OL Organic Letters

pubs.acs.org/OrgLett Letter

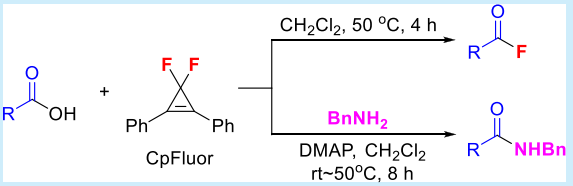
Deoxyfluorination of Carboxylic Acids with CpFluor: Access to Acyl Fluorides and Amides

Xiu Wang, Fei Wang, Fengfeng Huang, Chuanfa Ni, and Jinbo Hu*

Cite This: *Org. Lett.* 2021, 23, 1764–1768 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: 3,3-Difluoro-1,2-diphenylcyclopropene (CpFluor), a bench-stable fluorination reagent, has been developed in the deoxyfluorination of carboxylic acids to afford various acyl fluorides. This all-carbon-based fluorination reagent enabled the efficient transformation of (hetero)aryl, alkyl, alkenyl, and alkynyl carboxylic acids to the corresponding acyl fluorides under the neutral conditions. This deoxyfluorination method was featured by the synthesis of acyl fluorides with *in-situ* formed CpFluor, as well as the one-pot amidation reaction of carboxylic acids via *in-situ* formed acyl fluorides.

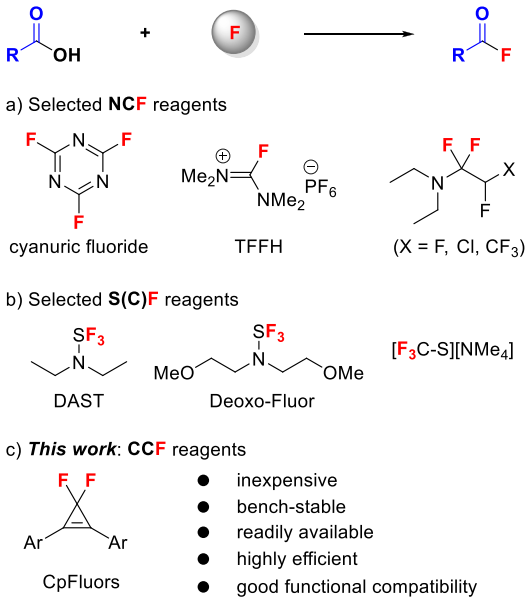


Recently, acyl fluorides have attracted much attention in organic synthesis, owing to their unique balance of stability and reactivity.[1] They are widely used as acyl,[2] aryl,[3] and fluoride sources.[4] Acyl fluorides are superior synthons compared to their corresponding carboxylic acid derivatives in terms of stability, reactivity, and transmetalation ability.[1,3] Therefore, the development of a reliable and general method to prepare acyl fluorides is highly appealing, among which the deoxyfluorination of carboxylic acids with a fluorination reagent has become a routine method.[1b−d] In this context, a bench-stable, readily available and efficient fluorination reagent is highly desirable.

Until now, two types of conventional fluorination reagents have been established in the synthesis of acyl fluorides. One is nitrogen-containing fluorination reagents (NCF reagents) (Scheme 1a),[5−8] such as cyanuric fluoride,[6] TFFH,[7] and perfluoroalkylamines.[8] The other is sulfur-containing fluorination reagents (S(C)F reagents) (Scheme 1b),[9−12] such as DAST,[10] Deoxo-Fluor,[11] and $(Me_4N)SCF_3$.[12] The introduction of a heteroatom is of great importance to stabilize and improve the reactivity of fluorination reagents for carbonyl compounds. However, these fluorination reagents have some drawbacks, such as sensitivity to air and moisture, tediousness, and costly synthetic routes, as well as the requirement of an additional base, which limit their applications in the synthesis of acyl fluorides.

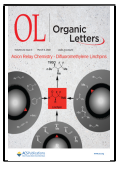
3,3-Difluoro-1,2-diarylcyclopropenes, a class of carbon-based fluorinating reagents (also called CpFluors), could be synthesized by stable and inexpensive 1,2-diarylalkynes with difluorocarbene reagents via [2 + 2] cycloaddition.[13] With our continuous efforts in organofluoine chemistry, we found that CpFluors could not only convert a variety of alcohols to alkyl fluorides[14] but also efficiently convert a diversity of carboxylic acids to acyl fluorides. Herein, we describe a practicable and straightforward approach to acyl fluorides via deoxyfluorination of carboxylic acids with CpFluor (Scheme 1c).

Scheme 1. Representative Fluorination Reagents in Deoxyfluorination of Carboxylic Acids



Encouraged by our previous work on deoxyfluorination of alcohols with CpFluors,[14] the deoxyfluorination of 3-methylbenzoic acid (**1a**) via nucleophilic attack of 3,3-difluoro-1,2-diphenylcyclopropene (CpFluor **2**) was evaluated

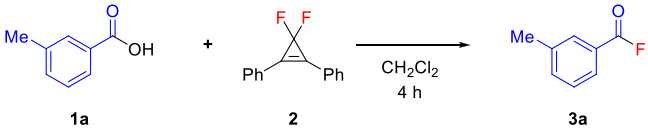
Received: January 18, 2021
Published: February 15, 2021



https://dx.doi.org/10.1021/acs.orglett.1c00190
Org. Lett. 2021, 23, 1764–1768

(Table 1). As expected, acyl fluoride **3a** was obtained in 13% yield at room temperature (entry 1). Conducting the reaction

Table 1. Optimization of the Reaction Conditions[a]



1a 2 3a

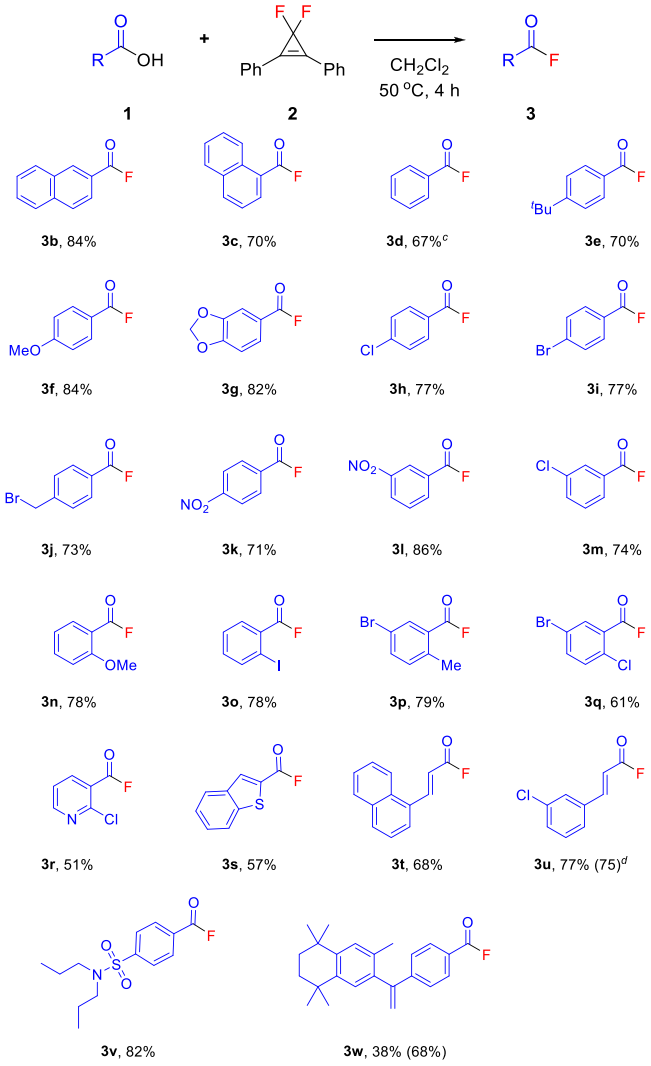
entry	2 (equiv)	temp (°C)	3a (%)[b]
1	1.2	25	13
2	1.2	30	53
3	1.2	50	57
4	1.2	70	53
5	1.6	50	76 (70)
6	2.0	50	65

[a]Reaction conditions: **1a** (0.5 mmol), CH_2Cl_2 (2.5 mL), 4 h. [b]Determined by ^{19}F NMR analysis of the crude mixture, using benzotrifluoride as an internal standard. An isolated yield is given in parentheses.

at an elevated temperature (50 °C) provided the desired product **3a** in 57% yield (entry 3). Furthermore, the use of 1.6 equiv of CpFluor **2** improved the yield of **3a** to 76% (entry 5). However, the use of 2 equiv of CpFluor **2** resulted in the formation of more anhydride, as well as a low yield of target product **3a** (entry 6), probably arising from the increased concentration of intermediate **I** at the initiation stage (see Scheme 4). Notably, no bases or additives are required in this deoxyfluorination process, and the byproduct 2,3-diphenylcycloprop-2-en-1-one (**5**) can be easily separated from the target molecule.

The generality of this protocol was explored with a wide range of carboxylic acids as shown in Scheme 2. Naphthyl substrates provided the corresponding acyl fluorides **3b** and **3c** in good yields. Nonsubstituted benzoyl fluoride **3d** was observed with moderate yield. In addition, benzoic acid bearing electron-donating groups such as *p*-*tert*-butyl, *p*-methoxyl, and acetyl substituents were well tolerated, affording aroyl fluorides **3e**−**3g** in 70−84% yields. The introduction of electron-withdrawing groups such as halogens, bromomethyl, and nitro groups onto benzoic acid in the *para*-position gave the target products **3h**−**3k** in 71%−77% yields. Benzoic acid with electronically diverse functional groups in the *ortho*- and *meta*-positions also successfully converted into the desired aroyl fluorides (**3l**−**3o**), which illustrated that the present reaction is insensitive to electronic effect and steric hindrance. In addition, disubstituted acyl fluorides **3p** and **3q** were obtained in 79% and 61% yields, respectively. Other heterocycles including pyridyl (**1r**) and benzothiophene (**1s**) were also compatible in this reaction. Particularly, alkenyl acyl fluorides (**3t** and **3u**) were accommodated during the reaction regardless of the electronic nature of the aromatic ring. To prove the utility of our method, carboxylic acid-containing drugs were examined; probenecid coupled with CpFluor yielded **3v** in 82% yield, whereas bexarotene only afforded **3w** in 38% isolated yield. The reaction could further be extended to the aliphatic and alkynyl carboxylic acids; however, low yields of desired products were observed due to the instability of the formed acyl fluorides during isolation by silica gel flash column chromatography.

Scheme 2. Deoxyfluorination of Carboxylic Acids[a,b]

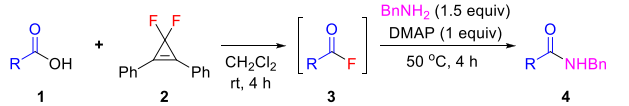


[a]Reaction conditions: **1** (0.5 mmol), **2** (0.8 mmol), CH_2Cl_2 (2.5 mL), 50 °C, 4 h. [b]Isolated yields. [c]^{19}F NMR yields using benzotrifluoride as an internal standard. [d]The isolated yield of the reaction performed on 1 mmol scale is given in parentheses.

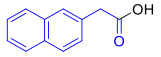
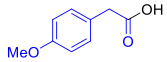
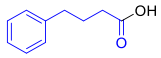
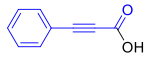
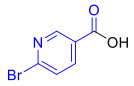
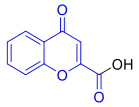
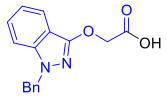
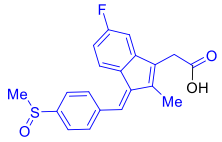
One-pot deoxyfluorination/amidation of several selected carboxylic acids were investigated using benzylamine as the substrate. Acyl fluorides were formed by an optimized deoxyfluorination procedure, followed by the addition of 1.5 equiv of benzylamine activated by 1 equiv of 4-dimethylaminopyridine (DMAP), and then direct amidation proceeded smoothly at 50 °C for another 4 h (Table 2). Notably, benzylic (**1x** and **1y**), aliphatic (**1z**), and alkynyl (**1aa**) carboxylic acids were well participated in the formation of acyl fluorides at room temperature, affording the corresponding acyl fluorides **3x**−**3aa** in good to excellent yields. Meanwhile, the one-pot amidation process furnished target products **4x**−**4aa** in moderate to good yields. On the other hand, representative aromatic carboxylic acid **1ab** and alkenyl carboxylic acid **1ac** were also subjected to the one-pot deoxyfluorination/amidation. Besides, carboxylic acid containing bioactive molecules, including bindazac **1ad** and sulindac **1ae**, were proved to be effective coupling partners at the elevated temperature, providing **4ad**−**4ae** in 78% and 75% yields, respectively. In some cases, in situ formed 2,3-diphenylcyclo-

https://dx.doi.org/10.1021/acs.orglett.1c00190
Org. Lett. 2021, 23, 1764−1768

Table 2. One-Pot Deoxyfluorination/Amidation of Carboxylic Acids via *in Situ* Formed Acyl Fluorides[a]



1 2 3 4

Compound	1	3 (%)[b]	4 (%)[c]
1x		79	55
1y		94	69
1z		85	83
1aa		82	65
1ab[d]		94	73
1ac[d]		78	41
1ad[d]		82	78
1ae[d]		83	75

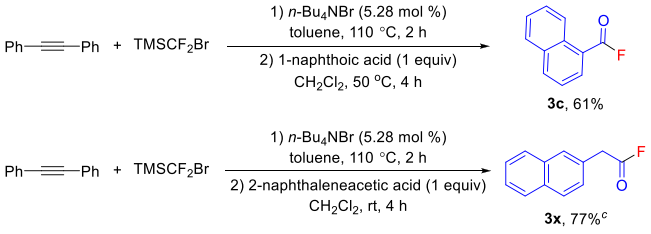
[a]Reaction conditions: **1** (0.5 mmol), **2** (0.8 mmol), CH_2Cl_2 (2.5 mL), rt, 4 h. Then $BnNH_2$ (1.5 equiv), DMAP (1 equiv), 50 °C, 4 h. [b]Determined by ^{19}F NMR analysis of the crude mixture, using benzotrifluoride as an internal standard. [c]Isolated yields. [d]Deoxyfluorination step was performed at 50 °C.

prop-2-en-1-one (**5**) in the deoxyfluorination step could also react with benzylamine, which decreased the amount of benzylamine for the amidation procedure and resulted in the low efficiency of the subsequent amidation.

To evaluate the utility of this approach, deoxyfluorination of carboxylic acids with *in situ* formed CpFluor was tested in Scheme 3. Initially, CpFluor **2** was prepared by [2 + 1] cycloaddition reaction of diphenyl acetylene with commercially available Me_3SiCF_2Br without further purification. Subsequently, 1 equiv of aromatic or benzylic carboxylic acid was directly added under the identical reaction conditions. Fortunately, 1-naphthoyl fluoride **3c** and 2-(naphthalen-2-yl)acetyl fluoride **3x** were obtained without a great loss compared to reaction with isolated CpFluor. This set of studies revealed that the present methodology is complementary to the deoxyfluorination of carboxylic acids without presynthesis of a fluorination reagent.

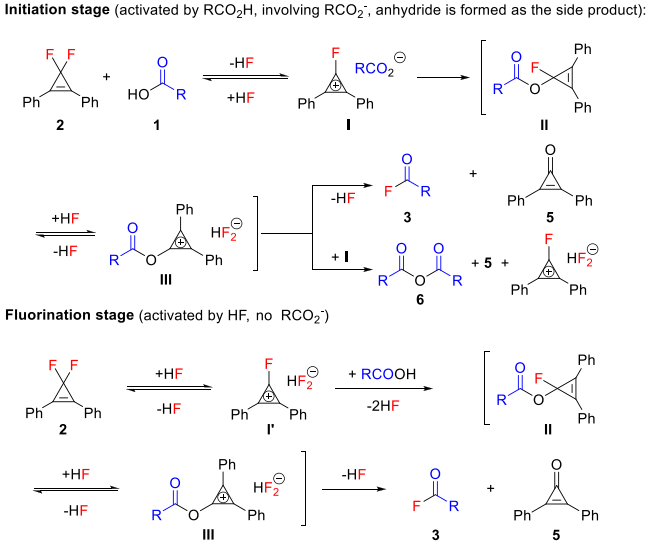
Based on our experimental results as well as the reported aromatic cation activation mode of *gem*-dihalocyclopropene in nucleophilic halogenation of alcohols and carboxylic acids,[14,15] the proposed mechanism of deoxyfluorination of carboxylic acids to acyl fluorides was reasoned as shown in Scheme 4. In the initiation stage, CpFluor (**2**) is prone to be in equilibrium with cyclopropenium salt **I** in the presence of carboxylic acids.

Scheme 3. Two-Step [2 + 1] Cycloaddition/Deoxyfluorination for the Synthesis of Acyl Fluorides[a,b]



[a]Reaction conditions: (1) diphenylacetylene (0.88 mmol), $TMSCF_2Br$ (1.32 mmol), $^nBu_4NBr$ (0.026 mmol), toluene (2.0 mL), 110 °C, 2 h; (2) Toluene was removed under the vacuum, added acid (0.5 mmol), CH_2Cl_2 (2 mL), rt or 50 °C, 4 h. [b]Isolated yields. [c]Determined by ^{19}F NMR analysis of the crude mixture, using benzotrifluoride as an internal standard.

Scheme 4. Proposed Mechanism



Intermediate **II** resulting from the combination of a cyclopropenium cation and carboxylate anion of **I** is activated by a proton to afford intermediate **III**, which further undergoes competitive nucleophilic substitution reaction with a carboxylate anion and bifluoride anion to provide anhydride **6** and acyl fluoride **3**, respectively. In the fluorination stage, the formation of a carboxylate anion is inhibited due to the accumulation of HF; thus, HF acts as the activator. In this stage, the formation of intermediate **III** is dominated by the direct attack of carboxylic acid **1** on the cyclopropenium cation and the formation of acyl fluoride **3** is the main pathway.

In summary, we have disclosed the high fluorination ability of *gem*-difluorocyclopropene in deoxyfluorination of carboxylic acids to synthesize a wide range of acyl fluorides. This deoxyfluorination method was featured by the synthesis of acyl fluorides with *in situ* formed CpFluor, as well as the one-pot amidation reaction of carboxylic acids via *in situ* formed acyl fluorides.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00190.

https://dx.doi.org/10.1021/acs.orglett.1c00190
Org. Lett. 2021, 23, 1764−1768

More detailed results of deoxyfluorination of carboxylic acids and characterization data of the representative starting materials and products (PDF)

AUTHOR INFORMATION

Corresponding Author

Jinbo Hu − *Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Shanghai 200032, China;* orcid.org/0000-0003-3537-0207; Email: jinbohu@sioc.ac.cn

Authors

Xiu Wang − *Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Shanghai 200032, China*

Fei Wang − *Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Shanghai 200032, China*

Fengfeng Huang − *Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Shanghai 200032, China*

Chuanfa Ni − *Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Shanghai 200032, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c00190

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the National Key Research and Development Program of China (2016YFB0101200), the National Natural Science Foundation of China (21632009), the Key Programs of the Chinese Academy of Sciences (KGZD-EW-T08), the Key Research Program of Frontier Sciences of CAS (QYZDJ-SSW-SLH049), and Shanghai Science and Technology Program (18JC1410601).

REFERENCES

(1) For recent reviews for transformations of acyl fluorides, see: (a) Blanchard, N.; Bizet, V. Acid Fluorides in Transition-Metal Catalysis: A Good Balance between Stability and Reactivity. *Angew. Chem., Int. Ed.* **2019**, *58*, 6814−6817. (b) Ogiwara, Y.; Sakai, N. Acyl Fluorides in Late-Transition-Metal Catalysis. *Angew. Chem., Int. Ed.* **2020**, *59*, 574−594. (c) Foth, P. J.; Malig, T. C.; Yu, H.; Bolduc, T. G.; Hein, J. E.; Sammis, G. M. Halide-Accelerated Acyl Fluoride Formation Using Sulfuryl Fluoride. *Org. Lett.* **2020**, *22*, 6682−6686. (d) Liang, Y.; Zhao, Z.; Taya, A.; Shibata, N. Acyl Fluorides from Carboxylic Acids, Aldehydes, or Alcohols under Oxidative Fluorination. *Org. Lett.* **2021**, *23*, 847−852.

(2) (a) Braden, R.; Himmler, T. Katalytische Reduktion von aromatischen Carbonsäurefluoriden zu Aldehyden. *J. Organomet. Chem.* **1989**, *367*, C12−C14. (b) Zhang, Y.; Rovis, T. A Unique Catalyst Effects the Rapid Room-Temperature Cross-Coupling of Organozinc Reagents with Carboxylic Acid Fluorides, Chlorides, Anhydrides, and Thioesters. *J. Am. Chem. Soc.* **2004**, *126*, 15964−15965. (c) Ogiwara, Y.; Maegawa, Y.; Sakino, D.; Sakai, N. Palladium-catalyzed Coupling of Benzoyl Halides with Aryltrifluorosilanes Leading to Diaryl Ketones. *Chem. Lett.* **2016**, *45*, 790−792. (d) Ogiwara, Y.; Sakino, D.; Sakurai, Y.; Sakai, N. Acid Fluorides as Acyl Electrophiles in Suzuki−Miyaura Coupling. *Eur. J. Org. Chem.* **2017**, *2017*, 4324−4327. (e) Boreux, A.; Indukuri, K.; Gagosz, F.; Riant, O. Acyl Fluorides as Efficient Electrophiles for the Copper-Catalyzed Boroacylation of Allenes. *ACS Catal.* **2017**, *7*, 8200−8204. (f) Ogiwara, Y.; Sakurai, Y.; Hattori, H.; Sakai, N. Palladium-Catalyzed Reductive Conversion of Acyl Fluorides via Ligand-Controlled Decarbonylation. *Org. Lett.* **2018**, *20*, 4204−4208. (g) Pan, F.-F.; Guo, P.; Li, C.-L.; Su, P.; Shu, X.-Z. Enones from Acid Fluorides and Vinyl Triflates by Reductive Nickel Catalysis. *Org. Lett.* **2019**, *21*, 3701−3705. (h) Ogiwara, Y.; Iino, Y.; Sakai, N. Catalytic C−H/C−F Coupling of Azoles and Acyl Fluorides. *Chem. - Eur. J.* **2019**, *25*, 6513−6516. (i) Wang, Z.; Wang, X.; Nishihara, Y. PPh_3-Assisted Esterification of Acyl Fluorides with Ethers via $C(sp^3)$−O Bond Cleavage Accelerated by TBAT. *Catalysts* **2019**, *9*, 574. (j) Han, J.; Zhou, W.; Zhang, P.-C.; Wang, H.; Zhang, R.; Wu, H.-H.; Zhang, J. Design and Synthesis of WJ-Phos, and Application in Cu-Catalyzed Enantioselective Boroacylation of 1,1-Disubstituted Allenes. *ACS Catal.* **2019**, *9*, 6890−6895.

(3) (a) Keaveney, S. T.; Schoenebeck, F. Palladium-Catalyzed Decarbonylative Trifluoromethylation of Acid Fluorides. *Angew. Chem., Int. Ed.* **2018**, *57*, 4073−4077. (b) Malapit, C. A.; Bour, J. R.; Brigham, C. E.; Sanford, M. S. Base-free nickel-catalysed decarbonylative Suzuki−Miyaura coupling of acid fluorides. *Nature* **2018**, *563*, 100−104. (c) Okuda, Y.; Xu, J.; Ishida, T.; Wang, C. A.; Nishihara, Y. Nickel-Catalyzed Decarbonylative Alkylation of Aroyl Fluorides Assisted by Lewis-Acidic Organoboranes. *ACS Omega* **2018**, *3*, 13129−13140. (d) Wang, Z.; Wang, X.; Nishihara, Y. Nickel-catalysed decarbonylative borylation of aroyl fluorides. *Chem. Commun.* **2018**, *54*, 13969−13972. (e) Sakurai, S.; Yoshida, T.; Tobisu, M. Iridium-catalyzed Decarbonylative Coupling of Acyl Fluorides with Arenes and Heteroarenes via C−H Activation. *Chem. Lett.* **2019**, *48*, 94−97. (f) Wang, X.; Wang, Z.; Liu, L.; Asanuma, Y.; Nishihara, Y. Nickel-Catalyzed Decarbonylative Stannylation of Acyl Fluorides under Ligand-Free Conditions. *Molecules* **2019**, *24*, 1671. (g) Wang, X.; Wang, Z.; Nishihara, Y. Nickel/copper-cocatalyzed decarbonylative silylation of acyl fluorides. *Chem. Commun.* **2019**, *55*, 10507−10510. (h) Zhang, C.; Zhao, R.; Dagnaw, W. M.; Liu, Z.; Lu, Y.; Wang, Z.-X. Density Functional Theory Mechanistic Insight into the Base-Free Nickel-Catalyzed Suzuki−Miyaura Cross-Coupling of Acid Fluoride: Concerted versus Stepwise Transmetalation. *J. Org. Chem.* **2019**, *84*, 13983−13991. (i) Malapit, C. A.; Bour, J. R.; Laursen, S. R.; Sanford, M. S. Mechanism and Scope of Nickel-Catalyzed Decarbonylative Borylation of Carboxylic Acid Fluorides. *J. Am. Chem. Soc.* **2019**, *141*, 17322−17330. (j) Kayumov, M.; Zhao, J.-N.; Mirzaakhmedov, S.; Wang, D.-Y.; Zhang, A. Synthesis of Arylstannanes via Palladium-Catalyzed Decarbonylative Coupling of Aroyl Fluorides. *Adv. Synth. Catal.* **2020**, *362*, 776−781.

(4) (a) Kalow, J. A.; Doyle, A. G. Enantioselective Ring Opening of Epoxides by Fluoride Anion Promoted by a Cooperative Dual-Catalyst System. *J. Am. Chem. Soc.* **2010**, *132*, 3268−3269. (b) Kalow, J. A.; Doyle, A. G. Mechanistic Investigations of Cooperative Catalysis in the Enantioselective Fluorination of Epoxides. *J. Am. Chem. Soc.* **2011**, *133*, 16001−16012. (c) Kalow, J. A.; Doyle, A. G. Enantioselective fluoride ring opening of aziridines enabled by cooperative Lewis acid catalysis. *Tetrahedron* **2013**, *69*, 5702−5709. (d) Ogiwara, Y.; Hosaka, S.; Sakai, N. Benzoyl Fluorides as Fluorination Reagents: Reconstruction of Acyl Fluorides via Reversible Acyl C−F Bond Cleavage/Formation in Palladium Catalysis. *Organometallics* **2020**, *39*, 856−861.

(5) Mukaiyama, T.; Tanaka, T. A Convenient Method for The Preparation of Carboxylic Acid Fluorides. *Chem. Lett.* **1976**, *5*, 303−306.

(6) (a) Olah, G. A.; Nojima, M.; Kerekes, I. Synthetic Methods and Reactions; IV. Fluorination of Carboxylic Acids with Cyanuric Fluoride. *Synthesis* **1973**, *1973*, 487−488. (b) Groß, S.; Laabs, S.; Scherrmann, A.; Sudau, A.; Zhang, N.; Nubbemeyer, U. Improved Syntheses of Cyanuric Fluoride and Carboxylic Acid Fluoride. *J. Prakt. Chem.* **2000**, *342*, 711−714.

(7) (a) Carpino, L. A.; El-Faham, A. Tetramethylfluoroformamidinium Hexafluorophosphate: A Rapid-Acting Peptide Coupling Reagent for Solution and Solid Phase Peptide Synthesis. *J. Am. Chem. Soc.* **1995**, *117*, 5401−5402. (b) Fiammengo, R.; Licini, G.; Nicotra, A.; Modena, G.; Pasquato, L.; Scrimin, P.; Broxterman, Q. B.; Kaptein, B. Duality of Mechanism in the Tetramethylfluoroformamidinium Hexafluorophosphate-Mediated Synthesis of N-Benzyloxycarbonylamino Acid Fluorides. *J. Org. Chem.* **2001**, *66*, 5905−5910.

(8) (a) Takaoka, A.; Iwakiri, H.; Ishikawa, N. *F*-Propene-Dialkylamine Reaction Products as Fluorinating Agents. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3377−3380. (b) Petrov, V. A.; Swearingen, S.; Hong, W.; Petersen, W. C. 1,1,2,2-Tetrafluoroethyl-*N*,*N*-dimethylamine: a new selective fluorinating agent. *J. Fluorine Chem.* **2001**, *109*, 25−31.

(9) (a) Hasek, W. R.; Smith, W. C.; Engelhardt, V. A. The Chemistry of Sulfur Tetrafluoride. II. The Fluorination of Organic Carbonyl Compounds. *J. Am. Chem. Soc.* **1960**, *82*, 543−551. (b) Markovskij, L. N.; Pashinnik, V. E.; Kirsanov, A. V. Stereoselective cis and trans Addition of Hydrogen Chloride to Olefins. *Synthesis* **1973**, *1973*, 787−789. (c) Beaulieu, F.; Beauregard, L.-P.; Courchesne, G.; Couturier, M.; LaFlamme, F.; L'Heureux, A. Aminodifluorosulfinium Tetrafluoroborate Salts as Stable and Crystalline Deoxofluorinating Reagents. *Org. Lett.* **2009**, *11*, 5050−5053. (d) L'Heureux, A.; Beaulieu, F.; Bennett, C.; Bill, D. R.; Clayton, S.; LaFlamme, F.; Mirmehrabi, M.; Tadayon, S.; Tovell, D.; Couturier, M. Aminodifluorosulfinium Salts: Selective Fluorination Reagents with Enhanced Thermal Stability and Ease of Handling. *J. Org. Chem.* **2010**, *75*, 3401−3411. (e) Singh, R. P.; Umemoto, T. 4-Fluoropyrrolidine-2-carbonyl Fluorides: Useful Synthons and Their Facile Preparation with 4-tert-Butyl-2,6-dimethylphenylsulfur Trifluoride. *J. Org. Chem.* **2011**, *76*, 3113−3121. (f) Smedley, C. J.; Barrow, A. S.; Spiteri, C.; Giel, M.-C.; Sharma, P.; Moses, J. E. Sulfur-Fluoride Exchange (SuFEx)-Mediated Synthesis of Sterically Hindered and Electron-Deficient Secondary and Tertiary Amides via Acyl Fluoride Intermediates. *Chem. - Eur. J.* **2017**, *23*, 9990−9995.

(10) (a) Kaduk, C.; Wenschuh, H.; Beyermann, M.; Forner, K.; Carpino, L. A.; Bienert, M. Synthesis of Fmoc-amino acid fluorides via DAST, an alternative fluorinating agent. *Lett. Pept. Sci.* **1996**, *2*, 285−288. (b) Gustafsson, T.; Gilmour, R.; Seeberger, P. H. Fluorination reactions in microreactors. *Chem. Commun.* **2008**, 3022−3024.

(11) (a) Lal, G. S.; Pez, G. P.; Pesaresi, R. J.; Prozonic, F. M. Bis(2-methoxyethyl)aminosulfur trifluoride: a new broad-spectrum deoxofluorinating agent with enhanced thermal stability. *Chem. Commun.* **1999**, 215−216. (b) Lal, G. S.; Pez, G. P.; Pesaresi, R. J.; Prozonic, F. M.; Cheng, H. Bis(2-methoxyethyl)aminosulfur Trifluoride: A New Broad-Spectrum Deoxofluorinating Agent with Enhanced Thermal Stability. *J. Org. Chem.* **1999**, *64*, 7048−7054. (c) White, J. M.; Tunoori, A. R.; Turunen, B. J.; Georg, G. I. [Bis(2-methoxyethyl)-amino]sulfur Trifluoride, the Deoxo-Fluor Reagent: Application toward One-Flask Transformations of Carboxylic Acids to Amides. *J. Org. Chem.* **2004**, *69*, 2573−2576.

(12) Scattolin, T.; Deckers, K.; Schoenebeck, F. Direct Synthesis of Acyl Fluorides from Carboxylic Acids with the Bench-Stable Solid Reagent $(Me_4N)SCF_3$. *Org. Lett.* **2017**, *19*, 5740−5743.

(13) (a) Xu, W.; Chen, Q.-Y. 3,3-Difluoro-1-iodocyclopropenes: A Simple Synthesis and Their Reactions. *J. Org. Chem.* **2002**, *67*, 9421−9427. (b) Oshiro, K.; Morimoto, Y.; Amii, H. Sodium Bromodifluoroacetate: A Difluorocarbene Source for the Synthesis of *gem*-Difluorocyclopropanes. *Synthesis* **2010**, *2010*, 2080−2084. (c) Wang, F.; Luo, T.; Hu, J.; Wang, Y.; Krishnan, H. S.; Jog, P. V.; Ganesh, S. K.; Praksh, G. K. S.; Olah, G. A. Synthesis of *gem*-Difluorinated Cyclopropanes and Cyclopropenes: Trifluoromethyltrimethylsilane as a Difluorocarbene Source. *Angew. Chem., Int. Ed.* **2011**, *50*, 7153−7157. (d) Wang, F.; Zhang, W.; Zhu, J.; Li, H.; Huang, K.-W.; Hu, J. Chloride ion-catalyzed generation of difluorocarbene for efficient preparation of *gem*-difluorinated cyclopropenes and cyclopropanes. *Chem. Commun.* **2011**, *47*, 2411−2413. (e) Li, L.; Wang, F.; Ni, C.; Hu, J. Synthesis of *gem*-Difluorocyclopropa(e)nes and O-, S-, N-, and P-Difluoromethylated Compounds with $TMSCF_2Br$. *Angew. Chem., Int. Ed.* **2013**, *52*, 12390−12394. (f) Deng, X.-Y.; Lin, J.-H.; Zheng, J.; Xiao, J.-C. Difluoromethylation and *gem*-difluorocyclopropenation with difluorocarbene generated by decarboxylation. *Chem. Commun.* **2015**, *51*, 8805−8808.

(14) Li, L.; Ni, C.; Wang, F.; Hu, J. Deoxyfluorination of alcohols with 3,3-difluoro-1,2-diarylcyclopropenes. *Nat. Commun.* **2016**, *7*, 13320−13331.

(15) (a) Kelly, B. D.; Lambert, T. H. Aromatic Cation Activation of Alcohols: Conversion to Alkyl Chlorides Using Dichlorodiphenylcyclopropene. *J. Am. Chem. Soc.* **2009**, *131*, 13930−13931. (b) Hardee, D. J.; Kovalchuke, L.; Lambert, T. H. Nucleophilic Acyl Substitution via Aromatic Cation Activation of Carboxylic Acids: Rapid Generation of Acid Chlorides under Mild Conditions. *J. Am. Chem. Soc.* **2010**, *132*, 5002−5003.

https://dx.doi.org/10.1021/acs.orglett.1c00190
Org. Lett. 2021, 23, 1764−1768