ChemPubSoc Europe

DOI: 10.1002/ejoc.201600088

EurJOC European Journal of Organic Chemistry

Full Paper

Fluorinated Michael Acceptors

Addition of Nucleophiles to Fluorinated Michael Acceptors

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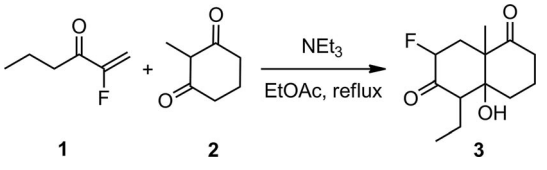
Abstract: A series of nucleophiles, including primary and secondary amines, primary alcohols, and thiols, as well as diethyl malonate and nitromethane, were added to different fluorinated Michael acceptors including 2-fluoroalk-1-en-3-ones and 2-fluoro-1-phenylprop-2-en-1-one. The resulting β-substituted α-fluoro ketones were isolated in 34–92 % yield, depending on the substrate and the nucleophile. The best yields were obtained with secondary amines and with *p*-methylthiophenol.

Introduction

The conjugate addition (1,4-addition) reactions of nucleophiles to the β-position of α,β-unsaturated carbonyl compounds (Michael addition[1]) and to other analogously activated π-systems are very frequently used in organic synthesis.[2] In the prototype reaction, stabilized carbanions add to α,β-unsaturated carbonyl compounds to form carbon–carbon bonds,[3] but hetero-nucleophiles can also be used.[4] The use of amines,[5] alcohols,[6] thiols,[7] or phosphines[8] as Michael donors has extended the scope of the reaction enormously; these nucleophiles can also be used in intramolecular reactions. In recent years, stereoselective Michael reactions for the synthesis of complex molecules have received much attention.[9]

Although fluorine-containing molecules play important roles in life sciences and materials science,[10] less attention has been paid to the use of Michael reactions for the synthesis of fluorinated compounds.[11] In most cases, the fluorine is located in the Michael donor molecules. Thus, in 2008, Prakash, Olah, and their coworkers reported the 1,4-addition of a series of α-substituted fluoro(phenylsulfonyl)methane derivatives to alkyl vinyl ketones and acrylates to form the target 4-fluorocarbonyl compounds.[12] In the same year, Shibata et al. reported the first enantioselective addition of fluorobis(phenylsulfonyl)methane to a series of α,β-unsaturated ketones catalyzed by a cinchona alkaloide.[13] One year later, the groups of Rios,[14] Wang,[15] and Córdova[16] studied the addition of the same molecule asymmetrically to α,β-unsaturated aldehydes, and Prakash, Olah, and coworkers described the related addition of α-fluoro-α-nitro(phenylsulfonyl)methane to chalcones.[17] In 2009, Rios reported the addition of 2-fluoromalonate,[18a] and two years later that of α-fluoro-α-nitro(phenylsulfonyl)methane[18b] to α,β-unsaturated aldehydes. These fluorinated Michael donors were also added enantioselectively to nitroolefins.[19] Recently, some β-trifluoromethylation reactions of α,β-unsaturated carbonyl compounds have been reviewed.[20]

Only a very few Michael additions to α-fluoro α,β-unsaturated carbonyl compounds have been reported to date. In an early report, Normant et al. reported on reactions with lithium dimethyl cuprate to give both 1,2- and 1,4-methylation products.[21] Elkik et al. described the reaction of 2-fluorohex-1-en-3-one (**1**) with 2-methylcyclohexane-1,3-dione (**2**) to give fluorinated ketone **3** by Michael addition and subsequent aldol reaction (Scheme 1), but the products were not fully characterized.[22]



Scheme 1. First reported Michael addition to an α-fluorinated α,β-unsaturated ketone.

Portella and coworkers used perfluorinated enones or their organosilicon synthetic equivalents to prepare heterocycles by reaction with bifunctional Michael donors,[23] and Schlosser et al. reported similar Michael additions of nitrogen, oxygen, and sulfur nucleophiles to monofluorinated α,β-unsaturated acrylates bearing an additional leaving group in the β-position to form various heterocycles.[24] Finally, 2-trifluoromethyl-acrylamides were reported to act as Michael acceptors in their reaction with amino acid esters to form peptidomimetics.[25] To the best of our knowledge, no other Michael additions to 2-fluoro-α,β-unsaturated carbonyl compounds have been reported to date. However, these compounds have frequently been used in other reactions such as [4+2]-cycloadditions[26] or olefin metathesis reactions.[27] In this paper, we present our results con-

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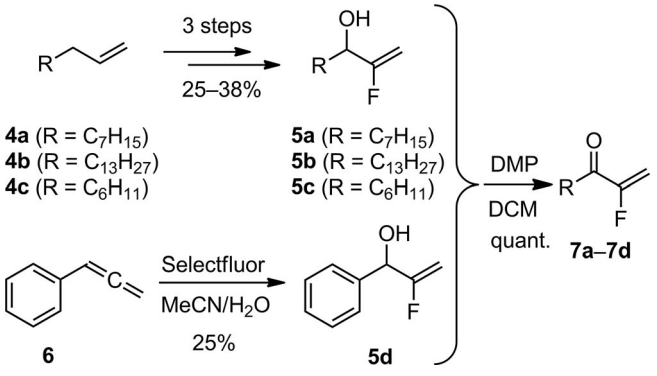
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201600088.

cerning the scope and limitations of the Michael addition of carbon, nitrogen, sulfur, and oxygen nucleophiles to selected 2-fluoro-alk-1-en-3-ones.

Results and Discussion

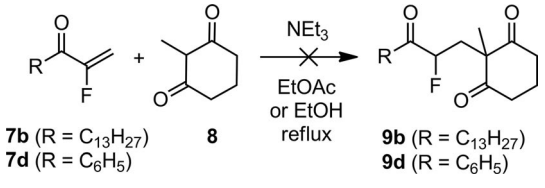
The precursors (i.e., **5a**–**5c**) of Michael acceptors **7a**–**7c** were prepared by our established three-step procedure starting from terminal alkenes **4a**–**4c**. Bromo- or iodofluorination followed by elimination of HBr/HI and subsequent allylic oxidation with SeO_2 yielded the corresponding 2-fluoroallylic alcohols (i.e., **5a**–**5c**).[28] Fluorinated allylic alcohol **5d** was prepared by a known sequence starting with dibromocyclopropanation of styrene, followed by a cyclopropylidene–allene rearrangement using a Grignard reagent to form phenylallene (**6**). Electrophilic fluorination with Selectfluor® in the presence of water resulted in the fluorination of the 2-position and introduction of a hydroxyl group at the benzylic position to give aromatic fluorinated allylic alcohol **5d** (Scheme 2).[29]



Scheme 2. Synthesis of starting 2-fluoroalk-1-en-3-ones **7**.

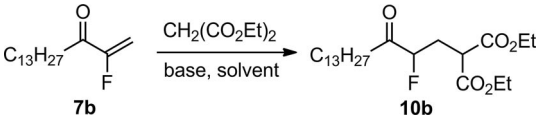
In contrast to earlier oxidations of such fluorinated allylic alcohols by Swern oxidation,[26c,26d] Dess–Martin periodinane (DMP) oxidation resulted in almost quantitative yields of the desired 2-fluoro-α,β-unsaturated carbonyl compounds (i.e., **7a**–**7d**) without purification (Scheme 2).

Ketones **7a**–**7d** were used as acceptors in subsequent Michael reactions. To our regret, acceptors **7b** and **7d** showed no conversion with 2-methylcyclohexane-1,3-dione (**8**) under the reaction conditions (trimethylamine, ethyl acetate, reflux for 8 h) reported before.[22] Leaving the reaction for longer (12 h) or using ethanol as solvent did not lead to any conversion (Scheme 3).



Scheme 3. Attempted Michael addition of 2-methylcyclohexane-1,3-dione (**8**) to **7b** and **7d**.

Therefore, we decided to treat **7b** with diethyl malonate as a typical Michael donor to form a new C–C bond (Scheme 4). Our efforts to find suitable reaction conditions are shown in Table 1.



Scheme 4. Michael addition of **7b** with diethyl malonate.

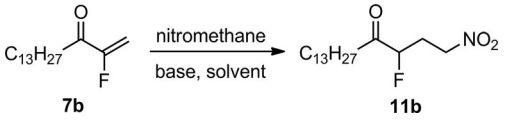
Table 1. Optimization of the conditions for the Michael addition of diethyl malonate to 2-fluorohexadec-1-en-3-one (**7b**) (n.r.: no reaction).

Entry	Base (equiv.)	Solvent	Temp.	Time [h]	Result
1	KOH (1.5)	EtOH	room temp.	6	n.r.
2	$CaCO_3$ (1.5)	EtOH	room temp.	8	n.r.
3	Et_3N (1.5)	EtOH	room temp.	24	n.r.
4	Et_3N (3.0)	EtOAc	reflux	8	n.r.
5	DBU (3.0)	EtOH	reflux	24	5 products
6	K_2CO_3 (1.5)	–	room temp.	3	**10b** (69 %)

Treatment of **7b** with diethyl malonate in the presence of potassium hydroxide or calcium carbonate in ethanol, or in the presence of triethylamine in ethanol or in ethyl acetate, did not lead to any reaction (Table 1, entries 1–4). Using diazabicycloundecane (DBU) as a strong organic base, substrate **7b** was fully converted. Signals of five fluorinated products were found in the ^{19}F NMR spectrum, but no signal for α-fluoro ketones in the typical range between $\delta = -180$ and -200 ppm was observed. However, these products could not be separated and identified. Finally, reaction of **7b** with an excess of diethyl malonate as cosolvent in the presence of potassium carbonate (1.5 equiv.) was complete (TLC) after 3 h at room temperature, giving the desired product (i.e., **10b**) in 69 % yield after purification (Table 1, entry 6). The ^{19}F NMR chemical shift of $\delta = -192$ ppm for the addition product is typical for fluorine bound to a secondary sp^3 carbon in a position α to a keto group. For substrate **7b**, a value of about $\delta = -117$ ppm was found. In the same way, also the other Michael acceptors (i.e., **7a**, **7c**, and **7d**) gave the desired addition products (i.e., **10a**, **10c**, and **10d**; Table 3). The unreacted diethyl malonate was recovered by distillation in all cases.

In addition, we examined the reactions of compounds **7** with nitromethane as another carbon nucleophile (Scheme 5). Compound **7b** did not react with nitromethane in the presence of triethylamine in ethanol at room temperature after 4 d, but the use of microwave irradiation at 100 °C for 1 h gave **11b** in 33 % yield. An extended reaction time of 6 d was necessary to fully transform the starting material using potassium carbonate (TLC; Table 2, entry 3). Thus, we also tried to accelerate this reaction by using microwave irradiation (Table 2, entry 4). After 3 h at 100 °C with microwave irradiation, all the starting material was consumed, but a complex mixture of unidentified fluorinated products was formed.

Under the conditions used in the reaction shown in Table 2, entry 3, the other fluorinated Michael acceptors (i.e., **7a**, **7c**, and **7d**) gave the corresponding nitromethane adducts without solvent at room temperature. In contrast, malodinitrile did not react, or gave a complex mixture of products under the conditions used (Table 3).



7b **11b**

Scheme 5. Michael addition of **7b** with nitromethane.

Table 2. Optimization of the conditions for the Michael addition of nitromethane to 2-fluorohexadec-1-en-3-one (**7b**).[a]

Entry	Base	Solvent	Temp.	Time	Result
1	Et_3N (1.5)	EtOH	room temp.	4 d	n.r.
2	Et_3N (1.5)	EtOH	100 °C (MW, 150 W)	1 h	**11b** (33 %)
3	K_2CO_3 (1.5)	–	room temp.	6 d	**11b** (41 %)
4	K_2CO_3 (1.5)	–	100 °C (MW, 150 W)	3 h	decomp.

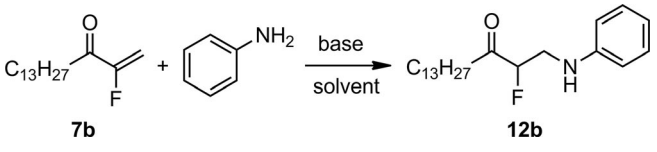
[a] Isolated yields in parentheses; n.r.: no reaction.

Table 3. Results of the Michael addition of carbon nucleophiles to enones **7**.[a]

Entry	Nucleophile	R			
		C_7H_{15} (**7a**)	$C_{13}H_{27}$ (**7b**)	C_6H_{11} (**7c**)	C_6H_5 (**7d**)
1	$CH_2(CO_2Et)_2$	**10a** (57 %)	**10b** (69 %)	**10c** (37 %)	**10d** (61 %)
2	CH_3NO_2	**11a** (52 %)	**11b** (41 %)	**11c** (45 %)	**11d** (50 %)
3	$CH_2(CN)_2$	–	c.m.	–	–

[a] Isolated yields in parentheses; c.m.: complex mixture.

Next, we turned our attention to nitrogen nucleophiles, and chose aniline as a model compound (Scheme 6). However, **7b** did not react with this aromatic amine in the presence of sodium carbonate without solvent. In the presence of DBU, without solvent or in DMF, complex mixtures of products were obtained, and no reaction occurred in other solvents such as THF, acetonitrile, Et_2O, EtOAc, CCl_4, and CH_2Cl_2. The starting material was recovered in some cases (Table 4, entries 1, 4).



7b **12b**

Scheme 6. Michael addition of aniline to **7b**.

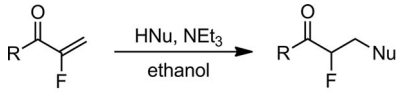
Table 4. Michael addition of aniline to **7b**, influence of bases and solvents.

Entry	Base	Solvent	Result[a]
1	K_2CO_3	–	n.r.
2	DBU	–	c.m.
3	DBU	DMF	c.m.
4	DBU	THF, MeCN, Et_2O, EtOAc, CCl_4, or CH_2Cl_2	n.r.
5	DBU	EtOH	**12b** (50 %)[b]
6	Et_3N	EtOH	**12b** (92 %)[c]

[a] Determined by ^{19}F NMR spectroscopy. [b] Full conversion of **7b**, 9 % of a side-product. [c] Isolated yield; n.r.: no reaction; c.m.: complex mixture.

However, the reaction could be carried out with DBU in ethanol as solvent, giving **12b** in nearly 50 % yield (by ^{19}F NMR spectroscopy). In addition, the oxy-Michael addition product of ethanol was also detected (9 % by ^{19}F NMR spectroscopy). These products could not be separated. In the presence of the weaker base NEt_3 (1.5 equiv.), the desired 2-fluoro ketone (i.e., **12b**) was isolated in 92 % yield after column chromatography.

Having achieved this promising result, we then examined the scope of the reaction using different amines and thiols with all the 2-fluoro-α,β-unsaturated carbonyl compounds **7** (Scheme 7, Table 5).



7a–7d **12a–d** to **17a–d**

Scheme 7. Michael addition of different nucleophiles to enones **7a**–**7d**.

Table 5. Michael addition of different nucleophiles to enones **7**.[a]

Entry	Nucleophile	R				
		OMe	C_7H_{15}	$C_{13}H_{27}$	C_6H_{11}	C_6H_5
1	aniline	c.m.[b]	**12a** (57 %)	**12b** (92 %)	**12c** (69 %)	**12d** (72 %)
2	*p*-anisidine	c.m.[c]	**13a** (81 %)	**13b** (80 %)	**13c** (83 %)	**13d** (80 %)
3	morpholine	c.m.[b]	**14a** (83 %)	**14b** (84 %)	**14c** (76 %)	**14d** (79 %)
4	piperidine	n.r.	**15a** (59 %)	**15b** (59 %)	**15c** (75 %)	**15d** (68 %)
5	3,5-bis(trifluoromethyl)aniline	–	–	n.r.	–	–
6	4-methylthiophenol	–	**16a** (86 %)	**16b** (88 %)	**16c** (88 %)	**16d** (83 %)
7	methyl L-NHBoc cysteinate	c.m.[c]	**17a** (54 %)	**17b** (58 %)	**17c** (88 %)	**17d** (83 %)
8	benzothiazol-2-thiol	–	–	n.r.	–	–

[a] Isolated yields in parentheses; n.r.: no reaction; c.m.: complex mixture. [b] With unidentified signals in the ^{19}F NMR spectra. [c] Without signals in the ^{19}F NMR spectra.

The reactions of **7a**–**7d** with aniline, anisidine, morpholine, and piperidine gave adducts **12a**–**12d**, **13a**–**13d**, **14a**–**14d**, and **15a**–**15d** in 57–92 % yield. Very good yields were also obtained for all reactions with 4-methylthiophenol to form **16a**–**16d**, and for the reactions of **7c** and **7d** with Boc-cysteine methyl ester to give **17c** and **17d**; moderate yields were obtained for the corresponding reactions of **7a** and **7b** (Table 4, entry 7). In all cases, 1:1 mixtures of the expected diastereomers were observed by ^{19}F NMR spectroscopy. In the ^1H and ^{13}C NMR spectra, the signals are very close to each other, or coincide, except for compound **17d** (see Supporting Information). The ^{19}F NMR spectra of crude products **17a** and **17b** did not show any fluorinated side-products or starting material. Thus, the lower yields seem to be due to loss of material during work-up. No reaction was observed with less nucleophilic amines or thiols (Table 4, entries 5 and 8). Furthermore, none of the amines or thiols tested gave Michael adducts with methyl 2-fluoroacrylate, although there are numerous reports of successful Michael reactions with fluorine-free methyl acrylate.[30] Methyl 2-fluoroacrylate did not react, or unknown fluorine-free compounds were formed, as the elimination of HF from methyl 2-fluoroacrylate seemed to be a competing process.

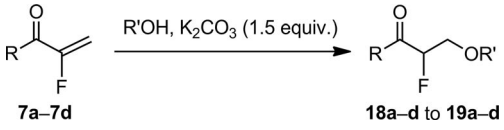
As mentioned above, in the case of the reaction of **7b** with aniline in the presence of DBU in ethanol (Table 4, entry 5), an oxy-Michael addition product was observed as an impurity. Therefore, finally, we tested alcohols as nucleophiles for the addition reactions with Michael acceptors **7**. The low nucleophilicity of alcohols and the reversibility of the addition step present challenges for oxy-Michael reactions.[9f] Thus, we used DBU as

the base for the reaction with ethanol. Although **7b** was fully converted, we were unable to separate **19b** from side-products. Thus, instead of DBU, we used K_2CO_3 (1.5 equiv.) as base, and an excess of ethanol. After stirring for 24 h at room temp., all the starting material was converted, and the desired product could be isolated in 32 % yield (Table 6, entry 2). We checked the reaction conditions with the other substrates and alcohols (Scheme 8, Table 6).

Table 6. Michael addition of alcohols to enones **7**.[a]

Entry	Alcohol	R			
		C_7H_{15}	$C_{13}H_{27}$	C_6H_{11}	C_6H_5
1	methanol	**18a** (34 %)	**18b** (44 %)	c.m.	c.m.
2	ethanol	**19a** (39 %)	**19b** (32 %)	**19c** (35 %)	c.m.
3	*tert*-butanol	c.m.	c.m.	–	–
4	benzyl alcohol	c.m.	c.m.	–	–

[a] Isolated yields in parentheses; c.m.: complex mixture.



Scheme 8. Michael addition of different alcohols to enones **7a**–**7d**.

The oxy-Michael addition worked successfully for methanol and ethanol as substrates, with yields ranging from 34–44 %. In contrast, the reactions of **7a** and **7b** with *tert*-butanol or benzyl alcohol, while showing complete conversion of the Michael acceptor, gave numerous fluorinated products, which could not be separated (Table 6, entries 3 and 4) due to their large number. In contrast to aza- or thio-Michael additions, the substituent R of the Michael acceptor and the R′ of the alcohol play important roles in these transformations. The reactions of aromatic compound **7d** and those of bulky alcohols led to complex product mixtures.

Conclusions

Michael additions of α-fluoro-α,β-unsaturated ketones **7** were investigated, and we observed the different behavior of aliphatic and aromatic Michael acceptors in reactions with various types of nucleophiles. The formation of carbon–carbon bonds was possible with malonates and nitromethane as nucleophiles. The formation of carbon–heteroatom bonds was possible with primary and secondary amines, with thiols, and with methanol and ethanol. The resulting new β-substituted α-fluoro ketones might be useful as building blocks for the construction of fluorinated heterocycles.

Experimental Section

General Remarks: All commercially sourced reagents were used without further purification. NMR spectra were recorded at 300 or 400 MHz (^{1}H), at 75 or 101 MHz (^{13}C), and at 282 MHz (^{19}F). Chemical shifts are reported in ppm downfield from TMS (^{1}H and ^{13}C), using $CDCl_3$ as an internal standard, and downfield from $CFCl_3$ (^{19}F). Signals were assigned with the help of GCOSY spectra (for ^{1}H NMR), and GHSQC and GHMBC spectra (for ^{1}H and ^{13}C NMR). Mass spectra were recorded with a Finnigan MAT 4200S instrument under ESI conditions. Column chromatography (silica gel, Merck 60, 0.040–0.063 mm) was used for purification. Fluorinated allylic alcohols were prepared according to refs.[6,7] Benzoquinone was added to α-fluorinated α,β-unsaturated ketones **7** in order to avoid decomposition.

General Procedure for Michael Additions of Carbon Nucleophiles: α-Fluorinated α,β-unsaturated carbonyl compound **7** (1.0 equiv.) was added to a solution of triethylamine (1.5 equiv.) and the nucleophile (1.0 equiv.). The reaction mixture was stirred until TLC indicated complete conversion. Then CH_2Cl_2 and H_2O (10 mL each) were added, and the mixture was shaken. After phase separation, the organic layer was washed with $NaHCO_3$ solution (5 wt.-%; 20 mL) and brine (20 mL), and dried with $MgSO_4$, and the solvent was evaporated in vacuo. The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 40:1 to 10:1) to give the desired product.

Ethyl 2-Ethoxycarbonyl-4-fluoro-5-oxododecanoate (10a): From 2-fluorodec-1-en-3-one (**7a**; 64 mg, 0.37 mmol), yield 69 mg (57 %), white solid, m.p. 39 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.9 Hz, 3 H, CH_3), 1.25–1.31 (m, CH_2 and 2 CH_3), 1.57–1.59 (m, 2 H, CH_2), 2.29 (dddd, J = 5.7, J = 9.5 Hz, J = 15.0 Hz, J = 16.6 Hz, 1 H, CH_2), 2.41–2.53 (m, 1 H, 1-CH_2), 2.58–2.63 (m, 2 H, CH_2), 3.57 (dd, J = 5.7, J = 8.9 Hz, 1 H), 4.17–4.28 (m, 4 H, 13/16-CH_2), 4.85 (ddd, J = 3.7, J = 9.5 Hz, J = 49.9 Hz, 1 H, 2-CHF) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0 (2 CH_3), 14.1 (CH_3), 22.6 (CH_2), 22.7 (CH_2), 26.9–29.6 (3 CH_2), 30.7 (d, J = 20.5 Hz, CH_2), 38.0 (2 CH_3), 47.6 (d, J = 3.0 Hz, CH_2), 61.8 (CH), 93.3 (d, J = 184.8 Hz, CHF), 168.4, 168.6, 208.6 (d, J = 23.4 Hz, CH) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –192.6 (dddt, J = 3.1, J = 16.2 Hz, J = 32.3 Hz, J = 49.6 Hz) ppm. HRMS (ESI): calcd. for $C_{17}H_{30}FO_5$ $[M + H]^+$ 355.1891; found 355.1891.

Ethyl 2-Ethoxycarbonyl-4-fluoro-5-oxooctadecanoate (10b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 57 mg (69 %), white solid, m.p. 47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.9 Hz, 3 H), 1.26–1.30 (m, 26 H), 1.57–1.59 (m, 2 H), 2.29 (dddd, J = 5.8, J = 9.5 Hz, J = 15.1 Hz, J = 16.6 Hz, 1 H), 2.51 (dddd, J = 3.7, J = 8.9 Hz, J = 15.1 Hz, J = 32.1 Hz, 1 H), 2.58–2.62 (m, 2 H), 3.57 (dd, J = 5.7, J = 8.9 Hz, 1 H), 4.17–4.27 (m, 4 H), 4.85 (ddd, J = 3.7, J = 9.5 Hz, J = 49.9 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0 (CH_3), 14.1 (CH_3), 22.6 (CH_2), 26.9–29.7 (CH_2), 30.7 (d, J = 20.5 Hz), 31.9 (CH_2), 38.1 (CH_2), 47.6 (d, J = 3.0 Hz, CH_2), 61.8 (CH), 93.4 (d, J = 184.9 Hz, CHF), 168.4, 168.6, 208.6 (d, J = 23.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –192.6 (dddt, J = 2.9, J = 16.7 Hz, J = 32.1 Hz, J = 49.7 Hz) ppm. HRMS (ESI): calcd. for $C_{23}H_{42}FO_5$ $[M + H]^+$ 417.3011; found 417.3010.

Ethyl 2-Ethoxycarbonyl-5-cyclohexyl-4-fluoro-5-oxopentanoate (10c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 58 mg, 0.36 mmol), yield 43 mg (0.14 mmol, 37 %), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25–1.31 (m, 12 H), 1.55–1.85 (m, 4 H), 2.39 (dddd, J = 5.7, J = 9.7 Hz, J = 15.0 Hz, J = 16.0 Hz, 1 H), 2.53 (dddd, J = 3.6, J = 8.9 Hz, J = 14.9 Hz, J = 33.0 Hz, 1 H), 2.75–2.85 (m, 1 H, 4-CH), 3.57 (dd, J = 5.7, J = 8.9 Hz, 1 H), 4.17–4.27 (m, 4 H), 4.95 (ddd, J = 3.5, J = 9.7 Hz, J = 49.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (2 CH_3), 25.4, 25.5 (2 CH_2), 25.7 (CH_2), 27.4, 28.0 (2 CH_2), 31.8 (d, J = 21.1 Hz, CFH_2), 46.0 (2 CH_2), 47.7 (d, J = 2.9 Hz, CH_2), 61.8, 92.6 (d, J = 185.3 Hz, CHF), 168.4, 168.6, 210.8 (d, J = 18.1 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –192.6 (dddd, J = 3.2, J = 16.2 Hz, J = 33.0 Hz, J = 49.5 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{26}FO_5$ $[M + H]^+$ 339.1584; found 339.1579.

Ethyl 2-Ethoxycarbonyl-4-fluoro-5-oxo-5-phenylpentanoate (10d): From 1-phenyl-2-fluoroprop-2-en-1-one (**7d**; 42 mg,

0.28 mmol), yield 37 mg (0.21 mmol, 69 %), white solid, m.p. 109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24–1.35 (m, 6 H), 2.39 (dddd, *J* = 4.6, *J* = 10.2 Hz, *J* = 15.0 Hz, *J* = 15.0 Hz, 1 H), 2.66 (dddd, *J* = 2.9, *J* = 10.0 Hz, *J* = 15.0 Hz, *J* = 35.0 Hz, 1 H), 3.74 (dd, *J* = 4.6, *J* = 9.9 Hz, 1 H), 4.17–4.34 (m, 4 H), 5.82 (ddd, *J* = 2.8, *J* = 10.2 Hz, *J* = 49.9 Hz, 1 H), 7.48–7.53 (m, 2 H), 7.60–7.65 (m, 1 H), 8.02–8.05 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (2 CH_3), 31.6 (d, *J* = 21.1 Hz, CH_2), 41.6, 47.6, 61.9, 90.5 (d, *J* = 182.5 Hz, CHF), 128.9, 133.6, 134.1, 168.7 (d, *J* = 9 Hz); 195.0 (d, *J* = 18.1 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –192.6 (ddd, = 15.3 Hz, *J* = 35.6, *J* = 50.1 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{19}FO_5Na$ $[M + Na]^+$ 333.1114; found 333.1111.

3-Fluoro-1-nitroundecan-4-one (11a): From 2-fluorodec-1-en-3-one (**7a**; 74 mg, 0.43 mmol), yield 52 mg (0.23 mmol, 52 %), brown oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 6.9 Hz, 3 H), 1.15–1.36 (m, 8 H), 1.54–1.60 (m, 2 H), 2.33–2.67 (m, 2 H), 2.62 (m, 2 H), 4.51 (m, 2 H), 4.88 (ddd, *J* = 4.0, *J* = 8.9 Hz, *J* = 49.1 Hz, CHF) ppm. ^{13}C NMR (153 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.5 (d, *J* = 4.3 Hz, CH_2), 22.6 (CH_2), 28.8, 28.9 (4 CH_2), 29.0 (CH_2), 70.5 (d, *J* = 4.3 Hz, CH_2), 92.1 (d, *J* = 185.9 Hz, CHF), 208.2 (d, *J* = 23.5 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –194.0 (dddt, *J* = 3.2, *J* = 17.1 Hz, *J* = 29.1 Hz, *J* = 49.3 Hz) ppm. HRMS (ESI): calcd. for $C_{11}H_{20}FNO_3Na$ $[M + Na]^+$ 256.1325; found 256.1323.

3-Fluoro-1-nitroheptadecan-4-one (11b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 26 mg (0.08 mmol, 41 %), yellow solid, m.p. 45 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 6.9 Hz, 3 H), 1.15–1.26 (m, 20 H), 1.47–1.56 (m, 2 H), 2.33–2.72 (m, 2 H), 2.65 (m, 2 H), 4.54 (m, 2 H), 4.88 (ddd, *J* = 4.0, *J* = 8.9 Hz, *J* = 49.2 Hz, CHF) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.6 (CH_2), 22.7 (CH_2), 28.9 (CH_2), 29.1–31.9 (9 CH_2), 38.3 (CH_2), 70.5 (d, *J* = 4.3 Hz, CH_2), 92.2 (d, *J* = 185.9 Hz, CHF), 208.2 (d, *J* = 23.6 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –193.9 (dddt, *J* = 3.2, *J* = 17.1 Hz, *J* = 28.8 Hz, *J* = 49.2 Hz) ppm. HRMS (ESI): calcd. for $C_{17}H_{36}FN_2O_3$ $[M + NH_4]^+$ 335.2710; found 335.2704.

1-Cyclohexyl-2-fluoro-4-nitrobutan-1-one (11c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 66 mg, 0.42 mmol), yield 41 mg (0.19 mmol, 45 %), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12–1.34 (m, 10 H), 2.34 (m, 1 H), 2.58 (m, 1 H), 2.77 (m, 1 H), 4.46 (m, 2 H), 4.92 (ddd, *J* = 3.9, *J* = 8.8 Hz, *J* = 48.9 Hz, 1 H, CHF) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.3, 24.5, 24.7 (3 CH_2), 28.4, 28.2 (2 CH_2), 45.1 (CH), 47.7 (d, *J* = 2.9 Hz, CH_2), 69.6 (d, *J* = 4.2 Hz, CH_2), 90.5 (d, *J* = 186.3 Hz, CHF), 209.5 (d, *J* = 22.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –195.0 (dddd, *J* = 3.6, *J* = 17.4 Hz, *J* = 29.0 Hz, *J* = 49.5 Hz) ppm. HRMS (ESI): calcd. for $C_{10}H_{16}FNO_3Na$ $[M + Na]^+$ 240.1012; found 240.1014.

2-Fluoro-4-nitro-1-phenylbutan-1-one (11d): From 1-phenyl-2-fluoroprop-2-en-1-one (**7d**; 29 mg, 0.20 mmol), yield 20 mg (0.01 mmol, 50 %), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.54–2.60 (m, 1 H), 2.72–2.88 (m, 1 H), 4.61 (dt, *J* = 5.9, *J* = 14.4 Hz, 1 H), 4.70 (ddd, *J* = 5.5, *J* = 8.7 Hz, *J* = 14.3 Hz, 1 H), 5.81 (ddd, *J* = 3.6, *J* = 9.0 Hz, *J* = 48.6 Hz, CHF), 7.49–7.55 (m, 2 H), 7.63–7.68 (m, 1 H), 7.98–8.02 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 29.3 (d, *J* = 21.4 Hz, CH_2), 70.2 (d, *J* = 4.2 Hz, CH_2), 89.4 (d, *J* = 183.6 Hz, CHF), 129.0 (2 CH), 129.0 (2 CH), 133.6 (CH), 134.4 (C), 194.4 (d, *J* = 18.7 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –193.9 (ddd, *J* = 17.2, *J* = 30.0 Hz, *J* = 47.9 Hz) ppm. HRMS (ESI): calcd. for $C_{10}H_{10}FNO_3Na$ $[M + Na]^+$ 234.0542; found 234.0548.

General Procedure for Michael Additions of Nitrogen and Sulfur Nucleophiles: Fluorinated α,β-unsaturated carbonyl compound **7** (1.0 equiv.) was dissolved in EtOH (4.0 mL). Triethylamine (1.5 equiv.) and the nucleophile were then added (1.5 equiv.) to the clear solution. The reaction mixture was stirred until TLC indicated complete conversion. Then, CH_2Cl_2 and H_2O (10 mL each) were added. The organic layer was separated, and washed with $NaHCO_3$ solution (5 wt.-%; 20 mL) and brine (20 mL). The organic phase was dried with $MgSO_4$, and the solvent was evaporated in vacuo. The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 10:1) to give the desired product.

2-Fluoro-1-(phenylamino)decan-3-one (12a): From 2-fluorodec-1-en-3-one (**7a**; 34 mg, 0.20 mmol), yield 30 mg (0.12 mmol, 57 %), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.7 Hz, 3 H), 1.27 (m, 8 H), 1.51–1.64 (m, 2 H), 2.50–2.74 (m, 2 H), 2.50–2.74 (m, 2 H), 4.94 (ddd, *J* = 49.5, *J* = 6.3 Hz, *J* = 3.6 Hz, 1 H, CHF), 6.68 (dd, *J* = 8.6, *J* = 1.0 Hz, 2 H), 6.73–6.81 (m, 1 H), 7.13–7.24 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 (CH_3), 21.5 (CH_2), 21.6 (CH_2), 28.0–30.6 (3 CH_2), 37.9 (CH_2), 44.6 (d, *J* = 21.0 Hz, CH_2), 93.4 (d, *J* = 186.3 Hz, CHF), 113.5 (C), 117.6 (C), 128.4 (C), 145.9 (C), 208.4 (d, *J* = 24.1 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.1 (dtt, *J* = 50.3, *J* = 23.7 Hz, *J* = 3.1 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{25}FNO$ $[M + H]^+$ 266.1915; found 266.1916; calcd. for $C_{16}H_{24}FNONa$ $[M + Na]^+$ 288.1740; found 288.1734.

2-Fluoro-1-(phenylamino)hexadecan-3-one (12b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg. 0.20 mmol), yield 64 mg (0.18 mmol, 92 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 6.9 Hz, 3 H), 1.16–1.21 (m, 20 H), 1.44–1.54 (m, 2 H), 2.44–2.65 (m, 2 H), 3.46 (ddd, *J* = 6.3, *J* = 14.4 Hz, *J* = 23.9 Hz, 1 H), 3.59 (ddd, *J* = 3.5, *J* = 14.4 Hz, *J* = 23.5 Hz, 1 H), 4.87 (ddd, *J* = 3.5, *J* = 6.3 Hz, *J* = 49.6 Hz, 1 H, CHF), 6.68 (dd, *J* = 1.0, *J* = 8.6 Hz, 2 H), 6.69 (tt, *J* = 1.0, *J* = 7.5 Hz, 1 H), 7.12 (dd, *J* = 7.4, *J* = 8.6 Hz, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.5 (CH_2), 22.7 (CH_2), 29.0, 29.4, 29.5, 29.5, 29.7 (8 CH_2), 38.9 (CH_2), 45.6 (d, *J* = 21.0 Hz, CH_2), 94.4 (d, *J* = 186.4 Hz, CHF), 113.5 (C), 118.6 (C), 129.4 (C), 146.9 (C), 209.4 (d, *J* = 24.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.6 (dtt, *J* = 3.0, *J* = 23.7 Hz, *J* = 50.3 Hz) ppm. HRMS (ESI): calcd. for $C_{22}H_{37}FNO$ $[M + H]^+$ 350.2854; found 350.2859; calcd. for $C_{22}H_{36}FNONa$ $[M + Na]^+$ 372.2673; found 372.2679.

1-Cyclohexyl-2-fluoro-3-(phenylamino)propan-1-one (12c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 39 mg, 0.25 mmol), yield 43 mg (0.17 mmol, 69 %), white solid, m.p. 43 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16–1.40 (m, 10 H), 2.86 (m, 1 H), 3.52 (ddd, *J* = 6.7, *J* = 14.4 Hz, *J* = 22.5 Hz, 1 H), 3.68 (ddd, *J* = 3.5, *J* = 14.4 Hz, *J* = 25.0 Hz, 1 H), 4.09 (br. s, 1 H), 5.03 (ddd, *J* = 3.5, *J* = 6.7 Hz, *J* = 49.8 Hz, 1 H, CHF), 6.68 (m, 2 H), 6.77 (m, 1 H), 7.20 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 25.6 (2 CH_2), 25.8 (CH_2), 28.0 (2 CH_2), 45.8 (d, *J* = 21.2 Hz, CH_2), 46.3 (CH), 93.8 (d, *J* = 187.0 Hz, CHF), 113.6 (C), 118.7 (C), 129.4 (C), 146.8 (C), 211.6 (d, *J* = 23.0 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –197.0 (dddd, *J* = 3.4, *J* = 22.8, *J* = 25.2, *J* = 50.1 Hz) ppm. HRMS (ESI): calcd. for $C_{15}H_{20}FNONa$ $[M + Na]^+$ 272.1421; found 272.1430.

2-Fluoro-1-phenyl-3-(phenylamino)propan-1-one (12d): From 2-fluoro-1-phenylprop-2-en-1-one (**7d**; 32 mg, 0.20 mmol), yield 35 mg (0.14 mmol, 72 %), yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.66 (ddd, *J* = 6.9, *J* = 14.5 Hz, *J* = 21.1 Hz, 1 H), 3.84 (ddd, *J* = 3.8, *J* = 14.5 Hz, *J* = 24.6 Hz, 1 H), 4.07 (br. s, 1 H), 5.76 (ddd, *J* = 3.8, *J* = 6.9 Hz, *J* = 48.9 Hz, 1 H, CHF), 6.66 (m, 2 H), 6.76 (m, 1 H), 7.19 (m, 2 H), 7.49 (m, 2 H), 7.61 (m, 1 H), 7.96 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.7 (d, *J* = 22.3 Hz, CH_2), 91.7 (d, *J* = 184.8 Hz, CHF), 113.4 (C), 118.6 (C), 128.6 (C), 128.9 (C), 129.4 (C), 134.1 (C), 134.4 (C), 146.8 (C), 195.6 (d, *J* = 22.3 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –192.4 (ddd, *J* = 20.9, *J* = 24.5 Hz, *J* = 48.7 Hz) ppm. HRMS (ESI): calcd. for $C_{15}H_{14}FNONa$ $[M + Na]^+$ 266.0957; found 266.0959.

2-Fluoro-1-[(4-methoxyphenyl)amino]decan-3-one (13a): From 2-fluorodec-1-en-3-one (**7a**; 50 mg, 0.20 mmol), yield 48 mg (0.16 mmol, 81 %), white solid, m.p. 53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, J = 6.8 Hz, 3 H), 1.20–1.26 (m, 8 H), 1.50–1.63 (m, 2 H), 2.46–2.62 (m, 2 H), 3.48 (ddd, J = 3.8, J = 11.2 Hz, J = 20.6 Hz, 1 H), 3.60 (ddd, J = 3.9, J = 11.3 Hz, J = 14.3 Hz, 1 H), 3.75 (s, 3 H), 4.93 (ddd, J = 3.5, J = 6.2 Hz, J = 49.6 Hz, 1 H, CHF), 6.53–6.59 (m, 2 H), 6.69–6.73 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.5 (CH_2), 21.6 (CH_2), 28.0 (2 CH_2), 30.6 (CH_2), 38.7 (CH_2), 45.7 (d, J = 20.9 Hz, CH_2), 54.7 (CH_3), 93.5 (d, J = 186.0 Hz, CHF), 113.9 (2 CH), 114.9 (2 CH), 139.9 (C), 151.9 (C), 208.5 (d, J = 24.2 Hz, C) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.2 to –196.5 (dm, J = 49.6 Hz) ppm. HRMS (ESI): calcd. for $C_{17}H_{27}FNO_2Na$ [M + Na]$^+$ 318.1845; found 318.1839.

2-Fluoro-1-[(4-methoxyphenyl)amino]hexadecan-3-one (13b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 68 mg (0.18 mmol, 80 %), white solid, m.p. 76 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.9 Hz, 3 H), 1.21–1.35 (m, 20 H), 1.51–1.60 (m, 2 H), 2.53–2.68 (m, 2 H), 3.75 (s, 3 H), 3.42–3.62 (m, 2 H), 2.73–2.83 (m, 2 H), 4.92 (ddd, J = 3.5, J = 6.3 Hz, J = 49.6 Hz, 1 H, CHF), 6.61–6.67 (m, 2 H), 6.75–6.82 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.5 (CH_2), 22.7 (CH_2), 26.7–31.9 (9 CH_2), 38.9 (CH_2), 46.8 (d, J = 20.9 Hz, CH_2), 55.7 (CH_3), 94.5 (d, J = 186.1 Hz, CH_2), 114.9 (C), 115.1 (C), 140.9 (C), 152.9 (C), 209.5 (d, J = 24.3 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.1 to –196.5 (dm, J = 49.5 Hz) ppm. HRMS (ESI): calcd. for $C_{23}H_{38}FNO_2Na$ [M + Na]$^+$ 402.2784; found 402.2779.

1-Cyclohexyl-2-fluoro-3-[(4-methoxyphenyl)amino]propan-1-one (13c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 36 mg, 0.23 mmol), yield 54 mg (0.18 mmol, 83 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08–1.78 (m, 10 H), 2.75 (m, 1 H), 3.37–3.67 (m, 2 H), 3.69 (s, 3 H), 5.11 (ddd, J = 3.2, J = 7.8 Hz, J = 49.4 Hz, 1 H, CHF), 6.75 (d, J = 9.0 Hz, 2 H), 6.91 (d, J = 8.9 Hz, 2 H, 12/14), 7.34 (s, 1 H, NH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 24.3 (CH_2), 24.5 (2 CH_2), 24.7 (CH_2), 27.0 (2 CH_2), 45.2 (CH), 47.9 (d, J = 20.8 Hz, CH_2), 54.6 (CH_3), 91.3 (d, J = 187.5 Hz, CHF), 114.0 (2 CH), 129.4 (2 CH), 135.0 (C), 154.5 (C), 209.5 (d, J = 22.3 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.0–196.4 (dm, J = 49.5 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{22}FNO_2Na$ [M + Na]$^+$ 302.1532; found 302.1533.

2-Fluoro-3-[(4-methoxyphenyl)amino]-1-phenylpropan-1-one (13d): From 2-fluoro-1-phenylprop-2-en-1-one (**7d**; 36 mg, 0.23 mmol), yield 54 mg (0.19 mmol, 80 %), brownish solid, m.p. 75 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.61 (ddd, J = 7.1, J = 14.4, J = 21.0 Hz, 1 H), 3.74 (s, 3 H), 3.84 (ddd, J = 3.6, J = 14.5 Hz, J = 25.2 Hz, 1 H), 4.07 (s, 1 H), 5.75 (ddd, J = 3.5, J = 7.0 Hz, J = 49.0 Hz, 1 H, CHF), 6.64 (m, 2 H), 6.79 (m, 2 H), 7.48 (m, 2 H), 7.61 (m, 1 H), 7.95 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.1 (d, d, J = 22.2 Hz, CH_2), 55.7 (s, CH_3), 91.8 (d, J = 184.4 Hz, CHF), 114.9 (2 CH), 115.0 (2 CH), 128.8 (2 CH), 128.9 (2 CH), 134.1 (CH), 134.4 (C), 140.8 (C), 152.9 (C), 195.7 (d, J = 19.3 Hz, C) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –193.0 (ddd, J = 20.5, J = 25.3 Hz, J = 48.8 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{16}FNO_2Na$ [M + Na]$^+$ 296.1063; found 296.1059.

2-Fluoro-1-morpholinodecan-3-one (14a): From 2-fluorodec-1-en-3-one (**7a**; 34 mg, 0.20 mmol), yield 43 mg (0.17 mmol, 83 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.7 Hz, 3 H, 10-CH_3), 1.20–1.29 (m, 8 H), 1.53–1.66 (m, 2 H), 2.45–2.56 (m, 2 H), 2.56–2.69 (m, 4 H), 2.75–2.91 (m, 2 H), 3.68 (t, J = 4.7 Hz, 4 H), 4.92 (ddd, J = 3.8, J = 4.9 Hz, J = 50.4 Hz, 1 H, CHF) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.5 (CH_2), 22.6 (CH_2), 29.0–31.6 (3 CH_2), 38.8 (CH_2), 54.2 (2 CH_2), 59.6 (d, J = 19.2 Hz, CH_2), 66.7 (2 CH_2), 95.5 (d, J = 187.2 Hz, CHF), 209.2 (d, J = 24.3 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –189.8 to –190.2 (m) ppm. HRMS (ESI): calcd. for $C_{14}H_{26}FNO_2Na$ [M + Na]$^+$ 282.1845; found 282.1838.

2-Fluoro-1-morpholinohexadecan-3-one (14b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 56 mg (0.17 mmol, 84 %), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.7 Hz, 3 H), 1.14–1.41 (m, 20 H), 1.55–1.66 (m, 2 H), 2.45–2.56 (m, 2 H), 2.57–2.68 (m, 4 H), 2.76–2.92 (m, 2 H), 3.69 (t, J = 4.7 Hz, 4 H), 4.93 (ddd, J = 3.4, J = 5.3 Hz, J = 50.4 Hz, 1 H, CHF) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7 (CH_2), 22.7 (CH_2), 29.2–31.9 (9 CH_2), 38.8 (CH_2), 50.7 (2 CH_2), 54.3 (2 CH_2), 60.0 (d, J = 19.2 Hz, CH_2), 95.5 (d, J = 187.2 Hz, CHF), 209.2 (d, J = 24.3 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.0 (dtt, J = 2.8, J = 27.9 Hz, J = 50.4 Hz) ppm. HRMS (ESI): calcd. for $C_{20}H_{38}FNO_2Na$ [M + Na]$^+$ 366.2784; found 366.2779.

1-Cyclohexyl-2-fluoro-3-morpholinopropan-1-one (14c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 36 mg, 0.23 mmol), yield 42 mg (0.17 mmol, 76 %), brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18–1.88 (m, 10 H), 2.86 (m, 1 H), 2.58 (m, 4 H), 2.82 (m, 2 H), 2.87 (m, 1 H), 3.69 (t, J = 4.7 Hz, 4 H), 5.02 (dm, J = 52.4 Hz, 1 H, CHF) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.5, 25.6 (2 CH_2), 25.8 (CH_2), 28.0 (2 CH_2), 46.3 (CH), 54.2 (2 CH_2), 59.8 (d, J = 19.4 Hz, CH_2), 66.9 (2 CH_2), 94.9 (d, J = 187.7 Hz, CHF), 211.5 (d, J = 23.9 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.6 to –191.0 (m) ppm. HRMS (ESI): calcd. for $C_{13}H_{22}FNO_2Na$ [M + Na]$^+$ 266.1532; found 266.1529.

2-Fluoro-3-morpholino-1-phenylpropan-1-one (14d): From 2-fluoro-1-phenylprop-2-en-1-one (**7d**; 39 mg, 0.25 mmol), yield 47 mg (0.19 mmol, 79 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.60 (m, 4 H), 2.99 (m, 2 H), 3.69 (t, J = 4.7 Hz, 4 H), 5.80 (ddd, J = 3.3, J = 6.2 Hz, J = 49.8 Hz, 1 H, CHF), 7.50 (m, 2 H), 7.61 (m, 1 H), 7.96 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 54.0 (CH_2), 60.0 (d, J = 20.7 Hz, CH_2), 66.8 (2 CH_2), 93.0 (d, J = 185.8 Hz, CHF), 128.7 (2 CH), 127.8 (2 CH), 133.8 (CH), 134.6 (C), 195.7 (d, J = 19.0 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –187.4 to –187.2 (dm, J = 49.9 Hz) ppm. HRMS (ESI): calcd. for $C_{13}H_{16}FNO_2Na$ [M + Na]$^+$ 260.1063; found 260.1064.

2-Fluoro-1-(piperidin-1-yl)decan-3-one (15a): From 2-fluorodec-1-en-3-one (**7a**; 34 mg, 0.20 mmol), yield 30 mg (0.12 mmol, 59 %), yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.9 Hz, 3 H), 1.28–1.39 (m, 8 H), 1.37–1.47 (m, 2 H), 1.48–1.65 (m, 6 H), 2.39–2.56 (m, 4 H), 2.56–2.64 (m, 2 H), 2.73–2.76 (m, 1 H), 2.80–2.83 (m, 1 H), 4.92 (ddd, J = 3.9, J = 5.3 Hz, J = 50.8 Hz, 1 H, CHF) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.6 (CH_2), 23.9 (CH_2), 26.0 (2 CH_2), 26.9 (CH_2), 29.0–31.7 (3 CH_2), 38.8 (CH), 55.1 (2 CH_2), 60.1 (d, J = 19.5 Hz, CH_2), 95.3 (d, J = 187.0 Hz, CHF), 209.5 (d, J = 24.0 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –189.1–189.6 (dm, J = 50.8 Hz) ppm. HRMS (ESI): calcd. for $C_{15}H_{28}FNONa$ [M + Na]$^+$ 280.2053; found 280.2049.

2-Fluoro-1-(piperidin-1-yl)hexadecan-3-one (15b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 40 mg (0.12 mmol, 59 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.9 Hz, 3 H), 1.21–1.35 (m, 22 H), 1.35–1.47 (m, 2 H, 5-CH_2), 1.51–1.63 (m, 4 H), 2.49 (m, 4 H), 2.57–2.65 (m, 2 H), 2.73–2.83 (m, 2 H), 4.92 (ddd, J = 3.8, J = 5.4 Hz, J = 50.8 Hz, 1 H, CHF) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7 (CH_2), 22.7 (CH_2), 24.0 (CH_2), 26.0 (2 CH_2), 29.2–31.9 (9 CH_2), 38.8 (CH_2), 38.7 (CH_2), 45.3 (CH), 55.1 (CH_2), 55.1 (CH_2), 60.2 (d, J = 19.5 Hz, CH_2), 95.3 (d, J = 186.9 Hz, CHF), 209.5 (d, J = 24.1 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –189.3 (dtt, J = 2.6, J = 27.9 Hz, J = 50.8 Hz) ppm. HRMS (ESI): calcd. for $C_{21}H_{40}FNONa$ [M + Na]$^+$ 364.2992; found 364.2998.

1-Cyclohexyl-2-fluoro-3-(piperidin-1-yl)propan-1-one (15c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 45 mg, 0.29 mmol),

yield 53 mg (0.22 mmol, 75 %), yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (m, 4 H), 1.46 (m, 2 H), 1.56 (m, 4 H), 1.69 (m, 2 H), 1.82 (m, 4 H), 2.50 (m, 4 H), 2.74 (m, 1 H), 2.83 (m, 2 H), 5.01 (ddd, *J* = 3.9, *J* = 5.5, *J* = 50.8 Hz, 1 H, CHF) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 24.0 (CH_3), 25.6 (2 CH_2), 25.8 (CH_2), 26.0 (2 CH_2), 27.8, 27.9 (2 CH_2), 46.3 (CH), 55.1 (2 CH_2), 60.4 (d, *J* = 19.4 Hz, CH_2), 94.8 (d, *J* = 187.5 Hz, CHF), 211.9 (d, *J* = 22.7 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.1 (ddt, *J* = 3.0, *J* = 27.4 Hz, *J* = 50.8 Hz) ppm. HRMS (ESI): calcd. for $C_{14}H_{24}FNONa$ $[M + Na]^+$ 264.1740; found 264.1734.

2-Fluoro-1-phenyl-3-(piperidin-1-yl)propan-1-one (15d): From 2-fluoro-1-phenylprop-2-en-1-one (**7d**; 53 mg, 0.20 mmol), yield 53 mg (0.22 mmol, 75 %), yellowish oil. ^{1}H NMR (101 MHz, $CDCl_3$): δ = 1.43 (m, 2 H), 1.57 (m, 4 H), 2.54 (m, 4 H), 2.89 (m, 1 H), 2.99 (m, 1 H), 5.80 (ddd, *J* = 4.0, *J* = 5.9 Hz, *J* = 50.4 Hz, 1 H, CHF), 7.49 (m, 2 H), 7.59 (m, 1 H), 7.97 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.9 (CH_2), 25.9 (2 CH_2), 54.9 (2 CH_2), 60.6 (d, *J* = 20.9 Hz, CH_2), 94.1 (d, *J* = 185.4 Hz, CHF), 128.7 (2 CH), 127.8 (2 CH), 134.5 (CH), 134.6 (C), 196.1 (d, *J* = 19.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –186.9 (dm, *J* = 50.5 Hz) ppm. HRMS (ESI): calcd. for $C_{14}H_{18}FNONa$ $[M + Na]^+$ 258.1270; found 258.1271.

2-Fluoro-1-(*p*-tolylthio)decan-3-one (16a): From 2-fluorodec-1-en-3-one (**7a**; 36 mg, 0.21 mmol), yield 53 mg (0.18 mmol, 86 %), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.24–1.31 (m, 8 H), 1.53–1.65 (m, 2 H), 2.33 (s, 3 H), 2.63 (td, *J* = 3.1, *J* = 7.3 Hz, 2 H), 3.19 (ddd, *J* = 7.2, *J* = 14.6 Hz, *J* = 22.7 Hz, 1 H), 3.37 (ddd, *J* = 3.7, *J* = 14.6 Hz, *J* = 24.7 Hz, 1 H), 4.84 (ddd, *J* = 3.7, *J* = 7.2 Hz, *J* = 49.2 Hz, 1 H, CHF), 7.10–7.14 (m, 2 H), 7.30–7.37 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 21.1 (CH_3), 22.5 (CH_2), 22.7 (CH_2), 29.0–31.7 (3 CH_2), 36.9 (d, *J* = 19.7 Hz, CH_2), 38.9 (CH_2), 93.9 (d, *J* = 188.4 Hz, CHF), 129.9 (2 CH), 130.8 (C), 131.4 (2 CH), 137.4 (C), 208.9 (d, *J* = 25.4 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.0 to –190.2 (dm, *J* = 49.1 Hz) ppm. HRMS (ESI): calcd. for $C_{17}H_{25}FSONa$ $[M + Na]^+$ 319.1508; found 319.1507.

2-Fluoro-1-(*p*-tolylthio)hexadecan-3-one (16b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 63 mg (0.18 mmol, 88 %), yellow solid, m.p. 45 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.9 Hz, 3 H), 1.21–1.33 (m, 20 H), 1.49–1.57 (m, 2 H), 2.32 (s, 3 H), 2.62 (m, 2 H), 3.18 (ddd, *J* = 7.2, *J* = 14.6 Hz, *J* = 22.5 Hz, 1 H), 3.37 (ddd, *J* = 3.7, *J* = 14.6 Hz, *J* = 24.7 Hz, 1 H), 4.84 (ddd, *J* = 3.7, *J* = 7.2 Hz, *J* = 49.2 Hz, 1 H, CHF), 7.11–7.13 (m, 2 H), 7.32–7.35 (m 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 21.0 (CH_3), 22.5 (CH_2), 22.7 (CH_2), 29.1–29.8 (9 CH_2), 31.9 (t, C-4), 45.6 (d, *J* = 21.0 Hz), 94.4 (d, *J* = 186.4 Hz, CHF), 113.5 (2 CH), 118.6 (2 CH), 129.4 (C), 146.9 (C), 209.4 (d, *J* = 24.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.1 (dtt, *J* = 3.0, *J* = 23.7 Hz, *J* = 50.3 Hz) ppm. HRMS (ESI): calcd. for $C_{23}H_{37}FOSNa$ $[M + Na]^+$ 403.2447; found 403.2448.

1-Cyclohexyl-2-fluoro-3-(*p*-tolylthio)propan-1-one (16c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 36 mg, 0.23 mmol), yield 49 mg (0.17 mmol, 88 %), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17–1.87 (m, 10 H), 2.33 (s, 3 H), 2.85 (m, 1 H), 3.18 (ddd, *J* = 7.5, *J* = 14.5 Hz, *J* = 21.4 Hz, 1 H, 1-CH_2), 3.38 (ddd, *J* = 3.6, *J* = 14.6 Hz, *J* = 26.0 Hz, 1 H, 1-CH_2), 4.92 (ddd, *J* = 3.6, *J* = 7.6 Hz, *J* = 49.9 Hz, 1 H, CHF), 7.09–7.30 (m, 2 H), 7.30–7.39 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.6 (CH_3), 25.4, 25.6, 25.7 (3 CH_2), 26.9 (CH_2), 27.4, 28.0 (2 CH_2), 37.0 (d, *J* = 21.8 Hz, CH_2), 46.4 (CH), 93.5 (d, *J* = 188.9 Hz, CHF), 128.5 (2 CH), 129.9 (C), 131.3 (2 CH), 137.3 (C), 211.1 (d, *J* = 23.1 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.8 (dddd, *J* = 3.3, *J* = 21.4 Hz, *J* = 25.4 Hz, *J* = 50.2 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{21}FOSNa$ $[M + Na]^+$ 303.1195; found 303.1188.

2-Fluoro-1-phenyl-3-(*p*-tolylthio)propan-1-one (16d): From 2-fluoro-1-phenylprop-2-en-1-one (**7d**; 25 mg, 0.17 mmol), yield 36 mg (0.13 mmol, 83 %), brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 2.85 (m, 1 H), 3.33 (ddd, *J* = 7.8, *J* = 14.7 Hz, *J* = 17.7 Hz, 1 H), 3.48 (ddd, *J* = 4.3, *J* = 14.7 Hz, *J* = 26.0 Hz, 1 H), 5.61 (ddd, *J* = 4.3, *J* = 7.7 Hz, *J* = 48.4 Hz, 1 H, CHF), 7.13 (d, *J* = 7.8 Hz, 1 H), 7.35 (d, *J* = 7.8 Hz, 1 H), 7.42–7.47 (m, 2 H), 7.57–7.62 (m, 1 H), 7.87 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.1 (CH_3), 37.1 (d, *J* = 22.8 Hz, CH_2), 91.2 (d, *J* = 186.8 Hz, CHF), 128.7 (CH), 129.0 (C), 130.0 (CH), 130.7 (CH), 131.8 (CH), 134.0 (C), 134.2 (CH), 137.6 (C), 211.1 (d, *J* = 23.1 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.8 (ddd, *J* = 17.7, *J* = 25.8 Hz, *J* = 48.3 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{15}FOSNa$ $[M + Na]^+$ 297.0725; found 297.0727.

Methyl (2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-[(2-fluoro-3-oxodecyl)thio]propanoate (17a): From 2-fluorodec-1-en-3-one (**7a**; 63 mg, 0.37 mmol), yield 82 mg (0.20 mmol, 54 %), yellow solid, m.p. 38 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.0 Hz, 3 H), 1.24–1.30 (m, 8 H), 1.45 (s, 9 H), 1.55–1.63 (m, 2 H), 2.61–2.66 (m, 2 H), 2.94 (m, 2 H), 3.04 (m, 2 H), 3.77 (s, 3 H), 4.54–4.56 (m, 1 H), 4.92 (ddd, *J* = 3.7, *J* = 6.7 Hz, *J* = 49.2 Hz, 1 H, CHF), 5.34–5.36 (m, 1 H, NH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.5 (CH_2), 28.3–29.0 (3 CH_2), 28.7 (3 CH_2), 33.9 (d, *J* = 21.5 Hz, CH_2), 35.6 (d, *J* = 9.4 Hz, CH_2), 39.0 (d, *J* = 5.3 Hz, CH_2), 45.7 (CH_2), 52.6 (CH_3), 52.2/53.3 (CH), 80.2 (C), 95.5 (d, *J* = 187.8 Hz, CHF), 155.1 (C), 171.3 (C), 208.6 (d, *J* = 24.4 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.1 (m) ppm. HRMS (ESI): calcd. for $C_{19}H_{34}FNO_5SNa$ $[M + Na]^+$ 430.2039; found 430.2036.

Methyl (2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-[(2-fluoro-3-oxohexadecyl)thio]propanoate (17b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 56 mg (0.11 mmol, 58 %), yellow solid, m.p. 47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.9 Hz, 3 H), 1.26–1.33 (m, 20 H), 1.45 (s, 9 H), 1.55–1.63 (m, 2 H), 2.58–2.71 (m, 2 H), 2.87–3.00 (m, 2 H), 2.99 (m, 2 H), 3.77 (s, 3 H), 4.52–4.59 (m, 1 H), 4.92 (ddd, *J* = 3.5, *J* = 6.9 Hz, *J* = 49.2 Hz, 1 H, CHF), 5.33–5.35 (m, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.5, 22.7 (2 CH_2), 28.7 (3 CH_3), 29.1–29.6 (9 CH_2), 33.9 (d, *J* = 21.6 Hz, CH_2), 35.5 (d, *J* = 1.8 Hz, CH_2), 39.0 (d, *J* = 5.3 Hz, CH_2), 45.3 (CH_2), 52.6 (CH_3), 52.2/53.3 (CH), 80.3 (C), 95.5 (d, *J* = 187.5 Hz, CHF), 155.1 (C), 171.3 (C), 208.6 (d, *J* = 24.6 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.1 (m) ppm. HRMS (ESI): calcd. for $C_{25}H_{46}FNO_5SNa$ $[M + Na]^+$ 514.2978; found 514.2970.

Methyl (2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-[(3-cyclohexyl-2-fluoro-3-oxopropyl)thio]propanoate (17c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 31 mg, 0.20 mmol), yield 42 mg (0.11 mmol, 54 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22–1.37 and 1.66–1.90 (m, 10 H), 1.45 (s, 9 H), 2.82–2.88 (m, 1 H), 2.90–3.10 (m, 4 H), 3.77 (s, 3 H), 4.54–4.56 (m, 1 H), 5.00 (ddt, *J* = 3.5, *J* = 6.9 Hz, *J* = 49.0 Hz, 1 H, CHF), 5.32–5.35 (m, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.4, 25.6 (2 CH_2), 25.8 (CH_2), 27.3, 28.1 (2 CH_2), 28.7 (3 CH_2), 34.0 (d, *J* = 21.5 Hz, CH_2), 35.6 (d, *J* = 10.5 Hz, CH), 46.3 (CH_2), 52.7 (CH_3), 52.2/53.3 (CH), 80.2 (C), 95.1 (dd, *J* = 187.7 Hz, CHF), 155.1 (C), 171.3 (C), 210.9 (d, *J* = 23.1 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –191.3, –191.4 (m) ppm. HRMS (ESI): calcd. for $C_{18}H_{30}FNO_5SNa$ $[M + Na]^+$ 414.1726; found 414.1716.

Methyl (2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-[(2-fluoro-3-oxo-3-phenylpropyl)thio]propanoate (17d): From 2-fluoro-1-phenylprop-2-en-1-one (**7d**; 26 mg, 0.17 mmol), yield 36 mg (0.15 mmol, 83 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 9 H), 3.02–3.19 (m, 4 H), 3.76 (s, 3 H), 4.56 (m, 1 H), 5.63–5.80 (m, 1 H, CHF), 5.34–5.36 (m, 1 H), 5.63–5.80 (m, 1 H), 7.49–7.52 (m, 2 H), 7.61–7.65 (m, 1 H), 7.97–7.99 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28. 3 (3 CH_2), 34.0 (d, *J* = 21.5 Hz, CH_2), 35.6 (d, *J* = 10.7 Hz, C), 41.7

(CH_2), 52.7 (CH_3), 53.2/53.3 (CH), 80.3 (C), 93.0 (d, J = 188.4 Hz, CHF; second diastereomer), 93.1 (d, J = 188.4 Hz, CHF), 128.8 (CH), 129.1 (d, CH), 134.1 (C), 134.2 (CH), 155.1 (C), 171.3 (C), 194.67 (d, J = 20.0 Hz, CHF), 194.68 (d, J = 20.0 Hz, CHF; second diastereomer) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –183.9, –184.0 (m) ppm. HRMS (ESI): calcd. for $C_{18}H_{24}FNO_5SNa$ $[M + Na]^+$ 408.1257; found 408.1248.

General Procedure for Michael Additions of Oxygen Nucleophiles: Fluorinated α,β-unsaturated carbonyl compound **7** (1.0 equiv.) was added to a solution of sodium carbonate (1.5 equiv.) and the nucleophile (1 mL). The reaction mixture was stirred until TLC indicated complete conversion. Then, CH_2Cl_2 and H_2O (10 mL each) were added. The organic layer was washed with $NaHCO_3$ solution (5 wt.-%; 20 mL) and brine (20 mL). The organic phase was dried with $MgSO_4$, and the solvent was evaporated in vacuo. The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 40:1 to 10:1) to give the desired product.

2-Fluoro-1-methoxydecan-3-one (18a): From 2-fluorodec-1-en-3-one **7a** (44 mg, 0.26 mmol), yield 17 mg (0.08 mmol, 34 %), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.6 Hz, 3 H), 1.20–1.33 (m, 8 H), 1.54–1.61 (m, 2 H), 2.64 (tdd, J = 3.1, J = 7.3 Hz, 2 H), 3.38 (s, 3 H), 3.78 (m, 2 H), 4.85 (dm, J = 49.4 Hz, 1 H, CHF) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.4 (CH_2), 29.0, 29.7 (2 CH_2), 31.7 (CH_2), 39.2 (CH_2), 67.3 (CH_3), 70.3 (d, J = 19.7 Hz, CH_2), 95.3 (d, J = 189.2 Hz, CHF), 208.9 (d, J = 25.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –190.0 to –190.2 (m) ppm. HRMS (ESI): calcd. for $C_{11}H_{21}FO_2Na$ $[M + Na]^+$ 227.1423; found 227.1425.

2-Fluoro-1-methoxyhexadecan-3-one (18b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 25 mg (0.08 mmol, 44 %), white solid, m.p. 43 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.9 Hz, 3 H), 1.24–1.30 (m, 20 H), 1.53–1.61 (m, 2 H), 2.56–1.68 (m, 2 H), 3.37 (s, 3 H), 3.69–3.82 (m, 2 H), 3.74–3.95 (dm, J = 49.4 Hz, 1 H, CHF) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 14.9 (CH_2), 22.4 (CH_2), 29.3–31.9 (9 CH_2), 39.3 (CH_2), 59.6 (CH_3), 72.2 (d, J = 19.6 Hz, CH_2), 95.1 (d, J = 189.2 Hz, CHF), 208.6 (d, J = 24.9 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.3 (dddt, J = 3.1, J = 24.9 Hz, J = 28.2 Hz, J = 49.3 Hz) ppm. HRMS (ESI): calcd. for $C_{17}H_{33}FO_2Na$ $[M + Na]^+$ 311.2362; found 311.2363.

1-Ethoxy-2-fluorodecan-3-one: (19a): From 2-fluorodec-1-en-3-one (**7a**; 40 mg, 0.27 mmol) Yield: 17 mg (0.08 mmol, 39 %), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.9 Hz, 3 H), 1.18 (t, J = 7.0 Hz, 3 H), 1.15–1.26 (m, 8 H), 1.56–1.62 (m, 2 H), 2.61–2.66 (m, 2 H), 3.45–3.59 (m, 2 H), 3.74–3.84 (m, 2 H), 4.79–4.92 (dm, J = 50.2 Hz, CHF) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 14.9 (CH_3), 22.4 (CH_2), 22.7 (CH_2), 29.0–29.8 (3 CH_2), 39.2 (CH_2), 67.3 (CH_3), 70.3 (d, J = 19.7 Hz, CH_2), 95.2 (d, J = 189.2 Hz, CHF), 208.9 (d, J = 25.5 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.1 (dtt, J = 3.1, J = 23.7 Hz, J = 50.4 Hz) ppm. HRMS (ESI): calcd. for $C_{12}H_{23}FO_2Na$ $[M + Na]^+$ 241.1580; found 241.1580.

1-Ethoxy-2-fluorohexadecan-3-one (19b): From 2-fluorohexadec-1-en-3-one (**7b**; 50 mg, 0.20 mmol), yield 19 mg (0.06 mmol), white solid, m.p. 45 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, J = 6.9 Hz, 3 H), 1.11 (t, J = 7.0 Hz, 3 H), 1.15–1.26 (m, 20 H), 1.47–1.56 (m, 2 H), 2.53–2.61 (m, 2 H), 3.39–3.51 (m, 2 H), 3.68–3.79 (m, 2 H), 4.70–4.86 (dm, J = 50.2 Hz, 1 H, CHF) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 14.9 (CH_3), 22.4 (CH_2), 22.5 (CH_2), 29.0–31.9 (9 CH_2), 39.2 (CH_2), 67.3 (CH_2), 70.3 (d, J = 19.7 Hz, CH_2), 95.3 (d, J = 189.1 Hz, CHF), 208.9 (d, J = 24.9 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.0 (dtt, J = 3.1, J = 23.7 Hz, J = 50.4 Hz) ppm. HRMS (ESI): calcd. for $C_{18}H_{35}FO_2Na$ $[M + Na]^+$ 325.2519; found 325.2513.

1-Cyclohexyl-3-ethoxy-2-fluoropropan-1-one (19c): From 1-cyclohexyl-2-fluoroprop-2-en-1-one (**7c**; 56 mg, 0.36 mmol), yield 26 mg (0.13 mmol, 36 %), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, J = 7.0 Hz, 3 H), 1.16–1.40 (m, 10 H), 2.86 (m, 1 H), 3.47–3.58 (m, 2 H), 3.75–3.85 (m, 2 H), 4.94 (m, 1 H, CHF) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (CH_3), 25.5, 25.6 (2 CH_2), 25.8 (CH_2), 28.0 (2 CH_2), 46.3 (CH_2), 67.2 (CH_2), 70.4 (d, J = 19.7 Hz, CH_2), 94.4 (d, J = 189.6 Hz, CHF), 211.2 (d, J = 23.3 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –196.6 to –197.0 (m) ppm. HRMS (ESI): calcd. for $C_{11}H_{19}FO_2Na$ $[M + Na]^+$ 225.1267; found 225.1267.

Acknowledgments

Financial support from the Deutsche Forschungsgemeinschaft (DFG) (SFB 656, project B01) is gratefully acknowledged.

Keywords: Fluorine · Enones · Michael addition · Nucleophilic addition

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Received: January 22, 2016
Published Online: March 14, 2016

