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α-Fluoroacrylonitriles: Horner–Wittig synthesis and conversion into 2-fluoroallylamines and C-(1-fluorovinyl)nitrones

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Abstract

α-Fluoroacrylonitriles **2** were synthesized in moderate to good yields by Horner–Wittig (HW) reaction of aldehydes and ketones with (diphenylphosphinoyl)fluoroacetonitrile (**1**), prepared in situ from commercially available fluoroacetonitrile and diphenylphosphinyl chloride. New synthetic applications of **2** are presented with the one-pot conversion into 2-fluoroallylamines **6** and *C*-(1-fluorovinyl)nitrones **8** through a diisobutylaluminum hydride (DIBALH)-reduction transimination protocol. The scope and limitations of this procedure are discussed.

Keywords: Horner–Wittig; Phosphine oxide; Fluorine; Nitrile; Transimination; Amine; Nitrone

1. Introduction

The concept of using fluorinated analogues of natural compounds has received much attention [1–3]. A class of compounds which can act as fluorinated building blocks are the α-fluoroacrylonitriles. On the one hand, the electron-poor double bond provides the possibility of applying both the Michael addition [4], and the Diels–Alder reaction [5]. On the other hand, the nitrile function can be converted into an ester through the Pinner reaction [6], or into an aldehyde by reduction with diisobutylaluminum hydride (DIBALH) and hydrolysis [7,8]. The resulting aldehydes were converted into mono-fluorinated dienes by Wittig reactions. However, applications have been hampered by the limited availability of α-fluoroacrylonitriles.

Various synthetic schemes have been designed for specific α-fluoroacrylonitriles [4,9–11]. The most general route is based on the Horner–Wadsworth–Emmons (HWE) reaction of a cyanofluoromethyl-substituted phosphonate with carbonyl compounds [7,8,12]. Reaction of fluoroacetonitrile with diethyl chlorophosphate in the presence of 2 eq. of base, followed by addition of aromatic aldehydes, yielded α-fluorocinnamonitrile derivatives with little stereoselectivity [8]. The likely intermediary phosphonate could not be identified [8]. The reaction failed for enolizable aldehydes, possibly caused by an unfortunate choice for the order of addition of the reagents [8]. Pure diethyl cyanofluoromethylphosphonate was obtained by electrophilic fluorination of diethyl cyanomethylphosphonate with commercially unavailable *N*-fluoro[bis(trifluoromethyl)]sulfonimide [12]. As it was found to be extremely sensitive to hydrolysis, it was best used immediately in the HWE reaction with aldehydes or ketones to prepare α-fluoroacrylonitriles in moderate yields, and with low (*E*)/(*Z*) selectivities [12].

The corresponding phosphine oxide was patented [13], but its application in the Horner–Wittig (HW) reaction has not been reported. In line with our research towards new α-fluorinated phosphine oxides [14,15], we were interested in its synthesis and properties.

2. Results and discussion

2.1. Synthesis of α-fluoroacrylonitriles

From a solution of fluoroacetonitrile and diphenylphosphinoyl chloride in THF, the anion of phosphine oxide **1** could be obtained as a clear, yellow or light-brown solution, by addition of 2 eq. of LDA or LiHMDS at −78 °C.[1] Reproducibility was better with LiHMDS. Reactions using LDA as the base were carried out on a 2 mmol scale, unless indicated otherwise; reactions using LiHMDS were

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[1] Formation of a dark solution resulted in lower yields, as well as in changes of stereoselectivity.

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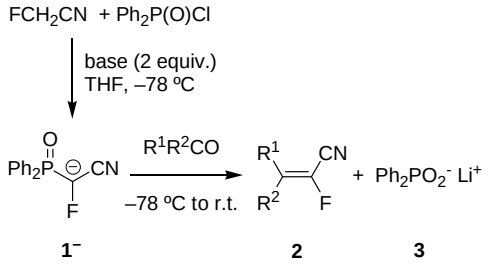


Scheme 1.

performed on a 6 mmol scale. After addition of the carbonyl compound $R^1R^2C{=}O$, the temperature was allowed to rise to room temperature. Gradually a suspension developed, signifying formation of α-fluoroacrylonitriles **2** and (poorly soluble) lithium diphenylphosphinate (**3**). This usually occurred between 0 and 10 °C, but at lower temperatures for **2d** (−5 °C), and **2l** (−40 °C). In contrast to the HWE synthesis, no heating is needed to obtain α-fluoroacrylonitriles **2** [8,12]. The general procedure is illustrated in Scheme 1. An attempt to isolate phosphine oxide **1** by quenching the reaction with acetic acid gave only impure compound in low yield.

After work-up, the crude mixture was analyzed by ^1H and ^{19}F NMR in order to determine the (*E*)/(*Z*) ratio of α-fluorinated α,β-unsaturated nitriles **2** formed. Subsequently, the compounds were purified by column chromatography. Results are listed in Table 1. For known compounds, literature data of the analogous HWE reactions are presented.

Yields of the HW reaction are comparable to those of the HWE reaction. The higher basicity of the phosphine oxide anion may explain the slightly lower yields found in some cases. Phenylacetaldehyde gave a very low yield of **2r**. In the major product, 2-fluoro-4-phenylbut-3-enenitrile (**4**), the double bond had shifted into conjugation with the phenyl group. A similar rearrangement has been noted for the reaction of the non-fluorinated analogue with 2-phenylpropanal [16]. Best yields were found for **2d** (73%) and **2l** (76%). In these cases, precipitation of phosphinate **3** showed the reaction to occur at relatively low temperatures, which obviously is advantageous. Possibly, anion $\mathbf{1}^-$ is unstable at temperatures over 0 °C.

The applicability of commercially available fluoroacetonitrile as a starting compound is considerably expanded by the HW approach described here, since in the HWE reaction it could only be successfully applied in the case of aromatic aldehydes [8]. Furthermore, diphenylphosphinoyl chloride is considerably less toxic than the acetylcholinesterase inhibitor diethyl chlorophosphate [17].

Stereoselectivity of the HW reactions is low, although sometimes clearly different from that of the HWE reaction. Benzaldehyde derivatives **2a–c**, and aliphatic aldehyde derivatives **2f–h** were formed with some preference for the (*Z*)-isomers, while with phosphonates, the outcome varied. Surprisingly, (*E*) selectivity was found for benzyloxyacetaldehyde derivative **2i**. With the remaining substrates, little or no stereoselectivity was found. The generally low and unpredictable stereoselectivities found

Table 1
Synthesis of α-fluoroacrylonitriles **2**

Entry	Substrate ($R^1R^2C{=}O$)	Base[a]	Yield (%)[b]	Yield HWE (%)[b]
a	Benzaldehyde	LDA[c]	53 (21:79)	54 (2:1) [12]
b	*p*-Methoxybenzaldehyde	LDA	50 (32:68)	52 (1:1) [8]
c	*p*-Tolualdehyde	LDA	46 (28:72)	51 (1:3) [8]
d	2-Pyridinecarboxaldehyde	LDA	73 (53:47)	53 (3:2) [12]
e	(*E*)-Cinnamaldehyde	LDA	45 (44:56)	38 (3:2) [12]
f	*n*-Heptanal	LDA	50 (26:74)	30 (1:1) [12]
g	3-Phenylpropanal	LDA	48 (26:74)	
g	3-Phenylpropanal	LiHDMS	51 (26:74)	
h	Cyclohexanecarboxaldehyde	LDA	42 (19:81)	
i	Benzyloxyacetaldehyde	LiHDMS	40 (79:21)	
j	Phenylacetaldehyde	LDA	42[d]	50 (2:3) [12]
k	*tert*-Butylcyclohexanone	LiHDMS	56	
l	1,4-Dioxaspiro[4,5]cyclodecan-8-one[e]	LiHDMS	76	
m	Cyclododecanone	LiHDMS	62	
n	Adamantanone	LiHDMS	31	
o	Acetophenone	LDA	44 (61:39)	58 (1:1) [12]
p	β-Ionone	LDA	41 (41:59)	46 (2:1) [12]
q	(*R*)-Carvone	LiHDMS	50 (68:32)[f]	
r[c]	α,α,α-Trifluoroacetophenone	LiHDMS	45[g] (50:50)	

[a] Reactions with LDA carried out on 2 mmol scale, with LiHMDS on 6 mmol scale.
[b] Yield of combined isomers, after column chromatography; (*E*)/(*Z*) ratio (determined from ^{19}F NMR of the crude product) given in parentheses.
[c] Reaction carried out on 1 mmol scale.
[d] Including rearranged product **4**; ***E*-1j**:***Z*-1j**:**4** = 22:22:56: original (*E*)/(*Z*) ratio unknown.
[e] 1,4-Cyclohexanedione mono-ethylene ketal.
[f] Stereochemistry determined on the basis of δ (H-3) and δ (F).
[g] Product could not be separated from starting ketone.

Table 2
Synthesis of 2-fluoroallylcarbamates **7** from α-fluoroacrylonitriles **2**

Entry	Substrate	Substrate (R^1R^2C=O) of **2**[a]	R^3	R^4	Yield (%)[b]
a	**2g**	3-Phenylpropanal (26:74)	PMB	Bn	64 (28:72)
b	**2i**	Benzyloxyacetaldehyde (79:21)	Me	*t*-Bu	35 (76:24)
c	**2k**	*tert*-Butylcyclohexanone	Me	*t*-Bu	53
d	**2k**	*tert*-Butylcyclohexanone	Bn	Bn	60[c]
e	**2k**	*tert*-Butylcyclohexanone	PMB	Bn	81[d]
f	**2l**	1,4-Dioxaspiro[4,5]cyclodecan-8-one	PMB	Bn	70[e]
g	**2m**	Cyclododecanone	Me	*t*-Bu	72[f]
h	**2m**	Cyclododecanone	Bn	*t*-Bu	n.d.[g]
i	**2m**	Cyclododecanone	PMB	Bn	65[h]
j	**2q**	(*R*)-Carvone (68:32)	PMB	Bn	77 (84:16)
k	**2r**	α,α,α-Trifluoroacetophenone (50:50)	Bn	Bn	50 (50:50)

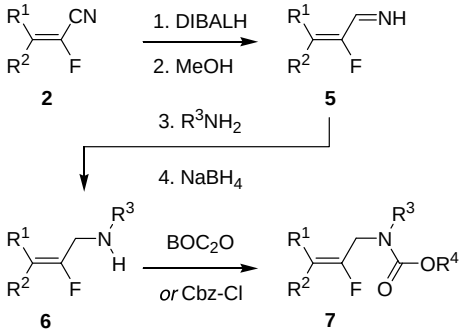
[a] (*E*)/(*Z*) ratio in parentheses.
[b] Yield of combined isomers, after column chromatography; (*E*)/(*Z*) ratio, determined by NMR-analysis of the crude product, in parentheses.
[c] Not obtained in pure form.
[d] Contained 10% of amine **6e**.
[e] Contained 13% of amine **6f**.
[f] Possibly contained some BOC_2O.
[g] Could not be separated from BOC_2O.
[h] Contained 13% of amine **6i**.

for α-fluoroacrylonitriles **2** contrast the high, consistent selectivities found for α-fluorinated acrylates [18], and vinyl sulfoxides [15]. Notably, the non-fluorinated diethyl phosphonate analogue, which was expected to be a good indicator for the stereochemistry of **1** [18], did not show much (*E*)/(*Z*)-selectivity either [16].

2.2. Transimination reactions with α-fluoroacrylonitriles

DIBALH reduction of **2** [7,8] presents an entry into a wide variety of products, using the DIBALH-reduction transimination protocol. This one-pot, multi-step method was developed in our laboratories for the derivatization of protected cyanohydrins [19–23].

The protocol is outlined in Scheme 2. Hydroalumination of the cyanide function in **2** afforded metallo-imines [7,8]. After addition of methanol, to destroy the excess of DIBALH and liberate the free primary imines **5**, addition of a primary amine R^3NH_2 (R^3: methyl, benzyl, *p*-methoxybenzyl (PMB)) led to transimination to the more stable secondary imine, under loss of NH_3. Finally, reduction of the imino group with sodium borohydride gave 2-fluoroallylamines **6**. Such amines have received attention from industrial research groups [24]. The corresponding carbamates were tested as peptide isosteres [25–27].



Scheme 2.

To facilitate work-up, crude amines **6** were converted directly into the *tert*-butoxycarbonyl (BOC, R^4: *t*-Bu) or benzyloxycarbonyl (Cbz, R^4: Bn) derivatives **7**, which were isolated as oils. Results are presented in Table 2.

The (*E*)/(*Z*) ratios of starting compounds **2** seemed not to be affected by transimination with primary amines, except for carvone derivative **2q**. Probably, in this case the intermediate imine underwent (*Z*) → (*E*) isomerization. Highest yields were obtained when transimination was performed with *p*-methoxybenzylamine (R^3: PMB), which also provides a convenient protecting group [28], and when benzyl chloroformate (R^4: Bn) was used to protect the amino function. In addition, pure products could be obtained more easily by column chromatography. Though yields were not as high as found for *O*-protected cyanohydrins [19–23], the reactions show that α-fluoroacrylonitriles **2** can be conveniently derivatized through the transimination procedure.[2]

Reaction of primary imines **5** with *N*-benzylhydroxylamine [29] yielded novel *C*-(1-fluorovinyl)nitrones **8** (Scheme 3). They were obtained, usually in high yields, as colorless solids. Results are listed in Table 3.

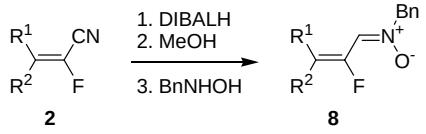
From aldehyde derivatives **2g** and **i**, nitrones **8** were formed as single isomers, with the carbon–carbon double bond in the (*Z*) configuration. This is probably due to failure of the (*E*)-isomers to react with benzylhydroxylamine. The yields can readily be explained by presuming a complete

[2] Imines can also be obtained by reaction of the nitrile with Grignard reagents (cf. [20,22,23]), but this procedure has not been investigated in the study presented here.

Table 3
Synthesis of *C*-(1-fluorovinyl)nitrones **8** from α−fluoroacrylonitriles **2**

Entry	Substrate[a]	Substrate (R^1R^2C=O) of **2**	Yield (%)[b]	(*E*)/(*Z*) (C=N)[c]
a	**2g** (26:74)	3-Phenylpropanal	79 (< 2:98)	< 2:98
b	**2i** (79:21)	Benzyloxyacetaldehyde	18 (< 2:98)	< 2:98
c	**2k**	*tert*-Butylcyclohexanone	81	10:90
d	**2l**	1,4-Dioxaspiro[4,5]cyclodecan-8-one	93	10:90
e	**2m**	Cyclododecanone	98	< 5:95 (20:80)
f	**2n**	Adamantanone	67	2:98 (4:96)

[a] (*E*)/(*Z*) ratio in parentheses.
[b] Yield of combined isomers, after column chromatography; (*E*)/(*Z*) ratio of C=C bond in parentheses (determined by ^{1}H NMR).
[c] For crude compound; for isolated compound in parentheses (if different) (determined by NMR).



Scheme 3.

conversion of the (*Z*)-isomers. Ketone derivatives **2k**–**n** reacted well, except α,α,α-trifluoroacetophenone derivative **2r**, which resisted transimination.

Nitrones **8e**, and to a lesser extent **8f**, which were formed as single isomers, showed some silica-induced (*Z*) → (*E*) isomerization.

Like their saturated analogues [30,31], the novel unsaturated α-fluorovinyl nitrones **8** are expected to engage in 1,3-dipolar cycloaddition reactions.

3. Conclusions

Horner–Wittig reaction of (diphenylphosphinoyl)fluoroacetonitrile (**2**), prepared in situ from commercially available compounds, with a wide range of carbonyl compounds yielded α-fluoroacrylonitriles **2** in moderate to good yields. No heating was required to complete the reaction. As in related Wittig-type syntheses, stereoselectivity was generally low. α-Fluoroacrylonitriles could be applied in one-pot transimination reactions to form 2-fluoroallylamines **6** and C-(1-fluorovinyl)nitrones **8**, usually in good yields. Straightforward conversion of α,β-unsaturated nitriles into asymmetric allylic amines is unprecedented.

4. Experimental

4.1. General procedures

Column chromatography was performed on Baker Silica Gel (0.063–0.200 mm). For TLC-analyses, Schleicher and Schuell F1500/LS 254 silica plates were used, visualized with ultraviolet light or $KMnO_4$. ^{1}H (200 MHz), ^{13}C (50 MHz), ^{31}P (80 MHz), and ^{19}F NMR (188 MHz) spectra were recorded on a Bruker AC-200 instrument, with $CDCl_3$ as the solvent. Chemical shifts are given relative to TMS (^{1}H, ^{13}C), $CFCl_3$ (^{19}F, external reference) or 85% phosphoric acid (^{31}P, external reference). Mass spectra were recorded on a Finnigan MAT 900 equipped with an electrospray interface (ESI), or with a Finnigan MAT TSQ70 triple quadrupole mass spectrometer equipped with a custom-made ESI. Exact masses were obtained on a Finnigan TSQ Quantum AM. GC/MS spectra were recorded on a Finnigan MAT ITD 700, coupled with a Packard 438A GC. Fluoroacetonitrile was obtained from Aldrich, and used without purification. $Ph_2P(O)Cl$, obtained from Acros Chimica, was used without purification; old batches were distilled before use. THF was distilled from $LiAlH_4$. Aldehydes were freshly distilled. Cyclododecanone was purified by column chromatography. LDA was prepared from *n*-BuLi (2.8 ml, 1.6 M in hexanes) and diisopropylamine (0.67 ml) in THF (5 ml) at 0 °C. Petroleum ether signifies the fraction boiling at 40–60 °C. ***CAUTION: Fluoroacetonitrile is highly toxic!***

4.2. (Diphenylphosphinoyl)fluoroacetonitrile (*1*)

Fluoroacetonitrile (0.11 ml, 2.0 mmol) and $Ph_2P(O)Cl$ (0.29 ml, 2.0 mmol) were dissolved in THF (25 ml) in an inert atmosphere. At −78 °C, LDA (2 eq.) or LiHMDS (4.0 ml, 1.0 M in THF) were added, leading to a yellow or light-brown solution of phosphine oxide anion $\mathbf{1}^-$. After stirring for 15 min at −78 °C, the reaction was quenched with HOAc (4 mmol) in Et_2O (10 ml). The temperature was raised to room temperature, and solvents were removed under reduced pressure. Column chromatography (eluent: EtOAc) yielded impure phosphine oxide **1**. During further attempts to purify the compound by column chromatography, it decayed.

^{1}H NMR: δ 5.67 (dd, 1H, $J_{FH} = 46.8$, $J_{HP} = 8.0$, H-2), 7.54–7.73 (m, 6H, H-arom.), 7.85–7.99 (m, 4H, H-arom.); ^{19}F NMR: δ −207.3; ^{31}P NMR: δ 25.7 (d, $J_{PF} = 52.5$).

4.3. Synthesis of α-fluoroacrylonitriles *2*, typical procedure

Anion $\mathbf{1}^-$ was prepared as described before. After stirring for 15 min at −78 °C, the carbonyl substrate (1.1 eq.) was added in portions (solids) or as a THF solution (ca. 5 ml), and

the temperature was allowed to rise to room temperature. After 1 h, saturated brine (15 ml) was added to the reaction mixture, and the aqueous layer was extracted with Et_2O (2× 10 ml). The combined organic layers were dried with $MgSO_4$. After filtration and evaporation of the solvents, the crude product was analyzed by ^1H and ^{19}F NMR. Column chromatography (eluent: petroleum ether/Et_2O, 10/1; or *n*-pentane/Et_2O 20/1; for **2d**: petroleum ether/Et_2O/Et_3N, 100/10/1; for **2l**: *n*-pentane/Et_2O, 20/1 → 4/1) yielded the pure α-fluoroacrylonitriles as (usually colorless) mixtures of isomers, with yields and (*E*)/(*Z*) ratios as listed in Table 1. α-Fluoroacrylonitriles **2** were difficult to analyze through LC/MS, causing exact mass analysis of new compounds **2i**, **k**, **m**, **q**, and **r** to fail. For all of these consecutive reactions (to carbamates **7** or nitrones **8**) led to products with an acceptable exact mass, indirectly proving the assumed structures.

4.4. 2-Fluoro-3-phenylacrylonitrile (**2a**) [12]

Oil; ^1H NMR: δ 6.46 (d, 0.8H, J_{FH} = 34.3, H-3, *Z*),[3] 7.07 (d, 0.2H, J_{FH} = 16.8, H-3, *E*), 7.36–7.44 (m, 3H, $H_{m,p}$), 7.52–7.59 (m, 2H, H_o); ^{13}C NMR: δ 112.9 (d, *J* = 51.3, C≡N, *E*), 113.1 (d, *J* = 47.3, C≡N, *Z*), 123.5 (d, J_{FC} = 7.6, CH-3, *Z*), 125.9 (d, J_{FC} = 24.4, CH-3, *E*), 128.3 (d, J_{FC} = 3.0, CH, *E*), 129.0 (CH_p, *Z*), 129.1 (CH_p, *E*), 130.1 (d, J_{FC} = 7.6, CH, *Z*), 130.4 (d, J_{FC} = 14.4, CH, *E*), 130.6 (d, J_{FC} = 3.0, CH, *Z*), 133.4 (C_i, *E*), 133.6 (C_i, *Z*); δ (CF, both isomers) not elucidated; ^{19}F NMR: δ −122.7 (*E*), −122.0 (*Z*).

4.5. 2-Fluoro-3-(4-methoxyphenyl)acrylonitrile (**2b**) [8]

Solid; ^1H NMR: δ 3.85 (s, 3H, Me), 6.39 (d, 0.7H, J_{FH} = 35.2, H-3, *Z*), 6.93 (d, 1.4H, *J* = 8.9, H_m, *Z*), 6.94 (d, 0.6H, *J* = 8.9, H_m, *E*), 7.01 (d, 0.3H, J_{FH} = 17.0, H-3, *E*), 7.51 (d, 1.4H, *J* = 8.9, H_o, *Z*), 7.55 (d, 0.6H, *J* = 8.7, H_o, *E*); ^{13}C NMR δ 55.2 (OMe), 112.9 (d, J_{FC} = 45.8, C≡N, *E*), 113.4 (d, J_{FC} = 45.8, C≡N, *Z*), 114.3 (CH_m, *Z*), 114.4 (CH_m, *E*), 120.1 (d, J_{FC} = 5.9, C_i, *E*), 122.6 (d, J_{FC} = 6.1, C_i, *Z*), 123.1 (d, J_{FC} = 6.1, CH-3, *Z*), 125.7 (d, J_{FC} = 24.4, CH-3, *E*), 129.9 (d, J_{FC} = 3.0, CH_o, *E*), 131.8 (d, J_{FC} = 9.2, CH_o, *Z*), 161.2 (C_p); δ (CF, both isomers) not elucidated; ^{19}F NMR: δ −127.3 (*E*), −126.5 (*Z*).

4.6. 2-Fluoro-3-(p-tolyl)acrylonitrile (**2c**) [8]

Oil; ^1H NMR: δ 2.39 (s, Me, *Z*), 2.41 (s, Me, *E*) {comb. 3H}, 6.42 (d, 0.7H, J_{FH} = 35.1, H-3, *Z*), 7.03 (d, 0.3H, J_{FH} = 16.8, H-3, *E*), 7.22 (d, 2H, *J* = 8.0, H_m), 7.45 (d, 1.3H, *J* = 8.0, H_o, *Z*), 7.48 (d, 0.7H, *J* = 8.0, H_o, *E*); ^{13}C NMR: δ 21.3 (Me, *E*), 21.6 (Me, *Z*), 112.6 (d, J_{FC} = 47.3, C≡N, *E*), 113.2 (d, J_{FC} = 45.8, C≡N, *Z*), 123.4 (d, J_{FC} = 6.1, CH-3, *Z*), 125.4 (d, J_{FC} = 24.4, CH-3, *E*), 125.1 (d, J_{FC} = 6.1, C_i, *E*), 127.1 (d, J_{FC} = 6.1, C_i, *Z*), 128.2 (d, J_{FC} = 3.0, CH, Tol, *E*), 129.6 (CH, Tol, *Z*), 129.7 (CH, Tol, *E*), 130.0 (d, J_{FC} = 7.6, CH, Tol, *Z*), 136.8 (d, J_{FC} = 415.0, CF, *E*), 137.0 (d, J_{FC} = 408.9, CF, *Z*), 141.2 (C_p, *Z*), 142.7 (C_p, *E*); ^{19}F NMR: δ −124.7 (*E*), −123.7 (*Z*).

4.7. 2-Fluoro-3-(2-pyridyl)acrylonitrile (**2d**) [12]

Solid; ^1H NMR: δ 6.71 (d, 0.4H, J_{FH} = 34.4, H-3, *Z*), 7.06 (d, 0.6H, J_{FH} = 16.1, H-3, *E*), 7.30–7.35 (m, 1H), 7.43 (d, 0.6H, *J* = 8.0, H-3′, *E*), 7.71–7.79 (m, 1.4H), 8.67–8.71 (m, 1H, H-6′); ^{13}C NMR: δ 111.9 (C≡N, *Z*), 112.8 (C≡N, *E*), 123.9, 124.0, 124.1, 124.2, 124.4, 124.6 (CH, Pyr/CH-3, 1 isomer), 125.8 (d, J_{FC} = 12.2, CH-3, 1 isomer), 132.6 (d, J_{FC} = 257.9, CF, *Z*), 133.5 (d, J_{FC} = 252.6, CF, *E*), 136.6 (CH, Pyr, 1 isomer), 136.7 (CH, Pyr, 1 isomer), 147.9 (d, J_{FC} = 10.7, C_i, *E*), 149.1 (d, J_{FC} = 7.6, C_i, *Z*), 149.7 (CH-6′, *E*), 149.9 (CH-6′, *Z*); ^{19}F NMR: δ −119.1 (*E*), −117.6 (*Z*).

4.8. 2-Fluoro-5-phenylpenta-2,4-dienenitrile (**2e**) [12]

Yellow oil; ^1H NMR: δ 6.39 (dd, 0.5H, J_{FH} = 30.7, *J* = 9.0, H-3, *Z*), 6.77–6.91 (m, 2H, H-4,5), 7.04 (dd, 0.5H, J_{FH} = 16.1, *J* = 11.0, H-3, *E*), 7.35–7.40 (m, 3H, $H_{m,p}$), 7.49 (m, 2H, H_o); ^{13}C NMR: δ 110.4 (d, J_{FC} = 45.8, C≡N, *E*), 113.0 (d, J_{FC} = 45.8, C≡N, *Z*), 117.0 (CH-5, *Z*), 117.9 (d, J_{FC} = 3.0, CH-5, *E*), 124.4 (d, J_{FC} = 10.7, CH-3, *Z*), 126.6 (d, J_{FC} = 36.9, CH-3, *E*), 127.1 (CH, Ph, *E*), 127.4 (CH, Ph, *Z*), 128.8 (CH_p, Ph), 129.4 (CH, Ph, *E*), 129.6 (CH, Ph, *Z*), 130.3 (d, J_{FC} = 248.7, CF), 132.7 (d, J_{FC} = 242.6, CF), 135.1 (C_i), 139.8 (d, J_{FC} = 4.6, CH-4, *Z*), 140.8 (d, J_{FC} = 10.7, CH-4, *E*); ^{19}F NMR: δ −127.8 (*E*), −126.9 (*Z*); GC/MS: m/z = 173 [M^+].

4.9. 2-Fluorononon-2-enenitrile (**2f**) [12]

Oil; ^1H NMR: δ 0.86–0.92 (m, 3H, CH_3), 1.29–1.55 (m, 8H, CH_2-5 to CH_2-8), 2.19–2.29 (m, 2H, CH_2-4), 5.78 (dt, 0.8H, J_{FH} = 32.9, *J* = 8.0, H-3, *Z*), 6.12 (dt, 0.2H, J_{FH} = 13.9, *J* = 8.8, H-3, *E*); ^{13}C NMR: δ 13.8 (CH_3), 22.4 (CH_2-8), 26.2 (CH_2-7, *E*), 27.8 (CH_2-6, *Z*), 28.4 (CH_2-5, *E*), 28.6 (CH_2-5, *Z*), 31.2 (CH_2-4), 110.9 (d, J_{FC} = 48.8, C≡N, *E*), 112.2 (d, J_{FC} = 48.8, C≡N, *Z*), 126.7 (d, J_{FC} = 15.3, CH-3, *E*), 127.1 (d, J_{FC} = 13.7, CH-3, *Z*), 132.0 (d, J_{FC} = 244.2, CF, *Z*), 132.5 (d, J_{FC} = 229.6, CF, *E*); ^{19}F NMR: δ −125.9 (*Z*), −124.0 (*E*).

4.10. 2-Fluoro-5-phenylpent-2-enenitrile (**2g**)

Oil; ^1H NMR: δ 2.54–2.65 (m, 2H, CH_2-4), 2.72–2.83 (m, 2H, CH_2-5), 5.75 (dt, 0.7H, J_{FH} = 32.5, *J* = 7.7, H-3, *Z*), 6.10 (dt, 0.3H, J_{FH} = 14.2, *J* = 8.4, H-3, *E*), 7.15–7.36 (m, 5H, Ph); ^{13}C NMR: δ 26.0 (CH_2-5, *Z*), 27.8 (CH_2-5, *E*), 33.7 (CH_2-4, *Z*), 34.4 (d, J_{FC} = 3.1, CH_2-4, *E*), 110.7 (d, J_{FC} = 48.8, C≡N, *E*), 112.1 (d, J_{FC} = 47.3, C≡N, *Z*), 125.5 (d, J_{FC} = 15.3, CH-3, *E*), 125.8 (d, J_{FC} = 12.2, CH-3, *Z*), 126.4 (CH_p), 128.1 (CH_o, *Z*), 128.2 (CH_o, *E*), 128.5 (CH_m), 132.1 (d, J_{FC} = 244.1, CF, *Z*), 132.7 (d,

[3] The coupling constant reported in literature is erroneous: cf. [12].

$J_{FC} = 241.1$, CF, *E*), 139.2 (C_i, *E*), 139.5 (C_i, *Z*); ^{19}F NMR: δ −122.8 (*E*), −124.5 (*Z*); GC/MS: $m/z = 176$ [$M^+ + H$], 154 [$M^+ - F$], 91 [$C_7H_7^+$]. HRMS calcd. for $C_{11}H_{11}FN$ ([$M + H$]$^+$): 176.0876, found: 176.0890.

4.11. 3-Cyclohexyl-2-fluoroacrylonitrile (**2h**)

Oil; ^{1}H NMR: δ 0.83–0.91 (m, 0.4H, CH_2-4′, *E*), 1.06–1.43 (m, 5.6H, CH_2-3′,5′; CH_2-4′, *Z*), 1.71–1.80 (m, 4H, CH_2-2′,6′), 2.22–2.36 (m, 0.2H, H-1′, *E*), 2.52–2.69 (m, 0.8H, H-1′, *Z*), 5.63 (dd, 0.8H, $J_{FH} = 33.6$, $J = 9.9$, H-3, *Z*), 5.99 (dd, 0.2H, $J_{FH} = 14.4$, $J = 10.8$, H-3, *E*); ^{13}C NMR: δ 25.0 (CH_2-3′,5′, *Z*), 25.2 (CH_2-4′, *E*), 25.3 (CH_2-4′, *Z*), 29.5 (CH_2-3′,5′, *E*), 31.4 (CH_2-2′,6′, *Z*), 32.2 (CH_2-2′,6′, *E*), 34.3 (CH-1′, *Z*), 36.0 (CH-1′, *E*), 110.9 (d, $J_{FC} = 47.3$, C≡N, *E*), 112.2 (d, $J_{FC} = 48.8$, C≡N, *Z*), 130.7 (d, $J_{FC} = 242.6$, CF, *Z*), 131.3 (d, $J_{FC} = 241.1$, CF, *E*), 131.4 (d, $J_{FC} = 13.7$, CH-3, *E*), 131.6 (d, $J_{FC} = 12.2$, CH-3, *Z*); ^{19}F NMR: δ −126.3 (*Z*), −126.2 (*E*); GC/MS: $m/z = 154$ [$M^+ + H$], 82 [$C_6H_{10}^+$], 67 [$C_5H_7^+$]. HRMS calcd. for $C_9H_{13}FN$ ([$M + H$]$^+$): 154.1032, found: 154.1030.

4.12. 4-Benzyloxy-2-fluorobut-2-enenitrile (**2i**)

Oil; ^{1}H NMR: δ 4.23 (dd, $J_{FH} = 2.6$, $J = 7.3$, CH_2-4, *E*), 4.26 (dd, $J_{FH} = 2.9$, $J = 6.6$, CH_2-4, *Z*) {comb. 2H}, 4.52 (s, $PhCH_2$, *Z*), 4.56 (s, $PhCH_2$, *E*) {comb. 2H}, 5.95 (dt, 0.2H, $J_{FH} = 32.9$, $J = 6.6$, H-3, *Z*), 6.26 (dt, 0.8H, $J_{FH} = 13.5$, $J = 7.3$, H-3, *E*), 7.35 (b, 5H, Ph); ^{13}C NMR: δ 61.6 (CH_2-4, *Z*), 63.5 (d, $J_{FC} = 7.6$, CH_2, *E*), 72.6 (CH_2Ph), 110.1 (d, $J_{FC} = 47.3$, C≡N), 122.4 (d, $J_{FC} = 16.8$, CH-3, *E*), 123.1 (d, $J_{FC} = 10.7$, CH-3, *Z*), 127.5 (CH_o, Ph), 127.7 (CH_p, Ph), 128.2 (CH_m, Ph), 133.7 (d, $J_{FC} = 245.7$, CF, *E*), 136.8 (C_i, Ph); δ (C≡N, CF, *Z*) not determined; ^{19}F NMR: δ −119.9 (*Z*), −118.6 (*E*); GC/MS: $m/z = 192$ [$M^+ + H$], 114 [$M^+ - C_6H_5$].

4.13. 2-Fluoro-4-phenylbut-2-enenitrile (**2j**) [12]

First fraction after chromatography, oil (yield: 18%); ^{1}H NMR: δ 3.56–3.63 (m, 2H, CH_2), 5.95 (dt, 0.5H, $J_{FH} = 31.8$, $J = 7.9$, H-3, *Z*), 6.29 (dt, 0.5H, $J_{FH} = 13.5$, $J = 8.6$, H-3, *E*), 7.16–7.39 (m, 5H, Ph); ^{19}F NMR: δ −125.7 (*Z*), −123.1 (*E*); GC/MS: $m/z = 161$ [M^+], 133 [$M^+ - HCN - H$], 115 [$M^+ - F - HCN$]. The second fraction consisted of main product (*E*)-2-fluoro-4-phenylbut-3-enenitrile (**4**): oil (yield: 24%); ^{1}H NMR: δ 5.69 (dd, 1H, $J_{FH} = 46.5$, $J = 7.3$, CH-2), 6.31 (ddd, 1H, $J_{FH} = 8.0$, $J = 16.1$, 7.3, H-3), 7.01 (dd, 1H, $J_{FH} = 5.5$, $J = 16.1$, H-4), 7.34–7.46 (m, 5H, Ph); ^{19}F NMR: δ −172.0; GC/MS: $m/z = 161$ [M^+], 142 [$M^+ - F$], 135 [$M^+ - CN$], 115 [$M^+ - F - HCN$]. HRMS calcd. for $C_{10}H_9FN$ ([$M + H$]$^+$): 162.0719, found: 162.0768.

4.14. (4-tert-Butylcyclohexylidene)fluoroacetonitrile (**2k**)

Oil; ^{1}H NMR: δ 0.87 (s, 9H, CMe_3), 0.98–1.29 (m, 3H), 1.75–2.17 (m, 4H), 2.64 (m, 1H), 2.97 (m, 1H); ^{13}C NMR: δ 25.9 (CH_2), 26.9 (CH_2), 27.0 (Me, *t*-Bu), 27.6 (CH_2), 29.0 (CH_2), 32.0 (C, *t*-Bu), 47.0 (CH), 111.4 (d, $J_{FC} = 47.3$, C≡N), 125.5 (d, $J_{FC} = 232.0$, CF), 139.2 (d, $J_{FC} = 12.2$, C-1); ^{19}F NMR: δ −135.2 (d, $J_{FH} = 2.9$); GC/MS: $m/z = 196$ [$M^+ + H$], 57 [$C_4H_9^+$].

4.15. (1,4-Dioxaspiro[4,5]dec-8-ylidene)fluoroacetonitrile (**2l**)

Oil; ^{1}H NMR: δ 1.71–1.82 (m, 4H, CH_2-6,10), 2.47–2.58 (m, 4H, CH_2-7,9), 3.98 (s, 4H, CH_2-2,3); ^{13}C NMR: δ 23.0 (CH_2-9), 26.1 (CH_2-7), 33.5 (CH_2-10), 34.1 (CH_2-6), 64.2 (CH_2-2,3), 106.9 (C-5), 111.2 (d, $J_{FC} = 47.3$, C≡N), 126.1 (d, $J_{FC} = 235.0$, CF), 136.9 (d, $J_{FC} = 12.2$, C-8); ^{19}F NMR: δ −132.5; GC/MS: $m/z = 197$ [M^+], 182 [$M^+ - Me$], 168 [$M^+ - CHO$]. HRMS calcd. for $C_{10}H_{13}FNO_2$ ([$M + H$]$^+$): 198.0930, found: 198.0979.

4.16. Cyclododecylidenefluoroacetonitrile (**2m**)

Oil; ^{1}H NMR: δ 1.35 (broad, 14H, CH_2-4 to CH_2–10), 1.52–1.64 (m, 4H, CH_2-3,11), 2.26–2.35 (m, 4H, CH_2-2,12); ^{13}C NMR: δ 22.2, 23.0, 23.3, 23.6, 23.8, 24.1, 24.6, 26.0, 29.4 (each CH_2), 111.7 (d. $J_{FC} = 47.3$, C≡N), 129.4 (d, $J_{FC} = 235.0$, CF), 139.2 (d, $J_{FC} = 9.2$, C-1); ^{19}F NMR: δ −127.8; GC/MS: $m/z = 224$ [$M^+ + H$].

4.17. Adamant-2-ylideneacetonitrile (**2n**)

Oil; ^{1}H NMR: δ 1.56–1.87 (m, 6H), 1.92–1.94 (m, 2H), 2.00–2.05 (m, 4H), 2.80 (b, 1H, CH), 3.16 (broad, 1H, CH); ^{13}C NMR: δ 27.4, 30.0, 33.0 (each CH), 36.1 (CH_2), 37.9 ($2CH_2$), 38.7 ($2CH_2$), 111.8 (d, $J_{FC} = 48.8$, C≡N), 122.7 (d, $J_{FC} = 231.9$, CF), 147.5 (d, $J_{FC} = 10.7$, C-2); ^{19}F NMR: δ −140.9; GC/MS: $m/z = 191$ [M^+]. HRMS calcd. for $C_{12}H_{15}FN$ ([$M + H$]$^+$): 192.1189, found: 192.1186.

4.18. 2-Fluoro-3-phenylbut-2-enenitrile (**2o**) [12]

Oil; ^{1}H NMR: δ 2.22 (d, 0.6H, $J_{FH} = 4.4$, CH_3, *E*), 2.30 (d, 0.4H, $J_{FH} = 4.4$, CH_3, *Z*), 7.42 (m, 5H, Ph); ^{13}C NMR: δ 16.3 (d, $J_{FC} = 3.0$, CH_3, *Z*), 17.8 (CH_3, *E*), 112.4 (d, $J_{FC} = 45.8$, C≡N), 127.4 (CH_o, *E*), 127.8 (d, $J_{FC} = 4.6$, CH_o, *Z*), 128.4 (CH_m, *E*), 128.7 (CH_m, *Z*), 128.7 (d, $J_{FC} = 242.6$, CF, *E*), 129.3 (d, $J_{FC} = 238.0$, CF, *Z*), 129.5 (CH_p), 132.8 (d, $J_{FC} = 9.2$, C-3, *E*), 133.3 (d, $J_{FC} = 3.0$, C_i, *E*), 134.1 (d, $J_{FC} = 3.0$, C_i, *Z*), 136.4 (d, $J_{FC} = 15.3$, C-3, *Z*); ^{19}F NMR: δ −127.9 (*E*), −124.6 (*Z*).

4.19. 3-Methyl-5-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2(E/Z),4(E)-pentadienenitrile (**2p**) [12]

Yellow oil; ^{1}H NMR: δ 1.02 (2 × CH_3, *Z*), 1.03 (2 × CH_3, *E*) {comb. 6H}, 1.43–1.50 (m, 2H, CH_2), 1.56–1.67 (m, 2H, CH_2), 1.72 (b, 3H, CH_3-2′), 2.01 (d, 2H, $J_{FH} = 3.6$, CH_3-3, *Z*), 2.05 (d, 1H, $J_{FH} = 3.6$, CH_3-3, *E*), 6.31 (dd, 0.6H,

$J = 16.1$, $J_{FH} = 2.2$, H-4, *Z*), 6.52 (m, 0.8H, H-4,5, *E*), 6.56 (m, 0.6H, H-5, *Z*); ^{13}C NMR: δ 10.3 (d, $J_{FC} = 3.0$, CH_3-3, *Z*), 13.1 (CH_3-3, *E*), 18.9 (CH_2-4′), 21.5 (CH_3-2′), 28.7 (2 × CH_3), 33.0 (CH_2-3′, *Z*), 33.1 (CH_2-3′, *E*), 34.0 (C-6′), 39.3 (CH_2-5′, *Z*), 39.4 (CH_2-5′, *E*), 111.9 (d, $J_{FC} = 38.2$, C≡N, *E*), 112.8 (d, $J_{FC} = 36.6$, C≡N, *Z*), 123.5 (d, $J_{FC} = 3.0$, CH-5, *E*), 125.6 (CH-5, *Z*), 131.2 (d, $J_{FC} = 7.6$, C-3, *E*), 132.2 (C, *E*), 133.0 (C, *Z*), 129.3 (d, $J_{FC} = 300.6$, CF, *E*), 133.8 (d, $J_{FC} = 15.3$, C-3, *Z*), 135.5 (d, $J_{FC} = 4.6$, CH-4, *E*), 135.6 (d, $J_{FC} = 10.7$, CH-4, *Z*), 136.6 (C, *Z*), 136.7 (C, *E*); δ (CF, *Z*) not elucidated; ^{19}F NMR: δ −133.1 (*E*), −132.3 (*Z*).

4.20. (R)-Fluoro-(5-isopropenyl-2-methylcyclohex-2-enylidene)acetonitrile (**2q**)

Oil; ^{1}H NMR: δ 1.75 (s, 3H, CH_3-3″), 1.99–2.03 (m, 3H, CH_3-2), 2.11 (s, 2H, CH_2), 2.16–2.24 (m, 2H, CH_2), 2.27–2.38 (m, 2H, CH_2), 2.61–2.71 (m, H-5′, *E*), 2.88–2.98 (m, H-5′, *Z*) {comb. 1H}, 4.76 (s, 1H, CH_2-1″), 4.82 (q, 1H, $J = 1.5$, CH_2-1″), 5.92 (m, H-3, *E*), 6.02 (m, H-3, *Z*) {comb. 1H}; ^{13}C NMR: δ 20.0 (CH_3-3″, *E*), 20.5 (CH_3-3″, *Z*), 21.5 (d, $J_{FC} = 9.2$, CH_3-2′), 28.3 (d, $J_{FC} = 6.1$, CH_2-6′, *Z*), 30.9 (CH_2-4′, *Z*) 31.3 (*E*), 31.5 (*E*), 39.3 (CH-5′, *Z*), 40.2 (CH-5′, *E*), 110.1 (CH_2-1″), 112.5 (d, $J_{FC} = 47.3$, C≡N), 124.9–130.0 (C's), 136.0 (CH-3′, *E*), 137.1 (CH-3′, *Z*), 146.4 (C-2″, *E*), 146.6 (C-2″, *Z*); ^{19}F NMR: δ −128.6 (*E*), −126.7 (*Z*); GC/MS: $m/z = 192$ [$M^+ + H$], 176 [$M^+ - Me$], 150 [$M^+ - Me - CN$], 136 [$M^+ - C_2H_5 - CN$].

4.21. 2,4,4,4-Tetrafluoro-3-phenylbut-2-enenitrile (**2r**)

Not separated from remaining α,α,α-trifluoroacetophenone; ^{1}H NMR: δ 7.33–7.56 (m, 5H, Ph); ^{13}C NMR: δ 109.3 (d, $J_{FC} = 44.2$, C≡N), 110.0 (d, $J_{FC} = 44.3$, C≡N), 125.4 (C), 125.6 (C), 128.7, 128.8, 129.1, 129.4, 129.5, 130.7, 131.1 (each CH), 131.7 (C), 132.1 (C), 136.5 (m, C-3), 137.6 (C-3); ^{19}F NMR: δ −111.5 (q, 1F, $J_{FF} = 14.1$, F-2, *Z*), −108.1 (q, 1F, $J_{FF} = 24.4$, F-2, *E*), −61.6 (d, 3F, $J_{FF} = 14.1$, F-4, *Z*), −61.2 (d, 3F, $J_{FF} = 24.4$, F-4, *E*); GC/MS: $m/z = 215$ [M^+].

4.22. Synthesis of 2-fluoroallylamines **6** and conversion into the corresponding carbamates **7**, typical procedures

To a solution of α-fluoroacrylonitrile **2** (1.0 mmol) in Et_2O (10 ml), DIBALH (1.0 M in hexanes, 1.6–2.0 eq.) was added through a syringe at −80 °C. After allowing the temperature to rise to 0 °C, the mixture was cooled to −100 °C, and MeOH (1 ml) was added. The appropriate amine (methylamine: 8 eq. (8.0N in ethanol); benzylamine: 5.5 eq. (neat); *p*-methoxybenzylamine: 3.2 eq. (neat)) was added after a few minutes, and the temperature was allowed to rise to room temperature. After 2.5 h, the mixture was cooled to −10 °C, $NaBH_4$ (6 eq.) was added, and stirring was continued for at least 3 h. The reaction mixture was poured into water, and extracted with Et_2O (3×). After washing the combined layers with saturated brine, and drying with $MgSO_4$, crude amine **6** was obtained after filtration and evaporation of the solvents. Amines **6** were immediately converted into the corresponding carbamates **7**. *BOC-protection*: *tert*-Butyl carbamates were prepared by dissolving crude amine **6** (ca. 1.0 mmol) in CH_2Cl_2 (10 ml), with Et_3N (1.0 ml) and excess di-*tert*-butyl dicarbonate (BOC_2O), and stirring overnight. Solvents were removed under reduced pressure; removal of remaining BOC_2O under high vacuum may be advantageous. *Cbz-protection*: Benzyl carbamates were prepared by overnight stirring of amine **6** in a biphasic system of CH_2Cl_2 and saturated aqueous $NaHCO_3$ (1/2, (v/v)) with excess benzyl chloroformate. Separation of the layers, and extraction of the aqueous layer with CH_2Cl_2, was followed by drying the organic layers with $MgSO_4$. Evaporation of the solvents gave crude carbamates **7**, which were purified by column chromatography (Et_2O/EtOAc, 95/5), and obtained as colorless oils, with yields and (*E*)/(*Z*) ratios as provided in Table 2.

4.23. Benzyl (E/Z)-(2-fluoro-5-phenylpent-2-enyl)-p-methoxybenzylcarbamate (**7a**)

^{1}H NMR: δ 2.22–2.30 (bm, 0.6H, CH_2-4, *E*), 2.35–2.45 (bm, 1.4H, CH_2-4, *E*), 2.66 (b, 2H, CH_2-5), 3.78 (s, 3H, OCH_3), 3.71–3.98 (bm, 2H, CH_2-1), 4.32–4.42 (bm, 2H, CH_2, PMB), 4.50–4.80 (bm, H-3), 5.18 (s, 2H, CH_2O), 6.80 (bd, 2H, $J = 8.0$, H_m, PMB), 7.00–7.32 (m, 7H, H-arom.); ^{13}C NMR: δ 24.8 (CH_2, *E*), 26.7 (b, CH_2, *Z*), 35.0 (CH_2, *E*), 35.7 (CH_2, *Z*), 41.4 (d, $J_{FH} = 29.0$, CH_2-1, 1 rotamer, *Z*), 41.9 (d, $J_{FH} = 24.3$, CH_2-1, 1 rotamer, *Z*), 45.5 (d, $J_{FH} = 32.0$, CH_2-1, 1 rotamer, *E*), 46.1 (d, $J_{FH} = 30.5$, CH_2-1, 1 rotamer, *E*), 48.4–48.7 (b, CH_2, PMB), 54.9 (OCH_3), 67.2 (CH_2O), 107.5 (d, $J_{FH} = 12.2$, CH-3, 1 rotamer, *E*), 108.0 (d, $J_{FH} = 13.2$, CH-3, 1 rotamer, *E*), 108.3–108.9 (m, CH-3, both rotamers, *Z*), 113.7 (CH_m, PMB), 125.8, 127.8–129.2 (CH, arom.), 136.4 (C), 140.6 (C, *Z*), 141.0 (C, *E*), 154.5, (d, $J_{FC} = 255.4$, CF), 156.0 (b, C=O), 158.8 (C_p, PMB); ^{19}F NMR: δ −116.2 (72%, *Z*), −109.8 (14%, *E*, 1 rotamer), −108.9 (14%, *E*, 1 rotamer); MS (ESI): $m/z = 456$ [$M^+ + Na$], 434 [$M^+ + H$]. HRMS calcd. for $C_{27}H_{29}FNO_3$ ([$M + H$]$^+$): 434.2131, found: 434.2142.

4.24. tert-Butyl (4-benzyloxy-2-fluorobut-2-enyl)methylcarbamate (**7b**)

^{1}H NMR: δ 1.45 (s, 6.75H, CH_3, *t*-Bu, *E*), 1.46 (s, 2.25H, CH_3, *t*-Bu, *Z*), 2.86 (s, 2.25H, NCH_3, *E*), 2.88 (s, 0.75H, NCH_3, *Z*), 3.99–4.16 (m, 4H, CH_2-1,4), 4.50 (s, 0.5H, $PhCH_2$, *Z*), 4.51 (s, 1.5H, $PhCH_2$, *E*), 4.96 (dt, 0.25H, $J_{FH} = 35.8$, $J = 7.7$, H-3, *Z*), 5.46 (dt, 0.75H, $J_{FH} = 20.5$, $J = 7.7$, H-3, *E*), 7.33 (b, 5H, Ph); ^{13}C NMR: δ 28.2 (CH_3, *t*-Bu), 34.1 (NCH_3), 45.1 (m, CH_2-1), 62.3 (d, $J_{FC} = 6.1$, CH_2-4, *Z*), 72.2 ($PhCH_2$), 79.9 (C, *t*-Bu), 104.4 (d, $J_{FC} = 12.2$, CH-3), 106.1 (m, CH-3), 127.6, 128.3, 128.7 (each CH, Ph), 137.8 (C_i, Ph); ^{19}F NMR: δ −112.6 (24%, *Z*),

−104.7 (38%, *E*, 1 rotamer), −103.8 (38%, *E*, 1 rotamer); MS (ESI): $m/z = 332$ $[M^+ + Na]$, 310 $[M^+ + H]$, 254 $[M^+ + H - C_4H_8]$, 210 $[M^+ + 2H - BOC]$. HRMS calcd. for $C_{17}H_{25}FNO_3$ ($[M + H]^+$): 310.1818, found: 310.1806.

4.25. *tert*-Butyl [2-(4-tert-butylcyclohexylidene)-2-fluoroethyl]methylcarbamate (**7c**)

^{1}H NMR: δ 0.84 (s, 9H, CH_3, *t*-Bu-4), 0.92–1.38 (m, 2H), 1.46 ({s, 9H, CH_3, *t*-BuO} + m, 1H), 1.52–1.67 (m, 1H), 1.82–1.89 (m, 3H), 2.47 (b, 1H), 2.85 (s, 3H, NCH_3), 2.77–2.92 (m, 1H), 4.03 (d, 2H, $J = 21.9$, CH_2-1); ^{13}C NMR: δ 25.5 (CH_2, *c*-Hex), 25.6 (CH_2, *c*-Hex), 27.4 (CH_3, *t*-Bu), 27.9 (CH_2, *c*-Hex), 28.0 (CH_2, *c*-Hex), 28.3 (CH_3, *t*-BuO), 32.3 (C, *t*-Bu-4), 33.6 (NCH_3), 44.3–45.6 (CH_2-1), 47.8 (CH-4′), 79.5 (C, *t*-BuO), 119.5 (b, C-1′), 147.5 (d, $J_{FC} = 244.1$, CF), 155.4 (C=O); ^{19}F NMR: δ −119.8, −119.3; MS (ESI): $m/z = 649$ $[(2M)^+ + Na]$, 336 $[M^+ + Na]$, 314 $[M^+ + H]$, 258 $[M^+ + H - C_4H_8]$, 238 $[M^+ - F - C_4H_8]$. HRMS calcd. for $C_{18}H_{33}FNO_2$ ($[M + H]^+$): 314.2495, found: 314.2439.

4.26. Benzyl benzyl-[2-(4-tert-butylcyclohexylidene)-2-fluoroethyl]carbamate (**7d**)

^{1}H NMR: δ 0.82 (s, 9H, CH_3), 0.89–1.01 (m, 1H), 1.55–1.84 (bm, 4H), 2.10–2.35 (bm, 1H), 1.81 (bd, $J = 11.7$, 1H), 4.02 (bd, 1H, $J_{FH} = 17.6$, CH_2-1, 1 rotamer), 4.12 (bd, 1H, $J = 21.9$, CH_2-1, 1 rotamer), 4.55 (bm, 2H, $PhCH_2N$), 5.18 (s, 1H, CH_2O, 2 rotamers), 5.18 (d, 0.5H, $J = 14.2$, CH_2O, 1 rotamer), 5.22 (d, 0.5H, $J = 14.2$, CH_2O, 1 rotamer), 7.28–7.78 (m, 10H, Ph); ^{13}C NMR: δ 25.1 (CH_2, *c*-Hex), 25.2 (CH_2, *c*-Hex), 27.1 (CH_3), 27.5 (CH_2, *c*-Hex), 27.7 (CH_2, *c*-Hex), 31.9 (C, *t*-Bu), 41.8 (d, $J_{FC} = 30.5$, CH_2-1, 1 rotamer), 42.5 (d, $J_{FC} = 30.5$, CH_2-1, 1 rotamer), 47.4 (CH-4′), 49.1 ($PhCH_2N$, 1 rotamer), 49.4 ($PhCH_2N$, 1 rotamer), 67.0 (CH_2O, 1 rotamer), 69.1 (CH_2O, 1 rotamer), 119.2–120.1 (2d, C-1′), 126.9–128.1 (CH-arom.), 136.3 (C, $PhCH_2O$), 137.2 (C, $PhCH_2N$), 146.5 (bd, $J = 244.9$, CF), 155.8 (C=O, 1 rotamer), 155.9 (C=O, 1 rotamer); ^{19}F NMR: δ −120.1, −119.0; MS (ESI): $m/z = 446$ $[M^+ + Na]$, 424 $[M^+ + H]$. HRMS calcd. for $C_{27}H_{35}FNO_2$ ($[M + H]^+$): 424.2652, found: 424.2675.

4.27. Benzyl [2-(4-tert-butylcyclohexylidene)-2-fluoroethyl]-p-methoxybenzylcarbamate (**7e**)

^{1}H NMR: δ 0.84, 0.85 (2 × *s*, 9H, CH_3), 0.87–1.17 (bm, 1H), 1.46–1.85 (bm, 5H), 2.16–2.39 (bm, 1H), 2.88 (bd, 1H, $J = 12.8$), 3.79 (s, 3H, OCH_3), 3.90–4.13 (2bm, 2H, CH_2-1), 4.47 (bs, CH_2, PMB), 5.18 (d, 1H, $J = 14.3$, $PhCH_2$), 5.21 (d, 1H, $J = 14.3$, $PhCH_2$), 6.82–6.85 (bm, 2H, H_m, PMB), 7.07–7.21 (bm, 2H, H_o, PMB), 7.33–7.36 (bm, 5H, Ph); ^{13}C NMR: δ 25.3 (CH_2, *c*-Hex), 25.4 (CH_2, *c*-Hex), 27.3 (CH_3, *t*-Bu), 27.7 (CH_2, *c*-Hex), 27.9 (CH_2, *c*-Hex), 32.1 (C, *t*-Bu), 41.7 (d, $J_{FC} = 32.0$, CH_2-1, 1 rotamer), 42.3 (d, $J_{FC} = 32.0$, CH_2-1, 1 rotamer), 47.6 (CH-4′), 48.6 (CH_2, PMB, 1 rotamer), 49.0 (CH_2, PMB, 1 rotamer), 54.8 (OCH_3), 67.1 ($PhCH_2$), 113.6 (CH_m, PMB), 119.5 (d, $J_{FC} = 13.7$, C-1′, 1 rotamer), 120.1 (d, $J_{FC} = 13.8$, C-1′, 1 rotamer), 127.6 (CH_o, PMB), 128.0, 128.1, 129.0 (each CH, Ph), 129.2 (C_i, PMB), 136.4 (C, Ph), 146.8 (d, $J_{FC} = 245.7$, CF), 155.9 (C=O, 1 rotamer), 156.1 (C=O, 1 rotamer), 158.7 (C_p, PMB); ^{19}F NMR: δ −120.4 (52%), −119.3 (48%); MS (ESI): $m/z = 476$ $[M^+ + Na]$, 454 $[M^+ + H]$, 320 $[M^+ - Cbz + 2H]$. HRMS calcd. for $C_{28}H_{37}FNO_3$ ($[M + H]^+$): 454.2757, found: 454.2766. Contained 10% of [2-(4-*tert*-butylcyclohexylidene)-2-fluoroethyl]-*p*-methoxybenzylamine (**6e**): ^{19}F NMR: δ −121.8; MS (ESI): $m/z = 320$.

4.28. Benzyl [2-(1,4-dioxaspiro[4,5]dec-8-ylidene)-2-fluoroethyl]-p-methoxybenzylcarbamate (**7f**)

^{1}H NMR: δ 1.58–1.72 (m, 4H, CH_2-6′,10′), 2.03–2.09 (bm, 50% of 2H, CH_2-9′, 1 rotamer), 2.20–2.28 (bm, 50% of 2H, CH_2-9′, 1 rotamer), 2.35–2.40 (bm, 2H, CH_2-7′), 3.79 (s, 3H, CH_3), 4.02–4.13 (m, 2H, CH_2-1), 4.48 (bs, 2H, CH_2, PMB), 5.19 (s, 2H, $PhCH_2$), 6.81–6.85 (bm, 2H, H_m, PMB), 7.06–7.18 (m, 2H, H_o, PMB), 7.33 (b, 5H, Ph); ^{13}C NMR: δ 22.2 (d, $J_{FC} = 7.6$, CH_2-9′), 24.5 (CH_2-7′), 34.2, 34.8 (CH_2-6′, CH_2-10′), 41.2–42.6 (m, CH_2-1), 48.6 (CH_2, PMB, 1 rotamer), 48.8 (CH_2, PMB, 1 rotamer), 54.9 (CH_3), 64.0 (CH_2-2′,3′), 67.2 ($PhCH_2$), 107.9 (C-5′), 113.7 (CH_m, PMB), 117.0–117.9 (m, C-8′), 127.6, 127.7, 128.2, 128.3 (b), 128.8 (b) (each CH), 129.0 (C_i, PMB), 136.3 (C, Ph), 147.5 (bd, $J_{FC} = 245.7$, CF), 155.9 (C=O, 1 rotamer), 156.0 (C=O, 1 rotamer), 158.7 (C_p, PMB); ^{19}F NMR: δ −118.4 (50%, 1 rotamer), −117.3 (50%, 1 rotamer); MS (ESI): $m/z = 495$ $[M^+ + K]$, 479 $[M^+ + Na]$. HRMS calcd. for $C_{26}H_{31}FNO_5$ ($[M + H]^+$): 456.2186, found: 456.2160. Probably contained 14% of [2-(1,4-dioxaspiro[4,5]dec-8-ylidene)-2-fluoroethyl]-*p*-methoxybenzylamine (**6f**): ^{1}H NMR: δ 3.81 (s, CH_3), 3.96 (s, CH_2-2′,3′), 6.90 (dd, $J = 8.6, 2.7$, H_m); ^{13}C NMR: δ 24.9, 25.0, 34.4 (CH_2-6′,7′,9′,10′), 50.2 (d, $J_{FC} = 30.5$, CH_2-1), 52.1 (CH_2, PMB), 107.7 (C-5′), 113.8 (CH_m, PMB), 113.9 (CH_m, PMB), 120.1 (d, $J_{FH} = 13.7$, C-8′), 129.4 (CH), 130.8 (CH), 159.6 (C_p, PMB); ^{19}F NMR: δ −119.5 (d, $J_{FH} = 20.7$).

4.29. *tert*-Butyl [2-(cyclododecylidene)-2-fluoroethyl]methylcarbamate (**7g**)

^{1}H NMR: δ 1.34 (b, 18H, *c*-Dod), 1.46 (s, 9H, CH_3, *t*-Bu), 2.07–2.18 (m, 4 H, CH_2-2′,12′, *c*-Dod), 2.85 (s, 3H, NCH_3), 4.06 (bd, 2H, $J_{FH} = 21.2$, CH_2); ^{13}C NMR: δ 22.3, 22.6, 23.2, 23.6, 23.9, 24.2, 24.7, 25.0 (each CH_2, *c*-Dod), 28.2 (CH_3, *t*-Bu), 33.4 (NCH_3), 44.9 (d, $J_{FC} = 30.5$, CH_2-1, 1 rotamer), 45.6 (d, $J_{FC} = 30.5$, CH_2-1, 1 rotamer), 79.4 (C, *t*-Bu), 119.3 (b, C-1′), 151.3 (bd, $J_{FC} = 250.2$, CF), 155.3 (C=O); ^{19}F NMR: δ −114.6 (50%), −113.2 (50%); MS (ESI): $m/z = 706$ $[(2M)^+ + Na]$, 364 $[M^+ + Na]$, 342 $[M^+ + H]$, 327 $[M^+ + H - Me]$, 286 $[M^+ + H - C_4H_8]$,

266 [$M^+ - F - C_4H_8$]. HRMS calcd. for $C_{20}H_{37}FNO_2$ ([$M + H$]$^+$): 342.2808, found: 342.2759.

4.30. tert-Butyl benzyl-[2-(cyclododecylidene)-2-fluoroethyl]carbamate (**7h**)

^{1}H NMR: δ 1.32 (b, 18H, *c*-Dod), 1.45 (bs, 9H, CH_3), 1.92 (b, 2H), 2.11 (b, 2H), 3.98 (bd, $J_{FH} = 21.2$), 4.08 (bd, $J_{FH} = 21.2$) {comb. 2H, CH_2-1}, 4.46 (b, 2H, $PhCH_2$), 7.20–7.30 (m, 5H, Ph); ^{13}C NMR: δ 22.2, 22.6, 23.2, 24.0, 24.9 (each CH_2, *c*-Dod), 27.0 (CH_3), 42.6 (d, $J_{FC} = 30.3$, CH_2-1), 49.1 (2b, $PhCH_2$), 79.6 (C, *t*-Bu), 119.3 (2d, C-1′), 126.8 (CH, Ph), 128.1 (CH, Ph), 137.9 (C, Ph), 153.2 (C=O); δ (CF) not determined; ^{19}F NMR: δ −114.9 (45%), −113.2 (55%); MS (ESI): $m/z = 857$ [$(2M)^+ + Na$], 835 [$(2M)^+ + H$], 440 [$M^+ + Na$], 418 [$M^+ + H$], 362 [$M^+ + H - C_4H_8$]. HRMS calcd. for $C_{26}H_{41}FNO_2$ ([$M + H$]$^+$): 418.3121, found: 418.3108.

4.31. Benzyl [2-(cyclododecylidene)-2-fluoroethyl]-p-methoxybenzylcarbamate (**7i**)

^{1}H NMR: δ 1.23–1.31 (b, 18H, *c*-Dod), 1.99–2.10 (bm, 4H, CH_2-2′,12′), 3.80 (s, 3H, CH_3), 4.04–4.15 (2d, 2H, $J_{FH} = 12.4$, CH_2-1), 4.48 (b, 2H, CH_2, PMB), 5.19 (s, 2H, CH_2O), 6.84 (bm, 2H, H_m, PMB), 7.09 (bd, 50% of 2H, H_o, PMB, 1 rotamer), 7.20 (bd, 50% of 2H, H_o, PMB, 1 rotamer), 7.33 (b, 5H, Ph); ^{13}C NMR: δ 22.0, 22.6, 23.0–24.9, 26.4, 27.0 (CH_2, *c*-Dod), 42.2 (d, $J_{FC} = 29.0$, CH_2-1, 1 rotamer), 42.8 (d, $J_{FC} = 33.1$, CH_2-1, 1 rotamer), 48.6 (CH_2, PMB, 1 rotamer), 49.1 (CH_2, PMB, 1 rotamer), 54.7 (CH_3), 67.1 (CH_2O), 113.5 (CH_m, PMB), 119.4 (d, $J_{FC} = 12.2$, C-1′, 1 rotamer), 119.8 (d, $J_{FC} = 12.2$, C-1′, 1 rotamer), 127.6–129.1 (CH, arom.), 130.8 (C_i, PMB), 136.3 (C, Ph), 150.5 (d, $J_{FC} = 245.7$, CF, 1 rotamer), 150.8 (d, $J_{FC} = 245.7$, CF, 1 rotamer), 155.8 (C=O, 1 rotamer), 156.0 (C=O, 1 rotamer), 158.6 (C_p, PMB); ^{19}F NMR: δ −115.8 (t, 49%, $J_{FH} = 21.3$, rotamer), −114.3 (t, 51%, $J_{FH} = 18.3$, rotamer); MS (ESI): $m/z = 504$ [$M^+ + Na$], 482 [$M^+ + H$]. HRMS calcd. for $C_{30}H_{41}FNO_3$ ([$M + H$]$^+$): 482.3070, found: 482.3063. *N*-protection incomplete, contained 13% of amine [2-(cyclododecylidene)-2-fluoroethyl]-*p*-methoxybenzylamine (**6i**): Identified signals provided; ^{1}H NMR: δ 1.76 (b, 4H, CH_2-2′,12′), 3.82 (s, 3H, CH_3); ^{13}C NMR: δ 51.0 (d, $J_{FC} = 29.0$, CH_2-1), 57.5 (CH_3), 113.7 (CH_m, PMB), 122.4 (d, $J_{FC} = 12.2$, C-1′), 125.8 (CH), 159.5 (C_p, PMB); ^{19}F NMR: δ −118.3 (t, $J_{FH} = 18.3$); MS could not confirm the nature of the side products.

4.32. Benzyl (R)-[2-(5-isopropenyl-2-methylcyclohex-2-enylidene)-2-fluoroethyl]-p-methoxybenzylcarbamate (**7j**)

^{1}H NMR: δ 1.65 (b, 3H, CH_3-2′), 1.98–2.01 (m, 3H, CH_3-3″), 2.16–2.36 (bm, 6H), 2.80 (bd, 1H, $J = 16.0$, H-5′), 3.79 (OCH_3, *E*), 3.81 (OCH_3, *Z*) {comb. 3H}, 3.93–4.20 (m, 2H, CH_2), 4.36–4.76 (m, 4H, $2CH_2$), 5.20 (s, 2H, CH_2O), 5.56 (b, 1H, H-3′, *E*), 5.60 (b, 1H, H-3′, *Z*), 6.82 (bd, $J = 8.0$, H_m, PMB, *E*), 6.90 (dd, $J = 8.8$, 1.5, H_m, PMB, *Z*) {comb. 2H}, 7.16–7.27 (m, 2H, H_o, PMB), 7.34–7.37 (m, 5H, Ph); ^{13}C NMR: δ 20.2 (CH_3, *E*), 20.4 (CH_3, *Z*), 23.1 (d, $J_{FC} = 12.2$, CH_3, *E*), 23.6 (CH_3, *Z*), 28.6 (d, $J_{FC} = 12.2$, CH_2-6′, *Z*), 29.5 (CH_2-4′, *Z*), 30.5 (d, $J_{FC} = 4.6$, CH_2-6′, *E*), 31.4 (CH_2), 40.2 (CH-5′, *Z*), 41.0 (CH-5′), 43.0 (d, $J_{FC} = 29.0$, CH_2-1, *E*, 1 rotamer), 43.6 (d, $J_{FC} = 29.0$, CH_2-1, *E*, 1 rotamer), 44.4 (m, CH_2-1, *Z*), 48.6 (CH_2, PMB, *E*, 1 rotamer), 49.1 (CH_2, PMB, *E*, 1 rotamer), 51.4 (d, $J_{FC} = 12.2$, CH_2, PMB, *Z*, 1 rotamer), 52.0 (d, $J_{FC} = 9.2$, CH_2, PMB, *Z*, 1 rotamer), 54.9 (OCH_3), 65.3 ($PhCH_2$, *Z*), 67.2 ($PhCH_2$, *E*), 109.1 (CH_2-1″), 113.7 (CH_m, PMB), 114.0 (CH_m, PMB), 127.7–128.6 (CH), 130.1 (d, $J_{FC} = 21.4$, CH-3′), 130.1 (C_i, PMB), 130.9 (d, $J_{FC} = 9.2$, CH-3′), 135.0 (C, Ph, *Z*), 136.4 (C, Ph, *E*), 144.7 (C-2″, *Z*), 148.3 (C-2″, *E*), 149.8 (d, $J_{FC} = 259.4$, CF), 150.1 (d, $J_{FC} = 245.7$, CF), 156.0 (b, C=O), 158.8 (C_p, PMB); ^{19}F NMR: δ −112.6 (12%, probably unprotected amine **6j**), −110.6 (36%), −109.3 (36%), −108.7 (8%), −107.2 (8%); MS (ESI): $m/z = 472$ [$M^+ + Na$], 450 [$M^+ + H$]. HRMS calcd. for $C_{28}H_{33}FNO_3$ ([$M + H$]$^+$): 450.2444, found: 450.2493.

4.33. Benzyl benzyl-(2,4,4,4-tetrafluoro-3-phenylbut-2-enyl)carbamate (**7k**)

^{1}H NMR: δ 3.87 (bd, 0.5H, $J_{FH} = 14.7$, CH_2-1, 1 rotamer), 3.99 (bd, 0.5H, $J_{FH} = 16.1$, CH_2-1, 1 rotamer), 4.36–4.44 (bm, 2.5H, $PhCH_2N$; CH_2-1, 1 rotamer), 4.60 (d, 0.5H, $J_{FH} = 5.8$, 1 rotamer), 5.15–5.17 (b, 2H, CH_2O), 6.99–7.45 (bm, 15H, H-arom.); ^{13}C NMR: δ 43.6–44.4 (CH_2-1), 46.0–48.1 (CH_2-1), 48.2 ($PhCH_2N$), 50.3–51.2 (CH_2-1), 66.8–72.5 (CH_2O), 126.2–130.0 (CH, Ph), 135.9–139.4 (C_i, C-3), 155.9, 156.2 (C=O); ^{19}F NMR (^{1}H decoupled): δ −102.1 (q, 55% of 1F, $J_{FF} = 24.4$, F-2, *Z*, 1 rotamer), −101.7 (q, 45% of 1F, $J_{FF} = 24.4$, F-2, *Z*, 1 rotamer), −97.0 (55% of 1F, $J_{FF} = 12.2$, F-2, *E*, 1 rotamer), −96.5 (45% of 1F, $J_{FF} = 12.2$ F-2, *E*, 1 rotamer), −59.7 (55% of 3F, $J_{FF} = 24.4$, F-4, *Z*, 1 rotamer), −59.3 (45% of 3F, $J_{FF} = 24.4$, F-4, *Z*, 1 rotamer), −57.0 (55% of 3F, $J_{FF} = 12.2$ F-4, *E*, 1 rotamer), −56.7 (45% of 3F, $J_{FF} = 12.2$, F-4, *E*, 1 rotamer); MS (ESI): $m/z = 909$ [$(2M)^+ + Na$], 466 [$M^+ + Na$], 444 [$M^+ + H$], 310 [$M^+ + H - Cbz$], 306 [$M^+ + Na - CF_3 - Bn$], 284 [$M^+ + H - CF_3 - Bn$]. HRMS calcd. for $C_{25}H_{22}F_4NO_2$ ([$M + H$]$^+$): 444.1587, found: 444.1564.

4.34. Synthesis of C-(1-fluorovinyl)nitrones **8**

With a solution of acrylonitrile **2** (1.0 mmol) in Et_2O (20 ml), reduction with DIBALH (2 eq.) was performed in similar manner as for amines **6**. After protonation with MeOH (1.0 ml), *N*-benzylhydroxylammonium chloride (1.1 eq.) was added, after which the mixture was allowed to reach room temperature, at which it was stirred for 3 h. The mixture was diluted with Et_2O, washed with water (10 ml) and brine (10 ml), and dried ($MgSO_4$). Column chromatography

(petroleum ether/Et_2O, 3/1 → 2/3) gave pure nitrones **8** as colorless solids, with yields and isomeric ratios as listed in Table 3. Silica-induced isomerization was noted for **8d** and **e**.

4.35. Benzyl-(2-fluoro-5-phenylpent-2-enylidene)amine N-oxide (*8a*)

^{1}H NMR: δ 2.50–2.62 (m, 2H, CH_2), 2.71–2.78 (m, 2H, CH_2), 4.93 (s, 2H, CH_2N), 6.94 (d, 1H, $J_{FH} = 8.0$, H-1), 7.04 (t, 0.5H, $J = 7.7$, H-3, other half eclipsed), 7.14–7.31 (m, 6.5H, H-arom., H-3, H-arom.), 7.40 (b, 4H, H-arom.); ^{13}C NMR: δ 25.8 (d, $J_{FC} = 4.6$, CH_2-4), 34.0 (CH_2-5), 70.3 (CH_2N), 116.0 (d, $J_{FC} = 10.7$, CH-3), 125.6 (CH, Ph), 126.5 (d, $J_{FC} = 58.0$, CH-1), 128.0 (CH, Ph), 128.6 (CH, Ph), 128.8 (CH, Ph), 128.9 (CH, Ph), 132.3 (C), 141.0 (C), 149.6 (d, $J_{FC} = 318.9$, CF); ^{19}F NMR: δ −121.6 (d, $J_{FH} = 30.5$; MS (ESI): $m/z = 306$ [$M^+ + Na$], 284 [$M^+ + H$]. HRMS calcd. for $C_{18}H_{19}FNO$ ([$M + H$]$^+$): 284.1451, found: 284.1493.

4.36. Benzyl-(2-fluoro-4-benzyloxybut-2-enylidene)amine N-oxide (*8b*)

^{1}H NMR: δ 4.29 (dd, 2H, $J_{FH} = 2.2$, $J = 7.3$, CH_2-4), 4.52 (s, 2H, $PhCH_2O$), 4.96 (s, 2H, CH_2N), 6.98 (d, 1H, $J_{FH} = 7.3$, H-1), 7.16 (t, 0.5H, $J = 7.3$, H-3, other half eclipsed), 7.26–7.39 (m, 6.5H, H-arom., H-3), 7.41 (b, 4H, H-arom.); ^{13}C NMR: δ 62.7 (d, $J_{FC} = 7.6$, CH_2N), 71.2 (CH_2-4), 72.2 ($PhCH_2O$), 112.7 (d, $J_{FC} = 11.2$, CH-3), 126.8 (d, $J_{FC} = 58.0$, CH-1), 127.6, 127.8, 128.3, 129.1, 129.4 (each CH, Ph), 132.0 (C), 137.9 (C); δ (CF) not elucidated; ^{19}F NMR, HRMS not measured.

4.37. Benzyl-[2-(4-tert-butylcyclohexylidene)-2-fluoroethylidene]amine N-oxide (*8c*)

^{1}H NMR: δ 0.83 (s, 8.1H, CH_3), 0.85 (s, 0.9 H, CH_3, *E*), 0.96–1.25 (m, 2H), 1.64–1.71 (bm), 1.84–1.88 (bm) {comb. 3H}, 2.20 (bd, 0.9H, $J = 13.2$), 2.45 (bd, 0.1H, $J = 14.2$, *E*), 2.97 (bd, 1H, $J = 14.2$), 4.94 (s, 2H, CH_2N), 7.03 (d, 0.9H, $J_{FH} = 12.4$, H-1), 7.28–7.36 (m, 2H, Ph), 7.37–7.49 (m, 3H, Ph), 7.57 (d, 0.1H, $J_{FH} = 21.5$, H-1, *E*); ^{13}C NMR: δ 26.0 (CH_2), 26.2 (CH_2), 27.2 (CH_3), 27.6 (CH_2), 28.3 (CH_2), 32.1 (C, *t*-Bu), 47.4 (CH-4′, *c*-Hex), 70.6 (CH_2N), 125.8 (d, $J_{FC} = 27.5$, CH-1), 127.2–128.9 (CH-arom.), 132.7 (C, Ph); δ (C-1′, CF) not assigned; ^{19}F NMR: δ −128.6 (90%, *Z*), −126.0 (10%, *E*); MS (ESI): $m/z = 607$ [$(2M)^+ + H$], 326 [$M^+ + Na$], 304 [$M^+ + H$]. HRMS calcd. for $C_{19}H_{27}FNO$ ([$M + H$]$^+$): 304.2077, found: 304.2062.

4.38. Benzyl-[2-(1,4-dioxaspiro[4,5]dec-8-ylidene)-2-fluoroethylidene]amine N-oxide (*8d*)

^{1}H NMR: δ 1.67–1.74 (m, 4H, CH_2-6′,10′), 2.15–2.20 (m, 1.8H, CH_2-9′), 2.28–2.35 (m, 0.2H, CH_2-9′, *E*), 2.46–2.52 (m, 2H, CH_2-7′), 3.95 (s, CH_2-2′,3′), 3.97 (s, CH_2-2′,3′) {comb. 4H}, 4.95 (s, 1.8H, CH_2N), 5.19 (s, 0.2H, CH_2N, *E*), 7.04 (d, 0.9H, $J_{FH} = 11.7$, H-1), 7.34–7.48 (m, 5H, Ph), 7.55 (d, 0.1H, $J_{FH} = 20.8$, H-1, *E*); ^{13}C NMR: δ 23.1 (d, $J_{FC} = 6.1$, CH_2-9′), 25.2 (d, $J_{FC} = 3.0$, CH_2-7′), 34.1, 34.4 (CH_2-6′, CH_2-10′), 64.1 (CH_2-2′,3′), 70.8 (CH_2N), 107.9 (C-5′), 125.4 (d, $J_{FC} = 32.0$, CH-1′), 125.6 (C-8′), 128.3 (CH, Ph, *E*), 128.8 (2CH, Ph), 128.9 (CH, Ph), 132.6 (C, Ph), 142.2 (d, $J_{FC} = 236.5$, CF); ^{19}F NMR: δ −125.5 (90%, *Z*), −123.1 (10%, *E*); MS (ESI): $m/z = 633$ [$(2M)^+ + Na$], 611 [$(2M)^+ + H$], 328 [$M^+ + Na$], 306 [$M^+ + H$]. HRMS calcd. for $C_{17}H_{21}FNO_3$ ([$M + H$]$^+$): 306.1505, found: 306.1496.

4.39. Benzyl-[2-(cyclododecylidene)-2-fluoroethylidene]amine N-oxide (*8e*)

Formed as a single isomer, isomerizing to a 4:1 mixture during purification by column chromatography: ^{1}H NMR: δ 1.17–1.44 (b, 16H, CH_2), 1.52 (m, 1.6H, CH_2, *Z*), 1.55 (m, 0.4H, CH_2, *E*), 1.96 (dd, 1.6H, $J = 7.3$, 5.8, CH_2, *Z*), 2.10 (t, 0.4H, 7.0, CH_2, *E*), 2.24 ({dt, 1.6H, $J = 7.3$, 2.2, CH_2, *Z*} + {m, 0.4H, CH_2, *E*}), 4.94 (s, 1.6H, CH_2Ph, *Z*), 5.20 (s, 0.4H, CH_2Ph, *E*), 6.99 (d, 0.8H, $J_{FH} = 14.6$, H-1, *Z*), 7.35–7.45 (m, 5H, Ph), 7.56 (d, 0.2H, $J_{FH} = 21.2$, H-1, *E*); ^{13}C NMR: δ 22.3, 22.7, 23.3, 23.5, 23.8 (3×), 24.8 (CH_2-2 to CH_2-11), 26.0 (d, $J_{FC} = 4.6$, CH_2-12), 27.4 (CH_2-1), 65.6 (d, $J_{FC} = 12.2$, CH_2Ph, *E*), 70.6 (CH_2Ph, *Z*), 125.6 (d, $J_{FC} = 24.4$, CH-1, *Z*), 127.4 (d, $J_{FC} = 21.4$, CH-1, *E*), 128.2 (CH, Ph, *E*), 128.5 (CH, Ph), 128.6 (CH, Ph), 128.9 (CH, Ph), 132.6 (C_i, Ph, *Z*), 133.3 (C, Ph, *E*), 144.0 (d, $J_{FC} = 238.0$, CF, *E*), 145.8 (d, $J_{FC} = 241.1$, CF, *Z*); ^{19}F NMR: δ −125.2 (*Z*), −121.9 (*E*); MS (ESI): $m/z = 663$ [$(2M)^+ + H$], 332 [$M^+ + H$]. HRMS calcd. for $C_{21}H_{31}FNO$ ([$M + H$]$^+$): 332.2390, found: 332.2372.

4.40. [2-(Adamant-2-ylidene)-2-fluoroethylidene]benzylamine N-oxide (*8f*)

Formed as a single isomer, isomerizing slightly during purification by chromatography; ^{1}H NMR: δ 1.76–1.94 (bm, 12H, Ada), 2.42 (b, 1H, CH), 2.67 (b, CH, *E*), 3.16 (b, 1H, CH), 4.94 (s, 2H, CH_2N), 5.30 (s, CH_2N, *E*), 7.04 (d, 1H, $J_{FH} = 13.2$, H-1), 7.34–7.49 (m, 5H, Ph), 7.55 (d, $J_{FH} = 21.9$, H-1, *E*); ^{13}C NMR: δ 27.6 (CH, *E*), 27.7 (CH-3′,5′), 29.4 (d, $J_{FC} = 6.1$, CH-1′), 31.9 (d, $J_{FC} = 3.0$, CH-3′), 36.5 (CH_2-6′), 38.2 ($2CH_2$), 38.6 ($2CH_2$), 70.8 (CH_2N), 125.5 (d, $J_{FC} = 27.5$, CH-1), 127.0 (d, $J_{FC} = 23.6$, CH-1, *E*), 128.3 (CH, Ph, *E*), 128.4, 128.8, 129.0 (CH, Ph), 132.8 (C), 137.0 (C-2′), 139.4 (d, $J_{FC} = 228.9$, CF); ^{19}F NMR: δ −133.4 (94%), −130.3 (6%); MS (ESI): $m/z = 599$ [$(2M)^+ + H$], 300 [$M^+ + H$]. HRMS calcd. for $C_{19}H_{23}FNO$ ([$M + H$]$^+$): 300.1764, found: 300.1781.

References

[1] J.T. Welch, Tetrahedron 43 (1987) 3123–3197.
[2] G. Resnati, Tetrahedron 49 (1993) 9385–9445.
[3] P. Bey, J.R. McCarthy, I.A. McDonald, in: J.T. Welch (Ed.), Effects of Selective Fluorination on Reactivity, ACS Symposium Ser. 456, Washington, DC, 1991.
[4] V. Tolman, P. Špronglová, Coll. Czech. Chem. Commun. 48 (1983) 319–326.
[5] V.A. Al'bekov, A.F. Benda, A.F. Gontar, G.A. Sokol'skii, I.L. Knunyants, Bull. Acad. Sci. USSR, Div. Chem. Sci. (1988) 765–769.
[6] B.L. Dyatkin, S.R. Sterlin, L.G. Zhuravkova, B.I. Martynov, I.L. Knunyants, J. Org. Chem. USSR 9 (1973) 1810–1814.
[7] E. Baader, W. Bartmann, G. Beck, P. Below, A. Bergmann, H. Jendralla, K. Keßeler, G. Wess, Tetrahedron Lett. 30 (1989) 5115–5118.
[8] T.B. Patrick, S. Nadji, J. Fluorine Chem. 49 (1990) 147–150.
[9] J. Cousseau, P. Albert, Bull. Soc. Chim. Fr. (1986) 910–915.
[10] L.S. Boguslavskaya, I.Y.U. Panteleeva, T.V. Morozova, A.V. Kartashov, N.N. Chuvatkin, Russ. Chem. Rev. 59 (1990) 906–917.
[11] N. Matsuo, A.S. Kende, Bull. Chem. Soc. Jpn. 64 (1991) 3193–3195.
[12] Z.-Q. Xu, D.D. DesMarteau, J. Chem. Soc. Perkin Trans. 1 (1992) 313–315.
[13] J. Tessier, J.P. Demoute, T. Van Thuong, Eur. Pat. Appl. EP 244 (1987) 417;
J. Tessier, J.P. Demoute, T. Van Thuong, Chem. Abstr. 107 (1987) 96889y.
[14] J.H. van Steenis, A. van der Gen, Eur. J. Org. Chem. (2001) 897–910.
[15] J.H. van Steenis, P.W.S. Boer, H.A. van der Hoeven, A. van der Gen, Eur. J. Org. Chem. (2001) 911–918.
[16] G. Etemad-Moghadam, J. Seyden-Penne, Synth. Commun. 14 (1984) 565–573.
[17] R.E. Lenga (Ed.), The Sigma–Aldrich Library of Chemical Safety Data, 2-Volume Set, second ed., Sigma–Aldrich, Milwaukee, WI, 1988.
[18] G. Etemad-Moghadam, J. Seyden-Penne, Bull. Soc. Chim. Fr. (1985) 448–454.
[19] P. Zandbergen, A.M.C.H. van den Nieuwendijk, J. Brussee, A. van der Gen, C.G. Kruse, Tetrahedron 48 (1992) 3977–3982.
[20] E.F.J. de Vries, P. Steenwinkel, J. Brussee, C.G. Kruse, A. van der Gen, J. Org. Chem. 58 (1993) 4315–4325.
[21] A.M.C.H. van den Nieuwendijk, J.C.J. Benningshof, V. Wegmann, R.A. Bank, J.M. te Koppele, J. Brussee, A. van der Gen, Bioorg. Med. Chem. Lett. 9 (1999) 1673–1676.
[22] J. Brussee, A. van der Gen, Recl. Trav. Chim. Pays-Bas 110 (1991) 25–26.
[23] A.M.C.H. van den Nieuwendijk, E.G.J.C. Warmerdam, J. Brussee, A. van der Gen, Tetrahedron: Asymmetry 6 (1995) 801–806.
[24] T. Allmendinger, C. Angst, H. Karfunkel, J. Fluorine Chem. 72 (1995) 247–253.
[25] T. Allmendinger, P. Furet, E. Hungerbühler, Tetrahedron Lett. 31 (1990) 7297–7300.
[26] L.G. Boros, B. de Corte, R.H. Gimi, J.T. Welch, Y. Wu, R.E. Handschumacher, Tetrahedron Lett. 35 (1994) 6033–6036.
[27] P.A. Bartlett, A. Otake, J. Org. Chem. 60 (1995) 3107–3111.
[28] P.J. Kocieński, in: D. Enders, R. Noyori, B.M. Trost (Eds.), Protecting Groups, Thieme, Stuttgart, 1994, pp. 223–227.
[29] E. Hulsbos, J. Marcus, J. Brussee, A. van der Gen, Tetrahedron: Asymmetry 8 (1997) 1061–1067.
[30] M. Ihara, T. Kawabuchi, Y. Tokunaga, K. Fukumoto, Heterocycles 40 (1995) 97–100.
[31] M. Ihara, Y. Tanaka, N. Takahashi, Y. Tokunaga, K. Fukumoto, J. Chem. Soc. Perkin Trans. 1 (1997) 3043–3052.