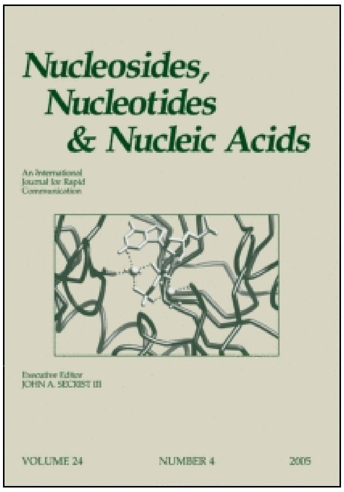

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SYNTHESIS AND ANTI-HIV ACTIVITY OF 6-SUBSTITUTED PURINE 2'-DEOXY-2'-FLUORORIBOSIDES[1)]

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ABSTRACT

3',5'-Di-*O*-protected 6-chloropurine arabinoside 4b was treated with diethylaminosulfur trifluoride (DAST) and subsequently deprotected with pyridinium *p*-toluenesulfonate to give 6-chloropurine 2'-deoxy-2'-fluororiboside 6a. The displacement with nucleophile afforded the 6-substituted congener 6b-e. Treatment of 5'-*O*-protected 6-chloropurine arabinoside 3c with DAST gave lyxo-epoxide 7.

INTRODUCTION

A series of 2'-deoxy-2'-fluoronucleosides have been prepared.[2)] One of these, 2'-deoxy-2'-fluorocytidine (dCfl), exhibited antiviral activity against herpes simplex virus (HSV).[3)] Because some 6-substituted purine nucleosides are known to show significant activity in cancer chemotherapy,[4)] we decided to evaluate the biological activity of 6-substituted purine 2'-deoxy-2'-fluororibosides. Also reported here are the one step synthesis of lyxo-epoxide from arabinoside.

This paper is dedicated to the late Professor Roland K. Robins who passed away during the summer of 1992.

SYNTHESIS

The syntheses of 2'-deoxy-2'-fluoronucleosides have been accomplished by several routes including nucleophilic displacement of 2'-*O*-trifluoromethanesulfonylarabinosides.[2] Recently, a method to introduce fluorine into the sugar moiety of nucleosides using DAST has been developed.[5] We adopted this reagent for the syntheses of 6-substituted purine 2'-deoxy-2'-fluororibosides.

An attempt at the conversion of **1a** to 2'-*O*-acetyl arabinoside **2** has been made by application of the method of Fukukawa *et al.*[6] Thus, treatment of **1a** with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane afforded the corresponding 3',5'-*O*-(tetraisopropyldisiloxane-1,3-diyl) derivative **1b**. Compound **1b** was allowed to react in pyridine with trifluoromethanesulfonyl chloride in the presence of 4-dimethylaminopyridine to give the 2'-*O*-triflate **1c** in high yield. An SN2 displacement with acetate anion at the 2'-position of **1c** was employed to obtain the 2'(*S*)(ara)-*O*-acetate **2**. At this stage, the silyl protecting group should be changed to a group which is stable under fluoride anion. Desilylation of **2** with 2 equivalent of tetrabutylammonium fluoride in the presence of acetic acid at 0° for 15 min afforded **3a**.[7] Since acyl protection causes neighboring group participation in the nucleophilic substitution of 3',5'-di-*O*-acetyl-2'-*O*- methanesulfonylarabinosides by azido anion, an etheral group has been chosen.[8a] Reaction of **3a** with 3,4-dihydro-2*H*-pyran and deacylation by ammonia in methanol gave 3',5'-di-*O*-protected arabinoside **4b**. Treatment of **4b** with DAST in the presence of pyridine in CH_2Cl_2 afforded **5** in 50% yield and recovered **4b** in 27% yield. No spot other than **4b** and **5** was observed on TLC. When the DAST reaction was tried in the absence of pyridine, the protecting group was partially removed from **4b** and **5**. Hydrolysis of **5** with pyridinium *p*-toluenesulfonate (PPTS) in ethanol gave 6-chloro-9-(2-deoxy-2-fluoro-β-D-ribofuranosyl)purine **6a**, a key intermediate for the synthesis of base-modified analogues. The ^{1}H-NMR spectrum of **6a** indicated that the 2'-fluorine caused a downfield shift of the 2'-proton and a large H2'-C-F geminal coupling (52.5Hz). Reaction of **6a** with liquid ammonia gave the known product **6b**, which was identical in all respects to the published data.[8b] Therefore, the structure of **6a** was unequivocally determined. Similar reactions of **6a** with various nucleophiles afforded 6-substituted congeners **6c-e** (Chart 1).

Tritylaion of **3a** gave 5'-*O*-trityl analog **3b** and subsequent deacetylation of the product afforded **3c**. When **3c** was treated with DAST in a similar manner to **4b**,

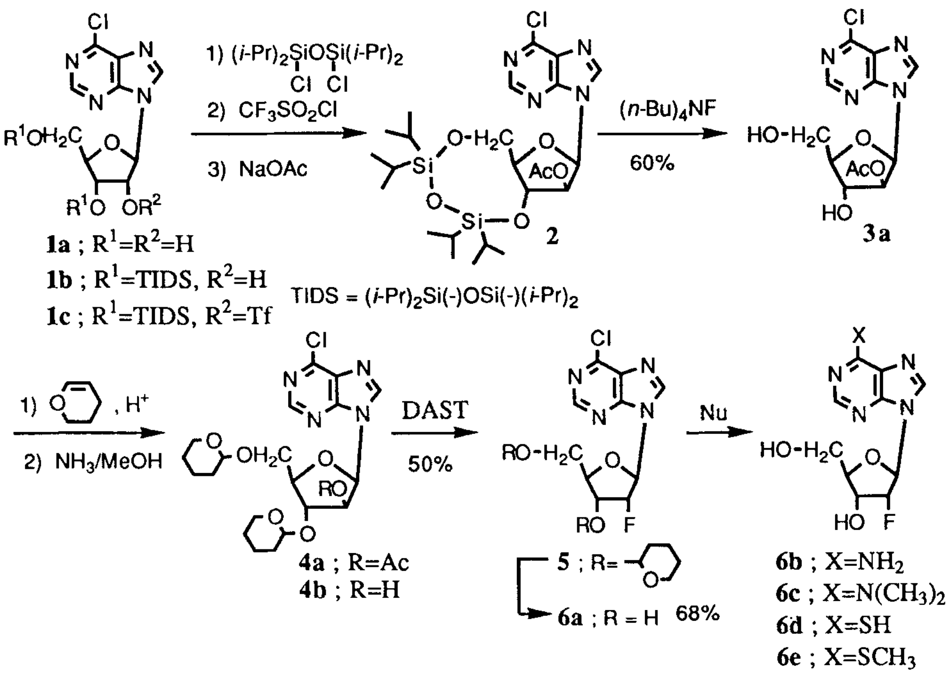


Chart 1

disappearance of the starting material was observed on TLC. Work-up of the reaction mixture gave *lyxo* epoxide **7** in 56% yield. The ^{1}H-NMR spectrum of the product showed that the signals derived from the sugar protons are close to those of 1-(2,3-anhydro-5-*O*-trityl-β-D-lyxofuranosyl)thymidine.[9] The structure of **7** was finally confirmed by an alternative synthesis. Treatment of **3b** with methanesulfonyl chloride gave 3'-*O*-mesylate **8**. Deacetylation and ring formation occurred on the treatment of **8** with liquid ammonia. The lyxo-epoxide **7** thus obtained was identical in all respects with the former sample. The reaction mechanism could be explained by the initial attachment of diethylaminosulfur difluoride group to the less hindered 3'-OH function followed by the intramolecular attack of 2'-OH (Chart 2).

BIOLOGICAL ACTIVITY

The antiviral activity of **6a-e** were assayed by HIV plaque reduction in CD4 expressing HeLa cell monolayers as previously described[10] (Table I). Both **6a** and **6b** displayed indications of activity against HIV-1 in this series. In contrast, **6c-e** proved

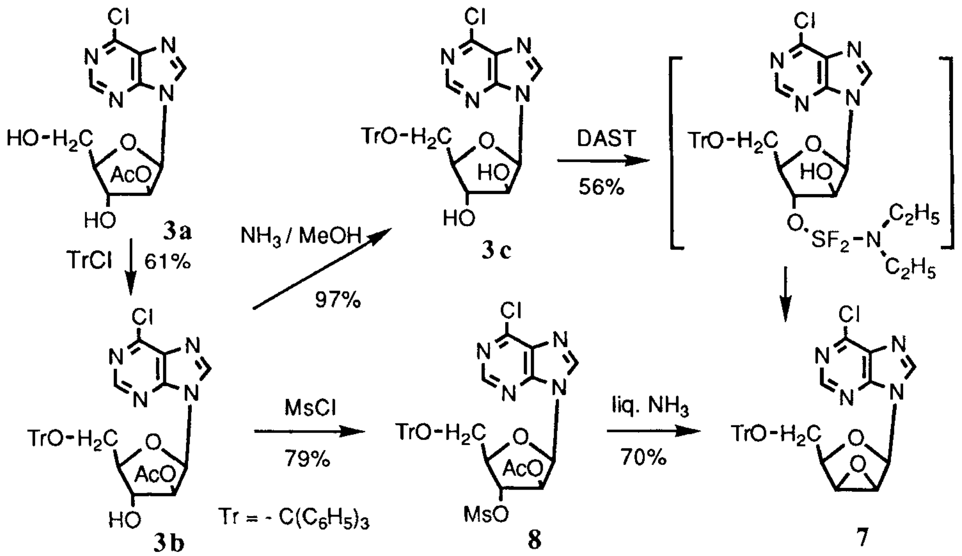


Chart 2

inactive against HIV-1 indicating that the exocyclic amino of adenine are essential for the antiviral effect of 2'-deoxy-2'-fluoro purinenucleosides. Because modified nucleosides may not serve as substrates for cellular nucleoside kinases, further modifications that would lead to phosphate or phosphonate derivatives should be attempted to increase potential anti-HIV activity.

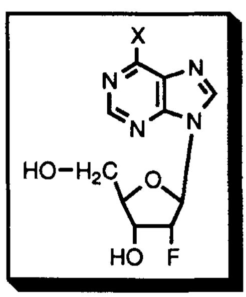
EXPERIMENTAL

Melting points (mp) were determined using a Yanagimoto micro-melting point apparatus (hot stage type) and are uncorrected. UV spectra were recorded with a Shimadzu UV-190 digital spectrometer. Low resolution mass spectra were obtained on a Shimadzu-LKB 9000B mass spectrometer in the direct-inlet mode. High resolution mass spectra were obtained on a JMS AX-500 spectrometer in the direct-inlet mode. ^{1}H-NMR spectra were recorded on either Varian UNITY 200 (200 MHz) or Varian UNITY 600 (600 MHz) in $CDCl_3$ (or dimethyl sulfoxide (DMSO)-d_6) with tetra-methylsilane as an internal standard. Merck Art 5554 plates precoated with silica gel 60 containing fluorescent indicator F_{254} were used for thin-layer chromatography and silica gel 60 (Merck 7734, 60 - 200 mesh) was employed for column chromatography.

Table 1. Inhibition of HIV-1 plaque formation by compounds **6a-d**

Compound	Concentration(μ M)	Average	% Reduction
6a	10	79	32
	1.0	116	0
	none	116	
6b	10	78	33
	1.0	120	0
6c	10	109	6
	1.0	119	0
6d	10	110	5

The assay was performed by inhibition of plaque formation in CD4 expressing HeLa cells using the HIV-1_{LA1} (LAV-1) virus



6 series
a ; X=Cl, **b** ; X=NH_2
c ; X=NMe_2, **d** ; X=SH

6-Chloro-9-(3,5-*O*-tetraisopropyldisiloxane-1,3-diyl-β-D-ribofuranosyl)purine (1b). 6-Chloropurine riboside **1a** (37.21 g, 0.13 mol) and imidazole (40.0 g, 1.1 eq.)were dissolved in DMF (130 m*l*), and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (46.0 m*l*, 1.1 eq.) was added to the solution and the mixture was stirred at room temperature for 1 h. The residue obtained after work-up of the solution was chromatographed over a column of silica gel G (5.0 × 29 cm) with $CHCl_3$ (3.7 *l*) and the residue thus obtained was crystallized from MeOH to give white crystals (47.52 g, 69%). Anal.cald. for $C_{22}H_{37}ClN_4O_5Si_2$: C,49.94 ; H,7.05 ; N,10.59. Found C,49.82 ; H,7.14 ; N,10.83. Ms m/z 485, 487 (M^+-C_3H_7) mp.106-108℃ UV: λ max 264.5nm, 250nm (sh) (MeOH), 264nm, 250nm (sh) (0.05N HCl) ^{1}H-NMR ($CDCl_3$) δ : 8.69 (1H, s, H8), 8.28 (1H, s, H2), 6.05 (1H, s, H1'), 5.02 (1H, t, H2', J=5.60Hz), 4.57 (1H, d, H3', J=5.60Hz), 3.99-4.18 (3H, m, H4' and H5'), 3.14 (1H, d, 2'-O<u>H</u>), 1.1 (28H, -C<u>H</u>(C<u>H</u>$_3$)$_2$×4).

6-Chloro-9-(3,5-*O*-tetraisopropyldisiloxane-1,3-diyl-2-*O*-triflyl-β-D-ribofuranosyl)purine (1c). Compound **1b** (14.3 g, 27.0 mmol) and 4-dimethylaminopyridine (5.40 g) were dissolved in a mixture of triethylamine (6.7 m*l*) and CH_2Cl_2 (270 m*l*), then ice-cooled. Trifluoromethanesulfonyl chloride (5.4 m*l*) was added to the solution and the mixture was stirred at room temperature for 30 min. The usual workup of the resulting solution and crystallization from MeOH gave white crystals (12.3 g, 69%). Anal.cald. for $C_{23}H_{36}F_3Cl\ N_4O_7SSi_2$: C,41.78 ; H,5.49 ; N,8.47. Found C,41.79 ; H,5.41 ; N,8.14. mp.101-102℃ UV: λ max 264nm, 250nm (sh) (MeOH), 263.5nm, 250nm (sh) (0.05N HCl) ^{1}H-NMR ($CDCl_3$) δ : 8.71 (1H, s, H8), 8.34 (1H, s, H2), 6.23 (1H, s, H1'), 5.67 (1H, d, H2', J=4.72Hz), 5.09 (1H, dd, H3', J=9.17Hz, J=4.72Hz), 4.00-4.26 (3H, m, H4', H5'), 1.1 (28H, -C<u>H</u>(C<u>H</u>$_3$)$_2$×4).

6-Chloro-9-(2-*O*-acetyl-3,5-*O*-tetraisopropyldisiloxane-1,3-diyl-β-D-arabinofuranosyl)purine (2). A solution of **1c** (20.04 g, 30.3 mmol) and NaOAc (12.4 g, 5 eq.) in DMF (10 m*l*) was stirred at room temperature overnight and filtered to remove insoluble materials. The usual workup of the filtrate and crystallization from MeOH gave white crystals (12.3 g, 78%). Anal.cald. for $C_{24}H_{39}ClN_4O_6Si_2$: C,50.47 ; H,6.88 ; N,9.81. Found C,50.62 ; H,7.25 ; N,9.89. Ms m/z 527, 529 (M^+-C_3H_7) mp.141-143 ℃ UV: λ max 264nm, 250nm (sh) (MeOH), 264nm, 250nm (sh) (0.05N HCl) ^{1}H-NMR ($CDCl_3$) δ : 8.72 (1H, s, H8), 8.35 (1H, s, H2), 6.52 (1H, d, H1', J=6.55Hz), 5.59

(1H, dd, H2', J=8.46Hz, J=6.55Hz), 4.90 (1H, t, H3', J=8.46Hz), 4.14 (2H, m, H5'), 3.97 (1H, m, H4'), 1.69 (3H, s, 2'-OCOC<u>H</u>$_3$), 1.1 (28H, -C<u>H</u>(C<u>H</u>$_3$)$_2$×4).

6-Chloro-9-(2-*O*-acetyl-β-D-arabinofuranosyl)purine (3a). To an ice-cooled solution of **2** (1.14 g, 2.0 mmol) in THF (10 m*l*) and acetic acid (0.23 m*l*) was added dropwise 1.0 M tetrabutylammonium fluoride solution in THF (4 m*l*, 4 eq.) and stirred at 0° for 10 min. The solution was concentrated to a small volume and subjected to a column of silica gel G (2.8 × 15 cm) using a 0 - 10% EtOH in $CHCl_3$ (1 *l*) as an eluent. The fraction was collected and the solution was evaporated to give a syrup, which was crystallized from EtOH to afford white crystals (395 mg, 60%). Anal.cald. for $C_{12}H_{13}ClN_4O_5$: C,43.84 ; H,3.96 ; N,17.05. Found C,43.86 ; H,4.00 ; N,16.94. mp. 179-180℃ UV: λ max 264nm, 250nm (sh) (MeOH), 264nm, 250nm (sh) (0.05N HCl) ^{1}H-NMR (DMSO-d_6) δ : 8.89 (1H, s, H8), 8.81 (1H, s, H2), 6.59 (1H, d, H1', J=5.86Hz), 5.90 (1H, d, 3'-O<u>H</u>, J=5.86Hz), 5.38 (1H, t, H2', J=5.86Hz), 5.14 (1H, t, 5'-O<u>H</u>, J=5.50Hz), 4.45 (1H, q, H3', J=5.86Hz), 3.93 (1H, m, H4'), 3.74 (2H, m, H5'), 1.68 (3H, s, 2'-OCOC<u>H</u>$_3$)

6-Chloro-9-(2-*O*-acetyl-3,5-di-*O*-(tetrahydro-2-pyranyl)-β-D-arabinofuranosyl)purine (4a). To a solution of **3a** (2.58 g, 7.85 mmol) in DMF (14 m*l*) and 3,4-dihydro-2*H*-pyran (6.8 m*l*) was added *p*-toluenesulfonic acid (2.74 g) and the solution was stirred at room temperature for 2 h. After neutralization with triethylamine (2 m*l*), the solution was subjected to the usual workup and silica gel chromatography to give a caramel (3.9 g, quantitative). UV: λ max 264nm, 250nm (sh) (MeOH).

6-Chloro-9-(3,5-di-*O*-(tetrahydro-2-pyranyl)-β-D-arabinofuranosyl)purine (4b). The acetate **4a** (3.92 g, 7.89 mmol) was dissolved in methanol (20 m*l*) saturated with ammonia and kept at 0° for 3 h. Evaporation of the solution afforded a caramel (3.42 g, 95%). Ms m/z 454, 456 (M^+) UV: λ max 264nm, 250nm (sh) (MeOH).

6-Chloro-9-(2-deoxy-2-fluoro-3,5-di-*O*-(tetrahydro-2-pyranyl)-β-D-ribofuranosyl)purine (5). To a cooled solution (- 60°) of **4b** (1.42 g, 3.12 mmol) in a mixture of CH_2Cl_2 (25 m*l*) and pyridine (3.2 m*l*) was added DAST (1.67 m*l*, 4 eq.) dropwise under N_2 atmosphere. Teflon equipments were used for flask and pipette. After 6 h at room temperature, the solution was poured into the stirred solution of 10% $NaHCO_3$ (50 m*l*) and diluted with CH_2Cl_2 (25 m*l*). The organic layer was washed with water (50 m*l* × 3), dried over $MgSO_4$ and evaporated to a small volume. The solution was chromatographed over a column of silica gel G (2.5 × 26 cm) with 0 - 68% AcOEt in hexane (2 *l*). From the first fraction **5** was obtained as a caramel (716 mg, 50%). UV: λ max 264nm, 250nm (sh) (MeOH). Starting material **4b** was recovered from the second fraction as a caramel (27%).

6-Chloro-9-(2-deoxy-2-fluoro-β-D-ribofuranosyl)purine (6a). A solution of **5** (716 mg, 1.57 mmol) in EtOH (30 m*l*) was stirred in the presence of pyridinium *p*-toluenesulfonate at 50° for 8 h and the solution was concentrated to 3 m*l*. The solution was chromatographed over a column of silica gel G (2.0 × 43 cm) with 0 - 12.5% AcOEt in $CHCl_3$ (2 *l*) to give white crystals (307 mg, 68%). Anal.cald. for $C_{10}H_{10}ClN_4O_3$: C,41.61 ; H,3.49 ; N,19.41. Found C,41.70 ; H,3.68 ; N,18.98. Ms m/z 288, 290 (M^+) mp. 209-212℃ UV: max 264nm, 250nm (sh) (H_2O), 264nm, 250nm (sh) (0.05N HCl) ^{1}H-NMR (DMSO-d_6) δ : 8.92 (1H, s, H8), 8.83 (1H, s, H2), 6.39 (1H, dd, H1', $J_{H1'-F}$=16.85Hz, $J_{H1'-H2'}$=1.83Hz), 5.78 (1H, d, 3'-O<u>H</u>, *J* =6.23Hz), 5.46 (1H, ddd, H2', $J_{H2'-F}$=52.75Hz, $J_{H2'-H3'}$=4.3Hz, $J_{H1'-H2'}$=1.83Hz), 5.18 (1H, br s, 5'-O<u>H</u>), 4.51 (1H, m, H3', $J_{H3'-F}$=22.34Hz), 4.02 (1H, m, H4'), 3.81, 3.63 (each 1H, m, H5').

2'-Deoxy-2'-fluoroadenosine (6b). Compound **6a** (100 mg, 0.35 mmol) was reacted with liquid ammonia (1 m*l*) in 10 m*l* of steel-bomb at 40° overnight. Ammonia was carefully evaporated and the solid was crystallized from MeOH to give white crystals (71 mg, 74%). Anal. cald. for $C_{10}H_{12}FN_5O_3$: C,44.61 ; H,4.49 ; N,26.01. Found C,44.25 ; H,4.54 ; N,25.77. Ms m/z 269 (M^+) mp. 209-212℃ UV: λ max 259nm (H_2O), 255.5nm (0.05N HCl), 259nm (0.05N NaOH) ^{1}H-NMR (DMSO-d_6) δ : 8.37 (1H, s, H8), 8.16 (1H, s, H2), 7.36 (2H, br s, 6-N<u>H</u>$_2$), 6.23 (1H, dd, H1', $J_{H1'-F}$=16.85Hz, $J_{H1'-H2'}$=2.93Hz), 5.72 (1H, d, 3'-O<u>H</u>, *J*=5.86Hz), 5.44 (1H, ddd, H2', $J_{H2'-F}$=52.76Hz, $J_{H2'-H3'}$=4.4Hz, $J_{H1'-H2'}$=2.93Hz), 5.28 (1H, t, 5'-O<u>H</u>, *J*=5.13Hz), 4.49 (1H, m, H3', $J_{H3'-F}$=17.71Hz), 3.99 (1H, m, H4'), 3.75, 3.59 (each 1H, m, H5').

2'-Deoxy-2'-fluoro-N^6,N^6-dimethyladenosine (6c). 50% Dimethylamine (0.20 m*l*, 6 eq.) was added to a solution of **6a** (100 mg, 0.35 mmol) in DMF (4 m*l*) and the solution was stirred at at room temperature for 2 h. After evaporation of the solution, the residue was chromatographed over a column of silica gel G (2.0 × 20 cm) with 0 - 5% EtOH in $CHCl_3$ (1.3 *l*) to give white crystals (72 mg, 69%). Anal. cald. for $C_{12}H_{16}FN_5O_3$: C,48.48 ; H,5.42 ; N,23.56. Found C,48.19 ; H,5.50 ; N,23.03. Ms m/z 297 (M^+) mp. 113-115℃ UV: λ max 273nm (MeOH), 267.5nm (0.05N HCl), 275nm

(0.05N NaOH) ^{1}H-NMR (DMSO-d_6) δ : 8.38 (1H, s, H8), 8.22 (1H, s, H2), 6.24 (1H, dd, H1', $J_{H1'-F}$=16.8Hz, J=2.31Hz), 5.70 (1H, d, 3'-O$\underline{H}$, J=6.92Hz), 5.42 (1H, m, H2', $J_{H2'-F}$=52.5Hz), 5.24 (1H, m, 5'-O$\underline{H}$), 4.46 (1H, m, H3', $J_{H3'-F}$=22.5Hz), 3.98 (1H, m, H4'), 3.68(2H, m, H5'), 3.45(6H, br s, 6-N(C$\underline{H}_3$)$_2$).

6-Mercapto-9-(2-deoxy-2-fluoro-β-D-ribofuranosyl)purine (6d). Hydrogen sulfide was introduced to a suspension of NaH (42 mg, 3 eq.) in DMF (5 m*l*) at 0 ° for 10 min and N_2 was passed into the solution to disperse the excess gas. 6-Chloro compound **6a** (100 mg, 0.35 mmol) was added to the solution and the mixture was stirred at room temperature for 1 h, then neutralized with acetic acid (0.06 m*l*). After bubbling N_2 gas for 30 min, the solution was evaporated to dryness and the residue was crystallized from EtOH to give white crystals (75 mg, 74%). Ms m/z 286 (M^+). mp. 270 ℃(dec.) UV: λ max 320nm, 224nm (H_2O), 322nm, 224nm (0.05N HCl), 311nm, 232nm (0.05N NaOH). ^{1}H-NMR (DMSO-d_6) δ : 8.31 (1H, s, H8), 8.13 (1H, s, H2), 6.18 (1H, dd, H1', $J_{H1'-F}$=16.6Hz, J=2.31Hz), 5.37 (1H, ddd, H2', $J_{H2'-F}$=52.8Hz, J=4.06Hz, J=2.31Hz), 4.44 (1H, m, H3', $J_{H3'-F}$=21.1Hz), 3.98 (1H, m, H4'), 3.66(2H, m, H5').

6-Methylmercapto-9-(2-deoxy-2-fluoro-β-D-ribofuranosyl)purine (6e). To a solution of **6a** (100 mg, 0.35 mmol) in anhydrous EtOH (5 m*l*) was added sodium thiomethoxide (15% solution in water, 0.46 m*l*, 3 eq.) and the solution was stirred at room temperature for 30 min. After evaporation of the solution, the residue was chromatographed over a column of silica gel G (2.3 × 15 cm) with 0 - 5% EtOH in $CHCl_3$ (1.1 *l*) to give a caramel (77 mg, 74%). Ms m/z 297 (M^+). UV: λ max 283nm, 289nm(sh) (MeOH), 289nm, 284nm(sh) (0.05N HCl), 284nm, 289nm(sh) (0.05N NaOH). ^{1}H-NMR (DMSO-d_6) δ : 8.75 (1H, s, H8), 8.63 (1H, s, H2), 6.33 (1H, dd, H1', $J_{H1'-F}$=17.0Hz, J=2.4Hz), 5.73 (1H, d, 3'-O$\underline{H}$, J=6.4Hz), 5.45 (1H, ddd, H2', $J_{H2'-F}$=52.8Hz, J=4.6Hz, J=2.4Hz), 5.13 (1H, m, 5'-O$\underline{H}$), 4.49 (1H, m, H3', $J_{H3'-F}$=22.5Hz), 3.99 (1H, m, H4'), 3.67(2H, m, H5'), 2.66(3H, s, 6-SC$\underline{H}_3$).

6-Chloro-9-(2-*O*-acetyl-5-*O*-trityl-β-D-arabinofuranosyl)purine (3b). A solution of **3a** (265 mg, 0.81 mmol) and trityl chloride (450 mg, 2 eq.) in pyridine (10 m*l*) was kept at room temperature overnight. The usual workup of the resulting solution gave a caramel (277 mg, 61%). UV: λ max 263nm (MeOH), 262nm (0.05N HCl) ^{1}H-NMR ($CDCl_3$) δ : 8.69 (1H, s, H8), 8.26 (1H, s, H2), 7.28-7.47 (15H, m, 5'-OC($C_6\underline{H}_5$)$_3$), 6.64 (1H, d, H1', J=5.9Hz), 5.27 (1H, t, H2', J=5.9Hz), 4.60 (1H, m, H3'), 4.19 (1H, q, H4', J=5.43Hz), 3.55 (2H, d, H5'), 1.76 (3H, s, 2'-OCOCH_3).

6-Chloro-9-(5-*O*-trityl-β-D-arabinofuranosyl)purine (3c). The acetate **3b** (200 mg, 0.35 mmol) was dissolved in methanol (50 m*l*) saturated with ammonia and kept at 0° for 3 h. Evaporation of the solution afforded a caramel (180 mg, 97%). UV: λ max 264nm (MeOH), 264nm (0.05N HCl) ^{1}H-NMR ($CDCl_3$) δ : 8.68 (1H, s, H8), 8.49 (1H, s, H2), 7.24-7.44 (15H, m, 5'-OC(C_6H_5)$_3$), 6.45 (1H, s, H1'), 4.38 (1H, s, 3'-OH), 4.32 (2H, s, H2' and H3'), 4.15 (1H, m, H4'), 3.70, 3.47 (each 1H, m, H5').

6-Chloro-9-(2-*O*-acetyl-3-*O*-mesyl-5-*O*-trityl-β-D-arabinofuranosyl)purine (8). Methanesulfonyl chloride (0.04 m*l*) was added to the solution of **3b** (135 mg, 0.24 mmol) in pyridine (5 m*l*) and the solution was stirred at room temperature for 3 h. The usual workup of the resulting solution gave a caramel (125 mg, 79%). UV: λ max 263nm, 250nm(sh) (MeOH), 263nm (0.05N HCl) ^{1}H-NMR ($CDCl_3$) δ : 8.50 (1H, s, H8), 8.23 (1H, s, H2), 7.24-8.49 (15H, m, 5'-OC(C_6H_5)$_3$), 6.60 (1H, d, H1', J=4.76Hz), 5.55(1H, dd, H3', J=4.64Hz, J=2.84Hz), 5.43(1H, dd, H2', J=4.76Hz, J=2.84Hz), 4.38 (1H, q, H4', J=4.64Hz), 3.56 (2H, d, H5', J=4.64Hz), 3.18 (3H, s, 3'-OSO_2CH_3), 1.89 (3H, s, 2'-OCOCH_3).

6-Chloro-9-(2,3-anhydro-5-*O*-trityl-β-D-lyxofuranosyl)purine (7).

Method 1. To a cooled solution (- 60°) of **3c** (321 mg, 0.61 mmol) in a mixture of CH_2Cl_2 (5 m*l*) and pyridine (1.3 m*l*) was added DAST (0.66 m*l*, 8 eq.) dropwise under N_2 atmosphere. After standing at room temperature for 2 h, the solution was treated in a similar manner described in a section of **5** to afford as white crystals (176 mg, 56%). Anal. cald. for $C_{29}H_{23}ClN_4O_3$: C,68.17 ; H,4.54 ; N,10.96. Found C,68.03 ; H,4.60 ; N,11.02. Ms m/z 510, 512 (M^+) mp.177-179℃ UV: λ max 264nm, 250nm(sh) (MeOH), 264nm (0.05N HCl) ^{1}H-NMR ($CDCl_3$) δ : 8.74 (1H, s, H8), 8.40 (1H, s, H2), 7.21-7.45 (15H, m, 5'-OC(C_6H_5)$_3$), 6.44 (1H, s, H1'), 4.30 (1H, t, H4', J=4.83Hz), 4.07 and 4.06 (1H, s, H2' and 1H, s, H3'), 3.46 (2H, m, H5').

Method 2. 3'-*O*-Mesylate **8** (150 mg) was reacted with liquid ammonia (1 m*l*) in 10 m*l* of steel-bomb at 0° for 30 min. Ammonia was carefully evaporated and the solid was crystallized from MeOH to give white crystals (83.5 mg, 70%). The product thus obtained was identical in any respect with sample obtained by method 1.

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