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# Chemoenzymatic Enantiodivergent Synthesis of 1,2-Dideoxy-2-amino-1-fluoro-*allo*-inositol.

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***Abstract***: Both enantiomers of dideoxyfluoroamino inositols (+)-**9** and (-)-**9** were synthesized from bromocyclohexadiene *cis*-diol **1** obtained by microbial oxidation of bromobenzene with toluene dioxygenase. Selective introduction of the amino group was achieved through $S_N2$ displacement of triflates **7**, **11**. Fluorine was selectively introduced via *trans*-diaxial epoxide opening with tetrabutylphosphonium fluoride dihydrofluoride (TBPF-DF). © 1999 Elsevier Science Ltd. All rights reserved.

**Keywords**: Biooxidation; Enantioselectivity; Fluoroamino Inositols; Toluene dioxygenase

## INTRODUCTION

Aminoglycoside antibiotics have gained wide use in the treatment of bacterial infections.[1-7] In recent years, there arose the need for antibiotics with a high rate of activity against resistant strains of bacteria coupled with minimal toxicity.[1-3,8] The aglycon moeity of antibiotics has been the target of many modifications [1-3,5,6] in hopes of increasing the activity of known antibiotics. We rationalized that any processes leading to enantiospecific synthesis of diverse aminocyclitols would be of interest since the products could be tested as substrates in the evaluation of various antibiotics of biological importance.[1]

Most of the work done in this field involves functionalization of known inositols.[1,9a-j] Several syntheses have utilized carba-sugars as starting material for the synthesis of aminocyclitols.[10,11] There are a few examples of aminoinositol synthesis in which the Diels-Alder reaction was utilized.[4,9k,l] Whereas most of these syntheses have been creative, they often involve resolution steps, and there is a limit to the scope of products that can be obtained. In contrast, the biocatalytic conversion of aromatics to the corresponding homochiral cyclohexadiene *cis*-diols allows for, through careful symmetry-based planning,[12,13] an efficient approach to functionalized inositols.

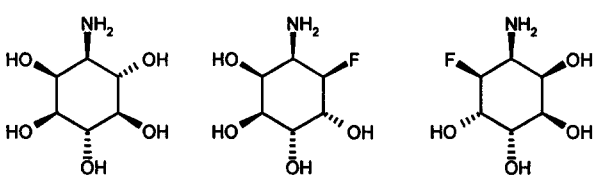


**Figure 1**

We describe herein an enantiodivergent chemoenzymatic synthesis of two dideoxyfluoroamino inositols, (+)-**9** and (-)-**9** from bromobenzene. Given that (-)-**9** resembles the structural features of the aminocyclitol

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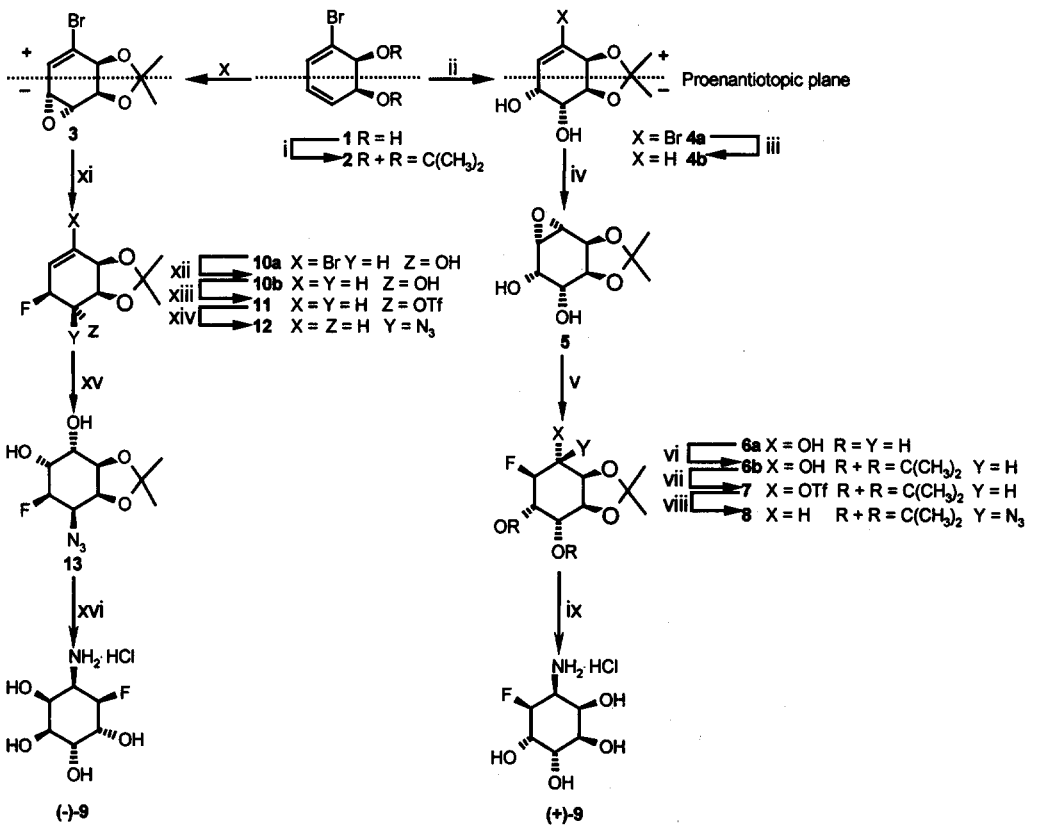
part of minosaminomycin,[7] Figure 1, (four of the six centers have identical absolute configuration) we thought it may be of interest to prepare fluoroamino cyclitols in both enantiomeric series for biological evaluation.

The isosteric and isoelectronic replacement of a hydroxy group with a fluorine atom was envisioned to be advantageous since it has been documented that introduction of fluorine in an antibiotic greatly enhances the antibacterial properties and remarkably reduces the toxicity to mammals.[2b] There are a few examples of diamino fluoroinositol synthesis most of which have been patented,[2,3] but no examples of monoamino fluoroinositols in the literature.

Since the pioneering work by Gibson,[13] cyclohexadiene *cis*-diols produced by the microbial oxidation of arenes with mutant strains of *P. putida*[13] have been used extensively in the synthesis of diverse natural products.[14] Toluene dioxygenase, the active enzyme in these aromatic oxidations, has been expressed in recombinant strains of *E. coli* JM109(pDTG601) for improved efficiency.[15] Recent reports from our laboratory have described the application of halocyclohexadiene *cis*-diols in the synthesis of cyclitols,[12,16] conduritols,[16] sugars,[17] alkaloids,[18] fluoroinositols,[19a] and fluorosugars.[19b] In this report, we take further advantage of the versatility of cyclohexadiene *cis*-diols to design a method for the synthesis of fluoroamino-*allo*-inositols.




**Scheme 1**

Synthesis of (+) **9** and (-) **9**. *Reagents and conditions*: i) DMP, acetone, TsOH (cat.). ii) $OsO_4$, NMO, $H_2O$, *t*-BuOH, 84%. iii) n-$Bu_3SnH$, AIBN, Benzene, reflux, 90%. iv) *m*-CPBA, $CH_2Cl_2$, reflux, 80%. v) TBPF-DF, 70%. vi) DMP, acetone, TsOH (cat.), 85%. vii) $Tf_2O$, pyridine, $CH_2Cl_2$, 90%. viii) $NaN_3$, DMF, 80%. ix) $H_2$/Pd-C, MeOH-HCl, 80%. x) *m*-CPBA, $CH_2Cl_2$, reflux, 80%. xi) TBPF-DF, 75%. xii) ) n-$Bu_3SnH$, AIBN, Benzene, reflux, 95%. xiii) $Tf_2O$, pyridine, $CH_2Cl_2$, 90%. xiv) $NaN_3$, DMF, 80%. xv) $OsO_4$, NMO, $H_2O$, *t*-BuOH, 75%. xvi) $H_2$/Pd-C, MeOH-HCl, 80%.

## RESULTS AND DISCUSSION

(5*S*,6*R*)-1-Bromocyclohexa-1,3-diene-5,6-diol (**1**) was prepared from bromobenzene using *E. coli* JM109(pDTG601). The biocatalytic microbial oxidation provides the diol precursor with excellent enantiomeric purity (>99% ee). In order to achieve enantiodivergence we altered the order of chemical events at the C3-C4 bond (diol formation versus epoxidation), in analogy with the description in our synthesis of (+)- and (-)-pinitol.[12,21] Bromodiene **1** possesses reflective symmetry, with respect to the functional groups similar to that of the two enantiomers of the target. The sequence of events in the two different pro-enantiotopic spaces, arbitrarily assigned here as (+) and (-) (Scheme 1), leads eventually to the enantiomeric pair.

One of the key steps in this synthesis was based on the selective opening of epoxides with fluoride ion. The fluorinating agent tetrabutylphosphonium fluoride dihydrofluoride (TBPF-DF) is known to open epoxides at the least hindered site through an $S_N2$-type process.[19a] The other significant step involved the appendage of an amino group via an $S_N2$ displacement of the triflate intermediates.

For the **(+)-9** enantiomer, *cis*-diol **4a** was prepared stereoselectively from the bromoacetonide (**2**) by oxidation with catalytic osmium tetroxide and *N*-methylmorpholine-*N*-oxide (NMO) as cooxidant.[20] Reduction of **4a** was achieved through treatment with n-$Bu_3SnH$ in benzene initialized by AIBN to give diol **4b**. The epoxide **5** was made according to literature methods.[22] The facial selectivity of the epoxidation was due both to the directing ability of the hydroxyl group on the α-face of the molecule and to the steric effect of the acetonide on the β-face. Opening of the epoxide with TBPF-DF gave only one regio- and stereo-isomer **6a**. The *cis*-diol of fluorohydrin **6a** was then protected with 2,2-dimethoxypropane (DMP) and tosic acid in acetone to yield the bis-acetonide **6b**. The lone hydroxyl group was then converted to a triflate, yielding compound **7**. $S_N2$ displacement of the triflate of **7** gave azide **8** as the sole product. One-pot hydrolysis of the acetonides, reduction of the azide to the amine and its subsequent protection as the hydrochloride salt **(+)-9** was achieved using $H_2$/ Pd-C in methanolic HCl.

Synthesis of (-)-1,2-dideoxy-2-amino-1-fluoro-alloinositol hydrochloride (**(-)-9**): The bromo-epoxide **3** was made according to literature methods.[22] Opening of the epoxide with TBPF-DF gave fluorohydrin **10a**[19a] as the only regio- and stereo- isomer. Reduction of **10a** was performed with n-$Bu_3SnH$/AIBN in benzene to afford the alkene **10b**.[19a] The hydroxyl group of **10b** was converted into the corresponding triflate **11** which was displaced with azide to afford **12**. Oxidation with osmium tetroxide yielded the diol **13** which was reduced with $H_2$/ Pd-C in methanolic HCl to generate the final product (**(-)-9**).

Fully stereocontrolled synthesis of dideoxyfluoroamino inositols **(+)-9** and **(-)-9** was accomplished through enzymatic and chemical transformation of bromobenzene. Enantiodivergence was achieved by changing the order of reagent application.[12,21] The advantage of our approach is our ability to synthesize a wide range of singly or doubly functionalized fluoroamino inositols from one precursor through selective opening of a suitably placed epoxide and displacement of appropriate leaving groups. Further endeavors in the application of chemoenzymatic synthesis as well as evaluation of biological profiles for **9** will be reported in due course.

## CONCLUSION

Fully stereocontrolled synthesis of dideoxyfluoroamino inositols **(+)-9** and **(-)-9** was accomplished through enzymatic and chemical transformation of bromobenzene. Enantiodivergence was achieved by changing the order of reagent application.[12,21] The advantage of our approach is our ability to synthesize a wide range of singly or doubly functionalized fluoroamino inositols from one precursor through selective opening of a suitably placed epoxide and displacement of appropriate leaving groups. Further endeavors in the application of chemoenzymatic synthesis as well as evaluation of biological profiles for **9** will be reported in due course.

## EXPERIMENTAL

All non-hydrolytic reactions were carried out under a nitrogen or argon atmosphere, with standard techniques for the exclusion of moisture. Glassware used for moisture sensitive reactions were flame dried with

an internal inert gas sweep. Analytical TLC was performed on Whatman K6F silica gel 60A plates. Flash chromatography was performed on chromatographic silica gel, 230-400 mesh (Lagand Chemical). Infrared spectra were recorded on a Perkin-Elmer FT-IR (KBr). Proton, fluorine and carbon NMR spectra were obtained on a Varian 300MHz spectrometer using $CDCl_3$/ TMS unless otherwise indicated in the experimental section.

Proton chemical shifts are reported in parts per million (ppm) relative to chloroform (7.24 ppm) or DMSO-$d_6$ (2.49 ppm). Carbon chemical shifts are reported in parts per million relative to the central line of the $CDCl_3$ triplet (77.0 ppm) or the central line of the DMSO-$d_6$ septet (39.7 ppm). Fluorine chemical shifts are reported relative to $CFCl_3$ (0.00 ppm). Coupling constants ($J$) are given in Hz. Optical rotations were recorded on a Perkin-Elmer 241 digital polarimeter ($10^{-1}$ deg. $cm^2$ $g^{-1}$). Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and they are uncorrected. High resolution mass spectra and elemental analyses were performed at the University of Florida and Atlantic Microlab, Inc.

**(1*S*,2*R*,3*S*,4*R*,5*R*,6*R*)-6-Fluoro-3,4-O-isopropylidinecyclohexane-1,2,3,4,5-pentol (6a).** To epoxide **5**[22] (1.00 g, 4.9 mmol) in a pyrex tube was added TBPF-DF (3.15 g, 9.9 mmol). The tube was sealed with a cap and the stirred mixture heated at 100 °C for 6 h. The residue was introduced onto a silica gel column and eluted with ethyl acetate:hexane (1/5) to give **6a** (0.70 g, 70%); mp: 145-147 °C; $[\alpha]_D^{30}$ + 15.8 ° (c 1.0, $CHCl_3$); $^1H$ NMR ( DMSO-$d_6$) δ: 1.3 (s, 3H), 1.4 (s, 3H), 3.5 (m, 1H), 3.6 (m, 1H), 3.9 (m, 2H), 4.1 (dd, J = 5.6, 3.9 Hz, 1H), 4.3 (dt, J = 52.5, 8.4 Hz, 1H), 5.2 (d, J = 5.9 Hz, 1H), 5.3 (d, J = 4.6 Hz, 1H), 5.4 (d, J = 6.1 Hz, 1H); $^{19}F$ NMR (DMSO-$d_6$) δ: -199.7 (dtd, J = 51.3, 17.1, 4.9 Hz); $^{13}C$ NMR (DMSO-$d_6$) δ: 25.8 (s), 28.2 (d, J = 3.0 Hz), 70.9 (d, J = 7.6 Hz), 71.2 (s), 75.0 (d, J=18.6 Hz), 78.0 (s), 80.0 (d, J = 10.0 Hz), 96.5 (d, J = 175.8 Hz), 109.6 (s); IR (KBr/ $cm^{-1}$): 1224, 1250, 1381, 2907, 2996, 3384; HRMS: $C_9H_{16}FO_5$ (M+H) Calcd. 223.2290, Found: 223.0981; Anal. Calcd. for $C_9H_{15}FO_5$: C, 48.65; H, 6.81; Found: C, 48.71; H, 6.86.

**(1*S*,2*R*,3*S*,4*R*,5*R*,6*S*)-6-fluoro-1,2,3,4-di-O-isopropylidenecyclohexane-1,2,3,4,5-pentol (6b).**

A mixture of **6a** (1.00 g. 4.5 mmol), 6.0 mL of acetone, a catalytic amount of *p*-TsOH and DMP (2.0 mL, 16 mmol) were stirred for 3 h at room temperature in a round bottom flask. The reaction was quenched with $NaHCO_3$ and the product extracted with ethyl acetate (3 X 30 mL). The organic layers were combined and dried over anhydrous $MgSO_4$. The residue was introduced onto a silica-gel column and eluted with ethyl acetate:hexane (3/1) to give **6b** (1.00 g, 85%); mp: 115-117 °C; $[\alpha]_D^{26}$ + 29.7 ° (c 1.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$) δ: 1.3 (s, 6H), 1.5 (s, 6H), 2.6 (s, 1H), 3.8 (dd, J = 17.6, 8.8 Hz, 1H), 4.2 (t, J = 7.1 Hz, 1H), 4.3 - 4.5 (m, 4H); $^{19}F$ NMR ($CDCl_3$, $CFCl_3$) δ: -199.5 (m); $^{13}C$ NMR ($CDCl_3$) δ: 25.1 (s), 27.6 (d, J = 7.1 Hz), 71.4 (d, J = 17.2 Hz), 75.8 (s), 76.0 (s), 76.1 (s), 76.3 (s), 77.8 (d, J = 8.0 Hz), 93.5 (d, 181.0 Hz), 110 (d, J = 5.8 Hz), 115.0 (s), 119.5 (s); IR (KBr/ $cm^{-1}$): 1147, 1216, 1260, 1376, 1468, 2943, 2995, 3441; HRMS: $C_{12}H_{20}FO_5$ (M+H) Calcd. 263.2868, Found: 263.1295; Anal. Calcd. for $C_{12}H_{19}FO_5$: C, 55.01; H, 7.30; Found: C, 55.27; H, 7.55.

**(1*S*,2*S*,3*R*,4*R*,5*S*,6*R*)-6-fluoro-5-azido-1,2,3,4,-di-O-isopropylidenecyclohexane-1,2,3,4-tetraol (8).** To a solution of **6b** (1.00 g, 3.8 mmol) in $CH_2Cl_2$ (10 mL) cooled to 0 °C in an ice bath was added $Tf_2O$ (1.2 mL, 7.0 mmol) dropwise over 3 min. Pyridine (1.4 mL, 17 mmol) was then added dropwise. The reaction mixture was allowed to warm to room temperature and the product extracted with ethyl acetate (3 x 10 mL). The organic layers were combined, washed with 0.1 M solution of $CuSO_4$ and dried over anhydrous $MgSO_4$. The solution containing the triflate **7** was added to a solution of DMF (15 mL) and $NaN_3$ (2.00 g, 30 mmol) and heated at 70 °C for 6 h. The reaction mixture was concentrated to afford a yellow oil which was crystallized from hexanes to yield white crystals of **8** (0.79g, 85 %); mp: 82 - 84 °C; $[\alpha]_D^{28}$ + 118.4 ° (c 2.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$) δ: 1.3 (d, 6.6 Hz, 6H), 1.4 (s, 3H), 1.5(s, 3H), 3.7 (ddd, J = 18.4, 4.7, 2.2 Hz, 1H), 4.5 - 4.7 (m, 5H); $^{19}F$ NMR ($CDCl_3$, $CFCl_3$) δ: -190.3 (m); $^{13}C$ NMR (DMSO-$d_6$) δ: 24.0 (d, J = 9.2 Hz), 25.6 (s), 26.6 (s), 58.7 (d, J = 17.2 Hz), 73.0 (d, J = 8.0 Hz), 74.5 (s), 74.8 (s), 75.4 (s), 75.9 (s), 90.8 (d, J = 183.0 Hz), 108.7 (s), 109.2 (s); IR (KBr/ $cm^{-1}$): 1162, 1214, 1276, 1377, 2117, 2984; HRMS: $C_{12}H_{19}FN_3O_5$ (M+H) Calcd. 288.2760, Found: 288.1360; Anal. Calcd. for $C_{12}H_{18}FN_3O_5$: C, 50.17; H, 6.31; N, 14.16; Found: C, 50.26; H, 6.29; N, 14.58.

**(+)-1,2-Dideoxy-2-amino-1-fluoro-*allo*-inositol hydrochloride ((+)-9).** The azide **8** (0.02 g, 0.07 mmol)) was added to a mixture of catalytic amount of 10% Pd-C and methanolic HCl solution (15 mL). The reaction vessel was evacuation and the solution was stirred under $H_2$ (50 psi) for 6 h. After completion of the

reaction (as observed by TLC), the suspension was filtered through Celite and concentrated under reduced pressure. The solid residue was recrystallized from dry acetone to give **(+)-9** (0.01g, 80%); $[\alpha]_D^{27}$ + 16.0 ° (c 2.0, MeOH); $^1$H NMR (DMSO-$d_6$) δ: 3.4 (br, 2H), 3.6 (m, 1H), 3.7 (m, 2H), 3.9 (t, J = 3.3 Hz, 1H), 4.0 (ddd, J = 9.9, 8.0, 3.0 Hz, 1H), 4.7 (ddd, J = 47.5, 8.0, 4.1 Hz, 1H), 5.3 (br, 1H), 5.5 (br, 1H), 7.8 (br, 2H); $^{19}$F NMR (DMSO-$d_6$): -199.80 (m); 13C NMR (DMSO-d6): 51.6 (s), 65.3 (s), 66.7 (s), 69.3 (s), 70.8 (s), 89.8 (d, J = 181 Hz); IR (KBr/ cm$^{-1}$): 1247, 1512, 1617, 2692, 2949, 3089, 3509; HPLC / APCI-MS: $C_6H_{13}FN_3O_4$ (M+H) Calcd. 182.1719; Found: 182.20; $C_6H_{13}ClFNO_4$ (M+Cl) Calcd. 216.67; Found: 216.6059; Anal. Calcd. for $C_6H_{12}FN_3O_4$: C, 33.11; H, 6.02; N, 6.44; Found: C, 33.25; H, 5.96; N, 6.35.

**(1*S*,2*S*,5*R*,6*R*)-6-azido-5-fluoro-1,2-O-isopropylidenecyclohex-3-ene-1,2-diol (12).** To **10b**[19a] (0.79 g, 3.7 mmol) in 10 mL $CH_2Cl_2$ cooled to 0 °C in an ice bath was added trifluoroacetic anhydride (0.95 mL, 6.7mmol.) dropwise over 2 min. Pyridine (0.44 mL 5.6 mmol) was added to the reaction mixture dropwise over 2 min and the reaction allowed to warm to room temperature. After 3 h the reaction was quenched with water and the product extracted with ethyl acetate (3 x 10 mL). The organic layers were combined and dried over anhydrous MgSO4. After filtration the solvent was removed, the crude product introduced onto a silica gel column and eluted with ethyl acetate: hexane (1/15) to obtain 1.1 g (90%) of the triflate **11**. The triflate (1.1 g, 3.4 mmol) was then added to 15 mL DMF and $NaN_3$ (2.00 g, 30 mmol) and the mixture heated to 70 °C. After 12 h the reaction was quenched with water and the product extracted with diethyl ether (3 x 10 mL). The organic layers were concentrated and the residue introduced onto a silica gel column and eluted with ethyl acetate:hexane (1/20) to give (0.61 g, 80%) of the azide **12** as white crystals; mp: 39-40 °C; $[\alpha]_D^{28}$ - 39.4 ° (c 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$) δ: 1.4 (s, 3H), 1.6 (s, 3H), 3.8 (dt, J = 14.1, 3.3 Hz, 1H), 4.4 - 4.5 (m, 1H), 4.5 - 4.6 (m, 1H), 5.1 (d, J = 48.3 Hz, 1H), 5.9 - 6.1 (m, 2H); $^{19}$F NMR ($CDCl_3$, $CFCl_3$) δ: -190.06 (dt, J = 48.3, 9.9 Hz); $^{13}$C NMR ($CDCl_3$) δ: 25.7 (s), 26.7 (s), 58.6 (d, J = 15.6 Hz), 71.1 (s), 72.9 (d, J = 6.0 Hz), 85.6 (d, J = 178.2 Hz), 111.6 (s), 126.1 (d, J = 22.2 Hz), 128.4 (d, J = 9.6 Hz); IR (KBr/ cm$^{-1}$): 1036, 1069, 1281, 1375, 2113, 3008; HRMS: $C_9H_{13}FN_3O_2$ (M+H) Calcd. 214.2342; Found: 214.0979; Anal. Calcd. for $C_9H_{12}FN_3O_2$: C, 50.70; H, 5.67; N, 19.71; Found: C, 50.89; H, 5.79; N, 19.37.

**(1*S*,2*R*,3*S*,4*R*,5*R*,6*R*)-6-azido-5-fluoro-1,2-O-isopropylidenecyclohexane-1,2,3,4-tetraol (13).**

A mixture of **12** (0.40 g, 1.87 mmol), $OsO_4$ solution in *t*-BuOH (2.0 mL, 0.02 M), $H_2O$ (one drop) and NMO (0.13 g, 0.96 mmol) was stirred at room temperature for 24 h. The reaction mixture was then concentrated under reduced pressure. The residue was introduced onto a silica-gel column and eluted with ethyl acetate: hexane (3/1) to give **13** (0.13 g, 75%) as a light yellow solid; mp: 112-113 °C; $[\alpha]_D^{26}$ - 17.8 ° (c 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, TMS) δ: 1.4 (s, 3H), 1.6 (s, 3H), 2.7 (s, 2H), 3.9 (dt, J = 24.0, 3.6 Hz, 1H), 4.1 (t, J = 2.7 Hz, 1H), 4.2 - 4.4 (m, 2H), 4.5 (t, 4.8 Hz, 1H), 4.9 (dt, J = 48.6, 4.2 Hz, 1H); $^{13}$C NMR ($CDCl_3$) δ: 32.2 (s), 34.1 (s), 64.1 (d, J = 16.1 Hz), 76.9 (s), 81.2 (d, J = 2.5 Hz), 83.4 (d, J = 35.2 Hz), 84.3 (d, J = 28.7 Hz), 98.7 (d, J = 184.3 Hz), 117.7 (s); $^{19}$F NMR ($CDCl_3$, $CFCl_3$) δ: - 199.3 (m); IR (KBr/ cm$^{-1}$): 1044, 1077, 1385, 2127, 2949, 3336, 3458; HRMS: $C_9H_{15}FN_3O_4$ (M+H) Calcd. 248.2432; Found: 248.0979; Anal. Calcd. for $C_9H_{14}FN_3O_4$: C, 43.72; H, 5.71; N, 17.00; Found: C, 44.01; H, 5.78; N, 16.76.

**(-)-1,2-Dideoxy-2-amino-1-fluoro-*allo*-inositol hydrochloride ((-)-9).** The azide **13** (0.04 g, 0.16 mmol) was added to a mixture of catalytic amount of 10% Pd-C and methanolic HCl solution (20 mL). The reaction vessel was evacuation and the solution was stirred under $H_2$ (48 psi) for 6 h. After completion of the reaction (as observed by TLC), the suspension was filtered through Celite and concentrated under reduced pressure. The solid residue was recrystallized from dry acetone to give compound **(-)-9** (0.03 g, 75%); $[\alpha]_D^{28}$ - 14.5 ° (c 1.1, MeOH); $^1$H NMR (DMSO-$d_6$) δ: 3.3 (s, 2H), 3.6 (m, 1H), 3.7, (m, 2H), 4.0 (m, 2H), 4.7 (ddd, J = 47.7, 7.2, 3.9 Hz, 1H), 5.3 (d, J = 4.8 Hz, 1H), 5.5 (br, 1H), 7.9 (br, 2H); $^{19}$F NMR (DMSO-$d_6$) δ: - 199.8 (m); $^{13}$C NMR (DMSO-$d_6$) δ: 51.5 (s), 65.2 (s), 67.0 (s), 69.2 (s), 70.8 (s), 89.9 (d, J = 170 Hz); IR (KBr/ cm$^{-1}$): 1260, 1501, 1620, 2704, 3102, 3498; HRMS: $C_6H_{13}FNO_4$ (M+H) Calcd. 182.17; Found: 182.08; Anal. Calcd. for : $C_6H_{12}FNO_4$: C, 33.11; H, 6.02; N, 6.44; Found: C, 32.93; H, 6.20; N, 6.20. Spectra for (-)-9 were recorded at very low concentrations.

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