Transition-Metal-Free Approach for *Z*-Vinyl Fluorides by Hydrofluorination of Alkynes bearing SF_4 and SF_5 Groups

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Abstract: The synthesis of vinyl fluorides plays a crucial role in various scientific disciplines, including pharmaceutical and materials sciences. Herein, we present a direct and stereoselective hydrofluorination method for the synthesis of the *Z* isomer of vinyl fluorides from alkynes containing unexplored SF_5 and SF_4 groups. Our strategy employed tetrabutylammonium fluoride (TBAF) as the fluorine source. It demonstrates high compatibility with aryls, biaryls, heteroaryls, and tert-alkyl groups, allowing the facile incorporation of SF_5 and SF_4 groups across the triple bond without any transition-metal catalysts. This approach avoids the potential decomposition of SF_5 or SF_4 units via coordination with transition metals or acidic protic sources. Remarkably, this transformation proceeded at room temperature without any additional additives, providing the *Z* isomer of the vinyl fluorides in excellent yield and high selectivity. The presence of a water molecule as a hydrate in TBAF is essential for an efficient conversion. This methodology opens new avenues for the synthesis of enchanted SF_5- and SF_4-containing fluorinated vinylic scaffolds, thereby providing advanced opportunities for novel drug discovery and fluorinated polymers.

Introduction

The diversification of fluorinated structural motifs through the development of innovative synthetic methodologies holds great significance in medicinal chemistry[1] as it expands the range of accessible molecules. In organic chemistry, pentafluoro-sulfanyl (-SF_5)[2] and tetrafluoro-sulfanyl (-SF_4-) [3] have attracted increasing attention as intriguing functional moieties. These groups consist of hypervalent sulfur(VI) atoms bonded to five or four fluorine atoms. The presence of sulfur and multiple fluorine atoms confer exceptional electronegativity and lipophilicity to these groups. Consequently, they serve as valuable and distinct modifying groups that alter the chemical and physicochemical properties of parent molecules. Furthermore, the SF_5 and SF_4 groups possessed notable bulk and size, which influenced their molecular interactions and spatial arrangements. Although both groups share some similarities, the SF_5 moiety is typically employed as the terminal group and is often regarded as a super trifluoromethyl (CF_3) group (Figure 1a), whereas the SF_4 moiety functions as a connecting element. Notably, the *trans*-SF_4 unit linearly linked two independent moieties, resembling an isosteric bridge akin to the alkyne, [1,1,1] bicyclopentane, cuban, or *p*-substituted phenyl connections (Figure 1b).[4] These unique structural properties have significant potential in pharmaceuticals, agrochemicals, and specialty materials, despite the limited availability of compounds featuring SF_5 and SF_4.

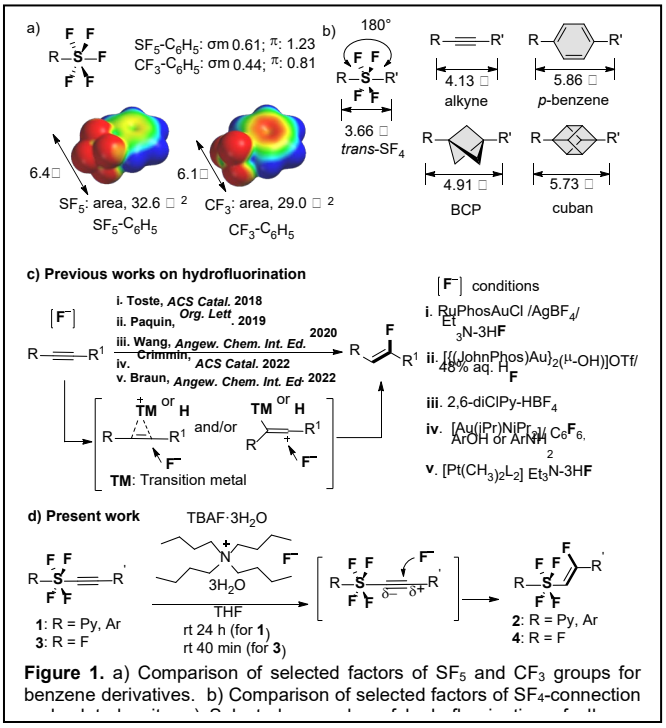
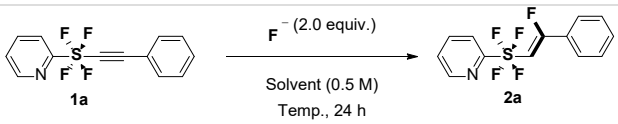


Figure 1. a) Comparison of selected factors of SF_5 and CF_3 groups for benzene derivatives. b) Comparison of selected factors of SF_4-connection

Vinyl fluorides with functionalized scaffolds bear structural similarities to amide bonds, and are prevalent in a wide range of bioactive compounds and materials.[5] Furthermore, fluoro-functionalized vinyl fluorides serve as valuable monomer units for the development of novel fluorinated polymers.[6] However, synthesizing vinyl fluorides with complex scaffolds remains a challenge in organic synthesis.[7] Among the various synthetic strategies, the hydrofluorination of alkynes has emerged as an intriguing approach, offering a direct route for the construction of highly functionalized vinyl fluorides (Figure 1c).[8] Nevertheless, the hydrofluorination of internal alkynes bearing fluorinated functional groups without using transition-metal catalysts remains unresolved. Pioneering studies by Sadighi et al.[8a] have

highlighted the significance of Au(I) complexes and N-heterocyclic carbene ligands in the trans-hydrofluorination of internal alkynes. Subsequently, Miller[8b] and Nolan[8c] expanded this approach by using Au complexes with Lewis base adducts of hydrogen fluoride. Since 2017, the field has progressed significantly (Figure 1c). Hammond et al. reported the hydrofluorination of propargyl sulfones using a Au complex, including JohnPhos, bistriflimide, and Olah's reagent, as an HF source.[8d] Toste et al.[8f] designed a Au-Ag co-catalyzed hydrofluorination of electron-withdrawing alkenes using triethylamine trihydrogen fluoride ($Et_3N{\cdot}3HF$) as the fluoride source. Paquin et al.[8g] further advanced this methodology using a dinuclear gold hydroxide complex with aqueous HF. They applied the method to the hydrofluorination of CF_3- and SF_5-alkynes, but the yields were low to moderate, and the substrate scope was not examined. These approaches involve Au complexes with HF reagents, likely because of the electrophilic nature of Au, which facilitates the coordination and activation of alkynes.[9] Crimmin et al. reported alkyne hydrofluorination under [Au(*i*Pr)NiPr$_2$] catalysis with perfluoroarene as the fluoride source to avoid the use of HF.[8i] Recently, Braun et al. used Pt complexes with HF to generate *Z*-vinyl fluorides.[8j,k] However, their wide applicability and scalability are restricted owing to the high cost of transition metal catalysts. In 2018, Fustero et al. developed the conjugate addition of fluoride to propargyl sulfones using tetra-n-butylammonium fluoride (TBAF) in the presence of NH_4Cl to provide β-fluoroalkyl sulfones with by-product formation of β-keto sulfones.[8e] Wang et al.[8h] described the transition metal-free hydrofluorination of alkynes. The highly electron-deficient and strongly acidic pyridinium salt of 2,6-dichlropyridinium tetrafluoroborates was employed for the generation of stereodivergent vinyl fluorides, albeit with a limited substrate scope. Based on an extensive literature search on hydrofluorination,[8-10] the coordination of alkyne triple bonds by transition metals or highly acidic protons is critical for generating reactive cationic intermediates or equivalents for hydrofluorination. Moreover, conjugated systems, such as propargyl sulfones, are required to activate alkynes. Presuming the demand for SF_5- and SF_4-compounds in drug discovery and novel materials,[2-3] we aimed to investigate a hydrofluorination strategy for internal alkynes bearing an SF_5 or SF_4 group at one end of the triple bond. This methodology enables the generation of highly functionalized SF_5- or SF_4-enriched vinyl fluorides from readily accessible SF_5- and SF_4-alkynes, respectively.[3,4,11] However, the steric hindrance and high electronegativity of SF_5 and SF_4 significantly affect the overall behavior of alkynes.[2-4,8e] In addition, the use of transition metals can be avoided because of the potential decomposition of SF_5 or SF_4 units by the coordination of transition metals to the fluoride moiety in SF_5 or SF_4.[12a] In addition, a highly acidic protic source can cause decomposition of SF_5 or SF_4 through the interaction of H^+ with the fluoride moiety in SF_5 or SF_4.[12b,4e] Nevertheless, in reported approaches using transition metals or highly acidic H^+, competition between coordination to alkyne moieties and the SF_5/SF_4 units is unavoidable. In this paper, we present a novel transition-metal-free approach for the synthesis of *Z-isomers* of vinyl fluorides from alkynes containing unexplored SF_5 and SF_4 groups. The choice of fluorinating reagent and solvent plays a critical role in achieving the desired hydrofluorination of SF_4- or SF_5-functionalized alkynes. TBAF trihydrate ($TBAF{\cdot}3H_2O$) was essential for the desired conversion, and the amount of water was critical for this transformation.

Table 1. Optimization of reaction conditions.[a]

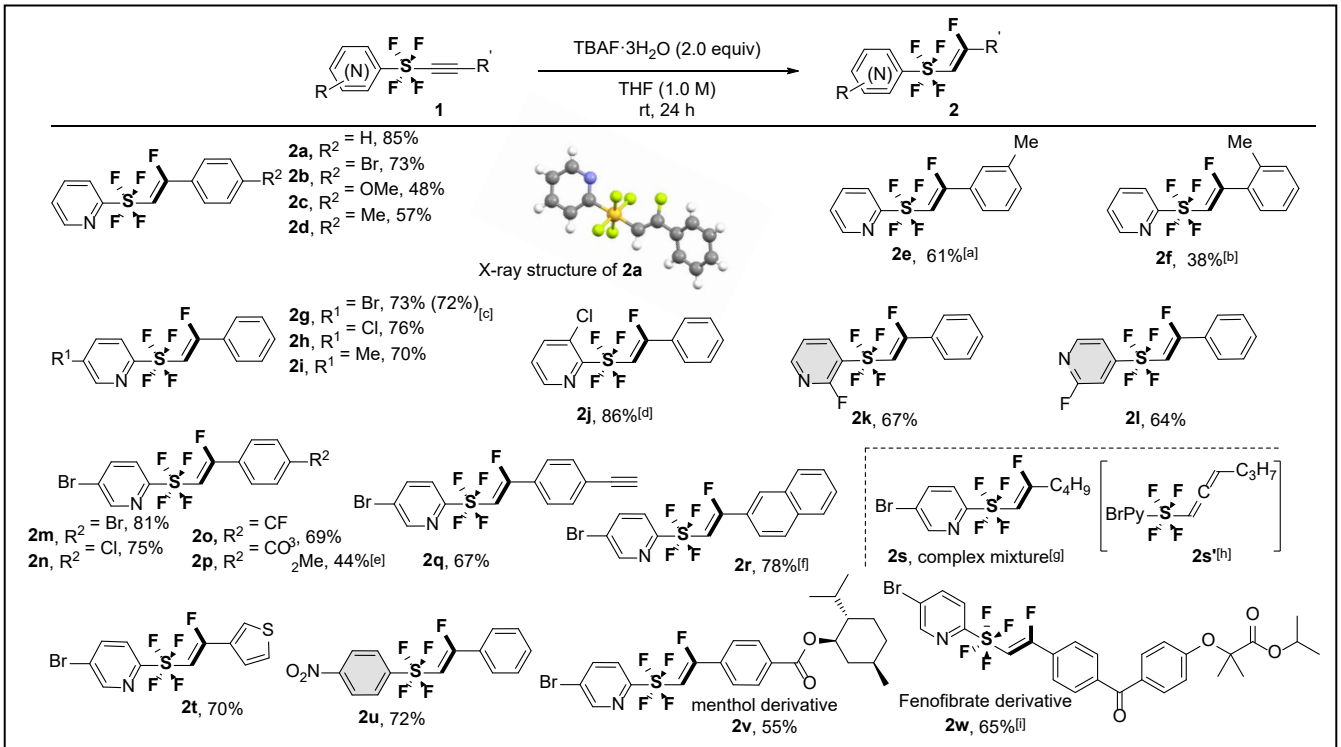


Entry	Fluorine source	Solvent	H_2O (equiv)	Temp. (°C)	Yield (%)
1	KF	THF		rt	N.R.
2	CsF	THF		rt	N.R.
3	KHF_2	THF		rt	N.R.
4	TBAF (1M in THF)	Toluene		rt	9
5	TBAF (1M in THF)	THF		rt	20
6	TBAF (1M in THF)	THF	3	rt	6
7	TBAF (1M in THF)	THF	10	rt	0
8	TBAF (1M in THF)	MeCN		rt	12
9	TBAF (1M in THF)	MeCN		50	68
10	TBAF (1M in THF)	DMSO		rt	44
11	TBAF (1M in THF)	DMSO		50	53
12	$TBAF{\cdot}3H_2O$	DMSO		rt	68
13	$TBAF{\cdot}3H_2O$	DCM		rt	23
14	$TBAF{\cdot}3H_2O$	Et_2O		rt	49
15	$TBAF{\cdot}3H_2O$	Toluene		rt	50
16	$TBAF{\cdot}3H_2O$	THF		rt	84
17	$TBAF{\cdot}3H_2O$	THF		50	73
18	$TBAF{\cdot}3H_2O$	Toluene		80	76
19	$TBAF{\cdot}3H_2O$	THF (1.0 M)		rt	87 (85[b])
20	$TBAF{\cdot}3H_2O$	THF (2.0 M)		rt	89
21	$TBAF{\cdot}3H_2O$ (1.5 equiv)	THF (2.0 M)		rt	83
22	$TBAF{\cdot}3H_2O$	THF (1.0 M)	3	rt	3
23	$TBAF{\cdot}3H_2O$	THF (1.0 M)	10	rt	0

[a] Reactions conducted on 0.1 mmol scale. Yields were determined by ^{19}F-NMR spectroscopy using $PhCF_3$ as an internal standard. [b] Isolated yield.

Results and Discussion

We began our exploration of hydrofluorination using 2-(tetrafluoro(phenylethynyl)-λ^6-sulfanyl)pyridine (**1a**) as a model substrate. Initially, various inorganic salts, such as KF, CsF, and KHF_2, were employed as fluorine sources in THF at room temperature for 24 h. However, no successful C-F bond formation was observed (entries 1-3). Next, we considered TBAF[8e] as a potential source of reactive “naked” fluoride anions with good solubility in organic solvents. The key factor of TBAF is the presence of alkyl hydrogen atoms in the countercation, which shelters its positive charge, thus weakening the electrostatic attraction to the fluoride anion.[13] Switching to TBAF (1.0 M solution in THF, maximum 10 wt.% water contaminated)[14] as a fluorine source in toluene resulted in 9% yield of SF_4-vinyl fluoride **2a** which was confirmed through ^{19}F NMR (entry 4), while 20% of **2a** was detected in THF (entry 5). As the 10% wt. % of water in this reaction scale (entry 5) corresponds to about 7 equiv of H_2O in the reaction mixture, we hypothesized that water is required to prompt protonation of the vinylic anion intermediate. Thus, we



Scheme 1. Substrate scope for the formation of vinyl fluorides **2.** Reaction conditions: **1** (0.2 mmol), TBAF·3H$_2$O (0.4 mmol) in THF (0.2 mL), under N_2 at room temperature. Isolated yields were shown. [a] 40 °C, 28 h. [b] 40 °C. [c] 1 mmol scale. [d] 50 °C. [e] 0.29 M in 1,4-dioxane. [f] 0.1 M. [g] 40 °C, 50 h. [h] **2s'** is a proposed structure (See SI). [i] 0.33 M.

added H_2O as an additive, and 3 and 10 equiv. However, the yield of **2a** decreased to 6 and 0%, respectively (entries 6-7). These results suggest that excess water is not effective for this transformation. Subsequently, the reaction was carried out in polar aprotic solvents. When acetonitrile (MeCN) was used, the reaction was slow, and only 12% yield of **2a** was obtained after 24 h (entry 8), while the yield increased to 68% at 50 °C (entry 9). Similar results were obtained when dimethyl sulfoxide (DMSO) was used as the solvent (entries 10 and 11). Subsequently, TBAF·3H$_2$O crystals were tested in various solvents, including DMSO, dichloromethane (DCM), diethyl ether (Et_2O), and toluene at room temperature. To our delight, Fluoride **2a** was obtained in selective *Z*-conformation in 68% yield in DMSO, whereas a lower yield was obtained in other solvents (entries 12-15). When THF was used as the solvent, 84% yield of targeted *Z* selective isomer was obtained after 24 h (entry 16). Increasing the reaction temperature to 50-80 °C did not improve the yield of the vinyl fluoride **2a** (entries 17-18). Changing the THF concentration slightly increased the yield of **2a** (entries 19-20). Lowering the amount of TBAF to 1.5 equiv lowered the yield of **2a** (entry 21). Screening under various conditions showed that TBAF·3H$_2$O in THF at room temperature was optimal for this reaction (entries 19 and 20). In the presence of 3 equiv. of H_2O impeded the fluorination process (3%, entry 22), and the reaction ceased when 10 equiv. in H_2O was added (0%, entry 23).

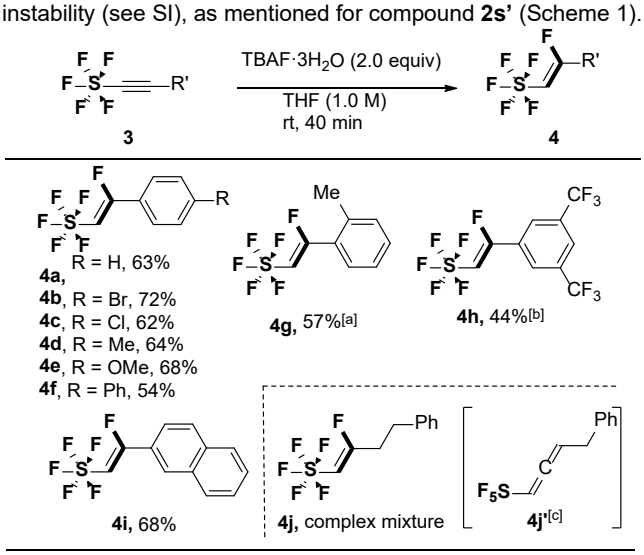
Under the optimized reaction conditions, we investigated the substrate scope of the hydrofluorination reaction (Scheme 1). When aryl-alkynyl-tetrafluoro-λ^6-sulfanylpyridines **1a-d** were employed under optimized reaction conditions with Br (**1b**), OMe (**1c**), Me (**1d**) at *p*-aryl position across the triple bond, the *Z*-selective vinyl fluorides **2a-d** were obtained in 48-85% yield. The formation of *Z*-isomer was confirmed by the X-ray crystallographic data of compound **2a** (CCDC 2279392).[15] The Substitution at the *m*-position of the aryl ring (**1e**) provided 61% yield **2e**, however, a lower yield (38%) was obtained with the *o*-Me substituted aryl group (**1f**), probably due to steric hindrance. Halogen (Br: **1g**, Cl: **1h**) or methyl (**1i**) substitution at 5-position of the pyridine ring of tetrafluoro-λ^6-sulfanyl pyridine provided the corresponding vinyl fluorides **2g-i** with selective *Z*-isomer in high yields (70-76%). The sterically demanding Cl substitution at the meta-position of the pyridine ring (**2j**) conducted a hydrofluorination reaction to provide the respective product **2j** in 86% yield. Phenyl-alkynyl-tetrafluoro-λ^6-sulfanylpyridines **1k** and **1l** with a meta- or para-connections between pyridine and the SF_4 units proceeded well under the optimized conditions to provide the desired vinyl fluorides **2k** and **2l** in 67% and 64% yields, respectively. Further substrate scope was explored using aryl-5-bromo-2-(tetrafluoro(phenylethynyl)-λ^6-sulfanyl)pyridines **1m-o**. The functional groups Br (**1m**), Cl (**1n**), and CF_3(**1o**) at the *p*-position of the aryl on the triple bond gave *Z*-selective vinyl fluorides **2m-o** in 69-81% yields. The ester group on the aryl group of **1p** was well tolerated and the desired vinyl fluoride **2p** (44%) was obtained using dioxane as the solvent instead of THF. It should be noted, when an ethynyl-substituted aryl substrate (**1q**) was employed under the screened reaction conditions, 67% yield of product **2q** was obtained, and the terminal aryl alkyne moiety remained unaffected. The reaction proceeded smoothly with naphthyl substitution on the other side of the triple bond to give the target product **2r** in 78% yield. The materially attractive thiophene-alkyne **1t** also reacted efficiently to afford **2t** in 70% yield. However, the non-aromatic substituted alkyne **1s**, with an aliphatic group at one end of the triple bond, was rather unreactive and gave a complex mixture after 50 h at 40 °C. Presumably, the α-proton of the alkyne moiety was removed, resulting in allene-type compound **2s'**, whereas the product could not be fully characterized owing to instability (see SI). The fruitful results with tetrafluoro-λ^6-sulfanylpyridine

motivated us to employ non-pyridyl, tetrafluoro phenyl-λ^6-sulfane **1u** under the designed reaction conditions to provide (Z)-tetrafluoro (2-fluoro-2-phenylvinyl) (4-nitrophenyl)-λ6-sulfane **2u** in 72% yield. It is noteworthy that in this hydrofluorination reaction, *Z*-vinyl fluorides **2** were formed exclusively with C-F bond formation opposite to the SF_4 group, irrespective of the groups attached on the other side of SF_4 alkyne **1**. Scale-up of the hydrofluorination reaction (1 mmol) of **1g** resulted in 72% of **2g**, which was almost the same yield as the small-scale reaction (73%).

Next, we applied the designed strategy to the synthesis of vinyl fluorides with natural product components. Treatment of menthol-linked alkyne **1v** underwent a successful transformation and provided the corresponding vinyl fluoride **2v** in 55% yield. This strategy has also been extended to the synthesis of vinyl fluorides containing drug moieties. Fenofibrate is a drug that decreases the levels of fatty substances in the blood. Interestingly, we designed the tetrafluorosulfanyl anion of fenofibrate drug **2w** with 65% yield. The functional groups present in fenofibrate **1w**, including aryl ketones, esters, and ethers, were well tolerated and remained intact in product **2w**.

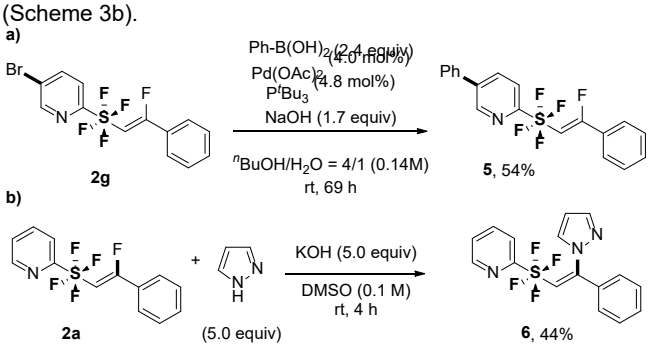
Based on the encouraging outcomes observed in the hydrofluorination reaction utilizing alkynyl tetrafluorosulfanyl pyridines, our focus shifted towards investigating hydrofluorination using alkynes featuring a pentrafluorosulfanyl substitution at the opposite terminus of the triple bond. The remarkable lipophilic properties of the SF_5 moiety make it a bioisosteric substitute for the CF_3 group, thereby establishing its significance in pharmaceutical exploration. Vinyl fluoride-containing CF_3 groups have attracted considerable interest as monomers in the synthesis of fluoropolymers. Consequently, vinyl fluorides appended to the SF_5 group have tremendous potential in the field of organic chemistry.

We initiated our investigation by subjecting fundamental phenyl-alkynyl-SF_5 compound **3a** to the screened reaction conditions employed for SF_4-alkynes. To our astonishment, hydrofluorination of **3a** occurred rapidly at room temperature within 40 min, affording the desired SF_5-enriched vinyl fluoride **4a** in a satisfactory yield of 63%. This reaction demonstrates the significantly enhanced reactivity of **3** towards hydrofluorination compared with that of SF_4-alkynes **1**. Encouraged by these findings, we expanded the substrate scope for the hydrofluorination of various SF_5-containing alkynes, **3** (Scheme 2). Remarkably, a range of SF_5-alkynes bearing p-substituted aryl groups underwent smooth conversions to the desired SF_5-vinyl fluorides **4** under identical conditions. Notably, halogen (Br: **3b**; Cl: **3c**)-, alkyl (Me: **3d**)-, and ether (OMe: **3e**)-substituted arylalkynes were all amenable to this transformation, furnishing the corresponding vinyl fluorides **4b** (72%), **4c** (62%), **4d** (64%), and **4e** (68%) in good yields. When the substrate scope was extended to include the π-extended *p*-biphenyl derivative **3f**, the desired SF_5-vinyl fluoride **4f** was obtained, albeit in a somewhat diminished yield of 54%. In contrast, the utilization of the sterically demanding *o*-methyl substrate **3g** resulted in a 57% yield of **4g**. Notably, despite the highly electron-withdrawing nature of the bis-trifluoromethylated phenyl group, SF_5-alkyne **3h** afforded **4h** in 44% yield. Furthermore, the β-naphthyl alkynyl-SF_5 compound **3i** underwent efficient conversion, providing the desired SF_5-vinyl fluoride **4i** in 68% yield. However, when the SF_5-alkyne possessing an aliphatic moiety at the terminal end of the triple bond (**3j**) was subjected to the reaction conditions, a complex mixture was obtained, presumably because of the reactivity of the alkynyl protons in substrate **3j** and vinylic protons in product **4j**. An allene-like compound **4j'** was detected based on NMR analysis; however, **4j'** could not be fully characterized owing to its instability (see SI), as mentioned for compound **2s'** (Scheme 1).

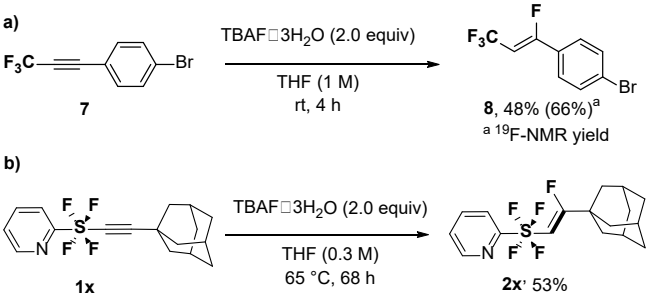


Scheme 2. Substrate scope of SF_5 alkyne **4**. Reaction conditions: **1** (0.2 mmol), TBAF · $3H_2O$ (0.4 mmol) in THF (0.2 mL), under N_2 at room temperature. Isolated yields were shown. [a] Reaction time was 5.5 h. [b] Reaction time was 3 h and the reaction was conducted with 0.13 mmol of **3**. [c] **4j'** was a proposed structure (See SI).

Using these novel *Z*-vinyl fluorides, we attempted two chemical transformations with **2**. First, we performed Suzuki coupling of the C_{sp2}–Br bond of pyridine in **2g** with phenylboronic acid in ^{n}BuOH/H_2O (4:1) in the presence of $Pd(OAc)_2$, P^{t}Bu$_3$, and NaOH at room temperature. The coupling product **5** was obtained in 54% yield (Scheme 3a). Next, the substitution reaction of the C_{sp2}-F bond on **2a** by pyrazole in DMSO in the presence of KOH at room temperature for 4h afforded the desired product **6** in 44% yield (Scheme 3b).



Scheme 3. Chemical transformations of **2**. a) at C-Br bond. b) at C-F bond.



Scheme 4. a) Hydrofluorination of CF_3-alkyne **7**. b) Hydrofluorination of SF_4-alkyne **1z** having tertiary alkyl group.

Notably, this method was effectively extended to the hydrofluorination of CF_3-alkyne **7**. Thus, under the same reaction

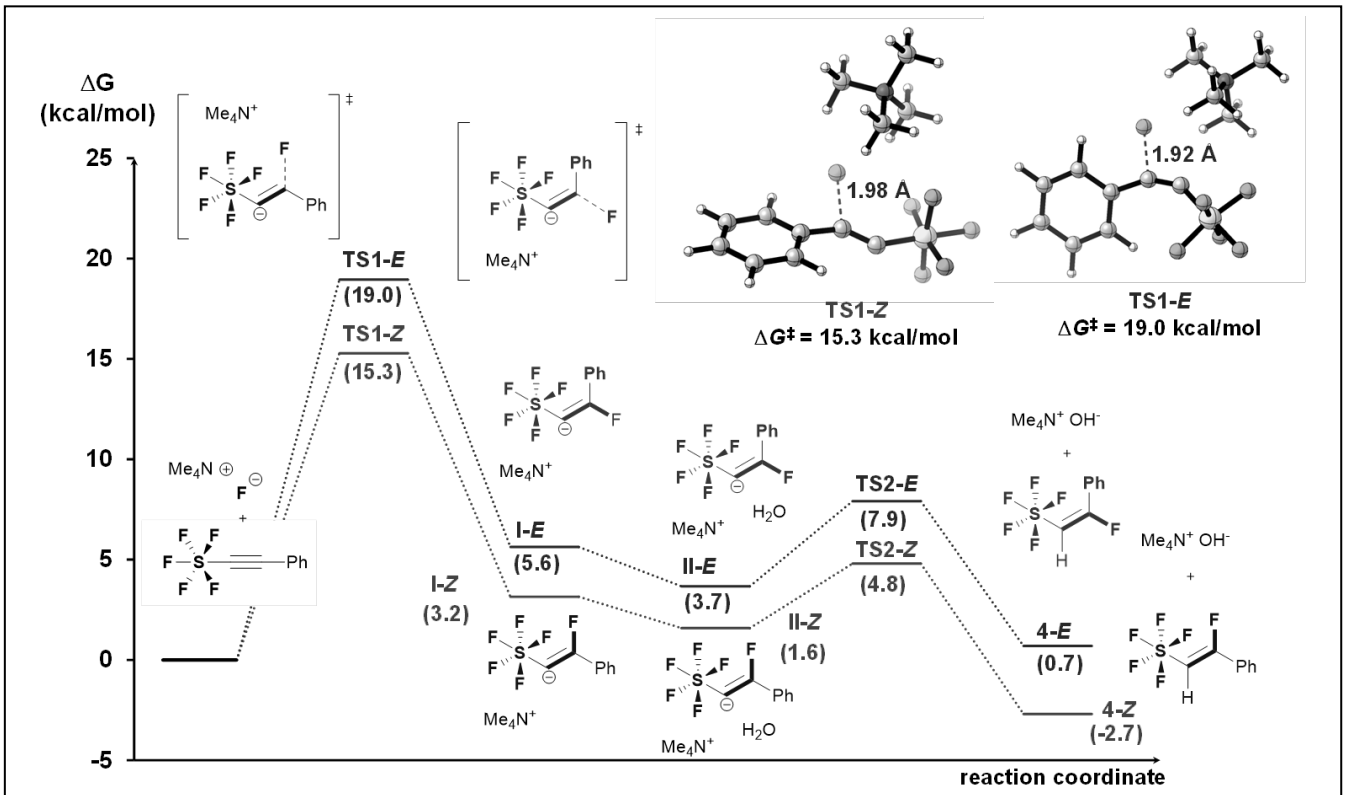
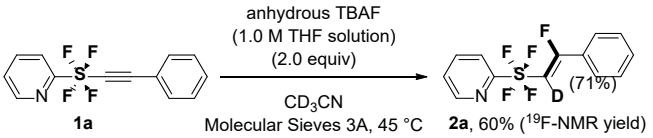


Figure 2. Gibbs energy profile for the reaction of **3a** (B3LYP-D3/Def2TZVPP), in THF. Tetramethylammonium (Me_4N^+) was used instead of nBu_4N^+ for computational simplicity.

conditions, the fluorination of CF_3-alkyne **7** proceeded smoothly to produce the desired *Z*-CF_3-vinyl fluoride **8** in 66% yield (48% isolated yield) within 4 h (Scheme 3a). Moreover, while the non-aromatic substituted alkyne **1s** failed to convert **2s** due to the deprotonation of α-proton (Scheme 1), the substrate **1x** with a tertiary aliphatic group was efficiently transformed into the hydrofluorination product **2x** in 53% after 68 h at 65 °C (Scheme 3b).

Based on the above results, we conclude that the hydrofluorination reaction of TBAF is strongly influenced by proton sources, such as H_2O and aprotic solvents (MeCN, DMSO). To elucidate the underlying reaction mechanism, deuterium labeling was performed to gain further insight (Scheme 5). When the hydrofluorination of **1a** was performed using the same TBAF (1.0 M THF solution) in CD_3CN at 45 °C, the desired vinylic fluoride **2a** was obtained in 60% yield, accompanied by a deuterium content of 71% (Scheme 3). This result indicates that MeCN and the contaminated water in TBAF in THF are proton sources. However, it was difficult to determine the exact role of water in this reaction. As shown in Table 1, TBAF·$3H_2O$ in THF afforded **2a** (87%, entry 19). However, it was observed that TBAF in THF solution (10 wt% water contaminated, approximately 7 equiv H_2O) showed limited efficacy in the hydrofluorination reaction (20%, entry 5). In addition, excess water stopped the conversion (entries 6, 7, 22, and 23), independent of TBAF·$3H_2O$ or TBAF in the THF solution.



Scheme 5. Deuterium-labeling experiment showing the location of **D** after hydrofluorination.

Based on the findings presented in Table 1, as well as additional experiments, including the deuterium labeling study outlined in Scheme 3 and existing literature reports, we propose a plausible mechanistic pathway for the generation of *Z*-vinylic fluorides bearing SF_4 (or SF_5) moieties from alkynes **1** (or **3**) and TBAF. We first calculated the Mulliken charges of the triple bond and, as expected, the SF_5 group polarizes the alkyne more than the Py-SF_4 group (Figure 3a). Notably, Cβ in both **1a** and **3a** is positive, and the polarizability between Cα and Cβ for **3a** is much higher than that of **1a** (δ: 0.377 for **1a** compared to 0.489 for **3a**), which could explain the superior reactivity of SF_5-**3a** compared to that of SF_4-**1a**. Thus, it is postulated that a fluoride species selectively attacks the positive Cβ of **1** (or **3**) (Figure 3b) via a *trans*-addition process, leading to the formation of an ionic pair of fluoro-vinyl anion intermediate **I** in the *Z*-configuration and nBu_4N cation (nBu_4N^+). These anionic species **I** are swiftly intercepted by water molecules present as hydrates within the TBAF solution to give vinyl fluorides **2** (or **4**) with tetrabutylammonium hydroxide (nBu_4NOH). Conversely, in an anhydrous environment, the unstable fluoro-vinyl anion intermediate **I** reverts to the starting alkyne **1** (or **3**) upon fluoride release, resulting in limited conversion. In fact, it has been suggested that the nucleophilic fluorination process is reversible. Thus, in the presence of potential protic sources such as TBAF·$3H_2O$ or MeCN (as a

solvent), vinylic anion **I** exhibits sufficient basicity to engage in protonation with H_2O or MeCN, giving rise to the desired product **2** (or **4**). This process differs from the reported hydrofluorination reaction pathway in which the coordination of transition metals or acidic protons over the triple bond of alkynes initiates the reaction process.

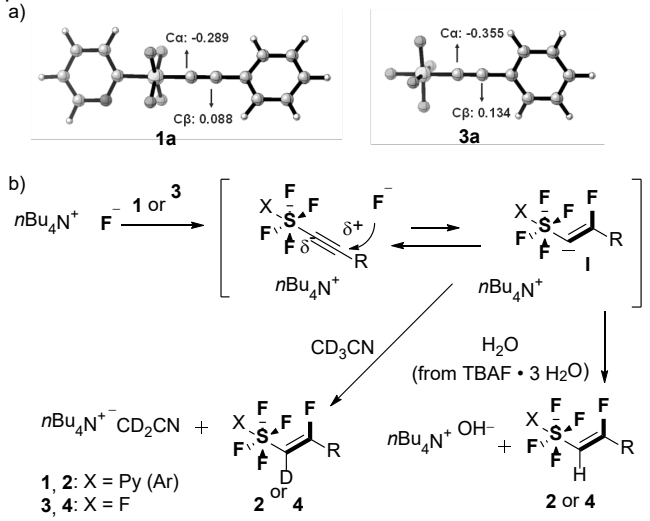
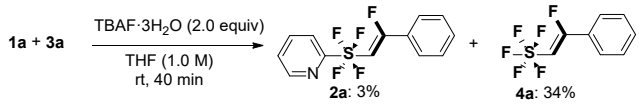


Figure 3. a) Mulliken charges of **1a** and **3a** determined by DFT calculations (B3LYP-D3/Def2TZVPP in THF). b) Proposed reaction mechanism.

Finally, DFT calculations were performed to confirm the proposed reaction mechanism.[16] To this end, DFT calculations were performed with Gaussian 16 using the hybrid B3LYP functional with dispersion correction (B3LYP-D3) and the valence triple-ζ-type basis set Def2TZVPP. The solvent effect (THF) was evaluated implicitly using the SMD continuum solvation model. Tetramethylammonium fluoride (TMAF) was used instead of TBAF for computational simplicity to reduce computational cost.[17] The Gibbs energy profile for the reaction of **3a** is shown in **Figure 2.** A comparison between the reaction leading to the vinyl anions *Z* and *E* intermediate **I** indicated the formation of **I-*Z*** ($\Delta G^{\ddagger}$ = 15.3 kcal/mol) is faster than that leading to **I-*E*** ($\Delta G^{\ddagger}$ = 19.0 kcal/mol), with **I-*Z*** being slightly more stable (ΔG_R =3.2 kcal/mol) than **I-*E*** (ΔG_R =5.6 kcal/mol). The energy difference of $\Delta G^{\ddagger}$ = 3.7 kcal/mol for both alternative reaction pathways is in line with a possible anionic reaction mechanism that yields the *Z*-configured vinyl anion with excellent diastereoselectivity. A closer look at the transition states structures reveals that the process leading to the formation of the *Z*-product, which proceeds via an earlier transition state (F···C distance of 1.98 Å vs 1.92 Å for **TS1-*Z*** and **TS1-*E***, respectively, Figure 2), has a lower activation barrier, in accordance with Hammond's postulate. Fast proton exchange with water through **TS2** delivered the desired product **4**. To exclude very fast interconversion, the barrier for interconversion of the formed products was calculated. The potential product interconversion shows a high barrier of interconversion with a $\Delta G^{\ddagger}$ = 49.8 kcal/mol, which is predicted to cause a very slow isomerization and equilibration of the formed products **4-*E*** and **4-*Z***. Protonation by CH_3CN, as shown by deuterium labeling experiments, was also investigated and was found to deliver the desired **4-*E*** and **4-*Z*** alkenes with similar exergonicities. Therefore, our theoretical calculations support a mechanistic proposal based on the nucleophilic attack of fluorides on SF_5-alkynes and the formation of the *Z*-isomer with excellent diastereoselectivity. The reactivity difference between SF_4-alkynes **1** and SF_5-alkynes **3** was investigated, and the computed Gibbs energy barrier for SF_4-alkyne with a pyridine ring was found to be 4.2 kcal/mol higher, in line with the experimental observation of longer reaction times for SF_4-alkyne derivatives. A comparison of both TS structures shows an earlier TS for the attack to alkyne **3** (1.98 Å) compared to the attack to Py-SF_4-alkyne **1** (1.91 Å), in line with a lower activation barrier for SF_5-alkyne **3**. Finally, a competitive experiment was conducted using a 1:1 mixture of **1a** and **3a** under optimized conditions for 40 min. In line with the higher reaction rate for **3a**, the corresponding SF_5-vinyl fluoride **4a** yielded 34%, whereas SF_4-vinyl fluoride **2a** was formed only 3% (Scheme 6).



Scheme 6. A competitive experiment. Reaction conditions: **1a** (0.1 mmol), **3a** (0.1 mmol), TBAF · $3H_2O$ (0.4 mmol) in THF (0.2 mL), under N_2 at room temperature for 40 min. ^{19}F-NMR yields were shown.

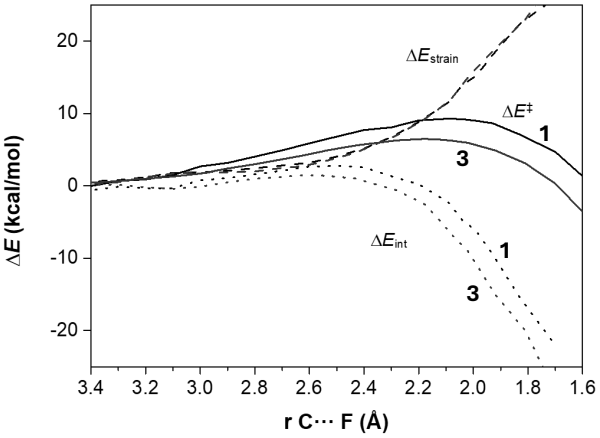


Figure 4. Activation strain diagrams computed (at B3LYP-D3/Def2TZVPP level of theory) along the IRC for the pathway via TS leading to the formation of the *Z*-product for the nucleophilic attack of fluoride at the β-carbon of alkyne **1** (black lines) and **3** (red lines).

To gain more insight into the difference in reactivity, we applied the activation strain model (ASM) developed by Houk and Bickelhaupt.[16] According to this approach, the activation energy for the attack of fluoride at the β-carbon of the alkyne can be decomposed into two contributions: the strain (ΔE_{strain}), which quantifies the energy required to distort the reactants, and the interaction (ΔE_{int}) terms. Figure 4 shows the corresponding activation strain diagram for the entire reaction coordination ζ (selected as the C···F bond-forming distance) for the nucleophilic attack of fluorine on the β-carbon of alkynes **1** and **3** leading to the formation of the *Z*-product. As shown in Figure 4, the ΔE_{strain} term is nearly identical for nucleophilic attack on both alkynes. However, the interaction term (ΔE_{int}) between the reactants is more stable for the process involving SF_5-alkyne **3**, indicating that this term is responsible for the experimentally observed higher reactivity of SF_5-alkynes. The higher interaction energy for SF_5-alkyne **3** can be correlated to a more accessible LUMO compared to Py-SF_4-alkyne **1** (-1.83 vs -1.63 eV, see Figure S1).

Although the exact influence of water on this process is unclear, our computational findings revealed a difference in the energy barrier for solvation with water. As demonstrated by the DFT calculations (Figure 5), the presence of one molecule of water led to a decrease in the barrier for the transition state without water (19.6 kcal/mol). As the number of water molecules increased, the Gibbs energy barrier increased, and the TS state became later as the C···F forming bond length decreased. Interestingly, the Gibbs energy barrier using water as the solvent increased to 27.1 kcal/mol, supporting the experimental observation that no reaction occurred with 10 equivalents of water at room temperature (Table 1, entries 7 and 23). These results imply that an appropriate amount of water is essential for a seamless transformation. However, further research is required to gain a comprehensive understanding, as the reactivity of fluoride is significantly influenced by hydrogen bonding.[13b,19]

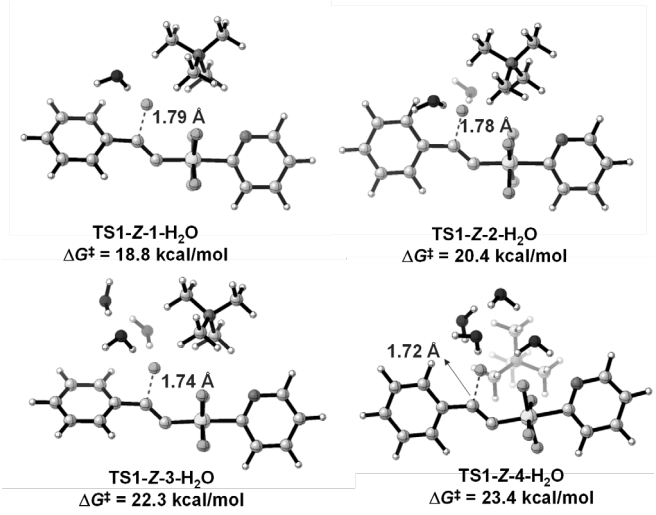


Figure 5. Optimized structures (showing the C···F forming bond length) and Gibbs activation barriers for TS leading to the *Z*-isomer with different water molecules (from 1 to 4).

In summary, we have identified a direct and stereoselective method for synthesizing the *Z* isomer of vinyl fluorides from alkynes containing unexplored SF_5 and SF_4 groups. Our proposed approach uses tetrabutylammonium fluoride (TBAF) as a fluorine source and is compatible with aryls, biaryls, and heteroaryls, allowing for the easy incorporation of SF_5 and SF_4 groups across the triple bond without the need for transition-metal catalysts. This transformation can occur at room temperature without any additional additives, yielding the *Z*-isomer of vinyl fluorides with a high efficiency and selectivity. The successful conversion of TBAF requires the presence of a water molecule as a hydrate. This study addresses these limitations by presenting a transition-metal-free strategy that avoids the potential decomposition of SF_5 or SF_4 units via coordination with transition metals or acidic protic sources. This approach provides new possibilities for the synthesis of fluorinated vinylic scaffolds containing SF_5 and SF_4, which may lead to the discovery of novel drugs and fluorinated polymers. Finally, it should be noted that the use of CF_3 molecules as refrigerants, blowing agents[20] and agrochemicals[21] is a contentious issue because of their propensity to decompose into environmentally detrimental trifluoroacetic acid. Moreover, the environmental consequences of employing highly CF_3- and CF_2-laden substances, such as perfluoroalkyl substrates (PFAS)[22] are also a subject of debate. Consequently, SF_5- and SF_4-molecules may be appealing alternatives to CF_3-substrates and related compounds. We are currently investigating in this direction.

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Keywords: fluorination• hydrofluorination • alkynes• pentafluorosulfanyl• tetrafluorosulfanyl

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[16] See Supporting Information for more computational details.

[17] The use of TBAF instead of TMAF also leads to the formation of the *Z* isomer with high selectivity, with an energy difference between the two competing TS of $\Delta\Delta G^{\ddagger}$ = 6.4 kcal/mol (Figure S2 in the Supporting Information).

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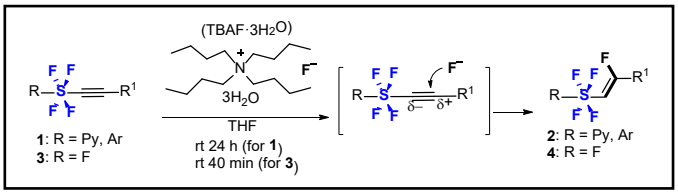

A transition-metal-free and stereoselective approach to the synthesis of *Z*-vinyl fluorides from alkynes containing unexplored SF_5 and SF_4 groups has been reported. TBAF·$3H_2O$ exhibits high compatibility, allowing for the easy incorporation of fluoride into SF_5 and SF_4 alkynes at room temperature. Competitive experiments and DFT calculations verified that SF_5 alkynes react much faster than SF_4 alkynes do.