Synthesis of N^4-β-D-glycoside cytosines and sugar N^4-acetylcytosin-1-ylmethylhydrazones as antiviral agents

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Reaction of monosaccharide aldoses with cytosine (**1**) gave stereoselectively β-*N*-glycosides **2a–d**, which were treated with acetic anhydride in pyridine to afford the corresponding acetylated derivatives **3a–d**. N^4-Acetylcytosine (**4**) was synthesised and treated with ethyl chloroacetate to give 1-(ethoxycarbonylmethyl)-N^4-acetylcytosine (**5**). Hydrolysis of the latter ester with hydrazine hydrate afforded the hydrazide derivative **6**. Condensation of the hydrazide with monosaccharide aldoses gave the corresponding sugar hydrazones **7a–f**. Acetylation of the hydrazones afforded the per-*O*-acetyl derivatives **8a–f**. The prepared compounds were tested for antiviral activity against hepatitis B virus (HBV) which showed moderate activities.

Keywords: cytosine, N^4-acetylcytosin, *N*-glycosides, antiviral activity

Glycosyl amines[1-6] are important because these occur as junctures in glycoproteins.[7,8] The chemical and structural nature of the derivatives formed from the reaction of a monosaccharide and different nitrogen bases depends upon the reaction conditions and the base used.[9] *N*-Glycosyl amines have better advantage in binding to metal ions over their saccharide counter parts, as these compounds provide additional binding centres. In view of such important aspects of *N*-glycosyl amines, herein we report the synthesis and characterisation of different *N*-glycosyl amines of simple saccharides using cytosine as an amine. Recently, the synthesis of acyclic nucleosides has attracted much attention.[10] Consequently, this significance and possible enhancement of biological activity resulting from the attachment of carbohydrate moieties to heterocycles and our interest in the synthesis of heterocyclic derivatives of carbohydrates,[11] attracted our attention to synthesise *C*-nucleosides using monosaccharide (N^4-acetylcytosine-1-yl)acetohydrazides.

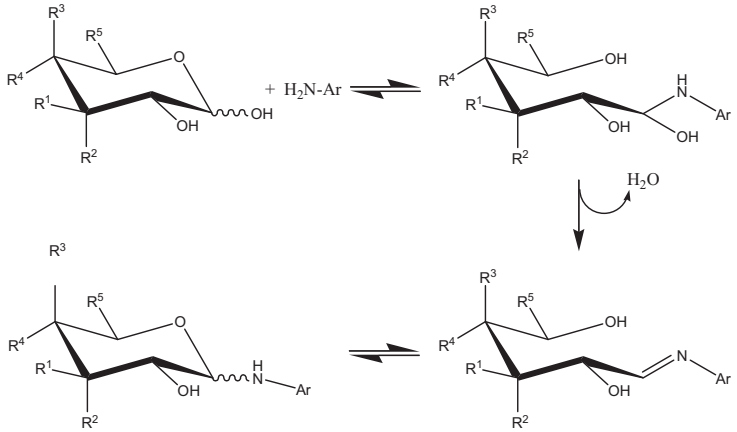
Results and discussion

Condensation of cytosine (**1**) with a number of monosaccharides (D-glucose, D-galactose, D-ribose, and D-xylose) in boiling ethanol and in the presence of a catalytic amount of glacial acetic acid gave stereoselectively 4-(β-D-glycopyranosylamino)pyrimidin-2(1*H*)-ones **2a–d** in 85-88% yields. In the ^{1}H NMR spectra of **2a–d**, the anomeric protons appear as doublet in the range δ 7.16–7.20 ppm, in which $J_{(1,2)}$ = 8.0 Hz. This value is consistent with the *β*-configuration of $^4C_1$ (D) conformation.[12]

The reaction of **2a–d** with acetic anhydride in pyridine at room temperature led to the acetylation of sugar hydroxyl groups without affecting the NH group to give tri- or tetraacetoxy-*β*-D-glycosides **3a–d** in 95–98% yields. The IR spectra of **3a–d** are characterised by two absorption bands at 3380–3395 and 1745–1755 cm^{-1} indicating the presence OAc and NH groups. In addition, the ^{1}H NMR spectra showed triplets at low field δ 5.15–5.20 ppm assigned as H-1' with $J_{(1,2)}$ = 9.0 Hz, which confirm the expected *β*-configuration of $^4C_1$ (D) conformation.

Refluxing of cytosine in acetic anhydride afforded the corresponding N^4-acetylcytosine (**4**),[13] which was treated with ethyl chloroacetate in acetone and anhydrous K_2CO_3 to afford 1-(ethoxycarbonylmethyl)-N^4-acetylcytosine (**5**) in 75% yield. Hydrazinolysis of the ethyl ester **5** gave (N^4-acetylcytosin-1-yl)acetohydrazide (**6**) in 89% yield.

Condensation of the hydrazides **6** with L-arabinose, D-ribose, D-xylose, D-glucose, D-galactose, and D-mannose gave the corresponding sugar hydrazones **7a–f** in 80-88% yield. The ^{1}H NMR spectra of the hydrazones **7a–f** confirmed the presence of sugar protons in the range δ 3.14–4.27 ppm and a doublet at δ 7.20–7.30 ppm corresponding to the proton at C-1 of the sugar. The assignments of NH and OH groups in these compounds were achieved by D_2O exchange. Acetylation of **7a–f** using acetic anhydride in pyridine at room temperature gave the corresponding acetylated derivatives **8a–f** 80–85% yields. The ^{1}H NMR spectra of the acetyl derivatives **8a–f** showed the *O*-acetyl-methyl groups at δ 1.95–2.10 ppm and the methine proton as doublet at δ 7.25–7.30 ppm.



Scheme 1

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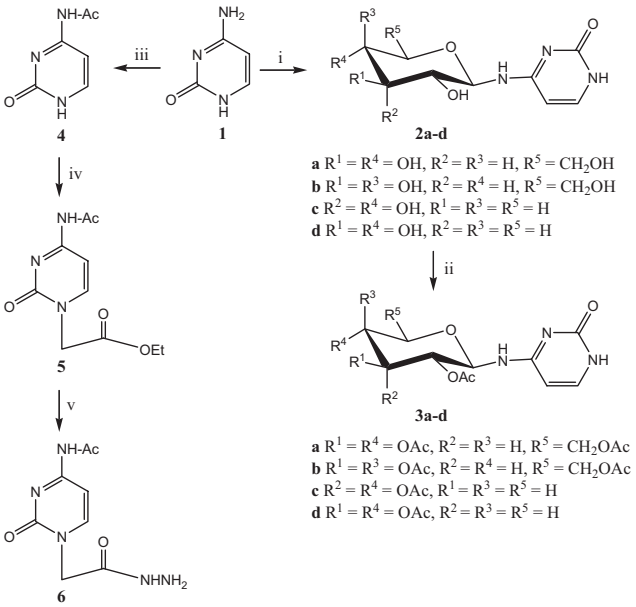
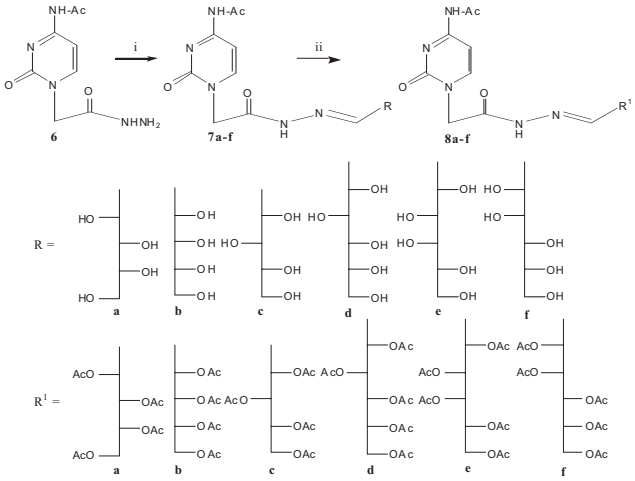


(i) Monosaccharide aldoses/EtOH/AcOH/reflux; (ii) Ac_2O/Py/r.t.; (iii) Ac_2O/reflux; (iv) $ClCH_2CO_2Et$/Acetone/K_2CO_3/reflux; (v) $N_2H_4.H_2O$/EtOH/reflux

Scheme 2



(i) Monosaccharide aldoses/EtOH/AcOH/reflux; (ii) Ac_2O/Py/r.t.

Scheme 3

Preliminary viral screening against hepatitis B virus (HBV) (Hep G2 2.2.15 cell method)[14] indicated that compounds **2a–c**, **3a**, **3b**, **7a–d**, **8a** and **8b** were found to be active against HBV replication with IC_{50} 80–90 μM and CC_{50} 85–95 μM. Compounds **2d**, **3c**, **7e**, and **8d** showed moderate viral replication inhibition and moderate cytotoxicity, while compounds **3d**, **7f**, **8c**, **8e**, and **8f** showed very low inhibition and high cytotoxicity.

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. IR spectra were recorded with a Perkin-Elmer model 1720 FTIR (KBr). ^{1}H NMR spectra were recorded on a Bruker AC 250 FT NMR spectrometer, 250 MHz 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. All commercially available reagents were used without further purification. Pyridine was distilled from CaH_2 and stored over molecular sieves. The microanalyses were performed at the microanalytical unit, Universität Konstanz, Germany. Viral screening against HBV was conducted at the National Liver Institute, Menoufia University, Shebin El Koam, Egypt.

4-(β-D-Glycopyranosylamino)pyrimidin-2(1H)-ones **2a–d**

A solution of the respective sugar (5 mmol) in ethanol (5 ml) was treated with **1** (0.55 g, 5 mmol) in ethanol (40 ml), and glacial acetic acid (0.1 ml). The mixture was heated under reflux for 2 h (TLC). The solid, which separated out on cooling, was filtered, washed with ethanol, and crystallised from ethanol to afford **2a–d** in 85–88% yields.

4-(β-D-Glucopyranosylamino)pyrimidin-2(1H)-one (**2a**): Yield 87%. M.p. 202–204°C. ^{1}H NMR (DMSO-d_6) δ: 3.25–3.60 (m, 2H, H-6'), 4.30–4.90 (m, 8H, H-2', H-3', H-4', H-5', 4xOH), 7.20 (d, 1H, J = 8.0 Hz, H-1'), 7.25 (d, 1H, J = 5.5 Hz, H-5), 7.72 (d, 1H, J = 5.5 Hz, H-6), 9.52 (brs, 1H, NH). MS: *m/z* (%) = 296 [(M^+ + Na), 39]. Anal. Calcd. for $C_{10}H_{15}N_3O_6$: C, 43.96; H, 5.53; N, 15.38. Found: C, 43.88; H, 5.23; N, 15.19%.

4-(β-D-Galactopyranosylamino)pyrimidin-2(1H)-one (**2b**): Yield 85%. M.p. 181–183°C. ^{1}H NMR (DMSO-d_6) δ: 3.25–3.60 (m, 2H, H-6'), 4.30–4.80 (m, 8H, H-2', H-3', H-4', H-5', 4xOH), 7.19 (d, 1H, J = 8.0 Hz, H-1'), 7.26 (d, 1H, J = 5.5 Hz, H-5), 7.88 (d, 1H, J = 5.5 Hz, H-6), 9.59 (brs, 1H, NH). MS: *m/z* (%) = 296 [(M^+ + Na), 44]. Anal. Calcd. for $C_{10}H_{15}N_3O_6$: C, 43.96; H, 5.53; N, 15.38. Found: C, 43.75; H, 5.29; N, 15.21%.

4-(β-D-Ribopyranosylamino)pyrimidin-2(1H)-one (**2c**): Yield 88%. M.p. 167–169°C. ^{1}H NMR (DMSO-d_6) δ: 3.20–3.50 (m, 2H, H-5'), 4.35–4.95 (m, 7H, H-2', H-3', H-4', 4xOH), 7.18 (d, 1H, J = 8.0 Hz, H-1'), 7.24 (d, 1H, J = 5.5 Hz, H-5), 7.89 (d, 1H, J = 5.5 Hz, H-6), 9.55 (brs, 1H, NH). MS: *m/z* (%) = 266 [(M^+ + Na), 30]. Anal. Calcd. for $C_9H_{13}N_3O_5$: C, 44.44; H, 5.39; N, 17.28. Found: C, 44.17; H, 5.22; N, 17.14%.

4-(β-D-Xylopyranosylamino)pyrimidin-2(1H)-one (**2d**): Yield 86%. M.p. 145–147°C. ^{1}H NMR (DMSO-d_6) δ: 3.10–3.40 (m, 2H, H-5'), 4.45–4.90 (m, 7H, H-2', H-3', H-4', 4xOH), 7.16 (d, 1H, J = 8.0 Hz, H-1'), 7.23 (d, 1H, J = 5.5 Hz, H-5), 7.81 (d, 1H, J = 5.5 Hz, H-6), 9.52 (brs, 1H, NH). MS: *m/z* (%) = 266 [(M^+ + Na), 27]. Anal. Calcd. for $C_9H_{13}N_3O_5$: C, 44.44; H, 5.39; N, 17.28. Found: C, 44.15; H, 5.24; N, 17.18%.

4-(2,3,4-Tri-O-acetyl)- and 4-(2,3,4,6-Tetra-O-acetyl-β-D-glycopyranosylamino)pyrimidin-2(1H)-ones **3a–d**

A mixture of **2a–d** (0.2 g), dry pyridine (3 ml) and acetic anhydride (3 ml) was stirred for 15 min at 0°C, then kept overnight at room temperature with stirring. The mixture was poured onto crushed-ice (30 g) and the precipitate was collected by filtration, washed repeatedly with water, dried, and recrystallised from ethanol–water (2: 8, *v/v*) to afford **3a–d** in 95–98% yields.

4-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosylamino)pyrimidin-2(1H)-one (**3a**): Yield 98%. M.p. 140–142°C. IR (cm^{-1}): 3390 (NH), 1750 (C=O). ^{1}H NMR (DMSO-d_6) δ: 1.95, 1.97, 1.99, 2.09 (4 s, 12H, 4xCH_3CO), 3.75–3.90 (m, 2H, H-6'), 4.60–5.00 (m, 4H, H-2', H-3', H-4', H-5'), 5.15 (d, 1H, J = 9.0 Hz, H-1'), 7.20 (d, 1H, J = 5.5 Hz, H-5), 7.70 (d, 1H, J = 5.5 Hz, H-6), 9.58 (brs, 1H, NH). MS: *m/z* (%) = 464 [(M^+ + Na), 25]. Anal. Calcd. for $C_{18}H_{23}N_3O_{10}$: C, 48.98; H, 5.25; N, 9.52. Found: C, 48.77; H, 5.17; N, 9.46%.

4-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosylamino)pyrimidin-2(1H)-one (**3b**): Yield 95%. M.p. 129–131°C. IR (cm^{-1}): 3370 (NH), 1745 (C=O). ^{1}H NMR (DMSO-d_6) δ: 1.94, 1.96, 1.99, 2.08 (4 s, 12H, 4xCH_3CO), 3.95–4.15 (m, 2H, H-6'), 4.70–5.00 (m, 4H, H-2', H-3', H-4', H-5'), 5.20 (d, 1H, J = 9.0 Hz, H-1'), 7.21 (d, 1H, J = 5.5 Hz, H-5), 7.73 (d, 1H, J = 5.5 Hz, H-6), 9.58 (brs, 1H, NH). MS: *m/z* (%) = 464 [(M^+ + Na), 22]. Anal. Calcd. for $C_{18}H_{23}N_3O_{10}$: C, 48.98; H, 5.25; N, 9.52. Found: C, 48.73; H, 5.11; N, 9.39%.

4-(2,3,4-Tri-O-acetyl-β-D-ribopyranosylamino)pyrimidin-2(1H)-one (**3c**): Yield 97%. M.p. 135–137°C. IR (cm^{-1}): 3396 (NH), 1755 (C=O). ^{1}H NMR (DMSO-d_6) δ: 1.97, 1.99, 2.05 (3 s, 9H, 3xCH_3CO), 3.80–4.00 (m, 2H, H-5'), 4.80–5.08 (m, 3H, H-2', H-3', H-4'), 5.17 (d, 1H, J = 9.0 Hz, H-1'), 7.25 (d, 1H, J = 5.5 Hz, H-5), 7.70 (d, 1H, J = 5.5 Hz, H-6), 9.60 (brs, 1H, NH). MS: *m/z* (%) = 392 [(M^+ + Na), 56]. Anal. Calcd. for $C_{15}H_{19}N_3O_8$: C, 48.78; H, 5.19; N, 11.38. Found: C, 48.66; H, 5.05; N, 11.22%.

4-(2,3,4-Tri-O-acetyl-β-D-xylopyranosylamino)pyrimidin-2(1H)-one (**3d**): Yield 96%. M.p. 120–122°C; IR (cm^{-1}): 3395 (NH), 1755 (C=O). ^{1}H NMR (DMSO-d_6) δ: 1.96, 1.98, 2.11 (3 s, 9H, 3xCH_3CO), 3.78–4.05 (m, 2H, H-5'), 4.75–4.95 (ms, 3H, H-2', H-3', H-4'), 5.18 (d, 1H, J = 9.0 Hz, H-1'), 7.20 (d, 1H, J = 5.5 Hz, H-5), 7.72 (d, 1H, J = 5.5 Hz, H-6), 9.61 (brs, 1H, NH). MS: *m/z* (%) = 392 [(M^+ + Na), 49]. Anal. Calcd. for $C_{15}H_{19}N_3O_8$: C, 48.78; H, 5.19; N, 11.38. Found: C, 48.70; H, 5.03; N, 11.20%.

1-(Ethoxycarbonylmethyl)-N^4-acetylcytosine (**5**)
A solution of **4**[13] (1.53 g, 10 mmol), dry acetone (100 ml), K_2CO_3 (1.38 g, 10 mmol) and ethyl chloroacetate (1.23 g, 10 mmol) was refluxed for 5 h (TLC) and then cooled to room temperature. The resulting precipitate was filtered and the filtrate was evaporated under reduced pressure. The residue was recrystallised from ethanol to give 1.79 g (75%) as yellow crystals. M.p. 180–181°C. ^{1}H NMR (DMSO-d_6) δ: 1.20 (t, 3H, J = 8.1 Hz, CH_3CH_2), 2.11 (s, 3H, CH_3CO), 4.18 (q, 2H, J = 8.1 Hz, CH_3CH_2), 4.61 (s, 2H, CH_2), 7.20 (d, 1H, J = 5.5 Hz, H-5), 8.05 (d, 1H, J = 5.5 Hz, H-6), 10.84 (brs, 1H, NH). Anal. Calcd. for $C_{10}H_{13}N_3O_4$: C, 50.21; H, 5.48; N, 17.56. Found: C, 50.04; H, 5.18; N, 17.33%.

(N^4-Acetylcytosin-1-yl)acetohydrazide (**6**)
A solution of **5** (2.39 g, 10 mmol) in ethanol (30 ml) was refluxed with hydrazine hydrate (1.25 g, 25 mmol) for 4 h. After cooling it to room temperature, a white solid appeared. This was recerystallised from ethanol to afford **6** (2.0 g, 89%). M.p. 258–260°C. ^{1}H NMR (DMSO-d_6) δ: 2.15 (s, 3H, CH_3CO), 4.20 (brs, 2H, NH_2), 4.34 (s, 2H, CH_2), 7.20 (d, 1H, J = 5.5 Hz, H-5), 7.62 (d, 1H, J = 5.5 Hz, H-6), 9.50 (brs, 1H, NH). Anal. Calcd. for $C_8H_{11}N_5O_3$: C, 42.67; H, 4.92; N, 31.10. Found: C, 42.50; H, 4.81; N, 30.94%.

Sugar 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazones **7a–f**
A solution of the respective sugar (10 mmol) in water (3 ml) was treated with a solution of **6** (2.25 g, 10 mmol) in ethanol (100 ml) and few drops of glacial acetic acid. The mixture was boiled under reflux for 4–5 h (TLC). The excess of ethanol was removed under reduced pressure and the residue was triturated with diethyl ether (15 ml). The product was filtered, washed with ether, and recrystallised from ethanol to give **7a–f** in 80–88% yield.

L-(+)-Arabinose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**7a**): Yield 88%. M.p. 150–151°C. ^{1}H NMR (DMSO-d_6) δ: 2.15 (s, 3H, CH_3CO), 3.14–3.40 (m, 3H, H-4', H-5'), 3.49 (s, 1H, H-3'), 3.60–3.65 (m, 1H, H-2'), 4.39–4.51 (m, 6H, CH_2, 4xOH), 7.22 (d, 1H, J = 5.5 Hz, H-5), 7.30 (d, 1H, J = 2.8 Hz, H-1'), 8.00 (d, 1H, J = 5.5 Hz, H-6), 9.88 (brs, 1H, NH). MS: m/z (%) = 380 [(M^+ + Na), 12].

D-(–)-Ribose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**7b**): Yield 80%. M.p. 140–142°C. ^{1}H NMR (DMSO-d_6) δ: 2.18 (s, 3H, CH_3CO), 3.14–3.52 (m, 5H, H-2', H-3', H-4', H-5'), 3.99–4.21 (brs, 4H, 4xOH), 4.37 (s, 2H, CH_2), 7.15 (d, 1H, J = 5.5 Hz, H-5), 7.25 (d, 1H, J = 2.8 Hz, H-1'), 8.02 (d, 1H, J = 5.5 Hz, H-6), 9.85 (brs, 1H, NH). MS: m/z (%) = 380 [(M^+ + Na), 16].

D-(+)-Xylose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**7c**): Yield 87%. M.p. 169–171°C; ^{1}H NMR (DMSO-d_6) δ: 2.14 (s, 3H, CH_3CO), 3.41–3.69 (brm, 3H, H-4', H-5'), 3.59–3.61 (m, 2H, H-2', H-3'), 4.35–4.88 (m, 6H, CH_2, 4xOH), 7.20–7.25 (m, 2H, H-5, H-1'), 8.01 (d, 1H, J = 5.5 Hz, H-6), 9.90 (brs, 1H, NH). MS: m/z (%) = 380 [(M^+ + Na), 34].

D-(+)-Glucose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**7d**): Yield 85%. M.p. 122–123°C. ^{1}H NMR (DMSO-d_6) δ: 2.18 (s, 3H, CH_3CO), 3.44–3.89 (m, 5H, H-3', H-4', H-5', H-6'), 4.27–4.88 (m, 8H, CH_2, H-2', 5xOH), 7.18 (d, 1H, J = 5.5 Hz, H-5), 7.27 (d, 1H, J = 2.8 Hz, H-1'), 8.07 (d, 1H, J = 5.5 Hz, H-6), 9.89 (brs, 1H, NH). MS: m/z (%) = 410 [(M^+ + Na), 11].

D-(+)-Galactose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**7e**): Yield 85%. M.p. 144–146°C; ^{1}H NMR (DMSO-d_6) δ: 2.13 (s, 3H, CH_3CO), 3.34–3.93 (m, 3H, H-5', H-6'), 4.12–4.23 (m, 3H, H-2', H-3', H-4'), 4.33–4.80 (m, 7H, CH_2, 5xOH), 7.15 (d, 1H, J = 5.5 Hz, H-5), 7.23 (d, 1H, J = 2.8 Hz, H-1'), 8.00 (d, 1H, J = 5.5 Hz, H-6), 9.88 (brs, 1H, NH). MS: m/z (%) = 410 [(M^+ + Na), 16].

D-(+)-Mannose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**7f**): Yield 82%. M.p. 166–167°C. ^{1}H NMR (DMSO-d_6) δ: 2.16 (s, 3H, CH_3CO), 3.44–3.78 (m, 6H, H-2', H-3', H-4', H-5', H-6'), 4.36–4.50 (m, 7H, CH_2, 5xOH), 7.17 (d, 1H, J = 5.5 Hz, H-5), 7.25 (d, 1H, J = 2.8 Hz, H-1'), 8.01 (d, 1H, J = 5.5 Hz, H-6), 9.86 (brs, 1H, NH). MS: m/z (%) = 410 [(M^+ + Na), 19].

Sugar tetra-O-acetyl- and Sugar penta-O-acetyl-2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazones **8a–f**
A cold solution of sugar hydrazones **7a–f** (1 mmol) in dry pyridine (3 ml) was treated with acetic anhydride (3 ml). The reaction mixture was left overnight with stirring, then poured onto crushed ice and the separated product was filtered off, washed with water, dried, and crystallised from *ethanol-water* (2: 8, *v/v*) to afford **8a–f** in 80–85% yields.

2,3,4,5-Tetra-O-acetyl-L-(+)-arabinose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**8a**): Yield 88%. M.p. 150–151°C. ^{1}H NMR (DMSO-d_6) δ: 1.95, 2.04, 2.10, 2.13, 2.15 (5 s, 15H, 5xCH_3CO), 4.17 (m, 2H, H-5'), 4.25 (m, 1H, H-4'), 4.50 (s, 2H, CH_2), 5.60 (m, 1H, H-3'), 5.75 (m, 1H, H-2'), 7.15 (d, 1H, J = 5.5 Hz, H-5), 7.25 (d, 1H, J = 2.5 Hz, H-1′), 8.05 (d, 1H, J = 5.5 Hz, H-6), 10.10 (brs, 1H, NH). MS: m/z (%) = 548 [(M^+ + Na), 22]. Anal. Calcd. for $C_{21}H_{27}N_5O_{11}$: C, 48.00; H, 5.18; N, 13.33. Found: C, 47.80; H, 5.00; N, 13.21%.

2,3,4,5-Tetra-O-acetyl-D-(–)-ribose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**8b**): Yield 80%. M.p. 140–142°C. ^{1}H NMR (DMSO-d_6) δ: 1.95, 2.03, 2.11, 2.13, 2.15 (5 s, 15H, 5xCH_3CO), 4.19 (m, 2H, H-5'), 4.33 (m, 1H, H-4), 4.53 (s, 2H, CH_2), 5.69 (m, 1H, H-3), 5.77 (m, 1H, H-2), 7.13 (d, 1H, J = 5.5 Hz, H-5), 7.27 (d, 1H, J = 2.5 Hz, H-1′), 8.00 (d, 1H, J = 5.5 Hz, H-6), 10.07 (brs, 1H, NH). MS: m/z (%) = 548 [(M^+ + Na), 31]. Anal. Calcd. for $C_{21}H_{27}N_5O_{11}$: C, 48.00; H, 5.18; N, 13.33. Found: C, 47.88; H, 5.07; N, 13.23%.

2,3,4,5-Tetra-O-acetyl-D-(+)-xylose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**8c**): Yield 87%. M.p. 169–171°C. ^{1}H NMR (DMSO-d_6) δ: 1.95, 2.03, 2.11, 2.12, 2.15 (5 s, 15H, 5xCH_3CO), 4.29 (m, 2H, H-5), 4.39 (m, 1H, H-4), 4.58 (s, 2H, CH_2), 5.74 (m, 1H, H-3), 5.88 (m, 1H, H-2), 7.12 (d, 1H, J = 5.5 Hz, H-5), 7.30 (d, 1H, J = 2.5 Hz, H-1′), 8.03 (d, 1H, J = 5.5 Hz, H-6), 10.00 (brs, 1H, NH). MS: m/z (%) = 548 [(M^+ + Na), 19]. Anal. Calcd. for $C_{21}H_{27}N_5O_{11}$: C, 48.00; H, 5.18; N, 13.33. Found: C, 47.77; H, 5.04; N, 13.19%.

2,3,4,5,6-Penta-O-acetyl-D-(+)-glucose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**8d**): Yield 85%. M.p. 122–123°C. ^{1}H NMR (DMSO-d_6) δ: 1.95, 2.00, 2.04, 2.10, 2.13, 2.15 (6 s, 18H, 6xCH_3CO), 4.00–4.11 (m, 2H, H-6), 4.50 (m, 1H, H-5′), 4.60 (s, 2H, CH_2), 4.70 (m, 1H, H-4), 5.15 (m, 1H, H-3), 5.45 (m, 1H, H-2), 7.12 (d, 1H, J = 5.5 Hz, H-5), 7.27 (d, 1H, J = 2.5 Hz, H-1′), 8.03 (d, 1H, J = 5.5 Hz, H-6), 10.00 (brs, 1H, NH). MS: m/z (%) = 620 [(M^+ + Na), 17]. Anal. Calcd. for $C_{24}H_{31}N_5O_{13}$: C, 48.24; H, 5.23; N, 11.72. Found: C, 48.09; H, 5.11; N, 11.53%.

2,3,4,5,6-Penta-O-acetyl-D-(+)-galactose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**8e**): Yield 85%. M.p. 144–146°C. ^{1}H NMR (DMSO-d_6) δ: 1.95, 2.00, 2.04, 2.10, 2.12, 2.15 (6 s, 18H, 6xCH_3CO), 4.08-4.22 (m, 2H, H-6), 4.59 (m, 1H, H-5′), 4.69 (s, 2H, CH_2), 4.76 (m, 1H, H-4), 5.18 (m, 1H, H-3), 5.40 (m, 1H, H-2), 7.13 (d, 1H, J = 5.5 Hz, H-5), 7.30 (d, 1H, J = 2.5 Hz, H-1), 8.03 (d, 1H, J = 5.5 Hz, H-6), 10.03 (brs, 1H, NH). MS: m/z (%) = 620 [(M^+ + Na), 19]. Anal. Calcd. for $C_{24}H_{31}N_5O_{13}$: C, 48.24; H, 5.23; N, 11.72. Found: C, 48.13; H, 5.10; N, 11.59%.

2,3,4,5,6-Penta-O-acetyl-D-(+)-mannose 2-[4-acetamido-2-oxopyrimidin-1(2H)-yl]acetylhydrazone (**8f**): Yield 82%. M.p. 166–167°C. ^{1}H NMR (DMSO-d_6) δ: 1.98, 2.02, 2.04, 2.11, 2.13, 2.15 (6 s, 18H, 6xCH_3CO), 4.13–4.33 (m, 2H, H-6), 4.57 (m, 1H, H-5′), 4.70 (s, 2H, CH_2), 4.79 (m, 1H, H-4), 5.20 (m, 1H, H-3), 5.47 (m, 1H, H-2), 7.14 (d, 1H, J = 5.5 Hz, H-5), 7.30 (d, 1H, J = 2.5 Hz, H-1), 8.06 (d, 1H, J = 5.5 Hz, H-6), 10.05 (brs, 1H, NH). MS: m/z (%) = 620 [(M^+ + Na), 24]. Anal. Calcd. for $C_{24}H_{31}N_5O_{13}$: C, 48.24; H, 5.23; N, 11.72. Found: C, 48.08; H, 5.14; N, 11.57%.

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