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Citation	Journal of Fluorine Chemistry, 142, 105-108 <a href="https://doi.org/10.1016/j.jfluchem.2012.07.001">https://doi.org/10.1016/j.jfluchem.2012.07.001</a>
Issue Date	2012-10
Doc URL	<a href="http://hdl.handle.net/2115/50357">http://hdl.handle.net/2115/50357</a>
Type	article (author version)
File Information	JFC142_105-108.pdf



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# *E*- or *Z*-Selective Synthesis of Trisubstituted (2-Fluoroalkenyl)iodonium Salts by the Reaction of (2-Fluoroalkenyl)iodonium Ylides with Aldehydes

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**Keywords:** (fluoroalkenyl)iodonium ylides, trisubstituted (2-fluoroalkenyl)iodonium salts, stereoselective synthesis

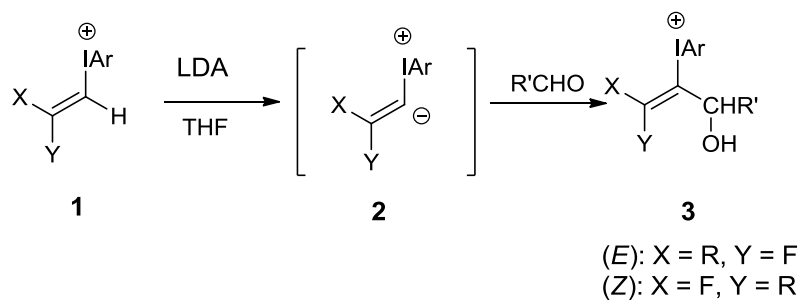
## **Abstract**

Trisubstituted (2-fluoroalkenyl)iodonium salts were prepared *E*- or *Z*-selectively by the reaction of (fluoroalkenyl)iodonium ylides generated from (fluoroalkenyl)iodonium salts with aldehydes.

## **1. Introduction**

Alkenyliodonium salts have been used as a versatile reagent in organic synthesis and many methods have been reported for their synthesis [1]. However, the stereoselective synthesis of acyclic alkenyliodonium salts having a substituent on the same carbon as the iodine is difficult and only few precedent works have been reported for their synthesis [2]. Recently, Ochiai *et al.* succeeded in preparing the (*E*)-isomer of trisubstituted (fluoroalkenyl)iodonium salts stereoselectively by the addition of iodotoluene difluoride to the unsymmetrical internal alkynes [3]. However, their method can't be applied to the synthesis of the corresponding

(*Z*)-isomers. Recently, we succeeded in the stereoselective synthesis of (fluoroalkenyl)boranes by using the unstable (2-fluoroalkenyl)iodonium ylides **2** generated from (2-fluoroalkenyl)iodonium salts **1** by the treatment with LDA [4]. As both (*E*)- and (*Z*)-(2-fluoroalkenyl)iodonium salts can be prepared stereoselectively, the methodology using **2** is considerably promising [5]. We report here the *E*- or *Z*-selective synthesis of trisubstituted (fluoroalkenyl)iodonium salts **3** by the reaction of **2** with aldehydes (**Scheme 1**).

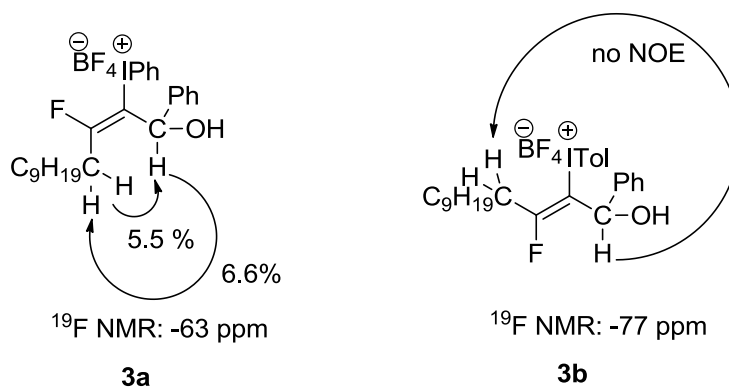


**Scheme 1.** The reaction of (2-fluoroalkenyl)iodonium ylide **2** with aldehyde

## 2. Results and discussion

When a THF solution of (*Z*)-(2-fluoro-1-dodecyl)(phenyl)iodonium salt **1a** [6] was treated with LDA in the presence of benzaldehyde at -78°C, a viscous liquid was obtained after a work-up procedure. The <sup>1</sup>H NMR spectra of the viscous liquid showed no vinylic proton, and the <sup>19</sup>F NMR spectra showed a singlet peak at -63 ppm. In NOE studies, 5.5%-6.6% interaction was observed between allylic protons and a benzylic proton. From these observations, the product was determined to be (*Z*)-(3-fluoro-1-hydroxy-1-phenyltridec-2-en-2-yl)(phenyl)iodonium salt **3a**. On the other hand, when the (*E*)-isomer of (2-fluoro-1-alkenyl)iodonium salt **1b** [7] was used

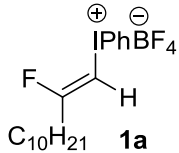
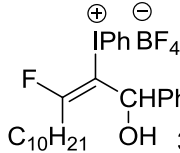
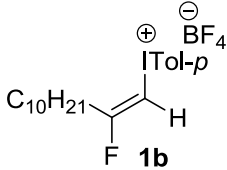
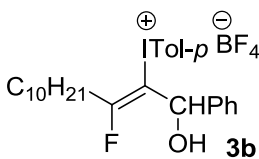
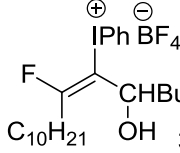
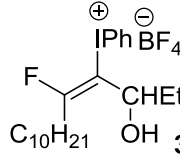
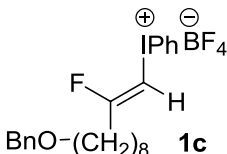
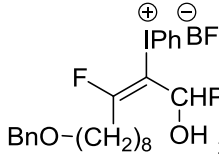
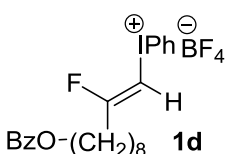
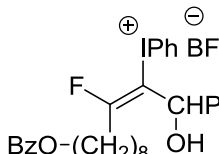
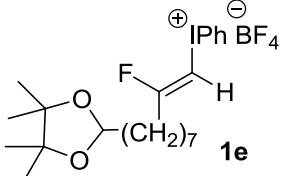
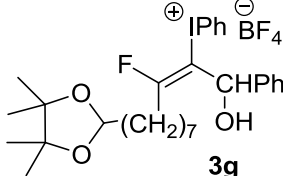
in the reaction with benzaldehyde, a product different from **3a** was obtained. In the  $^{19}\text{F}$  NMR spectra of this product, a singlet peak appeared at -77 ppm, and in NOE studies, no interaction was observed between allylic protons and a benzylic proton. From these observations, the product obtained from **1b** was determined to be (*E*)-(3-fluoro-1-hydroxy-1-phenyltridec-2-en-2-yl)(tolyl)iodonium salt **3b** (Scheme 2). Therefore, the generated ylides **2a** and **2b** reacted with benzaldehyde to give (*E*)- and (*Z*)-trisubstituted (fluoroalkenyl)iodonium salts **3a** and **3b**, respectively, without losing their original stereochemistry.



**Scheme 2.** NOE study of (*Z*)- and (*E*)-trisubstituted (fluoroalkenyl)iodonium salts **3a** and **3b**

Both aromatic and aliphatic aldehydes can be used in the reaction, and various hydroxyalkyl groups can be introduced to the vinylic carbon of the (fluoroalkenyl)iodonium salts. Furthermore, multi-functionalized trisubstituted (fluoroalkenyl)iodonium salts (**3e-g**) can be prepared by using functionalized (fluoroalkenyl)iodonium salts (**1c-e**) as the starting material (Entries 5-7, Table 1).

**Table 1**Reaction of (2-fluoroalkenyl)iodonium ylides **2** with aldehydes

Entry	Iodonium salt <b>1</b>	Aldehyde	Product	Yield (%) <sup>a</sup>
1	 C <sub>10</sub> H <sub>21</sub> <b>1a</b>	PhCHO	 C <sub>10</sub> H <sub>21</sub> <b>3a</b>	85
2	 C <sub>10</sub> H <sub>21</sub> <b>1b</b>	PhCHO	 C <sub>10</sub> H <sub>21</sub> <b>3b</b>	(68)
3	<b>1a</b>	<sup>t</sup> BuCHO	 C <sub>10</sub> H <sub>21</sub> <b>3c</b>	70
4	<b>1a</b>	EtCHO	 C <sub>10</sub> H <sub>21</sub> <b>3d</b>	79
5	 BnO-(CH <sub>2</sub> ) <sub>8</sub> <b>1c</b>	PhCHO	 BnO-(CH <sub>2</sub> ) <sub>8</sub> <b>3e</b>	75
6	 BzO-(CH <sub>2</sub> ) <sub>8</sub> <b>1d</b>	PhCHO	 BzO-(CH <sub>2</sub> ) <sub>8</sub> <b>3f</b>	83
7	 <b>1e</b>	PhCHO	 <b>3g</b>	(52)

<sup>a</sup>Isolated yield based on **1** used. In parentheses, <sup>19</sup>F NMR yield.

### 3. Conclusion

The (2-fluoroalkenyl)iodonium ylide generated from 2-(fluoroalkenyl)iodonium salt was shown to be used for the synthesis of the trisubstituted (2-fluoroalkenyl)iodonium salt by the reaction with aldehyde. It was also shown that the reaction proceeds stereoselectively and from (*E*)- and (*Z*)-(2-fluoroalkenyl)iodonium salts, the corresponding (*E*)- and (*Z*)-trisubstituted (fluoroalkenyl)iodonium salts were formed without loss of the original stereochemistry. Introduction of functional group to the product was also performed.

### 4. Experimental

#### 4.1. General

The IR spectra were recorded using a JASCO FT/IR-410. The  $^1\text{H}$  NMR (400 MHz) spectra,  $^{19}\text{F}$  NMR (376 MHz) spectra, and  $^{13}\text{C}$  NMR (100 MHz) were recorded in  $\text{CDCl}_3$  on a JEOL JNM-A400II FT NMR and the chemical shift,  $\delta$ , is referred to TMS ( $^1\text{H}$ ,  $^{13}\text{C}$ ) and  $\text{CFCl}_3$  ( $^{19}\text{F}$ ), respectively. The EI-high-resolution mass spectra were measured on a JEOL JMS-700TZ. *p*-Iodotoluene difluoride was prepared according to the literature [8]. 1-Alkynyliodonium salts were prepared from 1-alkyne according to the literature [9]. (*Z*)-(2-Fluoro-1-alkenyl)iodonium salts (**1a**, **1c-f**) were prepared from 1-alkynyliodonium salts according to the literature [6]. (*E*)-(2-Fluoro-1-dodecyl)iodonium salt (**1b**) was prepared from 1-dodecyne and *p*-iodotoluene difluoride according to the literature [7].

#### 4.2. General procedure for the reaction of **2** with aldehydes

To a THF solution (6 mL) of (2-fluoroalkenyl)iodonium salt **1** (0.5 mmol) and an aldehyde (0.7 mmol) was added a cooled THF solution (2 mL) of LDA (0.7 mmol) at -78 °C (for (*Z*)-isomer) or at -90°C (for (*E*)-isomer), and the mixture was stirred at -60 °C for 1.5h. After the addition of a 42% aqueous HBF<sub>4</sub> (2 mL), the cooling bath was removed and the mixture was stirred at room temperature for 1h. Then, the product was extracted with ether (10 mL X 3) and the combined organic layer was dried over MgSO<sub>4</sub>. After concentration under reduced pressure, the remained viscous liquid was washed with hexane. An upper hexane layer was removed by decantation (this operation was repeated twice). A volatile part was removed under high vacuum to give the (fluoroalkenyl)iodonium salt **3**.

4.2.1. (*Z*)-(3-Fluoro-1-hydroxy-1-phenyl-2-tridecen-2-yl)(phenyl)iodonium tetrafluoroborate (**3a**)

Viscous liquid. IR (neat): 3484, 2925, 1656, 1060 cm<sup>-1</sup>. <sup>1</sup>H NMR δ 0.88 (3H, t, *J* = 7.2 Hz), 1.15-1.40 (14H, m), 1.50-1.80 (2H, m), 2.75-2.89 (2H, dt, *J* = 23.6, 7.8 Hz), 5.67 (1H, d, *J* = 3.3 Hz), 5.30-6.00 (1H, brs), 7.10-7.49 (10H, m). <sup>13</sup>C NMR δ 13.9, 22.5, 26.0, 28.9, 28.9, 29.1, 29.2, 29.3, 30.0 (d, <sup>2</sup>*J*<sub>C-F</sub> = 24.8 Hz), 31.7, 69.2 (d <sup>3</sup>*J*<sub>C-F</sub> = 3.5 Hz), 109.9, 112.2 (d, <sup>2</sup>*J*<sub>C-F</sub> = 19.7 Hz) 125.6 (2C), 128.6, 128.8 (2C), 131.6 (2C), 132.3, 135.3 (2C), 138.6 (d, <sup>4</sup>*J*<sub>C-F</sub> = 2.4 Hz), 168.1 (d, <sup>1</sup>*J*<sub>C-F</sub> = 275.6 Hz). <sup>19</sup>F NMR δ -63.28 (1F, t, *J* = 22.9 Hz) -147.79 (s, 4F). HRMS (FAB, M<sup>+</sup>-BF<sub>4</sub>) calcd for C<sub>25</sub>H<sub>33</sub>FOI 495.1560, found 495.1540

4.2.2. (*E*)-(3-Fluoro-1-hydroxy-1-phenyl-2-tridecen-2-yl)(*p*-tolyl)iodonium tetrafluoroborate (**3b**)

Viscous liquid. IR (neat) 3480, 2925, 1651, 1059 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.88 (3H, t, *J* = 6.9 Hz), 1.00-1.65 (16H, m), 2.29 (3H, s), 2.85-3.00 (2H, m), 4.60-4.90 (1H, s), 6.00

(1H, s), 6.90-7.50 (9H, m).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  14.0, 21.1, 22.6, 25.8, 28.9, 29.19, 29.2, 29.3, 29.4, 31.8, 33.9 ( $d^2J_{\text{C-F}} = 24.4$  Hz), 67.2 ( $d^3J_{\text{C-F}} = 6.2$  Hz), 106.5, 117.0 ( $d^2J_{\text{C-F}} = 33.9$  Hz), 125.7 (2C), 128.3, 128.9 (2C), 132.5 (2C), 134.9 (2C), 139.0, 143.4, 169.5 ( $d^1J_{\text{C-F}} = 281.1$  Hz).  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -77.68 (1F, q,  $J = 18.0$  Hz), -147.05 (4F). HRMS (FAB,  $\text{M}^+ - \text{BF}_4$ ) calcd for  $\text{C}_{26}\text{H}_{35}\text{FOI}$  509.1717, found 509.1711.

4.2.3. (Z)-(5-Fluoro-3-hydroxy-2,2-dimethyl-4-pentadecen-4-yl)(phenyl)iodonium tetrafluoroborate (**3c**)

Viscous liquid. IR (neat) 3501, 2926, 1648, 1468, 1062  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR  $\delta$  0.87 (3H, t,  $J = 7.0$  Hz), 0.97 (9H, s), 1.20-1.70 (16H, m), 2.40-2.80 (2H, m), 4.17 (1H, s), 5.00-5.40 (1H, m), 7.40-8.00 (5H, m).  $^{13}\text{C}$  NMR  $\delta$  14.0, 22.6, 25.4 (3C), 26.0, 29.0 (2C), 29.2 (2C), 29.4, 31.0, 31.1 ( $d^2J_{\text{C-F}} = 24.8$  Hz), 31.8, 74.1, 108.1 ( $d^2J_{\text{C-F}} = 19.8$  Hz), 110.8, 132.3 (2c), 132.7, 135.2 (2C), 168.5 ( $d^1J_{\text{C-F}} = 275.7$  Hz).  $^{19}\text{F}$  NMR  $\delta$  -60.08 (1F, s), -148.31 (4F, s). HRMS (FAB,  $\text{M}^+ - \text{BF}_4$ ) calcd for  $\text{C}_{23}\text{H}_{37}\text{FOI}$  475.1873, found 475.1862.

4.2.4. (Z)-(5-Fluoro-3-hydroxy-4-pentadecen-4-yl)(phenyl)iodonium tetrafluoroborate (**3d**)

Viscous liquid. IR (neat) 3502, 2926, 1654, 1468, 1066  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR  $\delta$  0.77 (3H, t,  $J = 7.5$  Hz), 0.87 (3H, t,  $J = 7.2$  Hz), 1.20-1.90 (18H, m), 2.50-2.80 (2H, m), 4.22-4.28 (1H, m), 4.85 (1H, brs), 7.40-8.05 (5H, m).  $^{13}\text{C}$  NMR  $\delta$  9.5, 14.0, 22.6, 26.0, 28.9, 29.0, 29.2, 29.3, 29.4, 29.9, 30.4 ( $d^2J_{\text{C-F}} = 25.6$  Hz), 31.8, 70.7 ( $d^3J_{\text{C-F}} = 2.4$  Hz), 110.0, 111.2 ( $d^2J_{\text{C-F}} = 17.2$  Hz), 132.3 (2C), 132.7, 135.8 (2C), 168.3 ( $d^1J_{\text{C-F}} = 275.9$  Hz).  $^{19}\text{F}$  NMR  $\delta$  -61.41 (1F, t,  $J = 26.3$  Hz) -147.45 (4F, s). HRMS (FAB,  $\text{M}^+ - \text{BF}_4$ ) calcd for  $\text{C}_{21}\text{H}_{33}\text{FOI}$  447.1560, found 447.1588.

4.2.5. (Z)-(11-Benzyloxy-3-fluoro-1-hydroxy-1-phenyl-2-undecen-2-yl)(phenyl)iodonium tetrafluoroborate (**3e**)



Viscous liquid. IR (neat) 3482, 2932, 1541, 1060  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR  $\delta$  1.20-1.80 (12H, m), 2.75-2.95 (2H, m), 3.44 (2H, t,  $J = 6.8$  Hz), 4.47 (2H, s), 4.75-5.00 (1H, brs), 5.63 (1H, d,  $J = 3.4$  Hz), 7.05-7.50 (15H, m).  $^{13}\text{C}$  NMR  $\delta$  25.8, 25.9, 28.8 (2C), 29.0, 29.5, 30.0 (d,  $^2J_{\text{C-F}} = 25.1$  Hz), 69.1 (d,  $^3J_{\text{C-F}} = 3.6$  Hz), 70.3, 72.6, 110.0, 112.5 (d,  $^2J_{\text{C-F}} = 20.1$  Hz), 125.6 (2C), 127.4, 127.5 (2C), 128.2 (2C), 128.5, 128.7 (2C), 131.6 (2C), 132.2, 135.3 (2C), 138.4, 138.7 (d,  $^4J_{\text{C-F}} = 1.92$  Hz), 167.9 (d,  $^1J_{\text{C-F}} = 277.8$  Hz).  $^{19}\text{F}$  NMR  $\delta$  -63.69 (1F, t,  $J = 24.4$  Hz), -148.07 (4F, s). HRMS (FAB,  $\text{M}^+ - \text{BF}_4$ ) calcd for  $\text{C}_{30}\text{H}_{35}\text{FO}_2\text{I}$  573.1660, found 573.1644.

#### 4.2.6.

*(Z)-(11-Benzoyloxy-3-fluoro-1-hydroxy-1-phenyl-2-undecen-2-yl)(phenyl)iodonium tetrafluoroborate (3f)*

Viscous liquid. IR (neat) 3478, 2934, 1714, 1284,  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR  $\delta$  1.05-1.85 (12H, m), 2.70-3.00 (2H, m), 4.27 (2H, t,  $J = 6.6$  Hz), 5.69 (1H, s), 7.05-8.50 (15H, m).  $^{13}\text{C}$  NMR  $\delta$  25.6, 25.9, 28.4, 28.7 (2C), 28.8, 30.0 (d,  $^2J_{\text{C-F}} = 25.4$  Hz), 65.0, 69.2 (d,  $^3J_{\text{C-F}} = 3.4$  Hz), 109.9, 112.5 (d,  $^2J_{\text{C-F}} = 20.1$  Hz), 125.7 (2C), 128.2 (2C), 128.6, 128.8 (2C), 129.4 (2C), 130.1, 131.6 (2C), 132.3, 132.9, 135.4 (2C), 138.6, 166.8, 168.0 (d,  $^1J_{\text{C-F}} = 277.8$  Hz).  $^{19}\text{F}$  NMR  $\delta$  -63.55 (1F, t,  $J = 22.9$  Hz), -148.17 (4F). HRMS (FAB,  $\text{M}^+ - \text{BF}_4$ ) calcd for  $\text{C}_{30}\text{H}_{33}\text{FO}_3\text{I}$  587.1453, found 587.1454.

4.2.7. *(Z)-{3-Fluoro-1-hydroxy-1-phenyl-10-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)dec-2-en-2-yl}(phenyl)iodonium tetrafluoroborate (3g)*

Viscous liquid. IR (neat) 3480, 2979, 1651  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR  $\delta$  1.19 (12H, s), 1.26-1.73 (12H, m), 2.72-2.97 (2H, m), 5.02 (1H, t,  $J = 5.1$  Hz), 5.67 (1H, s), 7.17-7.47 (10H, m).  $^{13}\text{C}$  NMR  $\delta$  21.7 (2C), 23.9 (2C), 24.0, 25.9, 28.6, 28.8, 29.0, 30.0 (d,  $^2J_{\text{C-F}} = 25.0$  Hz), 36.0, 69.1 (d,  $^3J_{\text{C-F}} = 3.1$  Hz), 81.7 (2C), 100.6, 110.0, 112.5 (d,  $^2J_{\text{C-F}} = 19.3$  Hz), 125.63

(2C), 128.5, 128.8 (2C), 131.6 (2C), 132.3, 135.3 (2C), 138.6, 167.9 (d,  $^1J_{C-F}$  = 276.1 Hz).  $^{19}\text{F}$  NMR  $\delta$  -63.56 (1F, t,  $J$  = 22.8 Hz), -148.3 (4F, s). HRMS (FAB,  $\text{M}^+$ -BF<sub>4</sub>) calcd for C<sub>29</sub>H<sub>39</sub>FO<sub>3</sub>I 581.1922, found 581.1931.

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