Synthesis of 9-(2-Deoxy-2-fluoro-β-D-arabinofuranosyl)adenine Bearing a Selectively Removable Protecting Group

Tokumi MARUYAMA,*[,a] Satoshi TAKAMATSU,[b] Shigetada KOZAI,[a] Yoshiko SATOH,[a] and Kunisuke IZAWA[b]

Faculty of Pharmaceutical Sciences, Tokushima Bunri University,[a] Yamashiro-cho, Tokushima 770–8514, Japan and Amino Science Laboratories, Ajinomoto Co., Inc.,[b] 1–1 Suzuki-cho, Kawasaki-ku, Kawasaki City, Kanagawa 210–8681, Japan.
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A facile and practical method to introduce fluorine at the up-side of the 2′-carbon of nucleosides is described. 6-Chloropurine riboside 3 was converted to the 3′-*O*-benzoate 4a *via* a stannylene complex, then converted to the 3′-*O*-benzoyl-5′-*O*-tritylriboside 5a. In the presence of pyridine, migration of the 3′-benzoyl groups of 4a and 5a to 2′-OH was rather slow. Hence, 5a was reacted with diethylaminosulfur trifluoride (DAST) in CH_2Cl_2 in the presence of pyridine to give the 2′-deoxy-2′-fluoroarabinoside 6 in good yield. The 3′-*O*-benzoyl-5′-*O*-trityl protecting system was easy to deprotect selectively. Thus, treatment of 6 with ammonia in MeOH gave the 5′-*O*-trityl compound 7, which was subjected to esterification with phenyl chlorothionoformate, radical deoxygenation with tris(trimethylsilyl)silane and acid treatment to afford 9-(2,3-dideoxy-2-fluoro-β-D-*threo*-pentofuranosyl)adenine (FddA) 2. In addition, acid treatment of 7 gave 9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)adenine (FdaraA) 1.

Key words acyl migration; antiviral agent; nucleosides; protecting groups; regioselection

The importance of introducing a fluorine at the 2′(*S*)(ara) site of purine deoxynucleosides is well recognized since the 2′-deoxy-2′-fluoroarabinosides are biologically active and stable to chemical and purine nucleoside phosphorylase (PNP) catalyzed hydrolysis.[1)] For example, many pyrimidine analogs are active against herpes viruses,[2)] and purine analogs show selective T-Cell toxicity[3)] and antiparasitic activity.[4)] Moreover, 9-(2,3-dideoxy-2-fluoro-β-D-*threo*-pentofuranosyl)adenine (FddA) is an inhibitor of human immunodeficiency virus (HIV) reverse transcriptase.[5,6)] FddA is useful as an anti-HIV agent because of its effectiveness against resistant mutants of dideoxy nucleosides,[7,8)] its stability in the acidic solution[5)] which destroys 2′,3′-dideoxyinosine (ddI) and its ability to reach the brain.[9)]

As far as the synthesis of the 2′-deoxy-2′-fluoroarabinosides is concerned, it is very difficult to introduce a fluorine at the 2′(*S*)(ara) site of the nucleoside. One problem is the poor yield of 3′,5′-di-*O*-protection by the trityl group.[10,11)] Also, migration caused by intramolecular nucleophilic attack of N3 at the electrophilic C2′ has been reported during the reaction with diethylaminosulfur trifluoride (DAST).[11)] An attempt to condense the fluorinated sugar with purine failed to prevent formation of the α-anomer.[5b,12)] These difficulties prompted us to explore a new method of preparing 2′-deoxy-2′-fluoroarabinoside. An anti-AIDS compound, FddA, has been prepared by esterification followed by radical deoxygenation of 9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)adenine (FdaraA).[5b)] Recently, an alternative method for FddA was reported by Marquez and his co-workers, in which dehydration of 2′-deoxy-2′-fluoroadenosine and subsequent hydrogenation of the vinyl intermediate was described.[13)] However, 2′-deoxy-2′-fluoroadenosine is prepared *via* a multi procedure from adenosine by way of 9-(β-D-arabinofuranosyl)adenine[14)] and the dehydration step is still a problem. This led us to attempt to find an easier synthetic route for FddA.

In this report, the synthesis of 2′-deoxy-2′-fluoroarabinoside from the 3′-*O*-benzoate and radical deoxygenation of the product are described.

Synthesis The 2′,3′-*O*-di-*n*-butylstannylene complex is useful intermediate for introducing only one benzoyl group at the 2′-OH and/or 3′-OH.[15)] Thus, 6-chloropurine riboside **3**[16)] has been successively treated with di-*n*-butyltin oxide and excess benzoyl chloride (BzCl) in the presence of triethylamine (Et_3N) in MeOH. The resulting solution was subjected to the usual work-up, purification by silica gel chromatography, to give an inseparable mixture of **4a** and **4b**. However, crystallization from MeOH afforded pale yellowish crystals in 65% yield. At this point, the purity was checked by high performance liquid chromatography (HPLC), which revealed that this material is a mixture of the 3′-*O*-benzoate (96.1%) and 2′-*O*-benzoate (3.9%). It is already known that acylation of the riboside affords a mixture of the 2′-*O*-acylate and 3′-congener and the latter is obtainable by crystallization. This rule has been confirmed for the 3′,5′-di-*O*-acyl ribosides[17)] and the acidity of the 2′-OH of the ribonucleosides explains this result.[18,19)] Compound **4a** (96.1%) was reacted with trityl chloride (TrCl) in the presence of Et_3N and 4-dimethylaminopyridine (DMAP) in *N*,*N*-dimethylformamide (DMF). Thin-layer chromatography of the mixture showed spots for **5b** as well as **5a**, indicating migration of the benzoyl group from 3′-OH to 2′-OH in the reaction mixture. However, crystals from MeOH, which were mainly composed of the 3′-*O*-benzoate **5a**, were obtained in 71% yield. The purity of this product was shown to be 98.0% by HPLC.

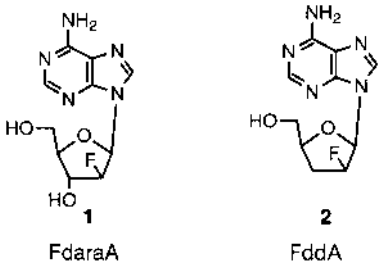

Fig. 1. The Nucleoside Analogs Bearing Fluorine

* To whom correspondence should be addressed.

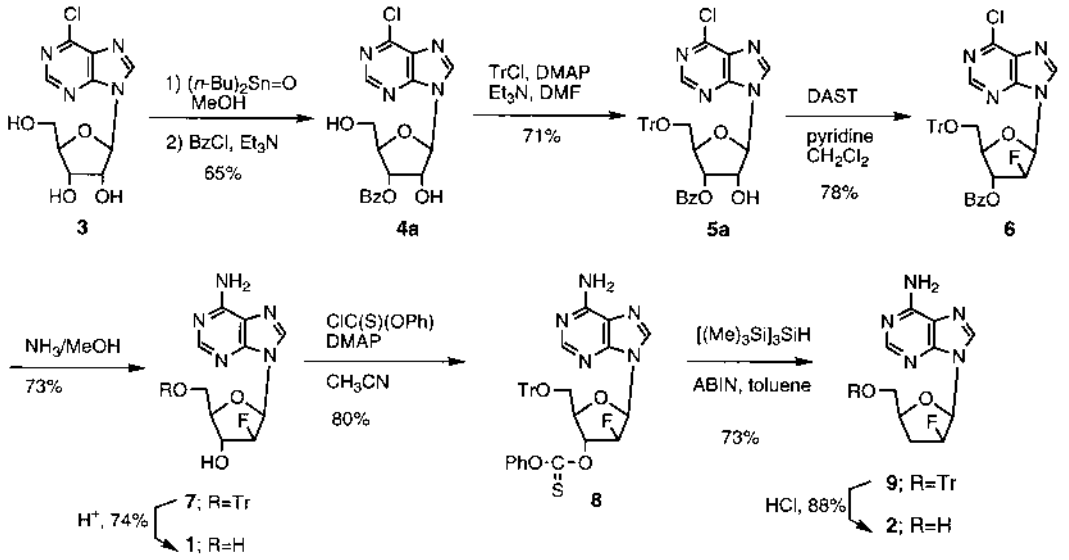

Chart 1

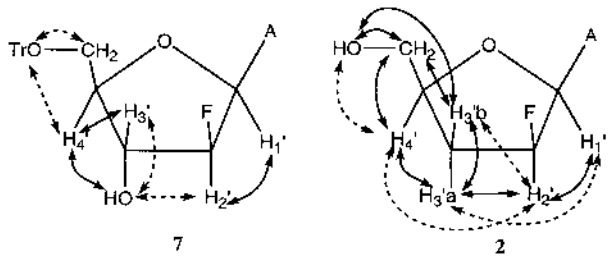

Fig. 2. NOESY Spectra of Compounds **2** and **7**

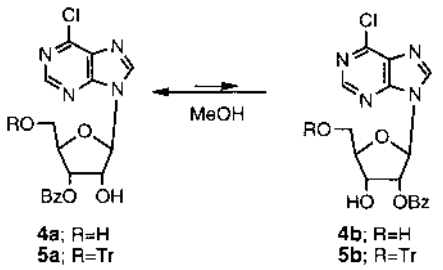

Chart 2

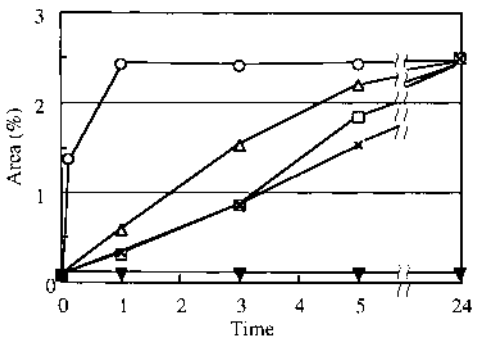

Fig. 3. Ratio of the 2′-*O*-Benzoate **4b** Mixed with 3′-*O*-Benzoate **4a** as a Function of Elapsed Time in MeOH Alone (—×—), and a 1 mM Solution of Et_3N (—○—), Imidazole (—△—), Pyridine (—□—) or HCl (—▼—)

Before reaction with DAST, the stability of the 3′-*O*-benzoyl group was checked hence reaction with DAST needs to be carried out in the presence of amine to protect the acid-labile 5′-*O*-trityl group. Thus, compound **5a** was heated under reflux in the presence of 6 eq pyridine in CH_2Cl_2 for 5 h. However only 3.1% of the 2′-*O*-benzoate **5b** was observed in the mixture. Accordingly, we attempted to react compound **5a** with DAST using the same solvents and obtained **6** in 78% yield. The 3′-*O*-benzoyl-5′-*O*-trityl protecting system has two advantages: it is easy to introduce the protecting group compared with di-*O*-trityl group and selective removal of either the 3′- or 5′-*O*-protecting group proceeds smoothly. Thus, displacement of the 6-chloro function and deprotection of the 3′-*O*-benzoyl group of compound **6** was achieved by treatment with ammonia in MeOH to give **7** as prisms in 73% yield. Part of the product was converted to the known product, 9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)adenine **1**, and the measured data were identical with published values.[11,20] Therefore, the structure of **7** was unequivocally confirmed as an 2′(*S*)-arabinoside structure. These results show that reaction of **5a** with DAST occurs without migration of the benzoyl group. Deoxygenation of the 3′-hydroxy group was achieved by the conventional method.[21] Compound **7** was esterified using phenyl chlorothionoformate to afford **8** in 80% yield. Then, the product was treated with tris(trimethylsilyl)silane in the presence of 2,2′-azobis(isobutyronitrile) (AIBN) in toluene under N_2 atmosphere to give **9** as white crystals in 73% yield. This was then treated with acid to give 9-(2,3-dideoxy-2-fluoro-β-D-*threo*-pentofuranosyl)adenine (FddA, **2**) as prisms in good yield. Data on this sample were identical in all respects with the published data[5,6] and the nuclear Overhauser effect spectroscopy (NOESY) spectrum also supported the structure of **2**.

Acyl Migration of the 3′-*O*-Benzoates 4a, 5a In HPLC analysis, the retention time of the 2′-*O*-benzoates **4b**, **5b** were determined as follows: To a solution of **4a** in dimethyl sulfoxide (DMSO)-d_6 a small amount of Et_3N was added to hasten the equilibrium, then the spectrum was recorded on a Varian UNITY 600 instrument. It appeared that this solution was a mixture of **4a** (80%) and **4b** (20%). The structure of **4b** was assigned as 2′-*O*-benzoate by the low-field shift of 2′-H (5.9 ppm). The major component had almost the same

Table 1. Selected Data for the Proton NMR Spectra of Compounds **4**, **5** in a Mixture of $CDCl_3$ and Et_3N

Compounds		H1′	H2′	H3′	H4′	H5′a	H5′b	2′(or 3′)OH	5′OH
4a (3′-*O*-Bz)	ppm	6.20	5.05	5.59	4.37—4.39	3.77—3.81	3.71—3.75	6.02	5.35
80%		d	q	dd	m	m	m	d	t
	J (Hz)	6.6	5.9	5.5, 2.7				6.0	5.5
4b (2′-*O*-Bz)	ppm	6.48	5.88	4.66	4.15—4.17	3.66—3.69	3.00—3.83	5.81	5.24
20%		d	dd	q	m	m	m	d	dd
	J (Hz)	4.9	5.2, 4.9	5.1				5.8	5.5, 5.2
5a (3′-*O*-Bz)	ppm	6.20	5.25	5.68	4.48—4.50	3.34—3.43		6.05—6.10	—
73%		d	q	dd	m	m		ND	
	J (Hz)	5.5	5.5	5.5, 4.4					
5b (2′-*O*-Bz)	ppm	6.51	6.05—6.10	4.87	4.28	3.34—3.43		5.83	—
27%		d	ND	q	dt	m		d	
	J (Hz)	3.6		6.1	6.9, 4.4			6.0	

ND; not determined.

spectrum as that of **4a** (Table 1). Then, this sample was analyzed by HPLC as described in experimental section and the benzoate ratio was estimated from the area of the peaks. The 2′-*O*-benzoate **4b** appeared at 12.8 min as a minor peak (21%) and the major one (79%) at 14.6 min was attributed to the 3′-*O*-benzoates **4a**. The benzoate ratio was in good agreement with the proton NMR results. Next, migration of the 3′-*O*-benzoate **4a** was explored in MeOH under acidic and basic conditions. Compound **4a** reached equilibrium rapidly in 1 mM Et_3N solution. However, the rate of migration was slow in 1 mM pyridine solution and similar to that in MeOH alone. In 1 mM imidazole solution, an intermediate value was obtained. Under acidic conditions, no migration was observed even after 1 d (Fig. 3). These results confirm the correctness of using 10 mM phosphoric acid–MeOH as an eluent. A solution of compound **5a** in a mixture of DMSO-d_6 and Et_3N was also brought to equilibrium and the spectrum recorded as described above. This revealed that the solution was a mixture of 2′-*O*-benzoate **5b** (27%) and 3′-*O*-benzoate **5a** (73%) (Table 1). Also, the retention times of **5b** and **5a** were determined as 6.7 and 8.4 min, respectively.

Conclusion

A protection of both 3′-OH and 5′-OH with a trityl group is impractical because of the low yield and lack of selectivity; also the 2′,5′-di-*O*-trityl product is inevitably formed. On the other hand, a benzoyl group can be successfully introduced on 3′-OH. It appears that the acyl migration of **4a** is slow in 1 mM pyridine in MeOH. In the case of **5a**, no acyl migration was observed even after refluxing for 5 h in a mixture of CH_2Cl_2 and pyridine. Thus, introduction of fluorine at C2′ was achieved in good yield. Also, this choice enabled selective deprotection of the 3′-*O*-benzoyl group and removal of the 3′-OH was carried out by radical deoxygenation. The target compound, FddA, was obtained after acid treatment. The present method is very useful for preparing FddA and related compounds from ribosides.

Experimental

General Melting points (mp) were determined using a Yanagimoto micro-melting point apparatus (hot stage type) and are uncorrected. UV spectra were recorded on 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) instrument in $CDCl_3$ (or DMSO-d_6) with tetramethylsilane as 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 used for column chromatography.

HPLC HPLC apparatus consisted of a CCPD pump (Tosoh Co.) and an SPD-M10A photo diode array UV-VIS detector (Shimadzu Co.). The HPLC conditions were as follows: Columns, a Cosmosil Guard Column 5C18-MS (4.6×10 mm, Nacalai Tesque Inc.) connected to a Cosmosil packed column 5C18-MS (4.6×150 mm, Nacalai Tesque Inc.); eluent, 10 mM phosphoric acid–MeOH (3 : 2) for **4a** or (1 : 4) for **5a**; flow rate, 1 ml/min; column temperature, 50 °C. To determine the retention time of the 2′-*O*-benzoates **4b**, **5b**, the following experiments were carried out: A solution of **4a** (10 mg) or **5a** (10 mg) in a mixture of DMSO-d_6 (0.7 ml) and Et_3N (1 μl) was kept at room temperature for 1 d, then the spectrum recorded on a Varian UNITY 600 (600 MHz) instrument with tetramethylsilane as internal standard. Then, these samples were analyzed by HPLC and the benzoate ratio was estimated from the area of the peaks.

6-Chloro-9-(3-*O*-benzoyl-β-D-ribofuranosyl)purine 4a A suspension of 6-chloropurine riboside **3** (14.34 g, 50 mmol) and di-*n*-butyltin (IV) oxide (12.45 g, 50 mmol) in MeOH (500 ml) was refluxed for 1 h, then Et_3N (34.8 ml, 250 mmol) was added. Benzoyl chloride (BzCl) (29.0 ml, 250 mmol) was added dropwise to the stirred solution. After 30 min, the solution was filtered to remove insoluble materials. The filtrate was evaporated and the residue was partitioned between ether (400 ml) and water (250 ml). The aqueous layer was washed twice with ether (200 ml) and the organic layers were combined, washed with water (100 ml), dried over $MgSO_4$, and concentrated to a small volume. The residual solution was chromatographed on a column of Silica gel G (6.5×35 cm) using CH_2Cl_2 (1 l) and 0—10% EtOH in CH_2Cl_2 (4 l). The fraction containing the monobenzoyl derivatives was concentrated to give a residue, which was crystallized from MeOH to afford the 3′-*O*-benzoate as crude crystals (12.67 g, 65%). This sample was analyzed by HPLC, and contamination of the 2′-*O*-benzoate **4b** (3.9%) was confirmed. Part of this sample (100 mg) was dissolved in a mixture of EtOH (4 ml), $CHCl_3$ (4 ml) and Et_3N (0.05 ml) and the solution was concentrated to afford white crystals (56 mg) in which the 2′-*O*-benzoate ratio was reduced to 1.1%. mp 174—177 °C. *Anal.* Calcd for $C_{17}H_{15}ClN_4O_5 \cdot 0.2H_2O$: C, 51.77; H, 3.94; N, 14.21. Found: C, 51.80; H, 3.99; N, 14.05. MS *m/z*: 360, 362 ($M^+ - CH_2O$), 285, 287 ($M^+ - C_6H_5CO$). UV λ_{max} (MeOH) nm: 264.5. ^{1}H-NMR ($CDCl_3$) δ: 8.97, 8.91 (each 1H, s, H-2, H-8), 7.5—8.1 (5H, m, C_6H_5CO), 6.16 (1H, d, *J*=6.5 Hz, H-1′), 5.95 (1H, m, 2′-OH), 5.55 (1H, dd, *J*=6.5, 2.4 Hz, H-3′), 5.28 (1H, br s, 5′-OH), 5.00 (1H, m, H-2′), 4.33 (1H, m, H-4′), 3.72 (2H, t, *J*=2.8 Hz, H-5′).

6-Chloro-9-(3-*O*-benzoyl-5-*O*-trityl-β-D-ribofuranosyl)purine 5a To a solution of **4a** (96.1%) (10.72 g, 25 mmol) in dry DMF (220 ml) was added Et_3N (11.0 ml, 78.9 mmol), DMAP (1.01 g, 8.25 mmol) and TrCl (23.00 g, 82.5 mmol) and the solution was kept at 50 °C overnight. After cooling, water (10 ml) was added to the solution and the solvent removed under reduced pressure. The residue was partitioned between $CHCl_3$ (300 ml) and water (150 ml) and the organic layer was washed with water (150 ml), dried over $MgSO_4$, and concentrated to a small volume. The residual solution was chromatographed on a column of Silica gel G (3.5×50 cm) using CH_2Cl_2 (1 l) and 0—2.5% EtOH in CH_2Cl_2 (4 l). Concentration of the solution gave a residue, which was crystallized from MeOH to afford white crystals

(11.21 g, 71%). HPLC showed they contained 2.0% 2′-*O*-benzoate (**5b**). mp 102—106 °C. *Anal.* Calcd for $C_{36}H_{29}ClN_4O_5 \cdot 0.8H_2O$: C, 66.78; H, 4.76; N, 8.65. Found: C, 66.86; H, 4.81; N, 8.43. MS *m/z*: 555, 557 ($M^+ - C_6H_5$), 389, 391 (M^+-trityl). UV λ_{max} (MeOH) nm: 264. ^{1}H-NMR ($CDCl_3$) δ: 8.69, 8.38 (each 1H, s, H-2, H-8), 7.2—8.05 (*ca.* 20H, m, C_6H_5CO, trityl), 6.18 (1H, d, J=6.1 Hz, H-1′), 5.74 (1H, dd, J=5.5, 2.5 Hz, H-3′), 5.29 (1H, m, H-2′), 4.59 (1H, m, H-4′), 3.95 (1H, d, J=4.5 Hz, 2′-OH), 3.53 (2H, t, J=3.6 Hz, H-5′).

Stability of Compound 5a A solution of **5a** (100 mg) in a solution of dry CH_2Cl_2 (4.1 ml) and pyridine (0.076 ml) was refluxed for 5 h. After cooling, part of the mixture (100 μl) was diluted with DMSO (2 ml) and the volatiles were removed under reduced pressure. The solution was then subjected to HPLC analysis, which showed that the solution consists of 2′-*O*-benzoate **5b** and 3′-*O*-benzoate **5a** in a ratio of 3.1 to 96.9.

6-Chloro-9-(3-*O*-benzoyl-2-deoxy-2-fluoro-5-*O*-trityl-β-D-arabinofuranosyl)purine 6 DAST (2.25 ml, 17 mmol) was added dropwise to an ice-cooled solution of **5a** (4.76 g, 7.5 mmol) in a solution of dry CH_2Cl_2 (100 ml) and pyridine (3.6 ml, 44.5 mmol). The solution was gradually warmed to room temperature and refluxed for 5 h. The whole was added dropwise to 5% $NaHCO_3$ (500 ml) and stirred for 20 min, then the organic layer was collected. The aqueous layer was washed with $CHCl_3$ (100 ml) and the organic layers were combined, washed with water (200 ml), dried over $MgSO_4$ and concentrated to a small volume. The residual solution was chromatographed on a column of Silica gel G (3.5×50 cm) using 0—12.5% AcOEt in benzene (4 l). Evaporation of the fraction gave a gum (3.71 g, 78%). MS *m/z*: 391, 393 (M^+-trityl), 375, 377 (M^+-trityloxy). UV λ_{max} (MeOH) nm: 263. ^{1}H-NMR ($CDCl_3$) δ: 8.76 (1H, s, H-2), 8.36 (1H, d, J=3.0 Hz, H-8), 7.2—8.1 (*ca.* 20H, m, C_6H_5CO, trityl), 6.66 (1H, dd, J=21.7, 2.7 Hz, H-1′), 5.70 (1H, dd, J=17.0, 3.0 Hz, H-3′), 5.28 (1H, m, J_{HCF}=50.0 Hz, H-2′), 4.42 (1H, m, H-4′), 3.62 (1H, dd, J=10.4, 5.2 Hz, H-5′a), 3.54 (1H, dd, J=10.4, 4.1 Hz, H-5′b).

9-(5-*O*-Trityl-2-deoxy-2-fluoro-β-D-arabinofuranosyl)adenine 7 A solution of **6** (3.15 g, 4.98 mmol) in MeOH (100 ml), saturated with ammonia at 0 °C, was kept in a sealed tube at 100 °C for 2 d. The solution was carefully evaporated and the residue was dissolved $CHCl_3$ (100 ml), then filtered to remove insoluble material. The filtrate was concentrated to a small volume and chromatographed on a column of Silica gel G (3.5×50 cm) using 3—10% EtOH in CH_2Cl_2 (4 l) to give prisms (1.87 g, 73%). mp 210.5—212.5 °C. *Anal.* Calcd for $C_{29}H_{26}FN_5O_3$: C, 68.09; H, 5.12; N, 13.69. Found: C, 68.06; H, 5.15; N, 13.70. MS *m/z*: 511 (M^+), 376 (M^+-adenine), 268 (M^+-trityl). UV λ_{max} (MeOH) nm: 258.5. ^{1}H-NMR (DMSO-d_6) δ: 8.15 (1H, s, H-2), 8.05 (1H, d, J=2.5 Hz, H-8), 7.37 (2H, br s, NH_2), 7.23—7.42 (15H, m, trityl), 6.46 (1H, dd, J=15.4, 4.7 Hz, H-1′), 6.02 (1H, d, J=5.2 Hz, 3′-OH), 5.22 (1H, ddd, J=52.5, 4.7, 3.6 Hz, H-2′), 4.48 (1H, ddt, J=19.2(d), 5.2(t), 3.6(d) Hz, H-3′), 4.04—4.07 (1H, m, H-4′), 3.24—3.38 (2H, m, H-5′).

9-(2-Deoxy-2-fluoro-β-D-arabinofuranosyl)adenine 1 A solution of **7** (100 mg, 0.195 mmol) in 80% trifluoroacetic acid (2 ml) was kept at room temperature for 10 min, then the solvent was removed under reduced pressure. The residue was partitioned between $CHCl_3$ (5 ml) and water (5 ml) and the aqueous layer was washed with $CHCl_3$ (5 ml). The solution was neutralized with Et_3N, and evaporated to give a solid, which was crystallized from EtOH to afford white crystals (39 mg, 74%). The sample data were identical in all respect to the published data. mp 229—232 °C (lit[1] 231—234 °C).

9-(3-*O*-Phenoxythiocarbonyl-5-*O*-trityl-2-deoxy-2-fluoro-β-D-arabinofuranosyl)adenine 8 To a suspension of **7** (419 mg, 0.82 mmol) and DMAP (273 mg, 2.23 mmol) in dry CH_3CN (10 ml) was added phenyl thionoformate (0.22 ml, 1.63 mmol) and the solution was stirred at room temperature for 3 h. The solution was concentrated to a small volume and chromatographed on a column of Silica gel G (2.5×32 cm) using 0—10% EtOH in $CHCl_3$ (1.2 l) to give a gum (406 mg, 80%). UV λ_{max} (MeOH) nm: 256, 230 (sh), λ_{max} (0.05 M HCl) nm: 255, 230 (sh). ^{1}H-NMR ($CDCl_3$) δ: 8.38 (1H, s, H-2), 8.08 (1H, d, J=3.3 Hz, H-8), 7.09—7.54 (*ca.* 20H, m, trityl, Ph), 6.60 (1H, dd, J=23.1, 2.6 Hz, 1H-1′), 5.95 (1H, dd, J=17.6, 2.2 Hz, H-3′), 5.80 (1H, br s, NH_2), 5.35 (1H, dd, J=52.0, 2.6 Hz, H-2′), 4.45 (1H, m, H-4′), 3.57 (2H, d, J=4.8 Hz, H-5′).

9-(5-*O*-Trityl-2,3-dideoxy-2-fluoro-β-D-*threo*-pentofuranosyl)adenine 9 To a suspension of **8** (386 mg, 0.63 mmol) in dry toluene (4 ml) was added ABIN (60 mg, 0.37 mmol) and tris(trimethylsilyl)silane (0.6 ml, 1.95 mmol) and the solution was heated at 100 °C under N_2 atmosphere for 30 min. After cooling, the resulting crystals were collected by filtration to give **7** (229 mg, 73%). mp 226—229 °C. *Anal.* Calcd for $C_{29}H_{26}FN_5O_2$: C, 70.29; H, 5.29; N, 14.13. Found: C, 70.20; H, 5.30; N, 14.24. MS *m/z*: 252 (M^+-trityl), 135 (adenine). UV λ_{max} (MeOH) nm: 258. ^{1}H-NMR ($CDCl_3$) δ: 8.36 (1H, s, H-2), 8.07 (1H, d, J=2.6 Hz, H-8), 7.1—7.6 (*ca.* 15H, m, trityl), 6.33 (1H, dd, J=17.0, 3.0 Hz, H-1′), 5.70 (2H, br s, NH_2), 5.22 (1H, m, J_{HCF}=43.6 Hz, H-2′), 4.4 (1H, m, H-4′), 3.46 (1H, dd, J=8.2, 5.9 Hz, H-5′a), 3.26 (1H, dd, J=8.2, 3.2 Hz, H-5′b), 2.2—2.65 (2H, m, H-3′).

9-(2,3-Dideoxy-2-fluoro-β-D-*threo*-pentofuranosyl)adenine 2 To a suspension of **9** (300 mg, 0.605 mmol) in MeOH (18 ml) was added conc. HCl (1.2 ml) and the solution was stirred at room temperature for 1.5 h, then Amberlite IR 400B (OAc^- form) (4 ml) was added. After stirring for 5 min, the solution was filtered to remove the resin and the filtrate was concentrated to 2 ml. This was then diluted with water (40 ml), washed three times with $CHCl_3$ (30 ml) and concentrated to give prisms (135 mg, 88%). The sample data were identical in all respect to the published data. mp 226.8—227.7 °C (lit[5] 227 °C). *Anal.* Calcd for $C_{10}H_{12}FN_5O_2$: C, 47.43; H, 4.78; N, 27.66. Found: C, 47.60; H, 4.94; N, 27.47. MS *m/z*: 253 (M^+), 164 (adenine+CHO). UV λ_{max} (MeOH) nm: 258. ^{1}H-NMR (DMSO-d_6) δ: 8.26 (1H, d, J=2.5 Hz, H-8), 8.16 (1H, s, H-2), 7.34 (2H, br s, NH_2), 6.32 (1H, dd, J=15.9, 4.1 Hz, H-1′), 5.43 (1H, ddt, J=54.4(d), 5.8(d), 3.5(t) Hz, H-2′), 5.06 (1H, dd, J=5.8, 6.0 Hz, 5′-OH), 4.16—4.20 (1H, m, H-4′), 3.58—3.65 (2H, m, H-5′), 2.52—2.62 (1H, m, H-3′a), 2.22—2.31 (1H, m, H-3′b).

References and Notes

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