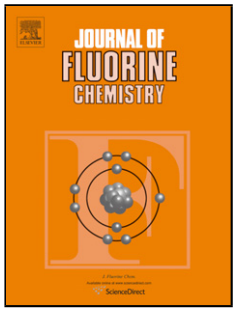

Title: Copper-catalyzed ligand free ring-opening amination of *gem*-fluorohalocyclopropanes—an efficient route toward 2-fluoroallylamines

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Copper-catalyzed ligand free ring-opening amination of *gem*-fluorohalocyclopropanes — an efficient route toward 2-fluoroallylamines

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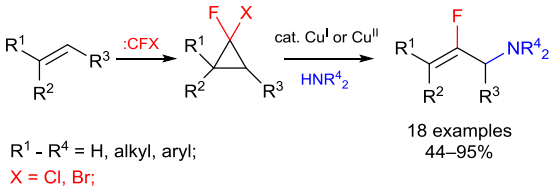
Graphical Abstract



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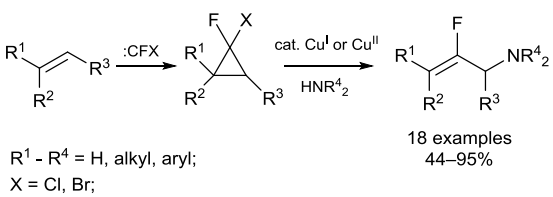

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Copper-catalyzed ring-opening amination of *gem*-chlorofluoro- and *gem*-bromofluorocyclopropanes easily prepared by carbenic cyclopropanation of olefins affords tertiary 2-fluoroallyl amines in moderate to excellent yields.

Highlights

- Copper-catalyzed cyclopropyl-allylic rearrangements of *gem*-fluorohalocyclopropanes.
- An effective approach to aryl-, alkyl substituted tertiary 2-fluoroallyl amines.
- Preparation of secondary 2-fluoroallyl amines using PMP-protective group.
- Synthesis of primary 2-fluoroallyl amines by Gabriel or Delepin amination of halides.

Abstract

Ring-opening amination of *gem*-chlorofluoro- and *gem*-bromofluorocyclopropanes with secondary alkyl, aryl amines or hydroxylamines catalyzed by copper(I) or copper(II) compounds with no additional ligands affords tertiary 2-fluoroallylamines or hydroxylamines in moderate to excellent yields. The reaction pathway involves isomerization of *gem*-fluorohalocyclopropanes to 2-fluoroallyl halides followed by *in situ* nucleophilic substitution of a halide by an *N*-nucleophile. The *p*-methoxyphenyl (PMP) protective group is efficient in the preparation of secondary 2-fluoroallylamines by this method. Primary 2-fluoroallylamines can only be obtained by a stepwise protocol including CuX-catalyzed isomerization of *gem*-fluorohalocyclopropanes to 2-fluoroallylic halides followed by amination.

Keywords: *gem*-fluorohalocyclopropanes, fluorohalocarbenes, copper catalysis, 2-fluoroallyl amines, ring-opening amination, cyclopropyl-allylic transformation

1. Introduction

The monofluoroalkenyl moiety is of continuously growing interest in modern medicinal chemistry [1]. It can be found in a wide range of biologically active compounds developed in the past few decades (figure 1). It manifests anticancer [2], antimicrobial [3], anti-HIV [4], anti-diabetic [5] and other types of pharmacological activities. Moreover, monofluoroalkenes can serve as promising bioisosters of amide bonds [6].

Rearrangements of *gem*-fluorohalocyclopropanes (halogen = fluorine, chlorine, bromine) were found to be efficient for the construction of the monofluoroalkenyl moiety [7]. *gem*-Fluorohalocyclopropanes are readily available by carbene cyclopropanation of olefins using a variety of inexpensive fluorohalocarbene sources [7] that makes these processes an attractive alternative to other synthetic routes toward monofluoroalkenes [8],[9].

However, the *gem*-fluorohalocyclopropyl moiety itself is rather stable at elevated temperatures and under ordinary acidic or basic conditions. The propensity of *gem*-fluorohalocyclopropanes to undergo ring-opening rearrangements can be dramatically increased by electron-donating substituents (e.g. alkoxy [10], amino [11] groups), by a negative charge at an α-position to the three-membered ring [12], or by incorporation into a strained polycyclic system [13].

Ring-opening of non-activated *gem*-fluorohalocyclopropanes under mild conditions still remains a challenge (scheme 1). In fact, thermolytic activation usually requires 350–650°C in a gas phase or 150–200°C in a liquid phase and leads to the formation of 2-fluoro-1,3-dienes [14] or fluoroarenes [15]. Silver(I) mediated conditions extensively studied by M. Schlosser, P. Weyerstahl, R. Kostikov and some other groups are applicable to a variety of *gem*-chlorofluoro- and *gem*-bromofluorocyclopropanes and give 2-fluoroallyl ethers, esters and alcohols [16]. However, these processes require stoichiometric amounts of relatively expensive silver(I) salts and this fact partially overrides the benefits generated by the availability of the starting fluorohalocarbene sources (i.e. $CHCl_2F$, $CHBr_2F$).

Recently we reported the first catalytic ring-opening of *gem*-chlorofluoro- and *gem*-bromofluorocyclopropanes in the presence of CuX (X = Cl, Br) [17]. These conditions made it possible to synthesize not only 2-fluoroallylic *O*-derivatives but also 2-fluoroallyl chlorides and bromides [18,19]. The recently reported [Pd^0]/^{t}Bu-XPhos-catalyzed ring-opening of *gem*-difluorocyclopropanes in the presence of various *O,N,C*-nucleophiles leading to the corresponding 2-fluoroallylic compounds should also be mentioned [20]. However, in addition to the fact that this protocol requires as much as 10 mol.% of $Pd(OTFA)_2$ and expensive ^{t}Bu-XPhos ligand, it is also limited only to monosubstituted *gem*-difluorocyclopropanes.

In this paper we report the development of ring-opening amination of *gem*-chlorofluoro- and *gem*-bromofluorocyclopropanes that can be effectively catalyzed by copper(I) or copper(II) compounds in aprotic solvents and requires no additional ligands [21].

2. Results

Optimization of the reaction conditions was performed using 7-chloro-7-fluoro- and 7-bromo-7-fluorobicyclo[4.1.0]heptanes (**1a** and **2a**) and morpholine as model substrates. The copper source, additional base/ligand or solvent were varied (see table 1). It is noteworthy that under all the conditions studied, only *endo*-Cl/Br-isomers (*endo*-Cl-**1a**, *endo*-Br-**2a**) reacted, while *exo*-Cl/Br-isomers remained unchanged.

We initially heated *endo*-Cl-**1a** in the presence of 3.0 equiv. of morpholine in dioxane at 100°C using 0.20 equiv. of CuCl as the catalyst. The reaction was completed in 24 hours and gave the target *N*-(2-fluorocyclohept-2-enyl)morpholine (**3aa**) in moderate yield (74%, entry 1). The major side product was identified as 2,2'-difluoro-3,3'-bicycloheptene (**4a**, 24% yield). It was formed as a mixture of two diastereomers in ca. 1/1 ratio. The formation of small amounts of 2-fluorocyclohepta-1,3-diene (**5a**) was also detected (2% yield).

When the reaction was carried out for only 5 hours (entry 2), the presence of 2-fluorocyclohept-2-enyl chloride **6a** in appreciable amounts (12% yield) and almost complete conversion of *endo*-Cl-**1a** were observed. A further decrease in the morpholine amount to 2.0 and 1.0 equiv. (entries 3,4) showed almost no influence on *endo*-Cl-**1a** conversion but resulted in a dramatic increase in chloride **6a** yields. Meanwhile, decreasing the CuCl amount lowered the conversion of *endo*-Cl-**1a** and increased the yield of **6a** (entry 5).

Changing the reaction solvent to DMSO resulted in almost complete conversion of chloride **6a** after 5 hours (entry 6). However, a slight decrease in the ring-opening rate of *endo*-Cl-**1a** was also observed. An important advantage of this solvent is a significant decrease in the yield of dimer **4a** from 24% in dioxane to only 10% in DMSO (entry 7).

These initial results are in very good agreement with the previously proposed mechanism for CuX catalyzed ring-opening isomerization of *gem*-fluorohalocyclopropanes and their rearrangements in the presence of *O*-nucleophiles [17b,c]. As applied to ring-opening amination, this mechanism involves a cyclopropyl-allylic transformation of halocyclopropane *endo*-Cl-**1a** by the well-known electrocyclic mechanism [22] to give 2-fluoroallyl chloride **6a** as a preliminary product of ion-pair return in intermediate **I** (schemes 2,3). The latter undergoes nucleophilic substitution with an amine to give 2-fluoroallyl amine **3aa**.

The formation of side product **4a** is likely a result of single-electron reduction of halide **6a** by copper-amine complexes followed by dimerization of 2-fluoroallyl radicals. Considering this, it is not surprising that replacement of dioxane with DMSO allowed us to reduce the amounts of halide **6a** and dimer **4a** formed, as DMSO is well known to promote S_N2 processes (entries 1,2 vs. 6,7).

Therefore, we decided to use *gem*-bromofluorocyclopropane *endo*-Br-**2a** for further optimizations assuming that much faster nucleophilic substitution in intermediate allyl bromide **7a** *vs.* allyl chloride **6a** would facilitate the formation of amine **3aa** [23]. Indeed, when *endo*-Br-**2a** was heated in the presence of 0.20 equiv. of CuBr and 3.0 equiv. of morpholine at 100°C for 5 hours in various solvents, complete conversions of cyclopropane *endo*-Br-**2a** and allyl bromide **7a** were achieved and amine **3aa** was obtained in good to excellent yields (entries 8–14). In most cases, the yield of side product **4a** did not exceed 5% (except in toluene, see entry 14). The best results were obtained in dioxane, DMSO and MeCN (entries 8–10), while in DMF, MeOH and HFIP (1,1,1,3,3,3-hexafluoro-*iso*-propanol) other side processes were detected. For example, in DMF (2-fluorocyclohept-2-enyl)dimethylamine **3ab** was formed in 10% yield (entry 11) due to the presence of free dimethylamine in the reaction mixture — the product of either thermal decomposition of DMF or its transamidation with morpholine. In MeOH, (2-fluorocyclohept-2-enyl)methyl ether **8a** was formed in 6% yield (entry 12), while in HFIP, diene **5a** was formed in 10% yield (entry 13).

Attempts were made to reduce the required excess of morpholine using additional bases or ligands. In fact, the reaction of *endo*-Br-**2a** with 1.2 equiv. of morpholine and additional

2.0 equiv. of NEt_3 in dioxane or DMSO gave amine **3aa** in good yields (entries 15,21). Under the same conditions, DIPEA (di-*iso*-propylethylamine) showed a slightly lower yield of **3aa** due to incomplete (95%) conversion of *endo*-Br-**2a** (entry 17). In both cases, no allyl bromide **7a** was detected. Conversely, inorganic bases (K_2CO_3, Cs_2CO_3, NaOH) lead to lower yields of amine **3aa** significantly (entries 18–20). Moreover, additional diamine ligands (Phen, TMEDA) dramatically increase the yields of side dimers **4a** (entries 22,23), while diphosphine ligand such as dppe and NHC-ligand IPr (1,3-bis(2,6-di-*iso*-propylphenyl)imidazol-2-ylidene) inhibit the ring-opening of *endo*-Br-**2a** (entries 24,25).

It is interesting that the amination can be catalyzed not only by cuprous halides but also by other Cu^{I} or Cu^{II} compounds [24]. In fact, *endo*-Br-**2a** could be effectively rearranged in the presence of 0.20 equiv. of Cu_2O, CuO, $Cu(OAc)_2$ or $Cu(acac)_2$ to give amine **3aa** in 74–84% yields (entries 26–29).

Next, solvent effect on the regioselectivity of ring-opening amination was studied. For this purpose, 2-chloro-2-fluoro- and 2-bromo-2-fluoro-1-phenylcyclopropanes (**1b** and **2b**) were chosen as model substrates (table 2). *N*-((*Z*,*E*)-3-Phenyl-2-fluoroallyl)morpholine *Z*,*E*-**3ba** and its regioisomer **9ba** are the major products in all the cases. The product of side reductive dimerization **4b** was formed as a mixture of 6 isomers (see table 2).

The best regioselectivity (**3ba**/**9ba** ratio) was achieved using *gem*-bromofluorocyclopropane **2b** in dioxane or DMSO (entries 6,7). In these cases, only traces of **9ba** and **4b** were formed. It should be noted that in polar aprotic solvents (MeCN and DMSO) known to facilitate S_N2 processes, more *E*-isomeric **3ba** was formed in comparison to the reactions in dioxane (see entries 2,3 *vs.* 1 and entries 7,8 *vs.* 6), whereas in polar protic solvents (MeOH and HFIP) known to facilitate S_N1 processes, more regioisomeric **9ba** was obtained (see entries 4,5 and 9,10).

With optimized conditions in hand, we studied the scope of copper-catalyzed ring-opening amination of *gem*-bromofluorocyclopropanes (see tables 3,4). In addition to the one-step amination protocol (scheme 4, method A), a two-step approach was explored that involved CuBr-catalyzed isomerization of *gem*-bromofluorocyclopropane to give 2-fluoroallylbromide followed by *one pot* nucleophilic substitution of bromine (scheme 4, method B).

In addition to cycloheptenyl- and 3-phenylallylamines **3aa** and **3ba**, *N*-(3,3-difluoro-2-fluoroallyl)morpholine **3ca** was obtained in 90% yield after heating of 1,1-diphenylcyclopropane **2c** in the presence of 0.20 equiv. of CuBr and 3.0 equiv. of morpholine at 100°C for 72 hours. The much longer reaction time is probably a result of larger steric

hindrance in the allyl cationic intermediate in the case of **2c** in comparison with monophenyl substituted cyclopropane **2b**.

The amination of *trans*-1-phenyl-2-methylcyclopropane **2d** involved significant side dehydrobromination of the intermediate allyl bromide. Therefore, *N*-((*Z*)-3-phenyl-1-methyl-2-fluoroallyl)morpholine *Z*-**3da** was obtained in only 44% yield (*Z*/*E* > 99). The corresponding *E*-isomeric amine *E*-**3da** was not detected, probably due to a higher propensity of the corresponding (*E*)-allyl bromide to dehydrobromination.

It is of interest that 2-fluoroallyl amines **3ea**, **3fa**, **3ga** can be obtained by amination of bicyclopropanes **2e,f** and spiroheptane **2g** only by one-step method A (table 3, entries 5–7) in moderate yields. The reactions of these cyclopropanes under CuBr-catalyzed isomerization conditions (method B) give only oligomeric products.

To make conclusions from these results, the two-step method B gave slightly better yields of allyl amines in the case of aryl substituted cyclopropanes **2b,c** as compared with the one-step method A, namely, >98% *vs.* 90–95% (table 3, entries 2,3). This difference is the result of the side reductive dimerization that occurs under the conditions of copper-catalyzed ring-opening of *gem*-bromofluorocyclopropanes in the presence of amines. On the contrary, the one-step method A is much more preferable for alkyl substituted cyclopropanes **2a,d–g** than method B (table 3, entries 1,4–7) due to the capture of labile intermediate allyl bromides [25] that form more stable allyl amines under reaction conditions A.

Ring-opening amination of phenylcyclopropane **2b** and spiroheptane **2g** with 1.2 equiv. of various secondary alkyl-, arylamines or hydroxylamines in the presence of 2.0 equiv. of DIPEA in dioxane or DMSO at 100°C gave the corresponding 2-fluoroallyl amines in moderate to good yields (see table 4). It should be noted that for **2b**, it is necessary to use the more sterically hindered base DIPEA instead of NEt_3 to obtain good yields of the allyl amine. In fact, when amination of **2b** was carried out with NEt_3 as the base, the formation of ammonium salt *Z*-**10b** in 40–50% yield was detected. In the case of **2g**, no significant benefits of DIPEA compared with NEt_3 were found.

Attempts to use *N*-acetylbenzylamine and *N*-Boc-glycine methyl ester as nucleophiles failed. In fact, no amidation products were obtained when reactions of cyclopropanes **2b** and **2g** were carried out using DIPEA as the base due to the low nucleophilicity of the amide

nitrogen. Instead, the corresponding allyl bromides *Z,E*-**7b** and dimers **4b** were obtained from phenylcyclopropane **2b**, while complete polymerization of the reaction mixtures was observed for spirohexane **2g**. The use of inorganic bases (K_2CO_3 or NaH) resulted in complete deactivation of the copper catalyst probably due to the formation of unreactive copper amidate complexes. Nevertheless, phenyl substituted allyl amide **3bi** and carbamate **3bj** were obtained by the two-step procedure (table 4, entries 7,8, method B).

Attempts were made to obtain secondary 2-fluoroallyl amines by our ring-opening amination method. However, it was found that the reaction of phenylcyclopropane **2b** with 0.5–1.2 equiv. of cyclohexylamine resulted in a mixture of mono- and diallylation products **11b** and **12b** in 1.2–7:1 ratio (scheme 5).

The *p*-methoxyphenyl (PMP) protective group was shown to be efficient for the selective preparation of secondary allyl amines. Using this group, the corresponding cyclohexylamino derivatives **11b** and **11g** were prepared from phenylcyclopropane **2b** or spirohexane **2g** in moderate to good overall yields (scheme 6).

Other protective groups were found to be inefficient. As shown above, various acyl, carbamate, and sulfonamide groups cannot be used under conditions of copper-catalyzed ring-opening amination, while the benzyl groups cannot be removed selectively. Thus, in the cases of *N*-benzyl- or *N*-(*p*-methoxybenzyl)-*N*-(2-fluoroallyl)amines, hydrogenation conditions using H_2 or HCO_2H as the reductants over Pd/C resulted in complex product mixtures with complete loss of fluorine. Under single-electron oxidative conditions using $(NH_4)_2[Ce(NO_3)_6]$, concurrent cleavage of 2-fluoroallyl and benzyl or *p*-methoxybenzyl groups was observed (scheme 7).

Attempts to obtain primary 2-fluoroallyl amines by CuBr catalyzed ring-opening amination of *gem*-fluorohalocyclopropanes (**1b,1h,2b**) either with phthalimide in the presence of bases (K_2CO_3, Cs_2CO_3), or with potassium phthalimide or urotropine, failed. Under all the conditions, CuBr was totally deactivated and no ring-opening products were detected.

Therefore, a stepwise procedure was used for the preparation of primary 2-fluoroallyl amines from *gem*-fluorohalocylopropanes. This included: (a) CuX catalyzed isomerization of cyclopropanes to 2-fluoroallyl halides; (b) introduction of an NH_2 group by Gabriel or Delepin methods (scheme 8) [26].

It should be noted that 2-fluoro-3-methylbut-2-enyl amine **13h** that we have synthesized is used for the preparation of new agrochemicals, potential drugs for the

treatment of ophthalmic diseases, potential anti-inflammatory drugs, as well as compounds exhibiting antiviral activity [27].

3. Conclusions

In summary, we have developed an efficient method for the preparation of various alkyl, aryl substituted tertiary 2-fluoroallyl amines and hydroxylamines in moderate to excellent yields by copper-catalyzed ring-opening amination of readily available *gem*-chlorofluoro- and *gem*-bromofluorocyclopropanes. The reaction pathway involves isomerization of *gem*-fluorohalocyclopropanes to 2-fluoroallylic halides — products of *gem*-fluorohalocyclopropane isomerization, followed by *in situ* nucleophilic substitution of a halide by an *N*-nucleophile. Using these conditions, it became possible to capture labile alkyl substituted 2-fluoroallyl halides that easily undergo dehydrohalogenation or various rearrangements and are therefore difficult to be obtained. The *p*-methoxyphenyl (PMP) protective group was found to be efficient for the preparation of secondary 2-fluoroallylamines by copper-catalyzed *gem*-fluorohalocyclopropane ring-opening. Primary 2-fluoroallylamines were only obtained by a stepwise protocol involving CuX-catalyzed isomerization of *gem*-fluorohalocyclopropanes to 2-fluoroallylic halides followed by Gabriel or Delepin amination.

4. Experimental

4.1. General information

All reagents were purchased from Acros, Aldrich or Alfa Aesar and used without further purification. Dioxane was distilled over Na-benzophenone ketyl anion-radical and stored over 4A Linde type molecular sieves. Anhydrous DMSO stored over 4A Linde type molecular sieves obtained from Acros was used without additional purification. *gem*-Fluorohalocyclopropanes were synthesized by cyclopropanation of corresponding olefins with $CHCl_2F$ or $CHBr_2F$ under PTC conditions as previously published [17] or analogously (see ESI for experimental procedures and characterization data for unpublished cyclopropanes).

4.2. General procedure for synthesis of (2-fluoroallyl)morpholines

Method A. A 4-ml screw neck vial was charged with *gem*-fluorobromocyclopropane (0.50 mmol) and CuBr (0.10 mmol). In a stream of argon dioxane (0.50 mL) was added

followed by morpholine (1.5 mmol). The vial was quickly sealed and the reaction mixture was stirred at 100°C for 5 hours. GC analysis of a reaction aliquot showed the completion of the reaction. CH_2Cl_2 and satd. NH_3 were added; the organic layer was washed with water, then with brine and dried over K_2CO_3. The solvents were removed in vacuo, affording a residue which was purified by flash column chromatography providing the desired product.

Method B. A 4-ml screw neck vial was charged with *gem*-fluorobromocyclopropane (0.50 mmol) and CuBr (0.10 mmol). In a stream of argon MeCN (0.50 mL) was added. The vial was quickly sealed and the reaction mixture was stirred at 100°C for 5 hours. GC analysis of a reaction aliquot showed the completion of the cyclopropane isomerization. Next, morpholine (1.5 mmol) was added and the reaction mixture was stirred at room temperature for additional 2 hours. The desired product was isolated as written above.

***N*-(2-Fluorocyclohept-2-enyl)morpholine (3aa)**

A colorless oil (method A: 86.5 mg, 87%; method B: 20.2 mg, 20%) was obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 100/1 to 4/1).

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.38–2.03 (m, 7H), 2.23 (m, 1H, C*H*H'-CH=), 2.54 (m, 4H, $2CH_2N$), 2.90 (m, 1H, CH-morpholine), 3.71 (m, 4H, $2CH_2O$), 5.46 (dddd., 1H, -CH=, $^3J_{HF}$ = 21.6 Hz, J_{HH} = 8.0, 5.4, 1.3 Hz). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –92.4 (br. t, $^3J_{HF}$ = 20 Hz) ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 21.7 (d, CH_2, J_{CF} = 11.1 Hz), 23.5 (s, CH_2), 26.3 (d, CH_2, J_{CF} = 9.1 Hz), 26.6 (d, CH_2, J_{CF} = 0.9 Hz), 51.1 (s, $2CH_2N$ (morpholine)), 65.7 (d, CH-morpholine, $^2J_{CF}$ = 27.4 Hz), 67.3 (s, $2CH_2O$ (morpholine)), 108.8 (d, -CH=, $^2J_{CF}$ = 21.1 Hz), 162.3 (d, -CF=, $^1J_{CF}$ = 251 Hz). MS (EI) *m/z* 200 ($[M+H]^+$, 10), 199 ($[M]^+$, 78), 198 ($[M-H]^+$, 9), 170 (100), 140 (19), 126 (12), 112 (20), 97 (20), 87 (71), 56 (21), 41 (12). HRMS (ESI), calcd. for $C_{11}H_{18}FNO$: *m/z* 200.1445 [$M+H^+$]. Found: *m/z* 200.1441 [$M+H^+$].

***N*-(2-Fluoro-3-phenylallyl)morpholine (3ba)**

A colorless oil (method A: 105.1 mg, 95% (*Z/E* = 85/15); method B: 108.7 mg, 98% (*Z/E* = 93/7)) was obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 50/1 to 5/1). ^{1}H, ^{19}F and ^{13}C NMR were fully consistent with previously published [9e].

***N*-(2-Fluoro-3,3-diphenylallyl)morpholine (3ca)**

A colorless solids (mp 103–104°C; method A: 133.4 mg, 90%; method B: 148.0 mg, 99%) were obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 50/1 to 3/1).

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 2.38–2.60 (m, 4H, $2CH_2$N-morpholine), 3.21 (d, 2H, CH_2N, $^{3}J_{HF}$ = 21.7 Hz), 3.62–3.78 (m, 4H, $2CH_2$O-morpholine), 7.09–7.44 (m, 10H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –105.6 (t, $^{3}J_{HF}$ = 21.7 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 53.2 (s, $2CH_2$N-morpholine), 57.0 (d, CH_2N, $^{2}J_{CF}$ = 25.3 Hz), 67.0 (s, $2CH_2$O-morpholine), 124.6 (d, =CPh_2, $^{2}J_{CF}$ = 13.6 Hz), 127.3 (s, CH-arom.), 127.6 (s, CH-arom.), 128.0 (s, 2CH-arom.), 128.4 (s, 2CH-arom.), 129.6 (d, 2CH-arom., J_{CF} = 5.1 Hz), 130.4 (d, 2CH-arom., J_{CF} = 3.0 Hz), 137.0 (s, C-arom.), 138.2 (d, C-arom., $^{3}J_{CF}$ = 7.5 Hz), 153.8 (d, –CF=, $^{1}J_{CF}$ = 264 Hz). MS (EI) *m/z* 297 ([M^+], 22), 276 (2), 266 (2), 239 (9), 220 (15), 211 (58), 209 (37), 196 (23), 191 (84), 178 (54), 165 (29), 133 (100), 100 (20), 86 (51), 56 (31). HRMS (ESI), calcd. for $C_{19}H_{20}FNO$: *m/z* 298.1602 [M+H^+]. Found: *m/z* 298.1613 [M+H^+].

***N*-(2-Fluoro-3-phenyl-1-methylallyl)morpholine (3da)**

A colorless oil (method A: 52.1 mg, 44% (*Z/E* > 99); method B: 35.5 mg, 30% (*Z/E* > 99)) was obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 50/1 to 3/1).

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.35 (d, 3H, CH_3, $^{3}J_{HH}$ = 6.9 Hz), 2.44–2.77 (m, 4H, $2CH_2$-morpholine), 3.13 (dq, CH(Me)N<, $^{3}J_{HF}$ = 22.7 Hz, $^{3}J_{HH}$ = 6.9 Hz), 3.64–3.83 (m, 4H, $2CH_2$-morpholine), 5.62 (d, –CH=, $^{3}J_{HF(trans)}$ = 39.6 Hz), 7.15–7.40 (m, 3H, arom.), 7.44–7.57 (m, 2H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –108.7 (dd, $^{3}J_{HF(trans)}$ = 39.6 Hz, $^{3}J_{HF}$ = 22.7 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 15.0 (d, CH_3, J_{CF} = 2.5 Hz), 50.5 (s, $2CH_2$-morpholine), 62.3 (d, <u>C</u>H(Me)N<, $^{2}J_{CF}$ = 24.2 Hz), 67.3 (s, $2CH_2$-morpholine), 108.1 (d, –CH=, $^{2}J_{CF}$ = 7.4 Hz), 127.3 (d, CH-arom., $^{6}J_{CF}$ = 2.3 Hz), 128.5 (s, 2CH-arom.), 128.6 (d, 2CH-arom., $^{4}J_{CF}$ = 7.7 Hz), 133.1 (d, C-arom., $^{3}J_{CF}$ = 2.2 Hz), 159.8 (d, –CF=, $^{1}J_{CF}$ = 274 Hz). HRMS (ESI), calcd. for $C_{14}H_{18}FNO$: *m/z* 236.1445 [M+H^+]. Found: *m/z* 236.1448 [M+H^+].

***N*-(2-Fluoro-3-cyclopropylallyl)morpholine (3ea)**

3ea was obtained only by method A. After flash column chromatography of the crude product (*n*-hexane/EtOAc, 3/1), the fractions contained **3ea** were evaporated with an excess of 4.0 M HCl in dioxane. A colorless solids of **3ea·HCl** (method A: 89.6 mg, 81% (*Z*/*E* = 72/28)) were obtained. When carried out by method B, starting cyclopropane **2e** reacted completely to give oligomeric products.

^{1}H NMR (200.1 MHz, DMSO-d$_6$) δ: (a mixture of *Z*,*E*-isomers) 0.36–0.53 (m, 2H, cyclopropyl), 0.68–0.92 (m, 2H, cyclopropyl), 1.51–1.80 (m, 1H, CH, cyclopropyl), 2.90–3.46 (m, 4H, 2CH$_2$-morpholine), 3.81–4.01 (m, 4H, 2CH$_2$-morpholine), 3.96 (d, 2H, CH$_2$N, *Z*-**3ea**, $^{3}J_{HF}$ = 21.2 Hz), 4.19 (d, 2H, CH$_2$N, *E*-**3ea**, $^{3}J_{HF}$ = 23.0 Hz), 4.90 (dd, –CH=, *Z*-**3ea**, $^{3}J_{HF(trans)}$ = 36.2 Hz, $^{3}J_{HH}$ = 10.0 Hz), 5.22 (dd, –CH=, *E*-**3ea**, $^{3}J_{HF(cis)}$ = 19.7 Hz, $^{3}J_{HH}$ = 10.3 Hz). ^{19}F NMR (188.3 MHz, DMSO-d$_6$) δ: –107.2 (td, $^{3}J_{HF}$ = 23.0 Hz, $^{3}J_{HF(cis)}$ = 19.7 Hz), –115.1 (dt, $^{3}J_{HF(trans)}$ = 36.2 Hz, $^{3}J_{HF}$ = 21.2 Hz). ^{13}C NMR (50.3 MHz, DMSO-d$_6$) δ: 6.4–6.9 (m, CH-cyclopropyl (*Z*-**3ea**) + CH$_2$-cyclopropyl (both isomers), 7.4 (d, CH-cyclopropyl (*E*-**3ea**), $^{3}J_{CF}$ = 9.9 Hz), 50.4 (s, CH$_2$-morpholine, *Z*-**3ea**), 50.6 (s, CH$_2$-morpholine, *E*-**3ea**), 51.9 (d, CH$_2$N, $^{2}J_{CF}$ = 28.7 Hz), 55.2 (d, CH$_2$N, *E*-**3ea**, $^{2}J_{CF}$ = 27.9 Hz), 62.9 (s, CH$_2$-morpholine, both isomers), 121.5 (d, –CH=, *Z*-**3ea**, $^{2}J_{CF}$ = 10.5 Hz), 122.0 (d, –CH=, *E*-**3ea**, $^{2}J_{CF}$ = 21.1 Hz), 148.0 (d, –CF=, *E*-**3ea**, $^{1}J_{CF}$ = 241 Hz), 148.7 (d, –CF=, *Z*-**3ea**, $^{1}J_{CF}$ = 249 Hz). HRMS (ESI), calcd. for C$_{10}$H$_{16}$FNO: *m/z* 186.1289 [*M*+H$^+$]. Found: *m/z* 186.1291 [*M*+H$^+$].

***N*-[2-Fluoro-3-(2,2-difluorocyclopropyl)allyl]morpholine (3fa)**

A colorless oil (method A: 81.1 mg, 73% (*Z*/*E* = 57/43))) was obtained after flash column chromatography (*n*-hexane/EtOAc, 1/1). When carried out by method B, starting cyclopropane **2f** reacted completely to give oligomeric products.

^{1}H NMR (300.1 MHz, CDCl$_3$) δ: 1.12–1.28 (m, 1H, CH$_2$-cyclopropyl, *Z*,*E*-**3fa**), 1.61–1.75 (m, 1H, CH$_2$-cyclopropyl, *Z*,*E*-**3fa**), 2.27 (m, 1H, CH-cyclopropyl, *E*-**3fa**), 2.52 (m, 1H, CH-cyclopropyl, *Z*-**3fa**, from {^{1}H-^{19}F}-HMBC), 2.46–2.57 (m, 4H, 2CH$_2$N-morpholine, *Z*,*E*-**3fa**), 3.07 (d, 2H, CH$_2$N, *Z*-**3fa**, $^{3}J_{HF}$ = 17.5 Hz), 3.22 (d, 2H, CH$_2$N, *E*-**3fa**, $^{3}J_{HF}$ = 20.6 Hz), 3.69–3.78 (m, 4H, 2CH$_2$O-morpholine, *Z*,*E*-**3fa**), 4.57 (dd, 1H, –CH=, *Z*-**3fa**, $^{3}J_{HF(trans)}$ = 34.5 Hz, $^{3}J_{HH}$ = 9.1 Hz), 5.05 (ddt, 1H, –CH=, *E*-**3fa**, $^{3}J_{HF(cis)}$ = 18.5 Hz, $^{3}J_{HH}$ = 9.1 Hz, $^{4}J_{HH}$ = 2.0 Hz). ^{19}F{^{1}H} NMR (282.4 MHz, CDCl$_3$) δ: (for *Z*-**3fa**) –109.6 (d, 1F, –

CF=, $^5J_{FF}$ = 2.1 Hz), –129.1 (dd, 1F, CF_2, $^2J_{FF}$ = 155.4 Hz, $^5J_{FF}$ = 2.1 Hz), –140.5 (d, 1F, CF_2, $^2J_{FF}$ = 155.4 Hz); (for *E*-**3fa**) –99.6 (d, 1F, –CF=, $^5J_{FF}$ = 1.6 Hz), –128.7 (dd, 1F, CF_2, $^2J_{FF}$ = 155.6 Hz, $^5J_{FF}$ = 1.6 Hz), –140.5 (dd, 1F, CF_2, $^2J_{FF}$ = 155.6 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 17.9–18.2 (m, CH_2-cyclopropyl, both isomers), 18.7 (ddd, CH-cyclopropyl, *Z*-**3fa**, J_{CF} = 13.3, 10.9, 6.6 Hz), 19.5 (dt, CH-cyclopropyl, *E*-**3fa**, J_{CF} = 13.2, 11.2 Hz), 53.3 (s, 2CH_2N-morpholine, both isomers), 55.9 (d, CH_2N, *Z*-**3fa**, $^2J_{CF}$ = 27.2 Hz), 59.2 (d, CH_2N, *E*-**3fa**, $^2J_{CF}$ = 26.5 Hz), 66.9 (s, 2CH_2O-morpholine, both isomers), 103.4 (ddd, –CH=, *Z*-**3fa**, J_{CF} = 12.6, 5.6, 1.9 Hz), 105.0 (ddd, –CH=, *E*-**3fa**, J_{CF} = 28.5, 5.5, 1.9 Hz), 112.8 (ddd, CF_2, $^1J_{CF}$ = 289, 285 Hz, $^4J_{CF}$ = 2.2 Hz), 113.2 (ddd, CF_2, $^1J_{CF}$ = 289, 283 Hz, $^4J_{CF}$ = 1.7 Hz), 158.2 (d, –CF=, $^1J_{CF}$ = 261 Hz), 158.4 (d, –CF=, $^1J_{CF}$ = 255 Hz). MS (EI) *m/z* 221 ([M^+], 40), 190 (3), 176 (5), 164 (8), 157 (15), 156 (16), 142 (12), 126 (39), 115 (49), 113 (25), 100 (100), 98 (48), 95 (28), 86 (49), 72 (12), 65 (14), 56 (27). HRMS (ESI), calcd. for $C_{10}H_{14}F_3NO$: *m/z* 222.1100 [*M*+H^+]. Found: *m/z* 222.1106 [*M*+H^+].

***N*-(2-Cyclopentylidene-2-fluoroethyl)morpholine (3ga)**

A colorless oil (method A: 76.5 mg, 77%) was obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 20/1 to 1/1). When carried out by method B, starting cyclopropane **2g** reacted completely to give oligomeric products.

^{1}H NMR (300.1 MHz, $CDCl_3$) δ: 1.57–1.75 (m, 4H, 2CH_2), 2.19–2.29 (m, 2H, CH_2), 2.32–2.42 (m, 2H, CH_2), 2.45–2.54 (m, 4H, CH_2N-morpholine), 3.12 (d, 2H, CH_2N, $^3J_{HF}$ = 22.1 Hz), 2.69–2.78 (m, 4H, CH_2O-morpholine). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –108.5 (t, $^3J_{HF}$ = 22.1 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 26.3 (s, CH_2), 27.0 (s, CH_2), 27.6 (d, CH_2, J_{CF} = 2.9 Hz), 28.7 (d, CH_2, J_{CF} = 4.6 Hz), 53.4 (s, 2CH_2N-morpholine), 57.5 (d, CH_2N, $^2J_{CF}$ = 27.4 Hz), 66.9 (s, 2CH_2O-morpholine), 123.9 (d, =CR_2, $^2J_{CF}$ = 17.1 Hz), 147.7 (d, –CF=, $^1J_{CF}$ = 245 Hz). MS (EI) *m/z* 199 ([M^+], 12), 168 (6), 154 (4), 140 (7), 126 (9), 112 (10), 100 (7), 97 (10), 93 (8), 87 (100), 86 (58), 79 (8), 57 (30), 56 (14). HRMS (ESI), calcd. for $C_{11}H_{18}FNO$: *m/z* 200.1445 [*M*+H^+]. Found: *m/z* 200.1444 [*M*+H^+].

4.3. General procedure for synthesis of various 2-fluoroallyl amines

Method A. A 4-ml screw neck vial was charged with *gem*-fluorohalocyclopropane (0.50 mmol), CuX (0.10 mmol) and HNR_2 or HNR_2·HCl (0.60 mmol). In a stream of argon dioxane (0.50 mL) was added followed by DIPEA (1.0 mmol). The vial was quickly sealed and the reaction mixture was stirred at 100°C for 5 hours. GC analysis of a reaction aliquot

showed the completion of the reaction. CH_2Cl_2 and satd. NH_3 were added, the organic layer was washed with water, then with brine and dried over K_2CO_3. The solvents were removed in vacuo, affording a residue which was purified by flash column chromatography providing the desired product.

Method B. A 4-ml screw neck vial was charged with *gem*-fluorohalocyclopropane (0.50 mmol) and CuX (0.10 mmol). In a stream of argon MeCN (0.50 mL) was added. The vial was quickly sealed and the reaction mixture was stirred at 100°C for 5 hours. GC analysis of a reaction aliquot showed the completion of the cyclopropane isomerization. Next, HNR_2 or $HNR_2 \cdot HCl$ (0.60 mmol) and K_2CO_3 (1.5 mmol) were added and the reaction mixture was stirred at room temperature for additional 2 hours. The desired product was isolated as written above.

***N*-Benzyl-*N*-(2-fluoro-3-phenylallyl)cyclohexylamine (3bc)**

A colorless oil (method A: 129.9 mg, 80% (*Z*/*E* = 82/18); method B: 153.1 mg, 95% (*Z*/*E* = 93/7)) was obtained after flash column chromatography (*n*-hexane/benzene 5/1 to *n*-hexane/EtOAc 25/1).

(A mixture of *Z*,*E*-isomers) ^{1}H NMR (300.1 MHz, $CDCl_3$) δ: 0.95–2.00 (m, 10H, 5CH_2-Chx), 2.51–2.70 (m, 1H, CHN-Chx), 3.30 (d, 2H, CH_2N, *Z*-**3bc**, $^3J_{HF}$ = 13.0 Hz), 3.43 (d, 2H, CH_2N, *E*-**3bc**, $^3J_{HF}$ = 22.0 Hz), 3.64 (s, 2H, CH_2Ph, *E*-**3bc**), 3.74 (s, 2H, CH_2Ph, *Z*-**3bc**), 5.70 (d, 1H, –CH=, *Z*-**3bc**, $^3J_{HF(trans)}$ = 39.3 Hz), 6.30 (d, 1H, –CH=, *E*-**3bc**, $^3J_{HF(cis)}$ = 21.3 Hz), 7.13–7.49 (m, 10H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –97.4 (td, *E*-**3bc**, $^3J_{HF}$ = 22.0 Hz, $^3J_{HF(cis)}$ = 21.3 Hz), –104.4 (dt, *Z*-**3bc**, $^3J_{HF(trans)}$ = 39.3 Hz, $^3J_{HF}$ = 13.0 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 26.2 (c., CH_2, both isomers), 26.4 (s, CH_2, both isomers), 29.1 (s, CH_2, *E*-**3bc**), 29.2 (s, CH_2, *Z*-**3bc**), 47.8 (d, CH_2N, *E*-**3bc**, $^2J_{CF}$ = 25.8 Hz), 51.4 (d, CH_2N, *Z*-**3bc**, $^2J_{CF}$ = 29.5 Hz), 54.0 (s, CH_2Ph, *E*-**3bc**), 54.1 (s, CH_2Ph, *Z*-**3bc**), 59.3 (s, CH-Chx, *Z*-**3bc**), 59.4 (s, CH-Chx, *E*-**3bc**), 107.2 (d, –CH=, *Z*-**3bc**, $^2J_{CF}$ = 6.9 Hz), 111.6 (d, –CH=, *E*-**3bc**, $^2J_{CF}$ = 27.9 Hz), 126.7–127.0 (m, CH-arom., both isomers), 128.0–129.0 (m, CH-arom., both isomers), 133.8 (d, C-arom., *Z*-**3bc**, $^3J_{CF}$ = 2.3 Hz), 133.8 (d, C-arom., *E*-**3bc**, $^3J_{CF}$ = 12.9 Hz), 140.7 (s, C-arom., Bn, both isomers), 159.4 (d, –CF=, *Z*-**3bc**, $^1J_{CF}$ = 269 Hz), 160.4 (d, –CF=, *E*-**3bc**, $^1J_{CF}$ = 256 Hz). MS (EI) *m/z* 323 ([M^+], 2), 280 (3), 267 (1), 232 (12), 176 (16), 135 (24), 133 (11), 115 (38), 109 (5), 91 (100), 83 (3), 65 (11), 55 (7). HRMS (ESI), calcd. for $C_{22}H_{26}FN$: *m/z* 324.2122 [*M*+H^+]. Found: *m/z* 324.2125 [*M*+H^+].

***N*-(4-Methoxybenzyl)-*N*-(2-fluoro-3-phenylallyl)cyclohexylamine (3bd)**

A yellow oil (method A: 133.9 mg, 76% (*Z*/*E* = 79/21); method B: 169.2 mg, 96% (*Z*/*E* = 93/7)) was obtained after flash column chromatography (*n*-hexane/benzene 5/1 to *n*-hexane/EtOAc 25/1).

(A mixture of *Z*,*E*-isomers) ^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 0.91–1.44 (m, 5H, Chx), 1.47–2.01 (m, 5H, Chx), 2.46–2.75 (m, 1H, >N-CH in Chx, both isomers), 3.29 (d, 2H, CH_2N, ***Z*-3bd**, $^{3}J_{HF}$ = 12.7 Hz), 3.41 (d, 2H, CH_2N, ***E*-3bd**, $^{3}J_{HF}$ = 22.1 Hz), 3.57 (s, 2H, CH_2Ph, ***E*-3bd**), 3.68 (s, 2H, CH_2Ph, ***Z*-3bd**), 3.78 (s, 3H, OCH_3, both isomers), 5.71 (d, 1H, =CH–, ***Z*-3bd**, $^{3}J_{HF(trans)}$ = 39.4 Hz), 6.31 (d, 1H, =CH–, ***E*-3bd**, $^{3}J_{HF(cis)}$ = 21.5 Hz), 6.75–6.91 (m, 2H, PMB), 7.12–7.38 (m, 5H, Ph + PMB), 7.40–7.52 (m, 2H, Ph). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –97.1 (td, ***E*-3bd**, $^{3}J_{HF}$ = 22.1 Hz, $^{3}J_{HF(cis)}$ = 21.5 Hz), –104.4 (dt, ***Z*-3bd**, $^{3}J_{HF(trans)}$ = 39.4 Hz, $^{3}J_{HF}$ = 12.7 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 26.2 (s, CH_2, both isomers), 26.4 (s, CH_2, both isomers), 28.9 (s, CH_2, ***E*-3bd**), 29.1 (s, CH_2, ***Z*-3bd**), 47.6 (d, CH_2N, ***E*-3bd**, $^{2}J_{CF}$ = 25.8 Hz), 51.1 (d, CH_2N, ***Z*-3bd**, $^{2}J_{CF}$ = 29.5 Hz), 53.2 (s, CH_2Ph, ***E*-3bd**), 53.4 (s, CH_2Ph, ***Z*-3bd**), 55.2 (s, OCH_3, both isomers), 59.0 (s, CH in Chx, ***Z*-3bd**), 59.1 (s, CH in Chx, ***E*-3bd**), 107.0 (d, =CH–, ***Z*-3bd**, $^{2}J_{CF}$ = 6.8 Hz), 11.5 (d, =CH–, ***E*-3bd**, $^{2}J_{CF}$ = 27.8 Hz), 113.5 (s, CH in PMB, ***E*-3bd**), 113.6 (s, CH in PMB, ***Z*-3bd**), 126.8 (s, CH-arom.), 128.0–129.9 (m, CH-arom., both isomers), 132.5 (s, C-arom.), 133.7 (d, C-arom., $^{3}J_{CF}$ = 2.2 Hz), 158.5 (s, C(OMe) in PMB, both isomers), 159.5 (d, =CF–, ***Z*-3bd**, $^{1}J_{CF}$ = 269 Hz), 160.4 (d, =CF–, ***E*-3bd**, $^{1}J_{CF}$ = 255 Hz). MS (EI) *m/z* 354 ($[M+H]^+$, 3), 353 ($[M^+]$, 12), 310 (1), 297 (1), 262 (8), 232 (2), 218 (1), 206 (13), 135 (5), 122 (9), 121 ($[MeOC_6H_4CH_2^+]$, 100), 115 (5), 91 (2). HRMS (ESI), calcd. for $C_{23}H_{28}FNO$: *m/z* 354.2228 [M+H^+]. Found: *m/z* 354.2224 [M+H^+].

***N*-(4-Methoxyphenyl)-*N*-(2-fluoro-3-phenylallyl)cyclohexylamine (3be)**

A yellow oil (method A: 144.5 mg, 85% (*Z*/*E* = 73/27); method B: 161.4 mg, 95% (*Z*/*E* = 93/7)) was obtained after flash column chromatography (*n*-hexane/benzene 5/1 to *n*-hexane/EtOAc 25/1).

(A mixture of *Z*,*E*-isomers) ^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 0.79–2.10 (m, 10H, CH_2 in Chx, both isomers), 3.25 (m, 1H, CH in Chx, ***E*-3be**), 3.53 (m, 1H, CH in Chx, ***Z*-3be**), 3.73 (s, 3H, OCH_3, ***E*-3be**), 3.75 (s, 3H, OCH_3, ***Z*-3be**), 3.93 (m, 2H, CH_2N, ***Z*-3be**), 4.07 (d, 2H, CH_2N, ***E*-3be**, $^{3}J_{HF}$ = 17.0 Hz), 5.71 (d, 1H, =CH–, ***Z*-3be**, $^{3}J_{HF(trans)}$ = 40.5 Hz), 6.30 (d, 1H, =CH–, ***E*-3be**, $^{3}J_{HF(cis)}$ = 21.0 Hz), 6.63–6.92 (m, 4H, PMP, both isomers),

7.11–7.54 (m, 5H, Ph, both isomers). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –102.7 (dt, *E*-**3be**, $^3J_{HF(cis)}$ = 21.0 Hz, $^3J_{HF}$ = 17.0 Hz), –107.7 (br. d, *Z*-**3be**, $^3J_{HF(trans)}$ = 40.5 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 26.8 – 25.4 (m, CH_2 in Chx, both isomers), 30.3 (s, CH_2 in Chx), 30.7 (s, CH_2 in Chx), 45.0 (d, CH_2N, *E*-**3be**, $^2J_{CF}$ = 25.3 Hz), 48.0 (d, CH_2N, *Z*-**3be**, $^2J_{CF}$ = 37.6 Hz), 55.5 (s, OCH_3, *E*-**3be**), 55.7 (s, OCH_3, *Z*-**3be**), 58.2 (s, CH in Chx, *Z*-**3be**), 59.9 (s, CH in Chx, *E*-**3be**), 105.8 (d, =CH–, *Z*-**3be**, $^2J_{CF}$ = 5.6 Hz), 110.8 (d, =CH–, *E*-**3be**, $^2J_{CF}$ = 27.3 Hz), 114.1 (s, CH in PMP, *E*-**3be**), 114.7 (s, CH in PMP, *Z*-**3be**), 116.0 (s, CH in PMP, *Z*-**3be**), 120.0 (s, CH in PMP, *E*-**3be**), 126.5–129.2 (m, CH in Ph, both isomers), 133.5 (d, C in Ph, *Z*-**3be**, $^3J_{CF}$ = 1.9 Hz), 133.7 (d, C in Ph, *E*-**3be**, $^3J_{CF}$ = 9.4 Hz), 142.6 (s, >N–C in PMP, *E*-**3be**), 143.1 (s, >N–C in PMP, *Z*-**3be**), 152.2 (s, C(OMe) in PMP, *Z*-**3be**), 153.4 (s, C(OMe) in PMP, *E*-**3be**), 158.9 (d, =CF–, *Z*-**3be**, *J* = 269 Hz), 159.7 (d, =CF–, *E*-**3be**, *J* = 257 Hz). MS (EI) *m/z* 340 ([M+H$^+$], 23), 339 ([M$^+$], 100), 296 (17), 283 (9), 282 (8), 248 (27), 204 (53), 192 (34), 148 (11), 135 (53), 122 (14), 115 (17), 109 (6), 92 (4), 77 (5), 55 (6), 41 (4). HRMS (ESI), calcd. for $C_{22}H_{26}FNO$: *m/z* 340.2071 [*M*+H$^+$]. Found: *m/z* 340.2073 [*M*+H$^+$].

***N*-Benzyl-*N*-(2-fluoro-3-phenylallyl)-4-methoxyaniline (3bf)**

A yellow oil (method A: 149.7 mg, 86% (*Z/E* = 68/32); method B: 167.1 mg, 96% (*Z/E* = 90/10)) was obtained after flash column chromatography (*n*-hexane/benzene 5/1 to *n*-hexane/EtOAc from 25/1 to 5/1).

(For *Z*-**3bf**): ^{1}H NMR (300.1 MHz, $CDCl_3$) δ: 3.70 (s, 3H, OCH_3), 4.09 (d, CH_2N, $^3J_{HF}$ = 8.6 Hz), 4.56 (s, 2H, CH_2Ph), 5.62 (d, –CH=, $^3J_{HF(trans)}$ = 39.7 Hz), 6.76–6.80 (m, 4H, PMP), 7.15–7.34 (m, 8H, arom.), 7.42–7.48 (m, 2H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –108.0 (dt, $^3J_{HF(trans)}$ = 39.7 Hz, $^3J_{HF}$ = 8.6 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 52.7 (d, CH_2N, $^2J_{CF}$ = 33.1 Hz), 54.9 (s, CH_2Ph), 55.7 (s, OCH_3), 107.1 (d, –CH=, $^2J_{CF}$ = 6.1 Hz), 114.8 (s, 2CH, PMP), 115.1 (s, 2CH, PMP), 126.8–127.4 (m, CH, arom.), 128.3–129.0 (m, CH, arom.), 133.1 (d, C-arom., $^3J_{CF}$ = 2.3 Hz), 138.6 (s, C-arom.), 143.2 (s, C-arom.), 152.4 (s, C-arom.), 156.9 (d, –CF=, $^1J_{CF}$ = 271 Hz). (For *E*-**3bf**): ^{1}H NMR (300.1 MHz, $CDCl_3$) δ: 3.67 (s, 3H, OCH_3), 4.20 (d, CH_2N, $^3J_{HF}$ = 18.4 Hz), 4.45 (s, 2H, CH_2Ph), 6.38 (d, –CH=, $^3J_{HF(cis)}$ = 21.1 Hz), 6.55–6.72 (m, 4H, PMP), 7.07–7.34 (m, 10H, 2Ph). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –104.4 (dt, $^3J_{HF(cis)}$ = 21.1 Hz, $^3J_{HF}$ = 18.4 Hz). (For both isomers): MS (EI) *m/z* 216 (4), 214 (3), 135 (74), 133 (34), 115 (100), 109 (11), 102 (6),

89 (9), 81 (14), 74 (7), 63 (15), 57 (13), 51 (13). HRMS (ESI), calcd. for $C_{23}H_{22}FNO$: *m/z* 348.1758 [*M*+H^+]. Found: *m/z* 348.1750 [*M*+H^+].

_N,O_-Dimethyl-_N_-(2-fluoro-3-phenylallyl)hydroxylamine (3bg)

A colorless oil (method A: 63.6 mg, 65% (*Z/E* = 71/29); method B: 82.6 mg, 85% (*Z/E* = 98/2)) was obtained after flash column chromatography (*n*-hexane/EtOAc, 20/1).

(For *Z*-**3bg**): ^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 2.67 (s, 3H, CH_3N), 3.44 (d, 2H, CH_2N, $^3J_{HF}$ = 18.0 Hz), 3.55 (s, 3H, OCH_3), 5.71 (d, 2H, –CH=, $^3J_{HF(trans)}$ = 38.5 Hz), 7.17–7.40 (m, 3H, arom.), 7.47–7.58 (m, 2H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –104.7 (dt, $^3J_{HF(trans)}$ = 38.5 Hz, $^3J_{HF}$ = 18.0 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 45.2 (s, CH_3N), 60.4 (s, CH_3O), 61.9 (d, CH_2N, $^2J_{CF}$ = 26.9 Hz), 109.8 (d, –CH=, $^2J_{CF}$ = 7.3 Hz), 127.4 (d, CH-arom., $^6J_{CF}$ = 2.3 Hz), 128.5 (s, 2CH-arom.), 128.7 (d, 2CH-arom., $^4J_{CF}$ = 7.5 Hz), 133.2 (d, C-arom., $^3J_{CF}$ = 2.8 Hz), 156.1 (d, –CF=, $^1J_{CF}$ = 268 Hz). (For *E*-**3bg**): ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –99.5 (dt, $^3J_{HF(cis)}$ = 21.8 Hz, $^3J_{HF}$ = 21.8 Hz). (For both isomers): MS (EI) *m/z* 195 ([M^+], 7), 162 (2), 135 (56), 133 (15), 115 (100), 109 (7). HRMS (ESI), calcd. for $C_{11}H_{14}FNO$: *m/z* 196.1132 [*M*+H^+]. Found: *m/z* 196.1134 [*M*+H^+].

Methyl _N_-(2-fluoro-3-phenylallyl)prolinate (3bh)

A colorless oil (method A: 114.6 mg, 87% (*Z/E* = 86/14); method B: 125.0 mg, 95% (*Z/E* = 96/4)) was obtained after flash column chromatography (*n*-hexane/EtOAc, 3/1).

(For *Z*-**3bh**): ^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.70–2.32 (m, 4H, $2CH_2$), 2.63 (m, 1H, $CHCO_2Me$), 3.10–3.84 (m, 4H, CH_2, CH_2N), 3.68 (s, 3H, OCH_3), 5.67 (d, 1H, –CH=, $^3J_{HF(trans)}$ = 38.5 Hz), 7.16–7.40 (m, 3H, arom.), 7.44–7.54 (m, 2H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –103.2 (dt, $^3J_{HF(trans)}$ = 38.5 Hz, $^3J_{HF}$ = 18.8 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 23.3 (s, CH_2), 29.6 (s, CH_2), 52.0 (s, NCH), 53.4 (s, NCH_2), 55.1 (d, CH_2N, $^2J_{CF}$ = 27.0 Hz), 64.7 (s, OCH_3), 109.1 (d, –CH=, $^2J_{CF}$ = 7.2 Hz), 127.3 (d, CH-arom., $^6J_{CF}$ = 2.2 Hz), 128.5 (s, 2CH-arom.), 128.7 (d, 2CH-arom., $^4J_{CF}$ = 7.4 Hz), 133.2 (d, C-arom., $^3J_{CF}$ = 2.8 Hz), 157.3 (d, –CF=, $^1J_{CF}$ = 270 Hz), 174.4 (s, C=O). (For *E*-**3bh**): ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –98.5 (д.т., $^3J_{HF(цис)}$ = 22.7 Hz, $^3J_{HF}$ = 22.7 Hz). (For both isomers): MS (EI) *m/z* 263 ([M^+], 3), 204 (33), 135 (100), 133 (24), 115 (93), 109 (9), 83 (4), 68 (11), 59 (5). HRMS (ESI), calcd. for $C_{15}H_{18}FNO_2$: 264.1394 [*M*+H^+], 286.1214 [*M*+Na^+]. Found: 264.1394 [*M*+H^+], 286.1205 [*M*+Na^+].

***N*-Acetyl-*N*-(2-fluoro-3-phenylallyl)benzylamine (3bi)**

Obtained by method B using NaH (0.60 mmol, dispersion in mineral oil, 55 w/w %) as the base. A colorless oil (method B: 121.6 mg, 86% (*Z*/*E* = 96/4)) was obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 50/1 to 3/1).

(For *Z*-**3bi**,*Z*-**3bi'**, rotamers, a ratio of 1/1): ^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 2.19 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 4.00 (d, 2H, AllCH_2N, $^{3}J_{HF}$ = 11.8 Hz), 4.26 (d, 2H, AllCH_2N, $^{3}J_{HF}$ = 16.7 Hz), 4.64 (s, 2H, CH_2Ph), 4.69 (s, 2H, CH_2Ph), 5.57 (d, 1H, –CH=, $^{3}J_{HF(trans)}$ = 38.5 Hz), 5.62 (d, 1H, –CH=, $^{3}J_{HF(trans)}$ = 38.5 Hz), 7.08–7.55 (m, 5H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –107.6 (dt, $^{3}J_{HF(trans)}$ = 38.5 Hz, $^{3}J_{HF}$ = 16.7 Hz), –109.5 (dt, $^{3}J_{HF(trans)}$ = 38.5 Hz, $^{3}J_{HF}$ = 11.8 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 21.6 (s, CH_3), 21.7 (s, CH_3), 45.9 (d, AllCH_2N, $^{2}J_{CF}$ = 29.7 Hz), 47.8 (s, CH_2Ph), 48.5 (d, AllCH_2N, $^{2}J_{CF}$ = 32.1 Hz), 51.3 (s, CH_2Ph), 108.5 (d, –CH=, $^{2}J_{CF}$ = 6.7 Hz), 109.3 (d, –CH=, $^{2}J_{CF}$ = 6.9 Hz), 126.4 (s, CH-arom.), 127.4–129.2 (m, CH-arom., 2Ph), 132.2 (d, C-arom., $^{3}J_{CF}$ = 2.8 Hz), 132.7 (d, C-arom., $^{3}J_{CF}$ = 2.7 Hz), 136.2 (s, C-arom., Bn), 137.0 (s, C-arom., Bn), 154.3 (d, –CF=, $^{1}J_{CF}$ = 269 Hz), 155.3 (d, –CF=, $^{1}J_{CF}$ = 269 Hz), 171.0 (s, *C*(O)CH_3), 171.2 (s, *C*(O)CH_3). (For *E*-**3bi**,*E*-**3bi'**, rotamers,a ratio of 1/1): ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –106.1 (dt, $^{3}J_{HF(cis)}$ = 21.6 Hz, $^{3}J_{HF}$ = 18.7 Hz), –107.9 (dt, $^{3}J_{HF(cis)}$ = 21.1 Hz, $^{3}J_{HF}$ = 18.5 Hz). (For both isomers): HRMS (ESI), calcd. for $C_{18}H_{18}FNO$: 284.1445 [$M+H^+$], 306.1265 [$M+Na^+$]. Found: 284.1445 [$M+H^+$], 306.2163 [$M+Na^+$].

Methyl *N*-(*tert*-butyloxycarbonyl)-*N*-(2-fluoro-3-phenylallyl)glycinate (3bj)

Obtained by method B using NaH (0.60 mmol, dispersion in mineral oil, 55 w/w %) as the base. A brown oil crystalized upon storage to yellowish solids (method B: 143.0 mg, 83% (*Z*/*E* = 96/4)) was obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 20/1 to 1/1)

(For *Z*-**3bj**,*Z*-**3bj'**, rotamers, a ratio of 1/1): ^{1}H NMR (300.1 MHz, $CDCl_3$) δ: 1.45 (s, 9H, 3CH_3, Boc), 1.49 (s, 9H, 3CH_3, Boc), 3.72 (s, 6H, OCH_3, both rotamers), 3.99 (s, 2H, C*H*$_2$$CO_2$Me), 4.09 (s, 2H, C*H*$_2$$CO_2$Me), 4.13 (d, 2H, CH_2N, $^{3}J_{HF}$ = 14.8 Hz), 4.19 (d, 2H, CH_2N, $^{3}J_{HF}$ = 16.2 Hz), 5.63 (s, 1H, –CH=, $^{3}J_{HF(trans)}$ = 38.3 Hz), 5.70 (d, 1H, –CH=, $^{3}J_{HF(trans)}$ = 38.3 Hz), 7.18–7.56 (m, 5H, arom.). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ: –108.8 (dt, $^{3}J_{HF(trans)}$ = 38.3 Hz, $^{3}J_{HF}$ = 16.2 Hz), –109.5 (dt, $^{3}J_{HF(trans)}$ = 38.3 Hz, $^{3}J_{HF}$ = 14.8 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 28.2 (s, CH_3, Boc). 28.3 (s, CH_3, Boc), 47.8 (s,

*C*H$_2$CO$_2$Me), 48.4 (s, *C*H$_2$CO$_2$Me), 48.9 (d, CH$_2$N, $^2J_{CF}$ = 30.4 Hz), 49.4 (d, CH$_2$N, $^2J_{CF}$ = 31.1 Hz), 52.0 (s, CO$_2$*C*H$_3$), 52.0 (s, CO$_2$*C*H$_3$), 81.0 (s, *C*Me$_3$, Boc), 81.1 (s, *C*Me$_3$, Boc), 108.3 (d, –CH=, $^2J_{CF}$ = 6.7 Hz), 109.0 (d, –CH=, $^2J_{CF}$ = 6.8 Hz), 127.3–128.9 (m, CH-arom., both isomers), 132.7 (m, C-arom., both rotamers), 155.0 (s, C=O, Boc), 155.3 (s, C=O, Boc), 155.5 (d, –CF=, $^1J_{CF}$ = 268 Hz, both rotamers), 170.2 (s, *C*O$_2$Me, both rotamers). (For ***E*-3bj**,***E*-3bj'**, rotamers, a ratio of 1/1): ^{1}H NMR (300.1 MHz, CDCl$_3$) (from {^{1}H,^{19}F}-HMBC) δ: 4.32 (d, 2H, CH$_2$N, $^3J_{HF}$ = 19.5 Hz), 4.38 (d, 2H, CH$_2$N, $^3J_{HF}$ = 18.9 Hz), 6.39 (d, –CH=, $^3J_{HF(cis)}$ = 20.6 Hz), 6.43 (d, –CH=, $^3J_{HF(cis)}$ = 21.0 Hz). ^{19}F NMR (282.4 MHz, CDCl$_3$) δ: –105.2 (dt, $^3J_{HF}$ = 20.5, 19.4 Hz), –106.3 (dt, $^3J_{HF}$ = 20.5, 19.2 Hz). (For both isomers): HRMS (ESI), calcd. for C$_{17}$H$_{22}$FNO$_4$: 346.1425 [M+Na^+], 362.1164 [M+K^+]. Found: 346.1423 [M+Na^+], 362.1162 [M+K^+].

***N*-Benzyl-*N*-(2-fluoro-2-cyclopentylidenethyl)cyclohexylamine (3gc)**

Obtained only by method A using DMSO as the solvent. A colorless oil (method A: 88.7 mg, 59%) was obtained after flash column chromatography (*n*-hexane/EtOAc, 50/1). When carried out by method B, starting cyclopropane **2g** reacted completely to give oligomeric products.

^{1}H NMR (200.1 MHz, CDCl$_3$) δ: 0.96–1.41 (m, 5H), 1.46–1.68 (m, 5H), 1.69–1.99 (m, 4H), 2.00–2.36 (m, 4H), 2.55 (m, 1H, CH in Chx), 3.22 (d, 2H, CH$_2$N, $^3J_{HF}$ = 21.5 Hz), 3.66 (s, 2H, CH$_2$Ph), 7.08–7.48 (m, 5H, Bn). ^{19}F NMR (188.3 MHz, CDCl$_3$) δ: –108.9 (t, $^3J_{HF}$ = 21.5 Hz). ^{13}C NMR (50.3 MHz, CDCl$_3$) δ: 26.3 (s, CH$_2$), 26.3 (s, CH$_2$), 26.5 (s, CH$_2$), 27.0 (s, CH$_2$), 27.6 (d, CH$_2$, J_{CF} = 3.3 Hz), 28.4 (d, CH$_2$, J_{CF} = 5.0 Hz), 29.1 (s, CH$_2$), 49.3 (d, CH$_2$N, $^2J_{CF}$ = 27.5 Hz), 53.9 (s, CH$_2$Ph), 59.6 (s, CH in Chx), 121.9 (d, =C<, $^2J_{CF}$ = 17.6 Hz), 126.5 (s, CH in Bn), 128.1 (s, CH in Bn), 128.4 (s, CH in Bn), 141.3 (s, C in Bn), 150.0 (d, =CF–, $^1J_{CF}$ = 246 Hz). MS (EI) *m/z* 302 ([M+H]$^+$, 5), 301 ([M]$^+$, 24), 300 ([M–H]$^+$, 5), 272 (6), 259 (13), 258 (73), 245 (35), 244 (69), 238 (3), 232 (19), 224 (5), 214 (9), 210 (8), 190 (12), 189 (50), 188 (12), 176 (34), 158 (25), 146 (34), 133 (6), 113 (6), 106 (4), 91 (100). HRMS (ESI), calcd. for C$_{20}$H$_{28}$FN: 302.2279 [M+H^+]. Found: 302.2283 [M+H^+].

***N*-(4-Methoxybenzyl)-*N*-(2-fluoro-2-cyclopentylidenethyl)cyclohexylamine (3gd)**

Obtained only by method A using DMSO as the solvent. A colorless oil (method A: 92.7 mg, 56%) was obtained after flash column chromatography (*n*-hexane/EtOAc, 25/1).

When carried out by method B, starting cyclopropane **2g** reacted completely to give oligomeric products.

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 0.94–1.38 (m, 5H), 1.47–1.69 (m, 5H), 1.69–1.97 (m, 4H), 2.03–2.38 (m, 4H), 2.53 (m, 1H, CH in Chx), 3.20 (d, 2H, CH_2N, $^{3}J_{HF}$ = 21.4 Hz), 3.59 (s, 2H, PMB), 3.79 (s, 3H, OMe), 6.77–6.90 (m, 2H, PMB), 7.21–7.32 (m, 2H, PMB). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –108.9 (t, $^{3}J_{HF}$ = 21.4 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 26.3 (s, CH_2), 26.3 (s, CH_2), 26.5 (s, CH_2), 27.0 (s, CH_2), 27.6 (d, CH_2, J_{CF} = 3.3 Hz), 28.4 (d, CH_2, J_{CF} = 5.1 Hz), 29.0 (s, CH_2), 49.0 (d, CH_2N, $^{2}J_{CF}$ = 27.4 Hz), 53.1 (s, CH_2 in PMB), 55.3 (s, OCH_3), 59.2 (s, CH in Chx), 113.5 (s, 2CH in PMB), 121.8 (d, =C<, $^{2}J_{CF}$ = 17.8 Hz), 129.4 (s, 2CH in PMB), 133.2 (s, C in PMB), 150.1 (d, =CF–, $^{1}J_{CF}$ = 246 Hz), 158.4 (s, C(OMe) in PMB). MS (EI) *m/z* 331 ([M]$^{+}$, 8), 288 (5), 275 (6), 274 (7), 219 (14), 206 (3), 176 (2), 121 (100). HRMS (ESI), calcd. for $C_{21}H_{30}FNO$: 332.2384 [$M+H^{+}$]. Found: 332.2378 [$M+H^{+}$].

***N*-(4-Methoxyphenyl)-*N*-(2-fluoro-2-cyclopentylidenethyl)cyclohexylamine (3ge)**

Obtained only by method A using DMSO as the solvent. A colorless oil (method A: 98.1 mg, 62%) was obtained after flash column chromatography (*n*-hexane/EtOAc, 25/1). When carried out by method B, starting cyclopropane **2g** reacted completely to give oligomeric products.

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 0.96–1.45 (m, 5H), 1.49–1.72 (m, 5H), 1.72–1.99 (m, 4H), 2.06–2.41 (m, 4H), 3.28 (m, 1H, CH in Chx), 3.75 (s, 3H, OMe), 3.83 (d, 2H, CH_2N, $^{3}J_{HF}$ = 15.6 Hz), 6.70–6.92 (m, 4H, PMP). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –111.3 (t, $^{3}J_{HF}$ = 15.6 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 26.0 (s, CH_2), 26.1 (s, CH_2), 27.2 (s, CH_2), 27.8 (d, CH_2, J_{CF} = 3.5 Hz), 28.1 (d, CH_2, J_{CF} = 5.0 Hz), 30.7 (s, CH_2), 46.9 (d, CH_2N, $^{2}J_{CF}$ = 30.0 Hz), 55.6 (s, OCH_3), 59.5 (s, CH in Chx), 114.2 (s, 2CH in PMP), 119.5 (s, 2CH in PMP), 120.5 (d, =C<, $^{2}J_{CF}$ = 17.6 Hz), 143.5 (s, C in PMP), 149.3 (d, =CF–, $^{1}J_{CF}$ = 246 Hz), 153.1 (s, C(OMe) in PMP). MS (EI) *m/z* 318 ([M+H]$^{+}$, 20), 317 ([M]$^{+}$, 100), 302 (2), 288 (4), 275 (8), 274 (40), 261 (28), 260 (33), 248 (8), 205 (27), 204 (37), 192 (7), 174 (15), 162 (42), 149 (13), 134 (15), 122 (7), 108 (5). HRMS (ESI), calcd. for $C_{20}H_{28}FNO$: 318.2228 [$M+H^{+}$]. Found: 318.2234 [$M+H^{+}$].

***N*-Benzyl-*N*-(2-fluoro-2-cyclopentylidenethyl)-4-methoxyaniline (3gf)**

Obtained only by method A using DMSO as the solvent. A colorless oil (method A: 104.4 mg, 64%) was obtained after flash column chromatography (*n*-hexane/EtOAc, 25/1). When carried out by method B, starting cyclopropane **2g** reacted completely to give oligomeric products.

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.52–1.66 (m, 4H, $2CH_2$), 2.03–2.15 (m, 2H, CH_2), 2.24–2.39 (m, 2H, CH_2), 3.71 (s, 3H, OCH_3), 3.99 (d, 2H, CH_2N, $^{3}J_{HF}$ = 18.4 Hz), 4.46 (s, 2H, CH_2Ph), 6.75–6.80 (m, 4H, PMP), 7.13–7.35 (m, 5H, Ph). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –111.7 (t, $^{3}J_{HF}$ = 18.4 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 26.1 (s, CH_2), 27.2 (s, CH_2), 27.7 (d, CH_2, J_{CF} = 3.1 Hz), 28.2 (d, CH_2, J_{CF} = 4.7 Hz), 50.6 (d, CH_2N, $^{2}J_{CF}$ = 28.6 Hz), 55.1 (s, CH_2Ph), 55.7 (s, OCH_3), 114.7 (s, 2CH-arom., PMP), 115.9 (s, 2CH-arom., PMP), 122.3 (d, $=CR_2$, $^{2}J_{CF}$ = 16.8 Hz), 126.8 (s, CH-arom.), 127.2 (s, 2CH-arom.), 128.5 (s, 2CH-arom.), 139.2 (s, C-arom.), 144.0 (s, C-arom.), 148.8 (d, –CF=, $^{1}J_{CF}$ = 247 Hz), 152.3 (s, C-arom.). MS (EI) *m/z* 325 ([M^+], 20), 213 (38), 168 (9), 134 (17), 122 (9), 113 (8), 104 (7), 91 (100), 77 (16), 65 (23), 59 (4), 51 (4). HRMS (ESI), calcd. for $C_{21}H_{24}FNO$: 326.1915 [$M+H^+$]. Found: 326.1907 [$M+H^+$].

Methyl *N*-(2-fluoro-2-cyclopentylidenethyl)prolinate (3gh)

Obtained only by method A using DMSO as the solvent. A colorless oil (method A: 64.0 mg, 53%) was obtained after flash column chromatography (*n*-hexane/EtOAc, gradient from 10/1 to 3/1). When carried out by method B, starting cyclopropane **2g** reacted completely to give oligomeric products.

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.58–1.71 (m, 4H), 1.75–2.01 (m, 3H), 2.07–2.40 (m, 5H), 2.56 (m, 1H, CH_2 in proline), 3.18 (m, 1H, CH_2 in proline), 3.28 (m, 1H, CH in proline), 3.33 (dd, 1H, CH_2N, $^{3}J_{HF}$ = 21.0 Hz, $^{2}J_{HH}$ = 14.1 Hz), 3.43 (dd, 1H, CH_2N, $^{3}J_{HF}$ = 24.6 Hz, $^{2}J_{HH}$ = 14.1 Hz), 3.72 (s, 3H, $–CO_2CH_3$). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –107.9 (t, 22.8 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 23.1 (s, CH_2), 26.2 (s, CH_2), 26.9 (s, CH_2), 27.5 (d, CH_2, J_{CF} = 3.3 Hz), 28.5 (d, CH_2, J_{CF} = 4.7 Hz), 29.5 (s, CH_2), 51.8 (s, OCH_3), 51.8 (d, CH_2N, $^{2}J_{CF}$ = 27.2 Hz), 53.5 (s, CH_2 in proline), 64.7 (s, CH in proline), 123.2 (d, =C<, $^{2}J_{CF}$ = 16.8 Hz), 148.8 (d, =CF–, $^{1}J_{CF}$ = 246 Hz), 174.4 (s, $–\underline{C}O_2Me$). MS (EI) *m/z* 241 ([$M]^+$, 2), 183 (5), 182 (35), 140 (1), 128 (1), 113 (4), 93 (4), 91 (4), 70 (100),

59 (4). HRMS (ESI), calcd. for $C_{13}H_{20}FNO_2$: 242.1551 [$M+H^+$]. Found: 242.1554 [$M+H^+$].

4.4. **Synthesis of secondary 2-fluoroallyl amines**

Amination of 2b with cyclohexylamine

According to reaction conditions A described in paragraph 4.3 from **1b** (0.5 mmol) and cyclohexylamine (0.6 mmol) after flash column chromatography following fractions were collected: (1) — eluted with *n*-hexane/EtOAc 50/1 — 25.2 mg of yellowish oil that contained on the basis of NMR and GC 30 w/w % of **12b** (*Z,Z*/*Z,E*/*E,E* = 80/20/<1, yield 8%) and 70 w/w % of dimers **4b** (yield 26%); (2) — eluted with *n*-hexane/EtOAc 1/1 — 66.0 mg of **11b** as a yellowish liquid (*Z*/*E* = 91/9, yield 56%).

In the same manner, from **1b** (1.0 mmol) and cyclohexylamine (0.5 mmol) after flash column chromatography following fractions were collected: (1) — eluted with *n*-hexane/benzene, gradient from 5/1 to 2/1 — 77.9 mg of **12b** as a colorless oil (*Z,Z*/*Z,E*/*E,E* = 61/35/4, yield 43% based on $CyNH_2$); (2) — eluted with *n*-hexane/EtOAc 1/1 — 57.2 mg of **11b** as a yellowish liquid (*Z*/*E* = 76/24, yield 49% based on $CyNH_2$).

***N*-(2-Fluoro-3-phenylallyl)cyclohexylamine (11b)**

(A mixture of *Z,E*-isomers) ^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 0.78–2.04 (m, 11H, 5 CH_2 in Chx + NH), 2.36–2.65 (m, 1H, CH in Chx, both isomers), 3.47 (d, 2H, CH_2N, *Z*-**11b**, $^3J_{HF}$ = 15.8 Hz), 3.57 (d, 2H, CH_2N, *E*-**11b**, $^3J_{HF}$ = 22.5 Hz), 5.65 (d, 1H, =CH–, *Z*-**11b**, $^3J_{HF(trans)}$ = 39.4 Hz), 6.33 (d, 1H, =CH–, *E*-**11b**, $^3J_{HF(cis)}$ = *J* = 20.9 Hz), 7.13–7.40 (m, 3H, arom.), 7.43–7.58 (m, 2H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –104.7 (td, *E*-**11b**, $^3J_{HF}$ = 22.5 Hz, $^3J_{HF(cis)}$ = *J* = 20.9 Hz), –107.7 (dt, *Z*-**11b**, $^3J_{HF(trans)}$ = 39.4 Hz, $^3J_{HF}$ = 15.8 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 24.9 (s, CH_2 in Chx, *E*-**11b**), 24.9 (s, CH_2 in Chx, *Z*-**11b**), 26.1 (s, CH_2 in Chx, *E*-**11b**), 26.1 (s, CH_2 in Chx, *Z*-**11b**), 33.3 (s, CH_2 in Chx, *E*-**11b**), 33.4 (s, CH_2 in Chx, *Z*-**11b**), 43.8 (d, CH_2N, *E*-**11b**, $^2J_{CF}$ = 26.9 Hz), 47.8 (d, CH_2N, *Z*-**11b**, $^2J_{CF}$ = 29.1 Hz), 55.4 (s, CH in Chx, *Z*-**11b**), 55.7 (s, CH in Chx, *E*-**11b**), 107.0 (d, =CH–, *Z*-**11b**, $^2J_{CF}$ = 7.6 Hz), 110.2 (d, =CH–, *E*-**11b**, $^2J_{CF}$ = 27.5 Hz), 127.0 (d, CH-arom., J_{CF} = 2.0 Hz), 128.4 (s, CH-arom.), 128.5 (d, CH-arom., J_{CF} = 7.4 Hz), 133.3 (d, C-arom., $^3J_{CF}$ = 2.5 Hz), 158.9 (d, =CF–, $^1J_{CF}$ = 267 Hz). MS (EI) *m/z* 233 ([M^+], 8), 213 (3), 190 (14), 142 (10), 135 (100), 133 (21), 115 (84), 109 (9), 98 (15), 86 (10), 77 (4), 55 (16). HRMS (ESI), calcd. for $C_{15}H_{20}FN$: 234.1653 [$M+H^+$]. Found: 234.1649 [$M+H^+$].

***N,N*-Bis(2-fluoro-3-phenylallyl)cyclohexylamine (12b)**

(A mixture of *Z,Z*-**12b**, *Z,E*-**12b**, *E,E*-**12b** in a ratio of 61/35/4):

^{1}H NMR (300.1 MHz, $CDCl_3$) δ: 0.93–1.37 (m, 5H, CH_2 in Chx), 1.46–1.97 (m, 5H, CH_2 in Chx), 3.32 (d, 2H, *Z*-AllCH_2N, *Z,E*-**12b**, $^3J_{HF}$ = 12.7 Hz), 3.43 (d, 4H, *Z*-AllCH_2N, *Z,Z*-**12b**, $^3J_{HF}$ = 12.9 Hz), 3.48 (d, 4H, *E*-AllCH_2N, *E,E*-**12b**, $^3J_{HF}$ = 22.5 Hz), 3.57 (d, 2H, *E*-AllCH_2N, *Z,E*-**12b**, $^3J_{HF}$ = 21.5 Hz), 5.64 (d, 1H, (*Z*)-CF=CH-, *Z,E*-**12b**, $^3J_{HF(trans)}$ = 39.5 Hz), 5.78 (d, 2H, (*Z*)-CF=CH-, *Z,Z*-**12b**, $^3J_{HF(trans)}$ = 39.4 Hz), 6.34 (d, 2H, (*E*)-CF=CH-, *E,E*-**12b**, $^3J_{HF(cis)}$ = 21.1 Hz), 6.37 (d, 1H, (*E*)-CF=CH-, *Z,E*-**12b**, $^3J_{HF(cis)}$ = 21.1 Hz), 7.12–7.53 (m, 10H, 2Ph). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –96.7 (td, 2F, (*E*)-CF=CH-, *E,E*-**12b**, $^3J_{HF}$ = 22.5 Hz, $^3J_{HF(cis)}$ = 21.1 Hz), –99.0 (td, 1F, (*E*)-CF=CH-, *Z,E*-**12b**, $^3J_{HF}$ = 21.5 Hz, $^3J_{HF(cis)}$ = 21.1 Hz), –105.1 (dt, 1F, (*Z*)-CF=CH-, *Z,E*-**12b**, $^3J_{HF(trans)}$ = 39.5 Hz, $^3J_{HF}$ = 12.7 Hz), –105.3 (dt, 2F, (*Z*)-CF=CH-, *Z,Z*-**12b**, $^3J_{HF(trans)}$ = 39.4 Hz, $^3J_{HF}$ = 12.9 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 25.8–26.5 (m, CH_2 in Chx, all isomers), 28.7–29.9 (m, CH_2 in Chx, all isomers), 47.8 (d, *E*-AllCH_2N, *Z,E*-**12b**, $^2J_{CF}$ = 25.6 Hz), 47.9 (d, *E*-AllCH_2N, *E,E*-**12b**, $^2J_{CF}$ = 26.8 Hz), 51.2 (d, *Z*-AllCH_2N, *Z,E*-**12b**, $^2J_{CF}$ = 28.9 Hz), 51.6 (d, *Z*-AllCH_2N, *Z,Z*-**12b**, $^2J_{CF}$ = 29.8 Hz), 60.1–60.5 (m, CH in Chx, all isomers), 107.4 (d, (*Z*)-CF=C<u>H</u>-, *Z,E*-**12b**, $^2J_{CF}$ = 8.8 Hz), 107.5 (d, (*Z*)-CF=C<u>H</u>-, *Z,Z*-**12b**, $^2J_{CF}$ = 6.8 Hz), 111.8 (d, (*E*)-CF=C<u>H</u>-, *Z,E*-**12b**, $^2J_{CF}$ = 27.3 Hz), 112.0 (d, (*E*)-CF=C<u>H</u>-, *E,E*-**12b**, $^2J_{CF}$ = 27.9 Hz), 126.8–127.2 (m, CH arom., all isomers), 128.3–129.1 (m, CH arom., all isomers), 133.5–133.8 (m, C arom., all isomers), 158.7 (d, (*Z*)-<u>C</u>F=CH-, *Z,E*-**12b**, $^1J_{CF}$ = 268 Hz), 158.9 (d, (*Z*)-<u>C</u>F=CH-, *Z,Z*-**12b**, $^1J_{CF}$ = 269 Hz), 159.9 (d, (*E*)-<u>C</u>F=CH-, *E,E*-**12b**, $^1J_{CF}$ = 254 Hz), 160.0 (d, (*E*)-<u>C</u>F=CH-, *Z,E*-**12b**, $^1J_{CF}$ = 256 Hz). MS (EI) *m/z* 367 ([M]$^+$, 4), 324 (2), 276 (7), 220 (20), 136 (10), 135 (100), 133 (27), 116 (10), 115 (97), 109 (15), 91 (8), 83 (5). HRMS (ESI), calcd. for $C_{24}H_{27}F_2N$: 368.2184 [$M+H^+$]. Found: 368.2190 [$M+H^+$].

Typical procedure for cleavage of PMP-group in 3be with $(NH_4)_2[Ce(NO_3)_6]$. Synthesis of *N*-(2-Fluoro-3-phenylallyl)cyclohexylamine (11b).

To a solution of 34.5 mg (0.099 mmol) of **3be** (*Z/E* =73/27) in 1.0 mL of MeCN 0.20 mL of water were added followed by 155.7 mg (0.28 mmol) of $(NH_4)_2[Ce(NO_3)_6]$. The reaction mixture was stirred at room temperature for 1 hour, diluted with satd. $NaHCO_3$ and satd. Na_2SO_3 and stirred for additional 10 min. Resulted mixture was extracted with CH_2Cl_2, combined extracts were dried over K_2CO_3 and concentrated. The residue was purified by

flash column chromatography (*n*-hexane/EtOAc = 1/1) affording 22.4 mg of **11b** as a yellowish liquid (*Z/E* = 72/28, yield 97%).

Synthesis of *N*-(2-Fluoro-2-cyclopentylidenethyl)cyclohexylamine (11g) by cleavage of PMP-group in 3ge with $(NH_4)_2[Ce(NO_3)_6]$

Using the procedure described above, from 30.4 mg of **3ge** after flash column chromatography (EtOAc) 20.8 mg of **11g** as a brown oil were obtained (yield 98%).

^{1}H NMR (300.1 MHz, $CDCl_3$) δ: 0.99–1.35 (m, 5H, CH_2), 1.41 (br. s, 1H, NH), 1.56–1.80 (m, 7H, CH_2), 1.80–1.92 (m, 2H, CH_2), 2.17–2.28 (m, 2H, CH_2), 2.29–2.39 (m, 2H, CH_2), 2.45 (m, 1H, CH in Chx), 3.37 (d, 2H, CH_2N, $^3J_{HF}$ = 20.9 Hz). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ: –115.6 (t, $^3J_{HF}$ = 20.9 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 25.1 (s, CH_2), 26.3 (d, CH_2, J_{CF} = 14.2 Hz), 27.0 (s, CH_2), 27.5 (d, CH_2, J_{CF} = 3.2 Hz), 28.4 (d, CH_2, J_{CF} = 5.1 Hz), 33.5 (s, CH_2), 45.2 (d, CH_2N, $^2J_{CF}$ = 28.7 Hz), 55.6 (s, CH in Chx), 120.8 (d, =C<, $^2J_{CF}$ = 17.5 Hz), 150.1 (d, =CF–, $^1J_{CF}$ = 243 Hz). MS (EI) *m/z* 211 ([M]$^+$, 12), 168 (42), 154 (7), 148 (16), 142 (2), 134 (2), 126 (4), 113 (22), 109 (10), 100 (24), 98 (27), 93 (30), 91 (25), 85 (12), 79(18), 77 (23), 70 (16), 67 (22), 59 (13), 56 (100). HRMS (ESI), calcd. for $C_{13}H_{22}FN$: 212.1809 [$M+H^+$]. Found: 212.1812 [$M+H^+$].

Cleavage of Bn and PMB-groups in 3bc,3bd,3gc,3gd with $(NH_4)_2[Ce(NO_3)_6]$

According to the procedure described for **3be**. Crude product mixtures after work-up were analyzed by ^{1}H, ^{19}F NMR, GC and GC/MS. Results are presented on Scheme 7.

(*Z*)-2-Fluoro-3-phenylprop-2-enal (13b)

(For *Z*-**13b**): ^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 6.61 (d, 1H, –CH=CF–, $^3J_{HF(trans)}$ = 34.1 Hz), 7.11–8.00 (m, 5H, arom.), 9.35 (d, 1H, –CH=O, $^3J_{HF}$ = 17.0 Hz). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –127.9 (dd, $^3J_{HF(trans)}$ = 34.1 Hz, $^3J_{HF}$ = 17.0 Hz). MS (EI) *m/z* 150 ([M$^+$], 64), 149 (100), 129 (4), 121 (30), 101 (62), 96 (39), 78 (36), 75 (43), 63 (20), 51 (37). (For *E*-**13b**): ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –125.1 (dd, $^3J_{HF(cis)}$ = 19.5 Hz, $^3J_{HF}$ = 17.1 Hz). MS (EI) *m/z* 150 ([M$^+$], 42), 149 (100), 121 (14), 101 (33), 96 (32), 78 (15), 75 (29), 63 (9), 50 (20).

4.5. Synthesis of primary 2-fluoroallyl amines

For synthesis and isolation of 2-fluoroallyl chlorides *Z*-**6b** and **6h**, see refs. [17a,b].

2-Fluoro-3-phenylallyl amine (*Z*-14b)

Method A. To a solution of 340 mg (2.0 mmol) of *Z*-**6b** (*Z/E* > 99.9) in 2.0 mL of DMF 370 mg (2.0 mmol) of potassium phthalimide were added. The reaction mixture was stirred at 100°C for 3 hours, then diluted with Et_2O, washed with water and brine, dried over K_2CO_3. After evaporation of volatiles and drying of a residue under high vacuum 560 mg of pure *N*-((*Z*)-2-fluoro-3-phenylallyl)phthalimide *Z*-**15b** as colorless solids (yield >99%).

^{1}H NMR (400.1 MHz, $CDCl_3$) δ: 4.53 (d, 2H, CH_2N, $^3J_{HF}$ = 15.4 Hz), 5.85 (d, 1H, –CH=, $^3J_{HF(trans)}$ = 37.9 Hz), 7.18–7.32 (m, 3H, Ph), 7.44–7.49 (m, *2*H, Ph), 7.68–7.75 (m, 2H, phthalimide), 7.85–7.90 (m, 2H, phthalimide).^{19}F NMR (282.4 MHz, $CDCl_3$) δ: –109.7 (dt, $^3J_{HF(trans)}$ = 37.9 Hz, $^3J_{HF}$ = 15.4 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 39.2 (d, CH_2N, $^2J_{CF}$ = 32.2 Hz), 109.5 (d, –CH=, $^2J_{CF}$ = 6.4 Hz), 123.6 (s, 2CH, phthalimide), 127.7 (d, CH, $^6J_{CF}$ = 1.8 Hz), 128.5 (s, 2CH), 128.8 (d, 2CH, $^4J_{CF}$ = 7.3 Hz), 132.1 (s, 2C, phthalimide), 132.5 (d, C, $^3J_{CF}$ = 2.7 Hz), 134.3 (d, 2CH, phthalimide), 153.6 (d, –CF=, $^1J_{CF}$ = 268 Hz), 167.5 (s, 2C=O). MS (EI) *m/z* 281 ([M^+], 41), 261 (100), 232 (69), 204 (26), 178 (9), 165 (5), 148 (4), 133 (35), 115 (10), 104 (24), 91 (4), 77 (14). HRMS (ESI), calcd. for $C_{17}H_{12}FNO_2$: *m/z* 304.0744 [*M*+Na^+]. Found: *m/z* 304.0742 [*M*+Na^+].

To a solution of 560 mg (2.0 mmol) of *Z*-**15b** in 6.0 mL of MeOH 102 μL (2.2 mmol) of $N_2H_4 \cdot H_2O$ were added. The reaction mixture was stirred at room temperature for 24 hours, then was filtered. Under cooling on an ice bath 1 mL (ca. 10 mmol) of conc. HCl was added and the resulted mixture was concentrated on a rotary evaporator. The residue was dissolved in 50 mL of water, filtered and washed with CH_2Cl_2. After that under cooling on an ice bath ca. 6M solution of NaOH was added to pH = 14. Resulted solution was saturated with NaCl and extracted with CH_2Cl_2. Extracts were combined, dried over K_2CO_3 and concentrated under reduced pressure. The residue was purified by 'bulb-to-bulb' distillation (8 mmHg, 120 to 150°C) to give 270 mg of *Z*-**14b** as a colorless liquid (*Z/E* >99.9, yield 95%).

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.48 (br. s, 2H, NH_2), 3.44 (d, 2H, CH_2N, $^3J_{HF}$ = 14.3 Hz), 5.63 (d, 1H, –CH=, $^3J_{HF(trans)}$ = 39.3 Hz), 7.13–7.58 (m, 5H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –109.8 (dt, $^3J_{HF(trans)}$ = 39.3 Hz, $^3J_{HF}$ = 14.3 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 43.7 (d, CH_2N, $^2J_{CF}$ = 30.8 Hz), 105.4 (d, –CH=, $^2J_{CF}$ = 7.6 Hz), 127.1 (d, CH-arom., $^6J_{CF}$ = 2.2 Hz), 128.4 (s, 2CH-arom.), 128.4 (d, 2CH-arom., $^4J_{CF}$ = 7.1 Hz), 133.2 (d, C-arom., $^3J_{CF}$ = 2.5 Hz), 160.8 (d, –CF=, $^1J_{CF}$ = 267 Hz). HRMS (ESI), calcd. for $C_9H_{10}FN$: *m/z* 152.0870 [*M*+H^+]. Found: *m/z* 152.0873 [*M*+H^+].

Method B. To a solution of 862 mg (5.1 mmol) of *Z*-**6b** (*Z*/*E* > 99.9) in 10 mL of CH_2Cl_2 1.05 g (5.1 mmol) of urotropine were added. The reaction mixture was stirred under reflux for 24 hours. Precipitate formed was filtered off, washed with CH_2Cl_2 and dried under high vacuum to give 1.55 g of *N*-(2-fluoro-3-phenylallyl)urotropinium chloride *Z*-**16b** as colorless solids (yield 99%).

^{1}H NMR (200.1 MHz, DMSO-d_6) δ: 4.14 (d, 2H, CH_2N^+, $^3J_{HF}$ = 22.9 Hz), 4.46–4.73 (m, 6H, urotropine), 5.27–5.49 (m, 6H, urotropine), 6.41 (d, 1H, –CH=, $^3J_{HF(trans)}$ = 39.0 Hz), 7.28–7.66 (m, 5H, arom.). ^{19}F NMR (188.3 MHz, DMSO-d_6) δ: –94.1 (dt, $^3J_{HF(trans)}$ = 39.0 Hz, $^3J_{HF}$ = 22.9 Hz). ^{13}C NMR (50.3 MHz, DMSO-d_6) δ: 56.4 (d, CH_2N^+, $^2J_{CF}$ = 28.0 Hz), 69.6 (s, 3CH_2, urotropine), 78.0 (s, 3CH_2, urotropine), 117.2 (d, –CH=, $^2J_{CF}$ = 4.8 Hz), 128.7 (s, 2CH-arom.), 128.7 (d, CH-arom., $^6J_{CF}$ = 2.0 Hz), 129.3 (d, 2CH-arom., $^4J_{CF}$ = 7.2 Hz), 131.4 (d, C-arom., $^3J_{CF}$ = 3.1 Hz), 147.6 (d, –CF=, $^1J_{CF}$ = 264 Hz). HRMS (ESI), calcd. for $C_{15}H_{20}FN_4^+$: *m/z* 275.1667 [M^+]. Found: *m/z* 275.1672 [M^+].

To a well stirred suspension of 1.50 g (4.8 mmol) of *Z*-**16b** in 10 mL of EtOH 2 mL (ca. 20 mmol) of conc. HCl were added. The reaction mixture was stirred under reflux for 24 hours, and then concentrated on a rotary evaporator. Work-up as above followed by 'bulb-to-bulb' distillation afforded 486 mg of *Z*-**14b** as a colorless liquid (*Z*/*E* >99.9, yield 67%).

2-Fluoro-3-methylbut-2-enyl amine (14h)

Method A. A mixture of 12.3 g (100 mmol) of 2-fluoro-3-methylbut-2-enyl chloride **6h**, 18.5 g (100 mmole) of potassium phthalimide and 100 mL of DMF was stirred at 100°C for 3 hours, then diluted with Et_2O, washed with water, brine, and dried over K_2CO_3. After evaporation of volatiles and drying of a residue under high vacuum 22.4 g of pure *N*-((*Z*)-2-fluoro-3-phenylallyl)phthalimide **15h** as colorless solids (yield 96%).

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.66 (d, 3H, CH_3, *J* = 3.4 Hz), 1.86 (d, 3H, CH_3, *J* = 3.0 Hz), 4.47 (d, 1H, =CH–, *J* = 20.4 Hz), 7.65–7.78 (m, 2H, arom.), 7.80–7.91 (m, 2H, arom.). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –119.7 (tqq, *J* = 20.4, 3.4, 3.0 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 15.9 (d, CH_3, *J* = 8.5 Hz), 17.6 (d, CH_3, *J* = 4.8 Hz), 35.2 (d, CH_2, *J* = 31.3 Hz), 113.3 (d, =*C*Me_2, *J* = 15.4 Hz), 123.4 (s, 2CH-arom.), 132.1 (s, 2C-arom.), 134.0 (s, 2CH-arom.), 148.0 (d, =CF–, *J* = 243 Hz), 167.8 (s, 2 C=O). MS (EI) *m*/*z* 233 ([M]$^+$, 20), 218 ([M–CH_3]$^+$, 4), 213 ([M–HF]$^+$, 100), 198 (12), 185 (31), 170 (33), 160 (38), 148 (7), 133 (12), 130 (27), 105 (19), 104 (15), 86 (14), 85 (13), 76 (15). HRMS

(ESI), calcd. for $C_{13}H_{12}FNO_2$: 234.0925 [M+H^+], 256.0744 [M+Na^+]. Found: 234.0920 [M+H^+], 274.0738 [M+Na^+].

To a solution of 22.4 g (96 mmol) of **15h** in 300 mL of MeOH 5.1 mL (106 mmol) of $N_2H_4 \cdot H_2O$ were added dropwise. The reaction mixture was stirred at room temperature for 24 hours, and then was filtered. Under cooling on an ice bath 20 mL (ca. 200 mmol) of conc. HCl was added and the resulted mixture was concentrated on a rotary evaporator. The residue was dissolved in 300 mL of water, filtered and washed with CH_2Cl_2. After that under cooling on an ice bath ca. 6M solution of NaOH was added to pH = 14. Resulted solution was saturated with NaCl and extracted with CH_2Cl_2. Extracts were combined, dried over K_2CO_3 and concentrated under reduced pressure (25°C, 100 mbar). The residue was distilled under reduced pressure to give 8.90 g of 2-fluoro-3-methylbut-2-enyl amine **14h** as a colorless liquid (bp 65–66°C/100 mmHg, yield 90%).

^{1}H NMR (200.1 MHz, $CDCl_3$) δ: 1.25 (br. s., 2H, NH_2), 1.62–1.67 (m, 6H, $2CH_3$), 3.40 (d, 2H, CH_2, J = 21.9 Hz). ^{19}F NMR (188.3 MHz, $CDCl_3$) δ: –120.0 (tqq, J = 21.9, 3.0, 3.0 Hz). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 15.3 (d, CH_3, J = 8.9 Hz), 17.1 (d, CH_3, J = 5.5 Hz), 39.1 (d, CH_2, J = 31.0 Hz), 108.1 (d, =CMe_2, J = 17.2 Hz), 154.3 (d, =CF–, J = 241 Hz). MS (EI) m/z 103 ([M^+], 30), 102 (16), 88 (100), 86 (90), 85 (49), 68 (25), 59 (25), 41 (26). HRMS (ESI), calcd. for $C_5H_{10}FN$: 104.0870 [M+H^+]. Found: 104.0867 [M+H^+].

Method B. To a solution of 16.8 g (120 mmol) of urotropine in 150 mL of CH_2Cl_2 12.3 g (100 mmol) of 2-fluoro-3-methylbut-2-enyl chloride **6h** were added dropwise. The reaction mixture was stirred under reflux for 24 hours. Precipitate formed was filtered off, washed thoroughly with CH_2Cl_2 and dried under high vacuum to give 23.4 g of *N*-(2-fluoro-3-methylbut-2-enyl)urotropinium chloride **16h** as colorless solids (yield 89%).

^{1}H NMR (200.1 MHz, DMSO-d_6) δ: 1.74 (d, 3H, CH_3, J = 3.2 Hz), 1.79 (d, 3H, CH_3, J = 2.5 Hz), 3.92 (d, 2H, CH_2, J = 24.8 Hz), 4.43–4.71 (m, 6H, $3CH_2$-urotropine), 5.26 (s, 6H, $3CH_2$-urotropine). ^{19}F NMR (188.3 MHz, DMSO-d_6) δ: –106.0 (t, J = 24.8 Hz). ^{13}C NMR (50.3 MHz, DMSO-d_6) δ: 16.3 (d, CH_3, J = 8.3 Hz), 18.1 (d, CH_3, J = 3.8 Hz), 52.4 (d, CH_2, J = 30.9 Hz), 69.6 (s, $3CH_2$-urotropine), 77.5 (s, $3CH_2$-urotropine), 123.2 (d, =CMe_2, J = 15.2 Hz), 142.2 (d, =CF–, J = 237 Hz). HRMS (ESI), calcd. for $C_{11}H_{20}FN_4^+$: 227.1667 [M^+]. Found: 227.1670 [M^+].

To a solution of 70 mL (ca. 700 mmol) of conc. HCl in 300 mL of EtOH and 60 mL of water 23.4 g (89 mmol) of **16h** were added. The reaction mixture was stirred under reflux for 24 hours, and then concentrated on a rotary evaporator. Work-up as above followed by distillation gave 5.41 g of **14h** as a colorless liquid (yield 59%).

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[23] Our preliminary experiments indicated that *gem*-bromofluorocyclopropanes undergo ring-opening under copper-catalysis in aprotic solvents with comparable rates to chlorine-containing ones. The detailed investigations of this phenomenon and comparing it with thermolytically induced or silver-mediated reactions are currently underway in our laboratory.

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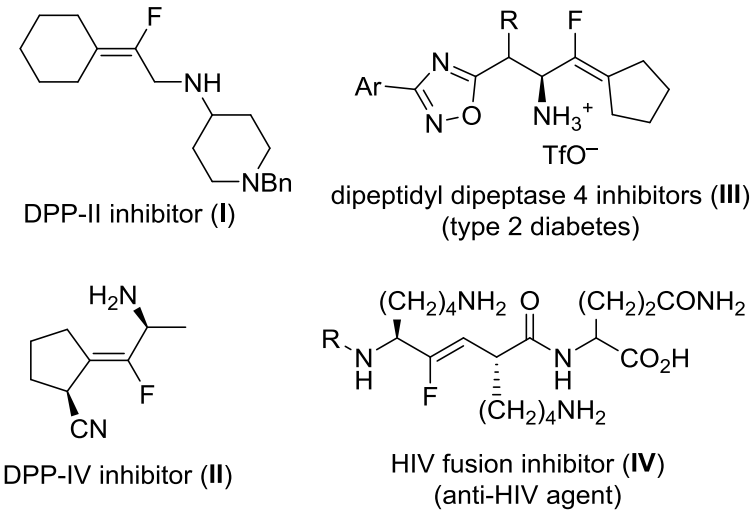
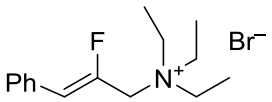
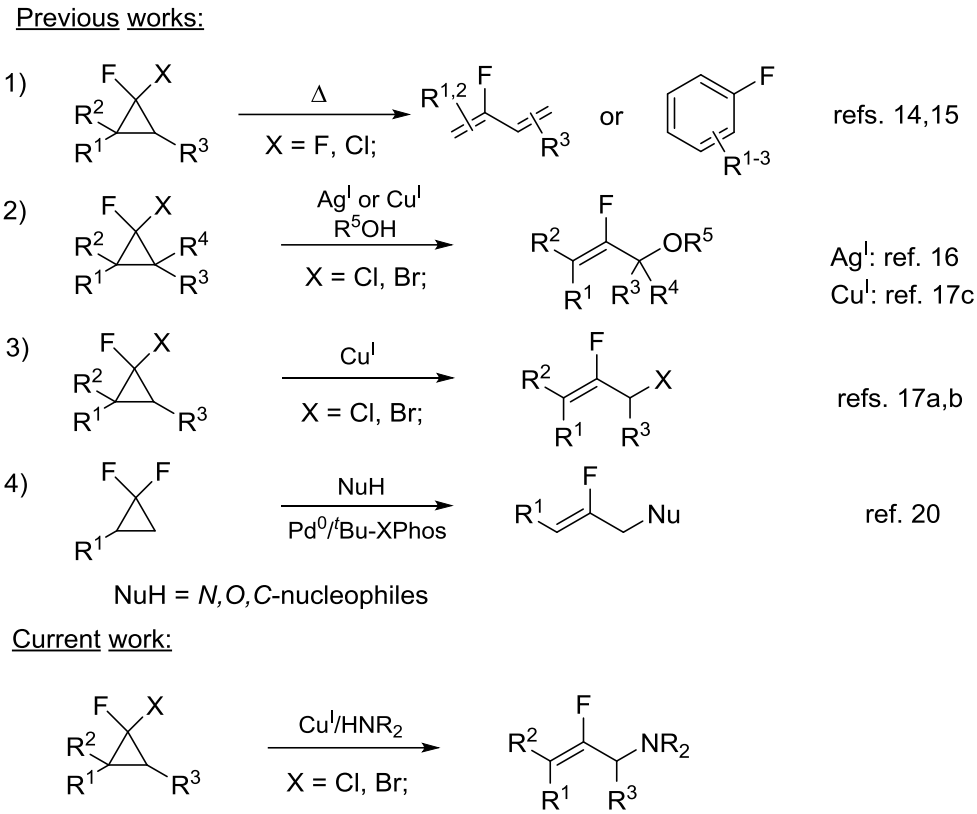


Fig. 1. Some biologically active monofluoroalkenes

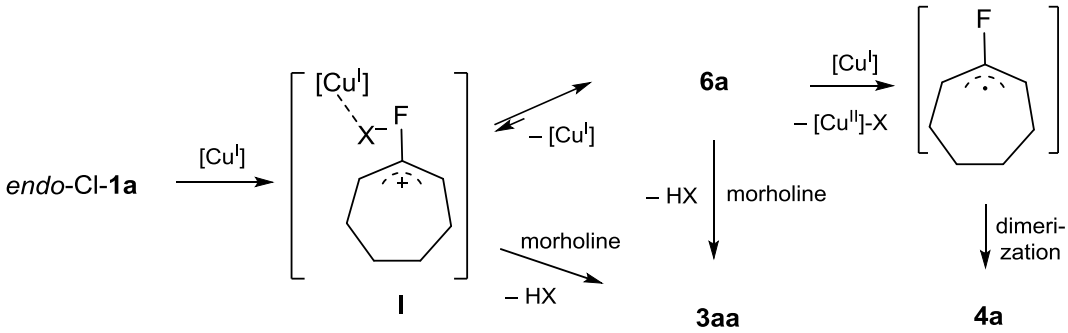


***Z*-10b**

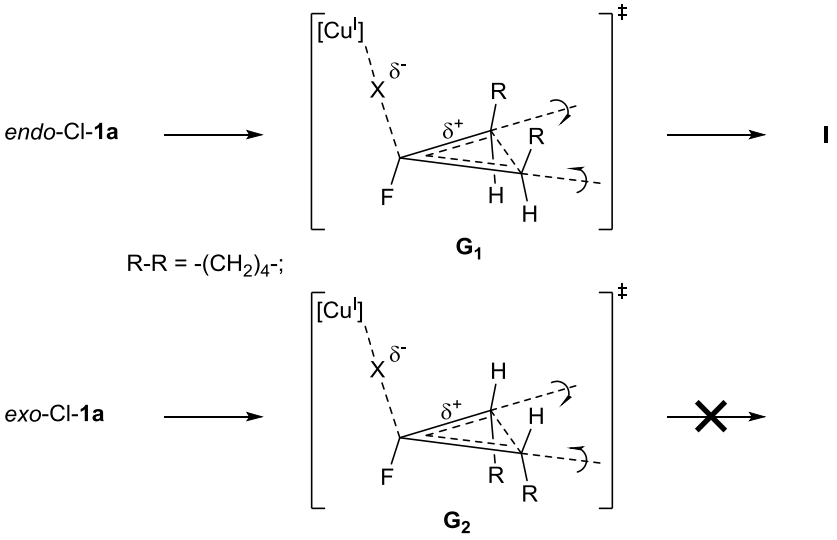
Fig. 2. Structure of ***Z*-10b**



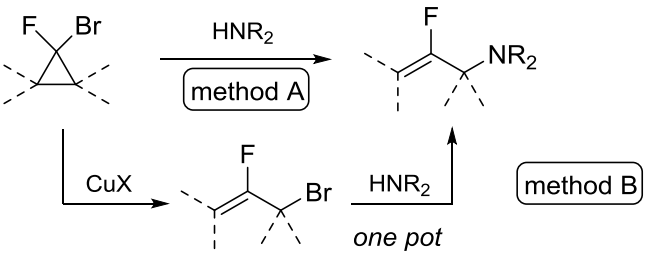
Scheme 1. Synthetic uses of non-activated *gem*-fluorohalocyclopropanes (R^1–R^5 = alkyl, aryl)



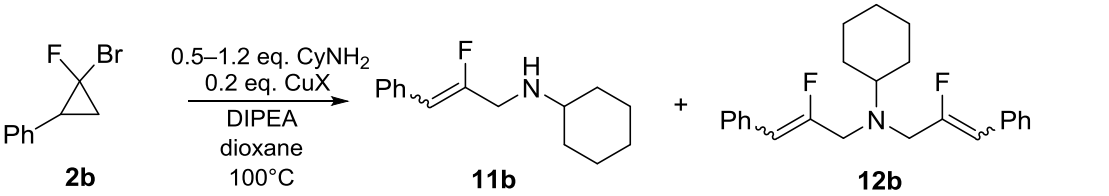
Scheme 2. A plausible scheme of copper-catalyzed ring-opening amination of *endo*-Cl-**1a**



Scheme 3. Proposed transition states for copper catalyzed ring-openings of *endo*-Cl-**1a** (**G1**) and *exo*-Cl-**1a** (**G2**)



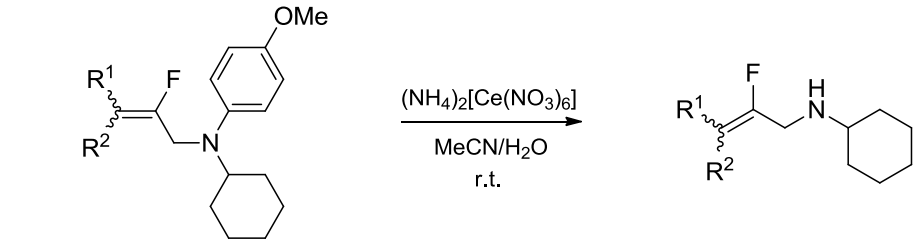
Scheme 4. Two synthetic strategies for the preparation of 2-fluoroallyl amines from *gem*-bromofluorocyclopropanes (the substituents are omitted for clarity)



1.2 eq. $CyNH_2$	56% (*Z*/*E*=91/9)	8% (*Z*,*Z*/*Z*,*E*/*E*,*E*=80/20/<1)
0.5 eq. $CyNH_2$	49%[a] (*Z*/*E*=76/24)	43%[a] (*Z*,*Z*/*Z*,*E*/*E*,*E*=61/35/4)

[a] Yields based on $CyNH_2$

Scheme 5. Ring-opening amination of **2b** with cyclohexylamine



R^1=Ph, R^2=H: **3be** (*Z*/*E*=73/27, 85% from **2b**)
R^1-R^2=-$(CH_2)_4$-: **3ge** (62% from **2g**)

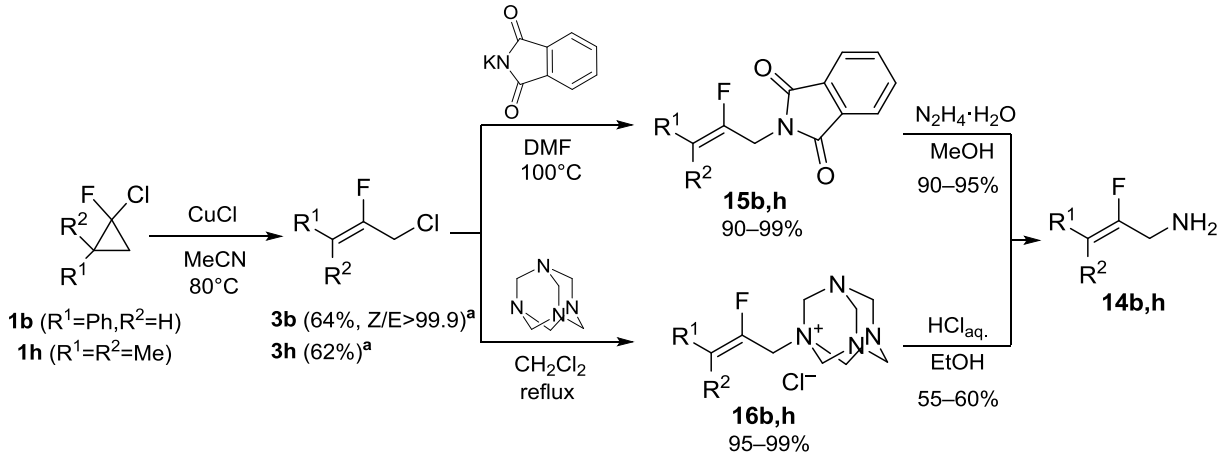
11b (*Z*/*E*=72/28, 97%)
11g (98%)

Scheme 6. Synthesis of secondary 2-fluoroallyl amines

R^1=Ph, R^2=H:	**3bc** (R=H, *Z*/*E*=95/5)	31% (*Z*/*E*=96/4)	50% (*Z*/*E*=96/4)	64%
	3bd (R=OMe, *Z*/*E*=79/21)[a]	32% (*Z*/*E*=90/10)	52% (*Z*/*E*=90/10)	64%
R^1-R^2=-$(CH_2)_4$-:	**3gc** (R=H)[b]	15%	(n.d.[d])	36%
	3gd (R=OMe)[c]	18%	(n.d.[d])	37%

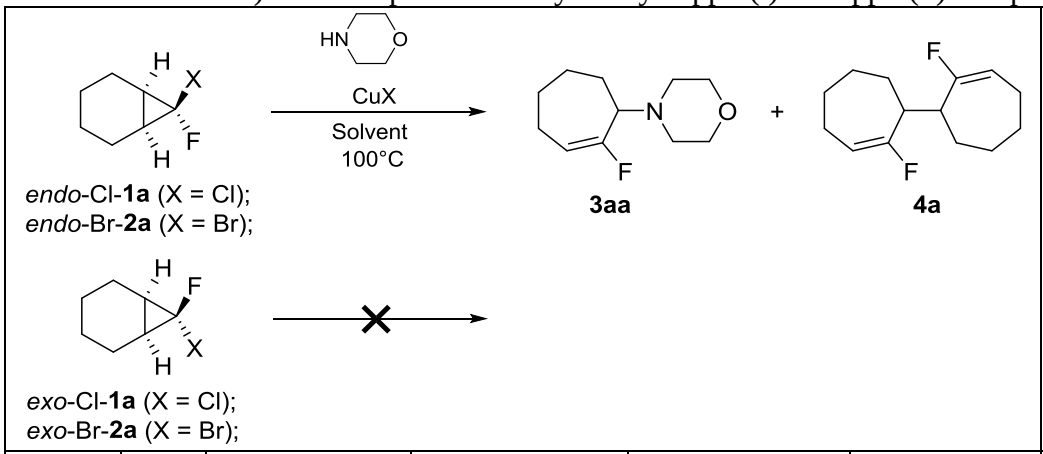
[a] 4% of *E*-**3bd** were recovered; [b] 34% of **3gc** were recovered; [c] 32% of **3gd** were recovered; [d] **13g** was not detected in the product mixture after work-up likely due to low boiling point;

Scheme 7. Cleavage of Bn and PMB-groups

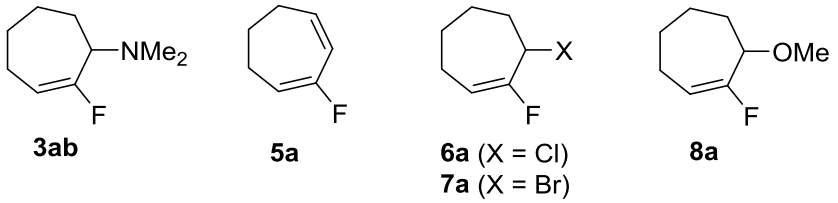


[a] Isolated yields after fractional distillation of isomer mixtures;
Scheme 8. Synthesis of primary 2-fluoroallyl amines

Table 1. Ring-opening amination of 7-chloro-7-fluoro- and 7-bromo-7-fluorobicyclo[4.1.0]heptanes (**1a** and **2a**) with morpholine catalyzed by copper(I) or copper(II) compounds [a,b]



Other products:

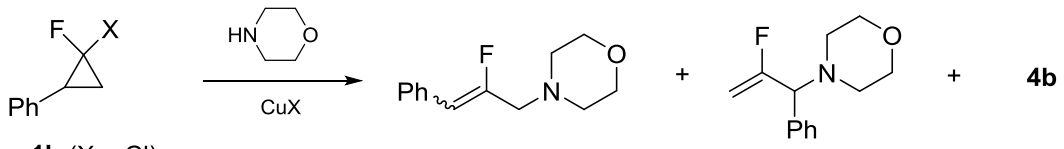


Entry	X	morpholine (equiv.)	[Cu] (equiv.)	Additive (equiv.)	Solvent	Recovery of *endo*-X-**1a/2a**, (%)	Yields, (%)				
							3aa	**4a**	**5a**	**6a/7a**	Other products
1[c]	Cl	3.0	CuCl (0.20)	—	dioxane	0	74	24	2	0	0
2	Cl	3.0	CuCl (0.20)	—	dioxane	6	68	11	2	13	0
3	Cl	2.0	CuCl (0.20)	—	dioxane	7	52	17	2	22	0
4	Cl	1.0	CuCl (0.20)	—	dioxane	8	33	12	3	44	0
5	Cl	3.0	CuCl (0.10)	—	dioxane	15	47	18	2	18	0
6	Cl	3.0	CuCl (0.20)	—	DMSO	12	76	8	2	1	1% [d]
7[c]	Cl	3.0	CuCl (0.20)	—	DMSO	0	86	10	3	0	1% [d]
8	**Br**	**3.0**	**CuBr (0.20)**	**—**	**dioxane**	**0**	**95 (87)[e]**	**3**	**2**	**0**	**0**
9	**Br**	**3.0**	**CuBr (0.20)**	**—**	**DMSO**	**0**	**94 (85)[e]**	**2**	**3**	**0**	**1% [d]**
10	Br	3.0	CuBr (0.20)	—	MeCN	1	92	5	2	0	0
11	Br	3.0	CuBr (0.20)	—	DMF	1	82	4	3	0	10% (**3ab**)
12	Br	3.0	CuBr (0.20)	—	MeOH	0	90	2	2	0	6% (**8a**)
13	Br	3.0	CuBr (0.20)	—	HFIP	0	87	< 0.5	10	0	1% [d]
14	Br	3.0	CuBr (0.20)	—	toluene	4	84	10	2	0	0

15	**Br**	**1.2**	**CuBr (0.20)**	**NEt_3 (2.0)**	**dioxane**	**0**	**80**	**16**	**4**	**0**	**0**
16	Br	1.2	CuBr (0.20)	NEt_3 (2.0)	—	3	82	12	3	0	0
17	Br	1.2	CuBr (0.20)	DIPEA (2.0)	dioxane	5	75	17	3	0	0
18	Br	1.2	CuBr (0.20)	K_2CO_3 (2.0)	dioxane	7	71	5	2	15	0
19	Br	1.2	CuBr (0.20)	Cs_2CO_3 (2.0)	dioxane	11	25	63	1	0	0
20	Br	1.2	CuBr (0.20)	NaOH (2.0)	dioxane	98	2	0	0	0	0
21	Br	1.2	CuBr (0.20)	NEt_3 (2.0)	DMSO	0	83	10	5	0	2% [d]
22	Br	1.2	CuBr (0.20)	Phen (0.20), NEt_3 (2.0)	dioxane	2	68	27	3	0	0
23	Br	1.2	CuBr (0.20)	TMEDA (0.20), NEt_3 (2.0)	dioxane	0	63	29	4	0	0
24	Br	1.2	CuBr (0.20)	dppe (0.20), NEt_3 (2.0)	dioxane	89	10	1	< 0.5	0	0
25	Br	1.2	(IPr)CuCl (0.20)	NEt_3 (2.0)	dioxane	87	10	0	0.6	2	0
26	Br	1.2	Cu_2O (0.20)	NEt_3 (2.0)	dioxane	0	74	22	4	0	0
27	**Br**	**1.2**	**CuO (0.20)**	**NEt_3 (2.0)**	**dioxane**	**< 0.5**	**84**	**11**	**4**	**0**	**0**
28	Br	1.2	$Cu(OAc)_2$ (0.20)	NEt_3 (2.0)	dioxane	0	79	17	4	0	0
29	Br	1.2	$Cu(acac)_2$ (0.20)	NEt_3 (2.0)	dioxane	0	76	21	4	0	0

[a] Reaction conditions: *endo*-X-**1a/2a** (0.50 mmole), CuX (0.10 mmol), morpholine (0.6–1.5 mmol) in 0.50 mL of a solvent were heated at 100°C for 5 hours. The yields were determined by ^{19}F NMR using 4-fluoroanisole (0.20 mmole) as the internal standard; [b] *endo*-X-**1a/2a** were used as a mixtures with *exo*-X-**1a/2a** (*endo*-Cl-**1a**/*exo*-Cl-**1a** = 65/35, *endo*-Br-**2a**/*exo*-Br-**2a** = 62/38); [c] Reaction time was 24 hours; [d] Unidentified products; [e] Isolated yield;

Table 2. Solvent effect on the regioselectivity of ring-opening amination of 2-chloro-2-fluoro- and 2-bromo-2-fluoro-1-phenylcyclopropanes (**1b** and **2b**) with morpholine catalyzed by CuX [a]



1b (X = Cl);
2b (X = Br);

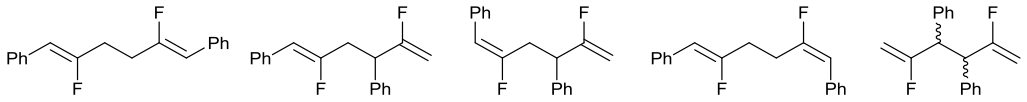
Z/E-**3ba**

9ba

Entry	X	Solvent	Yield **3ba**, (%)	*Z/E*	Yield **9ba**, (%)	Yield **4b**, (%) [b]
1	Cl	dioxane	80	75/25	6	14
2		DMSO	77	53/47	7	16
3		MeCN	80	58/42	11	9
4		MeOH	69	67/33	23	8
5		HFIP	63	73/27	30	4
6	Br	dioxane	97	85/15	1	2
7		DMSO	94	67/33	3	3
8		MeCN	96	71/29	4	0
9		MeOH	94	73/27	6	0
10		HFIP	87	76/24	8	5

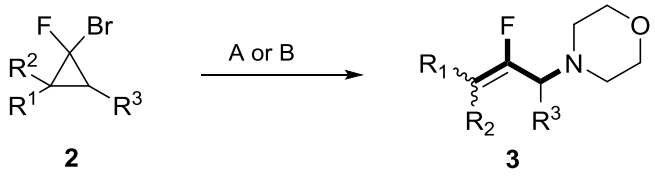
[a] Reaction conditions: **1b**/**2b** (0.50 mmole), CuBr (0.10 mmol), morpholine (1.5 mmol) in 0.50 mL of a solvent were heated at 100°C for 5 hours. In all the cases, full conversions of *syn*- and *anti*-**1b,2b** were achieved. The yields were determined by ^{19}F NMR using 4-fluoroanisole (0.20 mmole) as the internal standard;

[b] Isomers of **4b** formed (*Z,Z*-**4b**/α,*Z*-**4b**/α,*E*-**4b**/*Z,E*-**4b**/α,α-**4b**/α,α-**4b'** = 28/44/4/6/8/10):



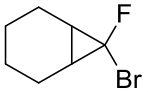
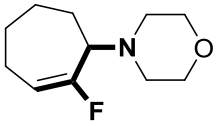
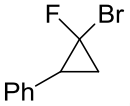
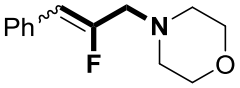
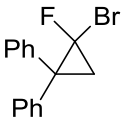
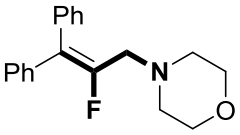
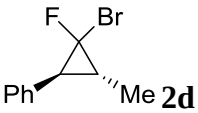
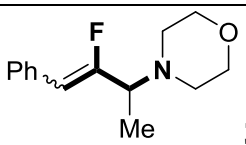
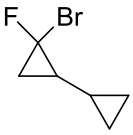
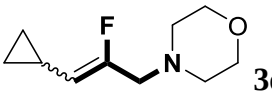
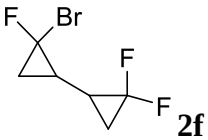
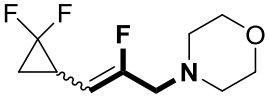
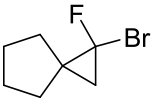
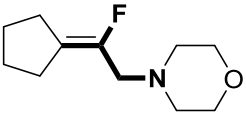
Z,Z-**4b** α,*Z*-**4b** α,*E*-**4b** *Z,E*-**4b** α,α-**4b,4b'**

Table 3. Synthesis of *N*-(2-fluoroallyl)morpholines



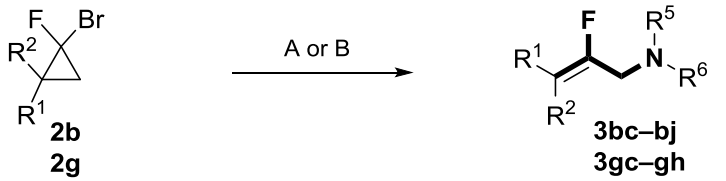
2 **3**

Reaction conditions:
A: morpholine (3 equiv.), CuBr (0.2 equiv.), dioxane, 100°C, 5 hours;
B: i) CuBr (0.2 equiv.), MeCN, 100°C, 5 hours;
ii) morpholine (3 equiv.), r.t., 2 hours;

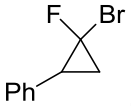
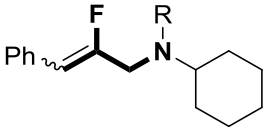
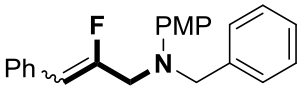
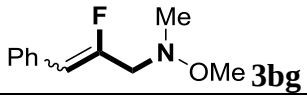
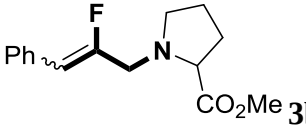
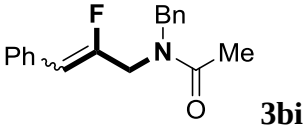
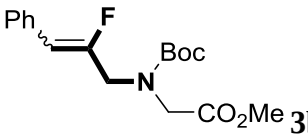
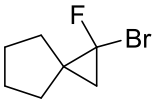
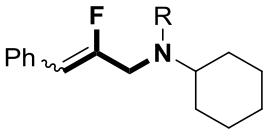
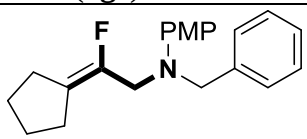
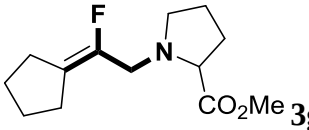
Entry	Cyclopropane	2-Fluoroallyl amine	Method A[a]		Method B[a]	
			Yield	*Z/E*	Yield	*Z/E*
1	 **2a**	 **3aa**	87%[b]	—	20%[b]	—
2	 **2b**	 **3ba**	95%	85/15	98%	93/7
3	 **2c**	 **3ca**	90%[c]	—	99%[c]	—
4	 **2d**	 **3da**	44%	> 99	30%	> 99
5	 **2e**	 **3ea**	81%	72/28	— [d]	—
6	 **2f**	 **3fa**	73%	57/43	— [d]	—
7	 **2g**	 **3ga**	77%[e]	—	— [d]	—

[a] Isolated yields and *Z/E* ratios; [b] Yield based on *endo*-Br-**2a**; [c] Reaction time was 72 hours; [d] Starting cyclopropanes **2e-g** reacted completely to give oligomeric products; [e] Reaction time was 24 hours;

Table 4. Synthesis of 2-fluoroallyl amines, amides, carbamates



Reaction conditions:
A: HNR^5R^6 or HNR^5R^6·HCl (1.2 equiv.), CuBr (0.2 equiv.), DIPEA (2–3 equiv.), dioxane, 100°C, 5 hours;
B: i) CuBr (0.2 equiv.), MeCN, 100°C, 5 hours;
ii) HNR^5R^6 (1.2 equiv.), K_2CO_3 (3 equiv.), MeCN, r.t., 2 hours;

Entry	Cyclopropane	2-Fluoroallyl amine	Method A[a]		Method B[a]	
			Yield	*Z/E*	Yield	*Z/E*
1	 **2b**	 R = Bn (**3bc**)	80%	82/18	95%	93/7
2		PMB (**3bd**)	76%	79/21	96%	93/7
3		PMP (**3be**)	85%	73/27	95%	93/7
4		 **3bf**	86%	68/32	96%	90/10
5		 **3bg**	65%[b]	71/29	85%	98/2
6		 **3bh**	87%	86/14	95%	93/7
7		 **3bi**	— [c]	—	86%[d]	96/4
8		 **3bj**	— [c]	—	83%[d]	96/4
9	 **2g**	 R = Bn (**3gc**)	59%[b]	—	— [e]	—
10		PMB (**3gd**)	56%[b]	—	— [e]	—
11		PMP (**3ge**)	62%[b]	—	— [e]	—
12		 **3gf**	64%[b]	—	— [e]	—
13		 **3gh**	53%[b]	—	— [e]	—

[a] Isolated yields and *Z/E* ratios; [b] DMSO as the solvent; [c] Allyl bromides **7b** (80–85%) and dimers

4b (15–20%) were observed; [d] 1.2 equiv. of NaH as the base; [e] **2g** reacted completely to give oligomeric products.