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Synthesis of 5-alkyl-3,4-difluorofuran-2(5*H*)-ones by lactonisation. Effects of substituents on cyclisation ability of fluorinated 4-hydroxyalkanoates. DFT calculations of the cyclisation energies

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Exo-trig lactonisations
DFT lactonisation energy

ABSTRACT

5-Alkyl-3,4-difluorofuran-2(5*H*)-ones were synthesised starting with radical addition of ethers to methyl 2,3,3-trifluoroprop-2-enoate, followed by alkyloxy bond cleavage, acid-catalyzed lactonisation and dehydrofluorination. For a study of substituent effects on lactonisation, methyl 4-bromo-2-chloro-2-fluorodecanoate and 2-chloro-2-fluoro-4,4-dimethoxybutanoate based on radical additions of methyl 2-bromo-2-chloro-2-fluoroacetate to oct-1-ene or vinyl acetate were prepared. DFT calculations of the transition state energies of the *exo-trig* cyclisations confirmed the observation that the ring closure became more feasible with increasing number of alkyls at C4 of the fluorinated 4-hydroxyesters.

1. Introduction

2-Fluoro- or 2,3-difluoro-α,β-unsaturated oxo compounds and esters belong to useful synthetic intermediates, which enable to synthesise various types of fluorine-containing compounds, e.g. [1]. 3-Fluoro- or 3,4-difluorofuran-2(5*H*)-ones (formally 2-fluoro- or 2,3-difluorobut-2-enolides) as a type of α,β-unsaturated systems can be utilised in an analogous way by nucleophilic additions or vinylic substitution of fluorine: *Podophyllotoxin* analogs were synthesised starting with 2-fluorobut-2-enolide [2], the fluorobutenolide cycle was modified by nucleophilic rearrangement [3] or nucleoside analogues possessing fluorobutenolide ring were prepared [4].

Fluorine atom as a substituent usually mimics hydroxy group [5] in bioactive compounds and frequently introduces new bioactivity, e.g. [6]. Tetronic (**1**) and ascorbic (**2**) acids belong to numerous bioactive natural butenolide derivatives [7]. Their analogues and derivatives have displayed interesting pharmaceutical properties [8]. The preparation of 2-fluorotetronic and fluorinated L-ascorbic acids for biomedical studies has been reported [9]. From this point of view, 5,5-dialkyl-3,4-difluorofuran-2(5*H*)-ones (**3**) can be understood as analogues of **1** or **2**. Similarly, 5-alkyl-3,4-difluorofuran-2(5*H*)-ones (**4**) are analogues of **1** and **2** and, in addition, they are potential novel synthetic intermediates. These compounds had not been synthesised so far and research of their synthesis has been the aim of this publication.

2. Results and discussion

2.1. Syntheses of 2,3-difluorobut-2-enolides

On the basis of our recent positive experience [10], we started the syntheses of the target products **4** (Fig. 1) with the radical addition of primary alkanols to trifluoroacrylate (**6**). The reaction is depicted in Scheme 1 and the results are summarised in Table 1. In the course of the radical additions of alkanols, the α-bonds C–H relatively to the hydroxyl group were cleaved specifically and the intermediate radicals added specifically to the β-carbon of the trifluoroacrylate. However, the radical additions (products **7–11**) were accompanied with nucleophilic additions (adducts **12–15**), which were dominant for ethanol (**13**, 60% rel.) and exclusive for methanol (**12**, 100% rel.). The portions of the nucleophilic additions

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0022-1139/

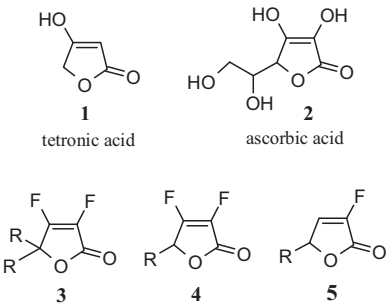


Fig. 1. Fluorinated analogues of tetronic and ascorbic acids.

were decreasing with the chain length (Table 1). This result is in a contrast with the radical additions of alkanols to tetrafluoroethene [11], hexafluoropropene [12] or 3,3-difluoroacrylate [13], where no products of nucleophilic additions were observed. The mixtures of the pairs of products **7–11** and the corresponding **12–15** were inseparable and therefore not employed in syntheses.

To avoid nucleophilic additions, aliphatic ethers were employed instead of alkanols (Scheme 1). The additions occurred at the α-positions relatively to the oxygen bridge (products **16–21**). In unsymmetrical ethers, higher alkyls were more reactive than the methyl group (products **22–23**, Table 2). The intermediate alkoxymethyl radicals **22a–23a** leading to the minor products **22–23** were very likely formed by the 1,3-hydrogen shift (Scheme 2) [14]. The monoadditions were accompanied by the additions of both α-bonds C–H to the acrylate (products **24–26**, Table 2). To suppress the double additions, the molar ratio ether/trifluoroacrylate should be 20/1 and higher. The additions of ether radicals were also completely regioselective to the β-carbon of the trifluoro-acrylate. Completely unsuccessful were attempts to carry out additions of ethers containing phenyl ring, e.g. anisole, phenetole or benzyl methyl ether, where, very likely, aromatic cycle caused quenching of the primary radicals. Completely unreactive was also methyl neopentyl ether due to steric reasons.

The cleavage of the ether linkage in 4-alkoxy-2,3,3-trifluoroalkanoates **16–21** was carried out using boron tribromide at r.t.

Table 1
Products of the addition of alkan-1-ols to trifluoroacrylate (**6**) under radical initiation.

R	Radical addition		Nucleophilic addition	
		% rel.		% rel.
H	**7**	0[a,b]	**12**	0[a], 100[b]
Me	**8**	40[a,b]	**13**	60[a,b]
Et	**9**	58[a], 45[b]	**14**	42[a], 55[b]
Hept	**11**	81[a], 71[b]	**15**	19[a], 29[b]

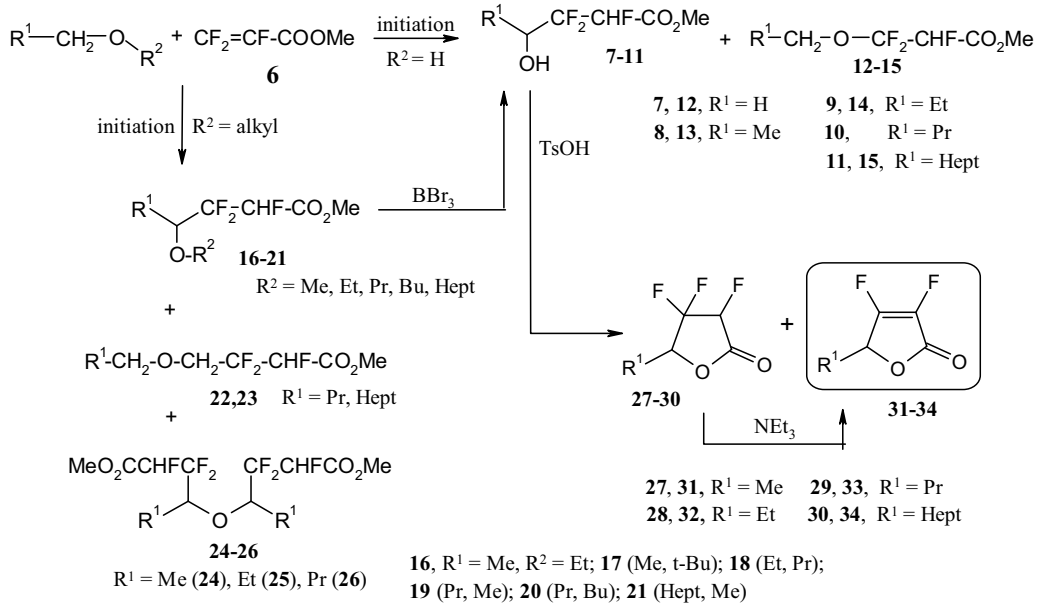
[a] UV.
[b] DBP/AIBN.

The resulting 4-hydroxyalkanoates **7–11** (Scheme 1) were obtained in moderate to good isolated yields (55–83%) (Table 3).

Methyl 2,3,3-trifluoro-4-hydroxyalkanoates **8–11** appeared to be relatively stable compounds that could be distilled or purified by column chromatography on silica gel. This behaviour is in sharp contrast with their 4-alkylated analogues, which cyclised spontaneously in solution when formed [10]. In light of the Baldwin predictions [15] the cyclisation of the 4-hydroxyesters should be easy. However, no cyclisation occurred by a long term treatment of **8–11** with conc. hydrochloric acid in methanol. A successful cyclisation was achieved using *p*-toluenesulfonic acid in boiling toluene. Difficult cyclisation was observed formerly for 5,5-difluoro-4-hydroxypentanoate [16] probably due to a lowered nucleophilicity of the hydroxylic oxygen (Table 4).

The formation of the main cyclisation products **27–30**, butanolides (dihydrofuranones) was accompanied by small amounts of the corresponding but-2-enolides (2(5*H*)-furanones) **31–34**, probably formed by thermal dehydrofluorination from the precursors **27–30**. The target difluorobutenolides **31–34** were obtained by dehydrofluorination of trifluorobutanolides **27–30** using triethylamine at r.t. (Table 5, [17]).

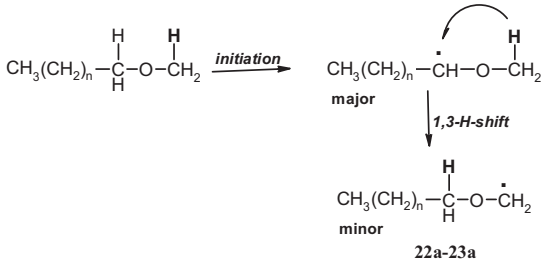
We attempted to synthesise difluorofuranones possessing functionalised alkyl at the 5-C. The results are summarised in Scheme 3. Radical addition of 2,2-dimethyl-1,3-dioxolane to trifluoroacrylate afforded the expected 1:1 adduct **35** in good yield (UV 65%, DBP/AIBN 75%). Its hydrolysis by HCl in refluxing methanol gave 4,5-dihydroxypentanoate **36** (yield 46%), but no butanolide.



Scheme 1. Overview of syntheses of 5-alkyl-3,4-difluorofuran-2(5*H*)-ones from aliphatic components.

Table 2
Addition of dialkyl ethers to trifluoroacrylate (**6**) under UV or radical initiation (Scheme 1).

Entry	R^1	R^2	Initiation	T (°C)	Time (h)	Main product			By-product	
							R^1	%		% rel.
1	Me	Et	UV	20	8	**16**	Me	51	**24**	42
2	Me	t-Bu	DBP/AIBN	70	16	**17**	Me	56	–	–
3	Et	Pr	DBP/AIBN	70	10	**18**	Et	62	**25**	24
4a	Pr	Me	UV	20	14	**19**	Pr	57	**22**	11
4b			DBP/AIBN	70	12	**19**	Pr	65	**22**	17
5	Pr	Bu	DBP/AIBN	90	10	**20**	Pr	58	**26**	29
6	Hept	Me	DBP/AIBN	90	12	**21**	Hept	49	**23**	14



Scheme 2. Rearrangement of intermediate ether radicals.

Lactonisation of dihydroxypentanoate **36** proceeded as in Scheme 1 under the catalysis of *p*-toluenesulfonic acid in refluxing toluene (Scheme 3) to give a mixture of the products **37–40**: both hydroxy groups participated in the lactonisation to afford 5-(**37**, **39**) and 6-membered lactones (**38**, **40**), the latter being highly prevailing. The saturated lactones **37–38** were transformed to the corresponding unsaturated ones **39–40** (Scheme 3) by triethylamine as above.

The transformation of tetrahydrofuran to 5-(halogenoalkyl)furanones **44** and **45** (Scheme 3) was successful: the only radical adduct **41** was specifically cleaved by boron tribromide to 7-bromo-4-hydroxyheptanoate (**42**). The lactonisation of **42** to **43** and subsequent dehydrofluorination of **43** to difluorofuranones **44** and **45** were realised in usual way (Scheme 3).

Table 3
Cleavage of the C–O linkage in 4-alkoxyalkanoates (**16–21**) using BBr_3.

4-Alkoxyester			Time (h)	Product		
	R^1	R^2			R^1	%
16	Me	Et	3	**8**	Me	83
17	Me	t-Bu	8	**8**	Me	55
18	Et	Pr	5	**9**	Et	70
19	Pr	Me	3	**10**	Pr	74
20	Pr	Bu	7	**10**	Pr	61
21	Hept	Me	3	**11**	Hept	68

Table 4
Lactonisation of 4-hydroxyesters **8–11**.

4-Hydroxy-ester		Time (d)	Products			
			Butanolide		Butenolide	
				%rel.		%rel.
8	Me	10	**27**	94	**31**	6
9	Et	8	**28**	95	**32**	5
10	Pr	8	**29**	91	**33**	9
11	Hept	2	**30**	92	**34**	8

2.2. Effects of substituents on cyclisation

Difficult cyclisation of 2,3,3-trifluoro-4-hydroxyesters **7–11** could be caused by a lowered nucleophilicity of the hydroxy oxygen due to the neighbour C-F bonds. To verify this effect we attempted to prepare 5-alkyl-3-fluorofuran-2(5*H*)-one (**5**, Scheme 4) or 5-alkyl-3-chloro-3-fluorofuran-2(5*H*)-one (**53**, Scheme 5) possessing the 3-CH_2 moiety. The attempted synthesis of **5** started with regiospecific radical addition of methyl bromochlorofluoroacetate to oct-1-ene to afford 4-bromo-2-chloro-2-fluorodecanoate (**47,** 51%, Scheme 4). Its transformation to 2-chloro-2-fluoro-4-hexyl-butanolide (**49**) was carried out in two ways: (1) the adduct **47** was refluxed in aqueous methanol and hydrochloric acid to be completely converted to **49** in 80 h (yield 70%); (2) the adduct **47** was hydrolysed to sodium salt **48**, which on heating in DMSO [17] afforded **49** (raw yield 82%). Dehydrochlorination of **49** by a series of agents (triethylamine, DABCO, DBU, potassium fluoride, potassium hydroxide, sodium carbonate, *tert*-butoxide) in various solvents (diethyl ether, tetrahydrofuran, DMF, DMSO, acetonitrile or toluene) was not successful, usually a rich mixtures of products were obtained.

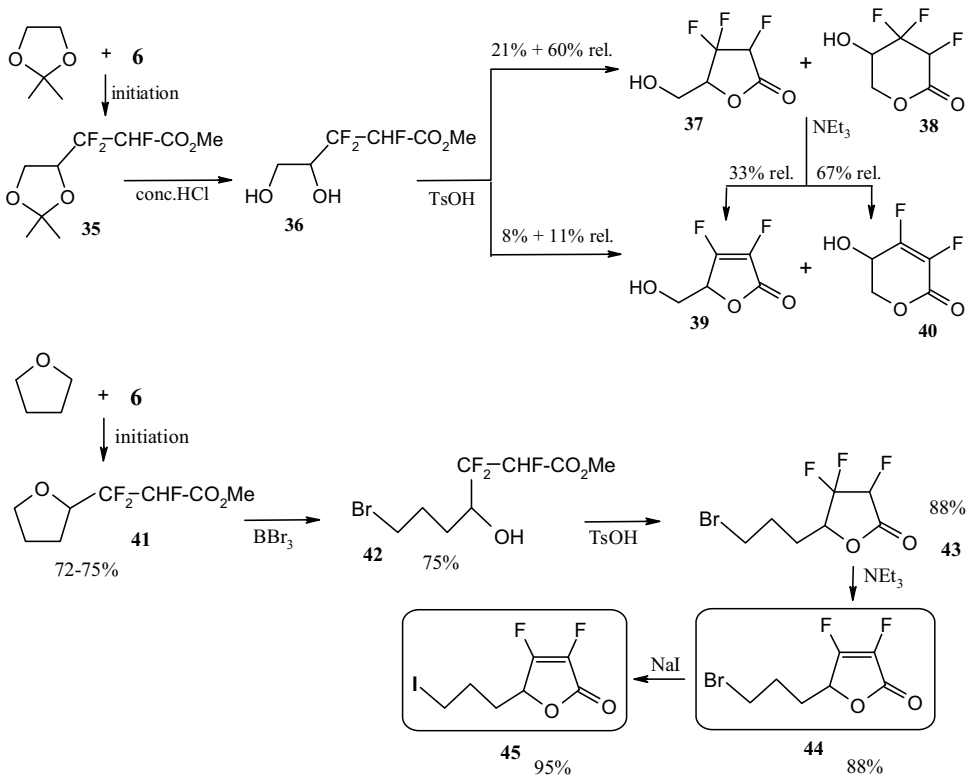
In attempted synthesis of butanolide **53**, regiospecific radical addition of methyl bromochlorofluoroacetate to vinyl acetate was used to afford 4-acetoxy-4-bromo-2-chloro-2-fluorobutanoate (**50**, yield 70%, Scheme 5). The yield of the 1:1 adduct was sensitive to the reaction temperature, at 100 °C telomers were obtained only. The adduct **50** was first transformed to the corresponding dimethyl acetal **51** and subsequently to the free acid **52**. We attempted to transform the all three compounds **50–52** to 2-chloro-2-fluoro-4-methoxybutanolide (**53**) using hydrochloric, polyphosphoric or *p*-toluenesulfonic acid in various solvents unsuccessfully: or the substrates were unreactive, or mixtures of products or polymers were obtained. This result is in a sharp contrast with easy lactonisations of acetalised 4-oxobutanoate moieties (also as a part of cyclic or saccharide structures) under an acid catalysis [18].

An overview on lactonisation reactions is given in Table 6. The lactonisations in entries 1 and 2a are nucleophilic substitution of chlorine by carboxylate oxygen, which is easier at the primary carbon in **54** than in **47**. A dramatic difference in lactonisation ability is met for the comparable structures **56** and **7–11** (entries 3

Table 5
Dehydrofluorination of butanolides using NEt_3.

Butanolide		Time (h)	Butenolide
			%[a]
27	Me	1	**31**	92
28	Et	1	**32**	96
29	Pr	1	**33**	89
30	Hept	1	**34**	93
43	$Br(CH_2)_3$	1	**44**	88

[a] Total isolated yield.



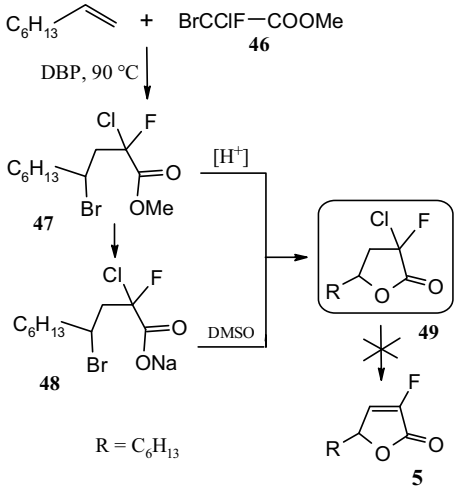
Scheme 3. Overview of syntheses of 5-alkyl-3,4-difluorofuran-2(5*H*)-ones using starting cyclic ethers.

and 4): while 4,4-dialkylated alkanoates **56** cyclise spontaneously, the monoalkylated analogues **7–11** require several-days refluxing under acid catalysis. In contrast, the compounds **50–52** as close analogues of **42** and functional derivatives of 2-chloro-2-fluoro-4-oxobutanoic acid at the same time did not afford the corresponding 4-methoxybutanolides.

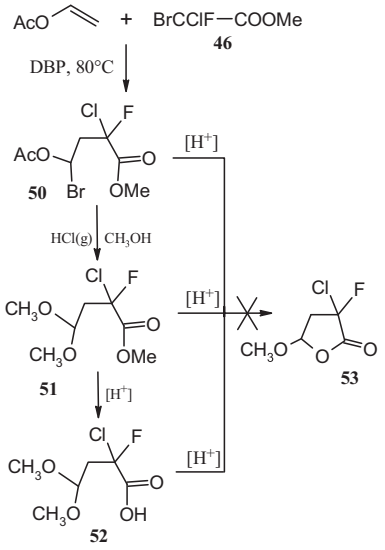
3. DFT calculations on lactonisation

For fluorinated hydroxycarboxylic acid with varied substitution on the C4 of the carbon chain, striking differences in the ability to cyclise prompted us to start a theoretical study of the lactonisation. We chose methyl 2,3,3-trifluoro-4-hydroxybutanoate (**7**) and methyl 2,3,3-trifluoro-4-hydroxy-4-methylpentanoate (**56a**) as the respective representatives of the non-cyclizing and easily cyclizing hydroxy ester. As the experimental cyclisations were performed under strongly acidic catalysis (TsOH) in non-polar toluene, the role of the solvent was neglected and the computations were performed for gas-phase approximation. Lactoniation of hydroxy esters is a type of transesterification [19].

We started the study with conformational search of fluorobutanoate **7** (Table 6). We concentrated on the potential key step, i.e. nucleophilic addition to protonated species **7H⁺**, and hence first decided to find its most stable conformation. Due to multiple substituent fluorine atoms, around 60 conformers were taken into account. In contrast to the expected anti conformer **7AH⁺**, the

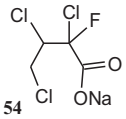
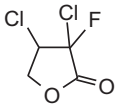
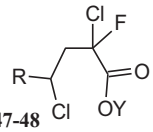
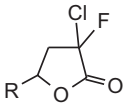
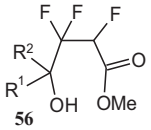
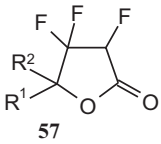
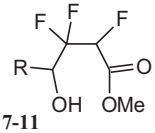
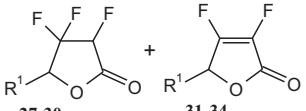
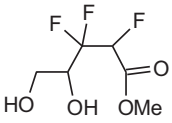
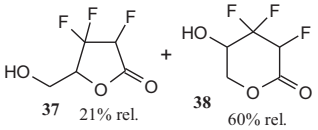
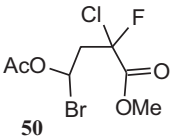
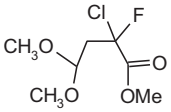
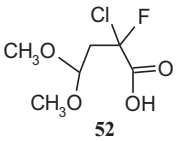


Scheme 4. Synthesis of 2-chloro-2-fluoro-4-hexyl butan-4-olide (**49**).



Scheme 5. Attempts to synthesise 2-chloro-2-fluoro-4-methoxybutan-4-olide (**53**).

Table 6
Overview on the lactonisation of 4-hydroxy- or/and 4-halogenoalkanoates to form butan-4-olides (furan-2(5*H*)-ones).

Entry	Starting compound	Reaction conditions	Product(s)	Character of cyclisation[a]	Refs.
1	 **54**	200 °C → 89% DMSO, 40 °C, 8 h → 41%	 **55**	Moderately easy	[17]
2a 2b	 **47-48** R = C_6H_{13}	Y = Na DMSO, 80 °C, 3 h → 82% Y = CH_3 HCl, H_2O, CH_3OH, reflux, 80 h → 70%	 **49** R = C_6H_{13}	Moderately easy difficult	
3	 **56** R^1, R^2 = Me, Et R^1-R^2 = $(CH_2)_5$	Spontaneously formed during photoaddition at 20 °C and work up	 **57**	Spontaneous	[10]
4	 **7-11** R = Me, Et, Pr, Hept	TsOH, toluene, reflux, 2–10 d → 88–96%	 **27-30** + **31-34** 5-8% rel.	Difficult	
5	 **36**	TsOH, toluene, reflux, 10 h → defined mixture	 **37** 21% rel. + **38** 60% rel.	Non-regioselective	
6	 **50**	HCl, H_2O, CH_3OH, r.t., 12 h → mixture	Unidentified mixture of products	Unfavourable	
7	 **51**	Various acids [H^+], H_2O, CH_3OH, reflux	Unidentified mixture of products	Unfavourable	
8	 **52**	Various acids [H^+], various solvents, reflux	Unidentified mixture of products	Unfavourable	

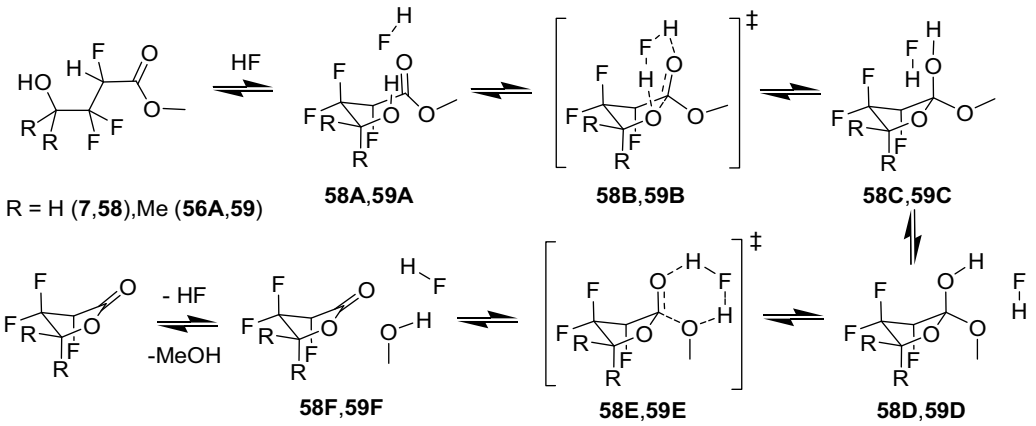
[a] All cyclisations are of *exo-trig* character [15].

gauche conformer **7BH$^+$** with the O–H–OH coordination proved to be most stable (Fig. 2). Further we found that the next structure on the potential lactonisation pathway, protonated monoalkylated orthoester **7CH$^+$**, is not a minimum on the potential energy surface (PES). Identical result was obtained when implicit solvent using SCRF methodology was included.

Recent computational publications addressing acidic hydrolysis of simple esters as ethyl acetate catalyzed with water-solvated proton [20] or sulfuric acid [21] encountered analogous problems. Instead of the traditional pathway including cationic intermediates, a "contact ion-pair" mechanism with neutral intermediates and transition states transferring protons between substrate and a catalyst was found to be energetically more favourable.

We found this approach to be perfectly applicable for our study. In the calculations, we employed two acids, hydrogen fluoride and methanesulfonic acid as a close substitute for 4-toluenesulfonic acid.

The computed lactonisation pathway catalysed with the former acid is depicted in Scheme 6. The reaction starts with coordination of HF to hydroxyester **7** or **56A** leading to the cluster **58A** or **59A**. The respective relative Gibbs free energies found are 0.0 kJ/mol (axial, anti), 27.3 kJ/mol (equatorial, anti), 30.3 kJ/mol (axial, syn) and 52.8 kJ/mol (equatorial, syn). For these four conformations, the whole reaction pathway according to Scheme 6 was computed. Due to clarity, only the pathway starting from the most stable conformer and giving transition states of lowest energies is



Scheme 6. "Contact ion-pair" mechanism of lactonisation catalyzed with HF.

depicted in Fig. 3. The simulated reaction continues from cluster **58A** or **59A** through cyclic transition state **58B** or **59B**, in which simultaneously one hydrogen atom is transferred from HF to the carbonyl group, while second hydrogen atom is moving from the hydroxyl group to the fluorine atom of HF. The movement of both hydrogens is accompanied by the attack of the hydroxy group to the carbonyl forming ortholacton/HF cluster **58C** or **59C**. The simulated reaction continues by recoordination of HF to the hydroxy group of ortholacton and the methoxy group yielding cluster **58D** or **59D**. The removal of methanol from the ortholacton is analogously accompanied by two hydrogen transfers from and to the fluorine atom of HF trough transition state **58E** or **59E** and the whole reaction pathway finishes with the formation of lactone and methanol coordinated to HF (**58F**, **59F**). Fig. 3 shows the potential energy surfaces of the simulated lactonisation of both substrates **7**, **56A**.

A comparison of both potential energy surfaces indicates that the energy of the first transition state plays negligible role in the preference for the cyclisation of the more substituted hydroxyester **57A**. Hence, it is the second part of the lactonisation process, i.e. the energy of the transition state of the decomposition of ortholactone cluster **59E** and even more the stability of the product cluster **59F**, which seems to play the major role in the preferred lactonisation. An analogous result was obtained when methanesulfonic acid was included in the calculations similarly to sulfuric acid [21] (see the Supporting information).

To summarise the calculations, in can be stated that computational analysis confirmed experimentally observed preference for the cyclisation of the more substituted hydroxyester **56A** (Scheme 6).

All computations were performed using the Gaussian 09W program [22] using the M06 functional [23] and SV(P) basis set [24]. For visualisations, GaussView program [25] was employed. Vibrational analysis was performed for all structures to obtain their standard Gibbs energies and characterise them as minima or transition states.

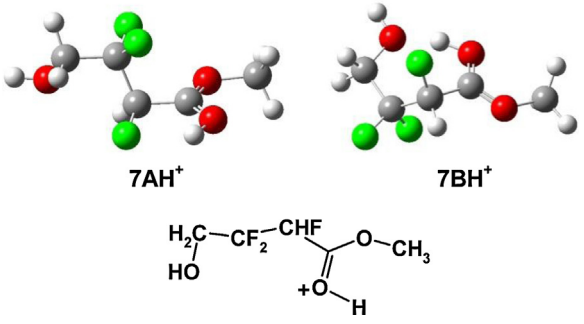


Fig. 2. Expected (**7AH$^+$**) and found (**7BH$^+$**) minimal energy conformations of protonated ester **7**.

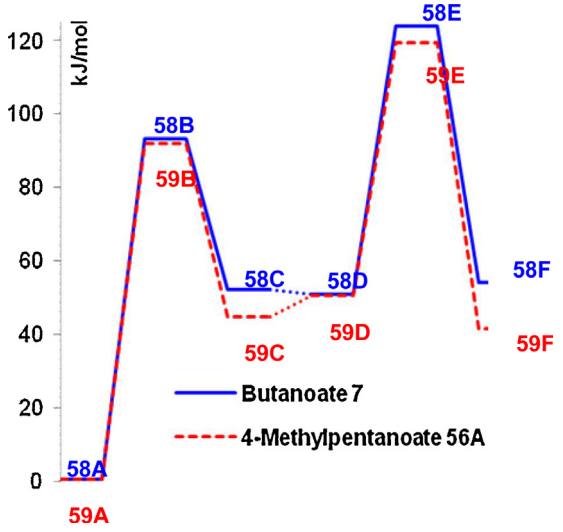


Fig. 3. Simulated HF-catalysed lactonisation of hydroxyesters **7** (cluster **58**, blue full line) and **56A** (cluster **59**, red dotted line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

4. Conclusions

The syntheses of 4-alkyl-2,3-difluorobut-2-enolides (5-alkyl-3,4-difluorofuran-2(5*H*)-ones) were developed starting with radical additions of ethers to methyl trifluoroacrylate. 2-Chloro-2-fluoro-4-hexylbutanolide was prepared using bromochlorofluoroacetate and oct-1-ene. DFT calculations of the transition state energies of the *exo-trig* cyclisations of halogenated 4-hydroxyalkanoates were carried out and confirmed the observation that the cyclisations become more feasible with increasing number of alkyls at C4.

5. Experimental

5.1. General

Unless noted otherwise, all starting materials were obtained from commercial suppliers and were used without further purification. Asymmetric ethers were prepared by the Williamson synthesis. Methyl 2,3,3-trifluoroacrylate (MTFA) was prepared according to Ref. [10].

NMR spectra were recorded on a Varian 300 HC (^{1}H, 300.1 MHz; ^{13}C, 75.5 MHz; ^{19}F, 276.5 MHz) instrument in $CDCl_3$. Chemical shifts δ (ppm) are relative to tetramethylsilane (^{1}H, 0.0 ppm), $CDCl_3$ (^{13}C, 77.0 ppm) or $CFCl_3$ (^{19}F, 0.0 ppm). For recording of ^{13}C NMR spectra the pulse sequences APT or DEPT were used. Coupling constants J are given in Hz. Mass spectra were recorded using a combination of Hewlett Packard GC HP 5890 series II gas chromatograph and a Hewlett Packard MS HP 5971 mass spectrometer (70 eV, EI). The capillary column for GC was DB5-MS. Purities of some compounds were measured using a Micromat HRGC 412 (HNU-Nordion, capillary column NB-30). Infrared spectra were recorded on a NICOLET 740 spectrophotometer.

5.2. Radical addition of alcohols to MTFA (**6**)

5.2.1. General procedures

Typical procedure A: MTFA (**6**, ca. 500 mg, 3.6 mmol) and alcohol (ca. 68 mmol) were added to an UV cuvette (5 mL). After bubbling nitrogen into the cooled (−50 °C) solution for 15 min, it was irradiated until full conversion of MTFA was observed (monitored by GC). The excess alcohol was evaporated or distilled off and CH_2Cl_2 (15 mL) was added to the residue. The mixture was washed twice with saturated water solution of $NaHCO_3$ (10 mL). The organic layer was dried over $MgSO_4$, filtered and CH_2Cl_2 was evaporated. The crude product was purified by column chromatography (silica gel 20 g, CH_2Cl_2).

Typical rocedure B: Nitrogen was bubbled into a mixture of MTFA (ca. 500 mg, 3.6 mmol) and alcohol (ca. 68 mmol) cooled to −20 °C for ca. 15 min. Dibenzoyl peroxide (DBP) and AIBN (2 mol%/2 mol% ratio) were added and the mixture was heated at 65 °C until complete conversion of MTFA was observed (monitored by GC). The final work-up of the reaction mixture was the same as in procedure A.

5.2.2. Reaction of MTFA with methanol: Product **12**

Procedure A: MTFA (488 mg, 3.49 mmol), methanol (2.20 g, 68.8 mmol), 6 h, no reaction occurred (monitored by ^{19}F NMR).

Procedure B: MTFA (501 mg, 3.58 mmol) and methanol (2.02 g, 63.1 mmol), 10 h, gave product **12** (527 mg, 3.06 mmol, 85.5%). For analysis see [26].

Methyl 2,3,3-trifluoro-3-methoxypropanoate (**12**): ^{1}H NMR ($CDCl_3$): δ 3.61 (s, 3*H*, CH_3O), 3.83 (s, 3*H*, CH_3O), 4.96 (dt, 1*H*, $^2J_{HF}$ = 46.7 Hz, $^3J_{HF}$ = 4.4 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 50.82 (t, CH_3O, $^3J_{CF}$ = 6.6 Hz), 52.96 (s, CH_3O), 85.59 (ddd, CHF, $^1J_{CF}$ = 198.1 Hz, $^2J_{CF}$ = 37.8 Hz, $^2J_{CF}$ = 34.9 Hz), 119.54 (dt, CF_2, $^1J_{CF}$ = 268.0 Hz, $^2J_{CF}$ = 23.5 Hz), 163.86 (d, C=O, $^2J_{CF}$ = 24 Hz) ppm. ^{19}F NMR ($CDCl_3$) δ −84.1 (dd, 1F, $^2J_{FF}$ = 134.6 Hz, $^3J_{FF}$ = 3.9 Hz), −86.2 (dd, 1F, $^2J_{FF}$ = 143.6 Hz, $^3J_{FF}$ = 5.9 Hz), −202.8 (d, 1F, $^2J_{HF}$ = 46.6 Hz) ppm.

5.2.3. Reaction of MTFA with ethanol: Products **8** and **13**

Procedure A: MTFA (491 mg, 3.51 mmol), ethanol (2.20 g, 68.8 mmol), 12 h, product as a mixture of **8** and **13** (503 mg, 2.70 mmol, 77.1%), ratio **8**/**13** = 37/67.

Procedure B: MTFA (496 mg, 3.54 mmol), ethanol (2.02 g, 63.1 mmol), 9 h, product as a mixture of **8** and **13** (469 mg, 2.52 mmol, 71.2%), ratio **8**/**13** = 41/59. $C_6H_9F_3O_3$ (186.13) (**8** + **13**): calcd C 38.72, H 4.87; found C 38.89, H 4.90.

Methyl 2,3,3-trifluoro-4-hydroxypentanoate (**8**). *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3*H*, $^3J_{HH}$ = 6.6 Hz), 3.06 (s, OH), 3.79 (s, 3*H*), 4.02–4.22 (m, 1*H*), 5.06 (ddd, 1*H*, CHF, $^2J_{HF}$ = 48 Hz, $^3J_{HF}$ = 13 Hz, $^3J_{HF}$ = 1 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 15.4 (d, CH_3, $^3J_{CF}$ = 2 Hz), 53.6 (s, OCH_3), 66.8 (dd, CH, $^2J_{CF}$ = 30 Hz, $^2J_{CF}$ = 25 Hz), 86.1 (dt, CF_2, $^1J_{CF}$ = 198 Hz, $^2J_{CF}$ = 30 Hz), 119.2 (ddd, CHF, $^1J_{CF}$ = 252 Hz, $^1J_{CF}$ = 255 Hz, $^2J_{CF}$ = 22 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −116.2 (dm, 1F, $^2J_{FF}$ = 266 Hz), −127.0 (dm, 1F, $^2J_{FF}$ = 266 Hz), −207.2 (dm, 1F, $^2J_{HF}$ = 47 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3*H*, $^3J_{HH}$ = 6.6 Hz), 3.06 (s, OH), 3.81 (s, 3*H*), 4.02–4.22 (m, 1*H*), 5.22 (ddd, 1*H*, CHF, $^2J_{HF}$ = 46 Hz, $^3J_{HF}$ = 20 Hz, $^3J_{HF}$ = 1 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 15.1 (d, CH_3, $^3J_{CF}$ = 3 Hz), 54.0 (s, OCH_3), 66.6 (dd, CH, $^2J_{CF}$ = 32, $^2J_{CF}$ = 25 Hz), 86.1 (dt, CF_2, $^1J_{CF}$ = 198, $^2J_{CF}$ = 30 Hz), 85.5 (ddd, CF_2, $^1J_{CF}$ = 192 Hz, $^2J_{CF}$ = 37 Hz), 119.3 (dt, CHF, $^1J_{CF}$ = 254 Hz, $^2J_{CF}$ = 26 Hz), 166.6 (ddd, C=O, $^2J_{CF}$ = 24 Hz, $^3J_{CF}$ = 4 Hz), 166.2 (ddd, C=O, $^2J_{CF}$ = 24 Hz, $^3J_{CF}$ = 10 Hz, $^3J_{CF}$ = 2 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −120.3 (dm, 1F, $^2J_{FF}$ = 266 Hz), 128.3 (dm, 1F, $^2J_{FF}$ = 266 Hz), −204.0 (dm, 1F, $^2J_{HF}$ = 45 Hz) ppm.

Methyl 3-ethoxy-2,*3,3-trifluoropropanoate* (**13**). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.28 (t, 3*H*, $^3J_{HH}$ = 7.2 Hz), 3.85 (s, 3*H*), 4.00 (q, 2*H*, $^3J_{HH}$ = 7.2 Hz), 4.96 (dt, 1*H*, CHF, $^2J_{HF}$ = 46.3 Hz, $^3J_{HF}$ = 5.5 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −81.3 (ddd, 1F, $^2J_{FF}$ = 144.8 Hz, $^3J_{FF}$ = 11 Hz, $^3J_{HF}$ = 4.9 Hz), −83.1 (ddd, 1F, $^2J_{FF}$ = 144.7 Hz, $^3J_{FF}$ = 14.8 Hz, $^3J_{HF}$ = 6.0 Hz), −202.6 (ddd, 1F, $^2J_{HF}$ = 52.7 Hz, $^3J_{FF}$ = 19.3 Hz, $^3J_{FF}$ = 17 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 185 (19) $[M-1]^+$, 155 (6.1), 149 (10.5), 133 (9.4), 123 (19), 115 (9), 105 (14), 93 (100), 75 (31), 57 (58).

5.2.4. Reaction of MTFA with propanol: Products **9** and **14**

Procedure A: MTFA (480 mg, 3.43 mmol), propan-1-ol (4.10 g, 68.3 mmol), 13 h, product as a mixture of **9** and **14** (518 mg, 2.59 mmol, 75.6%), ratio **9**/**14** = 58/42.

Procedure B: MTFA (512 mg, 3.66 mmol), propan-1-ol (4.04 g, 67.3 mmol), 12 h, product as a mixture of **9** a **14** (626 mg, 3.13 mmol, 85.6%), ratio **9**/**14** = 45/55. $C_7H_{11}F_3O_3$ (200.16) (**9** + **14**): calcd C 42.00, H 5.54; found C 42.10, H 5.48.

Methyl 2,3,3-trifluoro-4-hydroxyhexanoate (**9**). *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.01 (t, $^3J_{HH}$ = 7.4 Hz), 1.46–1.92 (m, 2*H*), 2.84 (s, OH), 3.82 (s, 3*H*), 3.79–3.94 (m, 1*H*), 5.17 (ddd, $^2J_{HF}$ = 45.6 Hz, $^3J_{HF}$ = 20.3 Hz, $^3J_{HF}$ = 3.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 9.6 (s, CH_3), 21.95 (s, CH_2), 52.97 (s, OCH_3), 71.13 (dd, $^2J_{CF}$ = 28.7 Hz, $^2J_{CF}$ = 29.8 Hz, CHOH), 84.81 (ddd, ds_2, $^1J_{CF}$ = 191.8 Hz, $^2J_{CF}$ = 30.4 Hz, CHF), 118.56 (ddt, $^1J_{CF}$ = 265.6 Hz, $^1J_{CF}$ = 269.1 Hz, $^2J_{CF}$ = 25.8, CF_2), 165.32 (d, $^2J_{CF}$ = 23.4 Hz, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −115.65 (ddt, 1F, $^2J_{FF}$ = 267.2 Hz, $^3J_{HF}$ = 4.6 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 12.2 Hz), −125.28 (ddt, 1F, $^2J_{FF}$ = 266.1 Hz, $^3J_{HF}$ = 18.6 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 7.7 Hz), −207.15 (ddd, 1F, $^2J_{HF}$ = 46.5 Hz, $^3J_{FF}$ = 12.3 Hz, $^3J_{FF}$ = 8.5 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.02 (t, $^3J_{HH}$ = 7.1 Hz), 1.46–1.92 (m, 2*H*), 3.06 (s, OH), 3.83 (s, 3*H*), 3.79–3.94 (m, 1*H*), 5.16 (ddd, $^2J_{HF}$ = 46.7 Hz, $^3J_{HF}$ = 12.1 Hz, $^3J_{HF}$ = 7.1 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 9.6 (s, CH_3); 21.78 (s, CH_2), 52.89 (s, OCH_3), 71.33 (dd, $^2J_{CF}$ = 24.6 Hz, $^2J_{CF}$ = 28.7 Hz, CHOH), 85.54 (dt, $^1J_{CF}$ = 195.2 Hz, $^2J_{CF}$ = 37.2 Hz, $^2J_{CF}$ = 29.2 Hz, CHF), 118.72 (dt, $^1J_{CF}$ = 239.9 Hz, $^2J_{CF}$ = 22.9 Hz, CF_2), 165.59 (dt, $^2J_{CF}$ = 21.1 Hz, $^2J_{CF}$ = 3.4 Hz, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −120.45 (dt, 1F, $^2J_{FF}$ = 267.3 Hz, $^3J_{HF}$ = $^3J_{FF}$ = 15.9 Hz), −126.22 (ddt, 1F, $^2J_{FF}$ = 268.2 Hz, $^3J_{HF}$ = 20.6 Hz, $^3J_{HF}$ = $^3J_{FF}$ = 2.5 Hz), −203.91 (ddd, 1F, $^2J_{HF}$ = 45.7 Hz, $^3J_{FF}$ = 9.6 Hz, $^3J_{FF}$ = 4.0 Hz) ppm.

Methyl 2,3,3-trifluoro-3-propoxypropanoate (**14**). ^{1}H NMR ($CDCl_3$): δ 0.92 (t, 3*H*, $^3J_{HH}$ = 7.1 Hz), 1.60–1.71 (m, 2*H*), 3.85 (s, 3*H*), 3.89 (t, 2*H*, $^3J_{HH}$ = 6.6 Hz), 4.97 (dt, 1*H*, CHF, $^2J_{HF}$ = 46.7 Hz, $^3J_{HF}$ = 4.9 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 10.01 (s, CH_3), 22.31 (s, CH_2), 53.01 (s, OCH_3), 65.99 (t, CH_2O, $^3J_{CF}$ = 5.4 Hz), 85.82 (ddd, CHF, $^1J_{CF}$ = 198.3 Hz, $^2J_{CF}$ = 38.6 Hz, $^2J_{CF}$ = 35.2 Hz), 119.38 (dt, CF_2, $^1J_{CF}$ = 268.0 Hz, $^2J_{CF}$ = 23.5 Hz), 164.10 (d, C=O, $^2J_{CF}$ = 23.8) ppm. ^{19}F NMR ($CDCl_3$): δ −80.54 (ddd, 1F, $^2J_{FF}$ = 144.1 Hz, $^3J_{FF}$ = 12.2 Hz, $^3J_{HF}$ = 4.9 Hz), −82.67 (ddd, 1F, $^2J_{FF}$ = 144.0 Hz, $^3J_{FF}$ = 14.6 Hz, $^3J_{HF}$ = 4.9 Hz), −202.16 (ddd, 1F, $^2J_{HF}$ = 47.6 Hz, $^3J_{FF}$ = 14.5 Hz, $^3J_{FF}$ = 12.2 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 180 (0.5) $[M-20]^+$, 171 (6.4), 142 (1.8), 141 (33), 139 (4.6), 123 (10), 113 (9.2), 109 (1.4), 93 (2.3), 92 (27), 91 (7.3), 82 (13), 79 (1.4), 69 (3.2), 63 (5.5), 59 (47).

*5.2.5. Reaction of MTFA with octan-1-ol: products **11** and **15***

Procedure A: MTFA (488 mg, 3.49 mmol) and octan-1-ol (8.61 g, 66.3 mmol), 14 h; as product, a mixture of **11** and **15** (655 mg, 2.43 mmol, 69.6%), ratio **11**/**15** = 81/19.

Procedure B: MTFA (505 mg, 3.61 mmol) and octan-1-ol (9.12 g, 70.2 mmol), 11 h, as product, a mixture of **11** and **15** (724 mg, 2.68 mmol, 74.4%), ratio **11**/**15** = 71/29. $C_{12}H_{21}F_3O_3$ (270.29): calcd C 53.33, H 7.83; found C 53.28, H 7.77.

*Methyl 2,3,3-trifluoro-4-hydroxyundecanoate (**11**). Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3*H*, $^3J_{HH}$ = 6.6 Hz), 1.18–1.86 (m, 12*H*), 2.28 (s, OH), 3.85 (s, 3*H*), 3.86–4.12 (m, 1*H*), 5.05–5.45 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 14.0 (s, CH_3), 22.6–31.7 (m, 6C, $(CH_2)_6$), 53.1 (s, CH_3), 69.7–70.6 (m, CH), 85.7 (dt, CHF, $^1J_{CF}$ = 195.8 Hz, $^2J_{CF}$ = 30.3 Hz), 115.1–122.2 (m, CF_2), 165.6 (d, C=O, $^2J_{CF}$ = 21.7 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −115.7 (ddt, 1F, $^2J_{FF}$ = 265.8 Hz, $^3J_{HF}$ = 12.0 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 4.7), −125.4 (ddt, 1F, $^2J_{FF}$ = 266.5 Hz, $^3J_{HF}$ = 18.5 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 8.3 Hz), −207.10 (ddd, 1F, $^2J_{HF}$ = 46.6 Hz, $^3J_{FF}$ = 12.4 Hz, $^3J_{FF}$ = 8.7 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3*H*, $^3J_{HH}$ = 6.0 Hz), 1.18–1.86 (m, 12*H*), 2.08 (s, OH), 3.87 (s, 3*H*), 3.86–4.12 (m, 1*H*), 5.05–5.45 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 14.0 (s, CH_3), 22.6–31.7 (m, 6C, $(CH_2)_6$), 53.0 (s, CH_3), 69.7–70.6 (m, CH), 85.1 (ddd, CHF, $^1J_{CF}$ = 192.4 Hz, $^2J_{CF}$ = 36.7 Hz, $^2J_{CF}$ = 29.8 Hz), 115.1–122.2 (m, CF_2), 165.2 (d, C=O, $^2J_{CF}$ = 25.2 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −120.3 (ddd, 1F, $^2J_{FF}$ = 267.5 Hz, $^3J_{HF}$ = 16.6 Hz, $^3J_{FF}$ = 13.6 Hz), −126.2 (ddd, 1F, $^2J_{FF}$ = 268.2 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 6.7 Hz, $^3J_{HF}$ = 4.2 Hz), −203.8 (dddd, 1F, $^2J_{HF}$ = 44.2, $^3J_{FF}$ = 16.7 Hz, $^3J_{HF}$ = 6.1 Hz, $^4J_{HF}$ = 2.4 Hz) ppm.

*Methyl 2,3,3-trifluoro-3-octyloxypropanoate (**15**)*. ^{1}H NMR (MHz, $CDCl_3$): δ 0.86 (t, 3*H*, $^3J_{HH}$ = 6.1); 1.49–1.71 (m, 12*H*), 3.85 (s, 3*H*), 3.92 (t, 2*H*, $^3J_{HH}$ = 6.6 Hz), 4.96 (dt, 1*H*, $^2J_{HF}$ = 46.8 Hz, $^3J_{HF}$ = 5.8 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 14.0 (s, CH_3); 25.5–31.7 (m, $(CH_2)_6$), 52.3 (s, CH_3), 64.5 (t, CH_2O, $^3J_{CF}$ = 5.7 Hz), 85.8 (ddd, CHF,$^1J_{CF}$ = 198.4 Hz, $^2J_{CF}$ = 38.4 Hz, $^2J_{CF}$ = 35.2 Hz), 119.4 (dt, CF_2, $^1J_{CF}$ = 268.0 Hz, $^2J_{CF}$ = 23.8 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −80.6 (ddd, 1F, $^2J_{FF}$ = 144.0 Hz, $^3J_{FF}$ = 11, $^3J_{HF}$ = 4.9 Hz), −82.7 (ddd, 1F, $^2J_{FF}$ = 144.1 Hz, $^3J_{FF}$ = 14.7 Hz, $^3J_{HF}$ = 6.1 Hz), −202.1 (ddd, 1F, $^2J_{HF}$ = 46.4 Hz, $^3J_{FF}$ = 14.7 Hz, $^3J_{FF}$ = 11 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 271 (10) $[M+1]^+$, 241 (19), 240 (11), 129 (9.2), 113 (19), 111 (17), 110 (14), 84 (18), 82 (19), 81 (14), 71 (76), 69 (40), 68 (22), 57 (100).

5.3. Radical addition of ethers to MTFA

5.3.1. General procedure

Typical procedure A: MTFA (ca. 14 mmol) and ether (ca. 270 mmol) were placed into a UV reactor and the mixture was purged with nitrogen at −50 °C for 15 min. and then irradiated. After full conversion of MTFA (monitored by GC) the excess of the ether was evaporated or distilled off and CH_2Cl_2 (15 mL) was added to the residue. The mixture was extracted twice with saturated water solution of $NaHCO_3$ (10 mL). The organic layer was dried over $MgSO_4$, filtrated and CH_2Cl_2 was evaporated. The crude product was distilled under vacuum or purified by column chromatography.

Typical procedure B: MTFA (ca. 15 mmol) and ether (ca. 290 mmol) were placed into a three-necked flask and the mixture was purged with nitrogen at −20 °C for 15 min. Then DBP (2 mol%) and AIBN (2 mol%) were added to the solution. The resulting mixture was heated under reflux until complete conversion of MTFA occurred (monitored by GC). The final work up of reaction mixture was the same as in procedure A.

*5.3.2. Reaction of MTFA with diethyl ether: Products **16** and **24***

Procedure A: MTFA (2.08 g, 14.4 mmol) and diethyl ether (21.1 g, 285 mmol) gave a mixture of mono-adduct **16** (1.63 g, 7.62 mmol, 51.1%) and bis-adduct **24** (971 mg, 36.9%). Crystallisation (hexane) afforded 22 mg of pure colourless crystals of bis-adduct **24** (mp 80–82 °C) as the *meso*-form.

*Methyl 4-ethoxy-2,3,3-trifluoropentanoate (**16**): Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.19 (t, 3*H*, $^3J_{HH}$ = 7.1 Hz), 1.29 (d, 3*H*, $^3J_{HH}$ = 6.1 Hz), 3.40–3.68 (m, 2*H*), 3.58–3.88 (m, 2*H*), 3.84 (s, 3*H*), 5.10 (ddd, 1*H*, $^2J_{HF}$ = 46.7 Hz, $^3J_{HF}$ = 12.1 Hz, $^3J_{HF}$ = 5.5 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 11.58 (dm, CH_3), 15.1 (s, CH_3), 2.7 (s, CH_3), 65.6 (s, CH_2), 72.8 (dd, CH, $^2J_{CF}$ = 23.5 Hz, $^2J_{CF}$ = 29.8 Hz), 85.4 (ddd, CHF, $^1J_{CF}$ = 193.5 Hz, $^2J_{CF}$ = 29.2 Hz, $^2J_{CF}$ = 32.7 Hz), 118.2 (ddd, CF_2, $^1J_{CF}$ = 257 Hz, $^1J_{CF}$ = 249.6 Hz, $^2J_{CF}$ = 24.1 Hz), 165.0 (dd, C=O, $^2J_{CF}$ = 24.1 Hz, $^3J_{CF}$ = 6.9 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −113.7 (ddt, 1F, $^2J_{FF}$ = 270.9 Hz, $^3J_{FF}$ = 12.2 Hz, $^3J_{HF}$ = 12.6 Hz, $^3J_{HF}$ = 5.1 Hz), −125.0 (ddt, 1F, $^2J_{FF}$ = 269.8 Hz, $^3J_{FF}$ = 7.1 Hz, $^3J_{FH}$ = 6.7 Hz, $^3J_{FH}$ = 17.3 Hz), −206.5 (ddd, 1F, $^2J_{HF}$ = 46.8 Hz, $^3J_{FF}$ = 12.6 Hz, $^3J_{FF}$ = 7 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.16 (t, 3*H*, $^3J_{HH}$ = 7.1 Hz), 1.29 (d, 3*H*, $^3J_{HH}$ = 6.1 Hz), 3.40–3.68 (m, 2*H*), 3.58–3.88 (m, 2*H*), 3.87 (s, 3*H*), 5.24 (ddd, 1*H*, CHF, $^2J_{HF}$ = 45.6 Hz, $^3J_{HF}$ = 20.9 Hz, $^3J_{HF}$ = 2.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 11.8 (dm, CH_3), 15.2 (s, CH_3), 52.8 (s, CH_3), 65.6 (s, CH_2), 72.7 (dd, CH, $^2J_{CF}$ = 25.2 Hz, $^2J_{CF}$ = 30.9 Hz), 84.8 (ddd, CHF, $^1J_{CF}$ = 190.6 Hz, $^2J_{CF}$ = 28.1 Hz, $^2J_{CF}$ = 37.2 Hz), 118.5 (ddd, CF_2, $^1J_{CF}$ = 255.2 Hz, $^1J_{CF}$ = 251.9 Hz, $^2J_{CF}$ = 23.5 Hz), 165.1 (d, C=O,$^2J_{CF}$ = 24.7 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.0 (dddd, 1F, $^2J_{FF}$ = 270.3 Hz, $^3J_{FF}$ = 12.4 Hz, $^3J_{HF}$ = 19.7 Hz, $^3J_{HF}$ = 5.6 Hz) ppm; −126.3 (dddd, 1F, $^2J_{FF}$ = 268.9 Hz, $^3J_{FF}$ = 6.3 Hz, $^3J_{FH}$ = 4.6 Hz, $^3J_{FH}$ = 18.5 Hz), −203.8 (dddd, 1F, $^2J_{FH}$ = 44.7 Hz, $^3J_{FF}$ = 13.2 Hz, $^3J_{FF}$ = 6.1 Hz, $^4J_{FF}$ = 4.2 Hz) ppm. $C_8H_{13}F_3O_3$ (214.18): calcd C 44.86, H 6.12; found C 44.93, H 6.23.

*Dimethyl 4,4′-oxybis(2,3,3-trifluoropentanoate) (**24**, meso-form)*. ^{1}H NMR ($CDCl_3$): δ 1.33 (d, 3*H*, $^3J_{HH}$ = 6.6 Hz), 3.84 (s, 3*H*), 4.29 (dtq, 1*H*, $^3J_{HF}$ = 12.7 Hz, $^3J_{HH}$ = 6.5 Hz, $^4J_{HF}$ = 1.1 Hz), 5.43 (ddd, 1*H*, $^2J_{HF}$ = 45.6 Hz, $^3J_{HF}$ = 14.3 Hz, $^3J_{HF}$ = 7.2 Hz) ppm. ^{13}C NMR (CDCl3): δ 12.6 (d, CH_3), 54.2 (s, OCH_3), 73.4 (dd, CH, $^2J_{CF}$ = 24.4 Hz, $^2J_{CF}$ = 30.9 Hz), 87.3 (dt, CHF, $^1J_{CF}$ = 192.6 Hz, $^2J_{CF}$ = 29.8 Hz), 120.3 (ddd, CF_2, $^1J_{CF}$ = 235.9 Hz, $^1J_{CF}$ = 244.7 Hz, $^2J_{CF}$ = 22.9 Hz), 166.4 (ddd, C=O, $^2J_{CF}$ = 23.8 Hz, $^3J_{CF}$ = 4.8 Hz, $^3J_{CF}$ = 3.2 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −114.3 (dm, 1F. $^2J_{FF}$ = 268.2 Hz), −133.6 (dddd, 1F, $^2J_{FF}$ = 268.1 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 7.3 Hz, $^3J_{FH}$ = 16.6 Hz), −207.1 (dt, 1F, CHF, $^2J_{FH}$ = 45.6 Hz, $^3J_{FF}$ = 10.1 Hz) ppm. GC–MS (EI): 355 (M^+ + 1.2.4), 314 (0.5), 213 (0.5), 169 (100), 183 (0.4), 149 (15.3), 121 (0.8), 95 (2.4), 71 (4.0), 59 (2.3), 43 (4.0). $C_{12}H_{16}F_6O_5$ (354.24): calcd C 40.69, H 4.55; found: C 40.85, H 4.61.

5.3.3. Reaction of MTFA with tert.*butyl ethyl ether: Product **17***

Procedure B: MTFA (2.10 g, 15.0 mmol) and *tert*-butyl ethyl ether (30.0 g, 294 mmol) gave 2.23 g (9.22 mmol, 61.4%) of product **17**.

*Methyl 4-tert-butoxy-2,3,3-trifluoropentanoate (**17**): Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.19 (s, 9*H*), 1.27 (d, 3*H*, $^3J_{HH}$ = 6.6 Hz), 3.83 (s, 3*H*), 3.95–4.13 (m, 1*H*), 5.01–5.31 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 15.5 (s, CH_3), 28.4 (s, CH_3), 52.7 (s, OCH_3), 66.2 (dd, CH, 2 × $^2J_{CF}$ = 26.3 Hz), 75.5 (s, O–C), 84.9 (dt, CHF, $^1J_{CF}$ = 192.4 Hz, $^2J_{CF}$ = 29.7 Hz), 118.6 (dt, CF_2, $^1J_{CF}$ = 245.1 Hz, $^2J_{CF}$ = 25.8 Hz), 165.2 (d, C=O, $^2J_{CF}$ = 24.7 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −114.2 (ddd, 1F, CF_2, $^2J_{FF}$ = 265.8 Hz, $^3J_{HF}$ = 20.2 Hz, $^3J_{FF}$ = 10.0 Hz), −121.3 (ddd, 1F, CF_2, $^2J_{FF}$ = 265.6 Hz, $^3J_{HF}$ = 22.6 Hz, $^3J_{FF}$ = 11.2 Hz); −205.6 (dt, 1F, CHF, $^2J_{HF}$ = 46.1 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 10.6 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.19 (s, 9*H*), 1.27 (d, 3*H*, $^3J_{HH}$ = 6.6 Hz), 3.84 (s, 3*H*), 3.95–4.13 (m, 1*H*), 5.01–5.31 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 16.6 (d, CH_3, $^3J_{CF}$ = 8.8 Hz), 28.3 (s, CH_3), 52.7 (s, OCH_3), 67.3 (dd, CH, $^2J_{CF}$ = 24.6 Hz, $^2J_{CF}$ = 30.0 Hz), 75.4 (s, O–C), 84.9 (ddd, CHF, $^2J_{CF}$ = 29.2 Hz, $^2J_{CF}$ = 97.9 Hz, $^1J_{CF}$ = 191.6 Hz), 118.5 (dt, CF_2, $^1J_{CF}$ = 258.6 Hz, $^2J_{CF}$ = 24.1 Hz), 165.0 (d, C=O, $^2J_{CF}$ = 24.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.1 (dddd, 1F, CF_2,

$^2J_{FF}$ = 269.9 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 18.3 Hz, $^3J_{HF}$ = 4.3 Hz); −121.3 (ddd, 1F, CF_2, $^2J_{FF}$ = 265.6 Hz, $^3J_{HF}$ = 22.6 Hz, $^3J_{FF}$ = 11.2 Hz); −123.5 (ddd, 1F, $^2J_{FF}$ = 270 Hz, $^3J_{HF}$ = 17.1 Hz, $^3J_{FF}$ = 7.8 Hz); −203.0 (ddd, 1F, CHF, $^2J_{HF}$ = 45.7 Hz, $^3J_{HF}$ = 13.5 Hz, $^3J_{FF}$ = 8.3 Hz) ppm. $C_{10}H_{17}F_3O_3$ (242.24): calcd C 49.58, H 7.08; found C 49.69, H 7.26.

*5.3.4. Reaction of MTFA with dipropyl ether: Products **18** and **25***

Procedure B: MTFA (2.17 g, 15.5 mmol) and dipropylether (30.1 g, 295 mmol) gave product **18** (2.32 g, 9.59 mmol, 61.8%) and product **25** (586 mg, 1.53 mmol, 19.8%).

*Methyl 4-propoxy-2,3,3-trifluorohexanoate (**18**). Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 0.89 (2x t, 3*H*, $^3J_{HH}$ = 4.4 Hz), 1.02 (t, 3*H*, $^3J_{HH}$ = 6.6 Hz), 1.45–1.80 (m, 4*H*), 3.40–3.62 (m, 3*H*), 3.83 (s, 3*H*), 4.92–5.29 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 10.04 (bs, CH_3), 10.38 (s, CH_3), 20.93 (s, CH_2), 23.09 (s, CH_2), 52.80 (s, OCH_3), 74.04 (s, OCH_2), 78.95 (d, OCH, $^2J_{CF}$ = 26.3 Hz), 85.32 (ddd, CHF, $^1J_{CF}$ = 191.7 Hz, $^2J_{CF}$ = 31.5 Hz, $^2J_{CF}$ = 5.7 Hz), 119.05 (dd, CF_2, $^1J_{CF}$ = 282.3 Hz, $^1J_{CF}$ = 257.1 Hz), 165.04 (d, C=O, $^2J_{CF}$ = 24.7 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −111.8 (ddd, 1F, $^2J_{FF}$ = 270 Hz, $^3J_{FF}$ = 6.1 Hz), −120.6 (ddt, 1F, $^2J_{FF}$ = 270.3), −205.5 (dt, 1F, CHF, $^2J_{HF}$ = 46.3 Hz) ppm.

Diastereoisomer B: δ 0.89 (2x t, 3*H*, $^3J_{HH}$ = 4.4 Hz), 1.02 (t, 3*H*, $^3J_{HH}$ = 6.6 Hz), 1.45–1.80 (m, 4*H*), 3.40–3.62 (m, 3*H*), 3.85 (s, 3*H*), 4.92–5.29 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 10.04 (bs, CH_3), 10.46 (s, CH_3), 21.50 (d, C*H*$_2$CH, $^3J_{CF}$ = 3.0 Hz), 23.19 (s, CH_2), 52.85 (s, OCH_3), 74.12 (s, OCH_2), 78.98 (dd, OCH, $^2J_{CF}$ = 50.5 Hz, $^2J_{CF}$ = 24.7 Hz), 85.28 (ddd, CHF, $^1J_{CF}$ = 193.5 Hz, $^2J_{CF}$ = 56.7 Hz, $^2J_{CF}$ = 30.9 Hz), 119.10 (ddd, CF_2, $^1J_{CF}$ = 250.8 Hz, $^1J_{CF}$ = 226.7 Hz, $^2J_{CF}$ = 6.4 Hz), 164.90 (dt, C=O, $^2J_{CF}$ = 24.0 Hz, $^3J_{CF}$ = 4.5 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −117.1 (ddt, 1F, $^2J_{FF}$ = 271.5 Hz, $^3J_{FF}$ = 7 Hz), −121.6 (dddd, 1F, $^2J_{FF}$ = 271.5 Hz, $^3J_{FF}$ = 15 Hz), −202.4 (dddd, 1F, CHF, $^2J_{HF}$ = 45.1 Hz) ppm. $C_{10}H_{17}F_3O_3$ (242.24): calcd C 49.58; H, 7.08; found C 49.79, H, 7.05.

*Dimethyl 4,4′-oxybis(2,3,3-trifluorohexanoate) (**25**). Mixture of diastereoisomers*: ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.80–1.00 (m, 6*H*), 1.41–1.79 (m, 4*H*), 3.37–3.66 (m, 2*H*), 5.01–5.38 (m, 2*H*) ppm. ^{19}F NMR ($CDCl_3$): δ −111.1–(−119.4) (m, 2F), −120.1–(−121.9) (m, 2F), -201.8-(-206.5) (2F) ppm. GC–EIMS: *m*/*z* (rel. int.): 381 (10) $[M-1]^+$, 324 (9.2), 323 (75), 303 (14), 283 (39), 244 (9.4), 183 (95), 163 (38), 143 (24), 111 (11), 103 (13), 93 (38), 91 (21), 59 (100). $C_{16}H_{24}F_6O_5$ (410.35): calcd C 43.99, H 5.27; found C 43.87, H 5.30.

*5.3.5. Reaction of MTFA with butyl methyl ether: Products **19** and **22***

Procedure A: MTFA (2.13 g, 15.2 mmol) and butyl methyl ether (29.1 g, 330.7 mmol) gave mixture of products **19** (89% rel.) and **22** (11% rel.), (2.43 g, 10.7 mmol, 70%).

Procedure B: MTFA (2.21 g, 15.8 mmol) and butyl methyl ether (27.8 g, 316.0 mmol) gave mixture of products **19** (83% rel.) and **22** (17% rel.), (2.71 g, 11.9 mmol, 75%).

$C_9H_{15}F_3O_3$ (228.21) (**19** + **22**): calcd C 47.37, H 6.63; found C 47.07, H 6.67.

Methyl 2,3,3-tri*fluoro-4-methoxyheptanoate* (**19**). *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 0.95 (t, 3*H*, $^3J_{HH}$ = 7.2 Hz), 1.50–1.72 (m, 4*H*), 3.43 (s, 3*H*), 3.72–3.85 (m, 1*H*), 3.65 (s, 3*H*), 5.14 (ddd, 1*H*, CHF, $^2J_{HF}$ = 46.2 Hz, $^3J_{HF}$ = 19.8 Hz, $^3J_{HF}$ = 3.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.93 (s, CH_3), 18.76 (s, CH_2), 30.16 (s, C*H*$_2$CH), 52.76 (s, OCH_3), 59.77 (s, OCH_3), 78.86 (dd, CH, $^2J_{CF}$ = 23.5 Hz, $^2J_{CF}$ = 2.3 Hz), 85.06 (ddd, CHF, $^1J_{CF}$ = 191.8 Hz, $^2J_{CF}$ = 30.3 Hz, $^2J_{CF}$ = 26.3 Hz), 118.8 (dt, CF_2, $^1J_{CF}$ = 256 Hz, $^2J_{CF}$ = 24.1 Hz), 164.5–165.3 (m, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −112.13 (ddt, 1F, $^2J_{FF}$ = 271.6 Hz, $^3J_{FH}$ = 10.7 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 7.6 Hz), −121.33 (ddt, 1F, $^2J_{FF}$ = 271.6 Hz, $^3J_{FH}$ = 15.3 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 9.2 Hz), −205.18 (ddd, 1F, CHF, $^2J_{FH}$ = 45.8 Hz, $^3J_{FF}$ = 11.2 Hz, $^3J_{FF}$ = 9.2 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 215 (0.05) $[M]^+$, 208 (0.05), 185 (8), 157 (1.5), 149 (5.5), 129 (3.5), 107 (5), 87 (73), 77 (5), 59 (24), 45 (100).

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.96 (t, 3*H*, $^3J_{HH}$ = 7.1 Hz), 1.50–1.72 (m, 4*H*), 3.47 (s, 3*H*), 3.72–3.85 (m, 1*H*), 3.60 (s, 3*H*), 5.08 (ddd, 1*H*, $^2J_{HF}$ = 46.7 Hz, $^3J_{HF}$ = 10.4 Hz, $^3J_{HF}$ = 9.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.93 (s, CH_3), 18.76 (s, CH_2), 29.73 (s, C*H*$_2$CH), 52.76 (s, OCH_3), 59.83 (s, OCH_3), 79.23 (dd, CH, $^2J_{CF}$ = 24.1 Hz, $^2J_{CF}$ = 4 Hz), 85.51 (ddd, CHF, $^1J_{CF}$ = 193.6 Hz, $^2J_{CF}$ = 30.3 Hz, $^2J_{CF}$ = 21.2 Hz), 118.93 (ddd, CF_2, $^1J_{CF}$ = 256.2 Hz, $^1J_{CF}$ = 256 Hz, $^2J_{CF}$ = 24.1 Hz), 164.51–165.3 (m, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −116.49 (dddd, 1F, $^2J_{FF}$ = 271.6 Hz, $^3J_{FH}$ = 18.3 Hz, $^3J_{FF}$ = 12.2 Hz, $^3J_{FH}$ = 4.6 Hz), −121.17 (dddd, 1F, $^2J_{FF}$ = 271.6 Hz, $^3J_{FH}$ = 18.3 Hz, $^3J_{FF}$ = 7.6 Hz, $^3J_{FH}$ = 3.1 Hz), −202.43 (dddd, 1F, CHF, $^2J_{FH}$ = 45.8 Hz, $^3J_{FF}$ = 13.7 Hz, $^3J_{FF}$ = 7.6 Hz, $^4J_{FH}$ = 3.1 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 215 (0.05) $[M]^+$, 208 (0.05), 185 (3), 157 (0.5), 149 (2), 129 (1.5), 107 (3.5), 87 (72), 77 (4), 59 (19), 45 (100).

*Methyl 4-butoxy-2,3,3-trifluorobutanoate (**22**).* ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.96 (t, 3*H*, $^3J_{HF}$ = 6.6 Hz), 1.32–1.48 (m, 4*H*), 3.48–3.60 (m, 2*H*), 3.48 (t, 2*H*, $^3J_{HH}$ = 7 Hz), 3.85 (s, 3*H*), 5.14 (ddd, 1*H*, $^2J_{HF}$ = 46.2 Hz, $^3J_{HF}$ = 12.6 Hz, $^3J_{HF}$ = 7.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.57 (s, CH_3), 18.95 (s, CH_2), 31.39 (s, CH_2), 68.16 (t, O*C*H$_2$CF$_2$, $^2J_{CF}$ = 29.8 Hz), 72.26 (s, CH_2O), 84.8 (ddd, CHF, $^1J_{CF}$ = 193.6 Hz, $^2J_{CF}$ = 32.1 Hz, $^2J_{CF}$ = 29.2 Hz), 117.85 (dt, CF_2, $^1J_{CF}$ = 250.2 Hz, $^2J_{CF}$ = 25.2 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −114.76 (dtt, 1F, $^2J_{FF}$ = 270.1 Hz, $^3J_{FH}$ = 13.7 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 7.6 Hz), −117.16 (dtt, 1F, $^2J_{FF}$ = 270.1 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 13.7 Hz, $^3J_{HF}$ = 10.7 Hz), −205.3 (dtt, 1F, CHF, $^2J_{HF}$ = 47.6 Hz, $^3J_{FF}$ = 10.7 Hz, $^4J_{HF}$ = 3.1 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 215 (0.25) $[M]^+$, 208 (2), 185 (0.5), 171 (0.5), 155 (44), 133 (6), 120 (2.5), 87 (13), 77 (7), 57 (100), 41 (40).

*5.3.6. Reaction of MTFA with dibutyl ether: Products **20** and **26***

Procedure B: MTFA (2.01 g, 14.4 mmol) and dibutyl ether (36.3 g, 279.2 mmol) gave product **20** (2.25 g, 8.33 mmol, 57.9%) and product **26** (718 mg, 1.75 mmol, 24.4%).

*Methyl 4-butoxy-2,3,3-trifluoroheptanoate (**20**). Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 0.84–1.0 (m, 6*H*), 1.25–1.75 (m, 8*H*), 3.44–3.68 (m, 3*H*), 3.84 (s, 3*H*), 5.11 (dt, 1*H*, $^2J_{HF}$ = 46.2 Hz, $^3J_{FF}$ = 10.4 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.76 (s, CH_3), 14.01 (s, CH_3), 18.87 (s, CH_2), 19.15 (s, CH_2), 30.64 (s, CH_2), 32.08 (s, CH_2), 52.38 (s, OCH_3), 72.04 (s, OCH_2), 77.08–78.04 (m, CH), 85.22 (dd, CHF, $^1J_{CF}$ = 191.8 Hz, $^2J_{CF}$ = 30.3 Hz), 118.98 (dt, CF_2, $^1J_{CF}$ = 250.8 Hz, $^1J_{CF}$ = 258.2 Hz, $^2J_{CF}$ = 23.5 Hz), 164.72 (d, C=O, $^2J_{CF}$ = 23.5 Hz) ppm. ^{19}F NMR ($CDCl_3$): diastereoisomer A: δ −112.78 (ddd, 1F, $^2J_{FF}$ = 269.5 Hz, $^3J_{HF}$ = 20.4 Hz, $^3J_{HF}$ = 10.6 Hz), −120.48 (ddd, 1F, $^2J_{FF}$ = 269.4 Hz, $^3J_{HF}$ = 23.5 Hz, $^3J_{HF}$ = 10.2 Hz), −205.51 (dt, 1F, CHF, $^2J_{HF}$ = 46.3 Hz, $^3J_{FF}$ = 10.8 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.84–1.0 (m, 6*H*), 1.25–1.75 (m, 8*H*), 3.44–3.68 (m, 3*H*), 3.86 (s, 3*H*), 5.15 (ddd, 1*H*, $^2J_{HF}$ = 46.2 Hz, $^3J_{FF}$ = 19.8 Hz, $^3J_{FF}$ = 3.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.76 (s, CH_3), 14.01 (s, CH_3), 18.83 (s, CH_2), 19.09 (s, CH_2), 30.06 (s, CH_2), 31.98 (s, CH_2), 52.38 (s, OCH_3), 71.94 (s, OCH_2), 77.08–78.04 (m, CH), 85.13 (ddd, CHF, $^1J_{CF}$ = 191.8 Hz, $^2J_{CF}$ = 60.7 Hz, $^2J_{CF}$ = 30.9 Hz), 118.91 (dt, CF_2, $^1J_{CF}$ = 253.6 Hz, $^2J_{CF}$ = 28.1 Hz), 164.63 (d, C=O, $^2J_{CF}$ = 23.5 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −117 (dddd, 1F, $^2J_{FF}$ = 271.4 Hz, $^3J_{HF}$ = $^3J_{FF}$ = 13.5 Hz, $^3J_{HF}$ = 4.6 Hz), −121.46 (dddd, 1F, $^2J_{FF}$ = 269.2 Hz, $^3J_{HF}$ = 18.3 Hz, $^3J_{HF}$ = 2.3 Hz, $^3J_{FF}$ = 2.2 Hz), −202.32 (ddt, 1F, CHF, $^2J_{HF}$ = 45.8 Hz, $^3J_{FF}$ = 7.7 Hz, $^4J_{HF}$ = 5.7 Hz) ppm. $C_{12}H_{21}F_3O_3$ (270.29): calcd C 53.33, H 7.83; found C 53.06, H 7.55.

Dimethyl 4,4′-oxybis(2,3,3-tri*fluoroheptanoate)* (**26**). *Mixture of diastereoisomers*: ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.79–0.98 (m, 6*H*, CH_3), 1.24–1.79 (m, 8*H*, CH_2CH_2), 3.74–3.83 (m, 6*H*, OCH_3), 3.85–4.07 (m, 2*H*, CH), 4.88–5.36 (m, 2*H*, CHF) ppm. ^{19}F NMR ($CDCl_3$): δ −111.97–(−121.68) (m, 4F, CF_2), −202.25–(−205.26) (m, 2F, CHF) ppm. GC–EIMS: *m*/*z* (rel. int.): 410 (0.1) $[M]^+$, 409 (32) $[M-1]^+$, 337 (15), 318 (4.3), 317 (17), 297 (100), 265 (17), 295 (21), 229 (23.4), 225 (49), 197 (98), 177 (19), 157 (64), 177 (19), 157 (64),

129 (34), 97 (25), 93 (21), 59 (79), 28 (40). $C_{16}H_{24}F_6O_5$ (410.35): calcd C 46.83, H 5.90; found C 47.35, H 6.08.

*5.3.7. Reaction of MTFA with 1-methoxyoctane: Products **21** and **23***

Procedure B: Reaction of MTFA (2.15 g, 15.4 mmol) and 1-methoxyoctane (46.6 g, 303.0 mmol) gave an inseparable mixture of products **21** (86% rel.) and **23** (14% rel.) (2.82 g, 9.59 mmol, 62.3%). $C_{13}H_{23}F_3O_3$ (284.32) (mixture of **21** and **23**): calcd C 54.93, H 8.10; found C 54.37, H 8.10.

*Methyl 4-methoxy-2,3,3-trifluoroundecanoate (**21**). Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 0.82 (t, 3*H*, $^3J_{HH}$ = 7.0), 1.15–1.65 (m, 12*H*), 3.36 (s, 3*H*), 3.41–3.52 (m, 1*H*), 3.67–3.88 (m, 1*H*), 3.77 (s, 3*H*), 5.01 (dt, 1*H*, $^2J_{HF}$ = 46.4 Hz, $^3J_{HF}$ = 10.9 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 14.0 (s, CH_3), 22.6–31.7 (m, 6C, $(CH_2)_6$), 52.8 (s, OCH_3), 59.8 (s, OCH_3), 79.3 (t, CH, $^2J_{CF}$ = 23.5 Hz), 85.5 (dt, CHF, $^1J_{CF}$ = 193.5 Hz, $^2J_{CF}$ = 30.9 Hz), 118.9 (dt, CF_2, $^1J_{CF}$ = 253.6 Hz, $^2J_{CF}$ = 24.6 Hz), 164.9 (d, C=O, $^2J_{CF}$ = 24 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −112.1 (ddt, 1F, $^2J_{FF}$ = 270.1 Hz, $^3J_{FH}$ = 10.7 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 7.6 Hz), −121.3 (ddt, 1F, $^2J_{FF}$ = 271.6 Hz, $^3J_{FH}$ = 15.3 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 9.2 Hz), −205.2 (ddd, 1F, CHF, $^2J_{FH}$ = 47.3 Hz, $^3J_{FF}$ = 10.7 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 285 (0.1) $[M + 1]^+$, 264 (0.3), 205 (1), 185 (7.3), 173 (6.2), 143 (70.6), 141 (7.3), 111 (21), 91 (5.7), 69 (100), 55 (41), 41 (42).

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.82 (t, 3*H*, $^3J_{HH}$ = 7 Hz), 1.15–1.65 (m, 12*H*), 3.40 (s, 3*H*), 3.41–3.52 (m, 1*H*), 3.67–3.88 (m, 1*H*), 3.79 (s, 3*H*), 5.07 (ddd, 1*H*, $^2J_{HF}$ = 46 Hz, $^3J_{HF}$ = 18.9 Hz, $^3J_{HF}$ = 3.1 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 14.0 (s, CH_3), 22.6–31.7 (m, 6 C, $(CH_2)_6$), 52.8 (s, OCH_3), 59.8 (s, OCH_3), 79.3 (dd, CH, $^2J_{CF}$ = 31.5 Hz, $^2J_{CF}$ = 24.1 Hz), 85.1 (ddd, CHF, $^1J_{CF}$ = 191.8 Hz, $^2J_{CF}$ = 36.1 Hz, $^2J_{CF}$ = 29.8 Hz), 117.9 (dt, CF_2, $^1J_{CF}$ = 250.8 Hz, $^2J_{CF}$ = 25.2 Hz), 164.8 (dd, C=O, $^2J_{CF}$ = 23 Hz, $^3J_{CF}$ = 6 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −116.4 (dddd, 1F, $^2J_{FF}$ = 271.6 Hz, $^3J_{FH}$ = 18.3 Hz, $^3J_{FF}$ = 13.7 Hz, $^3J_{FH}$ = 4.6 Hz), −121.1 (dddd, 1F, $^2J_{FF}$ = 271.6 Hz, $^3J_{FH}$ = 16.8 Hz, $^3J_{FF}$ = 7.6 Hz, $^3J_{FH}$ = 3.1 Hz), −202.4 (ddd, 1F, CHF, $^2J_{FH}$ = 45.8 Hz, $^3J_{FF}$ = 13.7 Hz, $^3J_{FF}$ = 7.6 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 285 (0.1) $[M + 1]^+$, 232 (0.3), 205 (1.7), 185 (15), 165 (2.3), 143 (68), 141 (7.3), 111 (19), 91 (5.7), 69 (100), 55 (37), 41 (35).

Methyl 4-o*ctyloxy-2,3,3-trifluorobutanoate* (**23**). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.82 (t, 3*H*, $^3J_{HH}$ = 5 Hz), 1.15–1.65 (m, 12*H*), 3.41–3.52 (m, 1*H*), 3.79 (s), 5.07 (ddd, 1*H*, $^2J_{HF}$ = 46.9 Hz, $^3J_{HF}$ = 13.2 Hz, $^3J_{HF}$ = 8.1 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 14.0 (s, CH_3), 22.6–31.7 (m, 6C, $(CH_2)_6$), 59.8 (s, OCH_3), 68.2 (t, OCH_2CF_2, $^2J_{CF}$ = 29.7 Hz), 72.6 (s, CH_2O), 84.8 (ddd, CHF, $^1J_{CF}$ = 193.5 Hz, $^2J_{CF}$ = 32.1 Hz, $^2J_{CF}$ = 29.7 Hz), 164.4–164.8 (m, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −114.8 (dtt, 1F, $^2J_{FF}$ = 270.8 Hz, $^3J_{FH}$ = 12.2 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 9.2 Hz), −117.4 (dtt, 1F, $^2J_{FF}$ = 270.1 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 21.4 Hz, $^3J_{HF}$ = 12.2 Hz), −205.3 (dt, 1F, CHF, $^2J_{HF}$ = 45.8 Hz, $^3J_{FF}$ = 9.2 Hz) ppm.

*5.3.8. Reaction of MTFA with 2,2-dimethyl-1,3-dioxolane: Product **35***

Procedure B: Reaction of MTFA (2.14 g, 15.3 mmol) and 2,2-dimethyl-1,3-dioxolane (30.8 g, 302.0 mmol) gave product **35** (2.44 g, 10.1 mmol, 65.8%).

*Methyl 3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,3,3-trifluoropropanoate (**35**). Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.36 (s,3*H*), 1.43 (s, 3*H*), 3.86 (s, 3*H*), 4.16 (2x dd, 1*H*, $^3J_{HH}$ = 7.2 Hz, $^2J_{HH}$ = 8.9 Hz), 4.28 (2x dd, 1*H*, $^3J_{HH}$ = 8.8 Hz, $^2J_{HH}$ = 8.9 Hz), 4.52 (ddt, 1*H*, $^3J_{HF}$ = 21 Hz), 5.15 (ddd, 1*H*, $^2J_{HF}$ = 46.5 Hz, $^3J_{HF}$ = 14.2 Hz, $^3J_{HF}$ = 4.7 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −115.4 (dt, 1F, $^2J_{FF}$ = 267 Hz, $^3J_{FF}$ = 13 Hz, $^3J_{FH}$ = 13 Hz), −125.8 (dddd, 1F, $^3J_{FF}$ = 6 Hz, $^3J_{FH}$ = 21.4 Hz, $^3J_{FH}$ = 5.2 Hz), −207.1 (ddd, 1F, $^2J_{HF}$ = 46.5 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.38 (s, 3*H*), 1.47 (s, 3*H*), 3.89 (s, 3*H*), 4.16 (2x dd, 1*H*, $^3J_{HH}$ = 7.2 Hz, $^2J_{HH}$ = 8.9 Hz), 4.28 (2x dd, 1*H*, $^3J_{HH}$ = 8.8 Hz, $^2J_{HH}$ = 8.9 Hz), 4.47 (ddt, 1*H*, $^3J_{HF}$ = 22 Hz), 5.2 (ddd, 1*H*, $^2J_{HF}$ = 45.7 Hz, $^3J_{HF}$ = 22.5 Hz, $^3J_{HF}$ = 2.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −122.1 (ddd, 1F, $^2J_{FF}$ = 266 Hz, $^3J_{FF}$ = 14.1 Hz, $^3J_{FH}$ = 22 Hz), −127.4 (dddd, 1F, $^3J_{FF}$ = 5.1 Hz, $^3J_{FH}$ = 22 Hz, $^3J_{FH}$ = 5.1 Hz), −203.9 (ddd, 1F, $^2J_{HF}$ = 45.7 Hz) ppm.

*5.3.9. Reaction of MTFA with tetrahydrofurane: Product **41***

Procedure A: Reaction of MTFA (1.94 g, 13.9 mmol) and THF (22.3 g, 309.7 mmol) gave product **41** (2.12 g, 10.0 mmol, 71.8%).

Procedure B: Reaction of MTFA (2.02 g, 14.4 mmol) and THF (20.2 g, 280.6 mmol) gave product **41** (2.23 g, 10.5 mmol, 75.3%).

*Methyl 2,3,3-trifluoro-3-(tetrahydrofuran-2-yl)-propanoate (**41**). Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): diastereoisomer A: δ 1.73–2.13 (m, 4*H*), 3.70–3.82 (m, 2*H*), 3.74 (s, 3*H*), 4.11–4.34 (m, 1*H*), 4.92–5.25 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 24.3 (s, CH_2), 24.6 (s, CH_2), 52.5 (s, OCH_3), 69.5 (s, CH_2O), 75.5 (dd, OCH, $^2J_{CF}$ = 33.1 Hz, $^2J_{CF}$ = 23.5 Hz), 85.7 (ddd, CHF, $^1J_{CF}$ = 195.8 Hz, $^2J_{CF}$ = 30.9 Hz, $^2J_{CF}$ = 28.1 Hz), 118.3 (ddt, CF_2, $^1J_{CF}$ = 255.9 Hz, $^1J_{CF}$ = 250.7 Hz, $^2J_{CF}$ = 21.7 Hz), 164.3–164.8 (m, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −115.3 (dt, 1F, $^2J_{FF}$ = 265.6 Hz, $^3J_{FF}$ = 13.6 Hz), −125.1 (ddt, 1F, $^2J_{FF}$ = 265.6 Hz, $^3J_{HF}$ = 23 Hz, $^3J_{FF}$ = 6.3 Hz), −207.4 (ddd, 1F, CF, $^2J_{HF}$ = 46.5 Hz, $^3J_{FF}$ = 12.7 Hz, $^3J_{FF}$ = 7.9 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.73–2.13 (m, 4*H*), 3.70–3.82 (m, 2*H*), 3.73 (s, 3*H*), 4.11–4.34 (m, 1*H*), 4.92–5.25 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 24.3 (s, CH_3), 24.6 (s, CH_3), 52.5 (s, OCH_3), 69.5 (s, CH_2O), 74.3 (dd, OCH, $^2J_{CF}$ = 33.7 Hz, $^2J_{CF}$ = 23.5 Hz), 84.9 (ddd, CHF, $^1J_{CF}$ = 191.2 Hz, $^2J_{CF}$ = 37.8 Hz, $^2J_{CF}$ = 27.5 Hz), 118.4 (dt, CF_2, $^1J_{CF}$ = 253 Hz, $^2J_{CF}$ = 25.7 Hz), 164.3–164.8 (m, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −120 (ddd, 1F, $^2J_{FF}$ = 266.8 Hz, $^3J_{FF}$ = 13.7 Hz, $^3J_{FH}$ = 21.2 Hz), −126.6 (ddd, 1F, $^2J_{FF}$ = 266.8 Hz, $^3J_{HF}$ = 22.9 Hz, $^3J_{FF}$ = 5.4 Hz), −205.0 (dddd, 1F, CF, $^2J_{HF}$ = 40 Hz, $^3J_{FF}$ = 13.7 Hz, $^3J_{FF}$ = 5.7 Hz, $^4J_{HF}$ = 2.6 Hz) ppm.

5.4. Cleavage of the ether bond

5.4.1. General procedure

A mixture of alkanoate (ca. 8 mmol) and dichloromethane (30 mL) was cooled to −50 °C and BBr_3 (ca. 10 mmol) was added dropwise. The reaction mixture was warmed to r.t. during 2 h while stirring until complete conversion of the starting alkenoate (monitored by ^{19}F NMR). The mixture was then very slowly poured into an ice-cold 20% solution of $NaHCO_3$ while vigorously stirring for additional 30 min. The organic layer was separated and washed twice with water (10 mL), dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was purified by column chromatography (20 g silica gel, CH_2Cl_2) or by vacuum distillation (**25**).

*5.4.2. Methyl-2,3,3-trifluoro-4-hydroxypentanoate (**8**)*

Reaction of alkoxyester **16** (10.5 g, 49 mmol) and BBr_3 (16 g, 63.7 mmol) gave product **8** (7.61 g, 40.9 mmol, 83.4%) as a colourless oil, bp 38–41 °C/0.8 mmHg.

Reaction of alkoxyester **17** (1.89 g, 7.8 mmol) with BBr_3 (2.54 g, 10.1 mmol) gave product **8** (0.8 g, 4.27 mmol, 54.8%).

*5.4.3. Methyl-2,3,3-trifluoro-4-hydroxyhexanoate (**9**)*

Reaction of alkoxyester **18** (2.02 g, 8.34 mmol) and BBr_3 (2.72 g, 10.8 mmol) gave product **9** (1.17 g, 5.85 mmol, 70.2%) as a colourless oil.

*5.4.4. Methyl 2,3,3-trifluoro-4-hydroxyheptanoate (**10**)*

Alkoxyester **19** (2 g, 7.4 mmol) and BBr_3 (2.41 g, 9.62 mmol) gave product **10** (1.17 g, 5.46 mmol, 73.8%) as a colourless oil.

Alkoxyester **20** (1.94 g, 7.18 mmol) and BBr_3 (2.34 g, 9.33 mmol) gave product **10** (0.94 g, 4.41 mmol, 61.4%) as a colourless oil.

Diastereoisomer A: ^{1}H NMR ($CDCl_3$): δ 0.94–0.97 (m, 6*H*), 1.28–1.75 (m, 4*H*), 2.48 (bs, OH), 3.83–3.87 (m, 3*H*), 3.88–4.06 (m, 1*H*), 5.26 (ddt, 1*H*, $^2J_{HF}$ = 45.6 Hz, $^3J_{HF}$ = 19.8 Hz, $^3J_{HF}$ = 3.3 Hz) ppm. ^{13}C

NMR ($CDCl_3$): δ 13.62 (s, CH_3), 18.44 (s, CH_2), 30.77 (s, CH_2), 53.07 (s, OCH_3), 69.80 (t, CH, $^2J_{CF}$ = 20.8 Hz), 85.59 (dt, CHF, $^1J_{CF}$ = 195.8 Hz, $^2J_{CF}$ = 30.9 Hz), 118.57 (ddt, CF_2, $^1J_{CF}$ = 251.4 Hz, $^1J_{CF}$ = 252 Hz, $^2J_{CF}$ = 22.3 Hz), 165.6 (d, C=O, $^2J_{CF}$ = 24.7 Hz) ppm. ^{19}F NMR ($CDCl_3$): diastereoisomer A: δ −115.59 (ddt, 1F, $^2J_{FF}$ = 270.4 Hz, $^3J_{HF}$ = 12.5 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 5.2 Hz), −125.18 (ddt, 1F, $^2J_{FF}$ = 266.3 Hz, $^3J_{HF}$ = 18.4 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 7.9 Hz), −206.98 (ddd, 1F, CHF, $^2J_{HF}$ = 46.7 Hz, $^3J_{FF}$ = 14.2 Hz, $^3J_{FF}$ = 4.7 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.94–0.97 (m, 6*H*), 1.28–1.75 (m, 4*H*), 2.67 (bs, OH), 3.83–3.87 (m, 3*H*), 3.88–4.06 (m, 1*H*), 5.16 (dm, 1*H*, $^2J_{HF}$ = 46.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 30.64 (s, CH_3), 30.77 (s, CH_2), 52.98 (s, OCH_3), 69.81 (t, CH, $^2J_{CF}$ = 28 Hz), 84.96 (ddd, CHF, $^1J_{CF}$ = 191.8 Hz, $^2J_{CF}$ = 37.2 Hz, $^2J_{CF}$ = 29.7 Hz), 118.72 (dt, CF_2, $^1J_{CF}$ = 253.6 Hz, $^2J_{CF}$ = 25.7 Hz), 165.26 (d, C=O, $^2J_{CF}$ = 26.3 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −120.45 (ddd, 1F, $^2J_{FF}$ = 267.4 Hz, $^3J_{HF}$ = 19.7 Hz, $^3J_{FF}$ = 13.8 Hz), −126.27 (dddd, 1F, $^2J_{FF}$ = 268.3 Hz, $^3J_{HF}$ = 19.9 Hz, $^3J_{HF}$ = 3.1 Hz, $^3J_{FF}$ = 6.9 Hz), −203.87 (dddd, 1F, CHF, $^2J_{HF}$ = 45.8 Hz, $^3J_{FF}$ = 13.7 Hz, $^4J_{HF}$ = 2 Hz, $^3J_{FF}$ = 5.9 Hz) ppm. $C_8H_{13}F_3O_3$ (214.18): calcd C 44.86, H 6.12; found C 44.78, H 6.10.

5.4.5. Methyl-2,3,3-trifluoro-4-hydroxyundecanoate (**11**)

Reaction of alkoxyester **21** (1.85 mg, 6.51 mmol) with BBr_3 (2.12 g, 8.46 mmol) gave product **11** (1.20 g, 4.43 mmol, 68.1%) as a colourless oil.

5.4.6. Methyl-8-bromo-2,3,3-trifluoro-4-hydroxyhexanoate (**42**)

Reaction of alkoxyester **41** (11.3 g, 53.3 mmol) with BBr_3 (17.3 g, 69.2 mmol) gave product **42** (11.8 g, 40.1 mmol, 75.2%) as a colourless oil. *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.64-2.21 (m, 4*H*), 2.83–3.99 (m, 2x OH), 3.44 (t, 3*H*, $^3J_{HH}$ = 6 Hz), 3.84 (s, 3*H*), 3.89–4.12 (m, 1*H*), 3.89–4.12 (m, 1*H*), 5.17 (ddd, 1*H*, $^2J_{HF}$ = 46.2 Hz, $^3J_{HF}$ = 12.6 Hz, $^3J_{HF}$ = 7.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 27.5 and 28.5 (2 x s, $(CH_2)_2$), 33 (s, $BrCH_2$), 53.2 (s, OCH_3), 69.5 (dd, CH, $^2J_{CF}$ = 29.2 Hz, $^2J_{CF}$ = 25.2 Hz), 85.5 (dt, CHF, $^1J_{CF}$ = 196.4 Hz, $^2J_{CF}$ = 30.3 Hz), 118.4 (ddd, CF_2, $^1J_{CF}$ = 255.9 Hz, $^1J_{CF}$ = 253.1 Hz, $^2J_{CF}$ = 23.5 Hz), 165.1 (d, C=O, $^2J_{CF}$ = 22.9 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −115.3 (ddt, 1F, $^2J_{FF}$ = 266.7 Hz, $^3J_{HF}$ = 12.6 Hz, $^3J_{FF}$ = 5 Hz), −125.1 (ddt, 1F, $^2J_{FF}$ = 266.7 Hz, $^3J_{HF}$ = 18.3 Hz, $^3J_{FF}$ = $^3J_{HF}$ = 8.2 Hz), −207 (ddd, 1F, $^2J_{HF}$ = 46.6 Hz, $^3J_{FF}$ = 12.2 Hz, $^3J_{FF}$ = 9 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.64–2.21 (m, 4*H*), 2.83–3.99 (m, 2x OH), 3.45 (t, 3*H*, $^3J_{HH}$ = 6 Hz), 3.86 (s, 3*H*), 3.89–4.12 (m, 1*H*), 5.18 (ddd, 1*H*, $^2J_{HF}$ = 47.8 Hz, $^3J_{HF}$ = 20.7 Hz, $^3J_{HF}$ = 2.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 27.5 and 28.5 (2 x s; $(CH_2)_2$), 32 (s, $BrCH_2$), 53.1 (s, OCH_3), 69.5 (dd, CH, $^2J_{CF}$ = 29.2 Hz, $^2J_{CF}$ = 25.2 Hz), 85 (ddd, CHF, $^1J_{CF}$ = 192.3 Hz, $^2J_{CF}$ = 36.1 Hz, $^2J_{CF}$ = 29.2 Hz), 118.5 (dt, CF_2, $^1J_{CF}$ = 254.2 Hz, $^2J_{CF}$ = 26.3 Hz), 165.6 (dt, C=O, $^2J_{CF}$ = 22.9 Hz, $^3J_{CF}$ = 3 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.9 (ddd, 1F, $^2J_{FF}$ = 268.6 Hz, $^3J_{HF}$ = 18.8 Hz, $^3J_{FF}$ = 15.4 Hz), −125.7 (ddd, 1F, $^2J_{FF}$ = 268.7 Hz, $^3J_{HF}$ = 19.4 Hz, $^3J_{FF}$ = 3.8 Hz), −203.7 (dddd, 1F, $^2J_{HF}$ = 45.8 Hz, $^3J_{FF}$ = 12.4 Hz, $^3J_{FF}$ = 6 Hz, $^4J_{HF}$ = 1.8 Hz) ppm. $C_8H_{12}F_3O_3Br$ (293.08): calcd C 32.78, H 4.13; found C 32.94, H 4.19.

5.4.7. Methyl 2,3,3-trifluoro-4,5-dihydroxypentanoate (**36**)

A mixture of alkoxyester **35** (2.15 g, 8.88 mmol), methanol (20 mL) and conc. HCl (6 mL) was refluxed for 20 h until complete conversion of **35** was observed (check by ^{19}F-NMR). Methanol was evaporated and the residue was dissolved in diethyl ether (30 mL). The mixture was washed with $NaHCO_3$ (20%, 10 mL). The water layer was extracted with ethyl acetate (10 mL) and the organic layer was dried over $MgSO_4$, filtered and evaporated. Product **36** was isolated by column chromatography (diethyl ether), yield 835 mg (4.14 mmol, 46.5%). *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 3.85 (s, 3*H*), 3.96 (s, OH), 4.09 (s, OH), 4.47 (dd, 1*H*, $^2J_{HH}$ = 15.1 Hz, $^3J_{HH}$ = 2.9 Hz), 4.51 (dd, 1*H*, $^2J_{HH}$ = 14.9 Hz, $^3J_{HH}$ = 3 Hz), 4.65 (dddd, 1*H*, $^3J_{HF}$ = 3 Hz, $^3J_{HF}$ = $^3J_{HH}$ = $^3J_{HH}$ = 6.1 Hz), 5.19 (ddd, 1*H*, $^2J_{HF}$ = 45.8 Hz, $^3J_{HF}$ = 12.2 Hz, $^3J_{HF}$ = 8.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −116.5 (dddd, 1F, $^2J_{FF}$ = 262.7 Hz, $^3J_{HF}$ = $^3J_{HF}$ = $^3J_{FF}$ = 10.1 Hz), −120.4 (ddt, 1F, $^2J_{FF}$ = 262.1 Hz, $^3J_{HF}$ = 10 Hz, $^3J_{FF}$ = 9.9 Hz, $^3J_{HF}$ = 13.8 Hz), −205.7 (ddd, 1F, $^2J_{HF}$ = 45 Hz, $^3J_{FF}$ = 10 Hz, $^3J_{FF}$ = 9.9 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 3.86 (s, 3*H*), 3.96 (s, OH), 4.11 (s, OH), 4.38 (dd, 1*H*, $^2J_{HH}$ = 13.8 Hz, $^3J_{HH}$ = 5 Hz), 4.43 (dd, 1*H*, $^2J_{HH}$ = 14 Hz, $^3J_{HH}$ = 5.2 Hz), 4.77 (dddd, 1*H*, $^3J_{HF}$ = 22.2 Hz, $^3J_{HF}$ = $^3J_{HH}$ = $^3J_{HH}$ = 6 Hz), 5.27 (ddd, 1*H*, $^2J_{HF}$ = 45 Hz, $^3J_{HF}$ = 19.9 Hz, $^3J_{HF}$ = 4.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −118.9 (dddd, 1F, $^2J_{FF}$ = 262.4 Hz, $^3J_{HF}$ = 20.4 Hz, $^3J_{FF}$ = 11.9 Hz, $^3J_{HF}$ = 4.1 Hz), −121.8 (ddt, 1F, $^2J_{FF}$ = 261.8 Hz, $^3J_{HF}$ = 16.2 Hz, $^3J_{FF}$ = 7.9 Hz, $^3J_{HF}$ = 8 Hz), −203.7 (ddd, 1F, $^2J_{HF}$ = 43.9 Hz, $^3J_{FF}$ = 12 Hz, $^3J_{FF}$ = 7.7 Hz) ppm. $C_6H_9F_3O_4$ (202.13): calcd C 35.65, H 4.49; found C 36.69, H 3.83.

5.5. Lactonisation of 4-hydroxyesters

5.5.1. General procedure

Hydroxyester and *p*-toluenesulfonic acid monohydrate (5 mol%) in toluene were refluxed until complete conversion of the hydroxyester (check by ^{19}F NMR). Toluene was evaporated and the residue was purified by column chromatography (silica gel 5 g, CH_2Cl_2) or distilled. The resulting mixtures of dihydrofuranone and furanone were analysed and used in the following dehydrofluorinating step without further purification.

5.5.2. 3,4,4-Trifluoro-5-methyldihydrofuran-2-one (**27**)

A mixture of hydroxyester **8** (7.05 g, 37.9 mmol) and TsOH.H_2O (360 mg, 1.89 mmol) in toluene (40 mL) was refluxed for 10 days to give a mixture of dihydrofuranone **27** and furanone **31** (5.37 g, 34.8 mmol, 92.0%) as a colourless oil. The ratio **27**/**31** was 94/6 and the ratio of diastereoisomers of **27** (A/B) was 65/35, b.p. 36–42 °C/0.8 mmHg.

Product **27**. *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.48 (dd, 3*H*, $^3J_{HH}$ = 6.6 Hz, $^4J_{FH}$ = 1.7 Hz), 4.63–4.76 (m, 1*H*), 5.34 (ddd, 1*H*, $^2J_{FH}$ = 48.4 Hz, $^3J_{FH}$ = 14.8 Hz, $^3J_{FH}$ = 7.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 11.4 (d, CH_3, $^3J_{CF}$ = 6.9 Hz), 75.3 (dd, CH, $^2J_{CF}$ = 29.8 Hz, $^2J_{CF}$ = 25.8 Hz), 82.8 (ddd, CHF, $^1J_{CF}$ = 207.2 Hz, $^2J_{CF}$ = 33.2 Hz, $^2J_{CF}$ = 18.9 Hz), 118.5 (dt, CF_2, $^1J_{CF}$ = 257.6 Hz, $^2J_{CF}$ = 14.9 Hz), 164.7 (dd, C=O, $^2J_{CF}$ = 21.7 Hz, $^3J_{CF}$ = 14.9 Hz) ppm. ^{19}F NMR ($CDCl_3$): diastereoisomer A: δ −122.0 (ddt, 1F, $^2J_{FF}$ = 235.8 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 7.2 Hz), −134.3 (ddt, 1F, $^2J_{FF}$ = 235.7 Hz, $^3J_{FF}$ = $^3J_{FH}$ = 15.7 Hz, $^3J_{FH}$ = 5.8 Hz), −219.4 (dt, 1F, CHF, $^2J_{FH}$ = 48.4 Hz, $^3J_{FF}$ = 7 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 134 (2.5) $[M-20]^+$, 119 (14), 105 (24), 91 (7.4), 88 (5.5), 77 (22), 71 (16), 64 (2.9), 63 (4.5), 51 (8.7), 44 (0.5), 43 (100).

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.48 (d, 3*H*, $^3J_{HH}$ = 6.6 Hz); 4.71–4.86 (m, 1*H*), 5.18 (dt, 1*H*, $^2J_{FH}$ = 48.9 Hz, $^3J_{FH}$ = 8.2 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 14.3 (dd, CH_3, $^3J_{CF}$ = 4.6 Hz, $^3J_{CF}$ = 4 Hz), 78.2 (t, CH, $^2J_{CF}$ = 28.1 Hz), 84 (ddd, CHF, $^1J_{CF}$ = 213 Hz, $^2J_{CF}$ = 27.5 Hz, $^2J_{CF}$ = 18.9 Hz), 118.7 (dt, CF_2, $^1J_{CF}$ = 257.6 Hz, $^2J_{CF}$ = 14.9 Hz), 164.5 (dd, C=O, $^2J_{CF}$ = 21.7 Hz, $^3J_{CF}$ = 9.7 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −121.1 (dm, 1F, $^2J_{FF}$ = 244.8 Hz), −124.8 (dm, 1F, $^2J_{FF}$ = 235.8 Hz), −219.4 (dt, 1F, $^2J_{FH}$ = 53.1 Hz, $^3J_{FF}$ = 13.2 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 134 (7.5) $[M-20]^+$, 119 (22), 105 (14), 91 (4.7), 88 (15.5), 77 (1.7), 71 (1.5), 64 (13), 51 (19), 43 (100).

5.5.3. 5-Ethyl-3,4,4-trifluorodihydrofuran-2-one (**28**)

Refluxing a mixture of hydroxyester **9** (1.12 g, 5.60 mmol) and TsOH.H_2O (51 mg, 0.27 mmol) in toluene (20 mL) for 8 days gave a mixture of dihydrofuranone **28** and furanone **32** (901 mg, 5.33 mmol, 95.9%) as a colourless oil. The ratio **28**/**32** was 95/5 and the ratio of diastereoisomers of **28** was 59/41.

Product **28**. ^{1}H NMR ($CDCl_3$): ^{1}H NMR ($CDCl_3$): δ 1.11 (t, 3*H*, $^{3}J_{HH}$ = 7.1 Hz), 1.12 (t, 3*H*, $^{3}J_{HH}$ = 7.7 Hz), 4.53–4.65 (m, 1*H*), 5.13 (dt, 1*H*, $^{2}J_{FH}$ = 48.9 Hz, $^{3}J_{FH}$ = 8.8 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 9.07 (s, CH_3), 22.28 (dd, 2x CH_2, $^{3}J_{CF}$ = 4 Hz), 82.81 (t, CH, $^{2}J_{CF}$ = 27.5 Hz), 83.13 (ddd, CHF, $^{1}J_{CF}$ = 206.6 Hz, $^{2}J_{CF}$ = 33.7 Hz, $^{2}J_{CF}$ = 33.7 Hz), 118.49 (dt, CF_2, $^{1}J_{CF}$ = 258.8 Hz, $^{2}J_{CF}$ = 16 Hz), 164.55 (ddd, C=O, $^{2}J_{CF}$ = 22.1 Hz, $^{3}J_{CF}$ = 4.8 Hz, $^{3}J_{CF}$ = 3.8 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −118.48 (dddd, 1F, $^{2}J_{FF}$ = 230.1 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 7.5 Hz), 124.13 (dddd, 1F, $^{2}J_{FF}$ = 247.9 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 7.7 Hz), −218.62 (dt, 1F, CHF, $^{2}J_{HF}$ = 48.5 Hz, $^{3}J_{FF}$ = 7 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 169 (19) $[M + 1]^+$, 149 (32), 139 (5.7), 129 (17), 119 (3.2), 111 (10), 103 (13), 95 (90), 91 (34), 82 (100), 77 (34), 73 (28), 64 (12), 57 (64), 51 (18), 47 (11), 41 (9.2), 29 (45).

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.66–2.00 (m, 2*H*), 4.37–4.50 (m, 1*H*), 5.30 (ddd, 1*H*, $^{2}J_{FH}$ = 48.4 Hz, $^{3}J_{FH}$ = 14.3 Hz, $^{3}J_{FH}$ = 8.2 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 8.81 (s, CH_3), 20.24 (d, CH_2, $^{3}J_{CF}$ = 6.3 Hz), 80.03 (dd, CH, $^{2}J_{CF}$ = 28.1 Hz, $^{2}J_{CF}$ = 24.6 Hz), 84.13 (ddd, CHF, $^{1}J_{CF}$ = 213.5 Hz, $^{2}J_{CF}$ = 26.9 Hz, $^{2}J_{CF}$ = 18.9 Hz), 118.79 (dt, CF_2, $^{1}J_{CF}$ = 258.8 Hz, $^{2}J_{CF}$ = 14.9 Hz), 162.4 (d, C=O, $^{2}J_{CF}$ = 21.2 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.12 (ddt, 1F, $^{2}J_{FF}$ = 247.7 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 13.7 Hz, $^{3}J_{FH}$ = 7.9 Hz), −133.45 (ddt, 1F, $^{2}J_{FF}$ = 238 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 15.2 Hz, $^{3}J_{FH}$ = 6 Hz), −216.8 (ddd, 1F, CHF, $^{2}J_{FH}$ = 48.9 Hz, $^{3}J_{FF}$ = 10.7 Hz, $^{3}J_{FF}$ = 6.9 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 169 (37) $[M + 1]^+$, 149 (88), 139 (7.2), 129 (39), 119 (6.5), 109 (11), 103 (23), 95 (100), 91 (39), 82 (94), 77 (37), 64 (11), 57 (60), 53 (13), 41 (85), 29 (17).

5.5.4. 3,4,4-Trifluoro-5-propyldihydrofuran-2-one (**29**)

Refluxing a mixture of hydroxyester **10** (1.14 g, 5.23 mmol) and $TsOH.H_2O$ (49 mg, 0.26 mmol) in toluene (10 mL) for 8 days gave a mixture of dihydrofuranone **29** and furanone **33** (851 mg, 4.68 mmol, 89.4%) as a colourless oil. The ratio **29**/**33** was 91/9 and the ratio of diastereoisomers of **29** was 61/39. *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 0.94–0.8 (m, 3*H*), 1.38–2.02 (m, 4*H*), 4.44–4.69 (m, 1*H*), 5.36 (ddd, 1*H*, $^{2}J_{FH}$ = 48.4 Hz, $^{3}J_{FH}$ = 14.3 Hz, $^{3}J_{FH}$ = 7.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.25 (s, CH_3), 17.72 (s, CH_2), 28.3 (d, CH_2, $^{3}J_{CF}$ = 5.2 Hz), 78.4 (dd, CH, $^{2}J_{CF}$ = 28.6 Hz, $^{2}J_{CF}$ = 22.9 Hz), 84.15 (ddd, CHF, $^{1}J_{CF}$ = 212.4 Hz, $^{2}J_{CF}$ = 26.9 Hz, $^{2}J_{CF}$ = 18.9 Hz), 118.91 (dt, CF_2, $^{1}J_{CF}$ = 257.6 Hz, $^{2}J_{CF}$ = 14.9 Hz), 164.83 (dd, C=O, $^{2}J_{CF}$ = 21.8 Hz, $^{3}J_{CF}$ = 16.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.42 (ddt, 1F, $^{2}J_{FF}$ = 237 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 7.4 Hz), −133.54 (ddt, 1F, $^{2}J_{FF}$ = 237.4 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 15.5 Hz, $^{3}J_{FH}$ = 6.3 Hz), −218.95 (dt, CHF, 1F, $^{2}J_{FF}$ = 48.4 Hz, $^{3}J_{FF}$ = 6.9 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 162 (0.01) $[M - 20]^+$, 154 (0.25), 139 (2.5), 117 (2.5), 111 (6.5), 103 (21), 91 (16), 82 (28), 77 (32), 60 (32), 56 (61), 41 (100).

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.94–0.98 (m, 3*H*), 1.38–2.02 (m, 4*H*), 4.44–4.69 (m, 1*H*), 5.18 (dt, 1*H*, $^{2}J_{FH}$ = 52.8 Hz, $^{3}J_{FH}$ = 10.4 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.12 (s, CH_3), 17.97 (s, CH_2), 30.66 (t, CH_2, $^{3}J_{CF}$ = 2.5 Hz), 81.45 (t, CH, $^{2}J_{CF}$ = 26.3 Hz), 83.05 (ddd, CHF, $^{1}J_{CF}$ = 206.6 Hz, $^{2}J_{CF}$ = 33.2 Hz, $^{2}J_{CF}$ = 18.3 Hz), 118.57 (dt, CF_2, $^{1}J_{CF}$ = 257.6 Hz, $^{2}J_{CF}$ = 16 Hz), 162.74 (dd, C=O, $^{2}J_{CF}$ = 25.2 Hz, $^{3}J_{CF}$ = 13.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.85 (dddd, 1F, $^{2}J_{FF}$ = 247 Hz, $^{3}J_{FF}$ = 15.3 Hz, $^{3}J_{FH}$ = 5.1 Hz, $^{3}J_{FH}$ = 6.6 Hz), −124.42 (ddt, 1F, $^{2}J_{FF}$ = 247 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 16.7 Hz), −217.18 (dt, 1F, CHF, $^{2}J_{FH}$ = 48.8 Hz, $^{3}J_{FF}$ = 7.7 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 154 (0.25), 139 (3), 133 (0.75), 120 (1.0), 111 (6.2), 103 (22), 95 (14), 91 (18), 77 (31), 72 (16), 60 (34), 56 (62), 41 (100).

5.5.5. 3,4,4-Trifluoro-5-heptyldihydrofuran-2-one (**30**)

Refluxing a mixture of hydroxyester **11** (1.05 g, 3.89 mmol) and $TsOH.H_2O$ (37 mg, 0.19 mmol) in toluene (20 mL) for 2 days gave mixture of dihydrofuranone **30** and furanone **34** (858 mg, 3.61 mmol, 92.8%) as a colourless oil. The ratio of **30**/**34** was 92/8 and the ratio of diasteromers of **30** (A/B) was 93/7. *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 0.82–0.98 (m, 3*H*), 1.19–1.88 (m, 12*H*), 4.41–4.59 (m, 1*H*), 5.33 (ddd, 1*H*, $^{2}J_{FH}$ = 48.4 Hz, $^{3}J_{FH}$ = 14.3 Hz, $^{3}J_{FH}$ = 7.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.9 (s, CH_3), 22.5–31.5 (m, $(CH_2)_6$), 78.8 (dd, CH, $^{2}J_{CF}$ = 29.7 Hz, $^{2}J_{CF}$ = 25.2 Hz), 84.1 (ddd, CHF, $^{1}J_{CF}$ = 213.5 Hz, $^{2}J_{CF}$ = 26.9 Hz, $^{2}J_{CF}$ = 18.9 Hz), 118.9 (dt, CF_2, $^{1}J_{CF}$ = 257.6 Hz, $^{2}J_{CF}$ = 14.9 Hz), 164.6 (dd, C=O, $^{2}J_{CF}$ = 22.3 Hz, $^{3}J_{CF}$ = 15.5 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.4 (ddt, 1F, $^{2}J_{FF}$ = 237.3 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 8 Hz), −133.6 (ddt, 1F, $^{2}J_{FF}$ = 237.1 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 15.4 Hz, $^{3}J_{FH}$ = 6.1 Hz), −219.1 (dt, 1F, $^{2}J_{FF}$ = 48.3 Hz, $^{3}J_{FF}$ = 6.7 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 218 (0.3) $[M - 20]^+$, 209 (0.3), 195 (3.3), 176 (3), 169 (3), 149 (3.5), 148 (8.3), 135 (4.5), 111 (6), 97 (7.5), 84 (25), 83 (17), 69 (34), 56 (74), 43 (100).

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.82–0.98 (m, 3*H*), 1.19–1.88 (m, 12*H*), 4.56–4.70 (m, 1*H*), 5.14 (dt, 1*H*, $^{2}J_{FH}$ = 48 Hz, $^{3}J_{FH}$ = 8.2 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.9 (s, CH_3), 22.5–31.5 (m, $(CH_2)_6$), 81.7 (t, CH, $^{2}J_{CF}$ = 26.9 Hz), 83.1 (ddd, CHF, $^{1}J_{CF}$ = 206.6 Hz, $^{2}J_{CF}$ = 33.7 Hz, $^{2}J_{CF}$ = 18.9 Hz) ppm, other signals overlapped with noise. GC–EIMS: *m*/*z* (rel. int.): 218 (0.5) $[M - 20]^+$, 209 (0.5), 195 (2), 189 (2), 176 (4.5), 155 (3), 148 (11), 135 (6.5), 111 (11.5), 109 (7.5), 84 (31), 69 (39), 56 (80.5), 43 (100).

5.5.6. 5-(3-Bromopropyl)-3,4,4-trifluorodihydrofuran-2-one (**43**)

Refluxing a mixture of hydroxyester **42** (10.05 g, 34.3 mmol) and $TsOH.H_2O$ (322 mg, 1.69 mmol) in toluene (50 mL) for 4 days gave a mixture dihydrofuranone **43** and furanone **44** (7.87 mg, 30.2 mmol, 88.1%) as a colourless oil in a ratio of **43**/**44** = 33/77 with the diasteromeric ratio of **43** A/B = 88/12, b.p. = 95–102 °C/0.1 mmHg. *Diastereoisomer A*: ^{1}H NMR ($CDCl_3$): δ 1.78–2.26 (m, 4*H*), 3.47 (s, 2*H*, $^{3}J_{HH}$ = 5), 4.62–4.79 (m, 1*H*), 5.33 (ddd, 1*H*, $^{2}J_{FH}$ = 48.4 Hz, $^{3}J_{FH}$ = 14.3 Hz, $^{3}J_{FH}$ = 7.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 25.4 (s, CH_2), 27.6 (d, CH_2CH, $^{3}J_{CF}$ = 23.4 Hz), 32 (s, $BrCH_2$), 78 (dd, CH, $^{2}J_{CF}$ = 30.3 Hz, $^{2}J_{CF}$ = 24.7 Hz), 83.9 (ddd, CHF, $^{1}J_{CF}$ = 214.1 Hz, $^{2}J_{CF}$ = 27.5 Hz, $^{2}J_{CF}$ = 18.9 Hz), 118.3 (dt, CF_2, $^{1}J_{CF}$ = 258.2 Hz, $^{2}J_{CF}$ = 24.1 Hz), 163.9–164.5 (m, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −119.9 (dm, 1F, $^{1}J_{FF}$ = 236 Hz), −133.2 (ddt, 1F, $^{2}J_{FF}$ = 236.1 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 16.4 Hz, $^{3}J_{FH}$ = 5.5 Hz), −219.5 (d, $^{2}J_{HF}$ = 48.2) ppm. GC–EIMS: *m*/*z* (rel. int.): 262 (12) $[M + 1]^+$, 260 (12) $[M - 1]^+$, 243 (2.4), 223 (2.4), 199 (5.2), 181 (76), 161 (35), 152 (5.2), 141 (27), 121 (20), 106 (26), 97 (58), 77 (73), 71 (35), 65 (17), 55 (33), 39 (100), 29 (31).

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 1.78–2.26 (m, 4*H*), 3.47 (s, 2*H*, $^{3}J_{HH}$ = 5), 4.49–4.62 (m, 1*H*), 5.16 (dt, 1*H*, $^{2}J_{FH}$ = 48.9 Hz, $^{3}J_{FH}$ = 8.8 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 25.3 (s, CH_2), 27.6 (bs, CH_2), 32 (s, $BrCH_2$, 80.8 (t, CH, $^{2}J_{CF}$ = 26.3 Hz), 82.9 (ddd, CHF, $^{1}J_{CF}$ = 206.6 Hz, $^{2}J_{CF}$ = 34.3 Hz, $^{2}J_{CF}$ = 18.3 Hz), 118.3 (dt, CF_2, $^{1}J_{CF}$ = 258.2 Hz, $^{2}J_{CF}$ = 25.8 Hz), 163.9–164.5 (m, C=O) ppm. ^{19}F NMR ($CDCl_3$): δ −119.3 (dm, 1F, $^{1}J_{FF}$ = 261.6 Hz), −124.5 (dddd, 1F, $^{2}J_{FF}$ = 246.2 Hz, $^{3}J_{FF}$ = $^{3}J_{FH}$ = 9.7 Hz), −218.2 (d, 1F, $^{2}J_{HF}$ = 49.2 Hz) ppm.

5.5.7. Lactonisation of methyl 2,3,3-trifluoro-4,5-dihydroxypentanoate (**36**)

Refluxing of dihydroxyester **36** (820 mg, 4.06 mmol) with $TsOH.H_2O$ (39 mg, 0.21 mmol) in toluene (5 mL) gave 543 mg of a mixture of dihydrofuranone **37** (21% rel.), furanone **39** (11% rel.), dihydropyranone **38** (60% rel.) and pyranone **40** (8% rel.). The ratio of diastereoisomers of **37** = 100/0 and ratio of diastereoisomers of **38** = 39/61. The mixture was separated from salts by short column chromatography (silica gel 5 g, diethyl ether). All attempts to separate products failed.

3,4,4-Trifluoro-5-hydroxymethyldihydrofuran-2-one (**37**). ^{19}F NMR ($CDCl_3$): δ −119.7 (dm, 1F, $^{2}J_{FF}$ = 246.4 Hz), −131.9 (dm, 1F, $^{2}J_{FF}$ = 246.8 Hz), −224.3 (dm, 1F, $^{2}J_{HF}$ = 23.6 Hz) ppm. GC–EIMS: *m*/*z* (rel. int.): 171 (1.6) $[M + 1]^+$, 151 (10), 133 (2.4), 120 (98), 105 (1.6), 91 (29), 71 (10), 63 (21), 44 (16), 37 (4), 31 (100).

3,4,4-Trifluoro-5-hydroxytetrahydropyran-2-one (**38**). *Diastereoisomer A*: ^{19}F NMR ($CDCl_3$): δ −115.3 (dm, 1F, $^{2}J_{FF}$ = 244), −123.3–(−124.3) (m, 1F), −217.5 (dm, 1F, $^{2}J_{HF}$ = 48.6 Hz);

Diastereoisomer B: ^{19}F NMR ($CDCl_3$): δ −118.0 (dm, 1F, $^2J_{FF}$ = 241.3 Hz), −123.3–(−124.3) (m, 1F), −218.73 (dm, 1F, $^2J_{HF}$ = 49.3 Hz) ppm. GC–EIMS: *m/z* (rel. int.): 171 (11) $[M + 1]^+$, 151 (4), 140 (7.3), 120 (35), 111 (4), 91 (30), 82 (19), 77 (12), 64 (13), 51 (15), 43 (45), 31 (100).

5.6. Dehydrofluorination

5.6.1. General procedure

A mixture of dihydrofuranone and furanone, diethylether and triethylamine (1.1 mol based on the content of dihydrofuranone) was stirred for 45 min at r.t, which led to complete conversion of dihydrofuranone to the targeted furanones (check by ^{19}F NMR). The mixture was neutralised with an equivalent of conc. HCl. The precipitated salts were filtered off and diethyl ether was evaporated. Crude furanone was purified by column chromatography (silica gel 10 g, CH_2Cl_2) or distilled under vacuum.

5.6.2. 3,4-Difluoro-5-methylfuran-2(5H)-one (**31**)

Reaction of a mixture of dihydrofuranone **27** and furanone **31** (5.20 g, 33.8 mmol) with triethylamine (3.76 g, 37.1 mmol) in diethyl ether (30 mL) afforded furanone **31** (4.77 g, 35.6 mmol, 91.7%), b.p. 40–41 °C/2 mmHg. ^{1}H NMR ($CDCl_3$): δ 1.59 (dd, 3*H*, $^3J_{HH}$ = 6.6 Hz, $^4J_{HF}$ = 1.1 Hz), 5.0 (ddq, 1*H*, $^3J_{HH}$ = 6.6 Hz, $^3J_{HF}$ = 5.5 Hz, $^4J_{HF}$ = 3.3 Hz) ppm. ^{13}C NMR ($CDCl_3$) δ 16.9 (s, CH_3), 70.1 (dd, CH, $^2J_{CF}$ = 19.8 Hz, $^3J_{CF}$ = 2.4 Hz), 127.4 (d, CF, $^1J_{CF}$ = 271.6 Hz), 157.6 (d, CF, $^1J_{CF}$ = 297.2 Hz), 162.5 (dd, C=O, $^2J_{CF}$ = 24.9 Hz, $^3J_{CF}$ = 12.8 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −126.4 (s, 1F), −164.7 (s, 1F) ppm. GC–EIMS: *m/z* (rel. int.): 134 (4.1) $[M]^+$, 119 (34), 105 (3.7), 91 (12), 88 (0.5), 77 (1.8), 71 (3.7), 64 (0.9), 63 (14), 51 (3.7), 44 (2.3), 43 (100). $C_5H_4F_2O_2$ (134.08): calcd C 44.79, H 3.01; found C 44.49, H 3.06.

5.6.3. 5-Ethyl-3,4-difluorofuran-2(5H)-one (**32**)

Reaction of a mixture of dihydrofuranone **28** and furanone **32** (852 mg, 5.07 mmol) with triethylamine (341 mg, 3.37 mmol) in diethyl ether (10 mL) afforded furanone **32** (721 g, 4.87 mmol, 96.0%). ^{1}H NMR ($CDCl_3$): δ 1.01 (t, 3*H*, $^3J_{HH}$ = 7.7 Hz), 1.77 (pseudo sept, 1*H*, $^3J_{HH}$ = 7.1 Hz), 1.96–2.1 (m, 1*H*), 4.9 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 7.85 (s, CH_3), 24.35 (s, CH_2), 74.37 (d, CH, $^2J_{CF}$ = 18.9 Hz,), 127.9 (d, CF, $^1J_{CF}$ = 273.9 Hz), 156.38 (d, CF, $^1J_{CF}$ = 290.3 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −126.16 (s, 1F), −163.67 (s, 1F) ppm. GC–EIMS: *m/z* (rel. int.): 149 (24.2) $[M + 1]^+$, 131 (2.4), 119 (100), 103 (3.2), 91 (23), 83 (4), 75 (4.8), 71 (10), 63 (10), 57 (44), 51 (6), 43 (48), 39 (9), 29 (22). $C_6H_6F_2O_2$ (148.11): calcd C 48.66, H 4.08; found C 48.60, H 4.12.

5.6.4. 3,4-Difluoro-5-propylfuran-2(5H)-one (**33**)

Reaction of a mixture of dihydrofuranone **29** and furanone **33** (805 mg, 4.42 mmol) with triethylamine (495 mg, 4.89 mmol) in diethyl ether (10 mL) afforded furanone **33** (637 mg, 3.93 mmol, 88.8%). ^{1}H NMR ($CDCl_3$): δ 0.94 (t, 3*H*, $^3J_{HH}$ = 8.1 Hz), 1.40–1.54 (m, 2*H*), 1.61–1.73 (m, 1*H*), 1.87–1.98 (m, 1*H*), 4.92 (ddt, 1*H*, $^3J_{HF}$ = 11 Hz, $^3J_{HH}$ = 4 Hz, $^4J_{HF}$ = 1.6 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 13.29 (s, CH_3), 17.16 (s, CH_2), 32.9 (s, CH_2), 73.35 (d, CH, $^2J_{CF}$ = 18.9 Hz), 127.58 (d, CF, $^1J_{CF}$ = 271.4 Hz), 156.76 (d, CF, $^1J_{CF}$ = 296.6 Hz), 162.47 (dd, C=O, $^2J_{CF}$ = 23.9 Hz, $^3J_{CF}$ = 11.9 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −124.53 (d, 1F, $^3J_{FF}$ = 4.4 Hz), −162.19 (d, 1F, $^3J_{FF}$ = 4.4 Hz) ppm. GC–EIMS: *m/z* (rel. int.): 162 (1.5) $[M]^+$, 144 (0.5), 134 (1), 133 (14), 120 (22), 106 (0.5), 97 (1.5), 91 (7.5), 85 (1), 71 (19), 63 (11), 57 (4), 43 (100). $C_7H_8F_2O_2Br$ (242.04): calcd C 51.86, H 4.97; found C 51.79, H 5.05.

5.6.5. 3,4-Difluoro-5-heptylfuran-2(5H)-one (**34**)

Reaction of a mixture of dihydrofuranone **30** and furanone **34** (786 mg, 3.30 mmol) with triethylamine (365 mg, 3.61 mmol) in diethyl ether (10 mL) afforded furanone **34** (679 g, 3.08 mmol, 93.4%). ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3*H*, $^3J_{HH}$ = 6.6 Hz), 1.14–1.62 (m, 10*H*), 1.63–1.78 (m, 1*H*), 1.92–2.07 (m, 1*H*), 5.49 (ddt, 1*H*, $^3J_{HH}$ = 7.5 Hz, $^3J_{HF}$ = 5 Hz, $^4J_{HF}$ = 3.9 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 14 (s, CH_3), 22.5–31.6 (m, $(CH_2)_6$), 73.6 (d, CH, $^2J_{CF}$ = 19.5 Hz), 127.7 (d, CF, $^1J_{CF}$ = 272.5 Hz), 156.8 (d, CF, $^1J_{CF}$ = 296.6 Hz), 162.6 (dd, C O, $^2J_{CF}$ = 25.2 Hz, $^3J_{CF}$ = 13.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −125.7 (dd, 1F, $^3J_{FF}$ = $^3J_{FH}$ = 3.8 Hz), −164 (d, 1F, $^3J_{FF}$ = 3.8 Hz) ppm. GC–EIMS: *m/z* (rel. int.): 203 (0.5) $[M - 15]^+$, 189 (1.5) $[M - 19]^+$, 183 (1), 169 (6), 155 (8), 144 (6), 133 (45), 119 (32), 111 (9.5), 97 (15), 97 (15), 82 (17), 69 (12), 57 (81), 55 (54). $C_{11}H_{16}F_2O_2$ (218.24): calcd C 60.54, H 7.39; found C 60.47, H 7.48.

5.6.6. 5-(3-Bromopropyl)-3,4-difluorofuran-2(5H)-one (**44**)

Reaction of a mixture of dihydrofuranone **43** and furanone **44** (7.21 g, 9.12 mmol) with triethylamine (1.12 g, 10.9 mmol) in diethyl ether (50 mL) afforded furanone **44** (6.78 g, 28.1 mmol, 88.3%), b.p. 100–102 °C/0.08 mmHg. ^{1}H NMR ($CDCl_3$): δ 1.76–2.28 (m, 4*H*), 3.44 (t, 2*H*, $^3J_{HH}$ = 6 Hz), 4.9–5.01 (m, 1*H*) ppm. ^{13}C NMR ($CDCl_3$): δ 27 (d, $BrCH_2CH_2$, $^4J_{CF}$ = 6.2 Hz), 29.7 (s, $BrCH_2$), 32 (d, CH_2CH, $^3J_{CF}$ = 7.4 Hz), 72.8 (d, CH, $^2J_{CF}$ = 18.8 Hz), 127.8 (d, CF, $^1J_{CF}$ = 270.9 Hz), 156.3 (d, CF, $^1J_{CF}$ = 294.8 Hz), 162.1 (dd, C=O, $^2J_{CF}$ = 25.1 Hz, $^3J_{CF}$ = 13.1 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −125.8 (dd, 1F, $^3J_{FF}$ = $^3J_{FH}$ = 3.2 Hz), −163.1 (dd, 1F, $^3J_{FF}$ = 5.2 Hz, $^3J_{FH}$ = 3.2 Hz) ppm. GC–EIMS: *m/z* (rel. int.): 242 (3.8) $[M + 1]^+$, 240 (4.4) $[M - 1]^+$, 213 (1.9), 211 (1.9), 186 (3.2), 184 (2.5), 162 (1.3), 160 (16), 151 (24), 149 (26), 133 (83), 132 (77), 120 (13), 119 (100), 117 (10), 106 (22), 97 (7), 95 (9), 91 (39), 90 (13), 75 (10), 71 (9), 63 (30), 57 (11), 51 (7.6), 41 (42). $C_7H_7F_2O_2Br$ (241.03): calcd C 34.88, H 2.93; found C 35.11, H 2.93.

5.6.7. 3,4-Difluoro-5-(3-iodopropyl)furan-2(5H)-one (**45**)

A mixture of furanone **44** (2.31 g, 9.59 mmol), dry NaI (2.88 g, 19.2 mmol) and acetone (50 mL) was reacted at r.t. under inert atmosphere until complete conversion of **44** (check by ^{19}F NMR). Precipitate was filtered off, the solvent evaporated (rotary evaporator) and the residue purified by column chromatography (silica gel 10 g, CH_2Cl_2) to afford **45** (2.62 g, 94.8%) as slightly yellow oil.

^{1}H NMR ($CDCl_3$): δ 1.77–2.22 (m, 4*H*), 3.22 (t, 3*H*, $^3J_{HH}$ = 6.6 Hz), 4.95 (ddt, 1*H*, $^3J_{HF}$ = 8.2 Hz, $^3J_{HF}$ = 5.2 Hz, $^4J_{HF}$ = 3.6 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 27.5 (s), 31.7 (bs), 72.4 (d, $^2J_{CF}$ = 18.6 Hz), 127.3 (d, $^1J_{CF}$ = 269.9 Hz), 155.95 (d, $^1J_{CF}$ = 296 Hz), 161.8 (dd, $^2J_{CF}$ = 24.9 Hz, $^3J_{CF}$ = 12.9 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −125.9 (s, 1F), −162.95 (s, 1F) ppm. GC–EIMS: *m/z* (rel. int.): 289 (4.8) $[M + 1]^+$, 271 (0.4), 243 (2.4), 197 (0.8), 161 (100), 141 (6.5), 119 (92), 85 (21), 77 (8.1), 57 (7.7), 39 (29), 31 (2.8). $C_7H_7F_2IO_2$ (288.03): calcd C 29.19, H 2.45; found C 29.41, H 2.63.

5.6.8. Dehydrofluorination of mixture of dihydrofuranone **37** and dihydropyranone **38**

Reaction of a mixture (508 mg, 2.99 mmol) of dihydrofuranone **37** (21%), furanone **39** (8%), dihydropyranone **38** (60%) and pyranone **40** (11%) with triethylamine (335 mg, 3.31 mmol) in diethyl ether (15 mL) afforded a mixture of furanone **39** and pyranone **40** (458 mg, 3.05 mmol, 90.1%) in a ratio of **39**/**40** = 33/67.

*3,4-Difluoro-5-(hydroxymethyl)furan-2(5H)-one (**39**). IR*: 1058 (primary OH), 1739, 1801, 3443 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.12 (d, 1*H*, $^2J_{HH}$ = 13 Hz), 4.48 (dd, 1*H*, $^2J_{HH}$ = 12.8 Hz, $^3J_{HH}$ = 3.2 Hz), 5.0 (dd, 1*H*, $^3J_{HH}$ = 4.8 Hz, $^3J_{HH}$ = 3 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −126.4 (dd, 1F, $^3J_{FF}$ = 3.7 Hz, $^3J_{HF}$ = 3.6 Hz); −161.8 (d, 1F, $^3J_{FF}$ = 3.7 Hz) ppm.

*3,4-Difluoro-5-hydroxy-5,6-dihydropyran-2-one (**40**). IR*: 1191 (secondary OH), 1765, 3443 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.89 (dd, 1*H*, $^2J_{HH}$ = 13 Hz, $^3J_{HH}$ = 3 Hz); 4.43 (dd, 1*H*, $^2J_{HH}$ = 12.8 Hz,

$^3J_{HH}$ = 4.2 Hz), 4.66 (ddd, 1*H*, $^3J_{HH}$ = 4.2 Hz, $^3J_{HH}$ = 3 Hz, $^3J_{HF}$ = 3.6 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −123.4 (dd, 1F, $^3J_{FF}$ = 9.8 Hz, $^3J_{HF}$ = 4.6 Hz), −155.1 (d, 1F, $^3J_{FF}$ = 3.7 Hz) ppm.

$C_5H_4F_2O_3$ (150.08): calcd C 40.01, H 2.69; found C 40.77, H 3.72.

5.7. Synthetic sequence to 3-chloro-3-fluoro-5-hexyldihydrofuran-2-one (**49**) and attempted 3-chloro-3-fluoro-5-methoxydihydrofuran-2-one (**53**)

5.7.1. Methyl 2-bromo-2-chloro-2-fluoroacetate (**46**)

For experimental details see Supplementary data.

5.7.2. Methyl 4-bromo-2-chloro-2-fluorodecanoate (**47**)

The reaction was carried out under argon in double-necked flask (25 mL) equipped with low temperature reflux condenser. A mixture of dibenzoyl peroxide (0.5 g, 2 mmol), halogenoacetate **46** (25.2 g, 0.123 mol) and oct-1-ene (5 g, 41 mmol) was cooled to −20 °C and deoxygenated with argon for 30 min. The mixture was then heated to 90 °C for 3.5 h while stirring. Unreacted components were then distilled off (bath 80 °C, 40 Pa), the residue was dissolved in dichloromethane (100 mL), filtered through silica gel and chromatographed ($CHCl_3$–petroleum ether 1:10) to afford separated diastereoisomers of **47** in total yield of 6.57 g (51%).

Diastereoisomer A: ^{1}H NMR ($CDCl_3$): δ 0.85 (t, CH_3, $^3J_{HH}$ = 6 Hz), 1.8 (m, 5-CH_2), 1.25 (m, 8*H*), 2.88 (ddd, H_a of 3-CH_2, $^2J_{HH}$ = 16 Hz, $^3J_{HH}$ = 7 Hz, $^3J_{HF}$ = 19 Hz), 3.05 (ddd, H_b of 3-CH_2, $^2J_{HH}$ = 16 Hz, $^3J_{HH}$ = 6 Hz, $^3J_{HF}$ = 19 Hz), 3.9 (s, OCH_3), 4.25 (m, CHBr) ppm. ^{19}F NMR ($CDCl_3$): δ −114.4 (t, CClF, $^3J_{HF}$ = 19 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.9 (t, CH_3, $^3J_{HH}$ = 6 Hz), 1.85 (m, 5-CH_2), 1.25 (m, 8*H*), 2.88 (ddd, H_a of 3-CH_2, $^2J_{HH}$ = 16 Hz, *J* = 4 Hz, *J* = 11 Hz), 3.06 (ddd, H_b of 3-CH_2, $^2J_{HH}$ = 16 Hz, *J* = 9 Hz, *J* = 27 Hz), 3.9 (s, OCH_3), 4.15 (m, CHBr) ppm. ^{19}F NMR ($CDCl_3$): δ −119.9 (m, CClF) ppm. $C_{11}H_{19}BrClFO_2$ (317.62) (mixture of diastereoisomers): calcd C 41.60, H 6.03; found C 41.78, H 6.22.

5.7.3. Sodium 4-bromo-2-chloro-2-fluorodecanoate (**48**)

A mixture of halogenodecanoate **47** (0.5 g, 1.57 mmol), sodium hydrogencarbonate (0.2 g, 2 mmol), methanol (4 mL) and water (3 mL) was refluxed for 12 h. Evaporation of solvents and drying under vacuum afforded the salt **48** (532 mg), which was used in cyclisation attempts.

^{1}H NMR (D_2O): δ 0.99 (t, CH_3, $^3J_{HH}$ = 7 Hz), 1.5 (m, 10*H*), 2.55 (m, 3-CH_2), 4.04 (m, CHBr) ppm. ^{19}F NMR (D_2O): diastereoisomer A: δ −118.7 (dd, CClF, $^3J_{HF}$ = 18 Hz, $^3J_{HF}$ = 27 Hz); diastereoisomer B: δ −109.4 (t, CClF, $^3J_{HF}$ = 17 Hz) ppm.

5.7.4. 2-Chloro-2-fluoro-4-hexyltetrahydrofuran-2-one (**49**)

Procedure A: A mixture of methyl halogenodecanoate **47** (4.29 g, 13.5 mmol), conc. hydrochloric acid (0.5 mL), methanol (25 mL) and water (2 mL) was refluxed for 80 h. The mixture was then neutralised with conc. solution of $NaHCO_3$ and the raw product **49** extracted with CFC-113. After evaporation of the solvent, pure **49** was isolated by column chromatography (toluene) in yield of 2.18 g (74%).

Procedure B: Sodium halogenodecanoate **48** (1 g, 3.07 mmol) was dispersed in dimethylsulfoxide (5 mL) and heated to 80 °C for 3 h while stirring. The mixture was then diluted with water and extracted with Freon 113. After evaporation of the solvent, pure **49** was isolated by column chromatography (toluene) in yield 0.511 g (66%).

Diastereoisomer A: ^{1}H NMR ($CDCl_3$): δ 0.88 (t, CH_3, $^3J_{HH}$ = 7 Hz), 1.75 (m, 5 x CH_2), 2.52 (ddd, H_a of 3-CH_2, $^2J_{HH}$ = 15 Hz, $^3J_{HH}$ = 7 Hz, $^3J_{HF}$ = 22 Hz), 3.09 (ddd, H_b of 3-CH_2, $^2J_{HH}$ = 15 Hz, $^3J_{HH}$ = 7 Hz, $^3J_{HF}$ = 19 Hz), 4.64 (ddt, CH, $^3J_{HH}$ = 6 Hz, $^3J_{HH}$ = 7 Hz, $^3J_{HH}$ = 8 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −114.4 (dd, CClF, $^3J_{HF}$ = 20 Hz, $^3J_{HF}$ = 22 Hz) ppm.

Diastereoisomer B: ^{1}H NMR ($CDCl_3$): δ 0.88 (t, CH_3, $^3J_{HH}$ = 7 Hz), 1.75 (m, 5 × CH_2), 2.39 (ddd, H_a of 3-CH_2, $^2J_{HH}$ = 14 Hz, $^3J_{HH}$ = 10 Hz, $^3J_{HF}$ = 15 Hz), 2.96 (dd, H_b of 3-CH_2, $^2J_{HH}$ = 14 Hz, $^3J_{HH}$ = 5 Hz), 4.53 (ddt, CH, $^3J_{HH}$ = 5 Hz, $^3J_{HH}$ = 8 Hz, $^3J_{HH}$ = 10 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ −119.2 (d, CClF, $^3J_{HF}$ = 15 Hz) ppm. $C_{10}H_{16}ClFO_2$ (222.69) (mixture of diastereoisomers): calcd C 53.94, H 7.24; found C 53.87, H 7.37.

5.7.5. Methyl 4-acetoxy-4-bromo-2-chloro-2-fluorobutanoate (**50**)

The reaction was carried out in the apparatus as for **47**. Dibenzoyl peroxide (0.2 g, 0.8 mmol) was dispersed in vinyl acetate (1.5 g, 17.4 mmol). Halogenoacetate **46** (10.73 g, 52.2 mmol) in flask was cooled to −20 °C and deoxygenated with argon for 30 min. Then was heated to 90 °C and the dispersion was added dropwise through septum while stirring, the mixture was then heated to 80 °C for 1 h. Volatile components were removed under reduced pressure (40 Pa, bath 80 °C) and the residue was chromatographed (toluene) to afford **50**, yield 3.15 g (61%). ^{1}H NMR (D_2O): δ 2.08 (t, CH_3), 3.4 (m, CH_2), 3.96 (s, OCH_3), 6.8 (m, CHBr) ppm. *Diastereoisomer A*: ^{19}F NMR (D_2O): δ −120.4 (dd, CClF, $^3J_{HF}$ = 13 Hz, $^3J_{HF}$ = 22 Hz) ppm.

Diastereoisomer B: ^{19}F NMR (D_2O): δ −116.7 (dd, CClF, $^3J_{HF}$ = 14 Hz, $^3J_{HF}$ = 20 Hz) ppm.

$C_6H_9BrClFO_2$ (247.49) (mixture of diastereoisomers): calcd C 29.12, H 3.67; found: C 28.97, H 3.84.

5.7.6. Methyl 2-chloro-2-fluoro-4,4-dimethoxybutanoate (**51**)

Under dry conditions, a mixture of butanoate **50** (3.55 g, 12.2 mmol) and methanol (1.5 g, 46.9 mmol) was stirred for 12 h under RT. The product **51** was extracted in CFC-113 and the extract neutralised with solid $NaHCO_3$. After filtration and evaporation of CFC, the product **51** was obtained by distillation in minimised apparatus, bp 87–88 °C/67 Pa, yield 1.21 g (46.8%). ^{1}H NMR (D_2O): δ 2.61 (ddd, H_a, CH_2, $^2J_{HH}$ = 14.5 Hz, $^3J_{HH}$ = 7.9 Hz, $^3J_{HF}$ = 29.6 Hz), 2.79 (ddd, H_b, CH_2, $^2J_{HH}$ = 14.5 Hz, $^3J_{HH}$ = 3.6 Hz, $^3J_{HF}$ = 8.9 Hz), 3.3 (s, OCH_3), 3.32 (s, OCH_3), 4.57 (dd, CH, $^3J_{HH}$ = 3.5 Hz, $^3J_{HH}$ = 8.9 Hz) ppm. ^{19}F NMR (D_2O): δ −117.6 (dd, CClF, *J* = 12.3 Hz, *J* = 25.8 Hz) ppm.

$C_7H_{12}ClFO_4$ (214.62): C 39.17, H 5.64, Cl 17.52, F 9.26; found C 39.04, H 5.26, Cl 18.53; F 9.76.

5.7.7. 2-Chloro-2-fluoro-4,4-dimethoxybutanoic acid (**52**) and its attempted cyclisation

Water solution of sodium hydroxide (0.151 M) was added dropwise to a mixture of dimethoxy-butanoate **51** (0.5 g, 1.72 mmol), methanol (5 mL), solution of sodium hydroxide (0.151 M, 10 mL) and drop of phenolphtaleine at 50 °C while stirring until pink coloration of the mixture. The solution was evaporated and the residue was dried in vacuum to obtain 0.521 g (100%) of sodium 2-chloro-2-fluoro-4,4-dimethoxybutanoate. ^{19}F NMR (D_2O): δ −107.9 (t, CClF, $^3J_{HF}$ = 20 Hz) ppm.

In a dropping funnel, water solution (1 mL) of sodium butanoate **51** (0.3 g, 1.35 mmol) was mixed with diethyl ether (10 mL) and hydrochloric acid was added to pH = 1. Organic layer was evaporated, the residue appeared to be a mixture of products (^{19}F NMR, GC, CC) and the separation of the expected product **53** was unsuccessful.

A mixture of sodium butanoate **51**, *p*-toluenesulfonic acid (110 mol% of **51**) and toluene was refluxed. Analysis of the reaction progress (^{19}F NMR, GC) identified formation of a mixture of products. Separation of the expected product **53** was unsuccessful.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2014.03.009.

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