New Derivatives of Pyrimidine Nucleosides: Synthesis, Physico-Chemical Properties and Biological Activity

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The paper reports the synthesis and physico-chemical data of eight new pyrimidine nucleosides C-4 substituted and two imidazo[1,2-*c*]pyrimidine nucleosides as well as preliminary results of their biological effects on neuroblastoma cells in culture.

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A number of modified pyrimidine nucleosides are known as minor components of nucleic acids, and some of them, exhibiting rather complex structures, have also been isolated from marine sponges and from microbiological sources.

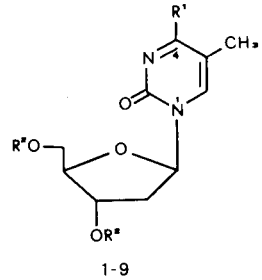
Metabolic derivatives of the major pyrimidine nucleosides seem to play an important biological role in the cell, especially in the organizational process of DNA and RNA, in their interactions and in the regulation of genetic expression.

Synthetic structural analogues may either interfere with nucleoside synthesis, interacting with enzymes of the nucleic acid metabolism, or exert their effects after incorporation, for example, into DNA [1,2]. In the latter instance this incorporation can lead to gene activation, as is the case of of 5-aza-2'-deoxycytidine, or can cause chain termination, as is the case of dideoxynucleotides or azidothymidine. Some of these analogues, which exert anticancer and/or antiviral activity, are currently used in therapy. New synthetic approaches with the aim of discovering compounds with useful biological activity are necessary to exploit the specificity differences, often unpredictable, of the enzymatic activity of invading agents and host cells [3-5].

The structural modifications of nucleosides that can be created are practically unlimited.

Nucleosides containing modified carbohydrate moieties have frequently been prepared *via* glycosilation of the base with a suitable derivative of the desired sugar. Alternatively, efforts have been made to develop specific chemical transformations suitable for introducing the desired modifications into the sugar moiety of nucleosides.

In a related way, base analogues have been prepared *via* *N*-glycosilation of suitably modified heterocycles or by structural transformation of the base moiety of existing nucleosides [6]. The latter approach has led to a method widely used in the preparation of antitumor agents involv-



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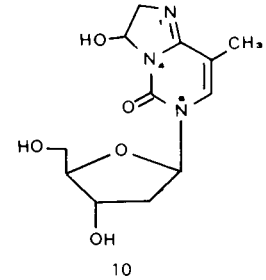

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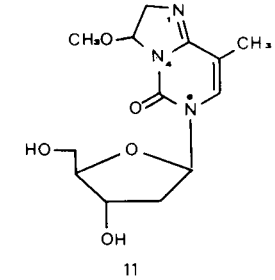

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	R^1	R^2
1	Cl	$-COCH_3$
2	$-NHNH_2$	$-H$
3	$-NH(CH_2)_2NH_2$	$-H$
4	$-NHCH_2COOEt$	$-COCH_3$
5	$-NH(CH_2)_2COOH$	$-COCH_3$
6	$-NHCH_2CH(OCH_3)_2$	$-COCH_3$
7	$-NHCH_2COOH$	$-H$
8	$-NH(CH_2)_2COOH$	$-H$
9	$-NHCH_2CH(OCH_3)_2$	$-H$

ing isosteric replacements in natural metabolites.

This paper deals with the synthesis and physicochemical characterization of eight pyrimidine nucleosides C-4 substituted, **2-9**, and two imidazo[1,2-*c*]pyrimidine nucleosides **10,11**. Data on the inhibitory effect that these compounds exert on the *in vitro* cell growth are also reported.

Synthesis of the derivatives was carried out on the basis of: a) the role of nitrogen atoms in the binding sites of biological systems, b) the occurrence in nature of several pyrimidinylaminoacids as antibiotics or as intermediates in the biosynthesis of nucleosides, and c) the potential capacity of imidazo[1,2-*c*]pyrimidine derivatives to either emulate or antagonize the function of the naturally occurring nucleosides [7-9].

Compounds **2-11** were synthesized from a C-4 chlorine derivative of thymidine (**1**), which proved to be a good synthon for different substitutions in the 4-position of the pyrimidine ring under very mild conditions [10,11].

Compound **1**, by treatment with anhydrous hydrazine (excess) and ethylendiamine (excess) for 2 and 5 hours at room temperature, afforded **2** and **3** in almost quantitative yields respectively. Structures **2** and **3** were assigned on the basis of their elemental analysis, uv, ms, ^{1}H- and ^{13}C-nmr. Furthermore, the structure of compound **2** was confirmed by its conversion into 6-(2-deoxy-β-D-*erythro*-pentofuranosyl)-8-methyltetrazolo[1,5-*c*]pyrimidin-5(6*H*)-one [11] by treatment with sodium nitrite/hydrochloric acid.

Compounds **4, 5** and **6** were synthesized by the reaction of compound **1** with glycine ethyl ester hydrochloride (dimethylformamide/triethylamine, 15 hours, 50°), 3-aminopropanoic acid (dimethylformamide/triethylamine, 15 hours, 50°) and 2,2-dimethoxyethylamine (acetonitrile, 1 hour, room temperature) respectively. Compounds **4-6** were purified by silica gel chromatography and their structures confirmed by elemental analysis, uv, ms, ^{1}H-and ^{13}C-nmr spectra.

Treatment of compounds **5** and **6** with concentrated ammonia/dioxane (1:1) for 24 hours at room temperature afforded the relative deacetyl derivatives **8** and **9**. Compound **4** in the same hydrolytic conditions, yielded the acid **7**. Structures **7-9** were confirmed by elemental analysis and spectroscopic data.

In order to obtain an imidazo[1,2-*c*]pyrimidine derivative *via* an intramolecular cyclization, we treated compound **9** with hydrochloric acid 0.5 *N* at 50° for 5 hours; after purification by silica gel chromatography, we obtained the compounds **10** and **11**. Spectroscopic analysis revealed that both are mixtures of epimers at C-3.

Preliminary analysis of the biological activity of compounds **2, 3, 7, 8, 9, 10** and **11** was made by determining their effect on murine 41 A 3 neuroblastoma cells in culture.

In order to evaluate the therapeutic potential of these compounds, we studied their effect on the growth of the neuroblastoma cells and on DNA synthesis. In both studies the cells were treated for 24 hours with the indicated compounds.

When the cells were treated with compounds **3, 8, 10** and **11** at a concentration of 10^{-4} *M*, the growth inhibition effect was 10%. Compound **9** had a growth inhibition effect of 15% and compounds **2** and **7** of 25%.

To evaluate the effect on DNA synthesis, the cells were treated with compounds **2** and **7** at a concentration of 10^{-5} *M*. Determination of the amount of radioactivity incorporated into DNA was made after a 4 hours pulse with methyl-^{3}H-thymidine (41 Ci/mmole). Compound **2** had a DNA synthesis inhibition effect of 7% and compound **7** of 15%.

EXPERIMENTAL

All the reagents for the synthesis are commercially available (Merck). The ^{1}H- and ^{13}C-nmr Fourier-transform spectra were recorded with a Bruker WM-250. The uv spectra were taken on a Perkin Elmer 550 S spectrophotometer. The ms were taken on a Kratos MS 50 instrument.

1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-4-hydrazino-5-methylpyrimidin-2(1*H*)-one (**2**).

Compound **1** (200 mg, 0.58 mmole) was treated with excess anhydrous hydrazine at room temperature for 2 hours. The resulting solution was dried *in vacuo* and dissolved in methanol. Thin layer chromatography analysis (silica gel, eluent chloroform/methanol 98:2) indicated that the starting compound **1** was completely converted into baseline material. The crude mixture was chromatographed on preparative layer chromatography (silica gel, eluent 1-butanol/acetic acid/water, 60:15:25); the band Rf 0.20 (uv light) eluted with methanol afforded 130 mg of **2** (89% yield). Recrystallization from methanol gave an analytically pure sample mp = 111-113°; $[\alpha]_D$ = 17.4 (c = 1, methanol); λ max (methanol) = 277 nm, (ε = 7200); ms: (chemical ionization) gave significant ions at m/z 257 $(MH)^+$, 141 (base moiety + 2H)$^+$, 99 (sugar moiety - H_2O)$^+$ and 81 (sugar moiety - $2H_2O$)$^+$; ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.28 (1H, bs, H-6), 6.00 (1H, dd, H-1'), 4.30 (1H, m, H-3'), 3.89 (1H, m, H-4'), 3.75 (2H, m, H_2-5'), 2.42 (1H, m, Ha-2'), 2.32 (1H, m, Hb-2'), 2.12 (3H, bs, CH_3-C-5); ^{13}C-nmr (perdeuteriomethanol, 62.9 MHz): δ 172.4 (C-2), 157.9 (C-4), 137.7 (CH-6), 104.1 (C-5), 88.8 (CH-1'), 87.2 (CH-3'), 72.2 (CH-4'), 63.0 (CH_2-5'), 41.6 (CH_2-2'), 12.8 (CH_3-C-5).

Anal. Calcd. for $C_{10}H_{16}N_4O_4$: C, 46.87; H, 6.29; N, 21.87. Found: C, 46.95; H, 6.34; N, 21.89.

1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-4-[(2-aminoethyl)-amino]-5-methylpyrimidin-2(1*H*)-one (**3**).

Compound **1** (200 mg, 0.58 mmole) was treated with an excess of anhydrous ethylendiamine (freshly distilled) at room temperature for 5 hours. The reaction mixture, dried *in vacuo*, was chromatographed on preparative layer chromatography (silica gel, 0.5 mm, eluent ethanol/water/ammonium hydroxide, concentrated, 80:16:4); the band Rf 0.4 (uv light) eluted with methanol afforded 130 mg of **3** (80% yield). Recrystallization from methanol gave an analytically pure sample mp 113-115°; $[\alpha]_D$ = 38.4 (c = 1, methanol); λ max (methanol): 278 nm (ε = 8100); ms: (chemical ionization) gave significant ions at m/z 285 $(MH)^+$, 267 (MH - H_2O)$^+$, 169 (base moiety + 2H)$^+$ and 117 (sugar moiety)$^+$; ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.80 (1H, bs, H-6), 6.29 (1H, dd, H-1'), 4.22 (1H, m, H-3'), 3.93 (1H, m, H-4'), 3.80 (2H, m, H_2-5'), 3.56 (2H, t, -CH_2-CH_2-NH_2), 2.87 (2H, t, -CH_2-CH_2-NH_2), 2.33 (1H, m, Ha-2'), 2.16 (1H, m, Hb-2'), 1.97 (3H, bs, CH_3-C-5); ^{13}C-nmr (deuterium oxide, 62.9 MHz): δ

166.8 (C-2), 159.9 (C-4), 139.3 (CH-6), 107.5 (C-5), 88.7 (CH-1'), 88.0 (CH-3'), 72.9 (CH-4'), 63.7 (CH_2-5'), 44.8 and 42.1 (-CH_2-CH_2-NH_2), 41.4 (CH_2-2'), 14.4 (CH_3-C-5).

Anal. Calcd. for $C_{12}H_{20}N_4O_4$: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.78; H, 7.13; N, 19.82.

1-(2-Deoxy-3,5-di-*O*-acetyl-β-D-*erythro*-pentofuranosyl)-4-[(ethoxycarbonylmethyl)amino]-5-methylpyrimidin-2(1*H*)-one (**4**).

Compound **1** (200 mg, 0.58 mmole) was treated in anhydrous dimethylformamide (3 ml) with 400 mg of glycine ethyl ester hydrochloride and 2 ml of anhydrous triethylamine and the mixture was stirred for 15 hours at 50°. After removal of the solvent *in vacuo* the solid residue was suspended in water and extracted with chloroform. The organic phase was evaporated to dryness *in vacuo* and the residue was chromatographed on preparative layer chromatography (silica gel, eluent chloroform/methanol, 95:5); the band Rf 0.5 (uv light) eluted with chloroform/methanol, 9:1, afforded 120 mg of **4** (50% yield). Recrystallization from methanol gave an analytically pure sample, mp = 157-158°; $[\alpha]_D$ = 24.4 (c = 1, chloroform); λ max (chloroform): 282 nm (ε = 7500); ms: (chemical ionization) gave significant ions at m/z 412 $(MH)^+$, 352 $(MH\text{-}CH_3COOH)^+$, 292 $(MH\text{-}2CH_3COOH)^+$ and 212 (base moiety + 2H)$^+$; ^{1}H-nmr (deuteriochloroform, 250 MHz): δ 7.34 (1H, bs, H-6), 6.36 (1H, dd, H-1'), 5.59 (1H, bt, -N*H*-CH_2-CO-), 5.28 (1H, m, H-3'), 4.33 (2H, d, -NH-CH_2-CO-), 4.30 (2H, m, H_2-5'), 4.26 (1H, m, H-4'), 4.30 (2H, q, CH_3-CH_2-O-), 2.62 (1H, m, Ha-2'), 2.40 and 2.10 (3H each, CH_3-CO-), 2.00 (1H, m, Hb-2'), 1.92 (3H, bs, CH_3-C-5), 1.28 (3H, t, CH_3-CH_2-O-); ^{13}C-nmr (deuteriochloroform, 62.9 MHz): δ 170.3 and 170.1 (2CH_3-*C*O-), 163.9 (-*C*OOEt), 162.7 (C-2), 155.6 (C-4), 136.6 (CH-6), 102.0 (C-5), 86.0 (CH-1'), 82.1 (CH-3'), 74.3 (CH-4'), 63.8 (CH_2-5'), 61.6 (CH_3-*C*H_2-O-), 42.8 (-*C*H_2-COOEt), 38.4 (CH_2-2'), 20.8 and 20.7 (2*C*H_3-CO-), 14.0 (*C*H_3-CH_2-O-), 12.9 (*C*H_3-C-5).

Anal. Calcd. for $C_{18}H_{25}N_3O_8$: C, 52.55; H, 6.13; N, 10.21. Found: C, 52.59; H, 6.18; N, 10.32.

1-(2-Deoxy-3,5-di-*O*-acetyl-β-D-*erythro*-pentofuranosyl)-4-[(2-carboxyethyl)amino]-5-methylpyrimidin-2(1*H*)-one (**5**).

Compound **1** (200 mg, 0.58 mmole) was treated in anhydrous dimethylformamide (4 ml) with 300 mg of 3-aminopropanoic acid and 2 ml of anhydrous triethylamine and the mixture was stirred for 15 hours at 50°. After removal of the solvent *in vacuo*, the mixture was dissolved in water and repeatedly liophylized, then it was suspended in chloroform/methanol 85:15 and the solid filtered. The eluate, dryed *in vacuo*, was chromatographed on preparative layer chromatography (silica gel, eluent chloroform/methanol 85:15); the band Rf 0.15 (uv light), eluted with chloroform/methanol 75:25, afforded 130 mg of **5** (56% yield). Recrystallization from methanol gave an analytically pure sample, mp = 118-121°; $[\alpha]_D$ = 12.9 (c = 1, methanol); λ max (methanol): 275 nm (ε = 7000); ms: (chemical ionization) gave significant ions at m/z 398 $(MH)^+$, 338 $(MH\text{-}CH_3COOH)^+$ and 198 (base moiety + 2H)$^+$. ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.51 (1H, bs, H-6), 6.22 (1H, dd, H-1'), 5.29 (1H, m, H-3'), 4.40 (2H, m, H_2-5'), 4.31 (1H, m, H-4'), 3.74 (2H, bt, -CH_2-CH_2-COOH), 2.58 (2H, bt, -CH_2-CH_2-COOH), 2.52 (1H, m, Ha-2'), 2.29 (1H, m, Hb-2'), 2.13 and 2.13 (3H each, s's, CH_3-CO-), 1.98 (3H, bs, CH_3-C-5); ^{13}C-nmr (perdeuteriomethanol, 62.9 MHz): δ 172.2 and 172.1 (2CH_3-*C*O-), 164.7 (C-2), 158.3 (C-4), 137.7 (CH-6), 105.4 (C-5), 87.4 (CH-1'), 83.6 (CH-3'), 76.0 (CH-4'), 65.0 (CH_2-5'), 38.5 (CH_2-2'), 38.3 (-CH_2-CH_2-COOH), 35.3 (-CH_2-*C*H_2-COOH), 20.8 (2*C*H_3-CO), 13.2 (*C*H_3-C-5).

Anal. Calcd. for $C_{17}H_{23}N_3O_8$: C, 51.38; H, 5.83; N, 10.58. Found: C, 51.39; H, 5.87; N, 10.63.

1-(2-Deoxy-3,5-di-*O*-acetyl-β-D-*erythro*-pentofuranosyl)-4-[(2,2-dimethoxyethyl)amino]-5-methylpyrimidin-2(1*H*)-one (**6**).

Compound **1** (200 mg, 0.58 mmole) was treated in anhydrous acetonitrile (3 ml) with 0.6 ml of 2,2-dimethoxyethylamine and the mixture allowed to stand for 1 hour at room temperature. The reaction mixture, dryed *in vacuo*, was chromatographed on preparative layer chromatography (silica gel, eluent chloroform/methanol 9:1); the band Rf 0.5 (uv light) eluted with chloroform/methanol 8:2 afforded 200 mg of **6** (85% yield). Recrystallization from methanol gave an analytically pure sample, mp = 113-115°; $[\alpha]_D$ = 34 (c = 1, chloroform); λ max (chloroform): 281 nm (ε = 7900); ms: (chemical ionization) gave significant ions at m/z 414 $(MH)^+$, 382 $(MH\text{-}CH_3OH)^+$, 350 $(MH\text{-}2CH_3OH)^+$, 214 (base moiety + 2H)$^+$ and 201 (diacetylated sugar moiety)$^+$; ^{1}H-nmr (deuteriochloroform, 250 MHz): δ 7.39 (1H, bs, H-6), 6.34 (1H, dd, H-1'), 5.23 [1H, bt, -N*H*-CH_2-$CH(OCH_3)_2$], 5.14 (1H, m, H-3'), 4.46 [1H, t, -CH_2-C*H*$(OCH_3)_2$], 4.31 (2H, m, H_2-5'), 4.21 (1H, m, H-4'), 3.66 [2H, bt, -CH_2-CH$(OCH_3)_2$], 3.37 (6H, s, OCH_3), 2.57 (1H, m, Ha-2'), 2.06 and 2.06 (3H each, s, CH_3CO), 2.04 (1H, m, Hb-2'), 1.90 (3H, bs, CH_3-C-5); ^{13}C-nmr (deuteriochloroform, 62.9 MHz): δ 170.2 and 170.1 (2CH_3-*C*O), 163.1 (C-2), 155.7 (C-4), 136.2 (CH-6), 102.2 [*C*H$(OCH_3)_2$], 101.8 (C-5), 85.9 (CH-1'), 81.9 (CH-3'), 74.2 (CH-4'), 63.8 (CH_2-5'), 54.4 (2-O*C*H_3), 43.2 [-*C*H_2-CH$(OCH_3)_2$], 38.2 (CH_2-2'), 20.7 and 20.6 (*C*H_3-CO-), 12.9 (*C*H_3-C-5).

Anal. Calcd. for $C_{18}H_{27}N_3O_8$: C, 52.29; H, 6.58; N, 10.16. Found: C, 52.39; H, 6.65; N, 10.21.

1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-4-[(carboxymethyl)amino]-5-methylpyrimidin-2(1*H*)-one (**7**).

Compound **4** (100 mg, 0.24 mmole) was treated with concentrated ammonia/dioxane (1:1) (10 ml) at room temperature for 24 hours. The resulting solution was dryed *in vacuo* and the residue was dissolved in water and liophylized. Thin layer chromatography analysis (silica gel, eluent: 1-butanol/acetic acid/water, 60:15:25) indicated that the compound **4** was completely converted into only one product (Rf 0.3, uv light) identified as **7**. Recrystallization from ethanol gave an analytically pure sample mp 110-113°; $[\alpha]_D$ = 37.0 (c = 1 in methanol); λ max (methanol): 277 nm (ε = 7800); ms: (chemical ionization) gave significant ions at m/z 300 $(MH)^+$, 282 $(MH\text{-}H_2O)^+$ and 184 (base moiety + 2H)$^+$; ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.85 (1H, bs, H-6), 6.28 (1H, dd, H-1'), 4.39 (1H, m, H-3'), 4.13 (2H, bs, -CH_2-COOH), 3.94 (1H, m, H-4'), 3.80 (2H, m, H_2-5'), 2.36 (1H, m, Ha-2'), 2.16 (1H, m, Hb-2'), 1.96 (3H, bs, CH_3-C-5); ^{13}C-nmr (perdeuteriomethanol, 62.9 MHz): δ 174.4 (COOH), 165.1 (C-2), 158.4 (C-4), 139.3 (CH-6), 105.0 (C-5), 88.8 (CH-1'), 87.5 (CH-3'), 72.0 (CH-4'), 62.8 (CH_2-5'), 44.5 (-*C*H_2-COOH), 41.9 (CH_2-2'), 12.9 (*C*H_3-C-5).

Anal. Calcd. for $C_{12}H_{17}N_3O_6$: C, 48.16; H, 5.73; N, 14.04. Found: C, 48.25; H, 5.81; N, 14.16.

1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-4-[(2-carboxyethyl)amino]-5-methylpyrimidin-2(1*H*)-one (**8**).

Compound **5** (100 mg, 0.25 mmole) was treated with concentrated ammonia/dioxane (1:1) (10 ml) at room temperature for 24 hours. The resulting solution was dryed *in vacuo* and the residue was dissolved in water and liophylized. Thin layer chromatography analysis (silica gel, eluent: 1-butanol/acetic acid/water, 60:15:25) indicated that the compound **5** was converted into corresponding deacetylated compound **8** (Rf 0.35, uv light, quantitative yield). Recrystallization from ethanol gave an analytically pure sample mp 135-138°; $[\alpha]_D$ = 25.0 (c = 1, methanol); λ max (methanol): 278 nm (ε = 7100); ms: (chemical ionization) gave significant ions at m/z 314 $(MH)^+$, 198 (base moiety + 2H)$^+$, 117 (sugar moiety)$^+$ and 81 (sugar moiety - $2H_2O$)$^+$; ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.78 (1H, bs, H-6), 6.30 (1H, dd, H-1'), 4.41 (1H, m, H-3'), 3.94 (1H, m, H-4'), 3.80 (2H, m, H_2-5'), 3.7 (2H, bt, -CH_2-COOH), 2.55 (2H, bt, -CH_2-CH_2-COOH), 2.33 (1H, m, Ha-2'), 2.18 (1H, m, Hb-2'), 1.97 (3H, bs, CH_3-C-5); ^{13}C-nmr (perdeuteriomethanol, 62.9 MHz): δ 180.2 (-COOH), 164.7 (C-2), 158.8 (C-4), 138.7 (CH-6), 105.0 (C-5), 88.8 (CH-1'), 87.4 (CH-3'), 72.1 (CH-4'), 62.9 (CH_2-5'), 41.8 (CH_2-2'), 38.7 (-CH_2-CH_2-COOH), 36.5 (-CH_2-*C*H_2-COOH), 12.9 (*C*H_3-C-5).

Anal. Calcd. for $C_{13}H_{19}N_3O_6$: C, 49.83; H, 6.11; N, 13.41. Found: C, 49.88; H, 6.10; N, 13.43.

1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-4-[(2,2-dimethoxyethyl)amino]-5-methylpyrimidin-2(1*H*)-one (**9**).

Compound **6** (100 mg, 0.24 mmole) was treated with concentrated ammonia/dioxane (1:1) (10 ml) at room temperature for 24 hours. The resulting solution was dryed *in vacuo* and the residue was dissolved in

water and liophylized. Thin layer chromatography analysis (silica gel, eluent: chloroform/methanol, 85:15) indicated that the compound **6** was completely converted into the corresponding deacetylated **9** (Rf 0.2, uv light). Recrystallization from ethanol/chloroform gave an analytically pure sample mp 130-132°; $[\alpha]_D$ = 43.0 (c = 1, methanol); λ max (methanol): 277 nm (ε = 8500); ms: (chemical ionization) gave significant ions at m/z 330 $(MH)^+$, 266 $(MH\text{-}2CH_3OH)^+$, 214 (base + 2H)$^+$ and 117 (sugar moiety)$^+$; ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.81 (1H, bs, H-6), 6.29 (1H, dd, H-1'), 4.70 [1H, t, -$CH_2CH(OCH_3)_2$], 4.40 (1H, m, H-3'), 3.94 (1H, m, H-4'), 3.80 (2H, m, H_2-5'), 3.59 [2H, d, -CH_2-$CH(OCH_3)_2$], 3.42 (6H, s, 2-OCH_3), 2.35 (1H, m, Ha-2'), 2.17 (1H, m, Hb-2'), 1.97 (3H, bs, CH_3-C-5); ^{13}C-nmr (perdeuteriomethanol, 62.9 MHz): δ 165.0 (C-2), 158.4 (C-4), 139.0 (CH-6), 104.7 (C-5), 103.6 [-$CH(OCH_3)_2$], 88.7 (CH-1'), 87.4 (CH-3'), 72.0 (CH-4'), 62.8 (CH_2-5'), 54.7 (2-OCH_3), 43.6 [-CH_2-$CH(OCH_3)_2$], 41.9 (CH_2-2'), 13.0 (CH_3-C-5).

Anal. Calcd. for $C_{14}H_{23}N_3O_6$: C, 51.05; H, 7.04; N, 12.76. Found: C, 51.00; H, 7.08; N, 12.82.

3-Hydroxy-2,3-dihydro-6-(2-deoxy-β-D-*erythro*-pentofuranosyl)-8-methylimidazo[1,2-*c*]pyrimidin-5(6*H*)-one (**10**) and 3-Methoxy-2,3-dihydro-6-(2-deoxy-β-D-*erythro*-pentofuranosyl)-8-methylimidazo[1,2-*c*]pyrimidin-5(6*H*)-one (**11**).

Compound **9** (100 mg, 0.30 mmole) was treated with hydrochloric acid 0.5 *N* (20 ml) at 50° for 5 hours. The resulting mixture was neutralized with excess Dowex AG1-X8 (OH^-) resin. The filtered solution was dryed *in vacuo* and the residue, dissolved in methanol was chromatographed on preparative layer chromatography (silica gel, 0.5 mm, eluent chloroform/-methanol, 83:17). The bands Rf 0.15 and 0.35 (uv light), eluted with chloroform/methanol 7:3, afforded respectively 30 mg of **10** (34% yield) and 15 mg of **11** (12% yield). The ^{1}H- and ^{13}C-nmr spectra showed that the products **10** and **11** are mixtures (in a ratio 2:1) of two epimers at C-3, through the splitting of some of the signals (H-7, H-1', C-1', C-4', C-5', CH_3-C-8 for **10** and C-3, C-3$_o$ and -OCH_3 for **11**).

The product **10** had: λ max (methanol): 279 nm (ε = 9300); ms: (chemical ionization) gave significant ions at m/z 266 $(MH\text{-}H_2O)^+$, 230 $(MH\text{-}3H_2O)^+$ 168 (base moiety + 2H)$^+$ 150 (base moiety + 2H-H_2O)$^+$ and 117 (sugar moiety)$^+$; ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.63 and 7.52 (1H, bs's, H-7), 6.37 and 6.31 (1H, dd's, H-1'), 4.67 (1H, m, H-3), 4.42 (1H, m, H-3'), 3.94 (1H, m, H-4'); 3.79 (2H, m, H_2-5'), 3.55 (2H, m, H_2-2), 2.18 (1H, m, Ha-2'), 2.03 (1H, m, Hb-2'), 1.80 (3H, bs, CH_3-C-8); ^{13}C-nmr (perdeuteriomethanol, 62.9 MHz): δ 157.0 (C-5), 151.3 (C-9), 138.9 (CH-7), 104.7 (C-8), 97.0 (C-3), 88.7 and 88.5 (CH-1'), 87.4 (CH-3'), 72.3 and 72.0 (CH-4'), 63.0 and 62.8 (CH_2-5'), 46.8 (CH_2-2), 41.9 (CH_2-2'), 13.1 and 12.8 (CH_3-C-8).

Anal. Calcd. for $C_{12}H_{17}N_3O_5$: C, 50.88; H, 6.05; N, 14.83. Found: C, 50.87; H, 6.14; N, 14.94.

The product **11** had: λ max (methanol): 280 nm (ε = 8800); ms: (chemical ionization) gave significant ions at m/z 298 $(MH)^+$, 182 (base moiety + 2H)$^+$, 150 (base moiety + 2H-CH_3OH)$^+$ and 117 (sugar moiety)$^+$; ^{1}H-nmr (perdeuteriomethanol, 250 MHz): δ 7.42 (1H, bs, H-7), 6.32 (1H, dd, H-1'), 5.70 (1H, m, H-3), 4.40 (1H, m, H-3'), 3.95 (2H, m, H_2-2), 3.90 (1H, m, H-4'), 3.76 (2H, m, H_2-5'), 3.49 (3H, s, -OCH_3), 2.20 (2H, m, H_2-2'), 1.94 (3H, bs, CH_3-C-8); ^{13}C-nmr (perdeuteriomethanol, 62.9 MHz): δ 156.6 (C-5), 150.3 (C-9), 134.3 (CH-7), 107.1 (C-8), 89.4 and 89.3 (C-3), 88.6 (CH-1'), 86.3 and 86.1 (CH-3'), 72.3 (CH-4'), 63.0 (CH_2-5'), 60.4 (CH_2-2), 57.1 and 56.9 (-OCH_3), 40.7 (CH_2-2'), 13.1 (CH_3-C-8).

Anal. Calcd. for $C_{13}H_{19}N_3O_5$: C, 52.51; H, 6.44; N, 14.13. Found: C, 52.56; H, 6.49; N, 14.21.

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