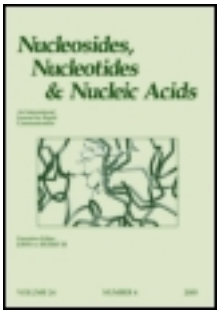

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Glycosylation of 2-Thiouracil Derivatives. A Synthetic Approach to 3-Glycosyl-2, 4-dioxypyrimidines

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Glycosylation of 2-Thiouracil Derivatives.

A Synthetic Approach to 3-Glycosyl-2,4-dioxypyrimidines

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Abstract: Reaction of 6-aryl-5-cyano-2-thiouracils **2a-d** with glycosyl halides **4a,b** under alkaline conditions gave the respective bisglycosylated derivatives **5a-h**. However, their deacetylation with ammonia in methanol caused a cleavage of the S-glycosyl residue and gave the N-3 glycosylated analogues **6a-h**.

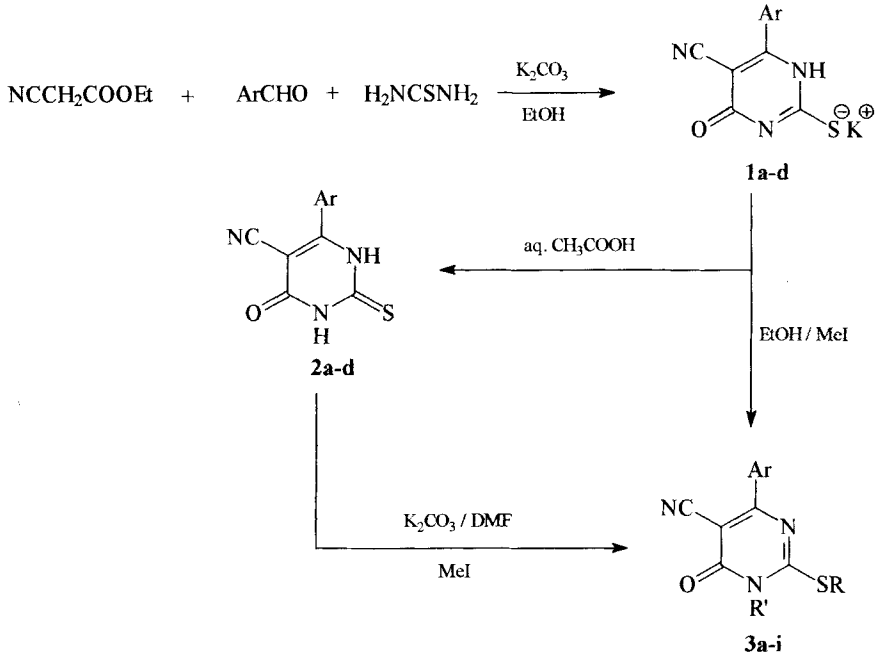
INTRODUCTION

Pyrimidines have occupied a unique place and have remarkably contributed to biological and medicinal chemistry. Various analogues of thiopyrimidines possess effective antibacterial, antifungal, antiviral, insecticidal, and miticidal activities[1-3]. Thiopyrimidine nucleosides are of interest owing to their occurrence as constituents of certain transfer ribonucleic acids (tRNA)[4]. A variety of pyrimidine nucleosides have shown interesting biological activities including antitumor activities[5,6], antiviral activity[7], virucidal against the herpes virus[8] and strain HF of HSV-1[9]. Among pyrimidine nucleosides[10], 5-iodo-2-deoxyuridine (IdUrd) has been in clinical use as a drug for years. The most active congeners among the 5-substituted 2'-deoxyuridine derivatives are (*E*)-5-(2-halogenovinyl)-2'-

deoxyuridines[11], which are particularly active against HSV-1 and varicella-zoster virus. The structure activity relationships among 5-substituted 2'-deoxyuridine analogues have been studied in some detail[12,13]. (2-Deoxy-D-glucosyl)uracil is an inhibitor of a nonspecific pyrimidine phosphorylase[14]. The versatile biological properties of pyrimidines and thiopyrimidines prompted us to investigate the synthesis, the antiviral activities and the antitumer activites of 6-aryl-5-cyano-2-alkylmercapto-3,4-dihydropyrimidin-4-ones **3a-h**, 6-aryl-5-cyano-3-(2',3',4',6'-tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosyl)-2-(2",3",4",6"-tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosylmercapto)-3,4-dihydropyrimidin-4-ones **5a-h** and 6-aryl-5-cyano-3-(β-D-gluco- and D-galactopyranosyl)-3,4-dihydropyrimidin-2,4-diones **6a-h**.

RESULTS AND DISCUSSION

The 6-aryl-5-cyano-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-ones **2a-d** were prepared in 28-42 % overall yield in two steps from the reaction of ethyl cyanoacetate with thiourea and aromatic aldehydes according to reported procedures[15,16]. The potassium salts could be isolated from the reaction whose acidification gave **2a-d**. A model study on the alkylation of **1a-d** and / or **2a-d** was carried out using iodomethane and ethyl bromoacetate by the reaction of one mole of the alkylating agents directly with the potassium salts of 6-aryl-5-cyano-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-ones **1a-d** or the reaction with **2a-d** in the presence of potassium carbonate in DMF whereby the same product **3a-h** was obtained in each case (Scheme 1). On the other hand, the use of two moles of the alkylating agents led to the dialkylated derivatives[17]. The structure of compounds **3a-h** was confirmed by the spectral data (IR, ^{1}H-NMR and MS). Their IR spectra showed a characteristic carbonyl group in the range 1633-1661cm^{-1}. Their ^{1}H-NMR spectra revealed the presence of an SMe or SCH_2 in the range 2.30-2.70 ppm and 4.10-4.30 ppm, respectively, as well as a broad singlet at δ 12.20 ppm due to the NH. These data as well as the mode of the reaction indicated that the

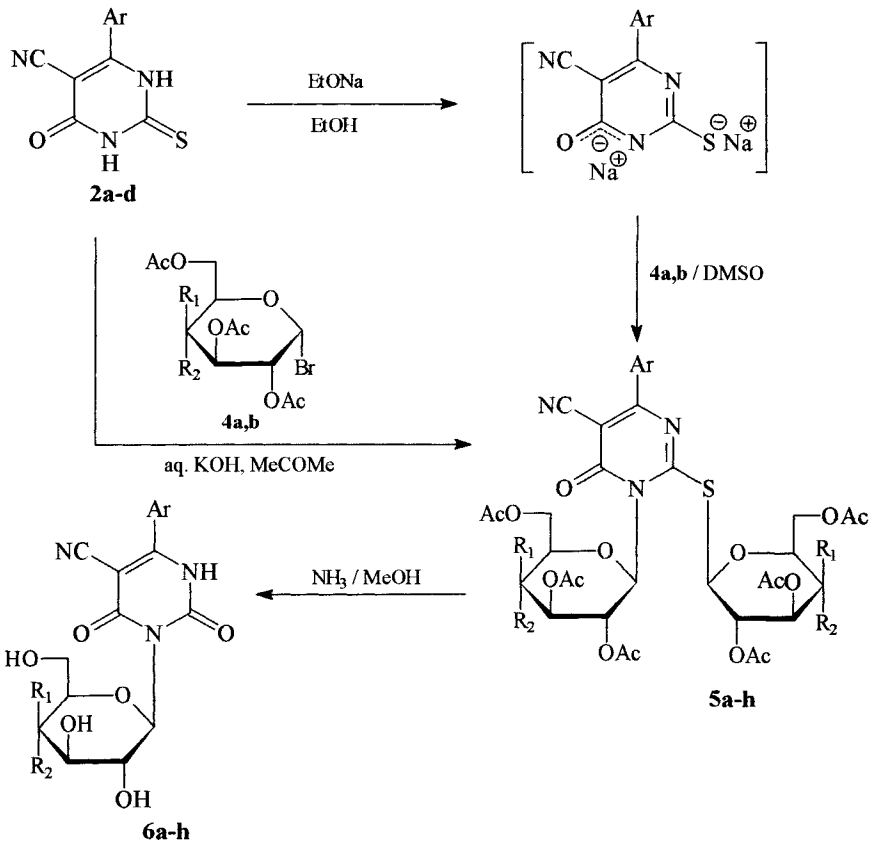


1-3	Ar	R	R'
a	Ph	Me	H
b	p-$MeOC_6H_4$	Me	H
c	p-MeC_6H_4	Me	H
d	p-ClC_6H_4	Me	H
e	Ph	CH_2CO_2Et	H
f	p-$MeOC_6H_4$	CH_2CO_2Et	H
g	p-MeC_6H_4	CH_2CO_2Et	H
h	p-ClC_6H_4	CH_2CO_2Et	H
i	Ph	Me	Me

Scheme 1

site of alkylation was the sulfur rather than the nitrogen and in the case of the disubstituted derivative the N-3 was the second position for alkylation.

Reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide **4a**[18] with **2a-d** or with the sodium salt of **2a-d** in the presence of aqueous potassium hydroxide gave the corresponding bisglucosides **5a-d**. Similarly, the reaction with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide **4b**[18] gave **5e-h**. The structures of compounds **5a-h** could be established and confirmed on the bases of their elemental analysis and spectral data. The elemental analysis as well as the mass spectra indicated the presence of the two glycosyl residues. Their IR spectra were characterized by the absence of signals for an NH groups and the presence of signals at 1660-1690 cm^{-1} due to the carbonyl of the pyrimidinone in addition to the acetoxy carbonyl groups at 1750-1760 cm^{-1}. The ^{1}H-NMR spectrum of **5f** showed the presence of two doublets at δ 5.85 and 6.30 ppm with spin-spin coupling constants of 10.63 and 7.96 Hz respectfully, that were assigned of H-1' and H-1". These coupling constants indicated their diaxial orientation with H-2' and H-2". Consequently, both glycosyl residues were in the β-configuration. Attempted deprotection of **5a-h** with ammonia in methanol, did not give the anticipated deacetylated derivatives but gave the nucleosides **6a-h,** respectively, indicating that a hydrolytic cleavage of the C-S bonds took place. The structures of compounds **6a-h** were confirmed by elemental analysis and spectral data. The IR absorption spectra of compound **6a** showed characteristic bands at 3346, 3226, 2210, 1725 and 1639 cm^{-1} due to the hydroxy groups of the glucose moiety, N_1-H, CN, C_2=O and C_4=O, respectively. The ^{1}H-NMR spectrum of compound **6a** revealed the presence of a broad singlet at δ 11.85 ppm due to N_1-H. The presence of a one doublet at δ 5.41 ppm ($J_{1',2'}$=10.10 Hz), indicated the presence of only one β-D-glucopyranose moiety. The four hydroxy groups of glucose moiety resonate at δ 4.61-5.36 ppm (exchangeable by D_2O). The ^{13}C-NMR spectrum of compound **6a** was characterized by a singlets at δ 88.00, 151.50 and 166.30 ppm were due to C-1', C-2 and C-4, respectively.



	Ar	R_1	R_2
5a	Ph	OAc	H
b	p-$MeOC_6H_4$	OAc	H
c	p-MeC_6H_4	OAc	H
d	p-ClC_6H_4	OAc	H
e	Ph	H	OAc
f	p-$MeOC_6H_4$	H	OAc
g	p-MeC_6H_4	H	OAc
h	p-ClC_6H_4	H	OAc

	Ar	R_1	R_2
6a	Ph	OH	H
b	p-$MeOC_6H_4$	OH	H
c	p-MeC_6H_4	OH	H
d	p-ClC_6H_4	OH	H
e	Ph	H	OH
f	p-$MeOC_6H_4$	H	OH
g	p-MeC_6H_4	H	OH
h	p-ClC_6H_4	H	OH

Scheme 2

TABLE 1 - THE SYNTHETIC DATA FOR THE COMPOUNDS PREPARED

Comp.	M.p. (°C)	Yield (%) a	Yield (%) b	Mol. formula (Mol. Mass)	Analysis (%) Calc./Found C	H	N	MS *m/z*
3a	267	86	78	$C_{12}H_9N_3OS$ (243.28)	Reference 15			
3b	>300	87	82	$C_{13}H_{11}N_3O_2S$ (273.31)	57.13 56.70	4.06 4.20	15.37 15.50	273 (M^+)
3c	>300	86	76	$C_{13}H_{11}N_3OS$ (257.31)	60.68 60.50	4.31 4.40	16.33 16.10	257 (M^+)
3d	295	84	80	$C_{12}H_8ClN_3OS$ (277.73)	51.90 52.10	2.90 2.80	15.13 15.00	277 (M^+)
3e	252	88	72	$C_{15}H_{13}N_3O_3S$ (315.35)	57.13 57.10	4.16 4.20	13.33 13.20	315 (M^+)
3f	232	86	79	$C_{16}H_{15}N_3O_4S$ (345.37)	55.64 55.40	4.38 4.10	12.17 12.40	345 (M^+)
3g	295	84	75	$C_{16}H_{15}N_3O_3S$ (329.37)	58.35 58.40	4.59 4.60	12.76 12.90	329 (M^+)
3h	210	85	78	$C_{15}H_{12}ClN_3O_3S$ (349.79)	51.51 51.80	3.46 3.40	12.01 11.90	349 (M^+)
5a	162	57	34	$C_{39}H_{43}N_3O_{19}S$ (889.84)	52.64 53.30	4.87 5.40	4.72 5.00	889 (M^+)
5b	198	53	37	$C_{40}H_{45}N_3O_{20}S$ (919.87)	52.23 52.50	4.93 4.90	4.57 4.80	919 (M^+)
5c	158	58	32	$C_{40}H_{45}N_3O_{19}S$ (903.87)	53.15 53.30	5.02 5.30	4.65 5.00	903 (M^+)
5d	170	55	38	$C_{39}H_{42}ClN_3O_{19}S$ (924.28)	50.68 51.00	4.58 4.90	4.55 4.70	924 (M^+)
5e	216	56	36	$C_{39}H_{43}N_3O_{19}S$ (889.84)	52.64 52.90	4.93 4.80	4.72 5.00	889 (M^+)
5f	215	52	35	$C_{40}H_{46}N_3O_{20}S$ (920.87)	52.23 51.90	5.03 5.20	4.57 4.90	919 (M^+)
5g	225	54	38	$C_{40}H_{46}N_3O_{19}S$ (904.87)	53.09 53.30	5.12 4.90	4.64 4.90	903 (M^+)
5h	214	59	36	$C_{39}H_{43}ClN_3O_{19}S$ (925.29)	50.68 50.80	4.58 4.50	4.55 4.80	924 (M^+)
6a	207	77	-	$C_{17}H_{17}N_3O_7$ (375.34)	54.40 54.70	4.57 4.80	11.20 11.40	375 (M^+)
6b	185	70	-	$C_{18}H_{19}N_3O_8$ (405.36)	53.33 53.60	4.72 4.50	10.37 10.70	405 (M^+)
6c	223	67	-	$C_{18}H_{19}N_3O_7$ (389.36)	55.53 55.90	4.92 5.10	10.79 10.50	389 (M^+)
6d	197	71	-	$C_{17}H_{16}ClN_3O_7$ (409.78)	49.83 50.10	3.94 4.10	10.25 10.50	409 (M^+)
6e	240	81	-	$C_{17}H_{17}N_3O_7$ (375.34)	54.40 54.70	4.57 4.40	11.20 11.40	375 (M^+)
6f	215	70	-	$C_{18}H_{19}N_3O_8$ (405.36)	53.33 53.50	4.72 4.80	10.37 10.10	405 (M^+)
6g	229	67	-	$C_{18}H_{19}N_3O_7$ (389.36)	55.53 55.70	4.92 5.00	10.79 11.10	389 (M^+)
6h	225	71	-	$C_{17}H_{16}ClN_3O_7$ (409.78)	49.83 50.00	3.94 3.80	10.25 10.60	409 (M^+)

a = method A; b = method B.

TABLE 2 - IR AND ^{1}H NMR DATA OF THE COMPOUNDS PREPARED

comp.	IR selected bands (cm^{-1})	^{1}H NMR (δ ppm) (DMSO)
3b	3414 (NH), 2219 (CN), 1650 (C_4O).	2.45 (3H, s, SMe), 3.86 (3H, s, OMe), 7.42 (2H, d, Ar-H), 8.15 (2H, d, Ar-H). 12.20 (1H, br.s, NH).
3c	3380 (NH), 2208 (CN), 1633 (C_4O).	2.38 (3H, s, SMe),2.41 (3H, s, Me), 7.22 (2H, d, Ar-H), 7.75 (2H, d, Ar-H), 12.25 (1H, br.s, NH).
3d	3380 (NH), 2208 (CN), 1633 (C_4O).	2.58 (3H, s, SMe), 7.60 (2H, d, Ar-H), 7.97 (2H, d, Ar-H), 12.20 (1H, br.s, NH).
3e	3456 (NH), 2223 (CN), 1736 (COOEt), 1661 (C_4O).	1.08 (3H, t, J=7.00 Hz, Me), 4.06 (2H, q, J=7.20 Hz, CH_2), 4.12 92H, s, SCH_2), 7.62 (3H, m, Ar-H), 7.93 (2H, m, Ar-H), 12.15 (1H, br.s, NH).
3f	3438 (NH), 2218 (CN), 1740 (COOEt), 1653 (C_4O).	1.12 (3H, t, J=7.10 Hz, Me), 4.07 (2H, q, J=7.10 Hz, CH_2), 4.13 (2H, s, SCH_2), 7.12 (2H, d, Ar-H), 7.97 (2H, d, Ar-H), 12.10 (1H, br.s, NH).
3g	3449 (NH), 2220 (CN), 1741 (COOEt), 1653 (C_4O).	-
3h	3454 (NH), 2219 (CN), 1739 (COOEt), 1661 (C_4O).	-
5a	2228 (CN), 1758 (MeCO), 1666 (C_4O).	1.81, 1.96, 1.98, 2.01, 2.07 (24H, 5s, 8 Ac), 3.99-4.15 (4H, m, H-6', H-6"), 4.20-4.43 (2H, m, H-5', H-5"), 4.98-5.22 (4H,m, H-4', H-4",H-3', H-3"), 5.58 (2H, m, H-2', H-2"), 6.00 (1H, d, J=10.58 Hz, H-1'), 6.50 (1H, d, J=7.98 Hz, H-1"), 7.58 (3H, m, Ar-H), 8.08 (2H, d, Ar-H).
5b	2226 (CN), 1758 (MeCO), 1672 (C_4O).	1.75, 1.97, 1.99, 2.00, 2.07 (24H, 7s, 8 Ac), 3.90 (3H, s, OMe), 3.98-4.15 (4H, m, H-6', H-6"), 4.20-4.15 (2H, m, H-5', H-5"), 4.85-5.20 (4H,m, H-4', H-4",H-3', H-3"), 5.50-5.65 (2H, m, H-2', H-2"), 6.15 (1H, d, J=10.75 Hz, H-1'), 6.50 (1H, d, J=8.10 Hz, H-1"), 7.40 (2H, m, Ar-H), 8.01(2H, d, Ar-H).
5c	2226 (CN), 1752 (MeCO), 1688 (C_4O).	1.74, 1.82, 1.97, 1.99, 2.02, 2.03 (24H, 6s, 8 Ac),2.43 (3H, s, Me), 4.05-4.15 (4H, m, H-6', H-6"), 4.20-4.45 (2H, m, H-5', H-5"), 5.11-5.19 (4H,m, H-4', H-4",H-3', H-3"), 5.58 (2H, m, H-2', H-2"), 6.00 (1H, d, J=10.68 Hz, H-1'), 6.49 (1H, d, J=7.90 Hz, H-1", 7.42 (2H, m, Ar-H), 7.98 (2H, d, Ar-H).
5d	2225 (CN), 1757 (MeCO), 1668 (C_4O).	1.80, 1.95, 1.98, 2.02, 2.07 (24H, 5s, 8 Ac), 3.98-4.45 (6H, m,H-5', H-5", H-6', H-6"), 4.99-5.30 (4H,m, H-4', H-4",H-3', H-3"), 5.56 (2H, m, H-2', H-2"), 6.00 (1H, d, J=10.50 Hz, H-1'), 6.50 (1H, d, J=7.95 Hz, H-1"), 7.60 (2H, m, Ar-H), 8.10 (2H, d, Ar-H).
5e	2228 (CN), 1756 (MeCO), 1669 (C_4O).	1.82, 1.96, 1.99, 2.02, 2.14, 2.17 (24H, 6s, 8 Ac), 4.01,4.12 (4H, 2d, J=7.42 Hz, H-6', H-6"), 4.45,

(CONTINUED)

TABLE 2 - IR AND ^{1}H NMR DATA OF THE COMPOUNDS PREPARED (CONTINUED)

		4.60 (2H, 2t, J=4.14 Hz, H-5', H-5"), 5.2-5.43 (6H, m, H-4', H4", H-3', H-3", H-2', H-2"), 5.86 (1H, d, J=11.20 Hz, H-1'), 6.34 (1H, d, J=8.70 Hz, H-1"), 7.55 (3H, m, Ar-H), 8.10 (2H, d,Ar-H).
5f	2227 (CN), 1755 (MeCO), 1670 (C_4O).	1.80, 1.97, 1.98, 2.00, 2.05, 2.15, 2.20 (24H, 7s, 8 Ac), 3.85 (3H, s, OMe), 4.02, 4.07 (4H, 2d, J=7.38 Hz, H-6', H-6"), 4.50, 4.60 (2H, 2t, J=4.20 Hz, H-5', H-5"), 5.10-5.45 (6H,m, H-4', H-4",H-3', H-3", H-2', H-2"), 5.85(1H, d, J=10.63 Hz, H-1'), 6.30 (1H, d, J=7.96 Hz, H-1"), 7.23 (2H, m, Ar-H), 8.10 (2H, d, Ar-H).
5g	2226 (CN), 1755 (MeCO), 1668 (C_4O).	1.84, 1.96, 1.98, 2.01, 2.15, 2.18 (24H, 6s, 8 Ac), 2.42 (3H, s, Me), 4.03,4.12 (4H, 2d, J=7.40 Hz, H-6', H-6"), 4.47-4.62 (2H, 2t, J=4.15 Hz, H-5', H-5"), 5.15-5.45 (6H,m, H-4', H-4",H-3', H-3", H-2', H-2"), 5.86 (1H, d, J=13.22 Hz, H-1'), 6.34 (1H, d, J=8.65 Hz, H-1"), 7.42 (2H, m, Ar-H), 7.98 (2H, d, Ar-H).
5h	2228 (CN), 1756 (MeCO), 1669 (C_4O).	1.82, 1.96, 1.98, 2.01, 2.05, 2.15, 2.20 (24H, 7s, 8 Ac), 4.00, 4.10 (4H, 2d, J=7.40 Hz, H-6', H-6"), 4.45, 4.60 (2H, 2t, J=4.15 Hz, H-5', H-5"), 5.15-5.40 (6H, m, H-4', H-4",H-3', H-3", H-2', H-2"), 6.00 (1H, d, J=10.95 Hz, H-1'), 6.35 (1H, d, J=7.60 Hz, H-1"), 7.60 (2H, m, Ar-H), 8.15 (2H, d, Ar-H).
6a	3346 (OH), 3226 (N_1H), 2210 (CN), 1725 (C_2O), 1639 (C_4O).	3.22-3.72 (6H, m, H-6', H-6", H-5', H4', H-3', H-2'), 4.61 (1H, t, 6'-OH), 5.07 (1H, d, 4'-OH), 5.19 (1H, s, 3'-OH), 5.36 (1H, s, 2'-OH), 5.41 (1H, d, J=10.10 Hz,H-1'), 7.53 (3H, m, Ar-H), 7.89 (2H, d, Ar-H), 12.00 (1H, br.s, NH).
6b	3355 (OH), 3235 (N_1H), 2212 (CN), 1728 (C_2O), 1649 (C_4O).	3.40-3.75 (6H, m, H-6', H-6", H-5', H4', H-3', H-2'), 3.85 (3H, s, OMe),4.59 (1H, t, 6'-OH), 4.68 (1H, d, 4'-OH), 4.92(1H, t, 3'-OH), 5.24 (1H, t, 2'-OH), 5.38 (1H, dd, J=4.56, 9.38 Hz, H-1'), 7.11 (2H, d, Ar-H), 7.95 (2H, d, Ar-H), 12.00 (1H, br.s, NH).
6c	3335 (OH), 3225 (N_1H), 2212 (CN), 1728 (C_2O), 1656 (C_4O).	2.38 (3H, s, Me), 3.22-3.72 (6H, m, H-6', H-6", H-5', H4', H-3', H-2'), 4.62 (1H, t, 6'-OH), 5.06 (1H, s, 4'-OH), 5.18 (1H, s, 3'-OH), 5.38 (1H, s, 2'-OH), 5.40(1H, d, J=10.50 Hz, H-1'), 7.62 (2H, d, Ar-H), 7.95 (2H, d, Ar-H), 12.00 (1H, br.s, NH).
6d	3338 (OH), 3223 (NH), 2211 (CN), 1726 (C_2O), 1656 (C_4O).	3.30-3.73 (6H, m, H-6', H-6", H-5', H4', H-3', H-2'), 4.52 (1H, t, 6'-OH), 4.68 (1H, s, 4'-OH), 4.93 (1H, s, 3'-OH), 5.28 (1H, d, J=5.30 Hz, 2'-OH), 5.33 (1H, d, J=9.92 Hz, H-1'), 7.60 (2H, d, Ar-H), 7.93 (2H, d, Ar-H), 12.00 (1H, br.s, NH).
6e	3346 (OH), 3226 (NH), 2210 (CN), 1725 (C_2O), 1639 (C_4O).	3.22-3.72 (6H, m, H-6', H-6", H-5', H4', H-3', H-2'), 4.61 (1H, t, 6'-OH), 5.07 (1H, d, 4'-OH), 5.19 (1H, s, 3'-OH), 5.36 (1H, s, 2'-OH), 5.41 (1H, d, J=10.10 Hz, H-1'), 7.53 (3H, m, Ar-H), 7.89 (2H, d, Ar-H), 12.00 (1H, br.s, NH).
6f	3348 (OH), 3219	3.40 (5H, m, H-6', H-6", H-5', H4', H-3'), 3.72 (1H, s, H-

TABLE 2 - IR AND ^{1}H NMR DATA OF THE COMPOUNDS PREPARED (CONTINUED)

	(NH), 2209 (CN), 1726 (C_2O), 1658 (C_4O).	2'), 3.84 (3H, s, OMe), 4.54 (1H, br.s, 6'-OH), 4.68 (1H, br.s, 4'-OH), 4.93 (1H, br.s, 3'-OH), 5.25 (1H, d, J=5.30 Hz, 2'-OH), 5.38 (1H, d, J= 10.08 Hz, H-1'), 7.10 (2H, d, Ar-H), 7.95 (2H, d, Ar-H), 12.00 (1H, br.s, NH).
6g	3335 (OH), 3225 (NH), 2212 (CN), 1728 (C_2O), 1656 (C_4O).	2.38 (3H, s, Me), 3.22-3.72 (6H, m, H-6', H-6", H-5', H4', H-3', H-2'), 4.62 (1H, t, 6'-OH), 5.06 (1H, s, 4'-OH), 5.18 (1H, s, 3'-OH), 5.38 (1H, s, 2'-OH), 5.40(1H, d, J=10.50 Hz, H-1'), 7.62 (2H, d, Ar-H), 7.95 (2H, d, Ar-H), 12.00 (1H, br.s, NH).
6h	3334 (OH), 3220 (NH), 2209 (CN), 1722 (C_2O), 1655 (C_4O).	3.17 (2H, m, H-6', H-6"), 3.45 (2H, m, H-5', H4'), 3.70 (1H, s, H-3'), 4.17 (1H, br.s, H-2'), 4.50 (1H, s, 6'-OH), 4.65 (1H, s, 4'-OH), 4.95 (1H, s, 3'-OH), 5.20 (1H, d, J=5.10 Hz, 2'-OH), 5.35 (1H, d, J=10.30 Hz, H-1'), 7.60 (2H, d, Ar-H), 8.00 (2H, d, Ar-H), 11.85 (1H, br.s, NH).

Antiviral Activity. No activity was found when the compounds **3a-h**, **5a-h** and **6a-h** were tested against HIV-1 (HTLV IIIB) in MT-4 cells.[19]

Atitumor activity. The 24 compounds were screened for antitumer activity against leukemia, non-small cell lung cancer, colon cancer, CNS cancer, melanoma, ovarian cancer, renal cancer, prostate cancer and breast cancer.[20] Only compound **5h** showed enough activity to be further tested in additional tumor systems.

EXPERIMENTAL

All evaporations were carried out under reduced pressure at 40 °C. All melting points are uncorrected. Aluminum sheets coated with silica gel 60 F_{254} (Merck) were used for TLC. Detection was affected by viewing under a short-wavelength UV lamp. IR spectra were obtained (KBr disc) on a Pye Unicam spectrum 1000. ^{1}H-NMR and ^{13}C-NMR spectra were measured on a Wilmad 270 MHz or on a Varian 500 MHz spectrometer for solutions in DMSO-d_6 with TMS as internal standard. The chemical shifts are given as δ values and the J values are given in Hz. Mass spectra were recorded on a Varian MAT 112 spectrometer. Analytical data were obtained from the Microanalytical Center at Cairo and Tanta Universities.

Potassium salts of 6-aryl-5-cyano-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-ones (1a-d). A mixture of thiourea (0.76 g, 10 mmol), ethyl cyanoacetate (1.13 g, 10 mmol), the appropriate aldehyde (10 mmol) and potassium carbonate (1.38 g, 10 mmol) in ethanol (30 ml) was refluxed for overnight and then cooled. The precipitate thus obtained was filtered off and recrystallized from ethanol (50 %) to give the products **1a-d** in 30-50 % yield as yellow solids.

6-Aryl-5-cyano-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-ones (2a-d). The potassium salt **1** was dissolved in water at 80 °C, filtered off and neutralized with glacialacetic acid. The light yellow precipitate was filtered off and washed with water. It was crystallized from a DMF-water mixture to give **2a-d**[15].

6-Aryl-5-cyano-2-(alkylmercapto)-3,4-dihydropyrimidin-4-ones (3a-h).

Method A: The potassium salt **1** (10 mmol) was suspended in ethanol (30 ml). To this suspension was added methyl iodide (10 mmol) or ethyl bromoacetate (10 mmol). The reaction mixture was stirred at room temperature. The white solid that separated was filtered off, washed with water and recrystallized from ethanol to give the products **3a-h**.

Method B: A solution of **2** (20 mmol) in DMF (10 ml) was stirred with potassium carbonate (10 mmol) and then treated with iodomethane (10 mmol) or ethyl bromoacetate (10 mmol). The reaction mixture was stirred for 4 h at r. t. and then diluted with water. The white solid was filtered off and recrystallized from ethanol to give the products **3a-h**.

6-Aryl-5-cyano-3-(2',3',4',6'-tetra-*O*-acet-yl-β-D-gluco- and D-galactopyranosyl)-2-(2",3",4",6"-tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosylmercapto)-3,4-dihydro-pyrimidin-4-ones (5a-h).

Method A: To a solution of **2** (10 mmol) in aqueous potassium hydroxide [1.23 g, 22 mmol, in distilled water (6 ml)] was added a solution of **4** (22 mmol) in acetone (30 ml). The reaction mixture was stirred for 4 h at r. t. until the starting material was consumed (TLC).

The mixture was evaporated under reduced pressure at 40 °C and the residue was washed with distilled water to remove the potassium bromide formed. The solid product was dried and crystallized from absolute ethanol to give the products **5a-h** in 50-60 % yield.

Method B : 6-Aryl-5-cyano-2-thiouracil **2** (10 mmol) was dissolved in 0.2 mM sodium ethoxide (100 ml) and then evaporated to dryness. The residue was dissolved in anhydrous dimethylsulphoxide (25 ml) containing **4** (20 mmol) and stirred at r. t. for 24 h. The reaction was then cooled, poured into water (200 ml) and extracted with chloroform (3 x 50 ml). The organic layer was washed with water (3 x 50 ml), dried over sodium sulfate and evaporated to dryness under *vacuum*. The resulting product was crystallized from ethanol to give the products **5a-h** in 30-40 % yield.

6-Aryl-5-cyano-3-(β-D-gluco- and D-galactopyranosyl)-3,4-dihydropyrimidin-2,4-diones (6a-h). The protected nucleoside **5** (2 g) was stirred in saturated NH_3/MeOH (50 ml) at r. t. for 24 h. The solvent was removed in *vacuo* and the residue was crystallized from methanol to give the deprotected nucleosides **6a-h**.

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