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α-Fluoroalkylation of carbonyl compounds mediated by a highly reactive alkyl-rhodium complex

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ABSTRACT

Treatment of silyl enol ethers of various carbonyl compounds with Et_2Zn and fluoroalkyl halides (R_f–X) in the presence of $RhCl(PPh_3)_3$ in DME gave the corresponding α-R_f carbonyl compounds. A highly reactive alkyl-rhodium complex which was derived from $RhCl(PPh_3)_3$ and Et_2Zn must be crucial in this reaction by accelerating the reaction rate and improving the yields dramatically. This reaction overcomes difficulties on the synthesis of α-R_f carbonyl compounds due to inverse polarization of R_f–X.

1. Introduction

In the search for various medicinal candidates, a synthesis of designed proteins and/or peptides has become an important project. Fluorinated amino acids, especially α-fluoroalkylated amino acids, are more stable than the corresponding non-fluorinated counterparts, and often used for these purposes [1]. However the effective syntheses of the fluorine-containing compounds, especially which have a fluoroalkyl (R_f) group at the α-position of a carbonyl group, are limited, and the development of their new synthetic methodology is highly desired [2–5]. The reason of the difficulty of the synthesis of α-R_f carbonyl compounds is attributed that the polarization of fluoroalkyl halides ($R_f^{\delta-}$–$X^{\delta+}$) is opposite to that of the alkyl halides ($R^{\delta+}$–$X^{\delta-}$), which makes it difficult to introduce R_f^+ unit to enolates [6]. Although Mikami and co-workers have already reported α-trifluoromethylation of ketones by using Li, Ti, or Zn enolates assisted by Et_3B/O_2, their applications were limited to aliphatic ketones [7]. More recently, MacMillan and co-workers reported α-fluoroalkylation of aldehydes via the enamines by using a photoredox catalyst under the visible light [8]. This methodology is a very innovative reaction, but the reaction vessel was needed to place near luminous source at under a cool bath.

Recently, we reported an α-trifluoromethylation of carbonyl compounds via trimethylsilyl enol ethers mediated by a highly reactive alkyl-rhodium complex that was derived from $RhCl(PPh_3)_3$ and Et_2Zn (Scheme 1) [9]. The reaction smoothly proceeded and gave various α-CF_3 carbonyl compounds in good yields. Thus, our reaction provided one of a breakthrough for the synthesis of them.

In this paper, we would like to report a further expansion of the scope of this reaction mediated by a highly reactive alkyl-rhodium complex to the synthesis of α-fluoroalkylated carbonyl compounds.

2. Results and discussion

2.1. Synthesis of α-fluoroalkylated ketones

Based on the previous condition [9b], various R_f–X (**1**) and 1-(trimethylsiloxy)cyclohexene as a model compound of the silyl enol ethers were treated with Et_2Zn in the presence of $RhCl(PPh_3)_3$. The results are summarized in Table 1.

As shown in entries 1–3, perfluoroalkyl iodides (**1a–c**) gave the corresponding products in moderate to good yields, although a mixture of **4a** and **5a** was obtained in entry 1. The latter was assumed to be formed during the work-up. We confirmed this by treating the mixture with alumina (pH = 9.0–11.0) overnight before purification. As expected, the dehydrofluorination of **4a** occurred and only **5a** was obtained. Since the ratio of **4a** and **5a** varied depending on a slight differences in the work-up conditions, here is only shown the yield of **5a** after complete dehydrofluorination. Interestingly, $C_{10}F_{21}$ group did not lead to the dehydro-

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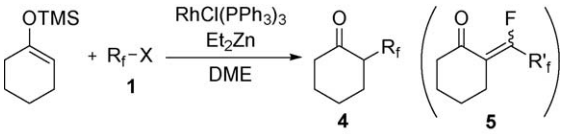
Table 1
α-Fluoroalkylation of cyclohexanone via its silyl enol ether.



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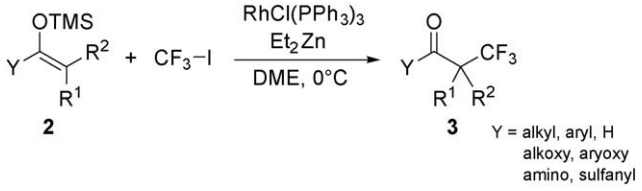
Entry	R_f–X	Temp. (°C)	Time (h)	Product	Yield (%)[a]
1	C_4F_9–1	0 to r.t.	24	**5a**	54 (66)[b,c]
2	$C_{10}F_{21}$–I	0	2	**4b**	77
3	C_6F_5–CF_2–I	0	23	**4c**	60
4	EtOOCCF$_2$–Br	0	5	**4d**	70 (82)[d]
5	EtOOCCF$_2$–Cl	0 to r.t.	24	**4d**	n.r.

[a] Isolated yield.
[b] ^{19}F NMR yield of the product (**5a**) calculated based on benzotrifluoride (BTF) as an internal standard.
[c] A mixture of the products was treated with alumina overnight.
[d] ^{19}F NMR yield calculated based on BTF as an internal standard.



Scheme 1.

fluorination contrary to the case of C_4F_9 group (entry 2). It may be attributed to the inflexibility of $C_{10}F_{21}$ group to form the rigid structure. On the other hand, ethyl bromodifluoroacetate (**1d**) gave the desired product (**4d**) in a good yield, while the reaction did not proceed with ethyl chlorodifluoroacetate (**1e**) even if the temperature was risen to room temperature (entries 4 and 5).

We have also reported that the α-fluoroalkylation of ketones proceeded by heating in 1,4-dioxane only in the presence of $RhCl(PPh_3)_3$ using the corresponding silyl enol ethers [10]. However the yield of products was low and dehydrofluorination also was observed in most cases because of the harsh condition in the previous report.

On the other hand, the addition of Et_2Zn improved the yield considerably, and suppressed the dehydrofluorination. The addition effect of Et_2Zn would be understood by our previous α-trifluoromethylation mechanism as shown in Fig. 1 [9b]. Namely, the oxidative addition of CF_3–I onto the highly reactive ethylrhodium complex (**6**), which was derived from $RhCl(PPh_3)_3$ and Et_2Zn, to form a Rh(III) complex (**7**) was followed by the coordination onto the π-bond of silyl enol ether (**2**). By subsequent insertion of the CF_3 unit into the olefin, another Rh(III) complex (**9**) was formed, which suffered from the reductive elimination to give the desired α-CF_3 product (**3**) along with loss of ethyltrimethylsilane (TMS–Et) or trimethylsilane (TMS–H) and ethylene.

We believe that this α-fluoroalkylation must proceed through the same mechanism. The oxidative addition of Cl–CF_2COOEt onto the complex (**6**) would be difficult due to the hard C–Cl bond, and this is the reason of non-reactivity of the Cl-ester, as shown in entry 5 in Table 1.

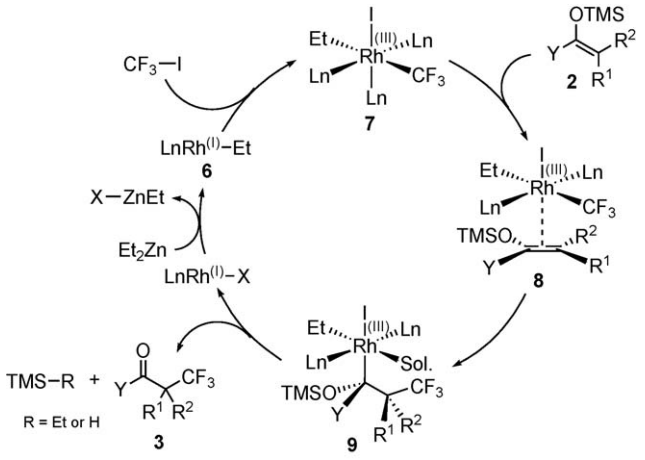


Fig. 1. Reaction mechanism of Rh-catalyzed α-trifluoromethylation.

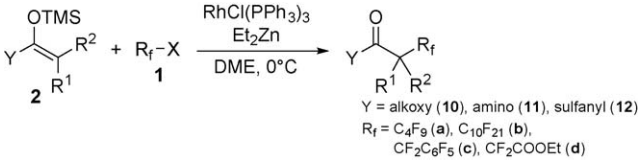
2.2. Synthesis of various α-fluoroalkylated carbonyl compounds

Next, we examined the several substrates for α-fluoroalkylation, and the results are summarized in Table 2. The yields and the reaction rates are well accorded with the order of electron density of the π-bond of the corresponding silyl enol ethers. Especially, the *N*,*O*-silyl ketene acetal from *N*-methyl-*N*-phenylisobutyramide reacted, though it has two methyl groups at the olefinic position that might cause a steric hindrance. In addition, it might be another reason of the low reactivity why there is less electron donation from nitrogen owing to the distortion by steric repulsion between TMS and amino groups. This result suggests that more electron rich silyl enol ethers would become to easily coordinate to the complex (**7**). Furthermore, it is understandable that the size of R_f–X also affects the yield.

On the other hand, the dehydrofluorinated product (**5a**) was obtained in a considerable yield in the reaction of C_4F_9–I with 1-(trimethylsiloxy)cyclohexene as mentioned above (entry 1 in Table 1). This result would be attributed to the enhanced acidity of α-hydrogen between ketone and R_f group, and this dehydrofluorination was suppressed in α-C_4F_9 ester (**10a**). This tendency becomes prominent by changing the functional group, and α-C_4F_9 thioester (**12a**) was obtained without dehydrofluorination.

Based on these results, we next tried to use the silyl enol ether derived from an aldehyde. An effective α-fluoroalkylation of aldehydes has hardly ever reported, while most of them suffer from cross-coupling reactions with sp^2-halides [11], radical reactions [12] or photochemical reaction [13]. The present transformation will become more useful from the above results, if the reactions would proceed with silyl enol ethers of aldehydes to give α-R_f aldehydes. As shown in Table 3, the increase of reaction rates was confirmed as expected, while the higher acidity of the α-hydrogen caused the dehydrofluorination of the products, α-R_f

Table 2
Various α-fluoroalkylated carbonyl compounds.



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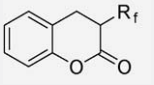
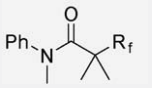
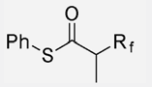
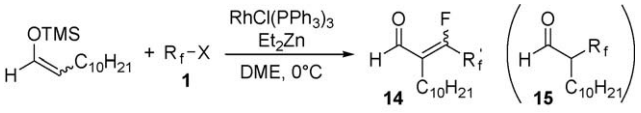
Entry	Product		Time (h)	Yield (%)[a]
1		C_4F_9 (**10a**)	3	44[b]
2		$C_{10}F_{21}$ (**10b**)	7	32
3		$CF_2C_6F_5$ (**10c**)	5	44
4		CF_2COOEt (**10d**)	3	66°
5		C_4F_9 (**11a**)	3	39
6		$C_{10}F_{21}$ (**11b**)	3	27
7		$CF_2C_6F_5$ (**11c**)	2	29
8		CF_2COOEt (**11d**)	3	42[c]
9		C_4F_9 (**12a**)	3	34
10		$C_{10}F_{21}$ (**12b**)	5	21
11		$CF_2C_6F_5$ (**12c**)	2	0
12		CF_2COOEt (**12d**)	3	0[c]

[a] Isolated yield.
[b] Dehydrofluorinated product (**13a**) was isolated in 14% as the by-product along with **10a**.
[c] $BrCF_2COOEt$ (**1d**) was used as the starting material.

Table 3
α-Fluoroalkylation of aldehydes.



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Entry	R_f–X	Temp. (°C)	Time (h)	Product	Yield (%)[a]
1	C_4F_9–I	0	1	**14a**	51
2	$C_{10}F_{21}$–I	0	1	**14b**	38
3	C_6F_5–CF_2–I	0	2	**14c**	24
4	$EtOOCCF_2$–Br	0	1	**14d**	0

[a] Isolated yield.

aldehydes (**14**). Unfortunately, the yields were not improved owing to the less stability and the higher reactivity, but we could confirm the formation of α-R_f aldehydes (Table 3).

3. Conclusions

We obtained various α-R_f carbonyl compounds which have been difficult to synthesize, especially it is rare for the direct α-fluoroalkylation of thioesters and aldehydes. Most results relevant to this α-fluoroalkylation supported the previous proposed mechanism which was mediated by a highly reactive alkyl-rhodium complex. Since the α-fluoroalkylation reaction can be widely applicable to various silyl enol ethers of carbonyl compounds, we expect that the reaction will play an important role in medicinal and/or material fields.

4. Experimental

4.1. General information

^1H NMR and ^{13}C NMR spectra were recorded on JNM-GX400 spectrometers. ^{19}F NMR spectra were recorded on Hitachi FT-NMR R-90H and JEOL-ECA-600SN spectrometers. Chemical shifts of ^1H NMR and ^{13}C NMR are reported in ppm from tetramethylsilane (TMS) as an internal standard. Chemical shifts of ^{19}F NMR are reported in ppm from benzotrifluoride (BTF) as an internal standard. All data are reported as follows: chemical shifts, relative integration value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; br, broad; m, multiplet), and coupling constants (Hz). Mass spectra were obtained on JEOL JMS-700T spectrometers. IR spectra were recorded on Hitachi 270-30 Infrared spectrophotometer. Melting points were measured on Yanagimoto micro melting point apparatus MP-S3 and uncorrected. Analytical gas–liquid chromatography (GLC) was carried out on Hitachi 263-50 gas chromatograph (column; 5% SE-30 3 mm × 2 m, carrier; N_2 at 30 mL/min). Peak areas were calculated on Shimadzu C-R5A Chromatopac.

The purity of products was certificated by ^1H NMR, and then HRMS was used as substitute for elemental analysis. ^{19}F NMR yields were calculated based on BTF as an internal standard. Dimethoxyethane (DME) was distilled from CaH_2 and stored over MS 4 Å. All commercially available reagents were used without further purification. All experiments were carried out under argon atmosphere unless otherwise noted.

4.2. General procedure

To a solution of $RhCl(PPh_3)_3$ (2 mol%) and ketene silyl acetal (**2**, 1.0 mmol) in DME (5 mL) was added R_f–X (**1**, 1.5 mmol) at 0 °C. Then 1.0 M Et_2Zn in hexane (1 mL, 1.0 mmol) was slowly added, and was stirred at the same temperature. The resulting mixture was quenched with 10% HCl, and extracted with AcOEt. The organic layer was washed with sat. NaCl and dried over $MgSO_4$. The solvent was removed *in vacuo*, then benzotrifluoride (BTF) was added in the residue. The yield was calculated from the integration ratio of the product and BTF on ^{19}F NMR. After the calculation, the residue was purified by column chromatography to give the corresponding α-fluoroalkylated carbonyl compound.

4.3. Spectroscopic data of α-R_f ketones

4.3.1. 2-Octafluorobutylidenecyclohexanone (5a); as the E-Z mixture

A colorless oil; ^1H NMR ($CDCl_3$) δ: 1.84–2.03 (4H, m), 2.56 (2H, t, *J* = 6.7 Hz), 2.62–2.70 (2H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −65.2 (1.6F, m), −64.5 (0.2F, m), −63.6 (0.4F, m), −58.1 (0.8F, m), −52.1 (1.6F, m), −51.9 (0.4F, m), −18.0 (0.6F, m), −17.9 (2.4F, m); MS *m*/*z*: 296 (M^+); HRMS Calcd for $C_{10}H_8OF_8$: 296.045 (M^+), Found: 296.045; IR (neat) cm^{-1}: 1730, 1680, 1356, 1302, 1188.

4.3.2. 2-Henicosafluorodecylcyclohexanone (4b)

Colorless crystals; M.p. 73.5–74.0 °C; ^1H NMR ($CDCl_3$) δ: 1.69–2.09 (5H, m), 2.26 (1H, m), 2.49 (2H, m), 3.20 (1H, m); ^{19}F NMR (90 MHz, $CDCl_3$) δ: −63.8 (2F, m), −59.9 (2F, m), −59.1 (2F, m), −58.9 (8F, m), −57.2 (2F, m), −51.1 (1F, m), −49.4 (1F, m), −18.0 (3F, m); MS *m*/*z*: 616 (M^+); HRMS Calcd for $C_{16}H_9OF_{21}$: 616.032 (M^+), Found: 616.031; IR (KBr) cm^{-1}: 1724, 1216, 1154.

4.3.3. 2-Perfluorobenzylcyclohexanone (4c)

A colorless oil; ^1H NMR ($CDCl_3$) δ: 1.71–1.78 (2H, m), 1.91–2.12 (3H, m), 2.27–2.35 (1H, m), 2.39–2.48 (2H, m), 3.34 (1H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −98.5 (2F, m), −88.5 (1F, m), −76.7 (2F, m), −41.5 (1F, ddt, *J* = 36.2 Hz), −26.0 (1F, dt, *J* = 15.5 Hz); MS *m*/*z*: 314 (M^+); HRMS Calcd for $C_{13}H_9OF_7$: 314.054 (M^+), Found: 314.055; IR (neat) cm^{-1}: 1726, 1372, 1330, 1222, 1038.

4.3.4. Ethyl 2,2-difluoro-2-(2-oxocyclohexyl)acetate (4d)

A colorless oil; ^1H NMR ($CDCl_3$) δ: 1.35 (3H, t, *J* = 7.2 Hz), 1.69 (2H, m), 1.86 (1H, m), 2.08 (2H, m), 2.35 (2H, m), 2.45 (1H, m), 3.33 (1H, m), 4.34 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 23.9, 25.3 (m), 26.5, 41.6 (m), 54.4 (m), 62.7, 114.1 (m), 163.6 (m), 206.4 (m); ^{19}F NMR (90 MHz, $CDCl_3$) δ: −55.3 (1F, dd, *J* = 273.8, 19.4 Hz), −46.2 (1F, dd, *J* = 273.8, 7.6 Hz); MS *m*/*z*: 220 (M^+); HRMS Calcd for $C_{10}H_{14}O_3F_2$: 220.091 (M^+), Found: 220.090; IR (neat) cm^{-1}: 1778, 1760, 1720, 1318, 1222, 1140.

4.4. Spectroscopic data of α-R_f esters

4.4.1. 3-Perfluorobutylchroman-2-one (10a)

A colorless oil; ^1H NMR ($CDCl_3$) δ: 2.80–3.30 (2H, m), 3.62 (1H, m), 7.08–7.35 (5H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −63.3 (2F, m), −57.9 (2F, m), −50.1 (2F, m), −18.1 (3F, m); MS *m*/*z*: 366 (M^+); HRMS Calcd for $C_{13}H_7O_2F_9$: 366.030 (M^+), Found: 366.030; IR (neat) cm^{-1}: 1784, 1360, 1236.

4.4.2. 3-Perfluorodecylchroman-2-one (10b)

Colorless crystals; M.p. 118.0 °C; ^1H NMR ($CDCl_3$) δ: 3.31 (2H, d, *J* = 8.0 Hz), 3.62 (1H, m), 7.10–7.34 (4H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −63.3 (2F, m), −59.9 (2F, m), −59.1 (2F, m), −58.8 (8F, m), −57.5 (2F, m), −51.2 (1F, m), −48.6 (1F, m), −18.0 (3F, m); MS *m*/*z*: 666 (M^+); HRMS Calcd for $C_{19}H_7O_2F_{21}$: 666.011 (M^+), Found: 666.011; IR (KBr) cm^{-1}: 1730, 1346, 1208, 1154, 1108.

4.4.3. 3-Perfluorobenzylchroman-2-one (10c)

A colorless oil; ^1H NMR ($CDCl_3$) δ: 3.39 (2H, m), 3.73 (1H, m), 7.05–7.33 (4H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −23.6 (1F, dt, *J* = 15.5 Hz), −43.4 (1F, ddt, *J* = 38.0 Hz), −76.6 to −76.7 (2F, m), −87.1 (1F, dt, *J* = 20.7 Hz), −97.8 to −97.9 (2F, m); MS *m*/*z*: 364 (M^+); HRMS Calcd for $C_{16}H_7O_2F_7$: 364.033 (M^+), Found: 364.033; IR (neat) cm^{-1}: 1760, 1332, 1258, 1234, 1162, 1094.

4.4.4. Ethyl difluoro-(2-oxochroman-3-yl)acetate (10d)

A colorless oil; ^1H NMR ($CDCl_3$) δ: 1.38 (3H, t, *J* = 7.24 Hz), 3.21 (1H, dd, *J* = 6.2, 6.8 Hz), 3.32 (1H, t, *J* = 14.5 Hz), 3.74 (1H, m), 4.41 (2H, q, *J* = 7.1 Hz), 7.07–7.33 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 22.6 (t, *J* = 4.4 Hz), 63.4, 116.8, 120.6, 125.1, 128.3, 128.6, 150.8, 162.6 (t, *J* = 30.0 Hz), 164.6, 164.7; ^{19}F NMR (90 MHz, $CDCl_3$) δ: −50.1 (2F, ddd, *J* = 19.4, 5.4, 4.6 Hz); MS *m*/*z*: 270 (M^+); HRMS Calcd for $C_{13}H_{12}O_4F_2$: 270.071 (M^+), Found: 270.071; IR (neat) cm^{-1}: 1758, 1334, 1228, 1172, 1108.

4.5. Spectroscopic data of α-R_f amides

4.5.1. 3,3,4,4,5,5,6,6,6-Nonafluoro-N,2,2-trimethyl-N-phenylpropionamide (11a)

A colorless oil; ^1H NMR ($CDCl_3$) δ: 1.20 (6H, s), 3.25 (3H, s), 7.17–7.45 (5H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −63.3 (2F, m), −59.4 (2F, m), −54.7 (2F, m), −17.9 (3F, m); MS *m*/*z*: 395 (M^+); HRMS Calcd for $C_{15}H_{14}ONF_9$: 395.093 (M^+), Found: 395.093; IR (neat) cm^{-1}: 1650, 1596, 1494, 1480, 1236, 1124.

4.5.2. 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-Henicosafluoro-N,2,2-trimethyl-N-phenyl-propionamide (11b)

Colorless crystals; M.p. 80.0–81.0 °C; ^1H NMR ($CDCl_3$) δ: 1.12 (6H, s), 3.25 (3H, s), 7.21–7.43 (5H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −63.3 (2F, m), −59.9 to −60.0 (2F, m), −59.1 (2F, m), −58.7 to −58.9 (8F, m), −53.7 (2F, m), −48.4 (2F, m), −18.0 (3F, m); MS *m*/*z*: 695 (M^+); HRMS Calcd for $C_{20}H_{14}ONF_{21}$: 695.074 (M^+), Found: 695.074; IR (KBr) cm^{-1}: 1656, 1592, 1238, 1143.

4.5.3. 2-Perfluorobenzyl-N,2,2-trimethyl-N-phenylpropionamide (11c)

Colorless crystals; M.p. 79.0–80.0 °C; ^1H NMR ($CDCl_3$) δ: 1.12 (6H, s), 3.21 (3H, s), 7.27–7.43 (5H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −99.0 to −99.1 (2F, m), −88.5 (1F, m), −75.1 to −75.3 (2F, m), −33.3 (2F, t, *J* = 31.0 Hz); MS *m*/*z*: 393 (M^+); HRMS Calcd for $C_{18}H_{14}ONF_7$: 393.096 (M^+), Found: 393.096; IR (KBr) cm^{-1}: 1653, 1586, 1248, 1142.

4.5.4. Ethyl 2,2-difluoro-3,3-dimethyl-4-(N-methyl-N-phenyl)-4-oxoacetate (11d)

Colorless crystals; M.p. 81.0–82.0 °C; ^1H NMR ($CDCl_3$) δ: 1.18 (6H, s), 1.39 (3H, t, *J* = 7.0 Hz), 3.21 (3H, s), 4.38 (2H, q, *J* = 7.0 Hz), 7.24–7.45 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 21.5 (t, *J* = 5.2 Hz), 41.2, 52.6 (dd, *J* = 22.6, 23.2 Hz), 62.2, 116.2 (t, *J* = 255.5 Hz), 128.4, 128.8, 129.4, 143.2, 164.2 (t, *J* = 32.4 Hz), 172.5 (t, *J* = 3.3 Hz); ^{19}F NMR (90 MHz, $CDCl_3$) δ: −50.2 (2F, s); MS *m*/*z*: 299 (M^+); HRMS Calcd for $C_{15}H_{19}O_3NF_2$: 299.133 (M^+), Found: 299.133; IR (KBr) cm^{-1}: 1754, 1652, 1226.

4.6. Spectroscopic data of α-R_f thioesters

4.6.1. S-phenyl 3,3,4,4,5,5,6,6,6-nonafluoro-2-methylhexanethioate (12a)

Colorless crystals; M.p. 41.0 °C; ^1H NMR ($CDCl_3$) δ: 1.53 (3H, d, *J* = 7.0 Hz), 3.56 (1H, m), 7.41–7.45 (5H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −63.2 (2F, m), −58.6 (2F, m), −52.2 (2F, m), −18.2 (3F, m); MS *m*/*z*: 384 (M^+); HRMS Calcd for $C_{13}H_9OF_9S$: 384.022 (M^+), Found: 384.022; IR (KBr) cm^{-1}: 1693, 1392, 1221.

4.6.2. S-phenyl 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-henicosafluoro-2-methyldodecanethioate (12b)

Colorless crystals; M.p. 68.0 °C; ^{1}H NMR ($CDCl_3$) δ: 1.53 (3H, d, J = 7.2 Hz), 3.56 (1H, m), 7.23–7.52 (5H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −63.3 (2F, m), −59.9 to −60.0 (2F, m), −59.2 (2F, m), −58.7 to −58.9 (8F, m), −55.0 (2F, m), −48.8 (2F, m), −18.0 (3F, m); MS m/z: 684 (M^+); HRMS Calcd for $C_{19}H_9OF_{21}S$: 684.004 (M^+), Found: 684.004; IR (KBr) cm^{-1}: 1696, 1394, 1238, 1138.

4.7. Spectroscopic data of α-R_f aldehydes

4.7.1. 2-(1,2,2,3,3,4,4,4-Octafluorobutylidene)dodecanal (14a); as the E–Z mixture

A colorless oil; ^{1}H NMR ($CDCl_3$) δ: 0.89 (3H, t, J = 7.1 Hz), 1.27–1.47 (16H, m), 2.30 (0.5H, m), 2.45 (1.5H, m), 9.98 (0.75H, m), 10.22 (0.25H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −64.7 to −64.4 (2F, m), −53.5 (0.2F, m), −49.5 to −49.4 (2F, m), −44.0 (0.8F, m), −17.7 (3F, m); MS m/z: 382 (M^+); HRMS Calcd for $C_{16}H_{22}OF_8$: 382.154 (M^+), Found: 382.154; IR (neat) cm^{-1}: 2924, 1694, 1228, 1122, 964, 736.

4.7.2. 2-(1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Icosafluorodecylidene)dodecanal (14b); as the E–Z mixture

Colorless crystals; M.p. 46.0 °C; ^{1}H NMR ($CDCl_3$) δ: 0.88 (3H, t, J = 6.5 Hz), 1.27–1.44 (16H, m), 2.31 (0.3H, m), 2.45 (1.7H, m), 9.99 (0.85H, m), 10.22 (0.15H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −63.4 to −63.3 (2F, m), −60.1 (2F, m), −59.9 (2F, m), −59.1-−59.9 (8F, m), −48.4-−48.3 (2F, m), −43.7-−44.6 (1F, m), −18.0 (3F, t, J = 9.7 Hz); MS m/z: 682 (M^+); HRMS Calcd for $C_{22}H_{22}OF_{20}$: 682.135 (M^+), Found: 682.135; IR (KBr) cm^{-1}: 2932, 1694, 1221, 1184.

4.7.3. 2-(1-Fluoro-1-pentafluorophenyl)ethylidenedodecanal (14c); as the E–Z mixture

A colorless oil; ^{1}H NMR ($CDCl_3$) δ: 0.88 (3H, t, J = 7.1 Hz), 1.21–1.51 (16H, m), 2.41–2.45 (2H, m), 10.00 (0.6H, m), 10.22 (0.4H, m); ^{19}F NMR (600 MHz, $CDCl_3$) δ: −93.4 (2F, m), −84.1 (1F, m), −73.9 to −73.8 (2F, m), −16.9 to −16.8 (1F, m); MS m/z: 380 (M^+); HRMS Calcd for $C_{19}H_{22}OF_6$: 380.157 (M^+), Found: 380.157; IR (neat) cm^{-1}: 2928, 2860, 1694, 1652, 1500, 1186.

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