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Streamlining Fluoroalkenyl Arene Synthesis Illuminated with Mechanistic Insights

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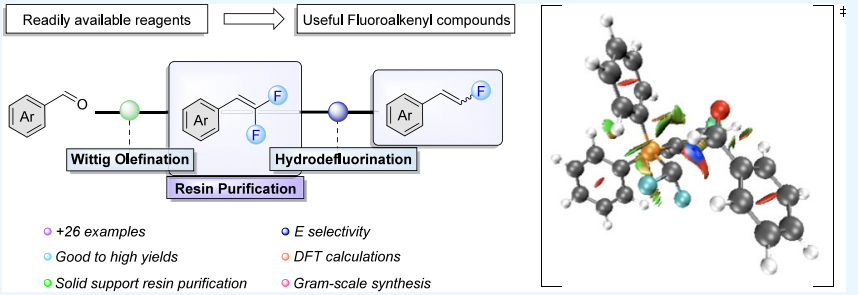

ABSTRACT: Fluorinated compounds are a staple of modern-day chemical innovation, and efficient strategies for their synthesis are highly valuable. In this chemical space, fluoroalkenes continue to be the object of much interest across diverse fields, including drug development and pharmaceuticals with active roles as bioisosteres. Herein, in expanding chemists' synthetic toolbox for constructing valuable organofluorine compounds, we report a "pipeline" strategy for the synthesis of fluorinated olefins, *viz.*, *gem*-difluoroalkenyl and monofluoroalkenyl arenes with high *E*-isomeric selectivity. The advantages of this streamlined synthetic protocol include mild reaction conditions, operational simplicity, broad substrate scope, and good to excellent yields, even at gram scales. Critical to this robust procedure is the use of widely available and inexpensive "scavenger" solid-support Merrifield peptide resin for removing phosphine impurities. Further computational investigations offering clarity into this reactivity are disclosed.

INTRODUCTION

Modern-day organic synthesis hinges upon efficiency and well-understood mechanisms for securing important chemical targets, such as organofluorine compounds. In this chemical space, growing interest in fluorinated compounds and strategies for their streamlined synthesis is of utmost importance.[1,2] In highlighting this status, is an impressive global market of fluorinated compounds, estimated at approximately 20 billion (USD) in the year 2022 and extensive applications in drug development, pharmaceutical synthesis, chemical biology, ion sensing, self-assembly, fluorescence, materials chemistry, and mechanochemistry.[1−3]

Prompting much of this attention is the innate makeup of fluorine, e.g., high electronegativity and small ionic radius (1.33 Å), making it the prototypical small atom with a "big ego".[4] Collectively, these attributes confer desirable physiochemical properties to organofluorine compounds. For example, organofluorine compounds benefit from fluorine's inherent ability to improve and finetune the solubility, lipophilicity, permeability, protein binding, and overall bioavailability of drug candidates.[1,5] As a result, approaches for the controlled and selective synthesis of organofluorine compounds are highly sought after.[6]

Among important organofluorine compounds, those containing monofluoroalkenyl groups find numerous applications[7] and serve as nonhydrolyzable biomimetics of amides (Scheme 1a)[8] as well as valuable fluorinated synthons for the synthesis of organofluorine compounds.[9] Likewise, *gem*-difluoroalkenyl groups are of great interest in various fields, especially in drug development, owing to their potential to act as carbonyl group bioisosteres for improving the bioavailability of drug candidates (Scheme 1b).[10] Moreover, attesting to the presence and significance of fluoroalkenyl groups in nature are a number of bioactive compounds (Scheme 1c,d).[10−12]

To date, considerable effort has been made to develop efficient methods for the preparation of *gem*-difluoroalkenyl compounds.[13] This has led to three general approaches for their construction, comprising (1) use of moisture-sensitive organometallic reagents such as *gem*-difluorovinyl lithium or borane reagents along with carbonyl electrophiles,[14] (2) *β*-elimination strategies requiring tedious multistep preparations of fluorinated precursors,[15] and (3) Julia, Horner−Wadsworth−Emmons (HWE), or Wittig reactions of aldehydes and

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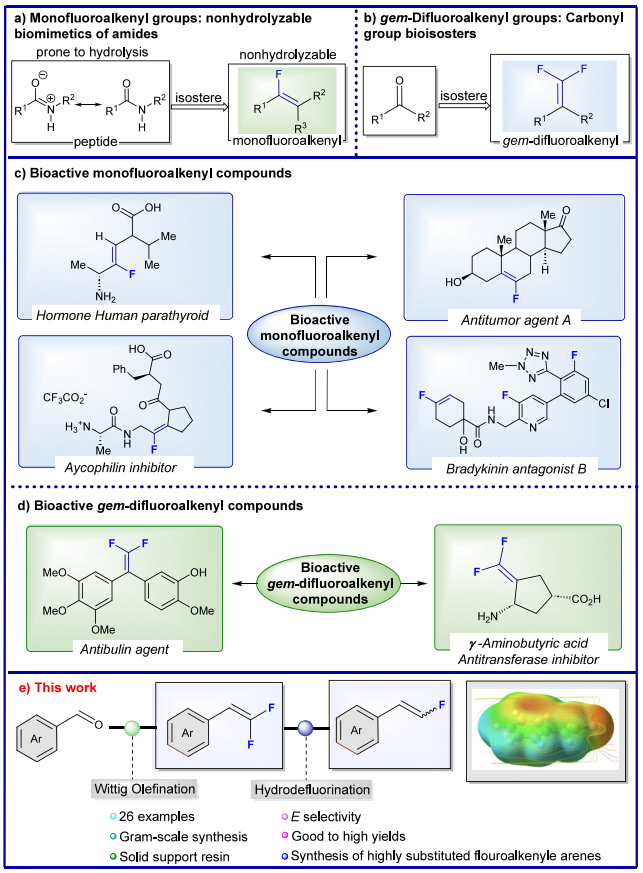
Scheme 1. (a) and (b) Fluoroalkenyl Bioisosters,[8,10] (c) and (d) Examples of Fluoroalkenyl-Containing Drugs and Natural Products,[9−12] and (e) Current Synthesis of *gem*-Difluoroalkenyl and Monofluoroalkenyl Arenes



ketones with CF_2 equivalents.[16] Of these approaches, the Wittig reaction is one of the most straightforward and widely used methods, although removal of stoichiometric byproduct triphenylphosphine oxide (TPPO) formed from these olefinations is often a serious limitation in practice.[17]

Meanwhile, efficient selective synthetic routes to preparing monofluoroalkenyl compounds continue to attract the attention of many researchers. Prior approaches to these valuable compounds have included C−F bond cleavage of *gem*-difluoroalkenes[18,19] under reductive conditions.[18a] Complementary to these synthetic approaches is the 1,2-addition of strongly nucleophilic organometallic species, e.g., organolithium or organomagnesium reagents, coupled to β-fluorine elimination, and protodemetalation to afford monofluoroalkenyl groups is known with limited scope.[21] Cross-metathesis employing Mo-alkylidene complexes and excess monosubstituted fluoroethylenes is also recently reported to furnish monofluoroalkenyl compounds.[22] Using noble transition metal catalysts, the monofluorination reaction of various di- and trisubstituted styrenes has been achieved with a combination of $RuCl_3$ catalyst and stoichiometric *N*-fluorobenzenesulfonimide (NFSI).[23] Furthermore, Wittig olefination[24] using phosphonium monofluoromethylides and Julia−Kocienski olefination[25] are classic methods for converting aldehydes and ketones to monofluoroalkenyl groups, although these methods generally suffer from poor *Z*- and *E*-alkene selectivity. The conversion of aldehydes into *Z*- and *E*-(1-fluoroalkenyl)-phosphonium salts followed by alkaline hydrolysis is also known although limited in scope and isolated yield.[26] Lastly, a transition metal-free decarboxylative fluorination of α,β-unsaturated carboxylic acids with an excess of base and costly Selectfluor affords β-fluorostyrene with low to moderate yields and *Z*-selectivity.[27]

Despite this significant progress, most previous methods suffer from one or more drawbacks. This includes narrow substrate scope, low isomer selectivity, lack of generality, overreduction, difficulty removing unreacted triphenylphosphine and byproduct TPPO, and use of transition metals. Thus, development of efficient modern-day methods for the synthesis of *gem*-difluoroalkenyl and monofluoroalkenyl compounds with high selectivity is desirable and needed.[28] In light of these limitations, herein, we wish to report a direct and practical method for the synthesis of *gem*-difluoroalkenyl and monofluoroalkenyl arenes with high *E*-isomeric selectivity. This operational simple "pipeline"-type approach uses plentiful, commercially available substrates and reagents, mild reaction conditions, and provides fluorinated alkenes products in good to excellent yields (Scheme 1e). Furthermore, is the strategic use of widely available and inexpensive solid-support Merrifield peptide resin as a scavenger for sequestering triphenylphosphine and byproduct TPPO, thus simplifying experimental purification of the fluorinated alkene products. Moreover, the utility of this procedure is demonstrated at gram scales showing its value for challenging TPPO removal. Collectively, this use represents the first report of solid-support resins being employed as scavengers for removing phosphine impurities from Wittig-type olefinations furnishing fluoroalkene products. Notably, TPPO is a byproduct of many common organic reactions often making product isolation difficult while negatively impacting reaction yields and making for time-consuming and tedious purification processes (e.g., chromatography) that, although efficacious on a small scale, halt progress and production in large-scale operations. Lastly, mechanistic studies providing clarity into this reactivity, e.g., the role of reactive ylide $Ph_3P=CF_2$ vs phosphonium stabilized α-carbanion $Ph_3P^+—CF_2^-$ or "free"-difluorocarbene in the synthesis of *gem*-difluoroalkenyl groups is disclosed. Noteworthy, the events for formation of ylide $Ph_3P=CF_2$, presumably via generation of difluorocarbene from sodium chlorodifluoroacetate ($ClCF_2CO_2Na$) and phosphine, have been investigated, although several significant facets of this reactivity remain uncertain and ill-defined.

RESULTS AND DISCUSSION

At the outset of this work, requiring fluoroalkenyl compounds for related studies probing the effect of fluorine substitution upon the reaction rates of olefins, we realized there was a need for efficient synthetic protocols for their preparation as well as limited commercial sources and often high cost of these organofluorine compounds. Moreover, our initial attempts using reported chemistries to prepare these compounds were plagued with challenges and failures. Foremost in this endeavor was the purification and isolation of fluorinated alkenyl compounds, which was complicated by issues of volatility, poor *E*- vs *Z*-alkene selectivity for monofluorinated alkenes, and difficulties in removal of byproducts hampering purification efforts. For instance, traditional Wittig olefination-based approaches leveraging the use of phosphines and difluorocarbene or synthetic equivalents were complicated by

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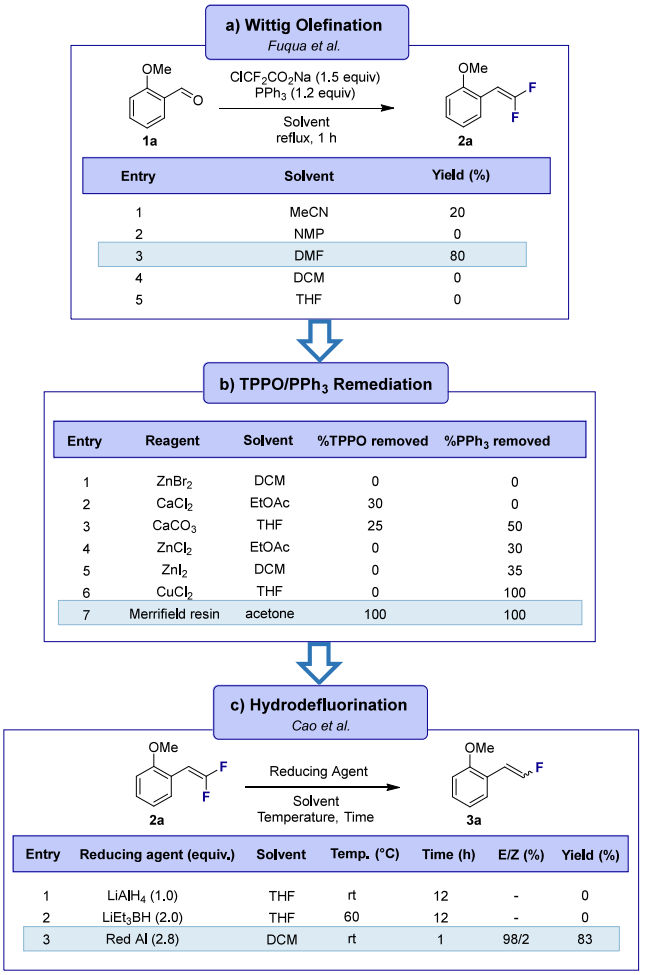
the formation of stoichiometric amounts of effluent TPPO and residual unreacted triphenylphosphine.

To overcome these limitations, we turned to optimization studies with the aim of developing a robust synthesis of monofluoroalkenyl arenes with high *E*-isomeric selectivity that also provided for the preparation of *gem*-difluoroalkenyl arenes. To this end, informed by the work of Fuqua and co-workers,[29] an initial solvent scan using benzaldehyde (**1a**), $ClClF_2CO_2Na$, and triphenylphosphine for Witting olefination revealed DMF as the optimal solvent at 80 °C (Scheme 2a). Subsequently, to

Scheme 2. Flowchart of Optimization Process for the Streamlined Synthesis of Monofluoroalkenyl Arenes[a]



Entry	Solvent	Yield (%)
1	MeCN	20
2	NMP	0
3	DMF	80
4	DCM	0
5	THF	0

Entry	Reagent	Solvent	%TPPO removed	%PPh_3 removed
1	$ZnBr_2$	DCM	0	0
2	$CaCl_2$	EtOAc	30	0
3	$CaCO_3$	THF	25	50
4	$ZnCl_2$	EtOAc	0	30
5	ZnI_2	DCM	0	35
6	$CuCl_2$	THF	0	100
7	Merrifield resin	acetone	100	100

Entry	Reducing agent (equiv.)	Solvent	Temp. (°C)	Time (h)	E/Z (%)	Yield (%)
1	$LiAlH_4$ (1.0)	THF	rt	12	-	0
2	$LiEt_3BH$ (2.0)	THF	60	12	-	0
3	Red Al (2.8)	DCM	rt	1	98/2	83

[a](a) Solvent scan for Witting olefination.[29] (b) Remediation of phosphines using salts and Merrifield resin. (c) Survey of reducing agents for hydrodefluorination.[32]

mitigate issues of removing byproduct TPPO generated from this Wittig olefination step—that in our hands proved reliable for forming *gem*-difluoroalkenyl arenes from aldehydes—we investigated precipitation of TPPO by complexation with metal halide salts. In this endeavor, it was anticipated that insoluble Lewis acid−TPPO adducts would form that could be removed from the crude reaction mixtures by filtration without the need for purification by column chromatography. In exploring the potential of this remediation strategy, several salts and different organic solvents were examined with our selection, in part directed by previous reported methods for removing TPPO[30] (Scheme 2b). From these investigations, limited success was achieved at small scales (100−500 mg) making this approach far from infallible with residual TPPO being ever present. Inspired by the excellent works of Lipshutz and Blomgren,[31] our efforts shifted to the use of inexpensive solid-support Merrifield peptide resin as a scavenger of unreacted PPh_3 and byproduct TPPO. To our satisfaction, upon scanning different solvents, time, and resin loadings, it was revealed that the use of Merrifield peptide resin under optimized conditions (entry 7, Scheme 2b) provided a reliable means for removing residual PPh_3 and TPPO. Indeed, this remediation step involved the simple addition of Merrifield peptide resin to the crude reaction mixture of Wittig olefination, stirring, filtration, and solvent removal.

Having a viable solution for TPPO removal and purification of *gem*-difluoroalkenyl arenes (Scheme 2b), our focus shifted to identifying conditions for selective hydrodefluorination while mindful of the work of Cao et al.[32] In this interest, various reducing agents were tested, including $LiAlH_4$ and $LiEt_3BH$, resulting in overreduction or a mixture of *E*- and *Z*-monofluoroalkenyl arene isomers (Scheme 2c, entries 1 and 2).[33] Notwithstanding, the use of 2.8 equiv of Red-Al in DCM to our satisfaction afforded monofluoroalkenyl arene **3a** with excellent *E*-selectivity along with a minor amount of the *Z*-isomer (Scheme 2c, entry 3).

SUBSTRATE SCOPE

We then sought to explore the generality of our fluoroalkenyl-forming protocol. Accordingly, various carbonyl substrates were reacted under the optimized reaction conditions (Scheme 2). First, benzaldehydes bearing various methoxy substituents at the *ortho*, *meta*, and/or *para* positions were tested to provide Wittig olefination products (**2a**−**2e**) in good yields. Likewise, *para*-benzyloxy- and ethyloxy-substituted products **2f** and **2g** were formed in good to moderate yields while piperonal reacted to afford *gem*-difluoroalkenyl arene **2h** in 80% yield. In a similar fashion, naphthyl-containing substrates were converted to targeted fluorinated alkenes (**2i**, **2j**), although 6-methoxy substitution (**2j**) led to a slight decrease in yield. Furthermore, *gem*-difluoroalkenes containing biphenyl and *para*-thiomethyl moieties (**2k**, **2l**) were generated in high yields while electron-deficient arenes (**2m**, **2n**) reacted to give products in moderate yields. In contrast, aryl ketone-derived products (**2o**, **2p**) were not formed resulting in the recovery of unreacted starting materials. Incidentally, critical for isolating these *gem*-difluoroalkenyl arenes in high purity was the strategic use of inexpensive solid-support Merrifield peptide resin as a scavenger for removing phosphine impurities.

Conversion of the synthesized *gem*-difluoroalkenyl compounds to *E*-isomeric monofluoroalkenyl compounds was subsequently achieved in moderate-to-high yields (**3a**−**3l**; 70−92% yield, *E*/*Z* up to 98/2). For example, the selective reduction of *gem*-difluoroalkenyl arenes with electron-donating groups, such as **2a**−**2g**, provided the desired *E*-monofluoroalkenyl arene products **3a**−**3g** in good to excellent yields. In addition, 1,3-benzodioxole (**3h**), naphthyl (**3i**), and 6-methoxynaphthyl (**3j**) arene products were prepared in high yields. Likewise, biphenyl derivative **3k** and *para*-thiomethyl **3l** were afforded with excellent *E*-selectivity in good to high yields. Meanwhile, the reaction of electron-deficient aromatic substrates with *para*-Cl and Br substitution resulted in the desired product along with inseparable impurities. Finally, our streamlined approach benefiting from the use of solid-support Merrifield resin as a PPh_3 and TPPO scavenger was applied to

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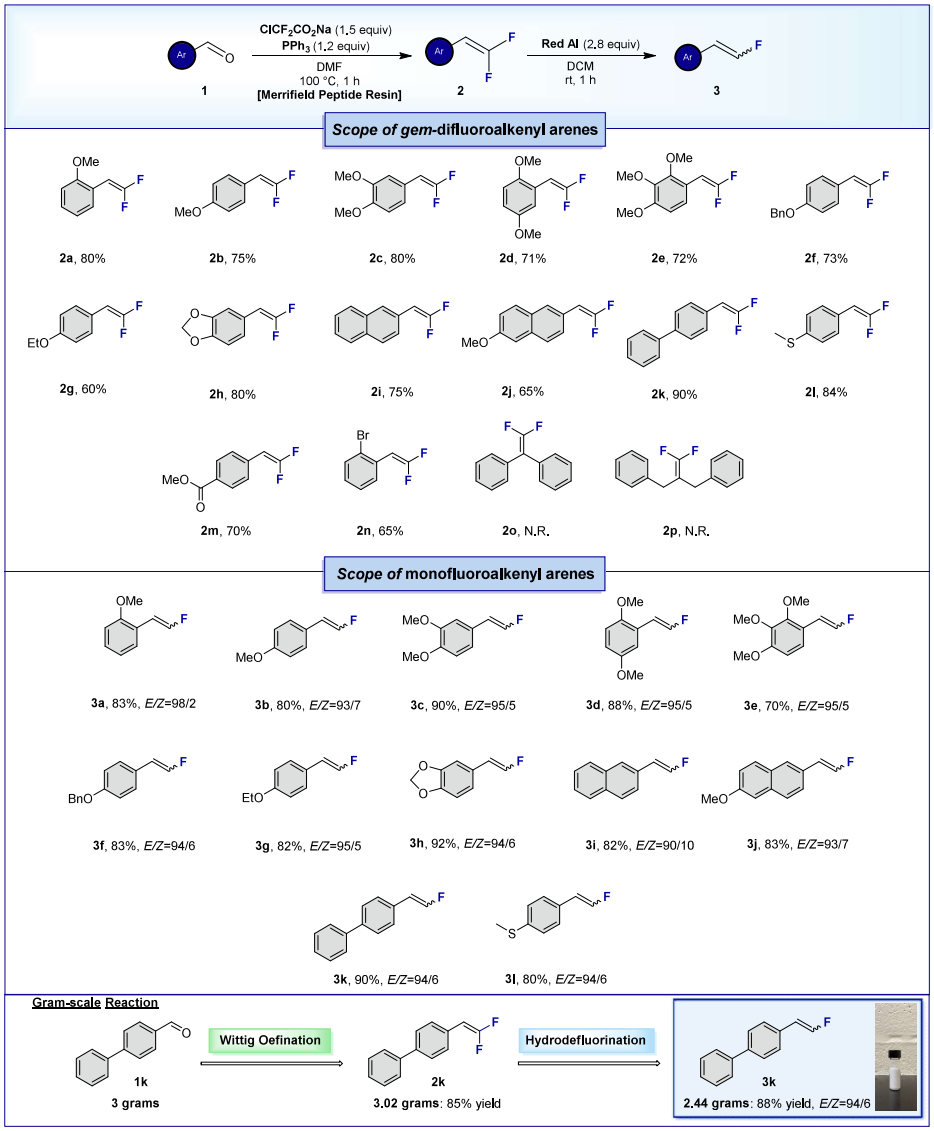
Table 1. Substrate Scope of *gem*-Difluoroalkenyl (2a−p) and Monofluoroalkenyl (3a−l) Arene Compounds[a,b]



[a]The E/Z selectivity of monofluoroalkenyl products was determined by ^{19}F NMR. [b]Yields reported based on isolated products.

the gram-scale synthesis of (E/Z)-monofluoroalkenyl arene **3k** in respectable yield with high selectivity (E/Z = 96:4) (Table 1).

In terms of the high levels of *E*-monofluoroalkene selectivity, this aspect may be rationalized by the computed transition-state $\mathbf{TS_{Red}1}$ with a Gibbs free activation energy ($\Delta G^{\ddagger}$) of approximately 20 kcal/mol relative to its precomplex (Scheme 3). The defining features of this structure correspond to an Al−H bond breaking and C−H bonding forming distances of 1.72 and 1.46 Å, with the chelated sodium cation nearby the arene ring.

Upon hydride transfer, a barrierless loss of fluoride anion to the Lewis acidic aluminum metal center with relief of a repulsive C−H•••F steric interaction between aryl and vinyl fluoride ensues as a highly favorable exergonic event (ΔG° = −83.7 kcal/mol), resulting in *E*-monofluoroalkenyl group formation.

Next, to better understand the underlying mechanism of these Wittig olefinations, with an emphasis placed upon difluorocarbene and ylide $Ph_3P = CF_2$ vs. phosphonium-stabilized α-carbanion $Ph_3P^+—CF_2^-$ reactivity, we turned to the use of dispersion-corrected DFT calculations at the (IEFPCM = DMF) ωB97X-D/6-31+G(d,p) level of theory[34,35] using the Gaussian 16 software package.[36] Notably, difluorocarbene has been the subject of various computational studies, confirming the ability of fluorine to impart significant stabilization while contributing to a large singlet (S) and triplet (T) state energy gap with the singlet being the ground state.[37] Meanwhile, the *in situ* trapping of difluorocarbene by triphenylphosphine to form ylide $Ph_3P = CF_2$[29] vs. "free" difluorocarbene is of interest.[38] In particular, previous studies probing the binding and structure of ylide $Ph_3P = CF_2$ or α-carbanion $Ph_3P^+—CF_2^-$ uncovered discrepancies and, furthermore, the potential role of explicit solvent participation in this reactivity was neglected.[39,40] Based upon these prior studies and aspects pertinent to this work, we investigated the following mechanistic scenarios: (1) $ClCCF_2CO_2Na$ decomposition to difluorocarbene ($:CF_2$) and capture by triphenylphosphine and/or solvent (mechanism A, pathway 1)[29,39,41] and (2) generation of (triphenylphosphonio)difluoroacetate

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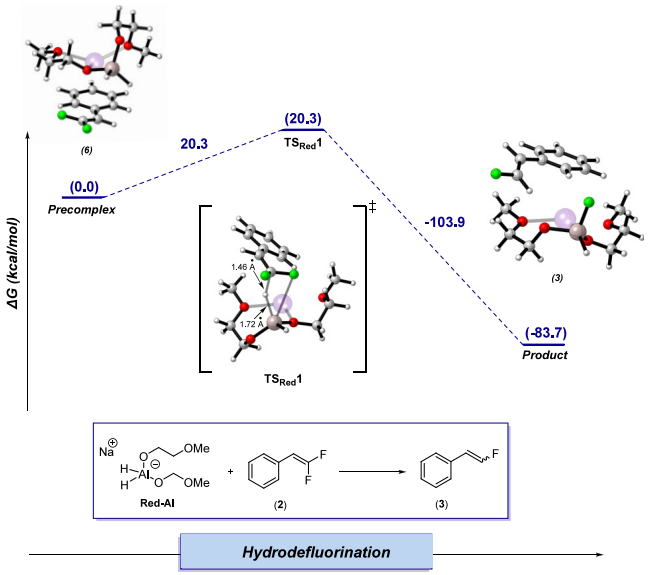
Scheme 3. Transition-State Geometry and Relative Energies for Red-Al-Mediated Hydrodefluoration[a]



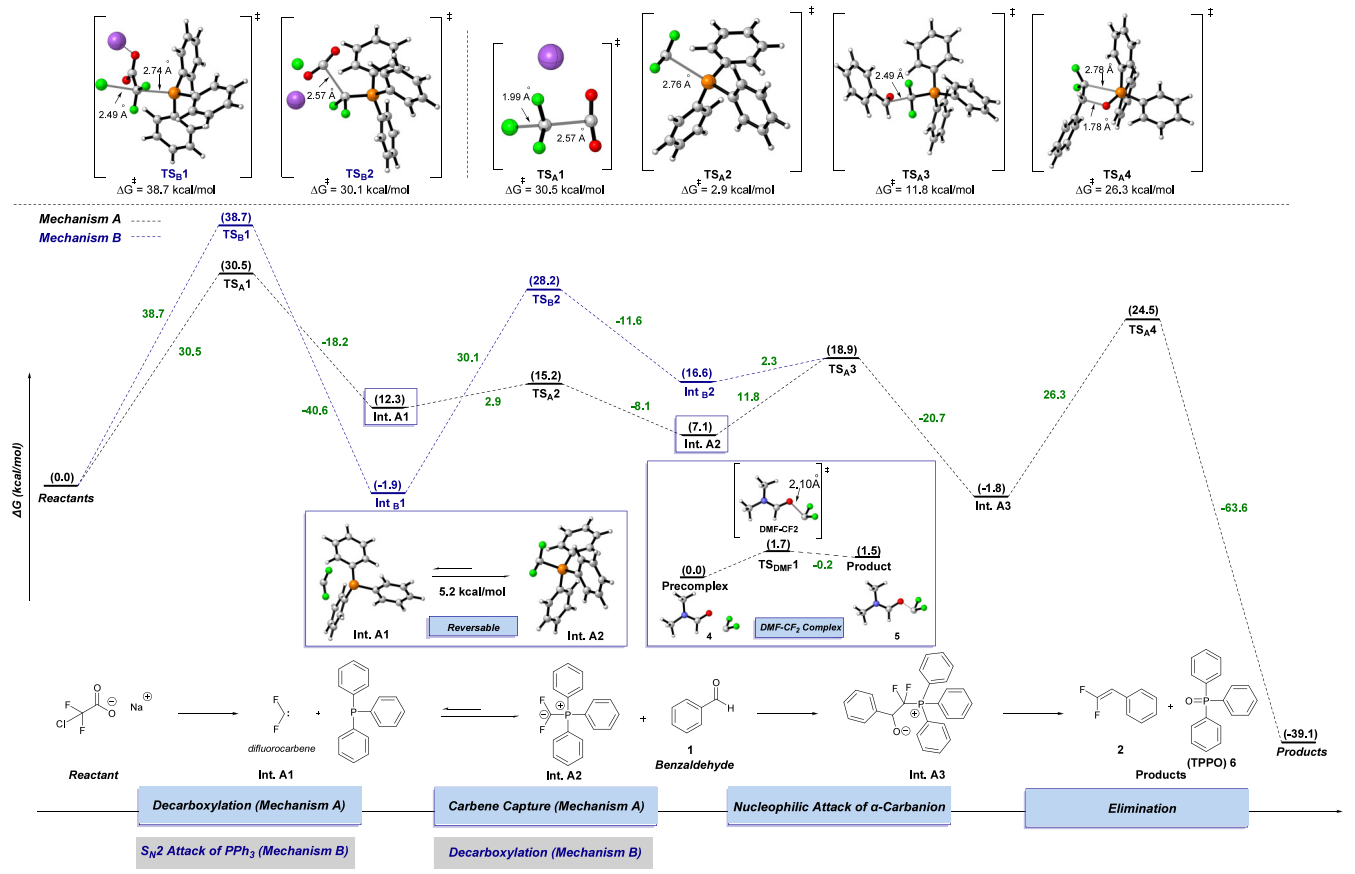
[a]All energies (kcal/mol) were computed at the (IEFPCM = DCM) ωB97X-D/6-31G(d,p) level of theory.[34,35]

(Ph_3P^+-$CF_2CO_2^-$, PDFA) and its subsequent decarboxylation (mechanism B, pathway 2).[39,40] Coupled to these processes were Wittig-type olefinations providing fluorinated alkene products. As a corollary, the following question prevailed: To what extent, if any, do alkali cations have in these olefination reactions, which are largely assumed to be innocuous, despite well-known salt effects in traditional Wittig olefinations?[42]

In exploring mechanism A (pathway 1), initial decarboxylation of $ClCF_2CO_2Na$ was found to be energetically demanding with Gibbs free activation barriers of approximately 30.5 kcal/mol via transition states $\mathbf{TS_A1}$ (Scheme 3). Noticeably, this decarboxylation transition state displayed elongated C−C and short C−Cl bond-breaking distances linked to the loss of CO_2. Next, carbene trapping by phosphine furnished intermediate **Int. A2** with a moderate barrier ($\Delta G^{\ddagger}$ = 2.9 kcal/mol) while, as an intriguing alternative for possibly increasing the lifetime of difluorocarbene, carbene capture by DMF, the experimental solvent, resulted in adduct **5** via $\mathbf{TS_{DMF}1}$ with a barrier of 1.7 kcal/mol.

As for intermediate **Int. A2**, this species is perhaps better defined as a phosphonium-stabilized α-carbanion Ph_3P^+—CF_2^- with a significant sp^3 character at carbon (C(1)) rather than an ylide $Ph_3P = CF_2$. Corroborating this view was the significant computed negative-charge buildup at carbon C(1) (Mulliken = −0.39 e) and the presence of a lone pair, as shown from the highest occupied molecular orbital (HOMO) and electrostatic potential (ESP) isosurfaces (Figure 1a). Furthermore, in probing α-carbanion stabilization, the role of sodium cation was found to be one of a bystander with a slightly unfavorable binding affinity of 3.8 kcal/mol, much like that of other cations (Figure 1b).

Scheme 4. Proposed Mechanism A (Favored) vs Mechanism B (Unfavored)[a]



[a]All energies (kcal/mol) were computed at the (IEFPCM = DMF) ωB97X-D/6-31+G(d,p) level of theory.[34,35]

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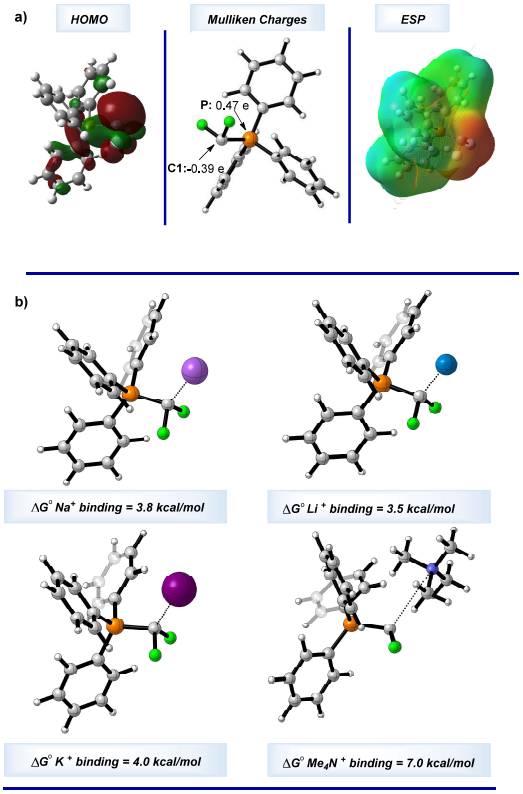

Figure 1. (a) Computed HOMO of phosphonium-stabilized α-carbanion $Ph_3P^+—CF_2^-$; Mulliken charge values of C1 and P for **Int. A2**; and electrostatic potential surface computed at the ωB97X-D/6-31+G(d,p) level of theory (isovalue = 0.05). (b) Computed phosphonium-stabilized α-carbanion $Ph_3P^+—CF_2^-$ complexation with Na^+, Li^+, K^+, and Me_4N^+ displaying unfavorable binding affinity.

Nucleophilic attack of α-carbanion $Ph_3P^+—CF_2^-$ (**Int. A2**), upon the carbonyl carbon of aldehyde **1**, then generates zwitterionic betaine intermediate **Int. A3** *via* $\mathbf{TS_A3}$ with an activation energy of 11.8 kcal/mol, linked to C−C bond formation measuring 2.49 Å. Irreversible retro-[2 + 2] elimination follows to generate 1,1-difluoroalkene (**2**) and TPPO via transition-state $\mathbf{TS_A4}$ ($\Delta G^{\ddagger}$ = 26.3 kcal/mol), a process driven by thermodynamically favorable P═O double bond formation with C−O and C−P bond breaking distances of 1.78 and 2.78 Å, respectively.

By contrast, mechanism B (pathway 2) proceeds with initial S_N2 attack of phosphine and chloride anion displacement incurring a barrier of 38.7 kcal/mol, making this pathway less competitive to mechanism A. Transition-state $\mathbf{TS_B1}$ for this transformation displayed C−P bond making and C−Cl bond breaking distances of 2.74 and 2.49 Å, respectively, with sodium cation aiding loss of the emerging nucleofuge chloride anion. The resulting zwitterion intermediate **Int. B1** then undergoes decarboxylation with an activation barrier $\mathbf{TS_B2}$ ($\Delta G^{\ddagger}$ = 30.1 kcal/mol) to afford α-carbanion $Ph_3P^+—CF_2^-$ (**Int. B2**). It is worth mentioning that these computed findings contrast with a previous work, reporting that the rate of thermal decomposition of $ClCF_2CO_2Na$ was accelerated by triphenylphosphine.[40] Next, like that of mechanism A, nucleophilic attack of α-carbanion $Ph_3P^+—CF_2^-$ upon the aldehyde electrophile (**1**) affords zwitterionic betaine-type intermediate **Int. A3** and ensuing irreversible retro-[2 + 2] elimination affords the *gem*-difluoroalkenyl product.

From these findings, several points deserve mention, including the findings relating to difluorocarbene formation and the role of solvent and phosphine binding in the mechanisms of these Wittig olefinations. Ultimately, as revealed from our calculations, this and other elements conspire to make pathway A favored. Finally, as a worthy alternative to existing approaches, our reported protocol offers a simple and efficient means for preparing fluorinated alkenes while demonstrating the value of resin technologies as useful tools for purification in organic synthesis.

CONCLUSIONS

In summary, we have reported an efficient, selective, and practical streamlined synthesis of *gem*-difluoroalkenyl and monofluoroalkenyl arenes in good to high yields. The success of this procedure, in part, benefits from the unique use of widely available and inexpensive solid-support Merrifield peptide resin for removal of phosphine impurities. What is more, in the broader context of informing future directions, computational findings offering clarity into this reactivity were disclosed. Lastly, owing to the practicality of this method for preparing fluoroalkenes of much interest in various fields, including in drug development and pharmaceuticals with roles as bioisosteres, it is anticipated that our streamlined approach will find greater use among chemists.

EXPERIMENTAL SECTION

General Information. Materials were obtained from commercial suppliers (Sigma-Aldrich and Oakwood Chemical) and were used without further purification unless otherwise stated. All solvents were purchased from Fisher Scientific and dried by distillation under a nitrogen atmosphere prior to use. All reactions were conducted under an inert atmosphere (N_2) in oven-dried glassware with magnetic stirring. Reactions were monitored by thin layer chromatography (TLC) performed on 200 μm silica-gel plates from Millipore-Sigma. Flash column chromatography was performed over Silicycle UltraPure silica gel (230−400 mesh). NMR spectra were obtained with a Bruker DPX 400 (^{1}H 400 MHz, ^{13}C 100.6 MHz, ^{19}F 376.6 MHz) in $CDCl_3$ unless specified otherwise. Chemical shifts were reported in parts per million (ppm, δ). Mass spectra were obtained on a Thermo Double Focusing Sector (DFS) Mass Spectrometer.

Synthesis of gem-Difluoroalkenyl Compounds (Procedure A). To a two-necked round-bottom flask equipped with a magnetic stir bar and charged with aldehyde (1 equiv), PPh_3 (1.2 equiv), and dry DMF (0.5 mol/L for aldehyde) was added a solution of sodium chlorodifluoroacetate (1.5 equiv) in DMF (2 mol/L) dropwise at 100 °C over 30 min (caution: During the course of the reaction, internal pressure increased due to vigorous liberation of CO_2 gas). The resulting mixture was heated at the same temperature under reflux for 1 h. After cooling to 0 °C, to the reaction mixture was added with water and extracted with Et_2O. The combined organic extract was washed with water and brine and then dried over Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford the corresponding *gem*-difluoroalkenyl products.

In procedure A (mentioned above), the scaled-up reaction was also applied using 3 g of 4-phenybenzaldehyde resulting in 4-(2,2-difluorovinyl)-biphenyl (**2k**) (3.02 g) clean product.

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Removal of PPh_3 and TTPO. To a cylindrical pressure vessel equipped with a magnetic stir bar and charged with a mixture of *gem*-difluoroalkene and PPh_3/ TTPO (1 equiv), sodium iodide (2 equiv), and acetone was added high-loading Merrifield peptide resin (0.5 g of resin for 1 mmol of PPh_3/ TPPO) and allowed to stir at room temperature. After 18 h, the mixture was filtered and washed with THF (3 × 3 mL) and acetone (3 × 3 mL).

Merrifield's peptide resin was obtained from Aldrich, catalog number 497061; 1% cross-linked, 100−200 mesh, containing 3.5−4.5 mmol/g Cl^-.

Synthesis of Monofluoroalkenyl Compounds (Procedure B). To a solution of *gem*-difluoroalkenes (1 equiv) in dry CH_2Cl_2 (8 mL) was added dropwise sodium bis(2-methoxyethoxy)aluminumhydride (Red-Al, a 60% w/w in toluene) (0.9 mL) at room temperature. The mixture was stirred at room temperature for 1 h. After the completion of reaction, the reaction was quenched with saturated ammonium chloride solution. The aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to give the corresponding monofluoro reduction products.

For the gram-scale reaction, using procedure B (mentioned above), to a solution of 4-(2,2-difluorovinyl)biphenyl (1.5 g, 6.94 mmol, 1 equiv,) in dry CH_2Cl_2 was added dropwise sodium bis(2-methoxyethoxy)aluminumhydride (Red-Al, a 60% w/w in toluene) (6.3 mL) at room temperature. The mixture was stirred at room temperature for 1 h. After the completion of reaction, the reaction was quenched with saturated ammonium chloride solution. The aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to give (*E*/*Z*)-4-(2-fluorovinyl)-1,1′-biphenyl (2.44 g) (**3k**).

*Characterization of gem-Difluoroalkenyl Compounds. 1-(2,2-Difluorovinyl)-2-methoxybenzene (**2a**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 5.68 (dd, *J* = 26.99, 4.31 Hz, 1H), 6.90 (d, *J* = 8.28 Hz, 1H), 6.98 (t, *J* = 7.55 Hz, 1H) 7.22-7.27 (m, 1H), 7.49 (dt, *J* = 7.70, 1.58 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.52, 76.23 (dd, *J* = 31.45, 12.62 Hz), 110.56, 119.21 (dd, *J* = 6.38, 6.38 Hz), 120.74, 128.23 (dd, *J* = 2.07, 1.39 Hz), 128.35 (dd, *J* = 9.27, 1.47 Hz), 156.17 (dd, *J* = 4.21, 1.40 Hz), 156.35 (d, *J* = 297.12, 286.64 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −84.0 (d, *J* = 32.16 Hz), −83.53 (d, *J* = 31.7 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*1-(2,2-Difluorovinyl)-4-methoxybenzene (**2b**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 5.24 (dd, *J* = 26.40, 3.77 Hz, 1H), 6.90 (d, *J* = 8.70, 2H), 7.28 (d, *J* = 8.54, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.26, 81.53 (dd, *J* = 29.28, 14.24 Hz), 114.18, 122.70 (dd, *J* = 6.19, 6.19 Hz), 128.78 (dd, *J* = 6.24, 3.49 Hz), 155.83 (dd, *J* = 296.75, 286.84 Hz), 158.56 (dd, *J* = 2.74, 2.06 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −86.44 (d, *J* = 38.0 Hz), −84.66 (d, *J* = 36.83 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*4-(2,2-Difluorovinyl)-1,2-dimethoxybenzene (**2c**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 3.91 (s, 3H), 5.23 (dd, *J* = 26.19, 3.91 Hz, 1H), 6.84−6.91 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.84, 55.90, 81.88 (dd, *J* = 29.31, 13.82 Hz), 110.59 (dd, *J* = 6.93, 3.01 Hz), 111.32, 120.42 (dd, *J* = 6.08, 4.17 Hz), 123.01 (dd, *J* = 6.21, 6.21 Hz), 148.16 (dd, *J* = 2.13, 1.47 Hz), 149.0, 155.84 (dd, *J* = 296.59, 286.9 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ − 86.07 (d, *J* = 36.60 Hz), −84.26 (d, *J* = 36.34 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[44]

*1-(2,2-Difluorovinyl)-2,5-dimethoxybenzene (**2d**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 3.82 (s, 3H), 5.67 (dd, *J* = 25.33, 5.82 Hz, 1H), 6.78 (dd, *J* = 8.96, 2.86 Hz, 1H), 6.83 (d, *J* = 8.93 Hz, 1H), 7.07 (d, *J* = 2.65 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.71, 56.22, 76.33 (dd, *J* = 30.33, 13.41 Hz), 111.73, 113.02, 114.10 (dd, *J* = 9.61, 2.13 Hz), 120.06 (dd, *J* = 5.62, 5.62 Hz), 150.64 (dd, *J* = 4.59, 1.73 Hz), 153.59, 156.34 (dd, *J* = 296.88, 288.03 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ − 83.13 (d, *J* = 30.94 Hz), −82.97 (d, *J* = 30.47 Hz) ppm. HRMS (EI): calc. for C10H10F2O2 [M]+ 200.185, found 200.0645.

*1-(2,2-Difluorovinyl)-2,3,4-trimethoxybenzene (**2e**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3H), 3.89 (s, 3H), 3.89 (s, 3H), 5.55 (dd, *J* = 26.36, 4.88 Hz, 1H), 6.70 (d, *J* = 8.8 Hz, 1H), 7.20 (dd, *J* = 8.8, 1.32 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 56.0, 60.85, 61.19, 75.97 (dd, *J* = 31.07, 13.44 Hz), 107.71, 117.04 (d, *J* = 5.86, 5.86 Hz), 122.59 (dd, *J* = 9.94, 1.41 Hz), 142.34, 151.07 (dd, *J* = 4.75, 1.77 Hz), 152.72 (dd, *J* = 1.69, 1.51 Hz), 156.24 (dd, *J* = 296.04, 286.50 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −84.55 (d, *J* = 34.23 Hz), −84.30 (d, *J* = 34.57 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[45]

*4-Benzyloxy-1-(2,2-difluorovinyl)benzene (**2f**).* ^{1}H NMR (400, $CDCl_3$) δ 5.09 (s, 2H), 5.23 (dd, *J* = 26.39, 3.83 Hz, 1H), 6.97 (d, *J* = 8.76 Hz, 2H), 7.28 (d, *J* = 8.56 Hz, 2H), 7.33−7.47 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 70.04, 81.55 (dd, *J* = 29.12, 14.15 Hz), 115.15, 122.99 (dd, *J* = 6.17, 6.17 Hz), 127.48, 128.05, 128.64, 128.82 (dd, *J* = 6.27, 3.52 Hz), 136.86, 155.86 (dd, *J* = 296.66, 286.66 Hz), 157.76 (dd, *J* = 4.11, 4.11 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ − 86.29 (d, *J* = 36.6 Hz), −84.48 (d, *J* = 36.49 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*1-(2,2-Difluorovinyl)-4-ethoxybenzene (**2g**).* ^{1}H NMR (400, $CDCl_3$) δ 1.44 (t, *J* = 7.04 Hz, 3H), 4.05 (dd, *J* = 13.98, 7.0 Hz, 2H), 5.23 (dd, *J* = 26.44, 3.88 Hz, 1H), 6.89 (dd, *J* = 6.77, 2.03 Hz, 2H), 7.27 (dd, *J* = 6.88, 2.0 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.80, 63.46, 81.56 (dd, *J* = 29.15, 14.13 Hz), 114.72, 122.53 (dd, *J* = 6.08, 6.08 Hz), 128.76 (dd, *J* = 6.22, 3.52 Hz), 155.80 (dd, *J* = 296.39, 286.47 Hz), 157.92 (dd, *J* = 2.07, 2.07 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ − 86.56 (d, *J* = 36.87 Hz), − 84.71 (d, *J* = 36.94 Hz); HRMS (EI): calc. for C10H10F2O [M]+ 184.19, found 184.0696.

*5-(2,2-Difluorovinyl)benzo[d][1,3]dioxole (**2h**).* ^{1}H NMR ($CDCl_3$) δ 5.22 (dd, *J* = 25.88, 3.90 Hz, 1H), 5.98 (s, 2H), 6.77 (dd, *J* = 8.10, 1.53 Hz, 1H), 6.80 (d, *J* = 8.02 Hz, 1H), 6.90 (d, *J* = 1.16 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 82.01 (dd, *J* = 29.86, 13.74 Hz), 101.15, 107.64 (dd, *J* = 7.79, 2.74 Hz), 108.47, 121.56 (dd, *J* = 4.97, 4.97 Hz), 124.12 (dd, *J* = 6.33, 6.33 Hz), 146.61 (dd, *J* = 2.87, 2.08 Hz), 148.01, 155.85 (dd, *J* = 296.90, 286.92 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ − 86.01 (d, *J* = 35.63 Hz), −83.80 (d, *J* = 35.78 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*2-(2,2-Difluorovinyl)naphthalene (**2i**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (dd, *J* = 26.21, 3.85 Hz, 1H), 7.45−7.53 (m, 3H), 7.77−7.85 (m, 4H); ^{13}C NMR (100.6 MHz,

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$CDCl_3$) δ 82.46 (dd, J = 29.23, 13.40 Hz), 125.38 (dd, J = 6.52, 2.23 Hz), 126.06, 126.44, 126.66 (dd, J = 5.66, 5.66 Hz), 127.65, 127.8, 128.37, 132.31, 133.45, 156.48 (dd, J = 298.76, 288.55 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ − 83.64 (d, J = 30.88 Hz), − 81.92 (d, J = 30.8 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[45]

*2-(2,2-Difluorovinyl)-6-methoxynaphthalene (**2j**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.95 (s, 3H), 5.42 (dd, J = 26.34, 3.92 Hz, 1H), 7.13 (d, J = 2.36 Hz, 1H), 7.17 (dd, J = 8.99, 2.50 Hz, 1H), 7.47 (d, J = 8.58 Hz, 1H), 7.69−7.74 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.31, 82.37 (dd, J = 29.19, 13.59 Hz), 105.68, 119.28, 125.55 (dd, J = 6.29, 6.29 Hz), 125.91 (dd, J = 6.55, 2.36 Hz), 126.50 (dd, J = 6.23, 4.86 Hz), 127.20, 128.93, 129.32, 133,48, 156.28 (dd, J = 297.81, 287.76 Hz), 157.88; ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −84.59 (d, J = 33.33 Hz), −82.74 (d, J = 33.22 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[44]

*4-(2,2-Difluorovinyl)biphenyl (**2k**).* ^{1}H NMR (400, $CDCl_3$) δ 5.34 (dd, J = 26.29, 3.74 Hz, 1H), 7.35−7.5 (m, 5H), 7.58−7.64 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 81.94 (dd, J = 29.18, 13.61 Hz), 126.96, 127.36, 127.43, 128.01 (dd, J = 6.34, 3.56 Hz), 128.84, 129.39 (dd, J = 6.54, 6.64 Hz), 139.83 (dd, J = 2.10, 2.10 Hz), 140.51, 156.37 (dd, J = 298.5, 288.59 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −83.82 (d, J = 30.92 Hz), −81.89 (d, J = 30.65 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*4-(2,2-Difluorovinyl)-1-(methylthio)benzene (**2l**).* ^{1}H NMR (400, $CDCl_3$) δ 2.51 (s, 3H), 5.25 (dd, J = 26.25, 3.73 Hz, 1H), 7.21−7.27 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.87, 81.76 (dd, J = 29.40, 13.73 Hz), 126.76, 127.18 (dd, J = 6.25, 6.25 Hz), 127.98 (dd, J = 6.37, 3.57 Hz), 137.15, 156.19 (dd, J = 297.92, 288.20 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −84.44 (d, J = 31.82 Hz), −82.26 (d, J = 31.9 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*Methyl 4-(2,2-Difluorovinyl)benzoate (**2m**).* ^{1}H NMR (400, $CDCl_3$) δ 3.94 (s, 3H), 5.36 (dd, J = 25.94, 3.60 Hz, 1H), 7.41 (d, J = 8.42 Hz, 2H), 8.02 (d, J = 8.44 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 52.1, 82.03 (dd, J = 29.82, 13.13 Hz), 127.42 (dd, J = 6.70, 3.55 Hz), 128. 59 (t, J = 2.22 Hz), 129.94, 135.16 (t, J = 6.83 Hz), 156.77 (dd, J = 300.54, 290.71), 166.66; ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −81.11 (d, J = 23.84 Hz), −79.18 (d, J = 23.85 Hz) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*1-Bromo-4-(2,2-difluorovinyl)benzene (**2n**).* ^{1}H NMR (400, $CDCl_3$) δ 5.70 (dd, J = 25.39, 3.74 Hz, 1H), 7.11−7.16 (m, 1H), 7.33 (t, J = 7.55 Hz, 1H), 7.52−7.62 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 81.66 (dd, J = 32.60, 12.13 Hz), 123.43 (dd, J = 5.54, 1.95 Hz), 127.57, 128.59, 129.15 (dd, J = 9.25, 1.08 Hz), 130.43 (dd, J = 7.85, 6.02 Hz), 132.94, 156.67 (dd, J = 298.84, 288.78 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$) δ −82.99 (d, J = 26.01 Hz), −81.74 (d, J = 26.18 Hz). The chemical shifts were consistent with those reported in the literature.[20d]

*Characterization of Monofluoroalkenyl Compounds. (E/Z)-1-(2-Fluorovinyl)-2-methoxybenzene (**3a**).* ^{1}H NMR (400 MHz, $CDCl_3$) for the major E-isomer: δ 3.89 (s, 3H), 6.52 (dd, J = 22.30, 11.17 Hz, 1H), 6.93 (dd, J = 13.07, 7.84, 2H), 7.20−7.27 (m, 2H), 7.42 (dd, J = 86.29, 11.19 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major E-isomer: δ 55.35, 110.49 (d, J = 18.32 Hz), 110.77, 120.74, 121.61 (d, J = 11.25 Hz), 128.37 (d, J = 2.03 Hz), 128.49 (d, J = 2.63 Hz), 151.57 (d, J = 257.45 Hz), 156.79 (d, J = 2.82 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −125.03 (s, E-isomer), −123.92 (s, Z-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[45]

*(E/Z)-1-(2-Fluorovinyl)-4-methoxybenzene (**3b**).* ^{1}H NMR (400 MHz, $CDCl_3$) for the major E-isomer: δ 3.83 (s, 3H), 6.37 (dd, J = 19.59, 11.34, 1H), 6.87 (dd, J = 6.76, 1.96 Hz, 2H), 7.11 (dd, J = 83.76, 11.32 Hz, 1H), 7.20 (d, J = 8.68 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major E-isomer: δ 55.30, 113.28 (d, J = 16.04 Hz), 114.25, 125.05 (d, J = 11.59 Hz), 127.30 (d, J = 2.89 Hz), 149.0 (d, J = 256.30 Hz), 159.09 (d, J = 1.46 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −132.68 (s, E-isomer), −125.36 (s, Z-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[42]

*(E/Z)-4-(2-Fluorovinyl)-1,2-dimethoxybenzene (**3c**).* ^{1}H NMR (400 MHz, $CDCl_3$) for the major E-isomer: δ 3.89 (s, 3H), 3.90 (s, 3H), 6.36 (dd, J = 19.46, 11.32 Hz, 1H), 6.80 (d, J = 21.01 Hz, 3H), 7.12 (dd, J = 83.57, 11.33 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major E-isomer: δ 55.86, 55.92, 109.0 (d, J = 2.34 Hz), 111.43, 113.62 (d, J = 16.21 Hz), 118.99 (d, J = 3.41 Hz), 125.39 (d, J = 11.82 Hz), 148.68 (d, J = 1.64 Hz), 149.16 (d, J = 256.97 Hz), 149.15; ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −132.29 (s, E-isomer), −125.04 (s, Z-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*(E/Z)-2-(2-Fluorovinyl)-1,4-dimethoxybenzene (**3d**).* ^{1}H NMR (400 MHz, $CDCl_3$) for the major E-isomer: δ 3.79 (s, 3H), 3.84 (s, 3H), 6.49 (dd, J = 22.0, 11.19 Hz, 1H), 6.77−6.85 (m, 3H), 7.41 (dd, J = 86.01, 11.29 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major E-isomer: δ 55.69, 55.91, 110.40 (d, J = 18.50 Hz), 111.85, 112.83 (d, J = 2.05 Hz), 114.15 (d, J = 2.65 Hz), 122.44 (d, J = 11.38 Hz), 151.18 (d, J = 2.91 Hz), 151.87 (d, J = 258.19 Hz), 153.60; ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −124.70 (s, E-isomer), −123.10 (s, Z-isomer) ppm.

*(E/Z)-1-(2-Fluorovinyl)-2,3,4-trimethoxybenzene (**3e**).* ^{1}H NMR (400 MHz, $CDCl_3$) for the major E-isomer: δ 3.86 (s, 3H), 3.88 (s, 3H), 3.88 (s, 3H), 6.44 (dd, J = 21.64, 11.26 Hz, 1H), 6.63 (d, J = 8.64 Hz, 1H), 6.90 (d, J = 8.62 Hz, 1H), 7.29 (dd, J = 85.79, 11.25 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major E-isomer: δ 55.99, 60.55, 60.82, 107.65, 109.58 (d, J = 18.39 Hz), 119.49 (d, J = 10.80 Hz), 122.0 (d, J = 2.34 Hz), 142.63,150.38 (d, J = 256.53 Hz), 151.31 (d, J = 2.94 Hz), 153.16 (d, J = 1.71 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −127.67 (s, E-isomer), −124.63 (s, Z-isomer) ppm. HRMS (EI): calc. for $C_{11}H_{13}FO_3$ $[M]^+$ 212.221, found 212.0841.

*(E/Z)-1-(Benzyloxy)-4-(2-fluorovinyl)benzene (**3f**).* ^{1}H NMR (400 MHz, $CDCl_3$) for the major E-isomer: δ 5.08 (s, 2H), 6.37 (dd, J = 19.57, 11.33 Hz, 1H), 6.94 (dd, J = 6.76, 1.96 Hz, 2H), 7.11 (dd, J = 83.83, 11.22 Hz, 1H), 7.19 (dd, J = 6.62, 2.18 Hz, 2H), 7.34−7.46 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major E-isomer: δ 70.06, 113.29 (d, J = 16.09 Hz), 115.23, 125.34 (d, J = 11.83 Hz), 127.33 (d, J = 2.97 Hz), 127.46, 128.04, 128.63, 136.86, 149.08 (d, J = 256.58), 158.29 (d, J = 1.43 Hz); ^{19}F NMR (376.6 MHz, CDCl3): δ −132.46 (s, E-isomer), −125.16 (s, Z-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[43]

*(E/Z)-1-(2-Fluorovinyl)-4-ethoxybenzene (**3g**).* ^{1}H NMR (400 MHz, $CDCl_3$) for the major E-isomer: 1.43 (t, J = 6.99 Hz, 3H), 4.05 (dd, J = 13.99, 7.0 Hz, 2H), 6.37 (dd, J = 19.64, 11.34 Hz, 1H), 6.86 (dd, J = 6.86, 1.94 Hz, 2H), 7.11 (dd, J = 83.81, 11.34 Hz, 1H), 7.18 (dd, J = 6.78, 2.02 Hz, 2H); ^{13}C

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NMR (100.6 MHz, $CDCl_3$) for the major *E*-isomer: δ 14.81, 63.48, 113.33 (d, J = 15.92 Hz), 114.81, 124.89 (d, J = 11.64 Hz), 127.29 (d, J = 2.90 Hz), 148.95 (d, J = 256.11 Hz), 158.48 (d, J = 1.81 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −132.89 (s, E-isomer), − 125.49 (s, *Z*-isomer) ppm. HRMS (EI): calc. for $C_{10}H_{11}FO$ $[M]^+$ 166.20, found 166.0786.

(E/Z)-5-(2-Fluorovinyl)benzo[d][1,3]dioxole (**3h**). ^{1}H NMR (400 MHz, $CDCl_3$) for the major *E*-isomer: δ 5.97 (s, 2H), 6.34 (dd, J = 19.32, 11.32 Hz, 1H), 6.71 (dd, J = 7.80, 1.71 Hz, 1H), 6.78 (d, J = 8.0 Hz, 2H), 7.09 (dd, J = 83.35, 11.31 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major *E*-isomer: δ 101.14, 105.75 (d, J = 2.08 Hz), 108.57, 113.70 (d, J = 16.55 Hz), 120.40 (d, J = 3.76 Hz), 126.57 (d, J = 11.86 Hz), 147.14 (d, J = 1.89 Hz), 148.07, 149.26 (d, J = 257.20 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −132.25 (s, *E*-isomer), −124.45 (s, *Z*-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[29]

(E/Z)-2-(2-Fluorovnyl)naphthalene (**3i**). ^{1}H NMR (400 MHz, $CDCl_3$) for the major *E*-isomer: δ 6.58 (dd, J = 19.45, 11.37 Hz, 1H), 7.21−7.52 (m, 4H), 7.67 (s, 1H), 7.74−7.84 (m, 3H); ^{13}C NMR (100.6 MHz, CDCl3) for the major *E*-isomer: δ 114.13 (d, J = 16.16 Hz), 123.35, 125.76 (d, J = 4.97 Hz), 125.93, 126.48, 127.70, 128.48, 130.12 (d, J = 11.80 Hz), 132.75, 133.59, 150.49 (d, J = 259.18 Hz); ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −129.41 (s, *E*-isomer), −121.75 (s, *Z*-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[46]

(E/Z)-2-(2-Fluorovinyl)-6-methoxynaphthalene (**3j**). ^{1}H NMR (400 MHz, $CDCl_3$) for the major *E*-isomer: δ 3.95 (s, 3H), 6.55 (dd, J = 19.60, 11.35 Hz, 1H), 7.13−7.21 (m, 2H), 7.37−7.60 (m, 3H), 7.70 (dd, J = 8.59, 2.81 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major *E*-isomer: δ 55.33, 105.86, 114.09 (d, J = 16.09 Hz), 119.21, 123.95 (d, J = 1.13 Hz), 125.58 (d, J = 4.73 Hz), 127.32, 127.86 (d, J = 11.60 Hz), 128.54 (d, J = 11.98 Hz), 129.02, 129.24, 132.13 (d, J = 9.83 Hz), 133.92, 149.94 (d, J = 258.15 Hz), 157.77; ^{19}F NMR (376.6 MHz, $CDCl_3$): δ −130.82 (s, *E*-isomer), −122.93 (s, *Z*-isomer) ppm. HRMS (EI): calc. for $C_{13}H_{11}FO$ $[M]^+$ 202.23, found 202.0790.

(E/Z)-4-(2-Fluorovinyl)-1,1′-biphenyl (**3k**). ^{1}H NMR (400 MHz, $CDCl_3$) for the major *E*-isomer: δ 6.46 (dd, J = 19.28, 11.37 Hz, 1H), 7.12−7.4 (m, 4H), 7.46 (t, J = 7.55 Hz, 2H), 7.56−7.62 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major *E*-isomer: δ 113.56 (d, J = 16.02 Hz), 126.57 (d, J = 2.98 Hz), 126.94, 127.43, 127.48, 128.85, 131.69 (d, J = 11.88 Hz), 140.37 (d, J = 2.04 Hz), 140.56, 150.23 (d, J = 259.53 Hz); ^{19}F NMR (376.6 MHz, CDCl3): δ −129.48 (s, E-isomer), −121.70 (s, Z-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[42]

(E/Z)-4-(2-Fluorovinyl)-1-(methylthio)benzene (**3l**). ^{1}H NMR (400 MHz, $CDCl_3$) for the major *E*-isomer: δ 2.50 (s, 1H), 6.37 (dd, J = 19.31, 11.37 Hz, 1H), 7.18 (dd, J = 83.21, 11.36 Hz, 1H), 7.20 (ddd, J = 13.52, 6.29, 2.34 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for the major *E*-isomer: δ 15.84, 113.38 (d, J = 16.27 Hz), 126.53 (d, J = 2.97 Hz), 126.87, 129.45 (d, J = 11.69 Hz), 137.73 (d, J = 2.04 Hz), 149.91 (d, J = 258.79 Hz);

^{19}F NMR (376.6 MHz, CDCl3): δ −130.41 (s, E-isomer), −122.32 (s, *Z*-isomer) ppm. The chemical shifts were consistent with those reported in the literature.[42]

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c01055.

General information; experimental sections; synthesis of *gem*-difluoroalkenyl compounds; synthesis of monofluoroalkenyl compounds; characterization of *gem*-difluoroalkenyl compounds; characterization of monofluoroalkenyl compounds; spectra; and computational methods (PDF)

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Author Contributions

S.R. conducted all experimental work (Schemes 1 and 2 and Table 1). Computational work was conducted by S.H. and T.D. (Schemes 3 and 4 and Figure 1).

Notes

The authors declare no competing financial interest.

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