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Approaches to the preparation of (*Z*)-1,2-difluorostilbenes☆

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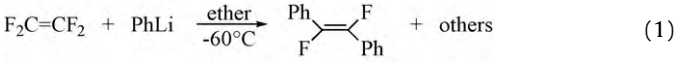
ABSTRACT

Methodology directed at the preparation of (*Z*)-1,2-difluorostilbenes has been evaluated. For symmetrical (*Z*)-1,2-difluorostilbenes, photochemical isomerization of the isomeric (*E*)-1,2-difluorostilbenes, and HPLC separation of the mixture of stilbene isomers is a reasonable route to a particular (*Z*)-stilbene. An alternative approach to both symmetrical and/or unsymmetrical (*Z*)-1,2-difluorostilbenes has been developed *via* stereospecific Pd(0) coupling of (*E*)-1,2-difluoro-aryl-ethenyltributylstannanes under Stille-Liebiskind conditions with aryl idodies. The requisite arylstannanes can be obtained *via* the reported route developed by Davis or *via* (*E*)-1,2-difluorovinyltributylstannane – a new route described in this work. The methodology tolerates almost any functionality in the aryl ring, is easily carried out, is stereospecific and provides the first general route to (*Z*)-1,2-difluorostilbenes.

1. Introduction

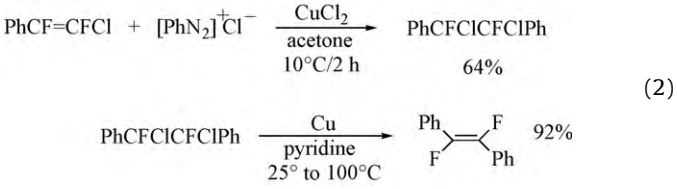
1,2-Difluorostilbenes have been of interest to organic chemists for several decades. These compounds have been tested and/or utilized in liquid crystal applications [1,2]. Poly(arylenevinylene)s with fluorinated vinylene units have also recently been investigated for fine-tuning of the electrical and optical properties in organic light-emitting diodes (OLEDs), and these polymers show the most bluefield photoluminescence emission in the solid state reported to date for poly(p-phenylenevinylene)s [3]. More recently, (*E*)-1,2-Difluorostilbenes have been demonstrated to be promising materials for high dielectric biaxiality ferroelectric mixtures [4].

Most of the reported work with 1,2-difluorostilbenes has been accomplished with the (*E*)-isomer. Dixon first reported the preparation of (*E*)-1,2-difluorostilbene *via* the reaction of tetrafluoroethene with phenyllithium in ether at −60 °C [5], Eq. (1).



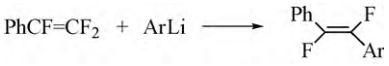
(1)

The yields are modest (~50%). Russian workers reported this same compound *via* the methodology outlined in Eq. (2) [6]. This route avoids the use of C_2F_4 and low temperatures.



(2)

Unsymmetrical (*E*)-1,2-difluorostilbenes have been prepared *via* the reaction of trifluorostyrenes and aryllithiums, Eq. (3) [1,2].



(3)

Initially, this methodology was somewhat limited due to the lack of a high yield method for the synthesis of suitable styrene precursors. However, recent reports have detailed useful routes to trifluorostyrene and substituted trifluorostyrenes [7–10] and this route has become a more useful approach to unsymmetrical (*E*)-1,2-difluorostilbenes.

As noted above, the symmetrical (*E*)-1,2-difluorostilbenes have been most commonly prepared from C_2F_4 and aryllithiums. The yields *via* this approach are modest, functionality in the aryllithiums is limited, and generally the stilbene is accompanied by more highly substituted vinyl derivatives. To circumvent the multiple substitution problem, the limitation of aryl functionality

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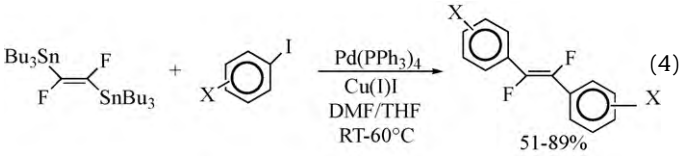
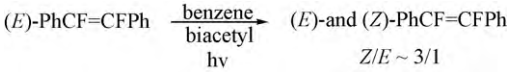
in the lithium reagent, and to avoid the use of C_2F_4 and low temperatures, we recently reported a highly efficient stereospecific route to (*E*)-1,2-difluorostilbenes *via* the palladium coupling of (*E*)-(1,2-difluoro-1,2-ethenediyl)bis [tributylstannane] with aryl iodides, as illustrated in Eq. (4) [11].



(4)

The bis[stannane] precursor is readily prepared in two steps from chlorotrifluoroethene [12]. The isolated yields are high and the methodology avoids the use of C_2F_4, tolerates a wider variety of functional groups than the organolithium approach and employs a cheap, safe olefin precursor.

In contrast to the extensive work on the preparation of (*E*)-1,2-difluorostilbenes, little progress has been made on synthetic routes to the isomeric (*Z*)-1,2-difluorostilbenes. The only route to this isomeric analog has been *via* the photochemical isomerization of the (*E*)-1,2-difluorostilbene [13], Eq. (5). This methodology generally produces a mixture of (*E*)- and (*Z*)-isomers, which were separated chromatographically.



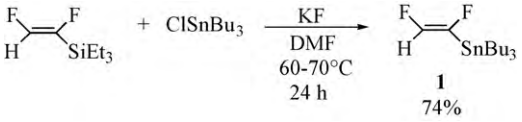
(5)

2. Results and discussion

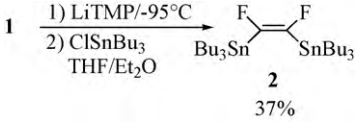
In the initial approach to a more general route to (*Z*)-1,2-difluorostilbenes we focused on several synthetic methods to evaluate routes that would accomplish our overall objective – namely, the successful preparation of (*Z*)-1,2-difluorostilbenes (both symmetrical and unsymmetrical analogues). We have not attempted to prepare an extensive list of the (*Z*)-stilbenes; instead we have attempted to develop a proof of principle to this class of compounds that would allow others to prepare the (*Z*)-stilbene of their choice.

2.1. (*Z*)-(1,2-Difluoro-1,2-ethenediyl)bis[tributylstannane], 2

The successful preparation of (*E*)-1,2-difluorostilbenes *via* Pd(0) coupling of aryl iodides with (*E*)-$Bu_3SnCF=CFSnBu_3$ [11] prompted us to investigate the viability of this approach for the synthesis of the corresponding (*Z*)-stilbenes. Thus, we prepared the requisite (*Z*)-(1,2-difluoro-1,2-ethenediyl)bis[tributylstannane] in modest yield as outlined below in Eqs. (6) and (7) [14,15].



(6)

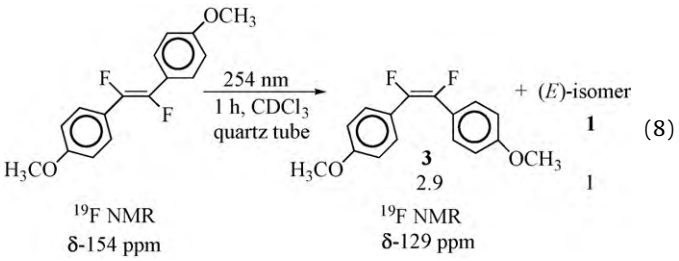


(7)

Attempted coupling of **2** with aryl iodides, such as 1-iodo-4-nitrobenzene and 4-iodoanisole, under conditions similar to the successful preparation of the (*E*)-stilbenes. $Pd(PPh_3)_4$/Cu(I)I/DMF failed to yield any (*Z*)-stilbene and extensive decomposition of **2** was noted. Thus, this synthetic route was not investigated further.

2.2. Photochemical isomerization

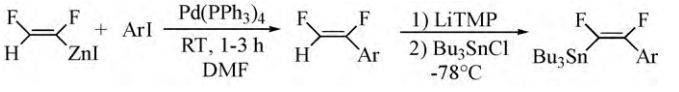
As noted above, Chinese workers had reported the photochemical isomerization of (*E*)-1,2-difluorostilbene in benzene and biacetyl(photosensitizer) with a 200 W mercury lamp [13] to give a 75/25 isomeric mixture of *Z*/*E* isomers. Since our recent methodology provided a high yield, short route to symmetrical (*E*)-1,2-difluorostilbenes [11], we were prompted to evaluate this route as a useful entry to the corresponding symmetrical (*Z*)-stilbenes. Recent advances in HPLC separation would immensely aid this approach. Thus, we prepared (*E*)-(1,2-difluoro-1,2-ethenediyl)bis[4-methoxybenzene] *via* the literature procedure [11]. Subsequent photochemical isomerization (254 nm, RT, quartz tube, $CDCl_3$, Rayonet UV Chamber, 1 h) was accompanied by a new singlet at δ −129 ppm [(*Z*)-stilbene] in the ^{19}F NMR spectrum. After 1 h the ratio of (*Z*/*E*) stilbenes was 2.9/1. Further irradiation did not change this ratio, Eq. (8). The two stilbene isomers could not be effectively separated by column chromatography, pentane eluant, [$R_f(Z) = 0.5$; $R_f(E) = 0.6$]. Therefore, the crude product was separated by HPLC (CH_3CN solvent) [16]. Removal of the solvent provided a 41% isolated yield of a colorless oil, identified *via* ^{19}F NMR, ^1H NMR, ^{13}C NMR and HRMS as (*Z*)-1,2-difluoro-1,2-ethenediyl)bis[4-methoxybenzene], **3** (cf. Experimental). The facile preparation of the (*E*)-stilbene makes this route practical for the preparation of an individual (*Z*)-1,2-difluorostilbene, but is somewhat tedious for the preparation of a series of (*Z*)-1,2-difluorostilbenes. However, we can recommend this route for any researcher interested in a particular symmetrical (*Z*)-1,2-difluorostilbene. Subsequently, we investigated alternative methodology that would employ a common precursor to a series of (*Z*)-1,2-difluorostilbenes.



(8)

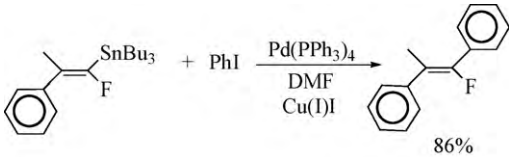
2.3. Preparation of (*E*)-1,2-difluoro-2-aryl-tributylstannylethenes

Recently, we reported a stereospecific route to (*E*)-1,2-difluoro-2-aryl-tributylstannylethenes from (*Z*)-1,2-difluorostyrenes [17], Eq. (9).

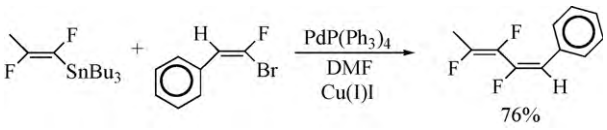


(9)

Since McCarthy had reported the successful preparation of (*Z*)-1-fluoro-1,2-diphenylpropene *via* Stille coupling of (*E*)-1-fluoro-2-phenyl-propenyltributylstannane, Eq. (10) [18,19], and we had observed successful Stille-Liebeskind cross-coupling reactions of (*Z*)-1,2-difluoro-1-tributylstannyl-1-propene with (*Z*)-1-bromo-1-fluorostyrene, Eq. (11) [20], arylation of [(*E*)-1,2-difluoro-2-aryl-tributylstannylethenes] seemed a potentially useful route to (*Z*)-1,2-difluorostilbenes [21]. The co-catalysis (Liebeskind conditions) [22] of Cu(I)I and $Pd(PPh_3)_4$ enhanced the overall yield of the reaction and minimized side product(s) formation [18,19].

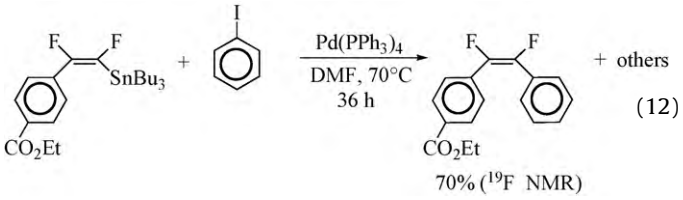


(10)



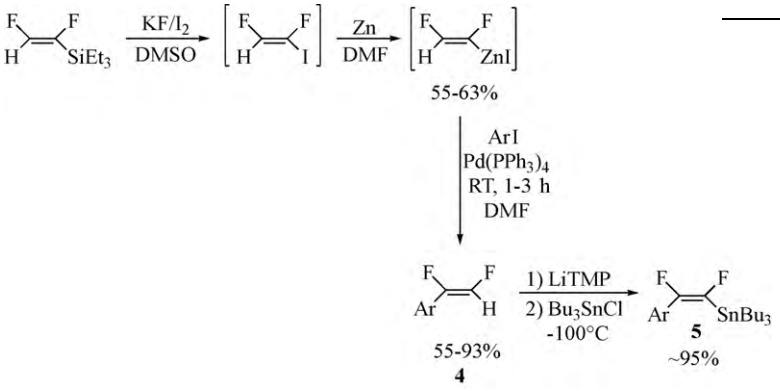
(11)

To test this idea, Davis [21] reacted (*E*)-1,2-difluoro-2-(4-carboethoxyphenyl)tributylstannylethene with iodobenzene with Pd(0) catalysis, Eq. (12) [21]. A 70% yield (^{19}F NMR) of the (*Z*)-1,2-difluorostilbene was obtained, along with 15% p-$EtO_2CC_6H_4CF$ = CFH and 15% others. Wesolowski subsequently investigated this reaction further employing Cu(I)I co-catalysis to improve the overall yield and selectivity [23].



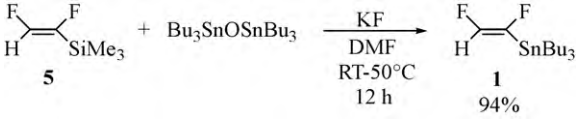
(12)

The requisite (*E*)-1,2-difluoro-2-aryl-tributylstannylethenes can be readily prepared by the method reported by Davis and Burton [17], as outlined in Eq. (13). This method works well and stereospecifically permits preparation of a variety of (*E*)-stannanes. The limiting step in this route is the synthesis of the (*E*)-CFH = CFI. Thus, we investigated an alternative precursor to the same (*Z*)-1,2-difluorostyrenes, **4**. Since we have demonstrated that fluorinated vinylsilanes can be easily converted (stereospecifically) to fluorinated vinylstannanes [14], we studied the use of (*E*)-(1,2-difluorovinyl)tributylstannane as an alternative to (*E*)-CFH=CFI.



(13)

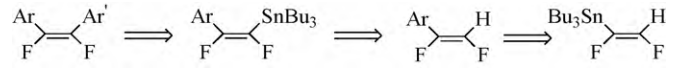
(*E*)-(1,2-difluorovinyl)tributylstannane, **1**, is readily prepared in high yield as outlined in Eq. (14). The vinylsilane, **5**, is readily prepared *via* our published methodology [24].



(14)

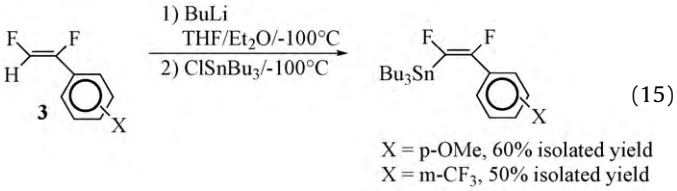
Retrosynthetic analysis for the preparation of (*Z*)-1,2-difluorostilbenes is outlined in Scheme 1.

To evaluate the utility of **1** for the preparation of (*Z*)-1,2-difluorostyrenes, **1** was cross-coupled with several aryl iodides under Stille-Liebeskind conditions. These results are summarized in Table 1.



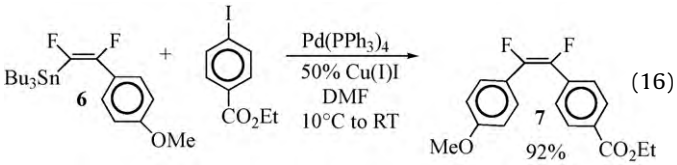
Scheme 1. Retrosynthetic analysis for the preparation of (*Z*)-1,2-difluorostilbenes.

Two representative examples of **4** were selected to test the proof of principle of our overall approach. The m-CF_3 and the p-OMe analogs [25] were converted to the corresponding vinylstannanes as illustrated below, Eq. (15).

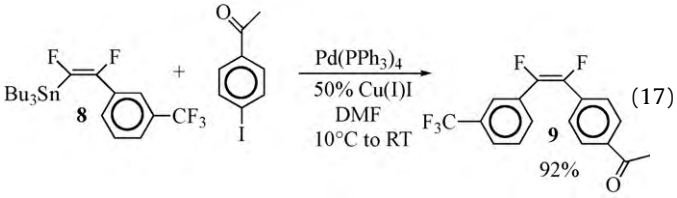


(15)

Subsequent Stille cross-coupling of our model substrates under Liebeskind conditions stereospecifically afforded the (*Z*)-1,2-difluorostilbenes in excellent yields, Eqs. (16) and (17).



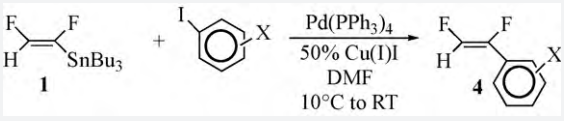
(16)



(17)

Thus, as illustrated above, arylation of (*E*)-1,2-difluoro-2-aryl-tributylstannylethenes provides a useful synthetic route to functionalized (*Z*)-1,2-difluorostilbenes [26].

Table 1
Stille cross-coupling reactions of **1** with aryl iodides.

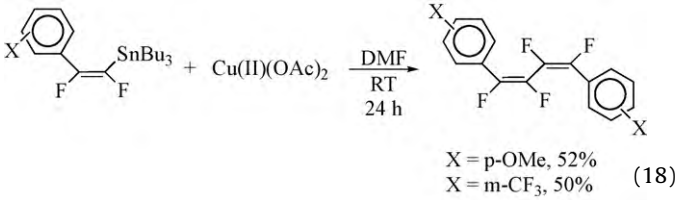


Entry	X	Yield (%)[a]
1	p-C(O)CH_3	75
2	p-OMe	92
3	m-CF_3	74
4	p-CH_3	66

[a] Isolated yields.

2.4. (Z,Z)-1,2,3,4-tetrafluoro-1,3-butadienes

In earlier work with fluorinated vinylstannanes, we had developed a useful procedure for the copper (II) mediated homocoupling of 1,2-difluorovinylstannanes [27]. Unfortunately, at that time, only one (*Z*,*Z*)-1,2-difluorovinylstannane was available to us. Since the (*Z*,*Z*)-1,2-difluorovinylstannanes, **6** and **8** were available to us in this work, we also reacted these vinylstannanes with $Cu(II)(OAc)_2$ and isolated modest yields of the respective, (*Z*,*Z*)-1,2,3,4-tetrafluoro-1,3-butadienes, as illustrated in Eq. (18).



(18)

3. Conclusions

Symmetrical (*E*)-1,2-difluorostilbenes can be photoisomerized at 254 nm in ~1 h to provide a mixture of (*E*)- and (*Z*)-1,2-difluorostilbenes significantly enriched in the (*Z*)-isomer. HPLC separation of these isomers provides a modest yield of pure symmetrical (*Z*)-1,2-difluorostilbenes. Since the (*E*)-1,2-difluorostilbenes can be readily prepared in high yield and wide tolerance of functionality in one step from (*E*)-$Bu_3SnCF=CFSnBu_3$, this route is a convenient route to an individual (*Z*)-1,2-difluorostilbene of the researcher's choice. An alternative approach to both symmetrical and/or unsymmetrical (*Z*)-1,2-difluorostilbenes has been developed *via* stereospecific Pd(0) coupling of (*E*)-1,2-difluoro-aryl-ethenyltributylstannanes under Stille-Liebeskind conditions with aryliodides. The requisite stannanes can be easily accessed from substituted (*Z*)-1,2-difluorostyrenes either *via* the reported route starting from (*E*)-HCF = CFI or *via* (*E*)-(1,2-difluorovinyl)tributylstannane – an alternative method developed in this work. Thus, any type of (*E*)- or (*Z*)-1,2-difluorostilbene can now be readily accessed.

In addition to the development of approaches to (*Z*)-1,2-difluorostilbenes, the (*Z*)-1,2-difluoro-aryl-ethenyltributylstannanes used herein can be readily stereospecifically converted to (*Z*,*Z*)-1,2,3,4-tetrafluoro-1,3-butadienes.

4. Experimental

4.1. General experimental procedures

Routine ^{19}F NMR spectra were recorded on a JEOL FX90Q Spectrometer (83.81 MHz) and high resolution data was obtained on a Bruker AC-300 Spectrometer (282.41 MHz). Chemical shifts have been reported in ppm relative to internal $CFCl_3$. Spectra of reaction mixtures were obtained in the ^7Li external lock mode. Quantitative determinations were carried out by integration relative to internal benzotrifluoride. Unless noted otherwise, $CDCl_3$ was used as the NMR lock solvent. Routine ^1H NMR (300.17 MHz) spectra and high resolution data were generally obtained on a Bruker AC-300 Spectrometer. Chemical shifts have been reported in ppm relative to internal TMS. Unless otherwise noted, $CDCl_3$ was used as the NMR lock solvent. High resolution $\{^1H\}$ ^{13}C NMR spectra were recorded on a Bruker AC-300 Spectrometer (75.48 MHz). Chemical shifts have been reported in ppm relative to internal TMS. Unless otherwise noted, $CDCl_3$ was used as the NMR lock solvent. Low resolution mass spectra were obtained using a TRIO-1 GC–MS instrument operated at 70 ev in the electron impact mode using a DB-1 column (0.25 mm ID × 15 m). High resolution mass spectra were obtained by the University of Iowa High Resolution Mass Spectrometry Facility.

Analytical GLPC were performed on a Hewlett–Packard Model 5890 equipped with a thermal conductivity detector and 3393A integrator. The column was packed with 5% OV-101 on chromosorb P. Flash column chromatography was carried out as described by Still et al. [28]. All melting points were determined in a 1.2 mm capillary tube in a Thomas–Hoover Unimelt apparatus and are uncorrected. DMF was dried overnight over CaH_2, then distilled at reduced pressure. Aryl iodides, stannane precursors, and routine commercial chemicals were used as received. $Pd(PPh_3)_4$ was prepared by Coulson's procedure [29]. Cu(I)I iodide (Aldrich) was purified by continuous extraction with anhydrous THF in a Soxhlet extraction apparatus as described by Posner [30]. Potassium fluoride and copper (II) acetate were dried by azeotropic distillation with benzene solvent and a Dean-Stark apparatus. Residual benzene was removed under reduced pressure.

4.2. Preparation of (E)-(1,2-difluorovinyl)tributylstannane, 1

A 250 ml two-neck flask, equipped with a stir bar, a thermometer, and a cold-water condenser attached to a nitrogen inlet adapter was charged with 1.10 g (19.0 mmol) of anhydrous potassium fluoride, 34.0 g (57 mmol) of bis(tributyltin)oxide and 60 ml of dry DMF. The flask was immersed in a 5-10 °C water bath, and 15.0 g (110 mmol) of (*E*)-(1,2-difluorovinyl)trimethylsilane was added *via* a syringe over 10 min. The cold bath was removed and the mixture was stirred for 2 h at room temperature, then for 12 h at 50 °C. Then, the reaction mixture was transferred to a 500 ml separatory funnel and partitioned between 150 ml of hexanes and 40 ml H_2O. The aqueous layer was extracted with 40 ml of hexanes, the hexanes layer combined and washed with 40 ml H_2O; the organic layer dried over $MgSO_4$ and concentrated by rotary evaporation. The crude vinylstannane was purified by distillation under reduced pressure through a jacketed short-path Vigreux column to give 36.5 g (94%) of **1**, bp. 96–97 °C/0.3 mm Hg, GLPC = 100%. ^{19}F NMR: δ −143.0 (dd, $^2J_{HF}$ = 77.3 Hz, $^3J_{FF}$ = 9.2 Hz), −147.1 (dd, $^3J_{HF}$ = 25.6 Hz, $^3J_{FF}$ = 9.5 Hz); ^{19}F $\{^1H\}$ NMR: δ −143.0 (d, $^3J_{FF}$ = 8.4 Hz), −147.1 (d, $^3J_{FF}$ = 9.0 Hz); ^1H NMR = δ 5.96 (dd, $^2J_{HF}$ = 77.2 Hz, $^3J_{HF}$ = 25.7 Hz, 1H) 5.96 (ddd, $^2J_{HF}$ = 77.3 Hz, $^3J_{HF}$ = 25.6 Hz). $^3J_{HSn}$ = 4.2 Hz, 1.48–1.60 (m, 6H), 1.32 (sextet, $^3J_{HH}$ = 7.4 Hz, 6H), 1.00–1.08 (m, 6H), 0.90 (t, $^3J_{HH}$ = 7.3 Hz, 9H); ^{13}C NMR: δ 154.9 (dd, $^1J_{CF}$ = 313.2 Hz, $^2J_{CF}$ = 7.3 Hz), 141.7 (dd, $^1J_{CF}$ = 282.4 Hz, $^2J_{CF}$ = 7.1 Hz), 28.9 (s), 28.9 (d, $^3J_{CSn}$ = 22.0 Hz). 27.2 (s), 27.2 (d, $^2J_{CSn}$ = 28.9 Hz), 13.7 (s), 10.0 (d, $^1J_{CSn}$ = 347.2 Hz). GC-MS, *m*/*z* (relative intensity): 297 (71), 296 (M^+-C_4H_9, 23), 295 (54), 241 (100).

4.3. Photochemical isomerization of (E)-(1,2-difluoro-1,2-ethenediyl)bis[4′-methoxybenzene]

A quartz NMR tube was charged with 13.7 mg (0.050 mmol) of (*E*)-(1,2-difluoro-1,2-ethenediyl)bis[4′-methoxybenzene] in 0.6 ml $CDCl_3$. The reaction solution was shaken manually until it became homogeneous. Then, the reaction solution was irradiated at 254 nm in a Rayonet UV chamber at ambient temperature for 1 h. ^{19}F NMR analysis of the reaction mixture indicated the formation of a new singlet at −129 ppm, which was later identified as (*Z*)-(1,2-difluoro-1,2-ethenediyl)bis[4′methoxybenzene] **3**. The ratio of the two isomers (*Z*/*E*) was 2.9/1. Further irradiation did not change the ratio. The reaction mixture was poured onto a silica gel column and eluted with a mixture of pentane and ether, $R_f(Z)$ = 0.5, $R_f(E)$ = 0.6. However, efficient separation of the two isomers could not be achieved. After recovery of the crude product mixture, the two isomers were separated by HPLC (elution with CH_3CN) [16].

Removal of the solvent at RT/1 mm Hg gave 4.8 mg (41%) of a colorless oil [(*Z*)-stilbene] **3**. ^{19}F NMR: δ −129.4 (s, 2F); ^{1}H NMR: δ 7.26 (dm, $^{3}J_{HH}$ = 9 Hz, 4H), 6.81 (dm, $^{3}J_{HH}$ = 9 Hz, 4H), 3.80 (s, 6H); ^{13}C NMR: δ 160.2 (s), 144.6 (dd, $^{1}J_{CF}$ = 246.2 Hz, $^{2}J_{CF}$ = 22 Hz), 129.5 (overlapping dd, $^{2}J_{CF}\sim^{3}J_{CF}$ = 3.6 Hz), 122.6 (2nd order spectrum due to virtual coupling), 113.9 (s), 55.3 (s). FTIR (CCl_4, cm^{-1}): 1609 (m), 1515 (s), 1298 (m), 1252 (vs), 1176 (m), 1029 (s). GC–MS, *m*/*z* (relative intensity): 276 (M^+, 100), 261 (80), 201 (24.7), 189 (13.9): UV ($CHCl_3$): 299 nm (ε = 6150 cm^{-1} M^{-1}), 248 (ε = 5525 cm^{-1} M^{-1}); HRMS: calc'd for $C_{16}H_{14}F_2O_2$: 276.0962; found: 276.0960.

4.4. Preparation of (Z)-1-(1,2-difluorovinyl)-(4-(methoxy)benzene)

A 100 ml two neck flask equipped with a stir bar, water condenser, rubber septum, and nitrogen inlet adapter was charged sequentially with 3.24 g (13.9 mmol) of p-iodoanisole, 1.32 g (6.93 mmol) of Cu(I)I, 0.32 g (0.28 mmol) of $Pd(PPh_3)_4$ and 20 ml of dry DMF. After stirring the mixture for 5 min, the flask was immersed in a 10 °C water bath and 6.35 g (18.0 mmol) of **1** was added *via* syringe over 10 min. The black mixture was stirred for 24 h at 35–40 °C. Then, the reaction mixture was diluted with 20 ml of Et_2O, treated with 2.0 g (34 mmol) of KF and dissolved in 15 ml of H_2O. The mixture was stirred for 15 min, the white precipitate (Bu_3SnF) was removed by filtration through a coarse-fritted funnel. The filtrate was transferred to a 250 ml separatory funnel containing 100 ml H_2O and 50 ml Et_2O. The aqueous layer was extracted with 2 × 30 ml Et_2O and the combined ether extracts were washed with 20 ml brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by silica gel chromatography (5% ethyl acetate in hexane, R_f = 0.23) afforded 2.16 g (92%) of the titled compound, GLPC = 100% as a clear, yellowish oil. The spectroscopic data obtained (^{19}F, ^{1}H, ^{13}C, GC–MS) were in good agreement with the data reported by Davis and Burton [17].

4.5. Preparation of (Z)-1-(1,2-difluorovinyl)-3-(trifluoromethyl)benzene

Similar to *4.4*, 35 ml DMF, 0.5 g (0.4 mmol) $Pd(PPh_3)_4$, 5.44 g (20.1 mmol) of 3-iodobenzotrifluoride, 1.90 g (10.0 mmol) of Cu(I)I, and 8.47 g (24.0 mmol) of **1** gave the crude product, which was distilled at partial pressure through a jacketed short-path Vigreux column to give 3.28 g (79%) of (*Z*)-1-(1,2-difluorovinyl)-3-(trifluoromethyl)benzene (containing ∼9% DMF impurity). This material was further purified by silica gel chromatography (pentane, R_f = 0.29) to give 3.06 g (74%) of the titled compound as a clear, colorless liquid, bp 64 °C/7 mm Hg. ^{19}F NMR: δ −63.5 (s, 3F), −143.1 (dd, $^{3}J_{HF}$ = 16.7 Hz, $^{3}J_{FF}$ = 10.8 Hz, 1F), −161.9 (dd, $^{2}J_{HF}$ = 72.0 Hz, $^{3}J_{FF}$ = 10.9 Hz, 1F); ^{19}F {^{1}H} NMR: δ −63.5 (s, 3F), −143.1 (d, $^{3}J_{FF}$ = 10.9 Hz, 1F), −161.9 (d, $^{3}J_{FF}$ = 10.7 Hz, 1F); ^{1}H NMR: δ 7.49–7.65 (m, 4H), 7.05 (dd, $^{2}J_{HF}$ = 71.9 Hz, $^{3}J_{HF}$ = 16.9 Hz, 1H); ^{13}C NMR: δ 147.9 (dd, $^{1}J_{CF}$ = 247.5 Hz, $^{2}J_{CF}$ = 11.7 Hz), 135.3 (dd, $^{1}J_{CF}$ = 259.8 Hz, $^{2}J_{CF}$ = 15.2 Hz), 131.9 (q, $^{2}J_{CF}$ = 32.9 Hz) 130.3 (d, $^{2}J_{CF}$ = 24.8 Hz), 129.8 (s), 126–127.1 (m), 126.2–126.5 (m), 124.2 (q, $^{1}J_{CF}$ = 272.5 Hz), 120.6–120.9 (m). GC–MS, *m*/*z* (relative intensity): 209 (M^+, 100). HRMS: calc'd for C_9HF_5, 208.0311, found, 208.0311.

4.6. Preparation of (Z)-1-(1,2-difluorovinyl)-4-(acetyl)benzene

Similar to *4.4*, 3.44 g (14.0 mmol) of 4-iodoacetophenone, 1.52 g (8.0 mmol) Cu(I)I, 0.32 g (0.28 mmol) $Pd(PPh_3)_4$, 20 ml of dry DMF, and 6.0 g (17 mmol) of **1** gave, after silica gel chromatography (20% ethyl acetate in hexanes, R_f = 0.26), a yellow-brown solid, which after recrystallization from pentane, gave 1.9 g (75%) of the titled compound as off-white needles, mp 46–47 °C. The spectroscopic data (^{19}F, ^{1}H, ^{13}C NMR, GC–MS) were in good agreement with the data reported by Davis and Burton [17].

4.7. Preparation of (Z)-1-(1,2-difluorovinyl)-4-(methyl)benzene

Similar to *4.4*, 35 ml dry DMF, 0.5 g (0.4 mmol) of $Pd(PPh_3)_4$, 4.36 g (20.0 mmol) of 4-iodotoluene, 1.90 g (20.0 mmol) of Cu(I)I and 8.47 g (24.0 mmol) of **1** gave a crude residue which was distilled at partial pressure through a jacketed short-path Vigreux column to give 2.17 g (70%) of (*Z*)-1-(1,2-difluorovinyl)-4-(methyl)benzene as a clear, colorless, liquid (containing ∼5% DMF impurity). This material was further purified by silica gel chromatography (pentane, R_f = 0.37) to yield 2.02 g (66%) of the titled compound as a clear, colorless liquid, bp 65 °C/4 mm Hg. The spectroscopic data (^{19}F, ^{1}H, ^{13}C NMR, GC–MS) were in good agreement with the data reported by Davis and Burton [17].

4.8. Preparation of (E)-1,2-difluoro-2-(4-methoxyphenyl)tributylstannylethene, 6

A 100 ml three-neck flask equipped with a stir bar, low temperature thermometer, rubber septum and nitrogen inlet adapter was charged with 1.50 g (8.82 mmol) of (*Z*)-1-(1,2-difluorovinyl)-4-methoxylbenzene, 10 ml THF and 10 ml Et_2O. The mixture was cooled to −105 °C in a pentane-liquid nitrogen bath, then n-BuLi (4.23 ml, 10.6 mmol, 2.5 M in hexanes) was added *via* a syringe maintaining the internal temperature at −100 to −105 °C throughout the addition. After complete addition of the n-BuLi, the resultant milky-yellow mixture was stirred at −100 to −105 °C for 1 h, then 4.13 g (12.7 mmol) of Bu_3SnCl (dissolved in 5 ml Et_2O) was slowly added *via* a syringe at −105 °C. After warming to room temperature overnight, volatile materials were removed in *vacuo*, and the crude residue was loaded directly onto a silica gel column (10%) ethyl acetate in hexanes, (R_f = 0.53) to give 2.41 g (60%) of, (*E*)-1,2-difluoro-2-(4-methoxyphenyl)tributylstannylethene, **6**, as a clear, colorless liquid. The spectroscopic data (^{19}F, ^{1}H, ^{13}C NMR, GC–MS) were in good agreement with the data reported by Davis and Burton [17].

4.9. Preparation of (E)-1,2-difluoro-2-(3-trifluoromethylphenyl)tributylstannylethene, 8

A 100 ml three-neck flask equipped with a stir bar, low temperature thermometer, rubber septum and nitrogen inlet adapter was charged with 2.88 g (13.8 mmol) of (*Z*)-1-(1,2-difluorovinyl)-3-(trifluoromethyl)benzene, 20 ml THF and 15 ml Et_2O. The mixture was cooled to −110 °C in a pentane-liquid nitrogen bath then n-BuLi (6.64 ml, 16.6 mmol, 2.5 M in hexanes) was added *via* syringe, maintaining the internal temperature at −105 to −110 °C throughout the addition. During the addition of the n-BuLi, the solution turned bright orange to blood red. After the addition was complete, the solution remained a brownish-red color. After the addition of n-BuLi was completed, the reaction mixture was stirred at −105 to −110 °C for 1 h; then 5.4 g (16.6 mmol) of Bu_3SnCl (dissolved in 5 ml of Et_2O) was slowly added *via* a syringe at −110 °C. The reaction mixture was then slowly warmed to room temperature overnight and the volatiles removed in *vacuo*. The crude stannane was loaded directly onto a silica gel column (hexanes, R_f = 0.34) to afford an 81:19 mixture of the titled compound and the starting material (as determined by ^{19}F NMR analysis). The starting material was removed by stirring the mixture for 12 h at 0.2 mm Hg to yield 3.40 g (50%) of the titled compound as a clear, colorless liquid: ^{19}F NMR: δ −63.3 (s, 3F), −114.9 (d, $^{3}J_{FF}$ = 5.3 Hz, 1F), −135.9 (d, $^{3}J_{FF}$ = 6.3 Hz, 1F), −135.9 (dd, $^{2}J_{FSn}$ = 174.5 Hz, $^{3}J_{FF}$ = 4.6 Hz), satellites due to natural

abundances of 7.68% ^{117}Sn and 8.58% ^{119}Sn isotopomers. ^{1}H NMR: δ 7.50–7.67 (m, 4H), 1.30–1.47 (m, 6H), 1.24 (sextet, $^3J_{HH}$ = 7.3 Hz, 6H), 0.90–0.95 (m, 6H), 0.84 (t, $^3J_{HH}$ = 7.2 Hz, 9H); ^{13}C NMR: δ 156.1 (d, $^1J_{CF}$ = 312.7 Hz), 154.6 (dd, $^1J_{CF}$ = 269.8 Hz, $^2J_{CF}$ = 12.4 Hz), 154.6 (ddd, $^1J_{CF}$ = 269.3 Hz, $^2J_{CSn}$ = 74.4 Hz, $^2J_{CF}$ = 12.3 Hz), 132.4 (dd, $^2J_{CF}$ = 26.8 Hz, $^3J_{CF}$ = 4.0 Hz), 131.3 (q, $^2J_{CF}$ = 32.9 Hz), 131.0 (s), 129.3 (s), 126.3 (d, $^3J_{CF}$ = 3.8 Hz), 124.5 (m), 124.0 (q, $^1J_{CF}$ = 272.3 Hz), 28.9 (s), 28.9 (d, $^3J_{CSn}$ = 20.4 Hz), 27.3 (s), 27.3 (d, $^2J_{CSn}$ = 62.3 Hz), 13.6 (s), 10.9 (s), 10.9 (d, $^1J_{CSn}$ = 352.5 Hz). GS–MS, *m*/*z* (relative intensity): 441 (M^+-C_4H_9, 27), 177 ($HSnBu^+$, 20), 169 (M^+-F_2SnBu_3, 100). HRMS: calc'd for $C_{17}H_{22}F_2{}^{120}Sn$ (M^+-C_4H_9) 441.0657, found 441.0664.

4.10. Preparation of (Z)-1,2-difluoro-4-carboethoxy-4′-methoxystilbene, 7

A 100 ml three-neck flask equipped with a stir bar, rubber septum, and a nitrogen inlet adapter was charged sequentially with 10 ml of dry DMF, 0.11 g (0.09 mmol, 5 mol%) of tetrakis(-triphenylphosphine) palladium (0) and 0.51 g (1.8 mmol) of ethyl-4-iodobenzoate. The mixture was stirred for 10 min, then 0.18 g (0.92 mmol, 50 mol%) of copper (I) iodide was added to the mixture. The flask was immersed in a cold-water bath (~10 °C), and l.10 g, (2.40 mmol) of **6** was added *via* a syringe over 5 min. After 10 min the cold-water bath was removed, and the dark solution was stirred for 24 h at room temperature. Then, the flask was charged with 0.5 g, (9 mmol) of KF and the reaction mixture was stirred an additional 24 h at RT. The reaction mixture was then loaded directly onto a silica gel column, eluted with 10% ethyl acetate in hexanes (R_f = 0.34) to give 0.54 g (92%) of the titled compound as a white solid, mp 53–55 °C. ^{19}F NMR: δ −121.0 (d, $^3J_{FF}$ = 15.0 Hz, 1F), −134.5 (d, $^3J_{FF}$ = 14 Hz, 1F). ^{1}H NMR: δ 7.93 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 7.37 (d, $^3J_{HH}$ = 8.6 Hz, 2H), 7.29 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 6.84 (d, $^3J_{HH}$ = 8.8 Hz, 2H), 4.36 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 3.81 (s, 3H), 1.37 (t, $^3J_{HH}$ = 7.1 Hz, 3H). ^{13}C NMR: δ 165.7 (s), 161.3 (s), 147.0 (dd, $^1J_{CF}$ = 251.3 Hz, $^2J_{CF}$ = 20.3 Hz), 144.0 (dd, $^1J_{CF}$ = 243.8 Hz, $^2J_{CF}$ = 22.2 Hz), 134.7 (d, $^2J_{CF}$ = 24.4 Hz), 130.9 (s), 130.3 (dd, $^3J_{CF}$ = $^4J_{CF}$ = 2.6 Hz), 129.6 (s), 127.3 (dd, $^3J_{CF}$ = $^4J_{CF}$ = 3.9 Hz), 121.8 (d, $^2J_{CF}$ = 24.1 Hz), 114.4 (s), 61.2 (s), 55.2 (s), 14.3 (s). GC-MS, *m*/*z* (relative intensity) 319 (M+1, 21), 318 (M+, 100). HRMS: calc'd for $C_{18}H_{16}F_2O_3$, 318.1068, found 318.1064.

4.11. Preparation of (Z)-1,2-difluoro-3-(trifluoromethyl)-4′-(acetyl)stilbene, 9

A 100 ml two-necked flask equipped with a magnetic stir bar, rubber septum, and nitrogen inlet adapter was charged sequentially with 10 ml of DMF, 0.14 g (0.13 mmol, 5 mol%) of tetrakis(triphenylphosphine)palladium(0) and 0.62 g (2.5 mmol) of 4-iodoacetophenone. After the mixture was stirred for 10 min; 0.25 g (1.3 mmol, 50 mol%) copper (I) iodide was added to the mixture. The flask was immersed in a cold-water bath (~10 °C) and 1.5 g (3.02 mmol) of **8** was added *via* a syringe over 5 min. After 10 min the cold-water bath was removed, and the dark solution was stirred for 24 h at room temperature. The flask was charged with 0.5 g (9 mmol) of KF, and the reaction mixture was stirred for a few hours at RT. Then, the reaction mixture was loaded directly onto a silica gel column and eluted with 10% ethyl acetate in hexanes (R_f = 0.4) to yield 0.75 g (92%) of (*Z*)-1,2-difluoro-3-(trifluoromethyl)-4′(acetyl)stilbene as an orange oil. ^{19}F NMR: δ −63.6 (s, 3F), −126.2 (d, $^3J_{FF}$ = 11.4 Hz, 1F), −128.1 (d, $^3J_{FF}$ = 11.6 Hz, 1F); ^{1}H NMR: δ 7.90 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 7.64 (d, $^3J_{HH}$ = 10.4 Hz, 2H), 7.42–7.51 (m, 4H), 2.60 (s, 3H); ^{13}C NMR: δ 197.1 (s), 145.6 (dd, $^1J_{CF}$ = 249.6 Hz, $^2J_{CF}$ = 20.8 Hz), 145.5 (dd, $^1J_{CF}$ = 250.3 Hz, $^2J_{CF}$ = 21.6 Hz), 138.0 (s), 133.9 (d, $^2J_{CF}$ = 23.7 Hz), 131.6 (s), 131.5 (q, $^2J_{CF}$ = 32.7 Hz), 130.7 (d, $^2J_{CF}$ = 24.5 Hz), 129.4 (s) 128.6 (s), 128.2 (dd, $^3J_{CF}$ = $^4J_{CF}$ = 3.9 Hz), 126.8 (d, $^3J_{CF}$ = 3.9 Hz), 125.1 (m) 123.7 (q, $^1J_{CF}$ = 272.4 Hz), 26.6 (s). HRMS: calc'd for $C_{17}H_{11}OF_5$ 326.0730, found 326.0718.

4.12. Preparation of (Z,Z)-1,2,3,4-tetrafluoro-1,4-bis(3-trifluoromethylphenyl)-1,3-butadiene

A 100 ml three-neck flask equipped with a stir bar, rubber septum and nitrogen inlet adapter was charged with 0.37 g (4.0 mmol) of copper (II) acetate, 10 ml dry DMF, 1.00 g (2.01 mmol) (*E*)-1,2-difluoro-2-(3-trifluoromethylphenyl)tributylstannylethene. After stirring for 24 h at RT, the reaction mixture was loaded directly onto a silica gel column (hexanes, R_f = 0.21) to yield 0.42 g (50%) of (*Z,Z*)-1,2,3,4-tetrafluoro-1,4-bis(3-trifluoromethylphenyl)-1,3-butadiene as a white solid: mp 60–63 °C. ^{19}F NMR: δ −63.8 (s, 6F), −119.1 (d, $^3J_{FF}$ = 8.0 Hz, 2F), −139.4 (d, $^3J_{FF}$ = 8.9 Hz, 2F); ^{1}H NMR: δ 7.57 (d, $^3J_{HH}$ = 7.5 Hz, 2H), 7.32–7.42 (m, 4H), 7.25 (bs, 2H); ^{13}C NMR: δ 150.3 (dm, $^1J_{CF}$ = 260.9 Hz), 137.6 (dddd, $^1J_{CF}$ = 256.3 Hz, $^2J_{CF}$ = 32.4 Hz, $^3J_{CF}$ = 23.7 Hz, $^4J_{CF}$ = 6.0 Hz,), 131.6 (q, $^2J_{CF}$ = 33.3 Hz), 13.3 (bs), 129.3 (s), 129.0 (d, $^2J_{CF}$ = 23.2 Hz), 127.4 (d, $^3J_{CF}$ = 3.0 Hz), 123.8 (bs), 123.4 (q, $^1J_{CF}$ = 272.7 Hz). GC-MS, *m*/*z* (relative intensity): 414 (M^+, 100), 69 (45). HRMS: calc'd for $C_{18}H_8F_{10}$ 414.0466, found 414.0440.

4.13. Preparation of (Z,Z)-1,2,3,4-tetrafluoro-1,4-bis(4-methoxyphenyl)-1,3-butadiene

Similar to *4.12*, 0.79 g (4.4 mmol) copper (II) acetate, 10 ml DMF, and 1.00 g (2.18 mmol) of (*E*)-1,2-difluoro-2-(4-methoxyphenyl)-tributylstannylethene were stirred at RT for 24 h. The reaction mixture was loaded directly onto a silica gel column (10% ethyl acetate in hexanes, R_f = 0.19) to give 0.38 g (52%) of the titled (*Z,Z*)-diene as a viscous, yellow-orange oil that solidified on standing to a yellow solid, mp 38–41 °C. ^{19}F NMR: δ −118.6 (d, $^3J_{FF}$ = 10.4 Hz, 2F) −140.6 (d, $^3J_{FF}$ = 10.9 Hz, 2F); ^{1}H NMR: δ 7.14 (dt, J = 9.3 Hz, J = 2.4 Hz 4H), 6.76 (dt, J = 9.4 Hz, J = 2.3 Hz, 4H), 3.79 (s, 6H); ^{13}C NMR: δ 161.3 (s), 151.4 (dm, $^1J_{CF}$ = 259.2 Hz), 136.1 (dm, $^1J_{CF}$ = 250.7 Hz), 128.6 (m), 120.4 (d, $^2J_{CF}$ = 23.6 Hz), 113.9 (s), 55.3 (s). GC-MS, *m*/*z* (relative intensity): 338 (M^+, 100). HRMS: calc'd for $C_{18}H_{14}F_4O_2$ 338.0930, found 338.0904.

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