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Report

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Monofluoromethyl-Substituted Sulfonium Ylides: Preparation, Structure-Reactivity Study and Substrate Scope

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Abstract. Structure-reactivity study of a family of electrophilic monofluoromethylating reagents based on sulfonium ylide skeleton with different steric hindrance and electron-withdrawing properties was described. These studies led us to discover two highly reactive reagents **3** with a cyclic malonate backbone and **6** with an electron-poor 1,1,1,5,5,5-hexafluoropentane-2,4-dione backbone. The high reactivity of reagent **6** allowed to highly selectively access either C-monofluoromethylated or O-monofluoromethylated β-ketoesters in high yields by the use of different bases. In addition, reactions of reagent **3** with a variety of nucleophiles including phenols, carboxylic acids, thiophenols or heteroaryl nucleophiles occurred in full conversion within 10 min at room temperature and the scopes for these reactions were reported in detail.

Background and Originality Content

Monofluoromethyl group (-CH_2F), which is generally considered as bioisostere of methyl, hydroxy, thiol or amino group,[1] has attracted recent intense interests in the field of medicinal chemistry, largely due to fluorine's unique properties related to its small size and strong electronegativity. It is now well-accepted that the incorporation of fluorine might change the target molecule's physical properties including conformation and dipole moment, which in turn would bring "magic effect" on the drug candidate's physiological properties such as lipophilicity and metabolic stability.[2,3] Consequently, development of efficient methods for the preparation of monofluoromethylated compounds is in high demand and represents a current great challenge.

Classic methods for the introduction of monofluoromethyl group generally involve two different strategies.[4] In the first strategy, a primary alcohol was treated with a fluorinating reagent such as DAST or its derivatives to afford the monofluoromethylated compounds.[5] Alternatively, in the second strategy, an alkyl electrophile such as alkyl halide or tosylate was nucleophilically replaced by a fluoride to generate the corresponding monofluoromethylated compounds.[6] A third, direct monofluoromethylating strategy that utilizes an electrophilic monofluoromethylating reagent to react with various nucleophiles for the formation of monofluoromethylated compounds, however, is less developed, owing mainly to the lack of highly reactive electrophilic monofluoromethylating reagent. Earlier direct monofluoromethylating strategy typically use fluoromethyl halides ($ClCH_2F$ or ICH_2F) as the monofluoromethyl source.[7] While chlorofluoromethane belongs to a family of ozone-depleting compounds and its future usage will be limited, iodofluoromethane, which exhibits higher reactivity than chlorofluoromethane, was mainly made from chlorofluoro-methane in low yield, even though it allowed the direct monofluoromethylation of various carbon-nucleophiles.[8] Later on, two radical monofluoromethylating reagents CH_2FSO_2Na (**I**)[9] and $(CH_2FSO_2)_2Zn$ (**II**)[10] that were able to monofluoromethylate electron-poor heteroarenes or alkenes

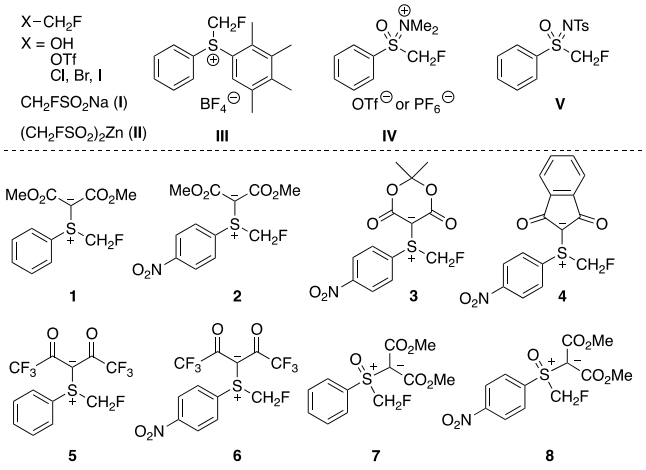


Figure 1 Reagents for monofluoromethylation.

were reported by Hu and Baran, respectively. Alternatively, to expand the scope of the substrates for the introduction of the monofluoromethyl group, three electrophilic monofluoromethylating reagents such as *S*-monofluoromethyl-*S*-phenyl-2,3,4,5-tetramethylphenylsulfonium tetrafluoroborate (**III**)[11] and *N*-((fluoromethyl)(oxo)(phenyl)-λ⁶-sulfaneylidene)-*N*-methylmethanaminium triflate or hexafluorophosphate (**IV**),[12] and *N*-dimethyl-*S*-monofluoromethyl-*S*-phenylsulfoximinium hexafluorophosphate (**V**),[13] were reported. Nevertheless, the reactivities of these reagents were moderate and the substrates were limited mainly to heteroatom-containing nucleophiles such as phenol, thiol, amine, phosphine, sulfonic and carboxylic acid. To overcome these limitations, in 2017, we reported the development of two electrophilic monofluoromethylating reagents **1** and **2** based on sulfonium ylide skeleton that allowed to monofluoromethylate a variety of primary, secondary and tertiary alcohols and soft carbon nucleophiles malonate derivatives for the first time in high yields, as well as those heteroatom nucleophiles (Figure 1).[14,15] We now report that the development of a general method for the preparation of a variety of monofluoromethylated sulfonium ylides **3**-**8** and structure activity relationship studies (SAR) showed that two new reagents **3** and **6** exhibited higher reactivity than the original reagents. As a result, the scope of the reaction can now be easily extended to monofluoromethylate β-ketoesters. In addition, using reagent **3** as the electrophilic monofluoromethylating reagent, the reaction time could be significantly shortened to within 15 min, which might have potential application in the preparation of ^{18}F-labelled compounds.

Results and Discussion

Design and preparation of monofluoromethylated sulfonium ylides. Our original method for the preparation of monofluoromethylated sulfonium ylides involves a Rh-catalyzed reaction of aryl monofluoromethylthioether with dimethyl 2-diazomalonate in dichloromethane at 40 °C for 24 h.[16] The reaction was quite efficient since only 0.1 mol% $Rh_2(esp)_4$ (esp = tetramethyl-1,3-benzenedipropionate) was required for full conversion. With an aim to identify a more reactive electrophilic monofluoromethylating reagent through structure activity relationship study (SAR), we then designed a few analogs of reagent **1** and **2** with a cyclic malonate **3** or 2-diazo-1*H*-indene-1,3(2*H*)-dione **4** or a more electron-poor 1,1,1,5,5,5-hexafluoropentane-2,4-dione backbone **5** and **6**. However, our initial efforts to synthesize these ylide derivatives under the standard reaction conditions were unsuccessful. Reaction of (4-nitrophenyl)fluoromethylthioether with 2-diazo-2,2-dimethyl-1,3-dioxane-4,6-dione or 2-diazo-1*H*-indene-1,3(2*H*)-dione were sluggish and less than 30% conversions were observed after 72 h at 60 °C in 1,2-dichloroethane with 1.0 mol% rhodium catalyst loading, while reaction using 3-diazo-1,1,1,5,5,5-hexafluoropentane-2,4-dione did not occur at all. We reasoned that since the rate determining step of the ylide formation reaction was the Rh-catalyzed decomposition of the diazonium compound to generate the corresponding carbene, if we could use a more reactive carbene precursor, the reaction would be accelerated, and the yield of the reaction could be improved. With these in mind, we then tried the reaction using a carbene precursor derived from hypervalent iodide. Notably, it was found that reaction of 2,2-dimethyl-5-(phenyl-λ³-iodaneylidene)-1,3-dioxane-4,6-dione with (4-nitrophenyl)fluoromethylthioether in 1,2-dichloroethane in the presence of 1.0 mol% $Rh_2(OAc)_4$ occurred smoothly after 12 h at ambient temperature to give the corresponding monofluoromethylsulfonium ylide **3** in 88% yield, as determined by ^{19}F NMR spectroscopy with an internal standard (Figure 2). The reaction could be scaled up to 5.0 mmol to give ylide **3** in 46% isolated yield. Likewise, ylide **4** was prepared in 5.0 mmol in 57% yield. Furthermore, ylides **5** and **6** were synthesized from reactions of 1,1,1,5,5,5-hexafluoro-3-(phenyl-λ³-iodaneylidene) pentane-2,4-dione with (phenyl)fluoromethylthioether and (4-nitrophenyl)fluoromethylthioether in 63% and 83% yields, respectively. Previous efforts to synthesize reagents **5** and **6** from the diazonium precursor 3-diazo-1,1,1,5,5,5-hexafluoropentane-2,4-dione under various conditions were unsuccessful.[13]

To assess whether the oxidation state of the sulfur in the ylide will have a beneficial effect on the reactivity of the reagent, we designed reagents **7** and **8** wherein the S atom in these two reagents are in S(VI) oxidation state. Reagents **7** and **8** were prepared by the reactions of dimethyl 2-diazomalonate with 1-((fluoromethyl)sulfinyl)benzene or 1-((fluoromethyl)sulfinyl)-4-nitrobenzene in 1,2-dichloroethane in the presence of 0.5 mol% $Rh_2(OAc)_4$ for 12 h at ambient temperature with good yields (64% and 40%, respectively).

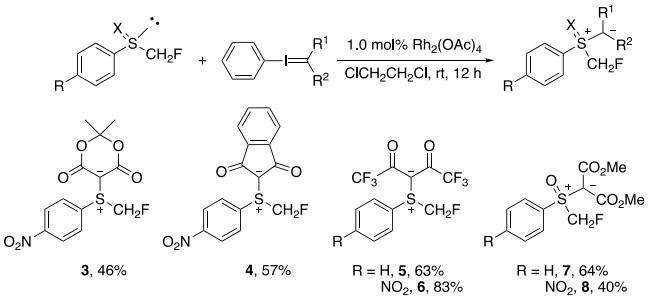
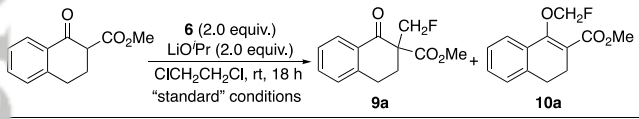


Figure 2 Preparation of ylides **3**-**8**.

X-ray structures of compounds 1-3 and 6-7. Monofluoromethylsulfonium ylides **1**-**8** are shelf-stable, white or yellow crystalline solids. Single crystals of ylides **1**-**3** and **6**-**7** were obtained by slow diffusion of petroleum ether to an ethyl acetate solution of the corresponding ylides at room temperature (Figure 3). Selected bond lengths and bond angles were shown in Table 1. It was found that the S(1)-C(CH_2F) bond length (1.8370(18) Å) in ylide **2** with a strong electron-withdrawing group was longer than that in ylide **1** (1.828(2) Å), while the bond length was further elongated with the malonate unit was replaced by a cyclic

malonate group of ylide **3**. Likewise, replacement of the malonate unit in ylide **1** by a more electron-poor 1,1,1,5,5,5 -hexafluoropentane-2,4-dione unit also led to elongate the bond length (1.8370(18) Å in ylide **2** vs 1.8453(17) Å in ylide **6**). In addition, it was found that the S(1)-C(CH_2F) bond length in ylide **7** with S(VI) oxidation state is longer than that in ylide **1**. Since the longer S(1)-C(CH_2F) bond length indicates the weaker S(1)-C(CH_2F) bond strength, we speculated that ylides **3**-**8** might exhibit higher electrophilicity and broader substrate scope than ylides **1**-**2**.

Scheme 1 Optimization of reaction of β-ketoester with reagent **6**.



entry	derivation from the "standard" conditions	yield (%)		
		TMSF	**9a**	**10a**
1	none	-	70	-
2	1.0 equiv of LiO^{i}Pr and reagent **6**	-	54	-
3	LiOH instead of LiO^{i}Pr	-	62	4
4	LiHMDS instead of LiO^{i}Pr	58	32	-
5	dioxane instead of $ClCH_2CH_2Cl$	-	50	18
6	BTPP	-	-	60

Reaction conditions: β-ketoester (0.1 mmol), reagent **6** (0.2 mmol), LiO^{i}Pr (0.2 mmol) in $ClCH_2CH_2Cl$ (1.0 mL) at room temperature for 18 h; [b]Yields were determined by ^{19}F NMR spectroscopy with trifluorotoluene as an internal standard.

C-Selective monofluoromethylation of β-ketoester.[17] In 2017, we discovered that reaction of 2-aryl or 2-alkyl-substituted malonate derivatives reacted with reagent **2** in NMP smoothly at room temperature after 4 h to give the corresponding carbon-monofluoromethylated malonates in high yields.[13] However, our efforts to extend the reaction of β-ketoesters failed since the reaction was rather sluggish and the formation of desired C-monofluoromethylated product was not detected. With the new monofluoromethylated ylides **3**-**8** in hand, we envisaged that these reagents might be electrophilic enough to enable the reaction. With these thoughts in mind, we attempted the reaction of β-ketoester derived from α-tetralone with reagent **6** because the S(1)-C(CH_2F) bond length in ylide **6** is the longest and likely **6** is the most electrophilic reagent in our list. A quick screening of the

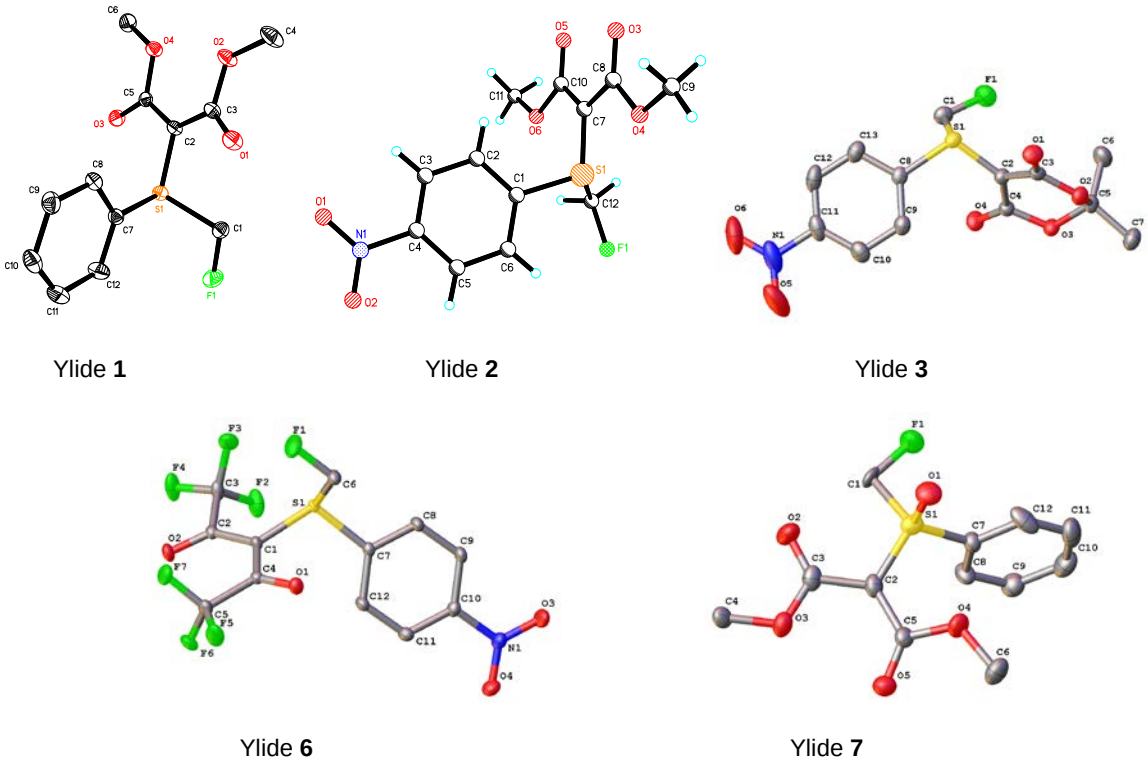


Figure 3 X-Ray structure of ylides **1**-**3** and **6**-**7**.

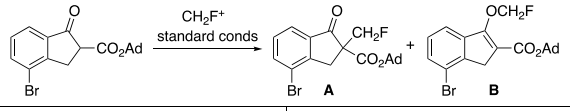
Table 1 Selected bond lengths and bond angles for single crystals of ylides **1**-**3** and **6**-**7**.

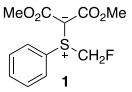
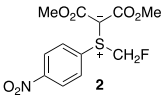
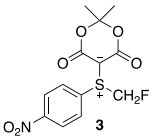
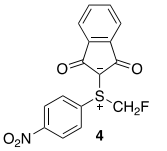
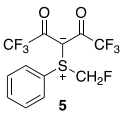
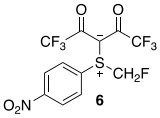
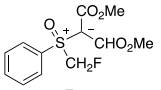
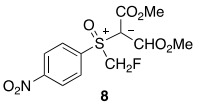
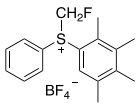
ylide	Bond length (Å)			Bond angle (°)	
	S(1)-C(CH_2F)	S(1)-C(Ar)	S(1)-C(=C)	C(CH_2F)-S(1)-C(Ar)	C(CH_2F)-S(1)-C(=C)
1	1.828(2)	1.787(2)	1.716(2)	100.32(10)	106.56(10)
2	1.8370(18)	1.7956(17)	1.7097(19)	101.90(8)	109.19(9)
3	1.844(2)	1.792(2)	1.7040(18)	96.64(9)	103.16(10)
6	1.8453(17)	1.7899(17)	1.7359(16)	101.24(8)	106.80(8)
7	1.842(9)	1.771(10)	1.696(11)	102.4(5)	108.3(5)

combination of the base and the solvent disclosed that reaction in 1,2-dichloroethane using 1.0 equivalent of LiO^{i}Pr as the base occurred smoothly to give the C-monofluoromethylated β-ketoester **9a** in 54% yield, while the formation of the O-monofluoromethylated compound **10a** was not observed. Increasing the amount of LiO^{i}Pr and reagent **6** to 2.0 equivalents led to the increase of the yield to 70% yield (Scheme 1, entry 1). Switching the base to LiOH gave slightly inferior yield (62%) with the formation of compound **10a** in 4% yield (Scheme 1, entry 3). Interestingly, when LiHMDS was used as the base, TMSF was observed to be the main product (58% yield) and compound **9a** was formed in 32% yield (Scheme 1, entry 4). In addition, when the reaction was conducted in an ether solvent such as dioxane, the formation of O-monofluoromethylated compound **10a** increased significantly to 18% (Scheme 1, entry 5). Surprisingly, when a strong organic base *tert*-butylimino tri(pyrrolidino)phosphorane (BTPP)[12] was used, the reaction occurred highly selectively to give O-monofluoromethylated compound **10a** in 60% yield (Scheme 1, entry 6).

Structure activity relationship study (SAR) of reagents 1-8. The success in identifying the right conditions for highly C-selective monofluoromethylation of β-ketoester promoted us to evaluate other electrophilic monofluoromethylating reagents under the optimized conditions. Consistent with our previous observation, reaction of β-ketoester derived from 1-indanone with reagents **1** and **2** occurred slowly to give the monofluoromethylated products in less than 24% yields with a high ratio formation of O-monofluoromethylated product **B** (Scheme 2, entries 1-2). Reactions with ylide **3** or **4** bearing a cyclic malonate or 1*H*-indene-1,3(2*H*)-dione subunit occurred much faster and gave the C-monofluoromethylated product **A** as the major product in 54-56% yields while the formation of O-monofluoromethylated product **B** was generated in less than 8% yields (Scheme 2, entries 3-4). Notably, reagents **5** and **6** containing a more electron-poor 1,1,1,5,5,5-hexafluoropentane-2,4-dione backbone exhibited dramatically different reactivity. While reaction with reagent **6** took place smoothly under the standard conditions to give the C-monofluoromethylated product **A** in 70% yield as well as the O-monofluoromethylated product **B** in 6% yield, reaction with reagent **5** did not occur at all (Scheme 2, entries 5-6). These results suggest the importance of the strong electron-withdrawing group (-NO_2) on the arene moiety of the ylide in promoting the reactivity of the reagent. To probe whether the oxidation state of the sulfur in the ylide can further promote the reactivity, we studied the reaction with reagents **7**-**8**. Nevertheless, reactions

Scheme 2 Structure activity study (SAR) of reagents **1**-**8** and reagent **III**.



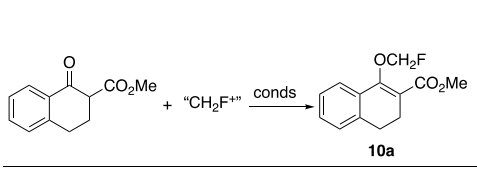
entry	reagent	yield (%) A	yield (%) B
1	 **1**	–	–
2	 **2**	14	10
3	 **3**	54	8
4	 **4**	56	6
5	 **5**	–	–
6	 **6**	70	6
7	 **7**	–	–
8	 **8**	–	–
9		28	68

[a]Reaction conditions: β-ketoester (0.1 mmol), reagent **1**-**9**, **III** (0.2 mmol), LiO^{i}Pr (0.2 mmol) in $ClCH_2CH_2Cl$ (1.0 mL) at room temperature for 18 h; [b]Yields were determined by ^{19}F NMR spectroscopy with trifluorotoluene as an internal standard.

were sluggish and the formation of monofluoromethylated products **A** or **B** was not observed (Scheme 2, entries 7-8). As a comparison, we also investigated the reaction of β-ketoester with Prakash's monofluoromethylating reagent **III**[11] under the standard conditions and found that the O-monofluoromethylated product **B** was generated as the major product and the C-monofluoromethylated product **A** was minor product with yields of 68% and 28%, respectively (Scheme 2, entry 9). These structure-activity studies suggest that decreasing the electron density on the sulfur atom of the ylide would significantly improve the electrophilicity of the reagent, while changing the oxidation state of the ylide from S(IV) to S(VI) does not have a beneficial effect on the reactivity of the reagent.

Scope of C-Selective monofluoromethylation of β-ketoesters with reagent 6. Having elucidated the key structural factors for the high reactivity of the monofluoromethylating reagents and the appropriate conditions for highly C-selective monofluoromethylating β-ketoester, we next studied the generality of the reaction toward other β-ketoesters. In general, β-ketoesters with both electron-donating (-OMe, Me) or withdrawing groups (-Cl, Br, F) all reacted to give the C-monofluoromethylated products in good to excellent yields, as shown in Scheme 3. It was found that the yield of the reaction was greatly affected by the steric hindrance of the ester group of β-ketoesters derived from 1-indanone. For example, reaction of *tert*-butyl ester derivative reacted in much higher yield (79%) than that of methyl ester derivative (Scheme 3, **9b** vs **9d**). In addition, the position of the substituent on β-ketoester also affected greatly the yield of the reaction. For instance, reactions of β-ketoesters with a methoxy group at 4-, 5- or 6-position occurred under the standard conditions to give the C-monofluoromethylated products **9g**-**i** in 70%, 98% and 68%

Scheme 4 Optimization for O-Selective monofluoromethylation of β-ketoesters and SAR study of ylides **1**-**6** and **8**.[a]



entry	reagent	base	solvent	yield (%)[b]
1	**6**	BTPP	CH_2Cl_2	58
2	**6**	BTPP	THF	20
3	**6**	BTPP	Dioxane	60
4	**6**	BTPP	DMF	-
5	**6**	BTPP	DMSO	-
6	**6**	BTPP	CH_3CN	-
7	**6**	DBU	Dioxane	-
8	**6**	Li_2CO_3	Dioxane	-
9	**6**	Na_2CO_3	Dioxane	-
10	**6**	K_2CO_3	Dioxane	16
11	**6**	Cs_2CO_3	Dioxane	50
12	**6**	BTPP	CH_2Cl_2	88 (80%[c])[d]
13	**1**	BTPP	CH_2Cl_2	14
14	**2**	BTPP	CH_2Cl_2	40
15	**3**	BTPP	CH_2Cl_2	84
16	**4**	BTPP	CH_2Cl_2	80
17	**5**	BTPP	CH_2Cl_2	20
18	**8**	BTPP	CH_2Cl_2	88[e]

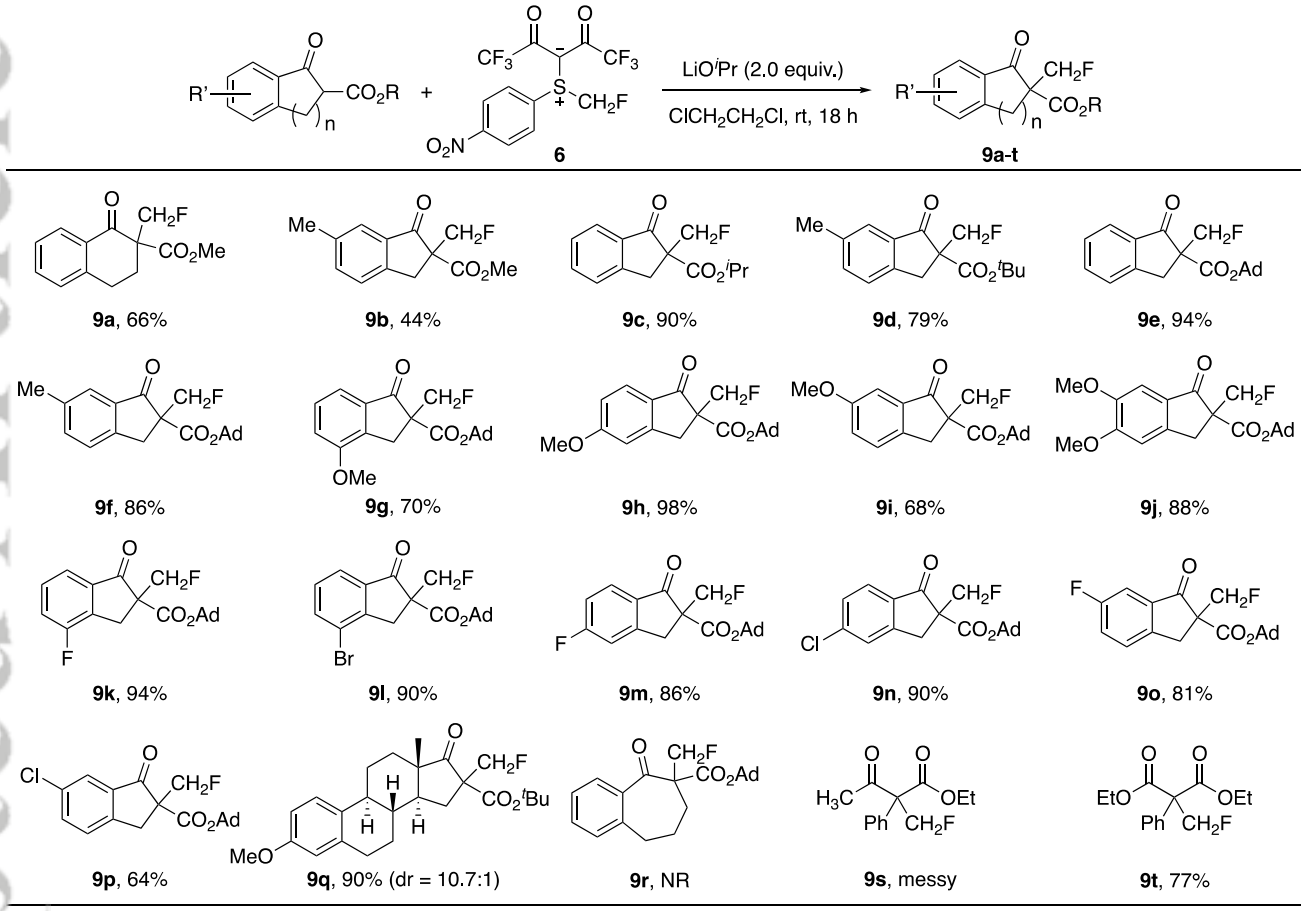
[a]Reaction conditions: β-ketoester (0.05 mmol), reagent **1-6**, **8** (0.05 mmol), base (0.05 mmol) in solvent (0.5 mL) at room temperature for 5.0 min; [b]Yields were determined by ^{19}F NMR spectroscopy with trifluorotoluene as an internal standard; [c]Isolated yield; [d]1.5 Equivalents of reagent **6** was used; [e]Reaction was conducted at room temperature for 2 h.

yields, respectively (Scheme 3, **9g**-**i**). Obviously, the resonance effect of the methoxy at 5-position enhanced the nucleophilicity of the enolate and consequently facilitate the monofluoromethylation. Notably, β-ketoester derived from estrone also reacted to give the corresponding product **9q** in 90% yield with a good diastereoselectivity (Scheme 3, **9q**). Efforts to extend the reaction to seven-membered β-ketoester, however, failed and less than 5% conversion was observed (Scheme 3, **9r**). Likewise, reactions of linear β-ketoesters were messy and the desired C-monofluoromethylated product was generated in less than 5% yield (Scheme 3, **9s**). Nevertheless, reaction of α−phenyl-substituted malonate ester occurred smoothly to give the desired C-monofluoromethylated product **9t** in 77% yield (Scheme 3, **9t**).

O-Selective monofluoromethylation of β-ketoesters with reagent 6. During the optimization for C-Selective monofluoromethylation of β-ketoesters with reagent **6**, we found that when a strong organic base BTPP was used, the O-monofluoromethylated compound **10a** was formed exclusively, which indicates that by choosing an appropriate base, we will be able to control the C- or O-selectivity for the monofluoromethylation reaction of β-ketoesters with reagent **6**. We then optimized the reaction conditions based on this initial

discovery. Carefully monitoring the reaction by ^{19}F NMR spectroscopy disclosed that the reaction occurred rather fast since full conversion was observed when the reactants and the solvent were mixed and rushed for NMR acquisition within 5 min (Scheme 4, entry 3). A quick screening of the solvents showed reactions in CH_2Cl_2 and dioxane occurred in high yields while reactions in other polar solvents such as DMF, DMSO or CH_3CN did not give the monofluoromethylated product at all (Scheme 4, entries 2-6). Considering that the solubility of the inorganic base in dioxane is higher than that in CH_2Cl_2, we next chose dioxane as the solvent to examine the effect of the inorganic bases. Nevertheless, reaction using bases such as Li_2CO_3, Na_2CO_3 or K_2CO_3 occurred

Scheme 3 Scope of C-Selective monofluoromethylation of β-ketoesters with reagent **6**.[a]



[a]Reaction conditions: β-ketoester (0.3 mmol), reagent **6** (0.6 mmol), LiO^{i}Pr (0.6 mmol) in $ClCH_2CH_2Cl$ (6.0 mL) at room temperature for 18 h; Isolated yields.

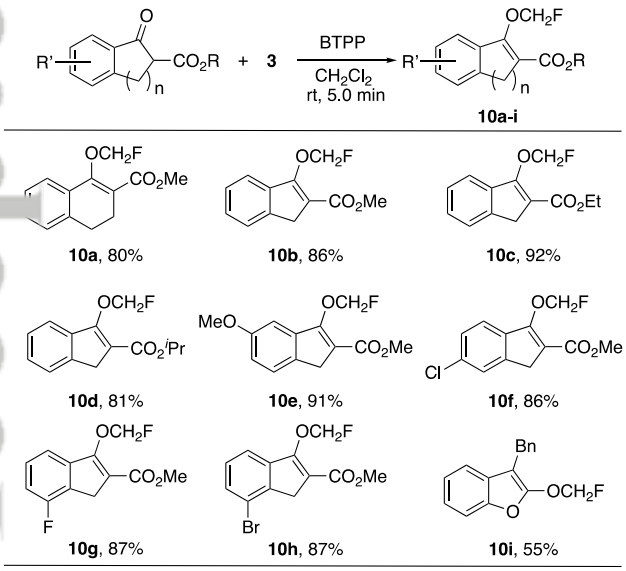
sluggishly and the formation of monofluoromethylated products were formed in less than 16% yield (Scheme 4, entries 8-10). Interestingly, reaction using Cs_2CO_3 occurred smoothly to give product **10a** in 50% yield (Scheme 4, entry 11). Further studies showed that using other organic base such as DBU was not effective (Scheme 4, entry 7). Finally, it was found that the yield of the reaction could be improved to 88% when 1.5 equivalents of reagent **6** was used (Scheme 4, entry 12).

At this stage, we conducted the structure activity relationship study (SAR) for O-Selective monofluoromethylation of β-ketoesters with monofluoromethylative ylide reagents. Not surprisingly, reagent **5** with analogous ylide skeleton as ylide **6** was much less reactive and gave the O-monofluoromethylated product in 20% yield (Scheme 4, entry 17), again highlighting the importance of the electron-withdrawing property of the nitro group on the reactivity of the ylide reagents. Similar to the cases of C-selective monofluoromethylation of β-ketoesters, reagents **1** and **2** were not effective monofluoromethylating reagents for O-Selective monofluoromethylation of β-ketoesters, giving the product **10a** in 14% and 40% yields, respectively (Scheme 4, entries 13-14). In contrast, reactions with ylide **3** or **4** bearing a cyclic malonate or 1*H*-indene-1,3(2*H*)-dione subunit occurred in comparable 84% and 80% yields, respectively (Scheme 4, entries 15-16). Finally, it was found that reaction with reagent **8** occurred

relatively slowly to give the desired compound **10a** after 2.0 h at room temperature in 88% yield (Scheme 4, entry 18).

Scope for O-Selective monofluoromethylation of β-ketoesters with reagent 3. Because of the comparable yields for O-Selective monofluoromethylation of β-ketoesters with reagent **6** and **3**, and the easy availability of the starting material for the preparation of ylide **3**, we next studied the scope of O-Selective monofluoromethylation of β-ketoesters with ylide **3**. As shown in Scheme 5, β-ketoesters derived from indanones with both electron-donating group (-OMe) or electron-withdrawing groups (-F, -Cl and -Br) all reacted smoothly to give the corresponding monofluoromethyl vinyl ethers in high yields (Scheme 5, **10e**, **10f**-**h**). We also found that the steric hinderance of the ester group in the β-ketoester did not have significant effect on the yield of the reaction. For example, β-ketoesters bearing methyl, ethyl or *iso*propyl group reacted with reagent **3** under the standard conditions to give the corresponding products **10b**-**d** in 86%, 92% and 81% yields, respectively (Scheme 5, **10b**-**d**). Furthermore, it was found that benzolactone also reacted under these conditions to give monofluoromethoxy-substituted benzofuran derivative **10i** in 55% yield (Scheme 5, **10i**). Currently, ^{18}F-labeled compounds have found widespread applications in positron emission tomography-computed tomography (PET/CT) for the diagnosis of the tumors and for the study of the pharmacokinetics of the drug molecules.[18] In general, it was required that the preparation of ^{18}F-labelled tracers should be highly efficient to full conversion within 15 mins because of the short lifetime of radioactive ^{18}F ($t_{1/2}$ = 110 min). The high efficiency in BTPP-promoted O-monofluoromethylation of β-ketoesters makes it potentially applicable in the preparation of ^{18}F-labeled monofluoromethyl vinyl ethers.

Scheme 5 Scope for O-Selective monofluoromethylation of β-ketoesters with ylide **3**.[a]

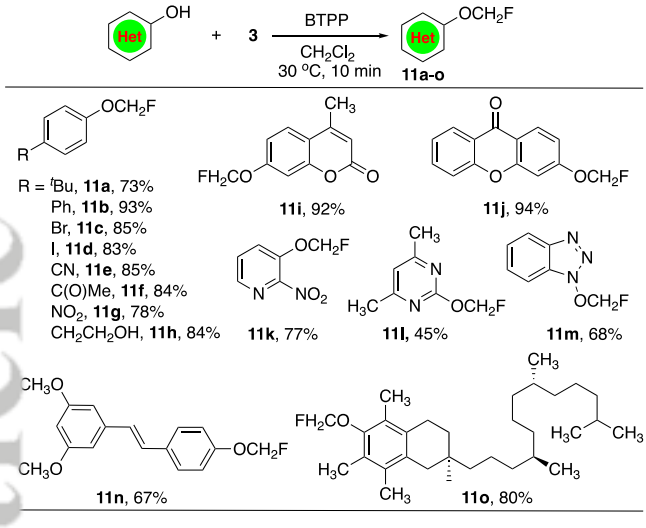


[a] Reaction conditions: β-ketoester (0.3 mmol), reagent **3** (0.3 mmol), BTPP (0.3 mmol) in CH_2Cl_2 (2.0 mL) at room temperature for 5.0 min; Isolated yield.

Monofluoromethylation of phenols with reagent 3. The high efficiency of the BTPP-promoted monofluoromethylation of β-ketoesters with regent **3** and its potential in the preparation of ^{18}F labeled radioactive tracers in PET-CT applications prompted us to study whether this protocol could be extended to other nucleophiles. Since fluoroalkoxy-substituted arenes and heteroarenes are commonly found in drug molecules, we first studied the reaction of phenols with reagent **3**. It was found that reactions of phenols with reagent **3** occurred slightly slower than those of β-ketoesters but full conversions were observed within 10 min at room temperature. As summarized in Scheme 6, reactions of both electron-rich or poor phenols all reacted to give the corresponding monofluoromethoxylated arenes in high yields. In addition, heterophenols such as 3-hydroxy-2-nitropyridine, 4,6-dimethylpyrimidin-2-ol and 1*H*-benzo[*d*][1,2,3]triazol-1-ol also reacted to give the desired products **11k**-**m** in high yields. Furthermore, because of the mild reaction conditions, various of common functional groups including Br (**11c**), I (**11d**), cyano (**11e**), enolizable ketone (**11f**), nitro (**11g**), hydroxyl (**11h**), ester (**11i**) were compatible. Finally, the reaction was applicable to natural molecules bearing a phenoxyl group. For example, reactions of antioxidants pterostilbene and D-δ-tocopherol with reagent **3** occurred to give the corresponding monofluoromethoxyarenes **11n** and **11o** in 67% and 80% yields, respectively (Scheme 6, **11n** and **11o**). The generality of the reaction toward to functionalized (hetero)phenols strongly supports that the reaction is potentially applicable in the preparation of monofluoromethoxylated (hetero)arenes and, more importantly, in the preparation of ^{18}F labeled radioactive tracers containing a monofluoromethoxylated (hetero)arene unit for PET-CT investigation.

Monofluoromethylation of carboxylic acids with reagent 3. Encouraged by the generality of the monofluoromethylative reaction of β-ketoesters and (hetero)phenols, we next tried the reaction of carboxylic acids with reagent **3** since carboxylic acids also bear a hydroxy group. It was found that the reaction conditions for phenols could be effectively applied to reaction with carboxylic acids. As summarized in Scheme 7, reactions of benzoic acids bearing both electron-donating or electron-withdrawing groups reacted under standard conditions

Scheme 6 Scope for monofluoromethylation of phenols with ylide **3**.[a]

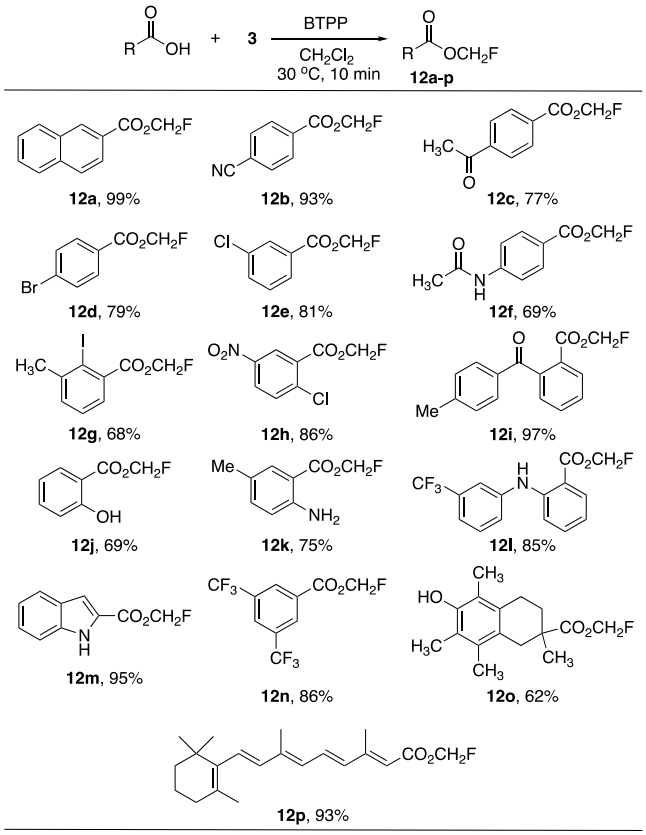


[a]Reaction conditions: phenol (0.3 mmol), reagent **3** (0.3 mmol), BTPP (0.3 mmol) in CH_2Cl_2 (2.0 mL) at room temperature for 10.0 min; Isolated yield.

give the corresponding monofluoromethyl esters in good to excellent yields. For example, reactions of 2-hydroxybenzoic acid and 2-chloro-5-nitrobenzoic acid with reagent **3** occurred after 10 min at room temperature to afford the corresponding monofluoromethyl esters **12j** and **12h** in 69% and 86% yields, respectively (Scheme 7, **12j** and **12h**). Heteroaryl carboxylic acid such as 1*H*-indole-2-carboxylic acid also reacted to give ester **12m** in 95% yield. Not only benzoic acids but also vinyl carboxylic acid or aliphatic carboxylic acids reacted to give the corresponding esters in high yields (Scheme 7, **12o**-**p**). More importantly, because of the higher acidity of the carboxylic acid, the carboxylic acid derivatives containing a free hydroxy, amino or amide group all reacted to give the monofluoromethyl esters while these functional groups remained intact and would allow to be connected with other pharmaceutically important structural motif for biologic activity assessment (Scheme 7, **12f**, **12j**-**l**). Likewise, enolizable ketone was also compatible with the reaction conditions (Scheme 7, **12c**). Furthermore, halogens such as chloride, bromide or iodide were tolerant, that could allow to expand the structural space of the potential drug molecules via classic transition metal-catalyzed cross-coupling.

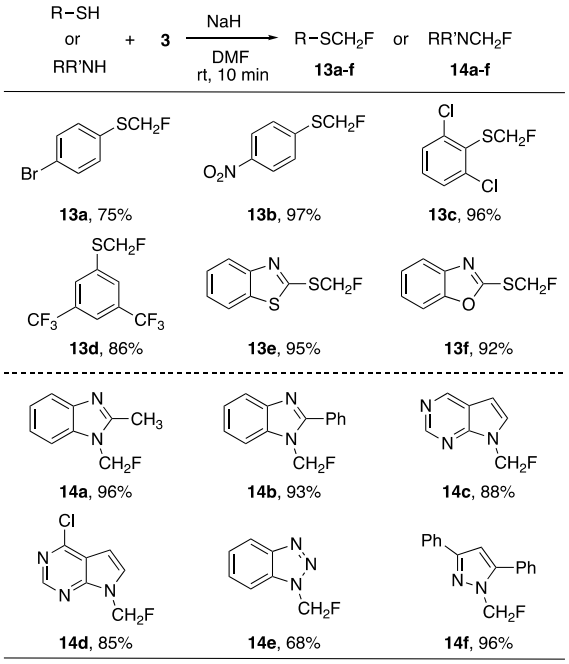
Monofluoromethylation of thiophenols and heteroaryl nitrogen nucleophiles with reagent 3. To further expand the scope of the nucleophiles that could react with electrophilic monofluoromethylating reagent based on ylide skeleton, we studied the reaction of sulfur and nitrogen nucleophilic atoms of heteroarenes with reagent **3**. However, reaction conditions developed for phenols or carboxylic acids were not suitable for these two types of nucleophiles. A quick survey of the commonly used bases led us to identify that NaH was an appropriate base for the reaction. Again, reactions of thiol and heteroaryl nitrogen nucleophile with reagent **3** were quick and full conversions were observed within 10 min at room temperature. As shown in Scheme 8, various aryl thiols and heteroaryl thiols reacted with reagent **3** to give the corresponding monofluoromethylthioethers in excellent yield. For instance, reactions of 4-nitrothiophenol and benzo[*d*]thiazole-2-thiol with reagent **3** occurred to afford monofluoromethylthioethers **13b** and **13e** in 97% and 95% yields, respectively (Scheme 8, **13b** and **13e**). Likewise, reactions of heteroaryl nitrogen nucleophiles with reagent **3** were highly efficient and high-yielding. For example, reactions of 7*H*-pyrrolo[2,3-*d*]pyrimidine and 1*H*-benzo[*d*][1,2,3]triazole with reagent **3** occurred under optimized conditions to give compound

Scheme 7 Scope for monofluoromethylation of carboxylic acids with ylide **3**.[a]



[a]Reaction conditions: carboxylic acid (0.3 mmol), reagent **3** (0.3 mmol), BTPP (0.3 mmol) in CH_2Cl_2 (2.0 mL) at 30 °C for 10 min; Isolated yields.

Scheme 8 Scope for monofluoromethylation of thiophenols and heteroaryl nitrogen nucleophiles with ylide **3**.[a]



[a]Reaction conditions: thiophenol or heteroarene (0.3 mmol), reagent **3** (0.3 mmol), NaH (0.33 mmol) in DMF (2.0 mL) at room temperature for 10 min; Isolated yields.

14c and **14e** in 88% and 68% yields, respectively (Scheme 8, **14c** and **14e**). The generality and the short reaction time of the monofluoromethylation reaction with thiols and heteroaryl nitrogen nucleophiles suggest that the current reaction might find applications in the preparation of ^{18}F-labeled tracer for further PET-CT investigations.

Conclusions

In summary, through structure-activity relationship study (SAR), we successfully elucidated the key structural factors that affect the electrophilicity and reactivity of the electrophilic monofluoromethylating reagents based on sulfonium ylide skeleton, and were able to identify two highly reactive electrophilic monofluoromethylating reagents **3** and **6** based on sulfonium ylide skeleton bearing either a cyclic malonate unit or strong electron-withdrawing 1,1,1,5,5,5-hexafluoropentane -2,4-dione backbone. With these two reagents, we successfully achieved the highly selective C-monofluoromethylation or O-monofluoromethylation of β-ketoesters by employing different bases LiO^iPr or BTPP. Furthermore, the high reactivity of these reagents allowed the high efficiency monofluoromethylating reactions of reagent **3** with a variety of nucleophiles such as phenols, carboxylic acids, thiophenols and heteroaryl nitrogen nucleophiles. Typically, these reactions occurred to full conversions within 10 min, thus paving the way for their future applications in the preparation of ^{18}F-labeled monofluoromethylated compounds. Expanding the scope of the reaction electrophilic monofluoromethylating reagents **1**-**8** with other nucleophiles are currently undergoing in our laboratory.

Experimental

General information. The ^{1}H, ^{19}F NMR spectra were obtained at 293 K on a 300 or 400 spectrometer, and chemical shifts were recorded relative to the solvent resonance. ^{19}F shifts were determined relative to $CFCl_3$ as outside standard and low field is positive. Coupling constants are reported in hertz. The following abbreviations were used to explain the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; br = broad.

All glassware was oven or flame dried for several hours prior to use. Solvents were freshly degassed according to the procedures in *Purification of Laboratory Chemicals* prior to use. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc., and were degassed and stored over activated 4 Å molecular sieves. Unless otherwise noted, all other reagents and starting materials were purchased from commercial sources and used without further purification. Reagent **1** and **2** were prepared according to our previous reported procedure.[14] Likewise, reagent **9** was prepared according to previous reported procedure.[11]

General procedure for preparation of reagent 3. Into a 50 mL round bottom flask equipped with a magnetic stirring bar was added (fluoromethyl)(4-nitrophenyl)thioether (711 mg, 5.00 mmol) and 1,2-dichloroethane (30.0 mL) under an atmosphere of nitrogen. To the mixture, $Rh_2(OAc)_4$ (22 mg, 1.0 mol%) and hypervalent iodonium ylide (3.1 g, 6.0 mmol,1.2 equiv.) was added. The mixture was stirred at room temperature for 12 h. The solvent was evaporated under vacuum and the residue was recrystallized from ethyl acetate/petroleum ether to give ylide **3** as a white solid.

5-[(Fluoromethyl)(4-nitrophenyl)-λ^4-sulfanylidene]-2,2-dimeth yl-1,3-dioxane-4,6-dione (**3**). White solid (575 mg, 46%), mp: 124 –126 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 8.45 (d, *J* = 9.0 Hz, 2 H), 8.04 (d, *J* = 8.7 Hz, 2 H), 6.64 (dd, *J* = 48.2, 6.9 Hz, 1 H), 6.13 (dd, *J* = 44.3, 6.9 Hz, 1 H), 1.77 (s, 6 H); ^{19}F NMR (471MHz, $CDCl_3$) δ -199.70 (dd, *J* = 48.3, 43.8 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4, 150.5, 134.0, 129.9, 125.5, 104.9, 91.0 (d, *J* = 229.8 Hz), 54.1, 26.3 ppm. IR (KBr): ν_{max} = 3105, 2998, 1665, 1531, 1316, 1199, 1051. 915, 853, 739 cm^{-1}. HRMS (ESI) for $C_{13}H_{12}FNO_6SNa$ ($M+Na^+$): Calcd: 352.0262; Found: 352.0259.

2-[(Fluoromethyl)(4-nitrophenyl)-λ^4-sulfanylidene]-1*H*-indene -1,3(2*H*)-dione (**4**). Yellow solid (720 mg, 57%), mp: 148 –150 °C. ^{1}H NMR (500MHz, $CDCl_3$, 293 K, TMS) δ 8.42 (d, *J* = 9.0 Hz, 2 H), 8.11 (d, *J* = 8.6 Hz, 2 H), 7.68 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.59 (dd, *J* = 5.4, 3.1 Hz, 2 H), 6.79 (dd, *J* = 47.9, 6.5 Hz, 1 H), 5.98 (dd, *J* = 44.3, 6.5 Hz, 1 H); ^{19}F NMR (471MHz, $CDCl_3$) δ -200.24 (dd, *J* = 47.5, 44.6 Hz, 1 F); ^{1}^{3}C NMR (126 MHz, $CDCl_3$) δ 188.9, 150.5, 138.9, 135.1, 132.6, 130.7, 125.5, 120.8, 88.8 (d, *J* = 233.6 Hz), 68.3 ppm. IR (KBr): ν_{max} = 3101, 1636, 1596, 1529, 1342, 1293, 852, 724 cm^{-1}.

MS (ESI): 332.0 ($M+H^+$). HRMS (ESI) for $C_{16}H_{11}FNO_4S$ ($M+H^+$): Calcd: 332.0387; Found: 332.0388.

1,1,1,5,5,5-Hexafluoro-3-[(fluoromethyl)(phenyl)-λ^4-sulfanylidene]pentane-2,4-dione (**5**). Yellow solid (1.1 g, 63%), mp: 75 –78 °C. Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.5). ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.70 (d, *J* = 7.3 Hz, 2 H), 7.67 –7.62 (m, 2 H), 6.70 (dd, *J* = 49.2, 7.6 Hz, 1 H), 6.06 (dd, *J* = 45.0, 7.6 Hz, 1 H); ^{19}F NMR (471MHz, $CDCl_3$) δ -72.12 (s, 6 F), -194.31 (t, *J* = 47.1 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6 (q, *J* = 36.0 Hz), 133.3, 131.0, 127.4, 125.3, 117.0 (q, *J* = 289.9 Hz), 94.0 (d, *J* = 228.5 Hz), 78.8 ppm. IR (KBr): ν_{max} = 3064, 2975, 1678, 1628, 1390, 1183, 1119, 1048, 768, 743 cm^{-1}. HRMS (ESI) for $C_{12}H_8F_7O_2S$ ($M+H^+$): Calcd: 349.0128; Found: 349.0126.

1,1,1,5,5,5-Hexafluoro-3-[(fluoromethyl)(4-nitrophenyl)-λ^4-sulfanylidene]pentane-2,4-dione (**6**). Yellow solid (8.7 g, 83%). mp: 115 –117 °C. ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 8.51 (d, *J* = 9.1 Hz, 2 H), 7.89 (d, *J* = 8.7 Hz, 2 H), 6.84 (dd, *J* = 49.4, 7.7 Hz, 1 H), 6.05 (dd, *J* = 44.4, 7.7 Hz, 1 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -72.18 (s, 6 F), -192.37 (dd, *J*= 49.3, 44.4 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4 (q, *J* = 36.3 Hz), 150.5, 132.3, 128.0, 125.9, 116.8 (q, *J* = 289.9 Hz), 94.7 (d, *J* = 232.1 Hz), 77.2 ppm. IR (KBr): ν_{max} = 3110, 1680, 1533, 1346, 1183, 1118, 1050, 853, 740 cm^{-1}. MS (ESI): 393.9 ($M+H^+$). HRMS (ESI) for $C_{12}H_7F_7NO_4S$ ($M+H^+$): Calcd: 393.9979; Found: 393.9978.

Dimethyl [(fluoromethyl)(oxido)phenyl-λ^6-sulfanylidene]propanedioate (**7**). White solid (650 mg, 64%, 3.5 mmol scale). mp: 117–119 °C. Eluent: ethyl acetate/petroleum ether (1:1, R_f = 0.3). ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.94 (d, *J* = 7.9 Hz, 2 H), 7.75 (t, *J* = 7.4 Hz, 1 H), 7.67 (t, *J* = 7.8 Hz, 2 H), 6.18 (dd, *J* = 46.2, 8.5 Hz, 1 H), 5.86 (dd, *J* = 47.7, 8.5 Hz, 1 H), 3.58 (s, 6 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -201.38 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 134.2, 133.9, 123.0, 127.5, 94.3 (d, *J* = 232.4 Hz), 74.1, 51.4 ppm. IR (KBr): ν_{max} = 2952, 1706, 1650, 1436, 1309, 1222, 1086, 772, 584 cm^{-1}. MS (ESI): 289.0 ($M+H^+$); HRMS (ESI) for $C_{12}H_{14}FO_5S$ ($M+H^+$): Calcd: 289.0540; Found: 289.0539.

Dimethyl [(fluoromethyl)(4-nitrophenyl)oxido-λ^6-sulfanylidene]propanedioate (**8**). White solid (670 mg, 40%, 5.0 mmol scale). mp:165 –167 °C. ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 8.40 (d, *J* = 9.0 Hz, 2 H), 8.15 (d, *J* = 8.8 Hz, 2 H), 6.21 (dd, *J* = 46.2, 8.7 Hz, 1 H), 5.94 (dd, *J* = 47.6, 8.7 Hz, 1 H), 3.65 (s, 6 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -200.77 (t, *J* = 46.8 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ164.5, 151.1, 140.6, 128.9, 125.0, 94.5 (d, *J* = 233.6 Hz), 74.5, 51.8 ppm. IR (KBr): ν_{max} = 3015, 2954, 1708, 1642, 1533, 1436, 1315, 1222. 1087, 730, 592 cm^{-1}. MS (ESI): 334.0 ($M+H^+$); HRMS (ESI) for $C_{12}H_{13}FNO_7S$ ($M+H^+$): Calcd: 334.0391; Found: 334.0391.

General procedure for C-Selective monofluoromethylation of β-ketoesters with reagent 6. Into a 25 mL Schlenk tube equipped with a magnetic stirring bar was added β-ketoester (0.3 mmol), LiOH or LiO^iPr (0.6 mmol), reagent **6** (0.6 mmol) and 1,2-dichloroethane (6.0 mL). The mixture was stirred at room temperature for 18 h. The solvent was evaporated under vacuum and the residue was purified by flash chromatograph to give compound **9a** (48 g, 67% yield) as a colorless liquid. Methyl 2-(fluoromethyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**9a**). Colorless liquid (48 mg, 67%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) 8.08 (d, *J* = 7.9 Hz, 1 H), 7.53 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.35 (t, *J* = 7.6 Hz, 1 H), 7.27 (d, *J* = 7.8 Hz, 1 H), 4.99 (dd, *J* = 46.6, 9.0 Hz, 1 H), 4.84 (dd, *J* = 46.9, 9.1 Hz, 1 H), 3.73 (s, 3 H), 3.19 (ddd, J = 16.4, 11.1, 4.7 Hz, 1 H), 3.02 (dt, *J* = 17.2, 4.7 Hz, 1 H), 2.65 (dt, *J* = 13.8, 4.7 Hz, 1 H), 2.44 (ddd, *J* = 13.8, 11.1, 4.8 Hz, 1 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -229.89 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 192.5 (d, *J* = 2.7 Hz), 169.7 (d, *J* = 6.8 Hz), 143.4, 134.1, 131.7, 128.9, 128.1, 127.0, 84.2 (d, *J* = 176.2 Hz), 58.5 (d, *J* = 20.1 Hz), 52.9, 28.4 (d, *J* = 4.0 Hz), 25.6 ppm. IR (KBr): ν_{max} = 2956, 1737, 1688, 1602, 1487, 1313, 1241, 1221, 1016, 749 cm^{-1}. MS (EI): 236 (M^+). HRMS (EI) for $C_{13}H_{13}FO_3$ (M^+): Calcd: 236.0849; Found: 236.0857.

Methyl 2-(fluoromethyl)-6-methyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**9b**). Colorless liquid (32 mg, 45%). Eluent: ethyl acetate/petroleum ether (1:10, Rf = 0.4). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) 7.57 (s, 1 H), 7.46 (d, *J* = 7.9 Hz, 1 H), 7.43 – 7.38 (m, 1 H), 4.87 (d, *J* = 48.0 Hz, 2 H), 3.70 (s, 3 H), 3.64 (d, *J* = 17.2 Hz, 1 H), 3.36 (d, *J* = 17.2 Hz, 1 H), 2.39 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.45 (t, *J* = 46.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 199.1 (d, *J* = 4.4 Hz), 168.9 (d, *J* = 9.6 Hz), 150.8, 138.1, 137.2, 135.1, 126.2, 124.8, 83.8 (d, *J* = 174.0 Hz), 61.5 (d, *J* = 21.0 Hz), 53.0, 33.9 (d, *J* = 3.4 Hz), 21.1 ppm. IR (KBr): ν_{max} = 2956, 1742, 1713, 1494, 1433, 1270, 1200, 1013, 823, 503 cm^{-1}. MS (EI): 236 (M^+). HRMS (EI) for $C_{13}H_{13}FO_3$ (M^+): Calcd: 236.0849; Found: 236.0857.

Isopropyl 2-(fluoromethyl)-6-methyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**9c**). Colorless liquid (68 mg, 90%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) 7.76 (d, *J* = 7.7 Hz, 1 H), 7.63 (t, *J* = 7.4 Hz, 1 H), 7.51 (d, *J* = 7.7 Hz, 1 H), 7.39 (t, *J* = 7.5 Hz, 1 H), 4.97-5.06 (m, 1 H), 4.87 (d, *J* = 48.0 Hz, 2 H), 3.67 (d, *J* = 17.3 Hz, 1 H), 3.39 (d, *J* = 17.3 Hz, 1 H), 1.22 – 1.15 (m, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.52 (t, *J* = 46.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 199.3, 167.8 (d, *J* = 9.5 Hz), 153.5, 135.7, 135.0, 127.9, 126.5, 124.9, 83.8 (d, *J* = 173.6 Hz), 69.8, 61.4 (d, *J* = 20.7 Hz), 34.3 (d, *J* = 3.5 Hz), 21.5 ppm. IR (KBr): ν_{max} = 2983, 1736, 1715, 1608, 1465, 1288, 1268, 1210, 1104, 1006, 927, 756 cm^{-1}. MS (EI): 250 (M^+). HRMS (EI) for $C_{14}H_{15}FO_3$ (M^+): Calcd: 250.1005; Found: 250.1003.

tert-Butyl 2-(fluoromethyl)-6-methyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**9d**). Brown liquid (65 mg, 78%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) 7.57 (s, 1 H), 7.46 (d, *J* = 7.8 Hz, 1 H), 7.41 (d, *J* = 7.9 Hz, 1 H), 4.89 (dd, *J* = 40.0, 8.0 Hz, 1 H), 4.84 (dd, *J* = 40.0, 8.0 Hz, 1 H), 3.60 (d, *J* = 17.0 Hz, 1 H), 3.34 (d, *J* = 17.0 Hz, 1 H), 2.40 (s, 3 H), 1.41 (s, 9 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.62 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 199.8 (d, *J* = 4.0 Hz), 167.5 (d, *J* = 10.3 Hz), 151.0, 137.8 136.9, 135.3, 126.1, 124.7, 83.9 (d, *J* = 172.8 Hz), 82.8, 62.3 (d, *J* = 20.3 Hz), 34.0 (d, *J* = 3.7 Hz), 27.8, 21.0 ppm. IR (KBr): ν_{max} = 2979, 2931, 1732, 1712, 1617, 1494, 1369, 1273, 1254, 1159, 1146, 1114, 1004, 843, 747, 504 cm^{-1}. MS (ESI): 301 ($M+Na^+$). HRMS (ESI) for $C_{16}H_{19}FNaO_3$ ($M+Na^+$): Calcd: 301.1210; Found: 301.1205.

Adamantyl 2-(fluoromethyl)-1-oxo-2,3-dihydro-1*H*-indene -2-carboxylate (**9e**). Colorless liquid (96 mg, 94%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.76 (d, *J* = 7.7 Hz, 1 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 7.50 (d, *J* = 7.7 Hz, 1 H), 7.38 (t, *J* = 7.8 Hz, 1 H), 4.88 (dd, *J* = 48.0, 8.0 Hz, 1 H), 4.8 (dd, *J* = 48.0, 8.0 Hz, 1 H), 3.63 (d, *J* = 17.2 Hz, 1 H), 3.37 (d, *J* = 17.1 Hz, 1 H), 2.11 (s, 3 H), 2.01 (s, 6 H), 1.59 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.81 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 200.0 (d, *J* = 4.1 Hz), 167.1 (d, *J* = 10.0 Hz), 153.5, 135.5, 135.2, 127.7, 126.4, 124.8, 83.8 (d, *J* = 172.8 Hz), 82.9, 62.1 (d, *J* = 20.4 Hz), 41.0, 36.0, 34.4 (d, *J* = 3.6 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2853, 1734, 1714, 1608, 1458, 1288, 1208, 1049, 1006, 756 cm^{-1}. MS (EI): 342 (M^+). HRMS (EI) for $C_{21}H_{23}FO_3$ (M^+): Calcd: 342.1631; Found: 346.1632.

Adamantyl 2-(fluoromethyl)-6-methyl-1-oxo-2,3-dihydro-1*H* -indene-2-carboxylate (**9f**). Colorless liquid (91 mg, 85%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.54 (s, 1 H), 7.42 (d, *J* = 8.9 Hz, 1 H), 7.37 (d, *J* = 7.8 Hz, 1 H), 4.86 (dd, *J* = 48.0, 8.0 Hz, 1 H), 4.79 (dd, *J* = 48.0, 8.0 Hz, 1 H), 3.56 (d, *J* = 17.1 Hz, 1 H), 3.30 (d, *J* = 17.0 Hz, 1 H), 2.37 (s, 3 H), 2.10 (s, 3 H), 2.00 (s, 6 H), 1.58 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.82 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 199.7 (d, *J* = 4.1 Hz), 167.1 (d, *J* = 10.0 Hz), 150.9, 137.7, 136.8, 135.3, 126.0, 124.6, 83.8 (d, *J* = 172.7 Hz), 82.7, 62.3 (d, *J* = 20.5 Hz), 40.9, 35.9, 34.0 (d, *J* = 3.5 Hz), 30.8, 21.0 ppm. IR (KBr): ν_{max} = 2912, 2853, 1731, 1712, 1617, 1494, 1457, 1283, 1198, 1049, 1006, 966, 873, 730, 503 cm^{-1}. MS (EI): 356 (M^+). HRMS (EI) for $C_{22}H_{25}FO_3$ (M^+): Calcd: 356.1788; Found: 356.1787.

Adamantyl 2-(fluoromethyl)-4-methoxy-1-oxo-2,3-dihydro -1*H*-indene-2-carboxylate (**9g**). Colorless liquid (75 mg, 67%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.34 (d, *J* = 3.8 Hz, 2 H), 7.05 (q, *J* = 4.3 Hz, 1 H), 4.87 (dd, *J* = 48.0, 8.0 Hz, 1 H), 4.82 (dd, *J* = 48.0, 8.0 Hz, 1 H), 3.90 (s, 3 H), 3.51 (d, *J* = 18.3 Hz, 1 H), 3.25 (d, *J* = 17.6 Hz, 1 H), 2.11 (s, 3 H), 2.01 (s, 6 H), 1.59 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -231.07 (t, *J* = 47.0 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 200.1, 167.2 (d, *J* = 10.4 Hz), 156.8, 142.5, 136.7, 129.3, 116.2, 115.6, 83.8 (d, *J* = 172.8 Hz), 82.8, 61.8 (d, *J* = 20.6 Hz), 55.5, 41.0, 36.0, 31.4 (d, *J* = 3.7 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2853, 1733, 1715, 1603, 1489, 1298, 1265, 1077, 1048, 1006, 969 cm^{-1}. MS (EI): 372 (M^+). HRMS (EI) for $C_{22}H_{25}FO_4$ (M^+): Calcd: 372.1737; Found: 372.1744.

Adamantylmethyl 2-(fluoromethyl)-5-methoxy-1-oxo-2,3 -dihydro-1*H*-indene-2- carboxylate (**9h**). Colorless liquid (108 mg, 97%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.37 (d, *J* = 8.3 Hz, 1 H), 7.20 (dd, *J* = 8.3, 2.6 Hz, 1 H), 7.16 (d, *J* = 2.5 Hz, 1 H), 4.87 (dd, *J* = 48.0, 8.0 Hz, 1 H), 4.78 (dd, *J* = 48.0, 8.0 Hz, 1 H), 3.52 (d, *J* = 16.8 Hz, 1 H), 3.27 (d, *J* = 16.8 Hz, 1 H), 2.10 (s, 3 H), 2.00 (s, 6 H), 1.59 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.92 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 199.7, 167.2 (d, *J* = 10.2 Hz), 159.6, 146.5, 136.4, 127.1, 125.0, 105.7, 83.8 (d, *J* = 172.6 Hz), 82.9, 62.7 (d, *J* = 20.5 Hz), 55.6, 41.0, 36.0, 33.8 (d, *J* = 3.5 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2853, 1731, 1712, 1493, 1279, 1264, 1049, 1026, 761, 731 cm^{-1}. MS (EI): 372 (M +). HRMS (EI) for $C_{22}H_{25}FO_4$ (M+): Calcd: 372.1737; Found: 372.1735.

Adamantyl 2-(fluoromethyl)-6-methoxy-1-oxo-2,3-dihydro -1*H*-indene-2-carboxylate (**9i**). Colorless liquid (76 mg, 68%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.68 (d, *J* = 8.6 Hz, 1 H), 6.90 (d, *J* = 8.2 Hz, 2 H), 4.84 (dd, *J* = 48.0, 8.0 Hz, 1 H), 4.80 (dd, *J* = 48.0, 8.0 Hz, 1 H), 3.58 (d, *J* = 17.3 Hz, 1 H), 3.29 (d, *J* = 17.2 Hz, 1 H), 2.11 (s, 3 H), 2.02 (s, 6 H), 1.59 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.60 (t, *J* = 47.1 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 197.6 (d, J = 4.4 Hz), 167.3 (d, *J* = 9.7 Hz), 166.0, 156.6, 128.3, 126.5, 115.9, 109.5, 83.9 (d, *J* = 172.4 Hz), 82.7, 62.4 (d, J = 20.3 Hz), 55.7, 41.0, 36.0, 34.3 (d, *J* = 3.5 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2852, 1730, 1709, 1600, 1490, 1457, 1262, 1049, 731 cm^{-1}. MS (EI): 372 (M^+). HRMS (EI) for $C_{22}H_{25}FO_4$ (M^+): Calcd: 372.1737; Found: 372.1747.

Adamantyl 2-(fluoromethyl)-5,6-dimethoxy-1-oxo-2,3 -dihydro-1*H*-indene-2-carboxylate (**9j**). White solid (106 mg, 88%), mp: 164–165 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.13 (s, 1 H), 6.88 (s, 1 H), 4.82 (dd, *J* = 48.0, 8.0 Hz, 1 H), 4.77 (dd, *J* = 48.0, 8.0 Hz, 1 H), 3.94 (s, 3 H), 3.86 (s, 3 H), 3.50 (d, *J* = 16.9 Hz, 1 H), 3.23 (d, *J* = 16.9 Hz, 1 H), 2.09 (s, 3 H), 2.00 (s, 6 H), 1.57 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -230.66 (t, *J* = 47.0 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 198.1 (d, J = 4.3 Hz), 167.4 (d, *J* = 9.8 Hz), 156.2, 149.7, 149.2, 127.8, 107.2, 104.9, 83.8 (d, *J* = 172.6 Hz), 82.7, 62.4 (d, *J* = 20.4 Hz), 56.3, 56.1, 41.0, 36.0, 34.1 (d, *J* = 3.4 Hz), 30.82 ppm. IR (KBr): ν_{max} = 2913, 2853, 1728, 1702, 1591, 1502, 1458, 1317, 1274, 1248, 1221, 1113, 1049, 1007, 965, 814, 869, 732 cm^{-1}. MS (EI): 402 (M^+). HRMS (EI) for $C_{23}H_{27}FO_5$ (M^+): Calcd: 402.1843; Found: 402.1848.

Adamantyl 4-fluoro-2-(fluoromethyl)-1-oxo-2,3-dihydro-1*H* -indene-2-carboxylate (**9k**). Yellow liquid (100 mg, 93%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.60 (d, *J* = 7.5 Hz, 1 H), 7.44 – 7.38 (m, 1 H), 7.33 (t, *J* = 8.2 Hz, 1 H), 4.95 (dd, *J* = 46.6, 9.2 Hz, 1 H), 4.82 (dd, *J* = 47.1, 9.2 Hz, 1 H), 3.66 (d, *J* = 17.4 Hz, 1 H), 3.40 (d, *J* = 17.4 Hz, 1 H), 2.14 (s, 3 H), 2.04 (s, 6 H), 1.63 (s, 6 H); ^{19}F NMR (471 MHz, CDCl3) δ -118.67 (dd, *J* = 8.6, 5.1 Hz, 1 F), -231.11 (t, *J* = 47.2 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.8 (d, *J* = 2.7 Hz), 166.5 (d, *J* = 10.2 Hz), 159.8 (d, *J* = 251.1 Hz), 139.3 (d, *J* = 19.8 Hz), 138.0 (d, *J* = 4.9 Hz), 129.8 (d, *J* = 6.6 Hz), 121.6 (d, *J* = 19.4 Hz), 120.5 (d, *J* = 3.9 Hz), 83.5 (d, *J* = 172.7 Hz), 83.3, 61.9 (d, *J* = 20.6 Hz), 41.0, 35.9, 30.8, 30.3 (d, *J* = 3.8 Hz) ppm. IR (KBr): ν_{max} = 2913, 2854, 1739, 1719, 1619, 1593, 1482, 1246, 1218, 1048, 1005, 879, 831, 808 cm-1. MS (EI): 360 (M^+). HRMS (EI) for C21H22F2O3 (M^+): Calcd: 360.1537; Found: 360.1532.

Adamantyl 4-bromo-2-(fluoromethyl)-1-oxo-2,3-dihydro -1*H*-indene-2-carboxyl-ate (**9l**). Yellow liquid (120 mg, 95%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^{1}H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.80 (d, J = 8.5 Hz, 1 H), 7.73 (d, J = 7.5 Hz, 1 H), 7.31 (t, *J* = 7.7 Hz, 1 H), 4.95 (dd, *J* = 46.6, 9.1 Hz, 1 H), 4.83 (dd, *J* = 47.1, 9.1 Hz, 1 H), 3.58 (d, *J* = 17.6 Hz, 1 H), 3.32 (d, *J* = 17.6 Hz, 1 H), 2.14 (s, 3 H), 2.04 (s, 6 H), 1.62 (s, 6 H); ^{19}F

NMR (471 MHz, $CDCl_3$) δ -230.85 (t, *J* = 47.0 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.2 (d, *J* = 3.9 Hz), 166.5 (d, *J* = 10.8 Hz), 153.2, 138.3, 137.1, 129.6, 123.6, 121.9, 83.5 (d, *J* = 172.9 Hz), 83.3, 62.1 (d, *J* = 20.3 Hz), 41.0, 36.0, 35.6 (d, *J* = 3.0 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2853, 1739, 1716, 1598, 1457, 1319, 1255, 1201, 1122, 1048, 1007, 732 cm^{-1}. MS (EI): 420 (M^+). HRMS (EI) for $C_{21}H_{22}BrFO_3$ (M^+): Calcd: 420.0736; Found: 420.0740.

Adamantyl 5-fluoro-2-(fluoromethyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxyl-ate (**9m**). White solid (86 mg, 79%), mp: 97–98 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.79 (dd, *J* = 8.5, 5.3 Hz, 1 H), 7.19 (d, *J* = 8.4 Hz, 1 H), 7.11 (t, *J* = 8.6 Hz, 1 H), 4.92 (dd, *J* = 14.0, 8.0 Hz, 1 H), 4.82 (dd, *J* = 48.0, 8.0 Hz, 1 H), 3.64 (d, *J* = 17.4 Hz, 1 H), 3.38 (d, *J* = 17.4 Hz, 1 H), 2.14 (s, 3 H), 2.03 (s, 3 H), 1.62 (s, 6 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -101.15 (dd, *J* = 15.7, 7.0 Hz, 1 F), -230.88 (t, *J* = 47.0 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9 (d, *J* = 4.0 Hz), 168.6, 166.8, 166.6 (d, *J* = 12.4 Hz), 156.5 (d, *J* = 10.6 Hz), 131.6, 127.1 (d, *J* = 10.8 Hz), 114.7 (dd, *J* = 359.2, 24.3 Hz), 83.6 (d, *J* = 172.7 Hz), 83.2, 62.3 (d, *J* = 20.3 Hz), 41.0, 36.0, 34.2 (d, *J* = 2.8 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2854, 1736, 1716, 1616, 1594, 1254, 1217, 1049, 1007, 962, 731, 651 cm^{-1}. MS (EI): 360 (M^+). HRMS (EI) for $C_{21}H_{22}F_2O_3$ (M^+): Calcd: 360.1537; Found: 360.1535.

Adamantyl 5-chloro-2-(fluoromethyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**9n**). White solid (102 mg, 90%), mp: 132 – 134 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.71 (d, J = 8.2 Hz, 1 H), 7.52 (s, 1 H), 7.38 (d, *J* = 8.1 Hz, 1 H), 4.92 (dd, *J* = 46.7, 9.2 Hz, 1 H), 4.80 (dd, *J* = 47.2, 9.2 Hz, 1 H), 3.62 (d, *J* = 17.3 Hz, 1 H), 3.37 (d, *J* = 17.3 Hz, 1 H), 2.13 (s, 3 H), 2.02 (s, 6 H), 1.62 (s, 6 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -230.90 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.4 (d, *J* = 3.8 Hz), 166.6 (d, *J* = 10.3 Hz), 154.9, 142.2, 133.7, 128.6, 126.7, 125.8, 83.5 (d, *J* = 172.6 Hz), 83.2, 62.2 (d, *J* = 20.4 Hz), 41.0, 35.9, 34.1 (d, *J* = 3.6 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2853, 1736, 1716, 1600, 1580, 1457, 1422, 1295, 1206, 1070, 1049, 1007, 836, 732 cm^{-1}. MS (EI): 376 (M^+). HRMS (EI) for $C_{21}H_{22}ClFO_3$ (M^+): Calcd: 376.1242; Found: 376.1247.

Adamantyl 6-fluoro-2-(fluoromethyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**9o**). Colorless liquid (88 mg, 81%), mp: 97 – 98 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). 1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.50 (dd, *J* = 8.4, 4.5 Hz, 1 H), 7.41 (dd, *J* = 7.4, 2.5 Hz, 1 H), 7.36 (td, *J* = 8.5, 2.5 Hz, 1 H), 4.93 (dd, *J* = 46.7, 9.1 Hz, 1 H), 4.81 (dd, *J* = 47.1, 9.1 Hz, 1 H), 3.60 (d, *J* = 17.0 Hz, 1 H), 3.36 (d, *J* = 17.0 Hz, 1 H), 2.14 (s, 3 H), 2.02 (s, 6 H), 1.62 (s, 6 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.95 (q, *J* = 7.5 Hz, 1 F), -231.00 (t, *J* = 46.9 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 166.7 (d, *J* = 10.6 Hz), 162.4 (d, *J* = 248.7 Hz), 149.0, 136.9 (d, *J* = 7.7 Hz), 127.8 (d, *J* = 7.8 Hz), 123.3 (d, *J* = 23.4 Hz), 110.4, 83.5 (d, *J* = 172.2 Hz), 83.2, 62.8 (d, *J* = 20.4 Hz), 41.0, 35.9, 33.9 (d, *J* = 3.8 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2913, 2854, 1737, 1716, 1488, 1457, 1296, 1262, 1214, 1048, 1007, 875, 767 cm^{-1}. MS (EI): 360 (M+). HRMS (EI) for $C_{21}H_{22}F_2O_3$ (M^+): Calcd: 360.1537; Found: 360.1534.

Adamantyl 6-chloro-2-(fluoromethyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**9p**). Colorless liquid (75 mg, 67%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.74 (d, *J* = 2.0 Hz, 1 H), 7.60 (dd, *J* = 8.2, 2.1 Hz, 1 H), 7.48 (d, *J* = 8.2 Hz, 1 H), 4.94 (dd, *J* = 46.6, 9.2 Hz, 1 H), 4.81 (dd, *J* = 47.1, 9.2 Hz, 1 H), 3.61 (d, *J* = 17.2 Hz, 1 H), 3.36 (d, J = 17.2 Hz, 1 H), 2.14 (s, 3 H), 2.03 (s, 6 H), 1.63 (s, 6 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -230.97 (t, *J* = 46.8 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.7 (d, *J* = 3.9 Hz), 166.6 (d, *J* = 10.7 Hz), 151.6, 136.7, 135.5, 134.2, 127.6, 124.5, 83.5 (d, *J* = 172.7 Hz), 83.3, 62.6, 41.0, 36.0, 34.0 (d, *J* = 3.8 Hz), 30.8 ppm. IR (KBr): ν_{max} = 2912, 2853, 1737, 1719, 1471, 1458, 1248, 1197, 1048, 1007, 871, 728 cm^{-1}. MS (EI): 376 (M^+). HRMS (EI) for $C_{21}H_{22}FClO_3$ (M^+): Calcd: 376.1242; Found: 376.1252.

16-(Fluoromethyl)-3-methoxy-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthrene-16-carboxylate (**9q**). Yellow solid (114 mg, 95%), mp: 105–108 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.22 (dd, *J* = 8.6, 0.9 Hz, 1 H), 6.75 (dd, *J* = 8.6, 2.8 Hz, 1 H), 6.68 (d, *J* = 2.7 Hz, 1 H), 4.72 (d, *J* = 47.3 Hz, 2 H), 3.80 (s, 3 H), 2.97 – 2.91 (m, 2 H), 2.50 – 2.39 (m, 2 H), 2.35 (dd, *J* = 13.0, 5.7 Hz, 1 H), 2.28 (td, *J* = 10.6, 4.3 Hz, 1 H), 2.11 – 1.92 (m, 2 H), 1.72 – 1.43 (m, 14 H), 1.06 (s, 3 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -226.70 (t, *J* = 47.3 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.9 (d, *J* = 2.8 Hz), 167.4 (d, *J* = 9.6 Hz), 157.7, 137.7, 131.8, 126.3, 113.9, 111.6, 85.1 (d, J = 175.7 Hz), 82.7, 62.2 (d, *J* = 20.1 Hz), 55.2, 49.5, 46.6, 43.9, 38.0, 31.8, 29.7 (d, *J* = 7.8 Hz), 27.9, 27.8, 26.5, 25.8, 13.9 ppm. IR (KBr): ν_{max} = 2977, 2932, 2837, 1750, 1721, 1609, 1576, 1500, 1455, 1369, 1281, 1248, 1147, 1042, 1014, 993, 910, 844, 733 cm^{-1}.

Diethyl 2-(fluoromethyl)-2-phenylmalonate (**9t**).[14] Colorless liquid (62 mg, 77%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (500 MHz, $CDCl_3$, 293 K, TMS) δ 7.51 – 7.28 (m, 5 H), 5.18 (s, 1 H), 5.09 (s, 1 H), 4.34 (q, *J* = 7.1, 2 H), 4.31 (q, *J* = 7.1, 2 H), 1.31 (t, *J* = 7.1 Hz, 6 H); ^{19}F NMR (471 MHz, $CDCl_3$) δ -223.77 (t, *J* = 46.7 Hz, 1 F); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1 (d, *J* = 5.7 Hz), 134.4, 128.5, 128.2, 128.0, 84.7 (d, *J* = 177.7 Hz), 63.7 (d, *J* = 19.2 Hz), 62.2, 14.0 ppm.

General procedure for O-Selective monofluoromethylation of β-ketoesters with reagent 3. Into a 10 mL Schlenk tube equipped with a magnetic stirring bar was added β-ketoester (0.3 mmol), BTPP (0.6 mmol), reagent **3** (0.3 mmol) and anhydrous dichloromethane (1.0 mL). The mixture was stirred at room temperature for 5.0 min. The solvent was evaporated under vacuum and the residue was purified by flash chromatograph to give compound **10a** (57 mg, 80% yield) as a colorless liquid.

Methyl 1-(fluoromethoxy)-3,4-dihydronaphthalene-2-carboxylate (**10a**). Colorless liquid (57 mg, 80%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.78 – 7.61 (m, 1 H), 7.33 – 7.22 (m, 2 H), 7.19 – 7.12 (m, 1 H), 5.63 (d, *J* = 55.2 Hz, 2 H), 3.79 (s, 3 H), 2.82 (t, *J* = 7.8 Hz, 2 H), 2.68 (t, *J* = 7.9 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -144.20 (t, *J* = 55.2 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 166.6, 158.3, 138.2, 131.2, 130.1, 127.2, 126.7, 125.0, 114.9, 105.3 (d, *J* =

220.3 Hz), 51.7, 27.4, 23.9 ppm. IR (KBr): ν_{max} = 2993, 2950, 1712, 1619, 1282, 1199, 1127, 972, 768 cm^{-1}. MS (EI): 236.0 (M^+). HRMS (ESI) for $C_{13}H_{13}FO_3$ (M^+): Calcd: 236.0849; Found: 236.0851.

Methyl 3-(fluoromethoxy)-1*H*-indene-2-carboxylate (**10b**).[12] White Solid (57 mg, 86%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.64 (d, *J* = 5.9 Hz, 1 H), 7.45 (d, *J* = 5.8 Hz, 1 H), 7.43 – 7.33 (m, 2 H), 5.94 (d, *J* = 53.8 Hz, 2 H), 3.81 (s, 3 H), 3.66 (s, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -145.05 (t, *J* = 53.8 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 164.3, 162.6, 141.8, 139.2, 128.9, 127.0, 124.3, 121.1, 114.7, 103.9 (d, *J* = 221.5 Hz), 51.47, 35.75 ppm.

Ethyl 3-(fluoromethoxy)-1*H*-indene-2-carboxylate (**10c**). Colorless oil (65 mg, 92%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.65 (d, *J* = 6.4 Hz, 1 H), 7.46 (d, *J* = 6.3 Hz, 1 H), 7.45 – 7.34 (m, 2 H), 5.94 (d, *J* = 54.4 Hz, 2 H), 4.29 (q, *J* = 6.9 Hz, 2 H), 3.69 (s, 2 H), 1.66 – 1.84 (m, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -145.03 (t, *J* = 53.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.9, 162.4, 141.8, 139.4, 128.9, 127.0, 124.3, 121.1, 115.3, 104.0 (d, *J* = 221.4 Hz), 60.3, 35.8, 14.3 ppm. IR (KBr): ν_{max} = 2985, 1697, 1598, 1578, 1367, 1254, 1172, 1124, 1042, 963, 758 cm^{-1}. MS (EI): 236 (M^+). HRMS (EI) for $C_{13}H_{13}FO_3$ (M^+): Calcd: 236.0849; Found: 236.0853.

Isopropyl 3-(fluoromethoxy)-1*H*-indene-2-carboxylate (**10d**).[12] Colorless oil (61 mg, 81%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.61 (dd, *J* = 7.1, 1.6 Hz, 1 H), 7.42 (d, *J* = 6.0 Hz, 1 H), 7.39 – 7.32 (m, 2 H), 5.91 (d, *J* = 54.0 Hz, 2 H), 5.14 (p, *J* = 6.2 Hz, 1 H), 3.64 (s, 2 H), 1.32 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -146.83 (t, *J* = 54.0 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.4, 162.2, 141.7, 139.5, 128.8, 127.0, 124.2, 121.0, 115.8, 104.1 (d, *J* = 221.3 Hz), 67.7, 35.9, 22.0 ppm.

Methyl 3-(fluoromethoxy)-5-methoxy-1*H*-indene-2-carboxylate (**10e**). Colorless oil (69 mg, 91%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.30 (d, *J* = 8.3 Hz, 1 H), 7.12 (d, *J* = 2.2 Hz, 1 H), 6.95 (dd, *J* = 8.3, 2.4 Hz, 1 H), 5.92 (d, *J* = 53.8 Hz, 2 H), 3.83 (s, 3 H), 3.79 (s, 3 H), 3.58 (s, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -145.03 (t, *J* = 53.8 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 164.2, 159.4, 140.5, 134.0, 125.0, 116.6, 115.8, 104.9, 04.0 (d, J = 221.4 Hz), 55.6, 51.5, 35.1 ppm. IR (KBr): ν_{max} = 2958, 2839, 1702, 1595, 1576, 1431, 1348, 1225, 1179, 1023, 972, 833 cm^{-1}. MS (EI): 252 (M^+). HRMS (EI) for $C_{13}H_{13}FO_4$ (M^+): Calcd: 252.0798; Found: 252.0804.

Methyl 6-chloro-3-(fluoromethoxy)-1*H*-indene-2-carboxylate (**10f**). Colorless oil (66 mg, 86%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.51 (d, *J* = 8.2 Hz, 1 H), 7.39 (s, 1 H), 7.32 (d, *J* = 9.6 Hz, 1 H), 5.91 (d, *J* = 53.6 Hz, 2 H), 3.79 (s, 3 H), 3.61 (s, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -145.30 (t, *J* = 53.6 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.9, 161.7, 143.2, 137.8, 135.3, 127.6, 124.7, 122.1, 114.9, 103.9 (d, *J* = 222.0 Hz), 51.6, 35.6 ppm. IR (KBr): ν_{max} = 2953, 1742, 1715, 1599, 1435, 1321, 1252, 1207, 1106, 1039, 982, 616 cm^{-1}. MS (EI): 256 (M^+). HRMS (EI) for $C_{12}H_{10}ClFO_3$ (M^+): Calcd: 256.0303; Found: 256.0305.

Methyl 7-fluoro-3-(fluoromethoxy)-1*H*-indene-2-carboxylate (**10g**)**.** White solid (63 mg, 87%), mp: 140–142 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.43 (d, *J* = 7.6 Hz, 1 H), 7.36 (td, *J* = 7.8, 4.8 Hz, 1 H), 7.09 (t, *J* = 8.5 Hz, 1 H), 5.94 (d, *J* = 53.6 Hz, 2 H), 3.83 (s, 3 H), 3.71 (s, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -120.28 (dd, *J* = 9.0, 4.7 Hz, 1 F), -145.49 (t, *J* = 53.6 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.9, 161.8, 158.5 (d, *J* = 248.5 Hz), 142.4 (d, *J* = 6.6 Hz), 129.3 (d, *J* = 6.9 Hz), 127.0 (d, *J* = 19.6 Hz), 117.3 (dd, *J* = 3.2, 1.4 Hz), 115.7 (d, *J* = 20.4 Hz), 115.4, 103.9 (d, *J* = 222.2 Hz), 51.7, 32.3 ppm. IR (KBr): ν_{max} = 3000, 2960, 1705, 1603, 1478, 1369, 1246, 1181, 1023, 993, 765 cm^{-1}. MS (EI): 240 (M^+). HRMS (EI) for $C_{12}H_{10}F_2O_3$ (M^+): Calcd: 240.0598; Found: 240.0607.

Methyl 7-bromo-3-(fluoromethoxy)-1*H*-indene-2-carboxylate (**10h**). White solid (79 mg, 87%), mp: 92 – 94 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.57 (d, *J* = 7.6 Hz, 1 H), 7.52 (d, *J* = 7.8 Hz, 1 H), 7.30 – 7.21 (m, 1 H), 5.86 (s, 2 H), 3.82 (s, 3 H), 3.61 (s, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -145.42 (t, *J* = 53.6 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.9, 161.7, 141.6, 140.8, 131.9, 128.9, 120.2, 119.2, 115.5, 103.9 (d, *J* = 222.2 Hz), 51.7, 37.2 ppm. IR (KBr): ν_{max} = 3003, 1711, 1593, 1564, 1440, 1360, 1332, 1286, 1232, 1185, 977, 761 cm^{-1}. MS (EI): 300 (M^+). HRMS (EI) for $C_{12}H_{10}BrFO_3$ (M^+): Calcd: 299.9797; Found: 299.9794.

3-Benzyl-2-(fluoromethoxy)benzofuran (**10i**). Colorless oil (42 mg, 55%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.33 (d, *J* = 8.2 Hz, 1 H), 7.26 – 7.19 (m, 5 H), 7.17 (dd, *J* = 8.0, 6.0 Hz, 2 H), 7.13 – 7.07 (m, 1 H), 5.76 (d, *J* = 52.6 Hz, 2 H), 3.94 (s, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -151.93 (t, *J* = 52.6 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 155.1, 148.9, 139.3, 129.2, 128.4, 128.3, 126.2, 123.1, 122.9, 119.4, 110.6, 101.1 (d, *J* = 227.6 Hz), 97.1, 28.1 ppm. IR (KBr): ν_{max} = 3060, 3027, 2920, 1800, 1619, 1495, 1462, 1229, 1125, 1061, 753, 699 cm^{-1}. MS (EI): 256 (M^+). HRMS (EI) for $C_{16}H_{13}FO_2$ (M^+): Calcd: 256.0900; Found: 256.0903.

General procedure for monofluoromethylation of phenols with reagent 3. Into a 10 mL Schlenk tube equipped with a magnetic stirring bar was added phenol (0.3 mmol), BTPP (0.6 mmol), reagent **3** (0.3 mmol) and anhydrous dichloromethane (1.0 mL). The mixture was stirred at room temperature for 10.0 min. The solvent was evaporated under vacuum and the residue was purified by flash chromatograph to give compound **11a** (40 mg, 73% yield) as a colorless liquid.

1-*tert*-Butyl-4-(fluoromethoxy)benzene (**11a**).[14] Colorless liquid (40 mg, 73%). Eluent: petroleum ether (R_f = 0.5). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.37 – 7.30 (m, 2 H), 7.00 (d, *J* = 8.6 Hz, 2 H), 5.68 (d, *J* = 54.9 Hz, 2 H), 1.30 (s, 9 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -148.03 (t, *J* = 54.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 154.5, 146.4, 126.5, 116.2, 101.0 (d, *J* = 218.0 Hz), 31.45 ppm.

4-(Fluoromethoxy)biphenyl (**11b**).[14] Colorless liquid (56 mg, 93%). Eluent: petroleum ether (R_f = 0.45). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.55 – 7.53 (m, 4 H), 7.42 (t, *J* = 7.3 Hz, 2 H), 7.32 (t, *J* = 7.3 Hz, 1 H), 7.14 (d, *J* = 8.4 Hz, 2 H), 5.73 (d, *J* = 54.6

Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -148.47 (t, *J* = 54.6 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 156.2, 140.4, 136.6, 128.8, 128.4, 127.1, 126.9, 116.9, 100.7 (d, *J* = 218.8 Hz) ppm.

1-Bromo-4-(fluoromethoxy)benzene (**11c**).[14] Colorless liquid (52 mg, 85%). Eluent: petroleum ether (R_f = 0.45). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.43 (d, *J* = 9.0 Hz, 2 H), 6.97 (d, *J* = 8.6 Hz, 2 H), 5.68 (d, *J* = 54.4 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -149.17 (t, J = 54.4 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 155.9, 132.6, 118.5, 116.1, 100.7 (d, *J* = 219.6 Hz) ppm.

1-(Fluoromethoxy)-4-iodobenzene (**11d**).[14] Colorless liquid (63 mg, 83%). Eluent: petroleum ether (R_f = 0.5). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.61 (d, *J* = 9.0 Hz, 2 H), 6.84 (d, *J* = 9.0 Hz, 2 H), 5.67 (d, *J* = 54.4 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -149.25 (t, *J* = 54.3 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 156.6, 138.6, 118.9, 100.5 (d, *J* = 219.7 Hz), 86.4 ppm.

4-(Fluoromethoxy)benzonitrile (**11e**).[14] Yellow liquid (39 mg, 85%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.5). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.65 (d, *J* = 9.0 Hz, 1H), 7.15 (d, *J* = 8.9 Hz, 1H), 5.76 (d, *J* = 53.6 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -151.12 (t, *J* = 53.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 159.6, 134.1, 118.5, 117.0, 107.1, 99.6 (d, *J* = 221.9 Hz).

1-(4-(Fluoromethoxy)phenyl)ethanone (**11f**).[14] White solid (42 mg, 84%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.5). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.94 (d, *J* = 8.9 Hz, 2 H), 7.20 – 6.98 (m, 2 H), 5.74 (d, *J* = 53.9 Hz, 2 H), 2.55 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -150.42 (t, *J* = 53.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 196.7, 160.2, 132.6, 130.6, 116.0, 99.8 (d, *J* = 220.7 Hz), 26.5 ppm.

1-(Fluoromethoxy)-4-nitrobenzene (**11g**).[14] Yellow solid (40 mg, 78%). Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.55). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.22 (d, *J* = 9.2 Hz, 2 H), 7.15 (d, *J* = 9.2 Hz, 2 H), 5.78 (d, *J* = 53.4 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -151.57 (t, *J* = 53.4 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 161.2, 143.5, 125.9, 116.4, 99.6 (d, *J* = 222.4 Hz) ppm.

2-(4-(Fluoromethoxy)phenyl)ethanol (**11h**). Colorless oil (43 mg, 84%). Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.35). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.17 (d, *J* = 8.3 Hz, 2 H), 7.02 (d, *J* = 8.3 Hz, 2 H), 5.68 (d, *J* = 54.8 Hz, 2 H), 3.81 (t, *J* = 6.5 Hz, 2 H), 2.82 (t, *J* = 6.5 Hz, 2 H), 1.57 (s, 1 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -148.31 (t, *J* = 54.7 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 155.4, 133.6, 130.2, 116.8, 100.9 (d, *J* = 218.3 Hz), 63.6, 38.3 ppm. IR (KBr): ν_{max} = 3354, 2932, 1611, 1512, 1224, 1095, 1046, 972, 825 cm^{-1}. MS (EI): 170 (M^+). HRMS (EI) for $C_9H_{11}FO_2$ (M^+): Calcd: 170.0743; Found: 170.0742.

7-(Fluoromethoxy)-4-methyl-2*H*-chromen-2-one (**11i**). White solid (58 mg, 92%), mp: 138 – 139 °C. Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.6). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.58 – 7.55 (m, 1 H), 7.06 – 7.00 (m, 2 H), 6.21 (s, 1 H), 5.77 (d, *J* = 53.7 Hz, 2 H), 2.42 (d, *J* = 1.2 Hz, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -150.86 (t, *J* = 53.7 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 160.7, 159.1 (d, *J* = 2.9 Hz), 154.8, 152.0, 125.9, 115.8, 113.4, 113.1 (d, *J* = 1.2 Hz), 104.3, 99.9 (d, *J* = 221.6 Hz), 18.7 ppm. IR (KBr): ν_{max} = 3070, 1732, 1614, 1392, 1371, 1272, 1199, 1089, 982, 868, 829, 455 cm^{-1}. MS (EI): 244 (M^+). HRMS (EI) for $C_{11}H_9FO_3$ (M^+): Calcd: 208.0536; Found: 208.0530.

3-(Fluoromethoxy)-9H-xanthen-9-one (**11j**). White solid (69 mg, 94%), mp: 134 – 136 °C. Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.6). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.38 – 8.21 (m, 2 H), 7.69 (t, *J* = 7.7 Hz, 1 H), 7.44 (d, *J* = 8.4 Hz, 1 H), 7.36 (t, *J* = 7.5 Hz, 1 H), 7.11 (s, 1 H), 7.06 (d, *J* = 10.6 Hz, 1 H), 5.81 (d, *J* = 53.6 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -151.28 (t, *J* = 53.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 176.2, 161.4 (d, *J* = 2.8 Hz), 157.5, 156.2, 134.6, 128.7, 126.7, 124.1, 121.8, 117.8, 117.7, 113.7, 103.8 (d, *J* = 1.4 Hz), 99.7 (d, *J* = 222.0 Hz) ppm. IR (KBr): ν_{max} = 3095, 3021, 2937, 1647, 1616, 1477, 1463, 1445, 1327, 1246, 1177, 1110, 1080, 976, 851, 764, 670 cm^{-1}. MS (EI): 244 (M^+). HRMS (EI) for $C_{14}H_9FO_3$ (M^+): Calcd: 244.0536; Found: 244.0543.

3-(Fluoromethoxy)-2-nitropyridine (**11k**). Yellow solid (40 mg, 77%), mp: 33 – 35 oC. Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.5). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.25 (s, 1 H), 7.76 (s, 1 H), 7.59 (s, 1 H), 5.77 (d, *J* = 53.0 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -151.15 (t, *J* = 52.9 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 149.6, 144.5, 142.7, 128.9, 127.8 (d, *J* = 1.6 Hz), 100.8 (d, *J* = 225.6 Hz) ppm. IR (KBr): ν_{max} = 3081, 2937, 1605, 1541, 1366, 1253, 1117, 991, 862, 814, 666 cm^{-1}. MS (EI): 172 (M^+). HRMS (EI) for $C_6H_5FN_2O_3$ (M^+): Calcd: 172.0284; Found: 172.0281.

1-(Fluoromethoxy)-1*H*-benzo[*d*][1,2,3]triazole (**11l**). Colorless oil (21 mg, 45%). Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.5). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 6.78 (s, 1 H), 6.07 (d, *J* = 51.8 Hz, 2 H), 2.43 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -156.64 (t, *J* = 51.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 169.8, 163.0, 115.9, 96.3 (d, *J* = 219.8 Hz), 23.8 ppm. IR (KBr): ν_{max} = 2961, 1913, 1339, 1261, 1092, 1019, 800, 418 cm^{-1}. MS (EI): 156.2 (M^+). HRMS (EI) for $C_7H_9FN_2O$ (M^+): Calcd: 156.0699; Found: 156.0695.

1-(Fluoromethoxy)-1*H*-benzo[*d*][1,2,3]triazole (**11m**). White solid (34 mg, 68%), mp: 35–37 °C. Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.5). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.98 (d, *J* = 8.9 Hz, 1 H), 7.61 (d, *J* = 8.3 Hz, 1 H), 7.56 – 7.47 (m, 1 H), 7.38 (t, *J* = 7.7 Hz, 1 H), 5.95 (d, *J* = 52.8 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -149.39 (t, *J* = 53.3 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 143.5, 128.8, 128.6, 125.0, 120.1, 109.1, 106.8 (d, *J* = 237.0 Hz) ppm. IR (KBr): ν_{max} = 3093, 2921, 1446, 1368, 1238, 1154, 1089, 1037, 989, 742, 612 cm^{-1}. MS (EI): 167 (M^+). HRMS (EI) for $C_7H_6FN_3O$ (M^+): Calcd: 167.0497; Found: 167.0496.

(E)-1-(4-(fluoromethoxy)styryl)-3,5-dimethoxybenzene (**11n**). Purple solid (58 mg, 67%), mp: 125–128 °C. Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.7). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.46 (d, *J* = 8.7 Hz, 2 H), 7.07 (d, *J* = 8.6 Hz, 2 H), 7.04 (d, *J* = 15.9 Hz, 1 H), 6.94 (d, *J* = 16.3 Hz, 1 H), 6.65 (d, *J* = 2.2 Hz, 2 H), 6.39 (t, *J* = 2.2 Hz, 1 H), 5.71 (d, *J* = 54.6 Hz, 2 H), 3.82 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -148.54 (t, *J* = 54.6 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 161.0, 156.3 (d, *J* = 3.0 Hz), 139.3, 132.7, 128.2, 127.9, 127.9, 116.8, 104.5, 100.6 (d, *J* = 218.9 Hz), 99.9, 55.3 ppm. IR (KBr): ν_{max} = 3396, 2937, 2836, 1597, 1510,

1458, 1424, 1227, 1150, 1092, 965, 833, 737 cm^{-1}. MS (EI): 288 (M^+). HRMS (EI) for $C_{17}H_{17}FO_3$ (M^+): Calcd: 288.1162; Found: 288.1165.

(R)-6-(fluoromethoxy)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-tr imethyltridecyl)ch roman (**11o**). Yellow oil (116 mg, 80%). Eluent: petroleum ether (R_f = 0.3). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 5.50 (d, *J* = 55.3 Hz, 2 H), 2.66 – 2.51 (m, 2 H), 2.17 (s, 3 H), 2.14 (s, 3 H), 2.10 (s, 3 H), 1.88 – 1.72 (m, 2 H), 1.61 – 1.01 (m, 24 H), 0.92 – 0.81 (m, 12 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -148.13 (t, *J* = 55.3 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 148.7, 146.7, 127.6, 125.9, 123.1, 117.6, 105.1 (d, *J* = 218.9 Hz), 75.0, 40.0, 39.4, 37.5, 37.4, 37.3, 32.8, 32.7, 31.2, 28.0, 24.8, 24.5, 23.9, 22.7, 22.6, 21.0, 20.7, 19.8, 19.7, 13.3, 12.5, 11.9 ppm. IR (KBr): ν_{max} = 2926, 2867, 1460, 1401, 1377, 1248, 1166, 1128, 1102, 975 cm^{-1}. MS (ESI): 463 ($M+H^+$). HRMS (ESI) for $C_{30}H_{52}FO_2$ ($M+H^+$): Calcd: 463.3946; Found: 463.3947.

General procedure for monofluoromethylation of carboxylic acids with reagent 3. Into a 10 mL Schlenk tube equipped with a magnetic stirring bar was added carboxylic acid (0.3 mmol), BTPP (0.6 mmol), reagent **3** (0.3 mmol) and anhydrous dichloromethane (1.0 mL). The mixture was stirred at room temperature for 10.0 min. The solvent was evaporated under vacuum and the residue was purified by flash chromatograph to give compound **12a** (55 mg, 89% yield) as a white solid. **Fluoromethyl 2-naphthoate 12a**. mp: 84–86 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.68 (s, 1 H), 8.08 (dd, *J* = 8.7, 1.7 Hz, 1 H), 7.95 (d, *J* = 8.1 Hz, 1 H), 7.88 (dd, *J* = 8.4, 6.0 Hz, 2 H), 7.65 – 7.59 (m, 2 H), 7.55 (t, *J* = 7.5 Hz, 1 H), 6.01 (d, *J* = 50.8 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -157.48 (t, *J* = 50.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 164.8, 135.9, 132.3, 132.0, 129.4, 128.7, 128.4, 127.7, 126.8, 125.6, 125.1, 93.9 (d, *J* = 220.5 Hz) ppm. IR (KBr): ν_{max} = 2995, 1735, 1473, 1352, 1285, 1195, 1152, 1095, 1000, 782, 769 cm^{-1}. MS (EI): 388 (M^+). HRMS (EI) for $C_{17}H_{15}ClF_2S_2O_2$ (M^+): Calcd: 388.0170; Found: 388.0180.

Fluoromethyl 4-cyanobenzoate (**12b**).[14] White solid (50 mg, 93%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.55). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.18 (d, *J* = 8.7 Hz, 2 H), 7.76 (d, *J* = 8.7 Hz, 2 H), 5.94 (d, J = 50.3 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -158.06 (t, *J* = 50.3 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.1, 132.3, 130.5, 117.6, 117.3, 94.0 (d, *J* = 222.7 Hz) ppm.

Fluoromethyl 4-acetylbenzoate (**12c**).[14] White solid (45 mg, 77%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.55). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.15 (d, *J* = 8.5 Hz, 2 H), 7.99 (d, *J* = 8.6 Hz, 2 H), 5.93 (d, *J* = 50.5 Hz, 2 H), 2.61 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -157.94 (t, *J* = 50.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 197.2, 163.8, 140.9, 132.1, 130.3, 128.2, 93.9 (d, *J* = 221.7 Hz), 26.8 ppm.

Fluoromethyl 4-bromobenzoate (**12d**). Yellow liquid (55 mg, 79%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.94 (d, *J* = 8.5 Hz, 2 H), 7.61 (d, *J* = 8.5 Hz, 2 H), 5.92 (d, *J* = 50.6 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -157.80 (t, *J* = 50.6 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.9, 131.9, 131.5, 129.2, 127.4, 93.8 (d, *J* = 221.4 Hz) ppm. IR (KBr): ν_{max} = 2292, 1747, 1591, 1474, 1399, 1265, 1162, 1101, 1010, 756, 566 cm^{-1}. MS (EI): 232.0 (M^+). HRMS (EI) for $C_8H_6BrFO_2$ (M^+): Calcd: 231.9535; Found: 231.9539.

Fluoromethyl 3-chlorobenzoate (**12e**). Yellow oil (46 mg, 81%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.3). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.06 (s, 1 H), 7.97 (d, *J* = 7.8 Hz, 1 H), 7.61 – 7.53 (m, 1 H), 7.41 (t, *J* = 7.9 Hz, 1 H), 5.93 (d, *J* = 50.5 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -157.89 (t, *J* = 50.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 163.5, 134.7, 133.9 , 130.2, 130.0, 129.8, 128.1, 93.8 (d, *J* = 221.8 Hz) ppm. IR (KBr): ν_{max} = 3074, 2994, 1749, 1577, 1473, 1429, 1279, 1252, 1116, 1011, 748 cm^{-1}. MS (EI): 188.1 (M^+). HRMS (EI) for $C_8H6ClFO_2$ (M^+): Calcd: 188.0040; Found: 188.0046.

Fuoromethyl 4-acetamidobenzoate (**12f**). White solid (44 mg, 69%), mp: 153–155 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.06 (d, *J* = 8.6 Hz, 2 H), 7.77 – 7.43 (m, 3 H), 5.93 (d, *J* = 50.8 Hz, 2 H), 2.22 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -157.44 (t, *J* = 50.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 168.5, 164.0, 143.0, 131.4, 123.7, 118.7, 93.7 (d, *J* = 220.3 Hz), 24.7 ppm. IR (KBr): ν_{max} = 3314, 3274, 3191, 3123, 1740, 1683, 1596, 1538, 1410, 1322, 1261, 1179, 1160, 1096, 1001, 769 cm^{-1}. MS (EI): 211.1 (M^+). HRMS (EI) for $C_{10}H_{10}FNO_3$ (M^+): Calcd: 211.0645; Found: 211.0652.

Fluoromethyl 2-iodo-3-methylbenzoate (**12g**). Yellow solid (60 mg, 68%), mp: 33–36 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.55 (dd, *J* = 7.6, 1.7 Hz, 1 H), 7.41 (dd, *J* = 7.5, 1.7 Hz, 1 H), 7.31 (t, *J* = 7.6 Hz, 1 H), 5.95 (d, *J* = 50.6 Hz, 2 H), 2.55 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -158.57 (t, *J* = 50.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 165.7, 143.9, 135.5, 132.9, 128.1, 127.8, 100.7, 94.1 (d, *J* = 221.9 Hz), 29.9 ppm. IR (KBr): ν_{max} = 2988, 1755, 1459, 1399, 1281, 1261, 1125, 1008, 750 cm^{-1}. MS (EI): 388 (M^+). HRMS (EI) for $C_9H_8FIO_2$ (M^+): Calcd: 293.9553; Found: 293.9555.

Fluoromethyl 2-chloro-5-nitrobenzoate (**12h**). Yellow solid (60 mg, 86%), mp: 62–64 °C. Eluent: ethyl acetate/petroleum ether (1:6, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.80 (d, *J* = 2.2 Hz, 1 H), 8.32 (dd, *J* = 8.7, 2.2 Hz, 1 H), 7.69 (d, *J* = 8.8 Hz, 1 H), 5.96 (d, *J* = 50.0 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -158.25 (t, *J* = 50.0 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 161.3, 146.1, 141.7, 132.8, 129.0, 127.8, 127.1, 94.1 (d, *J* = 224.2 Hz) ppm. IR (KBr): ν_{max} = 3118, 3097, 1751, 1609, 1518, 1463, 1357, 1276, 1164, 1012, 741, 595 cm^{-1}. MS (EI): 233.1 (M^+). HRMS (EI) for $C_8H_5ClFNO_4$ (M^+): Calcd: 232.9891; Found: 232.9896.

Fluoromethyl 2-(4-methylbenzoyl)benzoate (**12i**). Yellow solid (79 mg, 97%), mp: 65–67 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.5). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.10 (d, *J* = 7.6 Hz, 1 H), 7.71 – 7.61 (m, 3 H), 7.57 (t, *J* = 7.6 Hz, 1 H), 7.39 (d, *J* = 7.3 Hz, 1 H), 7.21 (d, *J* = 7.9 Hz, 2 H), 5.67 (d, *J* = 50.4 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -158.66 (t, *J* = 50.4 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 196.3, 164.0, 144.3, 142.7, 134.3, 133.2, 130.6, 129.6, 129.6, 129.3, 127.9, 127.4, 93.8 (d, *J* = 222.2 Hz), 21.7 ppm. IR (KBr): ν_{max} = 3028, 1731, 1694, 1661, 1602,

1487, 1274, 1089, 993, 932, 748, 715 cm^{-1}. MS (EI): 272.1 (M^+). HRMS (EI) for $C_{16}H_{13}FO_3$ (M^+): Calcd: 272.0849; Found: 272.0856.

Fluoromethyl 2-hydroxybenzoate (**12j**). White oil (35 mg, 69%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 10.29 (s, 1 H), 7.89 (dd, *J* = 8.0, 1.7 Hz, 1 H), 7.50 (ddd, *J* = 8.5, 7.2, 1.7 Hz, 1 H), 6.99 (dd, *J* = 8.4, 0.6 Hz, 1 H), 6.94 – 6.86 (m, 1 H), 5.94 (d, *J* = 50.3 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -157.99 (t, *J* = 50.4 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 168.3, 162.2, 136.8, 130.2, 119.4, 117.7, 111.0, 93.5 (d, *J* = 223.1 Hz) ppm. IR (KBr): ν_{max} = 3524, 2996, 2700, 1616, 1485, 1302, 1250, 1208, 1159, 1094, 1025, 758 cm^{-1}. MS (EI): 170.1 (M^+). HRMS (EI) for $C_8H_7FO_3$ (M^+): Calcd: 170.0379; Found: 170.0376.

Fluoromethyl 2-amino-5-methylbenzoate (**12k**). Yellow solid (41 mg, 75%), mp: 155–158 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.3). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.71 (s, 1 H), 7.14 (d, *J* = 8.3 Hz, 1 H), 6.60 (d, *J* = 8.4 Hz, 1 H), 5.90 (d, *J* = 51.1 Hz, 2 H), 5.61 (s, 2 H), 2.23 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -156.94 (t, *J* = 51.2 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 165.9, 149.3, 136.3, 130.8, 125.4, 116.7, 108.5, 93.3 (d, *J* = 219.6 Hz), 20.1 ppm. IR (KBr): ν_{max} = 3480, 3373, 1693, 1600, 1560, 1520, 1246, 1198, 1155, 1104, 988, 817, 786, 575 cm^{-1}. MS (EI): 388 (M^+). HRMS (EI) for $C_9H_{10}FNO_2$ (M^+): Calcd: 183.0696; Found: 183.0695.

Fluoromethyl 2-(3-(trifluoromethyl)phenylamino)benzoate (**12l**). Yellow solid (80 mg, 85%), mp: 70–73 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.5). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 9.45 (s, 1 H), 8.09 (d, *J* = 8.0 Hz, 1 H), 7.52 (s, 1 H), 7.49 – 7.40 (m, 3 H), 7.37 (d, *J* = 7.4 Hz, 1 H), 7.28 (d, *J* = 8.3 Hz, 1 H), 6.86 (t, *J* = 7.6 Hz, 1 H), 5.97 (d, *J* = 50.8 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -62.85 (s, 3 F), -157.31 (t, *J* = 50.7 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 166.4, 147.9, 141.0, 135.4, 132.1, 131.9 (q, *J* = 32.2 Hz), 123.0, 125.3, 120.2 (q, *J* = 3.9 Hz), 118.8 (q, *J* = 3.8 Hz), 118.3, 114.1, 110.8, 93.5 (d, *J* = 221.3 Hz) ppm. IR (KBr): ν_{max} = 3316, 3003, 1701, 1605, 1529, 1337, 1258, 1116, 997, 749, 693 cm^{-1}. MS (EI): 313.1 (M^+). HRMS (EI) for $C_{15}H_{11}F_4NO_2$ (M^+): Calcd: 313.0726; Found: 313.0731.

Fluoromethyl 1*H*-indole-2-carboxylate (**12m**). White solid (55 mg, 75%), mp: 120– 122 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.4). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 9.15 (s, 1 H), 7.71 (d, *J* = 8.1 Hz, 1 H), 7.43 (d, J = 8.4 Hz, 1 H), 7.40 – 7.34 (m, 2 H), 7.18 (t, *J* = 7.5 Hz, 1 H), 5.97 (d, *J* = 50.8 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -156.81 (t, *J* = 50.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 160.1, 137.6, 127.3, 126.3, 125.3, 122.9, 121.2, 112.1, 111.0, 93.7 (d, *J* = 221.8 Hz) ppm. MS (EI): 193.1 (M^+). HRMS (EI) for $C_{10}H_8FNO_2$ (M^+): Calcd: 193.0539; Found: 193.0531.

Fluoromethyl 3,5-bis(trifluoromethyl)benzoate (**12n**). Colorless liquid (75 mg, 86%). Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.54 (s, 2 H), 8.12 (s, 1 H), 5.99 (d, *J* = 50.1 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -63.19 (s, 6 F), -158.15 (t, *J* = 50.1 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 162.1, 132.5 (q, *J* = 34.2 Hz), 130.7, 130.1, 127.2 (dt, *J* = 6.7, 3.4 Hz), 122.6 (q, *J* = 272.9 Hz), 94.0 (d, *J* = 224.0 Hz) ppm. IR (KBr): ν_{max} = 3099, 3000, 1759, 1384, 1281, 1242, 1139, 1015, 916, 769, 683 cm^{-1}. MS (EI): 290 (M^+). HRMS (EI) for $C_{12}H_9FO_2$ (M^+): Calcd: 204.0587; Found: 204.0588.

Fluoromethyl 6-hydroxy-2,5,7,8-tetramethylchroman-2 -carboxylate (**12o**). White solid (52 mg, 62%), mp: 130–133 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.3). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 5.92 – 5.47 (m, 2 H), 4.28 (s, 1 H), 2.73 – 2.64 (m, 1 H), 2.57 (dt, *J* = 12.0, 6.0 Hz, 1 H), 2.52 – 2.45 (m, 1 H), 2.21 (s, 3 H), 2.17 (s, 3 H), 2.08 (s, 3 H), 1.94 (td, *J* = 13.2, 12.0, 6.4 Hz, 1 H), 1.68 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -157.96 (t, *J* = 50.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 172.1, 145.4, 145.2, 1226, 1213, 118.4, 116.6, 93.5 (d, *J* = 221.8 Hz), 76.7, 30.3, 25.0, 20.6, 12.1, 11.7, 11.11 ppm. IR (KBr): ν_{max} = 3545, 2938, 1762, 1457, 1416, 1261, 1232, 1167, 1113, 1004, 790, 565 cm^{-1}. MS (EI): 388 (M^+). HRMS (EI) for $C_{15}H_{19}FO_4$ (M^+): Calcd: 282.1267; Found: 282.1276.

(2E,4E,6E,8E)-fluoromethyl 3,7-dimethyl-9-(2,6,6-trimethyl cyclohex-1-enyl)nona-2,4,6,8-tetraenoate (**12p**). White solid (93 mg, 93%), mp: 80–83 °C. Eluent: ethyl acetate/petroleum ether (1:10, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.07 (dd, *J* = 15.0, 11.5 Hz, 1 H), 6.32 (s, 1 H), 6.28 (s, 1 H), 6.16 (s, 1 H), 6.12 (d, J = 5.0 Hz, 1 H), 5.79 (s, 1 H), 5.74 (d, *J* = 51.3 Hz, 2 H), 2.38 (s, 3 H), 2.06 – 1.93 (m, 5 H), 1.70 (s, 3 H), 1.61 (ddt, *J* = 12.4, 8.9, 4.7 Hz, 2 H), 1.51 – 1.43 (m, 2 H), 1.02 (s, 6 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -156.86 (t, *J* = 51.4 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 162.7, 154.7, 138.8, 135.7, 135.2, 132.5, 130.5, 128.3, 127.4, 114.2, 91.2 (d, *J* = 218.1 Hz), 37.6, 32.3, 31.2, 27.0, 19.8, 17.3, 12.2, 11.00 ppm. IR (KBr): ν_{max} = 2922, 1734, 1580, 1464, 1356, 1233, 1137, 999, 974 cm^{-1}. MS (EI): 388 (M^+). HRMS (EI) for $C_{21}H_{29}FO_2$ (M^+): Calcd: 332.2152; Found: 332.2154.

General procedure for monofluoromethylation of thiophenols with reagent 3. Into a 10 mL Schlenk tube equipped with a magnetic stirring bar was added thiophenol (0.3 mmol), NaH (0.33 mmol) and DMF (1.0 mL). The mixture was stirred at room temperature for 15 min. Reagent **3** (0.36 mmol) was added. The mixture was stirred at room temperature for 10.0 min. The solvent was evaporated under vacuum and the residue was purified by flash chromatograph to give compound **13a** (50 mg, 75% yield) as a colorless liquid. 4-Bromophenyl)(fluoromethyl) thioether (**13a**).[12] Colorless liquid (50 mg, 75%). Eluent: petroleum ether (R_f = 0.75). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.46 (d, *J* = 8.4 Hz, 2 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 5.69 (d, *J* = 52.7 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -182.35 (t, *J* = 52.7 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 133.5 (d, *J* = 2.8 Hz), 132.4, 132.4 (d, *J* = 2.1 Hz), 129.6 , 88.4 (d, *J* = 217.3 Hz) ppm.

(Fluoromethyl)(4-nitrophenyl)thioether (**13b**).[13] Yellow solid (54.5 mg, 97%). Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.17 (d, *J* = 8.7Hz, 2 H),7.56 (d, *J* =8.7Hz, 2 H), 5.83 (d, *J* = 52.2 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -184.83 (t, *J* = 52.1 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 146.8, 144.0 (d, *J* = 3.1 Hz), 128.7 (d, *J* = 2.3 Hz), 124.3, 86.3 (d, *J* = 218.6 Hz) ppm.

(2,6-Dichlorophenyl)(fluoromethyl)thioether (**13c**). Colorless liquid (61 mg, 96%). Eluent: petroleum ether (R_f = 0.75). ^1H NMR

(400 MHz, $CDCl_3$, 293 K, TMS) δ 7.42 (d, *J* = 8.1 Hz, 2 H), 7.31 – 7.08 (m, 1 H), 5.68 (d, *J* = 52.1 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -185.47 (t, *J* = 52.1 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 141.2 (d, *J* = 2.0 Hz), 130.9, 130.2 (d, *J* = 1.7 Hz), 128.8, 88.1 (d, *J* = 221.0 Hz) ppm. (KBr): ν_{max} = 3078, 2943, 1567, 1556, 1320, 1188, 976, 779, 734 cm^{-1}. MS (EI): 210 (M^+). HRMS (EI) for $C_7H_5Cl_2FS$ (M^+): Calcd: 209.9473; Found: 209.9478.

(3,5-Bis(trifluoromethyl)phenyl)(fluoromethyl)thioether (**13d**). Colorless liquid (72 mg, 86%). Eluent: petroleum ether (R_f = 0.75). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.90 (s, 2 H), 7.79 (s, 1 H), 5.79 (d, *J* = 52.2 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -63.12 (s, 6 F), -183.79 (t, *J* = 52.1 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 137.8 (d, *J* = 3.0 Hz), 132.5 (q, *J* = 33.7 Hz), 129.7, 124.2, 121.4 (dd, *J* = 7.2, 3.3 Hz), 87.1 (d, *J* = 219.2 Hz) ppm.

2-(Fluoromethylthio)benzo[*d*]thiazole (**13e**).[13] Yellow solid (57 mg, 95%). Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.96 (d, *J* = 8.4 Hz, 1 H), 7.80 (d, J = 8.0 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 1 H), 7.35 (t, *J* = 7.5 Hz, 1 H), 6.16 (d, *J* = 51.0 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -186.75 (t, *J* = 51.0 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 162.5, 153.1, 135.9, 126.5, 125.2, 122.5, 121.3, 85.0 (d, *J* = 222.2 Hz) ppm.

2-(Fluoromethylthio)benzo[*d*]oxazole (**13f**). Yellow solid (50.5 mg, 92%). Eluent: ethyl acetate/petroleum ether (1:5, R_f = 0.7). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.66 (d, *J* = 6.9 Hz, 1 H), 7.49 (d, *J* = 7.1 Hz, 1 H), 7.36 – 7.21 (m, 2 H), 6.16 (d, *J* = 50.5 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -188.55 (t, *J* = 50.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 161.1, 152.2, 141.7, 124.8, 124.8, 119.3, 110.4, 83.9 (d, *J* = 223.6 Hz) ppm. (KBr): ν_{max} = 3071, 3026, 1508, 1454, 1327, 1238, 1141, 1101, 969, 747, 726 cm^{-1}. MS (EI): 183.1 (M^+). HRMS (EI) for C_8H_6FNOS (M^+): Calcd: 183.0154; Found: 183.0156.

General procedure for monofluoromethylation of heteroaryl nitrogen nucleophile with reagent 3. Into a 10 mL Schlenk tube equipped with a magnetic stirring bar was added heteroaryl nitrogen nucleophile (0.3 mmol), NaH (0.33 mmol) and DMF (1.0 mL). The mixture was stirred at room temperature for 15 min. Reagent **3** (0.36 mmol) was added. The mixture was stirred at room temperature for 10.0 min. The solvent was evaporated under vacuum and the residue was purified by flash chromatograph to give compound **14a** (47 mg, 96% yield) as a yellow solid. 1-(Fluoromethyl)-2-methyl-1*H*-benzo[*d*]imidazole (**14a**).[12] Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.73 – 7.60 (m, 1 H), 7.36 – 7.32 (m, 1 H), 7.27 (d, *J* = 3.1 Hz, 1 H), 7.26 (d, *J* = 3.1 Hz, 1 H), 6.03 (d, *J* = 53.8 Hz, 2 H), 2.62 (s, 3 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -171.17 (t, *J* = 53.8 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 151.80 (d, *J* = 2.9 Hz), 142.7, 134.5 (d, *J* = 3.2 Hz), 123.3, 123.2, 119.6, 108.8, 80.5 (d, *J* = 200.1 Hz), 13.4 ppm.

1-(Fluoromethyl)-2-phenyl-1*H*-benzo[*d*]imidazole (**14b**).[14] Colorless liquid (64 mg, 95%). Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.94 – 7.79 (m, 3 H), 7.61 – 7.47 (m, 4 H), 7.42 – 7.33 (m, 2 H), 6.12 (d, *J* = 53.6 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -162.16 (t, *J* = 53.6 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 154.2, 143.1, 135.5, 130.7, 129.7, 129.1, 129.0, 124.2, 123.9, 120.5, 109.6, 81.9 (d, *J* = 198.7 Hz) ppm.

7-(Fluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**14c**).[14] Yellow liquid (40 mg, 88%). Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.55). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.98 (s, 1 H), 8.93 (s, 1 H), 7.34 (d, *J* = 3.7 Hz, 1 H), 6.64 (d, *J* = 2.8 Hz, 1 H), 6.26 (d, *J* = 53.3 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -163.98 (t, *J* = 53.3 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 152.6, 151.5 (d, *J* = 2.9 Hz), 150.1, 128.7 (d, *J* = 3.2 Hz), 119.5, 102.5, 81.1 (d, *J* = 200.3 Hz) ppm.

4-Chloro-7-(Fluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**14d**).[14] White solid (47 mg, 85%). Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.6). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.67 (s, 1 H), 7.37 (d, *J* = 3.7 Hz, 1 H), 6.67 (d, *J* = 2.9 Hz, 2 H), 6.23 (d, *J* = 52.8 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -164.58 (t, *J* = 52.7 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 152.9, 151.9, 128.9, 118.36 , 106.6, 102.2, 81.5 (d, *J* = 201.5 Hz) ppm.

1-(Fluoromethyl)-1*H*-benzo[*d*][1,2,3]triazole (**14e**).[14] White solid (40 mg, 88%). Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.52). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 8.10 (d, *J* = 8.3 Hz, 1 H), 7.65 (d, *J* = 8.2 Hz, 1 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 1 H), 6.58 (d, *J* = 52.5 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -167.97 (t, *J* = 52.5 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 146.6, 132.9 (d, *J* = 2.0 Hz), 129.0, 125.0, 120.6, 109.2, 83.5 (d, *J* = 204.3 Hz) ppm.

1-(Fluoromethyl)-3,5-diphenyl-1*H*-pyrazole (**14f**).[14] White solid (67 mg, 88%). Eluent: ethyl acetate/petroleum ether (1:3, R_f = 0.55). ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ 7.90 (d, *J* = 7.4 Hz, 2 H), 7.58 (d, *J* = 6.4 Hz, 2 H), 7.55 – 7.40 (m, 5 H), 7.38 (d, *J* = 7.2 Hz, 1 H), 6.75 (s, 1 H), 6.04 (d, *J* = 53.4 Hz, 2 H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -158.39 (t, *J* = 53.4 Hz, 1 F); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 153.21 (d, *J* = 1.9 Hz), 147.11 (d, *J* = 1.4 Hz), 132.7, 129.5, 129.4, 129.2, 129.0, 128.9, 128.6, 126.2, 105.3, 86.1 (d, *J* = 201.0 Hz) ppm.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2020xxxxx.

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Monofluoromethyl-Substituted Sulfonium Ylides: Preparation, Structure-Reactivity Study and Substrate Scope

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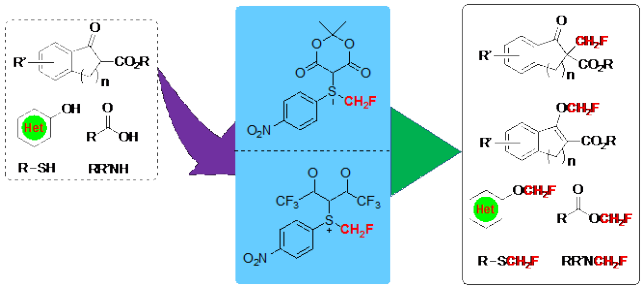

The development of two highly reactive reagents **3** with a cyclic malonate backbone and **6** with an electron-poor 1,1,1,5,5,5-hexafluoropentane-2,4-dione backbone through structure-activity relationship study (SAR) was reported. The high reactivity of reagents allowed to monofluoromethylate β-ketoesters with high C- or O-selectivity, as well as react with a variety of nucleophiles within 10 min at room temperature with broad substrate scope.