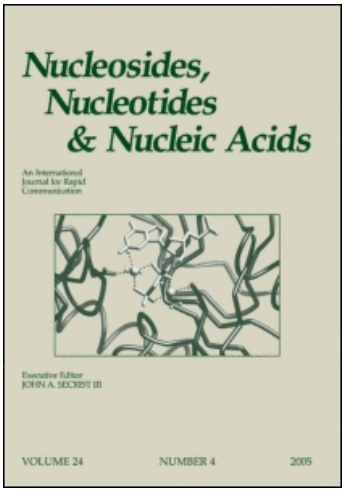

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NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS, 20(12), 1949–1960 (2001)

SYNTHESIS AND ANTI-HIV ACTIVITY OF NEW MODIFIED 1,2,3-TRIAZOLE ACYCLONUCLEOSIDES

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ABSTRACT

The synthesis of 1,2,3-triazole acyclonucleosides **7a-h** via 1,3-dipolar cycloaddition of N-9/N-1-propargylpurine/pyrimidine **2a-h** with azido-pseudo-sugar 4 is described and none of them had anti-HIV activity.

The synthesis and biological evaluation of modified nucleoside analogues have been a very active research area for a number of years[1]. In particular, several acyclonucleosides analogues are, presently, known as potent antiviral agents, among these ACV, HBG, DHPG[2,3], PMEA and HPMPA[4] derivatives. Furthermore, the importance of side-chain conformation in the interaction of acyclic nucleosides with enzymes has been noted[5], and differences in affinities for the viral thymidine kinase appear to be due to conformational factors.

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In addition, substances containing a five membered heterocyclic base are important targets in chemical synthesis because of their pronounced biological activities. Among them, ribavirin (virazole), which contains a substituted 1,2,4-triazole ring, represents the most successful one[1]. For instance, Alvarez et al[6]. have reported the synthesis and activity of a series of TSAO analogues, in which the thymine moiety of the lead compound (TSAO-T) was replaced by a series of 1,2,3-triazole substituted with different functional groups (amide, esters, ...) at the position 4 or 5. Several compounds of this class show potent anti-HIV-1 activities in comparison with the prototype (thymine) derivative, TSAO-T.

Based on these considerations and in continuation of our work on acyclonucleosides[7–9], we prepared a series of modified 1,2,3-triazole acyclonucleosides bearing a nucleobase at the position 4 or 5 of the triazole moiety. The idea behind these acyclic derivatives comes from a constraint imposed on side-chain flexibility by incorporation of 4 or 5-methylene-1,2,3-triazole as a spacer arm which would result in a better conformation for enzyme interaction[10].

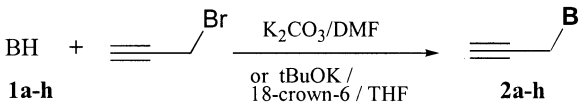
RESULTS AND DISCUSSION

The most common method described in literature for the preparation of 1,2,3-triazole rings is the 1,3-dipolar cycloaddition[11,12] between substituted acetylenes as dipolarophiles and alkyl azide derivatives. Thus, uracil **1a** was treated with propargyl bromide in the presence of K_2CO_3 in DMF[13], after 24 h reaction gave *N*-1-isomer **2a** and the *N*-1,*N*-3-dialkylated isomer as side product. The desired product was obtained via column chromatography in 50% yield (Table 1) (Sch. 1). These conditions were used for the preparation of **2b-d** and **2f-h** For the iodouracil derivative **2e** solid-liquid phase transfer

Table 1. *N*-Alkylation of Heterocyclic Bases with Propargyl Bromide

Base	Condition	Time (h)	Yield %[a]
Thymine	K_2CO_3/DMF	3	65
Uracil	K_2CO_3/DMF	3	50
5-Chlorouracil	K_2CO_3/DMF	1	56
5-Bromouracil	K_2CO_3/DMF	1	63
5-Iodouracil	tBuOK/18-Crown/THF	0.5	62
5-Fluorouracil	K_2CO_3/DMF	1	70
Adenine	K_2CO_3/DMF	2	70
N-2-Ac-guanine[b]	K_2CO_3/DMF	3	72

[a] yield of *N*-alkylated nucleobases (**2a-h**).
[b] ratio *N*-7:*N*-9 was 5:5.

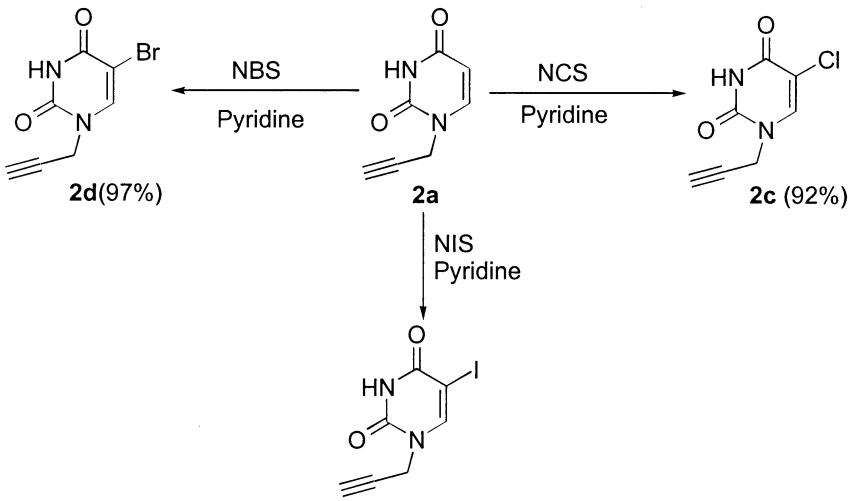


a: B = Thymin-1-yl, **b**: B = Uracil-1-yl, **c**: B = 5-Chlorouracil-1-yl, **d**: B= 5-Bromouracil-1-yl, **e**: B = 5-Iodouracil-1-yl, **f**: B = 5-Fluorouracil-1-yl, **g**: B = Adenin-9-yl, **h**: B = *N*-2-Acetylguanin-9-yl.

Scheme 1.

catalysis (tBuOK/18-crown-6/THF)[14] gave the desired product in 62% yield (Table 1).

An alternative route was explored to obtain the products **2c**, **2d** and **2e** using the *N*-1-propargyluracil **2a** as starting material, followed by halogenations at the C-5 position. Treatment of **2a** with *N*-bromo-, *N*-chloro- or *N*-iodosuccinimide in pyridine afforded the corresponding compounds **2c**, **2d** and **2e** in good yield (Sch. 2).

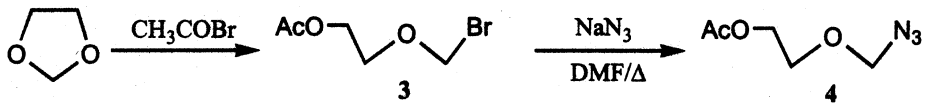


Scheme 2.

The structure of these compounds was confirmed using ^{1}H NMR, elemental analysis and UV spectroscopy.

Acyclic intermediate **3** was prepared according to the literature[15] and it was easily transformed to the corresponding azido derivative **4**[16] (Sch. 3).

We therefore investigated the cycloaddition of this azide **4** with electron deficient alkynes **2a-h**. It was necessary to select conditions which were sufficiently mild to avoid the thermal degradation of the azide. Thus cycloaddition of the azide **4** with **2a-h** occurred smoothly in refluxing toluene



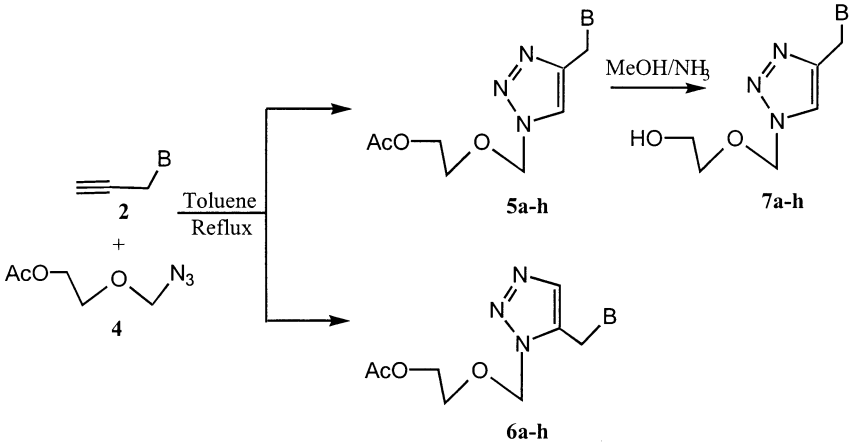
Scheme 3.

(110 °C) and the triazole acyclonucleosides **5a-h** and **6a-h** thus formed (Sch. 4), were separated using column chromatography, as a mixture of regioisomers. Only the major isomers **5a-h** were obtained as pure products.

It has been reported, that addition of azides to unsymmetrical acetylenes is determined by steric and electronic factors. In general, such addition tends to give mainly the isomers with electron-withdrawing groups at the 4-position and electron releasing groups at the 5-position. On the other hand, the sterically less hindered isomer tends to be the major isomer[7].

The structure of the two isomers was established by comparison of the chemical shift values for the triazole ring protons with those available from a known pair of 4- and 5-TSAO 1, 2, 3-triazole derivatives[7]. In the case of the 4-substituted isomers **5** the signal of H-5 proton appeared at lower field (7.74–8.23 ppm) than the signal of H-4 proton (6.90–7.75 ppm) in the 5-substituted derivatives **6**.

A common feature of many acyclic nucleoside analogues with antiviral activity, including ACV and HBG, is the presence of a primary alcoholic group. The later function and the nucleic acid base are essential for the antiviral activity. For this purpose deprotected products **7a-h** were obtained in good yield by treating compounds **5a-h** with ammonia in methanol at room temperature (Sch. 4).



a: B = Thymin-1-yl, **b**: B = Uracil-1-yl, **c**: B = 5-Chlorouracil-1-yl, **d**: B = 5-Bromouracil-1-yl, **e**: B = 5-Iodouracil-1-yl, **f**: B = 5-Fluorouracil-1-yl, **g**: B = Adenin-9-yl, **h**: B = N-2-Acetylguanin-9-yl.

Scheme 4.

Table 2. 1,3-Dipolar Cycloaddition of *N*-Propargyl Pyrimidine/Purine Derivatives with Acyclic Azide 4

Substrate	Yield %	Ratio* **5:6**
2a	74	91:9
2b	84	100:0
2c	70	100:0
2d	68	78:22
2e	82	100:0
2f	76	86:14
2g	65	74:26
2h	60	75:25

* The ratios were determined from ^{1}H NMR spectra.

Table 3. Chemical Shifts (δ, ppm) of H-5, H-4

Compound	H-5	H-4
5a/6a	7.74	6.90
5b/6b	8.06	–
5c/6c	8.23	–
5d/6d	8.09	7.73
5e/6e	8.09	–
5f/6f	8.08	7.70
5g/6g	8.08	7.65
5h/6h	8.00	7.75

Antiviral Activity

Compounds **2a-h**, **5a-f** and **7a-h** were evaluated for their inhibitory effect against the cytopathic effect of HIV-1 (III_B) and HIV-2 (ROD) in MT-4 cells[17]. No activity was observed against the replication of these viruses at compound concentrations up to 100 μg/mL.

EXPERIMENTAL

Melting points (mp) were determined on a electrothermal digital melting point apparatus and were uncorrected. Ultraviolet spectral (UV) were recorded with a Cary 219 spectrometer. The ^{1}H NMR spectra were recorded using a Brucker AC 250 MHz spectrometer. T (1,2,3-triazole) and B (heterocyclic base). Mass spectra (MS) were obtained with JEOL JMS DX 300 instrument using fast atomic bombardment (FAB^+). Thin layer chromato-

graphy was performed on plates of Kieselgel 60 F254 (Merck) and short-wave ultraviolet light (254 nm) was used to detect the UV-absorbing spots. Column chromatography separation was carried out on silica gel (0.063–0.2 mm, Merck). Elemental analysis was determined by the French Micro-analytical Central Service.

Preparation of *N*-1/*N*-9-propargylpyrimidine/Purine

Method A: To a suspension of heterocylic base (4 mmol) and anhydrous potassium carbonate (4 mmol) in 50 mL of DMF, was added 12 mmol of propargyl bromide. The mixture was stirred at room temperature for the required time. Removal of the solvent and column chromatography on silica gel afforded the pure product.

Method B: To a solution of **2b** (2 mmol) in pyridine (30 mL) was added *N*-halogenosuccinimide (NCS, NBS or NIS) (4 mmol). The mixture was stirred for 30 min at 100 °C and then a saturated aqueous $NaHCO_3$ solution (50 mL) was added. The mixture was extracted with $CHCl_3$ (3×50 mL). The organic phase was dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography.

Method C: To a solution of of 18-crown-6 (1 mmol) in dry THF (40 mL) under nitrogen atmosphere was added potassium tert-butoxide (10 mmol). Then the heterocyclic base (10 mmol) was added, and the reaction mixture was stirred at room temperature for 15 min. At this time propargyl bromide (10 mmol) was added dropwise with stirring. When the addition was finished, the mixture was stirred at 25 °C for 3 h. The residue was then filtered and evaporated to dryness in vaccuo and chromatographed on silica gel column.

N-1-Propargylthymine 2a

Method A: Eluent 99/1, v/v CH_2Cl_2/MeOH; yield 56%; mp 154–156°C (CH_2Cl_2/ether); ^{1}H NMR (DMSO-d_6) δ 1.76 (s, 3H, CH_3), 3.40 (t, 1H, CH, $J = 2.2$ Hz), 4.46 (d, 2H, CH_2-N, $J = 2.1$ Hz), 7.56 (s, 1H, H-6), 11.4 (s, 1H, NH); UV (MeOH) λ_{max} 271 nm; FAB-MS m/z 165 $(M+H)^+$.

N-1-Propargyluracil 2b

Method A: yield 50%; ^{1}H NMR (DMSO-d_6) δ 3.41 (t, 1H, CH, $J = 2.3$ Hz), 4.51 (d, 2H, CH2-N, $J = 2.3$ Hz), 5.62 (d, 1H, H-5, $J = 7.8$ Hz), 7.7 (d, 1H, H-6, $J = 7.8$ Hz), 11.3 (s, 1H, NH); UV (MeOH) λ_{max} 261 nm; mp 154–166°C (CH_2Cl_2/ether); FAB-MS m/z 151 $(M+H)^+$.

N-1-Propargyl-5-chlorouracil 2c

Method A: yield: 46%; **Method B**: yield 92%; mp 168–170°C (CH_2Cl_2/ether); ^{1}H NMR (DMSO-d_6) δ 3.46 (t, 1H, CH, $J = 2{,}4$ Hz), 4.50 (d, 2H, CH^2-N, $J = 2{,}4$ Hz), 8.20 (s, 1H, H-6), 11.86 (s, 1H, NH); UV(-MeOH) λ_{max} 276 nm; FAB-MS m/z 185 (M+H).$^+$

N-1-Propargyl-5-bromouracil 2d

Method A: yield 42%; **Method B**: yield 97%; mp 172–174°C (CH_2Cl_2/ether); ^{1}H NMR (DMSO-d_6) δ 3.45 (t, 1H, CH, $J = 2{,}4$ Hz), 4.51 (d, 2H, CH_2-N, $J = 2{,}4$ Hz), 8.26 (s, 1H, H-6), 11.91 (s, 1H, NH); UV (MeOH) λ_{max} 278 nm; FAB-MS m/z 230 (M+H).$^+$

N-1-Propargyl-5-iodouracil 2e

Method A: yield 62%; **Method B**: yield 50%; mp 179–181°C (CH_2Cl_2/ether); ^{1}H NMR (DMSO-d_6) δ 3.42 (t, 1H, CH, $J = 2{,}6$ Hz), 4.58 (d, 2H, CH_2-N, $J = 2{,}6$ Hz), 8.28 (s, 1H, H-6), 12,02 (s, 1H, NH), UV (MeOH) λ_{max} 282 nm; FAB-MS m/z 273 (M +H).$^+$

N-1-Propargyl-5-fluorouracil 2f

Method A: yield 52%; mp 146–148 °C (CH_2Cl_2/ether); ^{1}H NMR (DMSO-d_6) δ 3.46 (t, 1H, CH, $J = 2{,}4$ Hz), 4.60 (d, 2H, CH_2-N, $J = 2{,}4$ Hz), 8.25 (d, 1H, H-6, $J = 6{,}6$ Hz), 11.96 (s, 1H, NH); UV (MeOH) λ_{max} 270 nm; FAB-MS m/z 169 (M+H).$^+$

N-9-Propargyl-*N*-2-acetylguanine 2h

Method A: yield 35%; mp 285–286 °C (CH_2Cl_2/ether); ^{1}H RMN (DMSO-d_6) δ 2.00 (s, 3H, CH_3CON), 3.55 (t, 1H, CH, $J = 2.5$ Hz), 4.95 (d, 2H, CH_2-N, $J = 2.5$ Hz), 7.35(bs, 2H, NH_2), 8.08 (s, 1H, H-8); UV (H_2O) λ_{max} 259, 280 nm; FAB-MS m/z 233 (M+H).$^+$

N-9-Propargyladenine 2g[13]

Method A: yield 80%; ^{1}H NMR DMSO-d6) δ 3.55 (t, 1H, CH, $J = 2.5$ Hz), 5.07 (d, 2H, CH_2-N, $J = 2.5$ Hz), 7.35 (sl, 2H, NH_2), 8.20 and 8.25 (2s, 2H, H-2 and H-8); UV (MeOH) λ_{max} 260 nm; mp 213–214 °C (CH_2Cl_2/MeOH); FAB-MS m/z 174 (M+H).$^+$

General Procedure for the Synthesis of Compounds 5a-h

A solution of 12.5 mmol alkylazide and 2.5 mole of *N*-1/*N*-9-propargylpyrimidine/purine in anhydrous toluene (40 mL) were heated under reflux for 2 to 3 days (see Table 1). Evaporation of the solvent furnished a mixture of compounds **5** and **6**. Ratio of **5**/**6** was determined by ^{1}H NMR based on the integration of triazole protons H-4 (1,5-isomer) and H-5 (1,4-isomer), after purification by silica gel column chromatography.

1-[[1-((4-Acetoxyethoxy)methyl) -1,2,3-triazol-4-yl] methyl]thymine 5a. Yield 60% as a white solid; ^{1}H NMR ($CDCl_3$) δ 1.91 (s, 3, CH_3), 2.06 (s, 3, CH_3CO), 3.74 (t, 2, CH_2, $J = 4.6$ Hz), 4.18 (t, 2, CH_2), 4.99 (s, 2, T-CH_2-B), 5.71 (s, 2, O-CH_2-N), 7.35 (s, 1, H_6), 7.92 (s, 1, H-5′), 9.28 (s, 1, NH); MS (EI) m/z 323 (M^+); UV (MeOH) λ_{max} 272 nm, mp 152–154 °C (EtOH-ether), Anal. calcd. for $C_{13}H_{17}N_5O_5$: C, 48.30; H, 5.30; N, 21.66. found, C, 48.18; H, 5.27; N, 21.85.

1-[[1-((4-Acetoxyethoxy)methyl)-1,2,3-triazol-4-yl] methyl]uracil 5b. Yield 63%; ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 3, CH_3CO), 3.74 (t, 2, CH_2, $J = 4.0$ Hz), 4.18 (t, 2, CH_2), 5.01 (s, 2, T-CH_2-B), 5.72 (s, 2, O-CH_2-N), 5.74 (d, 1, H5, $J = 7.5$ Hz), 7.51 (d, 1, H-6), 7.91 (s, 1, H-5′), 9.26 (s, 1, NH); MS (EI) m/z 309 (M^+); UV (MeOH) λ_{max} 265 nm; mp 148–150 °C; Anal. calcd. for : $C_{12}H_{15}N_5O_5$: C, 46.60; H, 4.89; N, 22.64; found, C, 46.02; H, 4.89; N, 22.75.

1-[[1-((4-Acetoxyethoxy)methyl)-1,2,3-triazol-4-yl] methyl] 5-chlorouracil 5c. Yield 57%; ^{1}H NMR ($CDCl_3$) δ 2.05 (s, 3, CH_3CO), 3.74 (t, 2, CH_2, $J = 4.5$ Hz), 4.17 (t, 2, CH_2, $J = 4.5$ Hz), 5.00 (s, 2, T-CH_2-B), 5.72 (s, 2, O-CH_2-N), 7.80 (s, 1, H-6), 7.95 (s, 1, H-5′), 9.88 (s, 1, NH); MS (EI) m/z 343 (M^+); UV (MeOH) λ_{max} 278 nm; mp102–104 °C (EtOH-ether); Anal. calcd. for $C_{12}H_{14}N_5O_5Cl$: C, 41.93; H, 4.11; N, 20.37; found, C, 42.18; H, 4.09; N, 20.53.

1-[[1-((4-Acetoxyethoxy)methyl)-1,2,3-triazol-4-yl] methyl] bromouracil 5d. Yield 45%; ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 3, CH_3CO), 3.75 (t, 2, CH_2CH_2, $J = 4.6$ Hz), 4.18 (t, 2, $AcOCH_2$), 5.03 (s, 2, T-CH_2-B), 5.72 (s, 2, O-CH_2-N), 7.89 (d, 1, H-5′), 7.90 (s,1, H-6), 9.04 (s, 1, NH); MS (EI) m/z 387 (M^+); UV (MeOH) λ_{max} 279 nm; mp 143–145 °C (EtOH/ether); Anal. calcd. for $C_{12}H_{14}N_5O_5Br$: C, 37.13; H, 3.64; N, 18.04, found, C, 37.18; H, 3.53; N; 18.11.

1-[[1-((4-Acetoxyethoxy)methyl)-1,2,3-triazol-4-yl] methyl]iodouracil 5e. Yield 67%; ^{1}H NMR (DMSO-d_6) δ 2.0 (s, 3, CH_3CO), 3.60 (t, 2, CH_2, $J = 4.6$ Hz), 4.15 (t, 2, CH_2, $J = 4.6$ Hz), 5.0 (s, 2, T-CH_2-B), 5.80 (s, 2,

O-CH_2-N), 8.30 (s, 1, H-6), 8.38 (s 1, H-5′), 11.8 (s, 1, NH); MS (EI) m/z 435 (M^+); UV (MeOH) λ_{max} 282 nm; mp 147–149 °C (EtOH/ether), Anal. calcd. for $C_{12}H_{14}N_5O_5I$.: C, 33.12; H, 3.24; N, 16.09; found, C, 32.97; H, 3.26; N, 16.31.

1-[[1-((4-Acetoxyethoxy)methyl)-1,2,3-triazol-4-yl] methyl]fluorouracil 5f. Yield 54%, ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 3, CH_3CO), 3.75 (t, 2, CH_2, $J = 4.6$ Hz), 4.18 (t, 2, CH_2), 5.00 (s, 2, T-CH_2-B), 5.73 (s, 2, O-CH_2-N), 7.65 (d, 1, H-6), 7.93 (s, 1, H-5′), 9.71 (s, 1, NH); MS (EI) m/z 327 (M^+); UV (MeOH) λ_{max} 269 nm; mp 124–126 °C (EtOH); Anal. calcd. for $C_{12}H_{14}N_5O_5F$: C, 44.07; H, 4.31; N, 1.41; found, C, 44.23; H, 4.26; N, 21.52.

9-[[1-((4-Acetoxyethoxy)methyl)-1,2,3-triazol-4-yl] methyl]adenine 5g. Yield 47%, ^{1}H NMR (DMSO-d_6) δ 1.9 (s, 3, CH_3COO), 3.6 (t, 2, OCH_2), 4.0 (t, 2, OCH_2), 5.4 (t, 2, T-CH_2-B), 5.65 (s, 2, O-CH_2-N), 7.15 (bs, 2, NH2), 8.08 (s, 1, H-5′), 8.14 and 8.19 (2s, 2, H-2 + H-8); UV (EtOH): λ_{max} 261 nm; FAB-MS m/z 333 (M +H).

9-[[1-((4-Acetoxyethoxy)methyl)-1,2,3-triazol-4-yl]methyl]N-2-acetyl guanine 5h. Yield 42%, ^{1}H NMR ($CDCl_3$) δ 2.1 (s, 3, CH_3COO), 2.4 (s, 3, CH_3CON), 3.7 (t, 2, OCH_2), 4.2 (t, 2, OCH_2), 5.65 (t, 2, T-CH_2-B), 5.75 (s, 2, OCH_2N), 8.0 (s, 1, H-5′), 8.1 (s, 1, H-8); UV (H_2O) $\lambda_{max} = 256, 274$ nm; FAB-MS m/z 391 (M +H).$^+$

Deprotection Method

To 1 mole of the acetylated acyclonucleoside was added 45 mL of methanol saturated with ammonia at 0 °C. The flask was stopped tightly and the solution was stirred for 24 h at room temperature. Thin-layer chromatography indicated that complete deprotection of acyclonucleoside had occurred. Volatile materials were evaporated and the residue was purified by chromatography.

1-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl] thymine 7a. Yield 87%, ^{1}H NMR (DMSO-d_6) δ 3.46 (m, 4, CH_2CH_2), 4.57 (m, 1, OH), 4.91 (s, 2, T-CH_2-B), 5.69 (s, 2, OCH_2N), 7.62 (s, 1, H-6), 8.21 (s, 1, H-5′), 11.31 (s, 1, NH); MS (EI) m/z 281(M^+); UV (MeOH) λ 270 nm (ε 9400); mp 164–166 °C (EtOH); Anal. calcd. for $C_{11}H_{15}N_5O_4$.: C, 46.97; H, 5.38; N, 24.90, found, C, 46.96; H, 5.14; N, 24.94.

1-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl] uracil 7b. Yield 92%, ^{1}H NMR (DMSO-d_6) δ 3.40 (m, 2, CH_2), 3.74 (m, 2, CH_2OH), 4.67 (m, 1, OH), 4.95 (s, 2, T-CH_2-B), 5.70 (s, 2, OCH_2N), 7.75

(d, 1, H-6, $J = 7.4$ Hz), 8.21 (s, 1, H-5′), 11.29 (s, 1, NH); MS (EI) m/z 267 (M^+); UV (MeOH) λ_{max} 262 nm (ε 12200); mp 224–226 °C (EtOH), Anal. calcd. for $C_{10}H_{13}N_5O_4$.: C, 44.94; H, 4.90; N, 26.21; found, C, 44.73; H, 4.94; N, 26.48.

1-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl] 5-chlorouracil 7c. Yield 79%, ^{1}H NMR (DMSO-d6) δ 3.46 (m, 4, CH_2CH_2), 4.74 (m, 1, OH), 4.96 (s, 2, T-CH_2-B), 5.69 (s, 2, OCH_2N), 8.25–8.26 (2s, 2, H-5′, H-6), 11.86 (s, 1, NH); MS (EI) m/z 301(M^+); UV (MeOH) λ_{max} 277 nm (ε 10000), mp 144–146 °C (EtOH); Anal. calcd. for $C_{10}H_{12}N_5O_4Cl$: C, 39.81; H, 4.01; N, 23.21;. found, C, 39.85; H, 4.13; N, 23.22.

1-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl] 5-bromouracil 7d. Yield 82%, ^{1}H NMR (DMSO-d_6) δ 3.47 (m, 4, CH_2CH_2), 4.70 (m, 1, OH), 4.96 (s, 2, T-CH_2-B), 5.70 (s, 2, OCH_2N), 8.25 (s, 1, H-6), 8.35 (s, 1, H-5′), 11.83 (s,1,NH); MS (EI) m/z 346 (M^+); UV (MeOH) λ_{max} 280 nm (ε 9800); mp 217–219 °C (EtOH); Anal. calcd. for $C_{10}H_{12}N_5O_4Br$: C, 34.70; H, 3.49; N, 20.23;. found, C, 34.59; H, 3.52; N, 20.22.

1-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl] 5-iodouracil 7e. Yield 82%, ^{1}H NMR (DMSO-d_6) δ 3.50 (m, 4, CH_2CH_2), 4.74 (m, 1, OH), 4.99 (s, 2, T-CH_2-B), 5.73 (s, 2, OCH_2N), 8.27 (s, 1, H-6), 8.36 (s, 1, H-5′), 11.72 (s, 1, NH); MS (EI) m/z 394 (M^+); UV (MeOH) λ_{max} 282 nm (ε 4900); mp 160–162 °C (EtOH); Anal. calcd. for $C_{10}H_{12}N_5O_4I$.: C, 30.55; H, 3.08; N, 17.81; found, C, 30.61; H, 3.06; N, 17.86.

1-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl] 5-fluorouracil 7f. Yield 74%, ^{1}H NMR (DMSO-d_6) δ 3.46 (m, 4, CH_2CH_2), 4.72 (m, 1, OH), 4.91 (s, 2, T-CH_2-B), 5.70 (s, 2, OCH_2N), 8.21 (d, 1, H-6), 8.25 (s, 1, H-5′), 11.84 (s, 1, NH); MS (EI) m/z 286 (M^+); UV (MeOH) λ_{max} 269 nm (ε 8200); mp 125–127 °C (EtOH); Elem. Anal. calcd for $C_{10}H_{12}N_5O_4F$: C, 42.14; H, 4.24; N, 24.57. found, C, 42.26; H, 4.35; N, 24.29.

9-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl]adenine 7g. Yield 74%, ^{1}H NMR (DMSO-d_6) δ 3.4 (m, 4, CH_2CH_2), 4.65 (sl, 1, OH), 5,45 (s, 2, T-CH_2-B), 5.7 (s, 2, OCH_2N), 7.22 (bs, 2, NH_2), 8.05 (s, 1, H-5′), 8.20 and 8.25 (2s, 2, H-2 + H-8); UV (0.1N HCl) λ_{max} 260 nm; FAB-MS m/z 291 (M+H);$^+$ Anal. calcd. For $C_{11}H_{14}N_8O_2$: C, 45.51; H, 4.86; N, 38.60; found, C, 45.58; H, 4.97; N, 38.74.

9-[1-[(4-Hydroxyethoxy)methyl]-1,2,3-triazol-4-yl] methyl]guanine 7h. Yield 65%, ^{1}H NMR (DMSO-d_6) δ 3.5 (m, 4, CH_2CH_2), 4.65 (sl, 1, OH), 5.55 (s, 2, T-CH_2-B), 5.7 (s, 2, OCH_2N), 6.3 (bs, 2, NH_2), 8.0 (s, 1, H-5), 8.2 (s, 1, H-8); UV (H_2O) λ_{max} 256; 278 nm, FAB-MS m/z 307 (M+H).$^+$

Anal. calcd. for $C_{11}H_{14}N_8O_3$: C, 43.13; H, 4.61; N, 36.58; found, C, 43.24; H, 4.75; N, 36.64.

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