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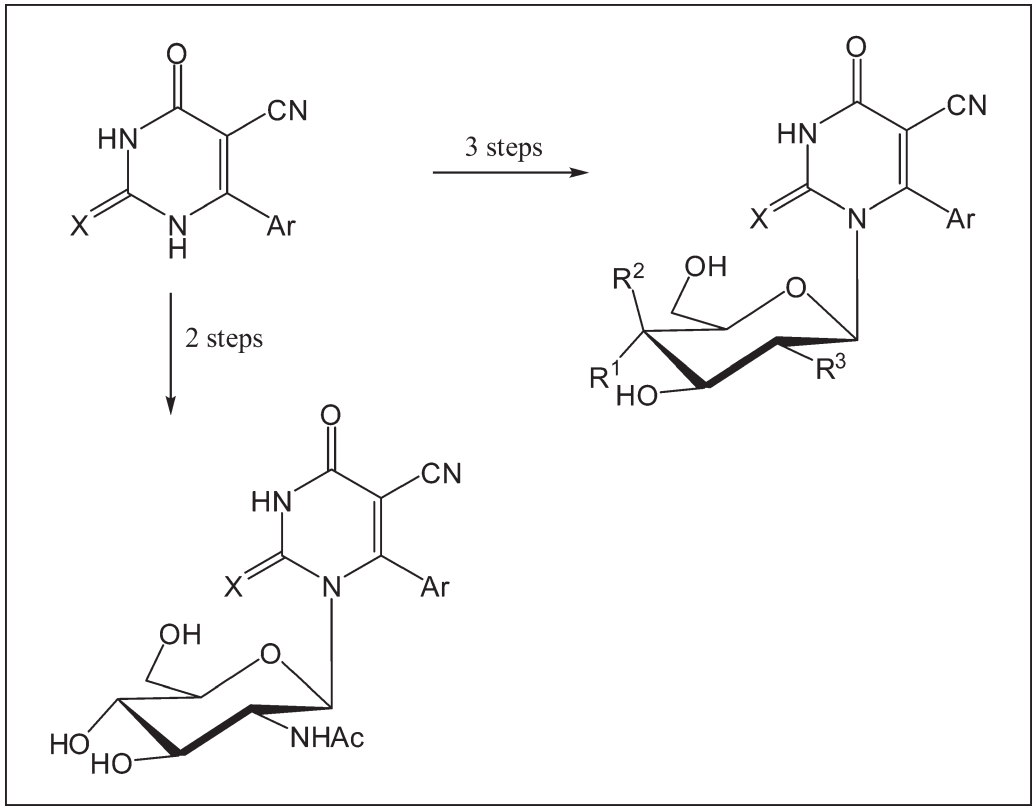

A number of *N*-substituted pyrimidine glycosides were synthesized by coupling reaction of the pyrimidine base with acetobromosugars followed by deprotection. The synthesized compounds were tested for their antiviral activity against Hepatitis B Virus (HBV). Plaque reduction infectivity assay was used to determine virus count reduction as a result of treatment with tested compounds which showed moderate to high anti viral activities.

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INTRODUCTION

Pyrimidines are an important class of compounds and have widespread applications from pharmaceuticals to materials [1]. They have been recognized as important heterocyclic compounds due to their diverse biological activities such as Tie-2 kinase inhibitors [2], HIV-1 inhibitor [3], antimalarial [4] secretive adenosine A1 receptor antagonist [5], anticancer [6,7], analgesic [8], and cardiovascular [9] activities. Furthermore, it has been found that 3,4-dihydropyrimidin-2(1*H*)-ones (DHPMs) have interesting multifaceted pharmacological profile as hepatitis B virus (HBV) replication inhibitors [10–12]. Moreover, the pyrimidine ring in an organic molecule also shows prominent activity as antagonist of both *a*1-adrenergic and serotonin-S2 receptors [13]. A number of synthetic pharmacophores with antibacterial [14], antifungal [15], and antimycotic activities [16] are based on the pyrimidyl motif. Also, pyrimidines are present in

numerous natural products and, significantly, in the pyrimidine and purineucleosides [17–20]. On the other hand, nucleoside analogs are structurally, metabolically, and pharmaco-dynamically related agents that have diverse biological actions and therapeutic effects including antiviral [21,22], and antitumor [23,24] activities. Furthermore, the acyclic nucleoside [25–28], analogues including modifications of both the acyclic glycon and aglycon parts have stimulated extensive research as biological inhibitors [29,30]. The importance of substituted hydroxyl alkyl chain conformation in the interaction of acyclic nucleosides with enzymes has been demonstrated [31]. Moreover, the 5-substituted derivatives of pyrimidine acyclonucleoside analogs have exhibited pronounced inhibitory properties with respect to uridine phosphorylase and have enhanced antitumor action [24]. Owing to the above significance and our interest in the synthesis of new and potent antiviral nucleoside analogs [32–34], herein we report the synthesis and anti HBV activity of new substituted pyrimidine acyclic nucleosides.

RESULTS AND DISCUSSION

Chemistry. 6-Aryl-5-cyanouracils (**1a–c**) were synthesized by base-catalyzed condensation followed by cyclization of ethyl cyanoacetate, urea, and aromatic aldehydes in 40–45% yields. By the same way, 6-aryl-5-cyano-2-thiouracils (**2a–c**) were synthesized by base-catalyzed condensation followed by cyclization of ethyl cyanoacetate, thiourea, and aromatic aldehydes in 45–52% yields. Treatment of **2a–c** with methyl iodide and sodium hydroxide in water and ethanol at 60°C afforded 6-aryl-5-cyano-2-(methylthio)uracils (**3a–c**) in 88–92% yields.

The sodium salts of **3a–c** were condensed with 2-acetamido-1-chloro-3,4,6-tri-*O*-acetyl-2-deoxy-D-glucose (**4**) in dry DMF. The reaction was proceeded at 90°C to give the desired 1-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-6-aryl-5-cyano-2-(methylthio)pyrimidin-4(1*H*)-ones (**5a–c**) in 76–81% yields. The structures of the nucleosides **5a–c** were determined on the basis of their respective IR, ^{1}H NMR, mass spectra, and microanalyses which were found to be consistent with the assigned structures by comparison with the structures of glycopyranoside analogues. Their IR spectra showed the *O*-acetyl groups at 1738–1742 cm^{-1}, the *N*-acetyl and *N*-CO at 1666–1672 cm^{-1} in addition to the bands corresponding to CN groups at 2205–2207 cm^{-1}. The ^{1}H NMR spectra of **5a–c** showed the anomeric protons as doublets at δ 5.70, 5.74, and 5.72 with *J* coupling of 9.5, 9.6, and 9.4 Hz, respectively, corresponding to a diaxial orientation of H-1′ and H-2′ protons which are indicative of the β-configuration. Deacetylation of **5a–c** in a mixture of methanol and ammonium hydroxide (25%) (1:1) at room temperature afforded the free nucleosides **6a–c** in 85–88% yields. Similarly, the free nucleosides **6a–c** showed, in their ^{1}H NMR spectra, the signals corresponding to the anomeric protons as doublets at δ 5.38, 5.39, and 5.35 with large $J_{1',2'}$ coupling constants (9.5, 9.6, and 9.5 Hz, respectively) clearly indicating that these compounds have also the β-configuration.

Condensation of the sodium salt of **3a–c** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**7**) in dry DMF at 90°C afforded 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1*H*)-ones (**8a–c**) in 78–83% yields. Their IR spectra showed characteristic absorption bands corresponding to *O*-acetyl groups at 1736–1742 cm^{-1}, the *N*-acetyl and *N*-CO groups at 1666–1670 cm^{-1} and the CN groups at 2204–2206 cm^{-1}. The ^{1}H NMR spectra of **8a–c** showed the anomeric protons as doublets at δ 6.42, 6.44, and 6.43 with *J* coupling of 8.2, 8.1, and 8.3 Hz, respectively, corresponding to a diaxial orientation of H-1′ and H-2′ protons which are indicative of the β-configuration. Deacetylation of **8a–c** in a mixture of methanol and ammonium hydroxide (25%) (1:1) at room temperature gave the free nucleosides **9a–c** in 88–92% yields. The free nucleosides **9a–c** showed, in their IR spectra absorption bands corresponding to the hydroxyl groups at 3386–3435 cm^{-1}. Their ^{1}H NMR spectra showed the signals corresponding to the anomeric protons as doublets at δ 5.74, 5.75, and 5.77 with *J* coupling of 7.8, 7.5, and 7.7 Hz, respectively clearly indicating that these compounds have also the β-configuration.

By the same way condensation of the sodium salt of **3a–c** with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**10**) in dry DMF at 90°C afforded 1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1*H*)-ones (**11a–c**) in 66–71% yields. The ^{1}H NMR spectra of **11a–c** showed the anomeric protons as doublets at δ 4.70, 4.74, and 4.73 with *J* coupling of 7.4, 7.5, and 7.4 Hz, respectively, corresponding to a diaxial orientation of H-1′ and H-2′ protons which are indicative of the β-configuration. The axial protons (H-4′) of the galactose moieties as doublets of doublets at δ 5.36, 5.33, and 5.37 with $J_{3',4'}$ coupling of 3.4, 3.3, and 3.5 Hz, and $J_{4',5'}$ coupling of 1.1, 1.0, and 1.2 Hz, respectively. Deacetylation of **11a–c** in a mixture of methanol and ammonium hydroxide (25%) (1:1) at room temperature gave the free nucleosides **12a–c** in 78–80% yields. The ^{1}H NMR spectra of the free nucleosides **12a–c** showed the anomeric protons as multiplets at δ 4.48, 4.54, and 4.50. The axial protons (H-4′) of the galactose moieties showed as multiplets at δ 3.88, 3.90, and 3.93, respectively (Figs. 1–3).

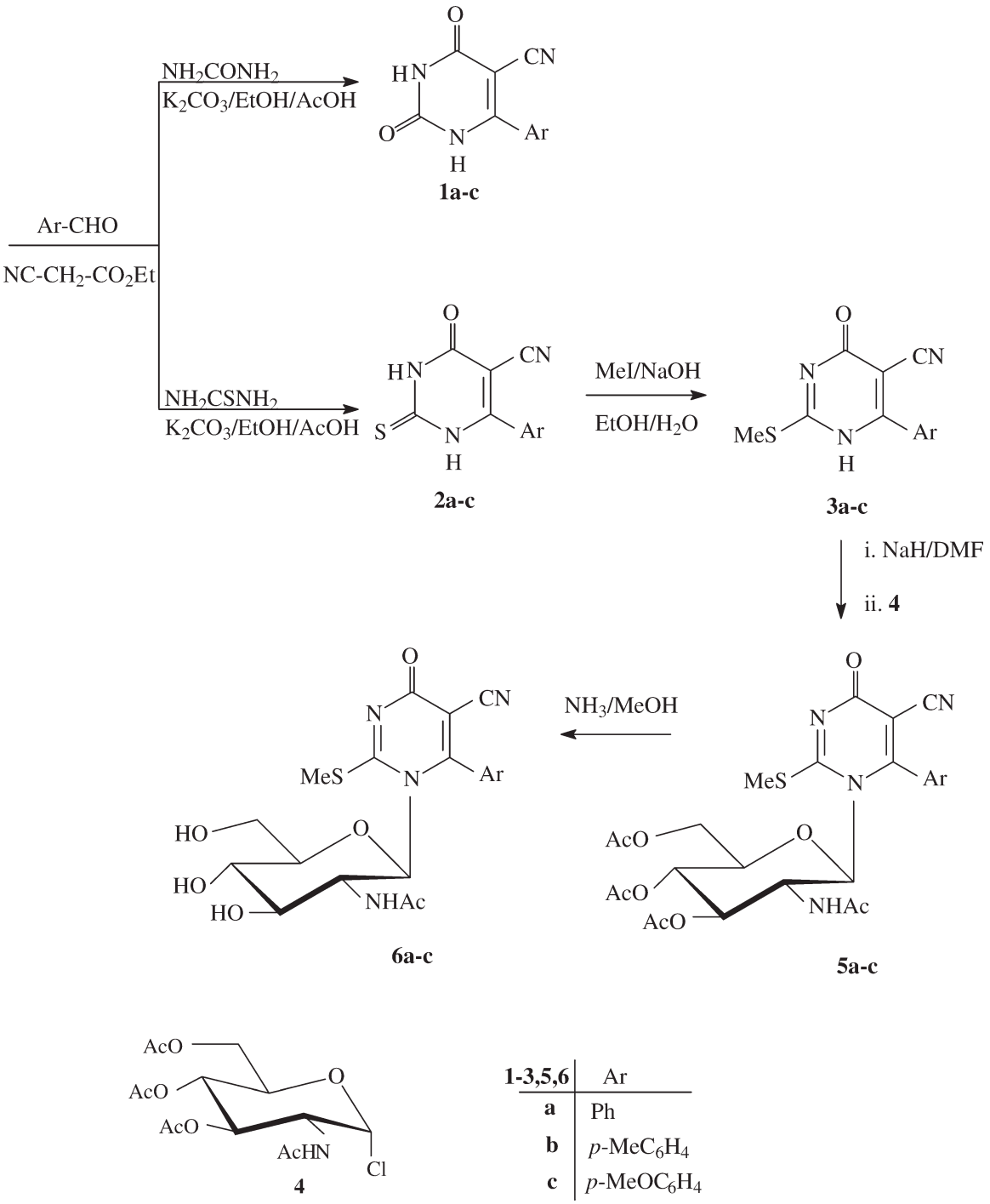

Figure 1. Synthesis rout of compounds **3–6.**

Glucosylation of the sodium salt of the 6-aryl-5-cyanouracils (**1a–c**) with **4** in dry DMF at 90°C gave the desired 1-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-6-aryl-5-cyanopyrimidin-4(1*H*)-ones (**13a–c**) in 75–80% yields. The glucosides **13a–c** showed, in their IR spectra, characteristic absorption bands corresponding to the NH and *O*-acetyl groups at 3317–3324 and 1737–1740 cm^{-1}, respectively. Their ^1H NMR spectra showed the anomeric protons as doublets at δ 5.49, 5.58, and 5.60 with *J* coupling of 9.3, 9.4, and 9.2 Hz, respectively, corresponding to a diaxial orientation of H-1′ and H-2′ protons which are indicative of the β-configuration. Deacetylation of **13a–c** in a mixture of methanol and ammonium hydroxide (25%) (1:1) at room temperature

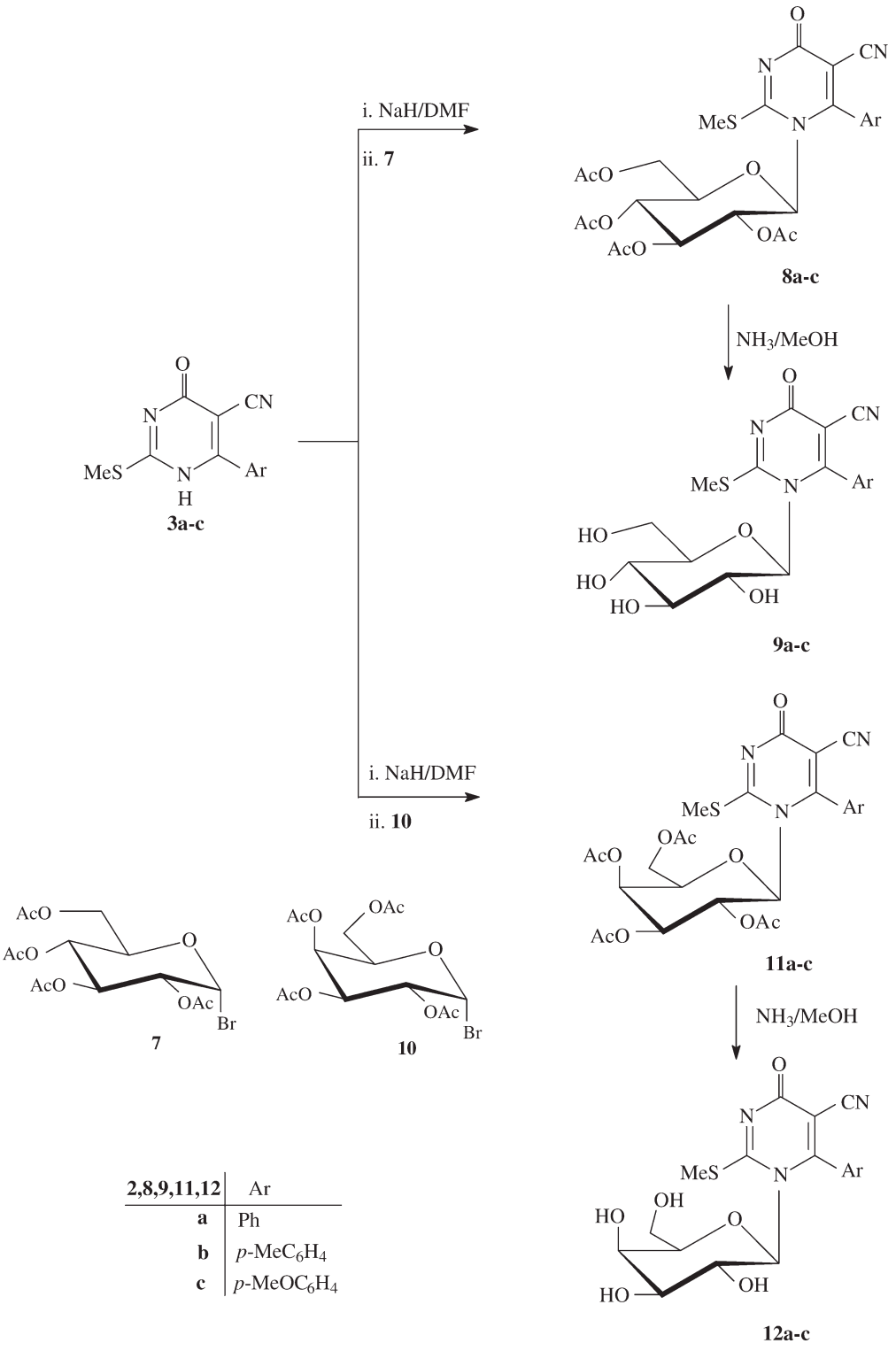

Figure 2. Synthesis of pyrimidine glycosides.

afforded the free nucleosides **14a–c** in 83–90% yields. The free nucleosides **14a–c** showed, in their ^{1}H NMR spectra, the signals corresponding to the anomeric protons as doublets at δ 5.36, 5.38, and 5.40 with *J* coupling constants (9.4, 9.6, and 9.5 Hz, respectively) clearly indicating that these compounds have also the β-configuration.

Antiviral activity. The synthesized compounds were tested for their antiviral activity against HBV using the

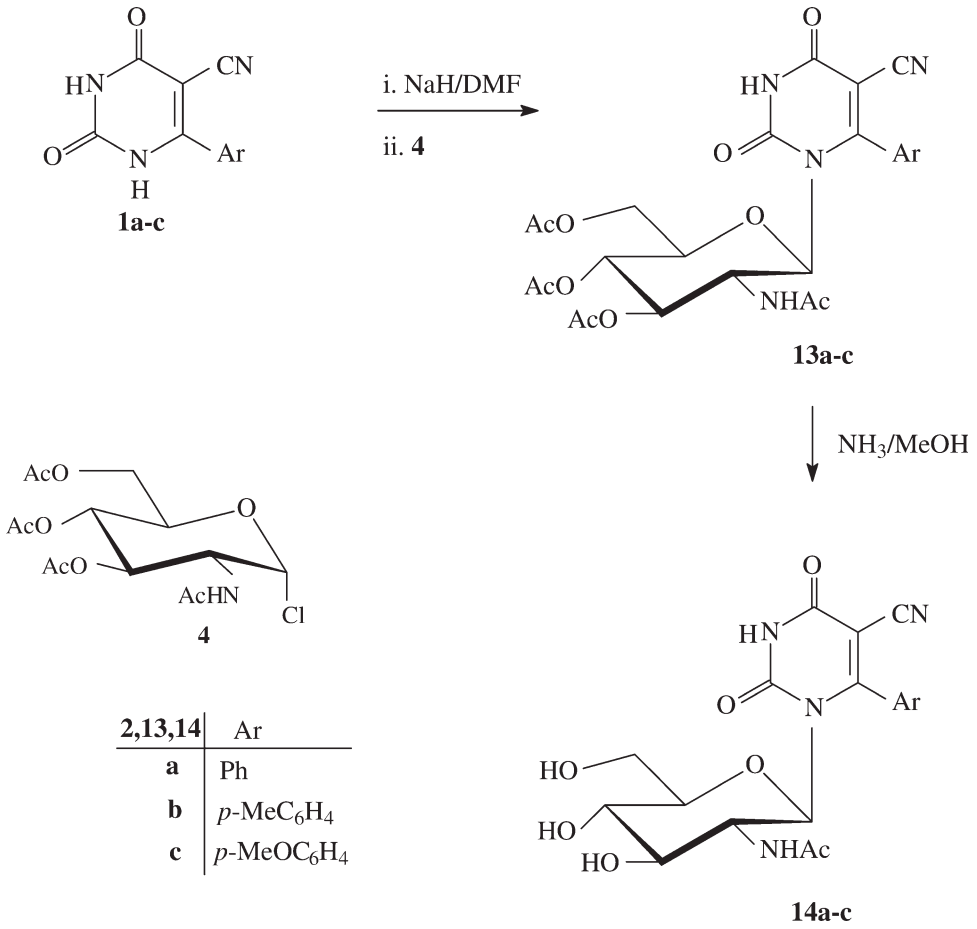

Figure 3. Glucosylation of cyanopyrimidines.

HepG2.2.2.15-cell line [35], a human hepatoplastoma cell line producing HBV viral particles [36]. The cell line was maintained in RPMI-1640 (Glutamax) (Gibco BRL Life Technologies, Paisly Scotland) culture medium containing 100 IU/mL nystatin (Gibco BRL Life technologies), 380 μg/mL G418 (genetecin) (Gibco BRL Life Technologies) and 10% fetal calf serum (FCS)(Gibco BRL Life Technologies). The transferred HEPG2.2.2.15 cells were kept in a tissue culture flask at 37°C and 5% CO_2. Subcultures were set up after a week by trypsination [(10% versin/trypsin (Biochrome KG, Berlin Germany)] and transferred to a 96-well tissue culture plate. Serial dilutions of the test compounds were added to the cell suspension and incubated for 6 days at 37°C and 5% CO_2. The antiviral activity and cytotoxic effect of the test compound was estimated by comparing the DNA content in the culture supernatant and the viability of the cells with the test compounds to those of HepG2.2.2.15 cells with no compounds added to their supernatant (blank cells). The drug lamivudine [(4-amino-1-[(2*R*,5*S*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one), GlaxoSmithKline, Uxbridge, UK] which is a potent selective inhibitor of HBV replication has been used as a standard positive control. Each compound was tested in triplicate.

DNA extraction. DNA extraction was done by incubating 10 μL of diluted supernatant with 10 μL of 0.2*M* NaOH at 37°C for 1 h, then carefully adding 9.6 μL of 0.2*M* HCl followed by addition of 90 μL of Tris-EDTA (TE) buffer [(2-amino-2-(hydroxymethyl)-1,3-propanediol-EDTA) (Gibco BRL Life Technologies)].

PCR-ELISA detection of HBV DNA. The DNA content in the cell culture supernatant was determined by PCR amplification of the HBV DNA using 1 μmol/L of each of the following primers: HCID-1 primer (5′-GGAAAGAAGTCAGAAGGCA-3′) and HCID-2 primer (5′-TTGGGGGAGGAGATTAGGTT-3′), in a reaction mixture containing 14 μL extracted supernatant, 4 mmol/L $MgCl_2$, 10 μmol/L DIG-11-dUTP (Roche, Munich, Germany), 190 μmol/L dTTP, 200 μmol/L dATP, dGTP, dCTP (Roche) 1.5 U Taq polymerase (Roche), in a total volume 50 μL. PCR reaction conditions were: 32 cycles of 10 min at 94°C, 30 s at 58°C and 30 s at 72°C with a 3 s increment for each cycle in a Perkin Elmer 480 thermal cycler (Perkin Elmer, Waltham, MA). The

Table 1

Cytotoxic effect (CC_{50}), inhibitory concentration (IC_{50}), and selective index (SI) of selected compounds.

Compd.	HBV DNA IC_{50} (μM)	Hep G2 2.2.15 CC_{50} (μM)	SI
Lamivudine	<0.1	>100	>1000
6a	1.31	>100	>76
6b	0.23	>100	>417
6c	0.28	>100	>357
9a	1.25	>100	>80
9b	0.66	>100	>151
9c	0.16	>100	>625
12a	1.56	>100	>64
12b	1.37	>100	>73
12c	1.19	>100	>84
14a	0.27	>100	>370
14b	0.20	>100	>500
14c	0.25	>100	>400

PCR product was detected by DIG-ELISA assay (Roche). The optical density (OD) from DNA of the test compound was compared to that of the blank culture.

Cytotoxicity assay. 3-(3,5-Dimethylthiazole-2-yl)-2,5-diphenyltetrazoliumbromide (MTT) (Sigma, St. Louis, MO) is a colorless substrate that is transferred to a colored product by any living cell but not by dead cells. The assay utilizes this compound to test for the viability of the cells with the test compound added compared to the viability of the blank cells [37].

Calculation of IC_{50}, CC_{50}, and SI values. The 50% inhibitory concentration (IC_{50}) of an antiviral drug was determined by plotting the DNA content of the serial dilutions of the tested compound versus the concentration of this compound. The 50% cytotoxic effect (CC_{50}) was calculated from the average viability of the cells in proportion to the concentration of the drug. The selective index (SI) could be calculated as CC_{50}/IC_{50}.

Antiviral activity. The synthesized compounds were tested for their antiviral activity against HBV using the HepG2.2.2.15-cell line, a human hepatoplastoma cell line producing HBV viral particles [38].

The results of the viral screening against HBV of selected compounds indicated that compounds 6b, 6c, 9b, 9c, 14a, 14b, and 14c showed moderate viral replication inhibition and mild cytotoxicity with SI >417, >357, >151, >625, >370, >500, and >400, respectively. On the other hand compounds 6a, 9a, 12a, 12b, and 12c showed very low inhibition and high cytotoxicity with SI >76, >80, >64, >73, and >84, respectively (Tables 1 and 2).

EXPERIMENTAL

General. Melting points were determined using a Büchi apparatus. IR spectra (KBr) were recorded with a Bruker-Vector22 instrument (Bruker, Bremen, Germany). ^{1}H NMR spectra were recorded with a Varian Gemini spectrometer at 300 and 200 MHz with TMS as internal standard. Chemical shifts were reported in δ scale (ppm) relative to TMS as a standard and the coupling constants (*J* values) are given in Hz. The progress of the reactions was monitored by TLC using aluminum silica gel plates 60 F_{245}. EImass spectra were recorded with a HP D5988 A 1000 MHz instrument (Hewlett, Packard, Palo Alto, CA). Antiviral activity against HBV was tested at the Liver Institute, Menoufia University, Shebien El-Kom Egypt.

6-Aryl-5-cyanouracils (1a-c) [39]. A mixture of aromatic aldehydes (0.1 mole), urea (6.0 g, 0.1 mole) ethyl cyanoacetate (11.3 g, 0.1 mole) and anhydrous K_2CO_3 (13.8 g, 0.1 mole) in absolute ethanol (150 mL) was refluxed for 20 h and then cooled. The obtained potassium salt was filtered off as a colorless solid. The potassium salt was dissolved in water at 80°C, filtered off and neutralized with glacial acetic acid. The precipitate was filtered off and washed with water. The precipitate was crystallized from a water-acetone mixture to give **1a–c**.

Table 2

Results of inhibition of HBV replication by selected compounds.

Compd.	Concentration (μM)	HBV DNA in supernatant
Lamivudine	1.0	0.25
	10.0	0.18
	100.0	0.15
6a	1.0	0.19
	10.0	0.16
	100.0	0.14
6b	1.0	0.75
	10.0	0.68
	100.0	0.61
6c	1.0	0.66
	10.0	0.60
	100.0	0.53
9a	1.0	0.21
	10.0	0.18
	100.0	0.15
9b	1.0	0.37
	10.0	0.31
	100.0	0.27
9c	1.0	0.80
	10.0	0.76
	100.0	0.69
12a	1.0	0.15
	10.0	0.13
	100.0	0.11
12b	1.0	0.18
	10.0	0.16
	100.0	0.12
12c	1.0	0.22
	10.0	0.20
	100.0	0.17
14a	1.0	0.68
	10.0	0.61
	100.0	0.56
14b	1.0	0.78
	10.0	0.72
	100.0	0.70
14c	1.0	0.73
	10.0	0.70
	100.0	0.63

5-Cyano-6-phenyluracil (1a). Yield: 40 %, m.p. 287–289°C (lit. 34%, m.p. 286–287°C).

5-Cyano-6-(4-methylphenyl)uracil (1b). Yield: 45%, m.p. 290–293°C (lit. 39%, m.p. 295–296°C).

5-Cyano-6-(4-methoxyphenyl)uracil (1c). Yield: 44%, m.p. 277–278°C (lit. 40%, m.p. 276–277°C).

6-Aryl-5-cyano-2-thiouracils (2a-c) [39]. A mixture of aromatic aldehydes (0.1 mole), thiourea (7.6 g, 0.1 mole) ethyl cyanoacetate (11.3 g, 0.1 mole) and anhydrous K_2CO_3 (13.8 g, 0.1 mole) in absolute ethanol (150 mL) was refluxed for 19 h and then cooled. The obtained potassium salt was filtered off as yellow solid. The potassium salt was dissolved in water at 80°C, filtered off and neutralized with glacial acetic acid. The light yellow precipitate was filtered off and washed with water. The precipitate was crystallized from a DMF-water mixture to give **2a–c**.

5-Cyano-6-phenyl-2-thiouracil (2a). Yield: 45%; m.p. 296–298°C (lit. 40%; m.p. 246–247°C).

5-Cyano-6-(4-methylphenyl)-2-thiouracil (2b). Yield: 50%; m.p. 260–263°C (lit. 42%; m.p. 245–246°C).

5-Cyano-6-(4-methoxyphenyl)-2-thiouracil (2c). Yield: 52%, m.p. 237–239°C (lit. 44%, m.p. 236–237°C).

6-Aryl-5-cyano-2-(methylthio)uracils (3a-c) [36]. A solution of substituted 2-thiouracils **2a–c** (0.05 mole), methyl iodide (3.11 ml, 0.05 mole) and sodium hydroxide (2 g, 0.05 mole) in water (50 mL) and ethanol (100 mL) was stirred at 60°C for 1 h. A white solid began to precipitate by cooling. The solid was filtered off, washed with water, dried and recrystallized from ethanol to give **3a–c** in 88–92% yields.

5-Cyano-2-(methylthio)-6-phenyluracil (3a). Yield: 90%, m.p. 267–269°C (lit. 86%, m.p. 267°C).

5-Cyano-6-(4-methylphenyl)-2-(methylthio)uracil (3b). Yield: 88%, m.p. 297–299°C (lit. 86%, m.p. > 300°C).

5-Cyano-6-(4-methoxyphenyl)-2-(methylthio)uracil (3c). Yield: 92%, m.p. > 300°C (lit. 87%, m.p. > 300°C).

2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranosyl chloride (4) [36]. Sodium (1.1 g, 47.5 mmol) was added in small pieces to 50 mL of methanol in a round-bottomed flask with cooling in an ice-bath. The solution was brought to 25°C and powdered 2-amino-2-deoxy-α-D-glucose hydrochloride (10.45 g, 48.52 mmol) was added. The mixture was gently swirled for 4–5 min, and then filtered through a Büchner funnel with very gentle suction. The filter was washed twice with 5-mL portions of methanol. The combined filtrate was treated with 6 mL (63 mmol) of acetic anhydride, and the flask was cooled under a tap for a few minutes to moderate the initial reaction. The clear solution was kept for overnight at room temperature and then refrigerated for 4 h at 0°C to complete crystallization. The product was filtered, washed with 10 mL of methanol and then with three 5 mL portions of ether, and dried well. The dried powder was placed in 250-mL round-bottomed flask and treated with 20 mL of acetyl chloride which was added drop wise through the top of the condenser with vigorous stirring. The mixture was stirred for 48 h without external heating at room temperature. Through the condenser, 80 mL of dichloromethane was added, then the solution was poured with vigorous stirring onto 80 g of ice and 20 mL of water. The organic solution was drawn off without delay into a beaker containing ice and 80 mL of saturated sodium bicarbonate solution. The organic layer was dried over Na_2SO_4, filtered, concentrated to 10 mL on a rotary evaporator at 50°C, and 100 mL of dry ether was added to the warm solution with swirling and left for 12 h at 5°C. The solid was collected by filtration, washed with dry ether and dried well. Pure 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**4**) was obtained; yield 13 g, 76 %; m.p. 125–126°C (lit. 70%, m.p. 127–128°C).

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1H)-ones (5a–c). A mixture of 2-(methylthio)uracils 3a–c (5 mmol) and 50% oil-immersed sodium hydride (0.24 g, 5 mmol) in DMF (30 mL) was stirred at 70–80°C for 1 h and then cooled to room temperature. α-Chloroacetamido sugar 4 (1.83 g, 5 mmol) was added to the mixture, and stirred at 90°C for 3–5 h. the mixture was evaporated till dryness under reduced pressure and the residue was recrystallized from absolute ethanol to give 5a–c in 76–81% yields.

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-5-cyano-2-(methylthio)-6-phenylpyrimidin-4(1H)-one (5a). Yield = 2.31 g, 81%; m.p. 190–191°C. ir (KBr) ν: 3310 (NH), 1738 (C=O), 1669 (C=O), 2205 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 1.77 (s, 3 H, NH*Ac*), 1.94, 1.99, 2.02 (3 s, 9 H, 3 OAc), 2.51 (s, 3 H, SCH_3), 3.97-4.10 (m, 3 H, H-5′, H-6′), 4.50 (m, 1 H, H-2′), 5.10 (m, 1 H, H-4′), 5.25 (t, 1 H, *J* = 9.5 Hz, H-3′), 5.70 (d, 1 H, *J* = 9.5 Hz, H-1′), 7.80 (d, 1 H, *J* = 7.5 Hz, *NH*Ac), 7.32-7.40 (m, 5 H, Ar—H). EI-MS: *m*/*z* = 572 [M^+]. Anal. Calcd for $C_{26}H_{28}N_4O_9S$ (572.58): C 54.53, H 4.92, N 9.78. Found: C 54.44, H 4.67, N 9.99.

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methylphenyl)-2-(methylthio)pyrimidin-4(1H)-one (5b). Yield = 2.22 g, 76%; m.p. 212–213°C. ir (KBr) ν: 3314 (NH), 1740 (C=O), 1672 (C=O), 2205 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.79 (s, 3 H, NHAc), 1.95, 1.99, 2.00 (3 s, 9 H, 3 OAc), 2.33 (s, 3 H, CH_3), 2.50 (s, 3 H, SCH_3), 3.95-4.15 (m, 3 H, H-5′, H-6′), 4.54 (m, 1 H, H-2′), 5.19 (m, 1 H, H-4′), 5.31 (t, 1 H, *J* = 9.5 Hz, H-3′), 5.74 (d, 1 H, *J* = 9.6 Hz, H-1′), 7.19 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.35 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.82 (d, 1 H, *J* = 7.5 Hz, *NH*Ac). EI-MS: *m*/*z* = 586 [M^+]. Anal. Calcd for $C_{27}H_{30}N_4O_9S$ (586.61): C 55.28, H 5.15, N 9.55. Found: C 55.12, H 4.99, N 9.37.

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methoxyphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (5c) Yield = 2.37 g, 79%; m.p. 233-234°C. ir (KBr) ν: 3312 (NH), 1742 (C=O), 1669 (C=O), 2207 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 1.78 (s, 3 H, NH*Ac*), 1.94, 1.99, 2.02 (3 s, 9 H, 3 OAc), 2.53 (s, 3 H, SCH_3), 3.48 (s, 3 H, OCH_3), 3.91-4.11 (m, 3 H, H-5′, H-6′), 4.53 (m, 1 H, H-2′), 5.22 (m, 1 H, H-4′), 5.34 (t, 1 H, *J* = 9.5 Hz, H-3′), 5.72 (d, 1 H, *J* = 9.4 Hz, H-1′), 7.18 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.30 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.77 (d, 1 H, *J* = 7.5 Hz, *NH*Ac). EI-MS: *m*/*z* = 602 [M^+]. Anal. Calcd for $C_{27}H_{30}N_4O_{10}S$ (602.61): C 53.81, H 5.01, N 9.29. Found: C 53.66, H 4.87, N 9.17.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1H)-ones (6a-c). A solution of 5a-c (0.5 g) in a 1:1 mixture (50 mL) of methanol and conc. ammonia (25%) was stirred at room temperature for 2 h. The reaction mixtures were concentrated under reduced pressure. The residue were recrystallized from methanol to furnish the title compounds 6a-c in 85-89% yields.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-cyano-2-(methylthio)-6-phenylpyrimidin-4(1H)-one (6a). Yield = 0.33 g, 85%; m.p. 263-264°C. ir (KBr) ν: 3412-3380 (OH), 3311 (NH),

1674 (C=O), 2205 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 1.68 (s, 3 H, NH*Ac*), 3.16-3.25 (m, 2 H, H-6′), 3.42-3.50 (m, 2 H, H-4′, H-5′), 3.73 (m, 1 H, H-3′), 3.84 (m, 1 H, H-2′), 5.18-5.31 (m, 3 H, 3 OH), 5.38 (d, 1 H, *J* = 9.5 Hz, H-1′), 7.35-7.40 (m, 5 H, Ar—H), 7.92 (d, 1 H, *J* = 8.5 Hz, NHAc). EI-MS: *m/z* = 446 [M^+]. Anal. Calcd for $C_{20}H_{22}N_4O_6S$ (446.47): C 53.80, H 4.96, N 12.54. Found: C 53.60, H 4.81, N 12.32.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methyl- phenyl)-2-(methylthio)-pyrimidin-4(1H)-one (6b). Yield = 0.34 g, 89%; m.p. 274-275°C. ir (KBr) ν: 3418-3385 (OH), 3316 (NH), 1670 (C=O), 2202 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 1.69 (s, 3 H, NH*Ac*), 2.30 (s, 3 H, CH_3), 2.51 (s, 3 H, SCH_3), 3.19-3.26 (m, 2 H, H-6′), 3.40-3.50 (m, 2 H, H-4′, H-5′), 3.77 (m, 1 H, H-3′), 3.89 (m, 1 H, H-2′), 5.21-5.31 (m, 3 H, 3 OH), 5.39 (d, 1 H, *J* = 9.6 Hz, H-1′), 7.23 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.39 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.90 (d, 1 H, *J* = 8.5 Hz, *NH*Ac). EI-MS: *m/z* = 460 [M^+]. Anal. Calcd for $C_{21}H_{24}N_4O_6S$ (460.50): C 54.77, H 5.25, N 12.16. Found: C 54.63, H 5.11, N 12.02.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methoxy-phenyl)-2-(methylthio)-pyrimidin-4(1H)-one (6c). Yield = 0.35 g, 88%; m.p. 260-262°C. ir (KBr) ν: 3429-3387 (OH), 3317 (NH), 1671 (C=O), 2205 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.69 (s, 3 H, NH*Ac*), 2.50 (s, 3 H, SCH_3), 3.29-3.50 (m, 7 H, H-4′, H-5′, H-6′, OCH_3), 3.75 (m, 1 H, H-3′), 3.85 (m, 1 H, H-2′), 5.20-5.35 (m, 3 H, 3 OH), 5.35 (d, 1 H, *J* = 9.5 Hz, H-1′), 7.23 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.37 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.91 (d, 1 H, *J* = 8.5 Hz, *NH*Ac). EI-MS: *m/z* = 476 [M^+]. Anal. Calcd for $C_{21}H_{24}N_4O_7S$ (476.50): C 52.93, H 5.07, N 11.75. Found: C 52.79, H 4.87, N 11.59.

2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl bromide (7) [40]. Glucose pentaacetate (12 g, 30.76 mmol) was dissolved in dry dichloromethane (24 mL) and placed in a 250-mL conical flask fitted with a glass stopper. Hydrogen bromide solution in acetic acid (24 mL) (45%, w/w HBr) was added and the reaction mixture was allowed to stand at room temperature for 2.5 h. The mixture was poured into ice-water and the flask was washed with dichloromethane. The organic layer was separated and washed with several portions of saturated aqueous $NaHCO_3$ until no effervescence occurs. The organic layer was washed with water, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was dissolved in dry ether, heating to 40°C and light petroleum (b.p. 40-60°C) was added slowly until a slight persistent cloudiness was occurred. A little amount of dry ether was added to give a clear solution which was left to cool slowly to room temperature and finally refrigerated. The purified product was filterted off and dried well to give **7**, yield 11 g, 87%; m.p. 85-86°C (lit. 88%, m.p. 88-89°C). The product should be stored in refrigerator without delay.

1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1H)-ones (8a-c). 2-(Methylthio)uracils 3a-c (5 mmol) were suspended in 25 mL dry DMF at room temperature. To this suspension 0.26 g NaH (50%, 5 mmol) was added and the mixture was stirred at 70-80°C for 0.5 h and cooled to room temperature. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (7) (2.26 g, 5.5 mmol) was added, and the mixture was stirred at room temperature for 3 h until the starting material was consumed (TLC) and then filtered. The residue resulted from evaporation of the filtrate under reduced pressure was purified by recrystallization from absolute ethanol to afford 8a-c in 78-83 yields.

1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-cyano-2-(methylthio)-6-phenylpyrimidin-4(1H)-one (8a). Yield = 2.23 g, 78 %; m.p. 166-168°C. ir (KBr) ν: 1736 (C=O), 1668 (C=O), 2204 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.02, 2.03, 2.04, 2.07 (4 s, 12 H, 4 OAc), 2.50 (s, 3 H, SCH_3), 4.09 (m, 2 H, H-6′), 4.22 (m, 1 H, H-5′), 5.06 (t, 1 H, $J_{3',4'}$ = 9.5 Hz, H-4′), 5.16 (t, 1 H, $J_{2',3'}$ = 9.2 Hz, H-2′), 5.58 (t, 1 H, $J_{2',3'}$ = 9.3 Hz, H-3′), 6.42 (d, 1 H, $J_{1',2'}$ = 8.2 Hz, H-1′), 7.35-7.40 (m, 5 H, Ar—H). EI-MS: *m/z* = 446 [M^+]. Anal. Calcd for $C_{26}H_{27}N_3O_{10}S$ (573.57): C 54.44, H 4.74, N 7.32. Found: C 54.23, H 4.61, N 7.25.

1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-cyano-6-(4-methylphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (8b). Yield = 2.31 g, 79%; m.p. 166-168°C. ir (KBr) ν: 1738 (C=O), 1666 (C=O), 2205 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 1.99, 2.02, 2.04, 2.06 (4 s, 12 H, 4 OAc), 2.38 (s, 3 H, CH_3), 2.52 (s, 3 H, SCH_3), 4.11 (m, 1 H, H-6′), 4.29 (m, 1 H, H-5′), 5.11 (m, 1 H, H-4′), 5.25 (m, 1 H, H-2′), 5.61 (m, 1 H, H-3′), 6.44 (d, 1 H, $J_{1',2'}$ = 8.1 Hz, H-1′), 7.20 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.40 (d, *J* = 10.3 Hz, 2 H, Ar-H). EI-MS: *m/z* = 587 [M^+]. Anal. Calcd for $C_{27}H_{29}N_3O_{10}S$ (587.60): C 55.19, H 4.97, N 7.15. Found: C 54.98, H 4.81, N 7.05.

1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-cyano-6-(4-methoxyphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (8c). Yield = 2.50 g, 83%; m.p. 189-191°C. ir (KBr) ν: 1742 (C=O), 1670 (C=O), 2206 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.98, 2.02, 2.05, 2.08 (4 s, 12 H, 4 OAc), 2.53 (s, 3 H, SCH_3), 3.48 (s, 3 H, OCH_3), 4.17 (m, 1 H, H-6′), 4.32 (m, 1 H, H-5′), 5.21-5.30 (m, 2 H, H-2′, H-4′), 5.66 (m, 1 H, H-3′), 6.43 (d, 1 H, $J_{1',2'}$ = 8.3 Hz, H-1′), 7.25 (d, *J* = 10.3 Hz, 2 H, Ar-H), 7.43 (d, *J* = 10.3 Hz, 2 H, Ar—H). EI-MS: *m/z* = 603 [M^+]. Anal. Calcd for $C_{27}H_{29}N_3O_{11}S$ (603.60): C 53.72, H 4.84, N 6.96. Found: C 53.60, H 4.80, N 7.08.

1-(β-D-Glucopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1H)-ones (9a-c). A solution of 8a-c (0.5 g) in a 1 : 1 mixture (50 mL) of methanol and conc. ammonia (25%) was stirred at room temperature for 2 h. The reaction mixtures were concentrated under reduced pressure. The residue were recrystallized from methanol to give 9a-c in 88-92% yields.

1-(β-D-Glucopyranosyl)-5-cyano-2-(methylthio)-6-phenylpyrimidin-4(1H)-one (9a). Yield = 0.32 g, 92 %; m.p. 170-171 °C. ir (KBr) ν: 3432-3386 (OH), 1670 (C=O), 2205 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.51 (s, 3 H, SCH_3), 3.28-3.31 (m, 4 H, H-3′, H-4′, H-5′, H-6′), 3.50 (m, 1 H, H-6′), 3.64 (m, 1 H, H-2′), 4.50 (brs, 1 H, 6′-OH), 5.00 (brs, 1 H, 4′-OH), 5.45 (m, 2 H, 2′-OH, 3′-OH), 5.74 (d, $J_{1',2'}$ = 7.8 Hz, H-1′), 7.30-7.40 (m, 5 H, Ar—H). EI-MS: *m/z* = 405 [M^+]. Anal. Calcd for $C_{18}H_{19}N_3O_6S$ (405.42): C 53.32, H 4.72, N 10.36. Found: C 53.09, H 4.63, N 10.17.

1-(β-D-Glucopyranosyl)-5-cyano-6-(4-methylphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (9b). Yield = 0.32 g, 90 %; m.p. 198-199°C. ir (KBr) ν: 3434-3389 (OH), 1672 (C=O), 2207 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.38 (s, 3 H, CH_3), 2.50 (s, 3 H, SCH_3), 3.35-3.45 (m, 5 H, H-3′, H-4′, H-5′, H-6′), 3.66 (m, 1 H, H-2′), 4.52 (brs, 1 H, 6′-OH), 5.07 (brs, 1 H, 4′-OH), 5.50 (m, 2 H, 2′-OH, 3′-OH), 5.75 (d, $J_{1',2'}$ = 7.5 Hz, H-1′), 7.25 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.45 (d, *J* = 10.3 Hz, 2 H, Ar-H). EI-MS: *m/z* = 419 [M^+]. Anal. Calcd for $C_{19}H_{21}N_3O_6S$ (419.45): C 54.40, H 5.04, N 10.01. Found: C 54.28, H 4.89, N 9.89.

1-(β-D-Glucopyranosyl)-5-cyano-6-(4-methoxyphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (9c). Yield = 0.31 g, 88 %; m.p. 218-220°C. ir (KBr) ν: 3435-3388 (OH), 1677 (C=O), 2207 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.50 (s, 3 H, SCH_3), 3.39-3.52 (m, 8 H, H-3′, H-4′, H-5′, H-6′, OCH_3), 3.63 (m, 1 H, H-2′), 4.48 (brs, 1 H, 6′-OH), 5.05 (brs, 1 H, 4′-OH), 5.55 (m, 2 H, 2′-OH, 3′-OH), 5.77 (d, $J_{1',2'}$ = 7.7 Hz, H-1′), 7.25 (d, J = 10.3 Hz, 2 H, Ar—H), 7.47 (d, J = 10.3 Hz, 2 H, Ar-H). EI-MS: m/z = 435 [M^+]. Anal. Calcd for $C_{19}H_{21}N_3O_7S$ (435.45): C 52.40, H 4.86, N 9.64. Found: C 52.27, H 4.80, N 9.53.

2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl bromide (10) [41]. Galactose pentaacetate (12 g, 30.76 mmol) was dissolved in dry dichloromethane (24 mL) and placed in a 250-mL conical flask fitted with a glass stopper. Hydrogen bromide solution in acetic acid (24 mL) (45%, w/w HBr) was added and the reaction mixture was allowed to stand at room temperature for 2.5 h. The mixture was poured into ice-water and the flask was washed with dichloromethane. The organic layer was separated and washed with several portions of saturated aqueous $NaHCO_3$ until no effervescence occurs. The organic layer was washed with water, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was dissolved in dry ether, heating to 40°C and light petroleum (b.p. 40-60°C) was added slowly until a slight persistent cloudiness was occurred. A little amount of dry ether was added to give a clear solution which was left to cool slowly to room temperature and finally refrigerated. The purified product was filtered off and dried well to give **10** (10 g, 79%). The product should be stored in refrigerator without delay.

1-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1H)-ones (11a-c). 2-(Methylthio)uracils 3a-c (5 mmol) were suspended in 25 mL dry DMF at room temperature. To this suspension 0.26 g NaH (50%, 5 mmol) was added and the mixture was stirred at 70-80°C for 0.5 h and cooled to room temperature. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide (10) (2.26 g, 5.5 mmol) was added, and the mixture was stirred at room at room temperature for 3 h until the starting material was consumed (TLC) and then filtered. The residue resulted from evaporation of the filtrate under reduced pressure was purified by recrystallization from absolute ethanol to afford 11a-c in 66-71 yields.

1-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-5-cyano-2-(methylthio)-6-phenylpyrimidin-4(1H)-one (11a). Yield = 2.03 g, 71 %; m.p. 143-144°C. ir (KBr) ν: 1737 (C=O), 1662 (C=O), 2205 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.02, 2.03, 2.07, 2.17 (4 s, 12 H, 4 OAc), 2.51 (s, 3 H, SCH_3), 3.86-3.92 (m, 1 H, H-5′), 4.06-4.18 (m, 2 H, H-6′), 4.70 (d, 1 H, $J_{1',2'}$ = 7.4 Hz, H-1′), 5.00 (m, 1 H, H-3′), 5.18 (m, 1 H, H-2′), 5.36 (dd, 1 H, $J_{3',4'}$ = 3.4 Hz, $J_{4',5'}$ = 1.1 Hz, H-4′), 7.30-7.40 (m, 5 H, Ar—H). EI-MS: m/z = 446 [M^+]. Anal. Calcd for $C_{26}H_{27}N_3O_{10}S$ (573.57): C 54.44, H 4.74, N 7.32. Found: C 54.27, H 4.51, N 7.20.

1-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-5-cyano-6-(4-methylphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (11b). Yield = 2.02 g, 69 %; m.p. 163-164°C. ir (KBr) ν: 1740 (C=O), 1667 (C=O), 2204 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 2.00, 2.03, 2.05, 2.14 (4 s, 12 H, 4 OAc), 2.33 (s, 3 H, CH_3), 2.50 (s, 3 H, SCH_3), 3.86-3.98 (m, 1 H, H-5′), 4.10-4.18 (m, 2 H, H-6′), 4.74 (d, 1 H, $J_{1',2'}$ = 7.5 Hz, H-1′), 5.15-5.20 (m, 2 H, H-2′, H-3′), 5.33 (dd, 1 H, $J_{3',4'}$ = 3.3 Hz, $J_{4',5'}$ = 1.0 Hz, H-4′), 7.21 (d, J = 10.3 Hz, 2 H, Ar—H), 7.41 (d, J = 10.3 Hz, 2 H, Ar-H). EI-MS: m/z = 587 [M^+]. Anal. Calcd for $C_{27}H_{29}N_3O_{10}S$ (587.60): C 55.19, H 4.97, N 7.15. Found: C 54.02, H 4.77, N 7.00.

1-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-5-cyano-6-(4-methoxyphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (11c). Yield = 1.99 g, 66 %; m.p. 205-206°C. ir (KBr) ν: 1744 (C=O), 1669 (C=O), 2207 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.01, 2.03, 2.05, 2.16 (4 s, 12 H, 4 OAc), 2.49 (s, 3 H, SCH_3), 3.50 (s, 3 H, OCH_3), 3.88-3.96 (m, 1 H, H-5′), 4.10-4.19 (m, 2 H, H-6′), 4.73 (d, 1 H, $J_{1',2'}$ = 7.4 Hz, H-1′), 5.10-5.20 (m, 2 H, H-2′, H-3′), 5.37 (dd, 1 H, $J_{3',4'}$ = 3.5 Hz, $J_{4',5'}$ = 1.2 Hz, H-4′), 7.22 (d, J = 10.3 Hz, 2 H, Ar—H), 7.40 (d, J = 10.3 Hz, 2 H, Ar—H). EI-MS: m/z = 603 [M^+]. Anal. Calcd for $C_{27}H_{29}N_3O_{11}S$ (603.60): C 53.72, H 4.84, N 6.96. Found: C 53.63, H 4.77, N 6.88.

1-(β-D-Galactopyranosyl)-6-aryl-5-cyano-2-(methylthio)-pyrimidin-4(1H)-ones (12a-c). A solution of 11a-c (0.5 g) in a 1 : 1 mixture (50 mL) of methanol and conc. ammonia (25%) was stirred at room temperature for 2 h. The reaction mixtures were concentrated under reduced pressure. The residue were recrystallized from methanol to give 12a-c in 78-80% yields.

1-(β-D-Galactopyranosyl)-5-cyano-2-(methylthio)-6-phenylpyrimidin-4(1H)-one (12a). Yield = 0.28 g, 80%; m.p. 210-211°C. ir (KBr) ν: 3435-3385 (OH), 1665 (C=O), 2204 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 2.50 (s, 3 H, SCH_3), 3.42-3.49 (m, 3 H, H-2′, H-3′, H-5′), 3.65-3.71 (m, 2 H, H-6′), 3.88 (m, 1 H, H-4′), 4.48 (m, 1 H, H-1′), 4.70 (brs, 1 H, 6′-OH), 5.05 (brs, 1 H, 4′-OH), 5.50 (m, 2 H, 2′-OH, 3′-OH), 7.30-7.40 (m, 5 H, Ar—H). EI-MS: m/z = 405 [M^+]. Anal. Calcd for $C_{18}H_{19}N_3O_6S$ (405.42): C 53.32, H 4.72, N 10.36. Found: C 53.22, H 4.60, N 10.24.

1-(β-D-Galactopyranosyl)-5-cyano-6-(4-methylphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (12b). Yield = 0.28 g, 80%; m.p. 237-239°C. ir (KBr) ν: 3436-3388 (OH), 1667 (C=O), 2206 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 2.33 (s, 3 H, CH_3), 2.52 (s, 3 H, SCH_3), 3.52-3.69 (m, 5 H, H-2′, H-3′, H-5′, H-6′), 3.90 (m, 1 H, H-4′), 4.54 (m, 1 H, H-1′), 4.74 (brs, 1 H, 6′-OH), 5.15 (brs, 1 H, 4′-OH), 5.55 (m, 2 H, 2′-OH, 3′-OH), 7.24 (d, J = 10.3 Hz, 2 H, Ar—H), 7.44 (d, J = 10.3 Hz, 2 H, Ar—H). EI-MS: m/z = 419 [M^+]. Anal. Calcd for $C_{19}H_{21}N_3O_6S$ (419.45): C 54.40, H 5.04, N 10.01. Found: C 54.32, H 4.95, N 9.94.

1-(β-D-Galactopyranosyl)-5-cyano-6-(4-methoxyphenyl)-2-(methylthio)-pyrimidin-4(1H)-one (12c). Yield = 0.28 g, 78 %; m.p. 243-245°C. ir (KBr) ν: 3439-3388 (OH), 1667 (C=O), 2207 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 2.51 (s, 3 H, SCH_3), 3.50-3.65 (m, 5 H, H-2′, H-3′, H-5′, H-6′), 3.93 (m, 1 H, H-4′), 4.50 (m, 1 H, H-1′), 4.77 (brs, 1 H, 6′-OH), 5.19 (brs, 1 H, 4′-OH), 5.59 (m, 2 H, 2′-OH, 3′-OH), 7.21 (d, J = 10.3 Hz, 2 H, Ar—H), 7.45 (d, J = 10.3 Hz, 2 H, Ar—H). EI-MS: m/z = 435 [M^+]. Anal. Calcd for $C_{19}H_{21}N_3O_7S$ (435.45): C 52.40, H 4.86, N 9.64. Found: C 52.33, H 4.77, N 9.49.

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-6-aryl-5-cyanopyrimidin-4(1H)-ones (13a-c). A mixture of 6-aryl-5-cyanouracils 1a-c (5 mmol) and 50% oil-immersed sodium hydride (0.24 g, 5 mmol) in DMF (30 ml) was stirred at 70-80°C for 1 h and then cooled to room temperature. α-Chloroacetamido sugar 4 (1.83 g, 5 mmol) was added to the mixture, and stirred at 90°C for 3-5 h. the mixture was evaporated till dryness under reduced pressure and the residue was recrystallized from absolute ethanol to give 13a-c in 75-80% yields.

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-phenylpyrimidin-4(1H)-one (13a). Yield = 2.11 g, 78 %; m.p. 150-151°C. ir (KBr) ν: 3317 (NH), 1737(C=O), 1668 (C=O), 2203 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.75 (s, 3 H, NH*Ac*), 1.94, 1.99, 2.00 (3 s, 9 H, 3 OAc), 3.95-4.11 (m, 3 H, H-5′, H-6′), 4.54 (m, 1 H, H-2′), 5.15 (m, 1 H, H-4′), 5.30 (m, 1 H, H-3′), 5.49 (d, 1 H, *J* = 9.3 Hz, H-1′), 7.77 (d, 1 H, *J* = 7.5 Hz, *NH*Ac), 7.37-7.47 (m, 5 H, Ar—H). EI-MS: *m*/*z* = 542 [M^+]. Anal. Calcd for $C_{25}H_{26}N_4O_{10}$ (542.50): C 55.35, H 4.83, N 10.32. Found: C 55.21, H 4.77, N 10.13.

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methylphenyl)-pyrimidin-4(1H)-one (13b). Yield = 2.22 g, 80 %; m.p. 242-243°C. ir (KBr) ν: 3319 (NH), 1738 (C=O), 1668 (C=O), 2205 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.76 (s, 3 H, NH*Ac*), 1.97, 2.00, 2.05 (3 s, 9 H, 3 OAc), 2.36 (s, 3 H, CH_3), 4.25-4.45 (m, 4 H, H-2′, H-5′, H-6′), 5.20-5.30 (m, 1 H, H-4′), 5.43 (m, 1 H, H-3′), 5.58 (d, 1 H, *J* = 9.4 Hz, H-1′), 7.21 (d, *J* = 10.3 Hz, 2 H, Ar-H), 7.39 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.80 (d, 1 H, *J* = 7.5 Hz, *NH*Ac). EI-MS: *m*/*z* = 556 [M^+]. Anal. Calcd for $C_{26}H_{28}N_4O_{10}$ (556.52): C 56.11, H 5.07, N 10.06. Found: C 56.00, H 4.89, N 9.97.

1-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methoxyphenyl)-pyrimidin-4(1H)-one (13c). Yield = 2.14 g, 75 %; m.p. 263-264°C. ir (KBr) ν: 3324 (NH), 1740 (C=O), 1672 (C=O), 2206 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.78 (s, 3 H, NH*Ac*), 1.96, 1.99, 2.02 (3 s, 9 H, 3 OAc), 3.53 (s, 3 H, OCH_3), 4.07-4.19 (m, 3 H, H-5′, H-6′), 4.33 (m, 1 H, H-2′), 5.32 (m, 1 H, H-4′), 5.50 (t, 1 H, *J* = 9.5 Hz, H-3′), 5.60 (d, 1 H, *J* = 9.2 Hz, H-1′), 7.19 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.33 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.79 (d, 1 H, *J* = 7.5 Hz, *NH*Ac). EI-MS: *m*/*z* = 572 [M^+]. Anal. Calcd for $C_{26}H_{28}N_4O_{11}$ (572.52): C 54.54, H 4.92, N 9.78. Found: C 54.32, H 4.81, N 9.57.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-6-aryl-5-cyano-pyrimidin-4(1H)-ones (14a-c). A solution of 13a-c (0.5 g) in a 1:1 mixture (50 mL) of methanol and conc. ammonia (25%) was stirred at room temperature for 8 h. The reaction mixtures were concentrated under reduced pressure. The residue were recrystallized from methanol to give 14a-c in 83-90% yields.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-phenyl-pyrimidin-4(1H)-one (14a). Yield = 0.34 g, 90%; m.p. 276-277°C. ir (KBr) ν: 4351-3986 (OH), 3315 (NH), 1668 (C=O), 2204 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.68 (s, 3 H, NH*Ac*), 3.32-3.50 (m, 4 H, H-4′, H-5′, H-6′), 3.77-4.88 (m, 2 H, H-2′, H-3′), 5.16-5.26 (m, 3 H, 3 OH), 5.36 (d, 1 H, *J* = 9.4 Hz, H-1′), 7.30-7.40 (m, 5 H, Ar—H), 7.90 (d, 1 H, *J* = 8.5 Hz, *NH*Ac). EI-MS: *m*/*z* = 416 [M^+]. Anal. Calcd for $C_{19}H_{20}N_4O_7$ (416.39): C 54.80, H 4.84, N 13.45. Found: C 54.60, H 4.71, N 13.37.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methyl- phenyl)-pyrimidin-4(1H)-one (14b). Yield = 0.34 g, 88%; m.p. 288-289°C. ir (KBr) ν: 4360-3990 (OH), 3317 (NH), 1669 (C=O), 2205 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.69 (s, 3 H, NH*Ac*), 2.38 (s, 3 H, CH_3), 3.19-3.29 (m, 4 H, H-4′, H-5′, H-6′, 3.70-3.80 (m, 2 H, H-2′, H-3′), 5.15-5.21 (m, 3 H, 3 OH), 5.38 (d, 1 H, J = 9.6 Hz, H-1′), 7.22 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.41 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.88 (d, 1 H, *J* = 8.5 Hz, *NH*Ac). EI-MS: *m*/*z* = 430 [M^+]. Anal. Calcd for $C_{20}H_{22}N_4O_7$ (430.41): C 55.81, H 5.15, N 13.01. Found: C 55.68, H 5.04, N 12.92.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-cyano-6-(4-methoxy- phenyl)-pyrimidin-4(1H)-one (14c). Yield = 0.32 g, 83%; m.p. 290-292°C. ir (KBr) ν: 4362-3995 (OH), 3324 (NH), 1674 (C=O), 2207 (CN) cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.73 (s, 3 H, NH*Ac*), 3.39-3.58 (m, 8 H, H-3′, H-4′, H-5′, H-6′, OCH_3), 3.88 (m, 1 H, H-2′), 5.20-5.30 (m, 3 H, 3 OH), 5.40 (d, 1 H, *J* = 9.5 Hz, H-1′), 7.21 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.39 (d, *J* = 10.3 Hz, 2 H, Ar—H), 7.90 (d, 1 H, *J* = 8.5 Hz, *NH*Ac). EI-MS: *m*/*z* = 446 [M^+]. Anal. Calcd for $C_{20}H_{22}N_4O_8$ (446.41): C 53.81, H 4.96, N 12.55. Found: C 53.60, H 4.83, N 12.33.

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