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An efficient room temperature preparation of bromo difluorovinylzinc reagent (CF₂=CBrZnCl) and a high yield one-pot synthesis of α -bromo- β , β -difluorostyrenes

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Abstract

A high yield room temperature preparation of the 1-bromo-2,2-difluorovinylzinc reagent [CF₂=CBrZnCl] (>89%) was achieved via insitu metallation of CF₃CH₂Br or CF₂=CHBr with LDA in presence of ZnCl₂. Palladium catalyzed cross-coupling of this zinc reagent with aryl iodides provides α -bromo- β , β -trifluorostyrenes (ArCBr=CF₂) in 64–86% isolated yields, in an essentially 'one-pot' procedure. © 2004 Elsevier B.V. All rights reserved.

 $\label{eq:keywords: 2-Bromo-1,1,1-trifluoroethane; 2-Bromo-1,1-difluoroethylene; Bromodifluorovinylzinc; Pd(0) coupling; Bromodifluorovinyllithium; $$\alpha$-Bromo-1,1-difluoroethylene; Bromo-1,1-difluoroethylene; Bromo-1,1-d$

1. Introduction

1,1-Difluoroalkenes (R₂C=CF₂) are important fluorinecontaining compounds both from the chemical as well as the biological point of view. They can be reduced to 1-monofluoroolefins [1,2]; some of them are potential enzyme inhibitors [3-7] and have exhibited cytotoxic activity [8,9]. Halogen containing 1,1-difluoroalkenes are useful building blocks in organofluorine chemistry not only due to the reactivity of the gem-difluoromethylene unit towards nucleophilic reagents but also due to the possible functionalization at the halogen (chlorine, bromine, iodine) site. Generally, olefins of the type $R_2C=CF_2$, where R = alkyl, aryl, perfluoroalkyl or hydrogen have been synthesized by Wittig type reactions [10,11], but this approach is not adaptable to the synthesis of $RCX=CF_2$, where X=CI, Br or I due to the acylation of Wittig reagents. Alternatively, this type of olefin can be prepared by the reaction of the Grignard reagent with CF₂=CFX; but such a reaction provides an undesired isomeric olefin or an exchange reaction occurs to give the trifluorovinyl organometallic compound [12]. In the early 1950s Cohen developed a preparative method for α -chloro- β , β -difluorostyrene by a multi step procedure [13]. But there are not many routes

available for the synthesis of α -bromo- β , β -difluorostyrenes and absolutely nothing for α -iodo- β , β -difluorostyrenes. The well-known method for α -chloro- β , β -difluorostyrene and α bromo- β , β -difluorostyrene is a two-step process—addition of halogen to RCH=CF₂ [14,15] followed by dehydrohalogenation [16]. The success of the dehydrohalogenation process depended on the base employed. A more selective base like Li₂CO₃ was used to improve the yield and to avoid undesired side products (Scheme 1). KO^tBu as base produced a marginal increase in the yield of the styrene.

Recent advancement in the synthesis of α,β,β -trifluorostyrenes via utilization of the trifluorovinylzinc reagent as a synthon, followed by Pd(0) catalyzed cross coupling with aryl iodides, included the synthesis α -halo- β,β -difluorostyrene by such strategy [17–20]. One such method was recently reported from this laboratory for the synthesis of α -bromo- β,β -difluorostyrenes via the formation of the CF₂=CBrZnX type zinc reagent followed by subsequent Pd(0) coupling with aryl iodides (Scheme 2) [21]. Even though it was possible to obtain α -bromo- β,β -difluorostyrenes in excellent isolated yield under mild conditions by this method, the stating materials for this preparation (CF₂=CX₂), their cost, availability and environmentally hazardous nature limited this procedure.

Recently HFC-134a and HCFC-133a have been identified as excellent synthetic precursors for the generation of tri-fluorovinyllithium and α -chloro- β , β -difluorovinyllithium

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



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

reagents at low temperature (Scheme 3) [22–24]. Various groups have demonstrated the synthetic potential of the trifluorovinyl or chlorodifluorovinyl anions thus generated, making them excellent alternatives for $CF_2=CFX$ or $CF_2=CX_2$ [25–28].

2. Results and discussion

We have recently developed an excellent room temperature preparation of the trifluorovinylzinc reagent from HFC-134a and the chlorodifluorovinyl zinc reagent from HCFC 133a by using an insitu metallation strategy in the presence of an amine medium [29,30]. Pd(0) catalyzed coupling of these zinc reagents with aryl iodides produced a cost-effective synthetic route for α , β , β -trifluorostyrenes and α -chloro- β , β -difluorostyrenes (Scheme 4).

Herein, we report an extension of this methodology for the synthesis of α -bromo- β , β -difluorostyrenes via the α -bromo- β , β -difluorovinylzinc reagent. The only previous report of the α -bromo- β , β -difluorovinylzinc reagent was from this laboratory where the zinc reagent was generated by zinc insertion reaction into CF₂=CBr₂ [21]. The success of generating the zinc reagent form CF₃CH₂Br or CF₂=CHBr depends on the selective metallation at the proton site rather than metal halogen exchange. It was of interest to determine

$$CF_{3}CH_{2}Br + 2 LDA \xrightarrow{ZnCl_{2}} [CF_{2}=CBrZnCl] \cdot Pr_{2}NH/THF$$

$$15-20 \circ C/THF \qquad 89\%$$

Scheme 5. Preparation of $\alpha\mbox{-bromo-}\beta\mbox{,}\beta\mbox{-difluorovinylzinc}$ reagent from $CF_3CH_2Br.$

the selectivity of the metallation under our reaction conditions; where the metallation-transmetallation process was performed in situ in the presence of zinc chloride using LDA as a base. Thus, when a THF solution of CF_3CH_2Br and anhydrous zinc chloride was treated with two equivalents of LDA at 15–20 °C, an 89% yield of CF_2 =CBrZnCl (Scheme 5) was formed (as detected by ¹⁹F NMR analysis of the reaction mixture).

The ¹⁹F NMR spectrum showed both the mono and bis zinc reagents complexed to diisopropylamine and THF. Addition of stoichiometric amount of TMEDA to the zinc reagent medium simplified the NMR spectrum as the zinc reagent complexes preferentially to TMEDA and thus makes the mono and bis clearly distinguishable. The ¹⁹F NMR showed chemical shifts at -69.8 (d, J = 54.4 Hz), -83.9 (d, J = 54.3 Hz) corresponding to the mono zinc reagent and peaks at -69.3 (d, J = 56.9 Hz), -85.3 (d, J = 57.5 Hz) corresponding to the bis zinc reagent (mono/bis: 70:30). The values were also in agreement with the reported values for the zinc reagent (CF₂=CBrZnBr) generated by zinc insertion to $CF_2=CBr_2$ [21]. The zinc reagent formation was further confirmed by addition of glacial acetic acid to the reaction mixture to give CF₂=CHBr (¹⁹F NMR: δ : -83.9, dd, J = 37.9, 19.7 Hz, 1F, -84.6, d, J = 37.8 Hz, 1F) quantitatively.

The zinc reagent $CF_2=CBrZnCl$ was also generated in 95% yield from $CF_2=CHBr$ by insitu treatment with 1.0 eq of LDA and zinc chloride at 15 °C (Scheme 6).

The increase in the yield of the bromodifluorovinylzinc reagent (>89% by the metallation of CF_3CH_2Br or $CF_2=CHBr$) compared to that of trifluorovinylzinc reagent (73% by the metallation of HFC-134a) under similar reaction conditions is attributed to the increased stability of the intermediate bromodifluorovinyllithium (CF₂=CBrLi) compared to trifluorovinyllithium (CF₂=CFLi) [29]. Since

$$CF_3CH_2X \xrightarrow{Base}_{-80 \ ^{\circ}C} [CF_3CXH]^- \xrightarrow{-F^-} [CF_2=CXH] \xrightarrow{Base} [CF_2=CX]^- \xrightarrow{E^+} CF_2=CXE$$

 $X = F, CI$

Scheme 3. Generation of trifluorovinyl and chlorodifluorovinyllithium by metallation of HFC-134a and HCFC-133a.

$$CF_{3}CH_{2}X + 2 LDA \xrightarrow{ZnCl_{2}} [CF_{2}=CXZnCl] \xrightarrow{R-[-]{-}} Pd(PPh_{3})_{4} \\ X = F, 73\% \\ X = Cl, 91\% \\ X = Cl, 65-85\% \\ X = Cl, 65-85\%$$

Scheme 4. Preparation of α,β,β -trifluorostyrenes and α -chloro- β,β -difluorostyrenes via trifluorovinyl/chorodifluorovinylzinc reagents.

CF=CHBr
$$\xrightarrow{1.0 \text{ LDA, ZnCl}_2}$$
 [CF₂=CBrZnCl]• ⁱPr₂NH/THF
15-20 °C/THF 95%

Scheme 6. Preparation of $\alpha\mbox{-bromo-}\beta\mbox{,}\beta\mbox{-difluorovinylzinc}$ reagent from $CF_2\mbox{=}CHBr.$



Scheme 7. Pd(0) catalyzed coupling of bromodifluorovinylzinc reagent with iodobenzene.

little was known about the nature and stability of the bromodifluorovinyllithium, we have performed a series of experiments to test its thermal stability. Bromodifluorovinyllithium, $[CF_2=CBrLi]$ was generated from $CF_2=CHBr$ at -80 °C using LDA in THF medium containing stoichiometric amount of TMEDA and the resulting clear solution was warmed to -10 °C (turned completely dark) and quenched with zinc chloride. This reaction produced an 81% yield of the zinc reagent. The reaction under similar conditions without TMEDA produced a 63% yield of the zinc reagent. These experiments, even though the solution turned dark during the warming process, demonstrated that most of the [CF₂=CBrLi] was intact even at -10 °C in both experiments. Similar experiments with [CF₂=CFLi] produced only $\sim 5\%$ yield of the zinc reagent. These experiments illustrate the increased stability of [CF₂=CBrLi] compared to [CF₂=CFLi] at temperatures near to room temperature. [CF₂=CBrLi] was also generated using *n*-BuLi in the absence of an amine in the medium at -80 °C. The resulting brown solution was warmed and quenched with $ZnCl_2$ at -10 °C to produce only a 24% yield of the zinc reagent. This confirms the increased stability of these fluorinated lithium reagents in an amine medium especially in the presence of TMEDA.

The zinc reagent generated by both routes were coupled with iodobenzene using $Pd(PPh_3)_4$ as catalyst to produce

Table 1

 $\begin{array}{l} \label{eq:constraint} Preparation of various α-bromo-β,β-difluorostyrenes$ \\ CF_3CH_2Br_{1.1\,eq.} + ZnCl_{21.0\,eq.} + LDA_{2.0\,eq.} \rightarrow \stackrel{(1)}{\underset{(2)}{}^{15-20\,^\circ\text{C}}} \text{ArCBr} = CF_2 \end{array}$

corresponding α -bromo- β , β -difluorostyrene in 76% isolated yield (Scheme 7).

After the successful synthesis of α -bromo- β , β -difluorostyrene, this methodology was successfully applied for the synthesis of a variety of substituted α -bromo- β , β -difluorostyrenes. Thus, the zinc reagent was generated from CF₃CH₂Br or CF₂=CHBr, and was treated with various aromatic iodides with electron donating and electron withdrawing groups in the ring using Pd(0) as catalyst at RT or heating at 65 °C to produce the styrenes in good isolated yields (Table 1). Reaction was smooth even with iodides having a bulky CF₃ *ortho* substituent (entry 7). Reaction with the heterocyclic iodide 2-iodothiophene was sluggish producing a mixture of styrene and traces of unreacted iodide (entry 9).

In conclusion, we have developed a high yield synthesis of α -bromo- β , β -difluorovinyl zinc reagent starting from the commercially available halocarbons CF₃CH₂Br or CF₂= CHBr by a metallation/insitu transmetallation process using LDA/ZnCl₂. Pd(0) catalyzed coupling reaction of this zinc reagent with various aryl iodides produced α -bromo- β , β -difluorostyrenes in excellent isolated yields. The metallation–coupling process could be performed either 'one-pot' or a stock solution of the zinc reagent prepared could be used for separate coupling reactions. Future reports will detail functionalization of these styrene derivatives.

3. Experimental

¹H, {¹H}¹³C and ¹⁹F 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 (CDCl₃, CFCl₃ or TMS). Unless noted otherwise, CDCl₃ 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

		(-)			
No.	Iodide (ArI)	Temp/time	α -Bromo- β , β -difluorostyrene	¹⁹ F NMR yield	Yield (%) ^a
1	C ₆ H ₅ I	RT, 12 h then 60 °C, 1 h	C ₆ H ₅ CBr=CF ₂	96	76
2	p-FC ₆ H ₄ I	RT, 14 h	p-FC ₆ H ₄ CBr=CF ₂	99	75
3	p-ClC ₆ H ₄ I	RT,14 h then 60 °C, 2 h	p-ClC ₆ H ₄ CBr=CF ₂	95	82
4	o-MeC ₆ H ₄ I	60 °C, 12 h	o-MeC ₆ H ₄ Br=CF ₂	99	86
5	m-NO ₂ C ₆ H ₄ I	RT, 22 h	$m-O_2NC_6H_4CBr=CF_2$	89	75
6	p-MeOC ₆ H ₄ I	65 °C, 5 h	<i>p</i> -MeOC ₆ H ₄ CBr=CF ₂	94	82
7	o-F3CC6H4I	65 °C, 15 h	o-F ₃ CC ₆ H ₄ CBr=CF ₂	96	74
8	p-IC ₆ H ₄ I	65 °C, 5 h	p-CF ₂ =CBrC ₆ H ₄ CBr=CF ₂	88	69
9 ^b	[Š—I	RT, 24 h then 60 $^\circ\text{C},$ 4 h	[S→CBr=CF ₂	84	64

^a Isolated yield of pure product.

^b This reaction was sluggish and the product styrene was contaminated with 4-5% 2-iodothiophene.

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 $63-200 \ \mu$ s). Tetrahydrofuran (THF) was dried by distillation from sodium benzophenone/ketyl at atmospheric pressure immediately prior to use. Pd(PPh₃)₄ was prepared by Coulson's procedure (Inorg. Synth. 13 (1972) 121–124). N₂ 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 the α -bromo- β , β -difluorovinylzinc reagent [CF₂=CBrZnCl]

A 100 ml two-necked RB fitted with a nitrogen tee and a septum was charged with diisopropylamine (70.0 ml, 50.0 mmol) and THF (20.0 ml). The mixture was cooled to 0 $^{\circ}$ C and 2.5 M *n*-BuLi (25.0 ml, 50.0 mmol) was slowly added over 20 min; the resulting mixture was allowed to stir for 10 min.

A 250 ml three-necked RB fitted with a condenser, septum and a low temperature thermometer were assembled while hot and flushed with nitrogen gas. It was charged with ZnCl₂ (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 CF₃CH₂Br (2.5 ml, 27.5 mmol) was added via a syringe. The pre-generated LDA was slowly added (25 min) through a cannula keeping the temperature between 15 and 20 $^{\circ}$ C (1.0 equivalent of LDA was used in the case of CF₂=CHBr; where CF₂=CHBr was condensed into the reaction mixture using a dryice/isopropanol condenser). The reaction mixture was stirred for 2 h at 20 °C and then allowed to settle. The ¹⁹F NMR of the pale vellow reaction mixture recorded at this stage showed formation of mono and bis zinc reagents complexed to THF and diisopropylamine along with traces of unreacted CF₃CH₂Br. The ¹⁹F NMR yield of the zinc reagent was 89%. TMEDA (0.1 ml) was added to the NMR tube and the ¹⁹F NMR of this solution showed mono and bis zinc reagents (mono/bis = 70:30) complexed only to TMEDA. ¹⁹F NMR of [CF₂=CBrZnCl]. TMEDA: δ -69.8 (d, J = 54.4 Hz, 1F), -83.9 (d, J = 54.3 Hz, 1F);¹⁹F NMR of $(CF_2=CBr)_2$ Zn.TMEDA: δ -69.3 (d, J = 56.9 Hz, 2F), -85.3 (d, J = 57.5 Hz, 2F).

3.2. General procedure for the Pd (0) catalyzed coupling reaction of the α -bromo- β , β -difluorovinylzinc reagent with aromatic iodides

To the zinc reagent, generated by the above procedure, was added the aromatic iodide (usually 0.80 eq) and tetrakistriphenylphosphinepalladium (1.5 mol%). The reaction mixture was either stirred at RT or heated at 60 °C using an oil bath. The reaction progress was monitored using ¹⁹F NMR by sampling small aliquots of the reaction mixture. After the reaction was completed, the mixture was triturated several times with pentane or hexane and the combined extracts evaporated on a rotary evaporator. The residual liquid was distilled under reduced pressure or purified by column chromatography over silica gel.

3.3. $C_6H_5CBr=CF_2$

Iodobenzene (3.6 g, 18.0 mmol) and Pd(PPh₃)₄ (0.358 g, 1.5 mol%) were added to the zinc reagent (22.5 mmol). The reaction mixture was stirred at RT for 12 h and then heated at 60 °C for 1 h, the color of the reaction mixture slowly changed from yellow to brown to black during this period. ¹⁹F NMR of the reaction mixture showed complete conversion with a 96% yield of α-bromo- β , β -difluorostyrene. The mixture was then triturated with pentane (6 × 25 ml). The lower black residue separated from the pentane extracts. The combined pentane extracts were evaporated under vacuum on rotary evaporator. The crude mixture was then carefully distilled under reduced pressure to obtain the pure α-bromo- β , β -difluorostyrene as a clear liquid in 76% (2.99 g, 13.7 mmol) yield. bp, 51–52 °C at 11 mm.

¹⁹FNMR (CDCl₃): δ –78.9 (d, J = 31.1 Hz, 1F), –85.1 (d, J = 31.2 Hz, 1F); ¹H NMR (CDCl₃): δ 7.44–7.48 (m, 2H), 7.26–7.37 (m, 3H); ¹³C NMR (CDCl₃): δ 153.2 (dd, J = 294.1, 286.5 Hz), 131.6 (d, J = 3.6 Hz), 128.9 (s), 128.8 (s), 128.5 (s), 79. 9 (dd, J = 30.5, 26.2 Hz); GC–MS: 220 (M⁺ + 2) (64), 218 (M⁺) (65), 139 (94), 119 (BP, 100), 99 (69), 87 (41), 63 (64), 62 (53); HRMS: calcd for C₈H₅F₂⁷⁹Br 217.9543 found 217.9546, calcd for C₈H₅F₂⁸¹Br 219.9522 found 219.9520.

3.4. p-FC₆H₄CBr=CF₂

Following the general procedure for the coupling reaction,1-fluoro-4-iodobenzene (3.89 g, 17.5 mmol), zinc reagent (21.4 mmol) and Pd(PPh₃)₄ (0.348 g, 1.5 mol%) at RT for 14 h followed by work-up and careful distillation under reduced pressure afforded the *p*-fluoro- α -bromo- β , β difluorostyrene as a clear liquid in 75% (3.1 g, 13.1 mmol) yield. bp, 45–48 °C at 11 mm.

¹⁹F NMR (CDCl₃): δ –79.0 (d, J = 33.1 Hz, 1F), -85.3 (d, J = 31.0 Hz, 1F), -112.1 (m, 1F); ¹H NMR (CDCl₃): δ 7.45 (m, 2H), 7.05 (m, 2H); ¹³C NMR (CDCl₃): δ 162.8 (d, J = 250.2 Hz), 153.3 (dd, J = 293.9, 286.7 Hz), 130.9 (m), 126.8 (s), 115.8 (d, J = 23.2 Hz), 79.0 (dd, J = 34.9, 25.8 Hz); GC–MS: 238 (M+2) (53), 236 (M⁺) (55), 157 (BP, 100), 137 (74), 107 (40), 87 (37), 81 (39); HRMS: calcd for C₈H₄F₃⁷⁹Br 235.9448 found 235.9447, calcd for C₈H₄F₃⁸¹Br 237.9428 found 237.9427.

3.5. p-ClC₆H₄CBr=CF₂

Following the general procedure for the coupling reaction, 1-chloro-4-iodobenzene (4.17 g, 17.5 mmol), zinc reagent (21.4 mmol) and Pd(PPh₃)₄ (0.348 g, 1.5 mol%) at RT for 14 h and then at 60 °C for 2 h, followed by work-up and

distillation under reduced pressure afforded the *p*-chloro- α bromo- β , β -difluorostyrene as a clear liquid in 82% (3.6 g, 14.3 mmol) yield. bp, 75 °C at 11 mm.

¹⁹FNMR (CDCl₃): δ -77.9 (d, J = 29.4 Hz, 1F), -84.2 (d, J = 29.0 Hz, 1F); ¹H NMR (CDCl₃): δ 7.31-7.35 (m, 2H), 7.39-7.43 (m, 2H); ¹³C NMR (CDCl₃): δ 153.3 (dd, J = 294.2, 286.4 Hz), 134.9 (s), 130.1 (t, J = 3.4 Hz), 128.8 (s), 79.0 (dd, J = 34.0, 25.6 Hz); GC-MS: 254 (M⁺ + 2) (61), 252 (M⁺) (48), 173 (86), 138 (BP, 100), 99 (41), 87 (57), 62 (46); HRMS: calcd for C₈H₄⁷⁹BrBr₃₅ClF₂ 251.9153 found 251.9151, calcd for C₈H₄⁸¹Br³⁵ClF₂ 253.9132 found 253.9129, calcd for C₈H₄⁸¹Br³⁷ClF₂ 253.9123 found 253.9129, calcd for C₈H₄⁸¹Br³⁷ClF₂ 255.9103 found 255.9107.

3.6. o-MeC₆H₄CBr=CF₂

Following the general procedure for the coupling reaction, 2-iodotoluene (3.83 g, 17.6 mmol), zinc reagent (22.0 mmol) and Pd(PPh₃)₄ (0.348 g, 1.5 mol%) at 60 °C for 12 h, followed by work-up and careful distillation under reduced pressure yielded the *o*-methyl- α -bromo- β , β -difluorostyrene as a clear liquid in 86% (3.52 g, 15.2 mmol) yield [21]. bp, 52–53 °C at 11 mm.

¹⁹FNMR (CDCl₃): δ -83.1 (d, J = 32.6 Hz, 1F), -84.5 (d, J = 33.5 Hz, 1F); ¹HNMR (CDCl₃): δ 7.20–7.30 (m, 4H), 2.33 (s, 3H); ¹³C NMR (CDCl₃): δ 152.7 (t, J = 289.1 Hz), 137.8 (d, J = 1.4 Hz), 130.9 (s), 130.6 (s), 130.5 (s), 129.9 (s), 126.2 (s), 76.8 (dd, J = 41.2, 25.7 Hz), 19.3 (s); GC–MS: 234 (M⁺ + 2) (62), 232 (M⁺) (63), 153 (64), 151 (62), 134 (52), 133 (BP, 100), 75 (51), 63 (50), 51 (57).

3.7. $m - O_2 NC_6 H_4 CBr = CF_2$

Following the general procedure for the coupling reaction, 1-iodo-3-nitrobenzene (4.38 g, 17.6 mmol), zinc reagent (22.0 mmol) and Pd(PPh₃)⁴ (0.348 g, 1.5 mol%) at RT for 22 h, followed by work-up and distillation under reduced pressure afforded the *m*-nitro- α -bromo- β , β -difluorostyrene as a pale yellow liquid in 75% (3.5 g, 13.2 mmol) yield. bp, 115–116 °C at 11 mm.

¹⁹FNMR (CDCl₃): δ –75.6 (d, J = 25.3 Hz, 1F), –82.0 (d, J = 26.4 Hz, 1F); ¹H NMR (CDCl₃): δ 8.40 (s, 1H), 8.21 (dm, J = 8.2 Hz, 1H), 7.80 (dm, J = 7.9 Hz, 1H), 7.63 (t, J = 7.8 Hz, 1H); ¹³C NMR (CDCl₃): δ 153.8 (dd, J = 297.5, 289.0 Hz), 148.2 (s), 134.5 (t, J = 3.2 Hz), 133.4 (d, J = 2.9 Hz), 129.7 (s), 123.8 (t, J = 3.4 Hz), 123.6 (s), 78.1 (dd, J = 33.1, 27.9 Hz); GC–MS: 265 (M⁺ + 2) (10), 263 (M⁺) (10), 138 (BP, 100), 99 (36), 87 (37), 62 (34); HRMS: calcd for C₈H₄F₂⁷⁹BrNO₂ 262.9393 found 262.9392, calcd for C₈H₄F₂⁸¹BrNO₂ 264.9373 found 264.9373.

3.8. p-MeOC₆H₄CBr=CF₂

Following the general procedure for the coupling reaction, 4-iodoanisole (3.9 g, 16.8 mmol), zinc reagent (20.5 mmol) and Pd(PPh₃)₄ (0.334 g, 1.5 mol%) at 65 °C for 5 h, followed by work-up and distillation under reduced pressure produced the *m*-methoxy- α -bromo- β , β -difluorostyrene as a clear liquid in79% (2.8 g, 13.7 mmol) yield. bp, 93–95 °C at 11 mm.

¹⁹FNMR (CDCl₃): δ –80.4 (d, J = 34.0 Hz, 1F), –86.6 (d, J = 34.6 Hz, 1F); ¹H NMR (CDCl₃): δ 7.40 (dm, J = 8.9 Hz, 2H), 6.88 (dm, J = 9.0 Hz, 2H), 3.80 (s, 3H); ¹³C NMR (CDCl₃): δ 160.0 (s), 153.0 (dd, J = 292.6, 285.6 Hz), 130.3 (t, J = 3.5 Hz), 123.9 (d, J = 4.1 Hz), 114.0 (s), 79.8 (dd, J = 34.3, 24.8 Hz), 55.4 (s); GC–MS: 250 (M⁺ + 2) (24), 248 (M⁺) (24), 169 (BP, 100), 154 (25), 126 (73), 125 (61), 99 (67). HRMS: calcd for C₉H₇F₂⁷⁹BrO 247.9648 found 247.9636, calcd for C₉H₇F₂⁸¹BrO 249.9628 found 249.9606.

3.9. o- $CF_3C_6H_4CBr=CF_2$

Following the general procedure for the coupling reaction, 2-iodobenzotrifluoride (4.56 g, 16.8 mmol), zinc reagent (21.0 mmol) and Pd(PPh₃)₄ (0.334 g, 1.5 mol%) at 65 °C for 15 h, followed by work-up and distillation under reduced pressure afforded the *o*-trifluoromethyl- α -bromo- β , β -difluorostyrene as a colorless liquid in 74% (3.55 g, 12.4 mmol) yield [21].(The ¹³C NMR values reported for this compound in [21] is not correct due to an error in reporting). bp, 51–53 °C at 11 mm.

¹⁹FNMR (CDCl₃): δ –61.4 (d, J = 5.4 Hz, 3F), -81.2 (m, 2F); ¹H NMR (CDCl₃): δ 7.71 (d, J = 7.6 Hz, 1H), 7.58 (m, 1H), 7.44–7.53 (m, 2H); ¹³C NMR (CDCl₃): δ 153.0 (t, J = 288.9 Hz), 133.0 (d, J = 2.4 Hz), 132.4 (s), 130.3 (s), 130.1 (s), 126.7 (q, J = 4.7 Hz), 123.5 (q, J = 273.4 Hz), 73.2 (dd, J = 41.2, 30.8 Hz); GC–MS: 288 (M⁺ + 2) (74), 286 (M⁺) (75), 207 (BP, 100), 187 (88), 157 (66), 138 (71), 99 (36), 87 (47), 69 (66).

3.10. Synthesis of p- F_2C = $BrCC_6H_4CBr$ = CF_2

Following the general procedure for the coupling reaction, 1,4-diiodobenzene (2.77 g, 8.4 mmol), zinc reagent (21.0 mmol) and Pd(PPh₃)₄ (0.324 g, 1.5 mol%) at 65 °C for 5 h, followed by work-up and distillation under reduced pressure yielded the bis- α -bromo- β , β -difluorostyrene as a colorless solid, which was crystallized from hexane 69% (2.08 g, 5.81 mmol) [21]. mp, 52–53 °C.

¹⁹FNMR (CDCl₃): δ -77.2 (d, J = 28.4 Hz, 2F), -83.6 (d, J = 28.2 Hz, 2F); ¹H NMR (CDCl₃): δ 7.53 (s, 4H); ¹³C NMR (CDCl₃): δ 153.5 (dd, J = 294.3, 288.0 Hz), 128.9 (t = not resloved), 79.4 (dd, J = 35.4, 28.1 Hz); GC-MS: 362 (M⁺ + 4) (2), 360 (M⁺ + 2) (4), 358 (M⁺) (2), 281 (3), 279 (4), 200 (34), 150 (30), 149 (34), 123 (35), 99 (BP, 100), 75 (87), 74 (46), 62 (39), 51(58).

3.11. 2-(2-Bromo-1,1-difluoroethenyl) thiophene

Following the general procedure for the coupling reaction, 2-iodothiophene (3.5 g, 16.8 mmol), zinc reagent (21.0 mmol) and Pd(PPh₃)₄ (0.334 g, 1.5 mol%) at RT for 24 h, followed by work-up and distillation under reduced pressure afforded the 2-(2-bromo-1,1-difluoroethenyl) thiophene as a colorless liquid in 64% (2.5 g, 11.2 mmol) yield. bp, 48–50 °C at 11 mm.

¹⁹FNMR (CDCl₃): δ –80.1 (d, J = 24.3 Hz, 1F), –80.4 (d, J = 25.1 Hz, 1F); ¹H NMR (CDCl₃): δ 7.35 (dd, J = 1.3, 5.3 Hz, 1H), 7.22 (dd, J = 1.2, 3.8 Hz, 1H), 7.02 (ddd, J = 1.0, 3.8, 4.9 Hz, 1H); ¹³C NMR (CDCl₃): δ 153.1 (dd, J = 298.3, 290.6 Hz), 132.9 (d, J = 7.8 Hz), 128.4 (t, J = 5.0 Hz), 127.3 (s), 127.1 (bs), 75.3 (dd, J = 34.4, 29.8 Hz); GC–MS: 226 (M + 2) (28), 224 (M⁺) (28), 210 (100), 145 (80), 127 (74), 111 (96), 101 (68), 83 (76), 57 (95); HRMS: calcd for C₆H₃⁷⁹BrF₂S 223.9107 found 223.9107, calcd for C₆H₃⁸¹BrF₂S 225.9086 found 225.9084.

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