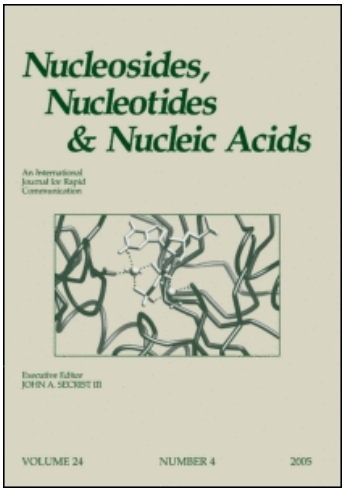


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# Synthesis of Bridged Pyrimidine Nucleosides and Triazo [4, 3-c] Pyrimidine Nucleoside Analogues

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# SYNTHESIS OF BRIDGED PYRIMIDINE NUCLEOSIDES AND TRIAZO [4,3-c] PYRIMIDINE NUCLEOSIDE ANALOGUES

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ABSTRACT

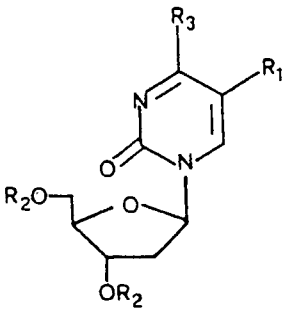
The synthesis and the spectral characterization of a number of $N^4$-$N^4$ bridged pyrimidine nucleosides and triazo [4,3-c] pyrimidine nucleoside analogues are reported.

## INTRODUCTION

Naturally occurring pyrimidine nucleosides and their derivatives play a very important role in the life of a cell and, therefore, it is not surprising that various pyrimidine nucleoside analogues exhibit important biological properties, such as anticancer and/or antiviral activity, inhibiting the DNA synthesis or interfering with enzymes of the nucleic acids metabolism[1-3].

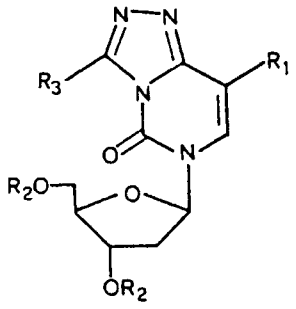
As a part of our studies on pyrimidine nucleoside analogues[4-6], we wish to report here the chemical synthesis and spectroscopic characterization of compounds 5-18.

The bridged nucleosides 7-14, could be of interest as models for studies of enzyme inhibition mechanism to explain



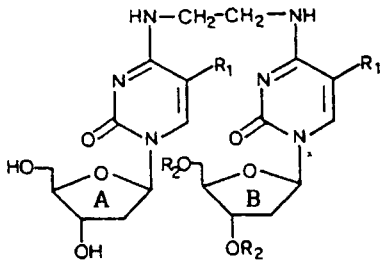
1 - 6

| Compound | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| 1 | $CH_3$ | $COCH_3$ | Cl |
| 2 | H | $COCH_3$ | Cl |
| 3 | $CH_3$ | H | $NHCH_2CH_2NH_2$ |
| 4 | $CH_3$ | H | $NHNH_2$ |
| 5 | H | H | $NHCH_2CH_2NH_2$ |
| 6 | H | H | $NHNH_2$ |



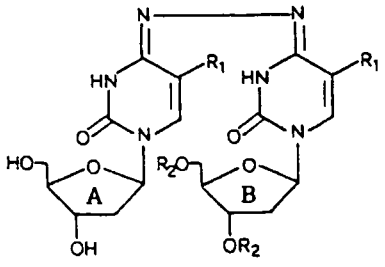
15 - 18

| Compound | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| 15 | $CH_3$ | $COCH_3$ | $CH_3$ |
| 16 | $CH_3$ | H | $CH_3$ |
| 17 | $CH_3$ | H | H |
| 18 | H | H | H |



7 - 10

| Compound | $R_1$ | $R_2$ |
|---|---|---|
| 7 | $CH_3$ | $COCH_3$ |
| 8 | H | $COCH_3$ |
| 9 | $CH_3$ | H |
| 10 | H | H |



11 - 14

| Compound | $R_1$ | $R_2$ |
|---|---|---|
| 11 | $CH_3$ | $COCH_3$ |
| 12 | H | $COCH_3$ |
| 13 | $CH_3$ | H |
| 14 | H | H |

the anticancer activity of certain alkylating bifunctional agents[7-9]. Moreover, studies concerning the effect on the growth of the neuroblastoma cells and on DNA synthesis, in order to evaluate the therapeutic potential of the new compounds are currently in progress.

As for the triazo[4,3-c]pyrimidine nucleosides 15-18, it is to be noted that nucleoside analogues which show an alterated nitrogen pattern are of wide biological interest[10]. In fact, the structural similarity of 15-18 with purine nucleosides could enable them to emulate or antagonize the biological functions of naturally occurring metabolites of this class. Particularly, we are going to synthesize oligodeoxyribonucleotides which incorporate compounds 16-18 in the recognition sequence of endodeoxyribonucleases with the aim of studying the interaction of the resulting oligomers with the pertinent enzymes[11,12].

Our approach to the synthesis of compounds 7-18 involves in the first step the reaction of the chlorinated compounds 1[4] and 2[5] with the appropriate nucleophilic reagent.

5[8], 1-(2-deoxy-ß-D-ribofuranosyl)-4-(2-aminoethyl)-aminopyrimidin-2(1H)-one, as well as 3[6], 1-(2-deoxy-ß-D-ribofuranosyl)-4-[(2-aminoethyl)amino]-5-methylpyrimidin-2(1H)--one, was prepared starting from 2 by reaction with ethylenediamine.This reagent also causes the aminolysis of the ester functions. The preparation of the hydrazino derivatives 4[6], 1-(2-deoxy-ß-D-ribofuranosyl)-4-hydrazino-5-methylpyrimidin-2(1H)-one, and 6, 1-(2-deoxy-ß-D-ribofuranosyl)-4-hydrazinopyrimidin-2(1H)-one, involved 1 and 2 as well, through the reaction with anhydrous hydrazine which causes the concomitant hydrazinolysis of the acetates. In the case of the bridged nucleosides 7 and 8, compounds 1 and 2 were reacted

Table 1. - $^1$H NMR (250 MHz) Chemical shifts* ( $\delta$ ) of compounds 7-14

| Position | 7 $CD_3OD$ | 8 $C_5D_5N$ | 9 $CD_3OD$ | 10 $C_5D_5N$ | 11 $CD_3OD$ | 12 $C_5D_5N$ | 13 $C_5D_5N$ | 14 $C_5D_5N$ |
|---|---|---|---|---|---|---|---|---|
| | | 6.12 d | | | | 5.92 d | | |
| 5 | | | | 5.96 d | | | | 5.83 d |
| | | 6.11 d | | | | 5.85 d | | |
| | 7.80 bs | 8.32 d | | | 7.25 bs | 7.79 d | | |
| 6 | | | 7.77 bs | 8.28 d | | | 7.59 bs | 7.76 d |
| | 7.49 bs | 7.85 d | | | 6.97 bs | 7.28 d | | |
| | 1.97 s | | | | 1.95 bs | | | |
| $CH_3$ | | | 1.95 bs | | | | 1.72 bs | |
| | 1.95 bs | | | | 1.95 bs | | | |
| A | 6.29 m | 6.96 dd | | | 6.30 dd | 6.97 dd | | |
| 1' | | | 6.29 dd | 7.03 dd | | | 7.00 dd | 6.98 dd |
| B | 6.29 dd | 6.74 dd | | | 6.26 dd | 6.66 dd | | |
| A | 2.35 m | 2.88- | | | 2.22 m | 2.60- | | |
| | 2.52 m | -2.37 | 2.17 m | 2.54 m | | -2.37 | | |
| 2' | | comp. | 2.35 m | 2.76 m | | comp. | 2.53 m | 2.51 m |
| | | sign. | | | | sign. | | |
| B | 2.25 m | | | | 2.27 m | | | |
| A | 4.39 m | 5.00 m | | | 4.43 m | 4.95 m | | |
| 3' | | | 4.42 m | 4.97 m | | | 4.98 m | 4.96 m |
| B | 5.28 m | 5.45 m | | | 5.27 m | 5.43 m | | |
| A | 3.95 m | 4.42 m | | | 3.91 m | 4.43 m | | |
| 4' | | | 3.95 m | 4.47 m | | | 4.43 m | 4.43 m |
| B | 4.30 m | 4.49 m | | | 4.26 m | 4.35 m | | |
| A | 3.81 | 4.20 m | | | 3.78 m | 4.13 m | | |
| 5' | | | 3.81 m | 4.18 m | | | 4.13 m | 4.12 m |
| B | 4.40 m | 4.56 m | | | 4.36 m | 4.51 m | | |
| | 2.13 s | 2.30 s | | | 2.16 s | 2.03 s | | |
| $2CH_3CO$ | | | | | | | | |
| | 2.12 s | 2.00 s | | | 2.12 s | 1.99 s | | |
| $CH_2CH_2$ | 3.71 bs | 3.95 bs | 3.70 bs | 3.90 s | | | | |

* The assignments of the signals of the sugar moieties A and B were supported by extensive spin decoupling experiments.

with 3 and 5 respectively in dimethylformamide at room temperature for 10 hrs.The bridged nucleosides 11 and 12 were synthesized by reaction of 1 and 2 with 4 and 6 respectively in dimethylformamide at 0°C for 8 hrs. Compounds 7, 8, 11 and 12 were purified by silica gel chromatography and their structures confirmed by elemental analyses and spectral data [ MS, $^1$H and $^{13}$C NMR (Tables 1-2), UV ].

Table 2. – $^{13}C$ NMR (62.9 MHz) Chemical shifts ( $\delta$ ) of compounds 7-14[a]

| Position | 7 $CD_3OD$ | 8 $C_5D_5N$ | 9 $CD_3OD$ | 10 $(CD_3)_2SO$ | 11 $CD_3OD$ | 12 $C_5D_5N$ | 13 $C_5D_5N$ | 14 $C_5D_5N$ |
|---|---|---|---|---|---|---|---|---|
| | 165.4 | 164.9 | | | 151.3 | | | |
| 2 | | | 165.5 | 163.4 | | b | b | b |
| | 165.3 | 164.8 | | | 151.2 | | | |
| | 159.3 | 157.3 | | | 149.5 | 149.0 | | |
| 4 | | | 158.4 | 155.0 | | | 148.6 | 147.8 |
| | 158.4 | 156.7 | | | 149.0 | 147.9 | | |
| | 105.3 | 96.4 | | | 111.3 | 102.3 | | |
| 5 | | | 104.8 | 94.7 | | | 109.0 | 101.7 |
| | 104.8 | 95.9 | | | 110.7 | 101.4 | | |
| | 138.9 | 140.8 | | | 131.1 | 134.0 | | |
| 6 | | | 138.9 | 139.9 | | | 130.7 | 132.6 |
| | 137.8 | 139.6 | | | 129.9 | 132.4 | | |
| | 13.2 | | | | 13.2 | | | |
| $CH_3$ | | | 13.1 | | | | 12.8 | |
| | 13.1 | | | | 13.1 | | | |
| | 88.7 | 88.9 | | | 88.4 | 88.6 | | |
| 1' | | | 88.8 | 87.1 | | | 88.6 | 88.8 |
| | 87.4 | 86.9 | | | 85.7 | 85.3 | | |
| | 41.9 | 42.2 | | | 40.5 | 40.8 | | |
| 2' | | | 41.9 | 40.4 | | | 40.7 | 40.9 |
| | 38.6 | 38.1 | | | 37.1 | 36.7 | | |
| | 87.4 | 86.9 | | | 85.7 | 85.3 | | |
| 3' | | | 87.5 | 84.8 | | | 85.2 | 85.2 |
| | 83.6 | 82.7 | | | 83.1 | 82.2 | | |
| | 72.0 | 71.4 | | | 72.4 | 71.7 | | |
| 4' | | | 72.0 | 70.3 | | | 71.7 | 71.9 |
| | 75.9 | 75.2 | | | 75.9 | 74.9 | | |
| | 62.8 | 62.5 | | | 63.1 | 62.6 | | |
| 5' | | | 62.9 | 61.3 | | | 62.6 | 62.7 |
| | 65.0 | 64.5 | | | 65.1 | 64.4 | | |
| | 20.7 | 20.7 | | | 20.8 | 20.6 | | |
| $2\underline{CH_3}CO$ | | | | | | | | |
| | 20.7 | 20.6 | | | 20.8 | 20.5 | | |
| | 41.8 | 40.9 | | | | | | |
| $CH_2\underline{CH_2}$ | | | 41.9 | b | | | | |
| | 41.8 | 40.9 | | | | | | |
| | 172.0 | 170.5 | | | 172.2 | 170.3 | | |
| $2CH_3\underline{CO}$ | | | | | | | | |
| | 172.0 | 170.5 | | | 172.2 | 170.3 | | |

a. confirmed by DEPT experiments.
b. submerged by the solvent signals.

Table 3. - $^{1}H$ NMR (250 MHz)[a] and $^{13}C$ NMR (62.9 MHz)[b] Chemical shifts of compounds 15-18.

| | 15 | | 16 | | 17 | | 18 | |
|---|---|---|---|---|---|---|---|---|
| Position | $\delta_C$ $CDCl_3$ | $\delta_H$ $CDCl_3$ | $\delta_C$ $CD_3OD$ | $\delta_H$ $CD_3OD$ | $\delta_C$ $CD_3OD$ | $\delta_H$ $CD_3OD$ | $\delta_C$ $CD_3OD$ | $\delta_H$ $C_5D_5N$ |
| 3 | 145.5 | | 156.1 | | 155.2 | 8.37 s | 155.2 | 8.39 s |
| 5 | 150.5 | | 165.5 | | 155.9 | | e | |
| 7 | 124.4 | 6.98 bs | 131.6 | 8.00 bs | 131.5 | 8.03 bs | 133.5 | 8.26 d |
| 8 | 106.9 | | 106.6 | | 107.1 | | 96.9 | 6.85 d |
| 9 | 149.2 | | 145.9 | | 146.3 | | 154.0 | |
| $\underline{CH}_3$-3 | 13.1c | 2.90 s | 14.0d | 2.54 s | | | | |
| $\underline{CH}_3$-8 | 12.9c | 2.38 bs | 13.0d | 2.31 bs | 13.0 | 2.34 bs | | |
| 1' | 85.6 | 6.44 dd | 89.4 | 6.53 dd | 89.4 | 6.54 dd | 90.0 | 6.56 dd |
| | | 2.23 m | | 2.49 m | | 2.37 m | | 2.38 m |
| 2' | 37.7 | | 41.9 | | 41.9 | | 42.2 | |
| | | 2.52 m | | 2.52 m | | 2.47 m | | 2.51 m |
| 3' | 82.5 | 5.26 m | 87.9 | 4.50 m | 88.0 | 4.52 m | 87.5 | 4.49 m |
| 4' | 74.0 | 4.31 m | 72.0 | 4.03 m | 71.9 | 4.04 m | 71.2 | 4.07 m |
| 5' | 63.5 | 4.40 m | 62.7 | 3.86 m | 62.6 | 3.87 m | 62.0 | 3.85 m |
| | 20.7 | 2.13 s | | | | | | |
| $\underline{CH}_3CO$ | | | | | | | | |
| | 20.7 | 2.15 s | | | | | | |
| | 170.0 | | | | | | | |
| $CH_3\underline{CO}$ | | | | | | | | |
| | 170.1 | | | | | | | |

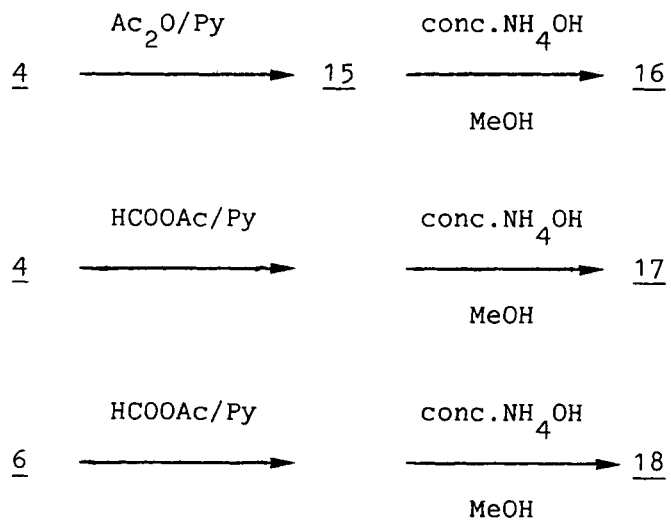
a. confirmed by spin decoupling experiments.
b. confirmed by DEPT experiments.
c. and d. assignments with identical superscript may be reversed.
e. submerged by solvent signals.

Particularly, in the case of 11 and 12, the UV spectra displayed a very large bathochromic shift in comparison with the starting material, thus indicating the presence of a highly conjugated system.

Compounds 7, 8, 11 and 12 were deacetylated by treatment with a solution of MeOH/concentrated ammonia (1:1) at room temperature for 12 hrs under stirring to give 9, 10[8], 13 and 14 respectively, in almost quantitative yields (NMR: Tables 1-2).

The syntheses of the triazo[4,3-c pyrimidine] nucleosides 15-18 were performed by reaction of the hydrazino derivatives 4 and 6 with acetic anhydride (pyridine, room temperature, 2 hrs), or acetic formic anhydride (pyridine, 0°, 3 hrs) and deacylation according to the scheme.

Scheme






In the case of the formyl derivatives, no intermediate purification step was included between the two reactions. The triazo[4,3-c]pyrimidine nucleosides were purified by silica gel chromatography and the structures were confirmed by elemental analyses and spectral data [MS, $^{1}H$ and $^{13}C$ NMR (Table 3), UV] .

In this paper we have further proved the versatility of the chlorine derivatives 1 and 2 as synthons for the preparation, in very satisfactory yields, of a large variety of pyrimidine deoxyribonucleosides C-4 substituted. Particularly, it is noteworth that the use of compounds 1 and 2 furnishes an alternative approach to the previously reported synthesis[7,8] of bridged nucleosides.

## EXPERIMENTAL

### General procedure

All the reagents for the syntheses are commercially available (Merck). The $^{1}H$ and $^{13}C$ NMR Fourier transform

spectra were recorded with a Bruker WM-250 instrument. The UV spectra were taken on a Perkin-Elmer 550S spectrophotometer. MS were taken on a Kratos MS 50 instrument. Chemical shifts were expressed in p.p.m. on the respect of the residual solvent signal. Optical rotations were measured with a Perkin-Elmer 141 polarimeter at 25°C.

1-(2-Deoxy-ß-D-rybofuranosyl)-4-(2-aminoethyl)-aminopyrimidin-2(1H)-one (5)

Compound 2 (200 mg, 0.61 mmol) was treated with excess of freshly distilled anhydrous ethylenediamine at room temperature for 5 hrs. The reaction mixture, dried in vacuo, was purified by PLC (silica gel 0.5 mm, eluent EtOH/$H_2O$/concentrated ammonia, 80:16:4). The band $R_f$ 0.4 (UV light) eluted with MeOH afforded 120 mg of 5 (78 % yield). Recrystallization from MeOH gave an analytically pure sample m.p. 145-148°; $[\alpha]_D$ = 51.4° (c = 1 in MeOH). Anal. Calcd. for $C_{11}H_{18}N_4O_4$ : C, 48.88; H, 6.71; N, 20.73. Found: C, 48.99; H, 6.73; N, 20.69. UV ( $\lambda_{max}$ in MeOH) 273 nm ( $\varepsilon$ = 8500). CI MS gave significant ions at m/z : 271 $(MH)^+$, 155 (M-sugar residue+2H)$^+$. $^1$H NMR ($CD_3OD$) : $\delta$ 7.92 (1H, d, H-6), 6.30 (1H, dd, H-1'), 5.90 (1H, d, H-5), 4.39 (1H, m, H-3'), 3.97 (1H, m, H-4'), 3.78 (2H, m, $H_2$-5'), 3.46 (2H, t, $-CH_2-CH_2-NH_2$), 2.83 (2H, t, $-CH_2-CH_2-NH_2$), 2.26 (1H, m, $H_a$-2'), 2.18 (1H, m, $H_b$-2'). $^{13}$C NMR ($CD_3OD$): $\delta$ 165.9 (C-2), 158.6 (C-4), 141.2 (CH-6), 97.1 (CH-5), 88.8 (CH-1'), 87.5 (CH-3'), 72.1 (CH-4'), 62.9 ($CH_2$-5'), 44.2 and 42.1 ($-CH_2-CH_2-NH_2$), 41.8 ($CH_2$-2').

1-(2-Deoxy-ß-D-ribofuranosyl)-4-hydrazinopyrimidin-2(1H)-one (6)

Compound 2 (200 mg, 0.61 mmol) was treated with excess of anhydrous hydrazine at room temperature for 2 hrs. The

resulting solution was dried in vacuo and dissolved in MeOH. The crude mixture was chromatographed by PLC (silica gel 0.5 mm, eluent 1-butanol/acetic acid/water, 60:15:25); the band $R_f$ 0.20 (UV light) eluted with MeOH afforded 120 mg of 6 (90% yield) as a white amorphous solid; $[\alpha]_D$ = 35° (c = 0.8 in MeOH). Anal. Calcd. for $C_9H_{14}N_4O_4$: C, 44.62; H, 5.83; N, 23.13. Found: C, 44.73; H, 5.71; N, 23.22. UV ($\lambda_{max}$ in MeOH) 274 nm ($\varepsilon$ =6500). CI MS gave significant ions at m/z: 243 $(MH)^+$, 127 (base moiety+2H)$^+$, 81 (sugar moiety-$2H_2O$)$^+$. $^1$H NMR ($CD_3OD$): $\delta$ 8.19 (d, 1H, H-6), 6.25 (1H, d, H-5), 6.03 (1H, dd, H-1'), 4.40 (1H, m, H-3') 3.98 (1H, m, H-4'), 3.78 (2H, m, $H_2$-5'), 2.35 (2H, m, $H_2$-2'). $^{13}$C NMR ($CD_3OD$): $\delta$ 157.3 (C-4), 145.6 (CH-6), 98.6 (CH-5), 89.5 (CH-1'), 88.4 (CH-3'), 72.3 (CH-4'), 63.0 ($CH_2$-5'), 41.9 ($CH_2$-2'), (C-2 not observed).

Synthesis of 7 (8)

A solution of the chlorine derivative 1 (2) (0.5 mmol) and 3 (5) (0.5 mmol) in anhydrous dimethylformamide (7 ml) was stirred at room temperature for 10 hrs. Removal of the solvent in vacuo yielded a residue which was purified by PLC (silica gel 0.5 mm, eluent $CHCl_3$/MeOH 85:15); the band $R_f$ 0.35 (0.30) (UV light), eluted with $CHCl_3$/MeOH (7:3), afforded the products 7 (8).

7: 82 % yield, m.p. 128-130° (from ethyl acetate/ $CHCl_3$); $[\alpha]_D$ =43.0° (c = 0.8 in MeOH).Anal. Calcd. for $C_{26}H_{36}N_6O_{10}$: C, 52.69, H, 6.12, N, 14.18. Found: C, 52.81, H, 6.14, N, 14.16. UV ($\lambda_{max}$ in MeOH) 281 nm ($\varepsilon$= 22000). FAB MS gave significant ions at m/z: 593 $(MH)^+$, 477 (M-deacetylated sugar+2H)$^+$, 277 (M-sugar residues +3H)$^+$.

8: 79% yield, m.p. 187-189° (from MeOH); $[\alpha]_D$ + 65.4° (c = 1 in MeOH ). Anal. Calcd. for $C_{24}H_{32}N_6O_{10}$ : C, 51.06; H, 5.71;

N,14.89. Found: C, 51.10; H, 5.66; N, 14.77. UV ( $\lambda_{max}$ in MeOH ) 274 nm ( $\varepsilon$ = 22000). FAB MS gave significant ions at m/z : 565 $(MH)^+$; 449 (M-deacetylated sugar+2H)$^+$, 365 ( M-diacetylated sugar+2H)$^+$, 249 (M-sugar residues+3H)$^+$.

Synthesis of 11 (12)

A solution of the chlorine derivatives 1 (2) (0.5 mmol) and 4 (6) (0.5 mmol) in anhydrous dimethylformamide (7 ml) was stirred at 0°C for 8 hrs. After removal of the solvent in vacuo, the solid residue was purified by PLC (silica gel 0.5 mm, eluent $CHCl_3$/MeOH 85:15). The band $R_f$ 0.4 (0.3) (UV light) eluted with $CHCl_3$/MeOH (3:2) afforded the compound 11 (12).

11: 75% yield; m.p. 113-115° (from benzene); $[\alpha]_D$ = -11.7° (c = 1 in MeOH). Anal. Calcd. for $C_{24}H_{32}N_6O_{10}$ : C, 51.06; H, 5.71; N, 14.89. Found: C, 51.15; H, 5.70; N, 14.98. UV ($\lambda$max in MeOH) 378 nm ( $\varepsilon$= 12700), 359 (25800), 342 (28500), 332 (22600), 246 (8600); FAB MS gave significant ions at m/z: 565 $(MH)^+$, 448 (M-deacetylated sugar+H)$^+$.

12: 70% yield; m.p. 126-127° (from MeOH); $[\alpha]_D$ = 4.5° (c = 1 in MeOH). Anal. Calcd. for $C_{22}H_{28}N_6O_{10}$ : C, 49.25; H, 5.26; N, 15.67. Found: C, 49.10; H, 5.30; N, 15.73. UV ( $\lambda_{max}$ in MeOH) 379 nm (s), 362 nm ($\varepsilon$= 17000), 344 (19500), 330 (s), 256 (7400). FAB MS gave significant ions at m/z : 537 $(MH)^+$, 420 (M-deacetylated sugar+H)$^+$.

Deacetylation of 7, 8, 11 and 12

Compounds 7, 8, 11 and 12 were treated with excess of a solution of concentrated ammonia/MeOH (1:1) at room temperature for 12 hrs under stirring. After removal of the solvent in vacuo the resulting mixture was dissolved in water and lyophilized. TLC analyses and spectroscopic data indicated

that the starting compounds had been completely converted into the deacetyl derivatives 9, 10, 13 and 14 respectively in almost quantitative yields.

9: m.p. 195-197° (from MeOH); $[\alpha]_D$ 63.6° (c = 1 in MeOH ). Anal. Calcd. for : $C_{22}H_{32}N_6O_8$ : C, 51.96; H, 6.34; N, 16.53. Found C, 51.84; H, 6.30, N, 16.48. UV ( $\lambda_{max}$ in MeOH), 280 nm ( $\varepsilon$ = 20000). FAB MS gave significant ions at m/z : 509 $(MH)^+$, 393 (M-deacetylated sugar+2H)$^+$, 277 (M-sugar residues+3H)$^+$.

10 : amorphous solid; $[\alpha]_D$ = 36.0 ( c = 1 in MeOH ). Anal. Calcd. for $C_{20}H_{28}N_6O_8$ : C, 49.99; H, 5.88; N, 17.49. Found: C, 50.12; H, 5.94; N, 17.35. UV ( $\lambda_{max}$ in MeOH) 275 nm ($\varepsilon$ = 16000). FAB MS gave significant ions at m/z : 481 $(MH)^+$, 249 (M- sugar residues+3H)$^+$.

13 : m.p. 195-198° (from EtOH); $[\alpha]_D$ = 3.4° (c = 1 in MeOH). Anal. Calcd for $C_{20}H_{28}N_6O_8$ : C, 49.99; H, 5.88; N, 17.49. Found : C, 50.07; H, 5.98; N, 17.39. UV ( $\lambda_{max}$ in MeOH) 379 nm, ($\varepsilon$=11000), 359 (22000), 343 (23800), 331 (19200), 248 (7800). FAB MS gave significant ions at m/z : 481 $(MH)^+$, 365 (M-deacetylated sugar+2H)$^+$.

14: amorphous solid; $[\alpha]_D$ = -10.5° (c = 1 in pyridine). Anal. Calcd. for $C_{18}H_{24}N_6O_8$ : C, 47.78; H, 5.35; N, 18.58. Found: C,47.65; H, 5.29; N,18.68. UV ( $\lambda_{max}$ in MeOH) 381 nm ( $\varepsilon$ = 7900), 361 (15700), 344 (18200), 332 (s), 255 (6800). FAB MS gave significant ions at m/z : 453 $(MH)^+$, 337 (M-deacetylated sugar+2H)$^+$.

Synthesis of 6-(2-deoxy-3,5-di-O-acetyl-ß-D-ribofuranosyl)-3,8-dimethyltriazo[4,3-c]pyrimidin-5(6H)-one (15).

200 mg of 4 were treated with excess of acetic anhydride (3 ml) in dry pyridine (6 ml) for 2 hrs at room temperature. After removal of the solvent in vacuo, the residue was chro-

matographed by PLC (silica gel 0.5 mm, eluent $CHCl_3$/MeOH 96:4); the band $R_f$ 0.5 ( UV light ) eluted with $CHCl_3$/MeOH (7:3) afforded 15 (70% yield); m.p. 140-141° (from $CCl_4$); $[\alpha]_D$ = 6.5° (c = 0.9 in $CHCl_3$). Anal. Calcd. for $C_{16}H_{20}N_4O_6$: C, 52.74; H, 5.53; N, 15.38. Found : C, 52.81; H, 5.49; N, 15.48. UV ( $\lambda_{max}$, $CHCl_3$) 266 nm ( $\varepsilon$ = 14500). CI MS gave significant ions at m/z: 365 $(MH)^+$, 245 $(MH-2CH_3COOH)^+$, 201 (diacetylated sugar)$^+$.

Deacetylation of 15

Compound 16 was obtained by treating 15 with excess of a solution of concentrated ammonia/MeOH (1:1) at room temperature for 6 hrs under stirring.After removal of the solvent in vacuo the residue was dissolved in water and lyophilizated to give pure 16 in almost quantitative yield; m.p. 99-103° (from $CHCl_3$); $[\alpha]_D$ 35.6° ( c= 1 in MeOH).
Anal. Calcd. for $C_{12}H_{16}N_4O_4$ : C, 51.42; H, 5.75; N, 19.99. Found : C, 51.46; H, 5.77; N, 20.03. UV ( $\lambda_{max}$ in MeOH) 274 nm ( $\varepsilon$ = 7000), 252 (4600). FAB MS gave significant ions at m/z : 281 $(MH)^+$, 165 (M-sugar residue + 2H)$^+$.

Synthesis of triazo[4,3-c]pyrimidine nucleosides 17 (18)

At 200 mg of the 4-hydrazinopyrimidine nucleoside 4 (6) in dry pyridine (6 ml) , 3 ml of acetic formic anhydride were added and the mixture was kept at 0° for 3 hrs. TLC analysis (silica gel, eluent $CHCl_3$/MeOH 95:5) indicated that the starting compound had been completely converted into a single product. After removal of the solvent in vacuo the solid residue was treated with excess of a solution of concentrated ammonia/MeOH ( 3:2 ) for 6 hrs under stirring. The crude mixture, dried in vacuo, was chromatographed by PLC (silica gel 0.5 mm, eluent $CHCl_3$/MeOH 8:2); the band (UV

light, $R_f$ 0.5 for compound 17, $R_f$ 0.45 for compound 18) eluted with $CHCl_3$/MeOH (1:1) afforded the desired products 17: (90 % yield); m.p. 161-162° ( from EtOH ); $[\alpha]_D$ = 42.7° ( c = 1 in MeOH ). Anal. Calcd. for : $C_{11}H_{14}N_4O_4$ : C, 49.62; H, 5.30; N, 21.04. Found : C, 49.71; H, 5.30; N, 21.06. UV ($\lambda_{max}$ in MeOH) 274 nm ($\varepsilon$= 8800), 254 (6600). FAB MS gave significant ions at m/z : 267 $(MH)^+$, 151 (M-sugar residues+2H)$^+$.

18 : (86 % yield); m.p. 165-169° ( from EtOH ); $[\alpha]_D$ = 46.5° (c = 1.1 in MeOH). Anal. Calcd. for $C_{10}H_{12}N_4O_4$ : C, 47.62; H, 4.80; N, 22.22. Found: C, 47.48; H, 4.87; N, 22.10. UV ( $\lambda_{max}$ in MeOH) 268 nm ( $\varepsilon$ = 4500), 252 nm (s). FAB MS gave significant ions at m/z : 253 $(MH)^+$, 137 (M-sugar residue + 2H)$^+$.



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