Carbofluorination of Alkenes with *gem*-Difluorinated Cyclopropanes as Bifunctional Reagents Enabled by Well-Define Rhodium Catalysts

Yaxin Zeng, Zhong-Tao Jiang, Yulei Zhu, Jinqi Chen, Han Zhang and Ying Xia*

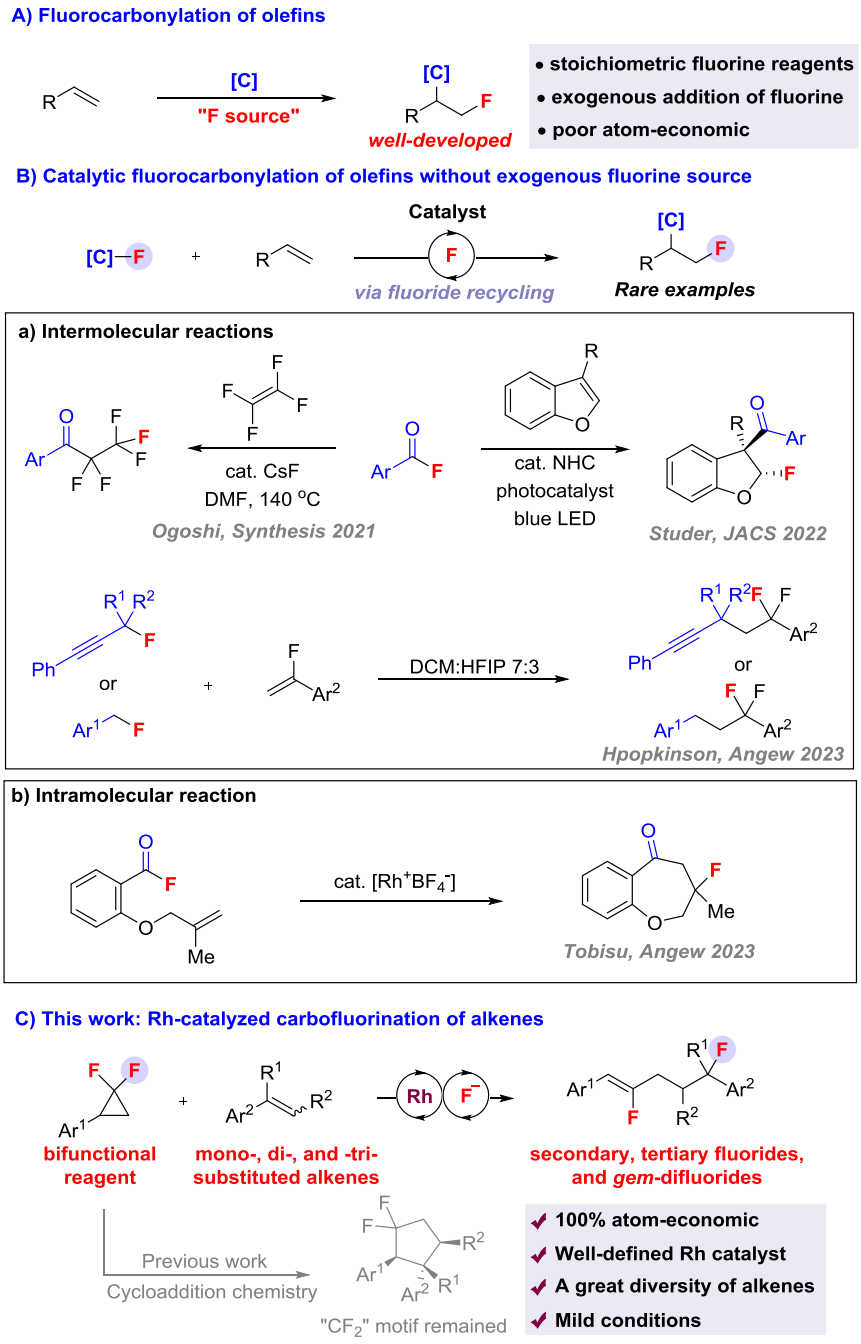
West China School of Public Health and West China Fourth Hospital, West China-PUMC C.C. Chen Institute of Health, and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, China
Email: xiayingscu@scu.edu.cn

Herein, we report a Rh-catalyzed carbofluorination of alkenes using *gem*-difluorinated cyclopropanes as bifunctional reagents. The developed method tolerates a wide range of alkenes, providing access to secondary, tertiary fluorides and *gem*-difluorides with 100% atom-economy under mild conditions. The resulting fluorides can be further transformed to yield C−C, C−N, and C−O bifunctionalization products. Cationic dicarbonyl rhodium tetrafluoroborate has been identified to be the only highly efficient catalyst in this reaction. Preliminary mechanistic studies reveal that the addition of fluorine atom to alkenes is mediated by tetrafluoroborate ion, which acts as a fluorine anion shuttle.

Alkenes are highly versatile and readily available feedstocks, and the bifunctionalization of alkenes is a powerful tool to allow for increasing the molecular complexity and diversity.[1] Among these intensive researches, the carbofluorination reactions of alkenes,[2] involving the formation of vicinal C−C bond and C−F bond, provide an attractive strategy for the assembly of fluorinated compounds. Given the significance of fluorinated molecules in pharmaceutical chemistry and materials science,[3] carbofluorination of alkenes has attracted great interest of synthetic community. However, this strategy typically requires the use of stoichiometric electrophilic or nucleophilic fluorination reagents (Scheme 1A).[4] In comparison, an alternative and more economical strategy is to use organofluorine compounds as dual functionalization reagents in catalytic reactions, which avoids the addition of exogenous fluorine sources (Scheme 1B). Strategies involving fluorine atom recycling and subsequent fluorination are highly advantageous in terms of atom and step economy in organofluorine chemistry. However, the challenge lies in the difficulty of achieving reincorporation of fluorides, as catalytic systems capable of breaking C−F bonds are typically unsuitable for the formation of C−F bonds. As a result, the development of catalytic carbofluorination reactions of alkene has been greatly limited.

Nevertheless, contemporary catalytic platforms have recently emerged to realize this challenging transformation. The first example of catalytic carbofluorination of olefins was reported by Ogoshi and co-workers in 2020, showing the synthesis of pentafluoroethyl ketones using acyl fluorides via CsF catalysis (Scheme 1Ba).[5] After that, the Studer group disclosed an intermolecular carbofluorination reactions of benzofurans and indoles with acyl fluorides by the use of a cooperative NHC/photoredox catalysis.[6] The Hopkinson group expanded the electrophile scope for catalytic carbofluorination to include progargyl and benzyl fluorides by taking advantage of the effect of fluorine-hydrogen bonding to activate the C−F bond.[7] More recently, Tobisu and co-workers reported on the intramolecular

carbofluorination of simple alkenes via a cation rhodium catalysis (Scheme 1Bb).[8] Despite these elegant reports in this area, current methods either restricted in intramolecular process, or suffered from specific alkene substrates and limited type of carbofluorination reagents. Therefore, the development of an intermolecularly catalytic strategy that can be applied to the carbofluorination of a great diversity of alkenes with readily available carbofluorination reagents is in high demand.[9]

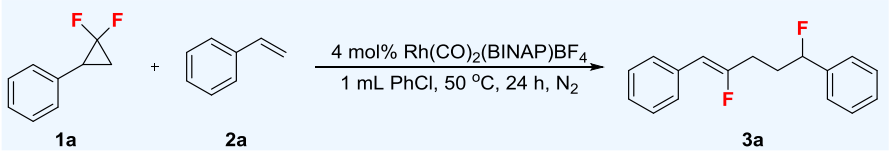


Scheme 1. (a) Carbofluorination of Alkenes. (b) Catalytic Carbofluorination of Alkenes without Exogenous Fluorine Source and Previously Reported Works. (c) This Work: Rh-Catalyzed Carbofluorination of Alkenes.

On the other hand, *gem*-difluorinated cyclopropanes (*gem*-DFCPs)[10] has become a commonly used substrate for the synthesis of monofluoro alkenes via ring-opening cross-coupling reactions under transition metal catalysis.[11] Such reactions involve a C−C bond activation and β-F elimination process

to provide the key fluoroallyl-metal intermediate, which exhibit versatile reactivity with various nucleophilic reagents.[12-16] However, the low nucleophilicity of fluoride ions has overshadowed the potential for fluorine atom recycling in the previous transformations of *gem*-DFCPs. Thus, one fluorine atom, originating from β-F elimination process, was always disposed of as waste. Until recently, our group reported a rhodium catalyzed [3+2] cycloaddition reaction of *gem*-DFCPs with internal alkenes, which is the first example with "CF_2" motif remaining under transition metal catalysis (Scheme 1C, bottom).[17,18] Building on our interest in the rhodium-catalyzed reactivity of *gem*-DFCPs, we turn our attention to the transformation with the retention or reconstruction of "CF_2" motif, particularly regarding how to control it via catalytic system. Herein, we present catalyst-controlled results of fluorindes recycling via C−F bond cleavage/formation. It was found that the well-define $[Rh(CO)_2(BINAP)BF_4]$ catalyst can efficiently achieve the carbofluorination reactions of a wide range of simple alkenes with *gem*-DFCPs the bifunctional reagents,[19] enabling the synthesis of secondary, tertiary fluorides and *gem*-difluorides with 100% atom-economy under mild condition.

Table 1. Optimization of reaction conditions[a]



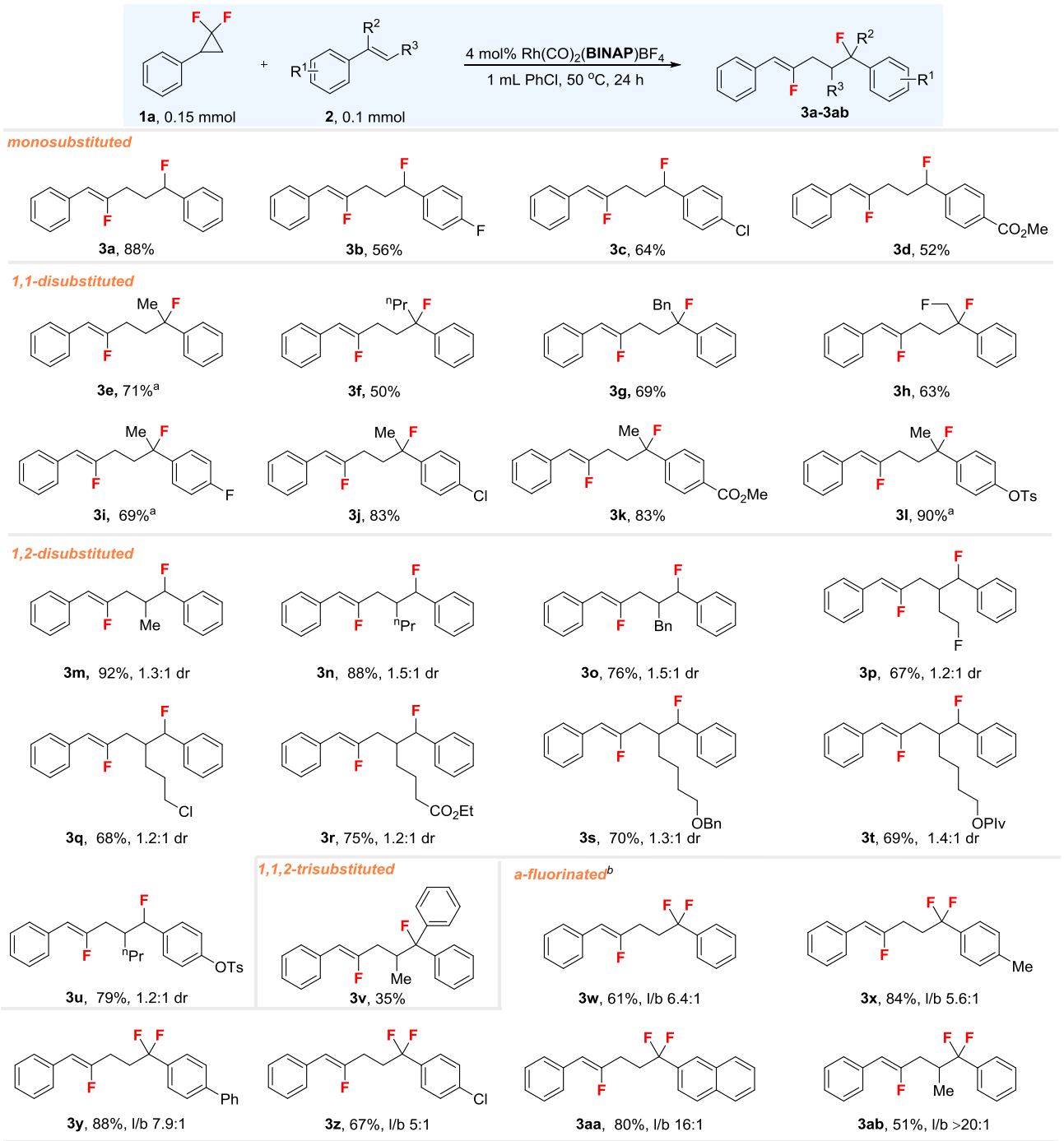
Entry	variations	Yield[b]
1	none	92% (88%)[c]
2	w/o $Rh(CO)_2(BINAP)BF_4$	0
3	$[Rh(CO)_2Cl]_2$, BINAP, and $AgBF_4$ instead of $Rh(CO)_2(BINAP)BF_4$	0
4	$[Rh(CO)_2Cl]_2$, dppp, and $AgBF_4$ instead of $Rh(CO)_2(BINAP)BF_4$	0
5	$[Rh(CO)_2Cl]_2$, dppf, and $AgBF_4$ instead of $Rh(CO)_2(BINAP)BF_4$	0
6	[Rh(CO)(BINAP)Cl] and $AgBF_4$ instead of $Rh(CO)_2(BINAP)BF_4$	0
7	$Rh(COD)(BINAP)BF_4$ instead of $Rh(CO)_2(BINAP)BF_4$	trace
8	1,4-Dioxane instead of PhCl	36%
9	$PhCF_3$ instead of PhCl	58%
10	PhF instead of PhCl	64%
11	40 °C instead of 50 °C	42%
12	16 h	54%

[a] Reaction performed on 0.1 mmol scale. [b] Yield was determined by ^1H NMR using 1,1,2,2-tetrachloroethane as the internal standard. [c] Isolated yield. BINAP, 1,1′-binaphthyl-2,2′-diphenyl phosphine; dppp, 1,3-bis(diphenylphosphino)propane; dppf, 1,1'-bis(diphenylphosphino)ferrocene.

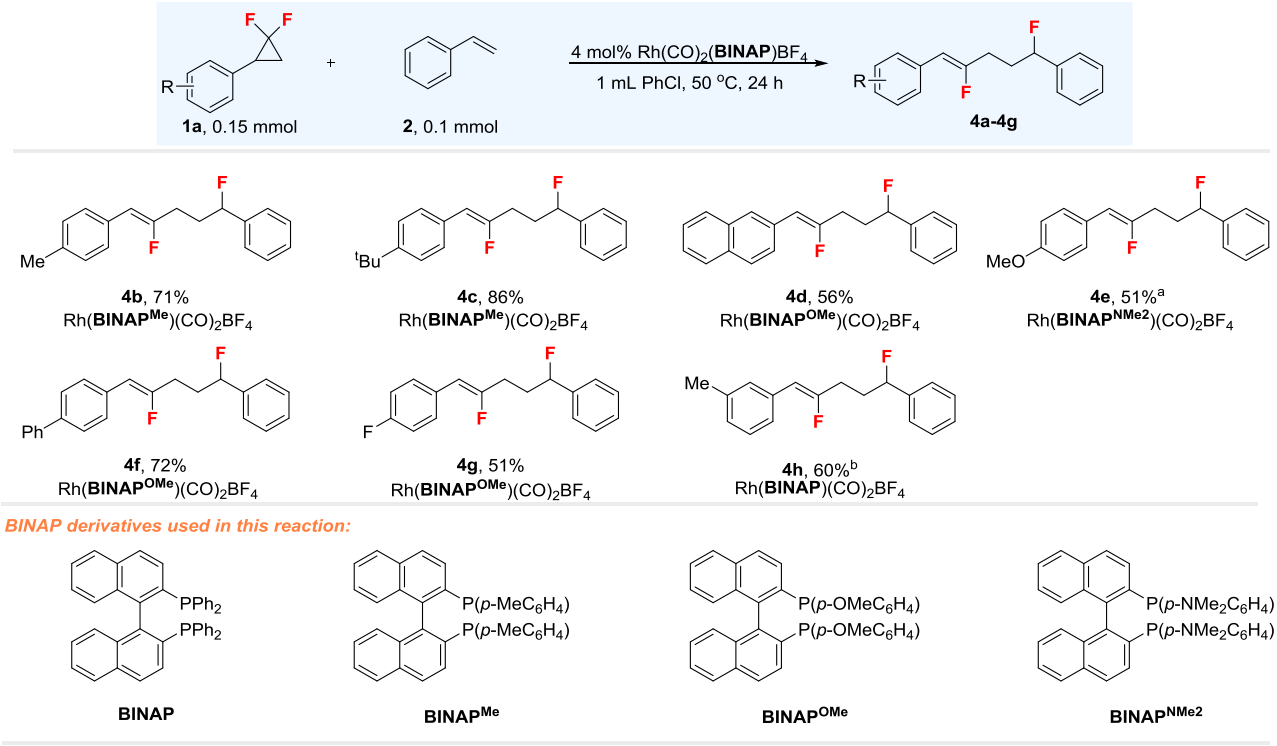
Our initial investigation used the readily available (2,2-difluorocyclopropyl)benzene **1a** and styrene **2a** as the substrates (Table 1). Optimization revealed that this reaction is conducted best with 4 mol% $[Rh(CO)_2(BINAP)BF_4]$ as the catalyst in PhCl at 50 °C for 24 h to produce the carbofluorination product **3a** in 88% isolated yield (entry 1). In the absence of the rhodium catalyst, this reaction didn't proceed (entry 2). We also investigated the use of a cationic Rh catalyst generated in situ from $[Rh(CO)_2Cl]_2$, bidentate phosphine ligands, and $AgBF_4$ in PhCl, but found it to be ineffective in this

reaction (entries 3-5). During the preparation of the catalyst solution mentioned above, we observed gas emission from the solid surface as it dissolved. This led us to realize that the presence of two carbon monoxide ligands bonded to the rhodium center is crucial for the activity of an effective cationic rhodium catalyst. To test this hypothesis, we synthesized [Rh(CO)(BINAP)Cl] to produce a rhodium catalyst with only one carbon monoxide ligand in situ with $AgBF_4$ in PhCl. As expected, no desired product was observed (entry 6). Additionally, [Rh(COD)(BINAP)BF_4] was found to be much less effective (entry 7). These results indicate that the presence of double carbon monoxide ligands attached to the rhodium center is essential for the success of the reactions. Furthermore, we also investigated the effect of different solvents, and found that PhCl was superior to other similar solvents such as $PhCF_3$ and PhF, while more polar solvents like 1,4-dioxane and THF resulted in significantly lower yields (entries 8-10). Decreasing the reaction temperature and shortening the reaction time led to worse results with incomplete conversion of the substrates (entries 11-12).

Having identified the optimized reaction conditions, we proceeded to investigate the scope of this carbofluorination reaction of alkenes (Scheme 2). Firstly, we examined a range of alkenes with *gem*-DFCP **1a**. As shown in Scheme 2, the styrene derivatives bearing electron-withdrawing group such as halogen (**3b**, **3c**) and ester (**3d**) afforded the desired products in moderate yields. 1,1-Disubstituted alkenes containing various substitution were compatible with this transformation, providing the corresponding tertiary fluorides in good yields (**3e-3l**). In some case of substrates (**3e**, **3i**, and **3l**), fluoroallylation of alkenes become the major pathway under standard reaction conditions, and reducing the reaction temperature to 40 ^{o}C resulted in a single carbofluorination product in good yields. Furthermore, 1,2-disubstituted alkenes also proceed smoothly under this catalytic system. Substrates decorated with methyl, propyl, benzyl, and functionalized alkyl substituents containing terminal halogen, ester, and ether group were tolerated and afforded **3m-3t** in good yields but with low diastereocontrol. Note that these 1,2-disubstituted alkenes exhibited high reactivity in our developed [3+2] cycloaddition reaction,[17] reflecting that current catalytic system displayed good chemoselectivity, despite the observation of a small amount of cycloaddition products (< 5%) in most case of 1,2-disubsituted alkenes. In addition, we found that tri-substituted alkenes can undergo this transformation, yielding a diaryl tertiary fluoride in acceptable yield (**3v)**. To further showcase the diversity of the product synthesized by this protocol, α-fluorostyrenes were employed in this reaction, which provide facile access to *gem*-difluorinated compounds. α-Fluorostyrene itself (**3w**) or substrates with functional groups encompassing methyl (**3x**), phenyl (**3y**), and chlorine (**3z**) at the *para*-position led to the formation of *gem*-difluorinated products in good yields with moderate regioselectivity. It is worth noting that 2-naphtyl and 1,2-disubstituted α-fluoroalkene were tolerated as well, delivering product **3aa** and **3ab** in good yields with good regioselectivity.

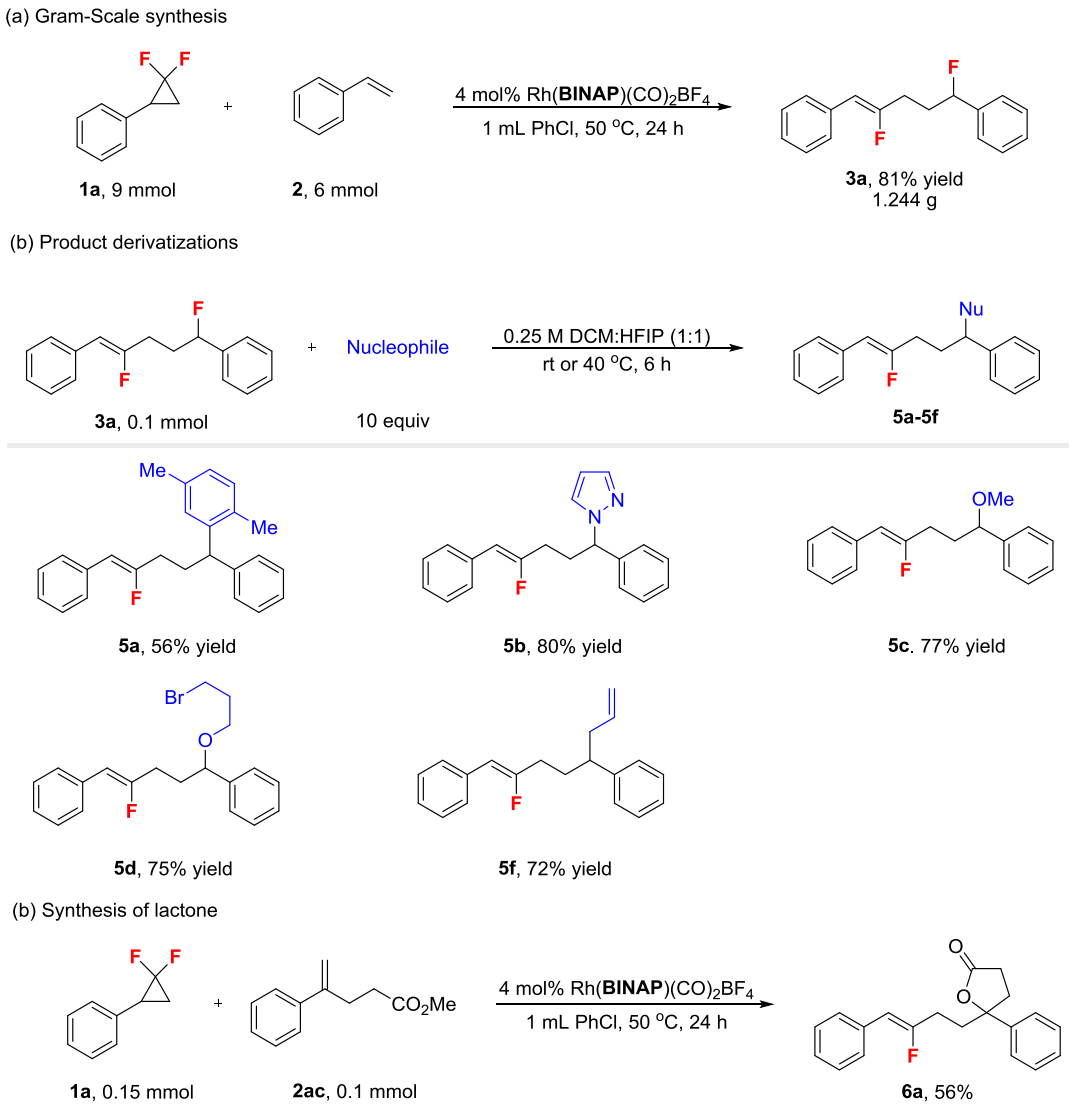


Scheme 2. Substrate Scope of Alkenes. Reaction conditions: **1a** (0.15 mmol), **2a** (0.1 mmol), $[Rh(CO)_2(BINAP)BF_4]_2$ (4 mol%) in PhCl (1 mL) at 50 °C for 24 h. All yields are the average of three runs. [a] 40 °C. [b] The ratio of l/b refers to the fluoroallyl regioselectivity (linear/branched).



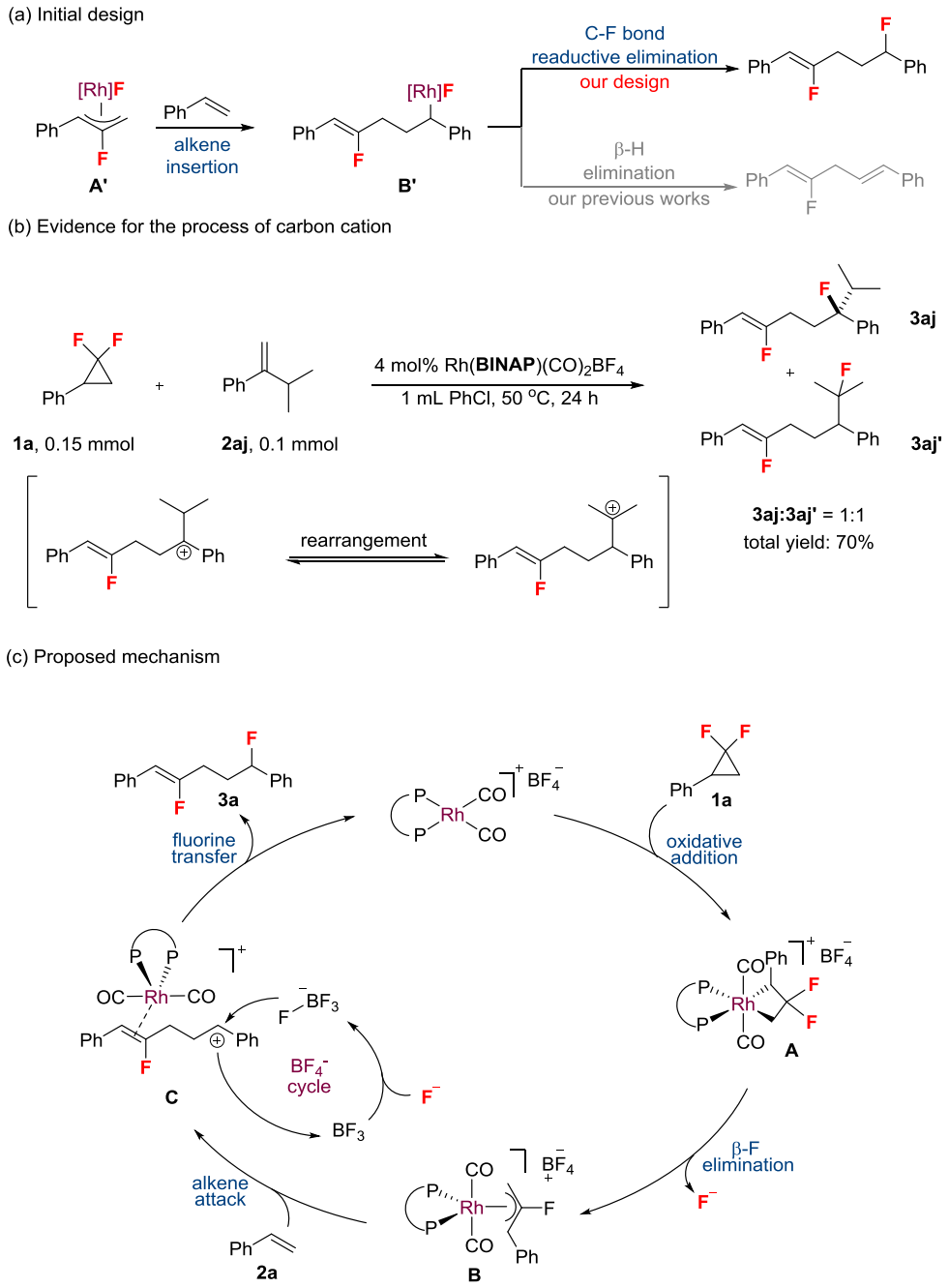
Scheme 3. Substrate Scope of *gem*-DFCPs. Reaction conditions: **1a** (0.15 mmol), **2a** (0.1 mmol), $[Rh(CO)_2(BINAP)BF_4]_2$ (4 mol%) in PhCl (1 mL) at 50 °C for 24 h. All yields are the average of three runs. [a] 48 h. [b] $PhCF_3$ as the reaction solvent.

After that, the reactivity of *gem*-DFCPs was evaluated with styrene as the partner (Scheme 3). Initially, we performed experiments using a series of *gem*-DFCPs under standard condition, but the results were unsatisfactory, except for the model substrate **1a**. The substituted *gem*-DFCPs lead to two outcomes: either a high conversion without the formation of desired products, or an extremely low conversion resulting in the recovery of the starting substrates. These results indicate that this reaction is sensitive to the electronic and steric hindrance effects of the substituents on *gem*-DFCPs. While substituted *gem*-DFCPs did not participate in the carbofluorination reaction using $Rh(CO)_2(BINAP)BF_4$ as the catalyst in our preliminary attempts, it was found that the rhodium catalyst produced from BINAP derivatives could facilitate the formation of product in certain substrate cases. When $Rh(CO)_2(BINAP^{Me})BF_4$ was employed as the catalyst, substrate bearing methyl- (**4b**) and tertiary butyl-substituents (**4c**) provided the target products in good yields. Additionally, 2-naphtyl *gem*-DCFP works well using $Rh(CO)_2(BINAP^{OMe})BF_4$ as the catalyst (**4d**). *gem*-DFCP with a strong electron-donating group (-OMe) required a more electron-rich ligand and longer reaction time (**4e**). Based on the results obtained, it can be inferred that the electron-rich substrate necessitates a rhodium catalyst with a higher electron density. Fluoro- and phenyl-substituted substrates (**4f**, **4g**) successfully underwent this reaction with $Rh(CO)_2(BINAP^{OMe})BF_4$ as the catalyst. Furthermore, the choice of reaction solvent is sometimes a critical parameter, with the *meta*-methyl substituted substrate exhibiting good reactivity and yielding the product in good yield when $PhCF_3$ was used as the solvent (**4h**).



Scheme 4. Synthetic Applications.

To explore the synthetic application of this protocol, we conducted the model reaction on a gram-scale, resulting in **3a** in 81% isolated yield (Scheme 4a). In addition, the benzyl C−F bond can undergo defluorinative coupling through hydrogen bonding with the use of HFIP as a hydrogen bond donor.[20] Friedel-Crafts reaction of **3a** with *p*-xylene generated a C−C bond coupling product **5a** in 56% yield. Treatment of **3a** with other types of nucleophiles efficiently forms C−C, C−N, C−O bonds (Scheme 4b). When methyl 4-phenylpent-4-enoate (**2ac**) was subjected to the standard reaction conditions, it successfully yielded compound **6a**, a lactone, in 56% yield (Scheme 4c). Taking together, our developed method not only offers general access to various benzyl fluorides, but also is able to achieve formal C−C, C−N, and C−O bifunctionalization of alkenes through post-transformation of the benzyl fluorides.



Scheme 5. Preliminary Mechanistic Studies and Proposed Mechanism.

In our previous work,[14c] styrene can attack the fluoroallyl rhodium intermediate **A'** through migratory insertion, giving a benzyl rhodium intermediate **B'**. This intermediate **B'** then undergoes β-H elimination to produce the fluoroallylation product. Initially, we considered the possibility of a C−F bond reductive elimination process in the benzyl rhodium intermediate, leading to the reincorporation of fluorine atom (Scheme 5a). To facilitate this process, we decided to use diphosphine ligands, which make the intermediate **B'** easier to reach a saturated coordination state and promote C−F bond reductive elimination. We tested a cationic Rh catalyst generated in situ from $[Rh(CO)_2Cl]_2$, bidentate phosphine ligands, and $AgBF_4$ in PhCl. However, this catalyst proved to be inefficient for the desired reactions (Table 1, entries 3-5), providing only a small amount of the target products occasionally. This unstable result inspires us to synthesize a cationic dicarbonyl Rh complex with a bidentate ligand, which exhibits excellent efficiency and selectivity for fluorides recovery. However, the actual reaction

mechanism was different from our initial expectations. When subjecting the (3-methylbut-1-en-2-yl)benzene as substrate to the standard reaction conditions, we observed the formation of benzyl fluorides and tertiary alkyl fluoride (Scheme 5b). This suggests the involvement of a carbon cation rearrangement in the reaction process. We also investigated the effect of different counter-anions and found that only tetrafluoroborate as an anion ensured the progress of the reaction (details are shown in the Supporting Information).

According to current findings and preceding research, we proposed a preliminary mechanism for this carbofluorination reaction (Scheme 4c). Firstly, the oxidative addition of *gem*-DFCP **1a** with $[Rh(CO)_2(BINAP)BF_4]$ catalyst gives the intermediate **A**, which then undergoes β-F elimination to deliver the fluoroallyl Rh species **B**. Subsequently, the outer-sphere nucleophilic attack of styrene **2a** on intermediate **B** can generate a benzylic cation **C**. This carbocation **C** finally leads to the production of fluoride **3a** by abstracting a fluoride from a BF_4^-, along with the formation of one molecular BF_3.[21] The resulting BF_3 can react with fluoride ions to form BF_4^- and regenerate the rhodium catalyst. This is our preliminary understanding of the reaction mechanism, and the detailed process will be further elucidated by combining it with DFT (density functional theory) calculations in the near future.

In conclusion, we have reported a Rh-catalyzed carbofluorination reaction of simple alkenes with *gem*-DFCPs as bifunctional reagents, providing access to various benzyl fluorides and *gem*-difluorides with 100% atom-economy. This approach has demonstrated the bifunctional reactivity of *gem*-DFCPs, distinguishing the fluorides recycling of *gem*-DFCPs from the prevailing defluorination coupling reaction. Furthermore, we have demonstrated the practicality of this transformation by conveniently coupling benzyl fluorides to form new C−C, C−N, and C−O bonds. Finally, the unique catalytic reactivity of the well-defined cationic dicarbonyl rhodium complex towards carbofluorination process over defluorinative allylation or cycloaddition in the reaction of *gem*-DFCPs with alkenes will provide more inspirations on how to tune the selectivity on transition-metal catalysis. Future work will focus on understanding the reaction mechanism and expanding the scope of the carbofluorination strategy using *gem*-DFCPs, and these works will be reported in due course.

ASSOCIATED CONTENT

Detailed experimental procedures, characterization data, copies of ^1H, ^{13}C and ^{19}F NMR spectra of products are reported in the Supporting Information.

AUTHOR INFORMATION

Corresponding Author

Ying Xia − West China School of Public Health and West China Fourth Hospital, West China-PUMC C.C. Chen Institute of Health, and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, China; Email: xiayingscu@scu.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work is supported by the National Natural Science Foundation (Grant 22001180) and the "Thousand Young Talents Program of China" (Grant 15-YINGXIA). Prof. Gang Lu from Shandong University is acknowledged for useful discussion on the reaction mechanism.

References:

(1) (a) McDonald, R. I.; Liu, G.; Stahl, S. S. Palladium(II)-Catalyzed Alkene Functionalization via Nucleopalladation: Stereochemical Pathways and Enantioselective Catalytic Applications. *Chem. Rev.* **2011**, *111*, 2981–3019. (b) Shimizu, Y.; Kanai, M. Recent Progress in Copper-Catalyzed Difunctionalization of Unactivated Carbon–Carbon Multiple Bonds. *Tetrahedron Lett.* **2014**, *55*, 3727–3737. (c) Chen, P.; Liu, G. Advancements in Aminofluorination of Alkenes and Alkynes: Convenient Access to β-Fluoroamines. *Eur. J. Org. Chem.* **2015**, *2015*, 4295–4309. (d) Tian, Y.; Chen, S.; Gu, Q.-S.; Lin, J.-S.; Liu, X.-Y. Amino- and Azidotrifluoromethylation of Alkenes. *Tetrahedron Lett.* **2018**, *59*, 203–215. (e) Alkene Difunctionalization Using Hypervalent Iodine Reagents: Progress and Developments in the Past Ten Years. *Molecules* **2019**, *24*, 2634. (f) Li, Z.-L.; Fang, G.-C.; Gu, Q.-S.; Liu, X.-Y. Recent Advances in Copper-Catalysed Radical-Involved Asymmetric 1,2-Difunctionalization of Alkenes. *Chem. Soc. Rev.* **2020**, *49*, 32–48.

(2) (a) Liu, G. Transition Metal-Catalyzed Fluorination of Multi Carbon–Carbon Bonds: New Strategies for Fluorinated Heterocycles. *Org. Biomol. Chem.* **2012**, *10*, 6243–6248. (b) Wolstenhulme, J. R.; Gouverneur, V. Asymmetric Fluorocyclizations of Alkenes. *Acc. Chem. Res.* **2014**, *47*, 3560−3570. (d) Zeng, Y.; Ni, C.; Hu, J. Recent Advances in the One-Step Synthesis of Distally Fluorinated Ketones. *Chem. Eur. J.* **2016**, *22*, 3210–3223. (c) Wang, X.; Lei, J.; Liu, Y.; Ye, Y.; Li, J.; Sun, K. Fluorination and Fluoroalkylation of Alkenes/Alkynes to Construct Fluoro-containing Heterocycles. *Org. Chem. Front.* **2021**, *8*, 2079–2109.

(3) (a) Müller, K.; Faeh, C.; Diederich, F. Fluorine in Pharmaceuticals: Looking Beyond Intuition. *Science*. **2007**, *317*, 1881−1886. (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. Fluorine in Medicinal Chemistry. *Chem. Soc. Rev.* **2008**, *37*, 320−330. (c) Kirk, K. L. Fluorination in Medicinal Chemistry: Methods, Strategies, and Recent Developments. *Org. Process Res. Dev.* **2008**, *12*, 305−321. (d) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. Fluorine in Pharmaceutical Industry: Fluorine-Containing Drugs Introduced to the Market in the Last Decade (2001−2011). *Chem. Rev.* **2014**, *114*, 2432−2506. (e) Champagne, P. A.; Desroches, J.; Hamel, J.-D.; Vandamme, M.; Paquin, J.-F. Monofluorination of Organic Compounds: 10 Years of Innovation. *Chem. Rev.* **2015**, *115*, 9073−9174. (f) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Aceña, J.; Soloshonok, V. A.; Izawa, K.; Liu, H. Next Generation of Fluorine-Containing Pharmaceuticals, Compounds Currently in Phase II-III Clinical Trials of Major Pharmaceutical Companies: New Structural Trends and Therapeutic Areas. *Chem. Rev.* **2016**, *116*, 422−518. (g) Qing, F.-L; Liu, X.-Y; Ma, J.-A; Shen, Q.; Song, Q.; Tang, P. A Fruitful Decade of Organofluorine Chemistry: New Reagents and Reactions. *CCS Chem.* **2022,** *4*, 2518−2549.

(4) McKnight, E. A.; Cadwallader, D.; Le, C. M. Carbofluorination of π-Bonds and Related

Reactions Involving Tandem C–C/C–F Bond Formation. *Eur. J. Org. Chem*. **2023**, e202300017.

(5) Ishida, N.; Iwamoto, H.; Sunagawa, D. E.; Ohashi, M.; Ogoshi, S. CsF-Catalyzed Fluoroacylation of Tetrafluoroethylene Using Acyl Fluorides for the Synthesis of Pentafluoroethyl Ketones. *Synthesis* **2021**, *53*, 3137–3143.

(6) Yu, X.; Meng, Q.-Y.; Daniliuc, C. G.; Studer, A. Aroyl Fluorides as Bifunctional Reagents for Dearomatizing Fluoroaroylation of Benzofurans. *J. Am. Chem. Soc.* **2022**, *144*, 7072–7079.

(7) Garg, A.; Gerwien, N. J.; Fasting, C.; Charlton, A.; Hopkinson, M. N. Formal Insertion of Alkenes Into C(sp^3)−F Bonds Mediated by Fluorine-Hydrogen Bonding. *Angew. Chem., Int. Ed.* **2023**, *62*, e202302860.

(8) Yoshida, T.; Ohta, M.; Emmei, T.; Kodama, T.; Tobisu, M. Cationic Rhodium(I) Tetrafluoroborate Catalyzed Intramolecular Carbofluorination of Alkenes via Acyl Fluoride C−F Bond Activation. *Angew. Chem., Int. Ed.* **2023**, *62*, e202303657.

(9) For such strategy of carbofluorination of other unsaturated molecules, see: (a) Fujimoto, H.; Kodama, T.; Yamanaka, M.; Tobisu, M. Phosphine-Catalyzed Intermolecular Acylfluorination of Alkynes via a P(V) Intermediate. *J. Am. Chem. Soc*. **2020**, *142*, 17323–17328. (b) Wang, F.; Nishimoto, Y.; Yasuda, M. Insertion of Diazo Esters into C–F Bonds toward Diastereoselective One-Carbon Elongation of Benzylic Fluorides: Unprecedented BF_3 Catalysis with C–F Bond Cleavage and Re-Formation. *J. Am. Chem. Soc.* **2021**, *143,* 20616–20612. (c) McKnight, E. A.; Arora, R.; Pradhan, E.; Fujisato, Y. H.; Ajayi, A. J.; Lautens, M.; Zeng, T.; Le, C. M. BF3–Catalyzed Intramolecular Fluorocarbamoylation of Alkynes via Halide Recycling. *J. Am. Chem. Soc.* **2023**, *145*, 11012– 11018.

(10) For selected reviews on *gem*-difluorinated cyclopropanes, see: (a) Dolbier, W. R.; Battiste, M. A. Structure, Synthesis, and Chemical Reactions of Fluorinated Cyclopropanes and Cyclopropenes. *Chem. Rev.* **2003**, *103*, 1071−1098. (b) Fedoryński, M. Syntheses of *gem*-Dihalocyclopropanes and Their Use in Organic Synthesis. *Chem. Rev.* **2003**, *103*, 1099−1132. (c) Adekenova, K. S.; Wyatt, P. B.; Adekenov, S. M. Beilstein. *J. Org. Chem.* **2021**, *17*, 245−272.

(11) For reviews on the ring-opening cross-coupling reactions of *gem*-DFCPs, see: (a) Lv, L.; Qian, H.; Li, Z. Catalytic Diversification of *gem*-Difluorocyclopropanes: Recent Advances and Challenges. *ChemCatChem.* **2022**, *14*, e202200890. (b) Zhu, Y.; Zeng, Y.; Jiang, Z.-T.; Xia, Y. Recent Advances in Transition-Metal-Catalyzed Cross-Coupling Reactions of *gem*-Difluorinated Cyclopropanes. *Synlett* **2023**, *34*, 1−13.

(12) For Pd catalysis with linear selectivity, see: (a) Xu, J.; Ahmed, E. A.; Xiao, B.; Lu, Q. Q.; Wang, Y. L.; Yu, C. G.; Fu, Y. Pd-catalyzed Regioselective Activation of *gem*-Difluorinated Cyclopropanes: a Highly Efficient Approach to 2-Fluorinated Allylic Scaffolds. *Angew. Chem., Int. Ed.* **2015**, *54*, 8231−8235. (b) Ni, J.; Nishonov, B.; Pardaev, A.; Zhang, A. Palladium-Catalyzed Ring-Opening Coupling of *gem*-Difluorocyclopropanes for the Construction of 2-Fluoroallylic Sulfones. *J. Org. Chem*. **2019**, *84*, 13646−13654. (c) Ahmed, E.-A. M.; Suliman, A. M.; Gong, T.-J.; Fu, Y. Access to Divergent Fluorinated Enynes and Arenes via Palladium-Catalyzed Ring-Opening Alkynylation of *gem*-Difluorinated Cyclopropanes. *Org. Lett.* **2020**, *22*, 1414−1419. (d) Suliman, A. M. Y.; Ahmed, E. M. A.; Gong, T.- J.; Fu, Y. Cu/ Pd-catalyzed cis-Borylfluoroallylation of Alkynes for the Synthesis of Boryl-Substituted Monofluoroalkenes. *Org.*

Lett. **2021**, *23*, 3259−3263. (e) Suliman, A. M.; Ahmed, E.-A. M.; Gong, T.-J.; Fu, Y. Three-Component Reaction of *gem*-Difluorinated Cyclopropanes with Alkenes and B_2pin_2 for the Synthesis of Monofluoroalkenes. *Chem. Commun.* **2021**, *57*, 6400−6403. (f) Xiong, B.; Chen, X.; Liu, J.; Zhang, X.; Xia, Y.; Lian, Z. Stereoselective *gem*-Difluorovinylation of *gem*-Difluorinated Cyclopropanes enabled by Ni/Pd Cooperative Catalysis. *ACS Catal.* **2021**, *11*, 11960−11965. (g) Fu, Z.; Zhu, J.; Guo, S.; Lin, A. Palladium-Catalyzed Allylic Alkylation Dearomatization of *beta*-Naphthols and Indoles with *gem*-difluorinated Cyclopropanes. *Chem. Commun*. **2021**, *57*, 1262−1265. (h) Zhou, P. X.; Yang, X.; Wang, J.; Ge, C.; Feng, W.; Liang, Y. M.; Zhang, Y. Palladium-Catalyzed C−H Allylation of Electron-Deficient Polyfluoroarenes with *gem*-Difluorinated Cyclopropanes. *Org. Lett.* **2021**, *23*, 4920−4924. (i) Yuan, W.; Li, X.; Qi, Z.; Li, X. Palladium-Catalyzed Synthesis of Functionalized Indoles by Acylation/Allylation of 2-Alkynylanilines with Three-Membered Rings. *Org. Lett.* **2022**, *24*, 2093−2098. (j) Sun, J.; Ye, H.; Sun, F.; Pan, Y.; Zhu, X.; Wu, X. Palladium-Catalyzed Allylation of P(O)H Compounds: Access to 2-Fluoroallylic Phosphorus Compounds. *Org. Lett.* **2023**, *25*, 5220-5225.

(13) For Pd catalysis with branched selectivity, see: (a) Lv, L.; Li, C.- J. Palladium-Catalyzed Defluorinative Alkylation of *gem*-difluorocyclopropanes: Switching Regioselectivity via Simple Hydrazones. *Angew. Chem. Int. Ed.* **2021**, *60*, 13098−13104. (b) Lv, L.; Qian, H.; Ma, Y.; Huang, S.; Yan, X.; Li, Z. Ligand-Controlled Regioselective and Chemodivergent Defluorinative functionalization of *gem*-difluorocyclopropanes with Simple Ketones. *Chem. Sci.* **2021**, *12*, 15511−15518. (c) Lv, L.; Qian, H.; Crowell, A. B.; Chen, S.; Li, Z. Pd/NHC-Controlled Regiodivergent Defluorinative Allylation of *gem*-Difluorocyclopropanes with Allylboronates. *ACS Catal.* **2022**, *12*, 6495−6505. (d) Wu, L.; Wang, M.; Liang, Y.; Shi, Z. Ligand-Controlled Palladium-Catalyzed Regiodivergent Defluorinative Allylation of *gem*-Difluorocyclopropanes via σ-Bond Activation. *Chin. J. Chem.* **2022**, *40*, 2345−2355. (e) Qian, H.; Nguyen, H. D.; Lv, L.; Chen, S.; Li, Z. Chemo-, Stereo- and Regioselective Fluoroallylation/Annulation of Hydrazones with *gem*-Difluorocyclopropanes via Tunable Palladium/NHC Catalysis. *Angew. Chem. Int. Ed.* **2023**, *62*, e202303271.

(14) For Rh catalysis, see: (a) Jiang, Z.-T., Huang, J., Zeng, Y., Hu, F.; Xia, Y. Rhodium Catalyzed Regioselective C−H Allylation of Simple Arenes via C−C Bond Activation of *gem*-Difluorinated Cyclopropanes. *Angew. Chem. Int. Ed.* **2021**, *60*, 10626−10631. (b) Jiang, Z.-T; Zeng, Y.; Xia, Y. Rhodium-Catalyzed Direct Allylation of Simple Arenes by Using *gem*-Difluorinated Cyclopropanes as Allyl Surrogates. *Synlett* **2021**, *32*, 1675–1682. (c) Zeng, Y.; Gao, H.; Zhu, Y.; Jiang, Z.-T.; Lu, G.; Xia, Y. Site-Divergent Alkenyl C−H Fluoroallylation of Olefins Enabled by Tunable Rhodium Catalysis. *ACS Catal*. **2022**, *12*, 8857−8867. (d) Zeng, Y.; Yang, H.; Du, J.; Huang, Q.; Huang, G.; Xia, Y. Rh-Catalyzed Regio-Switchable Cross-Coupling of *gem*-Difluorinated Cyclopropanes with Allylboronates to Structurally Diverse Fluorinated Dienes. *Chem. Sci.* **2022**, 13, 12419−12425.

(15) For Co catalysis, see: Ai, Y.; Yang, H.; Duan, C.; Li, X.; Yu, S. Cobalt-Catalyzed Fluoroallyllation of Carbonyls via C−C Activation of *gem*-Difluorocyclopropanes. *Org. Lett.* **2022**, *24*, 5051−5055.

(16) An electrochemical example, see: Zhao, B.; Pan, Z.; Pan, J.; Deng, H.; Bu, X.; Ma, M.; Xue, F.

Regiodivergent Electroreductive Defluorinative Carboxylation of *gem*-Difluorocyclopropanes. *Green Chemistry* **2023,** *25*, 3095−3102.

(17) For cycloaddition chemistry, see: Zeng, Y.; Xia, Y. Rhodium-Catalyzed Regio- and Diastereoselective [3+2] Cycloaddition of *gem*-Difluorinated Cyclopropanes with Internal Olefins. *Angew. Chem. Int. Ed.* **2023**, *62*, e202307129.

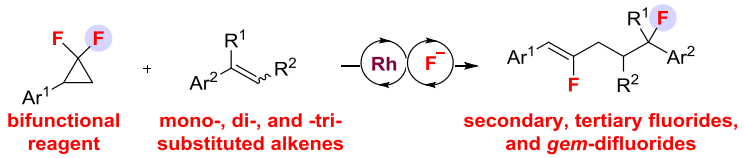
(18) The use of specific *gem*-DFCPs to synthesize *gem*-difluorinated cyclic molecules, see: (a) Liu, H.; Tian, L.; Wang, H.; Li, Z.-Q.; Zhang, C.; Xue, F.; Feng, C. A NovelType of Donor-Acceptor Cyclopropane with Fluorine as the Donor: (3 + 2)-Cycloadditions with Carbonyls. *Chem. Sci.* **2022**, *13*, 2686–2691. (b) Archer, G.; Cavalère, P.; Médebielle, M.; Merad, J. Photoredox Generation of Isothiouronyl Radical Cations: A New Platform in Covalent Radical Catalysis. *Angew. Chem. Int. Ed.* **2022**, *61*, e202205596.

(19) During the preparation of this manuscript, Liu and co-workers reported a fluorinative bifunctionalization of aziridinesand azetidines with *gem*-DFCPs under palladium catalysis: Li, D.; Shen, C.; Si, Z.; Liu, L. Palladium-Catalyzed Fluorinative Bifunctionalization of Aziridines and Azetidines with *gem*-Difluorocyclopropanes. *Angew. Chem. Int. Ed.* **2023**, e202310283.

(20) Champagne, P. A.; Benhassine, Y.; Desroches, J.; Paquin, J. Friedel–Crafts Reaction of Benzyl Fluorides: Selective Activation of C–F Bonds as Enabled by Hydrogen Bonding. *Angew. Chem. Int. Ed.* **2014,** *53*, 13835–13839.

(21) Cresswell, A. J.; Davies, S. G.; Roberts, P. M.; Tomson, J. E. Beyond the Balz−Schiemann Reaction: The Utility of Tetrafluoroborates and Boron Trifluoride as Nucleophilic Fluoride Sources. *Chem. Rev.* **2015**, *115*, 566−611.

Entry for the Table of Contents



bifunctional reagent

mono-, di-, and -tri-substituted alkenes

secondary, tertiary fluorides, and *gem*-difluorides

- 100% atom-economic
- Well-defined Rh catalyst
- A great diversity of alkenes
- Mild conditions