Synthesis of Polyfluorinated Tertiary Alcohols Using Ring Opening Reactions of 2,2-Bis(trifluoromethyl)oxirane[1]

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Abstract: This paper describes new reactions of 2,2-bis(trifluoromethyl)oxirane (**1**). Ring opening of **1** by oxygen, nitrogen, sulfur or carbon nucleophiles (Nu^-) proceeds regioselectively, with exclusive formation of tertiary alcohols: $NuCH_2C(CF_3)_2OH$. The reaction of **1** with strong acids (HX) is also regioselective and proceeds under mild conditions leading to the formation of $XCH_2C(CF_3)_2OH$ (X = FSO_2O, CF_3SO_2O, Cl, I). The addition of acetic acid to **1**, however, requires an elevated temperature and TaF_5 a catalyst. Highly selective reactions of **1** with nucleophilic or electrophilic reagents provide a simple and general route to materials containing $CH_2C(CF_3)_2OH$ group.

Key words, 2,2-bis(trifluoromethyl)oxirane, ring opening reactions, nucleophilic addition, electrophilic addition, epoxides

Introduction

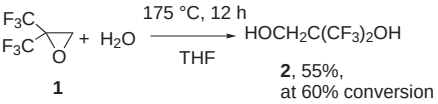
Development of a new generation of photoresist polymers for 157 nm microlithography requires preparation of polymers, which must be base-soluble, but at the same time highly transparent in the vacuum UV region of the spectrum. It has been demonstrated[2] that this goal can be achieved by the introduction of a $C(CF_3)_2OH$ fragment into the polymer backbone, since this group has low absorbance at 157 nm, and is acidic enough to provide the solubility of the polymer in conventional aqueous-base developers.

Methods to introduce the $C(CF_3)_2OH$ group into organic molecules are limited to reactions of hexafluoroacetone with organic substrates[3] or the reaction of the synthetic equivalents of trifluoromethyl anion,[4a,b] especially CF_3SiMe_3[4c] with carbonyl compounds. In search of a new methodology for introduction of the $C(CF_3)_2OH$ fragment into organic substrates we chose 2,2-bis(trifluoromethyl)oxirane (**1**), since ring opening reactions of **1** can potentially lead to materials containing the $CH_2C(CF_3)_2OH$ group. Similar reactions of its closest analogue, trifluoromethyloxirane, are indeed regiospecific, resulting in the formation of secondary α-trifluormethyl alcohols.[5]

Despite the fact that compound **1** was prepared for over 30 years ago (along with a few others epoxides of this type by the reaction of diazomethane with polyfluoroacetones [6–8]), the chemistry of 2,2-bis(trifluoromethyl)oxirane is still limited to very few transformations, i.e. interaction with ammonia and methylamine.[8] Recently developed simple and practical synthesis of **1**[9] made this material readily available on a multigram scale. The detailed investigation of reactivity of **1** is presented in this paper.

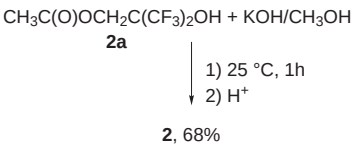
Reactions with Nucleophiles

The strong electron-withdrawing effect of two CF_3-groups in 2,2-bis(trifluoromethyl)oxirane (**1**) leads to the development of a substantial positive charge on the carbon bearing two hydrogen substituents and makes **1** susceptible to nucleophilic attacks. Even a relatively weak nucleophile, such as water, reacts with **1** in the absence of a catalyst, although only at elevated temperature (Scheme 1). The diol **2**[10] was isolated in this reaction as a 1:1 mixture with THF solvent.



Scheme 1

Separation of **2** and solvent proved to be difficult due to the combination of high solubility of **2** in water and formation of a complex between relatively acidic diol and THF. More convenient synthesis of **2** is based on hydrolysis of acetate **2a** under basic conditions (Scheme 2) (for preparation of **2a** see next section).



Scheme 2

The diol **2** was isolated after acidification of the reaction mixture by 10% hydrochloric acid and extraction with CH_2Cl_2 or Et_2O (see Experimental Part). The diol **2** contaminated with water could be a liquid,[10] however pure, water-free material was found to be a solid (mp 45–47 °C). At ambient temperature, epoxide **1** did not react with alcohols. However, the addition of **1** to a solution of alkoxides **3a**,**b** in THF resulted in fast, exothermic ring

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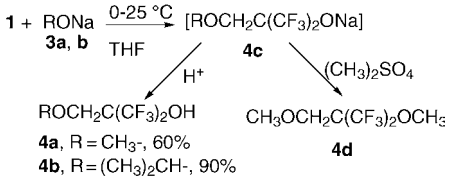
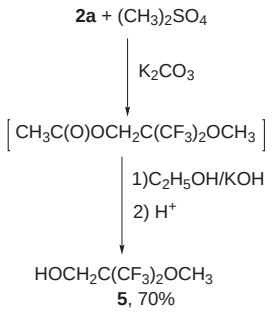


Scheme 3

opening reaction with the formation of compounds **4a**,**b**. The anion **4c** formed as an intermediate was intercepted and converted into the ether **4d** (Scheme 3).

The synthesis of hydroxyether **5** (isomer of **4a**) was conducted by methylation of the $C(CF_3)_2OH$ group of the ester **2a** with dimethyl sulfate, followed by deprotection of the primary alcohol function by basic hydrolysis (Scheme 4).



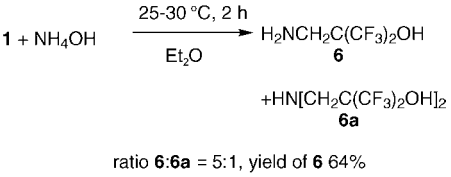
Scheme 4

Compound **2a** used in this experiment was prepared by the reported method involving radical addition of methyl acetate to hexafluoroacetone.[11]

Despite structural similarity of **4a** and **5**, there is a noticeable difference in chemical shifts of $C(CF_3)_2OH$ and $C(CF_3)_2OCH_3$ groups in ^{19}F NMR spectra. Introduction of a substituent to oxygen results in the substantial downfield shift of the resonance of $(CF_3)_2C$ (δ = –77.6 for **4a** and –71.5 ppm for **5**; in $CDCl_3$). Independent synthesis of **5** combined with NMR data of compounds **4a** and **5** allow unambiguous assignment of structure **4a** to the material formed in the reaction of **1** with sodium methoxide. The absence of a detectable amount of isomeric **5** in the crude reaction mixture (GC, NMR) is an indication of high regioselectivity of the ring-opening reaction of **1**. Attack of the nucleophile occurs on the CH_2 group of **1** leading to selective formation of the corresponding tertiary alcohol. It should be also pointed out that nucleophilic attack on perfluorinated oxiranes, such as oxides of hexafluoropropene[12a,b]or octafluoroisobutene,[12a,c] takes place at the *sterically hindered* carbon bearing trifluoromethyl group(s), with only a few exceptions reported for hexafluoropropene epoxide.[12a,13] For example, octafluoroisobutene epoxide reacts with Nu^- forming derivatives of hexafluoroisobutyric acid.[12c] In light of these data, the reactivity of **1** actually resembles the reactivity of trifluoromethyloxirane,[5] rather than octafluoroisobutene epoxide.

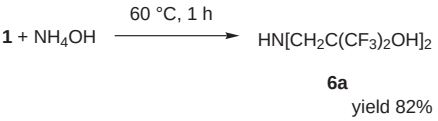
The reverse orientation of ring opening reactions of **1** (compared to octafluoroisobutene oxide) is a strong indication that in this case, the direction of the nucleophilic ring opening is governed by electronic, but not steric factors, as it was earlier suggested for reactions of trifluoromethyloxirane.[5a]

The reaction of **1** with *excess* of ammonia or ammonium hydroxide at low or ambient temperature gave primary amine **6**[8] as a major product, along with a smaller amount of secondary amine **6a** (Scheme 5).



Scheme 5

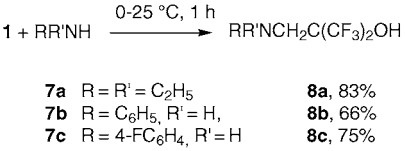
At higher temperature, in the reaction of **1** and NH_4OH, the amine **6a** was produced as the sole product in high yield (Scheme 6).



Scheme 6

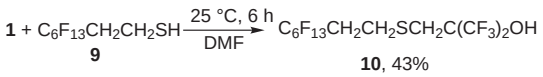
Surprisingly, the alkylation of **6a** by another equivalent of epoxide **1** was found to be difficult. Only a trace of the corresponding tertiary amine was detected in the reaction of **6a** and **1** at elevated temperature in a closed system (170 °C, diethyl ether) by GC/MS. This result can be explained in terms of steric hindrance created by two bulky $CH_2C(CF_3)_2OH$ substituents in the molecule of **6a**, since the reaction of trifluoromethyloxirane and NH_4OH was reported to give $N[CH_2CH(OH)CF_3]_3$ at ambient temperature.[14]

The epoxide **1** rapidly reacts with diethylamine (**7a**) and anilines **7b**,**c** under mild conditions in the absence of solvent to give the corresponding adducts **8a**–**c** in moderate to high yield (Scheme 7).



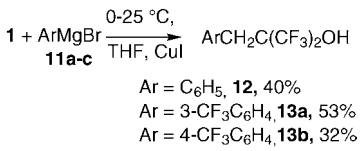
Scheme 7

The addition of thiol **9** to **1** proceeds at ambient temperature in dry DMF solvent without a catalyst leading to **10** (Scheme 8).



Scheme 8

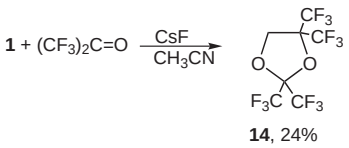
The reaction of **1** with methylmagnesium iodide was only briefly mentioned in Ref.[8] As it was found in this study, the reaction between **1** and *i*-PrMgCl or PhMgBr is surprisingly slow in diethyl ether or THF as solvent. In both cases the conversion of **1** did not exceed ~20% even after one week at ambient temperature. However, several years ago it was demonstrated that CuI could significantly accelerate the reaction of trifluoromethyloxirane with Grignard reagents.[15] The addition of a catalytic amount of CuI also had a drastic effect on the reaction of **1** with arylmagnesium bromides. The reaction in the presence of CuI catalyst rapidly proceeds at low temperature leading to the formation of aryl derivatives **12**,[16] **13a** and **13b** (Scheme 9).



Scheme 9

Moderate yields of **12**, **13a**,**b** in this reaction are the result of a side reaction, the formation of $BrCH_2C(CF_3)_2OH$[17] (confirmed by NMR of the crude reaction mixture). It should be also pointed out that the formation of the corresponding bromohydrin was previously reported in the reaction of trifluoromethyloxirane with $MgBr_2$ and CH_3MgBr.[18] The epoxide **1** seems to be more susceptible to attack by Br^- since the formation of the corresponding bromohydrin in the reactions of trifluoromethyloxirane with Grignard reagents catalyzed by CuI was not reported.[15]

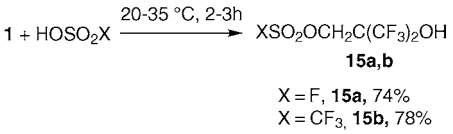
The reaction of **1** with hexafluoroacetone in the presence of dry CsF results in the formation of dioxolane **14** (Scheme 10).



Scheme 10

Reactions with Electrophiles

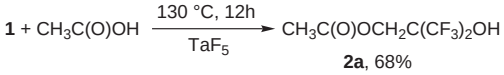
Electron-withdrawing effect of two trifluoromethyl groups attached to the carbon of the oxirane ring significantly decreases the basicity of the oxygen atom of epoxide **1**, resulting in reduced reactivity towards electrophiles. For example, compound **1** did not react with



Scheme 11

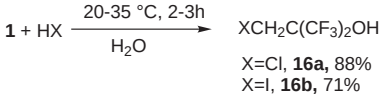
$BF_3{\cdot}OEt_2$, SbF_5 or glacial acetic acid at ambient temperature. On the other hand, the reaction of **1** with much stronger protic acids, trifluoromethanesulfonic or fluorosulfonic acid, proceeds rapidly at ambient or slightly elevated temperature, selectively leading to the corresponding β-hydroxysulfonates **15a**,**b** (Scheme 11).

It seems that epoxide **1** is more active in reaction with protic acids compared to perfluorinated epoxides. For example, hexafluoropropene oxide was reported to react with $HOSO_2F$ only at elevated temperature (>150 °C).[19] Acetic acid can be added to **1**, although this reaction proceeds only in the presence of Lewis acid catalyst at elevated temperature (Scheme 12).



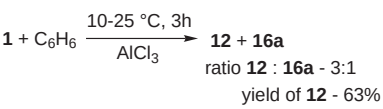
Scheme 12

This transformation provides an easy access to acetate **2a**, which was previously prepared by prolonged UV irradiation of a mixture of hexafluoroacetone and methyl acetate.[11] Similar to the reported reaction of 2,2-(chlorodifluoromethyl)oxirane with hydrobromic acid,[7] **1** rapidly reacts with concentrated hydrochloric or hydroiodic acids at 25–40 °C producing halohydrines **16a**[20] and **16b** (Scheme 13).



Scheme 13

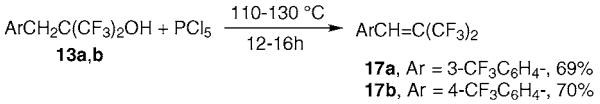
Analogous to trifluoromethyloxirane,[15] the epoxide **1** can be used as an alkylating agent for aromatic compounds. For example, the reaction between benzene, and **1** catalyzed by $AlCl_3$, resulted in the formation of **12**, along with chlorohydrin **16a** as a byproduct (Scheme 14). The formation of **16a**, probably is the result of addition of HCl to the epoxide catalyzed by $AlCl_3$.



Scheme 14

Compounds containing $CH_2C(CF_3)_2OH$ group could be converted into the corresponding olefins by elimination of water, using a method previously developed for the dehy-

dration of $CH_3C(CF_3)_2OH$.[21] Heating the compounds **13a,** or **13b** with excess PCl_5 resulted in the formation of olefins **17a**[22] or **17b** in good yields (Scheme 15).



Scheme 15

The conditions and yields for the reactions of **1** and the spectral data of compounds prepared are given in Tables 1 and 2.

Conclusion

The epoxide **1** has relatively high reactivity towards both nucleophilic and electrophilic reagents. Both types of ring-opening reactions of **1** are regioselective and proceed with formation of tertiary alcohols providing a simple method of the introduction the $CH_2C(CF_3)_2OH$ group into organic compounds and giving an access to a variety of new polyfluorinated tertiary alcohols.

Table 1 Conditions and Yields for the Reactions of 2,2-Bis(trifluoromethyl)oxirane (**1**)

Entry	Reagents (mol)	Solvent (mL)	Time (h)	Temp. (°C)	Product	Yield (%)	bp (°C)/mm Hg
1	**1** (0.1), H_2O (0.11)	THF (100)	12	175	**2**	55[a]	–
2	**1** (0.1), MeONa (0.1)	THF (100)	1	10–25	**4a**	60	62–63/110
3	**2a** (0.1), K_2CO_3 (0.11), Me_2SO_4 (0.1)	MeCN (100)	14	25	**5**	70[b]	125–126/760
4	**1** (0.1), **7a** (0.1)	Et_2O (100)	3	25–33	**8a**	83	71/5
5	**1** (0.055), **7c** (0.055)	CH_2Cl_2 (10)	16	25	**8c**	75	117–118/12 (mp 35–36)
6	**1** (0.025), **9** (0.025)	DMF (50)	25	16	**10**	43	25–26/0.1
7	**1** (0.1), **11a** (0.1), CuI (1 mol%)	THF (100)	0–25	14	**12**	40	101–103/53[c]
8	**1** (0.11), **11c** (0.1), CuI (1 mol%)	THF (100)	10–25	16	**13b**	32	92–93/10
9	**1** (0.2), CF_3SO_2OH (0.25)	–	0–25	3	**15b**	78	–
10	**1** (0.56), HCl (100 mL)[d]	–	25–85	16	**16a**	88	84–85/760
11	**1** (0.56), HI (100 mL)[e]	–	25–60	6	**16b**	71	41–42/55
12	**1** (0.055), C_6H_6 (0.26), $AlCl_3$ (0.004)	–	10	1	**12**	63[f]	–
13	**13a** (0.031), PCl_5 (0.04)	–	16	110–130	**17a**	69[g]	73–74/10

[a] Reaction was carried out in a 240 mL Hastelloy shaker tube, compound **2** was isolated as 1:1 mixture with THF; calculated yield (NMR).
[b] One-pot reaction; after dilution of the reaction mixture with H_2O (200 mL), the separated lower layer was treated with a 10% solution of KOH in MeOH (100 mL) for 30 min, diluted with H_2O (200 mL), the organic layer was separated, dried ($MgSO_4$) and distilled.
[c] According Ref.[16] isolated material was a colorless viscous oil.
[d] Concd HCl (36 wt%).
[e] Concd HI (48 wt%).
[f] The crude product also contained **16a** (ratio **12**:**16a** = 3:1, NMR).
[g] At 90% conversion (NMR).

Table 2 NMR and IR Data for New Compounds

Entry	Product	^{1}H NMR[a] δ, *J* (Hz)	^{19}F NMR[a] δ, *J* (Hz)	IR (cm^{-1})
1	**1**[b]	3.3 (s)	–73.3 (s)	1404, 1368[c]
2	**2**[d]	2.3(1 H, br s), 4.0 (2 H, s), 4.2 (1 H, br s)	–77.3 (s)	3490
3	**4a**[e]	3.5 (3 H, s), 3.8 (hept, *J* = 0.8), 4.3 (br s)	–77.5 (s)	3485
4	**4b**	1.3 (6 H, d, *J* = 6.0), 3.8 (1 H, m), 3.8 (2 H, m), 4.2 (1 H, br s)	–77.6 (s)	3426
5	**4d**	3.45 (3 H, s), 3.47(3 H, hept, *J* = 1.0), 3.9 (2 H, hept, *J* = 3.0)	–71.5 (s)	–
6	**5**[f]	2.5 (1 H, br s), 3.7 (3 H, hept, *J* = 1.1), 4.1 (2 H, s)	–73.9 (s)	3485
7	**6**	2.8 (3 H, br s), 3.3 (2 H, s)	–78.5	3395, 3333
8	**6a**	3.1 (3 H, br s), 3.2 (4 H, s)	–77.5 (s)	3400, 3380[g]
9	**8a**	1.0 (6 H, t, *J* = 7.6), 2.7 (4 H, q, *J* = 7.6), 2.8 (2 H, s), 6.7 (1 H, br s)	–78.6 (s)	3083, 2978, 2872
10	**8b**	3.8 (2 H, s), 4.3 (1 H, br s), 4.2 (1 H, br s), 6.8 (2 H, d, *J* = 8.0), 7.0 (1 H, t, *J* = 8.0), 7.3 (2 H, t, *J* = 8.0)	–78.0 (s)	–
11	**8c**	3.6 (2 H, s), 4.1 (1 H, br s), 6.9 (2 H, m, *J* = 9.0), 7.9 (2 H, t, *J* = 9.0)	–77.9 (3 F, s), –123.1 (1 F, m)	3424, 3378[g]
12	**10**	2.5 (2 H, m), 2.9 (2 H, m), 3.2 (2 H, s), 4.2 (1 H, br s)	–77.9 (6 F, s), –81.4 (3 F, t, *J* = 7.5), –114.6 (2 F, m), –122.4 (2 F, m), –123.3 (2 F, m), –123.8 (2 F, m), –126.6 (2 F, m)	3389
13	**13a**	2.8 (1 H, br s), 3.1 (2 H, s), 7.3 (2 H, m), 7.4 (2 H, m)	–63.2 (3 F, s), –76.5 (6 F, s)	3589
14	**13b**	3.0 (1 H, br s), 3.3 (2 H, s), 7.5 (2 H, d, *J* = 8.0), 7.6 (2 H, d, *J* = 8.0)	–62.1 (3 F, s), –76.4 (6 F, s)	3590
15	**14**[h]	4.7 (s)	–74.3 (6 F, hept, *J* = 0.5), –77.6 (6 F, hept, *J* = 0.5)	–
16	**15a**	4.1 (1 H, br s), 4.8 (2 H, s)	36.9 (1 F, s), –77.1 (6 F, s)	–
17	**15b**	3.3 (1 H, br s), 4.5 (2 H, s)	–74.7 (3 F, s), –76.2 (6 F, s)	3507, 1426
18	**16a**	3.6 (1 H, br s), 3.9 (2 H, s)	–76.1 (s)	3530
19	**16b**	3.2 (1 H, br s), 3.5 (2 H, s)	–75.8 (s)	3507
20	**17a**	7.6 (2 H, m), 7.7 (3 H, m)	–57.9 (3 F, q, *J* = 7.2), –63.4 (3 F, s), –64.3 (3 F, qd, *J* = 7.2, 1.2)	1669
21	**17b**	7.2 (1 H, s), 7.5 (2 H, m), 7.9 (2 H, m)	–57.9 (3 F, q, *J* = 7.0), –63.5 (3 F, s), –64.4 (3 F, qd, *J* = 7.0, 1.2)	1670

[a] In $CDCl_3$.
[b] ^{13}C{H} NMR ($CDCl_3$): δ = 46.8 (s), 55.0 (hept, *J* = 37 Hz), 120.8 (q, *J* = 275 Hz).
[c] Gas phase.
[d] Lit.:[10] ^{19}F NMR (standard CF_3CO_2H, in DMSO-d_6): δ = 11.68.
[e] ^{13}C{H} NMR (neat): δ = 59.2 (s), 68.1 (s), 75.3 (hept, *J* = 28 Hz), 122.9 (q, *J* = 289 Hz).
[f] In acetone-d_6; ^{13}C{H} NMR (neat): δ = 54.3 (s), 59.0 (s), 80.4 (hept, *J* = 26 Hz), 123.0 (q, *J* = 285 Hz).
[g] In KBr.
[h] ^{13}C{H} NMR (neat): δ = 70.1 (s), 84.6 (hept, *J* = 29 Hz), 105.2 (hept, *J* = 33 Hz), 119.8 (q, *J* = 291 Hz), 121.1 (q, *J* = 285 Hz).

^{19}F and ^{1}H NMR spectra were recorded on QE-300 (General Electric, 200 MHz) or Bruker DRX-400 instruments (376.8485 and 400.5524 MHz respectively) using $CFCl_3$ and TMS as an internal standard and $CDCl_3$ or acetone-d_6 as a lock solvents. IR spectra were recorded on a Perkin-Elmer 1600 FT spectrometer as films or KBr pellets. GC and GC/MS analysis were carried out on a HP 6890 instrument using HP FFAP capillary column (30 m) and TC (GC) or mass-selective (GC/MS) detectors.

Anhyd solvents, alcohols, NaH (98%), Et_2NH, anilines, BF_3-etherate, benzene, anhyd $AlCl_3$ (Aldrich); FSO_2OH, hexafluoroacetone, CF_3SO_2OH, SbF_5 (Synquest); $C_6F_{13}(CH_2)_2SH$ (Ciba-Geigy), $(CF_3)_2C{=}CH_2$ (DuPont) are commercially available and used without further purification. Reagents **11a**–**c** were prepared by the addition of the corresponding aryl bromides to Mg turnings (30% excess) in THF solvent at 30–40 °C. These solutions were filtered under N_2 and used immediately. The epoxide **1** was prepared according to reported procedure.[9] Due to its relatively low boiling point (39 °C,[8] 41–42 °C[9]) and high vapor pressure, most of the reactions were carried out in a reactor equipped with a dry-ice condenser to prevent loss of the epoxide.

Compounds **2**,[10] **2a**,[11] **6**,[8]**12**,[16] **16a**,[20] and **17a**[22] were identified by comparison of boiling points or NMR data with reported values.

Caution! Hexafluoroactone is a highly toxic material and should be handled in a well-ventilated hood to avoid contact with its vapor. The epoxide **1** and compounds prepared in this work are materials whose toxicological properties are not fully explored, and these materials should be handled accordingly.

Reactions with Nucleophiles; 3,3,3-Trifluoro-2-(trifluoromethyl)propane-1,2-diol (2) by Hydrolysis of 2a

Compound **2a** (48 g, 0.2 mol) was added dropwise to a stirred solution of KOH (30 g, 0.54 mol) in anhyd MeOH (150 mL) at 45–50 °C. The reaction mixture was kept at 50 °C for 30 min, cooled down to 10 °C and aq 20% HCl (200 mL) was slowly added. The mixture (pH ~1) was extracted with Et_2O (3 × 100 mL), the combined organic layers were dried ($MgSO_4$), the solvent was distilled off at atmospheric pressure, and the residue was distilled to give 27 g (68%) of **2**; bp 136–137 °C which crystallized on standing; mp 45–47 °C (Tables 1 and 2).

Anal. Calcd for $C_4H_4F_6O_2$: C, 24.26, H, 2.04. Found: C, 24.26, H, 1.96.

1,1,1,3,3,3-Hexafluoro-2-(isopropoxymethyl)propane-2-ol (4b); Typical Procedure

NaH (98%, 5 g, 0.21 mol) was placed in a 500-mL flask inside a dry box. Anhyd THF (100 mL) was introduced into the flask under a N_2 blanket using a syringe. A solution of *i*-PrOH (12 g, 0.2 mol) in anhyd THF (100 mL) was slowly added using an addition funnel to maintain the internal temperature at 30–35 °C. The reaction mixture was stirred for 1 h at 35 °C, cooled down to 15 °C and compound **1** (36 g, 0.2 mol) was added dropwise to keep the temperature of the reaction mixture below 20 °C. After 14 h, MeOH (10 mL) was added and the mixture was diluted with 10% HCl (500 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were dried ($MgSO_4$), the solvent was removed under vacuum and the residue was distilled to give 13 g of a fraction with bp 66–71 °C/100 mm Hg (mixture of **4b** and THF, 1:1) and 37 g of a fraction with bp 71–73 °C/100 mm Hg (**4b** 95%, 5% of THF). The calculated yield of **4b** was 90% (Table 2).

MS: *m*/*z* = 240 [M^+, $C_7H_{10}F_6O_2^+$].

1,1,1,3,3,3-Hexafluoro-2-(methoxymethyl)propane-2-ol (4a)

Compound **4a** was prepared similarly. Reaction condition, the ratio of reagents, analytical and spectroscopic data for **4a** are given in Tables 1 and 2.

1,1,1,3,3,3-Hexafluoro-2-methoxy-2-(methoxymethyl)propane (4d)

NaH (98%, 5 g, 0.21mol) was placed in a 500-mL flask inside a dry box. Anhyd THF (100 mL) was introduced into the flask under a N_2 blanket using a syringe. A solution of MeOH (7.1g, 0.22 mol) in anhyd THF (100 mL) was slowly added using an addition funnel to keep the temperature between 30–35 °C. The reaction mixture was stirred for 30 min, cooled down to 15 °C and compound **1** (36 g, 0.2 mol) was added dropwise to keep the temperature of the mixture at 15–20 °C. After 14 h, Me_2SO_4 (10 mL, 12.0 g, 0.095 mol) was added dropwise at 25–30 °C. After 1 h, the mixture was diluted with H_2O, the organic layer was separated, and dried ($MgSO_4$). The crude product (45 g, a mixture of 40% ether **4d** and 60% of alcohol **4a,** GC, NMR) was distilled to give 22 g of a fraction with bp 100–120 °C (mixture of **4d** and **4a,** 70:30). Pure **4d** was isolated by washing this fraction with 10% NaOH. Redistillation of the dried product afforded 15 g (33%) of **4d**; bp 120.3–120.5 °C (Table 2).

Anal. Calcd for $C_5H_6F_6O_2$: C, 31.57, H, 3.57. Found: C, 31.97, H, 3.51.

2-(Aminomethyl)-1,1,1,3,3,3-hexafluoropropane-2-ol (6)

Compound **1** (54 g, 0.3 mol) **1** was slowly added to a stirred mixture of 30% NH_4OH (100 mL) and Et_2O (100 mL) at 25–30 °C (~1 h). The reaction mixture was stirred for 2 h at 25 °C, the organic layer was separated, and the aqueous layer was extracted with Et_2O (2 × 50 mL). The organic layers were combined, dried ($MgSO_4$), the solvent was removed under vacuum (15–20 °C) and the crude solid product (mixture of **6** and **6a**, ratio 5:1, NMR) was distilled to give 37.8 g (64%) of **6**; bp 134–137 °C/760 mm Hg, which crystallized on standing; mp 75–76 °C (Lit.[7]mp 76–77 °C) (Table 2).

Anal. Calcd for $C_4H_5F_6NO$: C, 24.38, H, 2.56, N, 7.11. Found: C, 24.63, H, 2.27, N, 7.11.

1,1,1,3,3,3-Hexafluoro-2-({[3,3,3-trifluoro-2-hydroxy-2-(trifluoromethyl)propyl]amino}methyl)propan-2-ol (6a)

Compound **1** (80 g, 0.44 mol) was slowly added to a stirred 30% NH_4OH (20 mL) at 25–60 °C. The reaction mixture was kept at 60 °C for 1 h and cooled down to 25 °C. The crystallized crude product was dissolved in Et_2O (200 mL), the Et_2O solution was dried ($MgSO_4$), the solvent was removed under vacuum, and the crude product was recrystallized from hexane to give 68 g (82%) of **6a**; mp 90–91 °C (Table 2).

Anal. Calcd for $C_8H_7F_{12}NO_2$: C, 25.48, H, 1.87, N, 3.71. Found: C, 25.28, H, 1.64, N, 3.82.

2-(Anilinomethyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (8b); Typical Procedure

Compound **1** (15 g, 0.083 mol) was added dropwise to $C_6H_5NH_2$ (10 mL, 10.2 g, 0.11 mol) with stirring over a period of 1 h at 15–20 °C. After the addition was over, the reaction mixture was kept at 25 °C for 16 h and distilled to give 15 g (66%) of **8b**; bp 112–113 °C/10 mm Hg, which crystallized on standing; mp 34–35 °C (Table 2).

Anal. Calcd for $C_{10}H_9F_6NO$: C, 43.97, H, 3.32, F, 40.53. Found: C, 43.46, H, 3.26, F, 40.73.

Compounds 8a,c, and 10

These compounds were prepared similarly (Tables 1 and 2).

1,1,1,3,3,3-Hexafluoro-2-[3-(trifluoromethyl)benzyl]propan-2-ol (13a); Typical Procedure

To a solution of **11a** prepared by reacting Mg turnings (2.8 g) with 3-bromo-1-trifluoromethylbenzene (22.5 g, 0.1 mol) in anhyd THF (100 mL) was added CuI (0.2 g, 0.001 mol) at 10 °C, followed by slow addition of **1** (20 g, 0.11 mol). The reaction mixture was then

brought to r.t. After 12 h, it was diluted with aq sat. solution of NH_4Cl (300 mL), and extracted with CH_2Cl_2 (100 mL). The organic layer was dried ($MgSO_4$), the solvent was removed under vacuum and the residue (30 g) was distilled to give 17.2 g (53%) of **13a**; bp 88–89 °C/13 mm Hg (Table 2).

Anal. Calcd for $C_{11}H_7F_9O$: C, 40.51, H, 2.16, F, 54.42. Found: C, 40.64, H, 2.18, F, 54.32.

Compounds 12, 13a,b
These compounds were prepared similarly (Tables 1 and 2).

Reaction of 1 with Hexafluoroacetone; 2,2,4,4-Tetrakis(trifluoromethyl)-1,3-dioxolane (14)
CsF (9 g, 0.06 mol) was dried at 120 °C at reduced pressure (>0.1 mm Hg) in a 250 mL 3-neck round-bottom flask for 2 h. Anhyd MeCN (100 mL) was introduced under N_2 at r.t. into the reaction vessel and gaseous hexafluoroacetone (8 g, 0.047 mol) was introduced into the flask at 25–30 °C. The epoxide **1** was added to the resulting homogeneous solution dropwise (~20 min) and the mixture was stirred at r.t. for 12 h. It was diluted with H_2O (200 mL), the organic layer was separated, washed with H_2O (2×50mL), dried ($MgSO_4$) and fractionated to give 4 g (23.5%) of **14**; bp 70–72 °C/760 mm Hg (Table 2).

MS: m/z = 346 [M^+, $C_7H_2F_6O_2^+$].

Reactions of 1 with Electrophiles; 3,3,3-Trifluoro-2-hydroxy-2-(trifluoromethyl)propyl Fluorosulfate (15a)
Compound **1** (36 g, 0.2 mol) was added slowly (exothermic!) under stirring to $HOSO_2F$ (20 g, 0.2 mol) in a 50-mL glass flask at a rate, which allow to maintain the internal temperature at 30–35 °C. The reaction mixture was stirred for 30 min at 35–40 °C and was slowly poured onto ice. The organic layer was separated, dried ($MgSO_4$) and distilled under reduced pressure to give 44 g (79%) of **15a**; bp 72–74 °C/40 mm Hg (Table 2).

Compounds 15b, 16a,b
These compounds were prepared similarly (Tables 1 and 2).

3,3,3-Trifluoro-2-hydroxy-2-(trifluoromethyl)propyl Acetate (2a)
A 400 mL Hastelloy shaker tube was charged with TaF_5 (2 g, 0.007 mol), glacial AcOH (60 g, 1 mol) and **1** (180 g, 1 mol), evacuated at –78 °C and kept for 12 h at 120 °C. The crude reaction product was washed with H_2O (300 mL), separated, dried ($MgSO_4$) and distilled to give 192–216 g (80–90%) of **2a**; bp 75–76 °C/35 mm Hg (Lit.[11] mp 78 °C/35 mm Hg).

1-(Trifluoromethyl)-4-[3,3,3-trifluoro-2-(trifluoromethyl)prop-1-enyl]benzene (17b)
A mixture of **13b** (10 g, 0.03 mol) and PCl_5 (8.5 g, 0.04 mol) was heated in a glass flask till evaluation of HCl had ceased (~12 h). The reaction mixture was quenched with cold water and stirred at 20–50 °C for 1 h to reach the complete hydrolysis of $POCl_3$. The separated organic layer was dried ($MgSO_4$) and distilled to give 6.7 g (70%) of **17b**; bp 76–78 °C/12 mm Hg (Table 2)

Anal. Calcd for $C_{11}H_5F_9$: C, 42.88, H, 1.64, F, 55.49. Found: C, 42.66, H, 1.80, F, 55.30.

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References

(1) Publication No.: 8286.
(2) (a) Chiba, T.; Hung, R. J.; Yamada, S.; Trinque, B.; Yamachika, M.; Brodsky, C.; Patterson, K.; Hayden, V.; Jaminson, A.; Lin, S.-H.; Somervell, M.; Byers, J.; Coneley, W.; Willson, G. *J. Photopolym. Sci. Technol.* **2000**, *13*, 657. (b) French, R. H.; Feldman, J.; Zumsteg, F. C.; Crawford, M. K.; Feiring, A. E.; Petrov, V. A.; Schadt, F. L. III; Wheland, R. C. *Semiconductor Fabtech*, 14th Ed., 167; ICG Publishing Ltd.: London, **2001**.
(3) Krespan, C. G.; Middleton, W. J. *Fluorine Chem. Rev*. **1967**, *1*, 145.
(4) (a) Burton, D. J.; Morken, P. A. In *Methods of Organic Chemistry (Houben–Weyl)*, Vol. E10b/1; Baasner, B.; Hagemann, H.; Tatlow, J. C., Eds.; Thieme: Stuttgart, **2000**, Chap. 2.1.1.3, 483. (b) Furin, G. G. In *Methods of Organic Chemistry (Houben-Weyl)*, Vol. E10b/1; Baasner, B.; Hagemann, H.; Tatlow, J. C., Eds.; Thieme: Stuttgart, **2000**, Chap. 2.1.1.1, 402. (c) For a review on application of fluoroalkylsilanes in organic synthesis, see: Prakash, G. K. S.; Yudin, A. K. *Chem. Rev*. **1997**, *97*, 757.
(5) For reviews on the chemistry of trifluoromethyloxirane, see: (a) Katagiri, T. In *Enantiocontrolled Synthesis of Fluoro-Organic Compounds*; Soloshonok, V., Ed.; Wiley: New York, **1999**, Chap. 5, 161. (b) Katagiri, T.; Uneyama, K. *J. Fluorine Chem.* **2000**, *105*, 285.
(6) Dear, R. E. A.; Gilbert, E. E. (Allied Corporation) US Patent 3573330, **1971**; *Chem. Abstr*. **1971**, *74*, 141498.
(7) Simmons, H. E.; Wiley, D. W. *J. Am. Chem. Soc.* **1960**, *82*, 2288.
(8) Chang, I. S.; Willis, C. J. *Can. J. Chem.* **1977**, *55*, 2465.
(9) Petrov, V. A.; Feiring, A. E.; Feldmann, J. (to DuPont) WO 00/66575, PCT/US/00/11746, **2000**; *Chem. Abstr*. **2000**, *133*, 350691.
(10) Herrmann, W. A.; Eder, S. J. *Chem. Ber.* **1993**, *126*, 31.
(11) Howard, E. G.; Seargent, P. B.; Krespan, C. G. *J. Am. Chem. Soc.* **1967**, *89*, 1422.
(12) (a) Tarrant, P.; Allison, C. G.; Barthhold, K. P.; Stump, E. G. *Fluorine Chem. Rev*. **1971**, *5*, 77. (b) Millauer, H.; Schwertfeger, W.; Siegemund, G. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 161. (c) Knunyants, I. L.; Shokina, V. V.; Tuyleneva, V. V.; Cheburkov, Yu. A.; Aronov, Yu. E. *Izv. Akad. Nauk SSR., Ser. Khim.* **1966**, 1831; *Chem. Abstr*. **1967**, *66*, 94673.
(13) Watts, R. O'B.; Tarrant, P. *J. Fluorine Chem.* **1975**, *6*, 481.
(14) Voronkov, M. G.; Baryshok, V. P.; Tandure, S. N.; Vitkovskii, V. Y. U.; D'aykov, V. M.; Pestunovich, V. A. *J. Gen. Chem. USSR* **1978**, *48*, 2033.
(15) Takshashi, O.; Furuhashi, K.; Fukumasa, M.; Hirai, T. *Tetrahedron Lett*. **1990**, *31*, 7031.
(16) Ohno, F.; Kawashima, T.; Okazaki, R. *Chem. Commun.* **2001**, 463.
(17) Grushin, V. V.; Marshall, W. J.; Halliday, G. A.; Davidson, F.; Petrov, V. A. *J. Fluorine Chem., in* press.
(18) McBee, E. T.; Hathaway, C. E.; Roberts, C. W. *J. Am. Chem. Soc.* **1956**, *78*, 3851.
(19) Kolenko, I. P.; Filaykova, T. I.; Zapevalov, A. Ya.; Mochalina, E. P.; German, L. S.; Polishcuk, V. R. *Izv. Akad. Nauk., Ser. Khim.* **1979**, 667; *Chem. Abstr*. **1979**, *91*, 38866.
(20) Dear, R. E. A. *Synthesis* **1970**, 361.
(21) Dear, R. E. A.; Gilbert, E. E.; Murray, J. J. *Tetrahedron* **1971**, *27*, 3345.
(22) Burton, D. J.; Inouye, Y. *Tetahedron Lett.* **1979**, *20*, 3397.