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Chemoenzymatic Synthesis of Deoxyfluoroinositols: 5-Deoxy-5-fluoro-*myo*-inositol and 3-Deoxy-3-fluoro-L-*chiro*-inositol

Ba V. Nguyen, Chentao York, and Tomas Hudlicky *

Department of Chemistry, University of Florida, Gainesville, FL 32611-7200

Abstract: Two deoxyfluoroinositols were synthesized from bromocyclohexadiene *cis*-diol obtained by microbial oxidation of bromobenzene with *P. putida* (39D). The selective introduction of fluorine was accomplished by opening of the epoxide with tetrabutylphosphoniumfluoride dihydrofluoride (TBPF-DF). The synthesis of 5-deoxy-5-fluoro-*myo*-inositol **(1)** and 3-deoxy-3-fluoro-L-*chiro*-inositol **(2)** are described in detail. © 1997 Published by Elsevier Science Ltd.

INTRODUCTION

In recent years, inositols and phosphatidylinositols have been recognized for their various roles in cellular metabolism.[1] A number of unnatural fluorinated inositol analogs have been synthesized and used for probing the biochemistry of the inositol cycle,[2] cellular growth,[2l,p] and intracellular Ca^{2+} movement.[2n] The fluorine atom was introduced into the inositol in order to improve its physiochemical properties while retaining the donor hydrogen bonding capabilities.[3] Previous syntheses generally required fluorine functionalization of known inositols. Such strategy comprises multiple steps, laborious protection and deprotection sequences, and often renders the final fluoroinositols in low yields.[2] Consequently, enzymatic approaches to the syntheses of some fluorinated cyclitols have been reported.[4] Herein, we describe a chemoenzymatic synthesis of fluoroinositols **(1)** and **(2)** from bromobenzene.

Cyclohexadiene *cis*-diols, produced by microbial oxidation of arenes with mutant or recombinant strains of *P. putida*,[5] have been used extensively in the syntheses of diverse natural products.[6] Recent reports from our laboratory have demonstrated application of halocyclohexadiene *cis*-diols to synthesis of cyclitols,[7] aminocyclitols,[8] sugars,[9] aza-sugars,[10] conduritols,[11] and alkaloids.[8b,10b,12] These results have prompted us to take further advantage of the versatility of cyclohexadiene *cis*-diols in the design of a general method for the synthesis of fluorinated cyclitols.

RESULTS AND DISCUSSION

(5*S*,6*R*)-1-Bromocyclohexa-1,3-diene-5,6-diol **(3)** was prepared from bromobenzene using strains of *P. putida*.[5] The biocatalytic microbial oxidation provides the diol precursors with excellent enantiomeric purity (>99%). Epoxidation of diene *cis*-diol **(3)** is also stereo- and regioselective.[11,13] A strategy for the preparation

of fluoroinositols was formulated based on the opening of these epoxides with a fluoride anion. It is known that TBPF-DF opens epoxide rings at the less hindered site *via* an S_N2-type process,[11b] although it is possible that a S_N1-like mechanism operates at the allylic site in epoxides **(6a)** and **(6b)**.[7d] Thus, depending on the regio- and stereochemistry of the epoxide, TBPF-DF will lead to different regio- and stereoisomers of the corresponding fluoroinositol.

Synthesis of 5-deoxy-5-fluoro-*myo*-inositol **(1)**: Bromohydrin **(5)** was prepared by the addition of BrOH to the C_6-C_7 double bond of acetonide **(4)**. BrOH was generated *in situ* by the reaction of 5,5-dimethyl-2,4-dibromohydantoin and water. The mechanism of BrOH addition is electrophilic, with initial formation of the bromonium ion on the α-face of acetonide **(4)**. When bromohydrin **(5)** was treated with 1 eq. of aqueous NaOH the β–epoxide **(6a)** was generated. When excess aqueous NaOH was used the *trans*-diol **(7)** was obtained directly in high yield. The bromine of **(7)** was removed with *n*-Bu_3SnH in THF catalyzed by AIBN to give diols **(8)**. Selective epoxidation exclusively on the α-face with *m*-CPBA gave epoxide **(9)** by combination of the steric effect of the acetonide group on the β-side of the molecule and the directing influence of the hydroxyl group on the α-face at C_5. TBPF-DF as the fluoride source opened the epoxide at C_{5a} from the β-face of **(9)**.[14] The acetonide group of **(10)** was then removed by treatment with aq. HCl to give the desired 5-deoxy-5-fluoro-*myo*-inositol **(1)**.

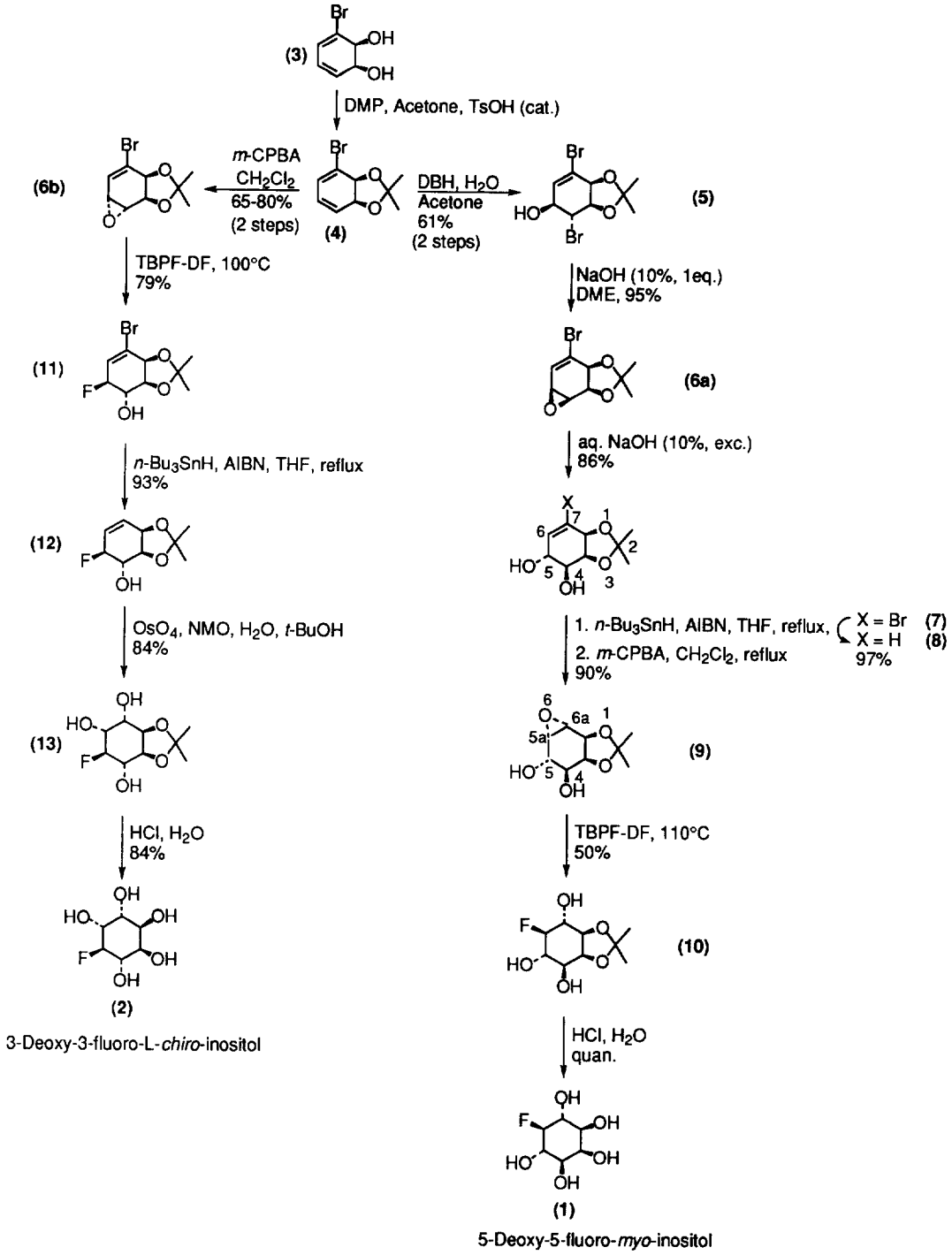
Synthesis of 3-deoxy-3-fluoro-L-*chiro*-inositol **(2)**: The bromo epoxide **(6b)** was made according to the literature methods.[13] Opening of the epoxide with TBPF-DF gave only one regio- and stereoisomer **(11)**. The bromine of **(11)** was again removed with *n*-Bu_3SnH/AIBN to afford alkene **(12)**, which was oxidized with osmium tetroxide. Deprotection of triol **(13)** gave 3-deoxy-3-fluoro-L-*chiro*-inositol **(2)**. At the stage of **(7)**, **(8)**, **(10)**, **(11)**, **(12)**, and **(13)**, a suitable group (acetate, phosphate etc.) could be introduced at one of the hydroxyl groups to maintain regioselective protection (as well as asymmetry in case of **(1)**) if such is desired after acetonide cleavage.

CONCLUSION

Enzymatic and subsequent chemical transformation of haloarenes provide for an efficient and fully stereocontrolled synthesis of deoxyfluoroinositols **(1)** and **(2)**. Compounds such as these may be useful in their phosphorylated form for further studies as phospholipase C inhibitors.[2b,c] This strategy has potential merit as a general method for the preparation of any fluorocyclitol by carefully designed introduction of epoxides and their opening on the periphery of cyclohexadiene *cis*-diols. A similar concept has recently been employed in the design of 2-, 3-, and 4-aminohexoses.[14]

EXPERIMENTAL SECTION

All reactions in aprotic solvents were carried out in an atmosphere of argon or nitrogen. Glassware used for moisture-sensitive reactions was dried under vacuum. Analytical TLC was performed on Whatman K6F silica gel 60 Å plates. Flash chromatography was performed on chromatographic silica gel, 230-400 mesh (FisherChemical). Infrared spectra were recorded on a Perkin-Elmer FT-IR. Proton, fluorine, and carbon NMR spectra were obtained on a Varian 300 MHz spectrometer using $CDCl_3$/TMS unless otherwise indicated in the


(3)
DMP, Acetone, TsOH (cat.)
(4)
m-CPBA
CH2Cl2
65-80%
(2 steps)
(6b)
DBH, H2O
Acetone
61%
(2 steps)
(5)
TBPF-DF, 100°C
79%
NaOH (10%, 1eq.)
DME, 95%
(11)
(6a)
n-Bu3SnH, AIBN, THF, reflux
93%
aq. NaOH (10%, exc.)
86%
(12)
OsO4, NMO, H2O, t-BuOH
84%
1. n-Bu3SnH, AIBN, THF, reflux,
2. m-CPBA, CH2Cl2, reflux
90%
X = Br (7)
X = H (8)
97%
(13)
(9)
HCl, H2O
84%
TBPF-DF, 110°C
50%
(10)
HCl, H2O
quan.
(2)
3-Deoxy-3-fluoro-L-chiro-inositol
(1)
5-Deoxy-5-fluoro-myo-inositol

experimental section or in the case of fluorine NMR spectra, a $CFCl_3$ standard was utilized. Optical rotations were recorded on a Perkin-Elmer 241 digital polarimeter. Melting points were obtained on Thomas-Hoover capillary melting point apparatus. High resolution mass spectra and elemental analyses were performed at the University of Florida.

(3a*R*,4*R*,5*S*,7a*S*)-4,7-Dibromo-2,2-dimethyl-4,5-dihydrobenzo[*d*][1,3]dioxol-5-ol (5). To the bromodiene diol **3** (5.0 g, 26.2 mmol) in acetone (20 mL) were added 2,2-dimethoxypropane (20 mL) and *p*-TsOH (57 mg, 0.30 mmol). The mixture was stirred for 30 min at room temperature and the solvent was evaporated. The residue was dissolved in acetone (50 mL) and water (10 mL), followed by addition of 1,3-dibromo-5,5-dimethyl hydantoin (DBH) (6.0 g, 17.5 mmol) at 0°C. The reaction mixture was stirred for 2 h at room temperature. Excess DBH was reduced with aqueous Na_2SO_3 (10%, 50 mL). After removal of the solvent, the residue was extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was subjected to column chromatography (silica gel, ethyl acetate/hexane : 1/ 5) to give 5.27 g of compound **5** in 61% yield; mp: 69-70°C; $[\alpha]_D^{28}$ = 13.8 (c 1.0, $CHCl_3$); ^{1}H NMR: 1.4 (s, 3H), 1.5 (s, 3H), 2.9 (d, J = 8.4 Hz, 1H), 4.3 (m, 2H), 4.6 (m, 1H), 4.7 (d, J = 5.4 Hz, 1H), 6.3 (d, J = 5.4 Hz, 1H); ^{13}C NMR: 26.3 (s), 27.8 (s), 48.6 (s), 70.6 (s), 76.1 (s), 77.8 (s), 111.9 (s), 123.5 (s), 131.1 (s); HRMS: $C_9H_{13}Br_2O_3$ (M+H) Calcd. 329.9189; Found: 329.9164.

(3a*S*,5a*S*,6a*S*,6b*S*)-2,2-Dimethyl-oxirano[2',3':3,4]benzo[*d*][1,3]dioxol-4-yl bromide (6a). Compound **5** (5.25 g, 16 mmol) was dissolved in 1,2-dimethoxyethane (20 mL), then aqueous NaOH (10%, 6.4 mL, 16 mmol) was added dropwise at 0°C. After stirring for 3 h at room temperature, the solvent was removed under reduce pressure and the residue was extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were washed with brine and dried over $MgSO_4$. After removal of the solvent, the crude products were purified by flash chromatography (silica gel, hexane/ethyl acetate : 7/1), to give 3.75 g of compound **6a** in 95% yield; mp: 76-77°C; $[\alpha]_D^{28}$ = - 76.2 (c 1.13, $CHCl_3$); ^{1}H NMR: 1.4 (s, 3H), 1.5 (s, 3H), 3.4 (dd, J = 4.5, 4.5 Hz, 1H), 3.6 (m, 1H), 4.5 (dd, J = 6.6, 2.4 Hz, 1H), 4.7 (dd, J = 6.6, 1.8 Hz, 1H), 6.7 (d, J = 4.5 Hz, 1H); ^{13}C NMR: 25.2 (s), 27.1 (s), 50.2 (s), 54.5 (s), 73.9 (s), 76.8 (s), 108.7 (s), 125.5 (s), 130.0 (s); HRMS: $C_9H_{12}BrO_3$ (M+H) Calcd. 247.9958; Found: 247.9947; Anal. Calcd. for $C_9H_{11}BrO_3$: C, 43.75; H, 4.49; Found: C, 43.57; H, 4.45.

(3a*S*,4*S*,5*R*,7a*S*)-7-Bromo-2,2-dimethyl-4,5-dihydrobenzo[*d*][1,3]dioxol-4,5-diol (7). To the bromoepoxide **6a** (0.108 g, 0.44 mmol) in dimethoxyethane (5 mL) was added aqueous NaOH (10%, 5 mL). The reaction mixture was heated at reflux for 3 h and then extracted with ethyl acetate (3x50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica gel, ethyl acetate/hexane: 3/1), to give 0.10 g of compound **7** in 86% yield; mp: 131-132°C; $[\alpha]_D^{28}$ = - 19.18 (c 1.13, MeOH); ^{1}H NMR: 1.4 (s, 3H), 1.4 (s, 3H), 2.1 (br, 2H), 3.7 (dd, J = 8.1, 2.4, Hz, 1H), 4.4 (dt, J = 8.1, 2.1 Hz, 1H), 4.5 (dd, J = 5.1, 2.7 Hz, 1H), 4.6 (dd, J = 5.1, 1.8 Hz, 1H), 6.1 (d, J = 1.8 Hz, 1H); ^{13}C NMR: 26.5 (s), 27.5 (s), 68.7 (s), 71.7

(s), 77.8 (s), 77.9 (s), 109.1 (s), 122.1 (s), 134.5 (s); HRMS: $C_9H_{14}BrO_4$ (M+H) Calcd. 266.007, Found: 266.009; Anal. Calcd. for $C_9H_{13}BrO_4$: C, 40.77; H, 4.94; Found: C, 40.88; H, 4.94.

(3a*R*,4*S*,5*R*,7a*R*)-2,2-Dimethyl-4,5-dihydrobenzo[*d*][1,3]dioxol-4,5-diol (8). To the compound **7** (1.27 g, 4.79 mmol) in dry THF was added n-Bu_3SnH (3 mL, 9.37 mmol) and AIBN (20 mg). The reaction was heated at reflux under argon for 10 h. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica gel, ethyl acetate/hexane: 3/1), to give 0.87 g of compound **8** in 97% yield; mp: 137-138°C; $[\alpha]_D^{28}$ = - 122.87 (c 1.0, MeOH); ^{1}H NMR: 1.4 (br, 6H), 2.4 (br, 2H), 3.6 (dd, J = 8.4, 2.7 Hz, 1H), 4.4 (m, 1H), 4.5 (m, 1H), 4.6 (m, 1H), 5.6 (m, 1H), 5.8 (m, 1H); ^{13}C NMR: 26.3 (s), 27.4 (s), 68.8 (s), 73.8 (s), 74.4 (s), 75.9 (s), 109.9 (s), 126.7 (s), 130.8 (s); HRMS: $C_9H_{15}O_4$ (M+H) Calcd. 187.0968, Found: 187.1000; Anal. Calcd. for $C_9H_{14}O_4$: C, 58.06; H, 7.53; Found: C, 57.94; H, 7.83.

(3a*S*,4*S*,5*R*,5a*S*,6a*S*,6b*R*)-2,2-Dimethyl-perhydrooxirano[2',3':3,4]benzo[*d*][1,3]dioxol-4,5-diol (9). To the compound **8** (0.60 g, 3.22 mmol) in CH_2Cl_2 (20 mL) was added, 1.6 g of *m*-CPBA (70%). The reaction mixture was stirred at room temperature for 1 h and then heated at reflux for another 3 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (silica gel, ethyl acetate/hexane: 3/1), to give 0.59 g of compound **9** in 90% yield; mp: 84-85°C; $[\alpha]_D^{29}$ = - 49.01 (c 0.91, $CHCl_3$); ^{1}H NMR: 1.3 (s, 3H), 1.4 (s, 3H), 2.3 (br, 2H), 3.2 (d, J = 3.5 Hz, 1H), 3.4 (d, J = 3.6 Hz, 1H), 3.8 (dd, J = 8.7, 2.4 Hz, 1H), 4.2 (d, J = 8.7 Hz, 1H), 4.4 (br, 1H), 4.5 (d, J = 5.7 Hz, 1H); ^{13}C NMR: 25.3 (s), 27.5 (s), 54.7 (s), 56.6 (s), 68.0 (s), 68.7 (s), 72.4 (s), 77.1 (s), 110.4 (s); HRMS: $C_9H_{15}O_5$ (M+H) Calcd. 203.0917, Found: 203.1006. Anal. Calcd. for $C_9H_{14}O_5$: C, 53.46; H, 6.93; Found: C, 53.33; H, 7.10.

(3a*S*,4*R*,5*S*,6*R*,7*R*,7a*S*)-6-Fluoro-2,2-dimethyl-perhydrobenzo[*d*][1,3]dioxol-4,5,7-triol (10). To the epoxide **9** (1 g, 4.95 mmol) in a Pyrex tube was added TBPF-DF (3.15 g, 9.9 mmol). The tube was capped and heated at 110°C for 3 days. The reaction mixture was introduced onto a silica gel column and eluted with hexane/ ethyl acetate (1:2) to give 0.55 g of **10** in 50% yield; mp: 147-148°C; $[\alpha]_D^{30}$ = 14.4 (c 0.94, MeOH); ^{1}H NMR (CD_3OD): 1.3 (s, 3H), 1.4 (s, 3H), 3.7 (m, 2H), 3.7 (m, 2H), 3.8 (m, 1H), 3.9 (dt, J = 51.6, 8.4 Hz, 1H); ^{19}F NMR (CD_3OD): - 197.5 (dt, J = 51.3, 12.2 Hz); ^{13}C NMR: 26.0 (s), 28.3 (s), 70.5 (d, J = 9.6 Hz), 72.3 (d, J = 17.7 Hz), 74.7 (d, J = 18.1 Hz), 77.6 (s), 79.9 (d, J = 10.6 Hz), 96.1 (d, J = 180.0 Hz), 110.9 (s); IR (cm^{-1}): 1222, 1248, 1377, 2928, 2998, 3454; HRMS: $C_9H_{16}FO_5$ (M+H) Calcd. 223.2290, Found: 223.0988; Anal. Calcd. for $C_9H_{15}FO_5$: C 48.61, H 6.81, Found: C 48.92, H 6.80.

5-Deoxy-5-fluoro-*myo*-inositol (1). A round bottomed 50 mL flask equipped with a stir bar and septum port, was charged with 10 mg (0.045 mmol) of **10**, 1.5 mL of water, and 0.1 mL of HCl (12N). After the reaction mixture was stirred at room temperature for 2 h, 2 mL of toluene was added, and the solvents were removed under vacuum to give 8 mg of compound **1** in 97% yield. ^{1}H NMR (D_2O, CD_3OD): 3.5 (d, J = 9 Hz, 2H), 3.8 (dt, J = 12.9, 9.6 Hz, 2H), 3.9 (m, 1H), 4.2 (dt, J = 51.9, 8.4 Hz, 1H); ^{19}F NMR (CD_3OD): - 201.0 (dt, J = 51.9, 14.2 Hz). All other data matched those in the literature.[2m,o]

(3a*S*,4*S*,5*S*,7a*S*)-7-Bromo-5-fluoro-2,2-dimethyl-4,5-dihydrobenzo[*d*][1,3]dioxol-4-ol (11). A dry tube equipped with a stir bar and a Teflon cap was charged with 1g (4.05 mmol) of **6b**[7d] and 3.8 g (12 mmol) of TBPF-DF. The reaction mixture was heated at 100°C for 24 h. After cooling to room temperature, the reaction mixture was introduced onto a silica gel column and eluted with hexane/ethyl acetate (1/1) to give 0.86 g (79% yield) of **11**; mp: 125-126°C; ^{1}H NMR: 1.4 (s, 3H), 1.5 (s, 3H), 2.9 (s, 1H), 3.9 (dt, J = 14.5, 7.2 Hz, 1H), 4.2 (dd, J = 6.7, 6.4 Hz, 1H), 4.7 (dm, J = 6.3 Hz, 1H), 4.8 (dddd, J = 49.7, 7.8, 2.1, 1.2 Hz, 1H), 6.3 (dd, J = 13.7, 2.0 Hz, 1H); ^{19}F NMR: - 189.5 (dt, J = 50.3, 13.7 Hz); ^{13}C NMR: 25.9 (s), 28.0 (s), 72.0 (d, J = 17.5 Hz), 76.8 (d, J = 11.5 Hz), 77.0 (s), 90.6 (d, J = 174.7 Hz), 111.6 (s), 120.7 (d, J = 12.2 Hz), 131.0 (d, J = 25.2 Hz); IR (cm^{-1}): 1084, 1161, 1225, 1378, 1648, 2872, 2931, 2989, 3448; HRMS: $C_9H_{13}BrFO_3$ (M+H) for ^{79}Br Calcd. 267.0031, Found: 267.0019, for ^{81}Br Calcd. 269.0010; Found: 269.0016; Anal. Calcd. for $C_9H_{12}BrFO_3$: C, 40.60; H, 4.55; Found: C, 40.72; H, 4.58.

(3a*R*,4*S*,5*S*,7a*R*)-5-Fluoro-2,2-dimethyl-4,5-dihydrobenzo[*d*][1,3]dioxol-4-ol (12). A round bottomed flask equipped with a stir bar and water condenser, was charged with 1.5 g (5.64 mmol) of **11**, 0.05 g (0.28 mmol) of AIBN, 3.28 g (11.28 mmol) of Bu_3SnH, and 15 mL of benzene. The reaction mixture was heated at reflux for 14 h. The reaction mixture was concentrated under reduced pressure and introduced onto a silica gel column and eluted with 200 mL hexane, then with hexane/ethyl acetate (1/1) mixture to give 0.99 g (93%) of **12**. ^{1}H NMR: 1.4 (s, 3H), 1.5 (s, 3H), 2.7 (d, J = 2.4 Hz, 1H), 3.8 (dtd, J = 14.2, 8.8, 2.4 Hz, 1H), 4.1 (dd, J = 9.0, 6.6 Hz, 1H), 4.6 (dm, J = 6.4 Hz, 1H), 5.0 (ddm, J = 50.5, 8.3 Hz, 1H), 5.9 (m, 1H), 6.0 (dm, J = 7.6 Hz, 1H); ^{19}F NMR: - 193.7 (dm, J = 51.3 Hz); ^{13}C NMR: 25.5 (s), 27.9 (s), 72.1 (s), 72.7 (d, J = 17.1 Hz), 76.9 (d, J = 12.1 Hz), 91.0 (d, J = 170.2 Hz), 111.0 (s), 124.7 (d, J = 9.6 Hz), 130.1 (d, J = 25.2 Hz); IR (cm^{-1}): 1223, 1369, 1646, 1703, 2856, 2918, 3429.

(3a*R*,4*R*,5*R*,6*S*,7*S*,7a*R*)-6-Fluoro-2,2-dimethyl-perhydrobenzo[*d*][1,3]dioxol-4,5,7-triol (13). A round bottomed flask equipped with a stir bar and an argon inlet, was charged with 0.10 g (0.532 mmol) of **12**, 6 mL (0.05 M) solution of OsO_4 in t-BuOH, 0.5 mL of H_2O, and 0.031 g (0.266 mmol) of NMO. The reaction was stirred at room temperature. After 24 h, the reaction mixture was concentrated under reduced pressure. The concentrated mixture was introduced onto a silica gel column and eluted with EtOAc (R_f = 0.5). The product was collected and dried under vacuum to give 0.10 g (84%) of **13**; $[\alpha]_D^{29}$ = - 100.7 (c 1.0, MeOH); mp: 117-118°C; ^{1}H NMR (DMSO-d_6): 1.4 (s, 3H), 1.5 (s, 3H), 3.6 (m, 1H), 3.7 (m, 1H), 4.0 (m, 2H), 4.2 (t, J = 4.6 Hz, 1H), 4.4 (dt, J = 52.5, 8.6 Hz, 1H), 5.4 (d, J = 5.9 Hz, 1H), 5.5 (d, J = 4.6 Hz, 1H), 5.6 (d, J = 5.9 Hz, 1H); ^{19}F NMR (DMSO-d_6): - 203.3 (dt, J = 51.3, 14.6 Hz); ^{13}C NMR (DMSO-d_6): 25.8 (s), 27.9 (s), 69.2 (d, J = 7.5 Hz), 69.4 (d, J = 17.9 Hz), 73.9 (d, J = 18.1 Hz), 77.1 (s), 78.9 (d, J = 11.1 Hz), 94.8 (d, J = 176.3 Hz), 108.4 (s); IR (cm^{-1}): 976, 1005, 1071, 1220, 1251, 1372, 2912, 2982, 3374; HRMS: $C_9H_{16}FO_5$ (M+H) Calcd. 223.0982 Found: 223.1020; Anal. Calcd. for $C_9H_{15}FO_5$: C, 48.63; H, 6.81; Found: C, 48.64; H, 6.71.

3-Deoxy-3-fluoro-L-*chiro*-inositol (2). A 50 mL round bottomed flask was charged with 0.16 g (0.72 mmol) of **13**, 3 mL of H_2O and 2 drops of HCl. The reaction mixture was stirred and monitored by TLC. After 30 min, the reaction mixture was concentrated under reduced pressure, introduced onto a silica gel column, and

eluted with EtOAc and then 2-propanol to give 0.11 g (84%) of **2**; mp: 206°C dec.; $[\alpha]_D^{29}$ = - 58.8 (c 1.1, MeOH); ^{1}H NMR (DMSO-d_6): 3.5 (m, 2H), 3.6 (m, 3H), 4.2 (dt, J = 53.5, 8.8 Hz, 1H), 4.6 (d, J = 4.9 Hz, 1H), 4.8 (d, J = 2.9 Hz, 1H), 4.9 (d, J = 6.1 Hz, 1H), 4.9 (s, 1H), 4.9 (d, J = 8.6 Hz, 1H); ^{19}F NMR (CD_3OD): - 201.0 (dm, J = 53.7 Hz); ^{13}C NMR (DMSO-d_6): 68.7 (d, J = 17.1 Hz), 70.2 (d, J = 9.6 Hz), 71.2 (d, J = 16.6 Hz), 71.9 (s), 72.3 (d, J = 9.6 Hz), 96.4 (d, J = 175.3 Hz); IR (cm^{-1}): 1011, 1116, 1358, 1473, 2884, 3336; HRMS: (M+H) $C_6H_{12}O_5F$ Calcd. 183.0669; Found: 183.0698; Anal. Calcd. for $C_6H_{11}O_5F$: C, 39.55; H, 6.09; Found: C, 39.46; H, 6.14.

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