Facile Synthesis of Substituted 1,1-Difluoroallenes via Carbonyl Difluorovinylidenation

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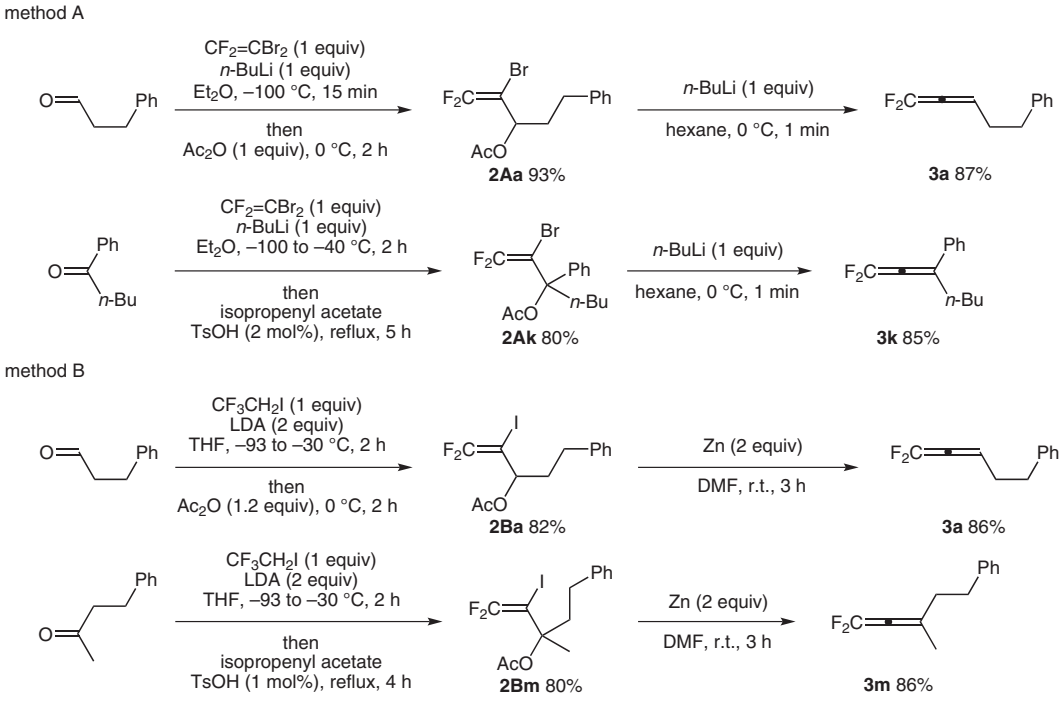
Received 22 November 2011; revised 11 December 2011

PSP No 217

Abstract: Two methods for the difluorovinylidenation of carbonyl compounds have been developed to synthesize 1,1-difluoroallenes bearing various substituents. The reaction of 1-bromo-2,2-difluorovinyllithium, generated from 1,1-dibromo-2,2-difluoroethylene and *n*-butyllithium, with aldehydes or ketones, and subsequent acetylation, gives 2-bromo-3,3-difluoroallylic acetates. Elimination of these acetates with *n*-butyllithium affords 1,1-difluoroallenes in high yield. 3,3-Difluoro-2-iodoallylic acetates are similarly prepared from aldehydes or ketones on treatment with 2,2-difluoro-1-iodovinyllithium, generated from 1,1,1-trifluoro-2-iodoethane and lithium diisopropylamide, followed by acetylation. These acetates readily undergo elimination with zinc metal to afford 1,1-difluoroallenes in high yield.

Key words: carbonyl compounds, metalation, difluorovinylidenation, 1,1-difluoroallenes



Scheme 1 Synthesis of 1,1-difluoroallenes by difluorovinylidenation of aldehydes or ketones

Introduction

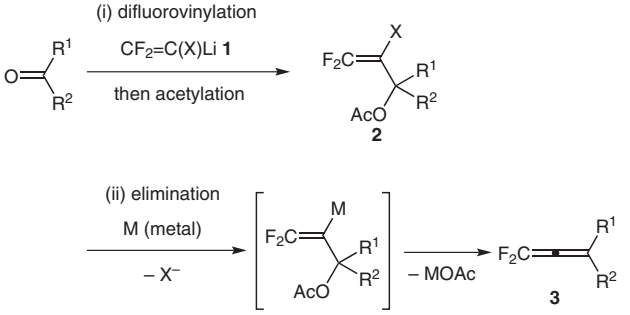
1,1-Difluoroallenes are highly attractive synthetic intermediates because of their fluorine substituents and cumulative double bonds. In addition, 1,1-difluoroallenes can serve as promising pharmaceuticals, as some non-fluorinated allenes have been used for therapeutic purposes.[1] To date, however, the synthetic methodology for 1,1-difluoroallenes bearing substituents has not been completely explored.[2–4]

We have recently reported facile methods for the synthesis of substituted 1,1-difluoroallenes via difluorovinylidenation of carbonyl compounds (Scheme 1).[5] A wide variety of 1,1-difluoroallenes were efficiently synthesized using these methods.

Our synthesis consists of two steps (Scheme 2): (i) The reaction of an aldehyde or ketone with a 2,2-difluoro-1-halovinyllithium **1** and subsequent acetylation to give the 3,3-difluoro-2-haloallylic acetate **2**. (ii) Metalation of

SYNTHESIS 2012, 44, 857–861
Advanced online publication: 16.01.2012
DOI: 10.1055/s-0031-1290157; Art ID: Z109011SS

acetate **2** with an appropriate reducing agent which causes elimination of the halide ion (X^-) and the acetate ion to furnish the desired 1,1-difluoroallene **3**. Depending on the reagents used for the difluorovinylation (the first step) and the elimination (the second step), two methods are available; namely, method A and B (see Scheme 1). Method B should have wide application because it includes a readily available starting material and facilitates the synthesis of 1,1-difluoroallenes bearing functionalities that are sensitive to *n*-butyllithium.



Scheme 2 Difluorovinylation–elimination sequence in 1,1-difluoroallene synthesis

Method A: Synthesis of 1,1-Difluoroallenes from 1,1-Dibromo-2,2-difluoroethylene (First-Generation Synthesis)[5a]

Initially, 1,1-dibromo-2,2-difluoroethylene (CF_2=CBr_2) was used as a difluorovinylation agent. 1,1-Dibromo-2,2-difluoroethylene was lithiated with 1 equivalent of *n*-butyllithium at –100 °C. Aldehydes or ketones were treated with the resulting vinyllithium, and then with acetic anhydride or with isopropenyl acetate/*p*-toluenesulfonic acid, respectively. Next, the isolated 2-bromo-3,3-difluoroallylic acetates **2A** (X = Br) were lithiated with *n*-butyllithium in hexane; elimination of lithium acetate occurred to afford the 1,1-difluoroallenes **3**.

Note that control of the temperature in the vinylation with dibromodifluoroethylene is crucial. The first lithiation at a temperature higher than –100 °C led to undesired 1,2-elimination of lithium fluoride from the intermediate 1-bromo-2,2-difluorovinyllithium. The second lithiation of allylic acetates **2A** must be performed in hexane to realize the elimination in high yield.

The resulting 1,1-difluoroallenes were purified by standard column chromatography (silica gel). The isolated difluoroallenes can be stored in a refrigerator (0 °C) for at least one month.

Method B: Synthesis of 1,1-Difluoroallenes from 1,1,1-Trifluoro-2-iodoethane (Second-Generation Synthesis)[5b]

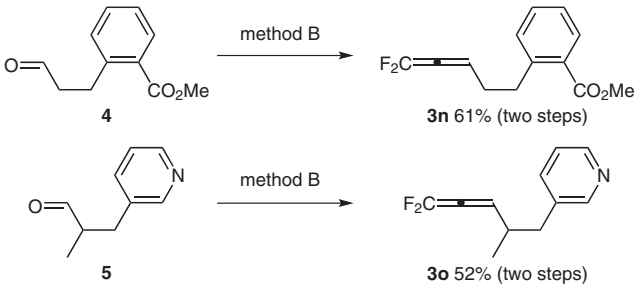
1,1-Dibromo-2,2-difluoroethylene, used in our first-generation synthesis, is an expensive, potential ozone-depleting substance and is now difficult to purchase because of the ban on its industrial manufacture. In addition, highly reactive *n*-butyllithium is required in both metalation steps of the alkenyl bromides.

The second-generation synthesis of 1,1-difluoroallenes was realized using 1,1,1-trifluoro-2-iodoethane (CF_3CH_2I) as a difluorovinylation agent.[6] This material is readily available because it is manufactured industrially for use as a refrigerant or fluorinated intermediate. 1,1,1-Trifluoro-2-iodoethane was treated with two equivalents of lithium diisopropylamide to generate 2,2-difluoro-1-iodovinyllithium. Aldehydes react with the iodovinyllithium, and then the formed alkoxides are trapped with acetic anhydride in a one-pot operation. In the case of ketones, the isolated allylic alcohols were acetylated with isopropenyl acetate and *p*-toluenesulfonic acid. The isolated 3,3-difluoro-2-iodoallylic acetates **2B** (X = I) were reduced with zinc metal (2 equiv). Elimination proceeds smoothly in *N*,*N*-dimethylformamide or tetrahydrofuran at room temperature, and the desired 1,1-difluoroallenes were obtained in high yield.

Reaction Scope

Yields of the synthesized acetates **2** and 1,1-difluoroallenes **3** using methods A and B are summarized in Table 1. A wide variety of monosubstituted 1,1-difluoroallenes were obtained from aldehydes, while the synthesis of disubstituted 1,1-difluoroallenes was accomplished by the difluorovinylidenation of ketones.

Although yields obtained in the two methods are nearly equal, method B is synthetically more favorable because it enables the synthesis of 1,1-difluoroallenes bearing functionalities that are sensitive to *n*-butyllithium. Aldehyde **4**, bearing an ester moiety, and aldehyde **5**, bearing a pyridine ring, were transformed to the corresponding 1,1-difluoroallenes **3n** and **3o** in 61% and 52% yield, respectively (Scheme 3).

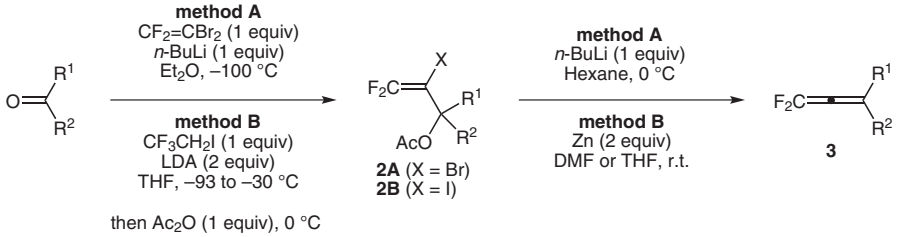


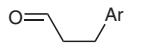
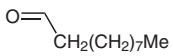
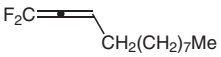
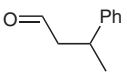
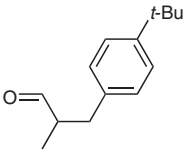
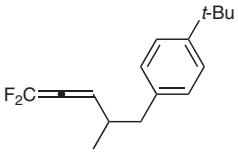
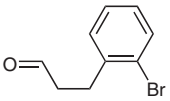
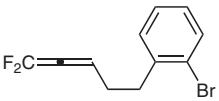
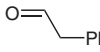
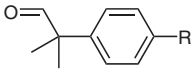
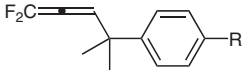
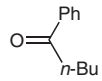
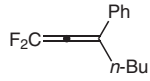
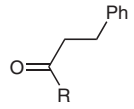
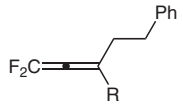
Scheme 3 Synthesis of 1,1-difluoroallenes with an ester moiety and a pyridine ring

Summary

Difluorovinylation of aldehydes or ketones is readily realized with 1-bromo-2,2-difluorovinyllithium (method A) and 2,2-difluoro-1-iodovinyllithium (method B), which is followed by acetylation to give 2-bromo-3,3-difluoroallylic acetates and 3,3-difluoro-2-iodoallylic acetates, respectively. The formed allylic acetates undergo facile elimination on treatment with *n*-butyllithium (method A) or zinc metal (method B) to afford 1,1-difluoroallenes in

Table 1 Synthesis of 1,1-Difluoroallenes from 1,1-Dibromo-2,2-difluoroethylene or 1,1,1-Trifluoro-2-iodoethane



Entry	Carbonyl compound	Difluoroallene		Yield (%) (method A)		Yield (%) (method B)	
				2A	**3**	**2B**	**3**
1			Ar = Ph	93 (**2Aa**)	87 (**3a**)	82 (**2Ba**)	86 (**3a**)
2			Ar = 1-Naph	84 (**2Ab**)	73[a] (**3b**)	83 (**2Bb**)	82 (**3b**)
3				n.a.[b]	n.a.[b]	84 (**2Bc**)	87 (**3c**)
4				83 (**2Ad**)	85 (**3d**)	81 (**2Bd**)	95 (**3d**)
5				86 (**2Ae**)	84 (**3e**)	87 (**2Be**)	92 (**3e**)
6				85 (**2Af**)	84 (**3f**)	n.a.[b]	n.a.[b]
7				85 (**2Ag**)	83 (**3g**)	n.a.[b]	n.a.[b]
8			R = H	n.a.[b]	n.a.[b]	83 (**2Bh**)	93 (**3h**)
9			R = Me	87 (**2Ai**)	82 (**3i**)	n.a.[b]	n.a.[b]
10			R = OMe	87 (**2Aj**)	81 (**3j**)	n.a.[b]	n.a.[b]
11				80[c] (**2Ak**)	85[a] (**3k**)	n.a.[b]	n.a.[b]
12			R = $(CH_2)_2$Ph	84[c] (**2Al**)	90 (**3l**)	n.a.[b]	n.a.[b]
13			R = Me	n.a.[b]	n.a.[b]	80[c] (**2Bm**)	86 (**3m**)

[a] ^{19}F NMR yield based on $PhCF_3$.
[b] n.a. = reaction not attempted.
[c] Acetylation was performed with isopropenyl acetate and *p*-TsOH.

high yield. Method B starts from the readily available 1,1,1-trifluoro-2-iodoethane, and allows the synthesis of 1,1-difluoroallenes bearing functionalities that are sensitive to *n*-butyllithium.

NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 500 or Avance 400 spectrometer. Chemical shift values are given in ppm relative to internal TMS (for ^1H NMR: δ = 0.00 ppm), $CDCl_3$ (for ^{13}C NMR: δ = 77.0 ppm), and C_6F_6 (for ^{19}F NMR: δ = 0.0 ppm). Mass spectra (EI–TOF or ESI–TOF) were measured on a JEOL JMS-T100GCV or JMS-T100CS mass spectrometer. IR spectra were recorded using the ATR (attenuated total reflectance) method on a Horiba FT-720 spectrophotometer. Column chromatography and preparative TLC were conducted on silica gel (Silica Gel 60 N, Kanto Chemical Co., Inc. for column chromatography and Wakogel B-5F, Wako Pure Chemical Industries for PTLC, respectively). All reactions were conducted under argon. THF, DMF, hexane, and Et_2O were dried by passage over a column of activated alumina followed by a column of Q-5 scavenger (Engelhard). Pentane was distilled from CaH_2.

2-Bromo-1,1-difluoro-5-phenylpent-1-en-3-yl Acetate (2Aa); Typical Procedure for Method A (from Aldehydes; Table 1, Entry 1)

To a soln of 1,1-dibromo-2,2-difluoroethylene (444 mg, 2.0 mmol) in Et_2O (16 mL) was added a Et_2O soln (2.0 mL) of *n*-BuLi (1.60 M in hexane; 1.28 mL, 2.0 mmol) at –100 °C under argon. The mixture was stirred for 15 min at that same temperature, then 3-phenylpropanal (0.28 mL, 2.0 mmol) was added. The mixture was stirred for an additional 15 min. After Ac_2O (0.19 mL, 2.0 mmol) was added, the mixture was allowed to warm to 0 °C over 2 h. The reaction was

quenched with sat. aq NH_4Cl (10 mL), and the products were extracted with Et_2O (3 × 15 mL). The combined organic layer was washed with brine (20 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (hexane–EtOAc, 20:1) to give **2Aa** as a colorless liquid; yield: 593 mg (93%).

IR: 3028, 2949, 1747, 1731, 1282, 1221, 1026, 700 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.98–2.08 (m, 1 H, CH_2), 2.07 (s, 3 H, CH_3CO), 2.11–2.17 (m, 1 H, CH_2), 2.58–2.62 (m, 2 H, CH_2), 5.44 (dddd, *J* = 7.3, 7.3 Hz, J_{HF} = 2.1, 2.1 Hz, 1 H, CH), 7.17 (dd, *J* = 7.8, 0.8 Hz, 2 H, ArH), 7.21 (tt, *J* = 7.8, 0.8 Hz, 1 H, ArH), 7.29 (dd, *J* = 7.8, 7.8 Hz, 2 H, ArH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.8, 31.1, 34.1, 68.3 (d, J_{CF} = 3 Hz), 81.0 (dd, J_{CF} = 35, 21 Hz), 126.3, 128.2, 128.6, 140.2, 154.2 (dd, J_{CF} = 294, 289 Hz), 169.7.

^{19}F NMR (470 MHz, $CDCl_3$): δ = 80.7 (br d, J_{FF} = 27 Hz, 1 F), 82.3 (br d, J_{FF} = 27 Hz, 1 F).

Anal. Calcd for $C_{13}H_{13}BrF_2O_2$: C, 48.92; H, 4.11. Found: C, 49.14; H, 4.34.

1,1-Difluoro-5-phenylpenta-1,2-diene (3a)

n-BuLi (1.60 M in hexane; 0.12 mL, 0.19 mmol) was added to a soln of acetate **2Aa** (60 mg, 0.19 mmol) in hexane (2.6 mL) at 0 °C under argon. The mixture was stirred for 1 min at that same temperature, then the reaction was quenched with aq NH_4Cl (3 mL), and the products were extracted with Et_2O (3 × 5 mL). The combined organic layer was washed with brine (10 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (pentane) to give **3a** as a colorless liquid; yield: 29 mg (87%).

IR: 3030, 2927, 2856, 2011, 1462, 1192, 744, 698 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.53–2.61 (m, 2 H, CH_2), 2.81 (t, *J* = 7.5 Hz, 2 H, CH_2), 6.47 (tt, *J* = 6.1 Hz, J_{HF} = 2.4 Hz, 1 H, =CH), 7.17–7.22 (m, 3 H, ArH), 7.30 (dd, *J* = 7.3, 7.3 Hz, 2 H, ArH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 33.8, 33.8, 121.4 (t, J_{CF} = 6 Hz), 126.2, 128.4, 128.5, 140.6, 152.8 (t, J_{CF} = 261 Hz), 170.1 (t, J_{CF} = 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = 59.9 (td, J_{FH} = 5, 2 Hz).

Anal. Calcd for $C_{11}H_{10}F_2$: C, 73.32; H, 5.59. Found: C, 73.16; H, 5.77.

2-Bromo-1,1-difluoro-3-phenylhept-1-en-3-yl Acetate (2Ak); Typical Procedure for Method A (from Ketones; Table 1, Entry 11)

To a soln of 1,1-dibromo-2,2-difluoroethylene (442 mg, 2.0 mmol) in Et_2O (16 mL) was added a Et_2O soln (2.0 mL) of *n*-BuLi (1.60 M in hexane; 1.28 mL, 2.0 mmol) at –100 °C under argon. The mixture was stirred for 15 min at that same temperature, then 1-phenylpentan-1-one (0.30 mL, 2.0 mmol) in Et_2O (3 mL) was added. The mixture was stirred for an additional 1 h, and then allowed to warm to –40 °C over 1 h. The reaction was quenched with sat. aq NH_4Cl (10 mL), and the products were extracted with Et_2O (3 × 15 mL). The combined organic layer was washed with brine (20 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (hexane–EtOAc, 10:1) to give 2-bromo-1,1-difluoro-3-phenylhept-1-en-3-ol. To a soln of the alcohol in isopropenyl acetate (3 mL) was added *p*-TsOH·H_2O (5 mg, 0.03 mmol). The mixture was refluxed for 5 h, then the reaction was quenched with sat. aq $NaHCO_3$ (2 mL). The products were extracted with Et_2O (3 × 3 mL). The combined organic layer was washed with brine (3 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (hexane–EtOAc, 30:1) to give **2Ak** as a colorless liquid; yield: 555 mg (80%, two steps).

IR: 2958, 2871, 1741, 1726, 1275, 1217, 962, 708 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.78 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.81–0.91 (m, 1 H, CH_2), 1.04–1.29 (m, 3 H, CH_2), 2.11 (dddd, *J* = 14.0, 11.9, 4.4 Hz, J_{HF} = 4.4 Hz, 1 H, CH_2), 2.20 (s, 3 H, CH_3CO), 2.94 (dddd, *J* = 14.0, 12.2, 4.4 Hz, J_{HF} = 3.4 Hz, 1 H, CH_2), 7.28–7.41 (m, 5 H, ArH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.8, 21.6, 22.5, 25.8 (d, J_{CF} = 2 Hz), 36.6 (d, J_{CF} = 7 Hz), 84.1 (dd, J_{CF} = 4, 2 Hz), 87.2 (dd, J_{CF} = 29, 23 Hz), 125.2, 127.7, 128.2, 141.4 (dd, J_{CF} = 2, 2 Hz), 153.4 (dd, J_{CF} = 297, 284 Hz), 168.6.

^{19}F NMR (470 MHz, $CDCl_3$): δ = 83.7 (ddd, J_{FF} = 34 Hz, J_{FH} = 4, 3 Hz, 1 F), 87.0 (d, J_{FF} = 34 Hz, 1 F).

Anal. Calcd for $C_{15}H_{17}BrF_2O_2$: C, 51.87; H, 4.94. Found: C, 51.83; H, 4.99.

1,1-Difluoro-3-phenylhepta-1,2-diene (3k)

The acetate **2Ak** was converted into the corresponding difluoroallene **3k** by the same procedure as used for acetate **2Aa**; yield: 85%.

IR: 2958, 2927, 1990, 1718, 1464, 1261, 1182, 769 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.42 (tq, *J* = 7.5, 7.4 Hz, 2 H, CH_2), 1.59 (tt, *J* = 7.5, 7.5 Hz, 2 H, CH_2), 2.69 (tt, *J* = 7.5 Hz, J_{HF} = 5.7 Hz, 2 H, CH_2), 7.33–7.40 (m, 3 H, ArH), 7.50–7.53 (m, 2 H, ArH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.0, 22.2, 29.7 (d, J_{CF} = 5 Hz), 33.0, 127.2, 128.5, 129.3, 134.8 (t, J_{CF} = 6 Hz), 135.7, 152.6 (t, J_{CF} = 259 Hz), 166.2 (t, J_{CF} = 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = 60.0 (t, J_{FH} = 6 Hz).

HRMS–FAB: *m/z* $[M + H]^+$ calcd for $C_{13}H_{15}F_2$: 209.1142; found: 209.1130.

1,1-Difluoro-2-iodo-5-phenylpent-1-en-3-yl Acetate (2Ba); Typical Procedure for Method B (from Aldehydes; Table 1, Entry 1)

To a soln of $(i\text{-Pr})_2NH$ (2.8 mL, 20 mmol) in THF (10 mL) was added *n*-BuLi (1.67 M in hexane; 12.0 mL, 20.0 mmol) over 10 min at 0 °C under argon. The resulting solution was allowed to stir for an additional 15 min, and then cooled to –93 °C in a cold hexane bath. To the cold LDA soln was added a soln of CF_3CH_2I (2.10 g, 10.0 mmol) in THF (5 mL) over 10 min, keeping the temperature between –93 °C and –85 °C. After the mixture was stirred for 20 min at that same temperature, a soln of 3-phenylpropanal (1.34 g, 10.0 mmol) in THF (5 mL) was added over 5 min, while keeping the temperature between –93 °C and –85 °C. The mixture was stirred for an additional 30 min, then warmed to –30 °C over 90 min. After Ac_2O (1.23 g, 12.0 mmol) was added, the mixture was allowed to warm to 0 °C over 2 h. The reaction was quenched with sat. aq NH_4Cl (20 mL), and the products were extracted with Et_2O (3 × 20 mL). The combined organic layer was washed with brine (20 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (hexane–EtOAc, 20:1). The acetate **2Ba** was obtained as a colorless liquid; yield: 3.01 g (82%).

IR: 3028, 2954, 1743, 1716, 1267, 1219, 1024, 698 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.87–1.93 (m, 1 H, CH_2), 2.05–2.17 (m, 1 H, CH_2), 2.07 (s, 3 H, CH_3CO), 2.58 (t, *J* = 7.2 Hz, 2 H, CH_2), 4.98 (t, *J* = 7.2 Hz, 1 H, CH), 7.17–7.22 (m, 3 H, ArH), 7.29 (dd, *J* = 7.3, 7.6 Hz, 2 H, ArH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.9, 30.9, 36.0, 53.8 (dd, J_{CF} = 25, 26 Hz), 68.9 (d, J_{CF} = 3 Hz), 126.2, 128.2, 128.5, 140.2, 154.0 (dd, J_{CF} = 286, 286 Hz), 169.6.

^{19}F NMR (470 MHz, $CDCl_3$): δ = 89.2 (d, J_{FF} = 22 Hz, 1 F), 90.2 (d, J_{FF} = 22 Hz, 1 F).

HRMS (ESI$^+$): *m/z* [M + Na]$^+$ calcd for $C_{13}H_{13}F_2IO_2Na$: 388.9826; found: 388.9830.

1,1-Difluoro-5-phenylpenta-1,2-diene (3a)

To a suspension of zinc powder (131 mg, 2.00 mmol) in DMF (3 mL) was added a soln of **2Ba** (366 mg, 1.00 mmol) in DMF (2 mL) at r.t. under argon, and the mixture was stirred for 3 h. The resulting mixture was filtered to remove the excess zinc and then diluted with Et_2O (20 mL) and brine (15 mL). The products were extracted with Et_2O (3 × 15 mL). The combined organic layer was washed with brine (15 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (pentane). Difluoroallene **3a** was obtained as a colorless liquid; yield: 155 mg (86%).

1,1-Difluoro-2-iodo-3-methyl-5-phenylpent-1-en-3-yl Acetate (2Bm); Typical Procedure for Method B (from Ketones; Table 1, Entry 13)

To a soln of (*i*-Pr)$_2$NH (1.1 mL, 8.00 mmol) in THF (5 mL) was added *n*-BuLi (1.67 M in hexane; 4.8 mL, 8.0 mmol) over 10 min at 0 °C under argon. The resulting solution was allowed to stir for an additional 15 min, and then cooled to –93 °C in a cold hexane bath. To the cold LDA soln was added a soln of CF_3CH_2I (840 mg, 4.00 mmol) in THF (2 mL) over 10 min, keeping the temperature between –93 °C and –85 °C. After the mixture was stirred for 20 min at that same temperature, a soln of 4-phenylbutan-2-one (593 mg, 4.00 mmol) in THF (2 mL) was added over 5 min, while keeping the temperature between –93 °C and –85 °C. The mixture was stirred for an additional 30 min, then warmed to –30 °C over 90 min. The reaction was quenched with sat. aq NH_4Cl (15 mL), and the products were extracted with Et_2O (3 × 15 mL). The combined organic layer was washed with brine (15 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (hexane–EtOAc, 10:1) to give 1,1-difluoro-2-iodo-3-methyl-5-phenylpent-1-en-3-ol. To a soln of the alcohol in isopropenyl acetate (3 mL) was added *p*-TsOH·H_2O (5 mg, 0.03 mmol). The mixture was refluxed for 4 h, then the reaction was quenched with sat. aq $NaHCO_3$ (15 mL). The products were extracted with Et_2O (3 × 15 mL). The combined organic layer was washed with brine (15 mL) and dried (Na_2SO_4). After the solvent was removed under reduced pressure, the residue was purified by column chromatography (hexane–EtOAc, 30:1) to give **2Bm** as a colorless liquid; yield: 1.22 g (80%, two steps).

IR: 3028, 2931, 2862, 1790, 1741, 1712, 1496, 1454, 1369, 1238, 1196, 1068, 1020, 700 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.87 (d, *J* = 4.6 Hz, 3 H, CH_3), 2.04 (s, 3 H, CH_3CO), 2.11–2.23 (m, 2 H, CH_2), 2.58 (t, *J* = 8.6 Hz, 2 H, CH_2), 7.18–7.20 (m, 3 H, ArH), 7.29 (dd, *J* = 7.0, 7.0 Hz, 2 H, ArH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.8, 22.9 (d, J_{CF} = 7 Hz), 30.0, 42.8 (d, J_{CF} = 2 Hz), 59.7 (dd, J_{CF} = 26, 22 Hz), 80.6 (d, J_{CF} = 3 Hz), 126.1, 128.3, 128.5, 140.8, 152.5 (dd, J_{CF} = 301, 281 Hz), 169.3.

^{19}F NMR (470 MHz, $CDCl_3$): δ = 89.0 (dq, J_{FF} = 33 Hz, J_{FH} = 5 Hz, 1 F), 97.3 (d, J_{FF} = 33 Hz, 1 F).

HRMS (ESI$^+$): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{15}F_2IO_2Na$: 402.9982; found: 402.9979.

1,1-Difluoro-3-methyl-5-phenylpenta-1,2-diene (3m)

The acetate **2Bm** was converted into the corresponding difluoroallene **3m** by the same procedure as used for acetate **2Ba**; yield: 86%.

IR: 3064, 2922, 2360, 2004, 1801, 1604, 1481, 1173, 1043, 995, 696 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.91 (t, *J* = 5.0 Hz, 3 H, CH_3), 2.40–2.48 (m, 2 H, CH_2), 2.74 (t, *J* = 8.2 Hz, 2 H, CH_2), 7.13–7.18 (m, 3 H, ArH), 7.25 (t, *J* = 7.6 Hz, 2 H, ArH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.8, 33.4, 38.6, 126.1, 128.3, 128.4, 132.3 (t, J_{CF} = 6 Hz), 141.0, 150.4 (t, J_{CF} = 260 Hz), 163.0 (t, J_{CF} = 35 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = 61.5 (tq, J_{FH} = 5, 5 Hz).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{12}H_{12}F_2$: 194.0907; found: 194.0909.

Acknowledgment

This research was partly supported by a Grant-in-Aid for Exploratory Research from MEXT, Japan. We thank Tosoh F-Tech, Inc. for providing 1,1,1-trifluoro-2-iodoethane.

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