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# Stereoselective Synthesis of (*Z*)-2-Fluoro-1-alkenyl(phenyl)iodonium Tetrafluoroborates

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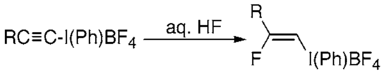
## ABSTRACT



**(*Z*)-2-Fluoro-1-alkenyl(phenyl)iodonium salts were stereoselectively prepared by the reaction of alkynyl(phenyl)iodonium salts with aqueous HF in good yields. The method is applicable to the synthesis of fluoroalkenyliodonium salts having functional groups such as ketone, ester, and chloride. (*Z*)-2-Fluoro-1-alkene, (*Z*)-2-fluoro-2-alkenoate, and (*Z*)-*β*-fluoroenyne could be stereoselectively prepared from the fluoroalkenyliodonium salt.**

Recently, palladium-catalyzed coupling reaction using fluorohaloalkenes[1] or fluoroalkenylmetals[2] has been used for the stereoselective synthesis of fluoroalkene derivatives that are of great interest as potent enzyme inhibitors.[3] (*E*)- or (*Z*)-1-Fluoro-1-alkenes and (*E*)-2-fluoro-1-alkenes have been stereoselectively prepared by the coupling reaction. However, the coupling reaction for (*Z*)-2-fluoro-1-alkene derivatives was still undeveloped, because an effective method for (*Z*)-2-fluoro-1-halo-1-alkenes or (*Z*)-2-fluoro-1-alkenyl metals was unknown. (*Z*)-2-Fluoro-1-alkenyliodonium salts (**2**) could be a precursor of various (*Z*)-2-fluoro-1-alkene derivatives; Ochiai et al. managed to synthesize **2** by the reaction of 1-alkynyliodonium salts **(1)** with CsF, but the yields were low (15−20%).[4] We wish to report here that **2** can be stereoselectively synthesized from the corresponding **1** in good yields and (*Z*)-2-fluoro-1-alkene derivatives can be prepared from **2**.

As it was reported that the reaction of metal fluorides with **1** was fruitless,[4] we examined the other fluoride sources such as $Et_3N-n$HF complexes and aqueous HF in the reaction with 1-dodecynyl(phenyl)iodonium tetrafluoroborate (**1a**) (Table 1).

An acidic complex, $Et_3N-5HF$,[5] was found not to be effective and **1a** remained unchanged after 24 h at room temperature (entry 1). On the other hand, $Et_3N-3HF$,[6] which affords a more nucleophilic fluoride, gradually reacted with **1a** at room temperature, and after 96 h the desired (*Z*)-2-fluoro-1-dodecenyliodonium salt (**2a**) was obtained in 71% yield (entry 2). With a more nucleophilic reagent, $Et_3N-2HF$,[7] the yield of **2a** decreased to 32% and further fluorination of **2a** took place to provide 1,2,2-trifluorododecane in 26% yield (entry 3). At 40 °C, the reaction of **1a**

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[4] (a) Ochiai, M.; Oshima, K.; Masaki, Y. *Chem. Lett*. **1994**, 871. (b) Ochiai, M.; Kitagawa, Y.; Toyonari, M.; Uemura, K.; Oshima, K.; Shiro, M. *J. Org. Chem*. **1997**, *62*, 8001.

[5] (a) Hayashi, E.; Hara, S.; Shirato, H.; Hatakeyama, T.; Fukuhara, T.; Yoneda, N. *Chem. Lett*. **1995**, 205. (b) Hara, S.; Kameoka, M.; Yoneda, N. *Synlett* **1996**, 529.

[6] Haufe, G. *J. Prakt. Chem*. **1996**, *338*, 99 and references therein.

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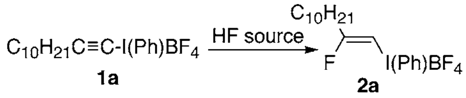
10.1021/ol027512y CCC: $25.00

**Table 1.** Reaction of 1-Dodecynyl(phenyl)iodonium Tetrafluoroborate **1a** with $Et_3N{-}n$HF or Aqueous HF



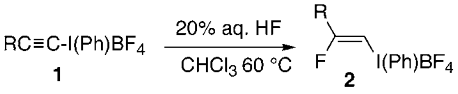
| entry | HF source | solvent | temp/°C | time/h | yield[a]/% |
|---|---|---|---|---|---|
| 1 | $Et_3N{-}5HF$ | $CH_2Cl_2$ | 20 | 24 | 0 |
| 2 | $Et_3N{-}3HF$ | $CH_2Cl_2$ | 20 | 96 | 71 |
| 3 | $Et_3N{-}2HF$ | $CH_2Cl_2$ | 20 | 44 | 32[b] |
| 4 | $Et_3N{-}3HF$ | $CH_2Cl_2$ | 40 | 12 | 71 |
| 5 | $Et_3N{-}3HF$ | $CHCl_3$ | 60 | 3 | 62 |
| 6 | 46% aq HF | $CHCl_3$ | 60 | 84 | 81 |
| 7 | 30% aq HF | $CHCl_3$ | 60 | 6 | 82 |
| 8 | 20% aq HF | $CHCl_3$ | 60 | 6 | 84 |
| 9 | 10% aq HF | $CHCl_3$ | 60 | 5 | 71 |

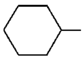
[a] Isolated yield based on **1a**. [b] 1,2,2-Trifluorododecane was also formed in 26% yield.

with $Et_3N{-}3HF$ completed in 12 h and **2a** could be obtained in 71% (entry 4). Aqueous HF was found to be more effective, and **1a** was converted to **2a** in 81% yield by the reaction with commercially available 46% aqueous HF at 60 °C for 84 h (entry 6). Finally, the best result was obtained by the reaction with 20% aqueous HF, and **2a** was obtained in 84% yield in 6 h (entry 8).[8]

The (*Z*)-stereochemistry of **2a** was determined from $^{1}$H NMR. A vinylic proton of **2a** appeared at 6.54 ppm as a doublet ($J_{H-F} = 33.18$ Hz), which was in good agreement with the reported data of (*Z*)-2-fluoroalkenyliodonium salt.[4]

**Table 2.** Synthesis of (*Z*)-2-Fluoro-1-alkenyl(phenyl)iodonium Tetrafluoroborate **2**

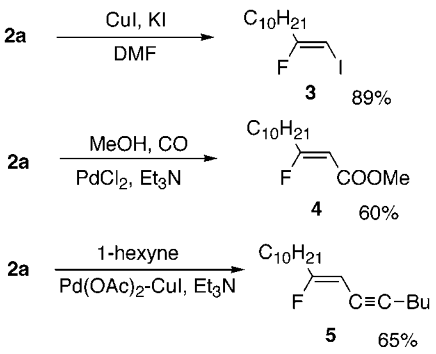


| entry | R | time/h | yield[a]/% |
|---|---|---|---|
| 1 | $C_{10}H_{21}$ (**1a**) | 6 | 84 |
| 2 | $^{t}Bu$ (**1b**) | 12 | 84 |
| 3 |  $-CH_2$ (**1c**) | 12 | 74 |
| 4 | $Cl\text{-}(CH_2)_9$ (**1d**) | 6 | 80 |
| 5 | $^{t}Bu\text{-}CO\text{-}(CH_2)_8$ (**1e**) | 6 | 72 |
| 6 | $^{i}PrOOC\text{-}(CH_2)_8$ (**1f**) | 6 | 76 |

[a] Isolated yield based on **1**.

Various (*Z*)-2-fluoro-1-alkenyliodonium salts **2** were prepared from the reaction of the corresponding alkynyliodonium salts **1**[9] with 20% aqueous HF (Table 2). Both (*Z*)-2-fluoro-1-alkenyliodonium salts having a sterically hindered alkyl group and those with a primary one could be prepared in good yield (entries 1 and 2). Furthermore, functional groups such as ketone, ester, and chloride on the substrate could tolerate the reaction conditions (entries 4−6). As expected, the (*Z*)-2-fluoro-1-alkene derivatives could be stereoselectively prepared from **2a** (Scheme 1). The conversion of **2a** to the corresponding iodide (**3**) was achieved by the treatment with CuI and KI.[4,10,11] Methyl (*Z*)-3-fluoro-2-undecenoate (**4**) was prepared in 60% yield by the reaction with CO and methanol in the presence of a Pd catalyst,[1c,9] and (*Z*)-1-(1-hexynyl)-2-fluoro-1-decene (**5**) was obtained in 65% yield by the Pd-catalyzed Sonogashira-type reaction with 1-hexyne.[1g]

**Scheme 1**



**Supporting Information Available:** Characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) **Representative Procedure for (*Z*)-2-Fluoro-1-alkenyl(phenyl)iodonium Salt (Table 1, entry 8).** 1-Dodecynyl(phenyl)iodonium tetrafluoroborate **1a** (228 mg, 0.5 mmol)[9] was dissolved in $CHCl_3$ (2 mL), and then 20% hydrofluoric acid (500 mg, 5 mmol) was added at room temperature. After vigorous stirring for 6 h at 60 °C, the reaction mixture was poured into a 5% aqueous solution of $NaBF_4$ (20 mL) and extracted with $CH_2Cl_2$ (10 mL) four times. The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was recrystallized from $CH_2Cl_2$−hexane and dried in vacuo to give pure (*Z*)-2-fluoro-1-dodecenyl(phenyl)iodonium tetrafluoroborate **2a** (84%, 200 mg, 0.42 mmol).

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