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Synthesis of N^2-Arylisocytidines and N^2-Aryl-2′-deoxyisocytidines

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Summary. 2-(Arylamino)pyrimidin-4-ones were synthesized, silylated, and condensed with 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranoside to afford the corresponding N^2-aryl protected isocytidines. Deprotection of the acetylated isocytidines using saturated NH_3 in *Me*OH solution gave 1-(β-D-ribofuranosyl)-2-(arylamino)-4-pyrimidinones. Methyl 2-deoxy-3,5-di-*O*-toluyl-α/β-D-ribofuranoside was prepared and condensed with the previously silylated bases to afford the anomeric mixture of protected nucleosides. The pure β-anomers were synthesized with better yield by treating the sodium salts of N^2-arylisocytosine derivatives with 2-deoxy-3,5-di-*O*-toluyl-α-D-ribofuranosyl chloride. Deprotection of the latter anomers afforded the corresponding free hydroxyl derivatives. The synthesized free nucleosides are under antiviral and oligonucleotide investigations.

Keywords. Cytosine; Isocytosine; Guanine; Isocytidine; 2′-Deoxyisocytidine.

Introduction

Isocytosine (2-amino-4-pyrimidinone) designates the pyrimidine part of guanine, and even though it is not involved directly as a carrier of the genetic code, it is of biological significance and its medical applications are numerous [1] (Fig. 1). A variety of 2-amino-4-pyrimidinones display anticancer, antiviral, or antibacterial properties [2–6], or are rendered as valuable agrochemicals [7–9]; specifically, platinum group metal complexes of isocytosine and derivatives attracted considerable attention because of their antitumor activity [10]. In addition, the isocytosine ring system has been explored as a molecular functionality for supramolecular assembly of H-bonded rod and layered organic materials [11], as a host for guests with suitable H-bonding abilities [12], or as color reagents for metal cations [13]. Nucleoside analogues bearing unnatural hydrogen bonding patterns have been proposed to expand the number of complementary nucleoside pairs available in nucleic acids [14, 15]. Several nucleoside pairs with complementary H-bonding patterns have been introduced into oligonucleotides [16–18]. In this paper we present the synthesis of N^2-arylisocytidines and N^2-aryl-2′-deoxyisocytidines.

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Results and Discussion

2-(Arylamino)pyrimidin-4-ones **2a**–**2c** were synthesized by refluxing 2-methylthiouracil (**1**) [19] with arylamines (aniline, *N*-methylaniline, and 4-chloroaniline) in glacial acetic acid. The products were recrystallized from *Ac*OH/H_2O to afford pale yellow powders in 75–90% yields. The ^{1}H NMR spectra showed H-5 and H-6 as doublet at $\delta = 6.17$–6.37 and 7.55–7.85 ppm. The ^{13}C NMR spectra showed the signals of C-5 and C-6 at $\delta = 109.4$–109.6 and 158.9–160.2 ppm. Silylation of these bases was carried out according to the *Wittenburg* method [20] by treating the 2-(arylamino)pyrimidin-4-ones **2a**–**2c** with 1,1,1,3,3,3-hexamethyldisilizane (*HMDS*) in presence of $(NH_4)_2SO_4$ as a catalyst at reflux temperature.

Condensation of 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranoside (**3**) with silylated bases using the trimethylsilyl trifluoromethanesulfonate (*TMS*-triflate) method of *Vorbrüggen et al.* [21] in dry *Me*CN at −30°C to room temperature for 2 h, gave the corresponding

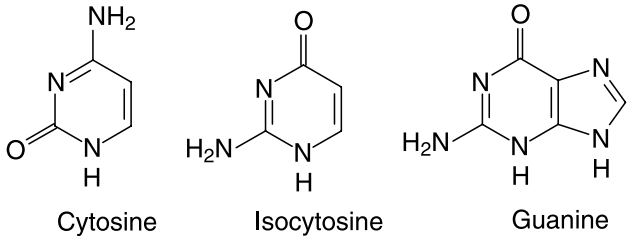
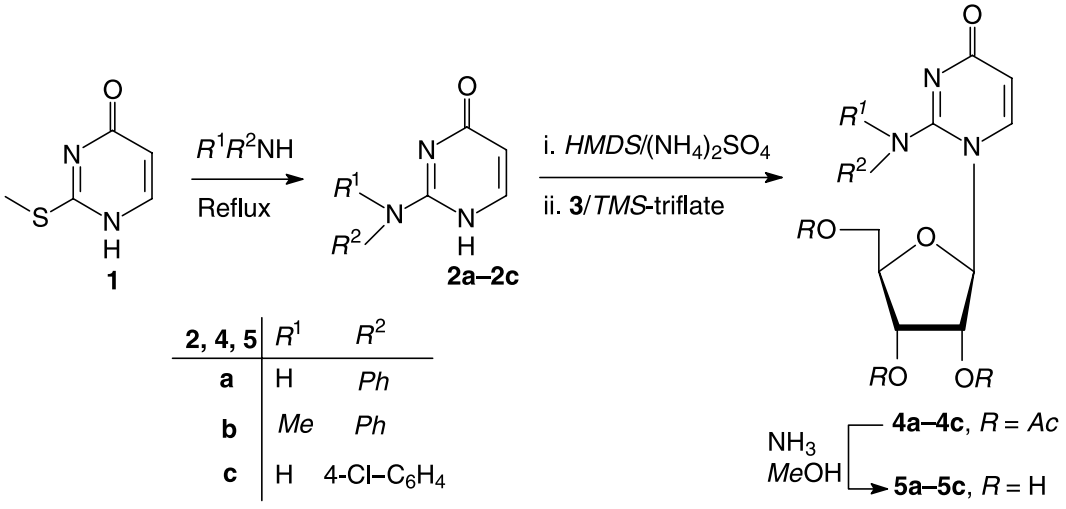
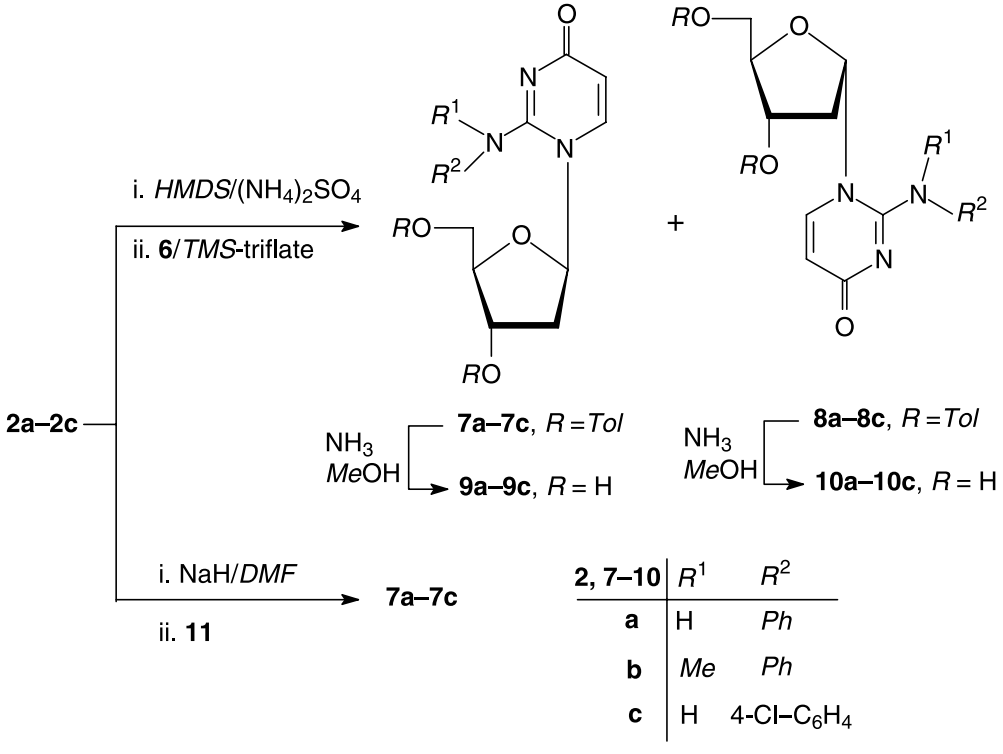


Fig. 1. Structures of cytosine, isocytosine, and guanine

N^2-aryl protected isocytidines **4a**–**4c** in 28–35% yields. The ^{1}H NMR spectra showed three singlets at $\delta = 2.04$–2.09, 2.10–2.12, and 2.16–2.18 ppm corresponding to *Me* of three *Ac* groups, while the anomeric proton appears as doublet at $\delta = 6.25$–6.28 ppm. The ^{13}C NMR spectra showed three signals at 20.3, 20.9, and 21.2 corresponding to *Me* of three *Ac* groups, while the three carbonyl groups of



Scheme 1



Scheme 2

Ac appear at $\delta = 169.3$, 169.7, and 170.1 ppm. Deprotection of **4a–4c** using saturated NH_3 in *Me*OH solution at room temperature gave 1-(β-D-ribofuranosyl)-2-(arylamino)-4-pyrimidinones **5a–5c** in 91–93% yields. ^{1}H and ^{13}C NMR spectra showed the disappearance of the acetyl groups (Scheme 1).

Methyl 2-deoxy-3,5-di-*O*-toluyl-α/β-D-ribofuranoside (**6**) was prepared from 2-deoxy-D-ribose [22]. Condensation of **6** with silylated bases **2a–2c** as described before afforded the anomeric mixture of protected nucleosides **7a–7c** and **8a–8c**. After separation and purification by silica gel column chromatography using 30% ether in *n*-hexane, the β-anomers **7a–7c** were obtained as the major products in 18–24% yields, while the α-anomers **8a–8c** as the minor products were isolated in 6–8% yields. The ^{1}H NMR spectra showed the presence of the anomeric proton of β-anomers **7a–7c** as multiplet in the range $\delta =$ 6.34–6.49 ppm, while for α-anomers **8a–8c** gave multiplet in the range $\delta = 6.14$–6.19 ppm. The anomeric protons as well as the rest of sugar protons were identified in comparison to the previously identified protons [23]. In order to synthesize the pure β-anmoers **7a–7c** with better yield than the previously mentioned method we treated the N^2-arylisocytosine derivatives **2a–2c** with NaH in dry *DMF* to form the corresponding sodium salts which were treated directly with 2-deoxy-3,5-di-*O*-toluyl-α-D-ribofuranosyl chloride (**11**) for 2 h to afford **7a–7c** in 29–38%. Deprotection of **7a–7c** and **8a–8c** was carried out with saturated NH_3 in *Me*OH solution at room temperature to afford the corresponding free hydroxyl derivatives **9a–9c** (92–94%) and **10a–10c** (92–93%) (Scheme 2). The synthesized free nucleosides **5a–5c** and **9a–9c** are under antiviral and oligonucleotide investigations.

Experimental

Melting points were determined using a *Kofler* block instrument. TLC was performed on plastic plates Silica Gel 60 F_{254} (E. Merck, layer thickness 0.2 mm). The detection was achieved by treatment with a solution of 15% H_2SO_4 in methanol, and heating at 150°C. NMR spectra were recorded on a Bruker AC 250 FT NMR spectrometer at 250 MHz for ^{1}H NMR and 62.9 MHz for ^{13}C NMR with *TMS* as an internal standard. MALDI-MS were measured with a KRATOS Analytical Compact, using 2,5-dihydroxybenzoic acid (*DHB*) as matrix. The $(M + Na)^+$ ion was peak matched using ions derived from the 2,5-dihydroxybenzoic acid matrix. The microanalyses were performed at the microanalytical unit, Odense University, Denmark, and were found to agree favourably with the calculated values.

General Procedure for the Synthesis of 2-(Arylamino) pyrimidin-4-ones ***2a–2c***

A mixture of 2.84 g **1** (20 mmol) and arylamines (30 mmol) in 60 cm^3 glacial acetic acid was refluxed for 10 h (TLC). The solvent was removed under reduced pressure and the residue was recrystallized from *Ac*OH/H_2O to afford **2a–2c** as pale yellow powders in 75–90% yield.

2-(Phenylamino)pyrimidin-4-one (**2a**, $C_{10}H_9N_3O$)
Yield 3.20 g (85%); Mp 217–219°C; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 6.37$ (d, $J = 3.7$ Hz, H-5), 7.19–7.43 (m, *Ph*-H, NH), 7.68 (d, $J = 6.8$ Hz, H-6), 8.55 (br s, NH) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 109.4$ (C-5), 122.8, 122.9, 130.2, 147.2 (*Ph*-C), 152.6 (C-2), 160.0 (C-6), 164.3 (C-4) ppm; MS: m/z (%) = 188 [($M^+ + 1$), 12.7].

2-[Methyl(phenyl)amino]pyrimidin-4-one (**2b**, $C_{11}H_{11}N_3O$)
Yield 3.01 g (75%); Mp 207–209°C; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 3.45$ (s, CH_3), 6.17 (d, $J = 3.0$ Hz, H-5), 7.34–7.68 (m, *Ph*-R, NH), 7.85 (d, $J = 6.1$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 31.9$ (CH_3), 109.6 (C-5), 122.9, 125.9, 129.6, 141.8 (*Ph*-C), 153.9 (C-2), 158.9 (C-6), 163.8 (C-4) ppm; MS: m/z (%) = 202 [($M^+ + 1$), 13.2].

2-(4-Chlorophenylamino)pyrimidin-4-one (**2c**, $C_{10}H_8ClN_3O$)
Yield 3.96 g (90%); Mp 248–250°C; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 6.35$ (d, $J = 3.8$ Hz, H-5), 7.05–7.55 (m, *Ph*-H, H-6, NH), 8.55 (br s, NH) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 109.4$ (C-5), 116.5, 125.6, 128.7, 141.5 (*Ph*-C), 152.6 (C-2), 160.2 (C-6), 164.3 (C-4) ppm; MS: m/z (%) = 222 [($M^+ + 1$), 12.8].

1-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-2-(arylamino)-4-pyrimidinones ***4a–4c***

A mixture of 3 mmol **2a–2c**, 30 cm^3 1,1,1,3,3,3-hexamethyldisilizane (*HMDS*), and 40 mg $(NH_4)_2SO_4$ (0.22 mmol) was heated under reflux overnight. The solvent was removed *in vacuo* to afford the silylated base which was dissolved in 20 cm^3 dry *Me*CN. **3** (0.95 g, 3 mmol) in 20 cm^3 dry *Me*CN were added and the mixture was cooled to −30°C. A solution of 0.25 cm^3 trimethylsilyl trifluoromethanesulfonate (1.24 mmol) in 5 cm^3 dry *Me*CN was added dropwise over 25 min to the reaction mixture with stirring. The reaction mixture was stirred at room temperature for 2 h until the total consuming of sugar (TLC). The solvent was removed under reduced pressure and the residue was dissolved in 100 cm^3 CH_2Cl_2 and washed with 3×50 cm^3 saturated aqueous solution of $NaHCO_3$ and 3×50 cm^3 H_2O. The organic layer was dried over Na_2SO_4 and evaporated *in vacuo* to give a crude dark brown product which was purified by silica gel column chromatography using ether/pet. ether (1/1, *v*/*v*).

1-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-2-(phenylamino)-4-pyrimidinone (**4a**, $C_{21}H_{23}N_3O_8$)
White foam (0.45 g, 34%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.09$, 2.12, 2.17 (3s, $3CH_3CO$), 4.09–4.34 (m, H-5′), 4.43 (m, H-4′), 5.71 (dd, $J = 5.0$, 6.0 Hz, H-3′), 5.91 (m, H-2′), 5.99 (d, $J = 4.0$ Hz, H-5), 6.25 (d, $J = 6.0$ Hz, H-1′),

7.22–7.40 (m, *Ph*-H), 7.53 (d, $J = 6.8$ Hz, H-6) ppm; ^{13}C NMR ($CDCl_3$, 250 MHz): $\delta = 20.3$, 20.9, 21.2 ($3CH_3CO$), 63.0 (C-5′), 70.6 (C-3′), 73.2 (C-2′), 80.4 (C-4′), 85.4 (C-1′), 105.8 (C-5), 121.9, 122.6, 129.9, 144.2 (*Ph*-C), 131.6 (C-6) 148.3 (C-2), 164.3 (C-4), 169.3, 169.7, 170.1 ($3CH_3CO$) ppm; MS: m/z (%) = 468 [($M^+ + Na$), 24.6].

1-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-2-(methyl(phenyl) amino)-4-pyrimidinone (**4b**, $C_{22}H_{25}N_3O_8$)
White foam (0.38 g, 28%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.08$, 2.12, 2.18, (3s, $3CH_3CO$), 3.44 (CH_3), 4.10–4.32 (m, H-5′), 4.42 (m, H-1′), 5.74 (dd, $J = 4.6$, 6.1 Hz, H-3′), 5.89 (m, H-2′), 5.97 (d, $J = 4.0$ Hz, H-5), 6.28 (d, $J = 6.0$ Hz, H-1′), 7.20–7.44 (m, *Ph*-H), 7.58 (d, $J = 6.5$ Hz, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 20.3$, 20.9, 21.2 ($3CH_3CO$), 34.2 (CH_3), 63.1 (C-5′), 70.6 (C-3′), 73.4 (C-2′), 80.5 (C-4′), 89.1 (C-1′), 106.0 (C-5), 124.7, 125.2, 129.6, 131.5, 142.1 (*Ph*-C), 131.5 (C-6),147.6 (C-2), 163.5(C-4), 169.3, 169.7, 170.1 ($3CH_3CO$) ppm; MS: m/z (%) = 482 [($M^+ + Na$), 25.9].

1-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-2-(4-chlorophenyl-amino)-4-pyrimidinone (**4c**, $C_{21}H_{22}ClN_3O_8$)
White foam (0.50 g, 35%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.04$, 2.10, 2.16 (3s, $3CH_3CO$), 4.11–4.33 (m, H-5′), 4.42 (m, H-1′), 5.71 (dd, $J = 4.3$, 5.8 Hz, H-3′), 5.94 (m, H-2′), 6.09 (d, $J = 3.8$ Hz, H-5), 6.26 (d, $J = 6.0$ Hz, H-1′), 7.22–7.67 (m, *Ph*-H, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 20.3$, 20.9, 21.2 ($3CH_3CO$), 63.2 (C-5′), 70.9 (C-3′), 73.2 (C-2′), 80.6 (C-4′), 85.4 (C-1′), 105.9 (C-5), 118.8, 124.9, 128.7, 144.1 (*Ph*-C), 131.6 (C-6) 146.2 (C-2), 163.3 (C-4), 169.3, 169.7, 170.1 ($3CH_3CO$) ppm; MS: m/z (%) = 502 [($M^+ + Na$), 24.6].

1-(β-D-Ribofuranosyl)-2-(arylamino)-4-pyrimidinones ***5a–5c***
A solution of **4a**–**4c** (0.6 mmol) in 30 cm^3 saturated NH_3/*Me*OH was allowed to stir overnight at room temperature. The mixture was concentrated and purified by column chromatography using 12% *Me*OH in CH_2Cl_2.

1-(β-D-Ribofuranosyl)-2-(phenylamino)-4-pyrimidinone (**5a**, $C_{15}H_{17}N_3O_5$)
White foam (0.18 g, 93%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 3.45$–3.71 (m, H-5′), 3.98 (m, H-4′), 4.25 (m, H-3′), 4.60 (m, H-2′), 4.99 (br s, HO-5′), 5.18 (br s, HO-3′), 5.41 (br s, HO-2′), 6.05 (d, $J = 3.5$ Hz, H-5), 6.12 (d, $J = 5.0$ Hz, H-1′), 7.32–7.45 (m, *Ph*-H), 7.55 (d, $J = 7.0$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 62.1$ (C-5′), 71.9 (C-3′), 73.9 (C-2′), 85.8 (C-4′), 87.9 (C-1′), 105.8 (C-5), 121.6, 122.5, 129.7, 143.4 (*Ph*-C), 133.2 (C-6) 147.2 (C-2), 164.6 (C-4) ppm; MS: m/z (%) = 320 [($M^+ + 1$), 18.5].

1-(β-D-Ribofuranosyl)-2-[methyl(phenyl)amino]-4-pyrimidinone (**5b**, $C_{16}H_{19}N_3O_5$)
White foam (0.19 g, 91%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 3.34$ (m, H-5′), 3.49 (s, CH_3), 3.51 (m, H-5′), 3.88 (m, H-4′), 4.45 (m, H-3′), 4.64 (m, H-2′), 5.09 (br s, HO-5′), 5.16 (br s, HO-3′), 5.39 (br s, HO-2′), 5.92 (d, $J = 3.6$ Hz, H-5), 6.15 (d, $J = 5.2$ Hz, H-l′), 7.28–7.51 (m, *Ph*-H), 7.58 (d, $J = 6.8$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 34.2$ (CH_3), 62.1 (C-5′), 71.9 (C-3′), 72.2 (C-2′), 86.7 (C-4′), 88.4 (C-1′), 106.0 (C-5), 124.7, 125.1, 129.5, 144.7 (*Ph*-C), 133.0 (C-6) 146.7 (C-2), 163.6 (C-4) ppm; MS: m/z (%) = 334 [($M^+ + 1$), 18.8].

1-(β-D-Ribofuranosyl)-2-(4-chlorophenylamino)-4-pyrimidinone (**5c**, $C_{15}H_{16}ClN_3O_5$)
White foam (0.19 g, 92.5%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): 3.35–3.60 (m, H-5′), 3.86 (m, H-4′), 4.24 (m, H-3′), 4.56 (m, H-2′), 5.05 (br s, HO-5′), 5.16 (br s, HO-3′), 5.38 (br s, HO-2′), 5.95 (d, $J = 3.6$ Hz, H-5), 6.10 (d, $J = 5.0$ Hz, H-1′), 7.12–7.34 (dd, $J = 4.0$, 8.0 Hz, *Ph*-H), 7.58 (d, $J = 6.8$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 62.1$ (C-5′), 72.0 (C-3′), 73.6 (C-2′), 84.9 (C-4′), 87.3 (C-1′), 105.8 (C-5), 118.7, 124.9, 128.6, 144.2 (*Ph*-C), 133.2 (C-6) 146.4 (C-2), 162.8 (C-4) ppm; MS: m/z (%) = 354 [($M^+ + 1$), 32.9].

1-(2-Deoxy-3,5-di-O,O-(4-methylbenzoyl)-α/β-D-ribofuranosyl)-2-(arylamino)-4-pyrimidinones ***7a–7c*** and ***8a–8c***
Method A: The appropriate base **2a**–**2c** (3 mmol) was treated with 30 cm^3 1,1,1,3,3,3-hexamethyldisilizane (*HMDS*) and 40 mg $(NH_4)_2SO_4$ (0.22 mmol) at 130°C for 20 h. The silylated compound was concentrated and used, without further purification, for *Vorbruggen* coupling. The silylated base was redissolved in 20 cm^3 *Me*CN, 1.15 g **6** (3 mmol) in 20 cm^3 dry *Me*CN were added, and the mixture was cooled to −30°C. Trimethylsilyl trifluoromethanesulfonate (0.25 cm^3, 1.24 mmol) in 5 cm^3 dry *Me*CN was added dropwise over 25 min to the reaction mixture with stirring overnight. After concentration, the residue was diluted with CH_2Cl_2. It was extracted with 3×50 cm^3 saturated $NaHCO_3$ and 3×50 cm^3 H_2O. The organic layer was dried over anhydrous Na_2SO_4 and purified by column chromatography using 30% ether in *n*-hexane to give α- and β-derivatives.

Method B: A solution of **2a**–**2c** (3 mmol) in 30 cm *DMF* was treated with 127 mg NaH (60% in mineral oil, 3.2 mmol). The solution was heated to 80 °C for 1 h. After cooling to room temperature, 1.17 g **11** (3 mmol) were added portionwise, and the reaction was stirred for 2 h. The reaction mixture was diluted with CH_2Cl_2 and washed with 3×50 cm^3 $NaHCO_3$ and 3×50 cm^3 H_2O. The organic layer was dried over anhydrous Na_2SO_4 and purified by column chromatography using 50% ether in *n*-hexane to give the β-derivative only.

1-(2-Deoxy-3,5-di-O,O-(4-methylbenzoyl)-β-D-ribofuranosyl)-2-(phenylamino)-4-pyrimidinone (**7a**, $C_{31}H_{29}N_3O_6$)
White foam (0.39 g, 24%, method A; 0.61 g, 38%, method B); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.38$, 2.46 (2s, $2CH_3$), 2.88–3.14 (m, H-2′), 4.48 (m, H-5′), 4.53 (m, H-4′), 4.71 (m, H-5′), 5.67 (m, H-3′), 5.94 (d, $J = 3.2$ Hz, H-5), 6.49 (m, H-1′), 7.10–8.04 (m, *Ph*-H, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 20.9$, 21.5 ($2CH_3$), 39.9 (C-2′), 64.1 (C-5′), 75.0 (C-3′), 81.7 (C-4′), 83.6 (C-1′), 105.8 (C-5), 121.8, 122.5, 129.8, 130.8, 132.4, 133.6, 135.5, 138.3, 143.5 (*Ph*-C, C-6), 146.3 (C-2), 164.82 (C-4), 165.2, 165.8 (2CO) ppm; MS: m/z (%) = 562 [($M^+ + Na$), 35.6].

1-(2-Deoxy-3,5-di-O,O-(4-methylbenzoyl)-β-D-ribofuranosyl)-2-[methyl(phenyl)amino]-4-pyrimidinone (**7b**, $C_{32}H_{31}N_3O_6$)
White foam (0.30 g, 18%, method A; 0.48 g, 29%, method B); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.36$, 2.44 (2s, $2CH_3$), 2.86–3.20 (m, H-2′), 3.50 (s, CH_3), 4.48 (m, H-5′), 4.52 (m, H-4′), 4.74 (m, H-5′), 5.65 (m, H-3′), 5.88 (d, $J = 3.2$ Hz, H-5), 6.34 (m, H-1′), 7.10–7.96 (m, *Ph*-H, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 20.9$, 21.5 ($2CH_3$), 34.2 (CH_3), 39.1 (C-2′), 64.0 (C-5′), 74.8 (C-3′), 81.6 (C-4′), 85.1 (C-1′), 106.0 (C-5), 124.7, 125.1, 126.1, 129.0, 129.5, 132.1, 143.5 (*Ph*-C, C-6), 146.8 (C-2), 165.5 (C-4), 165.3, 165.8 (2CO) ppm; MS: m/z (%) = 576 [($M^+ + Na$), 36.3].

1-(2-Deoxy-3,5-di-O,O-(4-methylbenzoyl)-β-D-ribofuranosyl)-2-(4-chlorophenylamino)-4-pyrimidinone (**7c**, $C_{31}H_{28}ClN_3O_6$)
White foam (0.32 g, 22%, method A; 0.50 g, 37%, method B); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.39$, 2.44 (2s, $2CH_3$), 2.92–3.20 (m, H-2′), 4.46 (m, H-5′), 4.51 (m, H-4′), 4.68 (m, H-5′), 5.70 (m, H-3′), 6.00 (d, $J = 3.4$ Hz, H-5), 6.44 (m, H-1′), 7.00–7.94 (m, *Ph*-H, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 20.9$, 21.5 ($2CH_3$), 39.9 (C-2′), 64.2 (C-5′), 75.1 (C-3′), 81.8 (C-4′), 84.4 (C-1′), 105.6 (C-5), 118.7, 124.9, 126.8, 128.6, 129.0, 132.2, 138.9, 143.5 (*Ph*-C, C-6), 146.5 (C-2), 164.7 (C-4), 165.34, 165.9 (2CO) ppm; MS: m/z (%) = 596 [($M^+ + Na$), 35.3].

1-(2-Deoxy-3,5-di-O,O-(4-methylbenzoyl)-α-D-ribofuranosyl)-2-(phenylamino)-4-pyrimidinone (**8a**, $C_{31}H_{29}N_3O_6$)
White foam (0.13 g, 8%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.30$ (m, H-2′), 2.40, 2.49 (2s, $2CH_3$), 2.62 (m, H-2′), 3.54–3.76 (m, H-5′), 4.50 (m, H-4′), 5.26 (m, H-3′), 5.95 (d, $J = 3.4$ Hz, H-5), 6.18 (m, H-1′), 7.14–7.96 (m, *Ph*-H, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 21.1$, 21.5 ($2CH_3$), 39.7 (C-2′), 63.9 (C-5′), 74.3 (C-3′), 86.2 (C-1′), 88.0 (C-4′), 105.7 (C-5), 122.0, 122.8, 129.1, 132.6, 138.4, 143.7 (*Ph*-C, C-6), 146.3 (C-2), 163.9 (C-4), 166.1, 166.8 (2CO) ppm; MS: m/z (%) = 562 [($M^+ + Na$), 35.5].

1-(2-Deoxy-3,5-di-O,O-(4-methylbenzoyl)-α-D-ribofuranosyl)-2-[methyl(phenyl)amino]-4-pyrimidinone (**8b**, $C_{32}H_{31}N_3O_6$)
White foam (0.10 g, 6%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.33$ (m, H-2′), 2.41, 2.46 (2s, $2CH_3$), 2.59 (m, H-2′), 3.46 (s, CH_3), 3.50–3.75 (m, H-5′), 4.55 (m, H-4′), 5.29 (m, H-3′), 5.90 (d, $J = 3.1$ Hz, H-5), 6.14 (m, H-1′), 7.14–7.90 (m, *Ph*-H, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 20.9$, 21.4 ($2CH_3$), 34.3 (CH_3), 39.8 (C-2′), 64.1 (C-5′), 74.3 (C-3′), 86.5 (C-1′), 87.9 (C-4′), 106.1 (C-5), 124.3, 125.4, 127.1, 129.1, 130.4, 133.7, 144.2 (*Ph*-C, C-6), 146.9 (C-2), 163.5 (C-4), 165.3, 165.8 (2CO) ppm; MS: m/z (%) = 576 [($M^+ + Na$), 36.7].

1-(2-Deoxy-3,5-di-O,O-(4-methylbenzoyl)-α-D-ribofuranosyl)-2-(4-chlorophenylamino)-4-pyrimidinone (**8c**, $C_{31}H_{28}ClN_3O_6$)
White foam (0.10 g, 7%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.34$ (m, H-2′), 2.39, 2.48 (2s, $2CH_3$), 2.65 (m, H-2′), 3.52–3.74 (m, H-5′), 4.53 (m, H-4′), 5.22 (m, H-3′), 6.01 (d, $J = 3.3$ Hz, H-5), 6.19 (m, H-1′), 7.05–7.96 (m, *Ph*-H, H-6) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 20.9$, 21.7 ($2CH_3$), 39.7 (C-2′), 63.8 (C-5′), 74.3 (C-3′), 86.5 (C-1′), 87.8 (C-4′), 105.4 (C-5), 119.0, 124.7, 129.1, 132.4, 138.8, 143.4 (*Ph*-C, C-6), 163.7 (C-4), 165.4, 165.9 (2CO) ppm; MS: m/z (%) = 596 [($M^+ + Na$), 35.4].

1-(2-Deoxy-α/β-D-ribofuranosyl)-2-(arylamino)-4-pyrimidinones ***9a–9c****, and* ***10a–10c***
Compounds **7a–7c** and **8a–8c** (0.2 mmol) in 10 cm^3 saturated NH_3/*Me*OH were stirred at room temperature for 16 h. The resulting solution was evaporated till dryness under reduced pressure. The residue was chromatographed on a silica gel column with 8% *Me*OH in CH_2Cl_2 to give **9a–9c** in 92–94% and **10a–10c** in 92–93% yields.

1-(2-Deoxy-β-D-ribofuranosyl)-2-(phenylamino)-4-pyrimidinone (**9a**, $C_{15}H_{17}N_3O_4$)
White foam (0.06 g, 94%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 2.55$–2.65 (m, H-2′), 3.49–3.75 (m, H-5′), 4.24 (m, H-4′), 4.48 (m, H-3′), 5.08, 5.22 (2s, 2OH), 5.98 (d, $J = 3.7$ Hz, H-5), 6.19 (dd, $J = 6.7$, 4.7 Hz, H-1′), 7.22–7.48 (m, *Ph*-H), 7.58 (d, $J = 6.8$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 39.6$ (C-2′), 61.6 (C-5′), 70.8 (C-3′), 84.8 (C-4′), 87.6 (C-1′), 105.8 (C-5), 121.6, 122.4, 130.1, 132.2, 137.8, 143.5 (*Ph*-C, C-6), 147.2 (C-2), 163.2 (C-4) ppm; MS: m/z (%) = 304 [($M^+ + 1$), 17.7].

1-(2-Deoxy-β-D-ribofuranosyl)-2-[methyl(phenyl)amino]-4-pyrimidinone (**9b**, $C_{16}H_{19}N_3O_4$)
White foam (0.06 g, 92%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 2.38$–2.54 (m, H-2′), 3.48 (s, CH_3), 3.49–3.72 (m, H-5′), 4.14 (m, H-4′), 4.42 (m, H-3′), 5.16, 5.25 (2br s, 2OH), 6.08 (d, $J = 3.7$ Hz, H-5), 6.27 (dd, $J = 6.6$, 4.5 Hz, H-1′), 7.28–7.53 (m, *Ph*-H), 7.64 (d, $J = 6.4$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 34.2$ (CH_3), 38.8 (C-2′), 61.6 (C-5′), 70.8 (C-3′), 85.6 (C-4′), 87.9 (C-1′), 106.1 (C-5), 125.6, 129.5, 132.6, 144.8 (*Ph*-C, C-6), 147.0 (C-2), 164.7 (C-4) ppm; MS: m/z (%) = 318 [($M^+ + 1$), 18.7].

1-(2-Deoxy-β-D-ribofuranosyl)-2-(4-chlorophenylamino)-4-pyrimidinone (**9c**, $C_{15}H_{16}ClN_3O_4$)
White foam (0.06 g, 94%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 2.52$–2.64 (m, H-2′), 3.46–3.70 (m, H-5′), 4.20 (m, H-4′), 4.42 (m, H-3′), 5.10, 5.19 (2br s, 2OH), 5.99 (d, $J = 3.8$ Hz, H-5), 6.26 (dd, $J = 6.4$, 4.8 Hz, H-1′), 7.06–7.51 (dd, $J = 8.2$, 4.3 Hz, *Ph*-H), 7.62 (d, $J = 7.0$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 39.6$ (C-2′), 62.0 (C-5′), 71.1 (C-3′), 84.8 (C-4′), 87.4 (C-1′), 105.8 (C-5), 118.7, 125.1, 128.6, 132.5, 137.8, 143.4 (*Ph*-C, C-6), 147.4 (C-2), 163.8 (C-4) ppm; MS: m/z (%) = 338 [($M^+ + 1$), 23.1].

1-(2-Deoxy-α-D-ribofuranosyl)-2-(phenylamino)-4-pyrimidinone (**10a**, $C_{15}H_{17}N_3O_4$)
White foam (0.06 g, 93%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 2.17$, 2.89 (m, H-2′), 3.11–3.29 (m, H-5′), 3.79 (m, H-4′), 4.42 (m, H-3′), 5.98 (d, $J = 3.5$ Hz, H-5), 6.24 (m, H-1′), 7.20–7.49 (m, *Ph*-H), 7.62 (d, $J = 6.7$ Hz, H-6) ppm; ^{13}C NMR

(*DMSO*-d_6, 62.5 MHz): $\delta = 40.7$ (C-2′), 62.8 (C-5′), 74.6 (C-3′), 87.8 (C-1′), 88.2 (C-4′), 105.5 (C-5), 122.9, 131.1, 133.2, 137.2, 143.7 (*Ph*-C, C-6), 147.3 (C-2), 163.8 (C-4) ppm; MS: m/z (%) = 304 [($M^+ + 1$), 17.7].

1-(2-Deoxy-α-D-ribofuranosyl)-2-[methyl(phenyl)amino]-4-pyrimidinone (**10b**, $C_{16}H_{19}N_3O_4$)
White foam (0.06 g, 93%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 2.24$, 2.84 (m, H-2′), 3.18–3.36 (m, H-5′), 3.52 (s, CH_3), 3.84 (m, H-4′), 4.39 (m, H-3′), 6.04 (d, $J = 3.4$ Hz, H-5), 6.21 (m, H-1′), 7.16–7.46 (m, *Ph*-H), 7.59 (d, $J = 6.6$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 34.6$ (CH_3), 40.6 (C-2′), 63.2 (C-5′), 74.7 (C-3′), 87.5 (C-1′), 87.9 (C-4′), 106.5 (C-5), 125.7, 128.9, 133.3, 144.4 (*Ph*-C, C-6), 146.9 (C-2), 163.8 (C-4) ppm; MS: m/z (%) = 318 [($M^+ + 1$), 18.8].

1-(2-Deoxy-α-D-ribofuranosyl)-2-(4-chlorophenylamino)-4-pyrimidinone (**10c**, $C_{15}H_{16}ClN_3O_4$)
White foam (0.06 g, 92%); ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 2.26$, 2.84 (m, H-2′), 3.18–3.30 (m, H-5′), 3.82 (m, H-4′), 4.39 (m, H-3′), 5.95 (d, $J = 3.5$ Hz, H-5), 6.22 (m, H-1′), 7.10–7.54 (dd, $J = 8.3$, 4.4 Hz, *Ph*-H), 7.64 (d, $J = 6.8$ Hz, H-6) ppm; ^{13}C NMR (*DMSO*-d_6, 62.5 MHz): $\delta = 40.4$ (C-2′), 62.6 (C-5′), 73.7 (C-3′), 87.5 (C-1′), 87.9 (C-4′), 105.6 (C-5), 119.4, 124.9, 129.1, 133.3, 137.7, 143.8 (*Ph*-C, C-6), 147.5 (C-2), 163.9 (C-4) ppm; MS: m/z (%) = 338 [($M^+ + 1$), 32.1].

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