Regioselective Opening of Simple Epoxides with Diisopropylamine Trihydrofluoride

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Treatment of benzyl ether derivatives of simple aliphatic epoxy alcohols with diisopropylamine trihydrofluoride gave mixtures of the corresponding fluorohydrins in good yields. Steric hindrance is a major factor in determining the regioselectivity of epoxide opening, although electronic effects cannot be ignored. Electronic effects are more dominant with pyridine polyhydrofluoride.

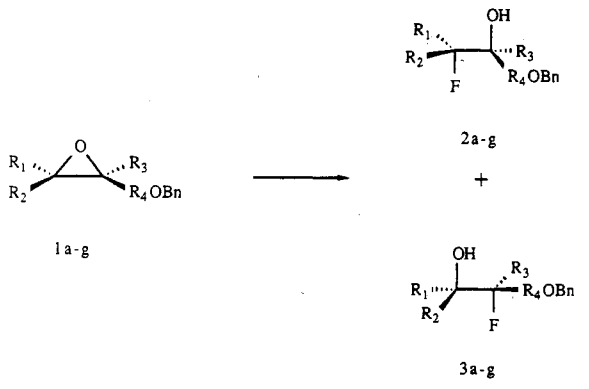
Pronounced biological effects are often seen when hydrogen atoms in natural metabolites are replaced by fluorine.[2] This behavior is usually attributed to several important properties of fluorine. It is the most electronegative of the elements,[3] and its powerful electron-withdrawing effect can profoundly alter the rate of a reaction when fluorine is placed near a reaction center.[4] In addition, fluorine is a good leaving group, and a large number of analogues have been discovered that inhibit enzymes irreversibly by covalent modification of nucleophilic moieties in the catalytic site.[5-7] Unlike other substitutions, replacement of hydrogen by a fluorine does not introduce large steric perturbations that might interfere with binding interactions to an enzyme or a receptor.

As part of a program to prepare and study fluorinated isoprenoids as inhibitors,[7] we became interested in procedures for the regioselective opening of simple aliphatic epoxides with hydrogen fluoride. Various reagents, where the reactivity of hydrogen fluoride was modified by a base or a Lewis acid, have been used to successfully fluorinate sterol epoxides.[8] Potassium fluoride/hydrogen fluoride in ethylene glycol was particularly useful for opening oxirane rings in carbohydrates,[8] and a variety of aryl-substituted glycidic esters and halogenated oxiranes gave fluorohydrins when treated with pyridinium polyhydrofluoride.[9,10] Trialkylammonium hydrofluoride salts were also reported to readily convert aryl glycidic esters and styrene oxides to fluorohydrins.[11-14] Simple aliphatic alicyclic oxiranes, however, are prone to polymerization and rearrangement.[15] We now describe experiments with several simple epoxides which gave good yields of the corresponding fluorohydrins upon treatment with diisopropylamine trihydrofluoride.[13]

Results and Discussion

Addition of substoichiometric quantities of amines to hydrogen fluoride substantially moderates the reactivity of the acid.[9,12,14] In searching for a mild selective electrophilic reagent for electrophilic addition of hydrogen fluoride to epoxides, we tried the diisopropylamine trihydrofluoride system reported by Jullien for opening styrene oxides[13] and phenyl-substituted glycidic esters.[14] The reagent was prepared by addition of 3 equiv of aqueous HF to the amine. The white crystalline salt obtained after lyophilization was stored in a desiccator until needed.

In a typical reaction, one equivalent of epoxide was heated with 1.5-2.0 equiv of diisopropylamine trihydrofluoride as a neat homogeneous melt at 110 °C for up to 30 h. At the end of that period, mixtures of regioisomeric fluorohydrins of the epoxides **1a-g** shown below were isolated in 60-80% yields. The mildness of the Jullien



	R_1	R_2	R_3	R_4
a	H	H	H	CH_2
b	CH_3	H	H	CH_2
c	CH_3	CH_3	H	CH_2
d	H	H	H	$C(CH_3)_2$
e	H	H	H	$(CH_2)_2$
f	H	H	CH_3	$(CH_2)_2$
g	H	H	H	$(CH_2)_3$

reagent, in comparison with other common sources of HF such as pyridinium polyhydrofluoride, is dramatically illustrated by comparative studies with **1a**. Seven hours at 110 °C were required to consume the epoxide with the diisopropylamine reagent. In contrast, the reaction with **1a** was complete in less than 15 min at −5 °C with pyridinium polyhydrofluoride, and the recoveries dropped noticeably at longer reaction times at that temperature.

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As illustrated in Table I, regioselectivities for diisopropylamine trihydrofluoride were generally good, and all of the isomeric fluorohydrins prepared in this study, including secondary alcohols **2b** and **3b**, were readily separated by flash chromatography. Steric hindrance is a major factor in determining the regioselectivity of epoxide opening. For example, fluoride adds to the less hindered carbon in the oxirane ring of all the epoxides except **1c**. Steric bulk adjacent to the ring is also important, as illustrated by the increased regioselectivity for **1d** versus **1a**. Increased alkyl substitution on the oxirane, however, eventually overwhelms steric control. In the series **1a–c**, the proportion of fluorohydrin **2** reached a minimum for **1b** and then increased slightly for **1c** with the introduction of a second methyl group at the same oxirane carbon. A similar effect is noted when comparing the regioselectivities of **1e** and **1f**. In the latter case, attack at the primary center is only slightly favored over the tertiary center. The more reactive pyridinium polyhydrofluoride reagent gave a much higher preference for fluoride attack at the more substituted epoxy carbon, as illustrated by **1a** and **1e**. Finally, the influence of the benzyloxy substituent is unclear. It appears to exert a modest electron-withdrawing influence since the regioselectivity drops from 15:1 for **1a** to 6:1 for **1e** as the group is moved away from the epoxide ring. However, the trend is reversed if one compares **1e** and **1g**.

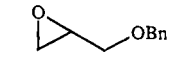
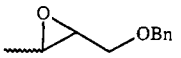
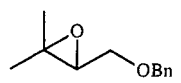
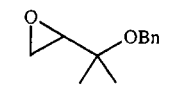
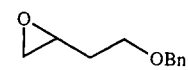
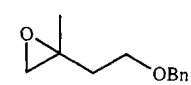
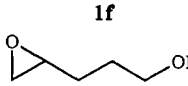
In summary, we found the Jullian formulation[13] of diisopropylamine and HF to be an excellent source of fluoride for opening simple aliphatic epoxides. Diisopropylamine trihydrofluoride is a mild, reasonably selective reagent for the conversion of this class of compounds to fluorohydrins with minimal complications from polymerization. All of the compounds in this study were benzyl derivatives of epoxy alcohols. That protecting group was stable to the diisopropylamine reagent; whereas, in preliminary experiments some trouble was experienced with more reactive sources of HF. The reactions with diisopropylamine trihydrofluoride were easy to run on gram quantities of material, and regioisomers were readily separated by flash chromatography.

Experimental Section

General. ^1H and ^{13}C NMR spectra are reported in parts per million downfield from internal TMS and ^{19}F spectra in parts per million downfield from trichlorofluoromethane. Infrared spectra were calibrated to the 1602-cm^{-1} absorption of polystyrene, and all absorptions are reported in wavenumbers (cm^{-1}). Analytical gas chromatography was carried out with a 12.5-m OV-1 WCOT and 20-m DB5 glass capillary columns. Silica gel flash chromatography was performed on grade 60, 235–400 mesh silica gel (Aldrich Chemical Co.) and TLC on silica gel 60 F-254 glass plates (American Scientific Products). Silica TLC plates were visualized under UV light, by iodine, or by dipping in a 10% solution of phosphomolybdic acid in ethanol followed by heating. Microanalyses were performed by MicAnal Inc. All reactions were conducted under an inert atmosphere of dry nitrogen.

Materials. Reagent grade hexanes were purified by washing with acid and base, filtered through neutral alumina, and distilled from glass. Reagent grade chloroform, diethyl ether, and ethyl acetate were distilled from glass. 3-Buten-1-ol, 2-buten-1-ol, 2-propen-1-ol, 2-methyl-3-buten-2-ol, 3-methyl-2-buten-1-ol, 3-methyl-3-buten-1-ol, 4-penten-1-ol, pyridinium polyhydrofluoride, and diisopropylamine were purchased from Aldrich Chemical Co. Hydrofluoric acid (48%) was purchased from J. T. Baker Chemical Co. and *m*-chloroperbenzoic acid from Lancaster Synthesis Ltd. Alcohols were converted to the corresponding benzyl ethers by routine procedures.[16]

Table I. Products of Oxirane Ring Opening

oxirane	reagent	product ratio[a] 2:3	yield, %
 **1a**	diisopropylamine trihydrofluoride	15:1	75[b]
	pyridine polyhydrofluoride	1.1:1	60[b]
 **1b**	diisopropylamine trihydrofluoride	5:1	79[b]
 **1c**	diisopropylamine trihydrofluoride	8:1	76[b]
 **1d**	diisopropylamine trihydrofluoride	25:1	62[b]
 **1e**	diisopropylamine trihydrofluoride	6:1	81[b]
	pyridine polyhydrofluoride	1:4	68[c]
 **1f**	diisopropylamine trihydrofluoride	1.5:1	78[b]
 **1g**	diisopropylamine trihydrofluoride	11:1	69[b]

[a] Determined by GLPC. Isomers were separated by flash chromatography on silica gel. [b] Sum of the isolated yields of isomers. [c] Yield of crude material.

General Procedure for Synthesis of Epoxides. In a flame-dried flask under a nitrogen atmosphere were combined 1 equiv of the olefin and 1.1 equiv of *m*-chloroperbenzoic acid in chloroform (0.15–0.35 M in olefin). The mixture was stirred at room temperature until the olefin was consumed as determined by GC (4–16 h). The mixture was extracted with three portions of 3 M sodium hydroxide solution, washed with water, and dried over magnesium sulfate. Solvent was removed in vacuo to afford a residue that was further purified by flash chromatography on silica gel.

1-(Benzyloxy)-2,3-epoxypropane (1a). 3-(Benzyloxy)-1-propene (2.00 g, 13.5 mmol) was treated with *m*-chloroperbenzoic acid (2.56 g, 14.8 mmol) for 12 h to yield 2.08 g (94%) of a colorless oil:[18] R_f 0.32 (hexanes/ethyl acetate, 3:1); ^1H NMR (90 MHz, $CDCl_3$) δ 2.57 (1 H, dd, $J_{H,H}$ = 4.9 Hz, $J_{H,H}$ = 2.4 Hz, H at C3), 2.76 (1 H, t, $J_{H,H}$ = 4.9 Hz, H at C3), 3.03 (1 H, m, H at C2), 3.40 (1 H, dd, $J_{H,H}$ = 11.2 Hz, $J_{H,H}$ = 5.5 Hz, H at C1), 3.74 (1 H, dd, $J_{H,H}$ = 11.2 Hz, $J_{H,H}$ = 3.0 Hz, H at C1), 4.56 (2 H, s, H at benzyl C), 7.30 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.26, 50.86, 70.79, 73.29, 127.76, 128.42, 137.85; IR (CCl_4) 3075, 3052, 3020, 2985, 2915, 2853, 1488, 1446, 1377, 1355, 1348, 1242, 1198, 1153, 1086, 1022, 905, 841, 722, 691 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{10}H_{12}O_2$ 164.0834, found 164.0824.

1-(Benzyloxy)-2,3-epoxybutane (1b). (*E,Z*)-1-(Benzyloxy)-2-butene (11.00 g, 67.8 mmol) was treated with *m*-chloroperbenzoic acid (12.87 g, 74.6 mmol) for 16 h to yield 10.3 g (85%) of a colorless oil:[19] R_f 0.39 (hexanes/ethyl acetate, 3:1); ^1H NMR (90 MHz, $CDCl_3$) δ 1.30 (3 H, d, $J_{H,H}$ = 6.0 Hz, H at C4), 2.80–3.00

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(2 H, m, H at C2 and C3), 3.30–3.80 (2 H, m, H at C1), 4.50 (2 H, s, H at benzyl C), 7.30 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.30, 52.10, 57.90, 70.30, 73.20, 127.59, 127.64, 127.80, 128.30; IR (CCl_4) 3075, 3053, 3020, 2980, 2920, 2851, 1489, 1446, 1372, 1355, 1321, 1240, 1198, 1118, 1082, 1022, 933, 898, 862, 722, 691 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{11}H_{14}O_2$ 178.0990, found 178.0961.

1-(Benzyloxy)-2,3-epoxy-3-methylbutane (1c). 4-(Benzyloxy)-2-methyl-2-butene (0.40 g, 2.27 mmol) was treated with *m*-chloroperbenzoic acid (0.43 g, 2.49 mmol) for 4 h to yield 0.36 g (91%) of a colorless oil:[20] R_f 0.56 (hexanes/ethyl acetate, 1:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.25 (3 H, s, H at methyl C), 1.23 (3 H, s, H at methyl C), 2.90 (1 H, t, $J_{H,H}$ = 5.2 Hz, H at C2), 3.60 (2 H, m, H at C1), 4.67 (2 H, d, $J_{H,H}$ = 3.0 Hz, H at benzyl C), 7.32 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.83, 24.67, 57.68, 62.06, 68.89, 73.22, 127.78, 128.42, 137.88; IR (CCl_4) 3074, 3045, 3014, 2965, 2948, 2912, 2843, 1486, 1442, 1368, 1350, 1300, 1233, 1194, 1074, 1018, 900, 860, 720, 690 cm^{-1}; MS (chemical ionization, methane), *m/z* (relative intensities) 91 (100.0), 107 (2.7), 115 (3.7), 131 (2.8), 145 (1.4), 157 (0.9), 175 (1.4), 181 (9.9), 182 (1.4), 191 (3.6), 193 (1.5) [M + 1].

2-(Benzyloxy)-3,4-epoxy-2-methylbutane (1d). 3-(Benzyloxy)-3-methyl-1-butene (3.00 g, 17.0 mmol) was treated with *m*-chloroperbenzoic acid (3.23 g, 18.7 mmol) for 14 h to yield 3.00 g (92%) of a colorless oil: R_f 0.40 (hexanes/ethyl acetate, 4:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.21 (3 H, s, H at methyl C), 1.28 (3 H, s, H at methyl C), 2.53–2.77 (2 H, m, H at C4), 2.10 (1 H, t, $J_{H,H}$ = 4.0 Hz, H at C3), 4.56 (2 H, s, H at benzyl C), 7.25 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.83, 23.32, 43.39, 57.64, 65.23, 127.25, 127.38, 128.29, 139.32; IR (CCl_4) 3052, 3020, 2972, 2923, 2860, 1598, 1578, 1489, 1462, 1446, 1377, 1354, 1262, 1233, 1198, 1156, 1078, 1050, 1022, 894, 864, 822, 705, 690 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{10}H_{13}O$ [M – C_2H_3O] 149.0963, found 149.0995.

1-(Benzyloxy)-3,4-epoxybutane (1e). 4-(Benzyloxy)-1-butene (12.00 g, 73.9 mmol) was treated with *m*-chloroperbenzoic acid (14.00 g, 81.3 mmol) for 14 h to yield 11.84 g (90%) of a colorless oil: bp 100–108 °C (1 mmHg) [lit.[21] bp 79–83 °C (1 mmHg)]; R_f 0.50 (hexanes/ethyl acetate, 1:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.73 (2 H, t, $J_{H,H}$ = 6.0 Hz, H at C2), 2.33 (1 H, dd, $J_{H,H}$ = 3.0 Hz, $J_{H,H}$ = 5.1 Hz, H at C4), 2.60 (1 H, t, $J_{H,H}$ = 5.1 Hz, H at C4), 2.75–3.07 (1 H, m, H at C3), 3.18 (2 H, t, $J_{H,H}$ = 6.0 Hz, H at C1), 4.45 (2 H, s, H at benzyl C), 7.26 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.1, 47.2, 50.2, 67.2, 73.3, 127.9, 128.7, 138.7; IR (CCl_4) 3080, 3060, 2988, 2915, 2850, 1488, 1476, 1448, 1355, 1254, 1090, 1022, 905, 825, 690 cm^{-1}.

1-(Benzyloxy)-3,4-epoxy-3-methylbutane (1f). 4-(Benzyloxy)-2-methyl-1-butene (3.5 g, 19.9 mmol) was treated with *m*-chloroperbenzoic acid (3.77 g, 21.8 mmol) for 5 h to yield 3.40 g (89%) of a colorless oil:[22] R_f 0.31 (hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.32 (3 H, s, H at C3'), 1.75–2.00 (2 H, m, H at C2), 2.58 (1 H, d, $J_{H,H}$ = 12.0 Hz, H at C4), 2.63 (1 H, d, $J_{H,H}$ = 12.0 Hz, H at C4), 3.53 (2 H, t, $J_{H,H}$ = 6.6 Hz, H at Cl), 4.46 (2 H, s, H at benzyl C), 7.29 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.53, 36.57, 54.00, 55.44, 66.62, 73.65, 127.61, 128.38, 138.25; IR (CCl_4) 3075, 3053, 3024, 2950, 2920, 2852, 1487, 1446, 1382, 1354, 1267, 1236, 1197, 1096, 1023, 900, 722, 705, 692 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.83; H, 8.49.

1-(Benzyloxy)-4,5-epoxypentane (1g). 5-(Benzyloxy)-1-pentene (3.00 g, 17.0 mmol) was treated with *m*-chloroperbenzoic acid (3.23 g, 18.7 mmol) in 50 mL of chloroform for 18 h to yield 2.63 g (80%) of a colorless oil: R_f 0.35 (hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.53–1.90 (4 H, m, H at C2 and C3), 2.40 (1 H, dd, $J_{H,H}$ = 3.0 Hz, $J_{H,H}$ = 5.1 Hz, H at C5), 2.67 (1 H, t, $J_{H,H}$ = 5.1 Hz, H at C5), 2.80–3.03 (1 H, m, H at C4), 3.49 (2 H, t, $J_{H,H}$ = 6.3 Hz, H at C1), 4.47 (2 H, s, H at benzyl C), 7.27 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.19, 29.30, 47.04, 52.05, 69.72, 72.88, 127.54, 127.60, 128.35, 137.26; IR (CCl_4) 3075, 3022, 2972, 2916, 2848, 1488, 1473, 1445, 1438, 1403, 1355, 1252, 1198, 1090, 1022, 934, 826, 722, 692 cm^{-1}; MS (CI, methane), *m/z* (relative intensities) 85.1 (20.0), 91.0 (28.0), 107.0 (5.5), 119.0 (1.9), 138.9 (1.2), 181.1 (1.8), 193.1 (0.5) [M + 1]. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.86; H, 8.46.

Diisopropylamine Trihydrofluoride. Diisopropylamine trihydrofluoride was prepared by a procedure similar to those previously described.[13,17] In a 250-mL Nalgene polyethylene bottle (wide screw cap) was placed 37.66 g (0.37 mol) of diisopropylamine and a stir bar. The bottle was cooled in a dry ice/isopropyl alcohol bath. Aqueous hydrogen fluoride solution (48%, 47.52 g, 1.12 mol) was added slowly over a period of 15 min with stirring. The resulting solution was allowed to warm to room temperature and lyophilized. A white crystalline solid (48.6 g, 81%) was obtained. The salt was stored in a desiccator at room temperature without noticeable decomposition for periods longer than 6 months.

General Procedure for Synthesis of Fluorohydrins. In a flame-dried flask under a nitrogen atmosphere were combined 1 equiv of epoxide and 1.5–2.0 equiv of diisopropylamine trihydrofluoride. The flask was tightly stoppered with a plastic cap and heated at 110 °C. The contents of the flask formed a viscous melt which was magnetically stirred. After starting material was consumed (8–29 h), as determined by GLPC, the yellow liquid solidified upon cooling to room temperature. The semisolid mass was extracted with at least 20 portions of diethyl ether. For large-scale reactions with over 20 mmol of oxirane, the mass was extracted with diethyl ether in a Soxhlet extractor for 12 h. The combined ether extracts were washed once with water, dried over magnesium sulfate, and passed through a short column of silica gel. Solvent was removed in vacuo to afford crude fluorohydrin. The mixture was analyzed by GLPC, and isomers were separated and purified by flash chromatography on silica gel. Yields were 62–81%.

Fluorohydrins from 1-(Benzyloxy)-2,3-epoxypropane (1a). Procedure A. 1-(Benzyloxy)-2,3-epoxypropane (**1a**) (0.38 g, 2.31 mmol) was treated with diisopropylamine trihydrofluoride (0.75 g, 4.63 mmol) at 110 °C for 7 h. Following workup and separation of isomers by flash chromatography (hexanes/ethyl acetate, 2:1), two colorless oils were obtained.

1-(Benzyloxy)-3-fluoropropan-2-ol (2a): 0.30 g (70%); R_f 0.29 (hexanes/ethyl acetate, 2:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.56 (1 H, s (br), OH), 3.54 (2 H, d, $J_{H,H}$ = 5.1 Hz, H at C1), 3.69–4.09 (1 H, m, H at C2), 4.32 (2 H, dd, $J_{H,F}$ = 48.0 Hz, $J_{H,H}$ = 5.1 Hz, H at C3), 4.53 (2 H, s, H at benzyl C), 7.31 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.28 (d, $J_{C,F}$ = 20.0 Hz), 70.00 (d, $J_{C,F}$ = 6.9 Hz), 73.55, 83.92 (d, $J_{C,F}$ = 169.2 Hz), 127.79, 127.94, 128.51, 137.61; ^{19}F NMR (282 MHz, $CDCl_3$) δ –234.85 (1 F, td, $J_{H,F}$ = 47.3 Hz, $J_{H,F}$ = 18.6 Hz); IR (CCl_4) 3565, 3430, 3075, 3052, 3020, 2940, 2900, 2854, 1490, 1447, 1354, 1324, 1245, 1209, 1086, 1014, 693 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{10}H_{13}FO_2$ 184.0896, found 184.0883.

3-(Benzyloxy)-2-fluoropropan-1-ol (3a): 20 mg (5%); R_f 0.17 (hexanes/ethyl acetate, 2:1); ^{1}H NMR (300 MHz, acetone-d_6) δ 3.700 (1 H, ddd, $J_{H,F}$ = 22.6 Hz, $J_{H,H}$ = 5.3 Hz), 3.704 (1 H, ddd, $J_{H,F}$ = 23.9 Hz, $J_{H,H}$ = 49.0 Hz), 3.737 (1 H, dddd, $J_{H,F}$ = 22.2 Hz, $J_{H,H}$ = 4.8 Hz, $J_{H,H}$ = 5.9 Hz), 3.753 (1 H, dddd, $J_{H,F}$ = 22.3 Hz, $J_{H,H}$ = 4.9 Hz, $J_{H,H}$ = 5.9 Hz), 4.075 (1 H, dd, $J_{H,H}$ = 5.9 Hz, $J_{H,H}$ = 5.9 Hz, OH), 4.558 (2 H, s, H at benzyl C), 4.675 (1 H, ddddd, $J_{H,F}$ = 48.95 Hz, $J_{H,H}$ = 5.3 Hz, $J_{H,H}$ = 4.0 Hz, $J_{H,H}$ = 4.8 Hz, $J_{H,H}$ = 4.9 Hz, H at C2), 7.345 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, acetone-d_6) δ 62.26 (d, $J_{C,F}$ = 23.4 Hz), 70.32 (d, $J_{C,F}$ = 22.8 Hz), 73.77, 94.04 (d, $J_{C,F}$ = 172.1 Hz), 128.28, 128.34, 129.07, 139.45; ^{19}F NMR (282 MHz, acetone-d_6) δ –198.09 (1 F, dm, $J_{H,F}$ = 49.7 Hz); IR (neat) 3400, 3080, 3055, 3021, 2922, 2860, 1492, 1450, 1363, 1305, 1249, 1203, 1094, 1043, 911, 843, 736, 695 cm^{-1}: Anal. Calcd for $C_{10}H_{13}FO_2$: C, 65.20; H, 7.11. Found: C, 64.95; H, 7.14.

Procedure B. 1-(Benzyloxy)-2,3-epoxypropane (**1a**) (0.40 g, 2.44 mmol) was treated with 0.5 mL of pyridine polyhydrofluoride (Aldrich) at –5 °C for 15 min. The reaction was carefully neutralized with saturated ammonium bicarbonate and extracted with ether. The ether extracts were dried over magnesium sulfate, the solvent was removed under vacuum, and the residue was analyzed by GLPC. The two components were separated on silica gel and found to be identical with **2a** (149 mg, 33%) and **3a** (121 mg, 27%) from procedure A.

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Fluorohydrins from 1-(Benzyloxy)-2,3-epoxybutane (1b). 1-(Benzyloxy)-2,3-epoxybutane (**1b**) (8.00 g, 44.9 mmol) was treated with diisopropylamine trihydrofluoride (18.1 g, 112.2 mmol) at 110 °C for 10 h. Following workup and separation of isomers by flash chromatography (hexanes/ethyl acetate, 3:1) two colorless oils were obtained.

1-(Benzyloxy)-3-fluorobutan-2-ol (2b): 5.83 g (66%); R_f 0.20 (hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.31 (3 H, dd, $J_{H,F}$ = 23.2 Hz, $J_{H,H}$ = 6.4 Hz, H at C4), 2.67 (1 H, s (br), OH), 3.43–3.60 (2 H, m, H at C1), 3.43–3.93 (1 H, d of quintet, $J_{H,F}$ = 47.7 Hz, $J_{H,H}$ = 6.2 Hz, H at C3), 4.50 (2 H, s, H at benzyl C), 7.28 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.73 (d, $J_{C,F}$ = 22.2 Hz), 70.29 (d, $J_{C,F}$ = 5.5 Hz), 72.24 (d, $J_{C,F}$ = 23.8 Hz), 73.47, 90.05 (d, $J_{C,F}$ = 167.5 Hz), 127.79, 127.87, 128.47, 137.67; ^{19}F NMR (282 MHz, $CDCl_3$) δ −186.34 (1 F, dqd, $J_{H,F}$ = 48.7 Hz, $J_{H,F}$ = 24.5 Hz, $J_{H,F}$ = 10.6 Hz); IR (CCl_4) 3560, 3460, 3075, 3053, 3022, 2973, 2922, 2860, 1490, 1446, 1370, 1304, 1234, 1200, 1152, 1090, 1056, 1022, 990, 930, 822, 853, 722, 694 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{11}H_{15}FO_2$ 198.1052, found 198.1064.

4-(Benzyloxy)-3-fluorobutan-2-ol (3b): 1.15 g (13%); R_f 0.32 (hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.20 (3 H, d, $J_{H,H}$ = 6.0 Hz, H at C1), 2.58 (1 H, s (br), OH), 3.66 (2 H, dd, $J_{H,F}$ = 24.6 Hz, $J_{H,H}$ = 4.5 Hz, H at C4), 3.73–4.10 (1 H, m, H at C2), 4.36 (1 H, dq, $J_{H,F}$ = 47.4 Hz, $J_{H,H}$ = 4.5 Hz, H at C3), 4.84 (2 H, s, H at benzyl C), 7.29 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.39 (d, $J_{C,F}$ = 5.2 Hz), 67.05 (d, $J_{C,F}$ = 23.5 Hz), 69.02 (d, $J_{C,F}$ = 22.7 Hz), 73.60, 94.50 (d, $J_{C,F}$ = 174.5 Hz), 127.78, 127.89, 128.48, 137.53; ^{19}F NMR (282 MHz, $CDCl_3$) δ −196.77 (1 F, dtd, $J_{H,F}$ = 48.2 Hz, $J_{H,F}$ = 24.3 Hz, $J_{H,F}$ = 12.4 Hz); IR (CCl_4) 3580, 3450, 3075, 3052, 3020, 2968, 2925, 1490, 1447, 1370, 1360, 1250, 1200, 1092, 1052, 1023, 990, 884, 721, 693 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{11}H_{15}FO_2$ 198.1052, found 198.1053.

Fluorohydrins from 1-(Benzyloxy)-3-methyl-2,3-epoxybutane (1c). 4-(Benzyloxy)-3-methyl-2,3-epoxybutane (**1c**) (0.70 g, 3.64 mmol) was treated with diisopropylamine trihydrofluoride (1.17 g, 7.28 mmol) at 110 °C for 12 h. Following workup and separation of isomers by flash chromatography (hexanes/ethyl acetate, 3:1) two colorless oils were obtained.

1-(Benzyloxy)-3-fluoro-3-methylbutan-2-ol (2c): 0.51 g (66%); R_f 0.30 hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.67 (6 H, d, $J_{H,F}$ = 21.9 Hz, H at C3′ and C4), 2.61 (1 H, d, J = 3.0 Hz, OH), 3.37–3.93 (3 H, m, H at C1 and C2), 4.56 (2 H, s, H at benzyl C), 7.31 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.04 (d, $J_{C,F}$ = 23.9 Hz), 23.47 (d, $J_{C,F}$ = 23.8 Hz), 70.20 (d, $J_{C,F}$ = 5.7 Hz), 73.51, 75.21 (d, $J_{C,F}$ = 25.1 Hz), 95.89 (d, $J_{C,F}$ = 177.1 Hz), 127.75, 127.85, 128.48, 137.71; ^{19}F NMR (282 MHz, $CDCl_3$) δ −149.83 (1 F, m); IR (CCl_4) 3580, 3460, 3080, 3055, 3032, 2975, 2910, 2868, 1490, 1448, 1376, 1365, 1222, 1198, 1146, 1102, 1022, 974, 895, 876, 849, 721, 692 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{12}H_{17}FO_2$ 212.1208, found 212.1246.

4-(Benzyloxy)-3-fluoro-2-methylbutan-2-ol (3c): 80 mg (10%); R_f 0.15 (hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.23 (6 H, s, H at C1 and C2′), 2.55 (1 H, s (br), OH), 3.73 (2 H, dm, $J_{H,F}$ = 24.3 Hz, H at C4), 4.40 (1 H, dt, $J_{H,F}$ = 48.6 Hz, H at C3), 4.56 (2 H, s, H at benzyl C), 7.32 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.25 (d, $J_{C,F}$ = 3.6 Hz), 25.52 (d, $J_{C,F}$ = 3.7 Hz), 69.29 (d, $J_{C,F}$ = 23.5 Hz), 71.29 (d, $J_{C,F}$ = 19.9 Hz), 73.65, 96.75 (d, $J_{C,F}$ = 177.1 Hz), 127.78, 127.89, 128.50, 137.45; ^{19}F NMR (282 MHz, $CDCl_3$) δ −197.08 (1 F, dt, $J_{H,F}$ = 48.5 Hz, $J_{H,F}$ = 24.4 Hz); IR (CCl_4) 3585, 3500, 3075, 3045, 3020, 2967, 2925, 2860, 1490, 1462, 1447, 1364, 1322, 1170, 1113, 1067, 1022, 985, 950, 903, 870, 722, 692 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{12}H_{17}FO_2$ 212.1208, found 212.1254; MS (EI, 17 eV), m/z (relative intensities) 91 (100.0), 107 (64.8), 108 (52.5), 109 (2.6), 113 (2.8), 117 (2.0), 119 (3.0), 120 (2.1), 134 (1.4), 146 (1.5), 149 (0.8), 150 (1.0), 151 (1.0), 155 (0.9), 170 (1.6), 179 (0.8), 193 (1.8), 198 (1.4), 199 (0.8), 212 (1.2) [M].

Fluorohydrins from 2-(Benzyloxy)-2-methyl-3,4-epoxybutane (1d). 2-(Benzyloxy)-2-methyl-2,3-epoxybutane (**1d**) (1.5 g, 7.80 mmol) was treated with diisopropylamine trihydrofluoride (2.51 g, 15.6 mmol) at 110 °C for 15 h. Following workup and flash chromatography (hexanes/ethyl acetate, 3:1) 1.02 g (62%) of 3-(benzyloxy)-1-fluoro-3-methylbutan-2-ol (**2d**) was obtained: R_f 0.34 (hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.27 (6 H, s, H at C3′ and C4), 2.73 (1 H, s (br), OH), 3.77 (1 H, dm, $J_{H,F}$ = 19.2 Hz, H at C2), 4.44 (2 H, s, H at benzyl C), 4.44 (1 H, ddd, $J_{H,F}$ = 48.3 Hz, $J_{H,H}$ = 9.6 Hz, $J_{H,H}$ = 6.3 Hz, H at C1), 4.62 (1 H, ddd, $J_{H,F}$ = 48.0 Hz, $J_{H,H}$ = 9.6 Hz, $J_{H,H}$ = 4.5 Hz, H at C1), 7.28 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.28, 21.53, 63.72, 63.80, 75.8 (d, $J_{C,F}$ = 17.8 Hz), 84.27 (d, $J_{C,F}$ = 166.7 Hz), 127.28, 127.42, 128.37, 138.93; ^{19}F NMR (282 MHz, $CDCl_3$) δ −232.81 (1 F, td, $J_{H,F}$ = 77.4 Hz, $J_{H,F}$ = 18.5 Hz); IR (CCl_4) 3595, 3550, 3080, 3055, 3020, 2968, 2925, 2880, 1491, 1460, 1447, 1383, 1358, 1270, 1148, 1100, 1045, 1005, 975, 903, 868, 722, 706, 692 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{10}H_{13}O$ [M − C_2H_4FO] 149.0963, found 149.0995; MS (EI, 17 eV), m/z (relative intensities) 91 (100.0), 92 (49.6), 101 (2.4), 105 (6.5), 106 (1.1), 107 (20.5), 108 (1.7), 113 (5.9), 117 (2.1), 120 (1.8), 144 (1.9), 149 (30.0), 150 (1.7), 151 (2.9), 155 (3.3), 159 (1.8), 163 (2.2), 170 (2.3), 179 (2.5), 212 (1.4) [M].

Fluorohydrins from 1-(Benzyloxy)-3,4-epoxybutane (1e). Procedure A. 4-(Benzyloxy)-3,4-epoxybutane (**1e**) (11.35 g, 63.7 mmol) was treated with diisopropylamine trihydrofluoride (20.53 g, 127.0 mmol) at 110 °C for 7 h. Following workup and separation of isomers by flash chromatography (hexanes/ethyl acetate/chloroform, 1:1:1) two colorless oils were obtained.

4-(Benzyloxy)-1-fluoro-2-butanol (2e): 8.7 g (69%); R_f 0.58 (hexanes/ethyl acetate/chloroform, 1:1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76 (2 H, q, $J_{H,H}$ = 5.9 Hz, H at C3), 3.30 (1 H, s (br), OH), 3.57–3.70 (2 H, m, H at C4), 3.90–4.10 (1 H, m, H at C2), 4.29 (1 H, ddd, $J_{H,H}$ = 5.9 Hz, $J_{H,H}$ = 9.4 Hz, $J_{H,F}$ = 47.7 Hz, H at C1), 4.35 (1 H, ddd, $J_{H,H}$ = 4.0 Hz, $J_{H,H}$ = 9.4 Hz, $J_{H,F}$ = 47.2 Hz, H at C1), 4.48 (2 H, s, H at benzyl C), 7.26–7.34 (5 H, m, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.0 (d, $J_{C,F}$ = 5.5 Hz), 67.7, 69.2 (d, $J_{C,F}$ = 19.9 Hz), 73.4, 86.8 (d, $J_{C,F}$ = 170.3 Hz), 128.05, 128.14, 128.82, 138.30; ^{19}F NMR (282 MHz, $CDCl_3$) δ −228.3 (1 F, td, $J_{H,F}$ = 47.0 Hz, $J_{H,F}$ = 19.0 Hz); IR (CCl_4) 3640–3100, 3600, 3080, 3057, 3012, 2940, 2852, 1490, 1450, 1357, 1090, 1015, 690 cm^{-1}; MS (CI, 2-methylpropane), m/z (relative intensities) 57 (133.3), 91 (100), 107 (25.0), 119 (1.7), 121 (2.5), 131 (3.6), 133 (2.6), 181 (5.2), 197 (5.6), 198 (5.6) [M], 199 (13.5) [M + 1]. Anal. Calcd for $C_{11}H_{15}FO_2$: C, 66.65; H, 7.63. Found: C, 66.33; H, 7.40.

4-(Benzyloxy)-2-fluoro-1-butanol (3e): 1.5 g (12%); R_f 0.49 (hexanes/ethyl acetate/chloroform, 1:1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76–2.01 (2 H, m, H at C3), 2.89 (1 H, s (br), OH), 3.56–3.30 (2 H, m, H at C4), 3.56–3.61 (2 H, m, H at C1), 4.49 (2 H, s, H at benzyl C), 4.72 (1 H, dm, $J_{H,F}$ = 47.0 Hz, H at C2), 7.26–7.34 (5 H, m, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.6 (d, $J_{C,F}$ = 20.5 Hz), 64.8 (d, $J_{C,F}$ = 22.0 Hz), 65.9 (d, $J_{C,F}$ = 5.5 Hz), 73.4, 92.2 (d, $J_{C,F}$ = 168.8 Hz), 128.1, 128.8, 138.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ −191.3 (1 F, dm, $J_{H,F}$ = 47.0 Hz); IR (CCl_4) 3610, 3440, 3085, 3060, 3030, 2925, 2860, 1450, 1360, 1095, 693 cm^{-1}; MS (CI, 2-methylpropane), m/z (relative intensities) 57 (100.0), 91 (100.0), 107 (40.1), 108 (8.5), 131 (6.5), 181 (30.3), 182 (4.8), 198 (5.0) [M], 199 (30.5) [M + 1]. Anal. Calcd for $C_{11}H_{15}FO_2$: C, 66.65; H, 7.63. Found: C, 66.40; H, 7.56.

Procedure B. 1-(Benzyloxy)-3,4-epoxybutane (**1e**) (0.10 g, 0.56 mmol) was mixed with 0.6 mL of pyridine polyhydrofluoride (Aldrich) at −78 °C. The solution was maintained at −40 to −50 °C for 1 h. The reaction was carefully neutralized with saturated sodium bicarbonate and extracted with ether. The ether extracts were dried over magnesium sulfate, and solvent was removed at reduced pressure to give 76 mg (68%) of a light yellow oil. Analysis of the residue by gas chromatography gave **2e** (20%) and **3e** (78%).

Fluorohydrins from 1-(Benzyloxy)-3-methyl-3,4-epoxybutane (1f). 1-(Benzyloxy)-3-methyl-3,4-epoxybutane (**1f**) (2.00 g, 10.4 mmol) was treated with diisopropylamine trihydrofluoride (3.35 g, 20.8 mmol) at 110 °C for 12 h. Following workup and separation of isomers by flash chromatography (hexanes/ethyl acetate, 3:1) two colorless oils were obtained.

4-(Benzyloxy)-1-fluoro-2-methylbutan-2-ol (2f): 1.03 g (47%); R_f 0.21 (hexanes/ethyl acetate, 3:1); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.22 (3 H, d, $J_{H,F}$ = 2.4 Hz, H at C2′), 1.85 (2 H, t, $J_{H,H}$ = 6.0 Hz, H at C3), 3.40 (1 H, s (br), OH), 3.68 (2 H, t, $J_{H,H}$ = 6.0 Hz, H at C4), 4.18 (2 H, d, $J_{H,F}$ = 47.7 Hz, H at C1), 4.50 (2 H, s, H at benzyl C), 7.28 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.93 (d, $J_{C,F}$ = 3.2 Hz), 36.67, 67.14, 71.70 (d, $J_{C,F}$ = 18.4 Hz), 73.67, 88.83 (d, $J_{C,F}$ = 174.4 Hz), 128.13, 128.26, 128.89, 138.01; ^{19}F NMR (282 MHz, $CDCl_3$) δ −227.66 (1 F, t, $J_{H,F}$ = 47.6 Hz); IR (CCl_4) 3596, 3500, 3080, 3060, 3035, 2975, 2918, 2898, 2860,

1494, 1452, 1412, 1388, 1364, 1333, 1260, 1097, 1029, 702 cm^{-1}; MS (CI, methane), m/z (relative intensities) 29.0 (72.8), 31.9 (21.3), 40.9 (13.1), 85.1 (6.9), 91.0 (60.3), 92.0 (5.2), 107.0 (3.9), 119.0 (1.7), 131.0 (0.8), 145.0 (0.9), 175.1 (1.1), 181.0 (1.1), 213.1 (0.8) [M + 1]; HRMS (EI, 17 eV), exact mass calcd for $C_{12}H_{17}FO_2$ 212.1208, found 212.1244.

4-(Benzyloxy)-2-fluoro-2-methylbutan-1-ol (3f): 0.69 g (31%); R_f 0.15 (hexanes/ethyl acetate, 3:1); ^1H NMR (90 MHz, $CDCl_3$) δ 1.34 (3 H, d, $J_{H,F}$ = 21.3 Hz, H at C2′), 1.98 (2 H, dt, $J_{H,F}$ = 17.7 Hz, $J_{H,H}$ = 6.0 Hz, H at C3), 2.70 (1 H, s (br), OH), 3.40–3.73 (4 H, m, H at C1 and C4), 4.83 (2 H, H at benzyl C), 7.28 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.49 (d, $J_{C,F}$ = 23.8 Hz), 36.85 (d, $J_{C,F}$ = 22.4 Hz), 65.80 (d, $J_{C,F}$ = 7.3 Hz), 67.91 (d, $J_{C,F}$ = 27.5 Hz), 73.57, 96.81 (d, $J_{C,F}$ = 168.7 Hz), 128.16, 128.24, 128.89, 138.00; ^{19}F NMR (282 MHz, $CDCl_3$) δ −155.04 (1 F, m (8 lines), $J_{H,F}$ = 19.6 Hz); IR (CCl_4) 3605, 3450, 3080, 3060, 3014, 2972, 2920, 2860, 1494, 1480, 1452, 1377, 1364, 1100, 1062, 1030, 887, 730, 702 cm^{-1}; MS (CI, methane), m/z (relative intensities) 29.0 (5.4), 85.1 (24.4), 91.0 (20.6), 107.0 (2.3), 181.0 (5.9), 193.1 (3.4), 213.1 (23.0) [M + 1]; HRMS (EI, 17 eV), exact mass calcd for $C_{12}H_{17}FO_2$ 212.1208, found 212.1200.

Fluorohydrins from 1-(Benzyloxy)-4,5-epoxypentane (1g). 1-(Benzyloxy)-4,5-epoxypentane (**1g**) (1.50 g, 7.80 mmol) was treated with diisopropylamine trihydrofluoride (3.35 g, 20.80 mmol) at 110 °C for 6 h. Following workup and separation of isomers by flash chromatography (hexanes/ethyl acetate/chloroform, 1:1:1) two colorless oils were obtained.

5-(Benzyloxy)-1-fluoropentan-2-ol (2g): 1.05 (63%); R_f 0.31 (hexanes/ethyl acetate/chloroform, 1:1:1); ^1H NMR (300 MHz, $CDCl_3$) δ 1.43–1.93 (4 H, m, H at C3 and C4), 2.95 (1 H, s (br), OH), 3.53 (2 H, t, $J_{H,H}$ = 5.8 Hz, H at C5), 3.80 (1 H, m, H at C2), 4.29 (1 H, ddd, $J_{H,F}$ = 47.8 Hz, $J_{H,H}$ = 9.3 Hz, $J_{H,H}$ = 6.4 Hz, H at C1), 4.38 (1 H, ddd, $J_{H,F}$ = 47.1 Hz, $J_{H,H}$ = 9.4 Hz, $J_{H,H}$ = 3.7 Hz, H at C1), 4.52 (2 H, s, H at benzyl C), 7.33 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.92, 29.55 (d, $J_{C,F}$ = 6.4 Hz), 70.09 (d, $J_{C,F}$ = 14.9 Hz), 86.81 (d, $J_{C,F}$ = 169.2 Hz), 127.76, 128.47, 137.97; ^{19}F NMR (282 MHz, $CDCl_3$) δ −230.72 (1 F, td, $J_{H,F}$ = 47.5 Hz, $J_{H,F}$ = 18.1 Hz); IR (CCl_4) 3589, 3410, 3075, 3053, 3020, 2935, 2850, 1489, 1448, 1354, 1266, 1197, 1090, 1021, 903, 784, 727, 692 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{12}H_{17}FO_2$ 212.1208, found 212.1210.

5-(Benzyloxy)-2-fluoropentan-1-ol (3g): 0.10 g (6%); R_f 0.25 (hexanes/ethyl acetate/chloroform, 1:1:1); ^1H NMR (90 MHz, $CDCl_3$) δ 1.39–1.95 (4 H, m, H at C3 and C4), 2.30 (1 H, s (br), OH), 3.39–3.62 (2 H, m, H at C5), 3.65 (2 H, dm $J_{H,F}$ = 20.7 Hz, H at C1), 4.47 (2 H, H at benzyl C), 4.52 (1 H, dm, $J_{H,F}$ = 48 Hz, H at C2), 7.29 (5 H, s, H at phenyl C's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.17 (d, $J_{C,F}$ = 4.6 Hz), 27.78 (d, $J_{C,F}$ = 20.7 Hz), 64.78 (d, $J_{C,F}$ = 22.0 Hz), 69.70, 72.93, 94.45 (d, $J_{C,F}$ = 168.2 Hz), 127.61 127.87, 128.39, 138.32; ^{19}F NMR (282 MHz, $CDCl_3$) δ −192.58 (1 F, m) IR (CCl_4) 3595, 3420, 3075, 3055, 3020, 2935, 2848, 1488, 1436, 1354, 1198, 1090, 1062, 1023, 903, 722, 692 cm^{-1}; HRMS (EI, 17 eV), exact mass calcd for $C_{12}H_{17}FO_2$ 212.1208, found 212.1197.

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Registry No. **1a**, 2930-05-4; *trans*-**1b**, 80374-37-4; *cis*-**1b**, 80374-36-3; **1c**, 71312-15-7; **1d**, 112482-34-5; **1e**, 94426-72-9; **1f**, 107127-75-3; **1g**, 112482-35-6; **2a**, 112482-36-7; **2b**, 112482-38-9; **2c**, 112482-40-3; **2d**, 112482-42-5; **2e**, 112482-44-7; **2f**, 112482-47-0; **2g**, 112482-49-2; **3a**, 112482-37-8; **3b**, 112482-39-0; **3c**, 112482-41-4; **3d**, 112482-43-6; **3e**, 112482-45-8; **3f**, 112482-48-1; **3g**, 112482-50-5; $((H_3C)_2CH)_2NH{\cdot}3HF$, 112482-51-6; $H_2C{=}CHCH_2OBn$, 14593-43-2; (*E*)-$BnOCH_2CH{=}CHCH_3$, 27299-30-5; (*Z*)-$BnOCH_2CH{=}CHCH_3$, 27299-31-6; $H_3CC(CH_3){=}CHCH_2OBn$, 22089-60-7; $H_2C{=}CHC(CH_3)_2OBn$, 112482-46-9; $H_2C{=}CH(CH_2)_2OBn$, 70388-33-9; $H_2C{=}C(CH_3)(CH_2)_2OBn$, 58558-53-5; $H_2C{=}CH(CH_2)_3OBn$, 81518-74-3; $((H_3C)_2CH)_2NH$, 108-18-9.

p,p′-Dinitrobenzhydryl Ethers, Acid and Base Stable Protecting Groups, Which Are Readily Removable in the Presence of Benzyl and Monomethoxytrityl Functions

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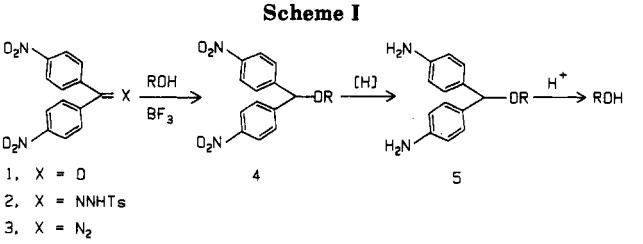
BF_3-catalyzed reaction of alcohols with bis(*p*-nitrophenyl)diazomethane gave the corresponding DNB ethers, from which blocking groups were selectively removed by catalytic hydrogenation using platinum or nickel boride or by chemical reduction, followed by mild acid hydrolysis (e.g., pH 4).

In connection with the synthesis of goniothalenol,[1] we required a protecting group that would survive strongly acidic (HCOOH, $ZnCl_2$/EtSH) and basic (PhMgBr) conditions, yet would be removable in the presence of a secondary benzyl group. As it happened, the protecting group we report on can also be removed in the presence of a monomethoxytrityl ether, which may make it useful as a carbohydrate or nucleotide protecting group.

Benzyl or benzhydryl ethers fulfill the stability conditions listed. It occurred to us that a *p,p′*-dinitrobenzhydryl (DNB) ether should be equally stable, yet be transformed by chemical or catalytic reduction to a very acid-labile diaminobenzhydryl ether (**4** to **5**, Scheme I).

Scheme I



Results and Discussion

Since the reaction of a sodium alkoxide with the known *p,p′*-dinitrobenzhydryl chloride[2] did not proceed in a

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