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# Copper-Catalyzed C($sp^2$)-H Difluoroalkylation of Aldehyde-Derived Hydrazones with Diboron as Reductant

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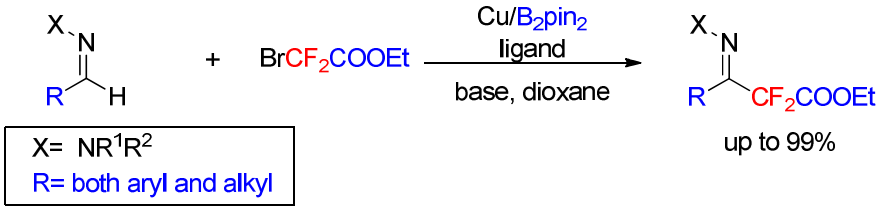
**Abstract**




An efficient and general method for C(sp2)-H difluoroalkylation of aldehyde-derived hydrazones via Cu(II)/B2pin2 catalyzed reaction between difluoroalkyl bromides and hydrazones was developed. In this reaction, both aromatic and aliphatic aldehyde-derived hydrazones could be achieved in good to excellent yields. For some heteroaromatic aldehyde-derived hydrazones, two fluoroacetates could be introduced onto the final products. Preliminary mechanism study manifested that a difluoroalkyl radical via SET pathway was involved in the reaction. And catalytic diboron reagent plays an indispensible role in this transformation.

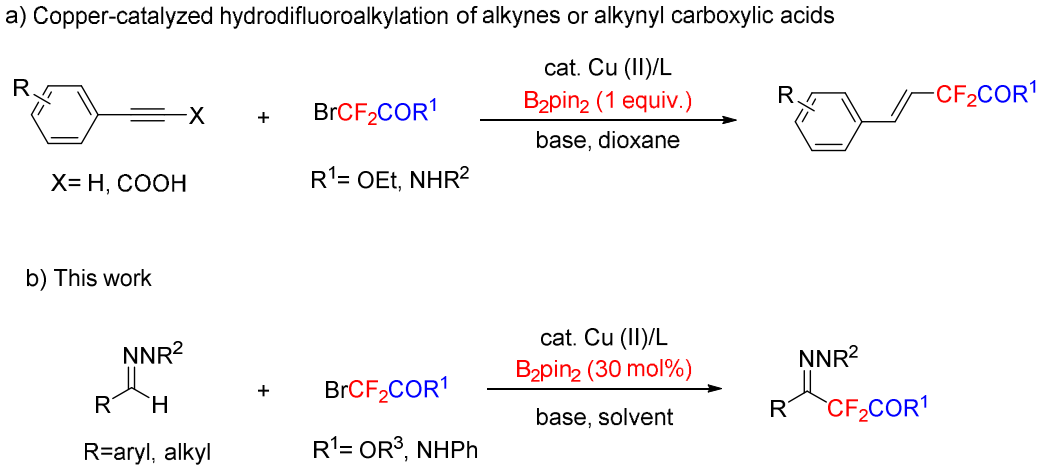
## INTRODUCTION

The incorporation of fluorinated functional groups into organic molecules has generated extraordinary research activity because of the enhanced metabolic stability, lipophilicity,

reactivity of the molecules compared to their nonfluorinated counterparts. [1-3] Although significant advances have been made on functionalized fluoroalkylation of aromatic compounds, [4-6] efficient and general methods for the synthesis of hydrazones containing difluorinated functional groups with high stereoselectivity through copper-catalyzed transformations are relatively rare.[9e] Aldehyde-derived hydrazones are an important intermediate in organic synthesis.[7] Conceptually, introduction of the $CF_2$ group into such a structual motif would open a good possibility to discover some novel bioactive molecules.

Recently, the fluoroalkyl radical addition of aldehyde-derived hydrazones has become an efficient tactic to synthesize α,α-difluoro-β-ketoesters. There are several known methods to achieve fluoroalkylated aldehyde-derived hydrazone compounds: a) visible-light photoredox-catalyzed cross coupling between aldehyde hydrazones and fluoroalkyl reagent (for example, with iridium or gold catalysts); [8] b) transition-metal-catalyzed cross coupling of aldehyde-derived hydrazones and fluoroalkyl halides. [9] In the latter case, Monteiro and co-workers reported an elegant Pd-catalyzed C-H alkylation of aldehyde-derived hydrazones with functional difluoromethyl bromides. [9d] Very recently, they also reported a Cu-catalyzed difluoroalkylation of aldehyde hydrazones.[9e] However, in both cases aliphatic aldehyde-derived hydrazones failed to provide difluoroacetated hydrazones, and expensive metals or ligands were essential to the success of the reactions. Inspired by our recent work on the Cu(II)/$B_2pin_2$-catalyzed hydrodifluoroacetylation of alkynes or phenylpropiolic acids with bromodifluoroacetate, in which difluoroalkyl radicals were generated via a single-electron transfer (SET) pathway (scheme 1a), [10] we envisioned that C($sp^2$)-H difluoroalkylation of aldehyde-derived hydrazones might be synthesized via the same novel radical generation

system: Cu/$B_2pin_2$, undoubtedly and ideally, if catalytic amount of $B_2pin_2$ was enough for the success of the transformation instead of stoichiometric amount, this reaction will become more attractive. Most interestingly, we successfully obtained C($sp^2$)-H difluoroalkylation of aldehyde-derived hydrazones with our Cu(II)-$B_2pin_2$ catalytic system in which only 30 mol% of $B_2pin_2$ was enough for this transformation and aliphatic aldehyde-derived hydrazones can also smoothly difluoroalkylated.



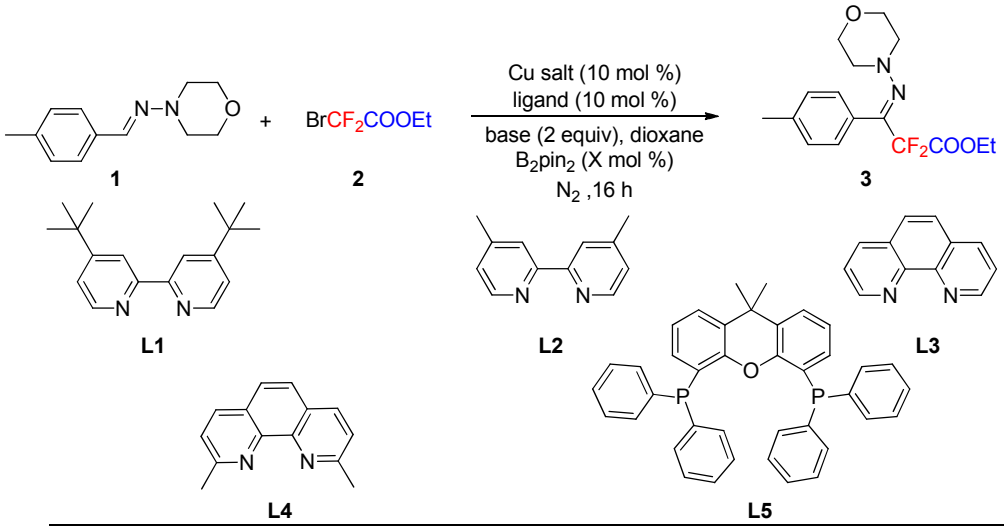

Scheme 1. Synthetic methods involving •$CF_2COOEt$ radical with Cu(II)/$B_2pin_2$ catalyst system.

**RESULTS AND DISCUSSIONS**

In order to examine our hypothesis, our investigation commenced with aldehyde hydrazones **1** and ethyl bromodifluoroacetate **2** as the model substrates with 1 equivalent of $B_2pin_2$ according to our previous work.[10] To our delight, the desired difluoroalkylated aldehyde hydrazones compounds **3** was obtained in 52% isolated yield at 80 $^oC$ using 10% $CuBr_2$ as catalyst, 10% DTBDPy as ligand, 1 equivalent of $B_2pin_2$ as additive and 2 equivalent of KOAc as base in 1,4-dioxane. Subsequently, other reaction parameters, such as base, loading of

$B_2pin_2$, Cu salt, ligand, reaction atmosphere were surveyed (table **1**, entry 1-24). Among the tested bases (table **1**, entry 1-7), $NaHCO_3$ showed the superior activity over others (KOAc, $K_2CO_3$, $Na_2CO_3$, NaOAc, KF, $Cs_2CO_3$), providing the desired product **3** in 93% isolated yield (table **1**, entry 1-7). Surprisingly, we found that the loading of $B_2pin_2$ could be dropped to 30 mol% without deteriorating the yield (table **1**, entry 9-10). However, lowering the loading of $B_2pin_2$ significantly reduced the yield (table **1**, 83%, entry 8). As we can see, CuCl, CuBr, $CuCl_2$ and $Cu(OAc)_2$ were all good catalysts when combined with ligand L1, yet $CuBr_2$ was the best among them (table **1**, entry 11-14). In terms of other ligands, the yields of the desired product dropped dramatically, and no desired one was observed when P ligand **L5** was used in the transformation (table 1, entry 15-18). Control experiments suggested that the additive $B_2pin_2$ is indispensable to the reaction since no reaction occurred in its absence (table **1**, entry 22). No desired product **3** was observed as well in the absence of copper catalyst, ligand or base (table **1**, entry 19-21), demonstrating that both copper salt, ligand and base play essential roles for the promotion of the reaction. This reaction is anaerobic and could not proceed under air or molecular oxygen (table **1**, entries 23 and 24).

**Table 1**. Optimization of the reaction conditions.



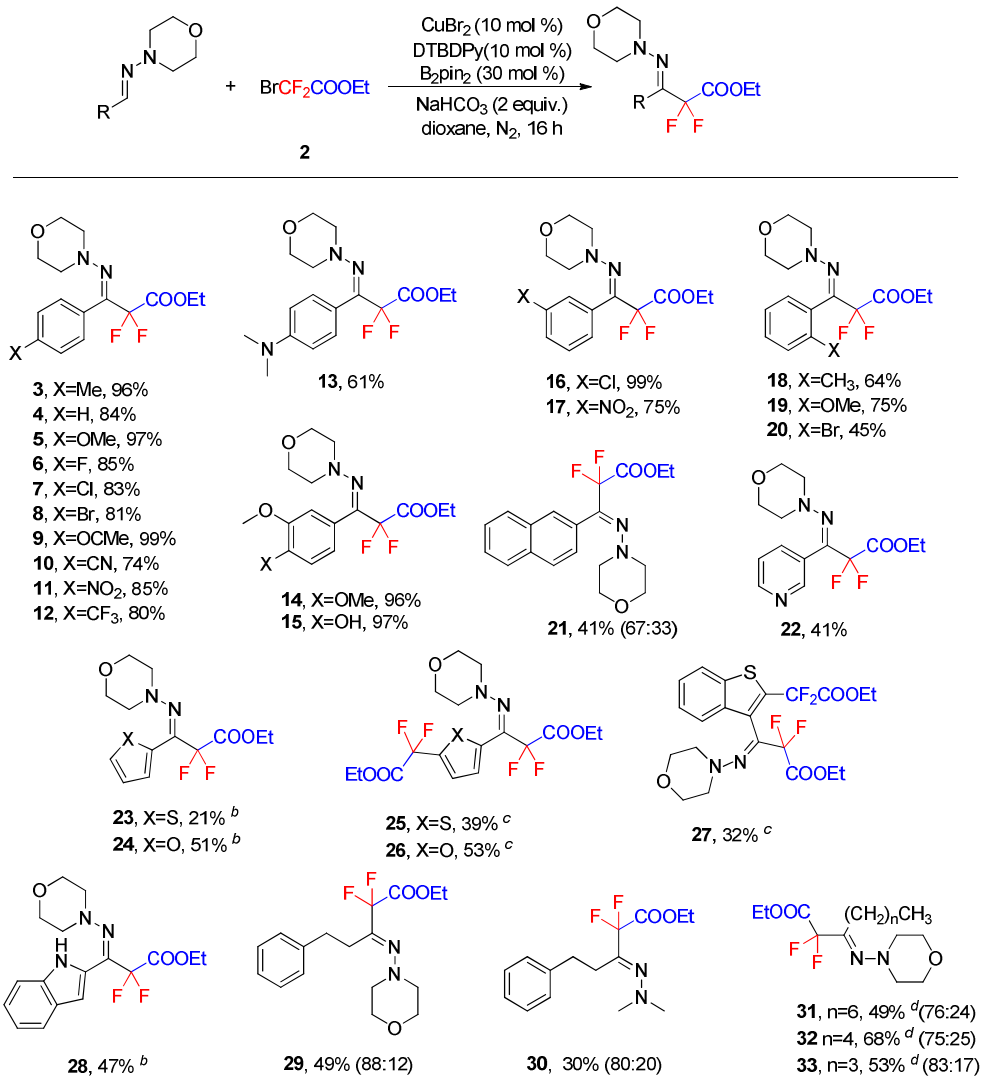

| entey | catalyst (10 mol%) | ligand (10 mol%) | base (2 equiv) | yield (%) |
|---|---|---|---|---|
| 1 | $CuBr_2$ | **L1** | KOAc | 52 |
| 2 | $CuBr_2$ | **L1** | $K_2CO_3$ | 72 |
| 3 | $CuBr_2$ | **L1** | $Na_2CO_3$ | 78 |
| 4 | $CuBr_2$ | **L1** | NaOAc | 77 |
| 5 | $CuBr_2$ | **L1** | $NaHCO_3$ | 96 (93 ) |
| 6 | $CuBr_2$ | **L1** | KF | 34 |
| 7 | $CuBr_2$ | **L1** | $Cs_2CO_3$ | 30 |
| 8[a] | $CuBr_2$ | **L1** | $NaHCO_3$ | 83 |
| 9[b] | $CuBr_2$ | **L1** | $NaHCO_3$ | >99 (96) |
| 10[c] | $CuBr_2$ | **L1** | $NaHCO_3$ | >99 |
| 11 | CuCl | **L1** | $NaHCO_3$ | 95 |
| 12 | CuBr | **L1** | $NaHCO_3$ | 89 |
| 13 | $CuCl_2$ | **L1** | $NaHCO_3$ | 93 |
| 14 | $Cu(OAc)_2$ | **L1** | $NaHCO_3$ | 91 |
| 15 | $CuBr_2$ | **L2** | $NaHCO_3$ | 75 |
| 16 | $CuBr_2$ | **L3** | $NaHCO_3$ | 18 |
| 17 | $CuBr_2$ | **L4** | $NaHCO_3$ | 8 |
| 18 | $CuBr_2$ | **L5** | $NaHCO_3$ | NR |
| 19 | - | **L1** | $NaHCO_3$ | NR |
| 20 | $CuBr_2$ | - | $NaHCO_3$ | NR |
| 21 | $CuBr_2$ | **L1** | - | NR |
| 22[d] | $CuBr_2$ | **L1** | $NaHCO_3$ | NR |
| 23[e] | $CuBr_2$ | **L1** | $NaHCO_3$ | NR |
| 24[f] | $CuBr_2$ | **L1** | $NaHCO_3$ | NR |

Reaction Condition:**1** (0.2 mmol), **2** (0.4 mmol), Cu salt(10 mol %), ligand (10 mol %), base (2 equiv.), $B_2pin_2$ (entry 1- 7, 1 equiv), $B_2pin_2$ (entry 11- 23, 30 mol%), dioxane (1 mL), at $N_2$, 16 h. [a] $B_2pin_2$ (20 mol %). [b] $B_2pin_2$ (30 mol %). [c] $B_2pin_2$ (40 mol %).[d] under air. [e] under $O_2$, [f] absence of $B_2pin_2$.GC yield by using *n*-dodecane as an internal standard. The isolated yield was listed in parathesis.

In order to test the scope of the method, a variety of aldehyde-derived hydrazones was surveyed (scheme 2). A series of difluoroacetylated aldehyde hydrazones was obtained in

good to excellent yields with versatile substituents on the aromatic rings regardless of the electron-donating or electron-withdrawing nature (**3-12**). Notably, 4-*N*, *N*-dimethyl product **13** was obtained in good yield under our standard conditions. Moreover, the position of substituents on the aromatic ring has less impact on the reactions albeit *ortho* ones with relatively lower yields (**16-20**). With multiple substituents on the aromatic rings, the

**Scheme 2**. Substrate scope of aldehyde-derived hydrazones for difluoroacetylation.

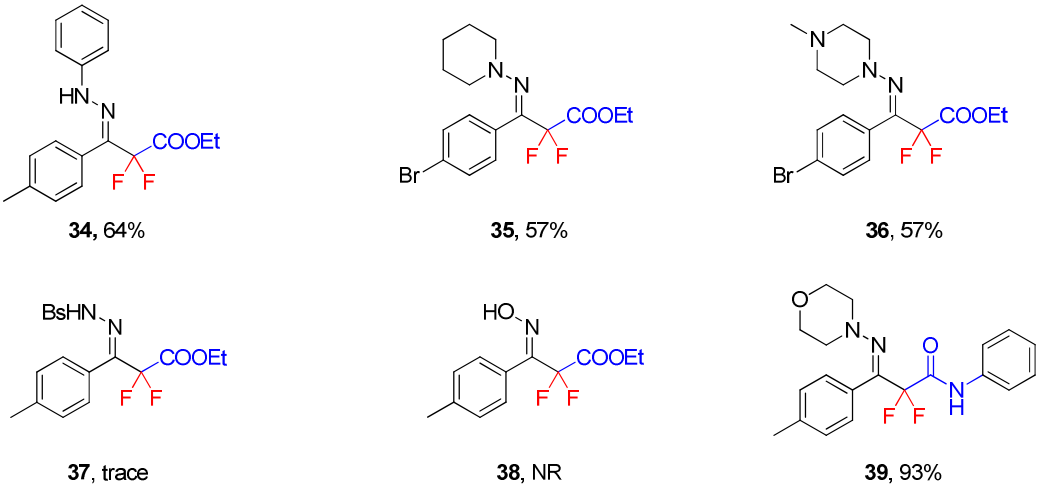



[a] Reaction Conditions: aldehyde-derived hydrazones (0.3 mmol), $BrCF_2COOEt$ (**2**) (0.6 mmol), $CuBr_2$ (10 mol%), DTBDPy (10 mol%), $NaHCO_3$ (2 equiv), $B_2pin_2$ (30 mol% ) dioxane (1 mL), 80 °C, 16 h, under $N_2$ in a Schlenck tube, all yields are those of isolated product. [b] Using 1 equivalent $BrCF_2COOEt$. [c] Using 2.5 equivalent $BrCF_2COOEt$. [d] Using $CuCl_2$ instead of $CuBr_2$. The ratio in parenthesis is the *E*/*Z* ratio.

corresponding products were also obtained with good yields (**14-15**). However, the reaction of naphthylaldehyde hydrazone gave a surprisingly low yield (**21**). Heteroaromatic aldehyde-derived hydrazones were also compatible under the standard conditions (**22-28**), interestingly, some bis-fluoroacetates were selectively synthesized from thiophene or furanyl or benzothiophene aldehyde-derived hydrazones (**23-27**). Importantly, aliphatic aldehyde hydrazones were good substrates in this transformation and the corresponding desired products were obtained in decent yields, albeit with relatively low stereoselectivities (**29-33**), which makes our method an alternative one for the reported Pd- or Cu-catalyzed difluoroalkylation of aldehyde-derived hydrazones, in which aliphatic aldehyde-derived hydrazones only rendered trace amount of desired products.[9d, 9e] It needs to be pointed out that our conditions were also applicable for the N,N-dimethyl aliphatic aldehyde-derived hydrazone and 30% of corresponding product **30** was obtained. However, when (E)-N-hexylidenemorpholin-4-amine was subjected under Monteiro's conditions[9e] in the presence of $B_2Pin_2$, the corresponding desired product was only obtained in 14% yield, much lower than the one under our current standard conditions (49% yield).

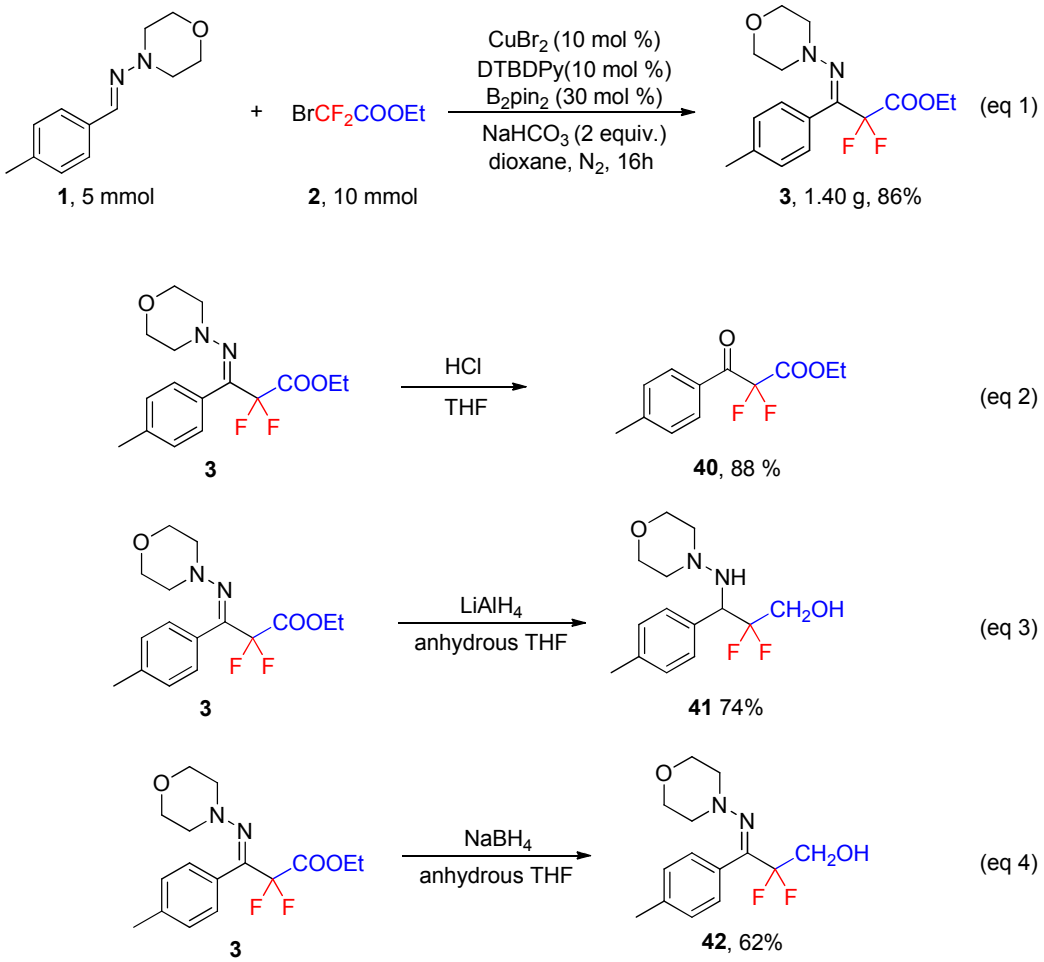
Next, we investigated the scope of *N*-substituent aldehyde hydrazones and the scope of difluoro regents (scheme **3**). Delightedly, the reactions were not just restricted to morpholine-derived hydrazones, phenylamine, piperidinyl and 4-methylpiperazinyl-derived hydrazones were also suitable candidates for this transformations, with corresponding desired products obtained in reasonable yields (**34-36**). Whereas the N-Bs (Bs = benzenesulfonyl) hydrazones (**37**) and oxime hydrazones (**38**) failed to furnish the desired product, probably due to their low HOMO level. Gratifyingly, the corresponding difluorinated hydrazone (**39**)

was obtained with excellent yield using bromodifluoroacetamide, which was prepared from bromodifluoroacetate **2** with phenylamine.[11]



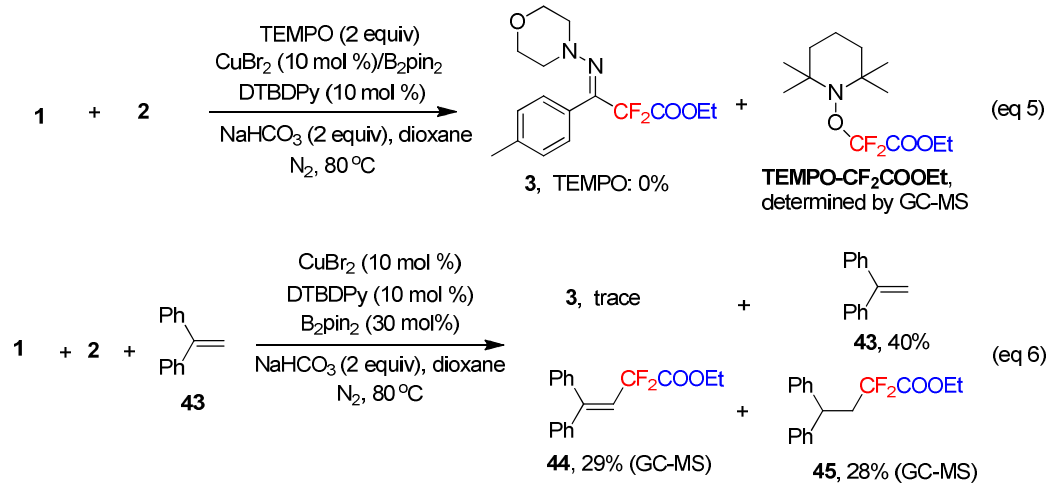

**Scheme 3.** Investigation of the effect of the N-substituents and bromodifluoroacetamide

Satisfyingly, this reaction could be easily scaled up to 5 mmol and desired product **3** was achieved in a high isolated yield of 86% in 1.4 gram (Scheme 4, eq 1), which illustrated the practicality and robustness of our transformation. Aldehyde-derived hydrazones is a facile important intermediate in organic chemistry which could be easily subjected for further structural manipulation. For instance, compound **3** could be hydrolyzed into *a*,*a*-difluoro-*β*-ketoester **40** in 88% yield (scheme 4, eq 2). And difluorinated hydrazine **41** was readily generated when compound **3** was subjected with lithium aluminum hydride in anhydrous THF (scheme 4, eq 3), in which ester group was also reduced simultaneously along with C=N bond to render an alcohol. Noteworthily, the ester group in compound **3** was transformed into hydroxyl group while the C=N double bond was untouched in compound **42** when compound **3** was treated with sodium borohydride (scheme 4, eq 4).




**Scheme 4.** The application of difluoroalkylation of aldehyde-derived hydrazones

Radical trapping experiments were subsequently performed in order to understand the mechanism of this Cu(II)/$B_2pin_2$-catalyzed C($sp^2$)-H difluoroalkylation of aldehyde-derived hydrazones. The desired product **3** was not obtained when radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was added, instead, TEMPO-$CF_2COOEt$ was generated in ca. 20% yield, implying that a radical pathway was involved in this reaction (eq 5). Furthermore, when 1-phenylstyrene (**43**) was added to the mixture of compound **1** and **2** under the standard conditions, desired product **3** was only formed in trace with 40% of compound **43** remained along with formation of compounds **44** and **45**. This result further confirmed the involvement of a free radical pathway in this transformation (eq 6).




On the base of the above control experiments, our previous work, [10] as well as precedent reports, [9e] a plausible mechanism is postulated (Figure 1). Initially, interaction between a Cu(II) salt **A** and $B_2pin_2$ generates a Cu(I)-Bpin species **B**.[10, 12, 14] Subsequently, an electrophilic fluoroalkyl radical from bromodifluoro reagent is formed via bromide abstraction by the copper(I) complex **B** with concomitant generation of copper(II) **C**.[10, 12b] The radical can be trapped by aldehyde-derived hydrazone to form the aminyl radical **D** which further converts into intermediate **E** via SET process.[8, 13] Then the removal of proton eventually produces the desired product **3**.

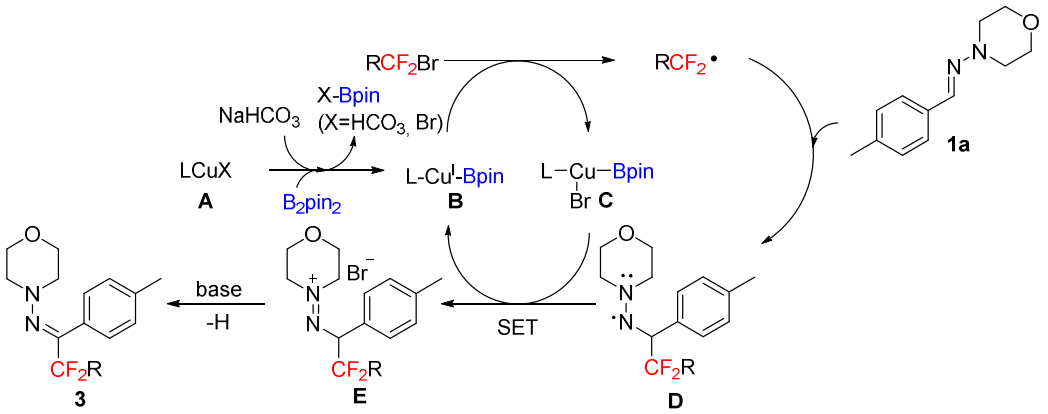



**Figure 1**. Plausible mechanistic pathway.

In summary, we described a novel, efficient C($sp^2$)-H difluoroalkylation of aldehyde-derived hydrazones via Cu(II)/$B_2pin_2$ catalyzed reaction between difluoroalkyl bromides and hydrazones. A broad range of functional groups was tolerated well under standard conditions with good to excellent yields. And aliphatic aldehyde-derived hydrazones are also good candidates in this method to render the corresponding products, which make our method as a complement protocol for the existing methods. Further applications about this transformation are under investigation in our laboratory.

## EXPERIMENTAL SECTION

**General information**: All reactions were accomplished in Schlenk tubes or round flasks under an atmosphere of $N_2$. Column chromatography was performed over silica gel (200-300 mesh). $^1$H NMR spectra were recorded on a 500 M spectrometer and chemical shifts (in ppm) were referred to $CDCl_3$ ($\delta$ = 7.26 ppm) as an internal standard. $^{13}$C NMR spectra were obtained by using the same NMR spectrometer and were calibrated with $CDCl_3$ ($\delta$ = 77.0 ppm). $^{19}$F NMR spectrometers were operated on the same NMR spectrometer ($CFCl_3$ as an external standard and low field is positive). The following abbreviations were used to illuminate the diversities: $\delta$ = chemical shifts, $J$ = coupling constant, s = singlet, d= doublet, t = triplet, q = quartet, m = multiplet. HRMS (EI) were measured with a quadrupole and TOF mass spectrometers. $CH_2Cl_2$ was distilled from $CaH_2$. All reagents and solvents were obtained from commercial suppliers, and used without further purification. Reactions were monitored by thin-layer chromatography (TLC), GC or GC-MS analysis. The products were purified by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

**The synthesis of aldehyde-derived hydrazones (1a -1ah)** [15]

Morpholin-4-amine (2.2 mmol), aldehyde (2.0 mmol) and anhydrous $MgSO_4$ (0.5 g) in $CH_2Cl_2$ (10 mL) was stirred overnight at room temperature until consumption of the raw material aldehyde (TLC tracking). After filtration of $MgSO_4$, the solvent was removed under reduced pressure and the residue was subjected to column chromatography to give the aldehyde-derivative hydrazone **(1a-1ah)** with good yields.

**General procedure for the synthesis of Difluoroalkylation of Aldehyde-Derived Hydrazones.** aldehyde hydrazone (0.3 mmol)，bis(pinacolato)diboron (30 mol%, 22.9 mg), $CuBr_2$ (10 mol%, 6.7 mg), 4, 4'-Dibutyl-2, 2'-bi-pyridyl (10 mol%, 8.1 mg), $NaHCO_3$ (2 equiv, 50.5 mg) were added to a 25 mL of Schlenk tube under air. Then the mixture was evacuated and backfilled with $N_2$ (3 times). Ethyl bromodifluoroacetate (2 equiv, 77 μL) and dioxane (1 mL) were added subsequently. The Schlenk tube was screw-capped and put into a pre-heated oil bath (80 $^oC$). The reaction mixture was cooled to room temperature after stirring for 16 h. After the reaction was finished, the mixture was concentrated under vacuum to remove dioxane, and the residue was purified by chromatography on silica gel (petroleum ether: ethyl acetate = 10:1-1:2) to afford the product**.**

(*E*)-N-(4-methylbenzylidene)morpholin-4-amine (**1a**).[16] Afforded **1a** (390 mg, 96%) as a white solid, m.p. 92-93 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.50 (d, $J$ = 8.1 Hz, 2H), 7.16 (d, $J$ = 7.9 Hz, 2H), 3.89 (t, $J$ = 5.0 Hz, 4H), 3.16 (t, $J$ = 5.0 Hz, 4H), 2.35 (s, 3H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): $\delta$ 138.3, 136.7, 133.2, 129.2, 126.2, 66.5, 52.0, 21.3.

(*E*)-N-benzylidenemorpholin-4-amine (**1b**).[17] Afforded **1b** (360 mg, 95%) as a white solid, m.p. 68-69 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.65 – 7.58 (m, 3H), 7.35 (t, $J$ = 7.5 Hz, 2H), 7.29 (ddd, $J$ = 7.3, 3.8, 1.2 Hz, 1H), 3.89 (t, $J$ = 5.0 Hz, 4H), 3.18 (t, $J$ = 5.0 Hz, 4H).

$^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): $\delta$ 136.2, 135.9, 128.5, 128.3, 126.2, 66.4, 51.8.

(*E*)-N-(4-methoxybenzylidene)morpholin-4-amine (**1c**).[18] Afforded **1c** (396 mg, 90%) as a white solid, m.p. 74-75 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.54 (d, $J$ = 8.8 Hz, 2H), 6.88 (d, $J$ = 8.8 Hz, 2H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.81 (s, 3H), 3.13 (t, $J$ = 5.0 Hz, 4H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): $\delta$ 159.9, 136.7, 128.7, 127.5, 114.0, 66.4, 55.2, 52.1.

(*E*)-N-(4-fluorobenzylidene)morpholin-4-amine (**1d**).[8a] Afforded **1d** (408 mg, 98%) as a white solid, m.p. 77-78 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.53 (m, 3H), 7.03 (t, $J$ = 8.7 Hz, 2H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.15 (t, $J$ = 5.0 Hz, 4H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): $\delta$ 162.8 (d, $J$ = 246.3 Hz), 135.0, 132.1 (d, $J$ = 2.5 Hz), 127.7 (d, $J$ = 5.0 Hz), 115.4 (d, $J$ = 8.8 Hz), 66.4, 51.8.

(*E*)-N-(4-chlorobenzylidene)morpholin-4-amine (**1e**).[8a] Afforded **1e** (426 mg, 95%) as a white solid, m.p. 94-95 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.46 (m, 3H), 7.30 (d, $J$ = 8.5 Hz, 2H), 3.86 (t, $J$ = 5.0 Hz, 4H), 3.15 (t, $J$ = 5.0 Hz, 4H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): $\delta$ 134.5, 134.4, 133.8, 128.6, 127.2, 66.3, 51.6.

(*E*)-N-(4-bromobenzylidene)morpholin-4-amine (**1f**).[8b] Afforded **1f** (472 mg, 88%) as a white solid, m.p. 128-129 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.50 (s, 1H), 7.47 -7.44 (m, 4H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.17 (t, $J$ = 5.0 Hz, 4H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): $\delta$ 134.9, 134.5, 131.6, 127.6, 122.4, 66.4, 51.7.

(*E*)-1-(4-((morpholinoimino)methyl)phenyl)ethanone (**1g**). Afforded **1g** (418 mg, 90%) as a yellow solid, m.p. 97-98 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.92 (d, $J$ = 8.4 Hz, 2H), 7.65 (d, $J$ = 8.4 Hz, 2H), 7.55 (s, 1H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.22 (t, $J$ = 5.0 Hz, 4H), 2.58 (s, 3H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): $\delta$ 197.5, 140.5, 136.3, 133.6, 128.7, 125.9, 66.3, 51.4,

26.6. HRMS: *m*/*z* (EI-TOF) calculated [M]: 232.1212, found: 232.1208.

(*E*)-4-((morpholinoimino)methyl)benzonitrile (**1h**).[19] Afforded **1h** (357 mg, 83%) as a white solid, m.p. 124-125 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.66 (d, $J$ = 8.4 Hz, 2H), 7.60 (d, $J$ = 8.4 Hz, 2H), 7.49 (s, 1H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.22 (t, $J$ = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 140.4, 132.4, 132.3, 126.2, 119.0, 110.8, 66.2, 51.3.

(*E)*-N-(4-nitrobenzylidene)morpholin-4-amine (**1i**).[9a] Afforded **1i** (423 mg, 90%) as a yellow solid, m.p. 145-146 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.15 (d, $J$ = 8.8 Hz, 2H), 7.68 (d, $J$ = 8.8 Hz, 2H), 7.50 (s, 1H), 3.87 (t, $J$ = 5.0 Hz, 4H), 3.24 (t, $J$ = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 146.8, 142.4, 131.4, 126.1, 123.8, 66.1, 51.1.

(*E*)-N-(4-(trifluoromethyl)benzylidene)morpholin-4-amine (**1j**).[8a] Afforded **1j** (475 mg, 92%) as a white solid, m.p. 75-76 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.68 (d, $J$ = 8.2 Hz, 2H), 7.58 (d, $J$ = 8.3 Hz, 2H), 7.55 (s, 1H), 3.89 (t, $J$ = 5.0 Hz, 4H), 3.21 (t, $J$ = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 139.4, 133.5, 129.7 (t, $J$ = 31.3 Hz), 125.1, 125.4 (t, $J$ = 3.8 Hz), 124.2 (t, $J$ = 270 Hz), 66.3, 51.5.

(*E)*-N-(4-(dimethylamino)benzylidene)morpholin-4-amine (**1k**).[20] Afforded **1k** (419 mg, 90%) as a pale yellow solid, m.p. 154-155 °C. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.61 (s, 1H), 7.50 (d, $J$ = 8.8 Hz, 2H), 6.69 (d, $J$ = 8.9 Hz, 2H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.11(t, $J$ = 5.0 Hz, 4H), 2.98 (s, 6H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 150.7, 138.7, 127.5, 124.1, 112.0, 66.5, 52.5, 40.3.

(*E*)-N-(3,4-dimethoxybenzylidene)morpholin-4-amine (**1l**).[21] Afforded **1l** (490 mg, 95%) as a white solid, m.p. 68-69 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.31 (d, $J$ = 1.8 Hz, 1H), 6.99 (dd, $J$ = 8.2, 1.8 Hz, 1H), 6.82 (d, $J$ = 8.2 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H),

3.87 (t, $J$ = 5.0 Hz, 4H), 3.14 (t, $J$ = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 149.5, 149.1, 136.7, 128.9, 120.4, 110.5, 107.2, 66.4, 55.8, 55.7, 52.0.

(*E*)-2-methoxy-4-((morpholinoimino)methyl)phenol (**1m**).[20] Afforded **1m** (420 mg, 89%) as a brown solid, m.p. 152-153 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.56 (s, 1H), 7.30 (d, $J$ = 1.5 Hz, 1H), 6.96 (dd, $J$ = 8.1, 1.4 Hz, 1H), 6.88 (d, $J$ = 8.1 Hz, 1H), 3.91 (s, 3H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.14 (t, $J$ = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 146.9, 146.4, 137.2, 128.5, 121.2, 114.1, 107.0, 66.5, 55.8, 52.1.

(*E*)-N-(3-chlorobenzylidene)morpholin-4-amine (**1n**).[8a] Afforded **1n** (430 mg, 96%) as a white solid, m.p. 43-44 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.62 (t, $J$ = 1.6 Hz, 1H), 7.48 (s, 1H), 7.42 (dt, $J$ = 7.4, 1.4 Hz, 1H), 7.26 (t, $J$ = 7.6 Hz, 1H), 7.25 – 7.21 (m, 1H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.18 (t, $J$ = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 137.9, 134.6, 133.9, 129.7, 128.0, 125.7, 124.4, 66.3, 51.6.

(*E*)-N-(3-nitrobenzylidene)morpholin-4-amine (**1o**).[22] Afforded **1o** (428 mg, 91%) as a yellow solid, m.p. 145-146 $^{o}$C. 1H NMR (500 MHz, $CDCl_3$) $\delta$ 8.41 (s, 1H), 8.07 (dd, $J$ = 8.1, 2.3 Hz, 1H), 7.88 (d, $J$ = 7.7 Hz, 1H), 7.54 (s, 1H), 7.48 (t, $J$ = 8.0 Hz, 1H), 3.88 (t, $J$ = 5.0 Hz, 4H), 3.22 (t, $J$ = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 148.6, 138.0, 132.0, 131.4, 129.3, 122.3, 120.6, 66.3, 51.4.

(*E*)-N-(2-methylbenzylidene)morpholin-4-amine (**1p**).[8b] Afforded **1p** (384 mg, 94%) as a brown solid, m.p. 64-65 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.81 – 7.77 (m, 1H), 7.21 – 7.18 (m, 2H), 7.17 – 7.12 (m, 1H), 3.91 (t, $J$ = 5.0 Hz, 4H), 3.19 (t, $J$ = 5.0 Hz, 4H), 2.43 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 135.4, 134.9, 133.7, 130.5, 128.1, 126.1, 125.5, 66.4, 51.9, 19.5.

(*E*)-N-(2-methoxybenzylidene)morpholin-4-amine (**1q**).[8a] Afforded **1q** (722 mg, 96%) as a pale yellow solid, m.p. 76-77 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.87 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.26 (dt, *J* = 7.5, 5.0 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 3.89 (t, *J* = 5.0 Hz, 4H), 3.85 (s, 3H), 3.18 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 157.0, 132.3, 129.4, 125.4, 124.4, 120.8, 110.7, 66.4, 55.4, 52.0.

(*E*)-N-(2-bromobenzylidene)morpholin-4-amine (**1r**). Afforded **1r** (509 mg, 95%) as a white solid, m.p. 77-78 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.87 (s, 1H), 7.52 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.28 (t, *J* = 5.0 Hz, 1H), 7.12 (td, *J* = 7.9, 1.7 Hz, 1H), 3.89 (t, *J* = 5.0 Hz, 4H), 3.22 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 134.6, 34.6, 132.8, 129.3, 127.4, 126.7, 123.2, 66.3, 51.7. HRMS: *m*/*z* (EI-TOF) calculated [M]: 268.0211, found: 268.0203.

(*E*)-N-(naphthalen-2-ylmethylene)morpholin-4-amine (**1s**).[18] Afforded **1s** (432 mg, 92%) as a white solid, m.p. 125-127 °C. $^1$H NMR (500 MHz, $CDCl_3$): *δ* 7.95 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.86 (s, 1H), 7.85 – 7.80 (m, 3H), 7.75 (s, 1H), 7.46- 7.45 (m, 2H), 3.92 (t, *J* = 5.0 Hz, 4H), 3.24 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 136.2, 133.7, 133.5, 133.4, 128.3, 128.0, 127.8, 126.6, 126.2, 126.0, 123.0, 66.4, 51.8

(*E*)-N-(pyridin-3-ylmethylene)morpholin-4-amine (**1t**). Afforded **1t** (330 mg, 86%) as a brown solid, m.p. 31-32 °C. $^1$H NMR (500 MHz, $CDCl_3$): *δ* 8.70 (d, *J* = 1.8 Hz, 1H), 8.47 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.96 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.52 (s, 1H), 7.25 (dd, *J* = 7.9, 4.8 Hz, 1H), 3.87 (t, *J* = 5.0 Hz, 4H), 3.19 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 149.0, 148.2, 132.3, 131.9, 131.8, 123.5, 66.3, 51.5. HRMS: *m*/*z* (EI-TOF) calculated [M]: 191.1059, found: 191.1057.

(*E)*-N-(thiophen-2-ylmethylene)morpholin-4-amine (**1u**).[23] Afforded **1u** (345 mg, 88%) as a brown solid, m.p. 92-93 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.2 (d, *J* = 5.0 Hz, 1H), 7.07 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.99 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.86 (t, *J* = 5.0 Hz, 4H), 3.13 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 141.5, 131.2, 127.1, 126.3, 125.5, 66.3, 51.8.

(*E*)-N-(furan-2-ylmethylene)morpholin-4-amine (**1v**). Afforded **1v** (299 mg, 83%) as a pale yellow solid, m.p. 53-54 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.41 (d, *J* = 0.8 Hz, 1H), 6.46 (d, *J* = 3.4 Hz, 1H), 6.43 – 6.38 (m, 1H), 3.85 (t, *J* = 5.0 Hz, 4H), 3.13 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 151.1, 142.7, 126.6, 111.3, 109.2, 66.2, 51.6. HRMS: *m*/*z* (EI-TOF) calculated [M]: 180.0899, found: 180.0894.

(*E*)-N-(benzo[b]thiophen-3-ylmethylene)morpholin-4-amine (**1w**). Afforded **1w** (423 mg, 86%) as a brown solid, m.p. 73-74 °C. $^1$H NMR (500 MHz, $CDCl_3$): *δ* 8.67 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.93 (s, 1H), 7.87 – 7.83 (m, 1H), 7.51 (s, 1H), 7.41 (dtd, *J* = 14.9, 7.2, 1.2 Hz, 2H), 3.92 (t, *J* = 5.0 Hz, 4H), 3.22 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 140.7, 136.3, 132.7, 132.4, 126.6, 124.9, 124.9, 124.6, 122.5, 66.4, 51.8. HRMS: *m*/*z* (EI-TOF) calculated [M]: 342.0827, found:246.0826.

(*E*)-N-((1H-indol-3-yl)methylene)morpholin-4-amine (**1x**).[24] Afforded **1x** (357 mg, 78%) as a pale white solid, m.p. 128-129 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.32 (d, *J* = 7.4 Hz, 1H), 7.99 (s, 1H), 7.34 (dd, *J* = 7.1, 1.1 Hz, 1H), 7.30 (d, *J* = 2.6 Hz, 1H), 7.25 – 7.23 (m, 1H), 7.22 – 7.17 (m, 1H), 3.93 (t, *J* = 5.0 Hz, 4H), 3.18 (t, *J* = 5.0 Hz, 4H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 136.7, 135.2, 125.5, 124.8, 123.0, 122.0, 120.7, 114.0, 111.1, 66.5, 52.6.

(*E*)-N-(3-phenylpropylidene)morpholin-4-amine (**1y**).[8a] Afforded **1y** (392 mg, 90%) as a clear colorless liquid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 10.1, 4.9 Hz, 2H), 7.24 – 7.17 (m, 3H), 6.97 (t, *J* = 5.3 Hz, 1H), 3.82 (t, *J* = 5.0 Hz, 4H), 2.94 (t, *J* = 5.0 Hz, 4H), 2.83(t, *J* = 7.5 Hz, 2H), 2.62 – 2.54 (m, 2H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 141.1, 140.6, 128.4, 128.3, 126.0, 66.4, 52.3, 34.6, 33.6.

(*E*)-ethyl 3-(2,2-dimethylhydrazono)-2,2-difluoro-5-phenylpentanoate (**1z**).[9a] Afforded **1z** (290mg, 48%) as a pale yellow liquid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.24 – 7.20 (m, 3H), 6.67 (t, *J* = 5.4 Hz, 1H), 2.84 – 2.79 (m, 2H), 2.73 (s, 6H), 2.60 – 2.52 (m, 2H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 141.4, 138.0, 128.4, 128.3, 125.9, 43.3, 34.7, 34.1

(*E*)-*N*-octylidenemorpholin-4-amine (**1aa**).[25] Afforded **1aa** (352mg, 83%) as a clear colorless liquid. $^1$H NMR (500 MHz, $CDCl_3$) δ 6.95 (t, *J* = 5.6 Hz, 1H), 3.80 (t, *J* = 5.0 Hz, 4H), 2.92 (t, *J* = 5.0 Hz, 4H), 2.25 – 2.19 (m, 2H), 1.46 (dt, *J* = 15.1, 7.4 Hz, 2H), 1.31 – 1.23 (m, 8H), 0.85 (t, *J* = 6.9 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 142.4, 67.0, 66.4, 52.5, 33.0, 31.7, 29.1, 29.0, 27.4, 22.6, 14.0.

(*E*)-N-hexylidenemorpholin-4-amine (**1ab**). Afforded **1ab** (302 mg, 82%) as a clear colorless liquid. $^1$H NMR (500 MHz, $CDCl_3$) *δ* 6.96 (t, *J* = 5.6 Hz, 1H), 3.80 (t, *J* = 5.0 Hz, 4H), 2.92 (t, *J* = 5.0 Hz, 4H), 2.26 – 2.18 (m, 2H), 1.52 – 1.40 (m, 2H), 1.33 – 1.26 (m, 4H), 0.87 (t, *J* = 7.5 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 142.4, 66.4, 52.5, 33.0, 31.3, 27.0, 22.4, 13.9. HRMS: *m/z* (EI-TOF) calculated [M]: 184.1576, found:184.1570.

(*E*)-N-pentylidenemorpholin-4-amine (**1ac**). Afforded **1ac** (296 mg, 87%) as a clear colorless liquid. $^1$H NMR (500 MHz, $CDCl_3$) δ 6.95 (t, *J* = 5.6 Hz, 1H), 3.80 (t, *J* = 5.0 Hz,

4H), 2.92 (t, $J$ = 5.0 Hz, 4H), 2.27 – 2.18 (m, 2H), 1.48 – 1.40 (m, 2H), 1.38 – 1.29 (m, 2H), 0.89 (t, $J$ = 7.3 Hz, 3H). $^{113}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 142.4, 66.4, 52.4, 32.7, 29.5, 22.2, 13.9. HRMS: $m/z$ (EI-TOF) calculated [M]: 170.1419, found:170.1415.

(*E*)-1-(4-methylbenzylidene)-2-phenylhydrazine (**1ad**).[26] Afforded **1ad** (412 mg, 98%) as a brown solid, m.p. 108-109 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.63 (s, 1H), 7.57 (d, $J$ = 8.1 Hz, 2H), 7.53 (s, 1H), 7.33 – 7.27 (m, 2H), 7.20 (d, $J$ = 8.0 Hz, 2H), 7.12 (dd, $J$ = 8.5, 0.9 Hz, 2H), 6.92 – 6.85 (m, 1H), 2.39 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 144.8, 138.4, 137.5, 132.5, 129.3, 129.2, 126.1, 119.9, 112.7, 21.4.

(*E*)-N-(4-bromobenzylidene)piperidin-1-amine (**1ae**). Afforded **1ae** (495 mg, 93%) as a white solid, m.p. 51-52 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.37 (m, 5H), 3.16 (t, $J$ = 5.0 Hz, 4H), 1.74 (dt, $J$ = 11.6, 5.8 Hz, 4H), 1.57 – 1.52 (m, 2H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 135.7, 132.7, 131.5, 127.3, 121.3, 51.9, 25.1, 24.1. HRMS: $m/z$ (EI-TOF) calculated [M]: 266.0419, found:266.0417.

(*E*)-N-(4-bromobenzylidene)-4-methylpiperazin-1-amine (**1af**). Afforded **1af** (489 mg, 87%) as a white solid, m.p.140-141 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.49 -7.45 (m, 5H), 3.20 (t, $J$ = 5.0 Hz, 4H), 2.60 (t, $J$ = 5.0 Hz, 4H), 2.35 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 135.2, 134.0, 131.5, 127.4, 121.7, 54.4, 50.8, 45.9. HRMS: $m/z$ (EI-TOF) calculated [M]: 281.0528, found: 281.0525.

(*E*)-4-methylbenzaldehyde oxime (**1ag**).[27] Afforded **1ag** (182 mg, 75%) as a white solid, m.p. 70-71 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.17 (s, 1H), 7.49 (d, $J$ = 8.1 Hz, 2H), 7.21 (d, $J$ = 8.0 Hz, 2H), 2.38 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 150.3, 140.3, 129.5, 129.0, 127.0, 21.4.

(*E*)-N'-(4-methylbenzylidene)benzenesulfonohydrazide (**1ah**).[8a] Afforded **1ah** (507 mg, 88%) as a white solid, m.p. 116-117 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.44 (s, 1H), 8.02 (s, 1H), 8.00 (d, $J$ = 1.4 Hz, 1H), 7.77 (s, 1H), 7.61 – 7.55 (m, 1H), 7.50 (dd, $J$ = 10.5, 4.7 Hz, 2H), 7.46 (d, $J$ = 8.1 Hz, 2H), 7.14 (d, $J$ = 8.0 Hz, 2H), 2.34 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): δ 148.4, 140.8, 138.1, 133.2, 130.3, 129.3, 129.0, 127.8, 127.3, 21.4.

2-Bromo-2,2-difluoro-N-phenylacetamide (**2b**).[9d] Afforded **2b** (488 mg, 98%) as a white solid, m.p. 83-84 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.57 (d, $J$ = 8.2 Hz, 2H), 7.39 (t, $J$ = 7.8 Hz, 2H), 7.24 (t, $J$ = 7.4 Hz, 1H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 157.5 (t, $J$ = 27.5 Hz), 135.3, 129.4, 126.24, 114.00, 111.5 (t, $J$ = 315.0 Hz). $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -60.6.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(p-tolyl)propanoate (**3**).[8a] The procedure was operated in general method. The reaction gave 63 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(p-tolyl)propanoate in 96 % isolated yield as a pale yellow solid (PE/EA=10:1), m.p. 68-69°C. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.37 (d, $J$ = 8.0 Hz, 2H), 7.21 (d, $J$ = 8.0 Hz, 2H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.60 (t, $J$ = 5.0 Hz, 4H), 2.93 (t, $J$ = 5.0 Hz, 4H), 2.37 (s, 3H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.7 (t, $J$ = 31.3 Hz), 141.1 (t, $J$ = 31.3 Hz), 139.7, 129.4, 128.5, 128.2, 114.32 (t, $J$ = 248.6 Hz), 65.98, 62.5, 54.1, 21.4, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.54.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-phenylpropanoate (**4**).[8a] The procedure was operated in general method. The reaction gave 79 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-phenylpropanoate in 87 % isolated yield as a clear yellow liquid (PE/EA=10:1). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, $J$ = 6.1, 2.6 Hz, 2H),

7.43 – 7.38 (m, 3H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.58 (t, $J$ = 5.0 Hz, 4H), 2.92 (t, $J$ = 5.0 Hz, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.64(t, $J$ = 31.3 Hz), 140.63 (t, $J$ = 30.0 Hz), 131.2, 129.7, 128.6, 128.6, 114.3 (t, $J$ = 247.5 Hz), 65.9, 62.5, 54.1, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.49.

(*E*)-ethyl 2,2-difluoro-3-(4-methoxyphenyl)-3-(morpholinoimino)propanoate (**5**). The procedure was operated in general method. The reaction gave 99 mg of (*E*)-ethyl 2,2-difluoro-3-(4-methoxyphenyl)-3-(morpholinoimino) propanoate in 97 % isolated yield as a pale yellow liquid (PE/EA=5:1). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.44 (d, $J$ = 8.8 Hz, 2H), 6.92 (d, $J$ = 8.9 Hz, 2H), 4.36 (q, $J$ = 7.1 Hz, 2H), 3.82 (s, 3H), 3.60 (t, $J$ = 5.0 Hz, 4H), 2.92 (t, $J$ = 5.0 Hz, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$) $\delta$ 163.7 (t, $J$ = 31.3Hz), 160.46, 141.5 (t, $J$ = 31.3Hz), 129.9, 123.0, 116.33, 114.35 (t, $J$ = 247.5Hz), 114.1, 66.0, 62.5, 55.2, 54.0, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$) δ -101.52. HRMS: *m*/*z* (EI-TOF) calculated [M]: 342.1391, found: 342.1388.

(*E*)-ethyl 2,2-difluoro-3-(4-fluorophenyl)-3-(morpholinoimino)propanoate (**6**).[8a] The procedure was operated in general method. The reaction gave 84 mg of (*E*)-ethyl 2,2-difluoro-3-(4-fluorophenyl)-3-(morpholinoimino) propanoate in 85 % isolated yield as a clear colorless liquid (PE/EA=10:1). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.48 (dd, $J$ = 8.6, 5.4 Hz, 2H), 7.11 (t, $J$ = 8.7 Hz, 2H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.60 (t, $J$ = 5.0 Hz, 4H), 2.91 (t, $J$ = 5.0 Hz, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.45 (t, $J$ = 31.3 Hz), 163.2 (d, $J$ = 248.8 Hz), 140.0 (t, $J$ = 31.3 Hz), 130.7 (t, $J$ = 7.5 Hz), 127.1 (t, $J$ = 2.5 Hz) 115.9 (t, $J$ = 21.3 Hz), 114.2 (t, $J$ = 247.5 Hz), 65.9, 62.6, 54.1, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.5, -109.8

(*E*)-ethyl 3-(4-chlorophenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**7**).[8a] The procedure was operated in general method. The reaction gave 86 mg of (*E*)-ethyl 2,2-difluoro-3-(4-chlorophenyl)-3-(morpholinoimino) propanoate in 83 % isolated yield as a pale yellow liquid (PE/EA=10:1). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.46 – 7.36 (m, 4H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.60 (t, $J$ = 5.0 Hz, 4H), 2.93 (t, $J$ = 5.0 Hz, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.64, 163.38 (t, $J$ = 32.5 Hz), 139.46 (t, $J$ = 31.3 Hz), 135.9, 130.09, 129.59, 129.09, 114.1 (t, $J$ = 247.5 Hz), 65.9, 62.6, 54.1, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): δ -101.3.

(*E*)-ethyl 3-(4-bromophenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**8**). The procedure was operated in general method. The reaction gave 95 mg of (*E*)-ethyl 2,2-difluoro-3-(4-bromophenyl)-3-(morpholinoimino) propanoate in 81 % isolated yield as a pale yellow liquid (PE/EA=10:1).$^1$H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, $J$ = 8.5 Hz, 2H), 7.36 (d, $J$ = 8.5 Hz, 2H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.60 (t, $J$ = 5.0 Hz, 4H), 2.93 (t, $J$ = 5.0 Hz, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.36 (t, $J$ = 31.3 Hz), 139.35 (t, $J$ = 32.5 Hz), 132.0, 130.2, 130.0, 124.2, 114.1 (t, $J$ = 251.3 Hz), 65.9, 62.6, 54.1, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.3. HRMS: *m*/*z* (EI-TOF) calculated [M]: 390.0391, found: 390.0386.

(*E*)-ethyl 3-(4-acetylphenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**9**). The procedure was operated in general method. The reaction gave 86 mg of (*E*)-ethyl 2,2-difluoro-3-(4-acetylhenyl)-3-(morpholinoimino) propanoate in 83 % isolated yield as a yellow liquid (PE/EA=5:1). $^1$H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, $J$ = 8.3 Hz, 2H), 7.58 (d, $J$ = 8.2 Hz, 2H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.58 (t, $J$ = 5.0 Hz, 4H), 2.92 (t, $J$ = 5.0 Hz, 4H),

2.61 (s, 3H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 197.2, 163.30 (t, $J$ = 31.3 Hz), 138.8 (t, $J$ = 31.3 Hz), 137.7, 136.0, 129.0, 128.4, 114.08 (t, $J$ = 248.8 Hz), 65.8, 62.7, 54.2, 26.6, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.1. HRMS: $m/z$ (EI-TOF) calculated [M]: 354.1391, found: 354.1385.

(*E*)-ethyl 3-(4-cyanophenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**10**). The procedure was operated in general method. The reaction gave 75 mg of (*E*)-ethyl 2,2-difluoro-3-(4-acetylhenyl)-3-(morpholinoimino) propanoate in 74 % isolated yield as a yellow solid (PE/EA=10:1). $^1$H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, $J$ = 8.5 Hz, 2H), 7.60 (d, $J$ = 8.4 Hz, 2H), 4.38 (q, $J$ = 7.1 Hz, 2H), 3.60 (t, $J$ = 5.0 Hz, 4H), 3.92 (t, $J$ = 5.0 Hz, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.0 (t, $J$ = 31.3 Hz), 137.7 (t, $J$ = 31.3 Hz), 136.0, 132.3, 129.5, 117.9, 114.0 (t, $J$ = 31.3 Hz), 113.6, 65.8, 62.8, 54.3, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -100.8. HRMS: $m/z$ (EI-TOF) calculated [M]: 377.1238, found: 337.1240.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(4-nitrophenyl)propanoate (**11**).[9d] The procedure was operated in general method. The reaction gave 91 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(4-nitrophenyl) propanoate in 85 % isolated yield as a yellow solid (PE/EA=10:1), m.p. 119-120 $^o$C. $^1$H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, $J$ = 8.8 Hz, 2H), 7.68 (d, $J$ = 8.7 Hz, 2H), 4.38 (q, $J$ = 7.1 Hz, 2H), 3.60 (t, $J$ = 5.0 Hz, 4H), 2.94 (t, $J$ = 5.0 Hz, 4H), 1.38 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.0 (t, $J$ = 30.0Hz), 148.3, 137.9, 137.2 (t, $J$ = 32.5 Hz), 129.9, 123.8, 113.93 (t, $J$ = 248.8Hz), 65.8, 62.8, 54.3, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): δ -100.7.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(4-(trifluoromethyl)phenyl)propanoate

(**12**).[8a] The procedure was operated in general method. The reaction gave 92 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(4-trifluoromethylphenyl) propanoate in 80% isolated yield as a yellow solid (PE/EA=10:1), m.p. 78-79 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, $J$ = 8.2 Hz, 2H), 7.61 (d, $J$ = 8.1 Hz, 2H), 4.38 (q, $J$ = 7.1 Hz, 2H), 3.60 (t, $J$ = 5.0 Hz, 4H), 2.93 (t, $J$ = 5.0 Hz, 4H), 1.38 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.3 (t, $J$ = 31.3 Hz), 138.5 (t, $J$ = 31.3 Hz), 135.0, 131.7 (q, $J$ = 32.5 Hz), 129.2, 125.6 (q, $J$ = 3.8 Hz), 123.6 (q, $J$ = 271.3 Hz), 114.1 (t, $J$ = 248.8 Hz), 65.9, 62.7, 54.2, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -63.0, -101.1.

(*E*)-ethyl 3-(4-(dimethylamino)phenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**13**). The procedure was operated in general method. The reaction gave 65 mg of (E)-ethyl 3-(4-(dimethylamino)phenyl)-2,2-difluoro-3-(morpholinoimino)propanoate in 61 % isolated yield as a clear colorless liquid (PE/EA=1:1). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, $J$ = 8.8 Hz, 2H), 6.68 (d, $J$ = 9.0 Hz, 2H), 4.36 (q, $J$ = 7.1 Hz, 2H), 3.63 (t, $J$ = 5.0 Hz, 4H), 3.00 (s, 6H), 2.94 (t, $J$ = 5.0 Hz, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.95 (t, $J$ = 31.9 Hz), 150.9, 143.38 (t, $J$ = 30.0 Hz), 129.4, 117.4, 114.67 (t, $J$ = 248.8 Hz), 111.40, 66.1, 62.4, 54.0, 40.0, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.3. HRMS: $m/z$ (EI-TOF) calculated [M]: 355.1707, found: 355.1706.

(*E*)-ethyl 3-(3,4-dimethoxyphenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**14**). The procedure was operated in general method. The reaction gave 107 mg of (E)-ethyl 3-(3,4-dimethoxyphenyl)-2,2-difluoro-3-(morpholinoimino)propanoate in 96 % isolated yield as a clear colorless liquid (PE/EA=5:1). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.07 (d, $J$ = 8.1 Hz, 1H), 7.03 (s, 1H), 6.88 (d, $J$ = 8.3 Hz, 1H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.90 (s, 3H), 3.87 (s, 3H),

3.60 (t, *J* = 5.0 Hz, 4H), 2.93 (t, *J* = 5.0 Hz, 4H), 1.37 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.7 (t, *J* = 31.3 Hz), 150.1, 148.9, 141.0 (t, *J* = 31.9 Hz), 123.0, 121.6, 114.4 (t, *J* = 248.1 Hz), 111.3, 111.0, 66.1, 62.5, 56.0, 55.8, 54.0, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.4. HRMS: *m*/*z* (EI-TOF) calculated [M]: 372.1497, found: 372.1500.

(*E)*-ethyl 2,2-difluoro-3-(4-hydroxy-3-methoxyphenyl)-3-(morpholinoimino)propanoate (**15**). The procedure was operated in general method. The reaction gave 100 mg of (E)-ethyl 3-(4-hydroxy-3-methoxyphenyl)-2,2-difluoro-3-(morpholinoimino)propanoate in 97 % isolated yield as a clear colorless liquid (PE/EA=3:1).$^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.05 – 7.00 (m, 2H), 6.93 (d, *J* = 8.2 Hz, 1H), 5.95 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 3.61 (t, *J* = 5.0 Hz, 4H), 2.93 (t, *J* = 5.0 Hz, 4H), 1.37 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.7 (t, *J* = 31.3Hz), 146.9, 146.5, 141.1 (t, *J* = 31.3Hz), 122.4, 114.7, 114.4 (t, *J* = 253.4Hz), 110.7, 66.1, 62.5, 56.1, 54.0, 24.8, 14.1. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.4. HRMS: *m*/*z* (EI-TOF) calculated [M]: 358.1340, found: 358.1342.

(*E*)-ethyl 3-(3-chlorophenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**16**).[8a] The procedure was operated in general method. The reaction gave 103 mg of (*E*)-ethyl 2,2-difluoro-3-(3-chlorophenyl)-3-(morpholinoimino) propanoate in 99% isolated yield as a pale yellow liquid (PE/EA=10:1).$^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.41 – 7.33 (m, 3H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.60 (t, *J* = 5.0 Hz, 4H), 2.94 (t, *J* = 5.0 Hz, 4H), 1.37 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.3 (t, *J* = 31.9Hz), 138.5 (t, *J* = 31.9Hz), 134.7, 132.9, 129.9, 129.9, 128.7, 126.9, 114.1 (t, *J* = 248.8 Hz), 65.9, 62.6, 54.2, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.2.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(3-nitrophenyl)propanoate (**17**). The

procedure was operated in general method. The reaction gave 81 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(3-nitrophenyl) propanoate in 75 % isolated yield as a yellow solid (PE/EA=10:1). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.38 (s, 1H), 8.28 (ddd, $J$ = 8.3, 2.2, 1.0 Hz, 1H), 7.82 (d, $J$ = 7.7 Hz, 1H), 7.64 (t, $J$ = 8.0 Hz, 1H), 4.39 (q, $J$ = 7.1 Hz, 2H), 3.61 (t, $J$ = 5.0 Hz, 4H), 2.95 (t, $J$ = 5.0 Hz, 4H), 1.39 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$) δ 163.0 (t, $J$ = 31.9 Hz), 148.2, 137.0 (t, $J$ = 31.2Hz), 134.6, 132.8, 129.8, 124.5, 123.8, 113.9 (t, $J$ =250.0 Hz), 65.8, 62.8, 54.3, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$) δ -100.84(d, $J$ = 9.4 Hz). HRMS: *m*/*z* (EI-TOF) calculated [M]: 357.1136, found: 357.1131.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(o-tolyl)propanoate (**18**). The procedure was operated in general method. The reaction gave 63 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(o-tolyl)propanoate in 64 % isolated yield as a clear colorless liquid (PE/EA=10:1). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.34 – 7.28 (m, 2H), 7.21 (t, $J$ = 8.1 Hz, 2H), 4.38 (q, $J$ = 7.1 Hz, 2H), 3.62 – 3.52 (m, 4H), 2.97 – 2.84 (m, 4H), 2.28 (s, 3H), 1.38 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.90 (t, $J$ = 32.5 Hz), 138.8 (t, $J$ = 31.3 Hz), 138.1, 131.2, 130.0, 129.7, 128.8, 125.7, 114.4 (t, $J$ = 247.5 Hz), 66.3, 62.5, 53.8, 19.7, 14.1. $^{19}$F NMR (471 MHz, $CDCl_3$) δ -101.0 (d, $J$ = 273.2 Hz), -103.3 (d, $J$ = 273.2 Hz). HRMS: *m*/*z* (EI-TOF) calculated [M]: 326.1442, found: 326.1441.

(*E*)-ethyl 2,2-difluoro-3-(2-methoxyphenyl)-3-(morpholinoimino)propanoate (**19**).[8a] The procedure was operated in general method. The reaction gave 77 mg of (*E*)-ethyl 2,2-difluoro-3-(2-methoxyphenyl)-3-(morpholinoimino) propanoate in 75 % isolated yield as a clear colorless liquid (PE/EA=5:1).$^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.37 (t, $J$ = 7.9 Hz, 1H), 7.24 (s, 1H), 6.96 (t, $J$ = 7.5 Hz, 1H), 6.90 (d, $J$ = 8.3 Hz, 1H), 4.36 (q, $J$ = 7.1 Hz, 2H), 3.83

(s, 3H), 3.57 (t, *J* = 5.0 Hz, 4H), 2.97 (t, *J* = 5.0 Hz, 4H), 1.36 (t, *J* = 7.1 Hz, 3H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): δ 164.1 (t, *J* = 33.1 Hz), 157.6, 135.0 (t, *J* = 31.1 Hz), 131.2, 130.5, 120.5, 114.2 (t, *J* =248.1 Hz), 111.12, 66.2, 62.4, 55.8, 53.4, 14.1. $^{19}F$ NMR (471 MHz, $CDCl_3$): *δ* -101.6, -103.2.

(*E*)-ethyl 3-(2-bromophenyl)-2,2-difluoro-3-(morpholinoimino)propanoate (**20**). The procedure was operated in general method. The reaction gave 53 mg of (*E*)-ethyl 2,2-difluoro-3-(2-bromophenyl)-3-(morpholinoimino) propanoate in 45 % isolated yield as a pale yellow liquid (PE/EA=10:1).$^1H$ NMR (500 MHz, $CDCl_3$): *δ* 7.61 (d, *J* = 8.0 Hz, 1H), 7.36 (dt, *J* = 14.8, 7.5 Hz, 2H), 7.31 – 7.26 (m, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.61 (t, *J* = 4.9 Hz, 4H), 3.01 (dtd, *J* = 17.0, 11.9, 4.7 Hz, 4H), 1.38 (t, *J* = 7.1 Hz, 3H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): *δ* 163.7 (t, *J* = 33.9 Hz), 133.5, 132.7, 131.3, 131.0, 127.2, 127.0, 124.3, 114.2 (t, *J* = 248.8 Hz), 66.3, 62.5, 53.4, 14.1. $^{19}F$ NMR (471 MHz, $CDCl_3$): *δ* -99.6 (d, *J* =268.5 Hz), -102.8 (d, *J* =268.5 Hz). HRMS: *m*/*z* (EI-TOF) calculated [M]: 390.0391, found: 390.0392.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(naphthalen-2-yl)propanoate (**21**, ***E***/***Z***=67:33). The procedure was operated in general method. The reaction gave 56 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(naphthalen-2-yl)propanoate in 51 % isolated yield as a pale yellow liquid (PE/EA=10:1). $^1H$ NMR (500 MHz, $CDCl_3$) *δ* 8.37 – 8.26 (m, 1H), 7.99 (s, 1H), 7.92 – 7.86 (m, 2H), 7.63 – 7.45 (m, 3H), 4.41 (q, *J* = 7.1 Hz, 3H), 3.60 (t, *J* = 5.0 Hz, 4H), 2.96 (t, *J* = 5.0 Hz, 4H), 1.40 (t, *J* = 7.1 Hz, 3H). $^{13}C\{1H\}$NMR (125 MHz, $CDCl_3$): *δ* 163.7 (t, *J* = 35.0 Hz), 140.7 (t, *J* = 32.5 Hz), 133.5, 132.8, 131.3, 128.5, 128.4, 128.4, 127.8, 127.3, 126.8, 125.4, 114.4 (t, *J* = 211.3 Hz), 66.0, 62.6, 54.3, 14.1. $^{19}F$ NMR

(471 MHz, $CDCl_3$): $\delta$ -101.1. HRMS: *m*/*z* (EI-TOF) calculated [M]: 362.1442, found: 362.1439.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(pyridin-3-yl)propanoate (**22**). The procedure was operated in general method. The reaction gave 38 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(pyridin-3-yl)propanoate in 41 % isolated yield as a pale yellow liquid (PE/EA=5:1). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.65 (d, *J* = 4.2 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.38 (dd, *J* = 7.8, 4.9 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.60 (t, *J* = 5.0 Hz, 4H), 2.94 (t, *J* = 5.0 Hz, 4H), 1.37 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.2 (t, *J* = 31.3Hz), 150.6, 149.4, 136.2, 127.7, 123.5, 114.00 (t, *J* = 248.1Hz), 65.8, 62.7, 54.2, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.3. HRMS: *m*/*z* (EI-TOF) calculated [M]: 313.1238, found: 326.1237.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(thiophen-2-yl)propanoate (**23**). The procedure was operated in general method. The reaction gave 21 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-3-(pyridin-3-yl)propanoate in 21 % isolated yield as a pale yellow liquid (PE/EA=7:1). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.26 – 7.23 (m, 1H), 6.96 (d, *J* = 3.8 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.86 (t, *J* = 5.0 Hz, 4H), 3.16 (t, *J* = 5.0 Hz, 4H), 1.35 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.2 (t, *J* = 35.0 Hz), 145.63, 132.6 (t, *J* = 30.0 Hz), 129.0, 128.4 (t, *J* = 5.6 Hz), 125.1, 111.6 (t, *J* = 248.7 Hz), 66.2, 63.4, 51.4, 13.9. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -93.9. HRMS: *m*/*z* (EI-TOF) calculated [M]: 318.0850, found: 318.0848.

(*E*)-ethyl 2,2-difluoro-3-(furan-2-yl)-3-(morpholinoimino)propanoate (**24**). The procedure was operated in general method. The reaction gave 46 mg of (*E*)-ethyl

2,2-difluoro-3-(furan-2-yl)-3-(morpholinoimino) propanoate in 51 % isolated yield as a pale yellow liquid (PE/EA=7:1). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 1H), 6.77 (dd, *J* = 3.4, 1.6 Hz, 1H), 6.57 (d, *J* = 3.5 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 3.86 (t, *J* = 5.0 Hz, 4H), 3.16 (t, *J* = 5.0 Hz, 4H), 1.36 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 162.3 (t, *J* = 33.8 Hz), 154.3, 143.5 (t, *J* = 33.1Hz), 124.8, 113.5, 108.59 (t, *J* = 246.9 Hz), 107.18, 66.2, 63.5, 51.2, 13.9. $^{19}$F NMR (471 MHz, $CDCl_3$): *δ* -102.2. HRMS: *m*/*z* (EI-TOF) calculated [M]: 302.1078, found: 302.1076.

(*E*)-ethyl-3-(5-(2-ethoxy-1,1-difluoro-2-oxoethyl)thiophen-2-yl)-2,2-difluoro-3-(morpholinoimino)propanoate (**25**). The procedure was operated in general method. The reaction gave 45 mg of (*E*)-ethyl-3-(5-(2-ethoxy-1,1-difluoro-2-oxoethyl)thiophen-2-yl)-2,2-difluoro-3-(morpholinoimino)propanoate propanoate in 39 % isolated yield as a pale yellow liquid (PE/EA=7:1). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.57 (m, 1H), 7.38 – 7.33 (m, 1H), 4.38 (q, *J* = 7.1 Hz, 4H), 3.84 (t, *J* = 5.0 Hz, 4H), 2.91 (t, *J* = 5.0 Hz, 4H), 1.37 (t, *J* = 7.1, 3H), 1.36 (t, *J* = 7.1, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 162.76 (t, *J* = 34.4 Hz), 162.3 (t, *J* = 30.0 Hz), 147.72 (t, *J* = 31.3 Hz), 138.9 (t, *J* = 33.8 Hz), 132.0 (t, *J* = 3.1 Hz), 130.2 (t, *J* = 1.9 Hz), 127.5 (t, *J* = 5.6 Hz), 113.8 (t, *J* = 252.5 Hz), 111.4 (t, *J* = 250.0 Hz), 65.8, 63.7, 63.0, 54.5, 13.9, 13.9. $^{19}$F NMR (471 MHz, $CDCl_3$): *δ* -94.2, -102.5. HRMS: *m*/*z* (EI-TOF) calculated [M]: 440.1029, found: 440.1033.

(*E*)-ethyl3-(5-(2-ethoxy-1,1-difluoro-2-oxoethyl)furan-2-yl)-2,2-difluoro-3-(morpholinoimino)propanoate **(26)**. The procedure was operated in general method. The reaction gave 68 mg of

(*E*)-ethyl3-(5-(2-ethoxy-1,1-difluoro-2-oxoethyl)furan-2-yl)-2,2-difluoro-3-(morpholinoimino )propanoate in 53 % isolated yield as a yellow liquid (PE/EA=7:1). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 6.84 (dd, $J$ = 3.4, 1.3 Hz, 1H), 6.81 (d, $J$ = 3.5 Hz, 1H), 4.38 (q, $J$ = 7.1 Hz, 2H), 4.36 (q, $J$ =7.1 Hz, 4H), 3.73 (t, $J$ = 5.0 Hz, 4H), 3.07 (t, $J$ = 5.0 Hz, 4H), 1.36 (t, $J$ = 7.1 Hz, 3H), 1.35 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$) δ 163.0 (t, $J$ = 31.9 Hz), 161.9 (t, $J$ = 33.1 Hz), 145.7 (t, $J$ = 34.4 Hz), 144.3, 127.5 (t, $J$ = 32.5 Hz), 114.8, 112.9, 112.9 (t, $J$ =124.4 Hz), 108.3 (t, $J$ = 248.1 Hz), 66.1, 63.8, 62.8, 53.9, 14.0, 13.8. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.9, -102.8. HRMS: *m*/*z* (EI-TOF) calculated [M]: 424.1257, found: 424.1258.

(*E*)-ethyl 3-(benzo[b]thiophen-3-yl)-2,2-difluoro-3-(morpholinoimino)propanoate (**27**). The procedure was operated in general method. The reaction gave 47 mg of (*E*)-ethyl 3-(benzo[b]thiophen-3-yl)-2,2-difluoro-3-(morpholinoimino)propanoate in 32 % isolated yield as a yellow liquid (PE/EA=7:1). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 1H), 7.80 – 7.73 (m, 1H), 7.52 – 7.46 (m, 2H), 4.48 – 4.32 (m, 4H), 3.59-3.47 (m, 4H), 3.20-2.80 (m, 4H), 1.40 (t, $J$ = 7.1 Hz, 3H), 1.35 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$) δ163.6 (t, $J$ = 31.9 Hz), 162.2 (t, $J$ = 33.7 Hz), 138.5, 138.3, 134.1 (t, $J$ = 27.5 Hz), 127.6 (t, $J$ = 3.8 Hz), 127.0, 125.7, 124.8, 124.8, 122.4, 114.1 (t, $J$ = 247.5 Hz), 111.7 (t, $J$ = 250.0 Hz), 66.2, 63.8, 62.7, 53.1, 14.1, 13.8. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -89.6 (dd, $J$ = 9.4，277.9 Hz) , -95.6 (dd, $J$ = 4.7，273.2Hz), -99.4 (d, $J$ = 9.4，268.5 Hz), -101.6 (dt, $J$ = 9.4，263.8 Hz). HRMS: *m*/*z* (EI-TOF) calculated [M]: 490.1186, found: 490.1190.

(*E*)-ethyl 2,2-difluoro-3-(1H-indol-3-yl)-3-(morpholinoimino)propanoate (**28**). The procedure was operated in general method. The reaction gave 58 mg of (*E*)-ethyl 2,2-difluoro-3-(1H-indol-3-yl)-3-(morpholinoimino)propanoate in 47 % isolated yield as a

yellow liquid (PE/EA=7:1).$^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.42 (d, $J$ = 8.1 Hz, 1H), 8.06 (s, 1H), 7.39 (d, $J$ = 8.2 Hz, 1H), 7.32 (t, $J$ = 7.6 Hz, 1H), 7.24 (d, $J$ = 7.7 Hz, 1H), 4.32 (q, $J$ = 7.1 Hz, 2H), 3.93 (t, $J$ = 5.0 Hz, 4H), 3.22 (t, $J$ = 5.0 Hz, 4H), 1.30 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 162.9 (t, $J$ = 35.6 Hz), 135.7, 131.3, 125.55, 125.31 (t, $J$ = 30.0 Hz), 125.2, 124.9, 123.8, 121.6, 114.6, 111.4, 111.12 (t, $J$ = 250.0 Hz), 66.5, 63.7, 51.9, 13.9. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.0. HRMS: $m/z$ (EI-TOF) calculated [M]: 351.1397, found: 351.1394.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-5-phenylpentanoate (**29**, ***E***/***Z***=88/12). The procedure was operated in general method. This compound is known.[8a] The reaction gave 50 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)-5-phenylpentanoate in 49% isolated yield as a clear colorless liquid (PE/EA=10:1).$^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.30 (q, $J$ = 7.3 Hz, 2H), 7.25 – 7.19 (m, 3H), 4.36 (q, $J$ = 7.1 Hz, 2H), 3.76 (t, $J$ = 5.0 Hz, 4H), 2.98- 2.94 (m, 2H), 2.84- 2.81 (m, 2H), 2.77 (t, $J$ = 5.0 Hz, 4H), 1.35 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 162.87 (t, $J$ = 31.3 Hz), 158.1 (t, $J$ = 29.4 Hz), 140.5, 128.6, 128.3, 126.4, 113.78 (t, $J$ = 250.6 Hz), 65.9, 62.7, 54.9, 31.7, 28.8, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -105.9.

(*E*)-ethyl 3-(2,2-dimethylhydrazono)-2,2-difluoro-5-phenylpentanoate (**30**, *E/Z*=80:20).[9d] The procedure was operated in general method. The reaction gave 27 mg of (*E*)-ethyl 3-(2,2-dimethylhydrazono)-2,2-difluoro-5-phenylpentanoate in 30% isolated yield as a clear colorless liquid (PE/EA=30:1). $^{1}$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.35 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 4.35 (q, $J$ = 7.1 Hz, 2H), 3.00 – 2.89 (m, 2H), 2.83 – 2.76 (m, 2H), 2.74 (s, 6H), 1.36 (t, $J$ = 7.2 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.5 (t, $J$ =31.3 Hz), 147.8 (t, $J$

=30.6 Hz), 140.8, 128.6, 128.25, 126.4, 114.8 (t, $J$ =247.5 Hz), 62.5, 46.9, 31.9, 28.6, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -104.6.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)decanoate (**31**, ***E***/***Z***=76:24). The procedure was operated in general method. The reaction gave 49 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)decanoate in 49% isolated yield as a clear colorless liquid (PE/EA=10:1). $^1$H NMR (500 MHz, $CDCl_3$) δ 4.36 (q, $J$ = 7.1 Hz, 1H), 3.80 (t, $J$ = 5.0 Hz, 4H), 2.85 (t, $J$ = 5.0 Hz, 4H), 2.55 – 2.47 (m, 2H), 1.67 - 1.63 (m, 3H), 1.42 – 1.26 (m, 11H), 0.90 (td, $J$ = 6.9, 2.6 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.1 (t, $J$ = 31.3 Hz), 161.81 (t, $J$ = 31.3 Hz), 113.8 (t, $J$ =250 Hz), 65.9, 62.6, 55.0, 31.6, 29.8, 28.7, 26.9, 25.5, 22.6, 14.0, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): δ -106.0. HRMS: *m*/*z* (EI-TOF) calculated [M]: 334.2068, found: 324.2070.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)octanoate (**32**, ***E***/***Z***=75:25). The procedure was operated in general method. The reaction gave 62 mg of (*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)decanoate in 68% isolated yield as a clear colorless liquid (PE/EA=10:1).$^1$H NMR (500 MHz, $CDCl_3$) δ 4.33 (q, $J$ = 7.1 Hz, 2H), 3.78 (t, $J$ = 5.0 Hz, 4H), 2.83 (t, $J$ = 5.0 Hz, 4H), 2.52 – 2.45 (m, 2H), 1.68 – 1.58 (m, 2H), 1.38 – 1.29 (m, 7H), 0.90 (t, $J$ = 6.9 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.1 (t, $J$ = 31.3Hz), 158.6 (t, $J$ = 29.4Hz), 113.8 (t, $J$ = 250.0Hz), 65.9, 62.6, 55.0, 32.0, 25.8, 25.2, 22.1, 14.0, 13.8. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -106.0. HRMS: *m*/*z* (EI-TOF) calculated [M]: 306.1755, found: 306.1750.

(*E*)-ethyl 2,2-difluoro-3-(morpholinoimino)heptanoate (**33**, E/Z=83:17). The procedure was operated in general method. The reaction gave 47 mg of (*E*)-ethyl

2,2-difluoro-3-(morpholinoimino)decanoate in 53% isolated yield as a clear colorless liquid (PE/EA=10:1). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 4.34 (q, $J$ = 7.1 Hz, 2H), 3.78 (t, $J$ = 5.0 Hz, 4H), 2.86 – 2.81 (t, $J$ = 5.0 Hz, 4H), 2.53 – 2.46 (m, 2H), 1.65 – 1.57 (m, 2H), 1.42 – 1.35 (m, 2H), 1.33 (t, $J$ = 7.2 Hz, 3H), 0.93 (t, $J$ = 7.3 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.1 (t, $J$ = 31.3 Hz), 158.4 (t, $J$ = 30.0 Hz), 113.8 (t, $J$ = 250.0 Hz), 66.0, 62.6, 55.0, 27.6, 26.6, 23.0, 14.0, 13.6. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -106.0. HRMS: $m/z$ (EI-TOF) calculated [M]: 292.1598, found: 292.1601.

(*E*)-ethyl 2,2-difluoro-3-(2-phenylhydrazono)-3-(p-tolyl)propanoate (**34**). The procedure was operated in general method. The reaction gave 60 mg of (*E*)-ethyl 2,2-difluoro-3-(2-phenylhydrazono)-3-(p-tolyl)propanoate in 60% isolated yield as a clear colorless liquid (PE/EA=4:1). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.81 (s, 1H), 7.36 (d, $J$ = 3.5 Hz, 3H), 7.23 (dd, $J$ = 8.5, 7.4 Hz, 2H), 6.94 – 6.87 (m, 3H), 4.49 (q, $J$ = 7.2 Hz, 2H), 2.45 (s, 3H), 1.44 (t, $J$ = 7.2 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 163.6 (t, $J$ = 32.5 Hz), 143.0, 140.6, 136.0 (t, $J$ = 31.3 Hz), 130.4, 129.2, 129.1, 123.84, 121.53, 113.9 (t, $J$ = 245 Hz), 113.3, 62.9, 21.5, 14.1. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.1. HRMS: $m/z$ (EI-TOF) calculated [M]: 362.1442, found: 362.1439.

(*E*)-ethyl 3-(4-bromophenyl)-2,2-difluoro-3-(piperidin-1-ylimino)propanoate (**35**). The procedure was operated in general method. The reaction gave 66 mg of (*E*)-ethyl 3-(4-bromophenyl)-2,2-difluoro-3-(piperidin-1-ylimino)propanoate in 57% isolated yield as a clear colorless liquid (PE/EA=8:1). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.53 (d, $J$ = 8.4 Hz, 2H), 7.35 (d, $J$ = 8.4 Hz, 2H), 4.37 (q, $J$ = 7.1 Hz, 2H), 2.93 (t, $J$ = 5.0 Hz, 4H), 1.50 – 1.41 (m, 6H), 1.38 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$163.8 (t, $J$ = 31.9 Hz),

135.49 (t, *J* = 31.9 Hz), 131.7, 130.8, 130.4, 123.6, 114.8 (t, *J* = 246.9 Hz) 62.5, 54.8, 24.7, 23.8, 14.0. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -100.4. HRMS: *m*/*z* (EI-TOF) calculated [M]: 388.0598, found: 388.0590.

(*E*)-ethyl 3-(4-bromophenyl)-2,2-difluoro-3-((4-methylpiperazin-1-yl)imino)propanoate (**36**). The procedure was operated in general method. The reaction gave 69 mg of (*E*)-ethyl 3-(4-bromophenyl)-2,2-difluoro-3-((4-methylpiperazin-1-yl)imino)propanoate in 57% isolated yield as a clear yellow liquid (PE/EA=1:1). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.99 (t, *J* = 5.0 Hz, 4H), 2.35 (t, *J* = 5.0 Hz, 4H), 2.23 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$163.6 (t, *J* = 31.3 Hz), 138.0 (t, *J* = 31.3 Hz), 131.9, 130.3, 127.7, 124.1, 114.4 (t, *J* = 248.1 Hz), 62.6, 53.8, 53.3, 45.6, 14.1. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.0. HRMS: *m*/*z* (EI-TOF) calculated [M]: 403.0707, found: 407.0703.

(*E*)-2,2-difluoro-3-(morpholinoimino)-N-phenyl-3-(p-tolyl)propanamide (**39**).[8a] The procedure was operated in general method. The reaction gave 105 mg of (*E*)-2,2-difluoro-3-(morpholinoimino)-N-phenyl-3-(p-tolyl)propanamide in 93% isolated yield as a white solid (PE/EA=5:1), m.p. 131-132 ºC. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.00 (s, 1H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.37 (dt, *J* = 7.5, 3.8 Hz, 4H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 3.58 (t, *J* = 5.0 Hz, 4H), 2.93 (t, *J* = 5.0 Hz, 4H), 2.38 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$161.6 (t, *J* = 28.9 Hz), 141.2 (t, *J* = 30.6 Hz), 139.8, 136.5, 129.4, 129.1, 128.5, 128.5, 125.2, 120.2, 114.37 (t, *J* = 251.3 Hz), 66.0, 54.2, 21.4. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -101.2.

Ethyl 2,2-difluoro-3-oxo-3-(p-tolyl)propanoate (**40**).[8a] Compound **3** was added into 25 mL

round bottom flask with 2 mL THF and 2 mL 0.6 M HCl. After the raw material **3** was consumed by TLC under room temperature. The crude production was diluted with ethyl ethylate and then scrubber with saturated NaCl solution (3 times). The organic layers dried over anhydrous $Na_2SO_4$, concentrated in vacuo, and purified by flash column chromatograph to give the pure production **40** (88%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): *δ* 184.9 (t, *J* = 27.5 Hz), 161.9 (t, *J* = 30.6 Hz), 146.5, 130.0 (t, *J* = 2.5 Hz), 129.7, 128.5, 109.8 (t, *J* = 263.1Hz), 63.7, 21.9, 13.8. $^{19}$F NMR (471 MHz, $CDCl_3$): *δ* -107.6.

2,2-Difluoro-3-(morpholinoamino)-3-(p-tolyl)propan-1-ol (**41**).[8a] **3** was added into 25 mL tube with 2 mL anhydrous THF under ice-bath. $LiAlH_4$ (10 equiv) was gradually added the mixture. Then the mixture was stirred under room temperature. After the raw material **3** was consumed by TLC. The crude production was diluted with ethyl ethylate and then scrubber with saturated NaCl solution (3 times). The organic layers dried over anhydrous $Na_2SO_4$, concentrated in vacuo, and purified by flash column chromatograph to give the pure production **41** (PE/EA= 4:1, 74%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 6.9 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 4.99 (s, 1H), 4.36 (dd, *J* = 22.5, 4.2 Hz, 1H), 4.00 (ddd, *J* = 29.6, 12.8, 3.9 Hz, 1H), 3.84 – 3.67 (m, 5H), 3.07 – 2.43 (m, 5H), 2.36 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$) δ 138.6, 131.8, 129.2, 128.6, 121.8 (t, *J* = 246.9 Hz), 66.7, 63.4 - 62.0 (m, 2C), 56.5, 21.1. $^{19}$F NMR (471 MHz, $CDCl_3$): *δ* -107.3 (d, *J* = 254.3 Hz), -119.9 (d, *J* = 254.3 Hz).

(*E*)-2,2-Difluoro-3-(morpholinoimino)-3-(p-tolyl)propan-1-ol (**42**). **3** was added into 25 mL tube with 2 mL anhydrous THF under ice-bath. $NaBH_4$ (10 equiv) was gradually added

the mixture. Then the mixture was stirred under room temperature.After the raw material **3**was consumed by TLC. The crude production was diluted with ethyl ethylate and then scrubber with saturated NaCl solution (3 times). The organic layers dried over anhydrous $Na_2SO_4$, concentrated in vacuo, and purified by flash column chromatograph to give the pure production **42** (PE/EA= 4:1, 62%).$^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.39 (d, $J$ = 8.0 Hz, 2H), 7.21 (d, $J$ = 8.0 Hz, 2H), 4.08 (td, $J$ = 11.8, 7.2 Hz, 2H), 3.62 (t, $J$ = 5.0 Hz, 4H), 3.05 (t, $J$ = 7.3 Hz, 1H), 2.90 (t, $J$ = 5.0 Hz, 4H), 2.37 (s, 3H). $^{13}$C{1H}NMR (125 MHz, $CDCl_3$): $\delta$ 146.4 (t, $J$ = 32.5 Hz), 139.7, 129.3, 128.6, 128.1, 118.2 (t, $J$ = 240.6 Hz), 66.0, 64.2, 63.9, 63.7, 54.3, 21.4. $^{19}$F NMR (471 MHz, $CDCl_3$): $\delta$ -103.7. HRMS: $m/z$ (EI-TOF) calculated [M]: 284.1336, found: 284.1339.

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**Notes**

The authors declare no competing financial interest.

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## ASSOCIATED CONTENT

### Supporting Information

$^{1}$H NMR, $^{13}$C NMR, and $^{19}$F NMR spectra for all products. The Supporting Information is available free of charge on the ACS Publications website.

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