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Photochemical Oxyfluoroalkylation of Styrenes by the Addition of Perfluoroalkyl Radicals in an Atmosphere of Oxygen

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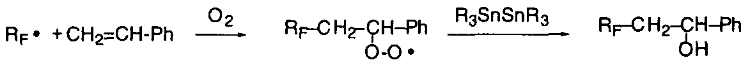
Absatract: The photochemical reaction of perfluoroalkyl iodide with α-methylstyrene and related compounds in the presence of hexabutylditin under oxygen atmosphere produces the fluoroalkylated alcohols in good yields. The reaction was photochemically initiated, and proceeded via a radical chain mediated by the ditin.

Keywords: oxyfluoroalkylation, fluoroalkyl radical, organofluorine compounds, hexabutylditin

Organofluorine compounds often show unique properties, and are widely used as medicines, pesticides, dyes or surfactants[1]. Especially, the substitution by a perfluoroalkyl group at particular positions of organic compounds may give rise to unique physical or biological properties which cannot be achieved by incorporating other functional groups. Free-radical chain addition of a perfluoroalkyl radical to olefins or acetylenes has long been known as an important and general methods for the introduction of perfluoroalkyl groups into carbon chains [2], and perfluoroalkyl iodides have been widely utilized as sources of perfluoroalkyl radicals [2, 3]. Recently, we found that a novel oxyfluoroalkylation of styrenes using fluoroalkyl iodides and molecular oxygen in the presence of organotin compounds produced fluoroalkylated peroxyl radicals which can be converted into the corresponding alcohols (Scheme 1). We now report here an efficient oxyfluoroalkylation of styrenes and related compounds under photochemical conditions.



$$R_F\bullet + CH_2{=}CH\text{-}Ph \xrightarrow{O_2} R_F\text{-}CH_2\text{-}\underset{O\text{-}O\bullet}{CH}\text{-}Ph \xrightarrow{R_3SnSnR_3} R_F\text{-}CH_2\text{-}\underset{OH}{CH}\text{-}Ph$$

Scheme 1

As shown in Scheme 2, a solution of $CF_3(CF_2)_5I$ (1 equiv.), styrene (3.0 equiv.), and 2.0 equiv. of $(Bu^n{}_3Sn)_2$ [4] in benzene was photoirradiated for 5 h under O_2 atmosphere using a metal halide lamp (>360 nm). The perfluoroalkyl iodide was completely consumed, and the alcohol **1** and the ketone **2** were obtained in 58% and 18% yields, respectively (Table 1, entry 1). The reaction of styrene with $CF_3(CF_2)_5I$ in the presence of $(Bu^n{}_3Sn)_2$ did not proceed without irradiation (entry 2), whereas a photochemical reaction occurred very slowly in the absence of $(Bu^n{}_3Sn)_2$ (entry 3). In addition, a similar reaction of styrene with $CF_3(CF_2)_5I$ in the presence of 1.1 equiv. of $(Bu^n{}_3Sn)_2$ produced **1** (32%) and **2** (8%), together with the recovered $CF_3(CF_2)_5I$ (49%) (entry 4).

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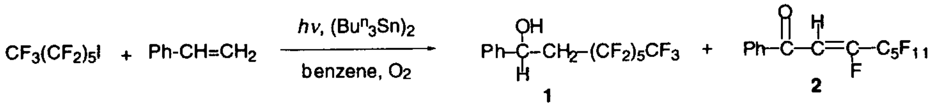
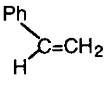
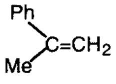
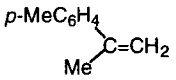
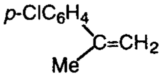
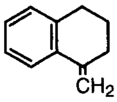


Scheme 2

Table 1. Photochemical oxygenative fluoroalkylation of styrenes[a)]

Entry	R_FI	Olefins	equiv. of $(Bu^n{}_3Sn)_2$	Products (Yield / %)[b)]
1	$CF_3(CF_2)_5I$		2.0	**1** (58); **2** (18)[c)]
2	$CF_3(CF_2)_5I$		2.0 (dark)	R_FI (~100)[d)]
3	$CF_3(CF_2)_5I$		0	R_FI (91)[d)]
4	$CF_3(CF_2)_5I$		1.1	**1** (32); **2** (8);[c)] R_FI (49)[d)]
5	$CF_3(CF_2)_3I$		2.2	**3a** (88)
6	$CF_3(CF_2)_5I$		2.0	**3b** (85)
7	$CF_3(CF_2)_9I$[e)]		2.0	**3c** (87)
8	$CF_3(CF_2)_3I$		2.2	**4a** (89)
9	$CF_3(CF_2)_5I$		2.0	**4b** (86)
10	$CF_3(CF_2)_9I$[e)]		2.0	**4c** (90)
11	$CF_3(CF_2)_3I$		2.2	**5a** (83)
12	$CF_3(CF_2)_5I$		2.0	**5b** (81)
13	$CF_3(CF_2)_9I$[e)]		2.0	**5c** (82)
14	$CF_3(CF_2)_3I$		2.0	**6a** (85)
15	$CF_3(CF_2)_5I$		2.0	**6b** (75)
16	$CF_3(CF_2)_9I$[e)]		2.0	**6c** (80)

a) Perfluoroalkyl iodides were completely consumed in 5 - 8 h except entry 2 - 4. The reaction mixtures were treated with Ph_3P in MeOH to ensure the conversion of the stannyl peroxides (**9** in Scheme 4) to the corresponding alcohol.

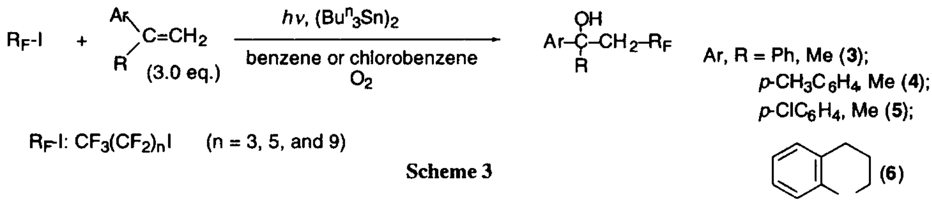
b)Yields were determined by ^{19}F-NMR using $PhCF_3$ as an internal standard.

c) The β-fluorine of **2** changed to OMe, when **2** was treated with MeOH.

d) Recovered $CF_3(CF_2)_5I$.

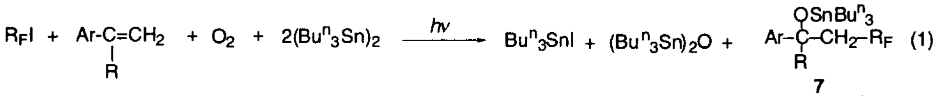
e) Chlorobenzene was used as a solvent for the low solvility of $CF_3(CF_2)_9I$ to benzene.

Taking into account the optimum conditions for the oxyfluoroalkylation of styrene, the photochemical reactions of fluoroalkyl iodides (1 equiv.) with α-methylstyrenes (3 equiv.) in the presence of $(Bu^n{}_3Sn)_2$ (2.0 - 2.2 equiv.) in benzene or chlorobenzene under O_2 atmosphere were carried out (Scheme 3) [5]. The results are summarized in Table 1 (entries 5 - 13). All photochemical reactions of α-methylstyrenes with fluoroalkyl iodides proceeded smoothly to produce the corresponding alcohols **3-5** in high yields. Interestingly, similar reactions of 5-methylenetetralin with fluoroalkyl iodides in the presence of $(Bu^n{}_3Sn)_2$ under O_2 atmosphere afforded the oxyfluoroalkylation products **6a-c** in good yields (entries 14 - 16). This is the first example of the simultaneous introduction of perfluoroalklyl and hydroxyl groups into styrenes using a perfluoroalkyl radical and molecular oxygen.

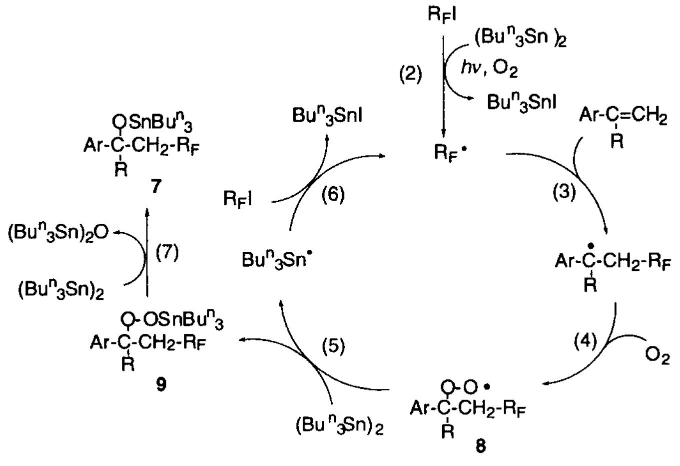


Scheme 3

The reaction mechanism of the oxyfluoroalkylation of styrenes is summarized in Scheme 4, and the overall reaction can be demonstrated in eq. 1. A radical chain reaction initiated by the photoirradiation is proposed for the formation of the alcoholates **7**. Since the reaction did not proceed in the absence of hexabutylditin, the radical chain reaction should be mediated by the ditin. Free-radical chain iodoperfluoroalkylation of olefins is known [2, 3]. However, in the reaction with styrene and α-methylstyrene, the benzyl and cumyl-type radicals produced by the addition of a perfluoroalkyl radical were too stable for the iodine abstraction from R_FI. Thus, the cumyl-type radical reacts with oxygen to give **8** (eqs. 3 and 4) [6], which can be converted to the alcoholate **7** via the stannyl peroxide **9** (eqs. 5 and 7). By the reaction of the peroxyl radical **8** with hexabutylditin, a tributyltin radical is produced (eq. 5) [7], and used again for the formation of a perfluoroalkyl radical to propagate the radical chain (eq. 6) [8]. The stannyl peroxide **9** is reduced to alcoholate **7** with $(Bu^n{}_3Sn)_2$ (eq. 7). Therefore, two equivalents of the ditin to R_FI are required in this reaction. As the reaction of the perfluoroalkyl radical with olefins is known to proceed very fast [9], it may react with styrenes much faster than with molecular oxygen [10]. Thus, this radical chain reaction gives the alcohol selectively.



$$R_FI + \text{Ar-}\underset{R}{C}\text{=}CH_2 + O_2 + 2(Bu^n{}_3Sn)_2 \xrightarrow{hv} Bu^n{}_3SnI + (Bu^n{}_3Sn)_2O + \underset{\mathbf{7}}{\text{Ar-}\overset{OSnBu^n{}_3}{\underset{R}{C}}\text{-}CH_2\text{-}R_F} \quad (1)$$



Scheme 4

Tributyltin hydride ($Bu^n{}_3SnH$) was examined instead of $(Bu^n{}_3Sn)_2$ as a radical chain mediator for the oxyfluoroalkylation; in the reaction of styrene with $CF_3(CF_2)_5I$ under similar conditions, a reduction product ($CF_3(CF_2)_5H$) was produced in 56% yield together with the alcohol **1** (22%). This is due to the competitive reactions between hydrogen abstraction from the hydride and the addition to styrene by the perfluoroalkyl radical. On the other hand, the perfluoroalkyl radical reacted with styrene selectively without the reaction with $(Bu^n{}_3Sn)_2$. Thus, the photochemical reaction using perfluoroalkyl iodide in combination with $(Bu^n{}_3Sn)_2$ under oxygen atmosphere affords a novel and efficient method for oxyfluoroalkylation.

References and Notes

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[5] Typical Procedure: A solution of perfluorobutyl iodide (280 mg, 0.6 mmol), α-methylstyrene (220 mg, 1.8 mmol), and $(Bu_3Sn)_2$ (770 mg, 1.2 mmol) in 5 ml benzene was irradiated using a metal halide lamp (National Sky-beam MT-70) in Pyrex tube under O_2 atmosphere until the iodide was completely consumed as determined by ^{19}F-NMR (5 h). The reaction mixture was treated with Ph_3P (80 mg, 0.3 mmol) in MeOH (1 ml) at room temperature for 30 min to ensure the conversion of the small amount of the remaining stannyl peroxide (**9** in Scheme 4) to the corresponding alcohol, and the yield of the alcohol was determined by ^{19}F-NMR using $PhCF_3$ as an internal standard. The alcohol was isolated in 61% yield using silica gel column chromatography (eluted with hexane / benzene = 3 / 1), followed by gel permeation chromatography to remove the tin compounds completely (JAI model LC-908 liquid chromatography equipped with JAIGEL-1H-20 and 2H-20 columns eluted by $CHCl_3$), and characterized by ^{1}H, ^{13}C, and ^{19}F-NMR, IR and MS; Colorless oil; ^{1}H-NMR(500.0 MHz : $CDCl_3$) δ 1.77 (s, 3H), 2.25 (s, 1H), 2.51-2.72 (m, 2H), 7.30 (m, 1H), 7.34 (m, 2H), 7.49 (m, 2H) ; ^{13}C-NMR(125.7 MHz : $CDCl_3$) δ30.21, 42.53 (t), 72.82, 124.31, 127.41, 128.47, 146.51; ^{19}F-NMR(470.4 MHz : $CDCl_3$) δ(ppm down field from external CF_3COOH) -6.41 (3F), -35.38 (d, J=267Hz, 1F),-37.76 (d, J=267Hz, 1F), -49.30 (2F), -50.69 (2F); IR (neat, cm^{-1}) 3588 (OH); Found: M+, 354.0668, $C_{13}H_{11}F_9O$ requires 354.0667.

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[8] The reaction was monitored by ^{119}Sn-NMR (186.4 MHz); two equivalents of the ditin to R_FI were completely consumed in 5 h photoirradiation, and the signal due to $(Bu^n{}_3Sn)_2O$ appeared (δ = 85.4 ppm from Me_4Sn). However, the signals assignable to $Bu^n{}_3SnI$ could not be observed in ^{119}Sn-NMR, probably because it was further converted to miscellaneous products under oxyfluoroalkylation conditions. In agreement with these observations, the decomposition of $Bu^n{}_3SnI$ occurred rapidly and the ^{119}Sn-NMR signal disappeared within 2 h, when the solution of $Bu^n{}_3SnI$ in benzene was irradiated under O_2 atmosphere.

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