Fluorinated Synthons: Reactivity of 1-R_F-Epoxy Ethers with Lewis Acids

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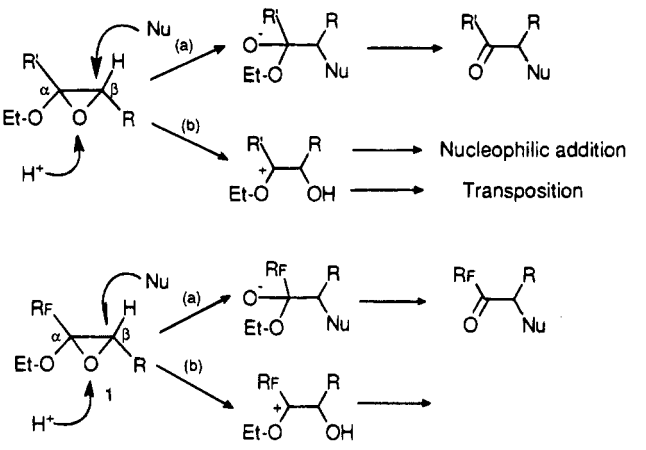
Fluorinated epoxy ethers **2**, **5**, **6**, and **12** react with Lewis acids to give different ring opening products, depending upon the structure and the experimental conditions. Both nucleophile-assisted and stepwise processes can occur. In all cases, except when a phenyl group stabilizes the Cβ secondary carbenium ion, the Cα–O bond is broken leading to addition, transposition, or cyclization products. $EtAlCl_2$ reacted with epoxy ethers **2a–c** providing chlorohydrins **3a** and the transposed products **4b,c** and **5b,c**. With epoxy ethers **6a–c** aldehydes **7a–c** were formed through a transposition. Epoxy ethers **9a–c** underwent ring opening to the chloroketones **10a–c** with $EtAlCl_2$ and $TiCl_4$ and **9a** gave the glycol ether **11a** with Me_3Al. Epoxy ether **12a** was transformed into a mixture of chlorohydrin **13a**$_1$ (*S*R**) and the cyclized product **14a** (*S*R**) with $TiCl_4$ or $EtAlCl_2$ at −78 °C. At room temperature, the cyclized products **14a** (*S*R**) or **15c** were selectively obtained in good yields from **12a** and **12c**, respectively, with $TiCl_4$.

The perfluoroalkyl group has unique features, such as high electronegativity, stability, and lipophilicity.[1] Perfluoroalkyl substituted organic compounds are becoming increasingly important in the development of new and more effective medicines and agrochemicals,[2] or new materials such as liquid crystals.[3] However, efficient methods for selective introduction of trifluoromethyl or perfluoroalkyl groups into organic compounds still remain a challenging problem.[4] For this purpose, synthetic strategies using fluorinated building blocks have been the subject of active investigation.[5] Toward this aim we have synthesized building blocks with perfluoroalkyl substituents such as 1-perfluoroalkyl enol ethers,[6] enamines,[7] or vinyl sulfides[8] from perfluoroalkyl carboxylic acids and employed them for the preparation of a variety of fluorinated compounds.[9,10] We are particularly interested in the 1-perfluoroalkyl epoxy ethers **1**, prepared by epoxidation of the corresponding 1-R_F enol ethers.[10a] These epoxy ethers can potentially be regarded as versatile building blocks in organic synthesis.

Scheme 1



In the reaction of nonfluorinated epoxides with a nucleophilic reagent, the favored attack site is the less hindered carbon. However, in the case of epoxy ethers, this S_N2 type ring opening (Scheme 1, path a) is disfavored because of the competing facile opening of the oxirane ring leading to a stable alkoxycarbenium ion (Scheme 1, path b).[11,12] The more important effect of a fluorinated substituent is the destabilization of the alkoxycarbenium ion. Consequently, the acid-catalyzed ring opening of **1** is expected to be less favored than in the case of nonfluorinated analogs, and the nucleophilic process leading to α-substituted ketones can compete (Scheme 1). This effect is well illustrated by the difference in reactivity of the two types of epoxy ethers with magnesium bromide. While nonfluorinated epoxy ethers react with $MgBr_2$ to provide α-alkoxy ketones resulting

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Table 1. Opening of Epoxy Ethers 2 by Lewis Acids

run	compd	Lewis acid (equiv.)	T, °C (t, h)	products[a]
1	**2a**	$EtAlCl_2$ (1.2)	0 (1)	**3a** 100 (76)[b]
2	**2a**	$EtAlCl_2$ (1.2)	−78 (1)	**3a**$_1$ 100 (78)
3	**2a**	Me_3Al (2)	0 (1)	**2a** 100
4	**2b**	$EtAlCl_2$ (1.2)	0 (1)	**4b** 65 (55), **5b** 35 (20)
5	**2b**	$EtAlCl_2$[c] (1.2)	−78 (1)	**3b**$_1$ 95 (86)[d]
6	**2b**	Me_3Al (2)	0 (1)	**2b** 100
7	**2c**	$EtAlCl_2$ (1.2)	0 (1)	**4c** 65 (60), **5c** 35 (30)
8	**2c**	$TiCl_4$ (2)	0 (1)	**3c** 100 (75)[b]
9	**2c**	Me_3Al (2)	0 (1)	**2c** 100

[a] GC analysis, the values in parenthesis are isolated yields. [b] Mixture (1:1) of the two diastereoisomers. [c] Reaction performed at −78 °C with $TiCl_4$ gave same results. [d] Reaction performed at −78 °C followed by 48 h at 0 °C gave a mixture of **4b** (39%), **5b** (23%), **3b**$_1$ (16%), and **3b**$_2$ (17%).

from a Wagner−Meerwein rearrangement,[13] fluoroalkyl substituted epoxy ethers **1** undergo nucleophilic ring opening leading to fluoroalkyl substituted α-bromo ketones.[10a] We have also previously described the nucleophilic opening of these compounds **1** to give α-amino ketones.[14]

We have then explored the acid-catalyzed opening of epoxy ethers **1** in the presence of Lewis acids. Since a mild Lewis acid, such as $MgBr_2$, was found to cause nucleophile induced ring opening, we decided to study Lewis acids of different nucleophilicities and electrophilicities such as alkyl aluminum reagents ($EtAlCl_2$ and Me_3Al) and titanium tetrachloride. Two main questions have to be considered, the first concerns the site of opening of the oxirane ring, the second is the subsequent behavior of the resulting carbenium ion.

The reaction outcome will be dependent on the nature of the R_F and R substituents. Therefore we have studied the reaction of epoxy ethers **2** (R = cyclohexylmethyl, a primary alkyl substituent) and **6** (R = cyclohexyl, a good migrating group). Epoxy ethers **8** (R = phenyl, able to stabilize an adjacent carbocation) and **12** (R = phenethyl), where the phenyl is a potential internal nucleophile, have been studied. The effect of the fluorinated chains (R_F = CF_3, C_2F_5, C_3F_7) was also investigated.

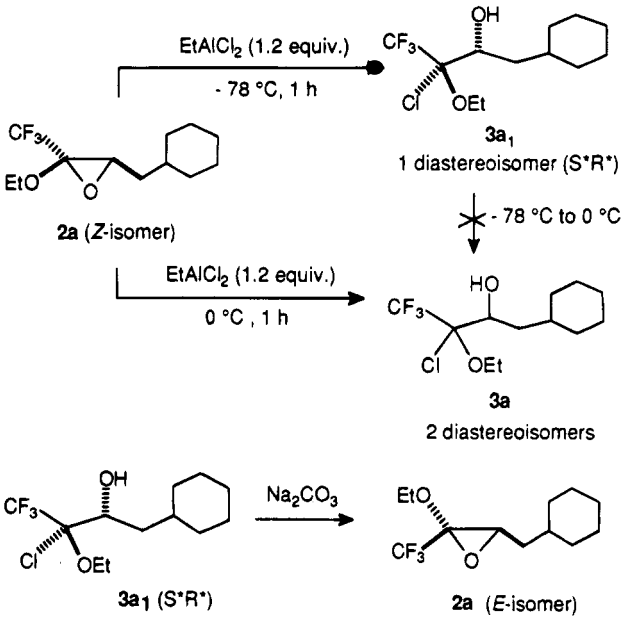
Results

The *Z*-epoxy ethers **2, 6, 8, 12** were prepared by epoxidation with mCPBA of the corresponding *Z*-enol ethers,[10a] obtained by Wittig olefination of ethyl perfluoroalkanoates.[6]

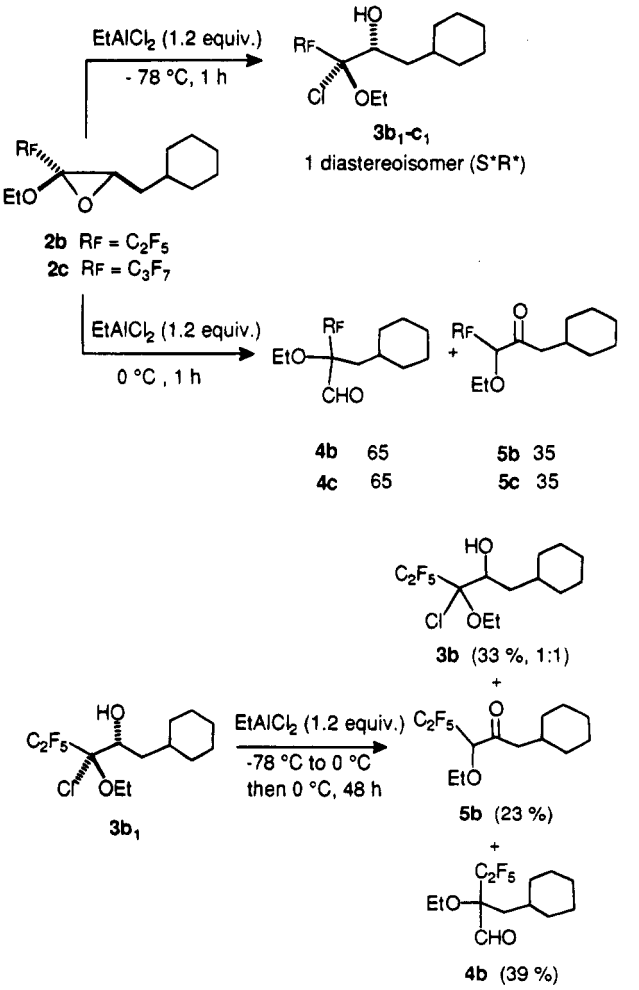
Reaction of Epoxy Ethers 2a−c (Table 1, Schemes 2 and 3). $EtAlCl_2$-induced opening of the *Z*-epoxy ether **2a** performed at 0 °C provided in good yield the chlorohydrin **3a** as a mixture (1:1) of two diastereomers (76%). At −78 °C the reaction led to a single chlorohydrin **3a**$_1$ (*S*R**). This chlorohydrin was stable in the reaction medium even when the temperature was raised to 0 °C. Its relative configuration has been deduced from the formation of the *E*-isomer of epoxy ether **2a** by treatment with aqueous sodium carbonate.

At 0 °C, *Z*-epoxy ethers **2b** (R_F = C_2F_5) and **2c** (R_F = C_3F_7) reacted with $EtAlCl_2$ or with $TiCl_4$ to give a mixture of transposed aldehydes **4** (major) and ketones **5** (minor) in good yields. However, when the reactions were performed at −78 °C, the (*S*R**) diastereoisomer of chlorohydrins **3b(c)** was isolated, with only traces of the other diastereoisomer. When the reaction temperature was raised from −78 °C to 0 °C, the (*S*R**) chlorohydrin **3b**$_1$ (or **3c**$_1$) turned slowly into a mixture of diastereo-

Scheme 2



Scheme 3



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Scheme 4

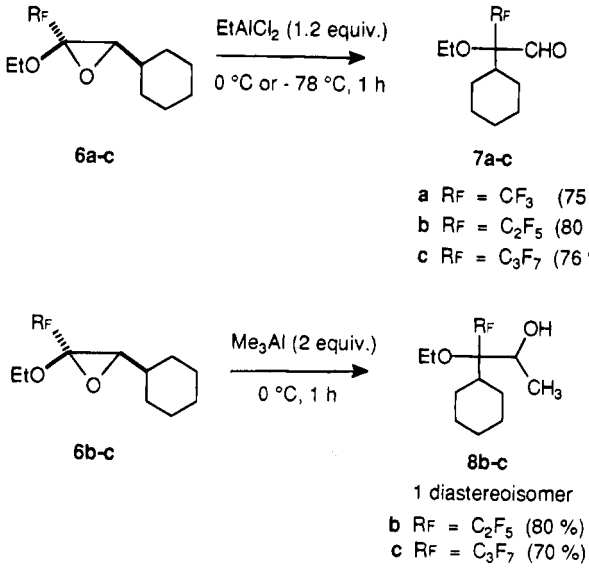


Table 2. Opening of Epoxy Ethers 6 by Lewis Acids

run	compd	Lewis acid (equiv)		T, °C (t, h)	products[a]
1	**6a**	$EtAlCl_2$	(1.2)	0 (1)	**7a** 96 (70)
2	**6a**	$EtAlCl_2$	(1.2)	−78 (2)	**7a** 98 (78)
3	**6a**	Me_3Al[b]	(2)[b]	0 (1)[b]	**6a** 100
4	**6b**	$EtAlCl_2$	(1.2)	0 (1)	**7b** 96 (68)
5	**6b**	$EtAlCl_2$	(1.2)	−78 (2)	**7b** 98 (80)
6	**6b**	Me_3Al	(2)	0 (1)	**8b** 94 (80)
7	**6c**	$EtAlCl_2$	(1.2)	0 (1)	**7c** 98 (76)
8	**6c**	Me_3Al	(2)	0 (1)	**8c** 90 (70)

[a] GC analysis, the values in parentheses are isolated yields. [b] Starting material was also recovered with 4 equiv of Me_3Al at 20 °C for 5 h.

isomers **3b** (or **3c**) and rearranged products **4b** and **5b** (or **4c** and **5c**). With Me_3Al, no reaction occurred with epoxy ethers **2a**−**c**.

Reaction of Epoxy Ethers 6a−c (Scheme 4, Table 2). $EtAlCl_2$-induced opening of epoxy ethers **6a**−**c** provided aldehydes **7a**−**c** derived from transposition, in good yield at 0 °C or at −78 °C. No reaction of epoxy ether **6a** with Me_3Al even at room temperature and with an excess of catalyst (4 equiv) was observed. However, epoxy ethers **6b** and **6c** underwent a facile reaction with Me_3Al at 0 °C to provide the rearranged ethoxy alcohols **8b** and **8c** (one diastereoisomer) in good yield, relative configuration of which has not been determined.

Reaction of Epoxy Ethers 9a−c (Scheme 5, Table 3). At −78 °C or at 0 °C, $EtAlCl_2$- or $TiCl_4$-induced opening of the epoxy ethers **9a**−**c** provided chloro ketones **10a**−**c** in 60−75% isolated yield. The Me_3Al-induced opening of **9a** afforded the ethoxy alcohol **11a** as a single diastereoisomer (60% yield). The relative configuration of the stereogenic centers in **11a** has not been determined.

Reaction of Epoxy Ethers 12a,c (Schemes 6−8, Table 4). At −78 °C, the epoxy ether **12a** reacted with $EtAlCl_2$ to give a mixture (9:1) of chlorohydrin **13a**$_1$ as a single (S^*R^*) diastereoisomer and *cis*-1-ethoxytetral-2-ol **14a**. At 0 °C, a mixture (1:1) of the diastereoisomeric chlorohydrins **13a** and the *cis*-**14a** were obtained. Even when the temperature was raised to 20 °C or when the reaction time was prolonged or when the number of equivalents of $EtAlCl_2$ was increased, the ratio of chlorohydrin and tetralol did not change. With $TiCl_4$ (2 equiv), the same stereoselective formation of chlorohydrin

Scheme 5

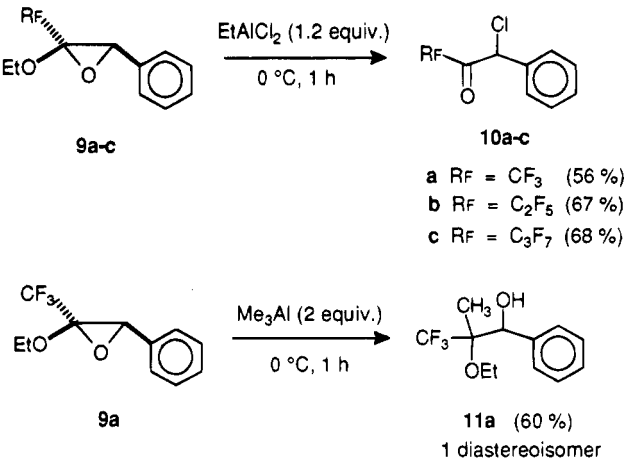
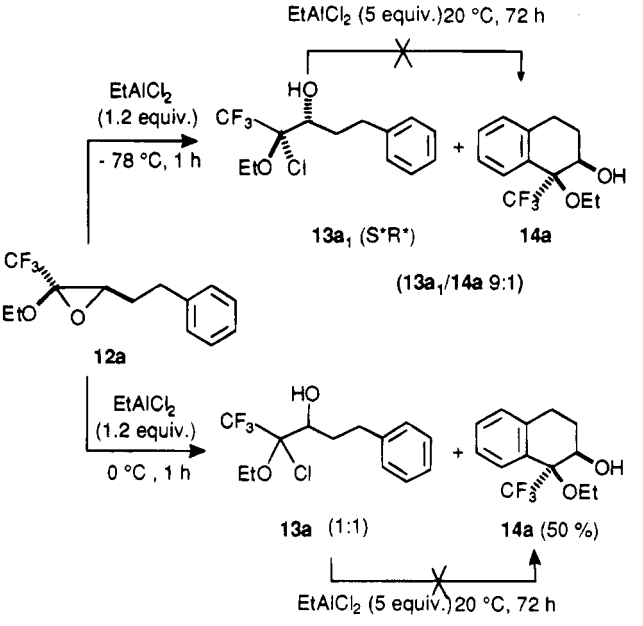


Table 3. Opening of Epoxy Ethers 9 by Lewis Acids

run	compd	Lewis acid (equiv)		T, °C (t, h)	products[a]
1	**9a**	$EtAlCl_2$	(1.2)	0 (1)	**10a** 70 (56)
1	**9a**	$EtAlCl_2$	(1.2)	−78 (3)	**10a** 68
3	**9a**	$TiCl_4$	(2)	0 (1)	**10a** 83 (75)
4	**9a**	Me_3Al	(2)	0 (1)	**11a**$_1$ 75 (60)[b]
5	**9b**	$EtAlCl_2$[c]	(1.2)	0 (1)	**10b** 67 (62)
6	**9c**	$EtAlCl_2$[c]	(1.2)	0 (1)	**10c** 68 (60)

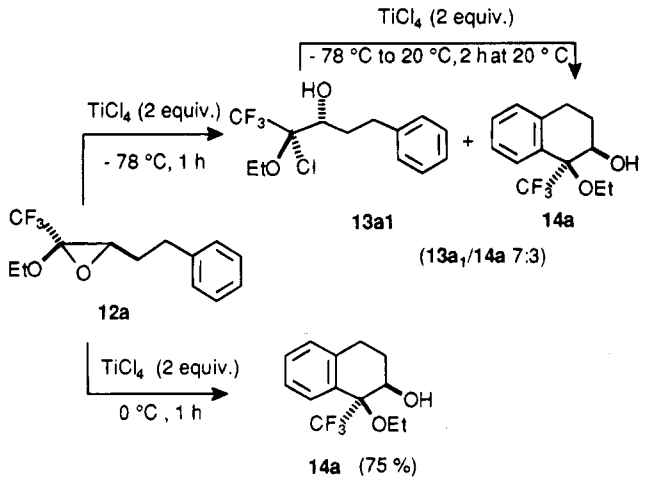
[a] GC analysis, the values in parentheses are isolated yields. [b] One single diastereoisomer. [c] Same results obtained when reaction was performed at −78 °C.

Scheme 6



13a$_1$ (S^*R^*) occurred at −78 °C, accompanied by the tetralol **14a**. When the reaction temperature was raised from −78 °C to 20 °C or when the reaction was directly performed at 0 °C, this tetralol **14a** was selectively obtained (75%). The relative configuration (S^*R^*) of **13a**$_1$ has been assigned by comparison of its ^{19}F NMR data to those of **3a**$_1$ (S^*R^*). The *cis* relative configuration of the hydroxyl group and ethoxy group in the tetralol **14a** was deduced from NMR data: the coupling constants between H-2 and H-3, H-3′ (^3J = 9.2 Hz and ^3J = 3.6 Hz), indicates an axial position for the H-2 hydrogen and thus an equatorial position for the hydroxy group. The strong heteronuclear Overhauser effect between CF_3 and H-2,

Scheme 7



Scheme 8

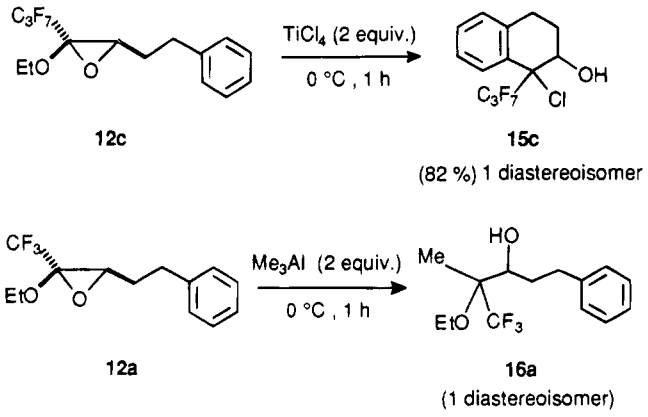


Table 4. Opening of Epoxy Ethers 12 by Lewis Acids

run	compd	Lewis acid (equiv)		T, °C (t, h)	products[a]
1	**12a**	$EtAlCl_2$	(1.2)	0 (1)	**13a** 56 (34),[b] **14a**$_1$ 44 (28)
2	**12a**	$EtAlCl_2$	(1.2)	−78 (1)	**13a**$_1$ 89, **14a**$_1$ 11
3	**12a**	$EtAlCl_2$	(5)	20 (72)	**13a** 52,[b] **14a**$_1$ 48
4	**12a**	$TiCl_4$	(2)	−78 (1)[c]	**13a**$_1$ 69, **14a**$_1$ 31
6	**12a**	$TiCl_4$	(2)	0 (1)	**14a**$_1$ 90 (75)
7	**12a**	Me_3Al	(2)	0 (1)	**16a** 96 (70)
8	**12c**	$TiCl_4$	(2)	0 (1)	**15c** (82)

[a] GC analysis, the values in parentheses are isolated yields. [b] Mixture 1:1 of two diastereoisomers. [c] Reaction performed at −78 °C and then 2 h at 20 °C provided selectively tetralol **14a**$_1$ in 95% (GC).

OH (presence of a H-bond) and the aromatic H-8 proton indicates a *cis* relationship between CF_3 and H-2 (Figure 1). The ethoxy group and the hydroxy group are in a *cis* relationship.

The reaction of epoxy ether **12c** with $TiCl_4$ (2 equiv) provided in high yield the unexpected 1-chlorotetral-2-ol **15c**. The relative configuration of the chlorine and the hydroxy group in **15c** has not been determined. The coupling constants of the H-2 hydrogen with hydrogens H-3 (^3J = 6 Hz and ^3J = 2.8 Hz) seem to indicate an equatorial configuration for H-2; in this equatorial position a heteronuclear Overhauser effect between the CF_2 groups and H-2 can be expected whatever the configuration of the fluorinated substituent (Figure 1). The epoxy ether **12a** reacted with Me_3Al to give the ethoxy alcohol **16a** as a single diastereoisomer. The strong heteronuclear Overhauser effect observed between the CF_3 group and H-3 and the hydroxy group, and the coupling constant (^3J = 6.4 Hz) between the hydrogen of

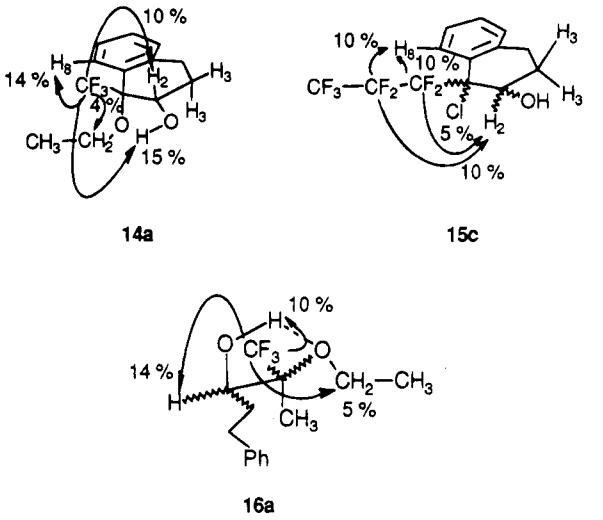


Figure 1. Heteronuclear Overhauser effects of **14a**, **15c**, and **16a**.

the hydroxy group and H-3 (Figure 1) are not sufficient evidence to allow us to assign the relative configuration in the ethoxy alcohol **16a**.

Discussion

The ring opening of the epoxy ether **2a** with $EtAlCl_2$ at 0 °C occurs by a stepwise process with the formation of an alkoxycarbenium ion, followed by an addition of a chloride anion to give a mixture (1:1) of the two diastereoisomeric chlorohydrins **3a**. This preferential formation of an α-trifluoromethylated alkoxy carbenium ion indicates that a secondary carbocation is less stable than an α-trifluoromethylated alkoxycarbenium ion. Conversely, at −78 °C, only one diastereoisomer of the chlorohydrin **3a** is obtained with retention of configuration. This strongly suggests that there is nucleophilic assistance of a chloride which is delivered from the Lewis acid epoxy ether complex. This proposed mechanism is confirmed by the results obtained by the treatment of epoxy ether **9a** with Me_3Al (see below). Epoxy ethers **2b** ($R_F = C_2F_5$) and **2c** ($R_F = C_3F_7$) react similarly to **2a** with $EtAlCl_2$ at −78 °C, leading stereoselectively to chlorohydrins **3b**$_1$ and **3c**$_1$, respectively, while the reaction at 0 °C occurs through a rearrangement process leading to aldehyde **4b** (and **4c**) and ketone **5b** (and **5c**). Although chlorohydrins **3b**$_1$ and **3c**$_1$ can themselves undergo rearrangement leading to the same products **4** and **5**, they are unlikely intermediates at 0 °C, since their rearrangement occurs only slowly (48 h at 0 °C). The striking difference in reactivity between CF_3- and C_2F_5- (or C_3F_7) substituted chlorohydrins can be compared to that recently reported by Tidwell *et al.* for the solvolysis of CF_3- and C_2F_5-substituted tosylates.[15,16]

Epoxy ethers **6a**−**c** react with $EtAlCl_2$ to give the transposed aldehydes **7a**−**c** (Scheme 4). The C_α−O bond is broken, possibly through the anchimeric assistance of the migrating group since the transposition occurs even at −78 °C. This is also supported by the fact that epoxy ethers **6b**,**c** undergo transposition with the mild Lewis acid Me_3Al. In this case the nucleophilic addition of a

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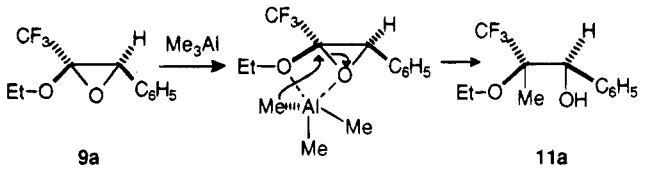
Scheme 9



methyl group occurs on the rearranged aldehyde, providing the glycol ethers **8b,c**. Methyl attack on the epoxide ring does not compete with the migration of the cyclohexyl group. Fluorinated α-alkoxy aldehydes **7** can be prepared in good yield by this reaction of epoxy ethers **6** with $EtAlCl_2$. This is an interesting alternative to the recently described route through the trimethylsilyl thiazole addition to perfluoroalkyl ketones.[17]

Unlike for epoxy ethers **2** and **6**, the opening of the oxirane ring of epoxy ethers **9a–c** with $EtAlCl_2$ or $TiCl_4$ took place with the breaking of the C_β–O bond (Scheme 5). This result indicates that stabilized benzylic cation is more stable than the alternative R_F-alkoxycarbenium ion. Formation of the benzylic cation is followed by nucleophilic addition of a chloride anion. However, Me_3Al brings about ring opening at the C_α site with the addition of a methyl group to the C_α carbon, indicating that with Me_3Al there is no formation of cation or ion pair and even no weakness of the Cβ–O bond. If the mechanism of substitution is S_N2 type, substitution should also occur on the secondary benzylic carbon.[10] This is not observed, suggesting that regioselectivity can be explained by an internal migration of a methyl group of the Lewis acid complexed with oxygen atoms of the epoxy ether. Although aluminum Lewis acids are not prone to make bidentate chelation, which places the methyl group closer to Cα, only this can explain this regioselectivity (Scheme 9). The same mode of attack has already been noted above for the introduction of chloride at Cα from epoxy ethers **2a–c** at −78 °C with $EtAlCl_2$ (Scheme 2). This similarity of reactions strongly suggests that in **11a** the relative configuration of the two stereocenters is *R*R**.

At −78 °C, $EtAlCl_2$ reacts with epoxy ether **12a** through two competitive processes leading to a mixture of (*S*R**) chlorohydrin **13a**$_1$ and the *cis*-tetralol **14a** (ratio **13a**$_1$/**14a** 9:1). As for chlorohydrin **3a**$_1$, the chlorohydrin **13a**$_1$ (*S*R**) results from a chloride-assisted opening of the oxirane ring. The nucleophilic attack of the phenyl group provides the cyclized *cis*-tetralol **14a**. Conversely when the reaction is performed at 0 °C, the two diastereoisomers of the chlorohydrin **13a** are obtained and the ratio **13a/14a** is decreased. Since the chlorohydrins **13a** cannot be cyclized into **14a** even in the presence of a large excess of $EtAlCl_2$ (5 equiv), they are not intermediates in the formation of the tetralol **14a**. So, at 0 °C, a stepwise process leading to **13a** competes with the assisted process leading to the *cis*-tetralol **14a**. Interestingly, in the treatment of **12a** at 0 °C with $TiCl_4$ the tetralol **14a** can be selectively obtained in very good yield. Unlike $EtAlCl_2$, $TiCl_4$ is able to transform the chlorohydrins **13a**$_1$ into the cyclized product **14a**. However, the reaction proceeds slower from chlorohydrins **13a** than from *Z*-epoxy ether **12a**.

In the reaction of epoxy ether **12a** with Me_3Al, the nucleophilic assistance of the methyl group to the opening of the oxirane ring is more efficient than the assistance of the phenyl group, and the introduction of a methyl group occurs, probably through the mechanism proposed for the formation of **11a**.

From epoxy ether **12c** and $TiCl_4$, chlorotetralol **15c** is obtained, instead of the expected ethoxytetralol, as a result of substitution of the benzylic ethoxy group by a chloride of the catalyst (Scheme 8).[18] In the C_3F_7-substrates the C–OEt bond is weaker than in the CF_3-tetralol **14a**.

We have demonstrated that fluorinated epoxy ethers can undergo nucleophilic opening to give α-substituted ketones[9c,13,14] as well as Lewis acid-catalyzed opening. In this latter case, depending on the temperature and on the Lewis acid, both nucleophilic-assisted and stepwise processes can occur. The nucleophilic-assisted process is much more favorable at low temperature but also competes at 0 °C with the stepwise process (reactions with Me_3Al, and cyclization). In the stepwise process, the cleavage of the Cα–O bond leading to a fluorinated alkoxycarbenium ion is favored, unless when a phenyl group stabilizes the Cβ secondary carbenium ion. Whatever the process, cleavage of the oxirane ring is accompanied by nucleophilic addition (or substitution), alkyl or hydride shifts, or cyclization process.

In conclusion, a fluorinated substituent deeply modifies the reactivity of an epoxy ether. The electron-donating effect of the alkoxy group balances the electron-withdrawing effect of the fluorinated moiety, so that a fluorinated epoxy ether reacts similarly to a nonfluorinated, nonfunctionalized epoxide toward nucleophiles and electrophiles.

Experimental Section

Standard spectral calibrations and spectral calibrations for ^1H (90, or 200 or 400 MHz), ^{19}F (84 or 373 MHz), and ^{13}C NMR (50 or 100 MHz) spectra were previously reported.[19] GC/MS analyses were obtained at 70 eV EI (capillary column CPSIL-5, 25 m). GC analysis was performed on a capillary column SE30, 10 or 25 m). $EtAlCl_2$, Me_3Al (solutions in hexanes) and $TiCl_4$ (1 M solution in CH_2Cl_2) were purchased from Aldrich Chemical Co.

Lewis Acid-Mediated Epoxy Ethers Ring Opening: General Procedure. Reactions were performed under anhydrous conditions under argon, with reaction volume adjusted to produce a solution about 0.1–0.15 M of perfluoroalkyl epoxy ether.[10a] The solution was cooled to the desired temperature and the Lewis acid in solution was added dropwise via a syringe through a septum cap. When the starting material had disappeared (followed by GC after rapid quenching of samples), ether (20 mL) was added and the mixture was hydrolyzed with saturated aqueous NH_4Cl and then allowed to warm to rt. The organic layer was separated, washed with aqueous $NaHCO_3$ until neutral and then twice with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was further purified by column chromatography (silica gel 60, 70–230 mesh) using pentane and pentane–diethyl ether as eluent.

Reaction of Epoxy Ether 2a: (a) With $EtAlCl_2$. Epoxy ether **2a** (200 mg, 0.79 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (0.95 mL of a 1 M solution in hexanes, 0.95 mmol) for 1 h at 0 °C, afforded, after workup and purification, the chlorohydrin **3a** (140 mg, 76%, mixture 1:1 of the two diastereoisomers) (100% GC).

The same reaction performed at −78 °C for 1 h afforded the pure **3a**$_1$ (78%) (100% GC).

(17) Bégué, J. P.; Benayoud, F.; Dondoni, A.; Boscarato, A.; Formaglio, P. *Synthesis* **1995**, 654–658.

(18) Bonnet-Delpon, D.; Charpentier-Morize, M.; Jacquot, R. *J. Org. Chem.* **1988**, *53*, 759–763.

(19) Bonnet-Delpon, D.; Abouabdellah, A. *Tetrahedron* **1994**, *41*, 11921–11932.

3-Chloro-1-cyclohexyl-3-ethoxy-4,4,4-trifluorobutan-2-ol R (3a): IR (neat) 3600 cm^{-1}; ^{19}F NMR δ −72.3 and −73.6; ^1H NMR δ 1.15 (t, J = 7 Hz, 3 H), 1.4 to 1.9 (m, 13 H), 2.4 (s, 1 H, OH), 3.85 (m, 2 H), 4.05 (m, 1 H); ^{13}C NMR δ 14.8 and 15.0, 26.0, 26.4, 26.6, 32.1, 33.0, 34.6, 36.3, 38.4 and 39.3, 63.5 and 63.9; 72.4 and 73.0, 101.7 and 103.1 (q, ^2J = 29 Hz, CCF_3), 122.4 (q, ^1J = 294 Hz, CF_3). Anal. Calcd for $C_{12}H_{20}F_3O_2Cl$: C, 49.91; H, 6.93. Found: C, 50.07; H, 7.03. **3a$_1$** (*RS,SR*): ^{19}F NMR δ −73.6; ^1H NMR δ 1.15 (t, J = 7 Hz, 3 H, 1.4 to 1.9 (m, 13 H), 2.4 (s, 1 H, OH), 3.85 (m, 2 H), 4.05 (m, 1 H); ^{13}C NMR δ 15.0, 26.0, 26.4, 26.6, 32.1, 33.0, 34.6, 39.3, 63.9; 73.0, 103.1 (q, ^2J = 29 Hz, C-CF_3), 122.4 (q, ^1J = 294 Hz, CF_3).

***(E)*-1-Ethoxy-1-trifluoromethyl-2-(methylcyclohexyl)-oxirane (2a):** Compound **3a$_1$** (40 mg, 0.14 mmol) and Na_2CO_3 dissolved in THF/MeOH (2 mL, 1/1) was stirred for 2 h at rt. After extraction (Et_2O), the organic layer was washed with brine and dried ($MgSO_4$) and solvents were evaporated to give pure epoxy ether **2a$_2$**. ^{19}F NMR δ −73.0; ^1H NMR δ 1.2 (t, ^3J = 7 Hz, 3 H), 1.5−2.0 (m, 13 H), 3.6 (m, 2 H); ^{13}C NMR δ 15.4, 26.1, 26.2, 26.4, 33.1, 33.3, 34.2, 36.3, 62.1, 82.2 (q, ^2J = 28 Hz), 122.3 (q, ^1J = 281.1 Hz, CF_3). The same reaction performed on the mixture (1:1) of chlorohydrins **3a** provide epoxy ethers **2a$_1$** and **2a$_2$** as a mixture (1:1).

(b) With Me_3Al. Epoxy ether **3a** (200 mg, 0.79 mmol) in CH_2Cl_2 (10 mL), treated with Me_3Al (0.79 mL of a 2 M solution in hexanes, 1.6 mmol) for 1 h at 0 °C, afforded, after workup and purification, starting material **2a** (100% GC).

Reaction of Epoxy Ether 2b: (a) With $EtAlCl_2$. Epoxy ether (200 mg, 0.66 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (0.80 mL of a 1 M solution in hexanes, 0.80 mmol) for 1 h at 0 °C, afforded, after workup and purification, a mixture of aldehyde **4b** (110 mg, 55%) and ketone **5b** (40 mg, 20%) (100% GC, **4b/5b** 65:35).

The same reaction performed at −78 °C for 1 h afforded **3b$_1$** (86%) (95% GC) and traces of the diastereoisomer **3b$_2$** (*S*S**).

The same reaction performed at −78 °C for 1 h and then 48 h at 0 °C afforded a mixture of **4b** (39%), **5b** (23%), **3b$_1$** (16%), and **3b$_2$** (17%) (GC determination).

2-(Cyclohexylmethyl)-2-ethoxy-3,3,4,4,4-pentafluorobutanal (4b): IR (neat) 1750 cm^{-1}; ^{19}F NMR δ −80.7 (3 F), −116.9 and −117.3 (2 F); ^1H NMR δ 1.1 (t, J = 6.8 Hz, 3 H), 1.1−2.0 (m, 13 H), 3.46 (q, J = 6.8 Hz, 2 H), 9.38 (s, 1 H); ^{13}C NMR δ 15.2, 25.7, 26.0, 26.1, 31.9, 33.9, 34.7, 60.9, 65.7, 83.5 (t, ^2J = 20.1 Hz, CC_2F_5), 196.9, C_2F_5 not observed. Anal. Calcd for $C_{13}H_{19}F_5O_2$: C, 51.65; H, 6.29. Found: C, 51.4; H, 6.18.

1-Cyclohexyl-3-ethoxy-4,4,5,5,5-pentafluoropentan-2-one (5b): IR (neat) 1731 cm^{-1}; ^{19}F NMR δ −82.8 (3 F), −119.8 (dd, $^2J_{FF}$ = 282 Hz, $^3J_{FH}$ = 18 Hz, 1F, CF_A), −126.5 (dd, ^2J = 282 Hz, $^3J_{FH}$ = 7 Hz, 1F, CF_B); ^1H NMR δ 1.0 (t, J = 6.8 Hz, 3 H), 1.2 to 2.0 (m, 13 H), 2.3 (dd, ^2J = 18 Hz, ^3J = 7 Hz, 2 H), 3.5 (q, J = 6.8 Hz, 2 H), 3.98 (dd, $^3J_{FAH}$ = 18 Hz, $^3J_{FBH}$ = 7 Hz, 1 H, CHC_2F_5); ^{13}C NMR δ 15.8, 26.9, 27.1, 31.8, 33.7, 33.8, 34.0, 47.7, 69.5, 82.0 (t, ^2J = 27 Hz, C-C_2F_5), 204.9, C_2F_5 not observed. Anal. Calcd for $C_{13}H_{19}F_5O_2$: C, 51.6; H, 6.29. Found: C, 51.4; H, 6.30.

3-Chloro-1-cyclohexyl-3-ethoxy-4,4,5,5,5-pentafluoropentan-2-ol (3b$_1$): IR (neat) 3600 cm^{-1}; ^{19}F NMR δ −79.3 (3 F), −113.8 (2 F), ^1H NMR δ 1.2 (t, J = 6.8 Hz, 3 H), 1.3 to 1.8 (m, 13 H), 1.9 (s, 1 H, O*H*); 3.8 (m, 2 H); 3.98 (s, 1 H); ^{13}C NMR δ 15.0, 26.1, 26.5, 26.6, 32.2, 34.2, 34.6, 39.2, 63.7, 73.1, 104.6 (t, ^2J = 22.2 Hz, C-C_2F_5), C_2F_5 not observed. Anal. Calcd for $C_{13}H_{20}F_5O_2Cl$: C, 46.1; H, 5.90. Found: C, 45.9; H, 5.79.

(b) With Me_3Al. Epoxy ether **2b** (200 mg, 0.66 mmol) in CH_2Cl_2 (10 mL), treated with Me_3Al (0.66 mL of a 2 M solution in hexanes, 1.32 mmol) for 1 h at 0 °C, afforded, after workup and purification, starting material **2b** (100% GC).

Reaction of Epoxy Ether 2c: (a) With $EtAlCl_2$. Epoxy ether **2c** (200 mg, 0.56 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (0.67 mL of a 1 M solution in hexanes, 0.67 mmol) for 1 h at 0 °C, afforded, after workup and purification, a mixture of aldehyde **4c** (120 mg, 60%) and ketone **5c** (60 mg, 30%) (100% GC, **4c/5c** 65:35).

2-(Cyclohexylmethyl)-2-ethoxy-3,3,4,4,5,5,5-heptafluoropentanal (4c): IR (neat) 1756 cm^{-1}; ^{19}F NMR δ −81.3 (3 F), −113.3 (d, ^2J = 272 Hz, 1 F, C*F*F), −115.3 (d, ^2J = 272 Hz, 1 F, CF*F*), −123.6 (2 F); ^1H NMR δ 1.2 (t, J = 6.8 Hz, 3 H); 1.25−2.0 (m, 13 H), 3.6 (q, J = 6.8 Hz, 2 H), 9.6 (s, 1 H); ^{13}C NMR δ 15.1, 26.0, 26.2, 32.6, 32.9, 34.4, 37.9, 59.4, 65.8, 89.8 (t, ^2J = 28 Hz, CC_3F_7); 192.0, C_3F_5 not observed. Anal. Calcd for $C_{14}H_{19}F_7O_2$: C, 47.72; H, 5.39. Found: C, 47.78; H, 5.41.

1-Cyclohexyl-3-ethoxy-4,4,5,5,6,6,6-heptafluorohexan-2-one (5c): IR (neat) 1731 cm^{-1}; ^{19}F NMR δ −81.3 (3 F); −119.2 (dd, $^2J_{FF}$ = 272 Hz, $^3J_{FH}$ = 19 Hz, 1 F, C*F*F), −121.3 (dd, $^2J_{FF}$ = 272 Hz, $^3J_{FH}$ = 7.5 Hz, 1 F, CF*F*), −126.3 (2 F); ^1H NMR δ 1.15 (t, J = 6.8 Hz, 3 H); 1.4 to 2.0 (m, 11 H), 2.5 (qd, ^2J = 17.5 Hz, ^3J = 7 Hz, 2 H); 3.75 (q, J = 6.8 Hz, 2 H), 4.18 (dd, ^3J = 19 Hz, ^3J = 7.5 Hz, 1 H, C*H*-C_3F_7); ^{13}C NMR δ 14.9, 25.7, 25.8, 31.8, 32.8, 33.8, 34.7, 46.7, 68.2, 77.0 (t, ^2J = 28 Hz, CC_3F_7), 198.5, C_3F_7 not observed. Anal. Calcd for $C_{14}H_{19}F_7O_2$: C, 47.72; H, 5.39. Found: C, 47.83; H, 5.42.

(b) With $TiCl_4$. Epoxy ether **2c** (200 mg, 0.56 mmol) in CH_2Cl_2 (10 mL), treated with $TiCl_4$ (1.12 mL of a 1 M solution in CH_2Cl_2, 1.12 mmol) for 1 h at 0 °C, afforded, after workup and purification, chlorohydrins **3c** (165 mg, 75%), (100% GC, mixture **3c$_1$/3c$_2$** 1:1). **3-Chloro-1-cyclohexyl-3-ethoxy-4,4,5,5,6,6,6-heptafluorohexan-2-ol (3c):** IR (neat) 3500 cm^{-1}; ^{19}F NMR δ −81.1 and −81.20 (3 F), −110.3 (2 F), −122.7, −125.4 and −122.6, −125.35 (two d, ^2J = 287.7 Hz, 2 F); ^1H NMR δ 1.05 (t, J = 6.8 Hz, 3 H), 1.2 to 1.8 (m, 13 H), 2.0 (broad s, 1 H, O*H*), 3.8 (q, J = 6.8 Hz, 2 H), 3.95 (m, 1 H); ^{13}C NMR δ 14.6 and 14.8, 25.1 and 25.9, 26.2 and 26.4, 29.6 and 31.7, 31.9 and 32.0, 33.8 and 34.1, 34.3 and 34.4, 39.0 and 39.1, 63.5 and 63.9, 73.1 and 73.2, 105.2 (t, ^2J = 22.2 Hz, CC_3F_7), C_3F_7 not observed. Anal. Calcd for $C_{14}H_{20}F_7ClO_2$: C, 43.2; H, 5.15. Found: C, 43.3; H, 5.27.

(b) With Me_3Al. Epoxy ether **2c** (200 mg, 0.56 mmol) in CH_2Cl_2 (10 mL), treated with Me_3Al (0.56 mL of a 2 M solution in hexanes, 1.12 mmol) for 1 h at 0 °C, afforded, after workup and purification, starting material **2c** (100 % GC).

Reaction of Epoxy Ether 6a: (a) With $EtAlCl_2$. Epoxy ether **6a** (200 mg, 0.84 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (1 mL of a 1 M solution in hexanes, 1 mmol) for 1 h at 0 °C, afforded, after workup and purification, alkoxy aldehyde **7a** (140 g, 70%) (96 % GC).

The same reaction performed at −78 °C for 2 h afforded **7a** (75%) (98% GC).

2-Cyclohexyl-2-ethoxy-3,3,3-trifluoropropanal (7a): IR (neat) 1750 cm^{-1}; ^{19}F NMR δ −66.6 (s, CF_3); ^1H NMR δ 1.2 (t, J = 7 Hz, 3 H), 1.5 to 2.2 (m, 11 H), 3.7 (q, J = 7 Hz, 2H), 9.6 (s, 1 H); ^{13}C NMR δ 15.2, 25.2, 25.4, 26.2, 26.7, 38.2, 41.0, 57.2, 86.4 (q, ^2J = 23.65 Hz, CCF_3); 124.4 (q, ^1J = 292 Hz, CF_3); 197.9. Anal. Calcd for $C_{11}H_{17}F_3O_2$: C, 55.4; H, 7.14. Found: C, 55.2; H, 7.27.

(b) With Me_3Al. Epoxy ether **6a** (0.200 g, 0.86 mmol) in CH_2Cl_2 (10 mL) treated with Me_3Al (1.75 mL of a 2 M solution in hexanes, 3.50 mmol) for 4 h at 0 °C, afforded, after workup and purification, the starting material **6a** (100 % GC).

Reaction of Epoxy Ether 6b: (a) with $EtAlCl_2$. 6b (200 mg, 0.69 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (0.83 mL of a 1 M solution in hexanes, 0.83 mmol) for 1 h at 0 °C, afforded, after workup and purification, the alkoxy aldehyde **7b** (136 mg, 68%).

The same reaction performed at −78 °C for 2 h afforded **7b** (80%) (98% GC).

2-Cyclohexyl-2-ethoxy-3,3,4,4,4-pentafluorobutanal (7b): IR (neat) 1760 cm^{-1}; ^{19}F NMR δ −80.3 (s, 3 F), −108.9 and −116.3 (q, ^2J = 272 Hz, 2 F); ^1H NMR δ 1.2 (t, J = 7 Hz, 3 H); 1.3 to 2.4 (m, 11 H); 3.6 (q, J = 7 Hz, 2 H); 9.5 (s, 1 H); ^{13}C NMR δ 15.1, 26.2, 26.25, 26.3, 26.35, 26.5, 39.1, 60.2; 83.8 (t, ^2J = 20.4 Hz, CC_2F_5), 197.4. Anal. Calcd for $C_{12}H_{17}F_5O_2$: C, 50.0; H, 5.90. Found: C, 49.9; H, 5.98.

(b) With Me_3Al. Epoxy ether **6b** (0.200 g, 0.69 mmol) in CH_2Cl_2 (10 mL) treated with Me_3Al (1.38 mL of a 2 M solution in hexanes, 0.69 mmol) for 1 h at 0 °C, afforded, after workup and purification, **8b** (168 mg, 80%) (94% GC). **3-Cyclohexyl-3-ethoxy-4,4,5,5,5-pentafluoropentan-2-ol (8b):** IR (neat) 3600 cm^{-1}; ^{19}F NMR δ −79.2 (s, 3 F), −108.0 and −113.1 (2 d, ^2J = 294 Hz, 2 F); ^1H NMR δ 1.16 (t, J = 6.9 Hz, 3 H), 1.4 (d, J = 6.7 Hz, 3 H), 1.4 à 2.1 (m, 11H), 2.87 (broad s, O*H*), 3.6 (q, J = 6.9 Hz, 2 H), 4.17 (q, J = 6.7 Hz, 1 H); ^{13}C NMR δ 15.2,

18.8, 26.6, 27.4, 27.9, 28.4, 30.9, 39.9, 59.9, 68.8, 83.3 (t, ^2J = 20.8 Hz, *C*-C_2F_5), 117.2 (qt, ^1J = 270 Hz; ^2J = 36.9 Hz, *C*F_2), 119.3 (qt, ^1J = 288.6 Hz, ^2J = 36.9 Hz, *C*F_3). Anal. Calcd for $C_{13}H_{21}F_5O_2$: C, 51.3; H, 6.90. Found: C, 51.0; H, 7.28.

Reaction of Epoxy Ether 6c: (a) With $EtAlCl_2$. Epoxy ether **6c** (200 mg, 0.59 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (0.7 mL of a 1 M solution in hexanes, 0.7 mmol) for 1 h at 0 °C, afforded, after workup and purification, the alkoxy aldehyde **7a** (152 mg, 76%) (98% GC). **2-Cyclohexyl-2-ethoxy-3,3,4,4,5,5,5-heptafluoropentanal (7c):** IR (neat) 1760 cm^{-1}; ^{19}F NMR δ −80.6 (s, 3 F), −109.9 and −111.2 (2 d, ^1J = 270 Hz, 2 F), −124.6 (2 F); ^{1}H NMR δ 1.05 (t, J = 7 Hz, 3 H), 1.22 to 2.24 (m, 11 H), 3.5 (q, J = 7 Hz, 2 H), 9.45 (s, 1 H); ^{13}C NMR δ 15.1, 26.3, 26.4, 26.6, 26.8, 27.0, 39.5, 60.3, 84.6 (t, ^2J = 28 Hz, *C*C_3F_7), 197.5, C_3F_7 not observed. Anal. Calcd for $C_{13}H_{17}F_7O_2$: C, 46.1; H, 5.02. Found: C, 45.4; H, 5.15.

(b) With Me_3Al. Epoxy ether **6c** (0.200 g, 0.59 mmol) in CH_2Cl_2 (10 mL) treated with Me_3Al (1.18 mL of a 2 M solution in hexanes, 0.59 mmol) for 1 h at 0 °C, afforded, after workup and purification, **8c** (146 mg, 70%, 90% GC). **3-Cyclohexyl-3-ethoxy-4,4,5,5,6,6,6-heptafluorohexan-2-ol (8c):** IR (neat) 3600 cm^{-1}; ^{19}F NMR δ −81.3 (3 F), −106.6 and −107.8 (2 d, J = 272 Hz, 2 F), −123.6 (2 F); ^{1}H NMR δ 1.25 (t, J = 6.8 Hz, 3 H), 1.45 (d, J = 6.7 Hz, 3 H); 1.6 to 2.3 (m, 11 H), 2.86 (broad s, 1 H, OH), 3.7 (q, J = 6.8 Hz, 2 H), 4.25 (q, J = 6.7 Hz, 1 H); ^{13}C NMR δ 15.3, 19.2, 26.9, 27.0, 27.5, 28.2, 28.6, 40.5, 60.3, 68.9, 90.0 (t, ^2J = 23 Hz, *C*C_3F_7), C_3F_7 not observed. Anal. Calcd for $C_{14}H_{21}F_7O_2$: C, 47.4; H, 5.93. Found: C, 47.3; H, 6.01.

Reaction of Epoxy Ether 9a. (a) With $EtAlCl_2$. Epoxy ether **9a** (200 mg, 0.86 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (1 mL of a 1 M solution in hexanes, 1 mmol) for 1 h at 0 °C, afforded, after workup and purification, the chloro ketone **10a** (0.124 g, 56%) (70% GC).

The same reaction performed at −78 °C for 3 h afforded **10a** (68% GC).

1-Chloro-1-phenyl-3,3,3-trifluoropropan-2-one (10a): IR (neat) 1780 cm^{-1}; ^{19}F NMR δ −75.3 (s); ^{1}H NMR δ 5.8 (s, 1H); 7.5 (m, 5H); ^{13}C NMR δ 59.6; 128.0 (q, ^1J = 296 Hz, CF_3); 128.4; 128.6; 129.1; 129.3; 129.5; 130.2; 186.0 (q, ^2J = 28 Hz). Anal. Calcd for $C_9H_6ClF_3O$: C, 48.5; H, 2.69. Found: C, 48.6; H, 2.72.

(b) With $TiCl_4$. Epoxy ether **9a** (200 mg, 0.86 mmol) in CH_2Cl_2 (10 mL), treated with $TiCl_4$ (1.75 mL of a 1 M solution in CH_2Cl_2, 1.75 mmol) for 1 h at 0 °C, afforded **10a** (166 mg, 75%) (83% GC).

(c) With Me_3Al. Epoxy ether **9a** (0.200 g, 0.86 mmol) in CH_2Cl_2 (10 mL) treated with Me_3Al (0.86 mL of a 2 M solution in hexanes, 1.75 mmol) for 1 h at 0 °C, afforded, after workup and purification, **11a** (128 mg, 60%) (75% GC). **2-Ethoxy-1-phenyl-2-(trifluoromethyl)propan-1-ol (11a):** IR (neat) 3600 cm^{-1}; ^{19}F NMR δ −78 (s); ^{1}H NMR δ 1.08 (t, J = 7 Hz, 3 H), 1.25 (s, 3 H), 2.78 (s, OH), 3.40 (q, J = 7 Hz, 2 H), 4.35 (s, 1 H), 7.20 (m, 5 H); ^{13}C NMR δ 14.9, 17.6, 63.3, 75.5, 82.8 (q, ^2J = 29.8 Hz, *C*CF_3), 127.0 (q, ^1J = 278 Hz, *C*F_3), 128.1, 128.3, 128.6, 128.8, 128.9, 129.2. Anal. Calcd for $C_{12}H_{15}F_3O_2$: C, 58.0; H, 6.04. Found: C, 58.1; H, 6.09.

Reaction of Epoxy Ether 9b. (a) With $EtAlCl_2$. Epoxy ether **9b** (200 mg, 0.70 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (0.84 mL of a 1 M solution in hexanes, 0.85 mmol) for 1 h at 0 °C, afforded, after workup and purification, the chloro ketone **10b** (168 mg, 62%) (67% GC). **1-Chloro-3,3,4,4,4-pentafluoro-1-phenylbutan-2-one (10b).** IR (neat) 1770 cm^{-1}; ^{19}F NMR δ −82.3 (3 F), −120.3 (2 F); ^{1}H NMR δ 5.8 (s, 1 H), 7.5 (m, 5 H); ^{13}C NMR δ 60.0, 100.0−124.0 (m, C_2F_5), 128.6, 128.7, 129.4, 129.7, 130.3, 131.8, 186.4 (t, ^2J = 27.8 Hz). Anal. Calcd for $C_{10}H_6F_5ClO$: C, 44.0; H, 2.20. Found: C, 44.1; H, 2.26.

Reaction of Epoxy Ether 9c. (a) With $EtAlCl_2$. Epoxy ether **9c** (200 mg, 0.60 mmol) in CH_2Cl_2 (10 mL) was treated with $EtAlCl_2$ (0.72 mL of a 1 M solution in hexanes, 0.72 mmol) for 1 h at 0 °C. This afforded, after workup and purification, the chloro ketone **3c** (193 mg, 60%) (68% GC). **1-Chloro-3,3,4,4,5,5,5-heptafluoro-1-phenylpentan-2-one (10c):** IR (neat) 1770 cm^{-1}; ^{19}F NMR δ −81.3 (3 F), −119.3 (dd, J = 270 Hz, 2 F); −127.3 (2 F); ^{1}H NMR δ 5.74 (s, 1 H), 7.45 m, 5 H); ^{13}C NMR δ 60.2, 128.2, 128.6, 129.4, 129.8, 130.3, 131.9, 187.4 (t, ^2J = 28 Hz), C_3F_7 not observed. Anal. Calcd for $C_{11}H_6ClF_7O$: C, 40.9; H, 1.82. Found: C, 40.8; H, 1.89.

Reaction of Epoxy Ether 12a: (a) With $EtAlCl_2$. Epoxy ether **12a** (200 mg, 0.76 mmol) in CH_2Cl_2 (10 mL), treated with $EtAlCl_2$ (0.9 mL of a 1 M solution in hexanes, 0.9 mmol) for 1 h at 0 °C, afforded, after workup and purification, **13a** (76 mg, 34%, mixture 1:1 of chlorohydrins **13a**) and **14a** (56 mg, 28%) (GC 28:28:44).

The same reaction performed with $EtAlCl_2$ (5 equiv) at 0 °C and then at 20 °C for 72 h afforded chlorohydrins **13a** (52%, mixture 1:1) and **14a** (48%).

The same reaction performed at −78 °C for 1 h afforded a mixture of pure **13a$_1$** and **14a** (89:11, GC).

The same reaction performed at −78 °C for 1 h and then at 20 °C for 2 h afforded the same results (**13a$_1$/14a**, 89:11, GC).

2-Chloro-2-ethoxy-5-phenyl-1,1,1-trifluoropentan-3-ol (13a): IR (neat) 3600 cm^{-1}; ^{19}F NMR δ −72 and −73.5 (3 F); ^{1}H NMR δ 1.1 (t, 7 Hz, 3 H), 1.7 (1 H, OH), 2.0 (m, 2 H), 2.35 (m, 2 H), 3.75 (m, 2 H), 3.8 (m, 1 H), 7.2 (m, 5 H); ^{13}C NMR δ 14.9 and 15.4, 31.9, 32.5, 63.5 and 63.8, 74.3 and 74.7, 100.8 and 102.6 (q, ^2J = 30 Hz, *C*-CF_3), 122.0 (q, ^1J = 290 Hz, *C*F_3), 126.6, 128.4, 129.5, 141.2. Anal. Calcd for $C_{13}H_{16}F_3O_2Cl$: C, 52.6; H, 5.39. Found: C, 52.6; H, 5.35. **13a$_1$**: ^{19}F NMR δ −73.5 (CF_3); ^{1}H NMR δ 1.1 (t, 7 Hz, 3 H), 1.7 (1 H, OH), 2.0 (m, 2 H), 2.35 (m, 2 H), 3.75 (m, 2 H), 3.8 (m, 1 H), 7.2 (m, 5 H); ^{13}C NMR δ 15.4, 31.9, 32.5, 63.8, 74.3, 102.7 (q, ^2J = 30 Hz, *C*CF_3), 122.3 (q, ^1J = 290 Hz, CF_3), 126.6, 128.4, 129.5, 141.2.

1-Ethoxy-1-(trifluoromethyl)-2-*cis*-tetralol (14a$_1$): IR (neat) 3600 cm^{-1}; ^{19}F NMR δ −74.6 (3 F); ^{1}H NMR δ 1.24 (t, J = 7 Hz, 3 H); 1.87 (m, ^2J = 13.5 Hz, $^3J_{H\text{-}3ax,H\text{-}2}$ = 9.2 Hz, 1 H, H-3_{ax}), 2.2 (m, ^2J = 13.5 Hz, $^3J_{H\text{-}3eq,H\text{-}2}$ = 3.6 Hz, $^3J_{H\text{-}4eq,H\text{-}3eq}$ = 6.6, $^3J_{H\text{-}4ax,H\text{-}3eq}$ = 5.4, 1 H, H-3_{eq}), 2.59 (d, $^3J_{OH,H\text{-}2}$ = 1.2 Hz, 1 H, O*H*); 2.72 (m, 1 H, *H-4$_A$*), 2.94 (m, 1 H, *H-4$_B$*), 3.53 (m, 1 H, OCH_AH$_B$); 3.7 (m, 1 H, OCH$_A$*H$_B$*); 4.40 (d, $^3J_{H\text{-}2,H\text{-}3ax}$ = 9.2 Hz, $^3J_{H\text{-}2,H\text{-}3eq}$ = 3.6 Hz, 1 H, H-2); 7.2 (m, 3 H, H-5, H-6, H-7); 7.68 (m, 1 H, H-8); ^{13}C NMR δ 15.4; 25.9; 27.5; 61.0; 67.0; 78.6 (q, ^2J = 25.4 Hz, *C*CF_3); 125.0 (q, ^1J = 286 Hz, CF_3), 126.2, 128.5, 128.9, 129.1, 129.5, 139.2. Anal. Calcd for $C_{13}H_{15}F_3O_2$: C, 60.0; H, 5.76. Found: C, 60.1; H, 5.79.

(b) With $TiCl_4$. Epoxy ether **12a** (200 mg, 0.76 mmol) in CH_2Cl_2 (10 mL), treated with $TiCl_4$ (1.52 mL of a 1 M solution in CH_2Cl_2, 1.52 mmol) for 1 h at 0 °C, afforded, after workup and purification, **14a** (150 mg, 75%).

The same reaction performed with $TiCl_4$ (1.52 mL of a 1 M solution in CH_2Cl_2, 1.52 mmol) for 1 h at −78 °C, afforded, after workup and purification, a mixture of chlorohydrin **13a$_1$** (69%) and tetralol **14a** (31%).

The same reaction performed with $TiCl_4$ (1.52 mL of a 1 M solution in CH_2Cl_2, 1.52 mmol) for 1 h at −78 °C and then 2 h at 20 °C afforded, after workup and purification, tetralol **14a** (95% GC).

(c) With Me_3Al. Epoxy ether **12a** (200 mg, 0.76 mmol) in CH_2Cl_2 (10 mL), treated with Me_3Al (0.76 mL of a 2 M solution in hexanes, 0.76 mmol) for 1 h at 0 °C, afforded, after workup and purification, **16a** (148 mg, 70%). **2-Ethoxy-2-methyl-5-phenyl-2-(trifluoromethyl)pentan-3-ol (16a):** IR 3600 cm^{-1}; ^{19}F NMR δ −74.4 (3 F); ^{1}H NMR δ 1.17 (t, J = 7 Hz, 3H), 1.37 (s, 3 H), 1.78 (m, ^2J = 14 Hz, $^3J_{H\text{-}4,H\text{-}3}$ = 2.3 Hz, 1 H, H-4_B), 1.93 (m, ^2J = 14.0 Hz, $^3J_{H\text{-}4A,H\text{-}3}$ = 10.4 Hz, 1 H, *H-4$_A$*), 2.06 (d, J = 6.36 Hz, O*H*), 2.65 (m, 1 H, H-5_A), 2.94 (m, H, *H-5$_B$*), 3.58 (q, J = 7 Hz, 3.7 (m, $^3J_{H\text{-}3,H\text{-}4A}$ = 10.4 Hz, $^3J_{H\text{-}3,H\text{-}4B}$ = 2.3 Hz, $^3J_{H\text{-}3,OH}$ = 6.2 Hz, 1 H, H-3), 7.25 (m, 5 H); ^{13}C NMR δ 13.4, 24.0, 32.5, 32.6, 59.9, 73.0, 79.0 (q, ^2J = 25 Hz, *C*-CF_3), 126.3 (q, ^1J = 290.5 Hz, *C*F_3), 125.9, 128.4, 128.5, 141.8. Anal. Calcd for $C_{14}H_{19}F_3O_2$: C, 60.8; H, 6.88. Found: C, 61.1; H, 6.81.

Reaction of Epoxy Ether 12c with $TiCl_4$. Epoxy ether **2c** (200 mg, 0.55 mmol) in CH_2Cl_2 (10 mL), treated with $TiCl_4$ (1.1 mL of a 1 M solution in CH_2Cl_2, 1.1 mmol) for 1 h at 0 °C, afforded, after workup and purification, **15c** (160 mg, 82%). **1-Chloro-1-(heptafluoropropyl)-2-tetralol (15c):** IR (neat)

3500 cm^{-1}; ^{19}F NMR δ −83.2 (dd, 3 F), −104.4 (m, 1 F, CF_AF_B-CF_3), −111.3 (m, 1 F, $CF_AF_BCF_3$), −123.1 (m, 2 F); ^1H NMR δ 2.20 (m, 2 H), 2.70 (s, 1 H, O*H*), 2.86 (m, 1 H, CH_AH_BPh), 3.10 (m, 1 H, CH_AH_BPh), 4.55 (dd, $^3J_{H\text{-}2,H\text{-}3A}$ = 5.9 Hz, $^3J_{H\text{-}2,H\text{-}3B}$ = 2.8 Hz, 1 H, C*H*OH), 7.20 (m, 3 H, H-5, H-6, H-7), 7.75 (m, 1 H, H-8); ^{13}C NMR δ 24.9, 25.9, 68.3, 75.5 (t, ^2J = 22 Hz, *C*-C_3F_7), 126.6, 128.6, 129.5, 131.0, 137.7, 137.9, C_3F_7 not observed. Anal. Calcd for $C_{13}H_{10}F_7ClO$: C, 44.50; H, 2.85; C, 44.63; H, 3.04.

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