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Journal of Fluorine Chemistry 75 (1995) 35–40

JOURNAL OF FLUORINE CHEMISTRY

Stereoselective synthesis of *Z* and *E* 3-*F*-alkyl 2-propenoates and derivatives

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Received 20 December 1994; accepted 19 May 1995

Abstract

The stereoselective preparation of 3-*F*-alkyl 2-propenoates and their derivatives is described. *E*-isomers are easily obtained by an in situ reduction–olefination from esters of *F*-acids and phosphonates or by a convenient dehydration of 3-*F*-alkyl 3-hydroxyesters. *Z*-isomers are known to be prepared by the hydrogenation of alkynes.

Keywords: Unsaturated ester; Unsaturated nitrile; *F*-Alkyl chain; Dehydration; *F*-Enoyl sultam

1. Introduction

Alkenes constitute an attractive class of synthons in organic hydrocarbon synthesis. They are often used in the preparation of biologically active compounds by epoxidation, hydroxylation, Diels–Alder reaction, cycloaddition, etc. A number of fluorinated products have been successfully employed as precursors in the preparation of fluorinated surfactants for biomedical application, oxygen carriage, diagnosis and drug delivery [1], and as fluorinated analogues [2] of pheromones [3], retinoids [4] and pyrethroids [5].

α,β-Unsaturated ketones or esters with a perfluoroalkyl group are of high interest having two non-equivalent electrophilic centres. The introduction of a long fluorinated chain changes both the reactivity and properties of these compounds. It is of great interest to obtain such compounds stereoselectively, to study their respective reactivities towards epoxidation, Diels–Alder reaction, dihydroxylation, etc.

We report here the stereospecific synthesis of α-*F*-alkylated β-functionalized (with an ester or cyano group, camphoryl group) *Z* and *E* α,β-unsaturated compounds.

2. Results and discussion

2.1. Preparation of Z-isomers

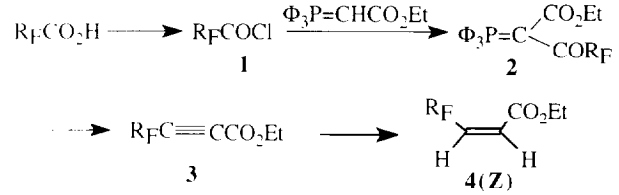
Z-Ethyl 3-*F*-alkyl 2-propenoates have already been prepared in the laboratory and described in the literature [6,7]. They can be obtained by controlled hydrogenation (with the Lindlar catalyst) of the corresponding alkyne **3** with good yields (90%) and 100% stereoselectivity [6]. We used the pyrolysis of triphenylphosphoranes to synthesize 3-*F*-alkyl 2-propynoates [7]. This is a simple method which can easily be adapted up to 50 g. The method is totally stereoselective but needs four steps from the starting *F*-acid (Scheme 1 and Table 1).

2.2. Preparation of E isomer

2.2.1. First method

β-*F*-Alkylated α,β-unsaturated esters are usually prepared from *F*-alkyl ketones or anhydrides by Wittig condensation por the Horner–Wadsworth–Emmons (HWE) reaction giving predominantly the *E*-isomer (Scheme 2) [8].

This method gives only C3 *gem*-disubstituted compounds and there is a problem with monosubstitution at this position which should be substituted by the *F*-alkyl chain. The obvious way is the condensation of an *F*-aldehyde with a phosphonoacetate carbanion. Fluorinated aldehydes are very unstable and easily give hydrolyzed products. Few general synthetic



Scheme 1. Preparation of *Z*-ethyl 3-*F*-alkyl 2,3-propenoates.

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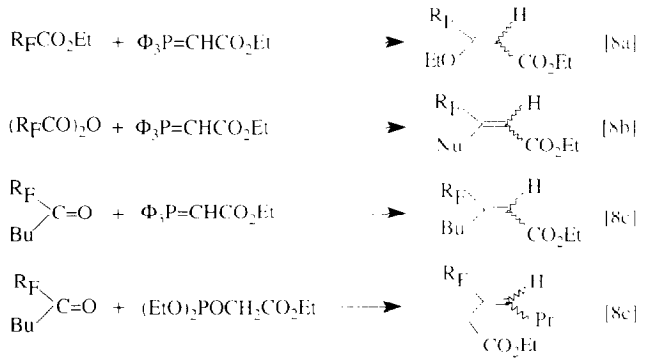
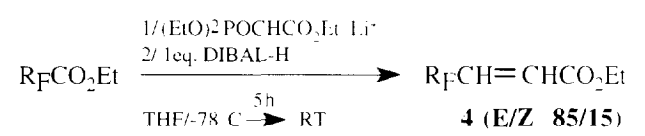
SSDI 0022-1139(95)03297-5

Table 1
Preparation of *Z*-ethyl 3-*F*-alkyl 2,3-propenoates (see Scheme 1)

R_F	Yield (%)				
	1	**2**	**3**	**4**(*Z*)	Overall
C_5F_{11} [a]	94	74	92	76	49
C_7F_{15} [b]	91	77	90	85	54



Scheme 2. Preparation of *F*-unsaturated esters.



Scheme 3. Preparation of *β*-*F*-alkyl *α*,*β*-unsaturated esters by the HWE reaction.

methods of fluorinated aldehydes are mentioned in the literature [9]. They are usually protected as the hemiacetal or acetal and prior deprotection is required. To overcome the problem of the isolation of these aldehydes, we have followed the method described by Takacs et al. [10]. The aldehyde is generated in situ by half-reduction of the *F*-ester with diisobutylaluminium hydride (DIBAL-H). The condensation step follows. A mixture of *Z*- and *E*-3-*F*-alkyl 2-propenoates **4** is obtained with a stereoselectivity of 85:15 in favour of the *E*-isomer [1]. The yield is about 55%. This route is not totally stereospecific but is a one-step reaction from the *F*-ester (Scheme 3) [11].

This reaction has also been extended to other phosphonates to give different alkenes. Diethyl cyanomethylphosphonate and triethyl 2-phosphonopropionate have been tested using the same conditions of temperature, solvent and reaction time. They gave the expected alkenes with correct yields but with different stereoselectivities. The cyano derivative **6** is obtained with 45%–50% yield and a stereoselectivity *Z*/*E* of 44:56. For the methylated olefin **5**, the yield is about 60%–80% and the *Z*/*E* ratio 80:20. These results are summarized in Table 2. We have no simple explanation for the difference

[1] The ratio of the two isomers is based on the integration of the respective peaks of the *α*-CF_2 group which exhibit different chemical shifts in this ^{19}F NMR spectra. The ratios of **5** and **6** are given by analogy and confirmed by the coupling constant of the ethylenic protons via ^1H NMR spectroscopy

Table 2
Synthesis of *β*-*F*-alkylated *α*-functionalized alkenes

Phosphonate	Product	R_F	Yield (%)	*Z*/*E* [a]
$(EtO)_2POCH_2CO_2Et$	$R_FCH{=}CHCO_2Et$ (**4**)	C_5F_{11}	53	15:85
		C_7F_{15}	56	18:82
$(EtO)_2POCH(CH_3)CO_2Et$	$R_FCH{=}CH(CH_3)CO_2Et$ (**5**)	C_5F_{11}	85	80:20
		C_7F_{15}	63	78:22
$(EtO)_2POCH_2CN$	$R_FCH{=}CHCN$ (**6**)	C_5F_{11}	50	44:56
		C_7F_{15}	44	44:56

[a] The *Z*/*E* ratio was estimated on the basis of ^{19}F NMR data.

in stereoselectivity. The steric effects of the various C2 substituents are not sufficient to explain these different stereoselective orientations.

2.2.2. Second method

The first method is interesting because it is a one-step reaction and can be used for the preparation of different kinds of alkenes. Although the stereoselectivity is good (*E*/*Z* = 80:20), it is not 100%. Another strategy is required for obtaining only the *E*-isomer. The literature describes the dehydration of 3-*F*-alkyl 3-hydroxypropanoates in acidic media (P_2O_5, H_2SO_4) [12] or the *β*-elimination of alcohol derivatives [13].

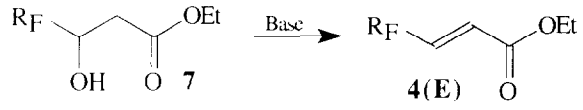
The method we report here is a direct dehydration of 3-*F*-alkyl 3-hydroxypropanoates **7** [14] in a mild basic medium (Scheme 4). The influence of the base, solvent and temperature has been optimized (Table 3). The best results have been obtained in K_2CO_3/EtOH(reflux) and in DBU/$CHCl_3$(reflux). Under these conditions, *E*-3-*F*-alkyl 2-propenoates **4** are obtained quantitatively with 100% stereoselectivity (Table 4).

2.3. Functionalization

Since the two *Z*- and *E*-isomers were obtained separately, our next aim was to induce a stereoface selectivity with chiral auxiliaries. There are a number of chiral auxiliaries available. The abundance, crystallinity and overall transformations induced by camphor (+)1− have attracted considerable interest. Thus, 10,2-bornane (−)3-sultam (XH) and its antipode (+)3−, accessible from inexpensive (+)1−1 and (−)1−1 camphor sulphonic acids via two simple operations is commonly used. This chiral auxiliary can be reacted with esters in different ways.

(i) The direct *N*-acylation of an acid chloride with NaH [15] (see Scheme 5):

(ii) The direct *N*-acylation of an ester with $AlMe_3$ [15] (see Scheme 6):



Scheme 4.

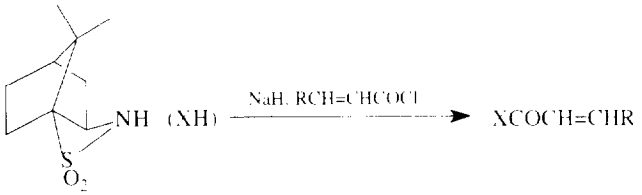
Table 3
Attempted dehydration of **7**

Exp. No.	Base	Base/substrate (equiv./equiv.)	Solvent	Temp. (°C)	Time	**7** [a]	**4**(*E*) [a]
1	$KHCO_3$	4	hexane	reflux	6 d	100	–
2	K_2CO_3	4	hexane	reflux	2 d	60	30
3	K_2CO_3	4	THF	reflux	5 d	100	–
4	K_2CO_3	2	$CHCl_3$	reflux	12 d	94	6
5	K_2CO_3	2	EtOH	reflux	26 h	–	100
6	DBU	4	hexane	reflux	7 d	100	–
7	DBU	4	THF	reflux	7 d	100	–
8	DBU	2	$CHCl_3$	reflux	1 d		100
9	DBU	2	EtOH	reflux	7 d	100	–

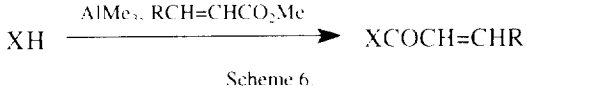
[a] Proportions determined on basis of ^{19}F NMR spectroscopy.

Table 4
Optimized results for the dehydration of **7**

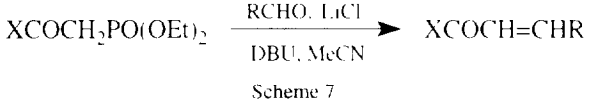
Base	Base/substrate (equiv./equiv.)	Solvent	Temp.	Time	R_F	Yield (%)	*Z*/*E*
K_2CO_3	2	EtOH	reflux	26 h	C_5F_{11}	90	0:100
					C_7F_{15}	89	0:100
DBU	2	$CHCl_3$	reflux	1 d	C_5F_{11}	95	0:100
					C_7F_{15}	92	0:100



Scheme 5



Scheme 6



Scheme 7

(iii) By a Horner–Wadsworth–Emmons reaction between a sulphonated phosphonate and aldehyde [16] (see Scheme 7):

Route (iii) was attractive because it was similar to the synthesis of the 3-*F*-alkyl 2-propenoates **4**. Attempts to prepare the *N*-enoyl sultam by direct reduction–olefination of the *F*-ester by DIBAL-H were unsuccessful however. In this reaction, the first step gives LiOH species which cleave the *N*-acylsultams: only the 10,2-bornane 3-sultam is recovered.

The *N*-(3-*F*-alkyl 2-propenyl) 10,2-bornane 3-sultam (**9**) is thus obtained by *N*-acylation of the acid chloride **8** in basic medium. The two steps are simple and the expected product is obtained in good yield and with the retention of the double-bond stereochemistry (Scheme 8).

3. Experimental details

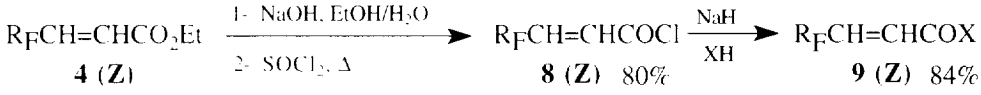
Gas chromatography was performed on a DELSI instrument (FID detector) fitted with a 3 m × 1/4 in column packed with 30% SE30 on Chromosorb. All GC analyses were performed as follows: 120 °C for 5 min, then heating at 5 °C min^{-1} up to 200 °C. Infrared spectra were obtained as KBr pellets or films on a Bruker IFS spectrometer. ^1H (200 MHz), ^{13}C (50.3 MHz) (internal reference Me_4Si) and ^{19}F (188.3 MHz) (internal reference $CFCl_3$, negative for upfield shifts) NMR spectra, all samples in $CDCl_3$ solution, were recorded on a Bruker AC-200 spectrometer. Combined gas chromatography/mass spectrometry was performed with an R10 Ribermag L10 instrument, EI (70 eV).

3.1. Synthesis of 3-F-alkyl 2-propenoates 4(Z) [7,11]

A mixture of 3-*F*-alkyl 2-propynoate (18 mmol) and Lindlar catalyst (1.8 mmol) in ethanol was placed in an autoclave. It was purged several times with N_2 and then H_2, and finally closed at a pressure of 7 bar of hydrogen and left under magnetic stirring for 24 h. After returning to atmospheric pressure, the solution was filtered on Celite and concentrated. The liquid product was purified by distillation under reduced pressure (yield, 85%).

Ethyl 3-*F*-pentyl 2-propenoate (**4aZ**): b.p. 95 °C/20 mmHg. IR (cm^{-1}): 1745 ν(CO); 1665 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.22 (t, $^3J = 7$ Hz, 3H, CH_3); 4.19 (q, $^3J = 7$ Hz, 2H, CH_2); 5.84 [q broad, $^3J = {}^3J(^1H–^{19}F) = 13$ Hz, 1H, CF_2–C*H*=]; 6.37 [dt, $^3J = 13$ Hz, $^4J(^1H–^{19}F) = 2.2$ Hz, 1H, C*H*–CO] ppm. ^{13}C NMR δ: 13.79 (CH_3); 61.66 (CH_2); 122.58 [t, $^2J(^{13}C–^{19}F) = 23.8$ Hz, CF_2–*C*]; 132.02 [t, $^3J(^{13}C–^{19}F) = 6$ Hz, *C*–CO]; 163.86 (CO) ppm. ^{19}F NMR δ: −81.6 (CF_3); −110.4 ($CF_{2\alpha}$); −123.3/−123.7 ($CF_{2\beta,\gamma}$); −127.0 ($CF_{2\omega}$) ppm.

Ethyl 3-*F*-heptyl 2-propenoate (**4bZ**): b.p. 120 °C/20 mmHg. IR (cm^{-1}): 1738 ν(CO); 1664 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.31 (t, $^3J = 7$ Hz, 3H, CH_3); 4.27 (q, $^3J = 7$ Hz, 2H, CH_2); 5.91 [q broad, $^3J = {}^3J(^1H–^{19}F) = 12.9$ Hz, 1H, CF_2–C*H*=]; 6.46 [dt, $^3J = 12.9$ Hz, $^4J(^1H–^{19}F) = 2$ Hz, 1H, C*H*–CO] ppm. ^{13}C NMR δ: 13.68 (CH_3); 61.69 (CH_2); 122.68 [t, $^2J(^1H–^{19}F) = 24.3$ Hz, CF_2–*C*]; 132.02 [t, $^3J(^1H–^{19}F) = 6$ Hz, *C*–CO]; 163.93 (CO) ppm. ^{19}F NMR δ: −81.6 (CF_3); −110.3 ($CF_{2\alpha}$); −122.2/



Scheme 8. Preparation of *N*-(3-*F*-alkyl 2-propenyl) 10,2-bornane 3-sultam (**9**).

−122.7/−123.4 ($4CF_2$); −126.8 ($CF_{2\omega}$) ppm. MS *m/z*(%): 441(4); 424(21); 423(100); 422(21); 421(58); 404(28); 401(14); 373(20.5); 181(5); 169(7.5); 157(7.5); 154(12); 149(13); 145(6); 136(5); 131(22); 126(8); 123(8); 121(19); 119(17); 107(10); 105(6); 104(60); 99(85); 95(11); 76(16); 75(9); 73(6); 76(14); 75(9); 73(6); 69(39); 55(5.5); 45(29).

3.2. Synthesis of ethyl 3-F-alkyl 2-propenoates 4(E): First method

n-Butyl-lithium (6 mmol, 1.6 N in hexane solution, 3.7 ml) was added dropwise to a cooled solution (−78 °C) of 6 mmol of $(EtO)_2P(O)CH_2CO_2Et$ in anhydrous THF (100 ml) under an inert atmosphere. After 1 h at −78 °C, 5 mmol of ethyl *F*-ester were added in one portion to the reaction medium; then 5 mmol of a DIBAL-H solution (1 M in THF, 5 ml) were added dropwise. The temperature was maintained at −78 °C during the operation. The mixture was allowed to warm up to room temperature over 5 h and then quenched with 10% HCl (75 ml). After the usual work-up, isomer *E* (*E*/*Z*=85:15) was separated by chromatography on silica gel (eluant: pentane/ether 8:2). From 1.7 g of ethyl *F*-hexanoate was obtained 1.1 g (yield, 53%) of **4a***E* while from 2.2 g of ethyl *F*-octanoate was obtained 1.3 g (yield, 56%) of **4b***E*.

Ethyl 3-*F*-pentyl 2-propenoate (**4a***E*): IR (cm^{-1}): 3000–2900 ν(CH); 1717 ν(CO); 1669 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.34 (t, ^3J=7 Hz, 3H, CH_3); 4.29 (q, ^3J=7 Hz, 2H, CH_2); 6.54 [dt, ^3J=16 Hz, $^4J(^1H–^{19}F)$=1.9 Hz, 1H, C*H*–CO]; 6.84 [dt, ^3J=16 Hz, $^3J(^1H–^{19}F)$=11.7 Hz, 1H, CF_2–C*H*] ppm. ^{13}C NMR δ: 14.05 (CH_3); 61.83 (CH_2); 130.68 [t, $^2J(^{13}C–^{19}F)$=23.2 Hz, CF_2–*C*]; 130.94 [t, $^3J(^{13}C–^{19}F)$=7.4 Hz, *C*–CO]; 163.65 (CO) ppm. ^{19}F NMR δ: −81.4 (CF_3); −114.1 ($CF_{2\alpha}$); −123.0 ($CF_{2\beta}$); −123.9 ($CF_{2\gamma}$); −126.8 ($CF_{2\omega}$) ppm.

Ethyl 3-*F*-heptyl 2,3-propenoate (**4b***E*): IR (cm^{-1}): 3000–2900 ν(CH); 1745 ν(CO); 1670 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.34 (t, ^3J=7 Hz, 3H, CH_3); 4.29 (q, ^3J=7 Hz, 2H, CH_2); 6.54 [dt, ^3J=16 Hz, $^4J(^1H–^{19}F)$=1.9 Hz, 2H, C*H*–CO]; 6.83 [dt, ^3J=16 Hz, $^3J(^1H–^{19}F)$=11.7 Hz, 1H, CF_2–C*H*] ppm. ^{13}C NMR δ: 14.05 (CH_3); 61.83 (CH_2); 130.78 [t, $^2J(^{13}C–^{19}F)$=23.8 Hz, CF_2–*C*]; 130.98 [t, $^3J(^{13}C–^{19}F)$=8.6 Hz, *C*–CO); 163.65 (CO) ppm. ^{19}F NMR δ: −81.6 (CF_3); −114.2 ($CF_{2\alpha}$); −122.1/−122.7/−123.4/−123.7 ($4CF_2$); −126.83 ($4CF_2$) ppm. MS *m/z*(%): 469(0.4); 441(14.5); 424(10); 423(100); 421(16.5); 404(5); 393(9); 373(10); 169(5); 149(9.6); 135(26); 131(15.5); 121(6); 119(11.5); 107(5.5); 104(40); 101(6); 100(8); 99(41); 93(8); 76(11); 69(29); 45(14).

3.3. Synthesis of ethyl 3-F-alkyl 2-methyl 2-propenoates 5(E)

The same procedure was applied to $(EtO)_2P(O)$-$C(CH_3)CO_2Et$. The *Z*- and *E*-isomers (*E*/*Z*=85:15) were separated by chromatography on silica gel (eluant: pentane/ether 8:2) (yield, 85%). From 1.7 g of ethyl *F*-hexanoate was obtained 0.3 g of **5a***E* and 1.3 g of **5a***Z* while from 2.2 g of ethyl *F*-octanoate was obtained 0.4 g of **5b***E* and 1.2 g of **5b***Z*.

Ethyl 3-*F*-pentyl 2-methyl 2-propenoate (**5a***E*): IR (cm^{-1}): 3000–2900 ν(CH); 1731 ν(CO); 1667 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.28 (t, ^3J=7 Hz, 3H, CH_2–CH_3); 2.09 (broad s, 3H, CH_3); 4.21 (q, ^3J=7 Hz, 2H, CH_2); 6.58 [broad t, $^3J(^1H–^{19}F)$=15.7 Hz, 1H, C*H*] ppm. ^{13}C NMR δ: 14.06 (CH_2–CH_3); 22.35 (CH_3); 62.06 (CH_2); 123.94 [t, $^2J(^{13}C–^{19}F)$=23.6 Hz, CF_2–*C*]; 142.35 (C=); 173.18 (CO) ppm. ^{19}F NMR δ: −81.2 (CF_3); −108.8 ($CF_{2\alpha}$); −123.0/−124.0 ($CF_{2\beta,\gamma}$); −126.7 ($CF_{2\omega}$) ppm. MS *m/z*(%): 382(M^+, 1.4); 367(4); 337(95.5); 335(15.5); 309(34); 135(13); 119(13); 115(54.5); 113(100); 101(15); 100(10.5); 90(36); 89(27.5); 87(23); 69(47.5); 51(8); 45(9.5).

Ethyl 3-*F*-pentyl 2-methyl 2-propenoate (**5a***Z*): IR (cm^{-1}): 3000–2800 ν(CH); 1743 ν(CO); 1677 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.23 (t, ^3J=7 Hz, 3H, CH_2–CH_3); 2.03 (broad s, 3H, CH_3); 4.18 (q, ^3J=7 Hz, 2H, CH_2); 5.48 [t, $^3J(^1H–^{19}F)$=14.3 Hz, 1H, C*H*] ppm. ^{13}C NMR δ: 13.75 (CH_2–CH_3); 21.54 (CH_3); 61.67 (CH_2); 115.06 [t, $^2J(^{13}C–^{19}F)$=23.0 Hz, CF_2–*C*]; 143.27 (C=); 167.47 (CO) ppm. ^{19}F NMR δ: −81.4 (CF_3); −109.6 ($CF_{2\alpha}$); −123.2/−123.7 ($CF_{2\beta,\gamma}$); −126.8 ($CF_{2\omega}$) ppm. MS *m/z*(%): 367(1); 337(38.5); 309(22); 140(7.5); 135(21.5); 131(11.5); 119(13.5); 115(46.5); 113(100); 109(8); 90(23.5); 89(23); 87(16); 69(37.5); 45(10).

Ethyl 3-*F*-heptyl 2-methyl 2-propenoate (**5b***E*): IR (cm^{-1}): 3000–2800 ν(CH); 1744 ν(CO); 1677 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.26 (t, ^3J=7 Hz, 3H, CH_2–CH_3); 2.04 (broad s, 3H, CH_3); 4.20 (q, ^3J=7 Hz, 2H, CH_2); 6.57 [broad t, $^3J(^1H–^{19}F)$=15.0 Hz, 1H, C*H*] ppm. ^{13}C NMR δ: 13.87 (CH_2–CH_3); 22.61 (CH_3); 61.93 (CH_2); 123.89 [t, $^2J(^{13}C–^{19}F)$=23.6 Hz, CF_2–*C*]; 141.55 (C=); 172.27 (CO) ppm. ^{19}F NMR δ: −81.5 (CF_3); −108.9 ($CF_{2\alpha}$); −122.2/−122.6/−123.3/−123.9 ($4CF_2$); −126.7 ($CF_{2\omega}$) ppm.

Ethyl 3-*F*-heptyl 2-methyl 2-propenoate (**5b***Z*): IR (cm^{-1}): 3000–2900 ν(CH); 1784 ν(CO); 1675 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 1.22 (t, ^3J=7 Hz, 3H, CH_2–CH_3); 2.03 (broad s, 3H, CH_3); 4.18 (q, ^3J=7 Hz, 2H, CH_2); 5.48 [broad t, $^3J(^1H–^{19}F)$=15.7 Hz, 1H, C*H*] ppm. ^{13}C NMR δ: 13.56 (CH_2–CH_3); 21.46 (CH_3); 61.60 (CH_3); 115.56 [t, $^2J(^{13}C–^{19}F)$=24.6 Hz, CH]; 143.21 [t, $^3J(^{13}C–^{19}F)$=6.2 Hz, C]; 167.42 (CO) ppm. ^{19}F NMR δ: −81.6 (CF_3); −109.6 ($CF_{2\alpha}$); −122.3/−122.7/−123.6 ($CF_{2\beta,\gamma}$); −126.9 ($CF_{2\omega}$) ppm.

3.4. Synthesis of 3-F-alkyl 2-propenenitriles 6(E)

The same experimental procedure was applied to $(EtO)_2P(O)CH_2CN$. The *Z*- and *E*-isomers (*E*/*Z*=85:15) were separated by chromatography on silica gel (eluant: pen-

tane/ether 8:2) (yield, 50%). From 1.7 g of ethyl *F*-hexanoate was obtained 0.4 g of **6a***E* and 0.5 g of **6a***Z* while from 2.2 g of ethyl *F*-octanoate was obtained 0.5 g of **6b***E* and 0.6 g of **6b***Z*.

3-*F*-Pentyl 2-propenenitrile (**6a***E*): IR (cm^{-1}): 2250 ν(CN); 1654 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 6.08 [dt, $^3J = 16.3$ Hz, $^4J(^1H–^{19}F) = 2.4$ Hz, 1H, C*H*–CN]; 6.60 [dt, $^3J = 16.3$ Hz, $^3J(^1H–^{19}F) = 11.2$ Hz, 1H, CF_2–C*H*] ppm. ^{13}C NMR δ: 110.81 [t, $^3J(^{13}C–^{19}F) = 11.1$ Hz, *C*–CN]; 113.71 (CN); 136.85 [t, $^2J(^{13}C–^{19}F) = 24.3$ Hz, CF_2–*C*] ppm. ^{19}F NMR δ: −81.4 (CF_3); −115.3 ($CF_{2\alpha}$); −123.0/−123.7 ($CF_{2\beta,\gamma}$); −126.9 ($CF_{2\omega}$) ppm. MS *m/z*(%): 321(0.5); 302(1.5); 169(2); 131(5); 119(14.5); 103(7.7); 102(100); 100 (15.5); 69(38); 52(6.5); 51(14).

3-*F*-Pentyl 2-propenenitrile (**6a***Z*): IR (cm^{-1}): 2250 ν(CN); 1654 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 6.00 [dt, $^3J = 12.1$ Hz, $^4J(^1H–^{19}F) = 2.6$ Hz, 2H, C*H*–CN]; 6.40 [dt, $^3J = 12.1$ Hz, $^3J(^1H–^{19}F) = 12.1$ Hz, 1H, CF_2–C*H*) ppm. ^{13}C NMR δ: 87.23 (CN); 109.74 [t, $^3J(^{13}C–^{19}F) = 7.3$ Hz, *C*–CN]; 135.45 [t, $^2J(^{13}C–^{19}F) = 24.6$ Hz, CF_2–*C*] ppm. ^{19}F NMR δ: −81.2 (CF_3); −112.4 ($CF_{2\alpha}$); −122.8/−123.3/−123.6 ($CF_{2\beta,\gamma}$); −126.7 ($CF_{2\omega}$) ppm. MS *m/z*(%): 321(1); 169(2.5); 131(5.5); 119(8.5); 103(4.5); 102(100); 100(13.6); 69(33.7); 52(7); 51(13).

3-*F*-Heptyl 2,3-propenenitrile (**6b***E*): IR (cm^{-1}): 2250 ν(CN); 1653 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 6.08 (dt, $^3J = 16.3$ Hz, $^4J_{^1H–^{19}F} = 2.4$ Hz, 1H, C*H*–CN); 6.60 [dt, $^3J = 16.3$ Hz, $^3J(^1H–^{19}F) = 11.2$ Hz, 1H, CF_2–C*H*] ppm. ^{13}C NMR δ: 110.81 [t, $^3J(^{13}C–^{19}F) = 10.8$ Hz, *C*–CN]; 113.63 (CN); 136.85 [t, $^2J(^{13}C–^{19}F) = 24.3$ Hz, CF_2–*C*] ppm. ^{19}F NMR δ: −81.4 (CF_3); −115.3 ($CF_{2\alpha}$); −122.6/−123.0/−123.7 ($4CF_2$); −126.9 ($CF_{2\omega}$) ppm.

3-*F*-Heptyl 2-propenenitrile (**6b***Z*): IR (cm^{-1}): 2250 ν(CN); 1653 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 5.95 [dt, $^3J = 11.8$ Hz, $^4J(^1H–^{19}F) = 2.7$ Hz, 2H, C*H*–CN]; 6.42 [dt, $^3J = 11.8$ Hz, $^3J(^1H–^{19}F) = 11.8$ Hz, 1H, CF_2–C*H*] ppm. ^{13}C NMR δ: 88.01 (CN); 109.51 [t, $^3J(^{13}C–^{19}F) = 7.4$ Hz, *C*–CN]; 135.30 [t, $^2J(^{13}C–^{19}F) = 24.5$ Hz, CF_2–*C*] ppm. ^{19}F NMR δ: −81.2 (CF_3); −112.3 ($CF_{2\alpha}$); −122.5/−123.2/−123.9 ($4CF_2$); −126.6 ($CF_{2\omega}$) ppm.

3.5. Synthesis of ethyl 3-F-alkyl 2-propenoates 4(E): Second method

A mixture of ethyl 3-*F*-alkyl 3-hydroxypropanoate (**7**) (14 mmol) and potassium carbonate (or DBU) (28 mmol) was heated in ethanol (or $CHCl_3$) at reflux over 24 h. After returning to room temperature, 50 ml of water was added. The fluorinated product was extracted with diethyl ether (3 × 30 ml). The extracts were concentrated and then purified by liquid chromatography on silica gel (eluant: pentane/ether 8:2). Spectroscopic data were similar to those given above.

3.6. Synthesis of 3-F-alkyl 2-propenoic acid (Z)

A solution of NaOH (50 ml, 2%) was added to 10 mmol of ethyl 3-*F*-alkyl 2-propenoate (**4**) in 10 ml of ethanol. The mixture was heated at reflux overnight. After returning to room temperature and usual work-up, the product was used without purification (yield, 91%).

3-*F*-Heptyl 2-propenoic acid (*Z*): b.p. 85 °C/40 mmHg. IR (cm^{-1}): 3500–2900 ν(OH); 1659 ν(CO); 1300–1100 ν(C–F). ^1H NMR δ: 5.92 [q, $^3J(^1H–^{19}F) = ^3J = 13$ Hz, 1H, CF_2–C*H*]; 6.45 [dt, $^3J = 13$ Hz, $^4J(^1H–^{19}F) = 3.1$ Hz, 1H, C*H*–CO] ppm.

3.7. Synthesis of 3-F-alkyl 2-propenoyl chloride (8bZ)

A mixture of *F*-alkylpropenoic acid (8 mmol) and 3 ml of $SOCl_2$ was heated at 80 °C until there was no longer elimination of HCl (about 1 h). After returning to room temperature, the excess of $SOCl_2$ was evaporated under reduced pressure and the acid chloride purified by distillation (yield, 80%).

3-*F*-Heptyl 2-propenoyl chloride (**8b***Z*): b.p. 67 °C/10 mmHg. IR (cm^{-1}): 1790 ν(CO); 1650 ν(C=C); 1300–1100 ν(C–F). ^1H NMR δ: 5.88 [q, $^3J(^1H–^{19}F) = ^3J = 13$ Hz, 1H, CF_2–C*H*]; 6.62 [dt, $^3J = 13$ Hz, $^4J(^1H–^{19}F) = 3$ Hz, 1H, C*H*–CO] ppm.

3.8. Synthesis of N-(3-F-heptyl 2-propenoyl) 10,2-bornane sultam (9bZ)

10,2-Bornane 3-sultam (XH) (6.2 mmol) in 10 ml of toluene was added dropwise to 9.3 mmol of NaH in 30 ml of toluene. After 1 h at room temperature, 6.2 mmol of acid chloride **8b***Z* in 10 ml of toluene were added dropwise. After 2 h, the mixture was quenched with 10% HCl. After the usual work-up and concentration, the product was purified by chromatography on silica gel (eluant: $CHCl_3$) (yield, 84%).

N-(3-*F*-Heptyl 2-propenyl) 10,2-bornane sultam (**9b***Z*): IR (cm^{-1}): 3050–2900 ν(CH); 1693 ν(CO); 1339 $\nu(SO_2)$; 1300–1100 ν(CF). ^1H NMR δ: 0.9–1.1 (2s, 6H, $2CH_3$); 1.3–1.6 (m, 2H, CH_2); 1.8–2.3 (m, 5H, CH_2–CH_2–CH); 3.92 (AB system, $J_{A,B} = 13$ Hz, 2H, CH_2–S); 3.93 (dd, $^3J = 4.5$ Hz, $^3J = 5.0$ Hz, 1H, CH); 5.92 [q, $^3J(^1H–^{19}F) = ^3J = 13$ Hz, 1H, CH–CF_2]; 6.75 [dt, $^3J = ^4J(^1H–^{19}F) = 13$ Hz, $^4J(^1H–^{19}F) = 2$ Hz, 1H, CH–CO] ppm. ^{13}C NMR δ: 19.89/20.40 ($2CH_3$); 37.78/32.90/26.44 ($3CH_2$); 44.73 (CH); 47.88/49.14 (2C); 52.78 (CH_2–S); 64.97 (CH); 123.58 [t, $^3J(^{13}C–^{19}F) = 23.4$ Hz, *C*–CF_2]; 132.22 [t, $^4J(^{13}C–^{19}F) = 5.6$ Hz, *C*–CO]; 161.99 (CO) ppm. ^{19}F NMR δ: −81.2 (CF_3); −110.7 ($CF_{2\alpha}$); −122.0/−122.5/−123.2 ($4CF_{2\beta}$); −126.6 ($CF_{2\omega}$) ppm. Analysis: $C_{18}H_{16}F_{15}NO_3S$ (611.36) requires: C, 35.36; H, 2.64; N, 2.29%. Found: C, 34.9; H 2.58; N, 2.33%.

4. Conclusions

We have shown that *Z*- and *E*-3-*F*-alkyl 2-propenoates may be obtained with 100% stereoselectivity (a) by controlled hydrogenation of the corresponding alkyne to obtain the *Z*-

isomer and (b) by mild basic dehydration of 3-*F*-alkyl 3-hydroxypropanoates to obtain the *E*-isomer. The reaction of the ester with a phosphonate via reduction–olefination gives the *E*-isomer predominantly in one step.

These compounds have three reaction centres: the two unsaturated centres and the ester function. These centres can react selectively. In a preceding work, we have shown the reactivity of the olefinic function towards epoxidation [11] and here we show that the ester can react with a chiral auxiliary to induce stereoface selectivity. Further work on the reactivities of these products is in progress.

Acknowledgements

We wish to thank the Centre National de la Recherche Scientifique and the Ministère de la Recherche et de la Technologie for their financial support and Atochem for a gift of *F*-alkyl products.

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