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Stereoselective Synthesis of Monofluoroalkyl α,β-Unsaturated Ketones From Allenyl Carbinol Esters Mediated by Gold and Selectfluor

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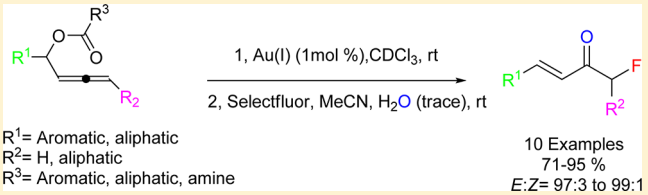
Supporting Information

ABSTRACT: Allenyl carbinol ester **3** isomerizes to an *E,Z* mixture of the corresponding diene **2** in the presence of gold catalyst **4**, but the resulting mixture yields monofluoroalkyl α,β-unsaturated ketone **1** with exclusive *E* selectivity and in high yields after reaction with Selectfluor.



Monofluoroalkyl α,β-unsaturated ketones **1** are important molecular synthons, as showcased by their widespread use in the syntheses of bioactive compounds (Figure 1).[1]

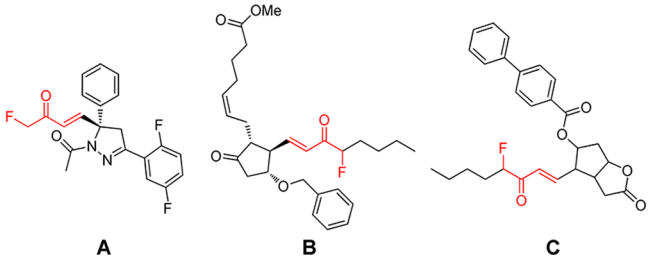


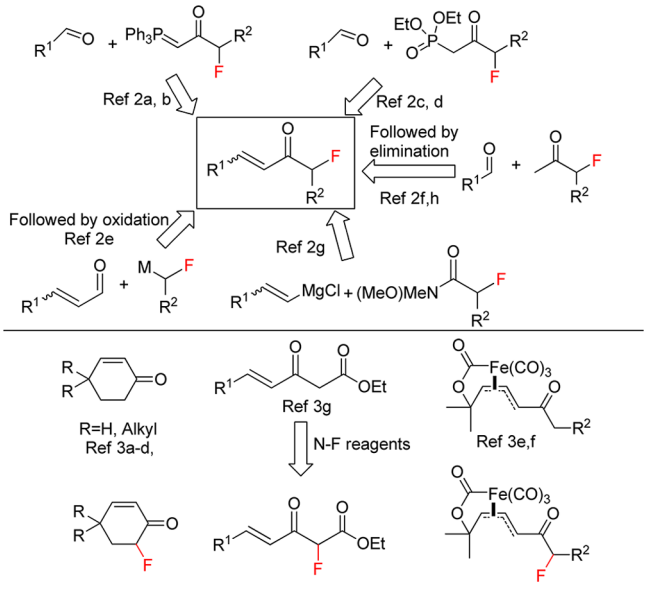
Figure 1. Monofluoroalkyl (*E*)-α,β-unsaturated ketones **A**,[1a] **B**,[1b] and **C**[1c] are important building blocks for bioactive agents.

Fluoroketone **1** is most commonly synthesized either by using a fluorine containing building block[2] or through fluorination of an unsaturated ketone.[3] But these methodologies have limitations. The former relies on a shallow pool of fluorine containing moieties (Scheme 1, top), whose preparation is not always trivial; a case in point is the synthesis of fluorine-containing Wittig reagents.[2a,b,4]

The fluorination of an unsaturated ketone is hampered because the regioselective fluorination of the starting unsaturated ketone is case specific (Scheme 1, bottom). Because of these limitations, it is not trivial to build libraries of fluoroalkyl α,β-unsaturated ketones.

Inspired by the works of Gouverneur[5] and Nevado[6] (Scheme 2, top), we envisioned a more efficient fluorination process to overcome the aforementioned drawbacks. Nevado and co-workers reported that propargyl acetate and Selectfluor, in the presence of gold catalyst, delivered α-fluoroenone (mixture of *E* and *Z*), and proposed that gold facilitated the 3,3-sigmatropic rearrangement of propargyl acetate, and that C−F bond may be formed through gold(III) reductive elimination. Gouverneur and co-workers researched a similar reaction and reported that

Scheme 1. Literature Syntheses of Monofluoroalkyl α,β-Unsaturated Ketones Using Fluorine-Containing Building Blocks (Top) or through Fluorination of Specific Ketones (Bottom)



the C−F bond formation did not involve gold catalysis. Instead, gold facilitated the isomerization of propargylic esters to give alleny acetate, which reacted with electrophilic fluorine followed by hydrolysis to give α-fluoroenone.

We posited that an electron rich 1,3-butadien-2-ol ester **2** could be a suitable substrate for electrophilic fluorination (Scheme 2, bottom) because it is readily made by the gold-catalyzed isomerization of allenyl carbinol ester **3** using Gagosz' methodology.[7] We are pleased to report that a stereomixture of

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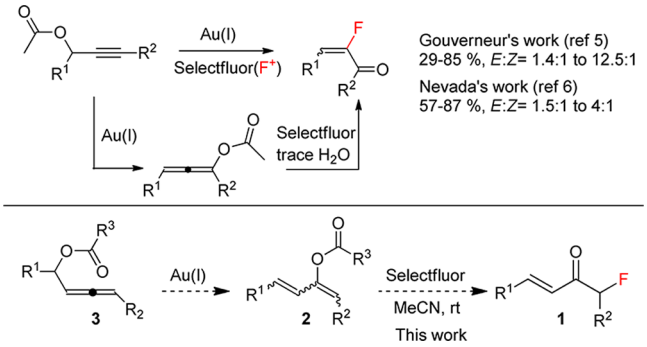
Scheme 2. Gold Catalyzed Isomerization of Alkyne and Allene and Subsequent Fluorination Strategy



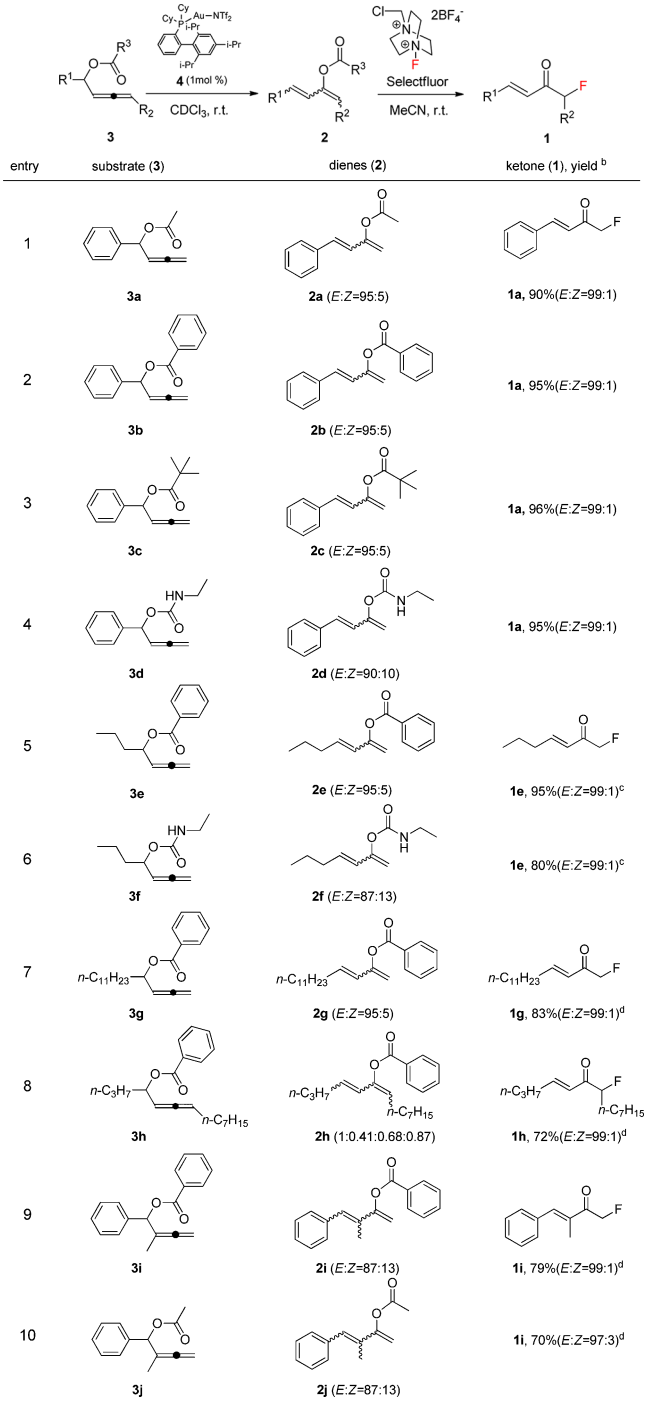
2 can be fluorinated at room temperature by Selectfluor to give fluoroalkyl α,β-unsaturated ketone **1** in high yields and with exclusive *E* stereoselectivity.

Our results are shown in Table 1. Gagosz and co-workers had reported that terminal allenyl carbinol ester **3** isomerizes to 1,3-butadien-2-ol ester **2** with moderate to good stereoselectivity in the presence of gold catalyst **4**. Indeed, in our hands carbinol ester **3a** isomerized to diene **2a** in $CDCl_3$ in the presence of catalyst **4**,[8] reacting readily with Selectfluor in MeCN to yield the corresponding fluorinated ketone **1a** in excellent yield and with exclusive *E* stereoselectivity.[9] It is noteworthy that diene **2a** (*E*:*Z* = 95:5) isomerizes to **1a** during the fluorination process, yielding exclusively the *E* isomer. Similarly, aromatic substrates **3b**, **3c** and **3d** isomerized to their corresponding dienes **2** as mixture of *E*/*Z* isomers, but upon fluorination, they afforded **1a** with high stereoselectivity and excellent chemical yields, regardless of the type of carboxylic acid derivative used. Aliphatic allenyl esters **3e** (entry 5), **3f** (entry 6) and **3g** (entry 7) were also examined. All of them isomerized efficiently and were fluorinated to give **1e** (*E*:*Z* = 99:1) (entries 5 and 6)[10] and **1g** (*E*:*Z* = 99:1) (entry 7) in very good yield. We were curious to know if an internal allenyl ester such as **3h** (entry 8) would behave similarly to terminal allene under our reaction conditions. We were pleasantly surprised to discover that even though **3h** isomerized readily to give a complex mixture of stereoisomers **2h** (1:0.41:0.68:0.87), this mixture still produced the desired **1h** in good yield, as a single *E*-isomer. Benzoate and acetate derivatives of 1,1-disubstituted allenyl esters **3i** and **3j** were also tested. Again, their isomerizations produced diene mixtures **2i** and **2j**, respectively, but after fluorination, only **1i** was obtained in very good yield and with exclusive *E* selectivity.

We decided to investigate the preparation of fluoroalkyl *E*,*E*-$\alpha,\beta,\gamma,\delta$-unsaturated ketone **1k** using our protocol, but unfortunately, this attempt failed because no isomerization of the two substrates tested, **3k** and **3l**, took place in the presence of gold catalyst **4** (Scheme 3).

A plausible mechanism for the isomerization of our diene mixture is proposed in Scheme 4. The electron-rich double bond of diene **2** attacks the electrophilic fluorine in Selectfluor to form cationic intermediate **C**, which immediately isomerizes to form the more stable intermediate **D**, and after hydrolysis with trace amounts of water present in the reaction media, it yields fluoroalkyl *E*-α,β-unsaturated ketone **1**. The reported electrophilic fluorination-nucleophilic addition reactions of glycals[11] and other substrates[5,6] using Selectfluor lend support to our proposed mechanism.

Table 1. Preparation of Monofluoroalkyl α,β-Unsaturated Ketones 1 from in Situ Generated Dienes 2[a]



entry	substrate (**3**)	dienes (**2**)	ketone (**1**), yield [b]
1	**3a**	**2a** (*E*:*Z*=95:5)	**1a**, 90%(*E*:*Z*=99:1)
2	**3b**	**2b** (*E*:*Z*=95:5)	**1a**, 95%(*E*:*Z*=99:1)
3	**3c**	**2c** (*E*:*Z*=95:5)	**1a**, 96%(*E*:*Z*=99:1)
4	**3d**	**2d** (*E*:*Z*=90:10)	**1a**, 95%(*E*:*Z*=99:1)
5	**3e**	**2e** (*E*:*Z*=95:5)	**1e**, 95%(*E*:*Z*=99:1)[c]
6	**3f**	**2f** (*E*:*Z*=87:13)	**1e**, 80%(*E*:*Z*=99:1)[c]
7	**3g**	**2g** (*E*:*Z*=95:5)	**1g**, 83%(*E*:*Z*=99:1)[d]
8	**3h**	**2h** (1:0.41:0.68:0.87)	**1h**, 72%(*E*:*Z*=99:1)[d]
9	**3i**	**2i** (*E*:*Z*=87:13)	**1i**, 79%(*E*:*Z*=99:1)[d]
10	**3j**	**2j** (*E*:*Z*=87:13)	**1i**, 70%(*E*:*Z*=97:3)[d]

[a]Reaction conditions: allenyl carbinol ester (**3**) (0.25 mmoL) and gold catalyst **4** (1.0 mol %) were dissolved in $CDCl_3$ (1 mL), stirred, and monitored by ^{1}H NMR until the reaction showed no more progress. After $CDCl_3$ removal under vacuum, Selectfluor (1.2 equiv) and acetonitrile (1.5 mL) were added to the diene mixture **2** and stirred for 3 h at rt. [b]Yield was calculated on starting allenyl carbinol ester (**3**). [c]^{19}F NMR yield due to their volatility, α,α,α-trifluorotoluene as internal standard. [d]Yield of allylic alcohol. Ketones were reduced to the corresponding allylic alcohol because of their instability toward silica gel. Allylic alcohols of **1g** and **1h** contain less than 3% of corresponding saturated alcohol; dr of the allylic alcohol (from **1h**) is 4:1.

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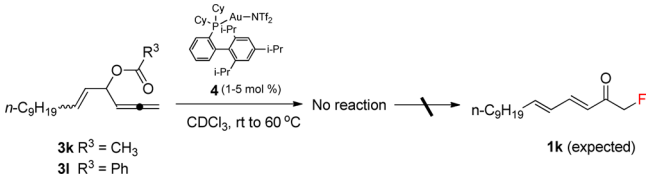
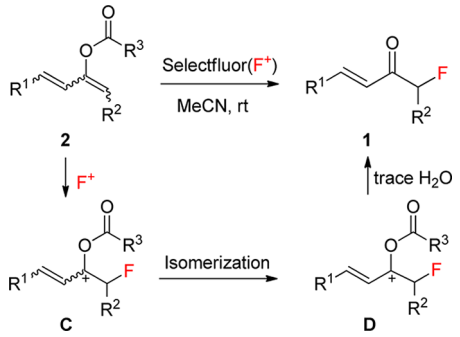
Scheme 3. Limitations of Our Protocol



Scheme 4. Proposed Mechanism for the Isomerization



In summary, our protocol can efficiently fluorinate a mixture of dienes **2** under mild conditions to give fluoroalkyl *E*-α,β-unsaturated ketones in good to excellent yield. Because the starting allenyl alcohols can be readily prepared using literature methodologies,[12] our protocol can be employed in the synthesis of a variety of fluoroalkyl *E*-α,β-unsaturated ketones. These ketones can, in turn, be further functionalized; for example, they can be converted into a fluorosugar precursor,[13] through dihydroxylation of its double bond.[2a]

EXPERIMENTAL SECTION

General Methods. The gold complex (**4**) and Selectfluor were purchased from Aldrich. All air and/or moisture sensitive reactions were carried out under argon atmosphere. Solvents (tetrahydrofuran, ether, dichloromethane and DMF) were chemically dried using a commercial solvent purification system. All other reagents and solvents were employed without further purification. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded at 500 (or 400), 126 (or 100) and 470 (or 376) MHz, respectively, using $CDCl_3$ (or CD_3CN) as a solvent. The chemical shifts are reported in δ (ppm) values relative to $CHCl_3$ (7.26 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR) and $CFCl_3$ (0 ppm for ^{19}F NMR). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz. FTIR spectra were recorded in ATR (attenuated total reflection) solid mode. Exact molecular weight of new compound was obtained by high-resolution mass spectrometry (TOF).

Preparation of Allenyl Alcohol. Allenyl alcohols precursor of **3a**, **3e** and **3g** were prepared by Crabbe reaction.[12b] Allenyl alcohol precursor of **3h** was prepared by Ma's methodology.[12a] Allenyl alcohol precursor of **3i** was prepared by Harada's methodology.[12c]

Typical Procedure for Crabbe Reaction. 1-Phenylprop-2-yn-1-ol (396.0 mg, 3.0 mmol), paraformaldehyde (180.0 mg, 6.0 mmol), diisopropylamine (834.0 μL, 6.0 mmoL), CuBr (257.4 mg, 1.8 mmol) and 1,4-dioxane (20 mL) were added into a 50 mL round-bottom reaction flask containing a stir bar, and the flask was equipped with reflux condenser. The reaction mixture was refluxed in oil bath for 2 h, cooled to room temperature, filtered through silica gel (about 15 g), and washed by mixture of hexanes and ethyl acetate (100 mL, ratio is 4:1). The solvent was removed in a vacuum, and the resulting residue was purified on a silica gel column, which was eluted by hexanes and ethyl acetate to give 1-phenylbuta-2,3-dien-1-ol (292.0 mg, 67%).

Typical Procedure for Ma's Methodology. Hex-1-yn-3-ol (556.2 μL, 5.0 mmol), octanal (779.5 μL, 5.0 mmol), morpholine (691.2 μL, 8.0 mmol), ZnI_2 (1276 mg, 4.0 mmol) and toluene (20 mL) were added into a 50 mL round-bottom reaction flask containing a stir bar, and the flask was equipped with refluxing condenser. The reaction mixture was refluxed for 8 h in oil bath, cooled to room temperature, filtered through silica gel (about 20 g), and washed by mixture of hexanes and ethyl acetate (120 mL, ratio is 4:1). The solvent was removed in a vacuum and the resulting residue was purified on a silica gel column, which was eluted by hexanes and ethyl acetate to give tetradeca-5,6-dien-4-ol (262.5 mg, 25%).

Typical Procedure for Harada's Methodology. Stannous chloride (568.8 mg, 3.0 mmol), 1-bromo-2-butyne (262.56 μL, 3.0 mmol), sodium iodide (450.0 mg, 3.0 mmol) and DMF (5 mL) were added into a 10 mL reaction flask containing a stir bar, and the reaction mixture was stirred for 1.5 h at room temperature. Then the reaction mixture was cooled at 0 °C, and benzaldehyde (305.7 μL, 3.0 mmol) in DMF (1 mL) was added dropwise and stirred for overnight. The reaction mixture was quenched by saturated ammonium chloride (20 mL), followed by diethyl ether extraction (25 mL × 4). The ether layers were combined and dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure; the resulting residue was subjected to silica gel chromatography eluted by hexanes and ethyl acetate system to yield 2-methyl-1-phenylbuta-2,3-dien-1-ol (384.0 mg, 80%).

Typical Procedure for Esterification of Allenyl Alcohol: Synthesis of 3a. 1-Phenylbuta-2,3-dien-1-ol (292.1 mg, 2.0 mmol) and triethylamine (417 μL, 3 mmol) were dissolved in dry dichloromethane (5.0 mL) at 0 °C, in which the acetyl chloride (213 μL, 3 mmol) was added slowly over a 5 min period, and the mixture was stirred for 10 min at 0 °C. The resulting solution was stirred for 5 h at room temperature, and then saturated ammonium chloride solution (20 mL) was added to the reaction mixture, followed by diethyl ether extraction (25 mL × 3). The ether layers were combined and dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure to yield **3a** (357.2 mg, 95%).

Spectroscopic Data for 3. *1-Phenylbuta-2,3-dien-1-yl acetate (**3a**).*[7] (357.2 mg, 95%), colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 6.31 (m, 1H), 5.45 (q, *J* = 6.8 Hz, 1H), 4.86 (m, 2H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.5, 171.2, 138.9, 128.5, 128.2, 126.9, 91.5, 77.8, 73.4, 21.1.

*1-Phenylbuta-2,3-dien-1-yl benzoate (**3b**).*[7] (450.2 mg, 90%), colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, J = 1.4, 7.1 Hz, 2H), 7.58 (dd, J = 1.3, 7.4 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 7.45 (d, J = 7.5 Hz, 2H), 7.40 (t, J = 7.0 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 6.56 (dt, J = 2.2, 6.7 Hz, 1H), 5.56 (q, J = 6.6 Hz, 1H), 4.90 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 208.7, 165.5, 139.3, 133.0, 130.3, 129.7, 128.5, 128.3, 128.2, 126.8, 91.7, 77.9, 74.0.

*1-Phenylbuta-2,3-dien-1-yl pivalate (**3c**).*[7] (425.5 mg, 93%), colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.29 (m, 5H), 6.28 (dt, *J* = 2.4, 6.6 Hz, 1H), 5.41 (q, *J* = 6.6 Hz, 1H), 4.88 (m, 2H), 1.24 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5, 177.4, 139.6, 128.4, 128.0, 126.9, 91.9, 77.5, 72.7, 38.9, 27.3.

*1-Phenylbuta-2,3-dien-1-yl ethylcarbamate (**3d**).* (386.3 mg, 89%), colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 6.23 (brs, 1H), 5.43 (q, *J* = 6.8 Hz, 1H), 4.84 (m, 2H), 3.21 (m, 2H), 1.12 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.47, 155.43, 139.75, 128.41, 128.06, 126.79, 92.06, 77.64, 73.72, 35.91, 15.17; HRMS (TOF) *m*/*z* (ES$^+$) calcd for $C_{13}H_{15}NNaO_2$ ([M + Na]$^+$) 240.0995, found 240.1000.

*Hepta-1,2-dien-4-yl benzoate (**3e**).*[7] (386.3 mg, 89%), colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08−8.05 (m, 2H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.44 (dd, *J* = 7.8 Hz, 2H), 5.55 (m, 1H), 5.40 (q, *J* = 6.6 Hz, 1H), 4.92−4.82 (m, 2H), 1.91−1.70 (m, 2H), 1.59−1.42 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5, 165.92, 132.8, 130.6, 129.6, 128.4, 91.1, 77.3, 72.1, 36.4, 18.6, 13.9.

*Hepta-1,2-dien-4-yl ethylcarbamate (**3f**).* (351.4 mg, 96%), colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.24 (m, 2H), 4.86 (m, 2H), 4.61 (brs, 1H), 3.23 (m, 2H), 1.64 (m, 2H), 1.38 (m, 2H), 1.14 (t, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125

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MHz, $CDCl_3$) δ 208.2, 155.9, 91.5, 76.8, 71.7, 36.5, 35.8, 18.5, 15.2, 13.8; HRMS (TOF) m/z (ES^+) calcd for $C_{10}H_{17}NNaO_2$ ($[M + Na]^+$) 206.1151, found 206.1154.

*Pentadeca-1,2-dien-4-yl benzoate (**3g**).* (577.4 mg, 88%), colorless liquid: ^{1}HNMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.6 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 8.0 Hz, 2H), 5.49 (q, J = 7.6 Hz, 1H), 5.32 (q, J = 6.4 Hz, 1H), 4.86 (m, 2H), 1.79 (m, 2H), 1.34 (m, 18H), 0.87 (t, J = 6.4 Hz, 3H); ^{13}CNMR (125 MHz, $CDCl_3$) δ 208.5, 165.9, 132.8, 130.6, 129.6, 128.3, 90.9, 77.3, 72.4, 34.3, 31.9, 29.6, 29.6, 29.6, 29.5, 29.4, 25.3, 22.6, 22.6, 14.1; HRMS (TOF) m/z (ES^+) calcd for $C_{22}H_{32}NaO_2^+$ ($[M + Na]^+$) 351.2295, found 351.2294.

*Tetradeca-5,6-dien-4-yl benzoate (**3h**).* (609.2 mg, 97%), yellow liquid: ^{1}HNMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.41 (t, J = 6.4 Hz, 2H), 5.47 (m, 1H), 5.27 (m, 2H), 1.99 (m, 2H), 1.82 (m, 2H), 1.33 (m, 12H), 0.95 (t, J = 7.2 Hz, 3H), 0.86 (m, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 203.99 (203.92), 165.9, 132.7 (132.6), 130.74 (130.72), 129.5, 128.3 (128.2), 93.8 (93.7), 91.6 (91.5), 72.8 (72.5), 36.5 (36.4), 31.8 (31.7), 29.1 (29.0), 29.07 (29.04), 29.0, 28.9 (28.5), 22.6 (22.5), 18.6, 14.1, 13.9 (13.8); HRMS (TOF) m/z (ES^+) calcd for $C_{21}H_{30}NaO_2^+$ ($[M + Na]^+$) 337.2138, found 337.2140.

*2-Methyl-1-phenylbuta-2,3-dien-1-yl benzoate (**3i**).* (477.8 mg, 81%), colorless liquid: ^{1}HNMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.44 (m, 4H), 7.38 (t, J = 7.8 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 6.46 (s, 1H), 4.84 (m, 2H), 1.73 (t, J = 3.2 Hz, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 206.6, 165.4, 138.6, 133.1, 130.3, 129.7, 128.4, 128.1, 126.9, 99.2, 76.7, 76.5, 14.9; HRMS (TOF) m/z (ES^+) calcd for $C_{18}H_{16}NaO_2^+$ ($[M + Na]^+$) 287.1043, found 287.1050.

*2-Methyl-1-phenylbuta-2,3-dien-1-yl acetate (**3j**).*[14] (354.4 mg, 86%), colorless liquid: ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.35 (m, 5H), 6.18 (s, 1H), 4.79 (s, 2H), 2.12 (s, 3H), 1.62 (t, J = 3.2 Hz, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 206.4, 169.9, 138.4, 128.5, 128.3, 127.4, 99.1, 76.7, 76.0, 21.1, 14.8; HRMS (TOF) m/z (ES^+) calcd for $C_{13}H_{14}NaO_2^+$ ($[M + Na]^+$) 225.0886, found 225.0890.

Isomerization of Allenyl Carbinol Esters (3) by Gold Complex (4). Allenyl carbinol esters (**3**) (0.25 mmol) and gold complex (**4**) (2.40 mg, 1 mol %) were dissolved in $CDCl_3$ (1 mL), stirred at room temperature, and monitored by ^{1}H NMR until no progress. All allenyl carbinol esters (**3a**−**3j**) efficiently isomerized into dienes (**2**), and NMR yield was at least 95%.

Fluorination of Dienes (2) with Selectfluor. $CDCl_3$ of the above reaction was carefully dried by rotary evaporator, and Selectfluor (106 mg, 0.3 mmol) and acetonitrile (1.5 mL) were added into the diene mixture (**2**) and stirred at room temperature for 3 h.

As for **1a**, the reaction mixture was subjected to short silica gel chromatography separation, which was eluted by gradient elution of hexanes and ethyl acetate.

As for **1e**, α,α,α-trifluorotoluene (0.1 mmoL) and 0.5 mL of CD_3CN were added into reaction mixture for ^{19}F NMR.

As for **1g**, **1h** and **1i**, the reaction mixture was filtered through silica gel (10 g), and washed by mixture of hexanes and ethyl acetate (4:1, 70 mL). Then, the solution was concentrated, and the remaining residue was dissolved in 2−3 mL of methanol. $CeCl_3{\cdot}7H_2O$ (186 mg, 0.4 mmol) was added into the methanol solution, the solution was placed at 0 °C (ice bath), and $NaBH_4$ (15 mg, 0.4 mmol) was added over 15 min. The reaction was stirred for another 20 min at room temperature. Then, the mixture was directly subjected to silica gel column separation eluted by hexane and ethyl acetate system.

*(E)-1-Fluoro-4-phenylbut-3-en-2-one (**1a**).*[2h] (37.0 mg, 90% for entry 1), amorphous solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 16.5 Hz, 1H), 7.61 (m, 2H), 7.44 (m, 3H), 7.03 (dt, J = 16.0, 2.0 Hz, 1H), 5.05 (dd, J = 47.5, 1.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.8 (d, J = 18.3 Hz), 145.1 (d, J = 3.1 Hz), 134.1, 131.2, 129.1, 128.7, 119.8, 84.8 (J = 184.1 Hz); ^{19}F NMR (470 MHz) δ −228.68 (dt, J = 47.5, 2.4 Hz); FTIR/cm^{-1} 3029, 2927, 1709, 1689, 1607, 1576, 1495, 1450, 1333, 1202, 1167, 1036, 998, 977, 748, 688.

*(E)-1-Fluorohept-3-en-2-one (**1e**).* (^{19}F NMR yield 95% for entry 5). NMR spectra was performed on mixture of **1e** and ethyl acetate: ^{1}H NMR (500 MHz, $CDCl_3$) (significant peaks) δ 7.05 (dt, J = 16.0, 6.6 Hz, 1H), 6.37 (d, J = 16.0 Hz, 1H), 4.97 (d, J = 47.5 Hz, 2H), 2.26 (m, 2H); ^{19}F NMR (470 MHz) δ −229.53 (t, J = 47.9 Hz).

*(E)-1-Fluoropentadec-3-en-2-ol, derived from (**1g**).* (50.6 mg, 83%), colorless liquid. Contains less than 3% saturated alcohol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (dt, J = 15.2, 8.0 Hz, 1H), 5.41 (dd, J = 15.6, 6.4 Hz, 1H), 4.45 (m, 0.5H), 4.34 (m, 2H), 4.20 (m, 0.5H), 2.04 (q, J = 6.8 Hz,1H), 1.25−1.39 (m, 18H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5 (d, J = 1.5 Hz), 125.8 (d, J = 8.5 Hz), 86.4 (d, J = 171.2 Hz), 71.5 (d, J = 19.4 Hz), 32.3, 31.9, 29.6, 29.6, 29.6, 29.4, 29.3, 29.1, 28.9, 22.7, 14.1; ^{19}F NMR (376 MHz) δ −225.54 (dt, J = 48.1, 17.7 Hz); FTIR (ATR)/cm^{-1} 3420, 2924, 2854, 1466, 1012; HRMS (TOF) m/z (ES^+) calcd for $C_{15}H_{29}FNaO$ ($[M + Na]^+$) 267.2095, found 267.2095.

*(E)-7-Fluorotetradec-4-en-6-ol (dr = 4:1), derived from (**1h**).* (41.4 mg, 72%), colorless liquid, containing less than 3% saturated alcohol. Major diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (dt, J = 15.2, 7.2 Hz, 1H), 5.42 (dd, J = 15.6, 7.6 Hz, 1H), 4.37 (m, 0.5H), 4.23 (m, 0.5H), 4.05 (m, 1H), 2.04 (m, 2H), 1.26−1.62 (m, 14H), 0.87 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 127.3 (d, J = 7.0 Hz), 96.6 (d, J = 171.1 Hz), 74.7 (d, J = 20.9 Hz), 34.4, 31.7, 30.9, 29.3, 29.1, 24.9, 22.6, 22.1, 14.0, 13.6; ^{19}F NMR (376 MHz) δ −192.30 (m); FTIR (ATR)/cm^{-1} 3427, 2926, 2857, 1464, 970; HRMS (TOF) m/z (ES^+) calcd for $C_{14}H_{27}FNaO$ ($[M + Na]^+$) 253.1938, found 253.1940.

*(E)-1-Fluoro-3-methyl-4-phenylbut-3-en-2-ol, derived from (**1i**).* (35.6 mg, 79% for entry 9), colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (m, 2H), 7.27 (m, 3H), 6.67 (s, 1H), 4.61 (dd, J = 9.0, 2.5 Hz, 0.5H), 4.51 (m, 2H), 4.39 (t, J = 7.5 Hz, 0.5H), 1.92 (d, J = 1.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9, 134.7 (d, J = 7.0 Hz), 128.9, 128.2, 127.7 (d, J = 1.6 Hz), 126.8, 85.7 (d, J = 172.2 Hz), 75.8 (d, J = 19.4 Hz), 14.6; ^{19}F NMR (470 MHz) δ −225.33 (dt, J = 47.5, 17.4 Hz); FTIR (ATR)/cm^{-1} 3397, 2977, 1723, 1448, 1055, 903, 751, 698; HRMS (TOF) m/z (ES^+) calcd for $C_{11}H_{13}FNaO$ ($[M + Na]^+$) 203.0843, found 203.0841. Stereochemistry was determined by ROSEY spectra.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C NMR, and IR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(9) We chose two steps in a one-pot reaction, because the gold-catalyzed isomerization is not effective in CD_3CN and Selectfluor has low solubility in $CDCl_3$. Diene **2a**, isolated from reaction mixture, can react efficiently with Selectfluor to give similar results.

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