ELSEVIER

Journal of Fluorine Chemistry 117 (2002) 161–166

JOURNAL OF FLUORINE CHEMISTRY

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Synthesis of 2-trifluoromethoxyethyl trifluoromethoxyacetate and derived 2-trifluoromethoxyacrylates

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Received 17 April 2002; received in revised form 27 May 2002; accepted 30 May 2002

Dedicated to Professor Lev M. Yagupolskii on the occasion of his 80th birthday.

Abstract

The synthesis of 2-trifluoromethoxyethyl trifluoromethoxyacetate **2** by oxidation of bis(2-trifluoromethoxyethyl)ether **1** followed by its anionic condensation with aldehydes, ketones and immonium salts under mild conditions, and further dehydration or deamination, enabled the preparation of 3-aryl and 3-alkyl-2-trifluoromethoxacrylates **8a–e** as well as the parent 2-trifluoromethoxyacrylate **8f**.

Keywords: Trifluoromethoxy group; Ether oxidation; Acrylates; Ester condensation; Aldehydes; Ketones; Eschenmoser salt

1. Introduction

The trifluoromethoxy group, which has been referred to as a super-halogen [1] or a pseudo-halogen [2], is perhaps the least well understood fluorine substituent [3]. A renewed interest seems to have arisen around this group, at least in the aromatic series [4]. In a recent publication in this journal [5], Rozen noted that: ''Aromatic trifluoromethyl ethers are well known and have many applications in the pharmaceutical and agricultural domains [...]. Aliphatic trifluoromethyl ethers, however, are rare and difficult to make''. This is mainly because there is no general direct method for the introduction of the OCF_3 group in aliphatic molecules [6]. Methyl trifluoromethoxy acetate for example has been prepared [7] using the carbonyl fluoride/sulfur tetrafluoride protocol ($ROH \rightarrow ROC(O)F \rightarrow ROCF_3$) [8]. Recent advances in the fluorodesulfurization reaction [5,9–11] enabled the preparation of some unfunctionalized aliphatic trifluoromethyl ethers under mild conditions (action of DBH and HF/pyridine to xanthates), avoiding the use of toxic reagents. Our own work in this area has shown that functional molecules bearing this group are now readily accessible by this methodology [12]. As a continuation of our efforts toward the elaboration of ready to use trifluoromethoxy bearing synthons, we address here the preparation of trifluoromethoxyacetate esters and the study of their transformation to 2-trifluoromethoxyacrylates derivatives. These compounds may find potential use in the preparation of polymers for example as core materials for optical waveguides [13].

2. Results and discussion

2.1. Preparation of 2-trifluoromethoxyethyl trifluoromethoxyacetate 2

We recently described the synthesis of bis(2-trifluoromethoxyethyl)ether **1** by action of DBH and HF/pyridine on a diethylene glycol bisxanthate, as well as its functionalization to 2-trifluoromethoxyethyl triflate [12]. We thought that this readily obtained compound may also be useful for the preparation of trifluoromethoxyacetate esters, provided that a suitable reagent could be found for its oxidation α to the central oxygen atom. Initial trials under Sharpless conditions [14] were unsuccessful, the starting material **1** being recovered unchanged after prolonged reaction time. Obviously a stronger oxidising agent was needed to effect the conversion to ester **2**. The powerful reagent dimanganese heptoxide was described as being able to oxidise smoothly simple aliphatic ethers in satisfactory yields at low temperature (−45 °C) [15]. In the case of ether **1**, we had to run the reaction at room temperature overnight to achieve complete conversion. Under these conditions and thanks to the symmetrical nature

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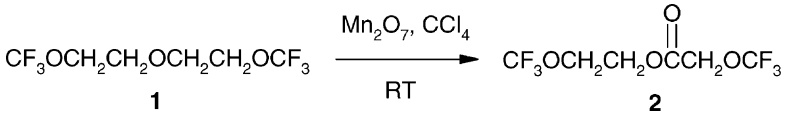
0022-1139/02/$ – see front matter
PII: S0022-1139(02)00152-5



Scheme 1.

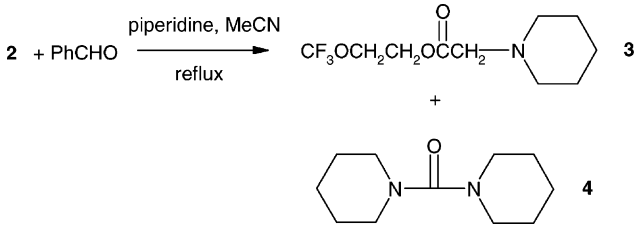
of ether **1**, the ester **2** could be obtained in 47% yield in a pure state after a simple filtration (Scheme 1).

2.2. Condensation of ester 2 with carbonyl compounds

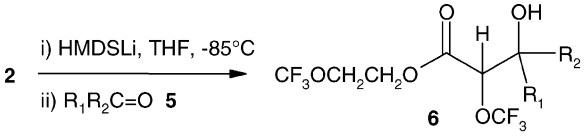
The chemistry of trifluoromethoxyacetates is poorly known [7]. We initially supposed, by analogy with our work on ethyl trifluoromethylthioacetate [16], that the Knoevenagel condensation of ester **2** with carbonyl compounds could be successful. Using the same conditions as before [16], we did not however observe the condensation of **2** with benzaldehyde (Scheme 2). Instead, we isolated the amino compound **3** as the major product (38%), resulting from the nucleophilic substitution of OCF_3 by piperidine. Thus, the behaviour of the trifluoromethoxy group in such reaction is closer to that expected for a chlorine atom rather than a fluorine atom or a trifluoromethylthio group. bis(Pentamethylene)urea **4** was also observed as a by product in this condensation. It possibly originates from further reaction of piperidine with carbonyl fluoride formed by decomposition of the trifluoromethoxide leaving group ($CF_3O^- \rightarrow COF_2 + F^-$).

Using conditions described earlier by our laboratory [17] for the preparation of the lithium enolate of ethyl fluoroacetate, later modified by Welch [18] (HMDSLi, THF, HMPA), we were however able to condense the anion of **2** with various carbonyl compounds **5a–e** (including a ketone **5e**) in satisfactory yields, provided that the temperature of the reaction medium is maintained at −85 °C (Scheme 3).

Using aldehydes **5a–d**, alcohols **6a–d** were thus obtained as inseparable mixtures of two diastereoisomers (55:45 to 70:30) retaining both trifluoromethoxy groups. No condensation product was observed using monomeric formaldehyde [19] under such conditions.



Scheme 2.



a : R_1 = Ph, R_2 = H
b : R_1 = 2-Furyl, R_2 = H
c : R_1 = Et, R_2 = H
d : R_1 = n-Hexyl, R_2 = H
e : R_1 = Me, R_2 = Me
f : R_1 = H, R_2 = H

Scheme 3.

2.3. Preparation of acrylates 8a–e by dehydration of alcohols 6a–e

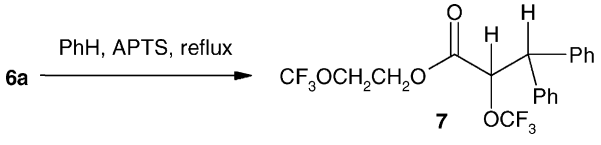
Alcohols **6a–e** obtained in the previous condensation proved unexpectedly stable towards dehydration conditions. In a preliminary attempt, we tried to dehydrate the phenyl derivative **6a** using azeotropic distillation of benzene in the presence of a trace of acid (PTSA). We did not observe however the clean formation of the desired acrylate **8a**. Instead, we isolated the diphenyl derivative **7** (74%) as the major product (Scheme 4).

Better results were obtained by holding a mixture of **6a**, powdered phosphorus pentoxide, and dry sand at 90 °C for 3 h, acrylate **8a** being isolated in 45% yield. Unfortunately, these dehydration conditions cannot be applied to alcohols **6b–e**. A more general method was found using thionyl chloride and pyridine as the dehydrating medium (Scheme 5) [20].

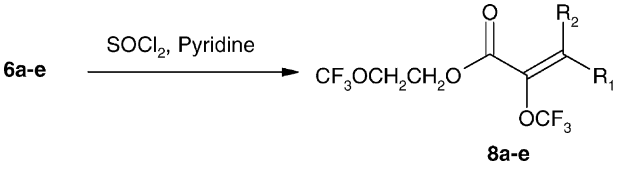
Using this combination of reagents, substituted acrylates **8a–e** were obtained in 20–95% yield with high *Z*-stereoselectivity (Table 1), as shown by the small $^3J_{(C=O,H)}$ coupling constants (2.2–4.4 Hz) between the carbonyl group and the vinylic hydrogen atom [21]. The lower yield was observed for the most sensitive substrate **8b** (entry 2).

2.4. Preparation of the parent acrylate 8f

As stated before, the parent acrylate **8f** (R_1 = H, R_2 = H) could not be obtained by condensation of the anion of **2** with formaldehyde. However, a related condensation could be



Scheme 4.

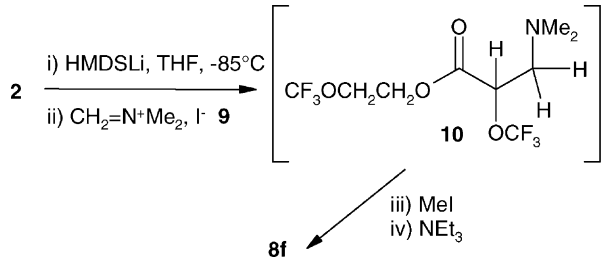


Scheme 5.

Table 1
Trifluoromethoxyacrylates derivatives **8** prepared

Entry	Product	Z/E[a]	Yield (%)[b]	$^3J_{C=O,H}$[c,d] (Hz)	$\delta_{H,acrylic}$ (ppm)
1	**8a**	100/0	54	4.4	7.49
2	**8b**	95/5	20	2.7	7.42
3	**8c**	97/3	86	2.2	6.77
4	**8d**	94/6	24	2.7	6.78
5	**8e**	–	95	–	–
6	**8f**	–	3	ND	5.74, 6.23

[a] Ratio determined by ^{19}F NMR analysis of the crude mixture.
[b] Isolated yields of *Z* isomer.
[c] For the *Z* isomer.
[d] Coupling constants were determined with simultaneous selective decoupling of the $CH_2O(CO)$ protons.



Scheme 6.

achieved using the Eschenmoser salt **9** (Scheme 6) albeit in low yield (Table 1, entry 6).

The intermediate amine **10** was not isolated. Upon quaternisation (MeI) followed by mild basic treatment (NEt_3), we observed the smooth formation of acrylate **8f**.

3. Conclusion

We have shown that trifluoromethoxyethyl trifluoromethoxyacetate **2** could be prepared by oxidation of fluorinated glyme **1**. Condensation of the anion of **2** with various carbonyl compounds or derivatives, followed by dehydration, afforded substituted or unsubstituted trifluoromethoxyacrylates **8a–f**.

4. Experimental

NMR spectra were recorded otherwise stated as $CDCl_3$ solutions, on a Bruker AC-300 spectrometer. Reported coupling constants and chemicals shifts were based on a first order analysis. Internal reference was the residual peak of $CHCl_3$ (7.27 ppm) for ^1H NMR (300 MHz), central peak of $CDCl_3$ (77 ppm) for ^{13}C NMR (75 MHz) spectra and internal $CFCl_3$ (0 ppm) for ^{19}F NMR (282 MHz) spectra. IR spectra were recorded as CCl_4 solutions on an Impact 400D Nicolet spectrophotometer. High resolution mass spectra were performed with a Finnigan MAT 95S spectrometer.

4.1. Oxidation of bis(2-trifluoromethoxyethyl)ether 1 by dimanganese heptoxide

A ca. 1 M solution of dimanganese heptoxide in CCl_4 (25 ml) was added to a solution of the fluorinated ether **1** (3 g, 12.4 mmol) in 40 ml CCl_4. The mixture was stirred overnight, filtered over a pad of Celite® and washed with diethylether. The filtrate was evaporated under vacuum to give 1.5 g (47%) of 2-trifluoromethoxyethyl trifluoromethoxyacetate (**2**) as a colourless liquid. Boiling point (Siwoloboff) 154–156 °C. Found: C, 28.07; H, 2.40%. $C_6H_6F_6O_4$ requires: C, 28.14; H, 2.36%. ^1H NMR δ (ppm): 4.16–4.21 and 4.42–4.47 (2× 2H, 2× m, CH_2CH_2); 4.56 (2H, s, $CF_3OCH_2C(O)$). ^{19}F NMR δ (ppm): −61.7 and −62.1 (2× s, CF_3). ^{13}C NMR δ (ppm): 62.68 ($C(O)OCH_2$); 62.7 (q, $J_{CF} = 3.7$ Hz, $CF_3OCH_2C(O)$); 121.39 and 121.44 (2× q, $J_{CF} = 257$ and 255 Hz, CF_3); 165.8 (C=O). IR (CCl_4) 1764 cm^{-1}. MS (EI) *m/z*: 257 ($M^{+\bullet}$, 1); 129 (13); 113 (42); 99 (100%).

4.2. Preparation of the anion of 2-trifluoromethoxyethyl trifluoromethoxyacetate 2

HMPA (0.34 ml, 2 mmol) followed by 2-trifluoromethoxyethyl trifluoromethoxyacetetate **2** (0.5 g, 2 mmol) was added to a solution of lithium bis(trimethylsilyl)amide (prepared from a solution of 5.9 mmol of hexamethyldisilazane in 20 ml THF and 5.9 mmol of methyllithium in diethylether under argon) cooled to −85 °C.

4.3. Condensation of 2-trifluoromethoxyethyl trifluoromethoxyacetate 2 with carbonyl compounds

4.3.1. Attempted condensation of 2-trifluoromethoxyethyl trifluoromethoxyacetate 2 with benzaldehyde in the presence of piperidine

A solution of ester **2** (0.3 g, 1.2 mmol), benzaldehyde (0.12 g, 1.13 mmol) and piperidine (0.24 ml, 2.4 mmol) in acetonitrile (20 ml) was refluxed for 3 days. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel; pentane/diethylether solvent gradient). Earlier fractions contained unreacted benzaldehyde followed by bis(pentamethylene)urea **4** identified by comparison of its spectral characteristics with published data. Further fractions (diethylether) were pooled and distilled (Kugelrohr, 150 °C, 10 mmHg) to give (110 mg, 38%) of 2-trifluoromethoxyethyl piperidinoacetate (**3**) as a colourless oil. ^1H NMR δ (ppm): 1.32–1.50 (2H, m, $NCH_2CH_2CH_2$); 1.53–1.70 (4H, m, NCH_2CH_2); 2.42–2.54 (4H, m, NCH_2); 3.16 (2H, s, NCH_2CO); 4.11–4.20 and 4.28–4.39 (4H, 2m, $CF_3OCH_2CH_2$). ^{19}F NMR δ (ppm): −61.6 (s, CF_3). ^{13}C NMR δ (ppm): 23.7 (1C, $NCH_2CH_2CH_2$); 25.7 (2C, NCH_2CH_2); 54.2 (2C, NCH_2); 59.9 and 61.3 ($CH_2C(O)OCH_2$); 64.9 (q, $J_{CF} = 3.2$ Hz, CF_3OCH_2); 121.4 (q, $J_{CF} = 255$ Hz, CF_3); 170.3 (C=O). IR (CCl_4) 1769 cm^{-1}. MS (EI) *m/z*: 255 ($M^{+\bullet}$, 3); 98 (100%).

*4.3.2. Condensation of the anion of 2-trifluoromethoxyethyl trifluoromethoxyacetate **2** with carbonyl compounds*

The anion of 2-trifluoromethoxyethyl trifluoromethoxyacetate **2** was prepared as before (Section 4.2). After 5 min stirring, the carbonyl compound **5** (2 mmol) was added rapidly at −85 °C. The reaction was then held at −78 °C for 30 min before the addition of a saturated ammonium chloride solution (4 ml). The temperature was raised to 20 °C and the mixture was diluted with hexane (60 ml) and water (20 ml). The organic layer was washed with diluted hydrochloric acid (2 M) until acidic, then with water and dried (4 Å molecular sieves). After the removal of the solvents, the residue was eluted on a silica gel column (40/60, diethylether/pentane) affording the condensation product **6**. Yields and part of the NMR data are shown in Table 1.

2-Trifluoromethoxyethyl 3-hydroxy-3-phenyl-2-trifluoromethoxypropionate **6a**. A 36% yield, oily mixture (40/60) of diastereoisomers. Found: C, 43.35; H, 3.39%. $C_{13}H_{12}F_6O_5$ requires: C, 43.11; H, 3.34%. ^{1}H NMR δ (ppm): 2.61 and 2.69 (1H, 2× br s, OH major and minor isomers); 3.90–4.15 (2H, m, CF_3OCH_2 both isomers); 4.20–4.43 (2H, m, $CF_3OCH_2CH_2$ both isomers); 4.73 and 4.79 (1H, 2× d, minor isomer $J = 5.6$ Hz and major isomer $J = 5.9$ Hz, CF_3OCH); 5.1–5.2 (1H, br s, PhC*H* both isomers); 7.4–7.5 (5H, br s, ArH). ^{19}F NMR δ: −60.47 and −61.75 (2× s, CF_3 major isomer); −60.5 and −61.73 (2× s, CF_3 minor isomer). ^{13}C NMR δ (ppm): (major isomer) 62.7 ($C(O)OCH_2$); 64.4 (q, $J_{CF} = 3.5$ Hz, CF_3OCH_2); 73.5 (CHOH); 78.2 (q, $J_{CF} = 2.3$ Hz, CF_3OCH); 121.2 and 121.4 (2× q, $J_{CF} = 258$ and 255 Hz, CF_3); 126.5 (2C, ArC); 128.6 (2C, ArC); 129.0 (ArC); 137.5 (quaternary ArC); 166.7 (C=O); (minor isomer) 62.3 (q, $J_{CF} = 3.5$ Hz, CF_3OCH_2); 62.7 ($C(O)OCH_2$); 73.8 (CHOH); 79.3 (q, $J_{CF} = 2.3$ Hz, CF_3OCH); 121.2 and 121.3 (2× q, $J_{CF} = 258$ and 255 Hz, CF_3); 126.5 (2C, ArC); 128.7 (2C, ArC); 129.1 (ArC); 136.7 (quaternary ArC); 166.6 (C=O). IR (CCl_4) 3677; 1752 cm^{-1}. MS (EI) *m/z*: 362 ($M^{+\bullet}$, 1); 345 (10); 107 (100%).

2-Trifluoromethoxyethyl 3-hydroxy-3-furyl-2-trifluoromethoxypropionate **6b**. A 50% yield, oily mixture (66/34) of diastereoisomers. Found: C, 37.77; H, 2.44%. $C_{11}H_{10}F_6O_6$ requires: C, 37.51; H, 2.86%. ^{1}H NMR δ (ppm): 2.70 and 2.78 (1H, 2× d, $J = 7.2$ and 8.2 Hz, OH major and minor isomers); 4.10–4.20 (2H, m, CF_3OCH_2 both isomers) 4.40–4.50 (2H, m, $CF_3OCH_2CH_2$ both isomers); 4.95 and 4.97 (1H, 2× d, minor isomer $J = 4.6$ Hz and major isomer $J = 5.9$ Hz, CF_3OCH); 5.10–5.20 (1H, m, C*H*OH both isomers); 6.36–6.40 (1H, m, 4-furyl-H both isomers); 6.41–6.50 (1H, m, 3-furyl-H both isomers); 7.43 (1H, br s, 5-furyl-H both isomers). ^{19}F NMR δ (ppm): −60.64 and −61.85 (2× s, CF_3 both isomers). ^{13}C NMR δ (ppm): (major isomer) 63.1 ($C(O)OCH_2$); 64.5 (q, $J_{CF} = 3.3$ Hz, CF_3OCH_2); 67.8 (CHOH); 76.5 (q, $J_{CF} = 2.2$ Hz, CF_3OCH); 109.1 and 110.6 (3- and 4-furyl-C); 123.2 and 123.3 (2× q, $J_{CF} = 258$ and 256 Hz, CF_3); 143.2 (5-furyl-C); 150.3 (2-furyl-C); 166.5 (C=O); (minor isomer) 62.9 ($C(O)OCH_2$); 64.5 (q, $J_{CF} = 3.8$ Hz, CF_3OCH_2); 68.4 (CHOH); 77.0 (q, $J_{CF} = 2.2$ Hz, CF_3OCH); 108.8 and 110.6 (3- and 4-furyl-C); 123.2 and 123.3 (2× q, $J_{CF} = 258$ and 256 Hz, CF_3); 143.1 (5-furyl-C); 150.2 (2-furyl-C); 166.4 (C=O). IR (CCl_4) 3480; 1758 cm^{-1}. MS (EI) *m/z*: 352 ($M^{+\bullet}$, 15); 266 (17); 69 (100%).

2-Trifluoromethoxyethyl 3-hydroxy-2-trifluoromethoxyvalerate **6c**. A 50% yield, oily mixture (70/30) of diastereoisomers. Found: C, 34.51; H, 3.91%. $C_9H_{12}F_6O_5$ requires: C, 34.41; H, 3.85%. ^{1}H NMR δ (ppm): 1.03 and 1.04 (3H, 2× t, major isomer $J = 7.6$ Hz and minor isomer $J = 7.3$ Hz, CH_3); 1.51–1.74 (2H, m, CH_2CHOH both isomers); 2.15 and 2.30 (1H, 2× br s, OH minor and major isomer); 3.88–4.01 (1H, m, C*H*OH both isomers); 4.16–4.23 (2H, m, CF_3OCH_2 both isomers); 4.36–4.57 (2H, m, $CF_3OCH_2CH_2$ both isomers); 4.59 and 4.61 (1H, 2× d, minor isomer $J = 3.3$ Hz and major isomer $J = 4.6$ Hz, CF_3OCH). ^{19}F NMR δ (ppm): −60.38 and −61.88 (2× s, CF_3 major isomer); −60.38 and −61.84 (2× s, CF_3 minor isomer). ^{13}C NMR δ (ppm): (major isomer) 9.5 (CH_3); 25.2 (CH_2CH_3); 62.6 ($C(O)OCH_2$); 64.5 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 72.9 (CHOH); 77.9 (q, $J_{CF} = 2.8$ Hz, CF_3OCH); 123.1 and 123.1 (2× q, $J_{CF} = 257$ and 256 Hz, CF_3); 167.0 (C=O); (minor isomer) 9.5 (CH_3); 25.8 (CH_2CH_3); 62.7 ($C(O)OCH_2$); 64.5 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 73.0 (CHOH); 77.4 (q, $J_{CF} = 2.6$ Hz, CF_3OCH); 123.1 and 123.2 (2× q, $J_{CF} = 258$ and 254 Hz, CF_3); 167.3 (C=O). IR (CCl_4) 3480; 1763 cm^{-1}. MS (EI) *m/z*: 314 ($M^{+\bullet}$, 1); 256 (100%).

2-Trifluoromethoxyethyl 3-hydroxy-2-trifluoromethoxynonanoate **6d**. A 24% yield, oily mixture (55/45) of diastereoisomers. Found: C, 42.48; H, 5.21%. $C_{13}H_{20}F_6O_5$ requires: C, 42.17; H, 5.45%. ^{1}H NMR δ (ppm): 0.85–0.95 (3H, m, CH_3 both isomers); 1.23–1.43 (8H, m, $(CH_2)_4$ both isomers); 1.50–1.70 (2H, m, CH_2CHOH both isomers); 2.5 (1H, br s, OH both isomers); 3.98–4.10 (1H, m, C*H*OH both isomers); 4.17–4.24 (2H, m, CF_3OCH_2 both isomers); 4.40–4.56 (2H, m, $CF_3OCH_2CH_2$ both isomers); 4.57 and 4.61 (1H, 2× d, minor isomer $J = 3.3$ Hz and major isomer $J = 4.3$ Hz, CF_3OCH). ^{19}F NMR δ (ppm): −60.36 and −61.88 (2× s, CF_3 major isomer); −60.38 and −61.91 (2× s, CF_3 minor isomer). ^{13}C NMR δ (ppm): (major isomer) 13.9 (CH_3); 22.5, 25.2, 28.9, 31.6, 32.7 (($CH_2)_5$); 62.6 ($C(O)OCH_2$); 64.5 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 71.7 (CHOH); 78.3 (q, $J_{CF} = 2.3$ Hz, CF_3OCH); 123.1 and 123.1 (2× q, $J_{CF} = 258$ and 256 Hz, CF_3); 167.3 (C=O); (minor isomer) 13.9 (CH_3); 22.5, 25.3, 28.9, 31.6, 32.0 (($CH_2)_5$); 62.7 ($C(O)OCH_2$); 64.51 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 71.6 (CHOH); 77.8 (q, $J_{CF} = 2.3$ Hz, CF_3OCH); 123.1 and 123.1 (2× q, $J_{CF} = 258$ and 256 Hz, CF_3); 167.9 (C=O). IR (CCl_4) 3454; 1767 cm^{-1}. MS (EI) *m/z*: 370 ($M^{+\bullet}$, 1); 256 (100%).

2-Trifluoromethoxyethyl 3-hydroxy-2-trifluoromethoxyisovalerate **6e**. A 31% yield, oil. Found: C, 34.15; H, 3.68%. $C_9H_{12}F_6O_5$ requires: C, 34.41; H, 3.85%. ^{1}H NMR δ (ppm): 1.34 and 1.35 (2× 3H, 2× s, $C(CH_3)_2$); 2.45 (1H, br s, OH); 4.18–4.23 (2H, m, CF_3OCH_2); 4.40–4.55 (2H, m, $CF_3OCH_2CH_2$); 4.45 (1H, s, CF_3OCH). ^{19}F NMR δ (ppm): −60.60 and −61.95 (2× s, CF_3). ^{13}C NMR δ

(ppm): 25.1 and 25.3 ($C(CH_3)_2$); 62.5 ($C(O)OCH_2$); 64.4 (q, $J_{CF} = 3.3$ Hz, CF_3OCH_2); 71.3 ($C(CH_3)_2$); 80.9 (q, $J_{CF} = 2.2$ Hz, CF_3OCH); 123.1 and 123.1 (2× q, $J_{CF} = 260$ and 257 Hz, CF_3); 167.3 (C=O). IR (CCl_4) 3677; 1767 cm^{-1}. MS (EI) *m/z*: 315 ($M^{+\bullet} + 1$, 55); 297 (52), 213 (63), 171 (92), 59 (100%).

*4.3.3. Dehydration of alcohols **6a–e** with p-toluenesulfonic acid*

A mixture of alcohol **6a** (20 mg, 0.053 mmol) in benzene (20 ml) containing *p*-toluenesulfonic acid was refluxed for 24 h in a Dean–Stark apparatus. The solvent was then removed under reduced pressure and the residue purified by TLC (SiO_2, dichloromethane) affording diphenyl adduct **7** (17 mg, 74%) as an oil: ^{1}H NMR δ (ppm): 3.75–3.97 (2H, m, CF_3OCH_2); 4.04–4.31 (2H, m, $CF_3OCH_2CH_2$); 4.52 (1H, d, $J_{CF} = 8.6$ Hz, CF_3OCH or $CHPh_2$); 5.24 (1H, d, $J_{CF} = 8.6$ Hz, $CHPh_2$ or CF_3OCH); 7.24–7.37 (10H, m, ArH). ^{19}F NMR δ (ppm): −60.5 and −61.7 (2× s, CF_3). ^{13}C NMR δ (ppm): 53.4 ($CHPh_2$); 62.5 ($CH_2OC(O)$); 64.3 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 77.8 (q, $J_{CF} = 2.5$ Hz, CF_3OCH); 121.2 and 121.4 (2× q, $J_{CF} = 258$ and 255 Hz, CF_3); 127.5 and 127.7 (2C, ArC); 128.3 and 128.5 (4C, ArC); 128.7 (4C, ArC); 137.8 and 138.0 (2C, ArC). MS (EI) *m/z*: 422 ($M^{+\bullet}$, 1); 167 (100%).

*4.3.4. Dehydration of alcohols **6a–e** with thionyl chloride*

Thionyl chloride (5 ml) was added dropwise to a stirred solution of the alcohol **6** (0.25 mmol) in dry pyridine (8 ml) cooled on an ice bath. The mixture was slowly raised to room temperature and stirred for 18 h. The reaction was quenched with ice and extracted with dichloromethane. The organic phase was washed with water and dried ($MgSO_4$). After removal of the solvents, the remaining residue was purified by column chromatography (silica gel; pentane/diethylether: 90/10).

2-Trifluoromethoxyethyl 3-phenyl-2-trifluoromethoxyacrylate (*Z*) **8a**. Oil; HRMS Found: 344.0479. $C_{13}H_{10}F_6O_4$ requires: 344.0483. ^{1}H NMR δ (ppm): 4.24-4.29 (2H, m, CF_3OCH_2); 4.49–4.55 (2H, m, $CF_3OCH_2CH_2$); 7.40–7.47 (3H, m, ArH); 7.49 (1H, s, =CH); 7.69–7.78 (2H, m, ArH). ^{19}F NMR δ (ppm): −57.6 (s, =C–OCF_3); −61.7 (s, CH_2OCF_3). ^{13}C NMR δ (ppm): 62.8 ($C(O)OCH_2$); 64.7 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 120.6 and 121.5 (2× q, $J_{CF} = 261$ and 255 Hz, CF_3); 128.8 (2C, ArC); 130.6 (quaternary ArC); 130.9 (2C, ArC); 130.95 (ArC); 132.3 (=CH); 134.0 (q, $J_{CF} = 1.9$ Hz, $=C=OCF_3$); 162.0 (C=O). IR (CCl_4) 1739; 1650 cm^{-1}. MS (EI) *m/z*: 344 ($M^{+\bullet}$, 100%).

2-Trifluoromethoxyethyl 3-furyl-2-trifluoromethoxyacrylate (*Z*) **8b**. Oil. HRMS Found: 335.0358. $C_{11}H_8F_6O_5$ requires: 335.0354. ^{1}H NMR δ (ppm): 4.22–4.28 (2H, m, CF_3OCH_2); 4.47–4.53 (2H, m, $CF_3OCH_2CH_2$); 6.57 (1H, dd, $J = 3.2$ and 1.7 Hz, 4-furyl-H); 7.03 (1H, d, $J = 3.3$ Hz, 3-furyl-H); 7.42 (1H, s, =CH); 7.61 (1H, d, $J = 1.7$ Hz, 5-furyl-H). ^{19}F NMR δ (ppm): −57.5 (s, =C-OCF_3); −61.7 (s, CH_2OCF_3). ^{13}C NMR δ (ppm): 62.8 ($C(O)OCH_2$); 64.8 (q, $J_{CF} = 3.8$ Hz, CF_3OCH_2); 112.9 (4-furyl-C); 118.1 (=CH); 120.7 (3-furyl-C); 122.6 and 123.3 (2× q, J_{CF} =260 and 255 Hz, CF_3); 131.3 (q, $J_{CF} = 2.2$ Hz, $=C$–OCF_3); 145.9 (5-furyl-C); 147.0 (2-furyl-C); 161.8 (C=O). IR (CCl_4) 1731; 1644 cm^{-1}. MS (EI) *m/z*: 344 ($M^{+\bullet}$, 100%).

2-Trifluoromethoxyethyl 3-ethyl-2-trifluoromethoxyacrylate (*Z*) **8c**. Oil. Found: C, 36.08; H, 3.51%. $C_9H_{10}F_6O_4$ requires: C, 36.50; H, 3.40%. ^{1}H NMR δ (ppm): 1.11 (3H, t, $J = 7.5$ Hz, CH_3); 2.37 (2H, quint., $J = 7.5$ Hz, CH_2CH=); 4.17–4.25 (2H, m, CF_3OCH_2); 4.42–4.48 (2H, m, $CF_3OCH_2CH_2$); 6.77 (1H, t, $J = 7.9$ Hz, =CH). ^{19}F NMR δ (ppm): −58.7 (s, =C–OCF_3); −61.7 (s, CH_2OCF_3). ^{13}C NMR δ (ppm): 13.0 (CH_3); 20.6 (=$CHCH_2$); 62.2 ($C(O)OCH_2$); 64.6 (q, $J_{CF} = 3.5$ Hz, CF_3OCH_2); 122.3 (q, $J_{CF} = 257$ Hz, CF_3); 123.2 (q, $J_{CF} = 254$ Hz, CF_3); 135.6 (q, $J_{CF} = 2.2$ Hz, $=C$–OCF_3); 139.0 (=CH); 161.2 (C=O). IR (CCl_4) 1747; 1660 cm^{-1}. MS (EI) *m/z*: 296 ($M^{+\bullet}$, 5); 113 (77); 84 (55); 69 (100%).

2-Trifluoromethoxyethyl 3-hexyl-2-trifluoromethoxyacrylate (*Z*) **8d**. Oil. Found: C, 44.62; H, 5.11%. $C_{13}H_{18}F_6O_4$ requires: C, 44.32; H, 5.155%. ^{1}H NMR δ: 0.86-0.96 (3H, m, CH_3); 1.25–1.55 (8H, m, $(CH_2)_4$); 2.35 (2H, dt, $J = 7.5$ and 7.4 Hz, CH_2CH=); 4.19-4.24 (2H, m, CF_3OCH_2); 4.43–4.48 (2H, m, $CF_3OCH_2CH_2$); 6.78 (1H, t, $J = 7.7$ Hz, =CH); ^{19}F NMR δ (ppm): −58.6 (s, =C–OCF_3); −61.8 (s, CH_2OCF_3). ^{13}C NMR δ (ppm): 13.9 (CH_3); 22.5, 26.3, 27.9, 28.9, 31.4 ($(CH_2)_5$); 62.5 ($C(O)OCH_2$); 64.7 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 120.6 (q, $J_{CF} = 259$ Hz, CF_3); 121.5 (q, $J_{CF} = 255$ Hz, CF_3); 123.2 (=C–OCF_3); 138.2 (=CH); 161.3 (C=O). IR (CCl_4) 1737; 1650 cm^{-1}. MS (CI, NH_3) *m/z*: 387 ($M^{+\bullet} + 2NH_3$, 25); 370 (100); 252 (6%).

2-Trifluoromethoxyethyl 3,3-dimethyl-2-trifluoromethoxyacrylate **8e**. Oil. Found: C, 36.07; H, 3.49%. $C_9H_{10}F_6O_4$ requires: C, 36.50; H, 3.40%. ^{1}H NMR δ (ppm): 1.99 and 2.21 (6H, 2s, CH_3); 4.18–4.24 (2H, m, CF_3OCH_2); 4.41–4.47 (2H, m, $CF_3OCH_2CH_2$). ^{19}F NMR δ (ppm): −58.9 (s, =C–OCF_3); −61.9 (s, CH_2OCF_3). ^{13}C NMR δ (ppm): 20.3 and 21.0 ($2CH_3$); 62.0 ($C(O)OCH_2$); 64.7 (q, $J_{CF} = 3.5$ Hz, CF_3OCH_2); 121.1 (q, $J_{CF} = 258$ Hz, CF_3); 121.6 (q, $J_{CF} = 255$ Hz, CF_3); 131.8 (q, $J_{CF} = 2.0$ Hz, $=C$–OCF_3); 136.30 ($=C(CH_3)_2$); 161.8 (C=O). IR (CCl_4) 1721; 1655 cm^{-1}. MS (CI, NH_3) *m/z*: 331 ($M^{+\bullet} + 2NH_3$, 35); 314 ($M^{+\bullet} + NH_3$, 100); 296 ($M^{+\bullet}$, 3%).

*4.4. Synthesis of 2-trifluoromethoxyethyl 2-trifluoromethoxyacrylate **8f***

The anion of 2-trifluoromethoxyethyl trifluoromethoxyacetate **2** was prepared as before (Section 4.2) from 4 mmol of ester. Solid Eschenmoser salt **9** (3.7 g, 20 mmol) was then slowly added. The mixture was stirred for 2.5 h at −78 °C before the addition of saturated ammonium chloride solution (4 ml), neutralization with 1 M hydrochloric acid and extraction with ethyl acetate. The organic phase was washed with water and dried ($MgSO_4$). After removal of the solvent, the residue was eluted on a silica gel column (pentane/diethyl-

ether: 60/40). The fraction with Rf 0.45 (160 mg) was collected and stirred for 12 h with methyl iodide (1 ml). Triethylamine (5 ml) was then added and the mixture was stirred for additional 12 h. After concentration, the residue was purified by TLC (SiO_2, pentane/diethylether: 90/10) to give 30 mg (0.11 mmol, 3%) of 2-trifluoromethoxyethyl 2-trifluoromethoxyacrylate **8f** as an oil. HRMS Found: 269.0256. $C_7H_7F_6O_4$ requires: 269.0249. ^{1}H NMR δ (ppm): 4.21–4.26 (2H, m, CF_3OCH_2); 4.46–4.51 (2H, m, $CF_3OCH_2CH_2$); 5.74 (1H, dq, $J_{HH} = 2.6$, $J_{HF} = 1.3$ Hz, =CHa); 6.23 (1H, dq, $J_{HH} = 2.6$, $J_{HF} = 1.3$ Hz, =CHb). ^{19}F NMR δ (ppm): −59.5 (s, =C–OCF_3); −61.7 (s, CH_2OCF_3). ^{13}C NMR δ (ppm): 63.0 (C(O)OCH_2); 64.5 (q, $J_{CF} = 3.4$ Hz, CF_3OCH_2); 121.9 (q, $J_{CF} = 259$ Hz, CF_3); 123.2 (q, $J_{CF} = 255$ Hz, CF_3); 114.7 (q, $J_{CF} = 1.1$ Hz, $=CH_2$); 142.3 (q, $J_{CF} = 1.7$ Hz, =*C*–OCF_3); 160.3 (C=O). IR (CCl_4) 1751; 1639 cm^{-1}.

Acknowledgements

This work enters in the frame of the European TMR programme ERB FMRX-CT970120, entitled ''Fluorine As a Unique Tool for Engineering Molecular Properties''.

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