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High regioselectivity in the alternative cleavage of terminal epoxides with different sources of nucleophilic fluoride

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Abstract

The ring-opening of epoxides derived from esters of 10-undecenoic acid using Olah's reagent yields predominantly the 10-fluoro-11-hydroxy derivatives, while the other regio isomers are obtained predominantly with mixtures of triethylamine trishydrogen fluoride and other amines. The best yields and best regioselectivity for the 11-fluoro-10-hydroxy compound, however, are found in conversion of the epoxide with potassium hydrogen difluoride/18-crown-6 in DMF.

Keywords: Terminal epoxides; Hydrofluorination; Olah's reagent; Triethylamine trishydrogen fluoride; Potassium hydrogen fluoride; Regioselectivity; NMR spectroscopy; Mass spectrometry

1. Introduction

Examination of the mechanism and selectivity of the conversion of terminal epoxides into the corresponding fluorohydrins has recently gained new interest from various authors [1,2]. The regioselective cleavage of terminal epoxides by nucleophilic fluoride is a major problem in the preparation of β-fluorinated alcohols, which are important precursors in the synthesis of the monofluorinated analogues of natural compounds. This increasing concern is mainly because partial substitution of hydrogen with fluorine leads to an interesting change in the chemical and biological properties of natural compounds [3]. However, the choice of fluorinating reagent, which should be both reactive and selective is quite difficult.

Systematic investigations into the regioselectivity and mechanism of this oxirane cleavage on the basis of different sources of nucleophilic fluoride are still very rare [1,4,5]. Our own investigations have concentrated on the monofluorination of the terminal epoxides of fatty acids in an attempt to develop a simple and effective conversion of oxirane derivatives into the regioisomeric fluorohydrins on the basis of the esters of unsaturated fatty acids. ω-Fluorinated fatty acids are natural compounds themselves [6], but in addition the regioisomeric fluorohydrins of terminally unsaturated fatty acids are important intermediates in the synthesis of fluorinated analogues of a large variety of different bioactive compounds.

All recent results [1] regarding the cleavage of oxirane by fluoride suggest a concurrence of an S_N1-type substitution by fluoride ion (following protonation of the epoxide) and an S_N2-type substitution by fluoride ion as a result of direct attack from the back-side of the oxirane (Scheme 1). Whether a free carbenium ion intermediate is involved in the S_N1-type substitution depends very much on the nature of the oxirane [1].

Herein we report our results on the formation of the desired regio isomers of the fluorohydrin of ethyl 10,11-epoxy-undecanoate (**1**) which served as the 'test' oxirane for our investigations. This can be easily prepared via a simple two-step procedure from undec-10-enoic acid by esterification with ethanol and subsequent epoxidation with *m*-chloroperoxybenzoic acid using standard procedures. As fluoride donors we used Olah's reagent (Py·9HF), triethylamine trishydrogen fluoride ($Et_3N \cdot 3HF$) and potassium hydrogen difluoride (KHF_2).

2. Results

In an initial investigation, we tried Olah's reagent (Py·9HF) with **1**. The reagent Py·9HF is one of the

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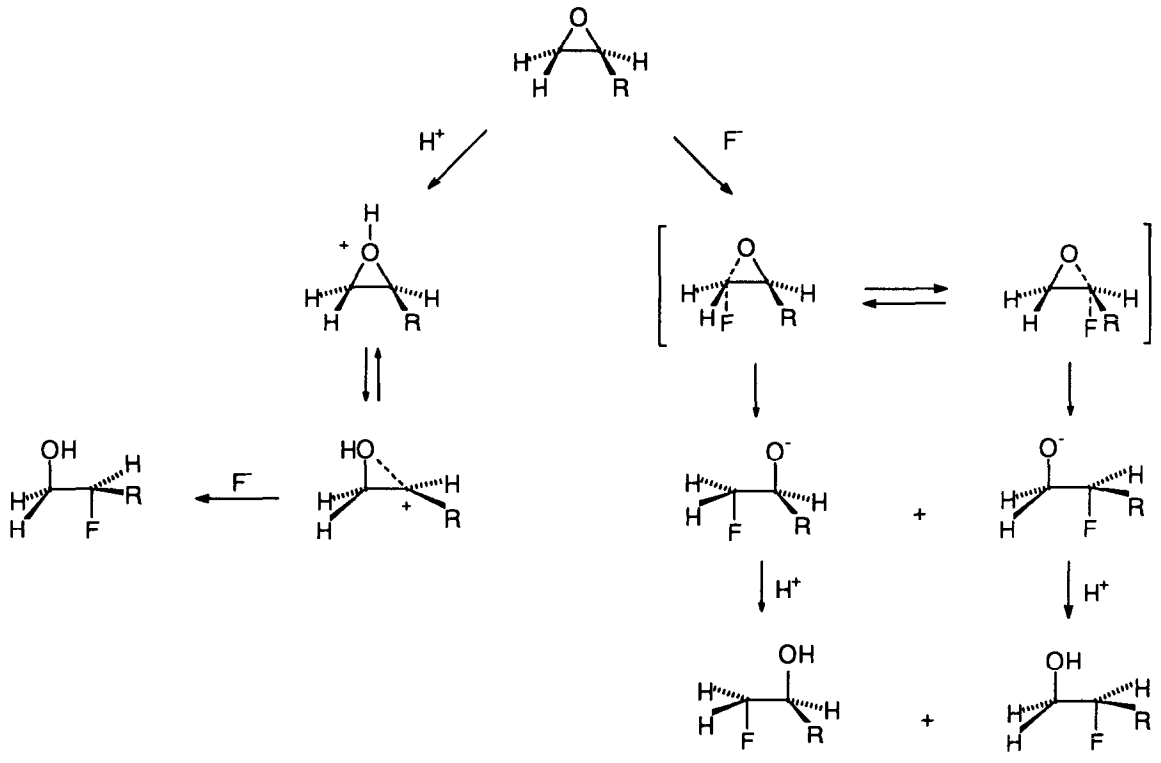
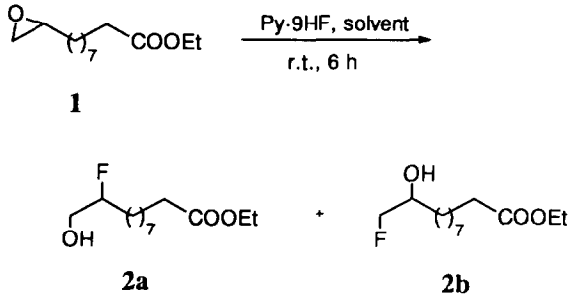


Scheme 1. Proposed mechanism for the hydrofluorination of terminal epoxides.

most acidic fluorinating reagents after anhydrous hydrogen fluoride. Solvents of different polarity were first used to explore their influence on the stability of the intermediates and hence on the selectivity of the reaction; secondly the nucleophilicity of fluoride was enhanced by the addition of pyridine (deprotonation of hydrogen fluoride) in order to force the system towards the opposite regio isomer **2b** (Scheme 2). The results obtained are documented in Tables 1 and 2.

A choice of quite non-polar solvents (entries 1 and 2) led neither to a drop in selectivity nor in yield. Hence, there is no indication for a free carbenium ion, which obviously corresponds with the results of Schlosser et al. [4c] and Umezawa et al. [1]. In cyclohexane (entry 1), Olah's reagent forms a two-phase system without any decrease in reactivity, which may be an indication of a reaction occurring within the very associated struc-



Scheme 2. Hydrofluorination of ethyl 10,11-epoxy-undecanoate (**1**) with py·9HF.

Table 1
Regioisomeric excess using Olah's reagent in different solvents

Entry No.	Solvent	HF (wt.%)	2a/2b (GLC)	Conversion (GLC) (%)	Yield (a+b) (%)
1	cyclohexane	65	92:8	>99	81
2	toluene	65	91:9	>99	78
3	dichloromethane	65	92:8	>99	83
4	acetone	65	–[a]	–[a]	–[a]

[a]Acetone adducts were formed.

Table 2
Regioisomeric excess using different Olah's reagent/pyridine mixtures

Entry No.	Solvent	HF (wt.%)	2a/2b (GLC)	Conversion (GLC) (%)	Yield (GLC) (%)
3	dichloromethane	65	92:8	>99	83
5	dichloromethane	60	83:17	>98	79
6	dichloromethane	50	74:26	>98	74
7	dichloromethane	40	55:45	≈5	not isolated
8	dichloromethane	30	≈50:50	≈2	not isolated

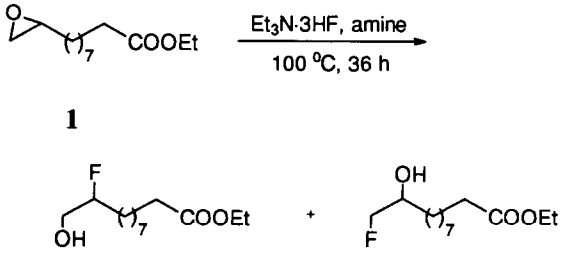
ture of the pyridine/HF phase [7]. Nevertheless, in all cases the favoured regio isomer is derived from the most stable cation (S_N1-type substitution by fluoride).

The addition of pyridine (entries 5–8), and thus the partial 'deprotonation' of Olah's reagent, results in a

shift of the regioisomeric ratio towards the opposite regio isomer, which certainly does not derive from a carbocationic species. Unfortunately, the reactivity drops enormously when HF of concentration 40 wt.% or lower is used. We therefore changed the reagent and used a fluorinating agent of low acidity, viz. triethylamine trishydrogen fluoride ($Et_3N \cdot 3HF$), which is a mild reagent which can be handled in normal glassware and can be distilled under reduced pressure [8]. It was originally synthesised in situ by Aranda, Jullien and Martin in 1965 [9], and was used for the cleavage of oxiranes. We used it as a defined reagent in earlier investigations on epoxide cleavages [10]. The use of pure $Et_3N \cdot 3HF$ in toluene (100 °C, 36 h) yielded 77% of fluorohydrins (**2a** + **2b**) in the ratio of **2a**/**2b** = 45:55.

To enhance the nucleophilicity of the fluoride ion within the reagent [11] and therefore to shift the regioisomeric ratio even more towards **2b**, we added different amounts of triethylamine [11] and of other amines (Scheme 3). Very basic and also very bulky amines were employed (Table 3).

The formation of by-products of higher molecular weight was observed in all cases. Attempts to vary other parameters especially during the work-up procedures



Scheme 3. Hydrofluorination of ethyl 10,11-epoxy-undecanoate (**1**) with $Et_3N \cdot 3HF$.

resulted in no change in the regioisomeric ratios or yields.

The results clearly show that the regioisomeric ratio is almost independent of:

(1) The basicity of the amine employed.
(2) The steric hindrance of the amine employed.
(3) The relative ratio of amine/$Et_3N \cdot 3HF$.

On deprotonation of HF within the HF/amine reagent, the mechanism changes (probably towards a thermodynamically directed attack of 'free' fluoride via an S_N2-like pathway [1,4]) and substitution occurs predominantly at the less hindered carbon. A maximum in the regioisomeric excess of **2c** was found at a ratio of **2a**/**2b** of ca. 1:4, which could represent thermodynamic equilibrium. This fact seems to be supported by semi-empirical calculations (AM1 [12]). More detailed calculation studies on the mechanism are in progress [13].

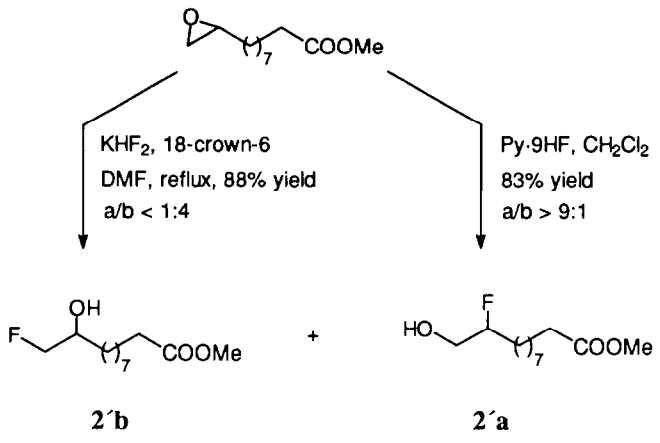
Unfortunately, the isolation of the fluorohydrins from the amine mixtures proved to be very difficult. Whilst regio isomer **2a** could be readily obtained in high yield with excellent regioisomeric excess (entry 3), further enhancement of the yield of **2b** (indicated in Table 3) proved to be impossible. This finding obviously corresponds with the results of Umezawa et al. [1]. Nevertheless we did not find any correlation of the ratio of **2a**/**2b** with the basicity or bulkiness of the amines added to the $Et_3N \cdot 3HF$ reagent.

To achieve a reasonable excess of the opposite regio isomer **2b** in high yield, we looked for methods employing different sources of highly nucleophilic fluoride, such as tetrabutylammonium fluoride or metal fluorides (e.g. caesium fluoride or potassium fluoride) for example, but without acceptable results. Finally we employed potassium hydrogen difluoride (KHF_2) and 18-crown-6 in DMF under reflux (previously used to convert sugar epoxides to fluorohydrins [14]). To the best of

Table 3
Regioisomeric excess using different $Et_3N \cdot 3HF$/amine mixtures without solvent

Entry No.	Amine	$Et_3N \cdot 3HF$/amine ratio	**2a**/**2b** (GLC)	Conversion (GLC) (%)	Isolated yield (**a** + **b**) (%)
9	triethylamine	1:2	24:76	82	44
10	pyridine	1:1	47:53	[a]	[a]
11	pyridine	1:2	30:70	[a]	[a]
12	$C_6H_5CH_2NH_2$	1:1.5	25:75	not determined	<2
13	$(C_6H_{11})_2NH$	1:1	20:80	96	23
14	Pr_2NH	1:1.2	18:82	97	23
15	Pr_2EtN	1:1	25:75	98	54
16	Pr_2EtN	1:2	27:73	98	18
17	DBU[b]	1:0.5	23:77	99	49
18	DBU[b]	1:1	20:80	99	40

[a]Over 70% formation of other products (not further characterised).
[b]DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.



Scheme 4. Reaction of methyl 10,11-epoxy-undecanoate with KHF_2.

our knowledge, this is the first application of this method to terminal, long-chain alkyl-substituted oxiranes and it turned out to be the most satisfactory method for obtaining a reasonable excess of **2b** in good yield.

We report herein our preliminary results [13] in employing this method. On treating the oxirane methyl ester **1'** (obtained similarly to **1**) with KHF_2/18-crown-6 in DMF under reflux for 36 h, we found a **2a'/2b'** ratio of less then 1:4, viz. 18:82. Hence, selective, conversion of the terminal epoxides of fatty acid esters into both regioisomeric fluorohydrins in high yield and satisfactory regioisomeric excess is possible by treating the oxirane either with Py·9HF in dichloromethane or KHF_2/18-crown-6 in DMF (Scheme 4). Both regio isomers could be readily obtained in pure form by flash chromatography on silica gel with cyclohexane/ethyl acetate (3:1) as eluent.

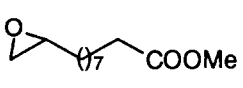
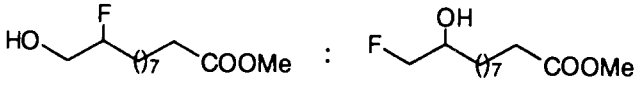
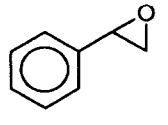
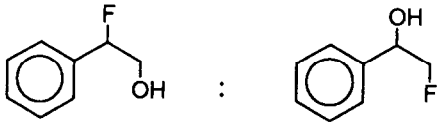
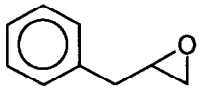
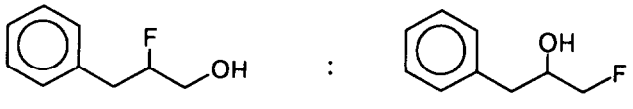
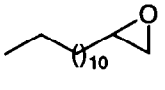
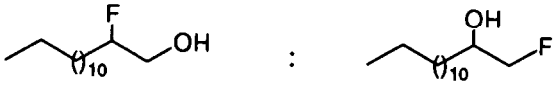
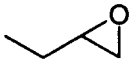
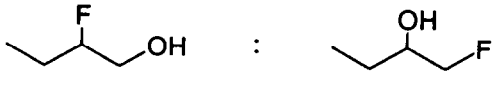
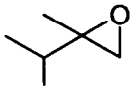
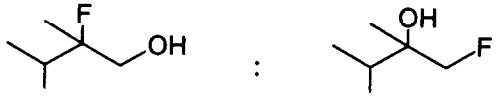
We also tried both types of conversion on methyl 9,10-epoxy-decanoate with exactly the same regiochemical results. Both methods should therefore be generally applicable to terminal oxiranes derived from esters of long-chain fatty acids.

Conversion by KHF_2/18-crown-6 in DMF to ensure the regioisomeric control of any oxirane ring-opening to a fluorohydrin and detailed studies of the mechanisms of such reactions are currently under intensive investigation within our group. Table 4 demonstrates our preliminary results on the regioisomeric ratios found for different substrates. All ratios were determined by ^{19}F NMR spectroscopy. Compounds were obtained in moderate yields which have not yet been optimized. Further substrates are currently being tested and detailed reaction conditions worked out [13].

3. Experimental

All melting points are reported uncorrected. Refraction indices were measured on a Zeiss, Jena, Abbé

Table 4
Regioisomeric ratios using KHF_2 on different substrates

Substrate	Regio isomers	^{19}F NMR ratio
		18:82
		25:75
		10:90
		20:80
		35:65
		20:80

refractometer. ^1H (300 MHz) and ^{13}C NMR spectra (75.5 MHz) were obtained using a Bruker WM 300 instrument. Chemical shifts are reported in ppm (δ) using TMS for ^1H and $CDCl_3$ for ^{13}C NMR as internal standards. ^{19}F NMR spectra (188.0 MHz) were obtained using a Bruker AC 200 instrument with α,α,α-trifluorotoluene (δ −63 ppm) as internal standard. Mass spectra (70 eV) were obtained using GLC–MS coupling with a Varian GC 3400/Varian Saturn IT (Ion Trap) data system NIST. GLC experiments were performed on a Hewlett Packard 5890 II gas chromatograph with a quartz capillary column (dimensions 0.33 mm×25 m) packed with 0.52 μm HP-1 (Hewlett Packard) using nitrogen as the carrier gas. Elemental analyses were undertaken by the Mikroanalytisches Laboratorium, OC, University of Münster. Thin layer chromatography was performed with Merck silica gel DC 60 F254 and flash chromatography with Merck silica gel 60 and cyclohexane/ethyl acetate (3:1) as the eluent system. $Et_3N \cdot 3HF$ was kindly donated by Hoechst A.G./Frankfurt. 10-Undecenoic acid and all other applied reagents were obtained from Janssen chemicals. All solvents were purified by distillation and stored over molecular sieves. CH_2Cl_2 was dried by distillation from P_2O_5 and stored over molecular sieves (0.4 nm).

3.1. Synthesis of esters and oxiranes

Methyl and ethyl undec-10-enoate have been synthesized by extractive esterification with methanol or ethanol, respectively, while the oxiranes were prepared using *m*-chloroperoxybenzoic acid in ether. All conversions followed standard procedures.

The physical constants obtained agree with those of commercially available ethyl undec-10-enoate and methyl undec-10-enoate, and those given in the literature for ethyl 10,11-epoxy-undecanoate [15] and methyl 10,11-epoxy-undecanoate [16].

3.2. Oxirane ring-opening with Olah's reagent (Py·9HF)

To a dry 100 ml polypropylene flask filled with argon was added 3 ml of Olah's reagent (Py·9HF, 100 mmol) and the flask and contents cooled to 0 °C. The epoxide (10 mmol) in 6 ml of dry CH_2Cl_2 was then carefully added. The temperature was allowed to reach room temperature when the solution was stirred for a further 6 h. The solution was then poured into 50 ml of ice-cooled 2 N aqueous ammonia solution and neutralized with a concentrated ammonia solution. The organic layer was separated and the aqueous layer extracted three times with small portions of CH_2Cl_2. Solid NaCl was then added and the aqueous layer again extracted twice. The combined organic layers were dried over Na_2SO_4. Removal of the CH_2Cl_2 gave the fluorohydrin **2a** together with about 8% of its regioisomer **2b** as yellowish, viscous oil. The isomers were separated by flash chromatography over silica gel using cyclohexane/ethyl acetate (3:1) as eluent.

Ethyl 10-fluoro-11-hydroxyundecanoate (**2a**): yield, **a**+**b** = 83%/pure **2a**, 63% (1.56 g); m.p. 7.5 °C, n_D^{21}, 1.4550. ^1H NMR ($CDCl_3$) δ: 1.25 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $COOCH_2CH_3$); 1.28–1.4 (br s, 10H, aliphat. H, 4-H_2 to 8-H_2); 1.45 (m, 2H, 9-H_2); 1.62 (m, 2H, 3-H_2), 2.28 (t, $^3J_{HH}$ = 7.4 Hz, 2H, 2-H_2); 2.78 (br s, 1H, $-CH_2-OH$); 3.65 (2 ddd, $^3J_{HF}$ = 23 Hz, 2H, 11-H_2); 4.12 (q, $^3J_{HH}$ = 7.1 Hz, 2H, $COOCH_2CH_3$); 4.54 (m, $^2J_{HF}$ = 49.4 Hz, 1H, 10-H) ppm. ^{13}C NMR ($CDCl_3$) δ: 14.25 ($COOCH_2CH_3$); 24.92 (d, $^3J_{CF}$ = 4 Hz, C-8) 24.97 (C-4); 29.1–29.7 (C-3 and C-5 to C-7); 31.1 (d, $^2J_{CF}$ = 20.4 Hz, C-9); 34.4 (C-2); 60.2 ($COOCH_2CH_3$); 64.9 (d, $^2J_{CF}$ = 21.9 Hz, C-11); 94.7 (d, $^1J_{CF}$ = 169.1 Hz, C-10); 173.95 ($COOCH_2CH_3$, C-1) ppm. ^{19}F NMR ($CDCl_3$) δ: −189.5 (m, $CH_2-CHF-CH_2OH$, 10-F) ppm. MS (GLC–MS, 70 eV, Ion Trap) *m/z* (%): 248 (0) [M^+]; 228 (100) [$M^+ - HF$]; 211 (10) [228 − H_2O]; 200 (8) [228 − C_2H_4, McLaff.]; 183 (45) [228-OCH_2CH_3]; 165 (30) [183 − H_2O]; 157 (10) [200-C_2H_3O]; 139 (40) [157 − H_2O]; 41 (90). Analysis: $C_{13}H_{25}FO_3$ (248.34) requires: C, 62.87; H, 10.15%. Found: C, 62.86; H, 10.46%.

Methyl 10-fluoro-11-hydroxyundecanoate (**2a'**): yield, **a'**+**b'** = 82%/pure **2a'**, 61% (1.47 g); m.p. 5 °C, n_D^{21}, 1.4525. ^1H NMR ($CDCl_3$) δ: 1.25–1.35 (br s, 10H, aliphat. H, 4-H_2 to 8-H_2); 1.45 (m, 2H, 9-H_2); 1.62 (m, 2H, 3-H_2); 2.28 (t, $^3J_{HH}$ = 7.5 Hz, 2H, 2-H_2); 2.4–2.7 (br s, 1H, $-CH_2-OH$); 3.65 (s, 3H, $COOCH_3$); 3.6–3.8 (2 ddd, 2H, 11-H_2); 4.55 (m, $^2J_{HF}$ = 49.7 Hz, 1H, 10-H) ppm. ^{13}C NMR ($CDCl_3$) δ: 24.9–25.1 (C-8 and C-4); 29.1–29.4 (C-3 and C-5 to C-7); 31.0 (d, $^2J_{CF}$ = 20.5 Hz, C-9); 34.9 (C-2); 51.4 ($COOCH_3$); 64.9 (d, $^2J_{CF}$ = 21.9 Hz, C-11); 94.8 (d, $^1J_{CF}$ = 168.3 Hz, C-10); 174.3 ($COOCH_3$) ppm. ^{19}F NMR ($CDCl_3$) δ: −189.5 (m, $-CHF-CH_2OH$, 10-F) ppm. MS (GLC–MS, 70 eV, Ion Trap). *m/z* (%): 234 (0) [M^+]; 215 (100) [$M^+ - F$]; 197 (15) [215 − H_2O]; 183 (45) [$M^+ - HF - OCH_3$]; 165 (35) [183 − H_2O]; 147 (20) [165 − H_2O]; 74 (18) [$C_3H_6O_2^+$]; 59 (20) [$COOCH_3^+$]; 41 (35); 39 (38). Analysis: $C_{12}H_{23}FO_3$ (234.31) requires: C, 61.51; H, 9.90%. Found: C, 61.57; H, 10.28%.

3.3. Oxirane ring-opening with triethylamine trishydrogen fluoride ($Et_3N \cdot 3HF$)

To a dry 100 ml flask was added 0.01 mol epoxide, 5.65 g (0.035 mol) of triethylamine trishydrogen fluoride $Et_3N \cdot 3HF$ and the molar amount given in Table 3 of another amine, and heated to 100 °C for 36 h. After cooling, the reaction mixture was continuously extracted with small quantities of ether. The combined organic layers were carefully washed twice with 2 N hydrochloric

acid (**hood!**), once with water and once with brine. The combined organic layers were dried over Na_2SO_4. Removal of the ether gave the regioisomeric fluorohydrins as yellowish, viscous oils. The isomers were separated by flash chromatography over silica gel using cyclohexane/ethyl acetate (3:1) as eluent.

Ethyl 11-fluoro-10-hydroxyundecanoate (**2b**): yield, **a**+**b**=54%/pure **2b**, 32.8% (0.82 g); m.p. 7 °C; n_D^{21}, 1.4470. ^{1}H NMR ($CDCl_3$) δ: 1.25 (t, $^2J_{HH}$=7.1 Hz, 3H, $COOCH_2CH_3$); 1.27–1.4 (br s, 10H, aliphat. H, 4-H_2 to 8-H_2); 1.45 (m, 2H, 9-H_2); 1.62 (m, 2H, 3-H_2); 2.14 (br s, 1H, $-CH_2-OH$); 2.28 (t, $^3J_{HH}$=7.5 Hz, 2H, 2-H_2); 3.8–3.92 (m, 1H, 10-H); 4.12 (q, $^3J_{HH}$=7.1 Hz, 2H, $COOCH_2CH_3$); 4.27 (ddd, $^2J_{HF}$=48.2 Hz, $^2J_{HH}$=9.42 Hz, $^3J_{HH}$=6.8 Hz, 1H, 11-H); 4.41 (ddd, $^2J_{HF}$=47.1 Hz, $^2J_{HH}$=9.42 Hz, $^3J_{HH}$=3 Hz, 1H, 11-H) ppm. ^{13}C NMR ($CDCl_3$) δ: 14.27 ($COOCH_2CH_3$); 24.95 (C-4); 25.3 (C-8); 29.1–29.5 (C-3 and C-5 to C-7); 31.9 (d, $^3J_{CF}$=6.4 Hz, C-9); 34.4 (C-2); 60.8 ($COOCH_2CH_3$); 70.5 (d, $^2J_{CF}$=17.8 Hz, C-10); 87.0 (d, $^1J_{CF}$=169.1 Hz, C-11); 173.9 ($COOCH_2CH_3$, C-1) ppm. ^{19}F NMR ($CDCl_3$) δ: −227.5 (dt, $^2J_{HF}$=47.6 Hz, $^3J_{HF}$=18.3 Hz, $-CH(OH)-CH_2-F$, 11-F) ppm. MS (GLC–MS, 70 eV, Ion Trap) *m/z* (%): 249 (25) [M^++H]; 229 (100) [M^+−F]; 215 (10) [M^+-CH_2F]; 211 (5) [229−H_2O]; 203 (5) [$M^+-H_2O-C_2H_4$, McLaff.]; 185 (15) [229−C_2H_3OH]; 183 (20) [229−$HOCH_2CH_3$]; 171 (18) [229−C_3H_5OH]; 165 (30) [183−H_2O]; 147 (30) [165−H_2O]; 43 (100) [$C_2H_3O^+$]; 41 (50). Analysis: $C_{13}H_{25}FO_3$ (248.34) requires: C, 62.87; H, 10.15%. Found: C, 62.87; H, 10.20%.

3.4. Oxirane ring-opening with KHF_2/18-crown-6 [14]

To an argon-covered solution consisting of 10.6 g (40 mmol) of 18-crown-6 and 7.8 g (100 mmol) of KHF_2 in 120 ml of refluxing dry DMF was added 25 mmol of epoxide in 40 ml of dry DMF. The solution was refluxed for an additional 36 h. After cooling, the solution was poured into 600 ml of ice water and was extracted five times with small quantities of CCl_4. The combined organic layers were repeatedly washed with water and dried with sodium sulfate. Evaporation of the solvent gave the fluorohydrin **2b′** together with about 18% of its regioisomer **a** as yellowish, viscous oil. The isomers were separated by flash chromatography over silica gel using cyclohexane/ethyl acetate (3:1) as eluent.

Methyl 11-fluoro-10-hydroxyundecanoate (**2b′**): Yield **a′**+**b′**=88%/pure **2b′**, 69% (4.05 g); m.p. 5 °C. ^{1}H NMR ($CDCl_3$) δ: 1.3 (br s, 10H, aliphat. H, 4-H_2 to 8-H_2); 1.46 (m, 2H, 9-H_2); 1.61 (m, 2H, 3-H_2); 2.3 (t, $^3J_{HH}$=7.5 Hz, 2H, 2-H_2); 2.55 (br s, 1H, $-CH(OH)-$); 3.66 (s, 3H, $-COOCH_3$); 3.78–3.94 (m, 1H, 10-H); 4.26 (ddd, $^2J_{HF}$=47.8 Hz, $^2J_{HH}$=9.4 Hz, $^3J_{HH}$=6.4 Hz, 1H, 11-H); 4.40 (ddd, $^2J_{HF}$=47.1 Hz, $^2J_{HH}$=9.4 Hz, $^3J_{HH}$=3 Hz, 1H, 11-H) ppm. ^{13}C NMR ($CDCl_3$) δ: 24.8 (C-4); 25.17 (C-8); 28.9–29.4 (C-3 and C-5 to C-7); 31.8 (d, $^3J_{CF}$=5 Hz, C-9); 34.0 (C-2); 51.3 ($COOCH_3$); 70.3 (d, $^2J_{CF}$=17.8 Hz, C-10); 86.9 (d, $^1J_{CF}$=167.1 Hz, C-11); 174.2 ($COOCH_3$, C-1) ppm. ^{19}F NMR ($CDCl_3$) δ: −228.2 (dt, $^2J_{HF}$=47.4 Hz, $^3J_{HF}$=18.4 Hz, $-CH(OH)-CH_2-F$, 11-F) ppm. MS (GLC–MS, 70 eV, Ion Trap) *m/z* (%): 235 (60) [M^++H]; 217 (25) [235−H_2O]; 215 (8) [235−HF]; 203 (10) [M^+-CH_3O]; 201 (12) [M^+-CH_2F]; 197 (9) [217−HF]; 185 (20) [203−H_2O]; 165 (30) [185−HF]; 147 (25) [165−H_2O]; 59 (25) [$COOCH_3^+$]; 55 (75); 43 (100). Analysis: $C_{12}H_{23}FO_3$ (234.31) requires: C, 61.51; H, 9.90%. Found: C, 61.43; H, 10.12%.

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