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Development of fluorination methods using continuous-flow microreactors

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Dedication with respect and congratulations to Professor Larry Overman on the receipt of the Tetrahedron Prize

ABSTRACT

The safe and reliable use of various fluorination methods including nucleophilic fluorination (DAST), trifluoromethylation (Ruppert's reagent) and electrophilic fluorination (Selectfluor®) in a continuous-flow microreactor is reported. Special attention was given to the use of in-line scavenging procedures in order to obtain clean products without the need for further purification.

1. Introduction

Fluorinated molecules are found in many commercially important products.[1] This is because fluorination can dramatically improve the properties of compounds especially against metabolic degradation in pharmaceutical or in agrochemical applications. However, the introduction of fluorine is not always straightforward and can add considerably to the cost of goods owing to the hazardous nature of the reagents used to introduce fluorine or the inherent expense of specific fluorinated building blocks.

In this work we report on the development of several methods to incorporate fluorine into various substrates using flow microreactor devices.[2] Flow chemical processes are becoming increasingly useful in the assembly of molecules since these methods readily accommodate automation and reaction optimization.[3] They can provide many efficiency gains through the generation of less waste, telescoped reaction processes,[4] and lower solvent usage when compared with more conventional batch reactions. Also their ability to contain hazardous, obnoxious or reactive intermediates adds to their value owing to their improved safety features.[5] Similarly by incorporating immobilized reagents and scavengers of by-products into the flow lines enhanced product purities are obtained without the need for routine unit operations such as crystallization, distillation, chromatography or aqueous work-up protocols.[6]

Flow chemistry has been shown to enhance many synthetic transformations; of particular importance is the introduction of fluorine into organic substrates.[7] Herein we report in full on the use of diethylaminosulfur trifluoride (DAST), (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo-[2.2.2]octane) *bis*(tetrafluoroborate) (Selectfluor®),

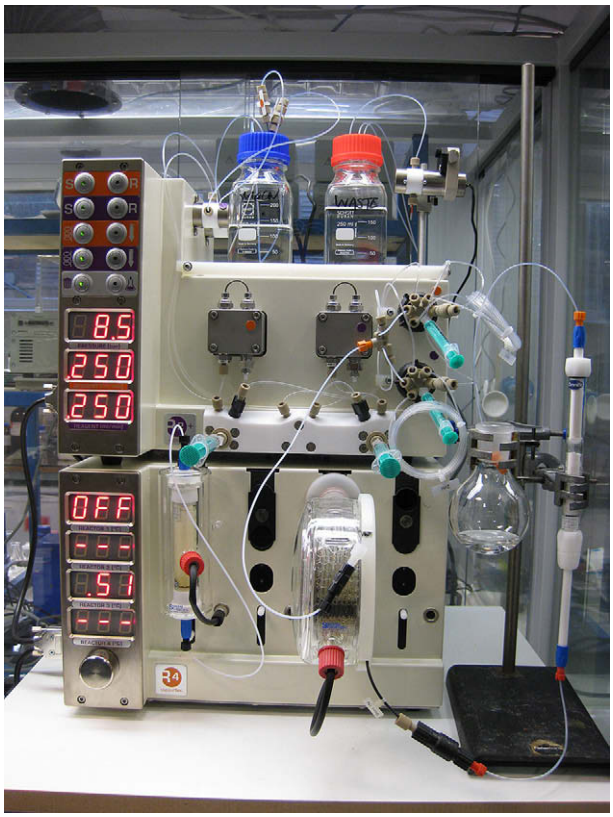

Figure 1. Vapourtec R2+R4 flow system.

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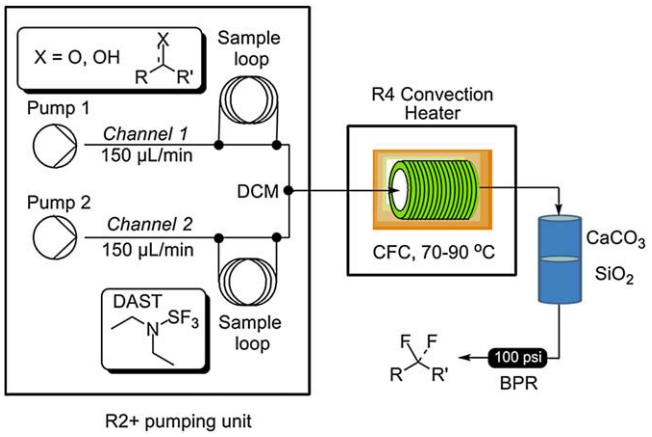


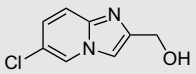
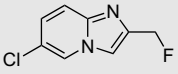
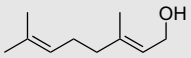
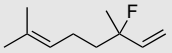
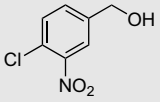
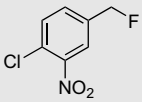
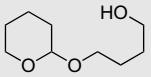
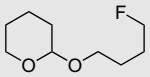
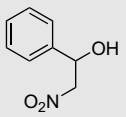
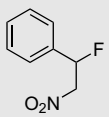
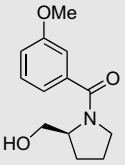
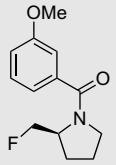
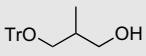
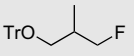
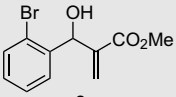
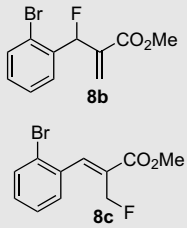
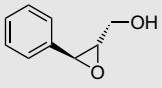
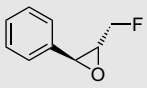
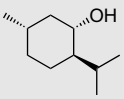
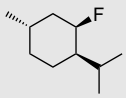
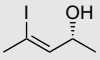
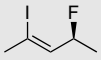
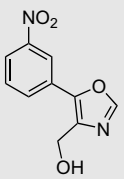
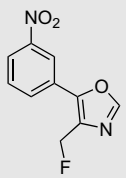
Scheme 1. General flow reactor schematic for DAST reactions.

and trimethylsilyl trifluoromethane (TMS-CF_3, Ruppert's reagent) as complimentary methods for the effective incorporation of fluorine moieties.

2. Results and discussion

In the first set of experiments we evaluated the use of DAST as a commonly used reagent to bring about the conversion of alcohols and carbonyl compounds to their corresponding fluoro derivatives. While this reagent is extremely effective it is problematic in that it is volatile, reacts violently with water and readily undergoes dismutation to SF_4 and $(Et_2N)_2SF_2$ when heated to temperatures in excess of 90 °C.[8] In addition the by-products of the reactions are corrosive and will readily etch standard laboratory glassware. Consequently, the use of DAST in a continuous-flow reactor using inert plastic flow tubes (PEEK, PTFE, PFA) provides flexibility, scale-up opportunity, and enhanced safety of operation. The flow reactor chosen for this study was the commercially available Vapourtec R2+/R4 modular device[9] (Fig. 1). This convenient set-up employs

Table 1
Fluorination products starting from alcohols; isolated yields

Entry	Starting material	Fluorination product	Yield (%)	Entry	Starting material	Fluorination product	Yield (%)
1	 **1a**	 **1b**	73	2	 **2a**	 **2b**	87
3	 **3a**	 **3b**	97	4	 **4a**	 **4b**	83
5	 **5a**	 **5b**	65	6	 **6a**	 **6b**	88
7	 **7a**	 **7b**	92	8	 **8a**	 **8b** **8c**	92
9	 **9a**	 **9b**	96	10	 **10a**	 **10b**	80
11	 **11a**	 **11b**	82	12	 **12a**	 **12b**	87

a self-calibrating dual pumping system and the ability to load the corrosive DAST reagent *via* a PFA injection loop mounted on the R2+ module. This reagent stream can be readily mixed in a T-piece joining the equivalent substrate flow stream and progressing into a convection flow coil (CFC, 9 mL volume, 1 mm i.d.) located on the R4 unit (Fig. 1). Temperatures of up to 90 °C were used with DCM as solvent with boiling suppressed using an in-line backpressure regulator (BPR) operating at 6.9 bar (100 psi).

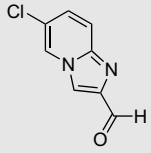
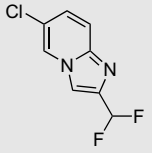
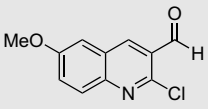
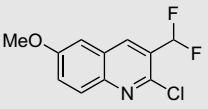
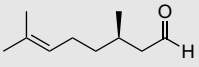
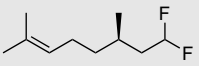
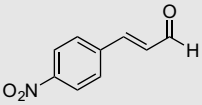
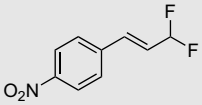
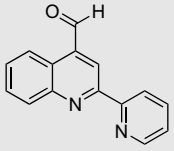
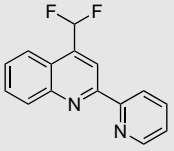
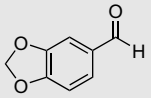
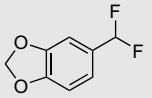
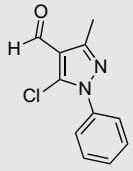
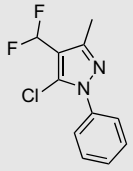
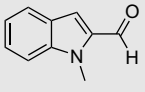
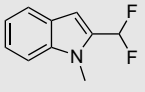
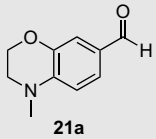
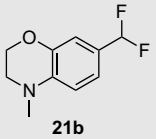
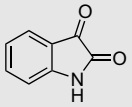
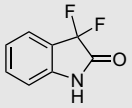
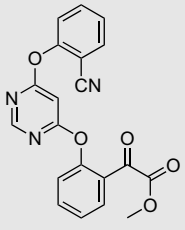
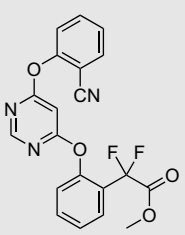
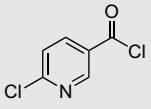
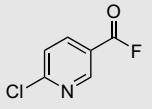
Typically, concentrations ranging between 0.5 and 1.0 M of the DAST reagent were used for these experiments (Scheme 1; X=O or OH). The DAST and the substrate were loaded into two identical sample loops (2 mL internal volume, PEEK, 0.16 mm i.d.), which were eluted at 150 μL/min per channel. The combined streams were then directed through the CFC, which was maintained at temperatures between 70 and 90 °C giving a heated residence time of 27 min.

The exiting flow stream from the CFC reactor was directed into a glass column (10 mm bore i.d., 150 mm length)[10] packed with a two compartment bed of powdered calcium carbonate (~2 g) followed by a plug of silica gel (~2 g) to effect quenching and removal of residual DAST and other side products. During this tandem quenching and scavenger step evolution of CO_2 was observed, but was easily contained within the reactor due to the presence of the BPR. The final product was then obtained without the need for further purification following evaporation of the solvent giving products with purities above 95% as determined by LC/MS and ^{1}H NMR. The exiting flow stream following sequestration was also analyzed for inorganic fluoride content using a standardized test kit[11] but no fluoride contaminants were detected.

The initial substrates examined for the reaction in flow using DAST in the apparatus described above were alcohols.[12] Accordingly, the primary alcohols **1a**–**12a** were reacted to give in good yields the corresponding monofluorides (Table 1).

What should be noted from the table is that many sensitive functionalities such as esters, acetals, amides, epoxides, ethers, and vinyl iodides remain intact during the reaction. In the case of geraniol (**2a**) the quaternary fluoride (**2b**) was produced as the sole

Table 2
Fluorination of carbonyl compounds using DAST; isolated yields

Entry	Starting material	Fluorination product	Yield (%)	Entry	Starting material	Fluorination product	Yield (%)
13	 **13a**	 **13b**	86	14	 **14a**	 **14b**	75
15	 **15a**	 **15b**	83	16	 **16a**	 **16b**	96
17	 **17a**	 **17b**	89	18	 **18a**	 **18b**	75
19	 **19a**	 **19b**	87	20	 **20a**	 **20b**	50
21	 **21a**	 **21b**	0	22	 **22a**	 **22b**	73
23	 **23a**	 **23b**	94	24	 **24a**	 **24b**	96

product, while in the case of the Baylis–Hillman adduct (**8a**) two allylic fluoride products (**8b**) and (**8c**, single isomer) were observed as a 1:1 mixture of regioisomers but in good overall combined yield. Substrate (**5a**) also proved problematic leading under the reaction conditions to a mixture of the desired product (**5b**) and the eliminated nitrostyrene (35% by crude ^{1}H NMR). However, this impurity could be easily removed by passage of the post reaction mixture through a column containing Quadrapure-BZA a high-loading macroporous benzyl amine resin (QP-BZA).[13]

In order to further expand the scope of this reaction we also examined the conversion of a small collection of aldehydes and ketones to their corresponding difluorides using the same flow procedure. In these experiments we used 2 equiv of the DAST reagent with the CFC operating at 80 °C. For electron-deficient aldehydes the reactions were generally rapid requiring residence times of only 27 min while electron-donating systems needed slightly longer reaction times of approximately 45 min equating to flow rates of 100 μL/min per channel. Once again the products were obtained in excellent yield and purity following the previously established in-line impurity scavenging process (Table 2).

With the electron-rich aldehyde (**20a**) we noticed only a 50% conversion to the desired product (**20b**) while starting material **21a** failed to react entirely. DAST is also known to be less efficient for the analogous conversion of ketones to their corresponding difluorides.[14] Nevertheless, for isatin (**22a**) and the commercially interesting α-ketoester (**23a**) good yields of the resultant difluorides were realized. Although in the case of isatin, owing to its poor solubility in DCM, this was first dissolved in MeCN and mixed with the DAST stream in the normal fashion. The results contained in Table 2 again demonstrate that the reaction is tolerant of many functional groups such as nitro's, alkenes, acetals, amines, nitriles, esters, and various heterocycles. In one isolated experiment we also showed that an acid chloride (**24a**) could be used as a precursor for the corresponding acid fluoride. While this reaction proceeded well giving **24b** in 96% isolated yield we were never able to further transform this to the trifluoride substitution product even using a 3 equiv excess of the DAST reagent at 100 °C.

Finally, we have also shown the DAST reagent to be particularly effective at dehydrating β-hydroxy amides and converting these to oxazolines. Starting from serinol-derived amides this method is also suitable to cyclodehydrate and subsequently fluorinate the substrate in a single operation furnishing fluoromethyl oxazoline (**28b**) in high yield (Table 3).

The experiments were conducted using a similar procedure as previously described using the two-reagent loop set-up. The substrate (0.25 M in DCM) and the DAST reagent (0.25 or 0.5 M) were combined in a T-piece at a combined flow rate of 300 μL/min then passed into the CFC (9 mL internal volume) heated at 70–80 °C. The dual quenching and scavenging process was performed upon the exiting flow stream, which following solvent evaporation furnished the cyclized products. Again, in these reactions the yields and purities of the products following the flow process were excellent and the embedded stereogenic centers remained unaffected during the transformation.

A popular alternative reagent to DAST for the fluorination of organic substrates is Selectfluor®.[15] This commercially available electrophilic fluorinating agent is a relatively stable crystalline solid, procurable at scale. The solid material is stable up to 100 °C[16] and can be used in a number of solvents of which MeCN is by far the most common owing to its ionic nature and solubility of about 50 mg/mL (0.14 M). In order to demonstrate the use of Selectfluor® under flow chemistry conditions in a microreactor format we have examined two different reactions. The first of these involves α-fluorination of activated carbonyl compounds to the corresponding fluoride (or difluoride in one case). In these examples the reactor configuration requires two independent injection loops, one loaded with a solution of Selectfluor® (0.1 M MeCN) and the other with the substrate (in MeCN). The reagents are pumped from the R2+ unit into a mixing T-piece and on into the CFC mounted on the Vapourtec R4 unit (CFC, 9 mL internal volume, 1 mm i.d.). The coil reactor is heated at between 100 and 120 °C and the material pumped at a combined flow rate of 300 μL/min giving a final residence time of 27 min. The product solution upon exiting the CFC cooled rapidly and was directly scavenged by passage through a mixed bed of Amberlyst 21 and 15 resins contained in a glass column (10 mm bore i.d., 150 mm length). In optimization of this process we determined that better overall yields and purities were obtained using the alternative Quadrapure-SA and -DMA scavenger resins.[13] These scavengers ensured the complete removal of excess reagents, by-products, and starting carbonyl compound *via* its enol form to give clean products in high yield and purities being in excess of 95% as determined by both LC/MS and ^{1}H NMR (Scheme 2).

The products of these fluorination reactions are listed in Table 4. Normally monofluorinated species are the primary products although with very reactive substrates such as the trifluoroacetyl derivative **34a** difluorination occurs rapidly to give **34b**. Consequently, in order to avoid mixed fluorination products **2** equiv of the Selectfluor® reagent was employed to drive this particular reaction to completion.

The second variant of the Selectfluor® process employs a similar reactor set-up but introduces olefinic substrates into the second channel together with wet acetic acid (<5 mol % water) to effect an overall fluoro-Ritter reaction process giving acetamide products (Table 5). A generic set of conditions using a flow rate of 150 μL/min per channel and a CFC (9 mL) temperature of 120 °C were determined. This generated the acetamide products in good overall yield and excellent purity. Interestingly, in the case of styrene **39a** the corresponding alcohol was obtained instead of the usual acetamide.

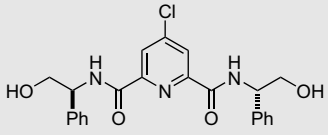
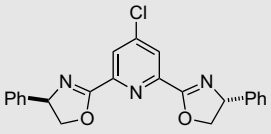
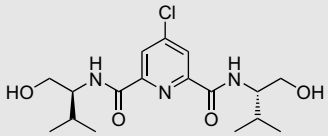
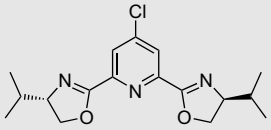
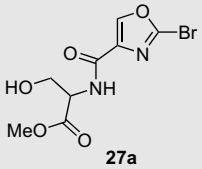
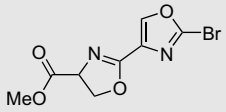
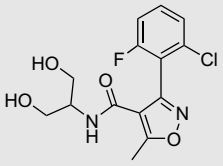
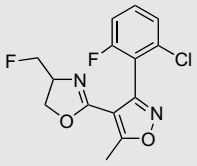
While only a limited number of examples have been investigated the reaction is interesting in that both fluorine and nitrogen substituents are installed into the starting material in a single operation. Additional investigations are currently underway to determine the substrate scope and to expand the range of nitrile nucleophiles.

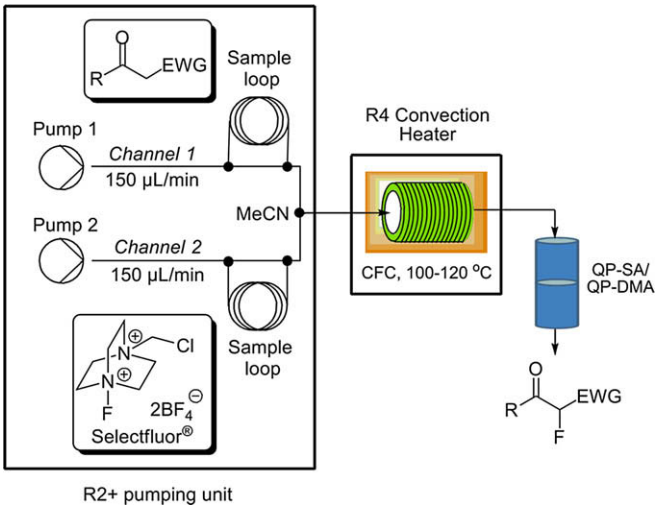
Finally, in order to introduce trifluoromethyl groups into organic precursors we have used the Ruppert reagent in a flow chemistry process. This was based upon an earlier study from our group[17] whereby we showed that the Ruppert reagent reacted with aldehydes to give trifluoromethyl addition products in the presence of an immobilized fluoride source. In this new work we demonstrate the use of a monolithic polymer[18] constructed in a flow tube to deliver fluoride and effect the addition reaction.

In order to prepare the ion-exchange type monolith[19] we firstly prepared a homogeneous mixture of vinyl benzyl chloride (30% v/v), divinyl benzyl chloride (20% v/v, as cross-linker), AIBN (1% w/w), and dodecanol (50% v/v) as the porogen (Scheme 3). After heating this mixture in an appropriately sized glass column (10 mm i.d. bore, 100 mm length) in the R4 unit at 80 °C for 20 h the monolith was allowed to cure and subsequently washed to elute any unreacted soluble monomers and the porogen. This yielded a white single-piece monolith (6.2 g dry weight) with a chloride loading of 4.1 mmol/g.[20] Further functionalization by displacement of the benzylic chloride with trimethylamine and subsequent ion-exchange using an aqueous solution of potassium fluoride furnished the desired fluoride monolith. During our investigations we also prepared the analogous triethylammonium fluoride monolith, however, its performance was much less in our trifluoromethylation reactions and gave significantly higher back-pressures.

The reactor configuration for effecting the reaction of the Ruppert reagent with aldehydes involved the usual two-injection loop system (2 mL internal volume) and T-piece mixing (Scheme 4). One sample loop was loaded with the aldehyde dissolved in THF (0.25 M, 1 equiv) and the other with the Ruppert reagent dissolved in the same solvent (0.3 M, 1.2 equiv). The combined reaction mixture was

Table 3
Cyclodehydration reactions using DAST; isolated yields

Entry	Starting material	Fluorination product	Yield (%)
25	 **25a**	 **25b**	95
26	 **26a**	 **26b**	92
27	 **27a**	 **27b**	91
28	 **28a**	 **28b**	87



Scheme 2. Flow schematic for Selectfluor® reactions.

flowed through the monolithic fluoride column and then pumped through two CFCs (2×10 mL internal volume, 1 mm i.d.) heated on the R4 unit at 40 °C giving residence times of about 2 h.

The addition products were subsequently purified using various scavenger resins. Excess Ruppert reagent was trapped using a bed of PS-benzaldehyde (Argonaut Technologies, 1.2 mmol/g, 3 equiv) in a glass tube (10 mm i.d. bore, 100 mm length). The intermediate silylated alcohol products were deprotected in-line using a QP-SA resin (3 mmol/g, 4 equiv.) in a second glass column (10 mm i.d. bore, 100 mm length) and finally any unreacted aldehyde was removed using a bed of PS-TsNHNH$_2$ (Argonaut Technologies, 2.84 mmol/g, 4 equiv) in a third glass tube (10 mm i.d. bore, 100 mm length). The alcohol products were subsequently isolated in good yield and purity following only evaporation of the solvent (Table 6).

By way of demonstrating the usefulness of the synthesized products from these reactions we also showed that **42b** could be oxidized using MnO_2 packed in a flow tube to afford the trifluoroacetyl derivative **51** in 93% isolated yield (Scheme 5). Alternatively, by passage of **42b** through the DAST microreactor arrangement described earlier we obtained the tetrafluoride derivative (**52**) in 89% yield. Unfortunately, treating **51** with 2 equiv of DAST at elevated temperatures (80 °C) did not furnish the expected pentafluoro compound.

3. Conclusion

In summary, we have demonstrated the safe and convenient application of a series of fluorination methods including nucleophilic fluorination, electrophilic fluorination and trifluoromethylation facilitated using a modular flow reactor. Although some of the reagents employed are known to be toxic and difficult to work with in batch-mode the flow set-up proved to be very reliable and easy to use. Applying in-line scavenging procedures to yield clean products (purities >95%) without the need of further work-ups were found to be of great benefit. In addition, the use of back-pressure regulators at the end of the flow stream allowed us to regularly superheat the solvent and hence accelerate the reactions.

4. Experimental section

4.1. General

All solvents were distilled prior to use and stored under argon. Melting points were determined using an OptiMelt automated melting point system available from Stanford Research Systems and

Table 4
α-Fluorination of activated carbonyls using Selectfluor®; isolated yields

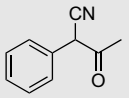
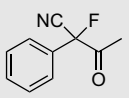
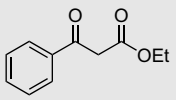
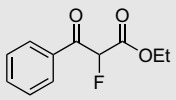
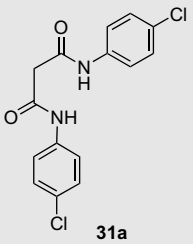
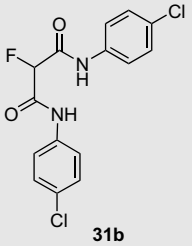
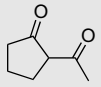
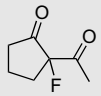
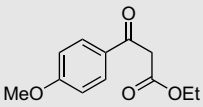
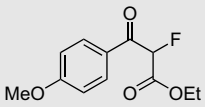
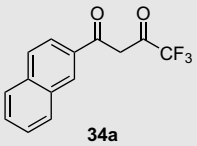
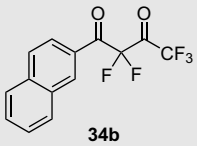
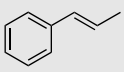
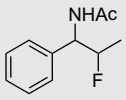
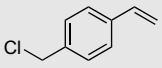
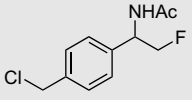
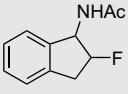
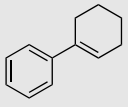
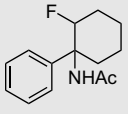
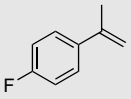
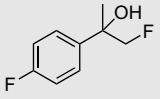
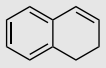
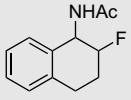
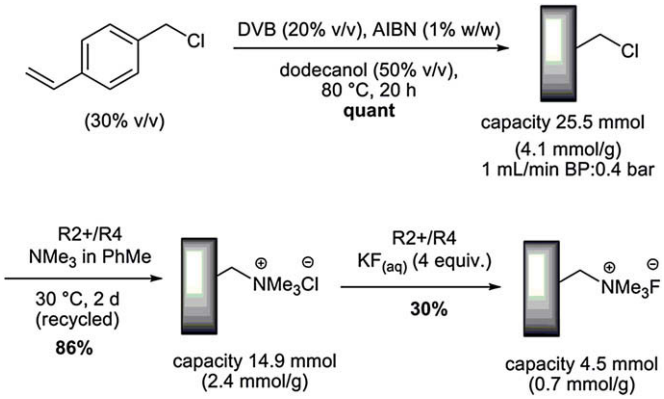
Entry	Starting material	Fluorination product	Yield (%)	Entry	Starting material	Fluorination product	Yield (%)
29	 **29a**	 **29b**	90	30	 **30a**	 **30b**	89
31	 **31a**	 **31b**	82	32	 **32a**	 **32b**	82
33	 **33a**	 **33b**	93	34	 **34a**	 **34b**	83

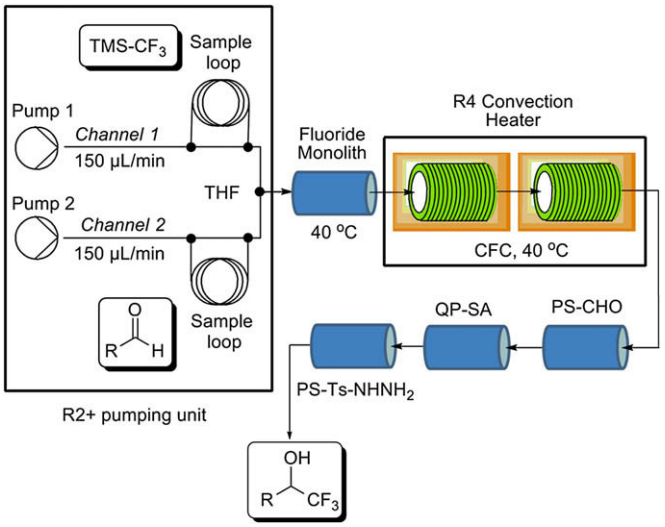
Table 5
Selectfluor® as fluorination reagent in Ritter reactions; isolated yields

Entry	Starting material	Fluorination product	Yield (%)	Entry	Starting material	Fluorination product	Yield (%)
35	 **35a**	 **35b**	97	36	 **36a**	 **36b**	83
37	 **37a**	 **37b**	86	38	 **38a**	 **38b**	96
39	 **39a**	 **39b**	86	40	 **40a**	 **40b**	91

are calibrated against Phenacetin (mp 136 °C). ^{1}H NMR spectra were recorded on a Bruker Avance DPX-400 or DRX-600 spectrometer with residual $CDCl_3$ as the internal reference. ^{13}C NMR

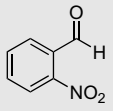
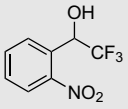
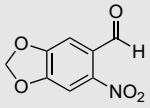
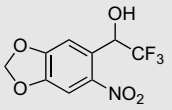
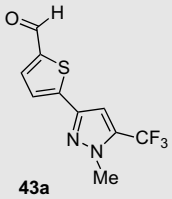
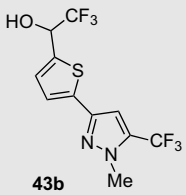
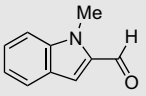
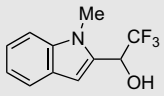
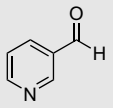
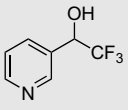
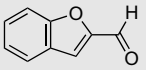
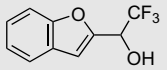
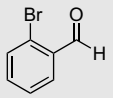
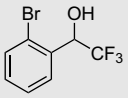
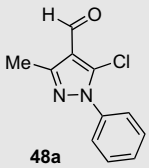
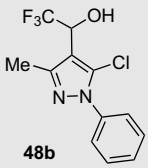
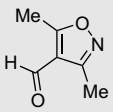
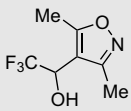
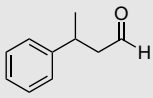
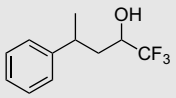


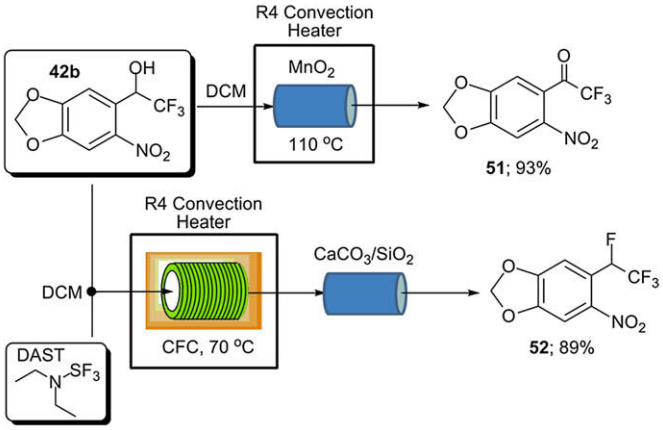
Scheme 3. Preparation of the fluoride monolith.



Scheme 4. General flow set-up for the trifluoromethylation reactions.

Table 6
Trifluoromethylation of aldehydes using Ruppert's reagent; isolated yields

Entry	Starting Material	Fluorination Product	Yield (%)	Entry	Starting Material	Fluorination Product	Yield (%)
41	 **41a**	 **41b**	84	42	 **42a**	 **42b**	76
43	 **43a**	 **43b**	88	44	 **44a**	 **44b**	79
45	 **45a**	 **45b**	86	46	 **46a**	 **46b**	84
47	 **47a**	 **47b**	80	48	 **48a**	 **48b**	87
49	 **49a**	 **49b**	88	50	 **50a**	 **50b**	83



Scheme 5. Derivatization of trifluoroethanols in flow.

spectra were also recorded in $CDCl_3$ on the same spectrometers with the central peak of the residual solvent as the internal reference using the deuterated solvent as internal deuterium lock. COSY, DEPT 135, HMQC, and HMBC spectroscopic techniques were used to aid the assignment of signals in the ^{13}C NMR spectra. IR spectra were recorded on a Perkin–Elmer SpectrumOne FT-IR spectrometer neat. Letters in the parentheses refer to relative absorbency of the peak: w, weak, <40% of the main peak; m, medium, 41–74% of the main peak; s, strong, >74% of the main peak. LC/MS analysis was performed on an Agilent HP 1100 chromatograph (Luna Max RP column) attached to an HPLC/MSD mass spectrometer. Elution was carried out using a reversed-phase gradient of MeCN/water with both solvents containing 0.1% formic acid. The gradient is described in Table 7. For HRMS an LCT Premier Micromass spectrometer was used.

Table 7
LC/MS conditions

Time (min)	MeCN (%)	Flow rate (mL/min^{-1})
0.00	5	1
3.00	95	1
5.00	95	1
5.50	5	1
8.00	5	1

4.1.1. General procedure for DAST reactions

Stock solutions of the substrate and DAST both dissolved in dry DCM (2 mL, 0.5–1 M) were prepared and injected into separate injection loops of the R2+ unit of the Vapourtec flow system. The reagent streams were combined in a standard T-piece and directed into a CFC heated at temperatures ranging between 70 and 90 °C using the R4 unit of the Vapourtec system. After leaving the CFC, the reaction mixture was passed into a glass column containing a plug of $CaCO_3$ (~2 g) and a plug of silica gel (~2 g) in order to quench and trap any fluoride by-products. The pure product was collected and isolated after evaporation of the solvent.

4.1.2. General procedure for Selectfluor® reactions

Using the R2+R4 flow reactor, solutions of the substrate (2 mL, 0.1 M in MeCN) and Selectfluor® (2 mL, 0.1 M in MeCN) were

loaded into individual 2 mL sample loops and combined in a T-mixing piece at flow rates between 0.1 and 0.2 mL/min. This reaction mixture was then directed through a CFC reactor heated at 120 °C giving residence times between 27 and 60 min. The out stream then entered an Omnifit glass column containing an excess of QP-DMA and QP-SA in order to remove the ionic Selectfluor® reagent by-product as well as residual starting material in case of activated enol compounds. The product was isolated after removal of the solvent under reduced pressure.

4.1.3. General procedure for Ruppert reactions

A solution of aldehyde (0.5 mmol, 1 equiv) in 2 mL of dry THF was prepared and combined in flow with a stream of Ruppert's reagent (0.6 mmol, 1.2 equiv) dissolved in 2 mL of dry THF using a T-piece. The reaction mixture was flowed through the monolithic fluoride column at ambient temperature and then pumped through two 10-mL CFCs heated on an R4 unit at 40 °C (residence time 100 min). After leaving the CFCs, the reaction mixture was purified using various scavenger resins in-line. Excess Ruppert's reagent was trapped using a bed of PS-benzaldehyde (Argonaut Technologies, 1.2 mmol/g, 3 equiv) in an Omnifit glass tube (10 mm i.d. bore, 100 mm length). Silylated alcohol product was deprotected in-line using an Amberlyst 15 (1 mmol/g, 4 equiv) in an Omnifit glass column (10 mm i.d. bore, 100 mm length) and finally the unreacted aldehyde was removed using a bed of PS-TsNHNH$_2$ (Argonaut Technologies, 2.84 mmol/g, 4 equiv) in an Omnifit glass tube (10 mm i.d. bore, 100 mm length). The pure product was collected and isolated after evaporation of the solvent.

4.2. 6-Chloro-2-(fluoromethyl)imidazo[1,2-*a*]pyridine (1b)

Prepared from 6-chloroimidazo[1,2-*a*]pyridine-2-yl-methanol (182 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 70 °C with a residence time of 27 min. The product was obtained as a white solid (73% yield, 95% purity). Yield: 73%, t_R=0.60 min, *m*/*z*=185.2 (M+H$^+$); ^{1}H NMR (600 MHz, CDCl$_3$): δ/ppm 8.17 (1H, s), 7.64 (1H, d, *J*=2.2 Hz), 7.55 (1H, d, *J*=9.6 Hz), 7.17 (1H, d, *J*=9.6, 2.2 Hz), 5.54 (2H, d, *J*=47.8 Hz); ^{13}C NMR (150 MHz, CDCl$_3$): δ/ppm 143.8 (C), 143.0 (C, d, *J*=20 Hz), 126.6 (CH), 123.7 (CH), 121.0 (C), 118.3 (CH), 111.6 (CH), 78.9 (CH$_2$, d, *J*=170 Hz); ^{19}F NMR (376 MHz, CDCl$_3$): δ/ppm −211.5 (s); IR (neat): ν 3064.4 (m), 2965.0 (w), 1519.9 (m), 1495.2 (m), 1430.7 (m), 1327.1 (s), 1185.7 (m), 1074.2 (s), 1023.8 (s), 1002.1 (s), 950.8 (s), 839.4 (m), 798.7 (s), 707.9 (s) cm^{-1}. HRMS calculated for $C_8H_7ClFN_2$: 185.0284, found: 185.0276.

4.3. 3-Fluoro-3,7-dimethylocta-1,6-diene (2b)

Prepared from geraniol (154 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 70 °C with a residence time of 27 min. The product was obtained as yellow oil after evaporation of solvent (82% yield, 95% purity). Yield: 82%, t_R=4.64 min, *m*/*z*=no mass detected. ^{1}H NMR (600 MHz, CDCl$_3$): δ/ppm 5.88 (1H, td, *J*=17.7, 11.0 Hz), 5.26 (1H, d, *J*=17.5 Hz), 5.05–5.15 (2H, m), 1.95–2.20 (2H, m), 1.68 (3H, s), 1.63–1.73 (2H, m), 1.59 (3H, s), 1.40 (3H, d, *J*=21.7 Hz); ^{13}C NMR (150 MHz, CDCl$_3$): δ/ppm 140.7 (CH, d, *J*=23 Hz), 131.8 (C), 123.8 (CH), 113.1 (CH$_2$, d, *J*=11 Hz), 95.9 (C, d, *J*=170 Hz), 40.3 (CH$_2$, d, *J*=23 Hz), 25.6 (CH$_3$), 25.2 (CH$_3$, d, *J*=26 Hz), 22.2 (CH$_2$, d, *J*=5 Hz), 17.5 (CH$_3$); ^{19}F NMR (376 MHz, CDCl$_3$): δ/ppm −208.1 (s); IR (neat): ν 2970. (s), 2917.3 (s), 1449.6 (s), 1410.9 (m), 1376.2 (s), 1188.0 (m), 1113.6 (m), 990.2 (s), 926.5 (s), 897.3 (s), 832.3 (m), 735.8 (m) cm^{-1}.

4.4. 1-Chloro-4-(fluoromethyl)-2-nitrobenzene (3b)

Prepared from (4-chloro-3-nitrophenyl)-methanol (187 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 70 °C with a residence time of 27 min. The product was obtained as a colorless oil (97% yield, 99% purity). Yield: 97%, t_R=4.42 min, *m*/*z*=no mass detected; ^{1}H NMR (600 MHz, CDCl$_3$): δ/ppm 7.86 (1H, s), 7.57 (1H, d, *J*=7.8 Hz), 7.51 (1H, d, *J*=7.8 Hz), 5.42 (2H, d, *J*=46.8 Hz); ^{13}C NMR (150 MHz, CDCl$_3$): δ/ppm 147.9 (C), 136.7 (C, d, *J*=18 Hz), 132.2 (CH), 131.2 (CH, d, *J*=6 Hz), 127.0 (C, d, *J*=2 Hz), 123.7 (CH, d, *J*=8 Hz), 82.2 (CH$_2$, d, *J*=170 Hz); ^{19}F NMR (376 MHz, CDCl$_3$): δ/ppm −213.3 (s). IR (neat): ν 3081.8 (w), 2961.2 (w), 1610.1 (w), 1571.7 (w), 1532.7 (s), 1480.9 (m), 1353.2 (s), 1218.5 (m), 1049.9 (m), 1023.7 (m), 892.9 (m), 829.0 (m), 807.2 (m), 753.6 (m), 670.0 (w) cm^{-1}. HRMS calculated for $C_7H_5NClO_2F$: 188.9982, found: 188.9987.

4.5. 2-(4-Fluorobutoxy)-tetrahydro-2*H*-pyran (4b)

Prepared from 4-(tetrahydro-2*H*-pyran-2-yloxy)-butan-1-ol (174 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 80 °C with a residence time of 50 min. The product was obtained as a colorless oil (83% yield, 95% purity). Yield: 83%, t_R=4.64 min, *m*/*z*=no mass detected; ^{1}H NMR (600 MHz, CDCl$_3$): δ/ppm 4.56 (1H, t, *J*=3.6 Hz), 4.47 (1H, t, *J*=6.0 Hz), 4.39 (1H, t, *J*=6.0 Hz), 3.85 (1H, td, *J*=6.6, 3.1 Hz), 3.70–3.80 (1H, m), 3.45–3.55 (1H, m), 3.33–3.43 (1H, m), 1.45–1.85 (10H, m); ^{13}C NMR (150 MHz, CDCl$_3$): δ/ppm 98.9 (CH), 84.0 (CH$_2$, d, *J*=163 Hz), 67.3 (CH$_2$), 62.3 (CH$_2$), 30.2 (CH$_2$, d, *J*=20 Hz), 29.3 (CH$_2$), 25.4 (CH$_2$), 22.0 (CH$_2$, d, *J*=7 Hz), 19.6 (CH$_2$); ^{19}F NMR (376 MHz, CDCl$_3$): δ/ppm −218.6 (s). IR (neat): ν 2941.4 (m), 2868.9 (m), 1738.9 (w), 1454.7 (w), 1353.1 (w), 1200.8 (w), 1242.1 (w), 1160.5 (w), 1121.9 (s), 1077.7 (s), 1033.4 (s), 991.9 (s), 905.5 (m), 869.9 (m), 814.0 (w), 734.4 (m) cm^{-1}.

4.6. (1-Fluoro-2-nitroethyl)benzene (5b)

Prepared from 2-nitro-1-phenyl-ethanol (167 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 80 °C with a residence time of 27 min. The product was obtained as yellow oil (65% yield, 95% purity) after scavenging by passage of the reaction mixture through a column of QP-BZA (500 mg; 2 mmol). Yield: 65%, t_R=4.35 min, *m*/*z*=no mass detected; ^{1}H NMR (600 MHz, CDCl$_3$): δ/ppm 7.35–7.50 (5H, m), 6.18 (1H, app. ddd, *J*=45.6, 9.7, 1.9 Hz), 4.80–4.90 (1H, m), 4.60 (1H, app. ddd, *J*=32.4, 13.8, 2.9 Hz); ^{13}C NMR (150 MHz, CDCl$_3$): δ/ppm 134.1 (C, d, *J*=20 Hz), 129.2 (2 CH, d, *J*=6 Hz), 129.1 (C), 125.7 (2×CH, d, *J*=6 Hz), 89.9 (CH, d, *J*=177 Hz), 79.3 (CH$_2$, d, *J*=27 Hz); ^{19}F NMR (376 MHz, CDCl$_3$): δ/ppm −179.6 (s). IR (neat): ν 2921.5 (m), 2852.6 (m), 1634.4 (m), 1556.8 (s), 1519.1 (s), 1450.0 (m), 1378.7 (m), 1342.6 (s), 1043.8 (m), 765.1 (m), 736.9 (m), 698.3 (m) cm^{-1}.

4.7. (*S*)-(2-(Fluoromethyl)pyrrolidin-1-yl)(2-methoxyphenyl)methanone (6b)

Prepared from (*S*)-(2-(hydroxymethyl)pyrrolidin-1-yl)(2-methoxyphenyl)methanone (117 mg, 0.5 mmol) and DAST (70 μL, 0.5 mmol) at 75 °C with a residence time of 27 min. The product was obtained as colorless oil after evaporation of solvent (88% yield, 95% purity). Yield: 88%, t_R=4.01 min, *m*/*z*=238.0 (M+H$^+$); ^{1}H NMR (600 MHz, CDCl$_3$): δ/ppm 7.33 (1H, t, *J*=7.2 Hz), 7.25 (1H, d, *J*=7.2 Hz), 6.96 (1H, t, *J*=7.2 Hz), 6.90 (1H, d, *J*=7.2 Hz), 4.77 (1H, ddd, *J*=48.6, 7.5, 4.2 Hz), 4.59 (1H, ddd, J=46.8, 9.3, 2.7 Hz), 4.44 (1H, m), 3.82 (3H, s), 2.00–2.13 (2H, m), 1.94 (1H, m), 1.78 (1H, m); ^{13}C NMR (150 MHz, CDCl$_3$): δ/ppm 168.2 (C), 155.2 (C), 130.4 (CH), 127.7 (CH), 127.2 (C), 120.8 (CH), 111.2 (CH), 83.1 (CH$_2$, d, *J*=170 Hz), 56.4 (CH, d, *J*=21 Hz), 55.6 (CH$_3$), 48.5 (CH$_2$), 27.0 (CH$_2$), 24.4 (CH$_2$); ^{19}F NMR (376 MHz, CDCl$_3$): δ/ppm −231.9 (s). IR (neat): ν 2968.2 (w), 2882.3 (w), 1625.6 (s), 1600.5 (s), 1492.2 (m), 1460.6 (s), 1437.3 (s), 1410.1 (s), 1280.6 (m), 1245.5 (s), 1108.6 (m), 1046.3 (m), 1015.0 (s), 890.4 (w), 754.1 (s) cm^{-1}; HRMS calculated for $C_{13}H_{17}NO_2F$: 238.1243, found: 238.1245.

4.8. ((3-Fluoro-2-methylpropoxy)methanetriyl)-tribenzene (7b)

Prepared from 2-methyl-3-(trityloxy)propan-1-ol (166 mg, 0.5 mmol) and DAST (70 μL, 0.5 mmol) at 70 °C with a residence time of 27 min. The product was obtained as colorless oil (93% yield, 95% purity). Yield: 93%, t_R: 5.23 min, m/z=318.0 (M−F); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.46–7.55 (6H, m), 7.32–7.37 (6H, m), 7.24–7.29 (3H, m), 4.40–4.60 (2H, m), 3.11–3.16 (2H, d, J=7.20 Hz), 2.12–2.22 (1H, m), 1.01–1.04 (2H, d, J=7.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 144.2 (C), 128.7 (CH), 127.8 (CH), 127.0 (CH), 86.0 (CH_2, d, J=165 Hz), 64.3 (CH_2, d, J=6 Hz), 52.1 (C), 35.2 (CH, d, J=18 Hz), 13.3 (CH_3, d, J=6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −226.4 (s); IR (neat): ν 3057.7 (m), 2963.7 (m), 1490.2 (m), 1448.8 (m), 1219.2 (w), 1154.4 (w), 1074.3 (s), 1032.5 (m), 1014.6 (m), 909.6 (m), 763.1 (s), 745.9 (s), 707.1 (s) cm^{-1}. HRMS calculated for $C_{23}H_{23}OFNa$: 357.1631, found: 357.1644.

4.9. (2*S*,3*S*)-2-(Fluoromethyl)-3-phenyloxirane[21] (9b)

Prepared from ((2*S*,3*S*)-3-phenyloxiran-2-yl)methanol (150 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 50 °C with a residence time of 27 min. The product was obtained as colorless oil (86% yield, 96% purity). Yield: 86%, t_R=3.84 min, m/z=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.28–7.40 (5H, m), 4.74 (1H, ddd, J=2.4, 10.8, 47.4 Hz), 4.51 (1H, ddd, J=4.8, 10.2, 46.8 Hz), 3.87 (1H, s), 3.30–3.34 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm 136.0 (C), 128.6 (2×CH), 128.5 (CH), 125.7 (2×CH), 82.5 (CH_2F, d, J=171 Hz), 59.7 (CH, d, J=23 Hz), 55.4 (CH, d, J=8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −228.6 (s); IR (neat) ν=1497.1 (w), 1456.0 (w), 1204.4 (w), 1067.8 (m), 998.0 (m), 881.9 (m), 840.1 (m), 748.2 (m), 696.8 (s) cm^{-1}.

4.10. (1*R*,2*S*,4*R*)-2-Fluoro-1-isopropyl-4-methylcyclohexane (10b)

Prepared from (1*S*,2*R*,5*S*)-2-2-isopropyl-5-methylcyclo-hexanol (156 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 70 °C with a residence time of 40 min. The product was obtained as colorless oil (80% yield, 95% purity). Yield: 80%, t_R=2.60 min, m/z=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 4.31 (1H, dtd, J=49.8, 10.8, 4.8 Hz), 2.00–2.15 (2H, m), 1.60–1.75 (2H, m), 1.40–1.50 (1H, m), 1.15–1.25 (1H, m), 0.80–1.10 (9H, m), 0.78 (3H, d, J=6.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 93.3 (CH, d, J=173 Hz), 48.1 (CH, d, J=78 Hz), 41.5 (CH_2, d, J=18 Hz), 34.1 (CH_2, d, J=20 Hz), 31.2 (CH, d, J=11 Hz), 26.5 (CH, d, J=3 Hz), 23.3 (CH_2, d, J=68 Hz), 22.0 (CH_3), 20.4 (CH_3), 17.0 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −175.1 (s); IR (neat) ν=2953.3 (m), 2923.3 (m), 2869.1 (m), 1455.9 (m), 1370.4 (w), 1191.0 (m), 939 (m), 902.5 (s), 848.9 (s), 743.4 (s) cm^{-1}.

4.11. (*S*,*Z*)-4-Fluoro-2-iodopent-2-ene (11b)

Prepared from (*R*,*Z*)-4-iodopent-3-en-2-ol (212 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 60 °C with a residence time of 27 min. The product was obtained as yellow oil (83% yield, 96% purity). Yield: 83%, t_R=4.51 min, m/z=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 5.70 (1H, m), 5.12 (1H, dquin, J=48.0, 6.6 Hz), 2.54 (3H, d, J=4.2 Hz), 1.40 (3H, dd, J=24.0, 6.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 135.0 (CH, d, J=24 Hz), 102.6 (C, d, J=14 Hz), 94.0 (CH, d, J=161 Hz), 33.8 (CH_3, d, J=2 Hz), 20.4 (CH_3, d, J=26 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −168.5 (s). IR (neat) ν=2972.3 (m), 2925.5 (m), 1648.5 (m), 1445.9 (m), 1404.3 (m), 1373.9 (m), 1250.4 (m), 1199.3 (m), 1085.2 (s), 882.8 (m) cm^{-1}.

4.12. 4-Fluoromethyl-5-(3-nitrophenyl)-oxazole (12b)

Prepared from (5-(3-nitrophenyl)oxazol-4-yl)methanol (220 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 65 °C with a residence time of 27 min. The product was obtained as brown solid (86% yield, 95% purity). Yield: 86%, t_R=4.16 min, m/z=245.8 (M+Na$^+$); ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 8.55 (1H, s), 8.26 (1H, d, J=8.0 Hz), 8.03 (1H, d, J=8.0 Hz), 7.98 (1H, s), 7.69 (1H, t, J=8.0 Hz), 5.51 (2H, d, J=48.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 150.2 (CH), 148.8 (C), 148.4 (C, d, J=7 Hz), 132.1 (C), 131.9 (CH, d, J=3 Hz), 130.3 (CH), 128.8 (C, d, J=3 Hz), 123.9 (CH), 121.2 (CH, d, J=3 Hz), 76.4 (CH_2, d, J=164 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −207.5 (s). IR (neat) ν=3098.6 (m), 1535.5 (s), 1504.6 (m), 1465.3 (m), 1402.6 (m), 1345.7 (s), 1326.5 (m), 1131.2 (m), 1024.1 (m), 972.8 (s), 952.6 (s), 872.9 (m), 806.2 (m), 768.4 (m), 742.5 (m), 732.9 (s), 683.3 (m), 667.9 (m) cm^{-1}. HRMS calculated for $C_{10}H_7N_2O_3F$: 222.0426, found: 222.0435.

4.13. 6-Chloro-2-(difluoromethyl)imidazo[1,2-*a*]-pyridine (13b)

Prepared from 6-chloroimidazo[1,2-*a*]pyridine-2-carbaldehyde (180 mg, 1 mmol) and DAST (280 μL, 2 mmol) at 80 °C with a residence time of 45 min. The product was obtained as a white solid (86% yield, 96% purity). Yield: 86%, t_R=3.62 min, m/z=203.2 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.20 (1H, s), 7.78 (1H, s), 7.59 (1H, d, J=9.6 Hz), 7.23 (1H, dd, J=9.6, 2.4 Hz), 6.85 (1H, t, J=55.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 143.8 (C), 141.3 (C, t, J=28 Hz), 127.4 (CH), 124.0 (CH), 121.8 (C), 118.7 (CH), 111.4 (CH, t, J=235 Hz), 110.9 (CH), ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −114.3 (s); IR (neat): ν 3089.0 (w), 2989.0 (w), 1562.6 (m), 1520.4 (m), 1504.5 (m), 1384.5 (m), 1307.0 (m), 1250.3 (m), 1169.1 (m), 1067.9 (s), 1000.6 (s), 981.9 (s), 852.0 (m), 794.5 (s), 765.4 (s), 703.7 (s) cm^{-1}; HRMS calculated for $C_8H_6ClN_2F_2$: 203.0182, found: 203.0178.

4.14. 2-Chloro-3-(difluoromethyl)-6-methoxyquinoline (14b)

Prepared from 2-chloro-6-methoxyquinoline-3-carbaldehyde (110 mg, 0.5 mmol) and DAST (140 μL, 1 mmol) at 80 °C with a residence time of 45 min. The product was obtained as a white solid (84% yield, 99% purity). Yield: 84%, t_R=4.64 min, m/z=244.3 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.36 (1H, s), 7.94 (1H, d, J=9.2 Hz), 7.46 (1H, dd, J=9.2, 2.7 Hz), 7.14 (1H, d, J=2.7 Hz), 7.02 (1H, t, J=54.6 Hz), 3.94 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 158.7 (C), 144.6 (C, t, J=5 Hz), 144.4 (C), 135.4 (CH, t, J=7 Hz), 129.8 (CH), 127.5 (C), 126.0 (C, t, J=23 Hz), 124.9 (CH), 111.7 (CH, t, J=239 Hz), 105.6 (CH), 55.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −116.1 (s). IR (neat): ν 3065.7 (w), 3020.1 (w), 1620.4 (m), 1594.3 (m), 1574.5 (m), 1498.2 (s), 1450.4 (m), 1420.4 (m), 1384.2 (m), 1338.0 (s), 1233.5 (s), 1203.4 (s), 1191.0 (s), 1167.8 (m), 1094.5 (s), 1060.1 (s), 1048.1 (s), 1024.1 (s), 959.0 (m), 926.9 (m), 838.4 (s), 828.3 (s), 743.8 (m) cm^{-1}; HRMS calculated for $C_{11}H_9NOF_2Cl$: 244.0341, found: 244.0346.

4.15. (*R*)-8,8-Difluoro-2,6-dimethyloct-2-ene[22] (15b)

Prepared from (*R*)-(+)-citronellal (154 mg, 1 mmol) and DAST (280 μL, 2 mmol) at 80 °C with a residence time of 45 min. The product was obtained as colorless oil (83% yield, 95% purity). Yield: 83%, t_R=5.23 min, m/z=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 5.85 (1H, tt, J=4.9, 56.9 Hz), 5.08 (1H, t, J=7.1 Hz), 2.00 (2H, m), 1.75–1.90 (1H, m), 1.66 (3H, s), 1.61 (3H, s), 1.50–1.70 (2H, m), 1.35–1.45 (1H, m), 1.20–1.30 (1H, m), 0.97 (3H, d, J=6.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 131.6 (C), 124.1 (CH), 117.1 (CH, t, J=237 Hz), 40.9 (CH_2, t, J=20 Hz), 37.0 (CH_2), 27.5 (CH, t, J=5 Hz), 25.6 (CH_3), 25.2 (CH_2), 19.5 (CH_3), 17.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −114.76 (s). IR (neat): ν 2960.2 (s), 2923.0 (s), 2856.0

(m), 1452.6 (m), 1401.4 (m), 1377.8 (m), 1120.9 (s), 1037.2 (s), 740.2 (m) cm^{-1}.

4.16. (*E*)-1-(3,3-Difluoroprop-1-enyl)-4-nitrobenzene (16b)

Prepared from (*E*)-3-(4-nitrophenyl)acrylaldehyde (177 mg, 1 mmol) and DAST (280 μL, 2 mmol) at 80 °C with a residence time of 45 min. The product was obtained as a yellow solid (96% yield, 95% purity). Yield: 96%, t_R=4.58 min, *m*/*z*=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.22 (2H, d, *J*=8.7 Hz), 7.59 (2H, d, *J*=8.7 Hz), 6.96 (1H, dt, *J*=16.2, 3.0 Hz), 6.35–6.43 (1H, m), 6.29 (1H, td, *J*=55.5, 5.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 148.1 (C), 140.6 (C), 134.5 (CH, t, *J*=12 Hz), 127.9 (2×CH), 125.2 (CH, t, *J*=24 Hz), 124.1 (2×CH), 114.2 (CH, t, *J*=233 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −112.0 (s). IR (neat): ν 1678.7 (w), 1665.0 (w), 1596.4 (m), 1514.9 (s), 1419.4 (w), 1383.8 (m), 1339.6 (s), 1297.5 (s), 1133.9 (s), 1110.0 (m), 1057.3 (m), 1007.2 (s), 971.7 (s), 955.9 (s), 865.4 (s), 820.5 (s), 746.3 (s), 709.7 (m), 683.2 (m) cm^{-1}.

4.17. 4-(Difluoromethyl)-2-(pyridine-2-yl)-quinoline (17b)

Prepared from 2-(pyridin-2-yl)-quinoline-4-carbaldehyde (117 mg, 0.5 mmol) and DAST (140 μL, 1 mmol) at 80 °C with a residence time of 45 min. The product was obtained as an off-white solid (89% yield, 97% purity). Yield: 89%, t_R=4.69 min, *m*/*z*=257.3 ($M+H^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.77 (1H, s), 8.76 (1H, d, *J*=4.8 Hz), 8.67 (1H, d, *J*=7.8 Hz), 8.26 (1H, d, *J*=7.8 Hz), 8.16 (1H, d, *J*=7.8 Hz), 7.89 (1H, t, *J*=7.8 Hz), 7.80 (1H, t, *J*=7.8 Hz), 7.65 (1H, t, *J*=7.8 Hz), 7.36–7.41 (1H, m), 7.18 (1H, t, *J*=54.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 155.8 (C), 155.4 (C), 149.2 (CH), 148.5 (C), 138.5 (C, t, *J*=21 Hz), 137.0 (CH), 130.7 (CH), 130.0 (CH), 128.0 (CH), 124.4 (CH), 124.0 (C), 123.6 (CH), 121.7 (CH), 116.6 (CH, t, *J*=8 Hz), 114.3 (CF_2H, t, *J*=240 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −113.7 (s). IR (neat): ν 3067.8 (w), 2921.3 (w), 1612.6 (w), 1590.3 (w), 1556.8 (w), 1510.7 (w), 1481.2 (w), 1441.7 (w), 1397.9 (m), 1367.1 (w), 1281.9 (m), 1242.6 (m), 1203.1 (m), 1166.6 (w), 1141.5 (w), 1109.0 (s), 1068.0 (m), 1045.0 (m), 1012.3 (s), 994.8 (s), 894.0 (s), 866.2 (s), 795.1 (s), 786.6 (s), 763.3 (s), 741.6 (s), 725.6 (s), 666.3 (m) cm^{-1}; HRMS calculated for $C_{15}H_{11}N_2F_2$: 257.0890, found: 257.0879.

4.18. 5-(Difluoromethyl)benzo[*d*][1,3]dioxole[23] (18b)

Prepared from piperonal (150 mg, 1 mmol) and DAST (280 μL, 2 mmol) at 80 °C with a residence time of 45 min. The product was obtained as a white solid (75% yield, 95% purity) after scavenging residual aldehyde starting material with PS-$TsNHNH_2$ (100 mg). Yield: 75%, t_R=4.35 min, *m*/*z*=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 6.95–6.99 (2H, m), 6.85 (1H, d, *J*=7.8 Hz), 6.54 (1H, t, *J*=56.6 Hz), 6.01 (2H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 149.5 (C), 148.0 (C), 128.3 (C, t, *J*=23 Hz), 120.1 (CH, t, *J*=7 Hz), 114.6 (CH, t, *J*=237 Hz), 108.2 (CH), 105.8 (CH, t, *J*=7 Hz), 101.5 (CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −108.2 (s). IR (neat): ν 2902.0 (w), 1505.9 (m), 1494.5 (m), 1450.2 (s), 1408.6 (m), 1351.3 (m), 1253.7 (s), 1137.9 (m), 1104.8 (m), 1061.9 (m), 1039.6 (s), 932.6 (m), 869.0 (m), 815.8 (m), 792.7 (m) cm^{-1}.

4.19. 5-Chloro-4-(difluoromethyl)-3-methyl-1-phenyl-1*H*-pyrazole (19b)

Prepared from 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde (220 mg, 1 mmol) and DAST (280 μL, 2 mmol) at 80 °C with a residence time of 45 min. The product was obtained as a white solid (87% yield, 97% purity). Yield: 87%, t_R=4.70 min, *m*/*z*=243.3 ($M+H^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.40–7.55 (5H, m), 6.68 (1H, t, *J*=54.2 Hz), 2.44 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 148 (C), 137.5 (C), 129.1 (2×CH), 128.7 (CH), 127.2 (C, t, *J*=8 Hz), 125.1 (2×CH), 112.1 (C, t, *J*=29 Hz), 110.8 (CH, t, *J*=230 Hz), 13.1 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −110.9 (s); IR (neat): ν 2924.3 (w), 1595.3 (w), 1559.9 (m), 1500.7 (m), 1485.5 (m), 1461.8 (m), 1422.9 (m), 1380.6 (m), 1363.8 (s), 1211.8 (m), 1077.1 (s), 1006.2 (s), 796.8 (s), 757.8 (s), 693.9 (s) cm^{-1}; HRMS calculated for $C_{11}H_{10}N_2F_2Cl$: 243.0501, found: 243.0511. Melting point: 56.5–58.2 °C.

4.20. 2-(Difluoromethyl)-1-methyl-1*H*-indole (20b)

Prepared from 1-methyl-1*H*-indole-2-carbaldehyde (159 mg, 1 mmol) and DAST (280 μL, 2 mmol) at 80 °C with a residence time of 45 min. The product was obtained as an off-white solid (50% yield, 97% purity) after scavenging residual aldehyde starting material with PS-$TsNHNH_2$ (150 mg). Yield: 50%, t_R=4.56 min, *m*/*z*=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.67 (1H, d, *J*=7.8 Hz), 7.39 (1H, d, *J*=7.8 Hz), 7.35 (1H, t, *J*=7.8 Hz), 7.17 (1H, t, *J*=7.8 Hz), 6.82 (1H, t, *J*=53.4 Hz), 6.75 (1H, br s), 3.88 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 138.7 (C), 131.0 (C, t, *J*=22.5 Hz), 126.2 (C), 123.8 (CH), 121.8 (CH), 120.2 (CH), 111.3 (CH, t, *J*=232.5 Hz), 109.6 (CH), 104.5 (CH, t, *J*=7.5 Hz), 30.8 (CH_3, t, *J*=2.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −109.6 (s). IR (neat): ν 2926.3 (w), 1556.6 (w), 1469.8 (m), 1401.1 (m), 1373.8 (m), 1347.6 (m), 1241.4 (w), 1185.5 (m), 1156.3 (m), 1144.2 (m), 1055.2 (m), 1004.6 (s), 911.2 (m), 850.2 (m), 795.6 (m), 751.1 (m), 737.4 (s), 671.3 (m) cm^{-1}. HRMS calculated for $C_{10}H_9NF_2$: 181.0703, found: 181.0698.

4.21. 3,3-Difluoroindolin-2-one[24] (22b)

Prepared from isatin (147 mg, 1 mmol, in MeCN) and DAST (280 μL, 2 mmol) at 80 °C with a residence time of 45 min. The product was obtained as a yellow solid (71% yield, 95% purity) after scavenging residual aldehyde starting material with PS-$TsNHNH_2$ (100 mg). Yield: 71%, t_R=3.92 min, *m*/*z*=170.2 ($M+H^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.46 (br s), 7.54 (1H, d, *J*=7.8 Hz), 7.45 (1H, t, *J*=7.8 Hz), 7.16 (1H, t, *J*=7.8 Hz), 6.96 (1H, d, *J*=7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 167.0 (C, t, *J*=30 Hz), 141.0 (C, t, *J*=7 Hz), 133.7 (CH), 125.1 (CH), 124.0 (CH), 120.3 (C, t, *J*=23 Hz), 111.6 (CH), 110.8 (CF_2, t, *J*=249 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −112.0 (s); IR (neat): ν 3175.3 (w), 3121.9 (w), 1747.2 (s), 1625.9 (s), 1475.1 (s), 1414.0 (w), 1318.9 (w), 1284.0 (m), 1207.2 (s), 1158.7 (m), 1130.0 (m), 1075.9 (s), 983.9 (m), 950.3 (m), 767.2 (s), 745.0 (m), 726.6 (s) cm^{-1}. HRMS calculated for $C_8H_5NOF_2Na$: 192.0233, found: 192.0231.

4.22. Methyl-2(2-(6-(2-cyanophenoxy)-pyrimidin-4-yloxy)-phenyl)-2,2-difluoroacetate (23b)

Prepared from methyl-2-(2-(6-(2-cyanophenoxy)-pyrimidin-4-yloxy)-phenyl)-2-oxoacetate (125 mg, 0.33 mmol) and DAST (94 μL, 0.66 mmol) at 80 °C with a residence time of 45 min. The product was obtained as colorless oil (94% yield, 95% purity). Yield: 94%, t_R=4.79 min, *m*/*z*=398.3 ($M+H^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.38 (1H, s), 7.80 (1H, dd, *J*=1.2, 7.8 Hz), 7.73 (1H, dd, *J*=1.2, 7.8 Hz), 7.69 (1H, td, *J*=1.2, 7.8 Hz), 7.60 (1H, t, *J*=7.8 Hz), 7.42 (1H, t, *J*=7.8 Hz), 7.39 (1H, t, *J*=7.8 Hz), 7.34 (1H, d, *J*=7.8 Hz), 7.28 (1H, d, *J*=7.8 Hz), 6.58 (1H, s), 3.79 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 170.7 (C), 170.2 (C), 163.7 (C, t, *J*=19 Hz), 157.8 (CH), 154.0 (C), 149.5 (C, t, *J*=5 Hz), 134.3 (CH), 133.6 (CH), 132.3 (CH), 127.0 (CH, t, *J*=8 Hz), 126.2 (CH), 126.1 (CH), 125.8 (C, t, *J*=5 Hz), 123.4 (CH), 123.1 (CH), 115.2 (C), 111.8 (CH, t, *J*=249 Hz), 107.4 (C), 93.5 (CH), 53.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −102.5 (s); IR (neat): ν 2233.7 (w), 1775.8 (m), 1594.4 (m), 1566.6 (s), 1486.5 (m), 1443.5 (s), 1379.3 (m), 1280.0 (m), 1244.7 (m), 1204.0 (m), 1143.9 (m), 1129.3 (s), 1078.0 (s), 1041.4 (m), 1000.6 (m), 984.4 (m), 844.1 (m), 761.9 (m), 737.0 (m) cm^{-1}; HRMS calculated for $C_{20}H_{14}N_3O_4F_2$: 398.0952, found: 398.0956.

4.23. 6-Chloronicotinoyl fluoride (24b)

Prepared from 6-chloronicotinoyl chloride (175 mg, 1 mmol) and DAST (140 μL, 1 mmol) at 70 °C with a residence time of 45 min. The product was obtained as an off-white solid (96% yield, 97% purity). Yield: 96%, t_R=2.01 min, m/z=159.9 (oxonium species); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.97 (1H, d, J=2.0 Hz), 8.23 (1H, dd, J=8.4, 2.0 Hz), 7.51 (1H, d, J=8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 158.1 (C), 155.1 (C, d, J=342 Hz), 152.5 (CH), 140.8 (CH, d, J=3 Hz), 125.0 (CH), 120.3 (C, d, J=63 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −149.9 (s); IR (neat): ν 3100.5 (w), 3046.6 (m), 1810.2 (s), 1586.5 (s), 1560.3 (m), 1454.5 (s), 1377.1 (m), 1293.6 (m), 1243.1 (s), 1147.9 (m), 1110.0 (s), 1040.4 (s), 995.8 (s), 853.8 (m), 796.7 (m), 754.5 (s), 708.7 (m), 686.3 (m) cm^{-1}.

4.24. 2,2′-(4-Chloropyridine-2,6-diyl)bis(4-phenyl-4,5-dihydrooxazole)[25] (25b)

Prepared from 4-chloro-N^2,N^6-bis(2-hydroxy-1-phenylethyl)-pyridine-2,6-dicarboxamide (110 mg, 0.25 mmol) and DAST (70 μL, 0.5 mmol) at 80 °C with a residence time of 45 min. The product was obtained as colorless oil (95% yield, 95% purity). Yield: 95%, t_R=4.95 min, m/z=404.3 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.34 (1H, s), 7.36 (2H, t, J=7.8 Hz), 7.28–7.35 (3H, m), 5.46 (1H, dd, J=9.6, 9.6 Hz), 4.93 (1H, dd, J=9.0, 9.0 Hz), 4.43 (1H, dd, J=10.2, 10.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 162.6 (C), 148.0 (C), 145.6 (C), 141.3 (C), 128.9 (2×CH), 127.9 (CH), 126.8 (2×CH), 126.4 (CH), 75.7 (CH_2), 70.3 (CH); IR (neat): ν 2930.3 (w), 1671.4 (s), 1639.4 (s), 1518.1 (s), 1454.2 (m), 1406.4 (m), 1379.9 (s), 1314.4 (m), 1235.1 (m), 1188.6 (m), 1148.0 (m), 1063.1 (m), 977.2 (w), 914.2 (w), 754.5 (m), 700.2 (w) cm^{-1}; HRMS calculated for $C_{23}H_{19}N_3O_2Cl$: 404.1166, found: 404.1169.

4.25. (4*S*,4′*S*)-2,2′-(4-Chloropyridine-2,6-diyl)bis(4-isopropyl-4,4-dihydrooxazole)[26] (26b)

Prepared from 4-chloro-N^2,N^6-bis((*S*)-1-hydroxy-3-methylbutan-2-yl)pyridine-2,6-dicarboxamide (371 mg, 1.0 mmol) and DAST (280 μL, 2.0 mmol) at 80 °C with a residence time of 45 min. The product was obtained as colorless oil (92% yield, 96% purity). Yield: 92%, t_R=4.57 min, m/z=335.9 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.18 (2H, s), 4.53 (2H, t, J=9.0 Hz), 4.22 (2H, t, J=8.4 Hz), 4.12–4.17 (2H, m), 1.85 (2H, app. sextet, J=6.6 Hz), 1.03 (6H, d, J=6.6 Hz), 0.93 (6H, d, J=6.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 161.4 (C), 148.0 (C), 145.5 (C), 125.8 (C), 72.8 (CH), 71.3 (CH_2), 32.8 (CH), 18.9 (CH_3), 18.3 (CH_3). IR (neat): ν 2960.0 (m), 2915.5 (m), 1642.2 (s), 1562.4 (s), 1467.6 (m), 1381.5 (s), 1366.2 (m), 1270.2 (m), 1236.9 (s), 1150.8 (m), 975.2 (s), 937.4 (s), 910.8 (m), 886.5 (m), 787.5 (s), 730.7 (s) cm^{-1}; HRMS calculated for $C_{17}H_{23}N_3O_2Cl$: 336.1479, found: 336.1494.

4.26. 4-Methyl-2-(2-bromooxazol-4-yl)-4,5-dihydrooxazole-4-carboxylate (27b)

A solution of methyl-2-(2-bromooxazole-4-carboxamido)-3-hydroxypropanoate (292 mg, 1 mmol) in 2 mL DCM was prepared and combined with a stream of DAST (140 μL, 1.0 mmol) dissolved in 2 mL DCM using a T-piece. This solution was pumped through the CFC at 80 °C with a residence time of 27 min. The product was obtained as off-white solid after removal of solvents. Yield: 91%, t_R=2.33 min, m/z=275.7 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.08 (1H, s), 4.80–4.89 (1H, m), 4.60–4.66 (1H, m), 4.50–4.54 (1H, m), 3.72 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 170.8 (C), 158.7 (C), 148.3 (C), 143.0 (CH), 131.7 (C), 69.8 (CH_2), 68.3 (CH), 52.7 (CH_3); IR (neat): ν 3144.9 (w), 2955.4 (w), 1738.5 (s), 1678.1 (m), 1585.0 (m), 1556.8 (m), 1523.5 (s), 1437.4 (m), 1364.5 (m), 1317.8 (m), 1278.3 (m), 1208.8 (s), 1178.4 (s), 1118.1 (s), 1090.2 (s), 1041.4 (m), 982.5 (s), 962.4 (m), 943.3 (m), 887.1 (m), 796.8 (m), 726.5 (m), 677.1 (m) cm^{-1}; HRMS calculated for $C_8H_8N_2O_4Br$: 274.9667, found: 274.9670.

4.27. 3-(2-Chloro-6-fluorophenyl)-4-(4-fluoromethyl)-4,5-dihydrooxazol-2-yl-5-methylisoxazole (28b)

Prepared from 3-(2-chloro-6-fluorophenyl)-*N*-(1,3-dihydroxypropan-2-yl)-5-methylisoxazole-4-carboxamide (328 mg, 1 mmol) and DAST (280 μL, 1 mmol) at 75 °C with a residence time of 27 min. The product was obtained as off-white solid (87% yield, 97% purity). Yield 87%, t_R=4.49 min, m/z=312.8 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.35–7.40 (1H, m), 7.28 (1H, d, J=8.4 Hz), 7.08 (1H, t, J=8.4 Hz), 4.38 (3H, m), 4.20 (2H, dt, J=8.4, 50.1 Hz), 2.76 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 173.1 (C), 160.7 (C, d, J=251 Hz), 158.6 (C), 155.0 (C), 135.3 (C, d, J=3 Hz), 131.4 (CH, d, J=9 Hz), 125.1 (CH, d, J=3 Hz), 117.6 (C, d, J=18 Hz), 114.0 (CH, d, J=23 Hz), 106.5 (C), 83.6 (CH_2, d, J=171 Hz), 68.7 (CH_2, d, J=5 Hz), 65.8 (CH, d, J=21 Hz), 13.1 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −110.0 (s), −230.7 (s); IR (neat): ν 2959.5 (w), 2906.5 (w), 1675.8 (s), 1615.9 (s), 1574.3 (s), 1457.4 (s), 1251.5 (s), 1103.2 (m), 1069.8 (m), 983.9 (m), 900.3 (s), 787.1 (s), 730.9 (m) cm^{-1}. HRMS calculated for $C_{14}H_{12}N_2O_2F_2Cl$: 313.0555, found: 313.0565.

4.28. 2-Fluoro-3-oxo-2-phenylbutanenitrile (29b)

Prepared from 3-oxo-2-phenylbutanenitrile (159 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) at 110 °C with a residence time of 27 min. The product was obtained as colorless oil (90% yield, 95% purity). Yield: 90%, t_R=4.29 min, m/z=176.8 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.53–7.57 (2H, m), 7.47–7.51 (3H, m), 2.31 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 195.4 (C, d, J=29 Hz), 131.0 (CH, d, J=2 Hz), 130.8 (C, d, J=24 Hz), 129.5 (2×CH), 124.9 (2×CH, d, J=6 Hz), 114.2 (C, d, J=33 Hz), 92.7 (C, d, J=198 Hz), 23.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −153.9 (s); IR (neat) ν=1741.7 (s), 1676.1 (w), 1494.3 (w), 1452.2 (m), 1419.6 (w), 1359.8 (m), 1216.1 (m), 1195.0 (m), 1123.6 (m), 1099.2 (m), 1070.4 (m), 926.2 (w), 754.5 (s), 737.7 (s), 695.5 (s) cm^{-1}.

4.29. Ethyl-2-fluoro-3-oxo-3-phenylpropanoate[27] (30b)

Prepared from ethyl-3-oxo-3-phenylpropanoate (192 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) at 120 °C with a residence time of 27 min. The product was obtained as colorless oil (89% yield, 95% purity). Yield: 89%, t_R=4.27 min, m/z=209.1 (M-H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$) δ/ppm 8.02 (2H, d, J=8.4 Hz), 7.62 (1H, t, J=8.4 Hz), 7.48 (2H, t, J=8.4 Hz), 5.87 (1H, d, J=48.6 Hz), 4.28 (2H, qd, J=2.4, 7.2 Hz), 1.23 (3H, t, J=7.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm 189.5 (C, d, J=20 Hz), 164.9 (C, d, J=24 Hz), 134.5 (CH), 133.4 (C, d, J=2 Hz), 129.5 (2×CH, d, J=2 Hz), 128.8 (2×CH), 89.9 (CHF, d, J=197 Hz), 62.6 (CH_2), 13.9 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −190.5 (s); IR (neat) ν=2985.6 (w), 1758.5 (s), 1693.2 (s), 1597.7 (m), 1449.7 (m), 1372.27 (m), 1242.5 (s), 1202.0 (s), 1096.1 (s), 1015.0 (s), 976.4 (m), 943.0 (w), 925.3 (w), 882.8 (m), 854.1 (w), 771.4 (w), 746.6 (w), 688.1 (s) cm^{-1}; HRMS calculated for $C_{11}H_{12}O_3F$: 211.0770, found: 211.0779.

4.30. N^1-N^3-*Bis*(4-chlorophenyl)-2-fluoromalonamide (31b)

Prepared from N^1,N^3-*bis*(4-chlorophenyl)malonamide (161 mg, 0.5 mmol) and Selectfluor® (195 mg, 0.55 mmol) at 120 °C with a residence time of 45 min. The product was obtained as off-white solid (82% yield, 96% purity). Yield: 82%, t_R=4.68 min, m/z=340.8 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.86 (2H, 2×NH), 7.52 (4H, d, J=9.0 Hz), 7.30 (4H, d, J=9.0 Hz), 5.50 (1H, CHF, d, J=48.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 162.4 (C, d, J=21 Hz),

134.7 (C), 130.7 (C), 129.2 (2×CH), 121.6 (2×CH), 86.3 (CHF, d, J=200 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −195.6 (s); IR (neat) ν=3283.4 (m), 3075.9 (w), 1714.8 (s), 1599.5 (s), 1532.3 (s), 1490.5 (s), 1402.4 (s), 1309.9 (m), 1245.4 (m), 1113.8 (m), 1091.8 (s), 1014.0 (m), 823.8 (s), 752.8 (m) cm^{-1}; HRMS calculated for $C_{15}H_{12}N_2O_2FCl_2$: 341.0260, found: 341.0272.

4.31. 2-Acetyl-2-fluorocyclopentanone (32b)

Prepared from 2-acetylcyclopentane (126 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) at 100 °C with a residence time of 45 min. The product was obtained as colorless oil (82% yield, 95% purity). Yield: 82%, t_R=3.12 min, m/z=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 2.45–2.55 (1H, m), 2.40 (2H, t, J=7.8 Hz), 2.32 (3H, app. d, J=5.4 Hz), 2.05–2.19 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm 209.0 (C, d, J=16 Hz), 205.8 (C, d, J=31 Hz), 100.8 (C, d, J=199 Hz), 35.7 (CH_2), 32.7 (CH_2, d, J=20 Hz), 26.5 (CH_3), 17.6 (CH_2, d, J=4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −160.9 (s); IR (neat) ν=2972.0 (w), 1759.2 (s), 1714.7 (s), 1420.0 (w), 1403.3 (w), 1358.9 (m), 1259.9 (w), 1166.5 (m), 1122.7 (m), 1032.4 (m), 983.9 (m), 914.3 (m), 815.0 (w) cm^{-1}.

4.32. Ethyl-2-fluoro-3-(4-methoxyphenyl)-3-oxo-propanoate (33b)

Prepared from ethyl-3-(4-methoxyphenyl)-3-oxopropanoate (222 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) at 120 °C with a residence time of 27 min. The product was obtained as colorless oil (93% yield, 98% purity). Yield: 93%, t_R=4.30 min, m/z =240.9 (M+H$^+$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.00 (2H, d, J=8.4 Hz), 6.93 (2H, d, J=8.4 Hz), 5.82 (1H, d, J=48.6 Hz), 4.20–4.30 (2H, m), 3.85 (3H, s), 1.22 (3H, t, J=7.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm 187.8 (C, d, J=2 Hz), 165.2 (C, d, J=2 Hz), 164.6 (C), 132.0 (2×CH), 126.3 (C), 114.1 (2×CH), 89.9 (CHF, d, J=197 Hz), 62.5 (CH_2), 55.5 (CH_3), 13.9 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −189.9 (s); IR (neat) ν=2985.7 (w), 1758.4 (s), 1682.4 (s), 1598.6 (s), 1574.5 (m), 1512.9 (m), 1466.8 (m), 1424.0 (m), 1251.8 (s), 1172.7 (s), 1092.0 (s), 1024.9 (s), 941.6 (m), 887.0 (m), 842.0 (s), 798.0 (m) cm^{-1}; HRMS calculated for $C_{10}H_{14}O_4F$: 241.0876, found: 241.0873.

4.33. 2,2,4,4,4-Pentafluoro-1-(naphthalen-2-yl)butane-1,3-dione (34b)

Prepared from 4,4,4-trifluoro-1-(naphthylen-2-yl)butane-1,3-dione (266 mg, 1 mmol) and Selectfluor® (780 mg, 2.2 mmol) at 110 °C with a residence time of 45 min. The product was obtained as off-white solid (83% yield, 98% purity). Yield: 83%, t_R=4.48 min, m/z =no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.71 (1H, s), 8.02 (1H, d, J=7.8 Hz), 7.97 (1H, d, J=8.4 Hz), 7.89 (1H, d, J=9.0 Hz), 7.87 (1H, d, J=8.4 Hz), 7.67 (1H, t, J=7.2 Hz), 7.58 (1H, t, J=7.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm 191.2 (C, t, J=29 Hz), 136.4 (C), 134.1 (CH, m), 132.1 (C), 130.4 (CH), 130.1 (CH), 128.7 (CH), 127.8 (CH), 127.3 (CH), 124.5 (C), 121.1 (C, q, J=308 Hz), 111.9 (C, t, J=267 Hz), 93.0 (C, qt, J=6, 33 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −81.1 (CF_2, t, J=11.3 Hz), −111.6 (CF_3, q, J=11.3 Hz); IR (neat) ν=1671.4 (s), 1625.9 (m), 1598.0 (m), 1468.4 (m), 1404.0 (m), 1366.6 (m), 1261.2 (m), 1196.5 (s), 1168.3 (s), 1108.2 (s), 1066.2 (s), 974.1 (m), 935.0 (m), 823.6 (m), 798.9 (s), 755.1 (m), 740.0 (m), 721.2 (m) cm^{-1}.

4.34. *N*-(2-Fluoro-1-phenylpropyl)acetamide (35b)

Prepared from (*E*)-prop-1-enylbenzene (118 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) in the presence of acetic acid (50 μL) at 120 °C with a residence time of 27 min. The product was obtained as colorless oil. Yield: 97%, t_R=3.87 min, m/z=175.8 (M−HF). *Major diastereoisomer*: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.26–7.35 (5H, m), 6.11 (1H, s), 5.10 (1H, ddd, J=2.4, 9.0, 26.4 Hz), 4.90–5.05 (1H, m), 2.08 (3H, s), 1.40 (3H, dd, J=6.6, 24.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 169.7 (C), 139.4 (C), 128.7 (2×CH), 127.8 (CH), 127.0 (2×CH), 92.2 (CH, d, J=173 Hz), 56.4 (CH, d, J=18 Hz), 23.3 (CH_3, s), 18.5 (CH_3, d, J=23 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −186.2 (s). *Minor diastereoisomer*: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.30–7.38 (5H, m), 6.21 (1H, s), 4.90–5.08 (2H, m), 2.02 (3H, s), 1.17 (3H, dd, J=6.0, 24.0 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 169.1 (C), 136.6 (C), 128.6 (2×CH), 128.4 (2×CH, d, J=2 Hz), 128.1 (CH), 91.9 (CH, d, J=173 Hz), 57.1 (CH, d, J=18 Hz), 23.4 (CH_3), 17.8 (CH_3, d, J=21 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −189.1 (s); IR (neat): ν=3316.0 (m), 2991.8 (w), 2935.9 (w), 1649.4 (s), 1538.5 (s), 1448.8 (m), 1371.7 (s), 1296.3 (m), 1274.1 (m), 1203.7 (m), 1066.2 (s), 1029.5 (m), 931.1 (m), 848.2 (m), 746.5 (s), 699.0 (s), 675.6 (s) cm^{-1}; HRMS: calculated for $C_{11}H_{15}NOF$: 196.1138, found: 196.1136.

4.35. *N*-(1-(4-(Chloromethyl)phenyl)-2-fluoroethyl)-acetamide (36b)

Prepared from 4-vinylbenzylchloride (152 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) in the presence of acetic acid (50 μL) at 120 °C with a residence time of 27 min. The product was obtained as a white solid, yield: 83%, t_R=3.82 min, m/z=229.8 (M+H$^+$); Melting point: 94.5–98.4 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.38 (2H, d, J=8.4 Hz), 7.33 (2H, d, J=8.4 Hz), 6.27 (1H, d, J=6.6 Hz), 5.25 (1H, app. ddt, J=4.2, 7.8, 25.8 Hz), 4.65 (app. dddd, J=3.6, 9.6, 20.4, 47.4 Hz), 4.57 (2H, s), 2.04 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 169.7 (C), 138.2 (C, d, J=3 Hz), 137.3 (C), 129.0 (2×CH), 127.4 (2×CH), 84.6 (CHF, d, J=171 Hz), 52.8 (CH, d, J=18 Hz), 45.7 (CH_2), 23.2 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −227.7 (s); IR (neat): ν=3290.9 (m), 1640.6 (s), 1542.8 (s), 1515.8 (s), 1442.4 (m), 1371.5 (m), 1295.7 (m), 1267.3 (m), 1108.6 (w), 1049.2 (w), 1019.1 (m), 899.9 (w), 833.3 (w), 794.2 (w), 737.6 (w), 679.7 (m); HRMS: calculated for $C_{11}H_{14}NOFCl$: 230.0748, found: 230.0752.

4.36. *N*-(2-Fluoro-2,3-dihydro-1*H*-inden-1-yl)acetamide (37b)

Prepared from 1*H*-indene (116 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) in the presence of acetic acid (50 μL) at 120 °C with a residence time of 27 min. The product was isolated as a white solid, yield: 86%, t_R=3.54 min, m/z=193.8 (M+H$^+$). *Major diastereoisomer*: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.20–7.35 (4H, m), 6.01 (1H, s), 5.62 (1H, ddd, J=4.1, 9.2, 26.1 Hz), 5.35 (1H, app. dt, J=3.7, 54.0 Hz), 3.05–3.39 (2H, m), 2.13 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 170.4 (C), 139.9 (C), 138.8 (C), 128.3 (CH), 127.4 (CH), 125.2 (CH), 123.8 (CH), 94.9 (CHF, d, J=180 Hz), 56.8 (CH, d, J=17 Hz), 37.4 (CH_2, d, J=23 Hz), 23.2 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −195.8 (s). *Minor diastereoisomer*: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.28–7.33 (4H, m), 5.45–5.55 (2H, m), 5.319 (1H, app. dt, J=3.0, 45.0 Hz), 3.35 (1H, app. dt, J=6.0, 21.6 Hz), 3.14 (1H, app. dt, J=6.0, 21.6 Hz), 2.08 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 169.8 (C), 139.6 (C), 139.2 (C), 129.1 (CH), 127.7 (CH), 125.3 (CH), 124.8 (CH), 98.1 (CH, d, J=195 Hz), 60.3 (CH_2), 37.2 (CH), 23.9 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −180.0 (s); IR (neat): ν=3275.2 (s), 1654.2 (s), 1555.0 (s), 1371.6 (m), 1293.5 (m), 1034.4 (m), 811.4 (m), 738.6 (s); HRMS: calculated for $C_{11}H_{12}NOFNa$: 216.0801, found: 216.0802.

4.37. *N*-(2-Fluoro-1-phenylcyclohexyl)acetamide (38b)

Prepared from cyclohexenylbenzene (158 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) in the presence of acetic acid (50 μL) at 120 °C with a residence time of 27 min. The product was obtained as colorless oil. Yield: 96%, t_R=4.10 min, m/z=236.1

($M+H^+$). *Major diastereoisomer*: ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.40 (2H, d, J=7.8 Hz), 7.35 (2H, t, J=7.8 Hz), 7.26 (1H, t, J=7.8 Hz), 5.85 (1H, s), 4.70 (1H, ddd, J=4.5, 10.8, 46.2 Hz), 3.14 (1H, m), 2.10 (3H, s), 2.00–2.08 (1H, m), 1.77–1.89 (3H, m), 1.56–1.62 (1H, m), 1.40–1.50 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 169.7 (C), 142.3 (C), 128.3 (2×CH), 127.2 (CH), 126.0 (2×CH), 96.3 (CH, d, J=181.5 Hz), 62.2 (C, d, J=15 Hz), 32.2 (CH_2, d, J=3 Hz), 28.2 (CH_2, d, J=20 Hz), 24.5 (CH_3), 23.3 (CH_2, d, J=11 Hz), 21.0 (CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −185.8 (s). *Minor diastereoisomer*: ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.75 (2H, d, J=7.8 Hz), 7.34 (2H, t, J=7.8 Hz), 7.26 (1H, t, J=7.8 Hz), 5.63 (1H, dd, J=4.8, 47.4 Hz), 5.53 (1H, s), 2.37–2.42 (1H, m), 2.17–2.22 (1H, m), 1.96 (3H, s), 1.80–1.93 (1H, m), 1.50–1.74 (5H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 169.3 (C), 142.8 (C), 128.3 (2×CH), 127.3 (CH), 126.7 (2×CH, d, J=4 Hz), 91.1 (CH, d, J=175 Hz), 60.3 (C, d, J=22 Hz), 31.5 (CH_2, d, J=2 Hz), 27.5 (CH_2, d, J=20 Hz), 24.4 (CH_3), 21.3 (CH_2), 20.0 (CH_2, d, J=4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −189.5 (s); IR (neat): ν=3308.5 (w), 2939.6 (m), 1655.2 (s), 1535.4 (m), 1446.0 (m), 1370.3 (m), 1293.9 (m), 1041.9 (m), 1028.7 (m), 909.3 (s), 728.7 (s), 696.4 (s) cm^{-1}; HRMS: calculated for $C_{14}H_{19}NOF$: 236.1451, found: 236.1461.

4.38. 1-Fluoro-1-(4-fluorophenyl)ethanol (39b)

Prepared from (1-fluoro-4-prop-1-en-2-yl)benzene (136 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) in the presence of acetic acid (50 μL) at 120 °C with a residence time of 27 min. The product was obtained as colorless oil. Yield: 86%, t_R=3.79 min, m/z=154.9 ($M-H_2O$). ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.42–7.50 (2H, m), 7.05 (2H, t, J=9.0 Hz), 4.41 (2H, ddd, J=9.6, 33.6, 48.0 Hz), 1.58 (3H, d, J=2.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 162.1 (C, d, J=245 Hz), 138.9 (C, t, J=4 Hz), 127.1 (2×CH, d, J=9 Hz), 115.1 (2×CH, d, J=21 Hz), 89.5 (CH_2, d, J=177 Hz), 73.5 (C, d, J=18 Hz), 25.3 (CH_3, d, J=3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −115.5 (s), −222.8 (s); IR (neat): ν=3426.0 (OH), 2985.6 (w), 1664.2 (w), 1603.4 (m), 1509.1 (s), 1461.1 (w), 1373.6 (w), 1225.1 (s), 1161.7 (m), 1012.8 (s), 873.2 (m), 834.8 (s), 815.3 (m), 725.4 (m) cm^{-1}; HRMS: calculated for $C_9H_8F_2$: 154.0594, found: 154.0589 (dehydrated species).

4.39. *N*-(2-Fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)acetamide (40b)

Prepared from 1,2-dihydronaphthalene (130 mg, 1 mmol) and Selectfluor® (390 mg, 1.1 mmol) in the presence of acetic acid (50 μL) at 120 °C with a residence time of 27 min. The product was obtained as colorless oil. Yield: 91%, t_R=3.77 min, m/z=208.0 ($M+H^+$). *Major diastereoisomer*: ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.25–7.27 (1H, m), 7.19–7.21 (2H, m), 7.11–7.13 (1H, m), 6.03 (1H, d, J=7.2 Hz), 5.37 (1H, dd, J=9.0, 31.2 Hz), 5.07 (1H, app. ddt, J=3.3, 50.4 Hz), 3.08 (1H, ddd, J=6.0, 12.0, 22.8 Hz), 2.76 (1H, dd, J=6.0, 16.2 Hz), 2.31–2.38 (1H, m), 2.14 (3H, s), 2.01 (1H, dddd, J=6.0, 12.6, 26.4, 42.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 170.2 (C), 136.0 (C), 133.6 (C), 128.5 (CH), 127.5 (CH), 127.4 (CH), 126.6 (CH), 89.3 (CH, d, J=171 Hz), 49.8 (CH, d, J=18 Hz), 26.6 (CH_2, d, J=21 Hz), 23.6 (CH_2, d, J=6 Hz), 23.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −202.1 (s). *Minor diastereoisomer*: ^1H NMR (600 MHz, $CDCl_3$): δ/ppm 7.26–7.28 (1H, m), 7.20–7.23 (2H, m), 7.11–7.14 (1H, m), 5.55 (1H, d, J=4.8 Hz), 5.22–5.30 (1H, m), 4.87 (1H, app. ddt, J=2.4, 7.8, 48.0 Hz), 2.96–3.04 (1H, m), 2.83 (1H, ddd, J=6.0, 12.0, 16.8 Hz), 2.15–2.24 (1H, m), 2.06 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 169.6 (C), 135.9 (C), 129.1 (CH). 128.7 (CH), 127.8 (CH), 127.0 (CH), 90.1 (CH, d, J=180 Hz), 51.4 (CH, d, J=27 Hz), 25.6 (CH_2, d, J=20 Hz), 25.0 (CH_2, d, J=8 Hz), 23.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −185.1 (s); IR (neat): ν=3243.0 (m), 3053.7 (m), 1635.9 (s), 1551.8 (s), 1492.3 (m), 1435.9 (m), 1373.1 (s), 1294.4 (m), 1061.9 (m), 1014.3 (m), 940.3 (m), 852.2 (m), 743.8 (s), 726.8 (m), 702.8 (m) cm^{-1}; HRMS: calculated for $C_{12}H_{15}NOF$: 208.1138, found: 208.1141.

4.40. 2,2,2-Trifluoro-1-(2-nitrophenyl)ethanol (41b)

Prepared from 2-nitrobenzaldehyde (151 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as yellow oil. Yield: 84%, t_R=4.20 min, m/z=222.1 ($M+H$); ^1H NMR (400 MHz, $CDCl_3$): δ/ppm 8.03 (1H, dd, J=0.8, 8.2 Hz), 7.97 (1H, d, J=7.9 Hz), 7.74 (1H, m), 7.59 (1H, m), 6.18 (1H, q, J=6.0 Hz), 2.94 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 148.6 (C), 133.6 (CH), 130.3 (CH), 129.5 (CH), 128.9 (C), 125.0 (CH), 123.9 (C, q, J=281 Hz), 66.9 (CH, q, J=32 Hz); IR (neat) ν=3482 (br), 2932 (w), 1701 (w), 1526 (s), 1348 (s), 1259 (m), 1173 (s), 1125 (s), 1100 (m), 1061 (m), 787 (m), 711(s) cm^{-1}; Microanalysis: C: 44.15, H: 2.96, N: 6.08%.

4.41. 2,2,2-Trifluoro-1-(5-nitrobenzo[*d*][1,3]dioxol-6-yl)ethanol (42b)

Prepared from 6-nitrobenzo[*b*][1,3]dioxole-5-carbaldehyde (195 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as yellow oil. Yield: 76%, t_R=4.27 min, m/z=no mass detected; ^1H NMR (400 MHz, $CDCl_3$): δ/ppm 7.52 (1H, s), 7.33 (1H, s), 6.10–6.25 (3H, m), 3.27 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 152.3 (C), 148.6 (C), 143.0 (C), 126.0 (C), 123.9 (C, q, J=281 Hz, CF_3), 108.2 (CH), 105.8 (CH), 103.4 (CH_2), 66.8 (CH, q, J=32 Hz); IR (neat) ν=3511 (br), 3134 (w), 2923 (w), 1618 (m), 1524 (s), 1507 (s), 1486 (s), 1332 (s), 1257 (s), 1169 (s), 1119 (s), 1076 (m), 1033 (s) cm^{-1}; Microanalysis: C: 40.65, H: 2.47, N: 5.27%.

4.42. 2,2,2-Trifluoro-1-(5-(4-(trifluoromethyl)-1-methyl-1*H*-pyrazol-3-yl)thiophen-2-yl)ethanol (43b)

Prepared from 5-(1-methyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl)thiophene-2-carbaldehyde (260 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as yellow solid. Yield: 89%, t_R=4.65 min, m/z=331.1 ($M+H^+$). Melting point: 100.6–103.1 °C. ^1H NMR (400 MHz, $CDCl_3$): δ/ppm 7.20 (1H, d, J=3.7 Hz), 7.11 (1H, d, J=3.7 Hz), 6.78 (1H, s), 5.24 (1H, q, J=6.4 Hz), 4.00 (3H, s), 3.43 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 145.2 (C), 136.4 (C), 136.2 (C), 133.5 (C, q, J=39 Hz), 127.8 (CH), 124.1 (CH), 123.1 (C, q, J=281 Hz, CF_3), 119.7 (C, q, J=281 Hz), 104.6 (CH), 69.3 (CH, q, J=34 Hz), 38.1 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −60.9 (s), −78.8 (s); IR (neat) ν=3253 (br), 2968 (w), 1543 (m), 1499 (m), 1427 (m), 1266 (s), 1256 (s), 1150 (m), 1114 (s), 1085 (s), 1038 (s), 926 (m), 808 (s), 695 (s) cm^{-1}; HRMS calculated for $C_{11}H_9N_2OF_6S$: 331.0340, found: 331.0336.

4.43. 2,2,2-Trifluoro-1-(1-methyl-1*H*-indol-2-yl)ethanol (44b)

Prepared from 1-methyl-1*H*-indole-2-carbaldehyde (159 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as orange oil. Yield=79%, t_R=4.47 min, m/z=230.1 ($M+H^+$); ^1H NMR (400 MHz, $CDCl_3$): δ/ppm 7.64 (1H, d, J=7.7 Hz), 7.26–7.40 (2H), 7.16 (1H, m), 6.70 (1H, s), 5.23 (1H, q, J=6.5 Hz), 3.77 (3H, s), 2.98 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 138.1 (C), 132.1 (C), 126.9 (C), 124.2 (C, q, J=281 Hz, CF_3), 122.9 (CH), 121.4 (CH), 120.2 (CH), 109.5 (CH), 102.4 (CH), 67.0 (CH, q, J=34 Hz), 30.4 (CH_3); IR (neat) ν=3301 (br), 2948 (m), 1615 (w), 1470 (m), 1352 (w), 1272 (m), 1169 (s), 1145 (s), 1120 (s), 1067 (w), 921 (w), 794 (w), 751 (m) cm^{-1}; HRMS calculated for $C_{11}H_{11}NOF_3$: 230.0793, found: 230.0790.

4.44. 2,2,2-Trifluoro-1-(pyridine-3-yl)ethanol (45b)

Prepared from nicotinaldehyde (107 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as white solid. Yield: 86%, t_R=0.46 min, m/z=177.6 ($M+H^+$); ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 8.61 (1H, br s), 8.57 (1H, br s), 7.90 (1H, d, J=7.9 Hz), 7.38 (1H, dd, J=4.9, 7.9 Hz), 5.08 (1H, q, J=6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 149.9 (CH), 148.4 (CH), 135.8 (CH), 130.9 (C), 124.1 (CF_3, q, J=280 Hz), 123.8 (CH), 50.5 (CH, q, J=32 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −78.1 (s); IR (neat) ν=3400–2800 (br), 2854.8 (m), 1602.3 (w), 1585.9 (w), 1432.2 (m), 1351.7 (m), 1266.4 (s), 1170.9 (s), 1132.0 (s), 1089.4 (m), 1046.8 (m), 1032.8 (m), 871.5 (m), 847.6 (w), 800.9 (m), 718.7 (s) cm^{-1}; HRMS calculated for $C_7H_7NO_3F$: 178.0480, found: 178.0480.

4.45. 1-(Benzofuran-2-yl)-2,2,2-trifluoroethanol (46b)

Prepared from benzofuran-2-carbaldehyde (146 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as yellow oil. Yield=84%, t_R=4.39 min, m/z=no mass detected; ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 7.61 (1H, d, J=7.7 Hz), 7.52 (1H, d, J=8.3 Hz), 7.36 (1H, t, J=7.7 Hz), 7.28 (1H, t, J=7.7 Hz), 6.90 (1H, s), 5.20 (1H, q, J=6.4 Hz), 2.79 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 155 (C). 149.4 (C), 127.4 (C), 125.5 (CH), 123.4 (C, q, J=281 Hz, CF_3), 123.4 (CH), 121.7 (CH), 111.6 (CH), 107.0 (CH), 67.8 (CH, q, J=34 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −77.7 (s); IR (neat) ν=3392 (br), 2978 (w), 2881 (w), 1455 (m), 1268 (m), 1253 (m), 1172 (s), 1140 (s), 1120 (s), 1067 (m), 964 (m), 813 (m), 749 (s), 741 (s), 700 (s) cm^{-1}; Microanalysis: C: 55.91; H: 3.61%.

4.46. 1-(2-Bromophenyl)-2,2,2-trifluoroethanol (47b)

Prepared from 2-bromobenzaldehyde (184 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as colorless oil. Yield=80%, t_R=4.45 min, m/z=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.68 (1H, d, J=7.8 Hz), 7.57 (1H, d, J=7.8 Hz), 7.37 (1H, t, J=7.8 Hz), 7.23 (1H, dt, J=1.8, 7.8 Hz), 5.58 (1H, q, J=6.6 Hz), 2.71 (1H, br s); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 134.3 (C), 132.8 (CH), 130.7 (CH), 129.4 (CH), 127.7 (CH), 124.7 (CF_3, q, J=281 Hz), 123.8 (C), 70.9 (CH, q, J=32 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −77.8 (s); IR (neat) ν=3382.7 (br), 2919.1 (m), 2850.7 (m), 1464.0 (m), 1440.4 (m), 1265.9 (m), 1174.4 (s), 1123.9 (s), 1080.0 (m), 1024.9 (m), 755.5 (m), 729.5 (m), 673.6 (m) cm^{-1}.

4.47. 1-(5-Chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2,2,2-trifluoroethanol (48b)

Prepared from 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde (220 mg, 1 mmol) and trimethyl(trifluoromethyl)-silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as white solid. Yield=87%, t_R=4.47 min, m/z=291.1 ($M+H^+$); melting point: 153.2–154.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 7.39–7.54 (5H, m), 5.06 (1H, q, J=7.2 Hz), 2.92 (1H, br s), 2.40 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 149.4 (C), 137.7 (C), 129.1 (2×CH), 128.6 (CH), 127.3 (C), 125.2 (2×CH), 124.7 (C, q, J=281 Hz, CF_3), 110.9 (C), 66.4 (CH, q, J=34 Hz), 13.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −78.1 (s); IR (neat) ν=3123 (br), 2934 (w), 2872 (w), 1599 (w), 1557 (w), 1505 (m), 1266 (m), 1175 (m), 1164 (m), 1131 (s), 1123 (s), 855 (m), 804 (s), 765 (s), 694 (s) cm^{-1}; HRMS calculated for $C_{12}H_{11}N_2OF_3Cl$: 291.0512, found: 291.0511.

4.48. 2,2,2-Trifluoro-1-(3,5-dimethylisoxazol-4-yl)-ethanol (49b)

Prepared from 3,5-dimethylisoxazole-4-carbaldehyde (125 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as yellow oil. Yield=88%, t_R=3.81 min, m/z=196 ($M+H$); ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 4.94 (1H, q, J=7.0 Hz), 3.73 (1H, br s), 2.43 (3H, s), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 168.9 (C), 159.3 (C), 124.6 (C, q, J=281 Hz, CF_3), 108.9 (C), 65.3 (CH, q, J=34 Hz), 11.5 (CH_3), 10.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −78.8 (s); IR (neat) ν=3333 (br), 2976 (m), 2878 (w), 1636 (m), 1428 (m), 1269 (s), 1170 (s), 1133 (s), 1087 (m), 1043 (s), 853 (m), 807 (m), 713 (m) cm^{-1}; HRMS calculated for $C_7H_9NO_2F_3$: 196.0585, found: 196.0585.

4.49. 1,1,1 Trifluoro-4-phenylpentan-2-ol (50b)

Prepared from 3-phenylbutanal (148 mg, 1 mmol) and trimethyl(trifluoromethyl)silane (156 mg, 1.1 mmol) at 40 °C with a residence time of 100 min. The product was obtained as yellow oil. Yield=83%; t_R=4.24 min, m/z=no mass detected. *Diastereoisomer 1*: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.33 (2H, t, J=7.6 Hz), 7.20–7.25 (3H, m), 4.00 (1H, sextet, J=6.5 Hz), 3.09 (1H, app. q, J=7.2 Hz), 2.08 (1H, br s), 1.88–1.97 (2H, m), 1.33 (3H, d, J=7.3 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 146.2 (C), 128.8 (2CH), 127.1 (2CH), 126.6 (CH), 127.7 (CF_3, q, J=289 Hz), 69.1 (CH, q, J=31 Hz), 38.1 (CH_2), 35.5 (CH), 23.2 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −80.1 (s). *Diastereoisomer 2*: ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.35 (2H, t, J=7.6 Hz), 7.15–7.25 (3H, m), 3.57 (1H, sextet, J=6.4 Hz), 3.03 (1H, app. q, J=7.2 Hz), 2.02 (1H, br s), 1.85–1.97 (2H, m), 1.31 (3H, d, J=7.3 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 144.8 (C), 128.7 (2CH), 126.8 (2CH), 126.5 (CH), 125.2 (CF_3, q, J=278 Hz), 68.5 (CH, q, J=30 Hz), 37.5 (CH_2), 35.4 (CH), 21.1 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −80.4 (s); IR (neat) ν=3409 (m), 2963.2 (w), 1494.7 (w), 1453.4 (w), 1275.9 (m), 1165.0 (m), 1134.2 (s), 907.9 (s), 763.5 (m), 731.5 (s), 699.8 (s) cm^{-1}.

4.50. 2,2,2-Trifluoro-1-(6-nitrobenzo[*d*][1,3]dioxol-5-yl)ethanone (51)

Prepared from 2,2,2-trifluoro-1-(5-nitrobenzo[*d*][1,3]-dioxol-6-yl)-ethanol (**42b**, 183 mg, 0.5 mmol) in DCM was flowed through a glass column (6.6 mm i.d.×10 cm, with adjustable end pieces) packed with manganese dioxide (870 mg, 10 mmol) heated at 110 °C with a residence time of 30 min. The product was obtained as yellow oil. Yield: 93%, t_R=4.51 min, m/z=no mass detected; ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.66 (1H, s), 6.84 (1H, s), 6.26 (2H, s). ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 183.0 (C, q, J=39 Hz), 153.5 (C), 150.8 (C), 141.4 (C), 126.4 (C), 115.4 (CF_3, q, J=285 Hz), 107.3 (CH), 104.8 (CH), 104.3 (CH_2); ^{19}F NMR (376 MHz, $CDCl_3$) δ/ppm −76.0 (s); IR (neat) ν=2922.2 (w), 1746.5 (m), 1606.4 (w), 1527.5 (m), 1507.7 (s), 1483.7 (s), 1433.3 (m), 1371.0 (m), 1333.6 (s), 1265.2 (s), 1208.4 (s), 1133.8 (s), 1033.0 (s), 921.7 (s), 875.9 (s), 773.5 (m), 738.1 (s) cm^{-1}.

4.51. 5-Nitro-6-(1,2,2,2-tetrafluoroethyl)benzo[*d*][1,3]-dioxole (52)

Prepared from 2,2,2-trifluoro-1-(5-nitrobenzo[*d*][1,3]-dioxol-6-yl)ethanol (**42b**, 183 mg, 0.5 mmol) and DAST (70 μL, 0.5 mmol) at 70 °C with a residence time of 27 min. The product was obtained as light brown oil. Yield: 89%, t_R=4.62 min, m/z=248.0 ($M-F$); ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 7.65 (1H, s), 7.19 (1H, s), 6.82 (1H, dq, J=5.4, 44.4 Hz), 6.20 (2H, app. d, J=7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 152.6 (C), 149.4 (C), 142.5 (C), 122.5 (C, d, J=23 Hz), 121.8 (CF_3, dq, J=29, 290 Hz), 107.4 (CH, d, J=15 Hz),

106.1 (CH), 103.7 (CH_2), 84.1 (CHF, dq, J=35, 185 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm −77.8 (d, J=11.3 Hz), −193.7 (q, J=11.3 Hz); IR (neat) ν=2922.0 (w), 1617.2 (w), 1529.8 (m), 1508.2 (s), 1487.6 (s), 1428.0 (m), 1358.8 (m), 1334.4 (s), 1309.1 (m), 1261.2 (s), 1188.5 (s), 1134.7 (s), 1060.1 (m), 1033.2 (s), 928.2 (m), 884.8 (m), 867.6 (m), 850.4 (m), 819.5 (m), 803.5 (m), 758.7 (m), 708.9 (m) cm^{-1}.

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