Convenient Synthesis of 2(1*H*)-Pyridinethione Glycosides

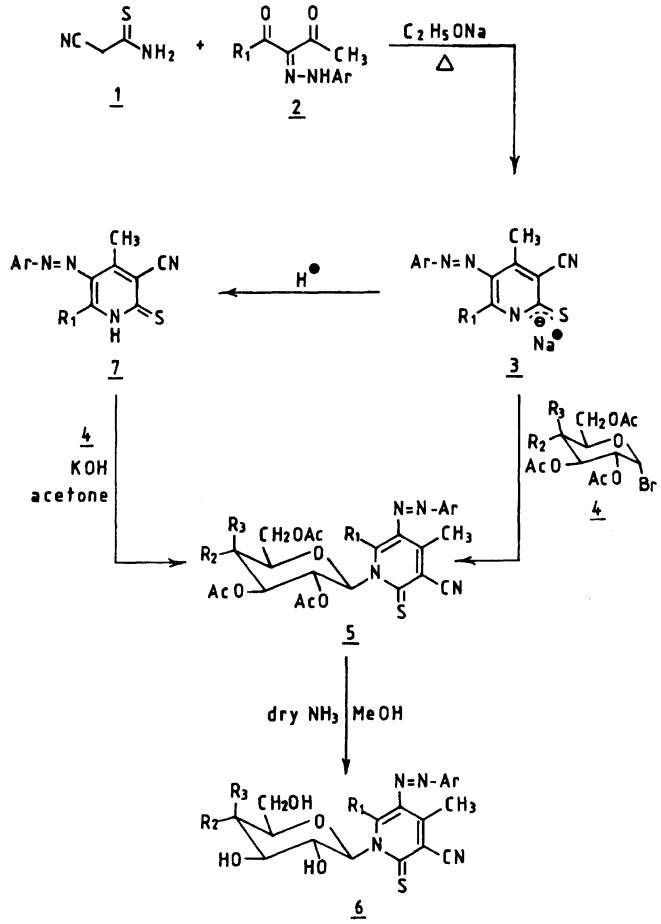
Galal E. H. ELGEMEIE,*,# Adel M. E. ATTIA,† Ali M. ELZANATE, and A. K. MANSOUR††
Chemistry Department, Faculty of Science, Cairo University (Bani Suef Branch), Bani Suef, Egypt
† Chemistry Department, Faculty of Education, Tanta University, Kafr El-Sheikh, Egypt
†† Chemistry Department, Faculty of Science, Cairo University, Cairo, Egypt
(Received September 21, 1993)

A novel synthesis of 2(1*H*)-pyridinethione glycosides utilizing 2(1*H*)-pyridinethiones or their sodium salts and α-tetra-*O*-acetyl-glucosyl or D-galactosyl bromides as starting components is described.

Among analogues of naturally occurring pyrimidine nucleosides modified in the heterocycle, the 5-aza and 6-aza analogues have demonstrated a broad spectrum of biological activity.[1] The 3-deazapyrimidine nucleosides, substituted analoguesly to naturally occurring pyrimidines, constitute another logical class of analogues with potential biological activity.[2] Although a number of *N*-glycosides of pyridines have been prepared, no pyridinethiones nucleosides had been synthesized or biologically evaluated prior to our studies. During the last decade we have been involved in a program aiming at the development of efficient and simple procedures for the synthesis of antimetabolites.[3—5] Several new approaches to mercaptopurine, pyrimidine and 5-deazafolic acid analogues were achieved during this work.[6—9] In conjunction with this we report here a novel synthesis of 2(1*H*)-pyridinethione glycosides utilizig the 2(1*H*) pyridinethiones **7** or their sodium salts **3**[10] as starting materials. Compounds **7** can be prepared by the reaction of arylhydrazones **2** of both acetylacetone and benzoylacetone with cyanothioacetamide **1** in boiling ethanolic sodium ethoxide. Compounds **3** reacted with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and D-galactopyranosyl bromides **4** in acetone to give the corresponding *N*-glucosides **5a**—**h** and *N*-galactosides **5i**—**p** (Scheme 1). Compounds **5a**—**p** could also be obtained in good yields by the reactions of 2(1*H*)-pyridinethiones **7** with **4** in the presence of aqueous potassium hydroxide. The structures of **5** were established and confirmed for the reaction products on the basis of their elemental analyses and spectral data (MS, IR, UV, ^{1}H NMR, ^{13}C NMR). Thus, structure **5b** was supported by its mass spectra, which showed the molecular formula $C_{28}H_{29}ClN_4SO_9$ (*m/z* 633). ^{1}H NMR spectroscopy was used to confirm this structure for the product. Thus, the ^{1}H NMR spectrum showed the anomeric proton as a doublet at δ=6.17 with a spin–spin coupling constant equal to 8.73 Hz, which corresponds to the diaxial orientation of H-1′ and H-2′ protons, indicating the presence of only the β-configuration. Another doublet appeared at δ=4.01, and was assigned to the CH_2 protons of the glucose part, while the other four protons of the glucopyranosyl ring resonate in the δ=4.20—5.60 region. The remaining four acetyl groups appear as four singlets at δ=1.98—2.02 and the two methyl groups of aglycone resonate at δ=2.56 and 2.66 (cf. Table 2). The ^{13}C NMR spectra were characterized by a signal at δ=82.25, corresponding to the C-1′ atom of the β-configuration. Four signals appear at δ=170.02—169.14 due to the four acetoxyl carbonyl carbon atoms of glucose, while four signals appearing at δ=20.51—22.21 are attributed to the acetoxyl methyl carbons. The two methyl carbon atoms of aglycone appear at δ=16.79 and 18.06. Another five signals at δ=62.90, 67.20, 68.57, 73.12 and 75.66 were assigned as C-6′, C-4′, C-2′, C-3′ and C-5′, respectively. The IR spectrum of **5b** was characterized by the absence of an NH group and the presence of an acetoxyl carbonyl at 1755 cm^{-1}. The UV spectra of compounds **5** prove that the reaction takes place at a nitrogen atom, thus leading selectively to the formation of *N*-glycosides, and excluding substitution at the sulfur atom. Thus, whereas the 2-(methylthio)pyridine derivative corresponding to pyridinethione **7c** shows one maximum at 357 nm, its *N*-glycosyl derivative **5c** exhibits two different UV absorption maxima at 278 and 369 nm. Moreover, the hydrolysis of compound **5c** with 9% HCl afforded the only 2(1*H*)-pyridinethione derivative **7c** as a sole product (2(1*H*)-pyridinone derivative is not formed) proving the existance of *N*-glycosides. Finally, when compounds **5** were treated with methanolic ammonia at 0 °C, the unprotected glycoside derivatives **6** were obtained. The structure of compounds **6** were established on the basis of elemental analyses and spectral data. Thus, the IR spectrum of **6b** showed a characteristic band at 3600—3200 cm^{-1} due to the hydroxyl groups of the glucose moiety. The ^{1}H NMR spectra revealed the presence of a doublet at δ=6.15 ($J_{1',2'}$=8.35 Hz), which was assigned to the anomeric proton of the glucose moiety, thus indicating the presence of only the β-configuration. The other six protons of glucose appear as a multiplet at δ=3.35—3.90, while the four hydroxyl groups of glucose part resonate at δ=4.52—5.68 (exchangeable by D_2O) (cf. Table 2).

In summary, we have achieved a highly regioselective synthesis of interesting 2(1*H*)-pyridinethione nucleosides by the reaction of 2(1*H*)-pyridinethiones or their sodium salts with α-glycosyl halides. These nucleosides seem to be promising for further chemical transformations as well as for biological evaluation studies.

#Present address: Chemistry Department, Faculty of Science, Qatar University, Doha, State of Qatar.



5	**a**	$Ar=C_6H_5$	$R_1=CH_3$	$R_2=OAc$	$R_3=H$
	b	$Ar=4\text{-}ClC_6H_4$	$R_1=CH_3$	$R_2=OAc$	$R_3=H$
	c	$Ar=4\text{-}CH_3C_6H_4$	$R_1=CH_3$	$R_2=OAc$	$R_3=H$
	d	$Ar=4\text{-}CH_3OC_6H_4$	$R_1=CH_3$	$R_2=OAc$	$R_3=H$
	e	$Ar=C_6H_5$	$R_1=C_6H_5$	$R_2=OAc$	$R_3=H$
	f	$Ar=4\text{-}ClC_6H_4$	$R_1=C_6H_5$	$R_2=OAc$	$R_3=H$
	g	$Ar=4\text{-}CH_3C_6H_4$	$R_1=C_6H_5$	$R_2=OAc$	$R_3=H$
	h	$Ar=4\text{-}CH_3OC_6H_4$	$R_1=C_6H_5$	$R_2=OAc$	$R_3=H$
	i	$Ar=C_6H_5$	$R_1=CH_3$	$R_2=H$	$R_3=H$
	j	$Ar=4\text{-}ClC_6H_4$	$R_1=CH_3$	$R_2=H$	$R_3=OAc$
	k	$Ar=4\text{-}CH_3C_6H_4$	$R_1=CH_3$	$R_2=H$	$R_3=OAc$
	l	$Ar=4\text{-}CH_3OC_6H_4$	$R_1=CH_3$	$R_2=H$	$R_3=OAc$
	m	$Ar=C_6H_5$	$R_1=C_6H_5$	$R_2=H$	$R_3=OAc$
	n	$Ar=4\text{-}ClC_6H_4$	$R_1=C_6H_5$	$R_2=H$	$R_3=OAc$
	o	$Ar=4\text{-}CH_3C_6H_4$	$R_1=C_6H_5$	$R_2=H$	$R_3=OAc$
	p	$Ar=4\text{-}CH_3OC_6H_4$	$R_1=C_6H_5$	$R_2=H$	$R_3=OAc$
6	**a**	$Ar=C_6H_5$	$R_1=CH_3$	$R_2=OH$	$R_3=H$
	b	$Ar=4\text{-}ClC_6H_4$	$R_1=CH_3$	$R_2=OH$	$R_3=H$
	c	$Ar=4\text{-}CH_3C_6H_4$	$R_1=CH_3$	$R_2=OH$	$R_3=H$
	d	$Ar=C_6H_5$	$R_1=C_6H_5$	$R_2=OH$	$R_3=H$
	e	$Ar=C_6H_5$	$R_1=CH_3$	$R_2=H$	$R_3=OH$
	f	$Ar=4\text{-}ClC_6H_4$	$R_1=CH_3$	$R_2=H$	$R_3=OH$
	g	$Ar=4\text{-}CH_3C_6H_4$	$R_1=CH_3$	$R_2=H$	$R_3=OH$
	h	$Ar=4\text{-}CH_3OC_6H_4$	$R_1=CH_3$	$R_2=H$	$R_3=OH$
	i	$Ar=C_6H_5$	$R_1=C_6H_5$	$R_2=H$	$R_3=OH$
	j	$Ar=4\text{-}ClC_6H_4$	$R_1=C_6H_5$	$R_2=H$	$R_3=OH$
	k	$Ar=4\text{-}CH_3C_6H_4$	$R_1=C_6H_5$	$R_2=H$	$R_3=OH$
	l	$Ar=4\text{-}CH_3OC_6H_4$	$R_1=C_6H_5$	$R_2=H$	$R_3=OH$

Scheme 1.

Table 1. Characterization Data for Compounds **5a**—**p** and **6a**—**1**

Compound (color)	Recryst. solvent	Mp θm/°C	Yield/% (a)	Yield/% (b)	Mol. formula	Found/Calcd (%) C	Found/Calcd (%) H	Found/Calcd (%) N	M^+ m/z
5a (Buff)	EtOH	175	83	75	$C_{28}H_{30}N_4SO_9$	56.4 56.2	4.8 5.0	9.3 9.4	598
5b (Yellow)	EtOH	185	80	72	$C_{28}H_{29}ClN_4SO_9$	53.2 53.1	4.8 4.6	9.0 8.9	633
5c (Yellow)	EtOH	195	81	73	$C_{29}H_{32}N_4SO_9$	56.6 56.9	5.4 5.2	9.1 9.2	612
5d (Yellow)	EtOH	180	78	69	$C_{29}H_{32}N_4SO_{10}$	55.1 55.4	5.2 5.1	9.1 8.9	628
5e (Yellow)	EtOH	198	76	67	$C_{33}H_{32}N_4SO_9$	60.3 60.0	4.7 4.8	8.7 8.5	660
5f (Buff)	EtOH	185	75	69	$C_{33}H_{31}ClN_4SO_9$	56.8 57.0	4.4 4.5	8.3 8.1	695
5g (Yellow)	EtOH	205	74	66	$C_{34}H_{34}N_4SO_9$	60.3 60.5	5.1 5.0	8.4 8.3	674
5h (Yellow)	EtOH	225	81	72	$C_{34}H_{34}N_4SO_{10}$	59.4 59.1	4.7 4.9	8.3 8.1	690
5i (Yellow)	EtOH	201	84	76	$C_{28}H_{30}N_4SO_9$	56.3 56.2	4.9 5.0	9.6 9.4	598
5j (Yellow)	EtOH	209	78	70	$C_{28}H_{29}ClN_4SO_9$	53.4 53.1	4.2 4.6	9.1 8.9	633
5k (Yellow)	EtOH	241	83	74	$C_{29}H_{32}N_4SO_9$	57.1 56.9	5.1 5.2	9.4 9.2	612
5l (Yellow)	EtOH	233	76	68	$C_{29}H_{32}N_4SO_{10}$	55.7 55.4	5.3 5.1	8.6 8.9	628
5m (Buff)	EtOH	164	78	69	$C_{33}H_{32}N_4SO_9$	60.4 60.0	4.5 4.8	8.7 8.5	660
5n (Buff)	EtOH	191	79	70	$C_{33}H_{31}ClN_4SO_9$	57.3 57.0	4.8 4.5	7.8 8.1	695
5o (Yellow)	EtOH	187	75	66	$C_{34}H_{34}N_4SO_9$	60.5 60.5	5.3 5.0	8.1 8.3	674
5p (Yellow)	EtOH	202	80	71	$C_{34}H_{34}N_4SO_{10}$	58.8 59.1	5.2 4.9	8.4 8.1	690
6a (Yellow)	MeOH	218	89		$C_{20}H_{22}N_4SO_5$	56.1 55.8	5.2 5.1	12.7 13.0	430
6b (Brown)	MeOH	213	87		$C_{20}H_{21}ClN_4SO_5$	51.9 51.7	4.7 4.5	12.3 12.0	465
6c (Brown)	MeOH	170	91		$C_{21}H_{24}N_4SO_5$	56.6 56.8	5.3 5.4	12.7 12.6	444
6d (Buff)	MeOH	224	86		$C_{25}H_{24}N_4SO_5$	61.2 61.0	4.6 4.9	11.7 11.4	492
6e (Yellow)	MeOH	219	92		$C_{20}H_{22}N_4SO_5$	55.5 55.8	5.4 5.1	13.3 13.0	430
6f (Brown)	MeOH	158	88		$C_{20}H_{21}ClN_4SO_5$	51.4 51.7	4.2 4.5	11.8 12.0	465
6g (Yellow)	MeOH	213	86		$C_{21}H_{24}N_4SO_5$	56.9 56.8	5.7 5.4	12.4 12.6	444
6h (Yellow)	MeOH	168	87		$C_{21}H_{24}N_4SO_6$	55.1 54.8	5.4 5.2	12.4 12.2	460
6i (Brown)	MeOH	136	89		$C_{25}H_{24}N_4SO_5$	61.4 61.0	4.7 4.9	11.2 11.4	492
6j (Brown)	MeOH	207	84		$C_{25}H_{23}ClN_4SO_5$	57.3 57.0	4.7 4.4	10.4 10.6	527
6k (Yellow)	MeOH	206	88		$C_{26}H_{26}N_4SO_5$	61.3 61.7	5.4 5.1	10.8 11.1	506
6l (Yellow)	MeOH	207	86		$C_{26}H_{26}N_4SO_6$	60.1 59.8	4.8 5.0	10.4 10.7	522

Table 2. IR and ^{1}H NMR Data for Compounds Listed in Table 1

Compound	IR (KBr) cm^{-1}	^{1}H NMR (DMSO) δ/ppm
5a	2225 (CN), 1762 (CO)	1.93—2.05 (4s, 12H, $4CH_3CO$), 2.58 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.95—4.18 (m, 2H), H-6′,6″), 4.25 (m, 1H, H-5′), 5.02 (t, J=9.6 Hz, 1H, H-4′), 5.21 (t, J=8.9 Hz, 1H, H-3′), 5.59 (t, J=9.1 Hz, 1H, H-2′), 6.20 (d, $J_{1'2'}$=7.9 Hz, H-1′), 7.66 (m, 3H, Ar-H), 7.94 (m, 2H, Ar-H).
5b	2218 (CN), 1755 (CO)	1.98—2.02 (4s, 12H, $4H_3CO$), 2.56 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 4.01 (d, J=10.8 Hz, 2H, H-6′,6″), 4.20 (m, 1H, H-5′), 5.01 (t, J=9.38 Hz, 1H, H-4′), 5.19 (t, J=9.4 Hz, 1H, H-3′), 5.58 (t, 9.2 Hz, 1H, H-2′), 6.17 (d, $J_{1'2'}$=8.73 Hz, H-1′), 7.72 (d, 2H, Ar-H), 7.96 (d, 2H, Ar-H).
5d	2223 (CN), 1761 (CO)	1.93—2.01 (4s, 12H, $4CH_3CO$), 2.47 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 4.01 (m, 2H, H-6′,6″), 4.21 (m, 1H, H-5′), 5.04 (t, J=9.1 Hz, 1H, H-4′), 5.17 (t, J=9.4 Hz, 1H, H-3′), 5.55 (t, J=9.61 Hz, 1H, H-2′), 6.16 (t, $J_{1'2'}$=7.35 Hz, H-1′), 7.18 (d, 2H, Ar-H), 7.93 (d, 2H, Ar-H).
5e	2224 (CN), 1762 (CO)	1.77—2.04 (4s, 12H, $4CH_3CO$), 2.52 (s, 3H, CH_3), 4.02 (m, 2H, H-6′,6″), 4.24 (m, 1H, H-5′), 5.01 (t, J=9.5 Hz, 1H, H-4′), 5.26 (t, J=8.76 Hz, 1H, H-3′), 5.65 (t, J=9.1 Hz, 1H, H-2′), 6.18 (d, $J_{1'2'}$=7.61 Hz, H-1′), 7.45 (m, 5H, Ar-H), 7.66 (m, 3H, Ar-H), 7.76 (m, 2H, Ar-H).
5f	2222 (CN), 1755 (CO)	1.74—2.03 (4s, 12H, $4CH_3CO$), 2.51 (s, 3H, CH_3), 3.97 (m, 2H, H-6′,6″), 4.21 (m, 1H, H-5′), 5.01 (t, J=9.16 Hz, 1H, H-4′), 5.23 (t, J=9.3 Hz, 1H, H-3′), 5.65 (t, J=9.9 Hz, 1H, H-2′), 6.17 (d, $J_{1'2'}$=8.12 Hz, H-1′), 7.46 (d, 2H, Ar-H), 7.67 (m, 5H, Ar-H), 7.77 (d, 2H, Ar-H).
5g	2219 (CN), 1760 (CO)	1.77—2.04 (4s, 12H, $4CH_3CO$), 2.43 (s, 3H, CH_3), 2.52 (s, 3H, CH_2), 4.05 (m, 2H, H-6′,6″), 4.26 (m, 1H, H-5′), 5.08 (t, J=9.35 Hz, 1H, H-4′), 5.26 (t, J=8.83 Hz, 1H, H-3′), 5.65 (t, J=9.4 Hz, 1H, H-2′), 6.19 (d, $J_{1'2'}$=7.5 Hz, H-1′), 7.46 (m, 4H, Ar-H), 7.69 (m, 5H, Ar-H).
5i	2218 (CN), 1755 (CO)	2.01—2.04 (4s, 12H, $4CH_3CO$), 2.58 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 4.14 (m, 3H, H-6′,6″ and H-5′), 5.35 (m, 3H, H-4′, H-3′ and H-2′), 6.02 (d, $J_{1'2'}$=8.65 Hz, H-1′), 7.56 (m, 3H, Ar-H), 7.91 (m, 2H, Ar-H).
5j	2220 (CN), 1760 (CO)	1.93—2.09 (4s, 12H, $4CH_3CO$), 2.59 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 4.14 (m, 3H, H-6′,6″ and H-5′), 5.36 (m, 3H, H-4′, H-3′ and H-2′), 6.01 (d, $J_{1'2'}$=8.55 Hz, H-1′), 7.55 (d, 2H, Ar-H), 7.87 (d, 2H, Ar-H).
5l	2216 (CN), 1756 (CO)	1.95—2.08 (4s 12H, $4CH_3CO$), 2.44 (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 4.05 (m, 2H, H-6′,6″), 4.43 (m, 1H, H-5′), 5.46 (m, 3H, H-4′, H-3′ and H-2′), 6.18 (d, $J_{1'2'}$=7.75 Hz, H-1′), 7.25 (d, 2H, Ar-H), 7.95 (d, 2H, Ar-H).
5m	2220 (CN), 1755 (CO)	1.76—2.04 (4s, 12H, $4CH_3CO$), 2.51 (s, 3H, CH_3), 4.03 (m, 2H, H-6′,6″), 4.28 (m, 1H, H-5′), 5.05 (t, J=9.1 Hz, 1H, H-4′), 5.30 (t, J=10.19 Hz, 1H, H-3′), 5.69 (t, J=10.66 Hz, 1H, H-2′), 6.20 (d, $J_{1'2'}$=7.5 Hz, H-1′), 7.47 (m, 5H, Ar-H), 7.64 (m, 3H, Ar-H), 7.78 (m, 2H, Ar-H).
5n	2220 (CN), 1750 (CO)	1.78—2.04 (4s, 12H, $4CH_3CO$), 2.53 (s, 3H, CH_3), 4.05 (m, 2H, H-6′,6″), 4.26 (m, 1H, H-5′), 5.03 (t, J=10.0 Hz, 1H, H-4′), 5.29 (t, J=9.68 Hz, 1H, H-3′), 5.68 (t, J=9.8 Hz, 1H, H-2′), 6.21 (d, $J_{1'2'}$=8.35 Hz, H-1′), 7.48 (m, 4H, Ar-H), 7.76 (m, 5H, Ar-H).
5o	2225 (CN), 1760 (CO)	1.79—2.08 (4s, 12H, $4CH_3CO$), 2.41 (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 4.01 (m, 2H, H-6′,6″), 4.45 (t, J=6.3 Hz, 1H, H-5′), 5.4 (m, 3H, H-4′, H-3′ and H-2′), 6.15 (d, $J_{1'2'}$=8.35 Hz, H-1′), 7.51 (m, 4H, Ar-H), 7.85 (m, 5H, Ar-H).

Table 2. (Continued)

Compound	IR (KBr) cm^{-1}	^1H NMR (DMSO) δ/ppm
6a	3600-3200 (OH), 2222 (CN)	2.65 (s, 3H, CH_3), 2.75 (s, 3H, CH_3), 3.24—3.53 (m, 6H, H-6′,6″, H-5′, H-4′, H-3′ and H-2′), 4.54 (t, J=9.16 Hz, 1H, 2′-OH), 4.86 (d, J=9.61 Hz, 1H, 3′-OH), 5.40 (m, 1H, 4′-OH), 5.71 (m, 1H, 6′-OH), 6.18 (d, $J_{1'2'}$=7.65 Hz, H-1′), 7.55 (m, 3H, Ar-H), 7.78 (m, 2H, Ar-H).
6b	3600-3150 (OH), 2225 (CN)	2.35 (s, 3H, CH_2), 2.46 (s, 3H, CH_3), 3.20—3.95 (m, 6H, H-6′,6″, H-5′, H-4′, H-3′ and H-2′), 4.55 (t, J=9.33 Hz, 1H, 2′-OH), 5.01 (d, J=9.61 Hz, 1H, 3′-OH), 5.26 (d, J=9.3 Hz, 1H, 4′-OH), 5.63 (m, 1H, 6′-OH), 6.05 (d, $J_{1'2'}$=7.85 Hz, H-1′), 7.56 (d, 2H, Ar-H), 7.84 (d, 2H, Ar-H).
6c	3600-3200 (OH), 2220 (CN)	2.32 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 3.20—3.68 (m, 6H, H-6′,6″, H-5′, H-4′, H-3′ and H-2′), 4.47 (t, J=9.4 Hz, 1H, 2′-OH), 5.06 (d, J=9.16 Hz, 1H, 3′-OH), 5.25 (d, J=9.73 Hz, 1H, 4′-OH), 5.57 (d, J=9.16 Hz, 1H, 6′-OH), 5.63 (d, $J_{1'2'}$=8.35 Hz, H-1′), 7.47 (d, 2H, Ar-H), 7.81 (d, 2H, Ar-H).
6d	3650-3200 (OH), 2218 (CN)	2.41 (s, 3H, CH_3), 3.35—3.89 (m, 6H, H-6′,6″, H-5′, H-4′, H-3′ and H-2′), 4.50 (t, J=9.37 Hz, 1H, 2′-OH), 4.71 (t, J=9.6 Hz, 1H, 3′-OH), 5.34 (m, 1H, 4′-OH), 5.66 (m, 1H, 6′-OH), 6.11 (d, $J_{1'2'}$=7.95 Hz, H-1′), 7.42 (m, 5H, Ar-H), 7.73 (m, 5H, Ar-H).
6f	3600-3200 (OH), 2220 (CN)	2.38 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.15—3.95 (m, 6H, H-6′,6″, H-5′, H-4′, H-3′ and H-2′), 4.45 (t, J=9.71 Hz, 1H, 2′-OH), 4.88 (d, J=9.46 Hz, 1H, 3′-OH), 5.20 (d, J=9.8 Hz, 1H, 4′-OH), 5.60 (m, 1H, 6′-OH), 6.18 (d, $J_{1'2'}$=8.25 Hz, H-1′), 7.68 (m, 4H, Ar-H).
6l	3650-3200 (OH), 2225 (CN)	2.42 (s, 3H, CH_3), 3.18—3.78 (m, 6H, H-6′,6″, H-5′, H-4′, H-3′ and H-2′), 3.96 (s, 3H, OCH_3), 4.50 (t, J=10.62 Hz, 1H, 2′-OH), 4.78 (d, J=9.7 Hz, 1H, 3′-OH), 5.05 (t, J=10.19 Hz, 1H, 4′-OH), 5.41 (d, J=10.66 Hz, 1H, 6′-OH), 5.66 (d, $J_{1'2'}$=7.85 Hz, H-1′), 7.19 (d, 2H, Ar-H), 7.43 (m, 5H, Ar-H), 7.78 (d, 2H, Ar-H).

Experimental

All of the evaporations were carried out under reduced pressure at 40 °C. The melting points are uncorrected. TLC aluminium sheet silica gel 60 F_{254} (Merck) was used for thin-layer chromatography. The detection was effected by viewing under a short-wavelength UV lamp. IR spectra were obtained (KBr disc) on a pye Unicam Spectra-1000. ^1H NMR and ^{13}C NMR spectra were measured on a Wilmad 270 MHz or on a Varian 400 MHz spectrometer for solutions in DMSO-d_6 using TMS as an external standard. The mass spectra were recorded on a Varian MAT 112 spectrometer. Analytical data were obtained from the Microanalytical data Center at Cairo University.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosyl)-5-arylazo-3-cyano-2(1*H*)-pyridinethiones 5. General Coupling Procedures. Method A. To a solution of 2(1*H*)-pyridinethione sodium salts **3a**—**h** (0.01 mol) in acetone (10 ml), a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or D-galactopyranosyl bromide **4** (4.521 gm, 0.011 mol) in acetone (20 ml) was added. The reaction mixture was stirred at room temperature until judged to be complete by TLC (30 min to 2 h). The mixture was evaporated under reduced pressure at 40 °C and crude glycoside was washed with distilled water to remove the formed sodium bromide. The product was dried and crystallized from the appropriate solvent (cf. Table 1).

Method B. To a solution of 2(1*H*)-pyridinethiones **7a**—**h** (0.01 mol) in aqueous potassium hydroxide (0.56 gm, 0.01 mol, in 6 ml of distilled water) was added a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or D-galactopyranosyl bromide **4** (4.521 mg, 0.011 mol) in acetone (30 ml). The reaction mixture was stirred at room temperature until judged to be complete by TLC (30 min to 2 h) then processed as described above.

1-(β-D-Gluco- and D-galactopyranosyl)-3-cyano-2-(1*H*)-pyridinethiones 6. General Procedure for Nucleoside Deacylation. Dry gaseous ammonia was passed through a solution of protected nucleoside **5** (0.5 gm) in dry methanol (20 ml) at 0 °C for about 0.5 h. The reaction mixture was then stirred at 0 °C until judged to be complete by TLC (3 to 6 h). The mixture was evaporated under reduced pressure at 40 °C to give a solid residue, which was crystallized from the appropriate solvent (cf. Table 1).

G. E. H. Elgemeie is deeply indebted to Professor Dr. M. Hudlicky, Professor Dr. R. H. White, Messrs K. C. Harich, G. Iannaccone and W. R. Bebout from Virginia Polytechnic Institute and State University, USA, for measuring the ^1H NMR and mass spectra, and to IOCD for supporting this collaborative activity.

References

1) J. Skoda, *Prog. Nucl. Acid. Res. Mol. Biol.*, **2**, 197 (1963); G. M. Timmis and D. C. Williams, "Chemotherapy of Cancer," Butterworths, London (1967).

2) A. Bloch, G. Dutschman, B. L. Currie, R. K. Robins, and M. J. Robins, *J. Med. Chem.*, **16**, 294 (1973).

3) G. E. H. Elgemeie and F. H. Abdelaal, *Heterocycles*, **24**, 349 (1986).

4) G. E. H. Elgemeie, A. H. Elghandour, and H. Elshimy,

J. Prakt. Chem., **331**, 466 (1989).
5) G. E. H. Elgemeie, A. M. Gohar, H. A. Regaila, and H. A. Elfahham, *Arch. Pham.* (*Weinheim*), **321**, 131 (1988).
6) G. E. H. Elgemeie and B. A. Hussein, *Tetrahedron*, **50**, 199 (1994).
7) G. E. H. Elgemeie, N M. Fathy, L. M. Faddah, and M. Y. Ebeid, *Arch. Pharm.* (*Weinheim*), **324**, 149 (1991).
8) G. E. H. Elgemeie, A. M. Elzanate, and A. K. Mansour, *J. Chem. Soc., Perkin Trans. 1*, **1992**, 1073.
9) G. E. H. Elgemeie, H. A. Regaila, and N. Shehata, *J. Chem. Soc., Perkin Trans. 1*, **1990**, 1267.
10) G. E. H. Elgemeie, A. M. Elzanate, and A. K. Mansour, *Bull. Chem. Soc. Jpn.*, **66**, 555 (1993).