Stereoselective Synthesis of Both Enantiomers of Trifluoro-γ-valerolactone and Pentafluoro-γ-caprolactone

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Both enantiomers of 5-(trifluoromethyl)dihydrofuran-2-one (**1a**) and 5-(pentafluoroethyl)dihydrofuran-2-one (**1b**) have been synthesised stereoselectively, in four steps, starting from chiral (*R*)- or (*S*)-3-[(4-methylphenyl)sulfinyl]propionic acid (**2**) and commercially available perfluorinated esters. Compound (+)-(*S*)-**1b** is the pentafluoro analogue of the aggregation pheromone of *Trogoderma glabrum*.

Introduction

The quasi-isosteric substitution of a fluorine atom for hydrogen in insect pheromones can alter the perception of the natural substrate by competitive binding of the fluorinated analogue with specific pheromone receptors, giving rise to disruption of the mating communication system.[1] This could represent an environmentally friendly, highly selective strategy for insect pest control,[2] and a clever alternative to insecticides, whose use is generally affected by serious ecological drawbacks.

The γ-lactone nucleus is a rather common substructure in pheromones. In this context, we have described a stereoselective synthesis of enantiomerically pure β-fluoroalkyl-γ-lactones,[3] based on a novel application of Marino's sulfoxide-directed lactonization.[4] Recently, we became interested in enantiomerically pure γ-fluoroalkyl-γ-lactones, such as **1a** and **1b** (Figure 1). The latter is a pentafluoro analogue of (+)-(*R*)-γ-caprolactone, a pheromone of several *Dermestidae* beetles.[5] In spite of their simple molecular structure, to the best of our knowledge only a couple of syntheses of enantiopure γ-perfluoroalkyl-γ-lactones have been described in the literature, in both cases concerning the trifluoromethyl (Tfm) derivative **1a**.[6,7] In this paper we present a stereoselective entry to 5-Tfm-dihydrofuran-2-one (*R*)-**1a**, 5-C_2F_5-dihydrofuran-2-one (*S*)-**1b**, and their enantiomers.

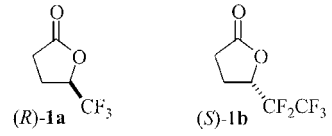
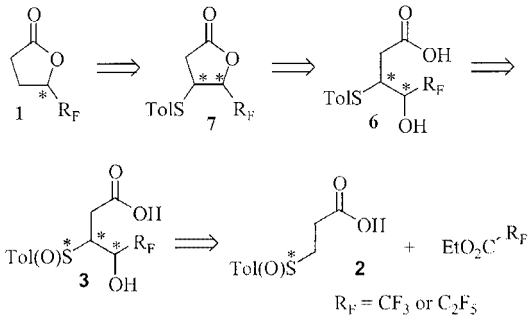


Figure 1. Enantiomerically pure 5-Tfm and 5-C_2F_5 γ-lactones

The strategy for the preparation of **1** (Scheme 1) is based on the assembly of enantiopure (*R*)- or (*S*)-3-(*p*-tolylsulfinyl)propionic acid (**2**) with commercially available perfluorinated acetic (R_F = CF_3) or propionic (R_F = C_2F_5) esters.[8] The stereogenic steps of the synthesis are: (1) the *C*-fluoroacylation of the *C*,*O*-dilithium derivative of **2**, and (2) the crucial carbonyl reduction of the intermediate β-ketosulfoxides to install the carbinolic stereocentre of the sulfinyl alcohols **3**.[9] Deoxygenation of the sulfinyl group to give **6**, followed by lactonization to **7**, and final reductive desulfenylation lead to the final targets **1**.



Scheme 1. Retrosynthetic analysis

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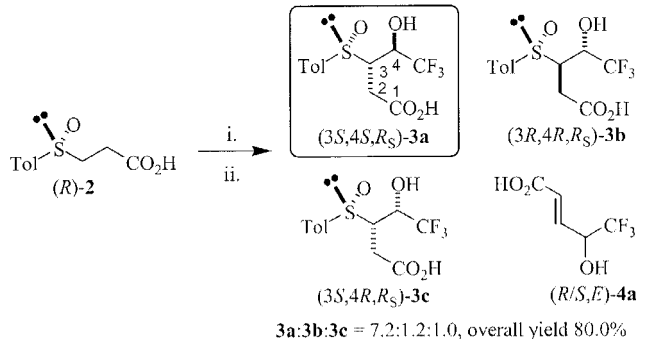
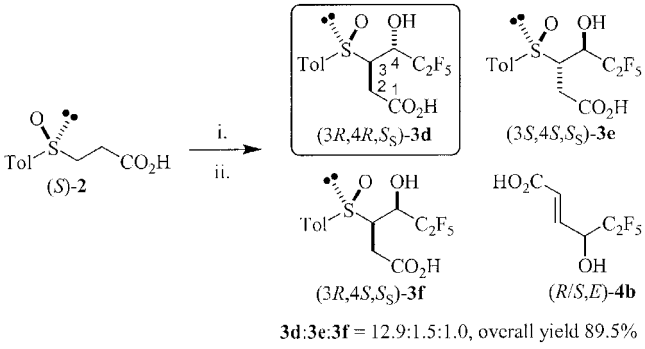
Results and Discussion

Synthesis of the β-Sulfinyl-γ-hydroxy Acids 3

The dilithium derivatives of enantiomerically pure (*R*)- or (*S*)-3-(sulfinyl)propionic acids **2** were condensed on ethyl trifluoroacetate (Scheme 2) and ethyl pentafluoropropionate (Scheme 3), respectively. Both reactions proceeded smoothly, although the intermediate 3-sulfinyl-4-oxo-4-fluoroalkylcarboxylic acids gave partial elimination of *p*-TolSOH during the workup, producing the α,β-unsaturated acids **4a,b** as by-products.



Scheme 2. Key: i) 1. LDA (2.0 equiv.), THF, −60 °C; 2. CF_3CO_2Et, THF, −70 °C; 3. 1 N HCl (pH 2); ii) 1. $NaBH_4$, THF/H_2O, 0 °C; 2. 1 N HCl (pH 2)

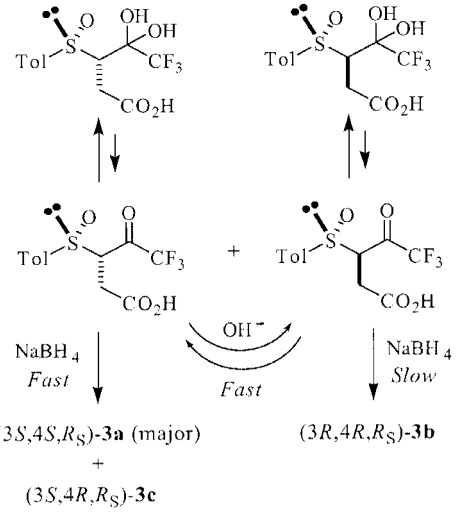


Scheme 3. Key: i) 1. LDA (2.0 equiv.), THF, − 60 °C; 2. $C_2F_5CO_2Et$, THF, − 70 °C; 3. 1 N HCl (pH 2); ii) 1. $NaBH_4$, THF/H_2O, 0 °C; 2. 1 N HCl (pH 2)

The crude products were rapidly treated with $NaBH_4$ to give the γ-fluoroalkyl-γ-hydroxy-β-sulfinylcarboxylic acids **3**,[10,11] which proved to be sufficiently stable to allow purification by flash chromatography (FC) and spectroscopic characterisation.[12]

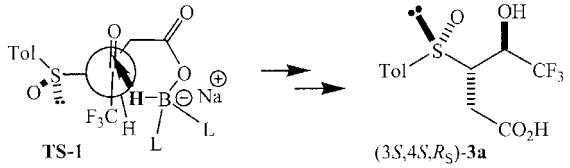
The two series of sulfinyl carbinols **3a−c** (Tfm derivatives) and **3d−f** (C_2F_5 derivatives), having opposite configurations due to the use of the enantiomeric starting materials (*R*)- and (*S*)-**2**, were produced with analogous stereochemical outcome and very good stereocontrol, which was totally unexpected on the basis of both our previous experience and literature reports on poorly stereoselective reductions of similar substrates by action of borohydrides.[9,13] In this case, three of the four possible diastereomers were obtained in very good overall yields, with a remarkable 3,4-*anti*-simple diastereoselectivity, in ratios **3a,b/3c** = 8.4:1.0 and **3d,e/3f** = 14.4:1.0.[14] The predominant diastereomers **3a** and **3d** were isolated by flash chromatography (FC) in 62 and 75% yields, and constituted 77 and 84%, respectively, of the whole mixtures of products, showing that the overall facial diastereocontrol was also very good.

A reasonable stereochemical outcome of the reaction is as follows. Fluoroacylation is probably a nonstereoselective process (Scheme 4), as already observed for analogous reactions,[9,13] affording a nearly equimolar mixture of two intermediate β-keto-sulfoxides epimers at C(3) in equilibrium with their *gem*-diol forms. Under the basic reduction conditions ($NaBH_4$, THF/H_2O) a stereoconvergent dynamic kinetic resolution should take place, whereby the oxo-form of the (3*S*)-diastereomer is reduced at a higher rate than the (3*R*)-diastereomer, which in turn is epimerised at C(3), regenerating the (3*S*)-substrate.[15]



Scheme 4. Stereoselective formation of **3a** by $NaBH_4$ reduction with dynamic kinetic resolution

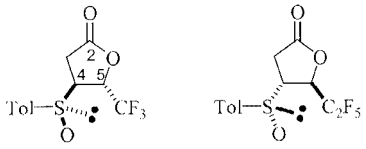
The good diastereocontrol in favour of **3a** may be due to the fact that hydride delivery takes place *intramolecularly* by action of an intermediate acyloxy borohydride (Scheme 5), which might be the actual reducing species, through the Felkin−Ahn model **TS-1**.[16] An analogous stereochemical outcome can be envisaged for the formation of the C_2F_5 derivative **3d**, through a quasi-enantiomeric model.



Scheme 5. Model for the stereoselective $NaBH_4$ reduction

Surprisingly, the lactonisation process did not take place spontaneously for **3a** and **3d**. In fact, at the end of the purification by FC on silica gel, only small amounts of *trans* sulfinyl lactones **5c** and **5f** (Figure 2) arising from the minor **3c** and **3f** *syn* precursors were detected. The *cis* sulfinyl lactones arising from the main diastereomeric *anti* alcohols **3a,d** were never detected. This is probably a result of the

steric strain induced by the bulky Tfm and C_2F_5 groups, which affects the *cis*-lactone isomers, making their formation from *anti*-**3a,b** and **3d,e** more difficult.

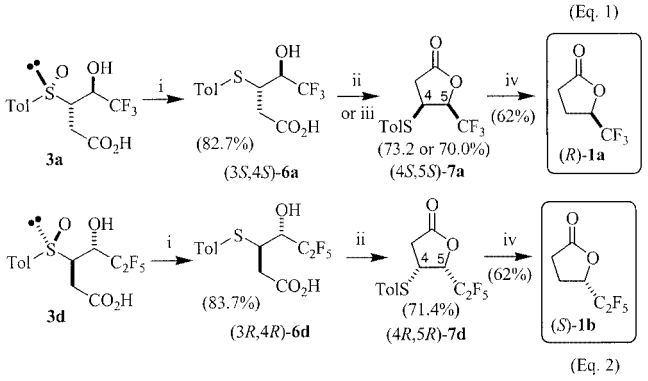


(4*S*,5*R*,R_S)-**5c** (4*R*,5*S*,S_S)-**5f**

Figure 2. Spontaneously formed *trans*-sulfinyllactones

Completion of the Synthesis of 1a,b

The thermal lability of the sulfinyl derivatives **3** led us to perform the next steps of the synthesis on their stable sulfenyl derivatives. The Drabowicz−Oae procedure[17] (trifluoroacetic anhydride, NaI) allowed us to obtain the *anti* 4-hydroxy-3-sulfenyl acids (3*S*,4*S*)-**6a** [Equation (1) in Scheme 6] and (3*R*,4*R*)-**6d** [Equation (2) in Scheme 6] from the corresponding major trifluoro and pentafluoro diastereomers **3a** and **3d**. Not surprisingly, very little of the spontaneous *cis* lactonization products (4*S*,5*S*)-**7a** and (4*R*,5*R*)-**7d** was detected after workup (4 and 1.2% isolated yields, respectively).



Scheme 6. Key: i) NaI, $(CF_3CO)_2O$, acetone, − 40 °C; ii) CH_3CO_2H, toluene, reflux, 4 h; iii) DCC, DMAP, CH_2Cl_2, 0 °C; iv) Raney Ni, H_2, $(CH_2OH)_2$, Δ, 2 h

On the other hand, the same reaction performed on mixtures of *anti*/*syn* (3*R*/*S*,4*R*,R_S)-**3b,c** (1.2:1.0) and (3*S*/*R*,4*S*,S_S)-**3e,f** (1.5:1.0) led to enantio- and diastereopure *trans*-lactonisation products derived only from the *syn* alcohols **3c** and **3f**.[18] Since the diastereoisomers **3b,c** and **3e,f** are rather difficult to separate from each other by FC, this finding provided us with a straightforward entry to their stereochemically pure derivatives.

Since the lactonisation of the major *anti*-sulfenyl derivatives **6a,d** did not take place spontaneously,[19] a way to perform this step was studied next. Among the different methods of lactonization of γ-hydroxycarboxylic acids described in the literature,[6a,6c,7,20] we chose the treatment with acetic acid in toluene, which required heating of the mixture for 4 h at reflux temperature.[21] The *cis*-lactones were obtained in good yields (73.2 and 71.4% for **7a** and **7d**, respectively). Even more conveniently, the Tfm substrate **6a** was treated with DCC (CH_2Cl_2, 0 °C, cat. DMAP, 5 min),[22] affording the lactone (4*S*,5*S*)-**7a** in similar yield (70%), without any detectable epimerisation.

Hydrogenolytic Removal of the p-*Tolylthio Group*

The final step was the reductive removal of the *p*-tolylthio group, which was performed by Raney-Ni hydrogenolysis in ethylene glycol at reflux temperature under H_2 atmosphere. Starting from the *cis* lactones **7a** and **7d**, the enantiopure desulfinylated γ-Tfm-γ-valerolactone (−)-(*R*)-**1a** and γ-pentafluoroethyl-γ-caprolactone (+)-(*S*)-**1b** were obtained (Scheme 6). The same reaction, performed on the corresponding *trans* lactones **7c** and **7f** led to the enantiomers (+)-(*S*)-**1a** and (−)-(*R*)-**1b**, respectively. The use of ethanol as solvent was less effective, affording significant amounts (ca. 20%) of ethyl 5,5,5-trifluoro-4-hydroxypentanoate or ethyl 5,5,6,6,6-pentafluoro-4-hydroxyhexanoate from **7a** and **7d**, respectively, by competitive solvolysis of the lactones **1a** and **1b**, probably due to the presence of the electron-withdrawing Tfm and C_2F_5 groups on C-4, which make the carboxy group strongly electrophilic.[23]

Concluding Remarks

A synthesis of both enantiomers of the trifluoro analogue of γ-valerolactone (**1a**) and the pentafluoro analogue of γ-caprolactone (**1b**) has been developed using sulfoxide chemistry. The key installation of the C(4) stereogenic centres, which was achieved by $NaBH_4$ reduction of β-keto-sulfoxide precursors, occurred with unexpectedly high stereocontrol, probably originating from an intramolecular hydride delivery by a transient carboxy-borohydride. A concomitant dynamic kinetic resolution ensured a very effective synthesis of the intermediate β-hydroxy sulfoxides **3a** and **3d**, which were converted into the title compounds in three further steps.

Experimental Section

General Details: Melting points (m.p.): uncorrected; capillary apparatus. Polarimetric analyses: PROPOL polarimeter. Analytical TLC: routinely used to monitor reactions, plates precoated with Merck silica gel 60 F_{254} of 0.25 mm thickness were used. Flash chromatography (FC): silica gel 60 (230−400 ASTM mesh). ^1H and ^{19}F NMR: Bruker AC 250 L (250 MHz) (^{19}F and ^{13}C), Bruker ARX400 (400 MHz) (^1H), chemical shifts in ppm (δ), tetramethylsilane (TMS) as internal standard for ^1H and ^{13}C nuclei (δ_H = 0.00 ppm), C_6F_6 external standard (δ_F = −162.90 ppm) for ^{19}F, coupling constants are expressed in Hz. MS: TSQ Finnigan Mat three-stage quadrupole instrument, DIS (Direct Inlet System) used for pure compounds. GC/MS: TSQ Finnigan Mat having a transfer line with Varian 3400 GC instrument. GC: DB-5 fused silica capillaries column [5% phenyl, 95% methyl silicone; 30 m × 0.25 mm; ϕ = 0.25 μm; carrier gas: He, 12 mL/min; temperature gradient operating: 40 °C (1 min) → 200 °C (1 min); 10 °C/min → 285 (24 min)]. IR: Perkin−Elmer System 2000 FT-IR (scan range: 15600 cm^{-1}; combined scan direction). THF was freshly distilled from Na/benzophenone, diisopropylamine was freshly distilled from CaH_2; in all other cases, commercially available reagent-grade

solvents were employed without purification. All reactions, where anhydrous organic solvents were employed, were performed under nitrogen, after flame-drying of the glass apparatus. Synthesis of (*R*)-3-(tolylsulfinyl)propionic acid (**2**) has already been described in detail[8b] and the synthesis of its (*S*)-**2** enantiomer was performed following the same procedure, starting from (−)-(*S*)-methyl *p*-tolyl sulfoxide.

Synthesis of β-Sulfinyl-γ-hydroxy Acids 3. General Procedure: A solution of 3-sulfinylpropionic acid (**2**) (10.0 mmol) in THF (30 mL) was added dropwise at − 60 °C to a solution of LDA (24.0 mmol) under argon atmosphere. The resulting yellow solution was cooled to −70 °C and added with neat fluorinated esters (CF_3CO_2Et or $CF_3CF_2CO_2Et$) (14.0 mmol). After 5 min, a saturated NH_4Cl solution was added, followed by a dilute HCl solution (until pH = 2). The mixture was extracted with EtOAc (3 × 50 mL), washed with water, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo at room temp. The residue was diluted with a H_2O/THF (1:4) solution (30 mL), the mixture was cooled to 0 °C and neat $NaBH_4$ (40.0 mmol) was added portionwise. The resulting clear solution was treated with 1 N HCl aqueous solution until pH 2, the organic layers were extracted with EtOAc (3 × 50 mL), washed with water, dried over anhydrous sodium sulfate, filtered and the solvents evaporated to dryness at room temp. under vacuum.

From (R_S)-2 and CF_3CO_2Et: (3*S*,4*S*,R_S)-**3a**/(3*R*,4*R*,R_S)-**3b**/(3*S*,4*R*,R_S)-**3c** = 7.2:1.2:1.0 (measured by ^1H and ^{19}F NMR spectroscopy in $CDCl_3$, CD_3COCD_3, and CD_3OD); 80.4% overall yield. The 4-hydroxyalkenoic acid (*R*/*S*,*E*)-**4a** was formed in variable amounts depending on the degree of elimination of *p*-TolSOH from **3a**−**c**.

5,5,5-Trifluoro-4-hydroxy-3-(tolylsulfinyl)pentanoic Acid [(3*S*,4*S*,R_S)-3a]: Yield 1.91 g (61.6%) obtained after FC ($CHCl_3$/EtOAc/AcOH, 70:30:1); R_f = 0.35. $[\alpha]_D^{20}$ = +143 (*c* = 1.1, CD_3OD). ^1H NMR (CD_3OD): δ = 2.41 (s, 3 H, CH_3), 2.58 (dd, ^2J = 17.6, ^3J = 7.2 Hz, 1 H, 2-H_a), 2.76 (dd, ^2J = 17.6, ^3J = 4.4 Hz, 1 H, 2-H_b), 3.44 (ddd, ^3J = 7.2, 4.4, 8.3 Hz, 1 H, 3-H), 4.44 (qd, $^3J_{H\text{-}F}$ = 8.4, ^3J = 8.3 Hz, 1 H, 4-H), 7.3 and 7.6 (m, 4 H, ArH) ppm. ^{19}F NMR (CD_3OD): δ = −74.8 (d, $^3J_{F\text{-}H}$ = 8.4 Hz) ppm. ^1H NMR (CD_3COCD_3): δ = 2.86 (s, 3 H, CH_3), 3.08 (dd, ^2J = 18.6, ^3J = 6.6 Hz, 1 H, 2-H_a), 3.28 (ddq, ^2J = 18.6, ^3J = 4.5, $^5J_{H\text{-}F}$ = 1.0 Hz, 1 H, 2-H_b), 3.90 (m, 1 H, 3-H), 5.08 (m, 1 H, 4-H), 7.8 and 8.0 (m, 4 H, ArH) ppm. ^{13}C NMR (CD_3OD): δ = 21.3 (s, CH_3), 27.6 (s, C-2), 63.1 (s, C-3), 70.7 (q, *J* = 31.7 Hz, C-4), 128.3 (q, *J* = 282.6 Hz, C-5), 128.2 (s, Ar*C*CH_3), 128.7 (s, ArC), 133.4 (s, Ar*C*S), 133.7 (s, ArC), 177.8 (s, C-1) ppm. ^{19}F (CD_3OD): δ = −74.4 (d, $^3J_{F\text{-}H}$ = 7.8 Hz) ppm. IR (neat): $\tilde{\nu}$ = 3210 cm^{-1}, 2956, 2395, 1724, 1687, 1416, 1243. MS (DIS EI, 70 eV): *m*/*z* (%) = 310 (8) [$M^{+\cdot}$], 292 (3) [$C_{12}H_{11}SO_3F_3^{+\cdot}$], 139 (28) [$C_7H_7SO^+$], 101 (17) [$C_4H_5O_3^+$], 91 (37) [$C_4H_5F_2^+$], 77 (42) [$C_6H_5^+$], 69 (100) [$CF_3^+$].

(3*R*/*S*,4*R*,R_S)-3b,c: Yield 580 mg (18.7%) obtained as a 1.2:1.0 mixture by FC ($CHCl_3$/EtOAc/AcOH, 70:30:1); R_f = 0.35.

(3*R*,4*R*,R_S)-3b: ^1H NMR (CD_3OD): δ = 2.19 (dd, ^2J = 17.6, ^3J = 7.2 Hz, 1 H, 2-H_a), 2.41 (s, 3 H, CH_3), 2.91 (ddq, ^2J = 17.6, ^3J = 4.4, $^5J_{H\text{-}F}$ = 1.2 Hz, 1 H, 2-H_b), 3.85 (ddd, ^3J = 7.2, 7.2, 4.4 Hz, 1 H, 3-H), 3.94 (qd, $^3J_{H\text{-}F}$ = 6.9, ^3J = 7.2 Hz, 1 H, 4-H), 7.3 and 7.7 (m, 4 H, ArH) ppm. ^{19}F NMR (CD_3OD): δ = −74.7 (d, $^3J_{F\text{-}H}$ = 6.9 Hz) ppm. ^1H NMR (CD_3COCD_3): δ = 2.73 (dd, ^2J = 18.0, ^3J = 7.5 Hz, 1 H, 2-H_a), 2.86 (s, 3 H, CH_3), 3.48 (ddq, ^2J = 18.0, ^3J = 4.5, $^5J_{H\text{-}F}$ = 1.2 Hz, 1 H, 2-H_b), 4.28 (ddd, ^3J = 8.4, 7.5, 4.5 Hz, 1 H, 3-H), 4.62 (qd, ^3J = 8.4, $^3J_{H\text{-}F}$ = 7.6 Hz, 1 H, 4-H), 7.7 and 8.1 (m, 4 H, ArH) ppm. ^{19}F NMR (CD_3COCD_3): δ = −74.3 (d, $^3J_{F\text{-}H}$ = 7.6 Hz) ppm.

(3*S*,4*R*,R_S)-3c: ^1H NMR (CD_3OD): δ = 2.41 (s, 3 H, CH_3), 2.71 (dd, ^2J = 18.2, ^3J = 6.6 Hz, 1 H, 2-H_a), 2.83 (dd, ^2J = 18.2, ^3J = 5.0 Hz, 1 H, 2-H_b), 3.65 (ddd, ^3J = 6.6, 5.0, 2.5 Hz, 1 H, 3-H), 4.43 (qd, $^3J_{H\text{-}F}$ = 7.5, ^3J = 2.5 Hz, 1 H, 4-H), 7.3 and 7.6 (m, 4 H, ArH) ppm. ^{19}F NMR (CD_3OD): δ = −76.0 (d, $^3J_{F\text{-}H}$ = 7.6 Hz) ppm. ^1H NMR (CD_3COCD_3): δ = 2.87 (s, 3 H, CH_3), 3.22 (ddq, ^2J = 18.9, ^3J = 6.0, $^5J_{H\text{-}F}$ = 0.5 Hz, 1 H, 2-H_a), 3.31 (dd, ^2J = 18.9, ^3J = 5.1 Hz, 1 H, 2-H_b), 4.11 (ddd, ^3J = 6.0, 5.1, 2.7 Hz, 1 H, 3-H), 5.14 (qd, ^3J = 8.0, $^3J_{H\text{-}F}$ = 2.7 Hz, 1 H, 4-H), 7.7 and 8.2 (m, 4 H, ArH) ppm. ^{19}F NMR (CD_3COCD_3): δ = −75.6 (d, $^3J_{F\text{-}H}$ = 8.0 Hz) ppm.

5,5,5-Trifluoro-4-hydroxy-2-pentenoic Acid [(*R*/*S*,*E*)-4a]: ^1H NMR (CD_3OD): δ = 4.68 (qdd, $^3J_{H\text{-}F}$ = 7.2, ^3J = 5.0, ^4J = 1.9 Hz, 1 H, 4-H), 6.26 (dd, ^3J = 15.7, ^4J = 1.9 Hz, 1 H, 2-H), 6.85 (dd, ^3J = 15.7, ^4J = 5.0 Hz, 1 H, 3-H) ppm. ^{13}C NMR (CD_3OD): δ = 73.2 (q, *J* = 30.9 Hz, C-4), 129.0 (q, *J* = 282.6 Hz, C-5), 139.2 (s, C-2), 143.7 (s, C-3), 176.0 (s, C-1) ppm. ^{19}F NMR (CD_3OD): δ = −77.4 (d, $^3J_{F\text{-}H}$ = 7.2 Hz) ppm.

4-(Tolylsulfinyl)-5-trifluoromethyldihydrofuran-2-one [(4*S*,5*R*,R_S)-5c]: Yield 292 mg (10%), formed during the FC ($CHCl_3$/EtOAc/AcOH, 70:30:1); R_f = 0.50. $[\alpha]_D^{20}$ = +159.5 (*c* = 0.4, $CHCl_3$); m.p. 95−97 °C (from diisopropyl ether). ^1H NMR ($CDCl_3$): δ = 2.44 (s, 3 H, CH_3), 2.49 (dd, ^2J = 18.6, ^3J = 9.8 Hz, 1 H, 3-H_a), 3.03 (dd, ^2J = 18.6, ^3J = 5.7 Hz, 1 H, 3-H_b), 3.61 (ddd, ^3J = 9.8, 5.7, 4.6 Hz, 1 H, 4-H), 5.07 (qd, $^3J_{H\text{-}F}$ = 6.0, ^3J = 4.6 Hz, 1 H, 5-H), 7.25 and 7.40 (m, 4 H, ArH) ppm. ^{19}F NMR ($CDCl_3$): δ = −79.1 (d, $^3J_{F\text{-}H}$ = 6.0 Hz) ppm.

From (*S*)-2 and $CF_3CF_2CO_2Et$: (3*R*,4*R*,S_S)-**3d**/(3*S*,4*S*,S_S)-**3e**/(3*R*,4*S*,S_S)-**3f** = 12.9:1.5:1.0 (determined by ^1H and ^{19}F NMR spectroscopy of the crude reaction mixture in CD_3OD); 89.5% global yields. The 4-hydroxyalkenoic acid (*R*/*S*,*E*)-**4b** was detected in a variable amount depending on the degree of elimination of *p*-TolSOH from **3d**−**f**.

5,5,6,6,6-Pentafluoro-4-hydroxy-3-(tolylsulfinyl)hexanoic Acid [(3*R*,4*R*,S_S)-3d]: Yield 2.7 g (75.0%), obtained after FC ($CHCl_3$/EtOAc/AcOH, 40:60:1.5); R_f = 0.35. $[\alpha]_D^{20}$ = −137 (*c* = 0.3, CD_3OD). IR (neat): $\tilde{\nu}$ = 3306 cm^{-1}, 1732, 1702, 1421, 1214, 1210, 1126, 1035. ^1H NMR (CD_3OD): δ = 2.40 (s, 3 H, CH_3), 2.63 (dd, ^2J = 18.2, ^3J = 7.0 Hz, 1 H, 2-H_a), 2.82 (ddd, ^2J = 18.2, ^3J = 4.5, ^4J = 1.4 Hz, 1 H, 2-H_b), 3.54 (ddd, ^3J = 7.0, 4.5, 5.5 Hz, 1 H, 3-H), 4.59 (ddd, $^3J_{H\text{-}F}$ = 21.5, 4.3, ^3J = 5.5 Hz, 1 H, 4-H), 7.1 and 7.5 (m, 4 H, ArH) ppm. ^{13}C NMR (CD_3OD): δ = 21.4 (s, CH_3), 27.6 (s, C-2), 63.05 (s, C-3), 69.4 (dd, *J* = 31.4, 20.3 Hz, C-4), 116.0 (tq, *J* = 257.1, 35.2 Hz, C-5), 120.5 (qt, *J* = 292.2, 35.2 Hz, C-6), 125.4 (s, ArC), 126.3 (s, Ar*C*CH_3), 130.9 (s, Ar*C*S), 131.3 (s, ArC), 173.5 (s, C-1) ppm. ^{19}F NMR (CD_3OD): δ = −80.3 (s, 3 F, CF_3), −116.8 (dd, $^2J_{F\text{-}F}$ = 275.9, $^3J_{F\text{-}H}$ = 4.3 Hz, 1 F, CF_a), −127.4 (dd, $^2J_{F\text{-}F}$ = 275.9, $^3J_{F\text{-}H}$ = 21.5 Hz, 1 F, CF_b) ppm. MS (DIS EI, 70 eV): *m*/*z* (%) = 361 (5) [M + H]$^+$, 360 (8) [$M^{+\cdot}$], 342 (5) [$C_{13}H_{11}SO_3F_5^{+\cdot}$], 140 (25) [$C_7H_8SO^{+\cdot}$], 139 (100) [$C_7H_7SO^+$], 101 (42) [$C_4H_5O_3^+$], 69 (8) [$CF_3^+$].

(3*S*/*R*,4*S*,S_S)-3e,f: Yield 522 mg (14.5%) obtained as a 1.5:1.0 mixture by FC ($CHCl_3$/EtOAc/AcOH, 70:30:1); R_f = 0.35.

(3*S*,4*S*,S_S)-3e: ^1H NMR (CD_3OD): δ = 2.25 (ddd, ^2J = 19.2, ^3J = 7.5, ^4J = 1.3 Hz, 1 H, 2-H_a), 2.40 (s, 3 H, CH_3), 2.89 (ddd, ^2J = 19.2, ^3J = 4.7, ^4J = 2.3 Hz, 1 H, 2-H_b), 3.91 (ddd, ^3J = 7.5, 4.7, 4.4 Hz, 1 H, 3-H), 4.23 (dddd, $^3J_{H\text{-}F}$ = 22.0, ^3J = 4.4, 2.3, 1.3 Hz,

1 H, 4-H), 7.1 and 7.5 (m, 4 H, ArH) ppm. ^{19}F NMR (CD_3OD): δ = −80.4 (s, 3F, CF_3), −122.7 (d, $^2J_{F\text{-}F}$ = 275.9 Hz, 1 F, CF_a), −129.3 (dd, $^2J_{F\text{-}F}$ = 275.9, $^3J_{F\text{-}H}$ = 22.0 Hz, 1 F, CF_b) ppm.

(3*R*,4*S*,*S*$_S$)-3f: ^{1}H NMR (CD_3OD): δ = 2.40 (s, 3 H, CH_3), 2.74 (ddd, ^2J = 19.5, ^3J = 10.0, ^4J = 0.9 Hz, 1 H, 2-H_a), 2.99 (ddd, ^2J = 19.5, ^3J = 4.5, ^4J = 0.5 Hz, 1 H, 2-H_b), 3.77 (m, 1 H, 3-H), 4.20 (m, 1 H, 4-H), 7.1 and 7.5 (m, 4 H, ArH) ppm. ^{19}F NMR (CD_3OD): δ = −80.5 (s, 3 F, CF_3), −116.8 (dd, $^2J_{F\text{-}F}$ = 275.8, $^3J_{F\text{-}H}$ = 5.6 Hz, 1 F, CF_a), −127.2 (dd, $^2J_{F\text{-}F}$ = 275.8, $^3J_{F\text{-}H}$ = 19.8 Hz, 1 F, CF_b) ppm.

5,5,6,6,6-Pentafluoro-4-hydroxy-2-hexenoic Acid [(*R*/*S*,*E*)-4b]: ^{1}H NMR (CD_3OD): δ = 4.80 (m, 1 H, 4-H), 6.25 (dd, ^3J = 13.7, ^4J = 1.2 Hz, 1 H, 2-H), 6.85 (dd, ^3J = 13.7, ^4J = 5.2 Hz, 1 H, 3-H) ppm. ^{13}C NMR (CD_3OD): δ = 69.7 (dd, J = 55.6, 25.9 Hz, C-4), 115.0 (tq, J = 257.1, 35.2 Hz, C-5), 120.2 (qt, J = 292.2, 35.2 Hz, C-6), 136.7 (s, C-2), 139.7 (s, C-3), 168.7 (s, C-1) ppm. ^{19}F NMR (CD_3OD): δ = −79.9 (s, 3 F, CF_3), −120.0 (dd, $^2J_{F\text{-}F}$ = 275.9, $^3J_{F\text{-}H}$ = 7.3 Hz, 1 F, CF_a), −127.3 (dd, $^2J_{F\text{-}F}$ = 275.9, $^3J_{F\text{-}H}$ = 15.9 Hz, 1 F, CF_b) ppm.

5-Pentafluoroethyl-4-(tolylsulfinyl)dihydrofuran-2-one [(4*R*,5*S*,*S*$_S$)-5f]: Yield 171 mg (5%), formed during the FC ($CHCl_3$/EtOAc/AcOH, 70:30:1); R_f = 0.45. $[\alpha]_D^{20}$ = −169 (c = 0.2, $CHCl_3$); m.p. 105−106 °C (from diisopropyl ether). ^{1}H NMR ($CDCl_3$): δ = 2.46 (s, 3 H, CH_3), 2.48 (ddd, ^2J = 18.6, ^3J = 9.8, ^4J = 4.6 Hz, 1 H, 3-H_a), 3.08 (dd, ^2J = 18.6, ^3J = 6.2 Hz, 1 H, 3-H_b), 3.74 (ddd, ^3J = 9.8, 6.2, 6.3 Hz, 1 H, 4-H), 5.20 (dddd, $^3J_{H\text{-}F}$ = 19.1, 1.6, ^3J = 6.3, ^4J = 4.6 Hz, 1 H, 5-H), 7.25 and 7.40 (m, 4 H, ArH) ppm. ^{19}F NMR ($CDCl_3$): δ = −83.3 (s, 3 F, CF_3), −125.8 (d, $^2J_{F\text{-}F}$ = 281.0 Hz, 1 F, CF_a), −132.0 (dd, $^2J_{F\text{-}F}$ = 281.0, $^3J_{F\text{-}H}$ = 19.1 Hz, 1 F, CF_b) ppm.

Sulfur Deoxygenation of β-Sulfinyl-γ-hydroxy Acids (3). General Procedure: A solution of trifluoroacetic anhydride (25.0 mmol) in acetone (20 mL) was added dropwise to a suspension of NaI (15.0 mmol) and **3** (5.0 mmol) in acetone (20 mL) cooled to −40 °C and stirred under argon atmosphere. A mixture of saturated aqueous solutions of Na_2SO_3 and $NaHCO_3$ was added dropwise to the resulting dark green slurry, the pH was adjusted to 2 by adding a 1 N HCl aqueous solution, the organic layers were extracted with EtOAc (3 × 25 mL), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo.

5,5,5-Trifluoro-4-hydroxy-3-(*p*-tolylthio)pentanoic Acid [(3*S*,4*S*)-6a]: Yield 82.7% from (3*S*,4*S*,*R*$_S$)-**3a**, isolated after FC ($CHCl_3$/EtOAc/AcOH, 90:10:1); R_f = 0.35. $[\alpha]_D^{20}$ = +5.5 (c = 0.5, $CHCl_3$); m.p. 80−82 °C (from diisopropyl ether). ^{1}H NMR ($CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 2.74 (dd, ^2J = 15.4, ^3J = 7.7 Hz, 1 H, 2-H_a), 2.90 (dd, ^2J = 15.4, ^3J = 5.4 Hz, 1 H, 2-H_b), 3.50 (br. s, 1 H, OH), 3.64−3.71 (m, 1 H, 3-H), 4.01−4.09 (m, 1 H, 4-H), 7.1 and 7.5 (m, 4 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.1 (s, CH_3), 37.1 (s, C-2), 46.8 (s, C-3), 71.0 (q, J = 30.6 Hz, C-4), 124.5 (q, J = 283.3 Hz, C-5), 128.7 (s, Ar*C*CH_3), 130.1 (s, ArC), 134.2 (s, ArC), 139.4 (s, Ar*C*S), 176.0 (s, C-1) ppm. ^{19}F NMR ($CDCl_3$): δ = −76.01 (d, $^3J_{H\text{-}F}$ = 7.0 Hz) ppm. IR (neat): $\tilde{\nu}$ = 3025 cm^{-1}, 2926, 1714, 1412, 1269, 1171, 1137. MS (DIS EI, 70 eV): m/z (%) = 294 (100) [$M^{+\cdot}$], 276 (13) [$C_{11}H_{11}SO_2F_3^{+\cdot}$], 196 (3) [$C_{10}H_{12}SO_2^{+\cdot}$], 195 (23) [$C_{10}H_{11}SO_2^+$], 177 (21) [$C_{10}H_9SO^+$], 153 (13) [$C_5H_7O_3F_2^+$], 149 (10) [$C_9H_9S^+$], 123 (16) [$C_7H_7S^+$].

4-*p*-Tolylthio-5-trifluoromethyldihydrofuran-2-one [(4*S*,5*S*)-7a]: Yield 4%, spontaneously formed from **6a** and isolated after FC ($CHCl_3$/EtOAc/AcOH, 90:10:1); R_f = 0.40. $[\alpha]_D^{20}$ = +32 (c = 0.25, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 2.73 (ddq, ^2J = 16.8, ^3J = 11.4, $^5J_{H\text{-}F}$ = 1.2 Hz, 1 H, 3-H_β), 2.86 (ddq, ^2J = 16.8, ^3J = 8.8, $^5J_{H\text{-}F}$ = 1.2 Hz, 1 H, 3-H_α), 4.16 (m, 1 H, 4-H), 4.87 (dq, $^3J_{H\text{-}F}$ = 7.6, ^3J = 7.6 Hz, 1 H, 5-H), 7.10 and 7.45 (m, 4 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.1 (s, CH_3), 34.1 (s, C-3), 43.4 (s, C-4), 77.0 (q, J = 32.0 Hz, C-5), 123.1 (q, J = 283.1 Hz, CF_3), 128.8 (s, Ar*C*CH_3), 130.4 (s, ArC), 132.9 (s, ArC), 139.1 (s, Ar*C*S), 171.9 (s, C-2) ppm. ^{19}F NMR ($CDCl_3$): δ = −73.4 (d, $^3J_{F\text{-}H}$ = 7.6 Hz) ppm. IR (neat): $\tilde{\nu}$ = 1709 cm^{-1}, 1212, 1210, 1120, 1006. MS (DIS EI 70 eV): m/z (%) = 276 (100) [$M^{+\cdot}$], 150 (15) [$C_9H_{10}S^{+\cdot}$], 135 (16) [$C_5H_5F_2O_2^+$], 123 (11) [$C_7H_7S^+$].

(4*S*,5*R*)-7c: Yield 80% from a (3*R*/*S*,4*R*,*R*$_S$)-**3b,c** mixture with 1.2:1.0 ratio, after FC ($CHCl_3$/EtOAc/AcOH, 90:10:1); R_f = 0.60. $[\alpha]_D^{20}$ = −55.5 (c = 0.15, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 2.57 (ddd, ^2J = 18.6, ^3J = 3.1, $^5J_{H\text{-}F}$ = 1.0 Hz, 1 H, 3-H_β), 3.04 (dd, ^2J = 18.6, ^3J = 8.3 Hz, 1 H, 3-H_α), 3.96 (ddd, ^3J = 8.3, 3.1, 2.5 Hz, 1 H, 4-H), 4.63 (qd, $^3J_{H\text{-}F}$ = 6.3, ^3J = 2.5 Hz, 1 H, 5-H), 7.15 and 7.40 (m, 4 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2 (s, CH_3), 30.9 (s, C-3), 41.3 (s, C-4), 79.8 (q, J = 32.9 Hz, C-5), 122.8 (q, J = 282.3 Hz, CF_3), 126.7 (s, Ar*C*CH_3), 130.9 (s, ArC), 134.2 (s, ArC), 140.0 (s, Ar*C*S), 170.8 (s, C-2) ppm. ^{19}F NMR ($CDCl_3$): δ = −79.5 (d, $^3J_{F\text{-}H}$ = 6.3 Hz) ppm. MS (DIS EI, 70 eV): m/z (%) = 276 (100) [$M^{+\cdot}$], 150 (18) [$C_9H_{10}S^{+\cdot}$], 135 (40) [$C_5H_5F_2O_2^+$], 123 (36) [$C_7H_7S^+$], 91 (33) [$C_4H_5F_2^+$], 77 (16) [$C_6H_5^+$], 69 (9) [CF_3^+].

5,5,6,6,6-Pentafluoro-4-hydroxy-3-(*p*-tolylthio)hexanoic Acid (3*R*,4*R*)-6d: Yield 82.7% from (3*R*,4*R*,*S*$_S$)-**3d**, isolated after FC ($CHCl_3$/EtOAc/AcOH, 90:10:1); R_f = 0.35. $[\alpha]_D^{20}$ = −5.9 (c = 1.9, $CHCl_3$). $[\alpha]_{365}^{20}$ = −23.5 (c = 1.9, $CHCl_3$); m.p. 105−107 °C (from diisopropyl ether). ^{1}H NMR ($CDCl_3$): δ = 2.33 (s, 3 H, CH_3), 2.77 (dd, ^2J = 17.2, ^3J = 7.9 Hz, 1 H, 2-H_a), 2.94 (dd, ^2J = 17.2, ^3J = 6.5 Hz, 1 H, 2-H_b), 3.45 (br. s, 1 H, OH), 3.77 (m, 1 H, 3-H), 4.12 (ddd, $^3J_{H\text{-}F}$ = 20.0, 3.6, ^3J = 5.6 Hz, 1 H, 4-H), 7.10 and 7.45 (m, 4 H, ArH), 10.2 (br. s, 1 H, COOH) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.1 (s, CH_3), 37.5 (s, C-2), 46.9 (s, C-3), 69.4 (dd, J = 28.5, 21.7 Hz, C-4), 113.7 (tq, J = 263.4, 36.54 Hz, C-5), 118.7 (qt, J = 286.7, 34.1 Hz, C-6), 127.6 (s, Ar*C*CH_3), 130.2 (s, ArC), 134.3 (s, ArC), 139.4 (s, Ar*C*S), 176.4 (s, C-1) ppm. ^{19}F NMR ($CDCl_3$): δ = −83.3 (s, 3 F, CF_3), −120.0 (dd, $^2J_{F\text{-}F}$ = 274.7, $^3J_{F\text{-}H}$ = 3.6 Hz, 1 F, CF_a), −132.0 (dd, $^2J_{F\text{-}F}$ = 274.7, $^3J_{F\text{-}H}$ = 20.0 Hz, 1 F, CF_b) ppm. MS (DIS EI, 70 eV): m/z (%) = 344 (100) [$M^{+\cdot}$], 326 (27) [$C_{13}H_{11}SO_2F_5^{+\cdot}$], 267 (9) [$C_{11}H_8SF_5^+$], 196 (6) [$C_{10}H_{12}SO_2^{+\cdot}$], 195 (36) [$C_{10}H_{11}SO_2^+$], 177 (56) [$C_{10}H_9SO^+$], 161 (10) [$C_4H_2OF_5^+$], 149 (37) [$C_9H_9S^+$], 123 (82) [$C_7H_7S^+$], 91 (72) [$C_4H_5F_2^+$], 77 (56) [$C_6H_5^+$], 69 (22) [$CF_3^+$].

5-Pentafluoroethyl-4-(*p*-tolylthio)dihydrofuran-2-one (4*R*,5*R*)-7d: Yield 1.2% from **6d**; R_f = 0.40. $[\alpha]_D^{20}$ = −39.5 (c = 0.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 2.76 (ddd, ^2J = 17.0, ^3J = 9.1, ^4J = 2.7 Hz, 1 H, 3-H_β), 2.86 (ddd, ^2J = 17.0, ^3J = 8.3, ^4J = 2.0 Hz, 1 H, 3-H_α), 4.19 (m, 1 H, 4-H), 4.95 (dddd, $^3J_{H\text{-}F}$ = 23.5, ^3J = 7.2, ^4J = 2.7, 2.0 Hz, 1 H, 5-H), 7.1 and 7.4 (m, 4 H, ArH) ppm. ^{13}C NMR ($CDCl_3$), δ = 21.1 ppm (s, CH_3), 34.9 (s, C-3), 44.6 (s, C-4), 75.4 (dd, J = 32.1, 22.1 Hz, C-5), 113.2 (tq, J = 264.0, 37.4 Hz, CF_2), 118.2 (qdd, J = 286.0, 35.7, 33.0 Hz, CF_3), 128.9 (s, Ar*C*CH_3), 130.2 (s, ArC), 133.2 (s, ArC), 139.2 (s, Ar*C*S), 171.6 (s, C-2) ppm. ^{19}F NMR ($CDCl_3$): δ = −82.7 (s, 3 F, CF_3), −118.9 (d, $^2J_{F\text{-}F}$ = 280.9 Hz, 1 F, CF_a), −130.5 (dd, $^2J_{F\text{-}F}$ = 280.9, $^3J_{F\text{-}H}$ = 23.5 Hz, 1 F, CF_b) ppm. MS (DIS EI, 70 eV): m/z (%) = 327 (18) [M + H]$^+$, 326 (100) [$M^{+\cdot}$], 161 (5) [$C_4H_2OF_5^+$], 150 (42) [$C_9H_{10}S^{+\cdot}$], 149 (37) [$C_9H_9S^+$], 135 (65) [$C_5H_5O_2F_2^+$], 123 (42) [$C_7H_7S^+$], 91 (26) [$C_4H_5F_2^+$], 77 (18) [$C_6H_5^+$].

(4*R*,5*S*)-7f: Yield 95% from (3*R*,4*S*,*S*$_S$)-**3f**, isolated after FC (*n*-hexane/diisopropyl ether, 4:1); R_f = 0.35. $[\alpha]_D^{20}$ = +50.5 (c = 1.2,

$CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 2.59 (ddd, ^2J = 18.6, ^3J = 2.6, $^5J_{H\text{-}F}$ = 1.5 Hz, 1 H, 3-H_β), 3.04 (dddd, ^2J = 18.6, ^3J = 8.7, $^5J_{H\text{-}F}$ = 1.3, 0.5 Hz, 1 H, 3-H_α), 4.07 (dddt, ^3J = 8.7, 3.1, 2.6, $^4J_{H\text{-}F}$ = 1.04 Hz, 1 H, 4-H), 4.73 (ddd, $^3J_{H\text{-}F}$ = 18.9, 4.0, ^3J = 2.6 Hz, 1 H, 5-H), 7.1 and 7.4 (m, 4 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2 (s, CH_3), 33.9 (s, C-3), 40.9 (s, C-4), 78.8 (dd, J = 32.1, 22.1 Hz, C-5), 116.0 (tq, J = 260.0, 37.6 Hz, CF_2), 121.0 (qdd, J = 286.0, 36.0, 32.0 Hz, CF_3), 126.7 (s, Ar*C*CH_3), 130.6 (s, ArC), 134.4 (s, ArC), 140.1 (s, Ar*C*S), 172.3 (s, C-2) ppm. ^{19}F NMR ($CDCl_3$): δ = −83.3 (s, 3 F, CF_3), −125.9 (dd, $^2J_{F\text{-}F}$ = 280.0, $^3J_{F\text{-}H}$ = 4.0 Hz, 1 F, CF_a), −132.45 (dd, $^2J_{F\text{-}F}$ = 280.0, $^3J_{F\text{-}H}$ = 18.9 Hz, 1 F, CF_b) ppm. MS (DIS EI, 70 eV): *m/z* (%) = 327 (8) $[M + H]^+$, 326 (100) $[(M)^{+\cdot}]$, 286 (7) $[C_{11}H_{11}SOF_5^{+\cdot}]$, 161 (8) $[C_4H_2OF_5^+]$, 150 (39) $[C_9H_{10}S^{+\cdot}]$, 149 (41) $[C_9H_9S^+]$, 135 (58) $[C_5H_5O_2F_2^+]$, 123 (38) $[C_7H_7S^+]$.

Synthesis of β-Sulfenyl-γ-lactones (7). General Procedure, Method A: A solution of sulfenylhydroxy acid **6** (1.0 mmol) and acetic acid (40 mmol) in toluene (20 mL) was refluxed for 24 h under N_2 atmosphere. Then the cooled solution was washed with a 5% aq $NaHCO_3$ solution (2 × 5 mL), water (2 × 5 mL), dried over anhydrous sodium sulfate, filtered and the solvents evaporated to dryness under reduced pressure. The residue was crystallised from diisopropyl ether providing the corresponding lactone **7**.

(4*S*,5*S*)-7a: Yield 73.2% from (3*S*,4*S*)-**6a**, isolated after FC (cyclohexane/diisopropyl ether, 3:2); R_f = 0.35. All the physical and spectroscopic data matched those described above.

(4*R*,5*R*)-7d: Yield 71.4% from (3*R*,4*R*)-**6d**, isolated after FC (cyclohexane/diisopropyl ether, 3:2); R_f = 0.35. All the physical and spectroscopic data matched those described above.

Method B: Neat DCC (1.1 mmol) was added to a stirred solution of (3*S*,4*S*)-**6a** (1.0 mmol) in CH_2Cl_2 (10 mL) cooled to 0 °C. Stirring was continued for 5 min, then neat DMAP (0.1 mmol) was added. A white solid precipitated immediately and was filtered off. The clear solution was concentrated to dryness.

(4*S*,5*S*)-7a: Yield: 70% after FC (cyclohexane/diisopropyl ether 1:1). $[\alpha]_D^{20}$ = +29 (*c* = 0.25, $CHCl_3$). All the physical and spectroscopic data matched those described above.

Synthesis of Butanolides 1. General Procedure: A black slurry of sulfenyl lactone **7** (1.0 mmol) and Raney-Ni (threefold excess by weight) in ethylene glycol (6 mL) was stirred under H_2 atmosphere at reflux for 2 h. After the starting compound was totally used up, the black powder was let to decant, the clear solution was poured into a vessel, water added and the organic products extracted with diethyl ether (3 × 5 mL). The combined ether solutions were then dried over anhydrous sodium sulfate, filtered and carefully concentrated at room temperature by blowing a gentle N_2 flow over the solution. The residue was purified by two alternative methods: (**A**) fractional distillation at atmospheric pressure, or (**B**) flash chromatography.

5-Trifluoromethyldihydrofuran-2-one [(*R*)-1a]: Yield 62% from (4*S*,5*S*)-**7a**, (**Method A**, b.p. ca. 80 °C). $[\alpha]_D^{20}$ = −14 (*c* = 0.7, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.30−2.78 (m, 4 H, 3-H_2 + 4-H_2), 4.78 (qdd, $^3J_{H\text{-}F}$ = 6.2, ^3J = 1.8, 1.6 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2 (s, C-4), 26.2 (s, C-3), 75.0 (q, J = 34.5 Hz, C-5), 123.5 (q, J = 279.9 Hz, CF_3), 174.7 (s, C-2) ppm. ^{19}F NMR ($CDCl_3$): δ = −80.7 (d, $^3J_{F\text{-}H}$ = 6.2 Hz) ppm. MS (GC EI, 70 eV): *m/z* (%) = 155 (3) $[M + H]^+$, 154 (9) $[M^{+\cdot}]$, 107 (8) $[C_3HO_2F_2^+]$, 95 (6) $[C_3H_2F_3^+]$, 85 (100) $[C_4H_5O_2^+]$, 69 (17) $[CF_3^+]$. GC/MS: t_1, *m/z* (%) = 5.23 min, 154 (98) $[M^+]$.

(*S*)-1a: Yield 55% from (4*S*,5*R*)-**7c** (**Method B**, *n*-pentane/ethyl ether, 4:1); R_f = 0.35 (*n*-pentane/ethyl ether, 3:2). $[\alpha]_D^{20}$ = +14 (*c* = 1.2, $CHCl_3$). All the spectroscopic data matched those described above for the enantiomer.

Ethyl 5,5,5-Trifluoro-4-hydroxypentanoate: Yield 20% when using EtOH as solvent with **7a**, by prolonging the reaction time to 3 h; R_f = 0.30 (*n*-pentane/ethyl ether, 3:2). ^1H NMR ($CDCl_3$): δ = 1.21 (t, ^3J = 6.8 Hz, 3 H, CH_3), 1.80−2.10 (m, 4 H, 2-H_2 + 3-H_2), 3.70 (br. s, 1 H, OH), 3.90−4.05 (m, 1 H, 4-H), 4.13 (q, ^3J = 6.8 Hz, 2 H, OCH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2 (s, CH_3), 24.9 (s, C-3), 29.7 (s, C-2), 60.9 (s, OCH_2), 69.5 (q, J = 31.3 Hz, C-4), 125.2 (q, J = 281.9 Hz, CF_3), 173.6 (s, C-1) ppm. ^{19}F NMR ($CDCl_3$): δ = −81.3 (d, $^3J_{F\text{-}H}$ = 6.2 Hz) ppm. MS (DIS EI, 70 eV): *m/z* (%) = 200 (3) $[M^{+\cdot}]$, 182 (9) $[C_7H_9O_2F_3^{+\cdot}]$, 155 (6) $[C_5H_6O_2F_3^+]$, 85 (100) $[C_4H_5O_2^+]$, 69 (17) $[CF_3^+]$.

5-Pentafluoroethyldihydrofuran-2-one (*S*)-1b: Yield 62% from (4*R*,5*R*)-**7d** (**Method B**, *n*-pentane/ethyl ether, 3:2); R_f = 0.35. $[\alpha]_D^{20}$ = +22.5 (*c* = 0.8, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.44−2.78 (m, 4 H, 3-H_2 + 4-H_2), 4.80−4.96 (m, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.7 (s, C-4), 26.2 (s, C-3), 74.3 (dd, J = 33.0, 23.2 Hz, C-5), 112.3 (tq, J = 259.0, 37.1 Hz, CF_2), 118.7 (qt, J = 284.9, 35.9 Hz, CF_3), 174.5 (s, C-2) ppm. ^{19}F NMR ($CDCl_3$): δ = −83.7 (s, 3 F, CF_3), −125.0 (dd, $^2J_{F\text{-}F}$ = 279.6, $^3J_{F\text{-}H}$ = 4.5 Hz, 1 F, CF_a), −132.3 (dd, $^2J_{F\text{-}F}$ = 279.6, $^3J_{F\text{-}H}$ = 18.5 Hz, 1 F, CF_a) ppm. MS (GC EI 70 eV): *m/z* (%) = 205 (100) $[M + H]^+$, 177 (6) $[C_5H_6OF_5^{+\cdot}]$, 109 (16) $[C_3H_3O_2F_2^+]$. GC/MS; t_1, *m/z* (%) = 5.51 min, 204 (98) $[M^+]$.

(*R*)-1b: Yield 66% from (4*R*,5*S*)-**7f** (**Method B**, *n*-pentane/ethyl ether, 3:2); R_f = 0.35. $[\alpha]_D^{20}$ = −23.5 (*c* = 1.1, $CHCl_3$). All the spectroscopic data matched those of the above described enantiomer.

Ethyl 5,5,6,6,6-Pentafluoro-4-hydroxyhexanoate: Yield 20% when using EtOH as solvent with **7d**, by prolonging the reaction time to 3 h; R_f = 0.30 (*n*-pentane/ethyl ether, 3:2). ^1H NMR ($CDCl_3$): δ = 1.26 (t, ^3J = 8.8 Hz, 3 H, CH_3), 1.90−2.15 (m, 2 H, 3-H_2), 2.45−2.65 (m, 2 H, 2-H_2), 4.05−4.20 (m, 1 H, 4-H), 4.17 (q, ^3J = 8.8 Hz, 2 H, OCH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.1 (s, CH_3), 24.1 (s, C-3), 29.7 (s, C-2), 60.9 (s, OCH_2), 69.4 (dd, J = 27.3, 23.3 Hz, C-4), 113.6 (tq, J = 257.0, 35.9 Hz, C-5), 119.2 (qt, J = 284.5, 35.9 Hz, C-6), 173.9 (s, C-1) ppm. ^{19}F NMR ($CDCl_3$): δ = −82.8 (s, 3 F, CF_3), −127.5 (dd, $^2J_{F\text{-}F}$ = 279.5, $^3J_{F\text{-}H}$ = 4.5 Hz, 1 F, CF_a), −133.8 (dd, $^2J_{F\text{-}F}$ = 279.5, $^3J_{F\text{-}H}$ = 19.0 Hz, 1 F, CF_a) ppm. MS (DIS EI, 70 eV): *m/z* (%) = 250 (7) $[M^{+\cdot}]$, 220 (22) $[C_6H_5O_3F_5^{+\cdot}]$, 205 (100) $[C_6H_6O_2F_5^+]$.

Supporting Information: Copies of ^1H NMR spectra of compounds **1a, 1b, 3a, 3d, 6a, 6d, 7a, 7d** and details on stereochemistry assignment experiments (15 pages). See footnote on page 1.

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