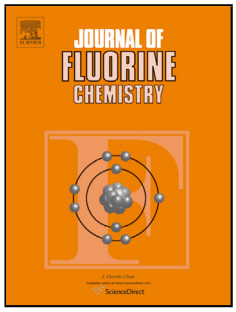

Title: Synthesis and pK_a Values of 2-(3- and 4-Pentafluorosulfanylphenyl)-2-fluorocyclopropylamines

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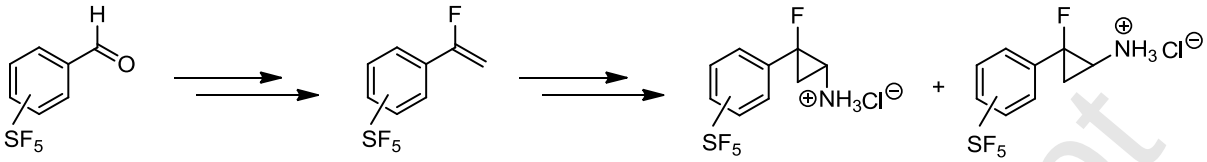
Graphical Abstract



Synopsis:

3- and 4-SF_5-substituted 2-fluoro-2-phenylcyclopropylamines were synthesized from the corresponding benzaldehydes in 7 steps and their pK_a values were determined.

Synthesis and pK_a Values of 2-(3- and 4-Pentafluorosulfanylphenyl)-2-fluorocyclopropylamines

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Abstract:

Starting from 3- and 4-pentafluorosulfanylbenzaldehydes, a series of *cis*- and *trans*-2-aryl-2-fluorocyclopropylamines bearing an SF_5 group in 3- or 4-position of the aryl ring were synthesized in 7 steps *via* the corresponding cyclopropanecarboxylic acids. While the pK_a values of the carboxylic acids are very little depending on the stereochemistry at the cyclopropane ring and the regiochemistry of the SF_5-substituents in the aryl ring, the pK_a of the corresponding 2-fluorocyclopropylamines is strongly dependent on the stereochemistry at the three-membered ring due to hyperconjugative effects of the C–F and the C–N bonds. Again, the regiochemistry of SF_5 substitution in the phenyl ring has almost no influence.

Keywords: α-Fluorostyrenes, 2-fluorocyclopropanecarboxylic acids, 2-fluorocyclopropylamines, pentafluorosulfanyl(SF5) substituent, pK_a values, stereochemistry, regiochemistry.

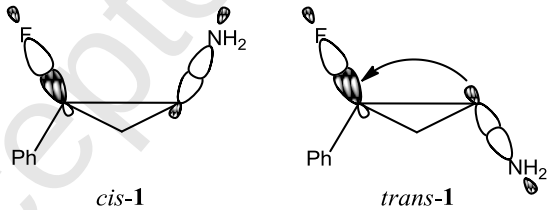
1. Introduction

The implementation of a pentafluorosulfanyl(SF_5) group into a molecule puts - just like the trifluoromethyl(CF_3) group - particular electronic effects on the compound [1]. Therefore, the SF_5 group is often dubbed as the "super-trifluoromethyl group" [2]. Comparing the electronegativity, the thermal and chemical stability, the lipophilicity or the steric demand, the SF_5 group is prevailing the CF_3 group in all these terms providing interesting possibilities for changing physicochemical properties and modifying biological effects of a molecule [3].

Looking at the electronic influence of the SF_5 substituent the electron withdrawing effect is similar to that of the CF_3 group regarding the 1s photoelectron spectra [4]. But the group electronegativity of the SF_5 substituent is higher with 3.65 compared to 3.36 of the CF_3 group [5]. Another important effect of the SF_5 group is its steric demand, which is close to that of the *tert*-butyl group and so being considerably bigger than that of a CF_3 group. However, CF_3

and the SF_5 substituted compounds often show very similar behavior in enzyme inhibition because they both represent a highly fluorinated surface having similar electrostatic properties, although the shapes appear different. While the CF_3 group appears as an inverted cone of electron density, the SF_5 group has a pyramidal electron density. Due to these facts, replacement of a CF_3 group with an SF_5 group is used to modify agrochemicals such as Trifluralin or pharmaceuticals like Fluoxetine, Fenfluramine and several others [6].

It is well known that the introduction of a fluorine atom or a fluorinated substituent close to another functional group has a great influence on the physicochemical properties such as pK_a and log D values or the dipole moment of the particular compound, which has unique relevance for medicinal chemistry and chemical biology [7-11]. In a previous work we reported about the effects of a monofluoro substituent and its relative configuration on the pK_a values of cyclopropylamines with fluorine taking a fixed position *cis* or *trans* to the amino function (Figure 1). Placing the fluorine atom in *trans*-position to the amino group results in a significantly more acidic compound compared to the *cis*-isomer **1** and to the corresponding fluorine free parent compounds. Based on computational studies, this was assigned to hyperconjugative overlapping of corresponding molecule orbitals and an electron-transfer from the σ(C–N) → σ*(C–F) in *trans*-**1** (Figure 1) is possible. Such an overlapping is not possible in *cis*-**1** resulting in a higher electron density of the amino group and hence in a higher *p*K$_a$ value [12].



cis-**1** pK_a = 7.35 *trans*-**1** pK_a = 6.98

Figure 1. Hypothetic orbital interactions in fluorinated phenylcyclopropylamine (*cis*/*trans* correlates to fluorine and the amino group) [9].

Furthermore, we found a decrease in the pK_a-values by substitution of the phenyl's *para*-position in fluorinated tranylcypromine analogues with electron withdrawing groups like fluorine, chlorine and the CF_3 group, which correlated with the *in vitro* activity of these compounds as monoamine oxidase inhibitors [13].

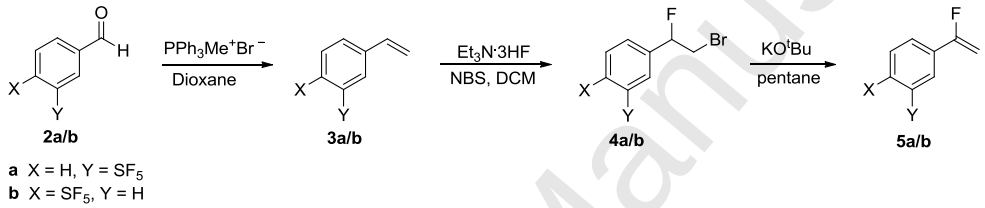
Within this paper, we report on synthesis and pK_a values of diastereomeric *meta*- and *para*-SF_5-substituted 2-aryl-2-fluorocyclopropanecarboxylic acids and corresponding

cyclopropylamines. The effects of combination of a fluorinated cyclopropane ring and the electron withdrawing SF_5 group in the phenyl ring will be discussed.

2. Results and discussion

2.1. Synthesis

Similarly to our earlier report [14], we synthesized 2-aryl-2-fluorocyclopropylamines bearing an SF_5 substituent in the 3- or 4-position. The synthetic sequence followed the route starting with a Wittig olefination of the commercially available 3- and 4-SF_5 substituted benzaldehydes **2a** and **2b**. Bromofluorination of the obtained styrenes **3a** and **3b** led to the bromofluorides **4a** and **4b**, which gave the α-fluorostyrenes **5a** and **5b** in good yields by HBr elimination (Scheme 1). The results of these reactions are depicted in Table 1.



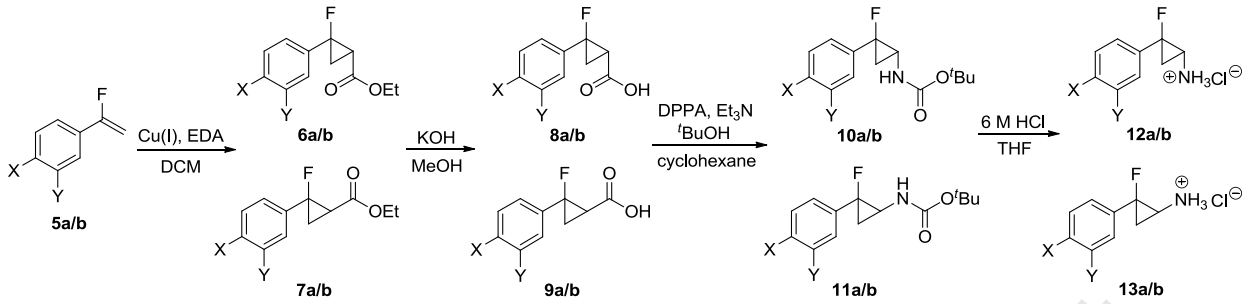
Scheme 1. Synthesis of α-fluoro-(3- and 4-pentafluorosulfanylphenyl)styrenes **5a** and **5b**.

Table 1. Results of the synthetic sequence towards α-fluoro-(3- and 4-pentafluorosulfanylphenyl)styrenes **5**

Entry	Compound	X	Y	Yield [%] **3**	Yield [%] **4**	Yield [%] **5**
1	**a**	H	SF_5	84	77	62
2	**b**	SF_5	H	70	~70*	75

* some amount of the HBr-elimination product **5b** detected

According to our earlier procedure [14] the copper(I)-catalyzed cyclopropanation with ethyldiazoacetate (EDA) in dichloromethane (DCM) gave the diastereomeric ethyl cyclopropylcarboxylates **6a/b** (*trans* regarding F and CO_2Et) and **7a/b** (*cis* regarding F and CO_2Et) in diastereomeric ratios of about 1.2:1 for compounds **a** and 1:1 for compounds **b** (GC). These mixtures were separated by column chromatography. Saponification of the single diastereomers gave the carboxylic acids **8a/b** and **9a/b**. The structure of **8b** and **9b** was determined by spectroscopic data and proved by X-ray analysis [15]. Succeeding Curtius-degradation with diphenylphosphoryl azide (DPPA) gave the Boc-protected cyclopropylamines **10a/b** and **11a/b**, which were finally deprotected with 6M hydrochloric acid in THF to yield the amine hydrochlorides **12a/b** and **13a/b** (Scheme 2). The yields of all reactions are given in Table 2.



Scheme 2. Synthesis of the 2-fluoro-(3/4-pentafluorosulfanylphenyl)cyclopropylamine hydrochlorides.

Table 2. Yields of compounds **6** to **13**

Entry	Comp.	X	Y	Yield [%]		Yield [%]		Yield [%]		Yield [%]	
				6	**7**	**8**	**9**	**10**	**11**	**12**	**13**
1	**a**	H	SF_5	32	23	59	72	89	87	100	96
2	**b**	SF_5	H	63% (1:1 GC)		46	30	46	45	95	94

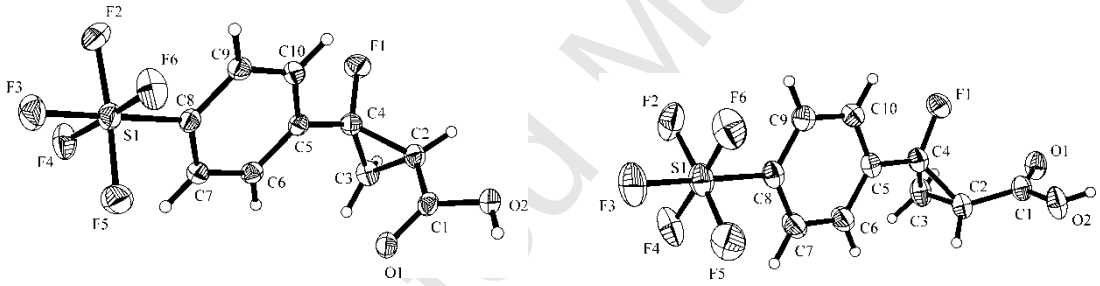
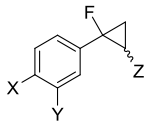


Figure 2. X-Ray structures of compounds **8b** and **9b**. Thermals ellipsoids are shown with 30% probability [15].

2.2. pK_a Values

The pK_a values of the carboxylic acids were measured in aqueous solution starting from basic pH (10 mL 0.1 M NaOH solution) against 0.1 M hydrochloric acid due to the insolubility of the carboxylic acids at pH 1. When precipitation of the acids starts, the automated titration was slowed down manually to give more exact titration curves. The amines were dissolved in 0.1 M KNO_3-solution and acidified with 0.5 mL of 2 M hydrochloric acid. The pK_a values were determined by titration with 0.1 M NaOH. The results of these measurements are depicted in Table 3.

Table 3. Results of pK_a measurements.

	Z = COOH		Z = NH_2	
	compound	pK_a	compound	pK_a[a]
X = Y = H	*trans*-**14**	3.98	*trans*-**1**	7.02 (6.98[b])
	cis-**15**	4.14	*cis*-**1**	7.23 (7.35[b])
X = H, Y = SF_5	**8a**	3.87	**12a**	6.31
	9a	3.88	**13a**	6.83
X = SF_5, Y = H	**8b**	3.71	**12b**	6.30
	9b	3.86	**13b**	6.77

[a] of the conjugated acid, [b] reference [16].

Comparison of the pK_a values of the diastereomeric 2-fluoro-2-phenylcyclopropanecarboxylic acids *trans*-**14** and *cis*-**15** and the corresponding amines *trans*-**1** and *cis*-**1** proved the *trans*-isomers to be about 0.2 pK_a units more acidic. Based on quantum chemical calculations, the higher acidity of *trans*- compared to *cis*-2-fluorocyclopropylamine was ascribed to a hyperconjugative interaction (Figure 1) leading to different local charge distribution and different hybridization of the nitrogen atom and hence to stronger proton affinity of the *cis*- over the *trans*-isomer [12]. This effect was found experimentally for the diastereomeric 2-fluoro-2-phenylcyclopropylamines [16].

The electron withdrawing effect of the SF_5 group leads to further acidification by about 0.8 pK_a units in case of the *trans*-2-fluoroamines **12a** and **12b** independently of the position of the SF_5 substituent in the aromatic ring. In case of the *cis*-compounds **13a** and **13b** the difference is about 0.5 pK_a units, regardless the regiochemistry (Table 3). Thus, this effect is mainly an inductive electron withdrawing effect of the SF_5-substituted aromatic ring. In literature, the pK_a values of 3- and 4-SF_5 substituted anilines were compared. The pK_a value of the anilinium ion (4.56) was lowered to 2.82 (3-SF_5) and 2.17 (4-SF_5), respectively. The much stronger electron withdrawing effect of the SF_5 group in *para*-position was assigned to d-orbital participation by the sulfur atom and/or hyperconjugation leading to higher acidity in case of the *p*-SF_5 aniline [17]. Such a hyperconjugation effect of the SF_5 group, if at all, is much weaker in the corresponding 2-aryl-2-fluorocyclopropylamines.

Compared to the fluorinated cyclopropanecarboxylic acids **14** and **15**, the difference is 0.1 and 0.2 pK_a units, respectively, for the *trans*-compounds **8a** and **8b** and about 0.3 pK_a units for the *cis*-isomers **9a** and **9b**. Again the position of the SF_5 group has almost no influence on the pK_a. Very little effect of regiochemistry was also found in 3- and 4-SF_5-benzoic acids [17].

3. Conclusion

A 7-steps synthetic sequence provided *cis*- and *trans*-2-aryl-2-fluorocyclopropylamines bearing an SF_5 substituent in *meta*- or *para*-position of the aryl ring in 6.7% (**12a**), 2.4% (**12b**), 5.5% (**13a**) or 1.5% (**13b**) overall yields starting from 3- and 4-pentafluorosulfanyl benzaldehydes via the diastereomeric 2-aryl-2-fluorocyclopropanecarboxylic acids, respectively. Compared to those of the *cis/trans* isomeric 2-fluoro-2-phenylcyclopropanecarboxylic acids **14** and **15**, the pK_a values of the SF_5-substituted 2-aryl-2-fluorocarboxylic acids **8** and **9** are slightly lowered. This effect is very little depending on the stereochemistry at the cyclopropane ring and the regiochemistry of the SF_5-substituents in the aryl ring. A much stronger effect on the pK_a is seen for the corresponding 2-fluorocyclopropylamines **12** and **13**. In contrast this effect is strongly dependent on the stereochemistry at the three-membered ring due to hyperconjugation of the C–F and the C–N bonds. Again, the position of SF_5 substitution in the phenyl ring has almost no influence showing that this effect is largely inductive in nature.

4. Experimental

4.1. General remarks

Melting points are uncorrected. NMR spectra were recorded on Bruker Avance II at 300 and 400 MHz, Bruker DRX at 300 MHz and Agilent DD2 at 500 and 600 MHz (^{1}H), at 25 °C. TMS (^{1}H and ^{13}C NMR) and CCl_3F (^{19}F NMR) were used as internal standards. Mass spectra (ESI-MS) were measured on a MicroTof Bruker Daltonics. The progress of reactions was monitored by TLC-plates (silica gel 60 F_{254}, Merck). Column chromatography was carried out on silica gel 60 (Merck, particle size 0.040–0.063 mm). The 3- and 4-pentafluorosulfanylbenzaldehydes **2a** and **2b** are commercially available at Fluorochem, UK. The known styrenes **3a** and **3b** were synthesized according to the protocol published in references [18,19]. The fluorinated phenylcyclopropanecarboxylic acids *trans*-**14** and *cis*-**15** were synthesized analogously to the sequence published in reference [14]. X-Ray diffraction: Data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection, COLLECT (B.V. Nonius, 1998); data reduction Denzo-SMN [20]; absorption correction, Denzo [21]; structure solution SHELXS-97 [22]; structure refinement SHELXL-97 [23] and graphics, XP (Bruker AXS, 2000). Thermals ellipsoids are shown with 30% probability, *R*-values are given for observed reflections, and *w*R^2 values are given for all reflections.

4.2. Wittig Olefination

*4.2.1. 3-Pentafluorosulfanylstyrene (**3a**)*

Similarly to the procedure given in ref. [18], 3-pentafluorosulfanylbenzaldehyde (3.48 g, 15.0 mmol) was stirred with methyltriphenylphosphonium bromide (6.0 g, 16.8 mmol, 1.1 eq.) and K_2CO_3 (4.00 g, 32.5 mmol) in 1,4-dioxane (10 mL) at 115 °C for 24 h. Then the solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, pentane) to give a colorless liquid. Yield: 2.90 g (12.6 mmol, 84 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.39 (d, $^3J_{H,H(cis)}$ = 10.9 Hz, 1 H, H_A), 5.82 (d, $^3J_{H,H(trans)}$ = 17.6 Hz, 1 H, H_B), 6.73 (dd, $^3J_{H,H(cis)}$ = 10.9, $^3J_{H,H(trans)}$ = 17.6 Hz, 1 H, 2-CH), 7.43 (m, 1 H, 5-CH), 7.54 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, 4-CH), 7.63 (ddd, $^4J_{H,H}$ = 1.1, $^4J_{H,H}$ = 2.3 Hz, $^4J_{H,H}$ = 8.2 Hz, 1 H, 6-CH), 7.54 (t, $^4J_{H,H}$ = 1.9 Hz, 1 H, 8-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 116.4 (s, 1-C), 123.8 (p, $^3J_{C,F}$ = 4.7 Hz, 6-C), 125.0 (p, $^3J_{C,F}$ = 4.7 Hz, 8-C), 128.8 (s, 5-C), 129.0 (s, 4-C), 135.2 (s, 2-C), 138.6 (s, 3-C), 154.4 (m, 7-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ 62.06 (d, $^2J_{F,F}$ = 150.2 Hz, 4 F, SF_{eq}), 83.70 (p, $^2J_{F,F}$ = 150.2 Hz, 1F, SF_{ax}).

*4.2.2. 4-Pentafluorosulfanylstyrene (**3b**)*

Similarly to the procedure given in ref. [19], 4-pentafluorosulfanylbenzaldehyde (0.65 g, 2.79 mmol) was stirred with methyltriphenylphosphonium bromide (1.09 g, 3.1 mmol, 1.1 eq.) and K_2CO_3 (804 mg, 5.83 mmol, 2 eq.) in 1,4-dioxane (10 mL) at 90 °C for 12 h. Then the solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, pentane) to give a yellowish liquid. Yield: 0.47 g (1.95 mmol, 70 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.41 (d, $^3J_{H,H(cis)}$ = 10.9 Hz, 1 H, H_A), 5.85 (d, $^3J_{H,H(trans)}$ = 17.6 Hz, 1 H, H_B), 6.72 (dd, $^3J_{H,H(cis)}$ = 10.9, $^3J_{H,H(trans)}$ = 17.6 Hz, 1 H, 2-CH), 7.46 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 4/8-CH), 7.70 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 5/7-CH). ^{19}F NMR (282 MHz, $CDCl_3$): δ 62.20 (d, $^2J_{F,F}$ = 150.6 Hz, 4 F, SF_{eq}), 83.19 (p, $^2J_{F,F}$ = 150.6 Hz, 1F, SF_{ax}).

4.3. Bromofluorination

*4.3.1. 2-Bromo-1-fluoro-1-(3-pentafluorosulfanylphenyl)ethane (**4a**)*

Similarly to the general procedure [24] **3a** (0.96 g, 4.14 mmol) was treated with triethylamine-trishydrofluoride ($Et_3N{\cdot}3HF$, 2.7 mL, 28.1 mmol, 7 eq.) and subsequently *N*-bromosuccinimide (NBS, 1.2 g, 7 mmol, 1.5 eq). Due to incomplete reaction pyridinium polyhydrogenfluoride (OHLA's reagent, Py·9HF, 1 mL, 4 mmol, 1 eq.) was added and the solution was stirred for 2 h. After neutralization with ammonia and extraction with pentane **4a** was isolated and purified by column chromatography (silica gel, pentane) to give a colorless liquid. Yield: 1.1 g (77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.66 (dd, $^3J_{H,H}$ = 4.9, $^3J_{H,F}$ = 22.0 Hz, 1 H, 1-CH_2Br), 3.67 (dd, $^3J_{H,H}$ = 6.6, $^3J_{H,F}$ = 17.7 Hz, 1 H, 1-CH_2Br), 5.70

(ddd, $^{3}J_{H,H}$ = 4.9, $^{3}J_{H,H}$ = 6.7, $^{2}J_{H,F}$ = 46.2 Hz, 1 H, 2-CHF), 7.50 (t, $^{3}J_{H,H}$ = 7.9 Hz, 1 H, 5-CH), 7.58 (d, $^{3}J_{H,H}$ = 7.9 Hz, 1 H, 6-CH), 7.74 (dd, $^{4}J_{H,H}$ = 1.9, $^{3}J_{H,H}$ = 8.9 Hz, 1 H, 4-CH), 7.77 (d, $^{4}J_{H,H}$ = 1.9 Hz, 1 H, 8-CH). ^{19}F NMR (282 MHz, $CDCl_3$): δ -175.83 (ddd, $^{3}J_{H,F}$ = 17.7, $^{3}J_{H,F}$ = 22.0, $^{2}J_{H,F}$ = 46.3 Hz, 1 F, 2-CHF), 62.91 (d, $^{2}J_{F,F}$ = 151.9 Hz, 4 F, SF_{eq}), 84.53 (p, $^{2}J_{F,F}$ = 151.9 Hz, 1F, SF_{ax}). MS (GC/EI), *m/z* (%): 330/328 (37/38) [M^+], 309/311 (3/3) [M^+-HF], 249 (3) [M^+-Br], 235 (100) [M^+-CH_2Br], 201 (4) [M^+-SF_5], 140 (1), 127 (20) [SF_5^+], 122 (8), 101 (4), 77 (5) [$C_6H_5^+$], 63 (1), 50 (2).

*4.3.2. 2-Bromo-1-fluoro-1-(4-pentafluorosulfanylbenzyl)ethane (**4b**)*

Similarly to the general procedure [24] **3b** (0.64 g, 2.80 mmol) was treated with triethylamine-trishydrofluoride ($Et_3N{\cdot}3HF$, 2.7 mL, 28.1 mmol, 10 eq.) and subsequently *N*-bromosuccinimide (NBS, 1.2 g, 7 mmol, 2.5 eq) to give **4b** as a colorless liquid. Yield: 0.55 g (~70%, HBr elimination product **5b** was also found). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.65 (m, 2 H, 1-CH_2Br), 5.70 (ddd, $^{3}J_{H,H}$ = 4.6, $^{3}J_{H,H}$ = 6.2, $^{2}J_{H,F}$ = 46.4 Hz, 1 H, 2-CHF), 7.48 (m, 2 H, 4/8-CH), 7.81 (m, 2 H, 5/7-CH). ^{13}C NMR (101 MHz, $CDCl_3$): δ 33.5 (d, $^{2}J_{C,F}$ = 27.6 Hz, 1-C), 91.4 (d, $^{1}J_{C,F}$ = 180.1 Hz, 2-C), 126.1 (d, $^{3}J_{C,F}$ = 7.2 Hz, 4/8-C), 126.5 (p, $^{3}J_{C,F}$ = 4.7 Hz, 5/7-C), 140.8 (d, $^{3}J_{C,F}$ = 20.8 Hz, 3-C), 154.2 (m, 6-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -176.96 (dt, $^{3}J_{H,F}$ = 19.5, $^{2}J_{H,F}$ = 46.3 Hz, 1 F, 2-CHF), -108.90 (dd, $^{3}J_{H,F}$ = 17.4, $^{3}J_{H,F}$ = 48.7 Hz, 1 F, HBr elimination product **5b**), 62.24 (d, $^{2}J_{F,F}$ = 150.1 Hz, 4 F, SF_{eq}), 83.23 (q, $^{2}J_{F,F}$ = 150.1 Hz, 1 F, SF_{ax}). MS (GC/EI), *m/z* (%): 309/311 (100/100) [M^+-HF], 263/265 (2/2), 230 (78) [309-Br], 182/184 (29/28) [309-SF_5], 127 (2) [SF_5^+], 122 (40) [$C_8H_7F^+$], 103 (47) [122-F], 77 (48) [$C_6H_4^+$], 51 (19).

4.4. HBr Elimination

*4.4.1. 1-Fluoro-3-pentafluorosulfanylstyrene (**5a**)*

Similarly to the procedure [25], **4a** (3.87 g, 11.8 mmol) was treated with potassium-*tert*-butanol (KO^tBu, 2.81 g, 25.0 mmol, 2.1 eq.) in refluxing pentane for 1 h. Bulb-to-bulb distillation gave **5a** as a colorless liquid. Yield: 2.41 g (62%). Bp 60 °C/0.07mbar. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.00 (dd, $^{2}J_{H,H}$ = 3.9, $^{3}J_{H,F(cis)}$ = 17.6 Hz, 1 H, H_A), 5.14 (dd, $^{2}J_{H,H}$ = 3.9, $^{3}J_{H,F(trans)}$ = 48.9 Hz, 1 H, H_B), 7.48 (tq, $^{5}J_{H,H}$ = 1.0, $^{3}J_{H,H}$ = 7.9 Hz, 1 H, 5-CH), 7.68 (m, 1 H, 6-CH), 7.74 (ddd, $^{5}J_{H,H}$ = 1.0, $^{4}J_{H,H}$ = 2.3, $^{3}J_{H,H}$ = 8.3 Hz, 1 H, 4-CH), 7.92 (t, $^{4}J_{H,H}$ = 2.0 Hz, 1 H, 8-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 91.7 (d, $^{2}J_{C,F}$ = 22.0 Hz, 1-C), 122.2 (dp, $^{3}J_{C,F}$ = 4.7, 7.4 Hz, 8-C), 126.7 (p, $^{3}J_{C,F}$ = 4.7 Hz, 6-C), 127.5 (d, $^{3}J_{C,F}$ = 6.6 Hz, 4-C), 129.0 (d, $^{4}J_{C,F}$ = 1.3 Hz, 5-C), 133.0 (d, $^{2}J_{C,F}$ = 29.8 Hz, 3-C), 154.5 (m, 7-C), 161.0 (d, $^{1}J_{C,F}$ = 250.7 Hz, 2-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -108.58 (dd, $^{3}J_{H,F(cis)}$ = 17.5,

$^3J_{H,F(trans)}$ = 49.0 Hz, 1 F, 2-CF), 62.02 (d, $^2J_{F,F}$ = 150.8 Hz, 4 F, SF_{eq}), 83.02 (p, $^2J_{F,F}$ = 152.1 Hz, 1 F, SF_{ax}). MS (GC/EI), *m/z* (%): 248 (100) [M^+], 229 (1) [M^+-HF], 140 (20), 138 (2), 101 ($C_8H_5^+$) 89 (4), 75 (12) [$C_6H_4^+$], 70 (1), 51 (1) [$C_4H_3^+$].

*4.4.2. 1-Fluoro-4-pentafluorosulfanylstyrene (**5b**)*

Similarly to the procedure [25] **4b** (0.50 g, 1.5 mmol) was treated with KO^{t}Bu (0.35 g, 3.1 mmol, 2 eq.) in refluxing pentane for 1 h. Bulb-to-bulb distillation gave **5b** as a colorless liquid. Yield: 0.28 g (75%). Bp 56 °C/0.07mbar. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.02 (dd, $^2J_{H,H}$ = 3.9, $^3J_{H,F(cis)}$ = 17.5 Hz, 1 H, H_A), 5.17 (dd, $^2J_{H,H}$ = 3.8, $^3J_{H,F(trans)}$ = 48.8 Hz, 1 H, H_B), 7.64 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 5/7-CH), 7.78 (m, 2 H, 4/8-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 92.5 (d, $^2J_{C,F}$ = 21.8 Hz, 1-C), 124.8 (d, $^3J_{C,F}$ = 7.0 Hz, 4/8-C), 126.3 (m, 5/7-C), 131.9 (m, 6-C), 135.0 (d, $^2J_{C,F}$ = 31.1 Hz, 3-C), 161.0 (d, $^1J_{C,F}$ = 251.3 Hz, 2-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -108.96 (dd, $^3J_{H,F(cis)}$ = 17.4, $^3J_{H,F(trans)}$ = 48.8 Hz, 1 F, 2-CF), 62.20 (d, $^2J_{F,F}$ = 150.6 Hz, 4 F, SF_{eq}), 83.02 (p, $^2J_{F,F}$ = 152.2 Hz, 1 F, SF_{ax}). MS (GC/EI), *m/z* (%): 248 (100) [M^+], 231 (49), 229 (4) [M^+-F], 203 (5) [M^+-C_2H_2F], 140 (16), 123 (62) [M^+-SF_5], 103 (7) [123-HF], 89 (31), 75 (42) [$C_6H_3^+$], 65 (59), 51 (1) [$C_4H_3^+$], 39 (16) [$C_3H_4^+$].

4.5. Cyclopropanation

4.5.1. Ethyl 2-fluoro-2-(3-pentafluorosulfanylphenyl)cyclopropylcarboxylates

Similarly to the protocol [14], to a solution of **5a** (2.34 g, 9.4 mmol) and $Cu(acac)_2$ (75 mg, 0.2 mmol) (reduced with 3 drops phenylhydrazine) in anhydrous CH_2Cl_2 (5 mL), a solution of EDA (2.77 g, 24.0 mmol, 2.6 eq.) in anhydrous CH_2Cl_2 (10 mL) was added at 40 °C via a syringe pump over a period of 5 h. After dilution with 100 mL CH_2Cl_2 the mixture was washed with sat. $NaHCO_3$ (2×50 mL) and H_2O (2×50 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator. Separation of the crude product by column chromatography (silica gel, pentane/Et_2O, 20:1) afforded the pure isomers **6a** and **7a** as colorless oils.

6a: Yield: 1.0 g (32%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03 (t, $^3J_{H,H}$ = 7.1 Hz, 3 H, 12-CH_3), 1.90 (ddd, $^2J_{H,H}$ = 7.3, $^3J_{H,H(cis)}$ = 10.4, $^3J_{H,F(cis)}$ = 19.3 Hz, 1 H, H_A), 2.03 (ddd, $^2J_{H,H}$ = 7.3, $^3J_{H,H(trans)}$ = 7.8, $^3J_{H,F(trans)}$ = 12.5 Hz, 1 H, H_B), 2.62 (ddd, $^3J_{H,H(trans)}$ = 7.8, $^3J_{H,H(cis)}$ = 10.5, $^3J_{H,F(cis)}$ = 18.1 Hz, 1 H, H_X), 3.94 (q, $^3J_{H,H}$ = 7.1 Hz, 2 H, 11-CH_2), 7.49 (t, $^3J_{H,H}$ = 8.1 Hz, 1 H, 7-CH), 7.63 (m, 1 H, 6-CH), 7.76 (m, 1 H, 8-CH), 7.88 (q, $^4J_{H,H}$ = 1.7 Hz, 1 H, 10-CH). ^{13}C NMR (101 MHz, $CDCl_3$): δ 13.9 (s, 12-C), 16.8 (d, $^2J_{C,F}$ = 10.1 Hz, 3-C), 28.2 (d, $^2J_{C,F}$ = 16.0 Hz, 2-C), 61.1 (s, 11-C), 82.3 (d, $^1J_{C,F}$ = 222.1 Hz, 4-C), 126.1 (q, $^3J_{C,F}$ = 4.8 Hz, 10-C), 126.7 (s, 8-C), 128.8 (s, 7-C), 131.4 (d, $^3J_{C,F}$ = 4.1 Hz, 6-C), 134.6 (d, $^2J_{C,F}$ = 20.9 Hz,

5-C), 153.8 (m, 9-C), 168.4 (d, $^{3}J_{C,F}$ = 1.8 Hz, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -157.22 (ddd, $^{3}J_{H,F(trans)}$ = 12.5, $^{3}J_{H,F(cis)}$ = 18.0, $^{3}J_{H,F(cis)}$ = 19.3 Hz, 1 F, 4-CF), 62.15 (dq, $^{4}J_{H,F}$ = 1.8, $^{2}J_{F,F}$ = 150.5 Hz, 4 F, SF_{eq}), 83.41 (p, $^{2}J_{F,F}$ = 150.5 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{12}H_{12}F_6O_2SNa^+$: 357.0354; found 357.0354. MS (GC/EI) *m*/*z* (%): 334 (46) [M^+], 315 (9) [M^+-F], 306 (8) [M^+-C_2H_4], 289 (15) [M^+-C_2H_5O], 279 (46), 261 (10) [M^+-$CO_2C_2H_5$], 251 (100) [$C_{10}H_7F_4OS^+$], 241 (9) [261-HF], 231 (20) [315-$C_4H_6O_2$], 206 (5), 203 (1) [$C_6H_4SF_5^+$], 178 (11), 162 (10), 158 (29), 151 (4), 133 (45), 132 (10) [M^+-$C_6H_4SF_5$], 127 (2), 115 (2), 89 (3), 83 (2), 75 (1), 55 (1).

7a: Yield: 0.71 g (23%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3 H, 12-CH_3), 1.69 (ddd, $^{2}J_{H,H}$ = 7.3, $^{3}J_{H,H(trans)}$ = 9.5, $^{3}J_{H,F(trans)}$ = 10.6 Hz, 1 H, H_B), 2.25 (ddd, $^{3}J_{H,F(trans)}$ = 3.1, $^{3}J_{H,H(trans)}$ = 7.9, $^{3}J_{H,H(cis)}$ = 9.3 Hz, 1 H, H_X), 2.38 (ddd, $^{2}J_{H,H}$ = 7.3, $^{3}J_{H,H(cis)}$ = 8.0, $^{3}J_{H,F(cis)}$ = 20.3 Hz, 1 H, H_A), 4.18 (m, 2 H, 11-CH_2), 7.36 (m, 1 H, 6-CH), 7.47 (m, 1 H, 7-CH), 7.67 (m, 2 H, 8/10-CH). ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.2 (s, 12-C), 19.3 (d, $^{2}J_{C,F}$ = 12.1 Hz, 3-C), 29.5 (d, $^{2}J_{C,F}$ = 11.4 Hz, 2-C), 61.5 (s, 11-C), 80.2 (d, $^{1}J_{C,F}$ = 229.0 Hz, 4-C), 122.2 (tq, $^{3}J_{C,F}$ = 4.5, 9.0 Hz, 10-C), 125.8 (p, $^{3}J_{C,F}$ = 4.0, 4.5 Hz, 8-C), 127.3 (d, $^{3}J_{C,F}$ = 6.4 Hz, 6-C), 129.3 (s, 7-C), 139.1 (d, $^{2}J_{C,F}$ = 21.9 Hz, 5-C), 154.3 (m, 9-C), 167.2 (d, $^{3}J_{C,F}$ = 2.3 Hz, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -190.28 (ddd, $^{3}J_{H,F(trans)}$ = 3.1, $^{3}J_{H,F(trans)}$ = 10.7, $^{3}J_{H,F(cis)}$ = 20.3 Hz, 1 F, 4-CF), 62.22 (d, $^{2}J_{F,F}$ = 150.4 Hz, 4 F, SF_{eq}), 83.54 (p,$^{2}J_{F,F}$ = 150.4 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{12}H_{12}F_6O_2SNa^+$: 357.0354; found 357.0353. MS (GC/EI) *m*/*z* (%): 334 (38) [M^+], 315 (10) [M^+-F], 306 (10) [M^+-C_2H_4], 289 (21) [M^+-C_2H_5O], 279 (50), 261 (12) [M^+-$CO_2C_2H_5$], 251 (100) [$C_{10}H_7F_4OS^+$], 241 (9) [261-HF], 231 (18) [315-$C_4H_6O_2$], 206 (5), 203 (1) [$C_6H_4SF_5^+$], 184 (1), 178 (11), 162 (10), 158 (20), 151 (4), 133 (40), 132 (10) [M^+-$C_6H_4SF_5$], 115 (2), 89 (3), 83 (2), 75 (1), 55 (1).

4.5.2. *Ethyl 2-fluoro-2-(4-pentafluorosulfanylphenyl)cyclopropylcarboxylates*

Similarly to the protocol [14], to a solution of **5b** (0.95 g, 3.8 mmol) and $Cu(acac)_2$ (75 mg, 0.2 mmol) (reduced with 3 drops of phenylhydrazine) in anhydrous CH_2Cl_2 (3 mL), a solution of EDA (1.61 g, 11.4 mmol, 3.0 eq.) in anhydrous CH_2Cl_2 (10 mL) was added at 40 °C via a syringe pump over a period of 5 h. After dilution with 50 mL CH_2Cl_2 the mixture was washed with sat. $NaHCO_3$ (2×50 mL) and H_2O (2×50 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator. Separation of the crude product (1:1 mixture of diastereomers **6b** and **7b**) by column chromatography (silica gel, cyclohexane/EtOAc, 40:1) was incomplete and provided a fraction with both diastereomers and pure fractions of **6b** and **7b** as colorless oils. Yield (all fractions): 0.74 g (63%).

6b: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3 H, 12-CH_3), 1.91 (ddd, $^{2}J_{H,H}$ = 7.4, $^{3}J_{H,H(cis)}$ = 10.5, $^{3}J_{H,F(cis)}$ = 19.5 Hz, 1 H, H_A), 2.03 (dt, $^{2}J_{H,H}$ = 7.4, $^{3}J_{H,H(trans)}$ = 7.9 Hz $^{3}J_{H,F(trans)}$ = 12.9 Hz, 1 H, H_B), 2.61 (ddd, $^{3}J_{H,H(trans)}$ = 7.9 Hz, $^{3}J_{H,H(cis)}$ = 10.5 Hz, $^{3}J_{H,F(cis)}$ = 18.4 Hz, 1H, H_X), 3.95 (q, $^{3}J_{H,H}$ = 7.0 Hz, 2 H, 11-CH_2), 7.56 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2 H, 6/10-CH), 7.75 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2 H, 7/9-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (s, 12-C), 17.0 (d, $^{2}J_{C,F}$ = 9.9 Hz, 3-C), 28.6 (d, $^{2}J_{C,F}$ = 16.0 Hz, 2-C), 61.1 (s, 11-C), 81.8 (d, $^{1}J_{C,F}$ = 221.6 Hz, 4-C), 125.8 (t, $^{4}J_{C,F}$ = 4.7 Hz, 7/9-C), 128.2 (d, $^{3}J_{C,F}$ = 5.0 Hz, 6/10-C), 136.9 (d, $^{2}J_{C,F}$ = 21.2 Hz, 5-C), 142.2 (m, 8-C), 168.4 (d, $^{3}J_{C,F}$ = 1.9 Hz, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -159.45 (ddd, $^{3}J_{H,F(trans)}$ = 12.6, $^{3}J_{H,F(cis)}$ = 18.4, $^{3}J_{H,F(cis)}$ = 19.5 Hz, 1 F, 4-CF), 62.23 (d, $^{2}J_{F,F}$ = 150.7 Hz, 4 F, SF_{eq}), 83.08 (p, $^{2}J_{F,F}$ = 150.7 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{12}H_{12}F_6O_2SNa^+$: 357.0354; found 357.0354. MS (GC/EI) *m*/*z* (%): 334 (21) [M^+], 315 (5) [M^+-F], 306 (21) [M^+-C_2H_5], 286 (8) [315-C_2H_5O], 279 (32), 261 (9) [M^+-$C_3H_5O_2$], 251 (73) [$C_{10}H_7F_4OS^+$], 231 (16) [251-HF], 207 (4) [M^+-SF_5], 179 (4) [306–SF_5], 162 (19) [$C_{10}H_7FO^+$], 151 (5), 134 (100) [$C_9H_7F^+$], 132 (60) [$C_6H_8FO_2^+$], 115 (11) [134-F], 89 (6), 83 (5), 55 (19).

7b: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3 H, 12-CH_3), 1.67 (ddd, $^{2}J_{H,H}$ = 7.2, $^{3}J_{H,H(cis)}$ = 9.5, $^{3}J_{H,F(trans)}$ = 10.6 Hz, 1 H, H_B), 2.23 (ddd, $^{3}J_{H,F(trans)}$ = 3.0, $^{3}J_{H,H(trans)}$ = 8.0, $^{3}J_{H,H(cis)}$ = 9.4 Hz, 1 H, H_X), 2.39 (ddd, $^{2}J_{H,H}$ = 7.2, $^{3}J_{H,H(trans)}$ = 8.0, $^{3}J_{H,F(cis)}$ = 20.3 Hz, 1 H, H_A), 4.24 (qm, $^{3}J_{H,H}$ = 7.1 Hz, 2 H, 11-CH_2), 7.36 (m, 2 H, 6/10-CH), 7.78 (m, 2 H, 7/9-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2 (s, 12-C), 19.6 (d, $^{2}J_{C,F}$ = 12.1 Hz, 3-C), 29.9 (d, $^{2}J_{C,F}$ = 11.3 Hz, 2-C), 61.5 (s, 11-C), 79.8 (d, $^{1}J_{C,F}$ = 229.2 Hz, 4-C), 124.1 (d, $^{3}J_{C,F}$ = 7.4 Hz, 6/10-C), 126.3 (m, 7/9-C), 141.6 (d, $^{3}J_{C,F}$ = 22.3 Hz, 5-C), 153.3 (m, 8-C), 167.0 (d, $^{3}J_{C,F}$ = 2.4 Hz, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -192.72 (ddd, $^{3}J_{H,F(trans)}$ = 3.0, $^{3}J_{H,F(trans)}$ = 10.6, $^{3}J_{H,F(cis)}$ = 20.5 Hz, 1 F, 4-CF), 62.38 (d, $^{2}J_{F,F}$ = 149.8 Hz, 4 F, SF_{eq}), 83.61 (p, $^{2}J_{F,F}$ = 149.8 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{12}H_{12}F_6O_2SNa^+$: 357.0354; found 357.0345. MS (GC/EI), *m*/*z* (%): 334 (14) [M^+], 315 (4) [M^+-F], 306 (18) [M^+-C_2H_5], 289 (8), 279 (29), 261 (9) [M^+-$C_3H_5O_2$], 251 (60) [$C_{10}H_7F_4OS^+$], 231 (13) [251-HF], 207 (4) [M^+-SF_5], 179 (3) [306–SF_5], 162 (22) [$C_{10}H_7FO^+$], 151 (5), 134 (100) [$C_9H_7F^+$], 132 (63) [$C_6H_8FO_2^+$], 115 (12) [134-F], 107 (7), 89 (6), 83 (5), 55 (19).

4.6. Saponification

*4.6.1. cis-2-Fluoro-2-(3-pentafluorosulfanylphenyl)-cyclopropylcarboxylic acid (**8a**)*

Similarly to the procedure [14] **6a** (1.1 g, 3.3 mmol) was treated with KOH (1.85 g, 33 mmol, 10 eq.) in methanol (15 mL) and stirred at room temperature for 12 h. Subsequently the mixture was diluted with ice/water (50 mL) and extracted with CH_2Cl_2 (2×20 mL). This

solution was discarded. The aqueous layer was acidified to pH 1 and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with H_2O (2×50 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the corresponding carboxylic acid **8a**. The acid was purified by recrystallization from CH_2Cl_2/pentane to give white needles. Yield: 0.6 g (59%). Mp 179 °C (CH_2Cl_2/pentane). ^{1}H NMR (300 MHz, MeOD): δ 1.92 (ddd, $^2J_{H,H}$ = 7.4, $^3J_{H,H(cis)}$ = 10.4, $^3J_{H,F(cis)}$ = 19.6 Hz, 1 H, H_A), 2.01 (ddd, $^2J_{H,H}$ = 7.4, $^3J_{H,H(trans)}$ = 7.8, $^3J_{H,F(trans)}$ = 12.7 Hz, 1 H, H_B), 2.62 (ddd, $^3J_{H,H(trans)}$ = 7.8, $^3J_{H,H(cis)}$ = 10.4, $^3J_{H,F(cis)}$ = 18.4 Hz, 1 H, H_X), 7.58 (m, 1 H, 7-CH), 7.73 (dd, $^4J_{H,F}$ = 1.4, $^3J_{H,H}$ = 7.8 Hz, 1 H, 6-CH), 7.83 (m, 1 H, 8-CH), 7.91 (q, $^4J_{H,F}$ = 1.8 Hz, 1 H, 10-CH). ^{13}C NMR (75 MHz, MeOD): δ 17.5 (d, $^2J_{C,F}$ = 10.2 Hz, 3-C), 29.2 (d, $^2J_{C,F}$ = 15.8 Hz, 2-C), 83.6 (d, $^1J_{C,F}$ = 220.7 Hz, 4-C), 127.0 (q, $^3J_{C,F}$ = 4.7 Hz, 8-C), 127.7 (m, 10-C), 130.2 (s, 7-C), 133.0 (d, $^3J_{C,F}$ = 4.3 Hz, 6-C), 136.4 (d, $^2J_{C,F}$ = 20.9 Hz, 5-C), 155.0 (t, $^2J_{C,F}$ = 17.3 Hz, 9-C), 171.9 (d, $^4J_{C,F}$ = 1.4 Hz, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -156.63 (ddd, $^3J_{H,F}$ = 12.7, $^3J_{H,F}$ = 18.6, $^3J_{H,F}$ = 19.6 Hz, 1 F, 4-CF), 62.12 (dq, $^3J_{H,F}$ = 1.9, $^2J_{F,F}$ = 150.4 Hz, 4 F, SF_{eq}), 83.45 (p, $^2J_{F,F}$ = 150.4 Hz, 1 F, SF_{ax}). HRMS (ESI), *m/z*: calcd. for $C_{10}H_8F_6O_2S{\cdot}Na^+$: 329.0041; found 329.0036. HRMS (ESI neg.), *m/z*: calcd. for $C_{10}H_7F_6O_2S^-$: 305.0076; found 305.0082; calcd. for $[C_{10}H_7F_6O_2S^-]_2+H^+$: 611.0215; found 611.0245.

*4.6.2. trans-2-Fluoro-2-(3-pentafluorosulfanylphenyl)-cyclopropylcarboxylic acid (**9a**)*

Similarly to the procedure [14] **7a** (0.71 g, 2.1 mmol) was treated with KOH (1.18 g, 21 mmol, 10 eq.) in methanol (15 mL) and stirred for 12 h at roomtemperature. Subsequently the mixture was diluted with ice/water (50 mL) and extracted with CH_2Cl_2 (2×20 mL). This solution was discarded. The aqueous layer was acidified to pH 1 and again extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with H_2O (2×50 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the corresponding carboxylic acid **9a**. For purification the acid was recrystallized from CH_2Cl_2/pentane to give white needles. Yield: 0.47 g (72%). Mp 147 °C (CH_2Cl_2/pentane). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78 (ddd, $^2J_{H,H}$ = 7.3, $^3J_{H,H(cis)}$ = 9.4, $^3J_{H,F(trans)}$ = 10.7 Hz, 1 H, H_B), 2.26 (ddd, $^3J_{H,F(trans)}$ = 2.6, $^3J_{H,H(trans)}$ = 7.8, $^3J_{H,H(cis)}$ = 9.4 Hz, 1 H, H_X), 2.41 (ddd, $^2J_{H,H}$ = 7.3, $^3J_{H,H(trans)}$ = 7.8, $^3J_{H,F(cis)}$ = 20.2 Hz, 1 H, H_A), 7.41 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, 8-CH), 7.51 (t, $^3J_{H,H}$ = 7.9 Hz, 1 H, 7-CH), 7.74 (m, 2 H, 6/10-CH), 11.64 (br s, 1 H, 1-COOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.6 (d, $^2J_{C,F}$ = 12.0 Hz, 3-C), 29.0 (d, $^2J_{C,F}$ = 11.4 Hz, 2-C), 80.7 (d, $^1J_{C,F}$ = 230.9 Hz, 4-C), 122.4 (dt, $^3J_{C,F}$ = 4.6, 7.9 Hz, 10-C), 126.0 (p, $^3J_{C,F}$ = 4.9 Hz, 8-C), 127.5 (d, $^3J_{C,F}$ = 6.2 Hz, 6-C), 129.3 (s, 7-C), 138.3 (d, $^2J_{C,F}$ = 21.9 Hz, 5-C), 154.2 (p, $^2J_{C,F}$ = 17.2 Hz, 9-C), 173.9 (s, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -188.38 (ddd,

$^3J_{H,F(trans)}$ = 2.6, $^3J_{H,F(trans)}$ = 10.8, $^3J_{H,F(cis)}$ = 20.4 Hz, 1 F, 4-CF), 62.19 (d, $^2J_{F,F}$ = 150.0 Hz, 4 F, SF_{eq}), 83.13 (p, $^2J_{F,F}$ = 150.0 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{10}H_8F_6O_2S{\cdot}Na^+$: 329.0041; found 329.0040. HRMS (ESI neg.), *m*/*z*: calcd. for $C_{10}H_7F_6O_2S^-$: 305.0076; found 305.0077; calcd. for $[C_{10}H_7F_6O_2S^-]_2+H^+$: 611.0215; found 611.0245.

*4.6.3. cis-2-Fluoro-2-(4-pentafluorosulfanylphenyl)-cyclopropylcarboxylic acid (**8b**)*

Similarly to the procedure [14] **6b** (1.38 g, 4.5 mmol) was treated with KOH (2.52 g, 45 mmol, 10 eq.) in methanol (15 mL) and stirred at room temperature for 12 h. Subsequently the mixture was diluted with ice/water and extracted with CH_2Cl_2 (2×20 mL). This solution was discarded. The aqueous layer was acidified to pH 1 and again extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with H_2O (2×50 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the corresponding carboxylic acid **8b**. The acid was purified by recrystallization from EtOAc/pentane to give white needles. Yield: 0.64 g (46%). Mp 128 °C (EtOAc/pentane). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.89-2.05 (m, 2 H, H_A/H_B), 2.57 (ddd, $^3J_{H,H(trans)}$ = 7.9, $^3J_{H,H(cis)}$ = 10.2, $^3J_{H,F(cis)}$ = 18.0 Hz, 1 H, H_X), 7.53 (d, $^3J_{H,H}$ = 8.0 Hz, 2 H, 6/10-CH), 7.74 (dp, $^4J_{H,F}$ = 1.1, $^3J_{H,H}$ = 8.1 Hz, 2 H, 7/9-CH), 9.91 (br s, 1 H, 1-COOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.6 (d, $^2J_{C,F}$ = 9.9 Hz, 3-C), 28.2 (d, $^2J_{C,F}$ = 16.9 Hz, 2-C), 82.3 (d, $^1J_{C,F}$ = 223.0 Hz, 1-C), 125.9 (t, $^3J_{C,F}$ = 4.7 Hz, 7/9-C), 128.3 (d, $^3J_{C,F}$ = 4.9 Hz, 6/10-C), 136.2 (d, $^2J_{C,F}$ = 20.8 Hz, 5-C), 152.8 (m, 8-C), 174.3 (d, $^3J_{C,F}$ = 1.7 Hz, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -157.6 (m, 1 F, 4-CF), 62.15 (d, $^2J_{F,F}$ = 150.0 Hz, 4 F, SF_{eq}), 83.32 (p, $^2J_{F,F}$ = 150.0 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{10}H_8F_6O_2S{\cdot}Na^+$: 329.0041; found 329.0036. HRMS (ESI neg.), *m*/*z*: calcd. for $C_{10}H_7F_6O_2S^-$: 305.0076; found 305.0067.

X-ray crystal structure analysis of **8b** (haf5673) [15]: formula $C_{10}H_8F_6O_2S$, M = 306.22, colorless crystal, 0.30 × 0.15 × 0.15 mm, a = 5.7172(3), b = 19.3208(8), c = 10.7850(4) Å, β = 104.516(3)°, V = 1153.29(9) Å^3, ρ_{calc} = 1.764 gcm^{-3}, μ = 3.285 mm^{-1}, empirical absorption correction (0.439 ≤ T ≤ 0.638), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, T = 223(2) K, ω and φ scans, 7791 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 Å^{-1}, 1989 independent (R_{int} = 0.034) and 1895 observed reflections [I>2σ(I)], 173 refined parameters, R = 0.033, wR^2 = 0.092, max. (min.) residual electron density 0.23 (-0.35) e.Å^{-3}, the hydrogen atoms were calculated and refined as riding atoms.

*4.6.4. trans-2-Fluoro-2-(4-pentafluorosulfanylphenyl)-cyclopropylcarboxylic acid (**9b**)*

Similarly to the procedure [14] **7b** (0.8 g, 2.6 mmol) was treated with KOH (1.45 g, 26 mmol, 10 eq.) in methanol (15 mL) and stirred at room temperature for 12 h. Subsequently the

mixture was diluted with ice/water (50 mL) and extracted with CH_2Cl_2 (2×20 mL). This solution was discarded. The aqueous layer was acidified to pH 1 and again extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with H_2O (2×50 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the corresponding carboxylic acid **9b**, which was purified by recrystallization from EtOAc/pentane to give white needles. Yield: 0.24 g (30%). Mp 146 °C (EtOAc/pentane). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.77 (ddd, $^2J_{H,H}$ = 7.3, $^3J_{H,H(cis)}$ = 9.4, $^3J_{H,F(trans)}$ = 10.7 Hz, 1 H, H_B), 2.26 (ddd, $^3J_{H,F(trans)}$ = 2.6, $^3J_{H,H(trans)}$ = 7.9, $^3J_{H,H(cis)}$ = 9.3 Hz, 1 H, H_X), 2.42 (ddd, $^2J_{H,H}$ = 7.3 $^3J_{H,H(trans)}$ = 7.9, $^3J_{H,F(cis)}$ = 20.2 Hz, 1 H, H_A), 7.38 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, 6/10-CH), 7.79 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 7/9-CH), 11.24 (br s, 1 H, 1-COOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.0 (d, $^2J_{C,F}$ = 12.0 Hz, 3-C), 29.4 (d, $^2J_{C,F}$ = 11.2 Hz, 2-C), 80.4 (d, $^1J_{C,F}$ = 230.8 Hz, 4-C), 124.4 (d, $^3J_{C,F}$ = 7.3 Hz, 6/10-C), 126.5 (m, 7/9-C), 140.9 (d, $^2J_{C,F}$ = 22.1 Hz, 5-C), 153.5 (m, 8-C), 173.5 (s, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -191.07 (ddd, $^3J_{H,F(trans)}$ = 2.6, $^3J_{H,F(trans)}$ = 10.8, $^3J_{H,F(cis)}$ = 20.4 Hz, 1 F, 4-CF), 62.34 (d, $^2J_{F,F}$ = 150.0 Hz, 4 F, SF_{eq}), 83.29 (p, $^2J_{F,F}$ = 150.0 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{10}H_8F_6O_2S{\cdot}Na^+$: 329.0041; found 329.0036. HRMS (ESI neg.), *m*/*z*: calcd. for $C_{10}H_7F_6O_2S^-$: 305.0076; found 305.0067.

X-ray crystal structure analysis of **9b** (haf5672) [15]: formula $C_{10}H_8F_6O_2S$, M = 306.22, colorless crystal, 0.50 × 0.17 × 0.03 mm, a = 17.1116(10), b = 5.1647(3), c = 13.5304(17) Å, β = 104.206(7)°, V = 1159.20(17) Å^3, ρ_{calc} = 1.755 gcm^{-3}, μ = 3.268 mm^{-1}, empirical absorption correction (0.291 ≤ T ≤ 0.908), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, T = 223(2) K, ω and φ scans, 7806 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 Å^{-1}, 1951 independent (R_{int} = 0.049) and 1663 observed reflections [I>2σ(I)], 173 refined parameters, R = 0.049, wR^2 = 0.158, max. (min.) residual electron density 0.29 (-0.23) e.Å^{-3}, the hydrogen atoms were calculated and refined as riding atoms.

4.7. Curtius degradation

*4.7.1. tert-Butyl cis-[2-fluoro-2-(3-pentafluorosulfanylphenyl)cyclopropyl]carbamate (**10a**)*

Similarly to the procedure [14] **8a** (0.31 g, 1.0 mmol) was treated with triethylamine (152 mg, 1.5 mmol, 1.5 eq.), *tert*-butanol (0.74 g, 10 mmol, 10 eq.) and diphenylphosphorylazide (DPPA, 824 mg, 3 mmol, 3 eq.) in dry cyclohexane (15 mL). After reflux for 12 h Boc_2O (328 mg, 1.5 mmol, 1.5 eq.) was added. Subsequently the mixture was diluted with EtOAc (50 mL) and washed with 5% citric acid (20 mL), sat. $NaHCO_3$ (20 mL), water (20 mL) and sat. NaCl solution (20 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the Boc-protected amine **10a**. Column chromatography (silica gel, cyclohexane/EtOAc, 10:1) and subsequent recrystallization from pentane/CH_2Cl_2 furnished

10a as a white solid. Yield: 334 mg (89%). Mp 118 °C (pentane/CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO): δ 1.08 (s, 9 H, 12/13/14-CH_3), 1.65 (ddd, $^3J_{H,H(trans)}$ = 6.1, $^2J_{H,H}$ = 9.4, $^3J_{H,F(trans)}$ = 13.8 Hz, 1 H, H_B), 1.81 (ddd, $^2J_{H,H}$ = 9.4, $^3J_{H,H(cis)}$ = 9.8, $^3J_{H,F(cis)}$ = 22.2 Hz, 1 H, H_A), 3.18 (ddd, $^3J_{H,H(trans)}$ = 6.1, $^3J_{H,H(cis)}$ = 9.8, $^3J_{H,F(cis)}$ = 13.4 Hz, 1 H, H_X), 7.15 (dt, $^4J_{H,H}$ = 1.1, $^3J_{H,H}$ = 8.5 Hz, 1 H, 6-CH), 7.65 (t, $^3J_{H,H}$ = 8.5 Hz, 1 H, 7-CH), 7.72 (s, 1 H, 10-CH), 7.86 (dt, $^4J_{H,H}$ = 2.0, $^3J_{H,H}$ = 7.6 Hz, 1 H, 8-CH). ^{13}C NMR (101 MHz, DMSO): δ 16.7 (d, $^2J_{C,F}$ = 10.8 Hz, 3-C), 27.6 (s, 12/13/14-C), 34.5 (d, $^2J_{C,F}$ = 18.3 Hz, 3-C), 78.0 (s, 11-C), 81.4 (d, $^1J_{C,F}$ = 216.7 Hz, 4-C), 119.8 (d, $^3J_{C,F}$ = 5.0 Hz, 6-C), 123.0 (dt, $^3J_{C,F}$ = 4.5, $^3J_{C,F}$ = 7.2 Hz, 10-C), 125.1 (m, 8-C), 129.2 (s, 7-C), 136.1 (d, $^2J_{C,F}$ = 20.8 Hz, 5-C), 152.5 (m, 9-C), 155.6 (s, 1-C). ^{19}F NMR (282 MHz, DMSO): δ -172.87 (ddd, $^3J_{H,F(cis)}$ = 13.4, $^3J_{H,F(trans)}$ = 13.8, $^3J_{H,F(cis)}$ = 22.3 Hz, 1 F, 4-CF), 62.37 (d, $^2J_{F,F}$ = 149.9 Hz, 4 F, SF_{eq}), 83.83 (p, $^2J_{F,F}$ = 150.0 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{14}H_{17}F_6NO_2SNa^+$: 400.0776; found 400.0778; calcd. for $(C_{14}H_{17}F_6NO_2S)_2Na^+$: 777.1661; found 777.1645. HRMS (ESI neg.), *m*/*z*: calcd. for $C_{14}H_{16}F_6NO_2S^-$: 376.0811; found 305.0811. MS (GC/EI), *m*/*z* (%): 377 (0) [M^+], 342 (1), 321 (2) [M^+-C_4H_8], 303 (1) [M^+-HOC_4H_9], 277 (11) [M^+-$CO_2C_4H_9$], 256 (16), 248 (1) [$C_{10}H_9F_3NOS^+$], 236 (2), 218 (1), 193 (3) [321-SF_5], 176 (1) [302-SF_5], 149 (3) [277-SF_5], 133 (5), 121 (2), 101 (5) [$CO_2C_4H_9^+$], 89 (2) [SF_3^+], 74 (2), 57 (100) [$C_4H_9^+$], 41 (16) [$C_3H_5^+$].

*4.7.2. tert-Butyl trans-[2-fluoro-2-(3-pentafluorosulfanylphenyl)cyclopropyl]carbamate (**11a**)*

Similarly to the procedure [14] **9a** (0.31 g, 1.0 mmol) was treated with triethylamine (152 mg, 1.5 mmol, 1.5 eq.), *tert*-butanol (0.74 g, 10 mmol, 10 eq.) and DPPA (824 mg, 3 mmol, 3 eq.) in dry cyclohexane (15 mL). After refluxing for 12 h Boc_2O (328 mg, 1.5 mmol, 1.5 eq.) was added. Subsequently the mixture was diluted with EtOAc (50 mL) and washed with 5% citric acid (20 mL), sat. $NaHCO_3$ (20 mL), water (20 mL) and sat. NaCl solution (20 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the Boc-protected amine **11a**. Column chromatography (silica gel, cyclohexane/EtOAc, 6:1) and subsequent recrystallization from pentane/EtOAc furnished **11a** as white solid. Yield: 329 mg (87%). Mp 128 °C (pentane/CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO): δ 1.39 (s, 9 H, 12/13/14-CH_3), 1.59 (ddd, $^3J_{H,H(trans)}$ = 6.5, $^2J_{H,H}$ = 8.4, $^3J_{H,F(cis)}$ = 22.7 Hz, 1 H, H_A), 1.74 (ddd, $^2J_{H,H}$ = 8.4, $^3J_{H,H(cis)}$ = 9.8, $^3J_{H,F(trans)}$ = 13.6 Hz, 1 H, H_B), 2.85 (ddd, $^3J_{H,F(trans)}$ = 3.6, $^3J_{H,H(trans)}$ = 6.5, $^3J_{H,H(cis)}$ = 9.8 Hz, 1 H, H_X), 7.57 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 6-CH), 7.65 (t, $^3J_{H,H}$ = 8.1 Hz, 1 H, 7-CH), 7.77 (s, 1 H, 10-CH), 7.86 (dd, $^4J_{H,H}$ = 2.5, $^3J_{H,H}$ = 8.2 Hz, 1 H, 8-CH). ^{13}C NMR (101 MHz, DMSO): δ 18.0 (d, $^2J_{C,F}$ = 11.0 Hz, 3-C), 28.0 (s, 12/13/14-C), 35.0 (d, $^2J_{C,F}$ = 9.9 Hz, 2-C), 78.3 (s, 11-C), 78.4 (d, $^1J_{C,F}$ = 218.6 Hz, 4-C), 119.8 (d, $^3J_{C,F}$ = 5.0 Hz, 6-C), 121.4 (dq,

$^3J_{C,F}$ = 4.2, $^3J_{C,F}$ = 5.3, $^3J_{C,F}$ = 10.7 Hz, 10-C), 124.9 (dq, $^3J_{C,F}$ = 7.9, $^3J_{C,F}$ = 9.3 Hz, 8-C), 129.8 (s, 7-C), 140.1 (d, $^2J_{C,F}$ = 21.0 Hz, 5-C), 153.2 (m, 9-C), 156.3 (s, 1-C). ^{19}F NMR (282 MHz, $CDCl_3$): δ -193.28 (ddd, $^3J_{H,F(trans)}$ = 3.6 , $^3J_{H,F(trans)}$ = 13.2, $^3J_{H,F(cis)}$ = 22.1 Hz, 1 F, 4-CF), 62.17 (d, $^2J_{F,F}$ = 150.2 Hz, 4 F, SF_{eq}), 83.12 (p, $^2J_{F,F}$ = 150.2 Hz, 1 F, SF_{ax}). HRMS (ESI), *m/z*: calcd. for $C_{14}H_{17}F_6NO_2SNa^+$: 400.0777; found 400.0778; calcd. for $(C_{14}H_{17}F_6NO_2S)_2Na^+$: 777.1661; found 777.1662. MS (GC/EI), *m/z* (%): 377 (0) [M^+], 342 (1), 321 (2) [M^+-C_4H_9], 303 (1) [M^+-HOC_4H_9], 277 (13) [M^+-$CO_2C_4H_9$], 256 (16), 248 (1) [$C_{10}H_9F_3NOS^+$], 236 (2), 218 (1), 209 (1), 193 (3) [321-SF_5], 176 (1) [302-SF_5], 149 (3) [277-SF_5], 133 (5), 121 (1), 101 (4) [$CO_2C_4H_9^+$], 89 (2) [SF_3^+], 74 (2), 57 (100) [$C_4H_9^+$], 41 (16) [$C_3H_5^+$].

*4.7.3. tert-Butyl cis-[2-fluoro-2-(4-pentafluorosulfanylphenyl)cyclopropyl]carbamate (**10b**)*

Similarly to the procedure [14] **8b** (0.64 g, 2.1 mmol) was treated with triethylamine (319 mg, 3.2 mmol, 1.5 eq.), *tert*-butanol (1.56 g, 21 mmol, 10 eq.) and DPPA (1.73 g, 6.3 mmol, 3 eq.) in dry cyclohexane (20 mL). After refluxing for 12 h Boc_2O (688 mg, 3.2 mmol, 1.5 eq.) was added. Subsequently the mixture was diluted with EtOAc (50 mL) and washed with 5% citric acid (20 mL), sat. $NaHCO_3$ (20 mL), water (20 mL) and sat. NaCl solution (20 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the Boc-protected amine **10b**. Column chromatography (silica gel, cyclohexane/EtOAc, 6:1) and subsequent recrystallization from pentane/EtOAc furnished **10b** as white solid. Yield: 362 mg (46%). Mp 185 °C (pentane/EtOAc). ^{1}H NMR (400 MHz, DMSO): δ 1.09 (s, 9 H, 12/13/14-CH_3), 1.71 (ddd, $^3J_{H,H(trans)}$ = 6.1, $^2J_{H,H}$ = 9.2, $^3J_{H,F(trans)}$ = 13.8 Hz, 1 H, H_B), 1.83 (ddd, $^2J_{H,H}$ = 9.2, $^3J_{H,H(cis)}$ = 10.1, $^3J_{H,F(cis)}$ = 22.3 Hz, 1 H, H_A), 3.19 (ddd, $^3J_{H,H(trans)}$ = 6.1, $^3J_{H,H(cis)}$ = 10.1, $^3J_{H,F(cis)}$ = 14.2 Hz, 1 H, H_X), 7.52 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, 6/10-CH), 7.88 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, 7/9-CH). ^{13}C NMR (101 MHz, DMSO): δ 17.1 (d, $^2J_{C,F}$ = 11.2 Hz, 3-C), 27.4 (s, 12/13/14-C), 34.8 (d, $^2J_{C,F}$ = 18.3 Hz, 2-C), 78.1 (s, 11-C), 81.0 (d, $^1J_{C,F}$ = 216.9 Hz, 4-C), 125.0 (m, 7/9-C), 126.0 (d, $^3J_{C,F}$ = 7.1 Hz, 6/10-C), 139.2 (d, $^2J_{C,F}$ = 18.7 Hz, 5-C), 151.8 (m, 8-C), 155.4 (s, 1-C). ^{19}F NMR (282 MHz, DMSO): δ -176.13 (ddd, $^3J_{H,F(trans)}$ = 13.8 Hz, $^3J_{H,F(cis)}$ = 14.2, $^3J_{H,F(cis)}$ = 22.3 Hz, 1 F, 4-CF), 64.53 (d, $^2J_{F,F}$ = 150.6 Hz, 4 F, SF_{eq}), 87.81 (p, $^2J_{F,F}$ = 150.6 Hz, 1 F, SF_{ax}). HRMS (ESI), *m/z*: calcd. for $C_{14}H_{17}F_6NO_2SNa^+$: 400.0776; found 400.0775. MS (GC/EI), *m/z* (%): 377 (0) [M^+], 342 (0) [362-HF], 321 (2) [M^+-C_4H_8], 303 (1) [M^+-HOC_4H_9], 284 (1) [303-F], 277 (8) [M^+-$CO_2C_4H_9$], 256 (9), 240 (1) [$C_9H_5SF_5^+$], 229 (1), 206 (1), 193 (2) [321-SF_5], 176 (3) [302-SF_5], 149 (3) [277-SF_5], 133 (4), 121 (2), 101 (3) [$CO_2C_4H_9^+$], 89 (2) [SF_3^+], 75 (1), 57 (100) [$C_4H_9^+$], 41 (15) [$C_3H_5^+$].

*4.7.4. tert-Butyl trans-[2-fluoro-2-(4-pentafluorosulfanylphenyl)cyclopropyl]carbamate (**11b**)*

Similarly to the procedure [14] **9b** (0.24 g, 0.8 mmol) was) was treated with triethylamine (121 mg, 1.2 mmol, 1.5 eq.), *tert*-butanol (0.60 g, 8 mmol, 10 eq.) and DPPA (659 mg, 2.4 mmol, 3 eq.) in dry cyclohexane (15 mL). After refluxing for 12 h Boc_2O (262 mg, 1.2 mmol, 1.5 eq.) was added. Subsequently the mixture was diluted with EtOAc (50 mL) and washed with 5% citric acid (20 mL), sat. $NaHCO_3$ (20 mL), water (20 mL) and sat. NaCl solution (20 mL). After drying ($MgSO_4$) the solvent was removed by rotary evaporator to give the corresponding Boc-protected amine **11b**. Column chromatography (silica gel, cyclohexane/EtOAc, 6:1) and subsequent recrystallization from pentane/EtOAc furnished **11b** as white solid. Yield: 131 mg (45%). Mp 190 °C (pentane/EtOAc). ^{1}H NMR (600 MHz, DMSO): δ 1.37 (s, 9 H, 12/13/14-CH_3), 1.65 (ddd, $^3J_{H,H(trans)}$ = 6.6, $^2J_{H,H}$ = 8.5, $^3J_{H,F(cis)}$ = 22.2 Hz, 1 H, H_A), 1.72 (ddd, $^2J_{H,H}$ = 8.5, $^3J_{H,H(trans)}$ = 9.9, $^3J_{H,F(trans)}$ = 13.7 Hz, 1 H, H_B), 2.86 (ddd, $^3J_{H,F(trans)}$ = 3.7, $^3J_{H,H(trans)}$ = 6.6, $^3J_{H,H(cis)}$ = 9.9 Hz, 1 H, H_X), 7.50 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 6/10-CH), 7.86 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 7/9-CH). ^{13}C NMR (151 MHz, DMSO): δ 19.0 (d, $^2J_{C,F}$ = 10.8 Hz, 3-C), 28.5 (s, 12/13/14-C), 36.4 (d, $^2J_{C,F}$ = 9.6 Hz, 2-C), 78.6 (d, $^1J_{C,F}$ = 218.1 Hz, 4-C), 78.7 (s, 11-C), 124.7 (m, 7/9-C), 126.3 (d, $^3J_{C,F}$ = 8.9 Hz, 6/10-C), 143.9 (d, $^3J_{C,F}$ = 20.9 Hz, 5-C), 152.0 (m, 8-C), 157.4 (s, 1-C). ^{19}F NMR (282 MHz, DMSO): δ -196.81 (dd, $^3J_{H,F(trans)}$ = 13.7, $^3J_{H,F(cis)}$ = 22.2 Hz, 1 F, 4-CF), 64.40 (d, $^3J_{H,F}$ = 150.6 Hz, 4 F, SF_{eq}), 87.42 (p, $^3J_{H,F}$ = 150.1, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_{14}H_{17}F_6NO_2SNa^+$: 400.0776; found 400.0770. HRMS (ESI neg.), *m*/*z*: calcd. for $C_{14}H_{16}F_6NO_2S^-$: 376.0811; found 305.0809. MS (GC/EI), *m*/*z* (%): 377 (0) [M^+], 321 (2) [M^+-C_4H_8], 304 (1) [M^+-OC_4H_9], 284 (1) [304-HF], 277 (7) [M^+-$CO_2C_4H_8$], 256 (9) [277-H-HF], 248 (2) [$C_8H_6F_6S^+$], 229 (1), 206 (1), 193 (1) [321-SF_5], 176 (2) [302-SF_5], 149 (1) [277-SF_5], 133 (4), 121 (2), 101 (3) [$CO_2C_4H_9^+$], 89 (2) [SF_3^+], 74 (2), 59 (16), 57 (100) [$C_4H_9^+$], 41 (15) [$C_3H_5^+$].

4.8. Deprotection

*4.8.1. cis-2-Fluoro-2-(3-pentafluorosulfanylphenyl)cyclopropylamine hydrochloride (**12a**)*

Similarly to procedure [14] **10a** (189 mg, 0.5 mmol) was treated with 6M HCl (3 mL) in THF (3 mL). After stirring for 12 h the solvents were removed under reduced pressure to yield the corresponding amine hydrochloride. Recrystallization from MeOH/Et_2O furnished **12a** as a white solid: Yield: 157 mg (100%). Mp 170 °C (MeOH/Et_2O, decomposition). ^{1}H NMR (300 MHz, MeOD): δ 1.90 (ddd, $^3J_{H,H(trans)}$ = 6.3, $^2J_{H,H}$ = 9.4, $^3J_{H,F(trans)}$ = 10.5 Hz, 1 H, H_B), 2.06 (ddd, $^2J_{H,H}$ = 9.3, $^3J_{H,H(cis)}$ = 10.2, $^3J_{H,F(cis)}$ = 20.3 Hz, 1 H, H_A), 3.49 (ddd, $^3J_{H,H(trans)}$ = 6.3, $^3J_{H,H(cis)}$ = 10.2, $^3J_{H,F(cis)}$ = 14.3 Hz, 1 H, H_x), 7.77 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 6-CH), 7.90 (d,

$^{3}J_{H,H}$ = 7.2 Hz, 1 H, 7-CH), 8.01 (ddd, $^{4}J_{H,H}$ = 1.2, $^{4}J_{H,H}$ = 2.2, $^{3}J_{H,H}$ = 8.3 Hz, 1 H, 5-CH), 8.14 (dd, $^{4}J_{H,H}$ = 1.8 Hz, 1 H, 9-CH). ^{13}C NMR (75 MHz, MeOD): δ 16.2 (d, $^{2}J_{C,F}$ = 13.0 Hz, 2-C), 32.9 (d, $^{2}J_{C,F}$ = 21.5 Hz, 1-C), 79.8 (d, $^{1}J_{C,F}$ = 221.0 Hz, 3-C), 128.3 (p, $^{3}J_{C,F}$ = 4.4 Hz, 7-C), 129.3 (dp, $^{3}J_{C,F}$ = 4.7, 6.9 Hz, 9-C), 131.4 (s, 6-C), 133.5 (d, $^{2}J_{C,F}$ = 20.1 Hz, 4-C), 134.1 (d, $^{3}J_{C,F}$ = 2.4 Hz, 5-C), 155.5 (p, $^{2}J_{C,F}$ = 17.9 Hz, 8-C). ^{19}F NMR (282 MHz, MeOD): δ -160.63 (dddd, $^{4}J_{H,F}$ = 1.4, $^{3}J_{H,F(trans)}$ = 10.6, $^{3}J_{H,F(cis)}$ = 14.4, $^{3}J_{H,F(cis)}$ = 20.4 Hz, 1 F, 3-CF), 63.04 (d, $^{2}J_{F,F}$ = 147.3 Hz, 4 F, SF_{eq}), 83.53 (p, $^{2}J_{F,F}$ = 147.3 Hz, 1 F, SF_{ax}). HRMS (ESI), *m/z*: calcd. for $C_9H_9F_6NSH^+$: 278.0433; found 278.0440; *m/z*: calcd. for $C_9H_8F_5NSH^+$ [MH-HF]: 258.0370; found 258.0378. Elemental analysis: calcd for $C_9H_{10}ClF_6NS$: C, 34.46; H, 3.21; N, 4.47; found: C, 34.37; H, 3.11; N, 4.35.

*4.8.2. trans-2-Fluoro-2-(3-pentafluorosulfanylphenyl)cyclopropylamine hydrochloride (**13a**)*

Similarly to the procedure [14] **11a** (151 mg, 0.4 mmol) was treated with 6M HCl (3 mL) in THF (3 mL). After stirring for 12 h the solvents were removed under reduced pressure to yield the corresponding amine hydrochloride. Recrystallization from MeOH/Et_2O furnished **13a** as a white solid. Yield: 121 mg (96%). Mp 180 °C (MeOH/Et_2O, decomposition). ^{1}H NMR (600 MHz, MeOD): δ 1.91 (ddd, $^{3}J_{H,H(trans)}$ = 6.2, $^{2}J_{H,H}$ = 9.4, $^{3}J_{H,F(cis)}$ = 22.9 Hz, 1 H, H_A), 1.95 (ddd, $^{3}J_{H,H(cis)}$ = 9.3, $^{2}J_{H,H}$ = 9.4, $^{3}J_{H,F(trans)}$ = 14.2 Hz, 1 H, H_B), 3.17 (ddd, $^{3}J_{H,F(trans)}$ = 0.9, $^{3}J_{H,H(trans)}$ = 6.2, $^{3}J_{H,H(cis)}$ = 9.3 Hz, 1 H, H_X), 7.61 (dd, $^{4}J_{H,H}$ = 1.5, $^{3}J_{H,H}$ = 8.1 Hz, 1 H, 5-CH), 7.66 (t, $^{3}J_{H,H}$ = 8.1 Hz, 1 H, 6-CH), 7.90 (ddt, $^{4}J_{H,H}$ = 0.8, $^{4}J_{H,H}$ = 1.5, $^{3}J_{H,H}$ = 7.6 Hz, 1 H, 7-CH), 7.93 (q, $^{4}J_{H,H}$ = 1.0, $^{4}J_{H,H}$ = 1.5 Hz, 1 H, 9-CH). ^{13}C NMR (75 MHz, MeOD): δ 18.1 (d, $^{2}J_{C,F}$ = 12.0 Hz, 2-C), 32.8 (d, $^{2}J_{C,F}$ = 9.9 Hz, 1-C), 78.7 (d, $^{1}J_{C,F}$ = 219.8 Hz, 3-C), 124.4 (dp, $^{3}J_{C,F}$ = 5.0, 9.9 Hz, 9-C), 127.7 (p, $^{3}J_{C,F}$ = 5.0 Hz, 7-C), 130.0 (d, $^{3}J_{C,F}$ = 5.7 Hz, 5-C), 131.1 (s, 6-C), 138.2 (d, $^{2}J_{C,F}$ = 20.9 Hz, 4-C), 155.3 (m, 8-C). ^{19}F NMR (564 MHz, MeOD): δ -189.61 (dd, $^{3}J_{H,F(trans)}$ = 14.1, $^{3}J_{H,F(cis)}$ = 22.9 Hz, 1 F, 3-CF), 62.91 (d, $^{2}J_{F,F}$ = 148.5 Hz, 4 F, SF_{eq}), 83.94 (p, $^{2}J_{F,F}$ = 148.5 Hz, 1 F, SF_{ax}). HRMS (ESI), *m/z*: calcd. for $C_9H_9F_6NSH^+$: 278.0433; found 278.0445; *m/z*: calcd. for $C_9H_8F_5NSH^+$ [MH-HF]: 258.0370; found 258.0379. Elemental analysis: calcd. for $C_9H_{10}ClF_6NS$: C, 34.46; H, 3.21; N, 4.47; found: C, 34.18; H, 3.11; N, 4.29.

*4.8.3. cis-2-Fluoro-2-(4-pentafluorosulfanylphenyl)cyclopropylamine hydrochloride (**12b**)*

Similarly to procedure [14] **10b** (334 mg, 0.9 mmol) was treated with 6M HCl (3 mL) in THF (3 mL). After stirring for 12 h the solvents were removed under reduced pressure to yield the corresponding amine hydrochloride. Recrystallization from MeOH/Et_2O furnished **12b** as a white solid. Yield: 263 mg (95%). Mp 170 °C (MeOH/Et_2O, decomposition). ^{1}H NMR (600

MHz, MeOD): δ 1.94 (ddd, $^{3}J_{H,H(trans)}$ = 6.3, $^{2}J_{H,H}$ = 9.4, $^{3}J_{H,F(trans)}$ = 10.7 Hz, 1 H, H_B), 2.05 (ddd, $^{2}J_{H,H}$ = 9.4, $^{3}J_{H,H(cis)}$ = 10.3, $^{3}J_{H,F(cis)}$ = 20.4 Hz, 1 H, H_A), 3.47 (ddd, $^{3}J_{H,H(trans)}$ = 6.3, $^{3}J_{H,H(cis)}$ = 10.3, $^{3}J_{H,F(cis)}$ = 14.5 Hz, 1 H, H_X), 7.83 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2 H, 5/9-CH), 8.00 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2 H, 6/8-CH). ^{13}C NMR (151 MHz, MeOD): δ 16.2 (d, $^{2}J_{C,F}$ = 12.8 Hz, 2-C), 33.1 (d, $^{2}J_{C,F}$ = 21.2 Hz, 1-C), 79.3 (d, $^{1}J_{C,F}$ = 220.9 Hz, 3-C), 128.0 (p, $^{3}J_{C,F}$ = 4.7 Hz, 6/8-C), 130.8 (d, $^{3}J_{C,F}$ = 4.1 Hz, 5/9-C), 136.1 (d, $^{2}J_{C,F}$ = 20.0 Hz, 4-C), 156.0 (p, $^{2}J_{C,F}$ = 18.1 Hz, 7-C). ^{19}F NMR (564 MHz, MeOD): δ -164.29 (ddd, $^{3}J_{H,F(trans)}$ = 10.7 Hz, $^{3}J_{H,F(cis)}$ = 14.5 Hz, $^{3}J_{H,F(cis)}$ = 19.8 Hz, 1 F, 3-CF), 62.79 (d, $^{2}J_{F,F}$ = 148.2 Hz, 4 F, SF_{eq}), 83.55 (p, $^{2}J_{F,F}$ = 148.1 Hz, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_9H_9F_6NSH^+$: 278.0433; found 278.0461; *m*/*z*: calcd. for $C_9H_8F_5NSH^+$ [MH-HF]: 258.0370; found 258.0379. Elemental analysis: calcd. for $C_9H_{10}ClF_6NS$: C, 34.46; H, 3.21; N, 4.47; found: C, 34.78; H, 3.20; N, 4.49.

4.8.4. *trans-2-Fluoro-2-(4-pentafluorosulfanylphenyl)cyclopropylamine hydrochloride (**13b**)*

Similarly to procedure [14] **11b** (60 mg, 0.2 mmol) was treated with 6M HCl (3 mL) in THF (3 mL). After stirring for 12 h the solvents were removed under reduced pressure to yield the corresponding amine hydrochloride. Recrystallization from MeOH/Et_2O furnished **13b** as a white solid. Yield: 50 mg (94%). Mp 190 °C (MeOH/Et_2O, decomposition). ^{1}H NMR (600 MHz, MeOD): δ 1.95 (m, 2 H, H_A/ H_B), 3.19 (m, 1 H, H_X), 7.57 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2 H, 5/9-CH), 7.90 (d, $^{3}J_{H,H}$ = 8.2 Hz, 1 H, 6/8-CH). ^{13}C NMR (151 MHz, MeOD): δ 18.8 (d, $^{2}J_{C,F}$ = 11.7 Hz, 2-C), 33.2 (d, $^{2}J_{C,F}$ = 9.7 Hz, 1-C), 78.4 (d, $^{1}J_{C,F}$ = 220.0 Hz, 3-C), 126.3 (d, $^{3}J_{C,F}$ = 6.9 Hz, 5/9-C), 127.6 (p, $^{3}J_{C,F}$ = 4.7 Hz, 6/8-C), 141.2 (d, $^{2}J_{C,F}$ = 21.0 Hz, 4-C), 154.9 (p, $^{2}J_{C,F}$ = 17.5 Hz, 7-C). ^{19}F NMR (564 MHz, MeOD): δ -193.86 (dd, $^{3}J_{H,F(trans)}$ = 15.4, $^{3}J_{H,F(cis)}$ = 21.7 Hz, 1 F, 3-CF), 62.98 (d, $^{2}J_{F,F}$ = 147.7 Hz, 4 F, SF_{eq}), 83.98 (p, $^{2}J_{F,F}$ = 147.6, 1 F, SF_{ax}). HRMS (ESI), *m*/*z*: calcd. for $C_9H_9F_6NSH^+$: 278.0433; found 278.0441. Elemental analysis: calcd. for $C_9H_{10}ClF_6NS$: C, 34.46; H, 3.21; N, 4.47; found: C, 34.64; H, 3.30; N, 4.38.

Supplementary information

Copies of the NMR spectra of all the synthesized compounds are available.

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Highlights:

- 3- and 4-SF_5-substituted benzaldehydes were transformed to the hitherto unknown styrenes by Wittig reactions.
- SF_5-substituted α-fluorostyrenes were synthesized by bromofluorination and subsequent HBr elimination.
- Copper(I)-catalyzed reactions with ethyldiazoacetate gave diastereomeric ethyl 2-aryl-2-fluorocyclopropanecarboxylates.
- the diastereomers were saponified and the acids were transformed to corresponding cyclopropylamines by Curtius degradation.
- pK_a values of the cyclopropanecarboxylic acids and the cyclopropylamines were determined.