A Facile Synthesis of 1,1-Difluoroallenes from Commercially Available 1,1,1-Trifluoro-2-iodoethane

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A Facile Synthesis of 1,1-Difluoroallenes from Commercially Available 1,1,1-Trifluoro-2-iodoethane

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Abstract: 1,1-Difluoroallenes are synthesized in good yield via zinc-promoted 1,2-elimination of 3,3-difluoro-2-iodoallylic acetates, which are prepared by the reaction of aldehydes or ketones with 1-iodo-2,2-difluorovinyllithium, generated from commercially available 1,1,1-trifluoro-2-iodoethane.

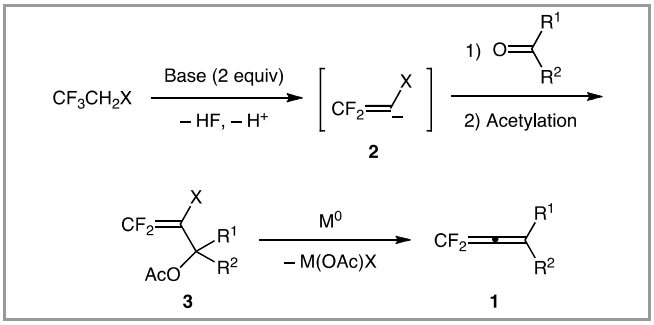
Key words: fluorinated allenes, metalation, carbanions, elimination, difluorovinylidenation.

1,1-Difluoroallenes have attracted much attention because of their unusual reactivities, which leads to them being used as synthetic building blocks for fluorinated molecules. The Diels–Alder and [3+2] cycloaddition reactions of 1,1-difluoroallenes with 1,3-dienes and 1,3-dipoles readily take place on the internal, non-fluorinated alkene moiety to give the corresponding *exo*-difluoromethylene compounds.[1] For example, 1,1-difluoroallene (CF_2=C=CH_2), with a low LUMO energy level, gives an excellent yield (>99%) of the cyclized product with cyclopentadiene under very mild conditions (–20 ºC, 1 min), while the non-fluorinated counterpart (CH_2=C=CH_2) requires vigorous conditions (200–230 °C) to give the product in a modest yield (49%).[1a,1f] [2+2] Cycloaddition reactions with alkenes and alkynes occur on the terminal, fluorinated alkene moiety to give ring fluorinated cyclobutane[2a] and cyclobutene[2b] derivatives. 1,1-Difluoroallenes also react with various nucleophiles to afford CF_2-terminal or internal addition products selectively, depending on the character of the nucleophile.[3]

Although the parent 1,1-difluoroallene (CF_2=C=CH_2) has been known since the 1950s,[4] very few synthetic methods for 3-substituted 1,1-difluoroallenes have been reported.[3a,5] Recently, we have developed a versatile synthetic method for 3-substituted 1,1-difluoroallenes **1** using two steps: (i) lithiation of 1,1-dibromo-2,2-difluoroethene with butyllithium generates 1-bromo-2,2-difluorovinyllithium (CF_2=CBrLi), which in turn, reacts with aldehydes or ketones to form 2-bromo-3,3-difluoroallylic acetates, and (ii) treatment of the bromoacetates with butyllithium gives 1,1-difluoroallenes *via* the 1,2-elimination of lithium acetate.[6]

However, there are two factors that limit the scope of this method: (a) the starting material, CF_2=CBr_2, is a high-cost, potential ozone-depleting substance, and is now unavailable because of the ban on its industrial manufacture, and (b) the highly nucleophilic alkyllithium is required in the preparation of 1,1-difluoroallenes, which restricts the choice of substrate. Here, we report an improved synthetic method for 1,1-difluoroallenes to overcome these issues using (A) an environmentally friendly and commercially available compound as the starting material, and (B) an effective process for carrying out a 1,2-elimination reaction under mild and tolerant reaction conditions.

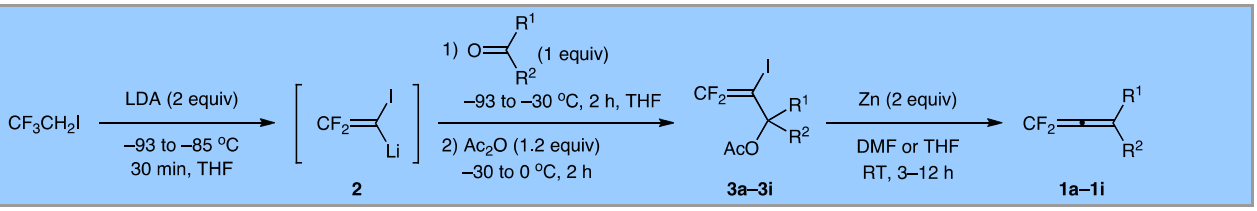
First, we considered that the key intermediate, a 1-halogenated 2,2-difluorovinyl anion **2** (Scheme 1), would be generated by the addition of two equivalents of a strong base to 1,1,1-trifluoro-2-haloethanes,[7-9] which bear two hydrogen atoms and are recognized to have much lower ozone depletion potential (ODP). These compounds are manufactured industrially for use as refrigerants or as fluorinated intermediates. Second, we proposed a different route to access the desired 1,1-difluoroallenes **1** from 3,3-difluoro-2-haloallylic acetates **3** (Scheme 1) on treatment with a zero-valent metal instead of the highly reactive alkyllithium, which would promote the 1,2-elimination from acetates **3** to form one more double bond under mild conditions. This sequence would expand the scope of the substrates.

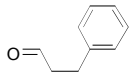
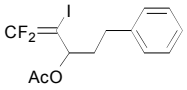
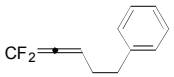
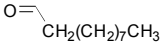
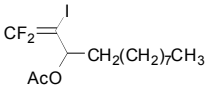
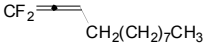
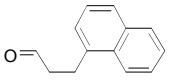
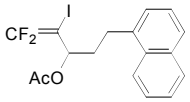
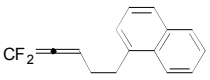
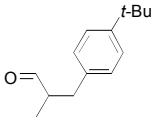
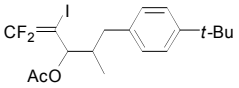
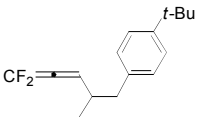
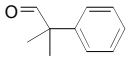
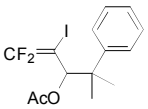
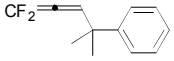
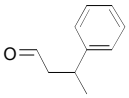
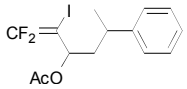
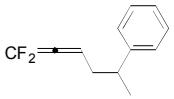
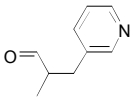
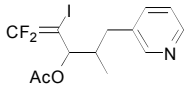
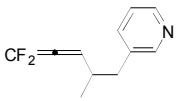
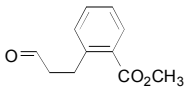
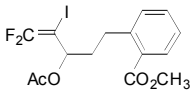
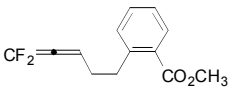
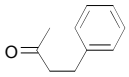
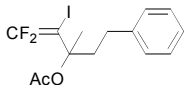
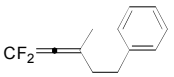


Scheme 1 A synthetic plan for 1,1-difluoroallenes from a 1,1,1-trifluoro-2-haloethane

We selected 1,1,1-trifluoro-2-iodoethane as the starting material because of its easy handling (bp. 55−56 °C). The lithiation of 1,1,1-trifluoro-2-iodoethane with two equivalents of LDA at low temperatures (–93 to –85 °C) successfully gave 2,2-difluoro-1-iodovinyllithium (**2**, Table 1).[10] Lithium species **2** then reacted with one equivalent of either an aldehyde or a ketone, and was subsequently acetylated with acetic anhydride (Table 1, Entries 1–8) or with isopropenyl acetate/TsOH (Entry 9) to afford 3,3-difluoro-2-iodoallylic acetates **3** in good yield.

Table 1 Synthesis of 1,1-Difluoroallenes **1** *via* Difluorovinylidenation of Carbonyl Compounds



Entry	Carbonyl Compound	3,3-Difluoro-2-iodoallylic Acetate **3**	Yield of **3** (%)	1,1-Difluoroallene **1**	Yield of **1** (%) (time)
1			**3a,** 82		**1a,** 86 (3 h)
2			**3b**, 84		**1b**, 87 (6 h)
3			**3c**, 83		**1c,** 82 (6 h)
4			**3d**, 87		**1d**, 92 (6 h)
5			**3e**, 83		**1e**, 93 (12 h)
6			**3f**, 81		**1f**, 95 (6 h)
7			**3g,** 73		**1g,** 71 (12 h)
8			**3h,** 82		**1h,** 74 (6 h)
9			**3i,** 80[a]		**1i,** 86 (8 h)

[a]Acetylation was performed with isopropenyl acetate/TsOH.[6]

Then, we found a facile and effective route by the zinc-promoted 1,2-elimination of acetates **3** under mild and tolerant reaction conditions (e.g., at room temperature for several hours) compared with the previously used *n*-BuLi-promoted 1,2-elimination.[6,11,12] The conditions of the zinc-promoted 1,2-elimination were optimized, as shown in Table 2. In most cases, 1,1-difluoroallenes **1** were obtained in good yield on treatment of acetates **3** with two equivalents of zinc, either in DMF or in THF, at room temperature for 3–12 hours (Table 2, Entries 1–6). However, 1,1-difluoroallene **1g** was only formed in DMF, and not in THF (Table 2, Entries 7 and 8), although the reason for this is not clear at present.[13] 3-Substituted 1,1-difluoroallenes with a primary alkyl group were produced readily using this method, while the yield decreased when the reaction period was extended by several hours (Table 2, Entries 1 and 2). In contrast, the yield of 1,1-difluoroallenes with a secondary or tertiary alkyl group at the 3-position remained steady, even after an extended reaction time (Table 2, Entries 3–5). This may be the result of the stability of 1,1-difluoroallenes.

Table 2 Optimization of the Zinc-promoted 1,2-Elimination

Entry	Acetate **3**	Zn (eq)	Solvent	Time	Yield of **1** (%)
1	**3a**	2	DMF	3 h	**1a**: 86
2	**3a**	2	DMF	6 h	**1a**: 72[a]
3	**3d**	2	DMF	3 h	**1d**: 83
4	**3d**	2	DMF	6 h	**1d**: 92

5	**3d**	2	DMF	12 h	**1d**: 90
6	**3d**	2	THF	6 h	**1d**: 88
7	**3g**	2	DMF	8 h	**1g:** 71
8	**3g**	4	THF	12 h	**1g:** trace[b]

[a]Allene **1a** partly decomposed to a complex mixture.
[b]Acetate **3g** was recovered quantitatively.

Owing to the mild conditions of the Zn-promoted 1,2-elimination, 1,1-difluoroallenes bearing a pyridine ring or an ester functionality were synthesized in good yield (Table 1, Entries 7 and 8). A 3,3-disubstituted 1,1-difluoroallene was obtained in high yield from a 1,1-disubstituted 2-iodo-3,3-difluoroallylic acetate, which was prepared from the corresponding ketone (Table 1, Entry 9).

In summary, we have developed a general and efficient method for the synthesis of 1,1-difluoroallenes from commercially available and environmentally friendly 1,1,1-trifluoro-2-iodoethane under mild reaction conditions. This facile and low-cost synthesis allows 1,1-difluoroallenes to be used as practical building blocks for the synthesis of a various useful fluorinated molecules. Their application is in progress in our laboratory and will be reported in due course.

NMR spectra were recorded on Bruker AVANCE-500 or Bruker AVANCE-400 in $CDCl_3$. Chemical shift values were given in ppm relative to internal $SiMe_4$ (for ^{1}H NMR: δ 0.00), $CDCl_3$ (for ^{13}C NMR: δ 77.0), and C_6F_6 (for ^{19}F NMR: δ 0.0). Mass spectra (EI-TOF or ESI-TOF) were measured on JEOL JMS-T100GCv or JMS-T100CS. IR spectra were recorded by ATR (attenuated total reflectance) method on a Horiba FT-720. Column chromatography and preparative thin layer chromatography (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 and DMF were dried by passing over a column of activated alumina followed by a column of Q-5 scavenger (Engelhard). 1,1,1-Trifluoro-2-iodoethane was obtained from Tosoh F-tech, Inc., and distilled from activated molecular sieves 4A. This compound can also be purchased from Tokyo Chemical Industry Co., Ltd. or Sigma-Aldrich Co. NMR and IR Spectra of compounds **1a**, **1c**, **1d**, and **1f** are in agreement with the published data.[6]

Synthesis of 1,1-difluoro-2-iodo-5-phenylpent-1-en-3-yl acetate (3a)

To a THF (10 mL) solution of diisopropylamine (2.8 mL, 20 mmol) was added butyllithium (12.0 mL, 1.67 M in hexane, 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 using a cold hexane bath. To this cold LDA solution was added a THF (5 mL) solution of CF_3CH_2I (2.10 g, 10.0 mmol) over 10 min, keeping the temperature between –93 °C and –85 °C. After stirring for 20 min at the same temperature, a THF (5 mL) solution of 3-phenylpropanal (1.34 g, 10.0 mmol) was added over 5 min, 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 acetic anhydride (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 saturated aqueous ammonium chloride, and the products were extracted with Et_2O. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (hexane–AcOEt, 20:1). The acetate **3a** was obtained as a colorless liquid (3.01 g, 82%).

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

^{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, 1F), 90.2 (d, J_{FF} = 22 Hz, 1F).

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

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

1,1-Difluoro-2-iodododec-1-en-3-yl acetate (3b)

840 mg of 1,1,1-trifluoro-2-iodoethane (4.00 mmol), 84% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (t, J = 6.9 Hz, 3H), 1.19–1.35 (broad, 14H), 1.52–1.61 (m, 1H), 1.65–1.74 (m, 1H), 2.07 (s, 3H), 4.94 (t, J = 7.2 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 14.0, 20.9, 22.6, 24.5, 28.9, 29.2, 29.30, 29.34, 31.8, 34.2, 54.1 (dd, J_{CF} = 24, 26 Hz), 69.3 (d, J_{CF} = 3 Hz), 153.9 (dd, J_{CF} = 286, 299 Hz), 169.6.

^{19}F NMR (470 MHz, $CDCl_3$): δ 88.3 (d, J_{FF} = 24 Hz, 1F), 89.6 (d, J_{FF} = 24 Hz, 1F).

IR (ATR): 2925, 2856, 1749, 1716, 1458, 1371, 1269, 1225, 1024, 962, 604 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{12}H_{19}F_2I$ $[M - AcOH]^+$: 328.0500; found: 328.0478.

1,1-Difluoro-2-iodo-5-(1-naphthyl)pent-1-en-3-yl acetate (3c)

840 mg of 1,1,1-trifluoro-2-iodoethane (4.00 mmol), 83% yield, a pale yellow liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.87–1.96 (m, 1H), 1.97 (s, 3H), 2.04–2.13 (m, 1H), 2.92 (t, J = 8.1 Hz, 2H), 5.00 (tdd, J = 6.4, 2.2, 1.4 Hz, 1H), 7.19 (d, J = 6.9 Hz, 1H), 7.28 (dd, J = 7.1, 7.1 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 7.0 Hz, 1H), 7.61 (d, J = 8.2 Hz, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.90 (d, J = 8.6 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 20.9, 28.1, 35.4, 53.8 (t, J_{CF} = 25 Hz), 69.2 (d, J_{CF} = 3 Hz), 123.4, 125.5, 126.0 (2C), 127.1, 128.9, 131.5, 133.9, 136.3, 154.1 (dd, J_{CF} = 299, 286 Hz), 169.6.

^{19}F NMR (470 MHz, $CDCl_3$): δ 89.4 (d, J_{FF} = 22 Hz, 1F), 90.3 (d, J_{FF} = 22 Hz, 1F).

IR (ATR): 3047, 2939, 1743, 1716, 1371, 1269, 1225, 1026, 966, 798 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{17}H_{15}F_2IO_2$ $[M]^+$: 416.0085; found: 416.0059.

5-(4-*tert*-Butylphenyl)-1,1-difluoro-2-iodo-4-methylpent-1-en-3-yl acetate (3d)

840 mg of 1,1,1-trifluoro-2-iodoethane (4.00 mmol), 87% yield (Diastereomer ratio = 1:1), a pale yellow liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.74 (d, *J* = 6.4 Hz, 1.5H), 0.91 (d, *J* = 6.2 Hz, 1.5H), 1.15–1.45 (m, 1H), 1.31 (s, 9H), 2.06 (s, 1.5H), 2.09 (s, 1.5H), 2.05–2.13 (m, 0.5H), 2.34 (dd, *J* = 13.5, 9.5 Hz, 0.5H), 2.67 (d, *J* = 12.2 Hz, 0.5H), 2.92 (d, *J* = 13.5 Hz, 0.5H), 4.70 (d, *J* = 10.0 Hz, 0.5H), 4.75 (d, *J* = 9.5 Hz, 0.5H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 14.5, 14.8, 20.8, 31.4, 34.3, 37.6, 38.0, 38.4, 39.1, 53.3 (dd, J_{CF} = 26, 26 Hz), 73.3 (d, J_{CF} = 3 Hz), 73.4 (d, J_{CF} = 3 Hz), 125.2, 128.7, 128.8, 136.0, 136.4, 148.9, 149.0, 154.3 (dd, J_{CF} = 298, 286 Hz), 154.4 (dd, J_{CF} = 297, 286 Hz), 169.7, 169.8.

^{19}F NMR (470 MHz, $CDCl_3$): δ 88.5 (d, J_{FF} = 23 Hz, 0.5F), 89.1 (d, J_{FF} = 22 Hz, 0.5F), 89.8 (d, J_{FF} = 23 Hz, 0.5F), 90.6 (d, J_{FF} = 22 Hz, 0.5F).

IR (ATR): 2962, 2871, 1741, 1716, 1510, 1462, 1369, 1269, 1225, 1020, 968, 606, 573 cm^{-1}.

HRMS (ESI^+): *m/z* calcd for $C_{18}H_{23}F_2IO_2Na$ $[M + Na]^+$: 459.0608; found: 459.0610.

1,1-Difluoro-2-iodo-4-methyl-4-phenylpent-1-en-3-yl acetate (3e)

840 mg of 1,1,1-trifluoro-2-iodoethane (4.00 mmol), 83% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.46 (s, 3H), 1.48 (s, 3H), 2.05 (s, 3H), 5.14 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.32 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.40 (d, *J* = 7.7 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 20.8, 24.9, 25.0 (d, J_{CF} = 9 Hz), 42.8, 48.0 (dd, J_{CF} = 25, 25 Hz), 74.5 (d, J_{CF} = 2 Hz), 126.7, 127.0, 128.0, 144.4, 153.8 (dd, J_{CF} = 298, 286 Hz), 169.3.

^{19}F NMR (470 MHz, $CDCl_3$): δ 91.1 (d, J_{FF} = 23 Hz, 1F), 91.3 (d, J_{FF} = 23 Hz, 1F).

IR (ATR): 2976, 1745, 1709, 1498, 1442, 1369, 1265, 1219, 1030, 980, 768, 698, 609 cm^{-1}.

HRMS (ESI^+): *m/z* calcd for $C_{14}H_{15}F_2IO_2Na$ $[M + Na]^+$: 402.9982; found: 403.0012.

1,1-Difluoro-2-iodo-5-phenylhex-1-en-3-yl acetate (3f)

840 mg of 1,1,1-trifluoro-2-iodoethane (4.00 mmol), 81% yield (Diastereomer ratio = 6:4), a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.28 (d, *J* = 7.0 Hz, 1.8H), 1.29 (d, *J* = 7.0 Hz, 1.2H), 1.80–1.88 (m, 1H), 1.95 (s, 1.8H), 1.98–2.05 (m, 0.4H), 2.06 (s, 1.2H), 2.06–2.12 (m, 0.6H), 2.62–2.69 (m, 0.6H), 2.70–2.78 (ddq, *J* = 7.0, 7.0, 7.0 Hz, 0.4H), 4.78 (dd, *J* = 6.5, 6.5 Hz, 0.6H), 4.84 (dd, *J* = 7.5, 7.5 Hz, 0.4H,), 7.16 (dd, *J* = 7.0, 5.0 Hz, 1.8H), 7.20 (dd, *J* = 7.5, 7.5 Hz, 1.2H), 7.28 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 20.8, 20.9, 21.7, 23.1, 35.8, 36.0, 42.3, 42.7, 54.0 (dd, J_{CF} = 25, 25 Hz), 54.2 (dd, J_{CF} = 26, 26 Hz), 68.0 (d, J_{CF} = 3 Hz), 126.5, 126.7, 126.8, 128.58, 128.61, 145.2, 145.5, 153.7 (d, J_{CF} = 299, 286 Hz), 153.9 (d, J_{CF} = 300, 286 Hz), 169.4, 169.5.

^{19}F NMR (470 MHz, $CDCl_3$): δ 88.8 (d, J_{FF} = 23 Hz, 0.4F), 89.6 (d, J_{FF} = 21 Hz, 0.6F), 89.7 (d, J_{FF} = 23 Hz, 0.4F), 90.2 (d, J_{FF} = 21 Hz, 0.6F).

IR (ATR): 3028, 2962, 1747, 1716, 1495, 1452, 1371, 1269, 1225, 1020, 978, 700 cm^{-1}.

HRMS (ESI^+): *m/z* calcd for $C_{14}H_{15}F_2IO_2Na$ $[M + Na]^+$: 402.9982; found: 403.0000.

1,1-Difluoro-2-iodo-4-methyl-5-(3-pyridyl)pent-1-en-3-yl acetate (3g)

840 mg of 1,1,1-trifluoro-2-iodoethane (4.00 mmol), 73% yield (Diastereomer ratio = 6:4), a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.75 (d, *J* = 7.0 Hz, 1.6H), 0.92 (d, *J* = 6.0 Hz, 1.4H), 2.10–2.11 (m, 4.4H), 2.40 (dd, *J* = 13.5, 9.5 Hz, 0.6H), 2.72 (d, *J* = 10.0 Hz, 0.4H), 2.99 (dd, *J* = 13.5, 4.5 Hz, 0.6H), 4.72 (d, *J* = 10.0 Hz, 0.6H), 4.78 (d, *J* = 9.5 Hz, 0.4H), 7.28 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 8.45 (s, 1H), 8.49 (d, *J* = 4.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 14.3, 14.6, 20.79, 20.83, 35.3, 35.6, 38.3, 39.0, 52.7 (dd, J_{CF} = 25, 25 Hz), 72.9 (d, J_{CF} = 3.5 Hz), 73.2 (d, J_{CF} = 3.2 Hz), 123.4, 134.8, 135.2, 136.8, 136.9, 147.3, 147.5, 150.0, 150.1, 154.4 (dd, J_{CF} = 299, 286 Hz), 154.5, (dd, J_{CF} = 299, 286 Hz), 169.59, 169.62.

^{19}F NMR (470 MHz, $CDCl_3$): δ 89.0 (d, J_{FF} = 22 Hz, 0.6F), 89.5 (d, J_{FF} = 21 Hz, 0.4F), 90.3 (d, J_{FF} = 22 Hz, 0.6F), 91.2 (d, J_{FF} = 21 Hz, 0.4F).

IR (ATR): 2968, 2933, 1736, 1714, 1425, 1371, 1265, 1221, 1024, 968, 793, 715 cm^{-1}.

HRMS (ESI^+): *m/z* calcd for $C_{13}H_{15}F_2INO_2$ $[M + H]^+$: 382.0116; found: 382.0117.

Methyl 2-(3-acetoxy-5,5-difluoro-4-iodopent-4-en-1-yl) benzoate (3h)

840 mg of 1,1,1-trifluoro-2-iodoethane (4.00 mmol), 82% yield, a pale yellow liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.86–1.92 (m, 1H), 2.04–2.13 (m, 1H), 2.08 (s, 3H), 2.90 (ddd, *J* = 15.5, 10.0, 5.5 Hz, 1H), 2.98 (ddd, *J* = 15.5, 10.0, 5.5 Hz, 1H), 3.91 (s, 3H), 5.02 (ddt, *J* = 7.0, 2.0, 2.0 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.28 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.44 (td, *J* = 7.5, 1.5 Hz, 1H), 7.91 (dd, *J* = 7.5, 1.4 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 20.9, 29.7, 36.2, 52.0, 53.9 (t, J_{CF} = 26 Hz), 69.2 (d, J_{CF} = 4 Hz), 126.4, 129.4, 130.9, 131.0, 132.2, 142.3, 154.0 (dd, J_{CF} = 299, 286 Hz), 167.7, 169.7.

^{19}F NMR (470 MHz, $CDCl_3$): δ 89.1 (d, J_{FF} = 23 Hz, 1F), 89.9 (d, J_{FF} = 23 Hz, 1F).

IR (ATR): 3068, 2952, 1747, 1716, 1435, 1373, 1259, 1228, 1088, 1026, 966, 712 cm^{-1}.

HRMS (ESI$^+$): *m/z* calcd for $C_{15}H_{15}F_2IO_4Na$ $[M + Na]^+$: 446.9881; found: 446.9879.

1,1-Difluoro-2-iodo-3-methyl-5-phenylpent-1-en-3-yl acetate (3i)

To a THF (5 mL) solution of diisopropylamine (1.1 mL, 8.00 mmol) was added butyllithium (4.8 mL, 1.67 M in hexane, 8.0 mmol) over 10 min at 0 °C under argon. The resulting solution was allowed to stir for an additional 15 min, then cooled to –93 °C using a cold hexane bath. To this cold LDA solution was added a THF (2 mL) solution of CF_3CH_2I (840 mg, 4.00 mmol) over 10 min, keeping the temperature between –93 °C and –85 °C. After stirring for 20 min at the same temperature, a THF (2 mL) solution of 4-phenylbutan-2-one (593 mg, 4.00 mmol) was added over 5 min, 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 saturated aqueous ammonium chloride, and the products were extracted with Et_2O. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (hexane–AcOEt, 10:1). This alcohol was used for the next step without further purification.

To a solution of the alcohol in isopropenyl acetate (3 mL) was added 4-methylbenzenesufonic acid monohydrate (5 mg, 0.03 mmol). After refluxing for 4 h, the reaction was quenched with saturated aqueous sodium hydrogen carbonate. The products were extracted with ether. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (hexane–AcOEt, 30:1). Acetate **3i** was obtained as a colorless liquid (1.22 g, 80%, two steps).

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

^{13}C NMR (126 MHz, $CDCl_3$): δ 21.8, 22.9 (d, J_{CF} = 7 Hz), 30.0, 42.8 (dd, 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, 1F), 97.3 (d, J_{FF} = 33 Hz, 1F).

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

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

Synthesis of 1,1-difluoro-5-phenylpenta-1,2-diene (1a)

To a suspension of zinc (powder, 131 mg, 2.00 mmol) in DMF (3 mL) was added a DMF (2 mL) solution of **3a** (366 mg, 1.00 mmol) at room temperature under argon. After stirring for 3 h, the resulting reaction mixture was filtered to remove the excess zinc and then diluted with Et_2O and brine. The products were extracted with Et_2O. The combined organic layer were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (pentane). Allene **1a** was obtained as a colorless liquid (155 mg, 86%).

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

^{13}C NMR (126 MHz, $CDCl_3$): δ 33.76, 33.77, 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 60.0 (td, J_{FH} = 5, 2 Hz, 2F).

IR (ATR): 3030, 2929, 2362, 2013, 1462, 1196, 744, 698 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{11}H_{10}F_2$ $[M]^+$: 180.0751; found: 180.0749.

1,1-Difluorododeca-1,2-diene (1b)

388 mg of **3b** (1.00 mmol), 87% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (t, *J* = 7.0 Hz, 3H), 1.27–1.30 (m, 12H), 1.49 (tq, *J* = 7.5, 7.0 Hz, 2H), 2.23 (ttd, *J* = 7.0, 6.3, 6.0 Hz, 2H), 6.42 (tt, *J* = 6.3 Hz, J_{HF} = 2.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 14.1, 22.7, 27.6, 28.9, 29.3, 29.4, 29.5, 31.9, 32.3 (t, J_{CF} = 2 Hz), 122.5 (t, J_{CF} = 6 Hz), 152.5 (t, J_{CF} = 261 Hz), 169.3 (t, J_{CF} = 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ 59.4 (td, J_{FH} = 6, 3 Hz, 2F).

IR (ATR): 2925, 2856, 2011, 1462, 1246, 1194, 721 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{12}H_{20}F_2$ $[M]^+$: 202.1533, found: 202.1516.

1,1-Difluoro-5-(1-naphthyl)penta-1,2-diene (1c)

416 mg of **3c** (1.00 mmol), 82% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 2.48–2.54 (m, 2H), 3.09 (t, *J* = 7.4 Hz, 2H), 6.36 (tt, *J* = 6.1 Hz, J_{HF} = 2.4 Hz, 1H), 7.16 (d, *J* = 6.6 Hz, 1H), 7.25 (dd, *J* = 7.6 Hz, 1H), 7.32–7.39 (m, 2H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 30.8, 33.0, 121.6 (t, J_{CF} = 5.5 Hz), 123.4, 125.5, 125.6, 126.0, 126.1, 127.1, 128.9, 131.6, 133.9, 136.6, 152.9 (t, J_{CF} = 261 Hz), 170.0 (t, J_{CF} = 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ 60.4 (dt, J_{FH} = 2, 5 Hz, 2F).

IR (ATR): 3062, 2941, 2009, 1745, 1458, 1186, 791 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{15}H_{12}F_2$ $[M]^+$: 230.0907; found: 230.0906.

5-(4-*tert*-Butylphenyl)-1,1-difluoro-4-methylpenta-1,2-diene (1d)

436 mg of **3d** (1.00 mmol), 92% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.05 (d, J = 6.6 Hz, 3H), 1.30 (s, 9H), 2.57 (dd, J = 13.0, 6.6 Hz, 1H), 2.59–2.68 (m, 1H), 2.75 (dd, J = 13.0, 7.6 Hz, 1H), 6.41 (ddd, J = 5.0 Hz, J_{HF} = 2.5, 2.5 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 18.5, 31.4, 34.3, 38.4, 41.6 (d, J_{CF} = 2 Hz), 125.2, 127.1 (dd, J_{CF} = 6, 6 Hz), 128.8, 136.4, 149.1, 153.5 (dd, J_{CF} = 261, 261 Hz), 168.6 (dd, J_{CF} = 36, 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ 60.0 (ddd, J_{FF} = 127 Hz, J_{FH} = 3, 3 Hz, 1F), 60.3 (ddd, J_{FF} = 127 Hz, J_{FH} = 3, 3 Hz, 1F).

IR (ATR): 2964, 2870, 2009, 1446, 1238, 1190, 937, 858 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{16}H_{20}F_2$ $[M]^+$: 250.1533; found: 250.1532.

1,1-Difluoro-4-methyl-4-phenylpenta-1,2-diene (1e)

380 mg of **3e** (1.00 mmol), 93% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.47 (s, 6H), 6.55 (t, J_{HF} = 2.8 Hz, 1H), 7.23–7.25 (m, 1H), 7.31–7.36 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 28.0, 42.4 (dd, J_{CF} = 2 Hz), 125.9, 126.6, 128.5, 131.0 (t, J_{CF} = 6 Hz), 146.2 (d, J_{CF} = 2 Hz), 153.3 (dd, J_{CF} = 262, 262 Hz), 167.1 (dd, J_{CF} = 36, 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ 61.1 (d, J_{HF} = 2 Hz, 2F).

IR (ATR): 2972, 2931, 2873, 2009, 1601, 1495, 1435, 1192, 958, 854, 760, 696 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{12}H_{12}F_2$ $[M]^+$ 194.0907, found: 194.0903.

1,1-Difluoro-5-phenylhexa-1,2-diene (1f)

380 mg of **3f** (1.00 mmol), 95% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.30 (d, J = 7.0 Hz, 3H), 2.44–2.60 (m, 2H), 2.95 (qdd, J = 7.1, 7.1, 7.1 Hz, 1H), 6.28 (dddd, J = 6.9, 6.9 Hz, J_{HF} = 2.4, 2.4 Hz, 1H), 7.18–7.23 (m, 3H), 7.30 (t, J = 6.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 21.6, 38.8, 40.7, 120.4 (dd, J_{CF} = 6, 6 Hz), 126.4, 126.9, 128.5, 145.7, 152.4 (dd, J_{CF} = 260, 260 Hz), 170.9 (dd, J_{CF} = 36, 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ 59.1 (br ddd, J_{FF} = 122 Hz, J_{FH} = 6, 4 Hz, 1F), 59.6 (br ddd, J_{FF} = 122 Hz, J_{FH} = 7, 4 Hz, 1F).

IR (ATR): 3030, 2964, 2009, 1726, 1603, 1495, 1458, 1240, 1190, 760, 698 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{12}H_{12}F_2$ $[M]^+$: 194.0907; found: 194.0906.

3-(5,5-Difluoro-2-methylpenta-3,4-dien-1-yl)pyridine (1g)

381 mg of **3g** (1.00 mmol), 71% yield, a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (d, J = 8.0 Hz, 3H), 2.60–2.72 (m, 2H), 2.81 (dd, J = 12.7, 6.0 Hz, 1H), 6.42 (dt, J = 8.0 Hz, J_{HF} = 2.6 Hz, 1H), 7.23 (ddd, J = 7.8, 4.8, 0.6 Hz, 1H), 7.49 (ddd, J = 7.8, 2.1, 1.9 Hz, 1H), 8.45 (d, J = 1.9 Hz, 1H), 8.48 (dd, J = 4.8, 1.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 18.5, 38.0 (t, J_{CF} = 2 Hz), 38.9 (t, J_{CF} = 2 Hz), 123.3, 126.0 (t, J_{CF} = 6 Hz), 134.8, 136.5, 147.7, 150.3, 153.4 (t, J_{CF} = 262 Hz), 169.4 (t, J_{CF} = 36 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ 60.5 (d, J = 120 Hz, 1F), 60.7 (d, J = 120 Hz, 1F).

IR (ATR): 2970, 2931, 2009, 1576, 1446, 1188, 1026, 939, 856, 796, 714 cm^{-1}.

HRMS (ESI$^+$): *m/z* calcd for $C_{11}H_{12}F_2N$ $[M + H]^+$: 196.0938; found: 196.0947.

Methyl 2-(5,5-difluoropenta-3,4-dien-1-yl)benzoate (1h)

424 mg of **3h** (1.00 mmol), 74% yield, a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 2.54–2.59 (m, 2H), 3.13 (t, J = 7.5 Hz, 2H), 3.88 (s, 3H), 6.49 (tt, J = 6.0 Hz, J_{HF} = 2.5 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 7.27 (dt, J = 7.5, 1.0 Hz, 1H), 7.42 (td, J = 7.5, 1.5 Hz, 1H), 7.92 (dd, J = 7.5, 1.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 32.6, 33.9, 51.9, 121.6 (t, J_{CF} = 6 Hz), 126.3, 129.3, 130.9, 131.1, 132.1, 142.6, 152.6 (t, J_{CF} = 261 Hz), 167.7, 169.7 (t, J_{CF} = 36 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ 60.0 (s, 2F).

IR (ATR): 2952, 2009, 1716, 1460, 1254, 1186, 1130, 1082, 962, 748, 708 cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{13}H_{12}F_2O_2$ $[M]^+$: 238.0805; found: 238.0805.

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

380 mg of **3i** (1.00 mmol), 86% yield, a colorless liquid.

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

^{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 = 5, 5 Hz, 2F).

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

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

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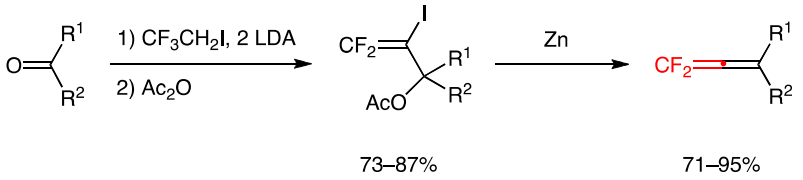
(10) The lithiation of CF_3CH_2I with *n*-BuLi instead of LDA at –93 to –85 °C led to a low yield of 2,2-difluoro-1-iodovinyllithium, probably due to iodine–lithium exchange reaction.

(11) For 2-bromo-3,3-difluoroallylic acetates, zinc-promoted 1,2-elimination also took place readily at room temperature and led to the formation of the corresponding 1,1-difluoroallenes.

(12) Magnesium was employed in THF to promote the 1,2-elimination of acetate **3d** in vain.

(13) When THF was used as a solvent, only a trace amount of **1g** was observed by the ^{19}F NMR measurement in spite of a large excess amount of zinc and an extended reaction time. A similar behavior was exhibited by some other acetates **3** without a heteroaromatic ring.

A Facile Synthesis of 1,1-Difluoroallenes from Commercially Available 1,1,1-Trifluoro-2-iodoethane



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