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Photoinduced addition and addition–elimination reactions of perfluoroalkyl iodides to electron-deficient olefins

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ABSTRACT

Photoinduced radical perfluoroalkylation of various simple electron-deficient olefins was achieved in the presence of an aqueous $Na_2S_2O_3$ solution. The reactions proceeded smoothly to give addition or addition–elimination products. The ability of the products to be used as radical precursors or Michael acceptors was also demonstrated.

1. Introduction

Perfluoroalkyl compounds have received considerable attention not only as pharmaceuticals but also as new materials, and the development of methods for their synthesis is desirable.[1] The radical addition of perfluoroalkyl iodides to olefins is one of the most efficient and direct methods for the introduction of perfluoroalkyl groups into organic compounds. Many examples of radical additions of perfluoroalkyl iodides to electron-rich olefins have been reported under various conditions and with high yields.[2] However studies on the addition of the perfluoroalkyl radical to electron-deficient olefins are scarce, despite the versatility of the products as fluorine-containing building blocks or monomers.[3] Although Burton et al. reported the photoinduced radical addition of perfluoroalkyl iodide with electron-deficient olefins, side reactions, such as oligomerization were observed in most cases, and the examples were limited to several acrylic derivatives.[3b] Thus, a novel, efficient perfluoroalkylation of electron-deficient olefins is desirable.

Recently, we reported an effective radical iodoperfluoroalkylation of acrylic acid derivatives bearing a chiral auxiliary in the presence of an aqueous $Na_2S_2O_3$ solution under UV irradiation.[4] The acrylic acid derivatives used in our previous study had a bulky chiral auxiliary and exhibited low reactivity toward oligomerization. Therefore, we were interested in whether our reaction conditions would be suitable for simple, easy-to-polymerize, electron-deficient olefins and would be a new, efficient synthetic method for fluorine-containing building blocks. In this context, we report herein an efficient photoinduced radical perfluoroalkylation of various simple electron-deficient olefins.

2. Results and discussion

First, the photoinduced reaction of perfluorohexyl iodide and various acrylic-type compounds was examined (Table 1). On the basis of the conditions used in our previous study, the reactions of **1a**–**k** (1 equiv) with perfluorohexyl iodide (5 equiv) were carried out in the presence of aqueous $Na_2S_2O_3$ under UV irradiation in CH_2Cl_2. The reactions of methyl, ethyl, and benzyl acrylates **1a**–**c** afforded the corresponding iodoperfluorohexylated products **2a**–**c** in good yields, respectively (entries 1–3). Under these conditions, the yields were not affected by the bulkiness of the alkyl moiety in the ester group, although Burton et al. reported that small acrylate, such as methyl acrylates afforded telomerized side products.[3b] Ethyl crotonate (**1d**) also gave the iodoperfluorohexylated product **2d** in 62% yield (entry 4). In addition, iodoperfluorohexylations of acrylic acid (**1e**), acrolein (**1f**), and alkyl vinyl ketones (**1g**, **1h**, **1i**) proceeded, although the yields of ketones (**2g**, **2h**, **2i**) were lower than the others (entries 5–9). Amide **1j**, nitrile **1k**, and sulfone **1l** also underwent the reaction (entries 10–12). However, the reaction of ethyl cinnamate (**1m**) gave the α-perfluoroalkylated conjugated olefin **3**.[5]

Second, the reactions of acrylates **1a** and **1c** with several fluoroalkyl iodides were investigated (Table 2). The addition of ethyl difluoroiodoacetate to ethyl acrylate (**1a**) afforded product **4a** in

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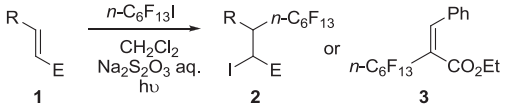
Table 1
Photoinduced reaction of perfluorohexyl iodide with acrylic-type compounds[6]

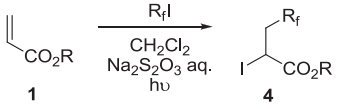


1 2 3

Entry	Substrate	Time (h)	Product	Yield (%)
1	Ethyl acrylate (**1a**)	1	**2a**	97
2	Methyl acrylate (**1b**)	1	**2b**	91
3	Benzyl acrylate (**1c**)	3	**2c**	76
4	Ethyl crotonate (**1d**)	1	**2d**	62[a]
5	Acrylic acid (**1e**)	3	**2e**	81
6	Acrolein (**1f**)	4	**2f**	87
7	Methyl vinyl ketone (**1g**)	1	**2g**	40
8	Ethyl vinyl ketone (**1h**)	1	**2h**	57
9	*n*-Pentyl vinyl ketone (**1i**)	1	**2i**	52
10	*N*,*N*-Dimethylacrylamide (**1j**)	3	**2j**	85
11	Acrylonitrile (**1k**)	5	**2k**	49
12	Phenyl vinyl sulfone (**1l**)	4	**2l**	87
13	Ethyl cinnamate (**1m**)	4	**3**	87

[a] Diastereomeric ratio of the products (70:30) was determined by ^{1}H NMR. The relative configurations of the products were not determined.

Table 2
Photoinduced reaction of fluoroalkyl iodides with electron-deficient olefins



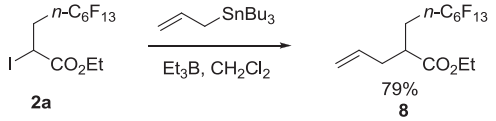
1 4

Entry	Substrate	R_f	Time (h)	Product	Yield (%)
1	Ethyl acrylate (**1a**)	CF_2CO_2Et	3	**4a**	80
2	Benzyl acrylate (**1c**)	CF_3	6	**4b**	50
3	Benzyl acrylate (**1c**)	*n*-C_3F_7	3	**4c**	87
4	Benzyl acrylate (**1c**)	^{i}C_3F_7	3	**4d**	89

80% yield (entry 1). Thus, this reaction could be effectively utilized for the synthesis of difluoro compounds. The reaction of **1c** with trifluoromethyl iodide also afforded the iodotrifluoromethylated product **4b**, although the yield was lower than those with other iodides (entry 2). The addition of *n*-perfluoropropyl and *i*-perfluoropropyl iodides to benzyl acrylate (**1c**) proceeded smoothly to give the corresponding iodoperfluoroalkylated products in good yields (entries 3 and 4, respectively).

Next, the radical perfluoroalkylation of α-substituted electron-deficient olefins **5a**–**d** was investigated (Table 3). In all these cases, the addition–elimination reaction occurred to afford olefinic products **6**. The reaction of ethyl methacrylate (**5a**) afforded **6a** in 91% yield (entry 1). A longer reaction time led to diperfluoroalkylation and gave the product **7** (entry 2). While the ester substrate **5b** gave **6b** in 81% yield with *E*/*Z*=54:46, the cyanide substrate **5c** exclusively afforded (*E*)-**6c** exclusively in 63% yield (entries 3 and 4). Reaction of diethyl itaconate (**5d**) proceeds with an *E*/*Z* selectivity of 40:60, and the *E*/*Z* isomers were easily separated by silica gel column chromatography (entry 5).

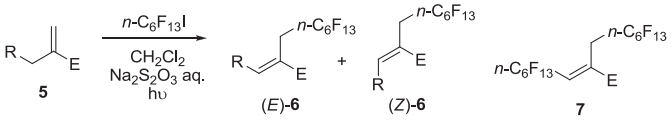
To demonstrate the applicability of the perfluoroalkyl products of this new addition reaction, the radical allylation of **2a** was then carried out using allyltributyltin and triethylborane. The iodoperfluoroalkylated product **2a** acted as a good radical precursor and was transformed to the desired product **8** in good yield (79%) (Scheme 1).



2a 8

Scheme 1.

Table 3
Photoinduced reaction of perfluorohexyl iodide with α-substituted electron-deficient olefins[6]



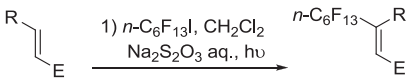
5 (*E*)-6 (*Z*)-6 7

Entry	Substrate	Time (h)	Product	Yield (%)	*E*/*Z*[a]
1	**5a** (R=H, E=CO_2Et)	1.5	**6a**	91	—
2	**5a** (R=H, E=CO_2Et)	16	**7**	76	100:0
3	**5b** (R=$PhCH_2$, E=CO_2Et)	2	**6b**	81	54:46
4	**5c** (R=$PhCH_2$, E=CN)	2	**6c**	63	100:0
5	**5d** (R=CO_2Et, E=CO_2Et)	8	**6d**	70	40:60

[a] *E*/*Z* ratio was determined by ^{1}H NMR. *E*/*Z* geometry was determined by NOE.

Because perfluoroalkylated olefins are useful fluorine-containing building blocks or monomers for fluorine-containing polymers,[6] we also investigated the one-pot addition–elimination reactions of perfluorohexyl iodide with acrylic-type olefins **1a**, **1d**, and **1h** (Table 4). When the photoirradiation reaction was completed, DBU was added to the reaction mixture, and the solution was stirred for an additional 1 h. The addition–elimination reaction proceeded smoothly to yield the corresponding (*E*)-olefins.[5b]

Table 4
One-pot addition–elimination reaction of perfluorohexyl iodide with electron-deficient olefins[a]

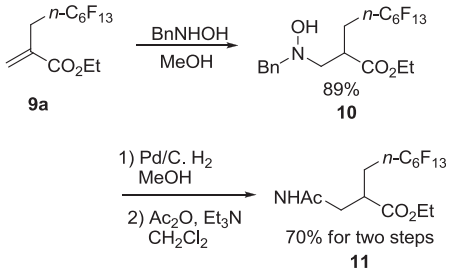


1 (*E*)-9

Entry	Substrate	Time (h)[b]	Product	Yield (%)
1	Ethyl acrylate (**1a**)	1+1	**9a**	82
2	Ethyl crotonate (**1d**)	1+1	**9b**	58
3	*N*,*N*-Dimethylacrylamide (**1h**)	4+1	**9c**	71

[a] After the photoinduced reaction was complete, DBU was added to the mixture and the solution was stirred at rt.
[b] (The reaction time of photoirradiation)+(the reaction time after the addition of DBU).

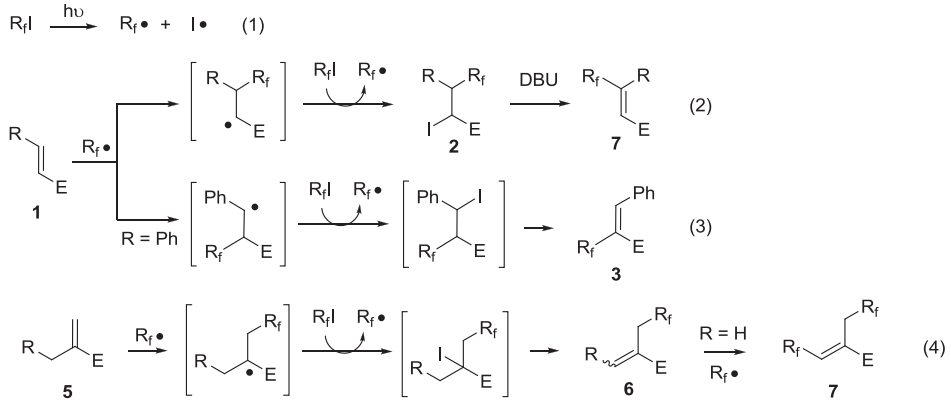
To demonstrate the synthetic utility of the perfluoroalkylated olefins, we carried out the synthesis of a β-amino ester prepared from the addition–elimination product **9a** (Scheme 2). The aza-Michael addition of *N*-benzylhydroxylamine to perfluoroalkylated olefin **9a** proceeded smoothly to give adduct **10** in 89% yield.[7] The reduction of the *N*-benzylhydroxylamino group followed by acetylation gave the perfluoroalkylated acetyl β-amino ester in good yield.



9a 10 11

Scheme 2.

The proposed mechanisms of the reactions are shown in Scheme 3. First, perfluoroalkyl iodide can be homolytically cleaved to generate a perfluoroalkyl radical under photoirradiation (Eq. 1).



Scheme 3.

Perfluorohexyl iodide exhibits an absorption maximum at 270 nm (Fig. 1). The photoinduced reactions were proceeded rapidly in a Pyrex tube or a quartz tube and the use of a 330–470 nm transmission filter also drive the reaction, although a longer reaction time is needed to complete the reaction (5 h). To confirm the generation of the perfluoroalkyl radical, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was reacted with perfluorohexyl iodide under photoirradiation in Pyrex tube, and TEMPO adduct **12** was obtained.[8] Moreover, when TEMPO was added in the standard reaction (Table 1, entry 1), the reaction did not proceed.

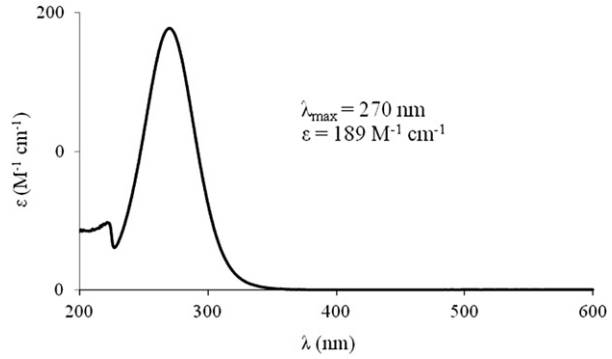
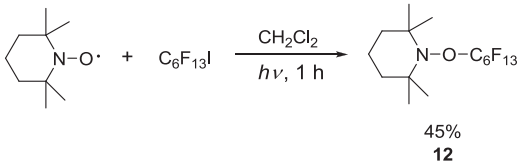


Fig. 1. UV–vis spectrum of $C_6F_{13}I$ in CH_2Cl_2.

Next, the formed perfluoroalkyl radical adds to the β-position of olefin **1** and a radical intermediate is formed. Finally, the iodine atom transfers from perfluoroalkyl iodide to the intermediate radical, regenerating the initial perfluoroalkyl radical and producing the iodoperfluoroalkylated product **2** (Eq. 2). In the case of the reaction with ethyl cinnamate (R=Ph), the perfluoroalkyl radical initially adds to the α-position of the olefin to afford a stable benzyl radical intermediate. After iodine atom transfer, the resulting iodide is eliminated to give the conjugated olefin **3** (Eq. 3). Moreover, the reaction with α-substituted olefin **5** also proceeds through the α-iodo ester, although the tertiary iodide is easily eliminated to give olefin **6** (Eq. 4). Despite the presence of relatively acidic fluoroalkylated side β-protons, dehydroiodination occurred on the R side of the methylene to give alkene **6**. The regioselectivity of the elimination is influenced by the fluorine substitution on the β-carbon.[9] Furthermore, in the case of methacrylic-type product **6** (R=H) with longer reaction time, a second radical addition occurred (Eq. 4) (Scheme 4).



Scheme 4.

3. Conclusion

We successfully carried out the photoinduced radical perfluoroalkylation of various simple electron-deficient olefins in the presence of an aqueous $Na_2S_2O_3$ solution. Perfluoroalkyl iodides reacted readily with various electron-deficient terminal and β-substituted olefins to afford iodoperfluoroalkylated products in high yields. The photoinduced reaction of α-substituted electron-deficient olefins gave olefinic products via an addition–elimination reaction. In addition, we demonstrated the ability of the products to serve as radical precursors or Michael acceptors, thus demonstrating the usefulness of the products as fluorine-containing building blocks.

4. Experimental section

4.1. General

All reactions were performed with a high-pressure Hg lamp (Ushio, 450W). ^{1}H NMR spectra were recorded on a JEOL AL-400 (400 MHz) or EX-400 (400 MHz) spectrometer with $CDCl_3$ or CD_3OD as the solvent and tetramethylsilane as an internal standard unless otherwise noted. ^{13}C NMR spectra were recorded on the instruments operating at 100.5 MHz with $CDCl_3$ or CD_3OD as the solvent and internal standard (δ 77.0). IR spectra were taken on a SHIMADZU FTIR-8700 spectrometer. Mass spectra (EI^+) were obtained on a JEOL JMS-700 mass spectrometer. Mass spectra (ESI) were obtained on a Thermo Exactive. Precoated Merck Kieselgel 60 F_{254} and Kanto silica gel 60 (spherical neutral) were used for thin layer chromatography and flash chromatography, respectively.

4.2. Typical procedure for photoinduced perfluoroalkylation

In a Pyrex glass tube were placed olefin (0.2 mmol), perfluoroalkyl iodide (1.0 mmol), and CH_2Cl_2 (5 mL). Then $Na_2S_2O_3$ (0.5 mmol, 79 mg) and water (1 mL) were added to the mixture. After sealing the tube, the mixture was shaked and then irradiated with a Hg lamp at room temperature. After the reaction was

completed, the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography to afford pure product.

*4.2.1. Ethyl 2-iodo-3-perfluorohexylpropanoate (**2a**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.29 (t, J=7.6 Hz, 3H, CH_3), 2.71 (m, 1H, $C_6F_{13}CHH$), 3.33 (m, 1H, $C_6F_{13}CHH$), 4.25 (q, J=7.6 Hz, 2H, OCH_2), 4.59 (dd, J=3.2, 10.8 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 5.4, 13.7, 38.6 (t, J=20.4 Hz, $C_6F_{13}C$), 62.5, 170.0; IR (neat, cm^{-1}) 2989, 1743, 1430, 1201, 1146, 961, 846, 730, 657, 530; MS m/z 546 (M^+, 100%), 473 (58), 363 (49), 327 (42), 203 (10); HRMS calcd for $C_{11}H_8F_{13}IO_2$ 545.9361, found 545.9349.

*4.2.2. Methyl 2-iodo-3-perfluorohexylpropanoate (**2b**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.73 (m, 1H, $C_6F_{13}CHH$), 3.33 (m, 1H, $C_6F_{13}CHH$), 3.80 (s, 3H, CH_3), 4.62 (dd, J=3.6, 10.4 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 4.4, 38.6 (t, J=20.7 Hz, $C_6F_{13}C$), 53.5, 170.6; IR (neat, cm^{-1}) 2961, 1748, 1441, 1238, 1207, 1146, 846, 699; MS m/z 532 (M^+, 67%), 473 (31), 386 (34), 59 (100); HRMS calcd for $C_{10}H_6F_{13}IO_2$ 531.9205, found 531.9230.

*4.2.3. Benzyl 2-iodo-3-perfluorohexylpropanoate (**2c**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.72 (m, 1H, $C_6F_{13}CHH$), 3.34 (m, 1H, $C_6F_{13}CHH$), 4.65 (dd, J=3.5, 10.6 Hz, 1H, CH), 5.19 (d, J=12.4 Hz, 1H, PhCHH), 5.22 (d, J=12.4 Hz, 1H, PhCHH), 7.37 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 5.1 (t, J=2.9 Hz, $C_6F_{13}CH_2C$), 38.7 (t, J=20.4 Hz, $C_6F_{13}C$), 68.4, 128.6, 128.8, 128.9, 134.8, 170.2; IR (neat, cm^{-1}) 3009, 1734, 1452, 1391, 1235, 1202, 1144, 698; MS m/z 481 (M^+–I, 65%), 107 (68), 91 (100); HRMS calcd for $C_{16}H_{10}F_{13}O_2$ 481.0473, found 481.0451.

*4.2.4. Ethyl 2-iodo-3-perfluorohexylbutanoate (**2d**).* Diastereomer mixture (70:30); colorless oil; IR (neat, cm^{-1}) 2989, 1740, 1464, 1375, 1240, 1148, 1029, 809,762, 699, 653, 531; MS m/z 560 (M^+, 100%), 487 (45), 433 (57), 405 (44), 385 (44), 341 (35), 337 (26); HRMS calcd for $C_{12}H_{10}F_{13}IO_2$ 559.9518, found 559.9518; *major isomer*: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J=7.2 Hz, 3H, CH_3), 1.43 (d, J=7.2 Hz, 3H, CH_3), 2.82 (m, 1H, CH), 4.23 (q, J=7.2 Hz, 2H, CH_2), 4.70 (d, J=6.6 Hz, 1H, ICH); ^{13}C NMR ($CDCl_3$) δ 1.2, 13.8, 20.1, 38.3 (t, J=20.4 Hz, $C_6F_{13}C$), 62.6, 170.3; *minor isomer*: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J=7.2 Hz, 3H, CH_3), 1.55 (d, J=7.2 Hz, 3H, CH_3), 2.87 (m, 1H, CH), 4.21 (q, J=7.2 Hz, 2H, CH_2), 4.80 (d, J=3.9 Hz, 1H, ICH); ^{13}C NMR ($CDCl_3$) δ 0.2, 13.9, 16.6, 43.2 (t, J=20.4 Hz, $C_6F_{13}C$), 62.4, 170.0.

*4.2.5. 2-Iodo-3-perfluorohexylpropanoic acid (**2e**).* Colorless plate crystal; mp 77.8 °C; ^{1}H NMR (CD_3OD) δ 2.62 (m, 1H, $C_6F_{13}CHH$), 3.15 (m, 1H, $C_6F_{13}CHH$), 4.76 (dd, J=3.6, 10.4 Hz, 1H, CH); ^{13}C NMR (CD_3OD) δ 6.2, 40.1 (t, J=21.4 Hz, $C_6F_{13}C$), 174.4; IR (KBr, cm^{-1}) 3006, 1717, 1430, 1363, 1204, 1146, 913; MS m/z 518 (M^+, 100%), 391 (30), 372 (36), 327 (55), 69 (75); HRMS calcd for $C_9H_4F_{13}IO_2$ 517.9048, found 517.9064.

*4.2.6. 2-Iodo-3-perfluorohexylpropanal (**2f**).* Colorless plate crystal; mp 39.5 °C (from hexane/AcOEt 5:1); ^{1}H NMR ($CDCl_3$) δ 2.68 (m, 1H, $C_6F_{13}CHH$), 3.34 (m, 1H, $C_6F_{13}CHH$), 4.89 (ddd, J=2.0, 5.2, 8.4 Hz, 1H, CH), 9.24 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$) δ 19.7, 34.1 (t, J=22.3 Hz, $C_6F_{13}C$), 188.1; IR (KBr, cm^{-1}) 2928, 1727, 1238, 1208, 1143, 708, 657; MS m/z 502 (M^+, 100%), 356 (24), 327 (60), 69 (33); HRMS calcd for $C_9H_4F_{13}IO$ 501.9100, found 501.9120.

*4.2.7. 3-Iodo-4-perfluorohexyl-2-butanone (**2g**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.47 (s, 3H, CH_3), 2.63 (m, 1H, $C_6F_{13}CHH$), 3.40 (m, 1H, $C_6F_{13}CHH$), 4.77 (dd, J=3.6, 14.2 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 15.9, 25.8, 36.4 (t, J=20.4 Hz, $C_6F_{13}C$), 199.6; IR (neat, cm^{-1}) 3006, 1723, 1428, 1363, 1239, 1146, 1074, 813, 708; MS m/z 516 (M^+, 11%), 370 (19), 43 (100), HRMS calcd for $C_{10}H_6F_{13}IO$ 515.9256, found 515.9244.

*4.2.8. 3-Iodo-4-perfluorohexyl-2-pentanone (**2h**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.18 (t, J=7.2 Hz, 3H, CH_3), 2.60 (dq, J=17.4, 7.2 Hz, 1H, CH_3CHH), 2.69 (m, 1H, C_6F_3CHH), 3.00 (dq, J=12.0, 7.2 Hz, 1H, CH_3CHH), 3.44 (m, 1H, C_6F_3CHH), 4.77 (dd, J=8.8, 3.6 Hz, 1H, CHI); ^{13}C NMR ($CDCl_3$) δ 8.5, 14.9, 32.1, 36.4 (t, J=20.4 Hz, $C_6F_{13}C$), 203.0; IR (neat, cm^{-1}) 2977, 1707, 1206, 1140, 704; HRMS (ESI$^+$) [M+Na$^+$] calcd for $C_{11}H_8F_{13}INa$ 552.9305, found 552.9307.

*4.2.9. 3-Iodo-4-perfluorohexyl-2-octanone (**2i**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J=6.8 Hz, 3H, CH_3), 1.39–1.26 (m, 4H, $CH_3C_2H_4$), 1.66 (qui, J=7.2 Hz, 2H, $C_3H_7CH_2$), 2.61 (dd, J=16.8, 7.2 Hz, 1H, C_4H_9CHH), 2.63 (m, 1H, C_6F_3CHH), 2.91 (dd, J=16.8, 7.2 Hz, 1H, C_4H_9CHH), 3.44 (m, 1H, C_6F_3CHH), 4.75 (dd, J=10.2, 3.2 Hz, 1H, CHI); ^{13}C NMR ($CDCl_3$) δ 13.8, 15.7, 22.3, 23.8, 31.0, 36.3 (t, J=21.0 Hz, $C_6F_{13}C$), 38.9, 202.3; IR (neat, cm^{-1}) 2960, 1715, 1352, 1245, 1145, 701; HRMS (ESI$^+$) [M+Na$^+$] calcd for $C_{14}H_{14}F_{13}INa$ 594.9774, found 594.9760.

*4.2.10. N,N-Dimethyl-2-iodo-3-perfluorohexylbutanamide (**2j**).* White powder; mp 50.7 °C (from hexane/AcOEt 5:1); ^{1}H NMR ($CDCl_3$) δ 2.74 (m, 1H, $C_6F_{13}CHH$), 2.99 (s, 3H, CH_3), 3.06 (s, 3H, CH_3), 3.58 (m, 1H, $C_6F_{13}CHH$), 4.78 (dd, J=3.1, 9.4 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 4.9, 36.8, 37.7, 38.4 (t, J=19.4 Hz, $C_6F_{13}C$), 168.6; IR (KBr, cm^{-1}) 3020, 1658, 1362, 1243, 1216, 1146, 757, 668; MS m/z 545 (M^+, 51%), 419 (14), 418 (100), 390 (84); HRMS calcd for $C_{11}H_9F_{13}INO$ 544.9522, found 544.9515.

*4.2.11. 2-Iodo-3-perfluorohexylpropionitrile (**2k**).* White powder; mp 59.8 °C (from hexane/AcOEt 5:1); ^{1}H NMR ($CDCl_3$) δ 2.88 (m, 1H, $C_6F_{13}CHH$), 3.12 (m, 1H, $C_6F_{13}CHH$), 4.50 (dd, J=4.4, 10.4 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ –20.3 (t, J=4.8 Hz, $C_6F_{13}CH_2C$), 40.3 (t, J=21.4 Hz, $C_6F_{13}C$), 117.7; IR (KBr, cm^{-1}) 2974, 1238, 1209, 1192, 1142, 799, 707, 527; MS m/z 499 (M^+, 100%), 372 (81), 180 (38), 69 (56); HRMS; calcd for $C_9H_3F_{13}IN$ 498.9103, found 498.9119.

*4.2.12. (1-Iodo-2-perfluorohexylethyl)sulfonylbenzene (**2l**).* White powder; mp 46.2 °C (from CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 2.80 (m, 1H, $C_6F_{13}CHH$), 3.41 (m, 1H, $C_6F_{13}CHH$), 5.01 (dd, J=1.6, 10.4 Hz, 1H, CH), 7.57 (t, J=7.6 Hz, 2H, Ph), 7.69 (t, J=7.6 Hz, 1H, Ph), 7.92 (d, J=7.6 Hz, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ 21.2, 35.2 (t, J=21.3 Hz, $C_6F_{13}C$), 129.4, 130.0, 133.6, 135.1; IR (KBr, cm^{-1}) 2975, 1450, 1368, 1335, 1239, 1210, 1083, 1073, 739, 709, 537, 525; MS m/z 614 (M^+, 23%), 125 (100), 77 (52); HRMS calcd for $C_{14}H_8F_{13}IO_2S$ 613.9083, found 613.9055.

*4.2.13. Ethyl (E)-2-perfluorohexyl-3-phenyl-2-propenoate (**3**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.17 (t, J=7.2 Hz, 3H, CH_3), 4.23 (q, J=7.2 Hz, 2H, CH_2), 7.30 (s, 1H, CH), 7.38 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.5, 62.1, 123.5 (t, J=22.3 Hz, $C_6F_{13}C$), 128.7, 128.9, 130.3, 132.5, 141.2 (t, J=8.7 Hz, $C_6F_{13}C{=}C$), 163.6 (t, J=2.0 Hz, C=O); IR (neat, cm^{-1}) 2989, 1739, 1734, 1641, 1452, 1362, 1235, 1199, 1146, 1082, 1026, 806, 697, 667; MS m/z 449 (M^+–OEt, 38), 449 (21), 177 (81), 84 (100); HRMS calcd for $C_{15}H_6F_{13}O$ 449.0211, found 449.0229.

*4.2.14. Diethyl 4,4-difluoro-2-iodopentanedioate (**4a**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.29 (t, J=7.2 Hz, 3H, CH_3), 1.37 (t, J=7.2 Hz, 3H, CH_3), 2.73 (m, 1H, CF_2CHH), 3.23 (m, 1H, CF_2CHH), 4.26 (q, J=7.2 Hz, 2H, OCH_2), 4.33 (q, J=7.2 Hz, 2H, OCH_2), 4.57 (dd, J=3.6, 10.0 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 7.2 (t, J=4.9 Hz, CF_2CH_2C), 13.6, 13.9, 41.6 (t, J=23.1 Hz, CF_2C), 62.3, 63.3, 114.2 (t, J=251.6 Hz, CF_2), 162.8 (t, J=31.3 Hz, $CF_2C{=}O$), 170.4; IR (neat, cm^{-1}) 2987, 1770, 1736, 1376, 1304, 1198, 1132, 1093, 1016, 855; MS m/z 350 (M^+, 19%), 304 (73),

249 (41), 223 (92), 195 (83), 167 (100); HRMS calcd for $C_9H_{13}F_2IO_4$ 349.9827, found 349.9799.

*4.2.15. Benzyl 2-iodo-4-trifluoromethylbutanoate (**4b**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.77 (m, 1H, CF_3CHH), 3.26 (m, 1H, CF_3CHH), 4.54 (dd, J=4.4, 9.8 Hz, 1H, CH), 5.20 (s, 2H, $PhCH_2$), 7.37 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 5.9 (q, J=3.3 Hz, CF_3CH_2C), 41.1 (q, J=29.7 Hz, CF_3C), 68.1, 125.2 (q, J=275.5 Hz, CF_3), 128.3, 128.6, 134.6, 169.7; IR (neat, cm^{-1}) 3037, 1734, 1457, 1260, 1151, 969, 753, 698; MS m/z 231 (M^+–I, 84%), 107 (66), 91 (100); HRMS calcd for $C_{11}H_{10}F_3O_2$ 231.0632, found 231.0654.

*4.2.16. Benzyl 2-iodo-3-perfluoropropylbutanoate (**4c**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.68 (m, 1H, C_3F_7CHH), 3.32 (m, 1H, C_3F_7CHH), 4.65 (dd, J=4.0, 10.8 Hz, 1H, CH), 5.19 (d, J=12.4 Hz, 1H, PhC*H*H), 5.22 (d, J=12.4 Hz, 1H, PhCH*H*), 7.37 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 4.9 (t, J=3.3 Hz, $C_3F_7CH_2C$), 38.2 (t, J=20.6 Hz, C_3F_7C), 68.2, 128.3, 128.6, 128.7, 134.6, 169.9; IR (neat, cm^{-1}) 3038, 1739, 1354, 1225, 1186, 1127, 909, 737, 698; MS m/z 331 (M^+–I, 71%), 107 (65), 91 (100); HRMS calcd for $C_{13}H_{10}F_7O_2$ 331.0569, found 331.0591.

*4.2.17. Benzyl 2-iodo-3-perfluoroisopropylbutanoate (**4d**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.69 (m, 1H, $^iC_3F_7CHH$), 3.42 (m, 1H, $^iC_3F_7CHH$), 4.66 (dd, J=3.2, 11.2 Hz, 1H, CH), 5.18 (d, J=12.8 Hz, 1H, PhC*H*H), 5.20 (d, J=12.8 Hz, 1H, PHCH*H*), 7.37 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 6.6 (d, J=4.2 Hz, $^iC_3F_7CH_2C$), 35.8 (d, J=18.9 Hz, $^iC_3F_7C$), 68.2, 128.4, 128.5, 128.6, 134.5, 169.9; IR (neat, cm^{-1}) 3038, 1743, 1648, 1225, 1154, 1120, 1054, 697; MS m/z 331 (M^+–I, 67%), 107 (67), 91 (100); HRMS calcd for $C_{13}H_{10}F_7O_2$ 331.0569, found 331.0544.

*4.2.18. Ethyl 2-(perfluorohexylmethyl)-2-propenoate (**6a**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.32 (t, J=7.2 Hz, 3H, CH_3), 3.19 (t, J=18.6 Hz, 2H, $^iC_3F_7CH_2$), 4.25 (q, J=7.2 Hz, 2H, OCH_2), 5.90 (s, 1H, =C*H*H), 6.55 (s, 1H, =CH*H*); ^{13}C NMR ($CDCl_3$) δ 14.2, 32.4 (t, J=22.4 Hz, $C_6F_{13}C$), 61.5, 129.4, 131.9, 165.5; IR (neat, cm^{-1}) 2990, 1729, 1639, 1366, 1319, 1241, 1067, 1027, 964, 813, 701; MS m/z 432 (M^+, 12%), 405 (16), 387 (100), 313 (28), 113 (61); HRMS calcd for $C_{12}H_9F_{13}O_2$ 432.0395, found 432.0397.

*4.2.19. Ethyl 2-(perfluorohexylmethyl)-4-phenyl-2-butenoate (**6b**).* E/Z=54:46 mixture; colorless oil; ^{13}C NMR ($CDCl_3$) δ 14.2 (2C), 28.1 (t, J=23.3 Hz, $C_6F_{13}C$), 35.4 (t, J=19.3 Hz, $C_6F_{13}C$), 35.6, 36.4, 61.2, 61.5, 121.2, 121.8, 126.7, 127.0, 128.7 (2C), 128.9, 129.0, 137.9, 139.2, 147.8, 149.0, 166.2, 166.5; IR (neat, cm^{-1}) 2987, 1717, 1653, 1365, 1307, 1241, 1146, 760, 707; MS m/z 522 (M^+, 100%), 477 (49), 476 (46), 449 (81); HRMS: calcd for $C_{19}H_{15}F_{13}O_2$ 522.0864, found 522.0850. *E*-isomer: major isomer; ^{1}H NMR ($CDCl_3$) δ 1.30 (q, J=7.2 Hz, 3H, CH_3), 3.56 (t, J=18.4 Hz, 2H, $C_6F_{13}CH_2$), 3.59 (d, J=7.6 Hz, 2H, $PhCH_2$), 4.23 (q, J=7.2 Hz, 2H, OCH_2), 7.17–7.35 (m, 6H, CH, Ph); *Z*-isomer: minor isomer; ^{1}H NMR ($CDCl_3$) δ 1.30 (q, J=7.2 Hz, 3H, CH_3), 3.16 (t, J=18.8 Hz, 2H, $C_6F_{13}CH_2$), 3.95 (d, J=7.6 Hz, 2H, $PhCH_2$), 4.29 (q, J=7.2 Hz, 2H, OCH_2), 6.35 (t, J=7.2 Hz, 1H, CH), 7.17–7.35 (m, 5H, Ph).

*4.2.20. (Z)-2-(Perfluorohexylmethyl)-4-phenyl-2-butenenitrile (**6c**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 3.03 (t, J=17.6 Hz, 2H, $C_6F_{13}CH_2$), 3.80 (d, J=7.6 Hz, 2H, $PhCH_2$), 6.61 (t, J=7.6 Hz, 1H, CH), 7.20 (d, J=8.0 Hz, 2H, Ph), 7.27 (t, J=8.0 Hz, 1H, Ph), 7.34 (t, J=8.0 Hz, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ 35.8 (t, J=22.4 Hz, $C_6F_{13}C$), 38.2, 103.0, 116.1, 127.1, 128.3, 128.9, 136.1, 154.3; IR (neat, cm^{-1}) 3034, 2226, 1604, 1498, 1456, 1434, 1352, 1239, 1146, 738, 699; MS m/z 475 (M^+, 53%), 156 (100); HRMS: calcd for $C_{17}H_{10}F_{13}N$ 475.0605, found 475.0583.

*4.2.21. Diethyl 2-(perfluorohexylmethyl)-2-butenenedioate (**6d**).* (*E*)-Isomer: minor, less polar isomer; colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.32 (t, J=6.8 Hz, 3H, CH_3), 1.34 (t, J=6.8 Hz, 3H, CH_3), 3.90 (t, J=18.8 Hz, 2H, $C_6F_{13}CH_2$), 4.27 (q, J=6.8 Hz, 2H, OCH_2), 4.31 (q, J=6.8 Hz, 2H, OCH_2), 7.09 (s, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 14.2 (2C), 28.0 (t, J=21.4 Hz, $C_6F_{13}C$), 61.6, 62.5, 133.2, 135.1, 165.0, 165.7; IR (neat, cm^{-1}) 2990, 1734, 1730, 1239, 1205, 1145, 1126, 1072, 1033, 735, 708; MS m/z 504 (M^+, 9%), 459 (97), 430 (75), 161 (100); HRMS: calcd for $C_{15}H_{13}F_{13}O_4$ 504.0606, found 504.0590; (*Z*)-isomer: major, more polar isomer; Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.31 (t, J=7.6 Hz, 6H, CH_3 ×2), 3.18 (t, J=18.0 Hz, 2H, $C_6F_{13}CH_2$), 4.24 (q, J=7.6 Hz, 2H, OCH_2), 4.29 (q, J=7.6 Hz, 2H, OCH_2), 6.24 (s, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.2, 35.2 (t, J=22.3 Hz, $C_6F_{13}C$), 61.6, 62.2, 130.8, 133.5, 164.5, 166.1; IR (neat, cm^{-1}) 2990, 1739, 1733, 1382, 1352, 1190, 1146, 1096, 1032, 829, 812, 733, 708; MS m/z 504 (M^+, 5%), 459 (25), 431 (100); HRMS: calcd for $C_{15}H_{13}F_{13}O_4$ 504.0606, found 504.0585.

*4.2.22. Ethyl 1-perfluorohexyl-2-(perfluorohexylmethyl)-2-propenoate (**7**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ1.37 (3H, t, J=7.6 Hz, OCH_2CH_3), 3.52 (2H, m, $C_6F_{13}CH_2$), 4.34 (2H, q, J=7.6 Hz, OCH_2), 6.99 (1H, m, $C_6F_{13}CH$=C); ^{13}C NMR ($CDCl_3$) δ 13.8, 28.8 (t, J_{C-F}=57.4 Hz, $C_6F_{13}C$), 63.2, 129.4 (t, J_{C-F}=60.8 Hz, $C_6F_{13}C$), 164.4; MS m/z 705 (M^+–OEt, 100%); HRMS calcd for $C_{16}H_3O_2F_{26}$ ([M-OEt]$^+$) 704.9769, found 704.9749.

4.3. Synthesis of ethyl 2-(perfluorohexylmethyl)-4-pentenoate (8)

To a solution of iodide **2a** (0.15 mmol) in dry CH_2Cl_2 (1.5 cm^3) were added allyltributyltin (0.30 mmol, 2 equiv) and Et_3B (1.06 mol dm^{-3} in hexane; 0.15 mmol, 1 equiv). The mixture was stirred at room temperature for 3 h. KF and water were added and the reaction mixture was stirred at room temperature for 3 h. After filtration, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel to give the product in 79% yield. ^{1}H NMR ($CDCl_3$) δ 1.27 (3H, t, J=7.3 Hz, OCH_2CH_3), 2.18 (1H, m, $C_6F_{13}CHH$), 2.34 (1H, m, CH_2=CHCH*H*), 2.46 (1H, m, CH_2=CHCH*H*), 2.67 (1H, m, $C_6F_{13}CHH$), 2.88 (1H, m, $C_6F_{13}CH_2CHCO_2$), 4.18 (2H, q, J=7.3 Hz, OCH_2), 5.11 (2H, m, CH_2=CH), 5.71 (1H, m, CH_2=C*H*); ^{13}C NMR ($CDCl_3$) δ 14.1, 36.9, 61.1, 118.6, 133.5, 173.5; IR (neat, cm^{-1}) 2934, 1742, 1241, 1193, 1146, 732, 708, 698, 655, 568; MS m/z 460 (M^+, 100%); HRMS calcd for $C_{14}H_{13}O_2F_{13}$ 460.0708, found 460.0732.

4.4. Typical procedure for iodoperfluoro alkylation–elimination

In a Pyrex glass tube were placed olefin (0.2 mmol), perfluoroalkyl iodide (1.0 mmol), and CH_2Cl_2 (5 mL). Then $Na_2S_2O_3$ (0.5 mmol, 79 mg) and water (1 mL) were added to the mixture. After sealing the tube, the mixture was shaked and then irradiated with a Hg lamp at room temperature. After the reaction was completed, DBU (0.3 mmol, 45 μL) was added and the reaction mixture was stirred at room temperature. The reaction mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography to afford pure product.

*4.4.1. Ethyl (E)-3-perfluorohexylpropenoate (**9a**).* Colorless oil; isomer; ^{1}H NMR ($CDCl_3$) δ 1.34 (q, J=7.6 Hz, 2H, CH_3), 4.29 (q, J=7.6 Hz, 2H, OCH_2), 6.53 (td, J=2.0, 15.6 Hz, 1H, =CH), 6.85 (td, J=11.6, 15.6 Hz, 1H, =CH); ^{13}C NMR ($CDCl_3$) δ 14.1, 61.8, 130.59 (t, J=24.0 Hz, $C_6F_{13}C$), 130.8 (t, J=9.0 Hz, C_6F_{13}=*C*), 163.4; IR (neat, cm^{-1}) 2991, 1738, 1371, 1319, 1240, 1199, 1146, 1031, 977, 720, 706, 535; MS m/z 373 (M^+–OEt, 100%), 371 (14), 354 (6); HRMS: calcd for $C_9H_2F_{13}O$ 372.9898, found 372.9884.

*4.4.2. Ethyl (E)-3-perfluorohexyl-2-butenoate (**9b**).* Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.32 (t, J=7.2 Hz, 3H, CH_2CH_3), 2.27 (s, 3H, CH_3), 4.24 (q, J=7.2 Hz, 2H, CH_2), 6.30 (s, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 13.6, 14.4,

61.5, 125.8 (t, J=8.9 Hz, $C_6F_{13}C$=C), 143.2 (t, J=21.5 Hz, $C_6F_{13}C$=C), 165.6; IR (neat, cm^{-1}) 2990, 1734, 1666, 1450, 1354, 1202, 1041, 888, 809, 746, 702, 648; MS m/z 432 (M^+, 26%), 404 (32), 387 (90), 58 (100); HRMS: calcd for $C_{12}H_9F_{13}O_2$ 432.0395, found 432.0415.

*4.4.3. (E)-N,N-Dimethyl-3-perfluorohexylpropenamide (**9c**).* Colorless oil; ^1H NMR ($CDCl_3$) δ 3.06 (s, 3H, CH_3), 3.14 (s, 3H, CH_3), 6.78 (td, J=13.2, 13.2 Hz, 1H, C*H*=CH), 7.02 (d, J=13.2 Hz, 1H, CH=C*H*); ^{13}C NMR ($CDCl_3$) δ 35.9, 37.4, 128.1 (t, J=22.3 Hz, $C_6F_{13}C$), 129.9 (t, J=7.8 Hz, C_6F_{13}CH=*C*), 163.2; IR (neat, cm^{-1}) 2942, 1679, 1645, 1499, 1404, 1366, 1239,1146, 1068, 970, 717; MS m/z 417 (M^+, 58%), 398 (28), 373 (35), 370 (39); HRMS calcd for $C_{11}H_8F_{13}NO$ 417.0398, found 417.0360.

4.5. Synthesis of ethyl 2-(perfluorohexylmethyl)-3-acetylaminopropane (11)

To a solution of olefin **9a** (0.2 mmol) in dry MeOH (4.0 cm^3) was added BnNHOH/HCl (0.22 mmol, 1.1 equiv) and Et_3N (0.4 mmol, 2 equiv). The mixture was stirred at room temperature for 8 h. After filtration, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel to give ethyl 2-(perfluorohexylmethyl)-3-*N*-benzylhydroxylaminopropane (**10**) in 89% yield. ^1H NMR ($CDCl_3$) δ 1.27 (t, 3H, J=7.2 Hz, Me), 2.39 (m, 1H, C_6F_{13}CH*H*), 2.67 (m, 1H, C_6F_{13}C*H*H), 2.92 (m, 1H, NCH*H*), 3.00 (m, 1H, NC*H*H), 3.20 (m, 1H, CH), 3.84 (d, 1H, J=12.0 Hz, PhH*H*), 3.86 (d, 1H, J=12.0 Hz, Ph*H*H), 4.19 (q, 2H, J=7.2 Hz, OCH_2), 4.87 (br s, 1H, OH), 7.33 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.0, 37.1, 60.9, 61.2, 65.0, 127.6, 128.4, 129.2, 172.7; IR (neat, cm^{-1}) 3414, 1733, 1652, 1240, 1200; HRMS (ESI^+) [M+H^+] calcd for $C_{19}H_{19}F_{13}NO_3$ 556.1157, found 556.1135.

To a solution of hydroxylamine **10** (0.2 mmol) in MeOH (5.0 cm^3) was added Pd/C (10%, 100 mg) and stirred under H_2 atmosphere at room temperature for 8 h. After filtration, the solvent was evaporated in vacuo. The residue was dissolved in dry CH_2Cl_2 (2.0 cm^3) and cooled to 0 °C. Then Et_3N (0.42 mmol, 2.1 equiv) and Ac_2O (0.42 mmol, 2.1 equiv) were sequentially added. After stirred at room temperature for 3 h, the mixture was evaporated in vacuo. The residue was purified by flash chromatography on silica gel to give ethyl 2-(perfluorohexylmethyl)-3-acetylaminopropane (**11**) in 70% yield. ^1H NMR ($CDCl_3$) δ 1.29 (t, 3H, J=7.2 Hz, CH_2CH_3), 2.00 (s, 3H, $C(O)CH_3$), 2.29 (m, 1H, C_6F_{13}CH*H*), 2.63 (m, 1H, C_6F_{13}C*H*H), 3.04 (m, 1H, CH), 3.56 (m, 2H, NCH_2), 4.21 (q, 2H, J=7.2 Hz, OCH_2), 5.86 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 14.0, 23.2, 38.4, 40.8, 61.6, 170.3, 172.7; IR (neat, cm^{-1}) 3320, 3099, 2998, 1732, 1658; HRMS (ESI^+) [M+Na^+] calcd for $C_{14}H_{14}F_{13}NO_3Na$ 514.0664, found 514.0644.

4.6. Photoinduced reaction of perfluoroalkyl ioded with TEMPO (12)

In a Pyrex glass tube were placed perfluoroalkyl iodide (0.1 mmol), TEMPO (0.1 mmol) and CH_2Cl_2 (2.5 mL). After sealing the tube, the mixture was shaked and then irradiated with a Hg lamp at room temperature for 1 h. After the reaction was completed, the mixture was concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography to afford pure product (**12**). ^1H NMR ($CDCl_3$) δ 1.19 (s, 12H, $CH_3\times4$), 1.55–1.64 (m, 6H, $CH_2\times3$); ^{13}C NMR ($CDCl_3$) δ 16.8, 20.7, 33.5 (t, J=4.8 Hz, OC), 40.4, 61.9; HRMS (ESI^+) [M+H^+] calcd for $C_{15}H_{19}F_{13}NO$ 5476.1254, found 476.1248.

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References and notes

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