Stereoselective $TiCl_4$-Promoted Nucleophilic Substitution at C-2 of (4*S*,5*S*)-2-Alkyl-4-methyl-5-trifluoromethyl-1,3-dioxolanes

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Abstract: $TiCl_4$-mediated nucleophilic ring-opening reactions of chiral acetals derived from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol proceed in a completely regioselective manner, leading to the break of the O1-C2 bond accompanied by a high degree of stereoselectivity. The use of triethylsilyl deuteride or allyltributyltin as nucleophiles gives access, after removal of the chiral auxiliary, to stereoselectively deuterated primary alcohols or homoallylic secondary alcohols, respectively, with high enantiomeric excesses.

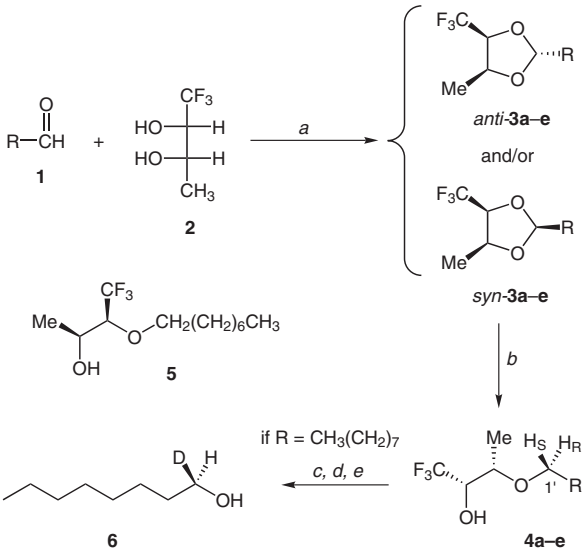
Key words: Acetals, ring opening, chiral auxiliary, allylations, stereoselectivity

The Lewis acid-promoted reactions of acetals derived from optically active diols are a powerful method for the stereoselective addition of nucleophiles to aldehydes.[1] These reactions have been deeply investigated as a tool for asymmetric synthesis[2] and a number of mechanistic features are now well established.[3]

We recently reported[3e] that the reductive ring-opening reaction of both 2-epimers of 1,3-dioxolanes **3** prepared from aromatic aldehydes (**1**, R = aryl) and (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**),[4] when carried out with triethylsilyl deuteride in the presence of $TiCl_4$, proceeds with an almost complete regioselectivity and a high degree of stereoselectivity (see **4** in Scheme 1, where R = aryl and H_R = D).

We report here that such procedure can be extended to deuteride reduction as well as to allylic substitution at the acetal carbon of trisubstituted 1,3-dioxolanes *syn*- and *anti*-**3** where R = alkyl, with maintenance of the selectivity previously observed.

Acetals *syn*- and *anti*-**3a–e** (see Table 1 for R) were obtained by refluxing the diol **2** with the appropriate aldehyde in toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid with azeotropic removal of water. Basic aqueous workup followed by flash column chromatography gave the dioxolanes **3a–e** as single *syn*- and *anti*-diastereomers. The configuration at the acetal carbon in each of them was assigned by ^{1}H NOESY experiments. The *syn*-diastereomer was obtained as major product in every case. The isolated quantities of *anti*- isomer, although enough for a complete NMR characterization of compounds *anti*-**3b**,**c**,**e**, were suitable for the subsequent ring-opening reactions only in the case of dioxolane **3c**. Attempts to provide the *anti*-isomer of dioxolane **3a** by acid-catalyzed equilibration of the corresponding *syn*-diastereomeric compound, under various experimental conditions, were unsuccessful.



Scheme 1 Reagents and conditions: (a) *p*-TsOH (cat. amount), toluene, reflux; (b) $TiCl_4$, Et_3SiH(D), CH_2Cl_2, –78 °C; (c) Swern oxidation; (d) NaH, wet THF, reflux; (e) TEA, diphenyl phopsphoroazidate (DPPA), THF, 1 M HCl, reflux. See Table 1 for alkyl residues.

Dioxolane *syn*-**3a** was subjected to reductive ring-opening reaction with Et_3SiH and $TiCl_4$ in dichloromethane at –78 °C to give compound **4a** as the only reaction product (Scheme 1). Its structure was confirmed by comparison with both the regioisomers **4a** and **5** prepared through independent routes. The former was obtained via protection of the hydroxyl group in 2-position of **2** as benzyl ether,[3e] subsequent alkylation of the remaining hydroxyl group with 1-bromooctane, and final hydrogenolysis to remove the protecting group. The latter was synthesized from (2*S*,3*S*)-3-benzyloxy-4,4,4-trifluorobutan-2-ol, an intermediate in the preparation of **2**,[4] by treatment with 1-bromooctane and NaH in DMF at 60 °C followed by removal of the benzyl group by hydrogenolysis.

Replacement of Et_3SiH with Et_3SiD (isotopic purity >99% D)[5] in the reduction of *syn*-**3a** furnished **4a** showing in the ^{1}H NMR spectrum a peak ratio of 96:4 for the two diastereotopic protons at C1′ (Scheme 1 and Table 1). The *R* configuration at the deuterated carbon in **4a** (H_R = D)

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was assigned on the basis of chemical degradation according to the procedure previously reported[3e] (Swern oxidation, subsequent haloform reaction and Curtius rearrangement; ca. 20% overall yield) and comparison of the resulting monodeuterated alcohol **6** with a sample of enantiopure (*S*)-(1-^{2}H)-octan-1-ol prepared enzymatically.[6] ^{1}H NMR spectra of (+)-MPTA esters[7] of the two enantiopure alcohols, together with that of the racemic monodeuterated alcohol, were used for comparison. The ee (85%) of **6** derived from dioxolane ring-opening was consistent with the diastereoselectivity in the deuteride reduction of the cyclic acetal **3a** (Table 1) in combination with the optical purity (ca. 95%) of the auxiliary used.[4]

In analogous experiments, summarized in Table 1, compounds **4b–e** (H_R = D) were obtained in good or moderate yields and high diastereoselectivity.

It can be noted that, as reported for benzylidene acetals,[3e] both epimers of **3c** gave the same absolute configuration at the deuterated carbon as well as comparable diastereoselectivity and chemical yield. The results presented here, together with those previously described, indicate that $TiCl_4$-catalyzed deuteride reductions of cyclic acetals derived from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol are characterized by complete regioselectivity, high diastereoselectivity and satisfactory yields independent of the 'activated' aldehyde (aromatic, aliphatic or α,β-unsaturated). Thus, a common mechanistic rationale can be assumed as described in the literature.[3e]

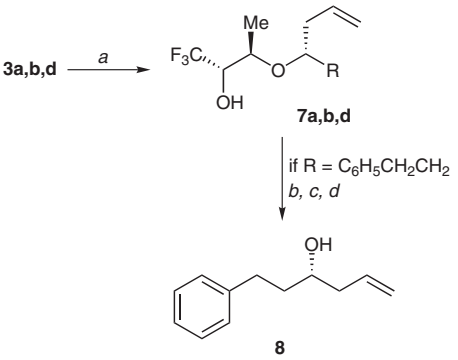
Table 1 $TiCl_4$-Mediated Reaction of Compounds *syn*-**3** with Et_3SiD to Give Compounds **4**

1,3-Dioxolane (*syn*-**3**)		Compound **4**	
Entry	R	Isolated yields (%)	Diastereomeric ratio (at C-1′)[a] *R*:*S*
a	$CH_3(CH_2)_6$	86	96:4
b	$C_6H_5CH_2CH_2$	84	97:3
c	$C_6H_5CH_2$	89 (85)[b]	97:3 (92:8)[b]
d	Cyclohexyl	67	97:3
e	(*E*)-C_6H_5CH=CH	62	93:7[c]

[a] Determined by integration of the two C-1′ protons in the ^{1}H NMR spectra on the assumption, based on the configuration of **6**, that the downfield signal was due to H_s and the isotopic abundance of every examined compound was >99% (as in Et_3SiD, compare ref. 5).
[b] Referred to the reaction of *anti*-**3**.
[c] Determined after conversion to compound **4b** by catalytic hydrogenation.

This conclusion prompted us to explore the synthetic potential of the regio- and stereoselectivity of ring-opening reactions of trifluoromethyl-substituted 1,3-dioxolanes with the involvement of *C*-nucleophiles. In this regard, the reaction of *syn*-**3b** with equimolar amounts of $TiCl_4$ and allyltriethylsilane under usual conditions afforded compound **7b** in 73% chemical yield. However, when an equivalent of allyltributyltin was added to a premixed solution of $TiCl_4$ and *syn*-**3b**, the isolated yield of **7b** increased to ca. 90% (Scheme 2).

Removal of the chiral auxiliary from **7b** as mentioned above (see Scheme 1 and ref. 3e), led to the homoallylic alcohol **8** (ca. 20% overall yield) which was shown to have the expected *S* configuration and 93% ee on the basis of its optical rotation[8] and ^{1}H NMR analysis in the presence of Eu(hfc)$_3$.



Scheme 2 Reagents and conditions: (a) $TiCl_4$, allyltributylstannane CH_2Cl_2, –78 °C; for (b)–(d) see reagents (c)–(e) of Scheme 1. See Table 1 for R.

In a similar manner, compounds **7a**,**d** were obtained in good yields starting from the corresponding *syn*-dioxolanes **3a**,**d**. It is to note that compounds **7a**,**b**,**d** were obtained in their diastereomeric pure form as the only reaction products. Only in the case of dioxolane **3d**, a small amount (<5% yield) of the diastereomeric allylated ether was isolated from the reaction mixture. This findings confirm that the reaction proceeds in a almost completely regio- and stereoselective fashion; minor diastereomeric allylic derivatives, if present, could be removed by chromatographic purification, affording the main reaction product in a diastereomerically pure form and in good chemical yields. Thus, the ee of the product depends entirely on the ee of the chiral auxiliary.[4]

TLC was performed on silica gel F_{254} precoated aluminum sheets (0.2 mm layer, Merck, Darmstadt, Germany); components were detected by spraying a ceric sulfate ammonium molybdate solution, followed by heating to ca. 150 °C. Silica gel (Merck, 40–63 μm) was used for flash chromatography (FC). ^{1}H and ^{13}C NMR spectra were recorded at 400.132 and 100.613 MHz on a Bruker AVANCE 400 spectrometer using a Xwin-NMR software package and at 300.133 and 75.469 on a Bruker AC 300 (Bruker, Karlsruhe, Germany) equipped with an ASPECT 3000 data system. Chemical shifts (δ) are given in ppm and were referenced to the signals of $CDCl_3$ (δ_H 7.25 and δ_C 77.00 ppm). ^{13}C NMR signal multiplicities were based on APT spectra. All reagents were of commercial quality or purified prior to use by standard methods.

Preparation of Dioxolanes *syn*- and *anti*-3a–e; General Procedure

A solution of (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**, 1.5 mmol), the appropriate aldehyde (1.6 mmol) and a catalytic amount of *p*-toluenesulfonic acid in toluene (3 mL), was refluxed for 1 h with re-

moval of water from the reaction mixture by means of a Dean–Stark apparatus. The mixture was cooled to r.t., diluted with EtOAc (10 mL), washed with sat. $NaHCO_3$ (2 × 10 mL), with a 10% solution of $NaHSO_3$ (2 × 10 mL) and with sat. NaCl solution (1 × 10 mL). After drying (Na_2SO_4), the solution was evaporated under reduced pressure and the residue was chromatographed by flash column chromatography with the appropriate eluent mentioned below.

(2*S*,4*S*,5*S*)-2-Heptyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*syn*-3a)

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and octanal in 89% yield.

FC: EtOAc–hexane, 1:20; $[\alpha]_D$ +30.83 (*c* 1.08, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3 H, *J* = 6.8 Hz, Me), 1.25–1.38 (m, 8 H, 4 CH_2), 1.42–1.48 (m, 2 H, CH_2), 1.49 (dq, 3 H, J_{HH} = 6.6 Hz, J_{HF} = 2.0 Hz, Me-4), 1.71–1.78 (m, 2 H, CH_2), 4.19 (dq, 1 H, $J_{HH} = J_{HF}$ = 6.6 Hz, H-5), 4.25 (dqq, 1 H, J_{HH} = 6.6 Hz, J_{HF} = 2.0 Hz, H-4), 4.99 (t, 1 H, *J* = 4.8 Hz, H-2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.48 (Me), 14.03 (Me), 22.58, 23.79, 29.11, 29.39, 31.71, 33.55 (7 CH_2), 74.07 (C-4), 74.83 (q, $^2J_{CF}$ = 30.5 Hz, C-5), 105.24 (C-2), 123.59 (q, J_{CF} = 280.5 Hz, CF_3).

Anal. Calcd for $C_{12}H_{21}F_3O_2$ (254.29): C, 56.68; H, 8.32. Found: C, 56.87; H, 8.03.

(2*S*,4*S*,5*S*)-4-Methyl-2-(2-phenylethyl)-5-(trifluoromethyl)-1,3-dioxolane (*syn*-3b) and (2*R*,4*S*,5*S*)- 4-Methyl-2-(2-phenylethyl)-5-(trifluoromethyl)-1,3-dioxolane (*anti*-3b)

***syn*-3b**

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and 3-phenylpropanal in 70% yield.

FC: EtOAc–hexane, 1:20; $[\alpha]_D$ +25.05 (*c* 1.01, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (dq, 3 H, J_{HH} = 6.5 Hz, J_{HF} = 1.8 Hz, Me), 2.03–2.08 (m, 2 H, CH_2), 2.76–2.80 (m, 2 H, CH_2Ph), 4.19 (dq, 1 H, $J_{HH} = J_{HF}$ = 6.5 Hz, H-5), 4.26 (dqq, 1 H, J_{HH} = 6.5 Hz, J_{HF} = 1.9 Hz, H-4), 5.00 (t, 1 H, *J* = 4.7 Hz, H-2), 7.19–7.22 (m, 3 H, aromatic H), 7.26–7.30 (m, 2 H, aromatic H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.50 (Me), 29.76 (CH_2), 34.95 (CH_2Ph), 74.23 (C-4), 74.99 (q, $^2J_{CF}$ = 32.6 Hz, C-5), 104.27 (C-2), 123.59 (q, J_{CF} = 281.7 Hz, CF_3), 125.95, 128.38, 141.18 (aromatic C).

Anal. Calcd for $C_{13}H_{15}F_3O_2$ (260.25): C, 60.00; H, 5.81. Found: C, 59.85; H, 5.62.

***anti*-3b**

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and 3-phenylpropanal in 10% yield.

FC: EtOAc–hexane, 1:20.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41–1.43 (m, 3 H, Me), 1.88–2.04 (m, 2 H, CH_2), 2.75 (t, 2 H, *J* = 8.5 Hz, CH_2Ph), 4.32 (dq, 1 H, $J_{HH} = J_{HF}$ = 6.4 Hz, H-5), 4.47 (br dq, 1 H, *J* = 6.4 Hz, H-4), 5.36 (t, 1 H, *J* = 5.0 Hz, H-2), 7.17–7.20 (m, 3 H, aromatic H), 7.26–7.30 (m, 2 H, aromatic H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.46 (Me), 30.19 (CH_2), 36.59 (CH_2Ph), 72.93 (C-4), 76.12 (q, $^2J_{CF}$ = 31.1 Hz, C-5), 105.20 (C-2), 124.34 (q, J_{CF} = 283.3 Hz, CF_3), 126.41, 128.74, 128.78, 141.52 (aromatic C).

Anal. Calcd for $C_{13}H_{15}F_3O_2$ (260.25): C, 60.00; H, 5.81. Found: C, 59.79; H, 5.95

(2*S*,4*S*,5*S*)-2-Benzyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*syn*-3c) and (2*R*,4*S*,5*S*)-2-Benzyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*anti*-3c)

***syn*-3c**

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and phenylacetaldehyde in 49% yield.

FC: EtOAc–hexane, 1:15; $[\alpha]_D$ +15.76 (*c* 0.59, EtOH).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (dq, 3 H, J_{HH} = 6.0 Hz, J_{HF} = 1.7 Hz, Me), 3.04 (d, 2 H, *J* = 5.1 Hz, CH_2Ph), 4.16 (dq, 1 H, $J_{HH} = J_{HF}$ = 7.0 Hz, H-5), 4.23–4.29 (m, 1 H, H-4), 5.16 (t, 1 H, *J* = 5.1 Hz, H-2), 7.19–7.42 (m, 5 H, aromatic H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.48 (Me), 40.67 (CH_2Ph), 74.28 (C-4), 74.95 (q, $^2J_{CF}$ = 30.9 Hz, C-5), 105.30 (C-2), 123.56 (q, J_{CF} = 279.0 Hz, CF_3), 126.85, 128.41, 129.68, 135.40 (aromatic C).

Anal. Calcd for $C_{12}H_{13}F_3O_2$ (246.23): C, 58.54; H, 5.32. Found: C, 58.19; H, 5.51.

***anti*-3c**

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and phenylacetaldehyde in 20% yield.

FC: EtOAc–hexane, 1:15.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (d, 3 H, *J* = 5.8 Hz, Me), 2.94 (d, 2 H, *J* = 4.4 Hz, CH_2Ph), 4.16–4.27 (m, 2 H, H-4 and H-5), 5.56 (t, 1 H, *J* = 4.4 Hz, H-2), 7.21–7.39 (m, 5 H, aromatic H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.93 (Me), 41.29 (CH_2Ph), 72.55 (C-4), 75.73 (q, $^2J_{CF}$ = 31.5 Hz, C-5), 105.36 (C-2), 123.81 (q, J_{CF} = 281.2 Hz, CF_3), 126.79, 128.35, 129.96, 135.23 (aromatic C).

Anal. Calcd for $C_{12}H_{13}F_3O_2$ (246.23): C, 58.54; H, 5.32. Found: C, 58.31; H, 5.44.

(2*S*,4*S*,5*S*)-2-Cyclohexyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*syn*-3d)

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and cyclohexanecarboxaldehyde in 63% yield.

FC: EtOAc–hexane, 1:16; $[\alpha]_D$ +32.90 (*c* 1.00, $CHCl_3$).

^{1}H NMR (400MHz, $CDCl_3$): δ = 1.06–1.28 (m, 5 H, cyclohexyl), 1.47 (dq, 3 H, J_{HH} = 6.6 Hz, J_{HF} = 1.8 Hz, Me), 1.58–1.70 (m, 2 H, cyclohexyl), 1.73–1.86 (m, 4 H, cyclohexyl), 4.17 (dq, 1 H, $J_{HH} = J_{HF}$ = 6.6 Hz, H-5), 4.22 (dqq, 1 H, J_{HH} = 6.6 Hz, J_{HF} = 2.0 Hz, H-4), 4.69 (d, 1 H, *J* = 5.1 Hz, H-2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.85 (Me), 25.98, 26.00, 26.67, 27.41, 27.54, 41.40 (cyclohexyl), 74.33 (C-4), 75.11 (q, $^2J_{CF}$ = 31.2 Hz, C-5), 108.37 (C-2), 124.00 (q, J_{CF} = 282.6 Hz, CF_3).

Anal. Calcd for $C_{11}H_{17}F_3O_2$ (238.25): C, 55.45; H, 7.19. Found: C, 55.60; H, 6.98.

(2*S*,4*S*,5*S*)-4-Methyl-2-[(*E*)-2-styryl]-5-(trifluoromethyl)-1,3-dioxolane (*syn*-3e) and (2*R*,4*S*,5*S*)- 4-methyl-2-[(*E*)-2-styryl]-5-(trifluoromethyl)-1,3-dioxolane (*anti*-3e)

***syn*-3e**

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and cinnamaldehyde in 65% yield.

FC: EtOAc–hexane, 1:16; $[\alpha]_D$ +11.73 (*c* 1.04, EtOH).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52–1.56 (m, 3 H, Me), 4.28 (dq, 1 H, $J_{HH} = J_{HF}$ = 7.1 Hz, H-5), 4.29–4.40 (m, 1 H, H-4), 5.50 (d, 1 H, *J* = 6.7 Hz, H-2), 6.16 (dd, 1 H, *J* = 16.0, 6.7 Hz, H-1′), 6.82 (d, 1 H, *J* = 16.0 Hz, H-2′), 7.29–7.38 (m, 3 H, aromatic H), 7.40–7.46 (m, 2 H, aromatic H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.50 (Me), 66.48 (C-4), 72.43 (q, $^2J_{CF}$ = 30.1 Hz, C-5), 104.84 (C-2), 123.67 (C-1′), 124.15 (q, J_{CF} = 281.0 Hz, CF_3), 128.36, 129.98, 134.01 (aromatic C), 136.90 (C-2′).

Anal. Calcd for $C_{13}H_{13}F_3O_2$ (258.24): C, 60.46; H, 5.07. Found: C, 60.51; H, 5.12.

***anti*-3e**

Pale yellow liquid, obtained from (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**) and cinnamaldehyde in 15% yield.

FC: EtOAc–hexane, 1:15.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (dq, 3 H, J_{HH} = 6.6 Hz, J_{HF} = 1.8 Hz, Me), 4.42 (dq, 1 H, J_{HF} = 7.6 Hz, J_{HH} = 6 Hz, H-5), 4.51–4.52 (m, 1 H, H-4), 5.90 (d, 1 H, *J* = 5.6 Hz, H-2), 6.16 (dd, 1 H, *J* = 15.6, 5.6 Hz, H-1′), 6.79 (d, 1 H, *J* = 15.6 Hz, H-2′), 7.28–7.38 (m, 3 H, aromatic H), 7.41–7.46 (m, 2 H, aromatic H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.22 (Me), 72.83 (C-4), 76.00 (q, $^2J_{CF}$ = 30.9 Hz, C-5), 104.69 (C-2), 124.20 (q, J_{CF} = 281.4 Hz, CF_3), 125.12 (C-1′), 127.36, 129.06 (aromatic C), 134.94 (C-2′), 135.89 (aromatic C).

Anal. Calcd for $C_{13}H_{13}F_3O_2$ (258.24): C, 60.46; H, 5.07. Found: C, 60.38; H, 4.97.

Reductive Ring-Opening Reactions of Acetals with $TiCl_4$/Et_3SiH(D); General Procedure

A 1 M solution of $TiCl_4$ in CH_2Cl_2 (0.26 mL) was added dropwise over ca. 2.5 min to a solution of the 1,3-dioxolane (0.50 mmol) and Et_3SiH(D) (0.55 mmol) in anhyd CH_2Cl_2 (2.5 mL) at –78 °C under N_2, and the mixture was stirred for 15 min. After quenching with MeOH (0.20 mL) and further stirring for 5 min while warming to r.t., the reaction mixture was diluted with CH_2Cl_2 (5 mL), washed with 1 M HCl (2 × 5 mL) and with sat. NaCl solution (1 × 5 mL), and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave the reaction product which was purified by flash chromatography with the eluents mentioned below.

(2*S*,3*S*)-1,1,1-Trifluoro-3-(octyloxy)butan-2-ol (4a)

Obtained from (2*S*,4*S*,5*S*)-2-heptyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*syn*-**3a**) in 86% yield.

Pale yellow liquid; FC: EtOAc–hexane, 1:9; $[\alpha]_D$ +2.25 (*c* 1.12, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 7.0 Hz, Me), 1.27 (d, 3 H, *J* = 6.4 Hz, Me), 1.28–1.38 (m, 10 H, 5 CH_2 octyl), 1.58 (dt, 2 H, *J* = 7.2 Hz, CH_2 octyl), 2.60 (d, 1 H, *J* = 5.2 Hz, OH), 3.36 (br t, 0.96 H, *J* = 7.2 Hz, CHD), 3.53 (br t, 0.04 H, *J* = 7.2 Hz, CHD), 3.67 (dq, 1 H, *J* = 6.4, 4.1 Hz, C*H*CH_3), 4.03–4.07 (m, 1 H, C*H*CF_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.94 (Me), 13.96 (Me), 22.53, 25.89, 29.12, 29.25, 29.56, 31.71 (CH_2), 69.08 (t, J_{CD} = 22.0 Hz, CHD), 71.75 (q, $^2J_{CF}$ = 29.5 Hz, *C*HCF_3), 73.60 (*C*HCH_3), 124.29 (q, J_{CF} = 281.2 Hz, CF_3).

(2*S*,3*S*)-1,1,1-Trifluoro-3-{[(1*R*)-3-phenylpropyl]oxy}butan-2-ol (4b)

Obtained from (2*S*,4*S*,5*S*)-4-methyl-2-(2-phenylethyl)-5-(trifluoromethyl)-1,3-dioxolane (*syn*-**3b**) in 84% yield.

Pale yellow liquid; FC: EtOAc–hexane, 1:12; $[\alpha]_D$ +22.36 (*c* 1.06, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (d, 3 H, *J* = 6.4 Hz, Me), 1.92 (dt, 2 H, *J* = 7.2 Hz, CH_2), 2.56 (d, 1 H, *J* = 5.6 Hz, OH), 2.72 (t, 2 H, *J* = 7.2 Hz, CH_2Ph), 3.40 (br t, 0.97 H, *J* = 7.2 Hz, CHD), 3.58 (br t, 0.03 H, *J* = 7.2 Hz, CHD), 3.69 (dq, 1 H, *J* = 4.0, 6.4 Hz, C*H*CH_3), 4.05 (ddq, 1 H, J_{HH} = 5.6, 4.0 Hz, J_{HF} = 7.4 Hz, C*H*CF_3), 7.20–7.23 (m, 2 H, aromatic H), 7.29–7.31 (m, 3 H, aromatic H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.15 (Me), 31.25, 32.31 (CH_2), 68.39 (t, J_{CD} = 22.5 Hz, CHD), 72.23 (q, $^2J_{CF}$ = 30.1 Hz, *C*HCF_3), 74.10 (*C*HCH_3), 125.05 (q, J_{CF} = 282.0 Hz, CF_3), 126.59, 129.10, 142.38 (aromatic C).

(2*S*,3*S*)-1,1,1-Trifluoro-3-[(1*R*)-2-phenylethoxy]butan-2-ol (4c)

Obtained from (2*S*,4*S*,5*S*)-2-benzyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*syn*-**3c**) in 89% yield.

Pale yellow liquid; FC: EtOAc–hexane, 1:9; $[\alpha]_D$ +9.13 (*c* 1.04, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, 3 H, *J* = 6.6 Hz, Me), 2.50 (br s, 1 H, OH), 2.90 (d, 2 H, *J* = 7.2 Hz, CH_2Ph), 3.59 (br t, 0.97 H, *J* = 7.2 Hz, CHD), 3.69 (dq, 1 H, *J* = 4.0, 6.6 Hz, C*H*CH_3), 3.83 (br t, 0.03 H, *J* = 7.2 Hz, CHD), 3.99 (dq, 1 H, J_{HH} = 4.0 Hz, J_{HF} = 7.2 Hz, C*H*CF_3), 7.23–7.27 (m, 3 H, aromatic H), 7.31–7.34 (m, 2 H, aromatic H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.13 (Me), 36.32 (CH_2Ph), 69.91 (J_{CD} = 22.0 Hz, CHD), 71.71 (q, $^2J_{CF}$ = 30.0 Hz, *C*HCF_3), 73.99 (*C*HCH_3), 124.29 (q, J_{CF} = 280.6 Hz, CF_3), 126.47, 128.48, 128.87, 138.58 (aromatic C).

Obtained from (2*R*,4*S*,5*S*)-2-benzyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*anti*-**3c**) in 85% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (d, 3 H, *J* = 6.6 Hz, Me), 2.60 (br s, 1 H, OH), 2.90 (d, 2 H, *J* = 7.2 Hz, CH_2Ph), 3.56 (br t, 0.92 H, *J* = 7.2 Hz, CHD), 3.71 (dq, 1 H, *J* = 4.0, 6.6 Hz, C*H*CH_3), 3.83 (br t, 0.08 H, *J* = 7.2 Hz, CHD), 3.99 (dq, 1 H, J_{HH} = 4.0 Hz, J_{HF} = 7.2 Hz, C*H*CF_3), 7.22–7.27 (m, 3 H, aromatic H), 7.30–7.34 (m, 2 H, aromatic H).

(2*S*,3*S*)-3-[(*R*)-Cyclohexylmethoxy]-1,1,1-trifluorobutan-2-ol (4d)

Obtained from (2*S*,4*S*,5*S*)-2-cyclohexyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (*syn*-**3d**) in 67% yield.

Pale yellow liquid; FC: EtOAc–hexane, 1:10; $[\alpha]_D$ +22.4 (*c* 1.12, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86–0.95 (m, 2 H, cyclohexyl), 1.14–1.21 (m, 2 H, cyclohexyl), 1.25 (d, 3 H, *J* = 6.4 Hz, Me), 1.51–1.57 (m, 2 H, cyclohexyl), 1.65–1.70 (m, 1 H, cyclohexyl), 1.69–1.80 (m, 4 H, cyclohexyl), 2.58–2.65 (br s, 1 H, OH), 3.17 (d, 0.97 H, *J* = 6.5 Hz, CHD), 3.35 (d, 0.03 H, *J* = 6.5 Hz, CHD), 3.64 (dq, 1 H, *J* = 6.4, 4.3 Hz, C*H*CH_3), 4.03 (dq, 1 H, J_{HF} = 7.3 Hz, J_{HH} = 4.3 Hz, C*H*CF_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.27 (Me), 25.91, 26.66, 29.78 (CH_2 cyclohexyl), 38.18 (CH cyclohexyl), 72.01 (q, $^2J_{CF}$ = 29.6 Hz, *C*HCF_3), 73.88 (*C*HCH_3), 74.95 (t, J_{CD} = 21.5 Hz, CHD), 125.54 (q, J_{CF} = 282.5 Hz, CF_3).

(2*S*,3*S*)-1,1,1-Trifluoro-3-{[(1*R*,2*E*)-3-phenylprop-2-en-1-yl]oxy}butan-2-ol (4e)

Obtained from (2*S*,4*S*,5*S*)-4-methyl-2-[(*E*)-2-styryl]-5-(trifluoromethyl)-1,3-dioxolane (*syn*-**3e**) in 62% yield.

Pale yellow liquid; FC: EtOAc–hexane, 1:8; $[\alpha]_D$ +8.24 (*c* 1.03, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (d, 3 H, *J* = 6.4 Hz, Me), 2.60 (d, 1 H, *J* = 5.6 Hz, OH), 3.84 (dq, 1 H, *J* = 4.0, 6.4 Hz, C*H*CH_3), 4.08–4.15 (m, 1 H, C*H*CF_3), 4.14 (dd, >0.90 H, *J* = 6.0, 1.4 Hz, CHD), 4.26 (dd, <0.10 H, *J* = 6.0, 1.4 Hz, CHD), 6.26 (dd, 1 H, *J* = 15.8, 6.0 Hz, vinylic H), 6.62 (dd, 1 H, *J* = 15.8, 1.4 Hz, vinylic H), 7.24–7.35 (m, 3 H, aromatic H), 7.38–7.40 (m, 2 H, aromatic H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.20 (Me), 69.44 (t, J_{CD} = 21.5 Hz, CHD), 71.96 (q, $^2J_{CF}$ = 30.0 Hz, *C*HCF_3), 72.90 (*C*HCH_3), 124.32 (q, J_{CF} = 282.3 Hz, CF_3), 125.12 (vinylic C), 126.50, 127.88, 128.56 (aromatic C), 133.11 (vinylic C), 136.35 (aromatic C).

Allylation Reactions of Dioxolanes with $TiCl_4$/Allyltributyltin; General Procedure

To a solution of the 1,3-dioxolane (0.5 mmol) in CH_2Cl_2 (2.5 mL), cooled to –78 °C, 1M $TiCl_4$ solution in CH_2Cl_2 (0.52 mL) was added dropwise over ca. 2.5 min. After 5 min, allyltributylstannane was added dropwise over 2 min and the mixture was stirred at –78 °C for 15 min. The reaction was quenched with MeOH (0.5 mL) and warmed to r.t. The mixture was diluted with CH_2Cl_2 (5 mL), washed with 1 M HCl (2 × 5 mL) and with sat. NaCl solution (1 × 5 mL) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the product was purified by flash column chromatography with the eluents mentioned below.

(2*S*,3*R*)-1,1,1-Trifluoro-3-{[(1*S*)-1-heptylbut-3-en-1-yl]oxy}butan-2-ol (7a)

Obtained from (2*S*,4*S*,5*S*)-2-heptyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (**3a**) in 80% yield.

Pale yellow liquid; FC: CH_2Cl_2; $[\alpha]_D$ +1.11 (*c* 1.02, EtOH).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 7.0 Hz, Me), 1.30–1.45 (m, 13 H, 5 CH_2 octyl and Me), 1.57–1.67 (m, 2 H, CH_2 octyl), 2.17–2.28 (m, 2 H, allylic CH_2), 2.93 (br, 1 H, OH), 3.38 (tt, 1 H, $J_1 = J_2 = 5.7$ Hz, CHO), 3.75 (dq, 1 H, *J* = 6.4, 3.4 Hz, C*H*CH_3), 3.98–4.07 (m, 1 H, C*H*CF_3), 5.02–5.08 (m, 2 H, vinylic H), 5.71–5.82 (m, 1 H, vinylic H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.56 (Me), 14.03 (Me), 22.60, 25.31, 29.20, 29.68, 31.77, 33.79, 38.81 (CH_2), 71.59 (*C*HCH_3), 72.05 (q, $^2J_{CF}$ = 30.1 Hz, *C*HCF_3), 78.07 (CHO), 117.19 (vinylic CH_2), 124.38 (q, J_{CF} = 281.1 Hz, CF_3), 134.56 (vinylic CH).

Anal. Calcd for $C_{15}H_{27}F_3O_2$ (296.37): C, 60.79; H, 9.18. Found: C, 60.63; H, 8.98.

(2*S*,3*R*)-1,1,1-Trifluoro-3-{[(1*S*)-1-(2-phenylethyl)but-3-en-1-yl]oxy}butan-2-ol (7b)

Obtained from (2*S*,4*S*,5*S*)-4-methyl-2-(2-phenylethyl)-5-(trifluoromethyl)-1,3-dioxolane (**3b**) in 85% yield.

Pale yellow liquid; FC: CH_2Cl_2–light petroleum, 1:1; $[\alpha]_D$ +1.04 (*c* 1.55, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (d, 3 H, *J* = 6.4 Hz, Me), 1.85 (dt, 2 H, *J* = 7.9, 5.8 Hz, $PhCH_2CH_2$), 2.32–2.36 (m, 2 H, allylic CH_2), 2.65 (br d, 1 H, *J* = 5.0 Hz, OH), 2.65 (dt, 1 H, *J* = 13.8, 7.9 Hz, CH_2Ph), 2.72 (dt, 1 H, *J* = 13.8, 7.9 Hz, CH_2Ph), 3.50 (tt, 1 H, $J_1 = J_2 = 5.8$ Hz, CHO), 3.80 (dq, 1 H, *J* = 6.4, 3.6 Hz, C*H*CH_3), 3.97–4.05 (m, 1 H, C*H*CF_3), 5.10–5.15 (m, 2 H, vinylic CH_2), 5.83 (ddt, 1 H, *J* = 18.0, 10.1, 7.1 Hz, vinylic H), 7.19–7.23 (m, 2 H, aromatic H), 7.28–7.33 (m, 3 H, aromatic H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.24 (Me), 31.92, 35.70, 39.25 (CH_2), 72.06 (*C*HCH_3), 72.54 (q, $^2J_{CF}$ = 30.2 Hz, *C*HCF_3), 77.64 (CHO), 117.94 (vinylic CH_2), 124.64 (q, J_{CF} = 282.3 Hz, CF_3), 126.39, 128.65, 128.89 (aromatic C), 134.64 (vinylic CH), 142.11 (aromatic C).

Anal. Calcd for $C_{16}H_{21}F_3O_2$ (302.33): C, 63.56; H, 7.00. Found: C, 63.42; H, 6.92.

(2*S*,3*R*)-3-{[(1R)-1-cyclohexylbut-3-en-1-yl]oxy}-1,1,1-trifluorobutan-2-ol (7d)

Obtained from (2*S*,4*S*,5*S*)-2-cyclohexyl-4-methyl-5-(trifluoromethyl)-1,3-dioxolane (**3d**) in 62% yield.

Pale yellow liquid; FC: EtOAc–light petroleum, 1:16; $[\alpha]_D$ +10.4 (*c* 1.00, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95–1.10 (m, 2 H, cyclohexyl), 1.10–1.30 (m, 3 H, cyclohexyl), 1.23 (d, 3 H, *J* = 6.4 Hz, Me), 1.44–1.53 (m, 1 H, cyclohexyl), 1.65–1.72 (m, 2 H, cyclohexyl), 1.73–1.81 (m, 3 H, cyclohexyl), 2.20–2.34 (m, 2 H, allylic CH_2), 2.56 (br d, 1 H, *J* = 5.8 Hz, OH), 3.19 (m, 1 H, CHO), 3.78 (dq, 1 H, *J* = 6.4, 3.0 Hz, C*H*CH_3), 4.05–4.13 (m, 1 H, C*H*CF_3), 5.05–5.12 (m, 2 H, vinylic CH_2), 5.82 (ddt, 1 H, *J* = 17.0, 10.4, 7.1 Hz, vinylic CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.90 (Me), 26.67, 26.92, 29.11 (CH_2 cyclohexyl), 36.09 (allylic CH_2), 41.25 (CH cyclohexyl), 72.34 (q, $^2J_{CF}$ = 29.8 Hz, *C*HCF_3), 72.40 (*C*HCH_3), 82.80 (CHO), 117.36 (vinylic CH_2), 124.60 (q, J_{CF} = 281.9 Hz, CF_3), 135.43 (vinylic CH).

Anal. Calcd for $C_{14}H_{23}F_3O_2$ (280.33): C, 59.98; H, 8.27. Found: C, 59.77; H, 8.11.

Alternative Synthesis of (2*S*,3*S*)-1,1,1-Trifluoro-3-(octyloxy)butan-2-ol (4a)

To a solution of (2*S*,3*S*)-1,1,1-trifluorobutane-2,3-diol (**2**, 302 mg, 2.09 mmol) in freshly distilled THF (10 mL), *t*BuOK (236 mg, 2.10 mmol) was added and the mixture was refluxed for 15 min. Benzyl bromide (0.25 mL, 2.10 mmol) was then added, the mixture was refluxed for 3 h, cooled to r.t., diluted with EtOAc (15 mL), washed with H_2O (2 × 10 mL), 1 M HCl (1 × 10 mL), and sat. NaCl (1 × 10 mL). The separated organic layer was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by flash chromatography (EtOAc–hexane, 1:5) to give (2*S*,3*R*)-3-benzyloxy-4,4,4-trifluorobutan-2-ol as pale yellow liquid, 250 mg (51% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (d, 3 H, *J* = 6.5 Hz, Me), 1.85 (br s, 1 H, OH), 3.81 (dq, 1 H, *J* = 7.1, 4.4 Hz, C*H*CF_3), 4.05 (dq, 1 H, *J* = 6.5, 4.4 Hz, C*H*CH_3), 4.63 (d, 1 H, *J* = 11.2 Hz, CH_2Ph), 4,90 (d, 1 H, *J* = 11.2 Hz, CH_2Ph), 7.36–7.40 (m, 5 H, aromatic H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.97 (Me), 66.32 (*C*HCH_3), 75.20 (*C*H_2Ph), 80.17 (q, $^2J_{CF}$ = 26.2 Hz, *C*HCF_3), 124.73 (q, J_{CF} = 283.5 Hz, CF_3), 128.14, 128.34, 128.59, 136.79 (aromatic C).

To a suspension of NaH (190 mg, 50% dispersion in mineral oil, 3.96 mmol) in DMF (5 mL), (2*S*,3*R*)-3-benzyloxy-4,4,4-trifluorobutan-2-ol prepared as above (250 mg, 1.05 mmol) was added, followed by bromooctane (0.28 mL, 1.60 mmol). The mixture was stirred at 60 °C for 1.5 h, cooled to r.t. and treated cautiously with H_2O until evolution of H_2 ceased. The solution was concentrated under reduced pressure, the residue was taken up in EtOAc (5 mL), washed with 1 M HCl (2 × 5 mL), with sat. NaCl solution (1 × 5 mL), and dried (Na_2SO_4). The solvent was removed under reduced pressure affording 580 mg of a chromatographically homogeneous yellow oil which was used in the subsequent step without further purification.

({[(1*R*,2*S*)-2-(Octyloxy)-1-(trifluoromethyl)propyl]oxy}methyl)benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 3 H, *J* = 6.8 Hz, Me), 1.15–1.40 (m, 13 H, 5 CH_2 and Me), 1.42–1.60 (m, 2 H, CH_2), 3.29 (dt, 1 H, *J* = 8.9, 6.4 Hz, CH_2O), 3.44 (dt, 1 H, *J* = 8.9, 6.4 Hz, CH_2O), 3.63 (dq, 1 H, *J* = 6.8, 4.1 Hz, C*H*CH_3), 3.80 (dq, 1 H, J_{HH} = 4.1, J_{HF} = 7.4 Hz, C*H*CF_3), 4.69 (d, 1 H, *J* = 11.3 Hz, $PhCH_2O$), 4.79 (d, 1 H, *J* = 11.3 Hz, $PhCH_2O$), 7.24–7.47 (m, 5 H, aromatic H).

To a suspension of Pd/C (210 mg, 10% Pd) in MeOH (15 mL) under an atmosphere of H_2, a solution of crude ({[(1*R*,2*S*)-2-(octyloxy)-1-(trifluoromethyl)propyl]oxy}methyl)benzene prepared as above (550 mg, 1.05 mmol) in MeOH (5 mL) was added and the reaction mixture was stirred overnight at r.t. The catalyst was filtered off, the methanolic solution was evaporated under reduced pressure and the residue was purified by flash chromatography (EtOAc–hexane, 1:9) to give the title compound **4a**.

Pale yellow liquid, 190 mg (68% yield); $[\alpha]_D$ +2.18 (*c* 0.55, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 6.8 Hz, Me), 1.27 (d, 3 H, *J* = 6.4 Hz, Me), 1.28–1.37 (m, 10 H, 5 CH_2 octyl), 1.55–1.60 (m, 2 H, CH_2 octyl), 2.63 (d, 1 H, *J* = 5.4 Hz, OH), 3.41 (dt, 1

H, J = 9.0, 6.4 Hz, CH_2O), 3.57 (dt, 1 H, J = 9.0, 6.8 Hz, CH_2O), 3.70 (dq, 1 H, J = 6.4, 4.0 Hz, C*H*CH_3), 4.07 (ddq, 1 H, J_{HH} = 5.4, 4.0 Hz, J_{HF} = 7.4 Hz, C*H*CF_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.43 (Me), 14.50 (Me), 23.02, 26.43, 29.60, 29.74, 30.18, 32.18 (CH_2 octyl), 69.92 (CH_2O), 72.26 (q, $^2J_{CF}$ = 29.6 Hz, *C*HCF_3), 74.05 (*C*HCH_3), 124.77 (q, J_{CF} = 282.2 Hz, CF_3).

(2*S*,3*S*)-4,4,4-Trifluoro-3-(octyloxy)butan-2-ol (5)

To a suspension of NaH (193 mg, 50% dispersion in mineral oil, 4 mmol) in DMF (5 mL), (2*S*,3*S*)-3-benzyloxy-4,4,4-trifluorobutan-2-ol[4] (252 mg, 1.05 mmol) was added, followed by bromooctane (0.28 mL, 1.6 mmol). The mixture was stirred at 60 °C for 1.5 h, cooled to r.t. and treated cautiously with H_2O until evolution of H_2 ceased. The solution was concentrated under reduced pressure, then the residue was taken up in EtOAc (10 mL), washed with 1 M HCl (2 × 8 mL) and with sat. NaCl solution (1 × 8 mL). After drying (Na_2SO_4) the solvent was removed under reduced pressure affording 580 mg of ({[(1*S*,2*S*)-2-octyloxy-1-(trifluoromethyl)propyl]oxy}methyl)benzene as chromatographically homogeneous yellow oil which was used in the subsequent step without further purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, 3 H, J = 6.8 Hz, Me), 1.28–1.42 (m, 13 H, 5 CH_2 octyl and Me), 1.53–1.61 (m, 2 H, CH_2 octyl), 3.59–3.83 (m, 4 H, CH_2O, C*H*CH_3 and C*H*CF_3), 4.50 (d, 1 H, J = 11.4 Hz, $PhCH_2O$), 4.59 (d, 1 H, J = 11.4 Hz, $PhCH_2O$), 7.33–7.49 (m, 5 H, aromatic H).

To a suspension of Pd/C (210 mg, 10% Pd) in MeOH (15 mL) under an atmosphere of H_2, a solution of the crude product prepared as above (550 mg, 1.05 mmol) in MeOH (5 mL) was added and the reaction mixture was stirred overnight at r.t. The catalyst was filtered off, the methanolic solution was evaporated under reduced pressure and the residue was purified by flash column chromatography (EtOAc–hexane, 1:6) giving **5**.

Pale yellow oil, 210 mg (77% yield); $[\alpha]_D$ – 4.25 (*c* 0.40, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3 H, J = 6.6 Hz, Me), 1.29–1.38 (m, 13 H, 5 CH_2 octyl and Me), 1.60–1.63 (m, 2 H, CH_2 octyl), 2.07 (br s, 1 H, OH), 3.58–3.67 (m, 2 H, CH_2O), 3.80–3.86 (m, 1,H, C*H*CH_3), 4.04 (dq, 1 H, J = 6.4, 4.5 Hz, C*H*CF_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.43 (Me), 18.35 (Me), 23.01, 26.25, 29.59, 29.68, 30.23, 32.18 (6 CH_2 octyl), 66.70 (*C*HCH_3), 74.46 (CH_2O), 81.42 (q, $^2J_{CF}$ = 27.3 Hz, *C*HCF_3), 125.13 (q, J_{CF} = 285.1 Hz, CF_3).

Removal of the Chiral Auxiliary from Compound 4a 3-[(*R*)-(1-^{2}H)Octyloxy]propanoic Acid

Obtained from (2*S*,3*S*)-1,1,1-Trifluoro-3-(octyloxy)butan-2-ol (**4a**) in 64% yield following the procedure described in ref. 3e.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.86 (t, 3 H, J = 6.7 Hz, Me), 1.23–1.36 (m, 10 H, 5 CH_2 octyl), 1.45 (d, 3 H, J = 6.9 Hz, Me), 1.60–1.63 (m, 2 H, CH_2 octyl), 3.44 (br t, 0.5 H, J = 6.5 Hz, CHD), 3.55 (br t, 0.5 H, J = 6.5 Hz, CHD), 3.97 (q, 1 H, J = 6.9 Hz, C*H*COOH), 8.00–8.50 (br, 1,H, COOH).

(*R*)-(1-^{2}H)Octan-1-ol (6)

Obtained from the above mentioned 3-[(*R*)-(1-^{2}H)octyloxy]propanoic acid in 32% yield following the procedure described in ref. 3e.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, 3 H, J = 6.7 Hz, Me), 1.22–1.35 (m, 10 H, 5 CH_2 octyl), 1.51–1.62 (m, 3 H, CH_2 octyl and OH), 3.61 (br t, 1 H, J = 6.6 Hz, CHD).

Removal of the Chiral Auxiliary from Compound 7b: Synthesis of (3*S*)-1-Phenylhex-5-en-3-ol (8)

2-{[(1*S*)-1-(2-Phenylethyl)but-3-en-1-yl]oxy}propanoic Acid

Obtained from (2*S*,3*R*)-1,1,1-trifluoro-3-{[(1*S*)-1-(2-phenylethyl)but-3-en-1-yl]oxy}butan-2-ol (**7b**) in 58% yield following the procedure described in ref. 3e.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (d, 3 H, J = 6.8 Hz, Me), 1.85–1.87 (m, 2 H, $PhCH_2CH_2$), 2.35 (m, 2 H, allylic CH_2), 2.69 (m, 2 H, $PhCH_2$), 3.50 (m, 1 H, CHO), 3.93 (m, 1 H, C*H*COOH), 5.10–5.16 (m, 2 H, vinylic CH_2), 5.78–5.80 (m, 1 H, vinylic CH), 7.15–7.31 (m, 5 H, aromatic H), 9.20–9.80 (br, 1 H, COOH).

(3*S*)-1-Phenylhex-5-en-3-ol (8)

Obtained from the above mentioned 2-{[(1*S*)-1-(2-phenylethyl)but-3-en-1-yl]oxy}propanoic acid in 33% yield following the procedure described in ref. 3e.

$[\alpha]_D$ – 19.24 (*c* 0.98, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.58 (br s, 1 H, OH), 1.74–1.86 (m, 2 H, $PhCH_2CH_2$), 2.10–2.14 (m, 2 H, allylic CH_2), 2.62–2.90 (m, 2 H, PhC*H*2), 3.60–3.74 (m, 1 H, CHO), 5.08–5.22 (m, 2 H, vinylic CH_2), 5.72–5.93 (m, 1 H, vinylic CH), 7.13–7.34 (m, 5 H, aromatic H).

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