

Glycosidopyrroles. part 4. 1- β -D-ribofuranosyl-pyrroles and indoles as potential antiviral agents

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Abstract

The preparation of new 1- β -D-ribofuranosylpyrroles of type 8 and a new method of synthesis of 1- β -D-ribofuranosylindoles of type 10, according to the scheme, is reported. All these new derivatives showed promising chemical and physical analogies with bioactive molecules but did not show any antiviral activity against HIV1.

Keywords: Ribofuranosyl-pyrroles, ribofuranosyl indoles, antiviral agents.

Introduction

Ribavirin, 1- β -D-ribofuranosyl-1,2,4-triazolo-3-carboxamide, is a broad spectrum antiviral agent¹ which also displays antitumor activity in mice.² It is a FDA approved anti-HIV drug with the trade name Virazole® and has attracted considerable attention because of a peculiar mechanism of action related to IMPDH inhibition via its anabolite 5-monophosphate.³ Ribavirin is also endowed with the capability of potentiating *in vitro* anti-HIV-1 activity of purine dideoxynucleosides. It is currently under clinical studies in combination with α -interferon for the treatment of patients with chronic hepatitis C.⁴

Recently, pyrazole nucleosides have been synthesized as carbon bioisosteres of ribavirin, and some of them, 4-substituted 3-carboxamido derivatives of type 1 (R=NH₂, R'=NO₂, Hal), emerged as selective *in vitro* inhibitors of human T and B leukemias and lymphomas and coxsackie B1 virus.⁵

It is well known that the activity of ribavirin is related to steric and hydrogen-bonding requirements at the primary amide at C-3 position. However in the second generation of the glycosidopyrazoles of type 1, it has been reported that the presence of the carboxamido function is not necessary for the appearance of the activity, since also 4-halo-3-methoxyesters showed activity against a panel of tumor cell lines, and in particular, 1- β -D-ribofuranosyl-4-iodo-3-

methoxycarbonylpyrazole (IPCAR, 1, R=OMe, R'=I) showed the wider spectrum of antiproliferative activity with low toxicity.⁶

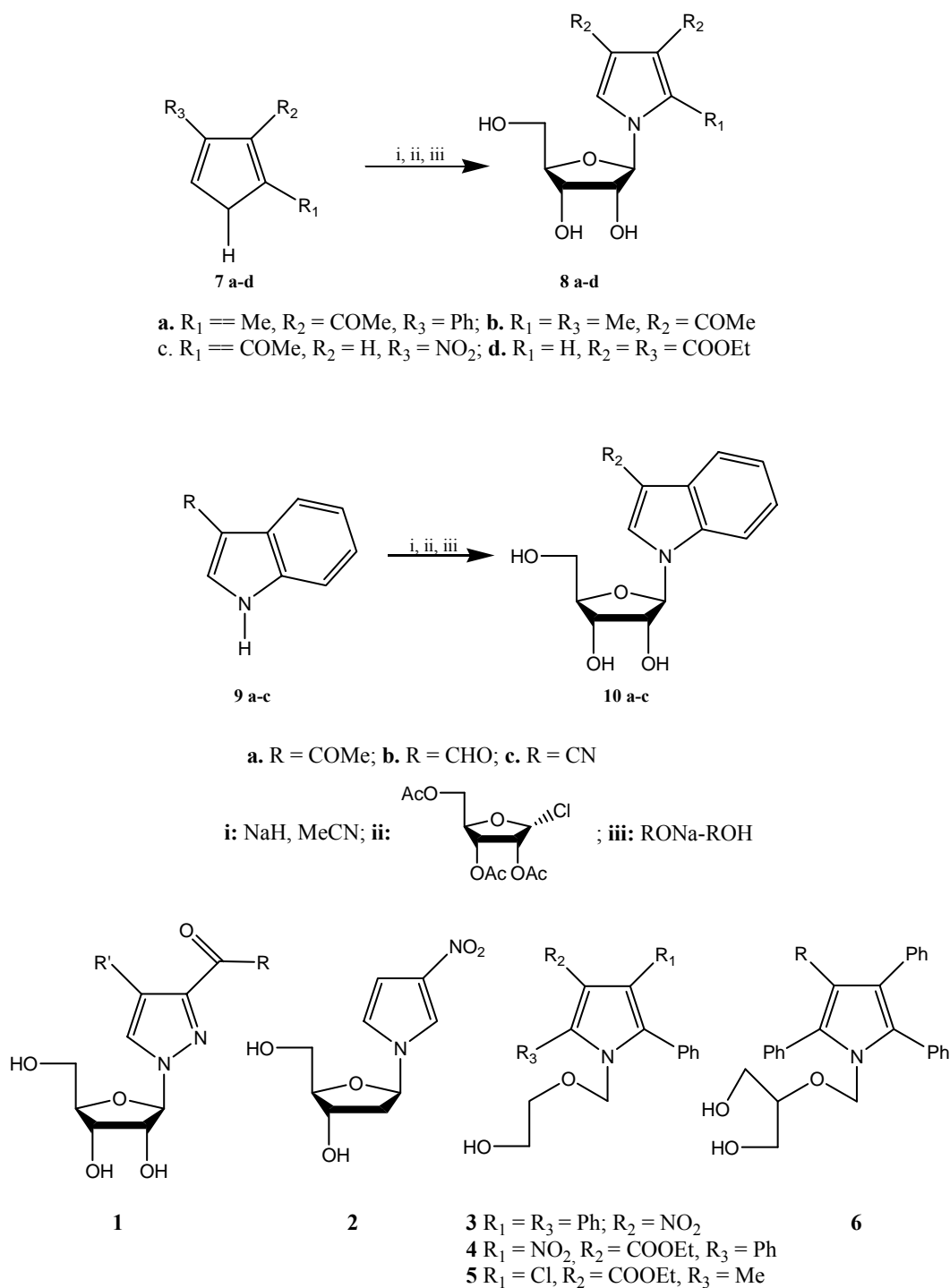
Interestingly, the switch from the triazole ring of ribavirin to the more electron richazole ring of pyrazole nucleosides results in increased antitumor activity, a trend that has already been observed with triazenoazoles.

Therefore nucleoside derivatives incorporating the pyrrole moiety, which can be considered dideaza analogues of ribavirin, could be developed as potential antiviral/anticancer agents.

Moreover this type of compounds can give a deeper insight on the interactions with DNA since recently the 1-(2'-deoxy- β -D-ribofuranosyl)-3-nitropyrrole (2) was demonstrated to behave as universal nucleoside.⁷ A unique property of this compound was its ability to replace long strings of contiguous nucleosides and still yield functional sequencing primers. Even if it does not resemble either a purine or pyrimidine nor does it contain a functional group of significant hydrogen bonding capacity, it showed an electronic distribution that resembled the average charge distribution of the DNA bases.

In connection with our studies on new compounds of biological interest incorporating the pyrrole and the related benzocondensed moieties, we have already reported⁸⁻¹⁰ the synthesis and the results of antiviral screening tests of acyclic glycosido-pyrroles and indoles in which the acyclic moieties of the well known antiviral agents Acyclovir and Ganciclovir were present.

All the tested 1-hydroxyethoxymethylpyrroles resulted generally inactive against either HIV-1 and HSV-1 and HSV-2, but showed considerable cytotoxicity.⁸ Only the 3-nitro-2,4,5-triphenyl derivative 3 was found to inhibit the HIV-1 replication at concentrations that were not cytotoxic for MT-4 cells and HSV-2 strain at concentrations slightly below those cytotoxic for Vero cells. Also derivatives 4 and 5 showed weak anti-HSV activity. A linear relationship between the observed cytotoxicity and the lipophilicity was found for this series of compounds: derivatives with high lipophilicity were also highly cytotoxic.



Scheme 1

In case of the 1-(1,3-dihydroxy-2-propoxy)methylpyrroles again the more interesting compounds belonged to the triphenyl substituted series of type 6.⁹ A slight selectivity, as shown by the SI

value (1.5-9.3), was found. Surprisingly the more active compound of the series was the 3-amino derivative (6, R = NH₂). Again the lipophilicity may play a role since all the active derivatives have similar polarity (log P in the range 4.5-6.0).

We also explored the influence of the benzocondensation in the 2 and 3 positions of the pyrrole ring and prepared a series of 1-hydroxyethoxymethylindoles.¹⁰ All these compounds did not show any antiviral activity, but once more the series of the 3-substituted derivatives with a phenyl in the 2 position of the ring resulted the most cytotoxic, with values decreasing in the order amino, bromo, nitro.

In this paper we report the synthesis of some new 1-β-D-ribofuranosyl-pyrroles and a new method for the preparation of 1-β-D-ribofuranosylindoles. Although ribofuranosylpyrroles have been synthesized, usually as key intermediates for the preparation of analogues of nucleosides, nothing is known in literature about their biological properties. In the indole series some glycosides have shown cytotoxic activity against human carcinomas.¹¹ However the more interesting derivatives were 1-arabinopyranosylindoles, which inhibited various types of carcinomas and sarcomas¹² and also have virucide properties,¹³ especially when electronwithdrawing groups are present in the indole moiety.

Results and Discussion

Ribofuranosylpyrroles. The synthesis of ribofuranosylpyrroles of type 8 involved the alkylation of the sodium salts (obtained with sodium hydride in acetonitrile) of the corresponding 1H derivatives 7a-d with 1-chloro-2,3,5-tri-O-acetyl-D-ribose. Removal of the protecting group was easily achieved by treatment with sodium alkoxide. This reaction represents a convenient method for the stereoselective glycosilation of pyrroles leading only to the single β-anomer as judged by ¹H NMR.¹⁴

However the yields are strongly influenced by the position and effects of the substituents on the pyrrole ring. In fact even if it has been claimed that glycosilation of pyrroles can be achieved with different 1-halo sugars,¹⁵ and that when using convenient ester-protected sugars the presence of at least an electronwithdrawing group adjacent to the pyrrole ring nitrogen is necessary,¹⁶ in our hands the reaction worked only with pyrroles unsubstituted in the α position.

Ribofuranosylindoles. A literature search revealed that all the syntheses of glycosidoindoles involved the so-called "indoline-indole" method, since it was stated that the usual syntheses of purine or pyrimidine nucleosides could not be employed by using indole derivatives as substrates.¹⁷ In fact all the glycosylation reactions were carried out with suitably protected carbohydrates on 2,3-dihydroindoles, followed by dehydrogenation.¹⁸ Although these methods allowed the isolation of glycosidoindoles in overall yields from moderate to good, these syntheses resulted rather tedious since often the starting indolines has to be prepared by reduction of the corresponding indoles. The direct glycosilation reaction of indoles leading to ribofuranosyl-indoles is hitherto unknown, in fact it has been reported that the reaction of indoles

with glycosyl halides containing acyloxy groups in the 2 position led to N- and C-nucleosides with the main product being alkylidene derivatives of the monosaccharides.¹⁹ In our hand however under the experimental conditions employed for the above mentioned pyrroles it was possible to isolate in good yields the 1- β -D-ribofuranosylindole derivatives 10a-c.

Molecular modelling. In order to evaluate the similarity of the whole molecule structures in terms of atomic potential charge, shape and lipophilicity, we run electrostatic calculations by using a semiempirical molecular package that can optimize the structure in vacuum. In Table 1 the matrix of the similarity indices for ribavirin, IPCAR, pyrrole nucleoside 2 and selected glycosidopyrrole/indole (8c and 10a) is reported. From these data it is possible to evidence the good correlation obtained for the pairs ribavirin/IPCAR (value in red) and compounds 2/8c (value in blue) in terms of charge distributions and the good similarity when comparing the lipophilicity of the pairs ribavirin/8c (value in red) and IPCAR/2 or 10a (values in blue). However the best results were obtained in the case of shape calculations that showed the expected structural analogies between the glycosidopyrroles/indoles and the reference compounds.

Selected glycosidopyrroles/indoles were also aligned with the reference bioactive compounds (ribavirin, IPCAR and pyrrole nucleoside 2) by using the algorithm of MacKay²⁰ in which quaternions are used to represent the rotation in space needed to overlay the two structures. Fitting obtained by superimposing the structures in the conformation of minimum of energy gave the R.M.S. distances between corresponding atoms in the range 0.0026-0.0138. (Figure 1). Fitting between ribavirin (red), IPCAR (green), compounds 2 (white), 8c (blue), and 10a (yellow)

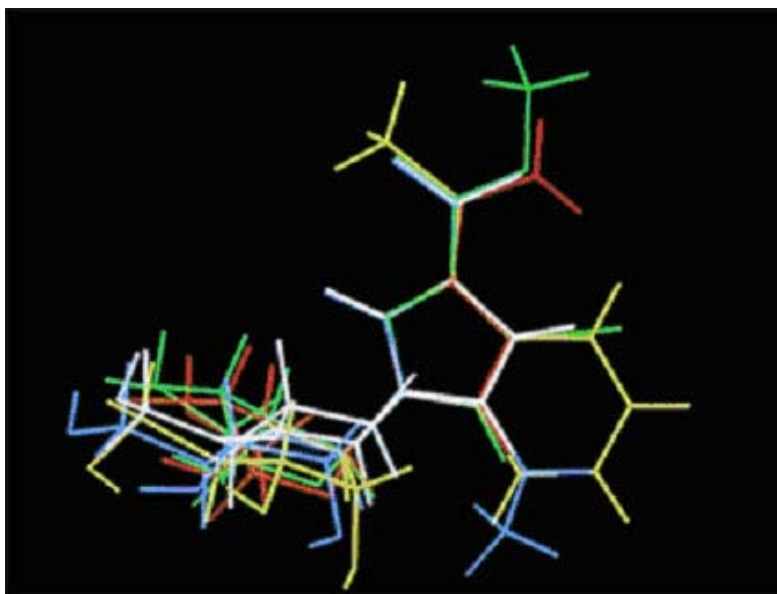


Figure 1

All these data suggest that the glycosidopyrroles and indoles possess electronic and steric requirement comparable to known anti-HIV-1 drugs. However, in spite of the promising

chemical and theoretical assumptions, these new derivatives were found inactive at concentrations as high as 200 μM when tested for antiviral activity against HIV-1 (data not shown).

Table 1. Similarity indices

Charge					
	RIBAVIRIN	IPCAR	2	8c	10a
RIBAVIRIN	1	0.8706	0.4122	0.0783	0.1429
IPCAR	0.8680	1	0.2459	0.1038	-0.0061
2	0.4079	0.2118	1	0.7682	0.1592
8c	0.2352	-0.0274	0.7817	1	0.2345
10a	0.1982	-0.0315	0.1620	0.2898	1
Shape					
	RIBAVIRIN	IPCAR	2	8c	10a
RIBAVIRIN	1	0.9289	0.8158	0.7725	0.7318
IPCAR	0.9227	1	0.7611	0.7635	0.7747
2	0.8211	0.7620	1	0.9077	0.8098
8c	0.5452	0.6733	0.9157	1	0.6644
10a	0.7469	0.7576	0.7899	0.6234	1
Lipophilicity					
	RIBAVIRIN	IPCAR	2	8c	10a
RIBAVIRIN	1	-0.6210	-0.7615	0.7992	-0.3125
IPCAR	-0.6181	1	0.8229	-0.2281	0.7728
2	-0.7615	0.8278	1	-0.3495	0.7401
8c	0.8343	-0.2179	-0.3565	1	0.1583
10a	-0.3751	0.8164	0.7318	0.2104	1

Experimental Section

General Procedures. All melting points were taken on a Büchi-Tottoli capillary apparatus and are uncorrected; IR spectra were determined in bromoform with a Jasco FT/IR 5300 spectrophotometer; ^1H and ^{13}C NMR spectra were measured respectively in DMSO- d_6 solution (TMS as internal reference), at 200 and 50.3 MHz, using a Bruker AC-E series 200 MHz NMR spectrometer. Column chromatography was performed with Merck silica gel 230-400 Mesh ASTM. Pyrroles 7a-c were prepared according to the literature,²¹ all the other starting material were commercially available. The calculations and molecular modelling was performed with

PIMMS, ASP, and Vamp packages supplied by Oxford Molecular Ltd. running on an Indigo II Silicon Graphics work station.

General method for the preparation of 1- β -D-ribofuranosyl-pyrroles 8a-d and indoles 10a-c

Sodium hydride (15 mmol, 55% oil dispersion) was added at room temperature to a solution of pyrroles 7a-d or indoles 9a-c (10 mmol) in acetonitrile (20 mL) under a nitrogen atmosphere. The reaction mixture was stirred for 3 h at room temperature. A solution of 1-chloro-2,3,5-tri-O-acetyl-D-ribofuranose²² (10 mmol) in acetonitrile (10 mL) was added dropwise and the reactants were stirred at room temperature for 1 h. Removal of the solid and evaporation of the solvent under reduced pressure gave a residue which was purified by column chromatography or by recrystallisation from ethanol. Only in the case of 7c and 9c it was possible to isolate pure 1-(2,3,5-tri-O-acetyl- β -D-ribofuranosyl derivatives. Otherwise the mixture, upon elution with dichloromethane : ethyl acetate (8:2) gave a syrup containing the protected glycosides and unreacted pyrrole or indole.

2-Acetyl-4-nitro-1-(2,3,5-tri-O-acetyl- β -D-ribofuranosyl)pyrrole. (80% yield), mp 160 °C; IR: 1710 and 1740 (CO), 1537 and 1342 (NO₂) cm⁻¹; ¹H NMR δ : 2.03 (3H, s, CH₃), 2.15 (6H, s, 2xCH₃), 2.51 (3H, s, CH₃), 4.41-4.46 (3H, m, 2xH-5' and H-4'), 5.29 (1H, dd, J = 7.8 Hz, J = 4.9 Hz, H-3'), 5.40 (1H, dd, J = 4.9 Hz, J = 2.0 Hz, H-2'), 6.56 (1H, d, J = 2.0 Hz, H-1'), 7.90 (1H, d, J = 2.0 Hz, H-3), 8.54 (1H, d, J = 2.0 Hz, H-5); ¹³C NMR δ : 20.21 (q, CH₃), 20.23 (q, CH₃), 20.47 (q, CH₃), 27.19 (q, CH₃), 61.67 (t, C-5'), 67.65 (d, C-3'), 74.54 (d, C-2'), 78.63 (d, C-4'), 89.73 (d, C-1'), 115.18 (d, C-3), 124.98 (d, C-5), 129.99 (s, C-4), 135.53 (s, C-2), 168.84 (s, CO), 169.21 (s, CO), 170.05 (s, CO), 188.97 (s, CO). Anal. Calcd. for C₁₇H₂₀N₂O₁₀: C, 49.52; H, 4.89; N, 6.79. Found: C, 49.62; H, 4.79; N, 6.30.

3-Cyano-1-(2,3,5-tri-O-acetyl- β -D-ribofuranosyl)indole. (70% yield), mp 123 °C; IR: 2222 (CN), 1742 (CO) cm⁻¹; ¹H NMR δ : 1.98 (3H, s, CH₃), 2.06 (3H, s, CH₃), 2.17 (3H, s, CH₃), 4.15 (1H, dd, J = 12.2 Hz, J = 5.4 Hz, H-3'), 4.32-4.38 (2H, m, 2xH-5'), 4.80-4.84 (2H, m, H-4' and H-2'), 6.07 (1H, s, H-1'), 7.31 (1H, dd, J = 7.5 Hz, J = 7.0 Hz, H-6), 7.38 (1H, dd, J = 8.1 Hz, J = 7.0 Hz, H-5), 7.66 (1H, d, J = 7.5 Hz, H-7), 7.73 (1H, d, J = 8.1 Hz, H-4), 8.30 (1H, s, H-2); ¹³C NMR δ : 20.40 (q, CH₃), 20.53 (q, CH₃), 24.27 (q, CH₃), 61.85 (t, C-5'), 71.09 (d, C-3'), 75.69 (d, C-2'), 77.38 (d, C-4'), 85.33 (s, C-3), 104.87 (d, C-1'), 113.46 (d, C-7), 114.88 (s, CN), 115.53 (s, C-3a), 118.87 (d, C-6), 122.50 (d, C-5), 124.24 (d, C-4), 128.12 (s, C-7a), 132.94 (s, CO), 133.84 (d, C-2), 169.63 (s, CO), 170.10 (s, CO). Anal. Calcd for C₂₀H₂₀N₂O₇: C, 60.00; H, 5.03; N, 7.00. Found: C, 60.02; H, 5.07; N, 6.98.

Removal of the protecting group: A solution of sodium methoxide (5 mmol) in methanol (10 mL) was added dropwise to a solution of tri-O-acetyl- β -D-ribofuranosyl-pyrrole or indole (5 mmol) in methanol (30 mL). The reactants were stirred at room temperature until disappearance of the starting materials (tlc monitoring, 15-30 min). Only in the case of pyrrole derivative d, the hydrolysis was carried out with sodium ethoxide in ethanol to avoid transesterification. Removal of the solvent in vacuo gave a crude residue which was purified by column chromatography (eluent dichloromethane ethyl : acetate 8:2) to give 8a-d and 10 a-c.

3-Acetyl-2-methyl-4-phenyl-1- β -D-ribofuranosylpyrrole (8a). (65% yield), oil; IR: 3300 (broad OH), 1710 (CO) cm^{-1} ; ^1H NMR δ : 1.86 (3H, s, CH_3), 1.96 (3H, s, CH_3), 3.22-3.81 (5H, m, H-2', H-3', H-4' and 2xH-5'), 4.48 (1H, t, $J = 5.4$ Hz, CH_2OH), 4.86 (1H, d, $J = 3.4$ Hz, OH), 5.48 (1H, d, $J = 3.6$ Hz, OH), 5.87 (1H, d, $J = 3.9$ Hz, H-1'), 6.86 (1H, s, H-5'), 7.27-7.37 (5H, m, C_6H_5); ^{13}C NMR δ : 12.26 (q, CH_3), 25.69 (q, CH_3), 59.62 (t, C-5'), 70.00 (d, C-3'), 79.34 (d, C-2'), 80.57 (d, C-4'), 104.19 (d, C-1'), 116.59 (d, C-5), 123.84 (s, C-3), 128.32 (d), 128.69 (d), 128.94 (d), 133.02 (s, C-4), 135.02 (s, C-2), 135.79 (s), 196.47 (s, CO). Anal. Calcd. for $\text{C}_{18}\text{H}_{21}\text{NO}_5$: C, 65.23; H, 6.39; N, 4.23. Found: C, 65.28; H, 6.33; N, 4.44.

3-Acetyl-2,4-dimethyl-1- β -D-ribofuranosylpyrrole (8b). (60% yield), oil; IR: 3290 (broad OH), 1715 (CO) cm^{-1} ; ^1H NMR δ : 1.79 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.32 (3H, s, CH_3), 3.13-3.79 (5H, m, H-2', H-3', H-4' and 2xH-5'), 4.74 (1H, t, $J = 5.1$ Hz, CH_2OH), 5.78 (1H, d, $J = 3.8$ Hz, OH), 5.98 (1H, d, $J = 3.8$ Hz, OH), 6.64 (1H, s, H-1'), 6.79 (1H, s, H-5); ^{13}C NMR δ : 13.12 (q, CH_3), 15.68 (q, CH_3), 25.69 (q, CH_3), 59.69 (t, C-5'), 70.06 (d, C-3'), 79.29 (d, C-2'), 80.57 (d, C-4'), 104.14 (d, C-1'), 116.67 (d, C-5), 117.69 (s, C-3), 123.03 (s, C-4), 133.61 (s, C-2), 195.08 (s, CO). Anal. Calcd. for $\text{C}_{13}\text{H}_{19}\text{NO}_5$: C, 57.97; H, 7.12; N, 5.20. Found: C, 57.76; H, 7.19; N, 5.58.

2-Acetyl-4-nitro-1- β -D-ribofuranosylpyrrole (8c). (100% yield), mp 145 $^\circ\text{C}$; IR: 3395 (broad OH), 1718 (CO), 1375 (NO_2), cm^{-1} ; ^1H NMR δ : 2.48 (3H, s, CH_3), 3.61-4.11 (5H, m, H-2', H-3', H-4' and 2xH-5'), 5.10 (1H, d, $J = 5.9$ Hz, OH), 5.39 (1H, t, $J = 4.9$ Hz, CH_2OH), 5.50 (1H, d, $J = 3.9$ Hz, OH), 6.35 (1H, s, H-1'), 7.81 (1H, d, $J = 2.0$ Hz, H-3), 8.96 (1H, d, $J = 2.0$ Hz, H-5); ^{13}C NMR δ : 27.42 (q, CH_3), 59.11 (t, C-5'), 67.54 (d, C-3'), 76.16 (d, C-2'), 83.65 (d, C-4'), 91.55 (d, C-1'), 114.85 (d, C-3), 125.84 (d, C-5), 129.93 (s, C-4), 135.00 (s, C-2), 188.97 (s, CO). Anal. Calcd. for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_7$: C, 46.15; H, 4.93; N, 9.79. Found: C, 46.20; H, 4.90; N, 9.39.

Ethyl 1- β -D-ribofuranosylpyrrole-3,4-dicarboxylate (8d). (50% yield), oil; IR: 3320 (broad OH), 1735 (CO) cm^{-1} ; ^1H NMR δ : 1.34 (6H, t, $J = 6.8$ Hz, 2x CH_2CH_3), 4.28 (4H, q, $J = 6.8$ Hz, 2x CH_2CH_3), 3.79-4.02 (5H, m, H-2', H-3', H-4' and 2xH-5'), 4.10-4.54 (3H, m, 3xOH), 5.86 (1H, d, $J = 3.9$ Hz, H-1'), 7.41 (2H, s, H-2 and H-5); ^{13}C NMR δ : 14.29 (q, CH_3), 60.05 (t, C-5'), 60.63 (t, CH_2), 70.34 (d, C-3'), 79.64 (d, C-2'), 80.52 (d, C-4'), 104.74 (d, C-1'), 116.66 (s, C-3 and C-4), 124.32 (d, C-2 and C-5), 163.87 (s, CO). Anal. Calcd. for $\text{C}_{15}\text{H}_{21}\text{NO}_8$: C, 52.47; H, 6.47; N, 4.28. Found: C, 55.12; H, 6.41; N, 4.42.

3-Acetyl-1- β -D-ribofuranosylindole (10a). (60% yield), oil; IR: 3260 (broad OH), 1702 (CO) cm^{-1} ; ^1H NMR δ : 1.96 (3H, s, CH_3), 3.37-3.93 (5H, m, H-2', H-3', H-4' and 2xH-5'), 4.48 (1H, d, $J = 4.3$ Hz, OH), 4.84 (1H, t, $J = 5.3$ Hz, CH_2OH), 5.49 (1H, d, $J = 6.4$ Hz, OH), 5.93 (1H, d, $J = 4.3$ Hz, H-1'), 7.25 (1H, dd, $J = 7.2$ Hz, $J = 6.4$ Hz, H-6), 7.29 (1H, dd, $J = 7.5$ Hz, $J = 7.2$ Hz, H-5), 7.74 (1H, d, $J = 6.4$ Hz, H-7), 8.22 (1H, d, $J = 7.5$ Hz, H-4), 8.27 (1H, s, H-2); ^{13}C NMR δ : 24.47 (q, CH_3), 59.59 (t, C-5'), 69.98 (d, C-3'), 79.47 (d, C-2'), 80.65 (d, C-4'), 104.50 (d, C-1'), 112.89 (d, C-7), 114.35 (s, C-3), 116.35 (s, C-3a), 121.64 (d, C-6), 122.26 (d, C-5), 123.41 (d, C-4), 126.86 (s, C-7a), 134.41 (d, C-2), 167.58 (s, CO). Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{NO}_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.81; H, 5.83; N, 4.87.

1- β -D-Ribofuranosylindole-3-carboxaldehyde (10b). (50% yield), oil; IR: 3330 (broad OH), 1690 (CO) cm^{-1} ; ^1H NMR δ : 3.35-4.09 (5H, m, H-2', H-3', H-4' and 2xH-5'), 4.47 (1H, d, $J = 4.3$ Hz, OH), 4.80 (1H, t, $J = 6.4$ Hz, CH_2OH), 5.46 (1H, d, $J = 6.4$ Hz, OH), 5.92 (1H, d, $J = 4.3$ Hz, H-1'), 7.23 (1H, dd, $J = 7.6$ Hz, $J = 7.2$ Hz, H-6), 7.30 (1H, dd, $J = 7.2$ Hz, $J = 6.4$ Hz, H-5), 7.79 (1H, d, $J = 7.6$ Hz, H-7), 8.12 (1H, d, $J = 6.4$ Hz, H-4), 8.35 (1H, s, H-2), 9.96 (1H, s, CHO); ^{13}C NMR δ : 59.55 (t, C-5'), 69.94 (d, C-3'), 79.56 (d, C-2'), 80.68 (d, C-4'), 104.53 (d, C-1'), 113.18 (d, C-7), 114.40 (s, C-3), 117.56 (s, C-3a), 120.98 (d, C-6), 122.67 (d, C-5), 124.05 (d, C-4), 134.77 (s, C-7a), 137.59 (d, C-2), 165.13 (d, CO). Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{NO}_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.68; H, 5.55; N, 5.35.

3-Cyano-1- β -D-ribofuranosylindole (10c). (100% yield), mp 98 $^\circ\text{C}$; IR: 3336 (broad OH), 2226 (CN) cm^{-1} ; ^1H NMR δ : 3.42-3.87 (5H, m, H-2', H-3', H-4' and 2xH-5'), 4.43 (1H, d, $J = 4.3$ Hz, OH), 4.83 (1H, t, $J = 6.1$ Hz, CH_2OH), 5.45 (1H, d, $J = 6.4$ Hz, OH), 5.91 (1H, d, $J = 4.3$ Hz, H-1'), 7.30 (1H, dd, $J = 7.5$ Hz, $J = 6.4$ Hz, H-6), 7.37 (1H, dd, $J = 7.5$ Hz, $J = 6.4$ Hz, H-5), 7.65 (1H, d, $J = 6.4$ Hz, H-7), 7.81 (1H, d, $J = 7.5$ Hz, H-4), 8.28 (1H, s, H-2); ^{13}C NMR δ : 59.52 (t, C-5'), 69.87 (d, C-3'), 79.48 (d, C-2'), 80.66 (d, C-4'), 85.00 (s, C-3), 104.54 (d, C-1'), 113.63 (d, C-7), 114.88 (s, CN), 115.53 (s, C-3a), 118.87 (d, C-6), 122.50 (d, C-5), 124.24 (d, C-4), 128.12 (s, C-7a), 133.84 (d, C-2). Anal. Calcd. for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.41; H, 5.18; N, 10.41.

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