Synthesis of 1-(3′-Azido-2′,3′-dideoxy-α-L-*threo*-pentofuranosyl)thymine as a Potential Anti-HIV Agent[1]

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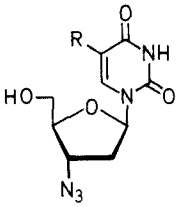
Starting from methyl 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranoside, a multistep synthesis of the C-4′ epimer of AZT is described. Glycosylation of silylated thymine with 2,3,5-tri-*O*-benzoyl-L-arabinofuranosyl acetate (**5**) affords the α-nucleoside **7** after debenzoylation. Deoxygenation at C-2′ of the selectively protected **8**, followed by displacement of a 3′-methanesulfonyl group by lithium azide leads to the title compound which did not exhibit antiviral activity against HIV-1.

Since the discovery of the human immunodeficiency virus (HIV) as the etiological agent of AIDS,[2] increasing efforts have been devoted to the synthesis and biological evaluation of compounds with potential anti-HIV activity. Most of those which have so far proved to be selective inhibitors of HIV replication are 2′,3′-dideoxy-3′-substituted nucleosides,[3,4] and one of them, 3′-azido-2′,3′-deoxythymidine (**1**, AZT) is currently used for the treatment of patients with AIDS. Although the exact mechanism of action of these nucleoside analogues is not fully understood, some structure–activity relationships of AZT analogues against HIV are already available from the base modified analogues **2**,[5,6] 2′-azido-2′,3′-dideoxy derivatives[7] and stereoisomers in which the azido group is *cis* to the thymine base.[4] None of these derivatives exhibit a higher anti-HIV activity than AZT. Since, to the best of our knowledge, no C-4′ epimer of 3′-azido-2′,3′-dideoxy nucleosides have been reported, we undertook the synthesis of **14**, in which the relative positions of the thymine base and the azido group are the same as in AZT, with C-4′ having the opposite configuration.



1 R = Me
2 R = H, F, Br, Cl, I

Compound **14** being an α-L-nucleoside analogue, and since L-nucleosides are not naturally occuring, we decided to develop a versatile methodology which could be employed for the synthesis of several nucleoside analogues. L-Arabinose, the sole L-pentose abundant in nature, was used as the starting material. Rather than coupling thymine with a 2-deoxy sugar derivative which would afford an α/β mixture of nucleosides,[8,9] we decided to couple the thymine base with a synthetic equivalent such as **5**. Here the participating group at C-2 is suitably positioned to favor the formation of the desired α-L-nucleoside which could be transformed into a 2′-deoxy nucleoside. Furthermore, the spatial arrangement of C-3 in **5** would allow the introduction of the azido group in the desired configuration by an S_N2 reaction, after protection of 5′-OH and activation of 3′-OH.

Although L- and D-arabinoses exist in the pyranose form, it is possible to obtain a mixture enriched in methyl arabinofuranosides by glycosylation of methanol under kinetic control.[10] Direct isolation of **3** from the resulting mixture is not possible, but **4** can be obtained in an acceptable yield (50%) by crystallization, after benzoylation of the crude mixture.

Acetolysis of **4** with a mixture of acetic anhydride and acetic acid[11] afforded **5** in 95% yield. The α/β-mixture was directly condensed with activated thymine[12] to give **6**. The nucleoside **6** was purified by column chromatography and characterized as the α-anomer by ^{1}H-NMR spectroscopic data (H-1′, $\delta = 6.25$, $J_{1',2'} = 3.1$ Hz). Debenzoylation[13] of **6** with sodium methoxide in methanol afforded **7**.

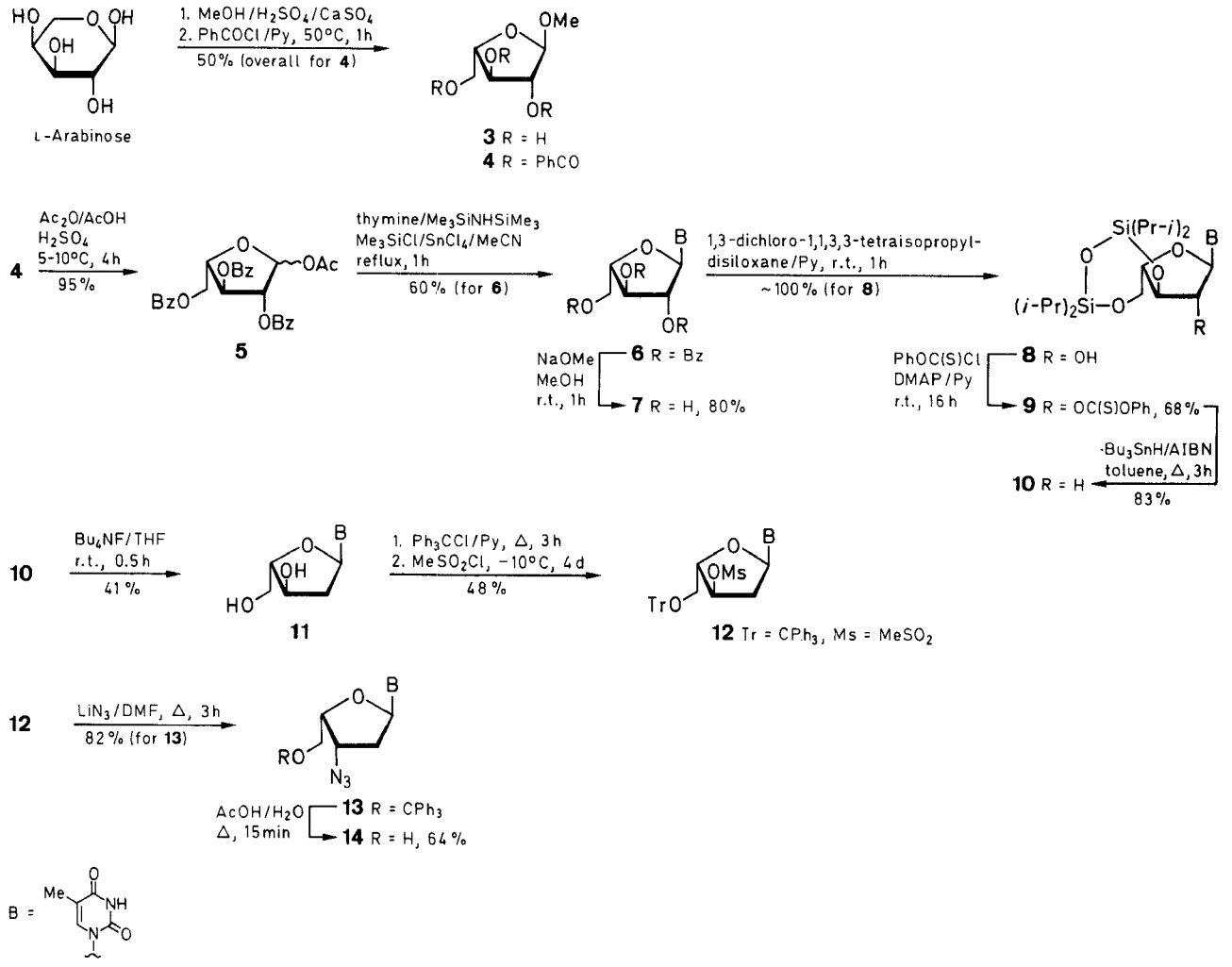
Differentiation of the 2′-OH was achieved by selective protection of the two other hydroxy groups with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane[14] to form **8**.

In order to limit undesired secondary reactions during the deoxygenation step, **8** was transformed into a *o*-phenyl thiocarbonate **9**[15] which upon treatment with tributyltin hydride under Barton's conditions[16] afforded **10** in good yield. Desilylation of **10** gave **11**, whose structure was confirmed by ^{1}H-NMR spectroscopy and comparison of the physical constants with those reported for the α-D-anomer.[17] Selective protection of the 5′-OH of **11** and activation of the 3′-OH was achieved in one-pot.[18] Nucleophilic displacement of the methylsulfonyl group of the resulting **12** with lithium azide[17] was clean and the protected azido compound **13** was the only product formed. It was detritylated under acid conditions to give the title compound **14**.

The inhibitory effects on the replication of HIV-1 were evaluated.[19] No appreciable antiviral effect could be detected for compound **14**.

Microanalyses were performed at the Service de Microanalyse of Pierre et Marie Curie University. Melting points were determined with Thomas-Hoover apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter. The ^{1}H-NMR spectra were recorded on a Bruker AM-250 spectrometer with TMS as internal standard. Reactions were monitored by analytical. TLC using 2 × 5 cm precoated aluminum plates silica gel 60 F_{254} (Merck) and detection by UV light and charring with H_2SO_4. For column chromatography, Merck silica gel 60 (230–400 Mesh) and anhydrous solvents were used. Preparative TLC was carried out with silica gel 60 GF_{254} (0.5 mm thickness) and distilled solvents. Solvents and reagents were purified and dried by standard procedures.

Methyl 2,3,5-Tri-*O*-benzoyl-α-L-arabinofuranoside (4):
This compound is prepared from L-arabinose as described by Fletcher for the α-D-isomer.[10] Compound **4** is obtained in 50%



yield by recrystallization; mp 101–102°C (abs. EtOH); $[\alpha]_D^{20}$ +19.4° (c = 2.05, $CHCl_3$) [Lit.[10] 100–101.5°C, $[\alpha]_D^{20}$ −20.5° (c = 2.05, $CHCl_3$) for the α-D-derivative].

1-*O*-Acetyl-2,3,5-tri-*O*-benzoyl-α- and β-L-arabinofuranosides (5):
A solution of **4** (8.0 g, 16.4 mmol) in glacial AcOH (84.5 mL) and Ac_2O (16.9 mL) is stirred at 5–10°C while conc. H_2SO_4 (4.9 mL) is added dropwise.[10] After completion of the reaction (4 h at r.t.) the mixture is poured into ice-water (300 mL) and extracted with $CHCl_3$ (2 × 100 mL). The extracts are combined, washed successively with sat. aq $NaHCO_3$ (2 × 50 mL) and water (50 mL), dried ($MgSO_4$), filtered and evaporated under reduced pressure. A syrup, containing the two anomers is obtained and used in the next step without purification; yield: 8.0 g (95%).

1-[2′,3′,5′-Tri-*O*-benzoyl-α-L-arabinofuranosyl]thymine (6):
To a mixture of thymine (2.06 g, 16.4 mmol) and **5** (8 g, 16.4 mmol) in anhydrous MeCN (150 mL) are successively added hexamethyldisilazane (2.74 mL, 13.1 mmol), $ClSiMe_3$ (1.6 mL, 13.1 mmol) and $SnCl_4$ (2.3 mL, 19.7 mmol).[12] The resulting clear solution is refluxed for 1 h when TLC indicates completion of the reaction. The mixture is concentrated to a small volume, diluted with CH_2Cl_2 (200 mL), washed with sat. aq $NaHCO_3$ (2 × 75 mL) and with water (3 × 50 mL). The organic phase is dried ($MgSO_4$), filtered and evaporated to give a white foam (7.53 g, 80%) which is chromatographed on a silica gel column ($CHCl_3$/acetone, 9:1). Evaporation of the appropriate fractions affords **6**; yield: 4.52 g (60%); mp 85°C; $[\alpha]_D^{20}$ −6.6° (c = 0.6, $CHCl_3$).

$C_{31}Hd_{26}O_9N_2$	calc.	C 65.26	H 4.56	N 4.91
(570.6)	found	65.47	4.61	4.67

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.95 (s, 3 H, CH_3), 4.60–4.80 (ddd, 2 H, $J_{5',5''}$ = 12 Hz, H-5′, 5″), 4.95 (m, 1 H, $J_{4',5'}$ = 5.9 Hz, $J_{4',5''}$ = 4.8 Hz, H-4′), 5.75 (t, 1 H, $J_{3',4'}$ = 3 Hz, H-3′), 5.95 (t, 1 H, $J_{2',3'}$ = 2.9 Hz, H-2′), 6.20 (d, 1 H, $J_{1',2'}$ = 3.1 Hz, H-1′), 7.30–8.20 (m, 15 H_{arom}), 8.80 (br s, 1 H, NH).

1-[α-L-Arabinofuranosyl]thymine (7):
A mixture of **6** (4.5 g, 7.89 mmol), MeOH (50 mL) and 1 M NaOMe in MeOH (7.9 mL) is kept at r.t.[13] After completion of the reaction (1 h), the mixture is concentrated to a small volume, and diluted with water (100 mL). The methyl benzoate is extracted with Et_2O (3 × 50 mL) and the aqueous phase is acidified to pH = 6 by IRN 77 resin (H^+ form). The resin is filtered and the water evaporated under reduced pressure affording of **7** pure enough for the next step; yield: 1.62 g (80%). An analytical sample is obtained by silica gel column chromatography. Elution with $CHCl_3$/MeOH (9:1) affords **7**; mp 62–65°C; $[\alpha]_D^{20}$ −39° (c = 1, MeOH).

$C_{10}H_{14}N_2O_6 \cdot 0.3\ H_2O$	calc.	C 45.45	H 5.30	N 10.60
(264.2)	found	45.15	5.96	10.40

^{1}H-NMR (DMSO-d_6/TMS): δ = 1.75 (d, 3 H, $J_{CH_3,H-6}$ = 1.2 Hz, CH_3), 3.40–3.60 (m, 2 H, H-5′,5″), 3.85–4.20 (m, 3 H, H-2′,3′,H-4′), 4.90 (t, 1 H, $J_{H,OH}$ = 5.5 Hz, 5′-OH), 5.45 (d, 1 H, $J_{H,OH}$ = 3.8 Hz, 2′-OH or 3′-OH), 5.65 (d, 1 H, $J_{H,OH}$ = 5.3 Hz, 2′-OH or 3′-OH), 5.75 (d, 1 H, $J_{1',2'}$ = 4.9 Hz, H-1′), 7.60 (d, 1 H, J_{H-6,CH_3} = 1.2 Hz, H-6), 11.30 (br s, 1 H, NH).

1-[3′,5′-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-α-L-arabinofuranosyl]thymine (8):
To a stirred suspension of **7** (1.6 g, 6.2 mmol) in pyridine (20 mL) is added 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane[14] (2.42 mL, 7.5 mmol). When TLC (EtOAc/MeOH, 20:1) shows completion of the reaction (5 h at r.t.), the solvent is evaporated and the residue is partitioned between EtOAc (3 × 50 mL) and water (50 mL). The extracts are combined, washed successively with 5% HCl (30 mL),

water (30 mL), sat. aq $NaHCO_3$ (30 mL) and water. The organic phase is dried ($MgSO_4$), filtered and evaporated. The resulting amorphous solid is of sufficient purity for direct use in the next step; yield: 3.09 g (~100%). An analytical sample is obtained by preparative TLC. Elution with EtOAc/MeOH (20:1) affords **8**; mp 99–101 °C; $[\alpha]_D^{20}$ +15.3° (*c* = 0.82, $CHCl_3$).

$C_{22}H_{40}O_7N_2Si_2$	calc.	C 52.80	H 8.00	N 5.60
500	found	52.57	8.02	5.55

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.00–1.10 [m, 28 H, 4 × (CH_3)$_2$CH], 190 (s, 3 H, CH_3), 3.80 (br s, 1 H, OH), 3.90–4.00 (m, 1 H, H-5″), 4.10 (m, 2 H, H-4′,5′), 4.30–4.50 (m, 2 H, H-3′,4′), 5.65 (d, 1 H, $J_{1',2'}$ = 4.3 Hz, H-1′), 7.40 (s, 1 H, H-6), 8.90 (br s, 1 H, NH).

1-[2′-*O*-Phenoxythiocarbonyl-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-L-arabinofuranosyl]thymine (9):

To a solution of **8** (2.67 g, 5.34 mmol) in anhydrous MeCN (50 mL) is added 4-(dimethylamino)pyridine (DMAP) (1.34 g, 10.35 mmol) and phenyl chlorothionoformate[15] (1.08 mL, 5.9 mmol). The solution is stirred at r.t. for 16 h. Solvent is evaporated and the residue is partitioned between EtOAc (2 × 100 mL) and water (60 mL). The extracts are combined, washed successively with 5% HCl (60 mL), water (60 mL), sat. aq $NaHCO_3$ (60 mL) and water. The organic phase is dried ($MgSO_4$), filtered and evaporated. The resulting oil (3.39 g, 100%) is chromatographed on a silica gel column. Elution with $CHCl_3$/MeOH affords **9**; yield: 2.31 g (68%); mp 80–83 °C; $[\alpha]_D^{20}$ −14.5° (*c* = 0.55, $CHCl_3$).

$C_{29}H_{44}N_2O_8Si_2S$	calc.	C 54.70	H 6.90	N 4.40
(636.9)	found	54.90	6.90	4.23

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.00–1.10 [m, 28 H, 4 × (CH_3)$_2$CH], 1.95 (d, 3 H, $J_{CH_3,H-6}$ = 1.1 Hz, CH_3), 4.00 (ddd, 2 H, $J_{5',5''}$ = 12 Hz, H-5′,5″), 4.35 (m, 1 H, H-4′), 4.75 (t, 1 H, $J_{3',4'}$ = 7.9 Hz, H-3′), 5.95 (d, 1 H, $J_{1',2'}$ = 5.3 Hz, H-1′), 6.30 (dd, 1 H, $J_{2',3'}$ = 7.2 Hz, H-2′), 7.30 (d, 1 H, J_{H-6,CH_3} = 1.1 Hz, H-6), 7.00–7.40 (m, 5 H_{arom}), 8.50 (br s, 1 H, NH).

3′,5′-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-α-L-thymidine (10).

To a mixture of **9** (2.18 g, 3.4 mmol), AIBN (0.109 g, 0.68 mmol, 0.2 equiv), in distilled toluene (72 mL) is added Bu_3SnH (9.14 mL, 10 equiv). The solution is deoxygenated with oxygen-free N_2 and then heated at 75 °C for 3 h.[15] The solvent is evaporated and the residue is chromatographed on silica gel column. Elution with Et_2O/petroleum ether (bp 45–65 °C) (4:1) affords **10**; yield: 1.37 g (83%); mp 178–180 °C; $[\alpha]_D^{20}$ −14.6° (*c* = 0.62, $CHCl_3$).

$C_{22}H_{40}N_2O_6Si_2$	calc.	C 54.50	H 8.26	N 5.78
(484.8)	found	54.63	8.25	5.69

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.00–1.10 [s, 28 H, (CH_3)$_2$CH], 1.95 (d, 3 H, $J_{CH_3,H-6}$ = 1 Hz, CH_3), 2.10–2.25 (m, 1 H, H-2″), 2.75–2.90 (ddd, 1 H, $J_{2',2''}$, 14.1 Hz, H-2′), 3.80 (ddd, 1 H, $J_{5',5''}$ = 12.5 Hz, H-5″), 4.00–4.10 (m, 2 H, H-4′,5′), 4.60 (m, 1 H, H-3′), 6.20 (t, 1 H, $J_{1',2'}$ = 6.3 Hz, $J_{1,2''}$ = 6.0 Hz, H-1′), 7.50 (d, 1 H, J_{H-6,CH_3} = 1 Hz, H-6), 8.00 (br s, 1 H, NH).

α-L-Thymidine (11):

A mixture of **10** (1.3 g, 2.76 mmol) and Bu_4NF (1.44 g, 5.52 mmol) in THF (2.76 mL) is stirred at r.t.[15]. After completion of the reaction (0.5 h), the solvent is evaporated, and the residue is partitioned between Et_2O and water. The aqueous phase is concentrated and applied to a column of silica gel. Elution with EtOAc/MeOH (9:1) affords **11**; yield: 0.275 g (41%); mp 187–188 °C [Lit.[17] mp 188–190 °C for the α-D derivative]; $[\alpha]_D^{20}$ −10° (*c* = 1.0, H_2O) Lit.[1] $[\alpha]_D^{18}$ +4.4° (*c* = 1.0, H_2O) for the α-D-derivative.

$C_{10}H_{14}N_2O_5$	calc.	C 49.50	H 5.80	N 11.60
(242.2)	found	49.38	5.82	11.43

UV (H_2O, pH 6): λ_{max} = 267 (7000), 206 mm (6600).

^{1}H-NMR (D_2O/TMS): δ = 1.75 (s, 3 H, CH_3), 1.95–2.10 (m, 1 H, H″), 2.50–2.65 (ddd, 1 H, $J_{2',2''}$ = 13.9 Hz, H-2′), 3.40–3.60 (ddd, 2 H, $J_{5',5''}$ = 12.3 Hz, $J_{4',5'}$ = 5.2 Hz, $J_{4',5''}$ = 3.8 Hz, H-5′,5″), 4.15–4.30 (m, 2 H, H-3′,4′), 6.00 (dd, 1 H, $J_{1',2'}$ = 7.4 Hz, $J_{1',2''}$ = 3.1 Hz), 7.60 (d, 1 H, J_{H-6,CH_3} = 1 Hz, H-6).

MS (CI/NH_3): *m/z* = 243 (M + 1, 100), 260 (M + 18, 29.4).

3′-*O*-Methylsulfonyl-5′-*O*-triphenylmethyl-α-L-thymidine (12).

A solution of **11** (163 mg, 0.67 mmol) and triphenylmethyl chloride (205 mg, 0.73 mmol) in pyridine (4 mL) is refluxed for 3 h. After completion of the reaction, the mixture is allowed to cool to r.t., and methanesulfonyl chloride (0.104 mL, 1.34 mmol) is added. The mixture is kept at −10 °C for 4 d.[18] The mixture is poured into ice-water (50 mL) under stirring. After stirring for 1 h, the nucleoside is extracted with $CHCl_3$ (2 × 25 mL). The $CHCl_3$ phase is washed with water (4 × 20 mL), dried ($MgSO_4$), filtered and evaporated. The resulting crude solid (314 mg, 83%) is purified by preparative TLC. Elution with EtOAc/petroleum ether (bp 45–65 °C) (2:1) affords pure **12**; yield: 180 mg (48%); mp 170–173 °C; $[\alpha]_D^{20}$ −8.3° (*c* = 0.3, $CHCl_3$).

$C_{30}H_{30}N_2O_7S$	calc.	C 64.05	H 5.34	N 4.98
(562.65)	found	64.10	5.40	4.64

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.93 (s, 3 H, CH_3), 2.40–2.50 (m, 1 H, H-2″), 3.00 (m, 4 H, CH_3SO_2, H-2′), 3.20–3.40 (ddd, 2 H, $J_{5',5''}$ = 10.6 Hz, H-5′,5″), 4.70–4.80 (m, 1 H, H-4′), 5.20 (m, 1 H, H-3′), 6.40 (dd, 1 H, $J_{1',2'}$ = 7.1 Hz, $J_{1',2''}$ = 5.0 Hz), 7.20 (s, 1 H, H-6), 7.25–7.40 (m, 15 H_{arom}), 8.20 (br s, 1 H, NH).

1-(3′-Azido-2′,3′-dideoxy-5′-*O*-triphenylmethyl-α-L-*threo*-pentofuranosyl)thymine (13):

A solution of **12** (21.8 mg, 50 μmol) and LiN_3 (7.5 mg, 152 μmol) in DMF (0.18 mL) is heated to reflux for 3 h.[1] After completion of the reaction, the mixture is poured into ice-water (5.5 mL). Crystallization of **13** is observed and the crystals (13.7 mg) are collected. Saturation of the mother liquors with NaCl and extraction with EtOH (2 × 15 mL) affords a second crop (7 mg) after drying and evaporation; total yield: 20.7 mg (80%); mp 87–89 °C; $[\alpha]_D^{20}$ +45° (*c* = 0.6, $CHCl_3$).

$C_{29}H_{27}N_5O_4$	calc.	C 68.35	H 5.34	N 13.74
(509.6)	found	68.15	5.20	13.55

IR (KBr): *ν* = 3050 (arom CH), 2100 (N_3), 1720–1650 (C=O), 710 cm^{-1} (arom CH).

^{1}H-NMR ($CDCl_3$/TMS: δ = 1.95 (s, 3 H, CH_3), 2.20 (ddd, 1 H, $J_{2',2''}$ = 14.1 Hz, H-2″), 2.60–2.80 (m, 1 H, H-2′), 3.30–3.40 (ddd, 1 H, $J_{5',5''}$ = 9.8 Hz, $J_{4',5'}$ = 4.8 Hz, $J_{4,5''}$ = 5.4 Hz, H-5″), 3.50–3.60 (m, 1 H, H-5′), 4.20–4.40 (m, 2 H, H-3′,4′), 6.00 (t, 1 H, $J_{1',2'}$ = 6.6 Hz, $J_{1',2''}$ = 6.5 Hz, H-1′9, 7.10 (s, 1 H, H-6), 7.20–7.40 (m, 15 H_{arom}), 8.10 (br s, 1 H, NH).

1-(3′-Azido-2′,3′-dideoxy-α-L-*threo*-pentofuranosyl)thymine (14):

A solution of **13** (18 mg, 3.53 μmol) in 80% aq AcOH (0.1 mL) is refluxed for 15 min.[18] Triphenylcarbinol is removed by precipitation with water (1.5 mL) and the solvent evaporated under reduced pressure affording **14**; yield: 6 mg (64%); TLC (EtOAc, R_f = 0.52); $[\alpha]_D^{20}$ +12.8° (*c* = 0.9, DMSO).

IR (KBr): *ν* = 3500 (OH), 2100 (N_3), 1720–1650 cm^{-1} (C=O).

^{1}H-NMR (D_2O/TMS): δ = 1.90 (s, 3 H, CH_3), 2.20–2.70 (m, 2 H, H-2′,2″), 3.20–3.50 (m, 2 H, H-5′,5″), 4.20 (m, 1 H, H-3′), 4.40 (m, 1 H, H-4′), 6.05 (t, 1 H, $J_{1',2'}$ = 6.5 Hz, $J_{1',2''}$ = 6.0 Hz, H-1′), 7.10 (s, 1 H, H-6).

MS (CI/NH_3): *m/z* = 268 (M^+ + 1, 12.9), 225 (M^+ − N_3, 2.5), 127 (B^+ + 2 H, 100).

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(2) Barré-Sinoussi, F.; Chermann, J.-C.; Rey, F.; Nugeyre, M.T.; Chamaret, S.; Gruest, J.; Danguet, C.; Axler-Blin, C.; Vézinet-Brun, F.; Rouzioux, C.; Rozenbaum, W.; Montagnier, L. *Science* **1983**, *220*, 868.
(3) Mitsuya, H.; Broder, S. *Nature* **1987**, *325*, 773.
(4) Herdewijn, P.; Pauwels, R.; Baba, M.; Balzarini, J.; De Clercq, E. *J. Med. Chem.* **1987**, *30* 2131.
(5) Lin, T.S.; Chen, M.S.; McLaren, C.; Guo, Y.S.; Ghazzouli, I.; Prusoff, W.H. *J. Med. Chem.* **1987**, *30*, 440.
(6) Lin, T.S.; Guo, J.Y.; Schinazi, R.F.; Chu, C.K.; Kiang, J.N.; Prusoff, W.H. *J. Med. Chem.* **1988**, *31*, 336.
(7) Warshaw, J.A.; Watanabe, K.A. *J. Med. Chem.* **1990**, *33*, 1663.
(8) Chu, C.K.; Beach, J.W.; Ullas, G.V.; Kosugi, Y. *Tetrahedron Lett.* **1988**, *29*, 5349.
(9) Fleet, G.W.J.; Son, J.C.; Derome, A.E. *Tetrahedron* **1988**, *44*, 625.
(10) Fletcher, H.G. *Methods Carbohydr. Chem.* **1963**, *2*, 228.
(11) See for example; Rosenthal, A.; Nguyen, L. *J. Org. Chem.* **1969**, *34*, 1029.
(12) Vorbrüggen, H.; Höfle, G. *Chem. Ber.* **1981**, *114*, 1256.
(13) Holy, A. *Coll. Czech. Chem. Commun.* **1972**, *38*, 100.
(14) Markiewicz, W.T.; Wiewiorowski, M. *Nucleic Acids Res.* **1978**, *6*, 185.
(15) Robins, M.J.; Wilson, J.S.; Hansske, F.; *J. Am. Chem. Soc.* **1983**, *105*, 4059.
(16) Barton, D.H.R.; McCombie, S.W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.
(16) Yamaguchi, T.; Saneyoshi, M. *Chem. Pharm. Bull.* **1984**, *32*, 1441.
(17) Palomino, E.; Meltsner, B.R.; Kessel, D.; Horwitz, J.P. *J. Med. Chem.* **1990**, *33*, 258.
(18) Dr. Klatzmann, La Pité Hospital, Paris. The assay procedure will be reported in a later paper together with other modified nucleosides.