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A new entry for the oxidation of fluoroalkyl-substituted methanol derivatives: Scope and limitation of the organoiodine(V) reagent-catalyzed oxidation

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ABSTRACT

Oxidation of various fluoroalkyl-substituted methanol derivatives under the influence of a catalytic amount of sodium 2-iodobenzenesulfonate and Oxone® in CH_3CN or CH_3NO_2 was investigated in detail. The efficiency of the newly developed oxidation was also evaluated by comparison to other oxidations, such as Dess–Martin, PDC, and Swern oxidation.

1. Introduction

Incorporation of fluorine atom(s) into organic molecules often changes their structure, stability, reactivity, and biological activity, and thereby frequently leads to the discovery of novel and potent applications in various domains from liquid crystalline materials to biologically active substances, peptide isosteres or enzyme inhibitors [1–7]. Consequently, the development of novel and convenient synthetic methods for the preparation of fluorine-containing materials has been becoming more and more important in fluorine chemistry [8–14].

Among various types of fluoroorganic molecules, fluoroalkylated ketones **1** have been well known as one of the most fundamental and valuable synthetic fluorinated units because of their great utility as an electrophile, and considerable studies on the preparation of **1** have been reported thus far [15–17].

The oxidation of fluoroalkyl-substituted methanol derivatives **2** to the corresponding ketones **1** would be one of the most attractive transformations in fluorine chemistry because the alcohols **2** can be easily prepared from numerous methods, such as the reductive coupling of commercially available fluoroalkyl halides **3** and various aldehydes [18,19], fluoride-catalyzed nucleophilic addition of $RfSiMe_3$ **4** with various aldehydes [20–22], and so on [23–25] (Fig. 1). However, it has been well recognized that the oxidation of the alcohols **2** is not trivial because they are significantly resistant to be oxidized due to a strongly electron-withdrawing effect of a fluoroalkyl group [26,27].

Therefore, very powerful oxidizing reagents, such as Dess–Martin periodinane **5** [28] or chromium reagents **6** and **7** [29], can be generally employed for the oxidation of such molecules in fluorine chemistry [30–33] (Fig. 2). From the viewpoint of safety, environmental load, and cost, however, more efficient as well as more practical oxidation methods have been highly required.

In this article we wish to disclose our recent studies on the hypervalent iodine-catalyzed oxidation [34–38] of fluorinated alcohols by using sodium 2-iodobenzenesulfonate (**8**) and Oxone® ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$), especially emphasizing scope and limitation of this oxidation, compared with other oxidation systems, such as Dess–Martin, PDC, and Swern oxidations.

2. Results and discussion

Initial studies focused on the oxidation of 2,2,2-trifluorophenethyl alcohol (**2a**: R = Ph) under the influence of a catalytic amount of sodium 2-iodobenzenesulfonate (**8**) and Oxone® ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$). Thus, treatment of **2a** with 0.6 equiv. of Oxone® in the presence of 1 mol% of **8** in CH_3CN at 70 °C for 3 h gave the corresponding ketone **1a** in 39%, together with 55% recovery of the starting material (Table 1, entry 1). Prolonged reaction time resulted in the increase of the yield up to 54% (entry 3). The increase of the catalysis loading (entry 4) and higher temperature (entry 5) led to satisfactory results, the ketone **1a** being obtained in up to 68% yield. Additionally, a significant improvement of the yield was observed when 0.9 equiv. of Oxone® was employed (entry 6). Further investigation on the catalysis

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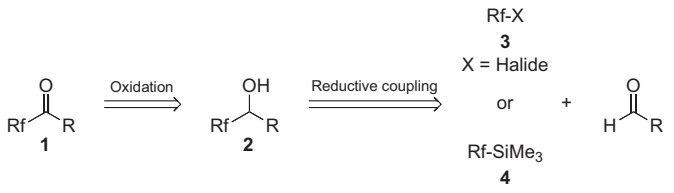


Fig. 1. Retrosynthesis of fluoroalkylated ketones **1**.

loading (entry 7) as well as the reaction time (entry 8) enabled us to afford the ketone **1a** in 97% yield.

This result encouraged us to investigate the oxidation of 1,1,1-trifluoroundecan-2-ol (**2b**: R = *n*-C_9H_{19}) under the same reaction conditions as described in entry 8. Unfortunately, the desired ketone **1b** was obtained in only 38% yield, and the starting alcohol was recovered in 48% yield (entry 9). Then, we reinvestigated the reaction conditions for the substrate **2b**. While the prolonged reaction time did not lead to a dramatic change in the yield (entry 10), changing the solvent from CH_3CN to CH_3NO_2 appreciably affected the yield (entry 11). Finally, the reaction at 110 °C proceeded very smoothly to give the desired ketone **1b** in excellent yield (entries 12 and 13). With the optimum reaction conditions in hand, we next examined the oxidation of various types of fluorinated alcohols. The results are collected in Table 2.

As shown in entries 1, 2, 5, 8, 10, the alcohols having an electron-donating group (MeO) as well as an electron-withdrawing group (Cl, NO_2, CF_3) on the benzene ring could participate very well in the oxidation, though isolated yields are very low in several cases due to the high volatility of the products. In the oxidation of the alcohols **2i** having a nitro group on the benzene ring, only the desired ketone **1i** could be easily isolated in high yield by silica gel column chromatography though ^{19}F NMR analysis of the reaction mixture revealed that the ketone **1i** as well as the corresponding hydrate **9i** were formed in a ratio of 1:1 (entry 8). Additionally, the position of the substituent on the benzene ring did not influence the reaction at all as described in entries 2–4 and entries 5–7. The trifluoromethylated allylic alcohol **2l** and propargylic alcohols **2m** and **2n** could be oxidized very smoothly to afford the corresponding ketones **1l**, **1m**, and **1n** in high to excellent yields (entries 11–13). As also described in Table 1, the trifluoromethylated alcohols **2b**, **2o**-**r**, having an aliphatic side chain, underwent a very smooth oxidation under the severe reaction conditions, such as 10 mol% of **8**/CH_3NO_2/110 °C/24 h, compared with that for 2,2,2-trifluorophenethyl alcohol derivatives (entries 14–18).

We also investigated the oxidation of the alcohols having various fluoroalkyl groups. As shown in entries 19–26, changing the fluoroalkyl group from trifluoromethyl group to nonafluorobutyl, pentafluoroethyl, and difluoromethyl groups did not cause a significant influence in the reaction, the desired ketones **1s**-**z** being obtained in excellent yields. Additionally, α,α,-difluoro-β-hydroxyesters **2aa** and **2ab** could also participate in the oxidation very well to give the corresponding 1,3-dicarbonyl compounds **1aa** and **1ab** (entries 27 and 28). Similarly, the oxidation of 2,2,3,3-tetrafluoro-1,4-diol derivative **2ac** took place very smoothly to afford the corresponding 1,4-dicarbonyl compound **1ac** in high yield (entry 29).

In this way, the newly developed oxidation was found to be much more effective for various types of fluorinated alcohols.

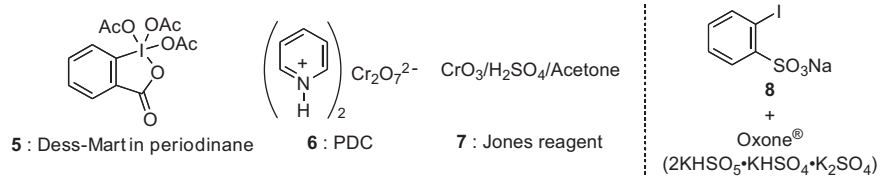


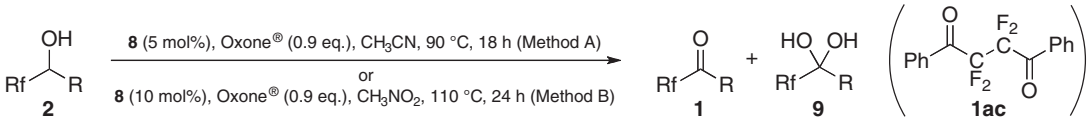
Fig. 2. Various oxidizing reagents.

Table 1
Investigation of the reaction conditions.

Entry	R	**8** X/mol%	Oxone® Y/eq.	Solvent	Temp.[a]/°C	Time/h	Yield of **1**[b]/%	Recovery of **2**[b]/%	Unidentified products[b]/%
1	Ph (**a**)	1	0.6	CH_3CN	70	3	39	55	2
2	Ph (**a**)	1	0.6	CH_3CN	70	12	52	43	2
3	Ph (**a**)	1	0.6	CH_3CN	70	24	54	43	3
4	Ph (**a**)	2	0.6	CH_3CN	70	24	61	33	3
5	Ph (**a**)	2	0.6	CH_3CN	90	12	68	28	2
6	Ph (**a**)	2	0.9	CH_3CN	90	12	86	10	3
7	Ph (**a**)	5	0.9	CH_3CN	90	12	94	2	3
8	Ph (**a**)	5	0.9	CH_3CN	90	18	97 (40)[c]	0	2
9	*n*-C_9H_{19} (**b**)	5	0.9	CH_3CN	90	18	38	48	6
10	*n*-C_9H_{19} (**b**)	5	0.9	CH_3CN	90	24	42	52	2
11	*n*-C_9H_{19} (**b**)	5	0.9	CH_3NO_2	90	24	75	17	2
12	*n*-C_9H_{19} (**b**)	5	0.9	CH_3NO_2	110	24	90	2	6
13	*n*-C_9H_{19} (**b**)	10	0.9	CH_3NO_2	110	24	92 (68)[c]	0	7

[a] Bath temperature.
[b] Determined by ^{19}F NMR. Values in parentheses are of isolated yield.
[c] Low yields were due to the high volatility of the products.

Table 2
The oxidation of various types of fluorinated alcohols.



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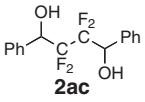
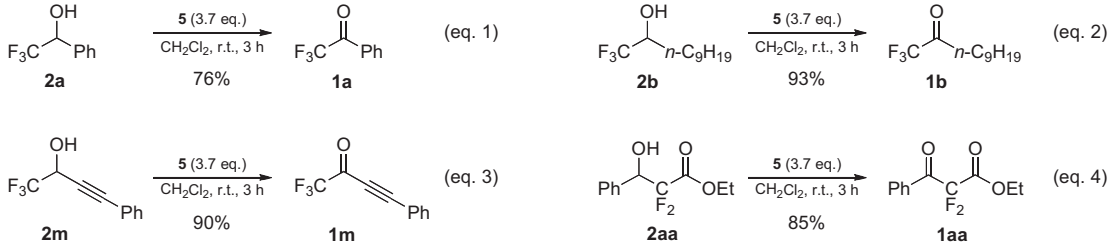
Entry	Rf	R		Method	Yield[a]/% of **1**	Yield[a]/% of **9**	Recovery[a]/% of **2**	References[b]
1	CF_3	Ph	(**a**)	A	97 (40)[c]	0	0	[39]
2	CF_3	*p*-$MeOC_6H_4$	(**c**)	A	99 (83)	Trace	0	[40]
3	CF_3	*m*-$MeOC_6H_4$	(**d**)	A	97 (83)	3	0	[40]
4	CF_3	*o*-$MeOC_6H_4$	(**e**)	A	96 (80)	4	0	[40]
5	CF_3	*p*-ClC_6H_4	(**f**)	A	89 (83)	8	0	[41]
6	CF_3	*m*-ClC_6H_4	(**g**)	A	97 (59)	3	0	[42]
7	CF_3	*o*-ClC_6H_4	(**h**)	A	98 (48)[c]	3	0	[43]
8	CF_3	*p*-$O_2NC_6H_4$	(**i**)	A	47 (83)[d]	49	0	[41]
9	CF_3	*o*-$O_2NC_6H_4$	(**j**)	B	Quant. (97)	0	0	[44]
10	CF_3	*p*-$F_3CC_6H_4$	(**k**)	A	59 (44)[c,e,f]	40	0	[15]
11	CF_3	(*E*)-PhCH=CH	(**l**)	A	75 (52)[e]	6	0	[41]
12	CF_3	PhC≡C	(**m**)	A	86 (62)	3	0	[39]
13	CF_3	*n*-C_6H_{13}C≡C	(**n**)	B	93 (80)	0	0	[45]
14	CF_3	*n*-C_9H_{19}	(**b**)	B	92 (68)	0	7	[39]
15	CF_3	$PhCH_2CH_2$	(**o**)	B	90	Trace	0	[13]
16	CF_3	PhCH(Me)	(**p**)	B	92	Trace	0	[46]
17	CF_3	*p*-(*t*-Bu)$C_6H_4CH_2CH$(Me)	(**q**)	B	92 (86)	0	0	New compound
18	CF_3	CH_2=CH–$(CH_2)_8$	(**r**)	B	84	0	15	[47]
19	*n*-C_4F_9	Ph	(**s**)	A	94 (76)[e]	0	0	[48]
20	*n*-C_4F_9	*p*-MeC_6H_4	(**t**)	A	98 (90)[e]	0	0	[49]
21	*n*-C_4F_9	*p*-$MeOC_6H_4$	(**u**)	A	97 (89)[e]	0	0	New compound
22	*n*-C_4F_9	*p*-ClC_6H_4	(**v**)	A	93 (89)[e]	0	0	New compound
23	*n*-C_4F_9	*o*-ClC_6H_4	(**w**)	A	96 (80)[e]	0	0	New compound
24	*n*-C_4F_9	(*E*)-PhCH=CH	(**x**)	A	88 (72)[e]	0	0	[50]
25	C_2F_5	Ph	(**y**)	A	94[e]	0	0	[18]
26	CHF_2	Ph	(**z**)	A	93[e]	0	0	[51]
27	CF_2CO_2Et	Ph	(**aa**)	A	97 (83)	3	0	[39]
28	CF_2CO_2Et	*n*-C_9H_{19}	(**ab**)	B	Quant. (83)	0	0	[52]
29			(**ac**)	A	98 (71)[g,h]	0	0	[53]

[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yield.
[b] The references for known compounds are listed.
[c] Low yields were due to the high volatility of the products.
[d] The reason that the isolated yield was higher than the one determined by ^{19}F NMR is because the hydrate was converted into the ketone during the silica gel column chromatography.
[e] The reaction was carried out for 24 h.
[f] Ten mol% of *pre*-IBS was used.
[g] The product, **1ac** was obtained.
[h] The reaction was carried out using 20 mol% of *pre*-IBS and 1.8 equiv. of Oxone®.

According to the literature, oxidation of **2a**, **2b**, **2m**, and **2aa** under the influence of 3.7 equiv. of Dess–Martin periodinane **5** in CH_2Cl_2 at room temperature for 3 h gives the corresponding ketones **1a**, **1b**, **1m**, and **1aa** in 76%, 93%, 90%, and 85%, respectively (Scheme 1, Eqs. (1)–(4)) [39]. These facts indicate that the present oxidation is comparable to Dess–Martin oxidation.

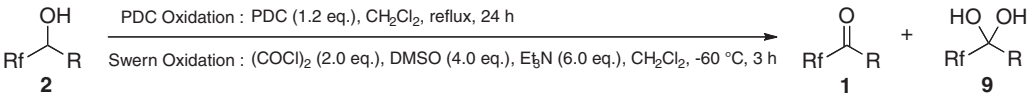
In order to prove the great utility of the present oxidation, we also examined PDC or Swern oxidation for some of fluorinated alcohols [54a–d] (Table 3).

In the case of the oxidation of the alcohols having an aryl group as R, both PDC as well as Swern oxidation proceeded very smoothly to give the corresponding ketone **1** as well as hydrate **9** in high to



Scheme 1. Oxidation of various fluorinated alcohols with Dess–Martin periodinane **5**.

Table 3
PDC and Swern oxidation of various types of fluorinated alcohols.



Entry	Rf	R		PDC oxidation			Swern oxidation		
				Yield[a]/% of **1**	Yield[a]/% of **9**	Recovery[a]/% of **2**	Yield[a]/% of **1**	Yield[a]/% of **9**	Recovery[a]/% of **2**
1	CF_3	Ph	(**a**)	62	29	3	93	7	0
2	CF_3	*p*-$MeOC_6H_4$	(**c**)	Quant.	0	0	Quant.	0	0
3	CF_3	*p*-ClC_6H_4	(**f**)	–	–	–	97	2	0
4	CF_3	*p*-$O_2NC_6H_4$	(**i**)	90	5	2	31	46	18
5	CF_3	*p*-$F_3CC_6H_4$	(**k**)	Quant.	0	0	85	10	4
6	CF_3	(*E*)-PhCH=CH	(**l**)	41	0	0	95	3	0
7	CF_3	PhC≡C	(**m**)	0	0	0	87	0	0
8	CF_3	*n*-$C_6H_{13}C$≡C	(**n**)	7	0	0		Complex mixture	
9	CF_3	*n*-C_9H_{19}	(**b**)	61	0	34	17	0	32
10	CF_2CO_2Et	Ph	(**aa**)	94	0	0	91	0	0
11	CF_2CO_2Et	*n*-C_9H_{19}	(**ab**)	58	0	40	46	0	0

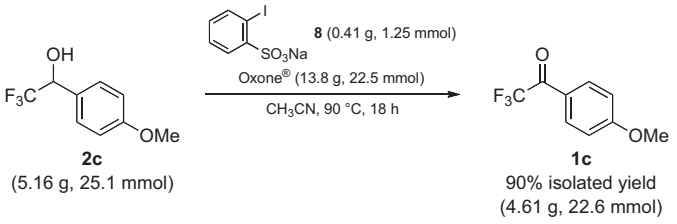
[a] Determined by ^{19}F NMR.

excellent yields (entries 1–5, 10). On the other hand, PDC oxidation of the allylic alcohol **2l** and the propargylic alcohols **2m**, **2n** took place very sluggishly to give the desired ketones **1l**, **1m**, and **1n** in very low yields (entries 6–8). In these cases, not only the corresponding hydrates were not obtained, but also the starting alcohols were not recovered at all. In sharp contrast to the PDC oxidation, Swern oxidation of **2l** and **2m** afforded the corresponding ketones in excellent yields (entries 6 and 7), while **2n** did not lead to the satisfactory result (entry 8). Furthermore, the fluorinated alcohols having an alkyl group as R were found to be less reactive under the PDC as well as Swern oxidation conditions, the starting alcohols being recovered in 30–40% (entries 9 and 11).

Finally, we attempted the hypervalent iodine(V)-catalyzed oxidation in a large scale (Scheme 2). Thus, 5.16 g of 1-(4-methoxyphenyl)-2,2,2-trifluoroethanol (**2c**, 25.1 mmol), 13.8 g of Oxone® (22.5 mmol), and 0.41 g of **8** (1.25 mmol) were dissolved in CH_3CN, and the whole was heated at 90 °C for 18 h. After the reaction mixture was allowed to cool to room temperature, the whole was filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give 4.61 g (22.6 mmol) of the corresponding ketone **1c** in 90% yield. In this way, the scale-up did not influence for the reaction efficiency at all.

In summary, we have demonstrated the hypervalent iodine(V)-catalyzed oxidation for various types of fluoroalkylated alcohols, compared with Dess–Martin, PDC and Swern oxidation. As a result, it was revealed that the newly developed oxidation could be applied for almost all types of fluorinated alcohols, and it was comparable to Dess–Martin oxidation, while PDC and Swern oxidation could not be employed for allylic, propargylic alcohols as well as the alcohols having an aliphatic side chain as R. Additionally, the present oxidation could be applied for a large-scale reaction without any decrease of the reaction efficiency.

The present oxidation also has much more advantages, like safety, environmental load-reducing and inexpensive system, very



Scheme 2. A catalytic oxidation in a large scale.

mild reaction conditions, easy workup, commercial availability of the reagents, and so on.

In this way, we have established very efficient and practical oxidation method for various types of fluorinated alcohols, which may be employed in a laboratory as well as an industry.

3. Experimental

^1H and ^{13}C NMR spectra were measured with a JEOL JNM-AL400 (399.65 MHz for ^1H and 100.40 MHz for ^{13}C) spectrometer in a chloroform-d ($CDCl_3$) solution with tetramethylsilane as an internal reference. A JEOL JNM-AL400 (376.05 MHz) was used to measure ^{19}F NMR spectra in $CDCl_3$ using $CFCl_3$ as an internal standard. Infrared spectra (IR) were taken on a Jasco FT/IR-4100type A spectrometer as film on a NaCl plate. High resolution mass spectra were taken with a JEOL JMS-700 MS spectrometer. Column chromatography was carried out on silica gel (Wako gel C-200) and TLC analysis was performed on silica gel TLC plates (Merck, Silica gel 60 F_{254}).

All reactions were carried out under an atmosphere of argon. Anhydrous tetrahydrofuran (THF) were purchased from Wako Pure Chemical Industries, Ltd. All chemicals were of reagent grade and, if necessary, were purified in the usual manner prior to use.

3.1. Preparation of sodium 2-iodobenzenesulfonate (8)

To a stirred suspension of 2-aminobenzenesulfonic acid (5.0 g, 28.9 mmol) and crushed-ice (20 g) in concentrated HCl (10 mL) was added NaNO2 (2.09 g, 30.3 mmol) in water (20 mL) slowly at 0 °C, and the whole was stirred for 20–30 min at below 5 °C. (Immediate precipitation of the diazonium salt was observed.) A solution of NaI (4.76 g, 31.8 mmol) in water (20 mL) was then added slowly with stirring at 0 °C. After the addition was complete, stirring was continued at 0 °C for 1 h, at room temperature for 1 h, and at 50 °C for 12 h to remove all N2. The mixture was cooled to room temperature, then concentrated *in vacuo*. The residue was recrystallized by distilled water, and thus obtained solid was washed with cold EtOH and Et2O to afford the desired sodium 2-iodobenzenesulfonate·H_2O (6.10 g, 18.8 mmol, 65%).

3.2. Preparation of the fluorinated alcohols 2

Typical procedure: a mixture of 10-undecenal (1.68 g, 10 mmol) and CF_3SiMe_3 (1.71 g, 1.9 mL, 12 mmol) in 15 mL of THF, which was cooled to 0 °C, was treated with 1 M THF solution

of TBAF (15 mol%, 15 mL, 1.5 mmol). The reaction mixture was brought to room temperature and stirred for 3 h. The resulting silyloxy compound was then hydrolyzed with aqueous HCl. Then, the mixture was extracted with ether (15 mL × 3), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: hexane/EtOAc = 7/1) to give 1,1,1-trifluoro-11-dodecen-2-ol (**2r**) (1.77 g, 7.43 mmol, 74%).

2r: ^{1}H NMR ($CDCl_3$) δ 1.30–1.38 (m, 12H), 1.53–1.71 (m, 2H), 2.04 (q, J = 7.10 Hz, 2H), 2.32 (br s, 1H), 3.84–3.94 (m, 1H), 4.93 (dm, J = 9.99 Hz, 1H), 4.99 (ddt, J = 16.78, 1.40, 1.40 Hz, 1H), 5.81 (ddt, J = 16.78, 9.99, 6.39 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 25.23, 29.22, 29.40, 29.52, 29.67, 29.68, 29.90, 70.86 (q, J = 30.86 Hz), 114.48, 125.56 (q, J = 281.02 Hz), 126.96, 139.53; ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ −80.55 (d, J = 7.10 Hz, 3F); IR (neat) 3376, 3078, 2928, 2857, 1641, 1466, 1392, 1279, 1172, 994, 910, 847, 723, 695 cm^{-1}; HRMS (EI) Calcd for (M^+) $C_{12}H_{21}F_3O$ 238.1544, Found 238.1544.

3.3. 1,1,1-Trifluoro-4-(4-tert-butylphenyl)-3-methylbutan-2-ol (2q)

Yield: 95% (d.r. *ca.* 56:44) ^{1}H NMR δ 0.85 and 0.92 (d, J = 6.79 and d, J = 6.79 Hz, 3H), 1.20 (s, 9H), 2.00–2.15 (m, 1H), 2.25–2.95 (m, 3H), 3.62–3.77 (m, 1H), 6.99 and 7.01 (d, J = 2.40 Hz and d, J = 2.60 Hz, 2H), 7.20 and 7.22 (d, J = 2.40 Hz and d, J = 2.60 Hz, 2H); ^{19}F NMR ($CDCl_3$, CCl_3F) δ −76.33 and −75.55 (d, J = 4.14 Hz, and d, J = 4.14 Hz, 3F); ^{13}C NMR($CDCl_3$) δ 13.24 and 15.62, 31.69 and 31.70, 34.70 and 36.42, 35.17 and 37.46, 39.75, 71.68 and 74.15 (q, J = 29.48 Hz and q, J = 29.22 Hz), 125.63 and 125.82, 125.85 and 125.87 (q, J = 282.96 Hz and q, J = 282.96 Hz), 129.07 and 129.37, 136.69 and 136.74, 149.41 and 149.64; IR (neat) 3348, 2964, 2871, 1911, 1800, 1710, 1662, 1516, 1464, 1364, 1271, 1166 cm^{-1}; HRMS (FAB+), Calcd for $C_{15}H_{21}F_3O$ (M+): 274.1544, Found 274.1552.

3.4. Typical procedure for the hypervalent iodine(V)-catalyzed oxidation

Method A: a mixture of 2,2,2-trifluoro-1-(4-methoxyphenyl)ethanol (**2c**) (0.206 g, 1.0 mmol) and sodium 2-iodobenzenesulfonate (**8**) (as monohydrate, 0.016 g, 0.05 mmol, 5 mol%), *powdered* Oxone® (0.554 g, 0.9 mmol) in CH_3CN (5 mL) was stirred at 90 °C under the atmosphere of air. After stirring for 18 h, the reaction mixture was allowed to cool to room temperature. The reaction mixture was filtered, being successively washed with ethyl acetate. The combined filtrates were washed with water (3× 10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: hexane/EtOAc = 10/1) to give 2,2,2-trifluoro-1-(4-methoxyphenyl)-1-ethanone (**1c**) (0.165 g, 0.81 mmol, 81% yield).

Method B: a mixture of 1,1,1-trifluoro-undecan-2-ol (**2b**) (0.136 g, 0.6 mmol) and **8** (as monohydrate, 0.019 g, 0.06 mmol, 10 mol%), *powdered* Oxone® (0.332 g, 0.54 mmol) in CH_3NO_2 (3 mL) was stirred at 110 °C under the atmosphere of air. After stirring for 24 h, the reaction mixture was allowed to cool to room temperature. The reaction mixture was filtered, being successively washed with ethyl acetate. The combined filtrates were washed with water (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: hexane/EtOAc = 10/1) to give 1,1,1-trifluoroundecan-2-one (**1b**) (0.092 g, 0.41 mmol, 68% yield).

3.5. 1,1,1-Trifluoro-4-(4-tert-butylphenyl)-3-methyl-2-butanone (1q)

Yield: 86%; ^{1}H NMR ($CDCl_3$) δ 1.26 (d, J = 6.79 Hz, 3H), 1.37 (s, 9H), 2.68 (dd, J = 13.79, 7.79 Hz, 1H), 3.15 (dd, J = 13.79, 5.99 Hz, 1H), 3.32 (m, 1H), 7.15 (d, J = 8.39 Hz, 2H), 7.38 (d, J = 8.39 Hz, 2H); ^{19}F NMR ($CDCl_3$, CCl_3F) δ −78.35 (s, 3F); ^{13}C NMR ($CDCl_3$) δ 16.11, 31.65, 34.75, 37.89, 43.17, 116.12 (q, J = 292.87 Hz), 120.49, 125.84, 135.18, 150.01, 195.13 (q, J = 33.60 Hz); IR (neat) 2965, 2871, 1759, 1518, 1462, 1365, 1290, 1268, 1203, 1153, 1109 cm^{-1}; HRMS (FAB+) Calcd for $C_{15}H_{19}F_3O$ (M+): 272.1388, Found 272.1378.

3.6. 2,2,3,3,4,4,5,5,5-Nonafluoro-1-(4-methoxyphenyl)-1-pentanone (1u)

Yield: 89%; ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3H), 6.98 (d, J = 8.19 Hz, 2H), 8.06 (d, J = 8.19 Hz, 2H); ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ −125.63 (s, 2F), −122.34 (s, 2F), −113.02 (s, 2F), −81.44 (d, J = 9.78 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 55.96, 105.84–114.39 (m, 3C), 114.71, 117.75 (qt, J = 285.70, 33.08 Hz), 124.75 (t, J = 2.06 Hz), 133.33, 165.80, 181.70 (t, J = 25.20 Hz); IR (neat) 3016, 2975, 2943, 2848, 1697, 1603, 1514, 1465, 1428, 1356, 1317, 1237, 1137 cm^{-1}; HRMS (FAB+) Calcd for $C_{12}H_7F_9O_2$ (M+): 354.0302, Found 354.0302.

3.7. 2,2,3,3,4,4,5,5,5-Nonafluoro-1-(4-chlorophenyl)-1-pentanone (1v)

Yield: 89%; ^{1}H NMR ($CDCl_3$) δ 7.52 (d, J = 8.99 Hz, 2H), 8.01 (d, J = 8.99 Hz, 2H); ^{19}F NMR δ −125.71 to −125.63 (m, 2F), −122.24 to −122.33 (m, 2F), −113.48 (t, J = 24.07 Hz, 2F), −81.40 (t, J = 19.55 Hz, 3F); ^{13}C NMR δ 105.81–114.25 (m, 3C), 117.63 (qt, J = 287.65, 33.03 Hz), 129.87, 130.17 (t, J = 2.51 Hz), 131.94, 142.84, 182.52 (t, J = 26.05 Hz); IR (neat) 1713, 1590, 1491, 1407, 1356, 1237, 1138 cm^{-1}; the molecular ion peak was not detected in HRMS.

3.8. 2,2,3,3,4,4,5,5,5-Nonafluoro-1-(2-chlorophenyl)-1-pentanone (1w)

Yield: 80%; ^{1}H NMR ($CDCl_3$) δ 7.35–7.43 (m, 1H), 7.48–7.58 (m, 3H); ^{19}F NMR δ −125.87 to −125.82 (m, 2F), −122.30 (s, 2F), −115.54 to −115.45 (m, 2F), −81.45 to −81.43 (m, 3F); ^{13}C NMR δ 106.08–113.24 (m, 3C), 117.62 (qt, J = 287.30, 32.90 Hz), 127.09, 129.31 (t, J = 3.75 Hz), 131.42, 133.05, 133.16, 133.86, 182.25 (t, J = 28.00 Hz); IR (neat) 1767, 1591, 1438, 1356, 1238, 1138 cm^{-1}; the molecular ion peak was not detected in HRMS.

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