d, *J* = 19.4 Hz), 55.5 (d, *J* = 6.0 Hz), 21.6 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.89 (td, *J* = 47.2, 20.6 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3433, 2959, 1653, 1501, 1379, 1167, 874, 568 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{17}H_{17}FNO_4S^+$ $[M+H]^+$ 350.0857, found 350.0855.



161m

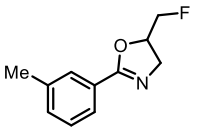
4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzaldehyde (161m), prepared from **160m** (94.5 mg, 0.5 mmol) following the general procedure GP5; white solid (33.1 mg, 32%); **m.p.** = 66 °C; **TLC:** R_f = 0.21 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.14 (d, *J* = 8.3 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H), 5.07 – 4.92 (m, 1H), 4.74 – 4.61 (m, 1H), 4.59 – 4.42 (m, 1H), 4.21 (dd, *J* = 14.8, 10.3 Hz, 1H), 3.94 (dd, *J* = 15.1, 7.6 Hz, 1H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 191.5, 163.4, 138.3, 132.1, 129.6, 129.0, 83.1 (d, *J* = 175.7 Hz), 78.3 (d, *J* = 19.4 Hz), 55.4 (d, *J* = 6.6 Hz) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -230.19 (td, *J* = 47.1, 20.5 Hz) ppm.

The analytical data are in accordance to those reported in the literature.[129]



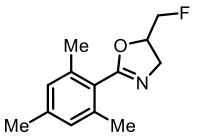
161n

5-(Fluoromethyl)-2-(o-tolyl)-oxazoline (161n), prepared from **160n** (87.6 mg, 0.5 mmol) following the general procedure GP5; colourless oil (42.5 mg, 44%); **TLC:** R_f = 0.28 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.25 (td, *J* = 7.5, 1.5 Hz, 1H), 7.18 – 7.12 (m, 2H), 4.83 – 4.71 (m, 1H), 4.57 – 4.45 (m, 1H), 4.45 – 4.32 (m, 1H), 4.08 (ddd, *J* = 14.9, 10.3, 1.5 Hz, 1H), 3.82 (dd, *J* = 14.8, 7.3 Hz, 1H), 2.51 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.4, 138.8, 131.2, 130.6, 129.8, 126.7, 125.5, 83.4 (d, *J* = 175.2 Hz), 76.6 (d, *J* = 19.5 Hz), 56.1 (d, *J* = 5.7 Hz), 21.6 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.58 (td, *J* = 47.1, 19.9 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3437, 2974, 1646, 1216, 1042, 756 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{11}H_{13}FNO^+$ $[M+H]^+$ 194.0976, found 194.0989.



161o

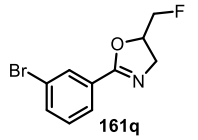
5-(Fluoromethyl)-2-(*m*-tolyl)-oxazoline (161o), prepared from **160o** (87.6 mg, 0.5 mmol) following the general procedure GP5; colourless oil (74.3 mg, 77%); **TLC:** R_f = 0.28 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.75 – 7.73 (m, 1H), 7.31 – 7.26 (m, 2H), 4.95 – 4.84 (m, 1H), 4.64 – 4.52 (m, 1H), 4.52 – 4.40 (m, 1H), 4.12 (ddd, *J* = 14.9 Hz, 10.2 Hz, 1.5 Hz, 1H), 3.84 (dd, *J* = 14.9 Hz, 7.5 Hz, 1H) , 2.37 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.1, 138.0, 132.2, 128.7, 128.2, 127.1, 125.3, 83.3 (d, *J* = 175.1 Hz), 77.5 (d, *J* = 19.6 Hz), 55.6 (d, *J* = 5.9 Hz), 21.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -228.87 (td, *J* = 47.1, 19.3 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3431, 2950, 1652, 1194, 1001, 712 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{11}H_{13}FNO^+$ $[M+H]^+$ 194.0976, found 194.0985.



161p

5-(Fluoromethyl)-2-(2,4,6-trimethylphenyl)-oxazoline (161p), prepared from **160p** (101.6 mg, 0.5 mmol) following the general procedure GP5; yellow oil (42.0 mg, 38%); **TLC:** R_f = 0.25 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86 (s, 2H), 4.91 – 4.80 (m, 1H), 4.70 – 4.55 (m, 1H), 4.55 – 4.41 (m, 1H), 4.17 (ddd, *J* = 14.6 Hz, 10.4 Hz, 1.6 Hz, 1H), 3.96 (dd, *J* = 14.5 Hz, 7.3 Hz, 1H), 2.30 (s, 6H), 2.28 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.4, 139.3, 137.0, 128.2, 125.5, 83.2 (d, *J* = 175.5 Hz), 77.1 (d, *J* = 19.4 Hz), 76.8, 55.7 (d, *J* = 6.0 Hz), 21.1, 19.6 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -231.25 (td, *J* = 47.3, 22.3 Hz) ppm;

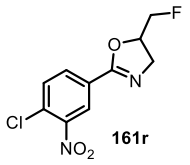
The analytical data are in accordance to those reported in the literature.[146]



161q

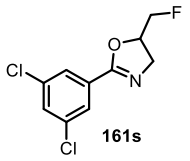
2-(3-Bromophenyl)-5-(fluoromethyl)-oxazoline (161q), prepared from **160q** (119.5 mg, 0.5 mmol) following the general procedure GP5; yellow oil (72.0 mg, 56%); **TLC:** R_f = 0.29 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 – 8.10 (m, 1H), 7.90 – 7.87 (m, 1H), 7.63 – 7.59 (m, 1H), 7.32 – 7.26 (m, 1H), 4.98 – 4.88 (m, 1H), 4.69 – 4.55 (m, 1H), 4.54 – 4.42 (m, 1H), 4.16 (ddd, *J* = 16.0, 10.7, 5.6 Hz, 1H), 3.88 (dt, *J* = 13.5, 6.6 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.7, 134.4,

131.1, 129.9, 129.2, 126.7, 122.3, 83.2 (d, *J* = 175.4 Hz), 77.8 (d, *J* = 19.5 Hz), 55.7 (d, *J* = 6.0 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.59 (td, *J* = 47.2, 20.2 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3437, 1651, 1567, 1254, 1060, 707 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{10}H_{10}BrFNO^+$ $[M+H]^+$ 257.9924, found 257.9928.



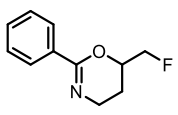
161r

2-(4-Chloro-3-nitrophenyl)-5-(fluoromethyl)-oxazoline (161r), prepared from **160r** (120.2 mg, 0.5 mmol) following the general procedure GP5; yellow solid (41.3 mg, 32%); **m.p.** = 82 °C; **TLC:** R_f = 0.22 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 2.0 Hz, 1H), 8.09 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 5.03 – 4.91 (m, 1 H), 4.72 – 4.57 (m, 1 H), 4.57 – 4.42 (m, 1 H), 4.19 (ddd, *J* = 15.2, 10.3, 1.5 Hz, 1H), 3.93 (dd, *J* = 15.3, 7.7 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.3, 147.9, 132.3, 132.1, 130.0, 127.4, 125.3, 83.00 (d, *J* = 175.9 Hz), 78.54 (d, *J* = 19.5 Hz), 55.81 (d, *J* = 6.1 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -230.78 (td, *J* = 47.1, 21.2 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3435, 1656, 1535, 1340, 1079, 836 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{10}H_9ClFN_2O_3^+$ $[M+H]^+$ 259.0280, found 259.0295.



161s

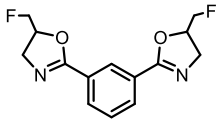
2-(3,5-Dichlorophenyl)-5-(fluoromethyl)-oxazoline (161s), prepared from **160s** (114.5 mg, 0.5 mmol) following the general procedure GP5; white solid (80.3 mg, 65%); **m.p.** = 67 °C; **TLC:** R_f = 0.29 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.0 Hz, 1H), 7.43 (t, *J* = 2.0 Hz, 1H), 4.97 – 4.85 (m, 1H), 4.67 – 4.53 (m, 1H), 4.52 – 4.39 (m, 1H), 4.13 (ddd, *J* = 15.2, 10.3, 1.5 Hz, 1H), 3.87 (dd, *J* = 15.2, 7.6 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.7, 135.1, 131.2, 130.1, 126.6, 83.04 (d, *J* = 175.8 Hz), 78.08 (d, *J* = 19.5 Hz), 55.69 (d, *J* = 6.0 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -230.06 (td, *J* = 47.0, 20.5 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3434, 1653, 1563, 1333, 1263, 1074, 805, 614 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{10}H_{10}Cl_2FNO^+$ $[M+H]^+$ 248.0040, found 248.0046.



161t

6-(Fluoromethyl)-2-phenyl-5,6-dihydro-4H-1,3-oxazine (161t), prepared from **160t** (87.6 mg, 0.5 mmol) following the general procedure GP5; white solid (25.1 mg, 26%); **m.p.** = 45 °C; **TLC:** R_f = 0.27 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 – 7.91 (m, 2H), 7.44 – 7.34 (m, 3H), 4.68 – 4.59(m, 1H), 4.57 – 4.42(m, 2H), 3.73 (ddd, *J* = 16.7, 5.4, 2.8 Hz, 1H), 3.61 (ddd, *J* = 16.5, 10.6, 5.2 Hz, 1H), 1.95 (ddt, *J* = 13.5, 5.6, 3.0 Hz, 1H), 1.85 (dtd, *J* = 13.5, 10.4, 5.4 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ155.1, 133.5, 130.5, 128.0, 127.0, 84.3 (d, *J* = 174.0 Hz), 73.0 (d, *J* = 20.5 Hz), 42.2, 22.3 (d, *J* = 5.7 Hz) ppm; **^{9}F NMR** (376 MHz, $CDCl_3$) δ -230.57 (td, *J* = 46.9, 19.6 Hz) ppm;

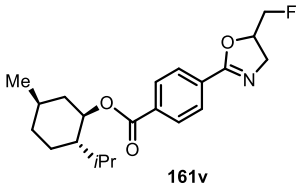
The analytical data are in accordance to those reported in the literature.[129]



161u

1,3-Bis(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzene (161u), prepared from **160u** (122.1 mg, 0.5 mmol) following the general procedure GP5; white solid (54.6 mg, 39%); **m.p.** = 92 °C; **TLC:** R_f = 0.21 (silica gel, 20:80 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 1.8 Hz, 1H), 8.07 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 1H), 4.97 – 4.85 (m, 1 H), 4.66 – 4.53 (m, 1 H), 4.52 – 4.40 (m, 1 H), 4.14 (ddd, *J* = 15.0, 10.3, 1.5 Hz, 2H), 3.87 (dd, *J* = 14.9, 7.6 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3, 131.0, 128.5, 127.9, 127.7, 83.2 (d, *J* = 175.4 Hz), 77.7 (d, *J* = 19.6 Hz), 55.8 (d, *J* = 5.8 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.67 (td, *J* = 47.2, 20.1 Hz) ppm;

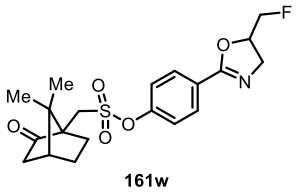
The analytical data are in accordance to those reported in the literature.[129]



161v

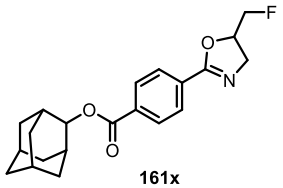
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzoate (161v), prepared from **160v** (171.6 mg, 0.5 mmol) following the general procedure GP5; colourless oil (130.0 mg, 72%); **TLC:** R_f = 0.23 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 23.4, 8.3 Hz, 4H), 4.98 – 4.86 (m, 1H), 4.66 – 4.53 (m, 1H), 4.52 – 4.40 (m, 1H), 4.15 (dd, *J* = 15.0, 10.3 Hz, 1H), 3.88 (dd, *J* = 15.1, 7.6 Hz, 1H), 2.10 (d, *J* = 12.0 Hz, 1H), 1.96 – 1.88 (m, 1H), 1.70 (d, *J* = 12.0 Hz, 2H), 1.57 – 1.51 (m, 2H), 1.16 – 1.05 (m, 2H), 0.94 – 0.85 (m, 7H), 0.77 (d, *J* = 6.9 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.3, 163.3, 133.3, 131.0, 129.4, 128.1, 83.1 (d, *J* = 175.5 Hz), 77.8 (d, *J* = 19.5 Hz), 75.18, 55.7 (d, *J* = 5.9 Hz), 47.13, 40.8, 34.2, 31.4, 26.4 (d, *J* = 2.0 Hz), 23.6 (d, *J* =

1.7 Hz), 21.9, 20.7, 16.4 (d, *J* = 1.8 Hz) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.60 (tdd, *J* = 47.2, 20.0, 11.6 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3413, 2956, 1714, 1274, 1118, 757 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{21}H_{29}FNO_3^+$ $[M+H]^+$ 326.2126, found 326.2128.



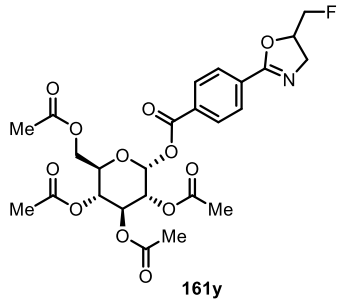
161w

4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)phenyl ((1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonate (161w), prepared from **160w** (195.6 mg, 0.5 mmol) following the general procedure GP5; colourless oil (100.2 mg, 49%); **TLC:** R_f = 0.27 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.7 Hz, 2H), 7.36 (d, *J* = 8.7 Hz, 2H), 5.00 – 4.94 (m, 1H), 4.71 – 4.55 (m, 1H), 4.52 – 4.39 (m, 1H), 4.21 – 4.11 (m, 1H), 3.90 (dd, *J* = 14.6, 7.4 Hz, 1H), 3.81 (d, *J* = 15.0 Hz, 1H), 3.20 (d, *J* = 15.0 Hz, 1H), 2.55 – 2.36 (m, 2H), 2.14 – 2.01 (m, 2H), 1.96 (d, *J* = 18.5 Hz, 1H), 1.77 – 1.67 (m, 1H), 1.49 – 1.41 (m, 1H), 1.13 (s, 3H), 0.89 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 213.8, 163.3, 151.6, 131.9, 130.3, 122.0, 83.1 (d, *J* = 175.8 Hz), 78.2 (d, *J* = 18.9 Hz), 58.1, 55.1 (d, *J* = 9.9 Hz), 48.0, 48.0, 42.8, 42.4, 26.8, 25.1, 19.8, 19.6 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -230.15 (td, *J* = 46.7, 20.1 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3405, 2961, 1747, 1654, 1504, 1374, 1151, 869, 754 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{20}H_{24}FKNO_5S^+$ $[M+K]^+$ 448.0991, found 448.0984.



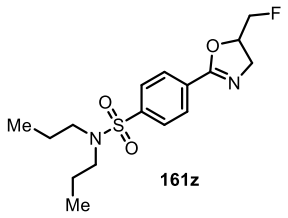
161x

(1r,3r,5r,7r)-adamantan-2-yl 4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzoate (161x), prepared from **160x** (169.6 mg, 0.5 mmol) following the general procedure GP5; white solid (119.7 mg, 67%); **m.p.** = 120 °C; **TLC:** R_f = 0.23 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.10 (q, *J* = 8.4 Hz, 4H), 5.19 (s, 1H), 5.05 – 4.98 (m, 1H), 4.74 – 4.60 (m, 1H), 4.58 – 4.43 (m, 1H), 4.23 (dd, *J* = 14.2, 10.6 Hz, 1H), 3.95 (dd, *J* = 14.8, 7.5 Hz, 1H), 2.13 (s, 4H), 1.89 – 1.78 (m, 8H), 1.64 (d, *J* = 12.2 Hz, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 163.6, 133.8, 130.7, 129.5, 128.2, 83.1 (d, *J* = 175.6 Hz), 78.0 (d, *J* = 21.4 Hz), 77.9, 55.4 (d, *J* = 5.5 Hz), 37.3, 36.3, 32.0, 31.9, 27.2, 26.9 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -230.12 (td, *J* = 47.0, 20.3 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3420, 2922, 1708, 1653, 1277, 1119, 706 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{21}H_{25}FNO_3^+$ $[M+H]^+$ 358.1813, found 358.1812.



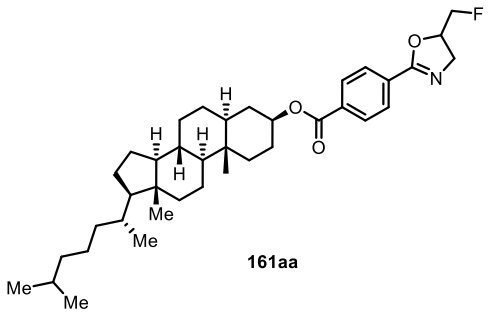
161y

(2R,3R,4S,5R,6R)-2-(acetoxymethyl)-6-((4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzoyl)oxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate (161y), prepared from **160y** (267.6 mg, 0.5 mmol) following the general procedure GP5; white solid (113.4 mg, 41%); **m.p.** = 120 °C; **TLC:** R_f = 0.15 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (s, 4H), 5.94 – 5.89 (m, 1H), 5.36 – 5.30 (m, 2H), 5.22– 5.15 (m, 1H), 5.06 – 5.01 (m, 1H), 4.74 – 4.69 (m, 1H), 4.62 – 4.46 (m, 1H), 4.31 (dd, *J* = 12.5, 4.4 Hz, 1H), 4.23 (t, *J* = 12.0 Hz, 1H), 4.14 – 4.10 (m, 1H), 3.98 – 3.93 (m, 1H), 2.05 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5, 170.0, 169.3, 169.2, 163.9, 163.7, 131.3, 130.2, 130.0 (s), 128.7, 92.5, 82.9 (d, *J* = 175.8 Hz), 78.6 (d, *J* = 17.0 Hz), 72.8, 72.5, 70.1, 67.8, 61.4, 54.8 (d, *J* = 2.1 Hz), 20.6, 20.5, 20.5 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -230.38 – -230.75 (m) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3445, 2958, 1750, 1242, 1082, 731 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{25}H_{28}FKNO_{12}^+$ $[M+K]^+$ 592.1227, found 592.1220.



161z

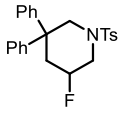
4-(5-(Fluoromethyl)-oxazolin-2-yl)-*N*,*N*-dipropylbenzenesulfonamide (161z), prepared from **160z** (162.1 mg, 0.5 mmol) following the general procedure GP5; yellow solid (126.6 mg, 74%); **m.p.** = 62 °C; **TLC:** R_f = 0.30 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 8.1 Hz, 2H), 4.96 – 4.88(m, 1H), 4.67 – 4.54 (m, 1H), 4.52 – 4.38 (m, 1H), 4.14 (dd, *J* = 15.2, 10.3 Hz, 1H), 3.88 (dd, *J* = 15.2, 7.6 Hz, 1H), 3.04 (t, *J* = 7.6 Hz, 4H), 1.49 (q, *J* = 7.5 Hz, 4H), 0.82 (t, *J* = 7.4 Hz, 6H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.6, 142.7, 130.8, 128.7, 126.8, 83.1 (d, *J* = 175.5 Hz), 78.0 (d, *J* = 19.4 Hz), 76.8, 55.7 (d, J = 6.1 Hz), 49.8, 21.7, 11.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -230.30 (td, *J* = 47.2, 20.9 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3676, 2967, 1653, 1336, 1160, 986, 600 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{16}H_{24}FN_2O_3^+$ $[M+H]^+$ 343.1486, found 343.1490.



161aa

(3S,5S,8R,9S,10S,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-(5-(fluoromethyl)-4,5-dihydrooxazol-2-yl)benzoate (161aa), prepared from **160aa** (287.7 mg, 0.5 mmol) following the general procedure GP5; white solid (210.7 mg, 71%); **m.p.** = 201 °C; **TLC:** R_f = 0.57 (silica gel, 50:50 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 – 8.03 (m, 4H), 5.03 – 4.90(m, 2H), 4.71 – 4.58 (m, 1H), 4.57 – 4.45 (m, 1H), 4.25 – 4.18 (m, 1H), 3.97 – 3.91 (m, 1H), 1.98 – 1.92 (m, 2H), 1.83 – 1.64 (m, 5H), 1.56 – 1.48 (m, 4H), 1.38 – 1.18 (m, 10H), 1.16 – 0.97 (m, 10H), 0.90 (d, *J* = 6.5 Hz, 4H), 0.86 – 0.85 (m, 9H), 0.65 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.2, 164.0, 133.9, 130.26 (s), 129.5, 128.3, 83.0 (d, *J* = 176.7 Hz), 78.3 (d, *J* = 17.4 Hz), 74.9, 56.4, 56.3, 55.0 (d, *J* = 5.3 Hz), 54.2 44.7, 42.6, 40.0, 39.5, 36.8, 36.1, 35.8, 35.5, 35.5, 34.1, 32.0, 28.6, 28.2, 28.0, 27.5, 24.2, 23.8, 22.8, 22.5, 21.2, 18.7, 12.3, 12.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -229.85 – -230.03 (m) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3419, 2935, 1715, 1653, 1278, 1118, 710 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{38}H_{57}FNO_3^+$ $[M+H]^+$ 594.4317, found 594.4308.

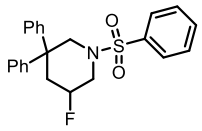
2.5 Analytical Data for the Aminofluorination of Alkenes



165a

5-Fluoro-3,3-diphenyl-1-tosylpiperidine (165a), prepared from **164a** (97.9 mg, 0.25 mmol) following the general procedure GP6; white solid (72.7 mg, 71%); **m.p.** = 160 °C; **TLC:** R_f = 0.27 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 7.2 Hz, 2H), 7.38 – 7.15 (m, 10H), 4.68 – 4.42 (m, 2H), 4.08 – 4.01 (m, 1H), 3.02 – 2.93 (m, 1H), 2.44 (d, *J* = 12.4 Hz, 1H), 2.43 (s, 3H), 2.36 – 2.28 (m, 1H), 2.23 – 2.13 (m, 1H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 145.3, 144.0, 143.1, 132.1, 129.9, 128.6, 128.6, 127.7, 127.7, 126.8, 126.5, 126.4, 85.5 (d, *J* = 173.8 Hz), 53.80, 49.8 (d, *J* = 31.1 Hz), 46.4 (d, *J* = 10.9 Hz), 41.0 (d, *J* = 18.7 Hz), 21.5 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -185.42 (d, *J* = 47.9 Hz) ppm.

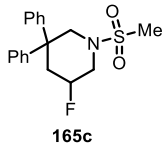
The analytical data are in accordance to those reported in the literature.[125]



165b

5-Fluoro-3,3-diphenyl-1-(phenylsulfonyl)piperidine (165b), prepared from **164b** (94.4 mg, 0.25 mmol) following the general procedure GP6; white solid (63.3 mg, 64%); **m.p.** = 172 °C; **TLC:** R_f = 0.27 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 – 7.80 (m, 2H), 7.67 – 7.63 (m, 1H), 7.59 – 7.55 (m, 2H), 7.53 – 7.51 (m, 2H), 7.40 – 7.36 (m, 2H), 7.33 – 7.19 (m, 6H), 4.69 – 4.49 (m, 2H), 4.11 – 4.06 (m, 1H), 3.04 – 2.98 (m, 1H), 2.49 (d, *J* = 12.3 Hz, 1H), 2.40 – 2.33 (m, 1H), 2.26 – 2.18 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.3, 143.1, 135.2, 133.1, 129.3, 128.7, 128.6, 127.7, 126.9, 126.5, 126.4, 85.5 (d, *J* = 174.0 Hz), 53.8, 49.8 (d, *J* = 31.1 Hz), 46.4 (d, *J* = 10.8 Hz), 41.0 (d, *J* = 18.7 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -185.40 (d, *J* = 47.6 Hz) ppm.

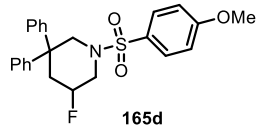
The analytical data are in accordance to those reported in the literature.[125]



165c

5-Fluoro-1-(methylsulfonyl)-3,3-diphenylpiperidine (165c), prepared from **164c** (78.9 mg, 0.25 mmol) following the general procedure GP6; white solid (35.0 mg, 42%); **m.p.** = 156 °C; **TLC:** R_f = 0.27 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 2H), 7.36 – 7.27 (m, 4H), 7.24 – 7.18 (m, 4H), 4.72 – 4.46 (m, 2H), 4.07 – 4.00 (m, 1H), 3.09 – 3.02 (m, 1H), 2.97 (d, *J* = 12.6 Hz, 1H), 2.82 – 2.76 (m, 1H), 2.74 (s, 3H), 2.44 – 2.33 (m, 1H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 145.1, 143.0, 128.7, 128.7, 127.5, 127.0, 126.6, 126.4, 85.4 (d, *J* = 174.6 Hz), 53.9, 49.7 (d, *J* = 30.6 Hz), 46.6 (d, *J* = 10.4 Hz), 41.1 (d, *J* = 18.7 Hz), 34.7 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -184.93 (d, *J* = 47.6 Hz) ppm.

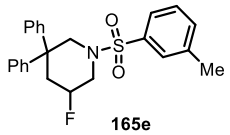
The analytical data are in accordance to those reported in the literature.[125]



165d

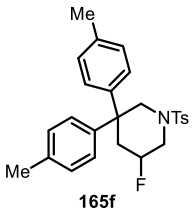
5-Fluoro-1-(4-methoxyphenylsulfonyl)-3,3-diphenylpiperidine (165d), prepared from **164d** (101.9 mg, 0.25 mmol) following the general procedure GP6; white solid (63.8 mg, 60%); **m.p.** = 188 °C; **TLC:** R_f = 0.15 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 – 7.71 (m, 2H), 7.51 – 7.49 (m, 2H), 7.39 – 7.35 (m, 2H), 7.32 – 7.27 (m, 2H), 7.25 – 7.17 (m, 4H), 7.03 – 6.99 (m, 2H), 4.67 –

4.47 (m, 2H), 4.08 – 4.03 (m, 1H), 3.89 (s, 3H), 3.02 – 2.96 (m, 1H), 2.46 (d, *J* = 12.3 Hz, 1H), 2.37 – 2.31 (m, 1H), 2.24 – 2.16 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.2, 145.4, 143.2, 129.8, 128.6, 128.6, 127.7, 126.8, 126.7, 126.5, 126.4, 114.4, 85.6 (d, *J* = 173.9 Hz), 55.6, 53.9, 49.8 (d, *J* = 30.9 Hz), 46.4 (d, *J* = 10.9 Hz), 41.0 (d, *J* = 18.6 Hz) ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -185.39 (d, *J* = 47.7 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3435, 1596, 1497, 1347, 1262, 1164, 564 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{24}H_{25}FNO_3S^+$ $[M+H]^+$ 426.1534, found 425.1528.



165e

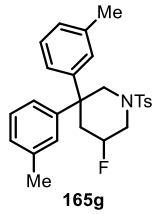
5-Fluoro-3,3-diphenyl-1-(*m*-tolylsulfonyl)piperidine (165e), prepared from **164e** (97.9 mg, 0.25 mmol) following the general procedure GP6; white solid (66.5 mg, 65%); **m.p.** = 145 °C; **TLC:** R_f = 0.33 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 – 7.59 (m, 2H), 7.54 – 7.51 (m, 2H), 7.46 – 7.44 (m, 2H), 7.40 – 7.37 (m, 2H), 7.33 – 7.28 (m, 3H), 7.26 – 7.19 (m, 3H), 4.69 – 4.50 (m, 2H), 4.11 – 4.07 (m, 1H), 3.05 – 2.95 (m, 1H), 2.51 (d, *J* = 12.5 Hz, 1H), 2.46 (s, 3H), 2.42 – 2.36 (m, 1H), 2.26 – 2.18 (m, 1H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 145.3, 143.1, 139.5, 135.1, 134.0, 129.1, 128.7, 128.6, 127.9, 127.7, 126.9, 126.5, 126.4, 124.9, 85.5 (d, *J* = 173.9 Hz), 53.7, 49.8 (d, *J* = 31.0 Hz), 46.5 (d, *J* = 10.8 Hz), 41.0 (d, *J* = 18.7 Hz), 21.4 ppm; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -185.40 (d, *J* = 47.7 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3435, 1600, 1348, 1162, 1043, 787, 699, 591 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{24}H_{25}FNO_2S^+$ $[M+H]^+$ 410.1585, found 410.1575.



165f

5-Fluoro-3,3-di-*p*-tolyl-1-tosylpiperidine (165f), prepared from **164f** (104.9 mg, 0.25 mmol) following the general procedure GP6; white solid (65.6 mg, 60%); **m.p.** = 218 °C; **TLC:** R_f = 0.33 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 1H), 7.37 – 7.31 (m, 4H),7.15 (d, *J* = 8.0 Hz, 1H), 7.09 – 7.03 (m, 4H), 4.65 – 4.46 (m, 2H), 4.06 – 4.01 (m, 1H), 2.97 – 2.90 (m, 1H), 2.43(s, 3H), 2.38 (d, *J* = 12.3 Hz, 1H), 2.30 (s, 3H), 2.29 (s, 3H), 2.30 – 2.26 (m, 1H), 2.17 – 2.08 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.0, 142.7, 140.2, 136.4, 135.9, 132.2, 129.8, 129.3, 129.2, 127.7, 127.5, 126.2, 85.7 (d, *J* = 173.6 Hz), 54.0, 49.8 (d, *J* = 31.1 Hz), 45.8 (d, *J* = 10.9 Hz), 41.1 (d, *J* = 18.5 Hz), 21.5, 20.8 (d, *J* = 6.9 Hz). **^{19}F NMR** (377 MHz, $CDCl_3$) δ -185.47 (d, *J* = 47.7 Hz) ppm.

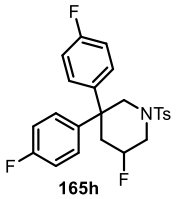
The analytical data are in accordance to those reported in the literature.[123]



165g

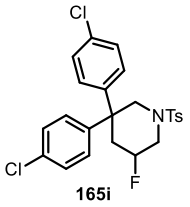
5-Fluoro-3,3-di-*m*-tolyl-1-tosylpiperidine (165g), prepared from **164g** (104.9 mg, 0.25 mmol) following the general procedure GP6; colourless oil (74.4 mg, 68%);**TLC:** R_f = 0.33 (silica gel, 90:10 hexane:EtOAc) [UV];**^{1}H NMR** (400 MHz, CDCl3) δ 7.67 – 7.65 (m, 2H), 7.34 – 7.27 (m, 4H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.04 – 6.95 (m, 4H), 4.64 – 4.45 (m, 2H), 4.07 – 4.02 (m, 1H), 3.00 – 2.94 (m, 1H), 2.43 (s, 3H), 2.38 (d, *J* = 12.4 Hz, 1H), 2.35 (s, 3H), 2.29 (s, 3H), 2.31 – 2.26 (m, 1H), 2.18 – 2.10 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.4, 144.0, 143.0, 138.1, 138.1, 132.3, 129.9, 128.5, 128.4, 128.3, 127.7, 127.6, 127.2, 127.0, 124.7, 123.4, 85.7 (d, *J* = 173.4 Hz), 53.9, 49.8 (d, *J* = 31.2 Hz), 46.2 (d, *J* = 11.0 Hz), 41.1 (d, *J* = 18.6 Hz), 21.7, 21.6, 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -185.40 (d, *J* = 47.7 Hz) ppm.

The analytical data are in accordance to those reported in the literature.[123]



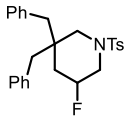
165h

5-fluoro-3,3-bis(4-fluorophenyl)-1-tosylpiperidine (165h), prepared from **164h** (106.9 mg, 0.25 mmol) following the general procedure GP6; white solid (61.3 mg, 55%); **m.p.** = 208 °C; **TLC:** R_f = 0.22 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.64 (m, 2H), 7.45 – 7.40 (m, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.12 – 7.09 (m, 2H), 7.06 – 7.00 (m, 2H), 6.98 – 6.92 (m, 2H), 4.62 – 4.43 (m, 1H), 4.38 – 4.33 (m, 1H), 4.03 – 3.98 (m, 1H), 2.90 – 2.82 (m, 1H), 2.47 – 2.41 (m, 4H), 2.39 – 2.32 (m, 1H), 2.20 – 2.12 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 17.3 Hz), 160.2 (d, *J* = 16.9 Hz), 144.2, 140.9 (d, *J* = 3.3 Hz), 138.8, 132.0, 129.9, 129.4 (d, *J* = 7.9 Hz), 128.1 (d, *J* = 8.0 Hz), 127.7, 115.6 (d, *J* = 10.8 Hz), 115.4 (d, *J* = 10.9 Hz), 85.2 (d, *J* = 174.7 Hz), 54.1, 49.7 (d, *J* = 30.7 Hz), 45.6 (d, *J* = 10.6 Hz), 41.2 (d, *J* = 18.8 Hz), 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -115.28, -115.74, -185.50 (d, *J* = 47.8 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3434, 1600, 1509, 1347, 1236, 1164, 837 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{24}H_{23}F_3NO_2S^+$ $[M+H]^+$ 446.1396, found 446.1391.



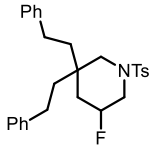
165i

3,3-bis(4-chlorophenyl)-5-fluoro-1-tosylpiperidine (165i), prepared from **164i** (115.1 mg, 0.25 mmol) following the general procedure GP6; white solid (58.6 mg, 49%); **m.p.** = 207 °C; **TLC:** R_f = 0.22 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.63 (m, 2H), 7.39 – 7.30 (m, 6H), 7.25 – 7.22 (m, 2H), 7.08 – 7.05 (m, 2H), 4.62 – 4.42 (m, 1H), 4.33 (d, *J* = 12.4 Hz, 1H), 4.01 – 3.96 (m, 1H), 2.87 – 2.81 (m, 1H), 2.44 (d, *J* = 7.9 Hz, 1H), 2.43 (s, 3H), 2.38 – 2.32 (m, 1H), 2.19 – 2.11 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.3, 143.3, 141.4, 133.1, 132.8, 132.0, 130.0, 129.1, 129.0, 128.8, 127.8, 127.7, 85.1 (d, *J* = 175.1 Hz), 53.8, 49.7 (d, *J* = 30.6 Hz), 45.8 (d, *J* = 10.6 Hz), 40.9 (d, *J* = 19.3 Hz), 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -185.42 (d, *J* = 47.7 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3435, 1634, 1494, 1348, 1167, 1094, 818 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{24}H_{23}Cl_2FNO_2S^+$ $[M+H]^+$ 478.0805, found 478.0800.



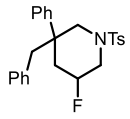
165j

3,3-dibenzyl-5-fluoro-1-tosylpiperidine (165j), prepared from **164j** (104.9 mg, 0.25 mmol) following the general procedure GP6; white solid (54.7 mg, 50%); **m.p.** = 157 °C; **TLC:** R_f = 0.22 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 2H), 7.33 – 7.29 (m, 4H), 7.28 – 7.18 (m, 6H), 7.11 – 7.09 (m, 2H), 5.05 – 4.87 (m, 1H), 3.40 – 3.32 (m, 1H), 3.06 (d, *J* = 11.5 Hz, 1H), 2.86 – 2.70 (m, 4H), 2.63 – 2.52 (m, 2H), 2.42 (s, 3H), 1.76 – 1.66 (m, 1H), 1.50 – 1.42 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.9, 136.8, 136.6, 132.6, 131.1, 130.9, 129.7, 128.2, 128.0, 127.6, 126.6, 126.4, 85.9 (d, *J* = 175.6 Hz), 52.2, 49.7 (d, *J* = 27.7 Hz), 43.9, 43.0, 38.4 (d, *J* = 6.0 Hz), 36.4 (d, *J* = 18.4 Hz), 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -181.02 ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3436, 1599, 1344, 1168, 706, 553 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{24}H_{29}FNO_2S^+$ $[M+H]^+$ 438.1898, found 438.1902.



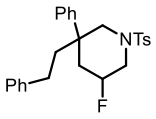
165k

5-fluoro-3,3-diphenethyl-1-tosylpiperidine (165k), prepared from **164k** (111.9 mg, 0.25 mmol) following the general procedure GP6; white solid (65.2 mg, 56%); **m.p.** = 133 °C; **TLC:** R_f = 0.22 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.65 (m, 2H), 7.35 – 7.30 (m, 6H), 7.24 – 7.19 (m, 6H), 4.94 – 4.76 (m, 1H), 3.66– 3.59 (m, 1H), 3.17 (d, *J* = 11.8 Hz, 1H), 2.80 – 2.53 (m, 6H), 2.45 (s, 3H), 1.96 – 1.82 (m, 2H), 1.80 – 1.63 (m, 3H), 1.56 – 1.45 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.7, 141.9, 141.9, 133.4, 129.8, 128.5, 128.5, 128.3, 128.3, 127.5, 126.0, 125.9, 85.5 (d, *J* = 175.6 Hz), 53.9, 50.1 (d, *J* = 28.3 Hz), 39.5 (d, *J* = 17.8 Hz), 38.2, 37.4 (d, *J* = 6.5 Hz), 36.6, 29.5, 29.4, 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -181.94 (d, *J* = 47.5 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3443, 1600, 1344, 1162, 699, 551 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{28}H_{33}FNO_2S^+$ $[M+H]^+$ 466.2211, found 466.2195.



165l
trans :*cis* =57:43

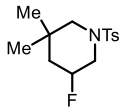
3-benzyl-5-fluoro-3-phenyl-1-tosylpiperidine (165l), prepared from **164l** (101.4 mg, 0.25 mmol) following the general procedure GP6; white solid (65.2 mg, 56%); **m.p.** = 133 °C; **TLC:** R_f = 0.22 (silica gel, 90:10 hexane:EtOAc) [UV]; *major diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.66 (m, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.35 – 7.27 (m, 3H), 7.26 – 7.22 (m, 2H), 7.17 – 7.10 (m, 3H), 6.64 – 6.62 (m, 2H), 4.71 – 4.52 (m, 1H), 3.90 (d, *J* = 12.1 Hz, 1H), 3.66 – 3.60 (m, 1H), 2.99 (d, *J* = 13.3 Hz, 1H), 2.86 (d, *J* = 13.3 Hz, 1H), 2.74 (d, *J* = 12.1 Hz, 1H), 2.66 – 2.52 (m, 2H), 2.48 (s, 3H), 1.82 – 1.74 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.9, 141.5, 135.8, 132.6, 130.4, 129.8, 128.4, 127.7, 127.6, 126.8, 126.6, 126.5, 85.3 (d, *J* = 175.1 Hz), 53.2, 50.0 (d, *J* = 29.4 Hz), 48.6, 43.0 (d, *J* = 8.0 Hz), 39.9 (d, *J* = 18.1 Hz), 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -182.86 (d, *J* = 47.9 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3435, 1599, 1345, 1166, 702, 552 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{25}H_{27}FNO_2S^+$ $[M+H]^+$ 424.1741, found 424.1741.



165m
trans :*cis* =52:48

5-fluoro-3-phenethyl-3-phenyl-1-tosylpiperidine (165m), prepared from **164m** (104.9 mg, 0.25 mmol) following the general procedure GP6; white solid (68.9 mg, 63%); **m.p.** = 165 °C; **TLC:** R_f = 0.22 (silica gel, 90:10 hexane:EtOAc) [UV]; *minor diastereomer*: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.36 – 7.27 (m, 6H), 7.24 – 7.16 (m, 2H), 7.08 – 7.05 (m, 2H), 5.09 – 4.90 (m, 1H), 4.11 – 4.06 (m, 1H), 3.97 – 3.92 (m, 1H), 2.62 – 2.54 (m, 2H), 2.45 (s, 3H), 2.40 – 2.31 (m, 2H), 2.28 – 2.07 (m, 3H), 1.77 – 1.68 (m, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.9, 143.7, 141.7, 133.2, 129.9,

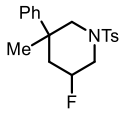
128.7, 128.4, 128.3, 127.5, 126.9, 125.9, 125.5, 85.5 (d, *J* = 174.3 Hz), 54.0, 49.9 (d, *J* = 30.4 Hz), 42.2 (d, *J* = 9.9 Hz), 39.3, 39.1 (d, *J* = 18.0 Hz), 30.0, 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -184.43 (d, *J* = 47.8 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3443, 1599, 1347, 1165, 701, 553 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{26}H_{29}FNO_2S^+$ $[M+H]^+$ 438.1898, found 438.1906.



165n

5-Fluoro-3,3-dimethyl-1-tosylpiperidine (165n), prepared from **164n** (66.8 mg, 0.25 mmol) following the general procedure GP6; white solid (16.4 mg, 23%); **m.p.** = 90 °C; **TLC:** R_f = 0.27 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 1H), 7.33 (d, *J* = 7.7 Hz, 1H), 4.89 – 4.65 (m, 1H), 3.64 – 3.54 (m, 1H), 2.95 (d, *J* = 13.0 Hz, 1H), 2.63 (dt, *J* = 11.3, 7.8 Hz, 1H), 2.43 (s, 3H), 2.39 (d, *J* = 11.5 Hz, 1H), 1.77 – 1.65 (m, 1H), 1.35 (td, *J* = 12.9, 8.7 Hz, 1H), 1.03 – 1.02 (m, 6H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.7, 133.5, 129.7, 127.5, 85.8(d, *J* = 175.3 Hz), 56.6, 49.7 (d, *J* = 28.5 Hz), 42.6 (d, *J* = 17.4 Hz), 31.8 (d, *J* = 7.3 Hz), 27.8 (d, *J* = 1.8 Hz), 25.9, 21.5 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -183.08 (d, *J* = 43.7 Hz) ppm.

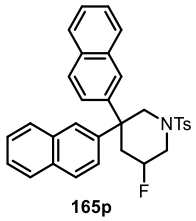
The analytical data are in accordance to those reported in the literature.[125]



165o
cis :*trans* =82:18

5-fluoro-3-methyl-3-phenyl-1-tosylpiperidine (165o), prepared from **164o** (82.4 mg, 0.25 mmol) following the general procedure GP6; white solid (33.9 mg, 39%); **m.p.** = 118 °C; **TLC:** R_f = 0.33 (silica gel, 90:10 hexane:EtOAc) [UV];**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 2H), 7.36 – 7.31 (m, 6H), 7.28 – 7.23 (m, 1H), 5.11 – 4.85 (m, 1H), 4.12 – 4.04 (m, 1H), 3.72 – 3.68 (m, 1H), 2.47 (d, *J* = 11.6 Hz, 1H), 2.43 (s, 3H), 2.36 – 2.25 (m, 2H), 1.84 – 1.72 (m, 1H), 1.45 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 145.9, 143.9, 133.3, 129.8, 128.6, 127.5, 126.9, 125.0, 85.9 (d, *J* = 173.9 Hz), 55.5, 49.9 (d, *J* = 30.4 Hz), 41.4 (d, *J* = 17.8 Hz), 39.0 (d, *J* = 10.3 Hz), 25.4, 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -184.98 (d, *J* = 48.0 Hz) ppm.

The analytical data are in accordance to those reported in the literature.[122]



165p

5-fluoro-3,3-di(naphthalen-2-yl)-1-tosylpiperidine (165p), prepared from **164p** (122.9 mg, 0.25 mmol) following the general procedure GP6; white solid (51.0 mg, 40%); **m.p.** = 198 °C; **TLC:** R_f = 0.22 (silica gel, 90:10 hexane:EtOAc) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.97 (d, *J* = 7.3 Hz, 1H), 7.82 – 7.74 (m, 5H), 7.69 (d, *J* = 8.1 Hz, 3H), 7.55 – 7.44 (m, 4H), 7.34 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.20 (dd, *J* = 8.7, 2.0 Hz, 1H), 4.74 (d, *J* = 12.3 Hz, 1H), 4.60 – 4.52 (m, 1H), 4.14 – 4.09 (m, 1H), 3.20 – 3.14 (m, 1H), 2.57 (d, *J* = 12.3 Hz, 1H), 2.46 – 2.38 (m, 5H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.1, 142.3, 140.2, 133.2, 133.1, 132.2, 132.1, 131.9, 129.9, 128.6, 128.4, 128.4, 128.1, 127.7, 127.4, 127.3, 127.0, 126.4, 126.3, 126.2, 126.2, 125.8, 125.4, 124.4, 85.7 (d, *J* = 174.2 Hz), 54.0, 49.9 (d, *J* = 30.9 Hz), 46.7 (d, *J* = 10.9 Hz), 40.9 (d, *J* = 19.0 Hz), 21.5 ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -185.39 (d, *J* = 47.7 Hz) ppm; **IR** (neat) $\tilde{\nu}_{max}$ = 3433, 1598, 1345, 1164, 747, 553 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{32}H_{29}FNO_2S^+$ $[M+H]^+$ 510.1898, found 510.1891.

2.6 NMR Investigations on the Formation of $ArIF_2$ Species

An undivided Teflon® cell equipped with a platinum anode (1×1.2 cm^2) and a platinum cathode (1×1.2 cm^2) was charged with CD_2Cl_2 (3.6 mL). Py·HF (0.2 mL) and NEt_3·3HF (0.2 mL) were added followed by 4-*tert*-butyliodobenzene (**154**, 0.30 mmol, 1.2 eq). The electrolysis was carried out at room temperature under constant current (24 mA) until 3.5 F/mol of electricity has passed.

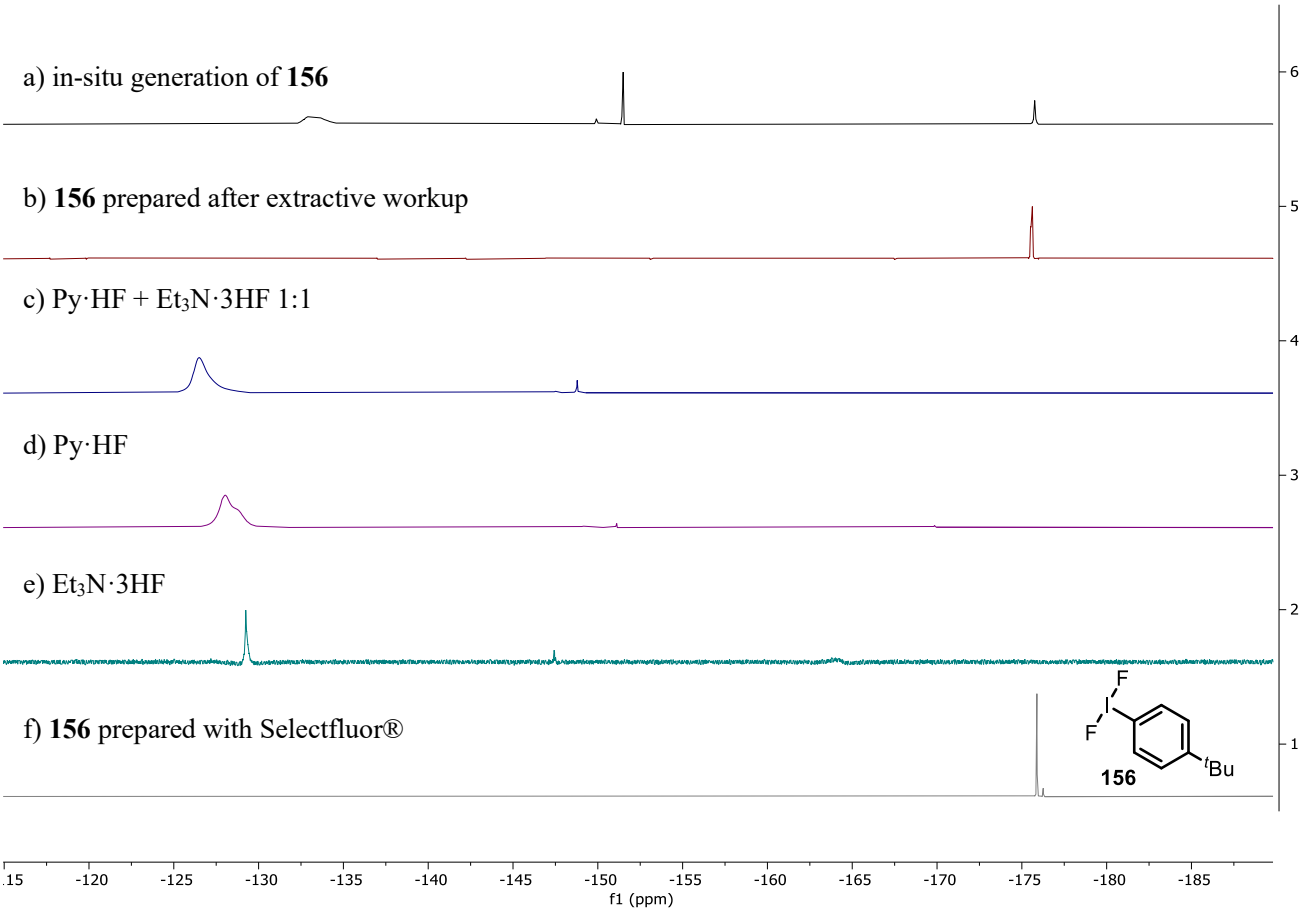


Figure 4. ^{19}F NMR study of the formation of *t*BuC$_6$H$_4$IF$_2$ (156) under electrochemical reaction conditions. a) The solution was taken up without workup in an NMR tube, diluted with CD_2Cl_2 and quickly analyzed by NMR. b) The reaction mixture was poured into a sat. $NaHCO_3$ solution (50 mL) and extracted with DCM (3×10 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was dissolved in CD_2Cl_2 and subjected to NMR analysis. c) 50:50 mixture (v/v) of Py·HF and Et_3N·3HF in CD_2Cl_2. d) Py·HF in CD_2Cl_2. e) Et_3N·3HF in CD_2Cl_2. f) **156** generated with Selectfluor®.

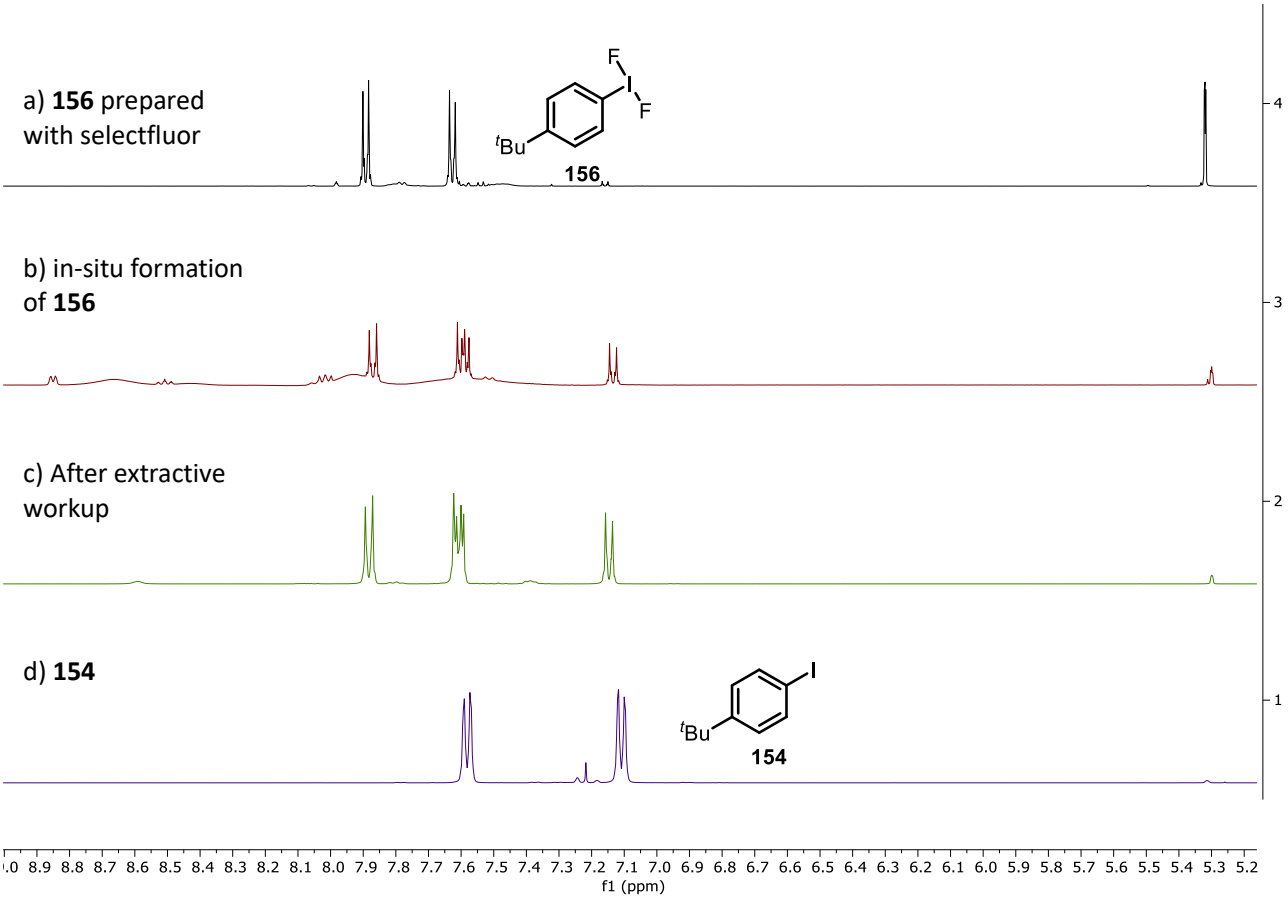


Figure 5. ^{1}H NMR study of the formation of ^{t}BuC$_6$H$_4$IF$_2$ (156) under electrochemical reaction conditions. a) **156** generated by selectfluor and measured in CD_2Cl_2. b) The solution was taken up without workup in an NMR tube and quickly analyzed by NMR. c) The reaction mixture was poured into sat. $NaHCO_3$ solution and extracted with DCM (3×10 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was dissolved in CD_2Cl_2 and subjected to NMR analysis. d) 4-*tert*-butyliodobenzene (**154**) in CD_2Cl_2.

2.7 Cyclic Voltammetry Experiments

Cyclic voltammograms were measured on an ElectraSyn 2.0 from *IKA*. The working electrode was a glassy carbon disc, the counter electrode a metal plate with platinum coating (6 cm × cm × 0.1 cm); a silver wire in an aqueous 3 M KCl solution (Ag/AgCl) acted as reference electrode. The compound (25.0 µmol, 1.0 eq.) and nBu$_4$NPF$_6$ (194 mg, 500 µmol, 20 eq.) were dissolved in DCM (5 mL, 5 mM) and the cyclic voltammogram was measured with the following parameters: Segment: 3; Initial V: 0.0; Direction: Rising; Upper V: 3.3/4.5; Lower V: -1.0; Final V: 0.0; Sweep [mVs^{-1}]: 200.

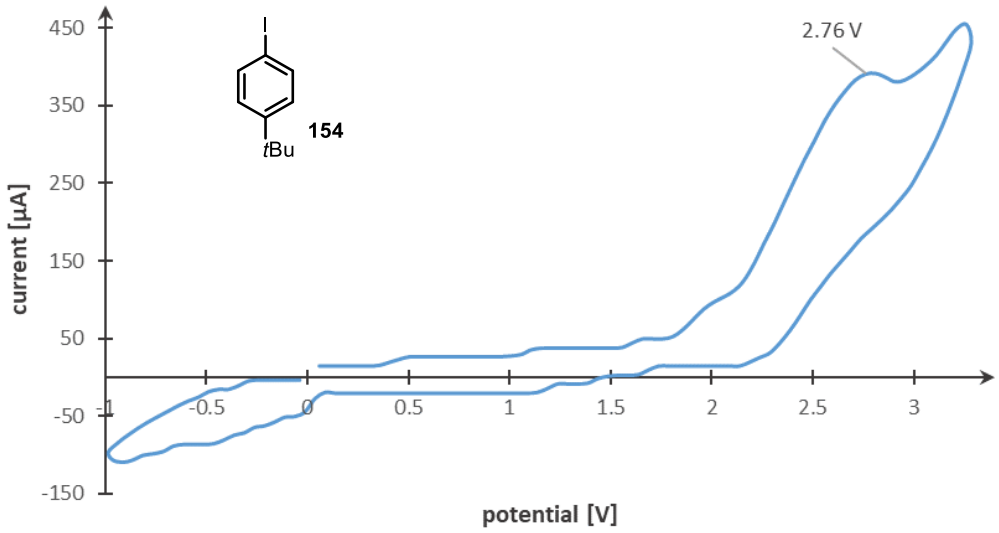


Figure 6. CV measurement of 4-*tert*-butyliodobenzene (**154**) + nBu$_4$NPF$_6$ in DCM.

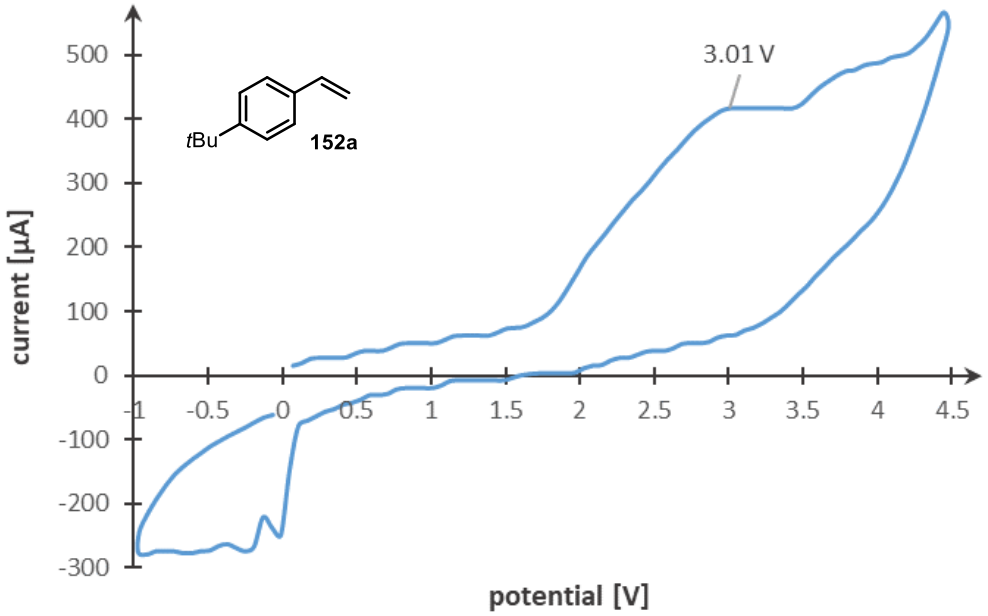


Figure 7. CV measurement of 4-*tert*-butylstyrene (**152a**) + nBu$_4$NPF$_6$ in DCM.

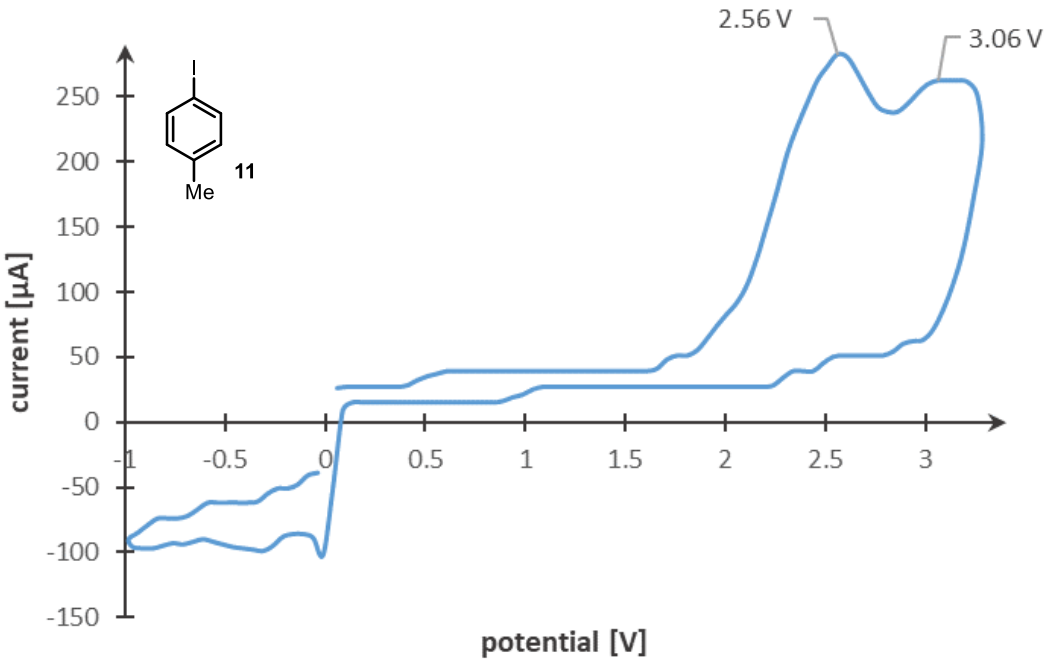


Figure 8. CV measurement of 4-iodotoluene (**11**) + nBu$_4$NPF$_6$ in DCM.

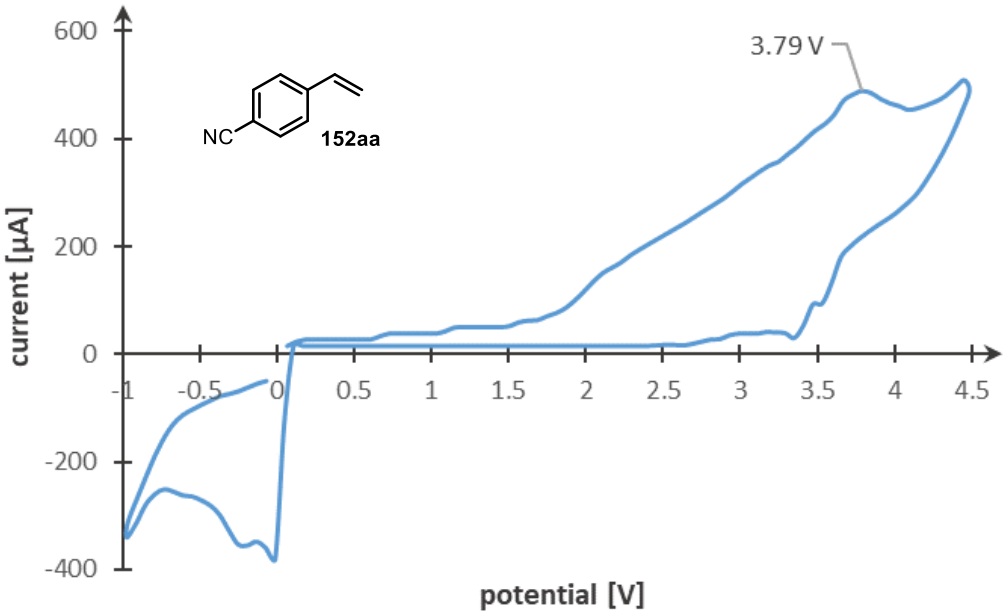


Figure 9. CV measurement of 4-cynostyrene (**152aa**) + nBu$_4$NPF$_6$ in DCM.

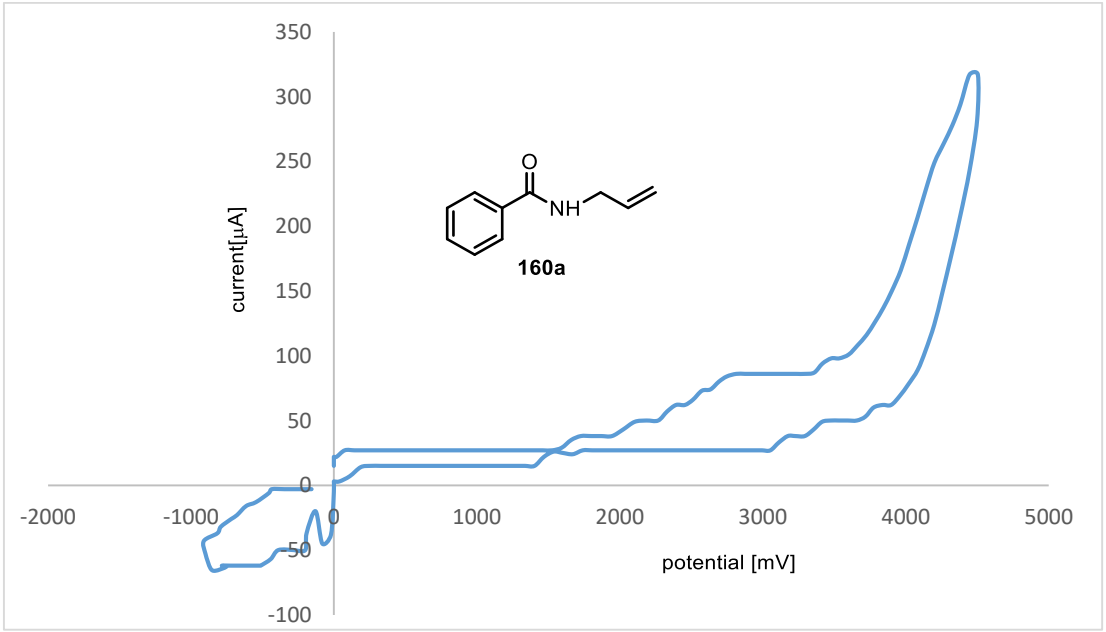


Figure 10. CV measurement of *N*-allylbenzamide (**160a**) + nBu$_4$NPF$_6$ in DCM.

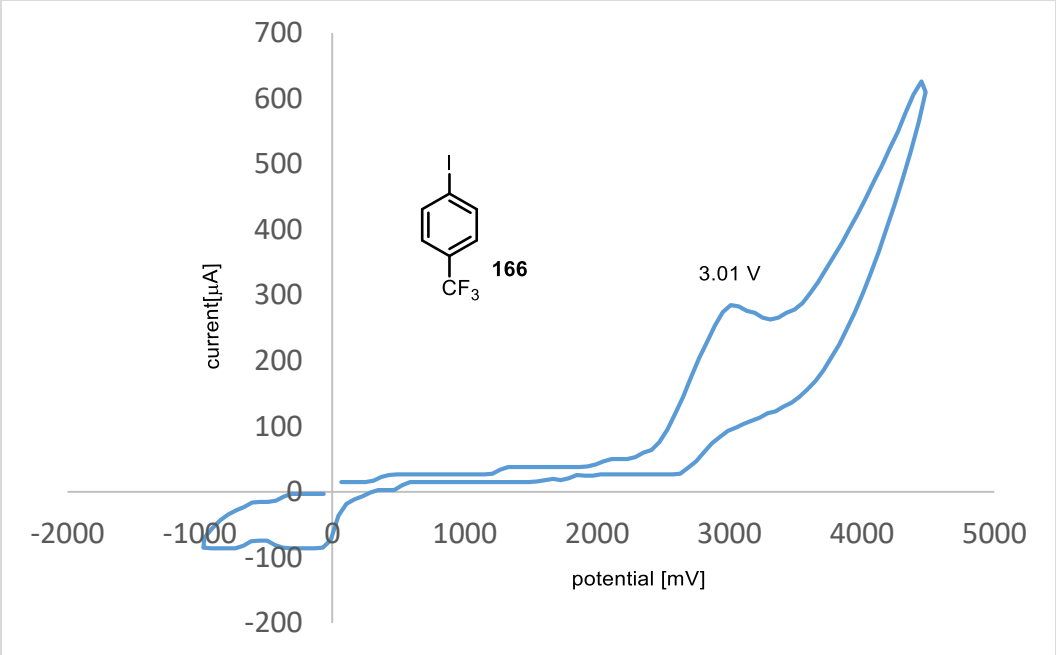


Figure 11. CV measurement of 4-iodobenzotrifluoride (**166**) + nBu$_4$NPF$_6$ in DCM.

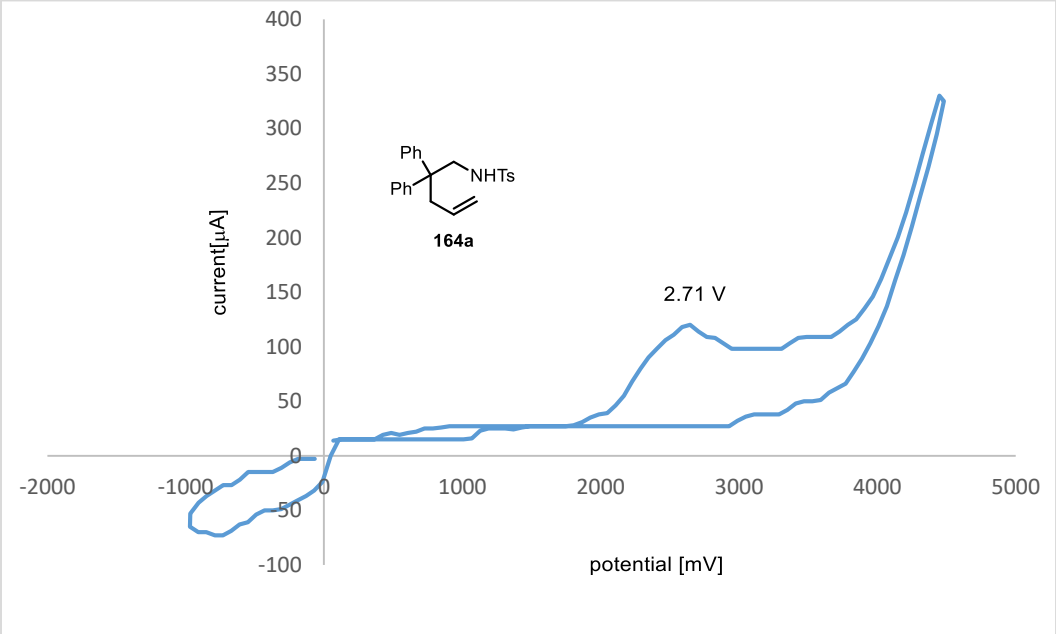


Figure 12. CV measurement of **164a** + nBu$_4$NPF$_6$ in DCM.

IV Abbreviations

Ac	Acetyl
AcOH	Acetic acid
Add.	Additives
aq	Aqueous
Ar	Argon
Bn.	Benzyl
Boc.	*t*-butoxycarbonyl
Bu	Butyl
Bs	Benzenesulfonyl
Bz	Benzoyl
ca.	circa
cat.	catalyst
calcd.	calculated
conc. (c)	concentrated
$CDCl_3$	Chloroform-*d*
CV	Cyclic Voltammetry
d	day(s)
DCM	dichloromethane
DCC	dicyclohexylcarbodiimide
DMF	dimethylformamide
d.r.	diastereomer ratio
Dest	destilliert (distilled)
DIAD	diisopropylazodicarboxylate
DMSO	dimethyl sulfoxide
eq	Equivalent(s)
ee	enantiomeric excess
EI	electron ionization
ESI	electrospray ionization
EtOH	ethanol
Et_2O	diethyl ether
EtOAc	ethyl acetate
EDG	Electron Donating Group

EWG	Electron Withdrawing Group
Et_3N	triethylamine
Et	Ethyl-
e.g.	exempli gratia
et al.	et alia
g	gram
HRMS	High-resolution mass spectrometry
h	hour(s)
H_2O	water
HF	hydrofluoric acid
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
HPLC	High-pressure liquid chromatography
Hz	hertz
IR	Infrared spectroscopy
i-Pr	Isopropyl
IUPAC	International Union of Pure and Applied Chemistry
J	coupling constant
K	Kelvin
L	liter
LDA	Lithiumdiisopropylamide
m	*meta*
mA	milliampere
*m*CPBA	*m*-chloroperoxybenzoic acid
m.p.	melting point
Me	Methyl
Ms	Mesyl (methane sulfonyl)
$MgSO_4$	magnesium sulfate
m.p.	melting point
MeCN	acetonitrile
MeOH	methanol
MHz	Megahertz
mg	milligram(s)
mL	milliliter
min	minute(s)

mmol	millimole
MS	mass spectrometry
n.r.(n.d.)	no reaction (not detected)
$NaHCO_3$	sodium bicarbonate
Na_2SO_4	sodium sulfate
NMR	Nuclear Magnetic Resonance
Ns	*p*-nitrobenzenesulfonyl
o	*ortho*
OMe	methoxy
p	*para*
PEG	Poly(ethylene glycol)
PG	protecting group
Py	pyridine
ppm	parts per million
Quant.	quantitative
rt	room temperature
rfx	reflux
R_f	Retention factor
s	second(s)
Sat.	saturate
SCE	saturated calomel electrode
S_N2	second-order nucleophilic substitution
T	temperature
THF	tetrahydrofuran
Ts	*p*-toluenesulfonyl
*t*Bu	*tert*-butyl
TLC	thin layer chromatography
TBAF	tetra-*n*-butyl ammonium fluoride
TFA	trifluoroacetic acid
TFE	trifluoroethanol
UV	ultraviolet
δ	chemical shift
µ	micro
$\tilde{\nu}_{max}$	maximum wave number
°C	degree Celsius

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