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The first preparation of the α-iodo-β,β-difluorovinylzinc reagent (CF_2=CIZnCl) and a high-yield one-pot synthesis of α-iodo-β,β-difluorostyrenes

R. Anilkumar, Donald J. Burton*

Department of Chemistry, The University of Iowa, Iowa City, IA 52242, USA

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Dedicated to Professor Richard D. Chambers on the occasion of his 70th birthday.

Abstract

The α-iodo-β,β-difluorovinylzinc reagent (CF_2=CIZnCl) was synthesized in >87% yield via room-temperature metallation of the commercially available CF_3CH_2I with LDA in the presence of $ZnCl_2$. This novel zinc reagent upon palladium-catalyzed cross-coupling with aryl iodides produced α-iodo-β,β-trifluorostyrenes (ArCI=CF_2) in 62–80% isolated yield.

Keywords: 2-Iodo-1,1,1-trifluoroethane; Iododifluorovinylzinc; Pd(0) coupling; Trifluorovinyllithium; Iododifluorovinyllithium; α-Iodo-β,β-difluorostyrene

1. Introduction

Fluoroolefins containing the terminal difluoromethylene (R_2C=CF_2) group are useful building blocks due to their unique reactivities in ionic as well as radical reactions [1–5] and their ability to form monovinylfluorides upon reduction [6,7]. They have also been shown to exhibit unique biological properties especially for certain mechanism-based enzyme inhibitors [8–12]. 1,1-Difluoroolefins, bearing a halogen (chlorine, bromine or iodine) at the α-position, are interesting compounds as they have significant synthetic potential due to the possible functionalization both at the terminal olefinic site as well as at the halogen site. Various methods have been developed for the preparation of 1,1-difluoroolefins and most of these methods utilize introduction of either a =CF_2 or a –CX=CF_2 group into the organic molecule, though there are exceptions. The most versatile method to introduce a =CF_2 group is via Wittig olefination chemistry, where olefins of the type R_2C=CF_2, where R = alkyl, aryl, perfluoroalkyl or hydrogen, have been synthesized in moderate to good yields [13–15]. But this approach is not adaptable to the synthesis of RCX=CF_2 (X = Cl, Br or I), due to acylation of the Wittig reagent. Organometallic routes for the 1,1-difluoroolefin involves incorporation of a two carbon difluoroolefinic unit (–CX=CF_2) into a precursor either by addition of stabilized difluorovinyl anions to suitable electrophiles [16–21] or by metal-catalyzed cross-coupling of difluorovinyl synthons with aryl or alkenyl iodides [22–26].

Traditionally α-halo-β,β-difluorostyrenes were prepared by a two-step process: addition of halogen to RCH=CF_2 [27,28] followed by dehydrohalogenation [29]. Though this method is not general, use of a more selective base like Li_2CO_3 or KO^tBu improved the yield of the α-halo-β,β-difluorostyrene significantly (Scheme 1).

A more general route for fluorinated styrenes employs Pd(0)-catalyzed coupling of fluorovinyl synthons with aryl iodides under mild reaction conditions [22–26,30–34]. This approach was initially utilized in this laboratory for the synthesis of α,β,β-trifluorostyrenes, where Pd(0)-catalyzed coupling reaction of trifluorovinyl zinc or tin reagents with aryl iodides produced the corresponding styrenes [30–33]. By a similar approach, various α-bromo-β,β-difluorostyrenes were also synthesized in excellent isolated yields by the Pd(0)-catalyzed coupling reaction of CF_2=CBrZnX

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* Corresponding author. Tel.: +1 319 335 1368; fax: +1 319 335 1270.
E-mail address: donald-burton@uiowa.edu (D.J. Burton).

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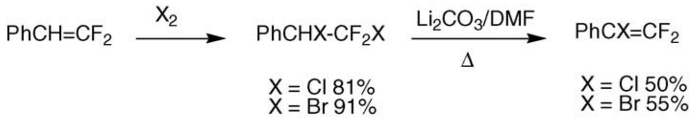
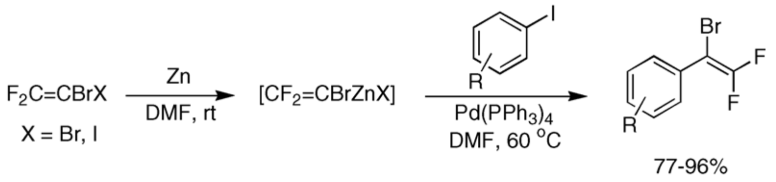
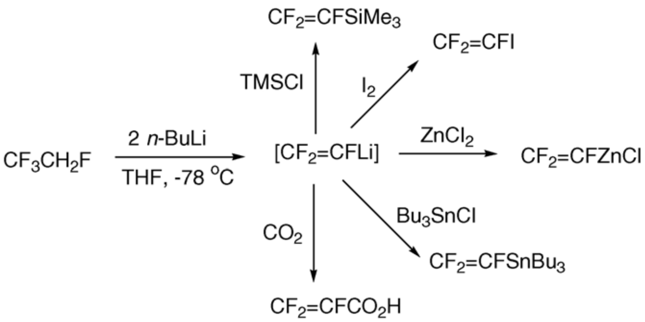


Scheme 1. Preparation of α-halo-β,β-difluorostyrenes by dehydrohalogenation.



Scheme 2. Preparation of α-bromo-β,β-difluorostyrenes by zinc insertion followed by Pd(0)-catalyzed coupling.



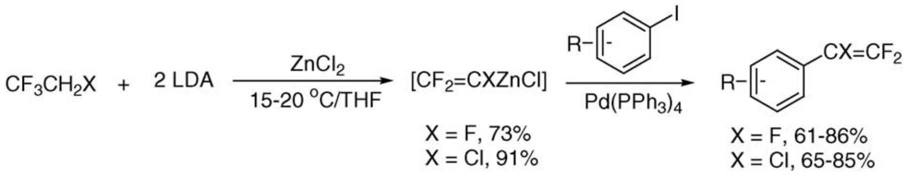
Scheme 3. Generation of trifluorovinyllithium from HFC-134a and its reaction with various electrophiles.

(generated by the zinc insertion into $CF_2{=}CBr_2$) with aryl iodides (Scheme 2) [34].

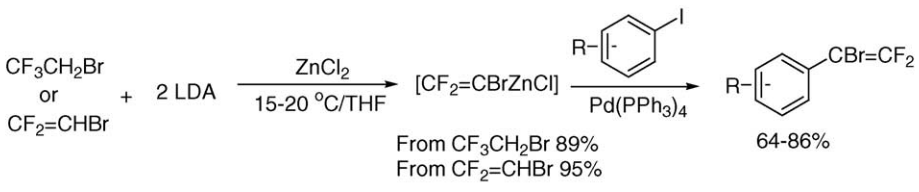
Recent work of Coe and co-workers demonstrated the halocarbon HFC-134a as an excellent synthetic precursor for the preparation of trifluorovinyllithium at low temperature (Scheme 3) [35–38]. The trifluorovinyllithium thus produced reacted with various electrophiles to produce the corresponding substituted products (Scheme 3). They have also identified HCFC-133a as a precursor for the generation of α-chloro-β,β-difluorovinyllithium at low temperature [36–38].

Utilizing the synthetic potential of these environmentally friendly halocarbons, we have recently developed an excellent synthetic route for α,β,β-trifluorostyrenes and α-chloro-β,β-difluorostyrenes [39–41]. Here, the trifluorovinylzinc reagent ($CF_2{=}CFZnCl$) and the α-chloro-β,β-difluorovinyl zinc reagent ($CF_2{=}CXZnCl$, X = Cl, Br) were generated by LDA metallation of a THF solution of $ZnCl_2$ and HFC-134a or HCFC-133a at room temperature. The vinyl zinc reagents thus generated were coupled with aryl iodides to produce α,β,β-trifluorostyrenes and α-chloro-β,β-difluorostyrenes in excellent isolated yields (Scheme 4). An extension of this methodology was later applied for the synthesis of α-bromo-β,β-difluorostyrenes [42]. Here the α-bromo-β,β-difluorovinylzinc reagent ($CF_2{=}CBrZnCl$), generated by metallation of CF_3CH_2Br or $CF_2{=}CHBr$, was coupled with aryl iodides to produce α-bromo-β,β-difluorostyrenes (Scheme 5).

Herein, we report a further extension of this methodology for the synthesis of α-iodo-β,β-difluorostyrenes via the α-iodo-β,β-difluorovinylzinc reagent.



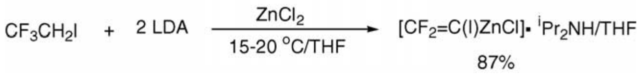
Scheme 4. Preparation of α,β,β-trifluorostyrenes, α-chloro-β,β-difluorostyrenes via the corresponding fluorovinylzinc reagents generated from HFC-134a or HCFC-133a.



Scheme 5. Preparation of α-bromo-β,β-difluorostyrenes via $CF_2{=}CBrZnCl$.

2. Results and discussion

After the successful synthesis of α-bromo-β,β-difluorostyrenes by our metallation-coupling methodology, we investigated whether α-iodo-β,β-difluorostyrenes could be prepared by this route, as they would potentially be useful for further functionalization at the iodine site. Also the α-iodo-β,β-difluorovinylzinc reagent and the α-iodo-β,β-difluorostyrenes were hitherto unknown in the literature, and the method could essentially yield a useful route for the synthesis of these compounds. Commercially available 1-iodo-2,2,2-trifluoroethane (CF_3CH_2I) was chosen as a precursor for the α-iodo-β,β-difluorovinylzinc reagent. It was of interest to examine whether there are competing reactions resulting in two different zinc reagents during the metallation of CF_3CH_2I. Metallation at the hydrogen site was expected to produce the iodozinc reagent ($CF_2{=}CIZnCl$), whereas metallation at the iodine site would result in the hydrozinc reagent ($CF_2{=}CHZnCl$) [43]. Though metallation at the halogen sites was not observed in the LDA metallation of CF_3CH_2Cl and CF_3CH_2Br [41,42], metallation of the iodine site might be expected for CF_3CH_2I due to the more labile C–I bond. Thus, via the conditions standardized for the metallation of HFC-134a, a THF solution of CF_3CH_2I and anhydrous zinc chloride was treated with 2.0 equiv. of LDA at 15–20 °C (Scheme 6). The yellow-colored reaction mixture was subjected to ^{19}F NMR analysis using $PhCF_3$ as the internal standard and showed the exclusive formation of the α-iodo-β,β-difluorovinylzinc reagent in 87% yield. No product resulting from the metallation at the iodine site ($CF_2{=}CHZnCl$) was detected by ^{19}F NMR [43].



Scheme 6. Preparation of α-iodo-β,β-difluorovinylzinc reagents.

The ^{19}F NMR spectrum also revealed the presence of both *mono* ($CF_2{=}CIZnCl$) and *bis* zinc reagents $[(CF_2{=}CI)_2Zn]$ complexed to diisopropylamine and THF. Addition of a stoichiometric amount of TMEDA to the reaction medium simplified the ^{19}F NMR spectrum with preferential complexation of the zinc reagents to TMEDA, which makes the *mono* and *bis* zinc reagents clearly distinguishable. The ^{19}F NMR spectra of the zinc reagent showed peaks at −58.0 (d, $J = 53$ Hz, 1F), −71.8 (d, $J = 53$ Hz, 1F) corresponding to the *mono* zinc reagent and peaks at −57.0 (d, $J = 56$ Hz, 2F), −73.2 (d, $J = 56$ Hz, 2F) corresponding to the *bis* zinc reagent (*mono*/*bis*: 85:15). Hydrolysis of the zinc reagent with glacial acetic acid produced $CF_2{=}CHI$ quantitatively (−73.2, d, $J = 31$ Hz, 1F; −77.6, dd, $J = 31$, 25 Hz, 1F) and thus confirmed the formation of $CF_2{=}CIZnCl$.

The zinc reagent was then reacted with iodobenzene and catalytic Pd(0) at r.t. for 24 h to produce α-iodo-β,β-difluorostyrene in 79% isolated yield (Table 1, entry 1). It was noticed that the coupling reaction of the iodobenzene with $CF_2{=}CIZnCl$ at r.t. was not as facile as that of other halozinc reagents. The difference in reactivity could be explained by a closer examination at the transmetallation process in the palladium cycle. A few literature reports, available on the mechanistic studies on the transmetallation step of palladium cycle, enlighten the major role played by the steric effects during the transmetallation process [44–47]. Though iodine at the α-carbon is expected to increase the reactivity of the zinc reagent electronically towards the transmetallation process, its bulkiness could create considerable steric crowding in the transition state resulting in a slower transmetallation process and thus a less facile coupling process. In order to facilitate faster reaction, the coupling reaction of the iododifluorovinylzinc reagent and 1-fluoro-4-iodobenzene was attempted under heating conditions (60 °C, 12 h) and resulted in a mixture of products with partial decomposition of the iododifluorovinylzinc

Table 1

Entry	Iodide (ArI)	Temp/time	α-Iodo-β,β-difluorostyrenes[a]	NMR yield	Yield (%)[b]
1	C_6H_5I	r.t., 12 h then 60 °C, 2 h	$C_6H_5CI{=}CF_2$	92	79
2[c]	p-FC_6H_4I	r.t., 12 h then 65 °C, 2 h	p-$FC_6H_4CI{=}CF_2$	92	71
3	m-FC_6H_4I	r.t., 18 h then 60 °C, 2 h	m-$FC_6H_4CI{=}CF_2$	88	73
4[d]	p-ClC_6H_4I	r.t., 14 h then 65 °C, 3 h	p-$ClC_6H_4CI{=}CF_2$	89	78
5	o-MeC_6H_4I	r.t., 18 h then 60 °C, 5 h	o-$MeC_6H_4CI{=}CF_2$	85	72
6	m-$NO_2C_6H_4I$	r.t., 15 h then 65 °C, 4 h	m-$O_2NC_6H_4CI{=}CF_2$	86	78
7	m-$MeOC_6H_4I$	r.t., 5 h then 65 °C, 2 h	m-$MeOC_6H_4CI{=}CF_2$	90	80
8	m-$F_3CC_6H_4I$	r.t., 24 h then 60 °C, 1 h	m-$F_3CC_6H_4CI{=}CF_2$	85	67
9	o-$F_3CC_6H_4I$	65 °C, 48 h	o-$F_3CC_6H_4CI{=}CF_2$	48	–
10[e]	p-IC_6H_4I	r.t., 24 h then 65 °C, 4 h	p-$CF_2{=}CIC_6H_4CI{=}CF_2$	–	62

$CF_3CH_2I \xrightarrow[15-20\,^{\circ}C/THF]{LDA,\,ZnCl_2} [CF_2{=}CIZnCl] \xrightarrow[r.t.\ to 65\,^{\circ}C]{ArI,\,Pd(PPh_3)_4} ArCI{=}CF_2$.

[a] All the styrenes gave satisfactory ^{1}H, ^{13}C, ^{19}F NMR, HRMS data.

[b] Isolated yield.

[c] Product styrene contaminated with 4% iodide.

[d] Product styrene contaminated with 2% iodide.

[e] Reaction was sluggish product styrene contaminated with traces of monostyrene and 1,4-diiodobenzene.

reagent. ^{19}F NMR analysis of this reaction mixture showed a considerable amount of reduced product (CF_2=CHI) along with coupled product and unreacted 1-fluoro-4-iodobenzene. In order to check the thermal stability of the iododifluorovinylzinc reagent under Pd(0) catalysis, a blank coupling reaction experiment with no aromatic iodide was performed. Thus, a THF solution of the iododifluorovinylzinc reagent, heated at 60 °C with a catalytic amount of Pd(0) for 12 h, produced 40% of the reduced product (CF_2=CHI) and no unreacted zinc reagent was detected. Thus, heating of the reaction mixture for long time to facilitate faster reaction destroyed the zinc reagent to a great extent. So a balance was struck, where slightly fewer equivalents of iodide (0.7 equiv.) and the zinc reagent were stirred at r.t. in the presence of Pd(0) catalyst, and the reaction was monitored via ^{19}F NMR. After significant amount of conversion (~80%) of the zinc reagent to styrene, the mixture was heated at 60 °C for a shorter period to effect complete conversion.

After the successful coupling reaction of the iododifluorovinylzinc reagent with iodobenzene and 1-fluoro-4-iodobenzene under these modified conditions (Table 1, entries 1 and 2), the same sequence was performed with other aromatic iodides to test the generality of this method. Reactions were successful with both electron-donating and electron-withdrawing aromatic iodides to produce the corresponding substituted α-iodo-β,β-difluorostyrenes in excellent isolated yields (Table 1, entries 2–10).

For some aromatic iodides, the coupling reaction was very sluggish especially with *o*-iodobenzotrifluoride, where no coupled product was detected when the reaction mixture was stirred at r.t. for 5 h. However, heating the reaction mixture at 65 °C for 2 days produced 48% (by ^{19}F NMR) of the coupled product (entry 9). ^{19}F NMR analysis of this reaction mixture also showed a large amount of unreacted iodide along with a significant amount of reduced product. Coupling reaction using 1,4-diiodobenzene was also slightly sluggish at r.t. and produced the corresponding *bis* styrene in 62% isolated yield (entry 10).

In conclusion, a high-yield room-temperature preparation of the α-iodo-β,β-difluorovinylzinc reagent (CF_2=CIZnCl) was achieved via reaction of CF_3CH_2I with LDA in the presence of $ZnCl_2$. The α-iodo-β,β-difluorovinylzinc reagent thus generated was coupled with aryl iodides using Pd(0) catalysis to produce α-iodo-β,β-trifluorostyrenes in excellent isolated yields under mild conditions. This method serves as the first preparation of the α-iodo-β,β-difluorovinylzinc reagent and the first general synthetic route for α-iodo-β,β-difluorostyrenes. Future reports will describe the functionalization of these α-iodo-β,β-difluorostyrenes.

3. Experimental

^{1}H, {^{1}H}^{13}C and ^{19}F NMR spectra were recorded on a Brucker AC-300 or a WM 360 Spectrometer. Chemical shifts have been reported in ppm relative to an internal reference ($CDCl_3$, $CFCl_3$ or TMS). Unless noted otherwise, $CDCl_3$ was used as the NMR lock solvent. Low-resolution mass spectra were obtained using a Voyeger GC–MS instrument operated at 70 eV in the electron impact mode, using a 15 m CB-5 column. The reported fragment peaks correspond to the most abundant ions, in addition to the parent ion(s). High-resolution mass spectra (HRMS) were obtained by the University of Iowa high-resolution mass spectrometry facility. Column chromatography was carried out using silica gel purchased from Em Science (Silica Gel 60, particle size 63–200 μm). Tetrahydrofuran (THF) was dried by distillation from sodium benzophenone/ketyl at atmospheric pressure immediately prior to use. $Pd(PPh_3)_4$ was prepared by Coulson's procedure [48]. N_2 was used without further purification. All other reagents and chemicals were obtained from commercial sources and used directly. All boiling points were measured during distillation and are uncorrected.

3.1. General procedure for the synthesis of α-iodo-β,β-difluorovinylzinc reagent (CF_2=CIZnCl)

A 100 mL 2-necked RB flask fitted with a nitrogen tee and a septum was charged with diisopropylamine (7.0 mL, 50.0 mmol) and THF (20.0 mL). This solution was cooled to 0 °C and 2.5 M *n*-BuLi (25.0 mL, 50.0 mmol) was added slowly over 20 min. The resulting solution was allowed to stir for an additional 10 min.

A 250 mL three-necked RB flask fitted with a condenser, septum and a low-temperature thermometer was assembled while hot and flushed with nitrogen. The flask was charged with $ZnCl_2$ (3.4 g, 25.0 mmol) and THF (15.0 mL). The saturated solution was cooled to 15 °C using a cold-water bath and CF_3CH_2I (2.7 mL, 27.5 mmol) was added via a syringe. The pre-generated LDA was then slowly added (25 min) through a cannula keeping the temperature between 15 and 20 °C. The reaction mixture was stirred for 2 h at 20 °C and then allowed to settle. The ^{19}F NMR spectrum of the zinc reagent recorded at this stage showed the formation of zinc reagents complexed to THF and diisopropylamine along with traces of unreacted CF_3CH_2I. A small amount of *bis* zinc reagent was also detected along with the *mono* zinc reagent (*mono*/*bis*: 85:15). The ^{19}F NMR yield of the zinc reagent was 87% (versus $PhCF_3$ as an internal standard).

^{19}F NMR of (CF_2=CIZnCl)·TMEDA: −58.0 (d, $J = 53$ Hz, 1F), −71.8 (d, $J = 53$ Hz, 1F). ^{19}F NMR of $(CF_2{=}CI)_2Zn$·TMEDA: −57.0 (d, $J = 56$ Hz, 2F), −73.2 (d, $J = 56$ Hz, 2F).

3.2. General procedure for the coupling reaction of the α-iodo-β,β-difluorovinylzinc reagent with aromatic iodides

To the zinc reagent generated in the previous experiment (CF_2=CIZnCl), was added the aromatic iodide (usually

0.7–0.75 equiv.) and the tetrakistriphenylphosphinepalladium (usually 2 mol%). The mixture was stirred at r.t. for a prolonged time (until an ~80% conversion) and then heated at 60 °C. The reaction progress was monitored using ^{19}F NMR by sampling small aliquots of the reaction mixture. After complete conversion, the reaction mixture was triturated several times with pentane or hexane and the combined extracts evaporated on a rotary evaporator. The crude product was purified by distillation under reduced pressure or by column chromatography over silica gel.

3.3. Synthesis of $C_6H_5CI{=}CF_2$

Iodobenzene (3.6, 17.7 mmol) and $Pd(PPh_3)_4$ (0.423 g, 1.5 mol%) were added to the zinc reagent (22.0 mmol). The reaction mixture was stirred at r.t. for 12 h (>80% conversion) followed by heating at 60 °C for 2 h. ^{19}F NMR analysis of the reaction mixture showed complete conversion of the zinc reagent to the corresponding styrene (92% yield based on ^{19}F NMR) along with a trace amount of reduced product. The mixture was then triturated with hexane (6 × 20 mL). The combined hexane extracts were subjected to rotary evaporation under vacuum. The crude mixture was then carefully distilled under reduced pressure to obtain the pure α-iodo-β,β-difluorostyrene as a clear liquid in 79% (3.7 g, 13.9 mmol) yield.

b.p.: 72–75 °C at 12 mmHg. ^{19}F NMR ($CDCl_3$): δ −71.0 (d, $J = 25$ Hz, 1F), −78.2 (d, $J = 26$ Hz, 1F); ^{1}H NMR ($CDCl_3$): δ 7.22–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 152.9 (dd, $J = 298$, 283 Hz), 133.9 (s), 129.7 (s), 128.7 (s), 128.5 (s), 48.5 (dd, $J = 58$, 28 Hz); GC–MS: 266 [M^+] (14), 139 (42), 127 (BP, 100), 119 (46), 99 (33), 63 (33); HRMS: Calcd. for $C_8H_5F_2I$, 265.9404; found 265.9404.

3.4. Synthesis of p-$FC_6H_4CI{=}CF_2$

Following the general procedure for the coupling reaction, 1-fluoro-4-iodobenzene (4.0 g, 18.0 mmol), zinc reagent (22.0 mmol) and $Pd(PPh_3)_4$ (0.358 g, 1.5 mol%) were stirred at r.t. for 12 h (>75% conversion) followed by heating at 60 °C for 2 h to give the corresponding styrene in 92% yield (by ^{19}F NMR) along with a trace amount of reduced product and unreacted iodide. The reaction mixture was triturated several times with pentane. Evaporation of the solvent followed by careful distillation under reduced pressure afforded the *p*-$FC_6H_4CI{=}CF_2$ as a clear liquid in 71% (3.64 g, 12.8 mmol) yield.

b.p.: 63–65 °C at 11 mmHg. ^{19}F NMR ($CDCl_3$): δ −71.0 (d, $J = 25$ Hz, 1F), −78.2 (d, $J = 25$ Hz, 1F), −112.5 (m, 1F); ^{1}H NMR ($CDCl_3$): δ 7.40 (m, 2H), 7.01 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 162.5 (d, $J = 251$ Hz), 153 (dd, $J = 298$, 284 Hz), 131.5 (m), 130.0 (s), 115.6 (d, $J = 21$ Hz), 46.9 (dd, $J = 32$, 27 Hz); HRMS: Calcd. for $C_8H_4F_3I$, 283.9310, found 283.9306.

3.5. Synthesis of p-$ClC_6H_4CI{=}CF_2$

Following the general procedure for the coupling reaction, 1-chloro-4-iodobenzene (4.3 g, 18.0 mmol), zinc reagent (22.0 mmol) and $Pd(PPh_3)_4$ (0.449 g, 2.0 mol%) were stirred at r.t. for 14 h (>75% conversion) followed by heating at 65 °C for 3 h to give the corresponding styrene in 89% yield (by ^{19}F NMR). The reaction mixture was triturated several times with hexane. Evaporation of the solvent followed by distillation under reduced pressure afforded the *p*-$ClC_6H_4CI{=}CF_2$ as a clear liquid in 78% (4.23 g, 14.1 mmol) yield.

b.p.: 96–98 °C at 11 mmHg. ^{19}F NMR ($CDCl_3$): δ −70.2 (d, $J = 24$ Hz, 1F), −77.4 (d, $J = 24$ Hz, 1F); ^{1}H NMR ($CDCl_3$): δ 7.38–7.35 (m, 2H), 7.32–7.28 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 153.0 (dd, $J = 291$, 284 Hz), 134.6 (s), 130.1 (t, $J = 3$ Hz), 128.8 (s), 47.1 (dd, $J = 32$, 27 Hz); GC–MS: 302 [$M^+ + 2$] (32), 300 [M^+] (46), 173 (96), 138 (BP, 100), 127 (45), 87 (37), 62 (35); HRMS: Calcd. for $C_8H_4{}^{35}ClF_2I$, 299.9014; found 299.9011; Calcd. for $C_8H_4{}^{37}ClF_2I$, 301.8989; found 301.8987.

3.6. Synthesis of m-$O_2NC_6H_4CI{=}CF_2$

Following the general procedure for the coupling reaction, 1-iodo-3-nitrobenzene (4.1 g, 16.5 mmol), zinc reagent (22.0 mmol) and $Pd(PPh_3)_4$ (0.410 g, 2.0 mol%) were stirred at r.t. for 15 h (>50% conversion) followed by heating at 60 °C for 4 h to give the styrene in 86% yield (by ^{19}F NMR) along with a trace amount of reduced product. The reaction mixture was triturated several times with hexane. Evaporation of the solvent followed by distillation under reduced pressure afforded the corresponding styrene as a pale yellow liquid that solidified upon cooling. Recrystallization from hexane produced*m*-$O_2NC_6H_4CI{=}CF_2$ as pale yellow needles in 78% (4.0 g, 12.9 mmol) yield.

m.p.: 40–42 °C. ^{19}F NMR ($CDCl_3$): δ −68.3 (d, $J = 20$ Hz, 1F), −75.3 (d, $J = 20$ Hz, 1F); ^{1}H NMR ($CDCl_3$): δ 8.33 (t, $J = 2$ Hz, 1H), 8.16 (dm, $J = 8$ Hz, 1H), 7.78 (dm, $J = 7.6$ Hz, 1H), 7.55 (t, $J = 7.6$ Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 153.7 (dd, $J = 300$, 285 Hz), 148.2 (s), 135.8 (t, distorted), 136 (t, $J = 2$ Hz), 128 (s), 124.8 (t, $J = 2$ Hz), 123.5 (s), 45.7 (dd, $J = 31$, 26 Hz); GC–MS: 311 [M^+] (92), 184 (47), 138 (BP, 100), 126 (24), 88 (30); HRMS: Calcd. for $C_8H_4F_2INO_2$, 310.9255; found 310.9257.

3.7. Synthesis of m-$MeOC_6H_4CI{=}CF_2$

Following the general procedure for the coupling reaction, 4-iodoanisole (4.0 g, 17.2 mmol), zinc reagent (23.0 mmol) and $Pd(PPh_3)_4$ (0.429 g, 2.0 mol%) were stirred at r.t. for 5 h (>80% conversion) followed by heating at 65 °C for 2 h to give the corresponding styrene in 90% yield (by ^{19}F NMR) along with a small amount of reduced product. The mixture was triturated several times with hexane. Evaporation of the solvent followed by distillation under reduced pressure afforded the *m*-MeOC$_6$H$_4$CI=CF$_2$ as a clear liquid in 80% (4.10 g, 13.8 mmol) yield.

b.p.: 133–136 °C at 12 mmHg. ^{19}F NMR (CDCl$_3$): δ −70.8 (d, J = 24 Hz, 1F), −77.4 (d, J = 26 Hz, 1F); ^{1}H NMR (CDCl$_3$): δ 7.23 (t, J = 8 Hz, 1H), 7.01 (d, J = 8 Hz, 1H), 6.96 (s, 1H), 6.81 (dd, J = 8, 3 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (CDCl$_3$): δ 159.5 (s), 153.0 (dd, J = 298, 284 Hz), 135.2 (s), 129.6 (s), 122.0 (t, J = 2 Hz), 115.5 (d, J = 2 Hz), 114.4 (s), 48.2 (dd, J = 31, 26 Hz), 56.4 (s); GC–MS: 296 [M$^+$] (89), 169 (78), 154 (BP) (100), 138 (27), 126 (83), 107 (33), 99 (59), 87 (38), 75 (53); HRMS: Calcd. for C$_9$H$_7$F$_2$IO, 295.9510; found 295.9517.

3.8. Synthesis of *m-FC$_6$H$_4$CI=CF$_2$*

Following the general procedure for the coupling reaction, 1-fluoro-3-iodobenzene (3.7 g, 16.7 mmol), zinc reagent (22.2 mmol) and Pd(PPh$_3$)$_4$ (0.443 g, 2.0 mol%) were stirred at r.t. for 18 h followed by 60 °C for 2 h to give the corresponding styrene in 88% yield (by ^{19}F NMR) along with a trace amount of reduced product. The reaction mixture was triturated several times with pentane. Evaporation of the solvent followed by careful distillation under reduced pressure afforded the *m*-FC$_6$H$_4$CI=CF$_2$ as a clear liquid in 73% (3.45 g, 12.1 mmol) yield.

b.p.: 64–65 °C at 12 mmHg. ^{19}F NMR (CDCl$_3$): δ −69.7 (d, J = 22 Hz, 1F), −76.6 (d, J = 22 Hz, 1F), −112.9 (m, 1F); ^{1}H NMR (CDCl$_3$): δ 7.14–7.34 (m, 3H), 6.98 (dt, J = 8, 1 Hz, 1H); ^{13}C NMR (CDCl$_3$): δ 162.3 (d, J = 247 Hz), 153.1 (dd, J = 301, 284 Hz), 135.9 (d, J = 9 Hz), 130.0 (dd, J = 23, 4), 125.4 (q, J = 4 Hz), 116.8 (dt, J = 23, 4 Hz), 115.6 (d, J = 20 Hz), 47.0 (dd, J = 30, 29 Hz); GC–MS: 284 [M$^+$] (89), 157 (97), 137 (BP, 100), 127 (71), 107 (76), 87 (74), 81 (66), 57 (61); HRMS: Calcd. for C$_8$H$_4$F$_3$I, 283.9310; found 283.9312.

3.9. Synthesis of *m-F$_3$CC$_6$H$_4$CI=CF$_2$*

Following the general procedure for the coupling reaction, 3-iodobenzotrifluoride (3.67 g, 13.5 mmol), zinc reagent (18.0 mmol) and Pd(PPh$_3$)$_4$ (0.354 g, 2.0 mol%) were stirred at r.t. for 28 h followed by heating at 65 °C for 1 h to give the corresponding styrene in 85% yield (by ^{19}F NMR) along with a small amount of reduced product. The reaction mixture was triturated several times with hexane. Evaporation of the solvent followed by distillation under reduced pressure afforded the *m*-F$_3$CC$_6$H$_4$CI=CF$_2$ as a colorless liquid in 67% (3.0 g, 9.0 mmol) yield.

b.p.: 70–71 °C at 12 mmHg. ^{19}F NMR (CDCl$_3$): δ −63.3 (s, 3F), −69.4 (d, J = 22 Hz, 1F), −76.6 (d, J = 21 Hz, 1F); ^{1}H NMR (CDCl$_3$): δ 7.7 (s, 1H), 7.62 (d, J = 8 Hz, 1H), 7.54 (d, J = 8 Hz, 1H), 7.45 (t, J = 8 Hz, 1H); ^{13}C NMR (CDCl$_3$): δ 153.5 (dd, J = 301, 285 Hz), 135.0 (t, J = 2 Hz), 133.1 (s), 131.3 (q, J = 32 Hz), 129.3 (s), 126.7 (m), 125.5 (m), 123.8 (q, J = 272 Hz), 47.0 (dd, J = 32, 27 Hz); GC–MS: 334 [M$^+$, BP, 100], 315 (11), 207 (84), 187 (83), 138 (57), 127 (56); HRMS: Calcd. for C$_9$H$_4$F$_5$I, 333.9278; found 333.9280.

3.10. Synthesis of *o-MeC$_6$H$_4$CI=CF$_2$*

Following the general procedure for the coupling reaction, 2-iodotoluene (3.76 g, 17.2 mmol), zinc reagent (23.0 mmol) and Pd(PPh$_3$)$_4$ (0.423 g, 1.5 mol%) were stirred at r.t. for 18 h (50% conversion) followed by heating t 60 °C for 4 h to give the styrene in 85% yield (by ^{19}F NMR) along with a trace amount of reduced product. The reaction mixture was triturated several times with pentane. Evaporation of the solvent followed by careful distillation under reduced pressure yielded the *o*-MeC$_6$H$_4$CI=CF$_2$ as a clear liquid in 72% (3.49 g, 12.5 mmol) yield.

b.p.: 65–67 °C at 11 mmHg. ^{19}F NMR (CDCl$_3$): δ −75.4 (d, J = 26 Hz, 1F), −77.0 (d, J = 25 Hz, 1F); ^{1}H NMR (CDCl$_3$): δ 7.13–7.24 (m, 4H), 2.26 (s, 3H); ^{13}C NMR (CDCl$_3$): δ 152.3 (dd, J = 294, 285 Hz), 137.2 (d, J = 3 Hz), 133.2 (s), 130.6 (s), 130.4 (d, J = 2 Hz), 129.5 (s), 126.3 (s), 44.8 (dd, J = 34, 29 Hz), 19.6 (s); GC–MS: 280 [M$^+$] (63), 153 (71), 133 (100, BP), 127 (36), 51 (38); HRMS: Calcd. for C$_9$H$_7$F$_2$I, 279.9561; found 279.9570.

3.11. Synthesis of *p-F$_2$C=ICC$_6$H$_4$CI=CF$_2$*

Following the general procedure for the coupling reaction 1,4-diiodobenzene (2.8 g, 8.6 mmol), zinc reagent (23.0 mmol) and Pd(PPh$_3$)$_4$ (0.457 g, 2.0 mol%) were stirred at r.t. for 24 h followed by heating at 65 °C for 4 h to give the corresponding *bis* styrene along with traces of *mono* styrene and reduced product. The reaction mixture was triturated several times with hexane; evaporation of the solvent followed by distillation under reduced pressure yielded the *p*-F$_2$C=ICC$_6$H$_4$CI=CF$_2$ as a low melting solid 62% (2.4 g, 5.3 mmol).

b.p.: 99–104 °C at 12 mmHg. ^{19}F NMR (CDCl$_3$): δ −69.6 (d, J = 21 Hz, 2F), −76.9 (d, J = 23 Hz, 2F); ^{1}H NMR (CDCl$_3$): δ 7.42 (s, 4H); ^{13}C NMR (CDCl$_3$): δ 153.1 (dd, J = 299, 285 Hz), 134.1 (bs), 129.7 (dd, J = 3.6, 2.4 Hz), 47.6 (dd, J = 31, 27 Hz); GC–MS: 454 [M$^+$, 10], 327 (14), 200 (19), 127 (100, BP), 99 (26); HRMS: Calcd. for C$_{10}$H$_4$F$_4$I$_2$, 453.8339; found 453.8344.

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