Stereospecific preparation of (1E,3E,5E)-3.4-difluoro-1,6-diphenylhexatriene and (2E,4E,6E)-diethyl-4,5-difluoroocta-2,4,6-trienedioate

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ABSTRACT

Palladium(0) catalyzed coupling of β-bromostyrene (E/Z = 89/11) with (E)-(1,2-difluoro-1,2-ethene-diyl)bis[tributylstannane], **1**, in DMF at room temperature stereospecifically gave only (1E,3E,5E)-3,4-difluoro-1,6-diphenylhexatriene. Similarly, palladium(0) catalyzed coupling of (E)-ethyl 3-bromoacry-late as the vinyl halide precursor stereospecifically gave (2E,4E,6E)-diethyl-4,5-difluoroocta-2,4,6-trienedioate. This work demonstrates that a non-fluorine-containing vinyl bromide will selectively undergo coupling with **1** and enable the stereospecific preparation of a mixed polyene system. The (E)-ethyl 3-bromoacrylate coupling with **1** illustrates that mixed functionalized hexatriene systems can be easily accessed *via* this methodology. The X-ray structure of (2E,4E,6E)-diethyl-4,5-difluoroocta-2,4,6-trienedioate confirmed its structure.

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1. Introduction

Recently we have described the preparation of a new bis synthon, (E)-1,2-difluoroethenediyl)bis[tributylstannane], **1** [1,2]. This synthon is readily prepared from chlorotrifluoroethene in four steps—only two isolation steps are required. The overall isolated yield of **1** from chlorotrifluoroethene is 73%. Subsequent work by Italian workers reported a modified route to **1** [3]. Their procedure required four isolation steps, utilized the more expensive triethylsilylchloride and gave a significantly overall lower yield of **1**.

Bisstannane **1** reacts readily with aryl halides, with Pd(0) catalysis, to provide a useful stereospecific route to symmetrical (E)-1,2-difluorostilbenes [1]. Similarly, **1** has been utilized for the preparation of poly(arylenevinylene) [3]. With a vinyl halide, such as iodotrifluoroethene, **1** with Pd(0) catalysis, gave the first direct route to (E)-1,3,5-octafluorohexatriene [4]. Similarly, Gao prepared (1E,3E,5E)-1,2,3,4,5,6,hexafluoro-1,6-diphenylhexatriene *via* Pd(0) coupling of **1** with (Z)-1-iodo-2-phenyl-1,2-difluoroethene [5].

Bisstannane **1** could be easily elaborated to (1Z,3E,5Z)-(1,2,3,4,5,6)-hexafluoro-1,3,5-hexenetriyl)bis[tributylstannane], which can be utilized for the stereospecific introduction of three fluorinated ethenyl groups in one step [4].

2. Results and discussion

2.1. Preparation of (1E,3E,5E)-3,4-difluoro-1,6-diphenylhexatriene, 2

In the examples cited in references [1–5], the coupling partner with **1** was either a fluorine-containing vinyl iodide or an aryl iodide. To illustrate that a non-fluorine-containing vinyl halide would enable one to stereospecifically prepare a mixed polyene system and to demonstrate that a vinyl iodide was not a necessary requirement for the vinyl halide component, we utilized β-bromo styrene as the vinyl halide precursor. We employed a mixture of isomers in this preparation (E/Z = 89/11). We have previously demonstrated that with a similar isomeric system (namely aryl or alkyl 1-bromo-1-fluoroalkenes) that the less hindered isomer could be selectively coupled (with Pd(0) catalysis) [6–8]. The recovered more hindered 1-bromo-1-fluoroalkene could be similarly coupled at higher temperatures or longer reaction times. The use of the mixture of E/Z β-bromostyrenes would allow us to test whether the 1-fluorine was necessary for activation of the 1-bromine or necessary for selective coupling. When the E/Z mixture of β-bromostyrenes was coupled (Pd(0)) catalysis with **1**, only the (1E,3E,5E)-3,4-difluoro-1,6-diphenylhexatriene, 2 was isolated (cf. experimental for details of characterization) as outlined in Eq. (1).
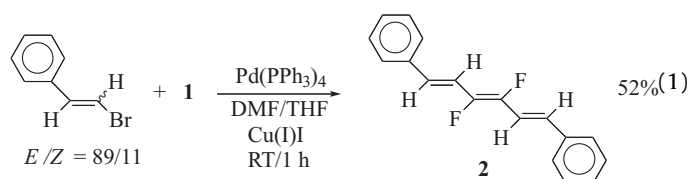

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This successful coupling reaction illustrated that a hydrocarbon vinyl bromide (rather than the less available vinyl iodides) could be utilized to prepare mixed polyene systems, and that a vinyl fluorine is not a necessary requirement to selectively couple the less hindered isomer in the vinyl bromide.

2.2. Preparation of (2E,4E,6E)-diethyl-4,5-difluoroocta-2,4,6-trienedioate, 3

To demonstrate that functionalized hexatrienes could be usefully prepared by this methodology, we employed (E)-ethyl-3-bromoacrylate as the vinyl halide precursor. The results of this coupling reaction are illustrated in Eq. (2).
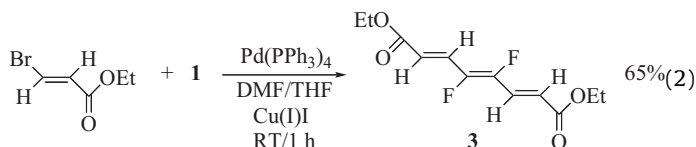
The structure of **3** was confirmed by ^{19}F, ^{1}H, ^{13}C NMR, HRMS and X-ray crystallography (Fig. 1).

2.3. X-ray structural determination of 3

X-ray data for **3** were collected at −120 °C using a Bruker (nee Siemens) 1K CCD system equipped with a sealed tube Mo source and a graphite monochromator. The structure was solved and refined using the Shelxtl [9] software package, refinement by full-matrix least squares on F^2, scattering factors from Int. Tables Vol. C, Tables 4.2.6.8 and 6.1.1.4.

Crystallographic data (excluding structural factors) for this structure have been deposited with the Cambridge Crystallographic Data Center as CCDC793891.[1]

The molecules are positioned on an inversion center (only half the molecule is crystallographically unique) and join via weak (less than van der Waals contact, H···O = 2.72 Å) C(10)–H(10B)···O (2) interactions (C–H = 0.98 Å, H···O = 2.65 Å, C···O = 3.430 (2), C–H···O = 136°) to form molecular tapes in the (−1,0,1) crystallographic plane (Fig. 2). This arrangement positions the H (2) atoms near the F (4) atoms on adjacent molecules within the tapes. This close contact of 2.71 Å is greater than van der Waals contact (H···F = 2.67 Å indicating F plays little role in the crystal packing.

A search in the Cambridge Structural Database (CSD), Version 5.31, November 2009; Allen, 2002 [10] for H_{vinyl}···F_{vinyl} intermolecular interactions yielded only three instances with the H···F distance less than van der Waal contact plus 0.1 Å [11–13].

The molecular tapes stack in the (2,0,1) crystallographic direction in an approximately perpendicular fashion (the tape direction is approximately perpendicular in alternating layers) such that the carbonyl groups (>C1=O2) are situated above and below the double bond (>C2=C3<) of adjacent molecules in the stacking direction allowing for pi-pi type interactions (3.594 Å between centroids of the C1=O2 and C2=C3 double bonds) between layers.

3. Experimental

3.1. General experimental procedures

All glassware was oven-dried prior to use. ^{19}F NMR (282.44 MHz), ^{1}H NMR (300.17 MHz) and {^{1}H} ^{13}C NMR (75.48 MHz) were recorded on an AC-300 spectrometer in CDCl$_3$
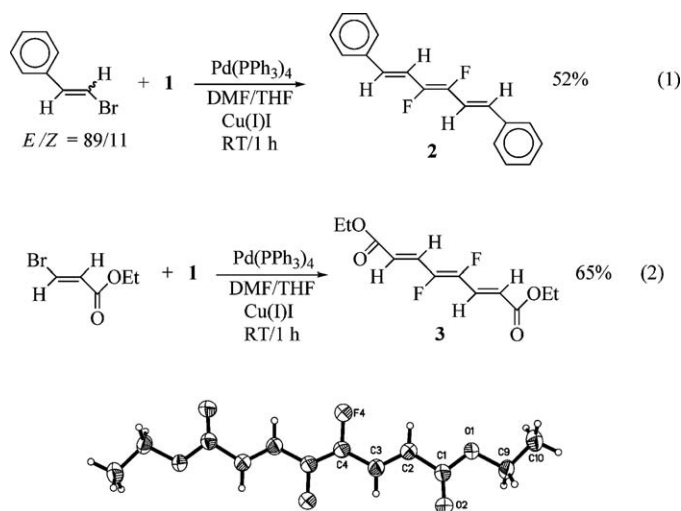
Fig. 1. Thermal ellipsoid drawing of **3** with C, O and F ellipsoids shown at the 50% level and H atoms shown as spheres of arbitrary diameter.

solvent. The chemical shifts are reported in parts per million downfield to the TMS internal standard for ^{1}H NMR and {^{1}H} ^{13}C NMR. The chemical shifts are reported in parts per million upfield to the CFCl$_3$ internal standard for ^{19}F NMR. FTIR spectra were recorded as CCl$_4$ solutions and reported in wavenumbers (cm^{-1}). Low resolution GC-MS spectra were obtained at 70 eV in the electron-impact mode on a TRIO-1-CG-MS instrument. GLPC analysis were performed on 5% OV-101 on a chromosorb P column with a thermal conductivity detector. High-resolution mass spectral determinations were made at the University of Iowa High Resolution Mass Spectrometry Facility. All reactions were carried out under an atmosphere of nitrogen. THF was distilled from a sodium benzophenone ketyl. DMF (CaH$_2$) was distilled at reduced pressure. Cu(I)I was purified by Kaufman's procedure [14]. Pd(PPh$_3$)$_4$ was prepared by Coulon's procedure [15]. (E)-Bu$_3$SnCF=CFSnBu$_3$, **1**, was prepared by the reported procedure [2]. 3-Bromoacrylate and β-bromostyrene were purchased from Aldrich and used as received. All other reagents and/or solvents were obtained from common commercial sources. All mps were obtained in a 1.2 mm capillary tube on a Thomas-Hoover Unimelt apparatus and are uncorrected. UV spectra were recorded using the cuvette cell compartment of a Beckman model 168 photodiode array detector. CHCl$_3$ was used as the cell solvent.

3.2. Preparation of (1E,3E,5E)-3,4-difluoro-1,6-diphenylhexatriene, 2

A one-neck 10 ml round bottom flask equipped with a Teflon-coated stir bar and attached to a nitrogen tee, was charged with
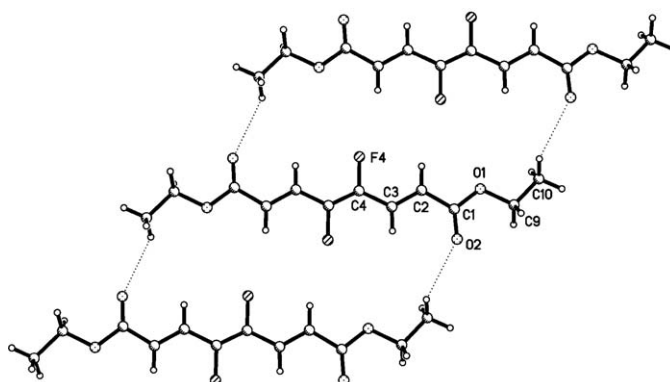
Fig. 2. Drawing showing the weak molecular tape forming interactions.

0.96 g (1.5 mmol) of (E)-(1,2-difluoro-1,2-ethenediyl)bis[tributyl-stannane], 0.55 g (3.0 mmol; E/Z = 89/11) β-bromostyrene, 1.5 ml THF, 1.5 ml DMF, 0.1 g (0.5 mmol, 0.2 equiv.) Cu(I)I and 0.08 g (0.07 mmol, 2 mol.%) Pd(PPh$_3$)$_4$. The reaction mixture was stirred at room temperature. A strongly exothermic reaction occurred and the reaction mixture gradually turned to a dark solution. After the reaction mixture had stirred for 24 h, it was extracted with ether (4 × 30 ml) and the ether extracts washed with water (4 × 20 ml). The organic layer was separated and dried over anhydrous MgSO$_4$. Removal of the solvent by rotary evaporation yielded a residue, which was eluted with pentane through a silica gel column, R_f = 0.2. Fractions with identical R_f values were collected. Removal of the solvent at RT/1 mm Hg yielded 0.21 g (52%) of shiny yellow crystals, mp 166–167 °C. ^{19}F NMR: δ −158.99 (dd $^3J_{HF}$ = 17 Hz, $^4J_{HF}$ = 14 Hz, 2F); {^{1}H} ^{19}F NMR: δ −158.6 (s, 2F); ^{1}H NMR: δ 7.48 (m, 4H), 7.35 (m, 4H), 7.28 (m, 2H), 7.00 (ddd as dt, $^3J_{HF}$ = 17 Hz, $^3J_{HH}$ = 16 Hz, $^4J_{HF}$ = 14 Hz, 2H),6.87 (d, $^3J_{HH}$ = 16 Hz); {1H} ^{13}C NMR: δ 148.32 (2nd order spectrum due to virtual coupling), 136.19 (s), 129.01 (t, $^3J_{CF}$ = 4 Hz), 128.81 (s), 128.47 (s), 126.98 (s), 113.65 (t, $^2J_{CF}$ = 8 Hz). FTIR (CCl$_4$, cm^{-1}) 3063 (m), 3027 (m), 1494 (m), 1450 (m), 1251 (vs), 1200 (m), 1031 (m). GC-MS, m/z (relative intensity): 269 (M$^+$+1, 18), 268 (M$^+$, 100), 247 (20), 91 (83); UV (CHCl$_3$): 384 nm (ε = 15,700 cm^{-1} M^{-1}), 364 nm (ε = 19,840 cm^{-1} M^{-1}), 255 nm (ε = 2120 cm^{-1} M^{-1}). HRMS: calc'd for C$_{18}$F$_2$H$_{14}$ 268.1064, obsvd 268.1073.

3.3. Preparation of (2E,4E,6E)-diethyl-4,5-difluoroocta-2,4,6-trienedioate, 3

A one-neck 5 ml round bottom flask equipped with a Teflon-coated stir bar and attached to a nitrogen tee, was charged with 0.64 g (1 mmol) of (E)-(1,2-difluoro-1,2-ethenediyl)bis[tributyl-stannane], 0.38 g (2 mmol, GLPC purity = 98%) of (E)-ethyl 3-bromoacrylate, 1 ml THF, 1 ml DMF, 0.1 g (0.5 mmol, 0.2 equiv.) Cu(I)I and 0.05 g (0.04 mmol; 2 mol.%) Pd(PPh$_3$)$_4$. The mixture was stirred at room temperature. A strongly exothermic reaction occurred and the reaction mixture gradually turned to a dark solution. ^{19}F NMR was utilized to follow the progress of the reaction. After the reaction mixture was stirred for 1 h, ^{19}F NMR analysis of the reaction mixture confirmed the disappearance of the signal due to (E)-(1,2-difluoro-1,2-ethenediyl)bis[tributylstan-nane]. The reaction mixture was extracted with ether (4 × 50 ml) and the combined ether layers washed with water (5 × 30 ml). The organic layer was separated and dried over anhydrous MgSO$_4$. The MgSO$_4$ was removed via gravity filtration, and the solvent was removed via rotary evaporation. The resultant residue was eluted consecutively with hexane (R_f ∼ 0) then ether (R_f = 0.8) on a silica

gel column. Fractions with identical R_f values were collected and the solvent removed by rotary evaporation to give a light yellow solid. Recrystallization of the solid from ethanol, followed by removal of solvent at RT/1 mm Hg afforded 0.17 g (65%) of colorless crystals of 3, mp 61–62 °C. ^{19}F NMR: δ −151.59 (dd, $^3J_{HF}$ = 17 Hz, $^4J_{HF}$ = 14.6 Hz, 2F); {H} ^{19}F NMR δ = −151.59 (s, 2F); ^{1}H NMR δ 7.50 (ddd, $^3J_{HF}$ = 17.1 Hz, $^3J_{HH}$ = 15.5 Hz, $^4J_{HF}$ = 14.6 Hz, 2H), 6.31 (d, $^3J_{HH}$ = 15.5 Hz, 2H), 4.27 (q, $^3J_{HH}$ = 7.2 Hz, 4H), 1.33 (t, $^3J_{HH}$ = 7.2 Hz, 6H); {H} ^{13}C NMR: δ 165.44 (s), 149.29 (2nd order NMR spectrum), 127.52 (t, $^2J_{CF}$ = 8 Hz), 121.93 (t, $^3J_{CF}$ = 3 Hz), 61.14 (s), 14.23 (s). FTIR (CCl$_4$, cm^{-1}) 2981 (m), 1722 (vs), 1630 (s), 1368 (m), 1311 (vs), 1263 (s), 1249 (s), 1174 (vs), 1046 (s). GC-MS m/z (relative intensity): 260 (M$^+$, 24), 215 (50), 186 (28), 164 (59), 159 (46), 139 (82), 136 (48), 115 (73), 114 (100). HRMS: calc'd for C$_{12}$H$_{14}$F$_2$O$_4$ 260.0860, obsvd 260.0839.

4. Conclusions

(1E,3E,5E)-3,4-Difluoro-1,6-diphenylhexatriene and (2E,4E,6E)-diethyl-4,5-difluoroocta-2,4,6-trienedioate were stereospecifically prepared by Pd(0) catalyzed coupling in DMF at RT of (E)-(1,2-ethenediyl)bis[tributylstannane] with β-bromostyrene and (E)-ethyl 3-bromoacrylate, respectively. The structure (2E,4E,6E)-diethyl-4,5-difluoroocta-2,4,6-trienedioate was confirmed by X-ray analysis.

Acknowledgements

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