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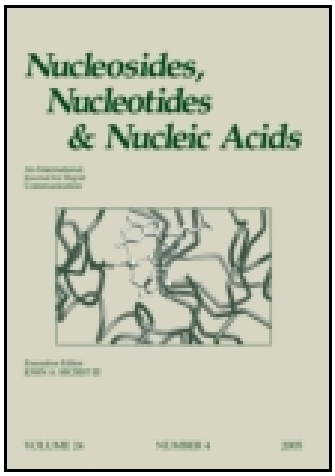

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NUCLEIC ACID COMPONENTS AND THEIR ANALOGUES: A NOVEL AND EFFICIENT METHOD FOR THE SYNTHESIS OF A NEW CLASS OF BIPYRIDYL AND BIHETEROCYCLIC-NITRO GEN THIOGLYCOSIDES FROM PYRIDINE-2(1H)-THIONES

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NUCLEIC ACID COMPONENTS AND THEIR ANALOGUES: A NOVEL AND EFFICIENT METHOD FOR THE SYNTHESIS OF A NEW CLASS OF BIPYRIDYL AND BIHETEROCYCLIC-NITROGEN THIOGLYCOSIDES FROM PYRIDINE-2(1*H*)-THIONES

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ABSTRACT

A novel synthesis of a new class of bipyridyl and biheterocyclic-nitrogen thioglycosides utilizing the reactions of heterocyclic substituted pyridine-2(1*H*)-thiones and α-bromoglucose or α-bromogalactose tetraacetate as starting components is described.

Key Words: Pyridine thioglycosides; Pyridine-2(1*H*)-thiones; Coupling reactions; Biheterocyclic thioglycosides

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Pyridinethione nucleosides were recently reported by us to exert inhibitory effects on both DNA and RNA containing viruses.[1–5] On the basis of these findings, it was of interest to prepare modified analogues to search for more effective agents. This paper describes the synthesis of nonclassical bipyridyl and biheterocyclic-nitrogen thioglycosides. As far as we know, these are the first reported examples of biheterocyclic thioglycosides. The sequence of reactions followed in the preparation of the designed compounds, is summarized in the following schemes (Charts 1–4). Thus, it was found that heating of cyclopentanone, cyclohexanone, cycloheptanone or cyclooctanone with cyanothioacetamide and a catalytic amount of ammonium acetate/acetic acid in benzene for 3 h with azeotropic removal of water gave the corresponding cycloalkylidenecyanothioacetamides **1** in good yields. Compounds **1** reacted with pyridylmethylenemalononitriles **2** in refluxing ethanol containing catalytic amounts of piperidine for 2 h to give the bipyridyl derivatives **5a–h**. The structures of compounds **5** are established on the basis of their elemental analyses and spectral data. Thus, **5c** revealed a molecular formula $C_{15}H_{13}N_3S$ ($m/z = 267$). The ^1H NMR spectrum of **5c** showed a broad scale at δ 14.12 ppm assigned to the NH proton. The formation of **5** from **1** and **2** is assumed to proceed via addition of the active methylene group of **1** to the olefenic bond of **2** to give the intermediate **3**. This Michael adduct **3** then cyclizes via malononitrile elimination to give the intermediate dihydropyridine derivative **4**, which is oxidized under the reaction conditions to yield the fused pyridinethiones **5**. The interesting course of the reaction between the cycloalkylidene-cyanothioacetamides **1** and the pyridylmethylenemalononitriles **2** prompted us to investigate the reaction between the pyridylmethylene(cyano)thioacetamides **6a,b** and the cycloalkylidenemalononitriles **7a–d** under the same conditions. The obtained products were shown to be the same as those resulting from the reaction of **1** with **2** by their m.p.s and spectral data. The mechanism of the reaction of **6** with **7** is assumed to proceed through the formation of the initial adduct **8**, which lead to intermediates **9** and subsequently to the products **5**, as the same produced by the reaction of **1** with **2**. Compounds **5** could be coupled with different classes of sugar halides to give a novel ring system of glycosides. Thus, it was found that compounds **5a–h** reacted with 2,3,4,6-tetra-O-acetyl-α-D-gluco- and -galacto-pyranosyl bromides **13a,b** in the presence of aqueous potassium hydroxide to give the corresponding *S*-glucosides **15a–h** and *S*-galactosides **15i–p**, respectively. The structures of the reaction products **15** were established on the basis of their elemental analyses and spectral data (MS, IR, UV, ^1H NMR, ^{13}C NMR). Thus, the analytical data for **15c** revealed a molecular formula $C_{29}H_{31}N_3O_9S$ ($m/z = 597$). The ^1H NMR spectrum of **15c** show the anomeric proton as a doublet at δ 6.15 ppm with a spin-spin coupling constant of 11.28 Hz corresponding to a diaxial orientation of H-1′ and H-2′ protons and indicating the β-configuration. The other six protons of the glucopyranosyl ring resonated in the δ 3.99–5.53 ppm region. The remaining

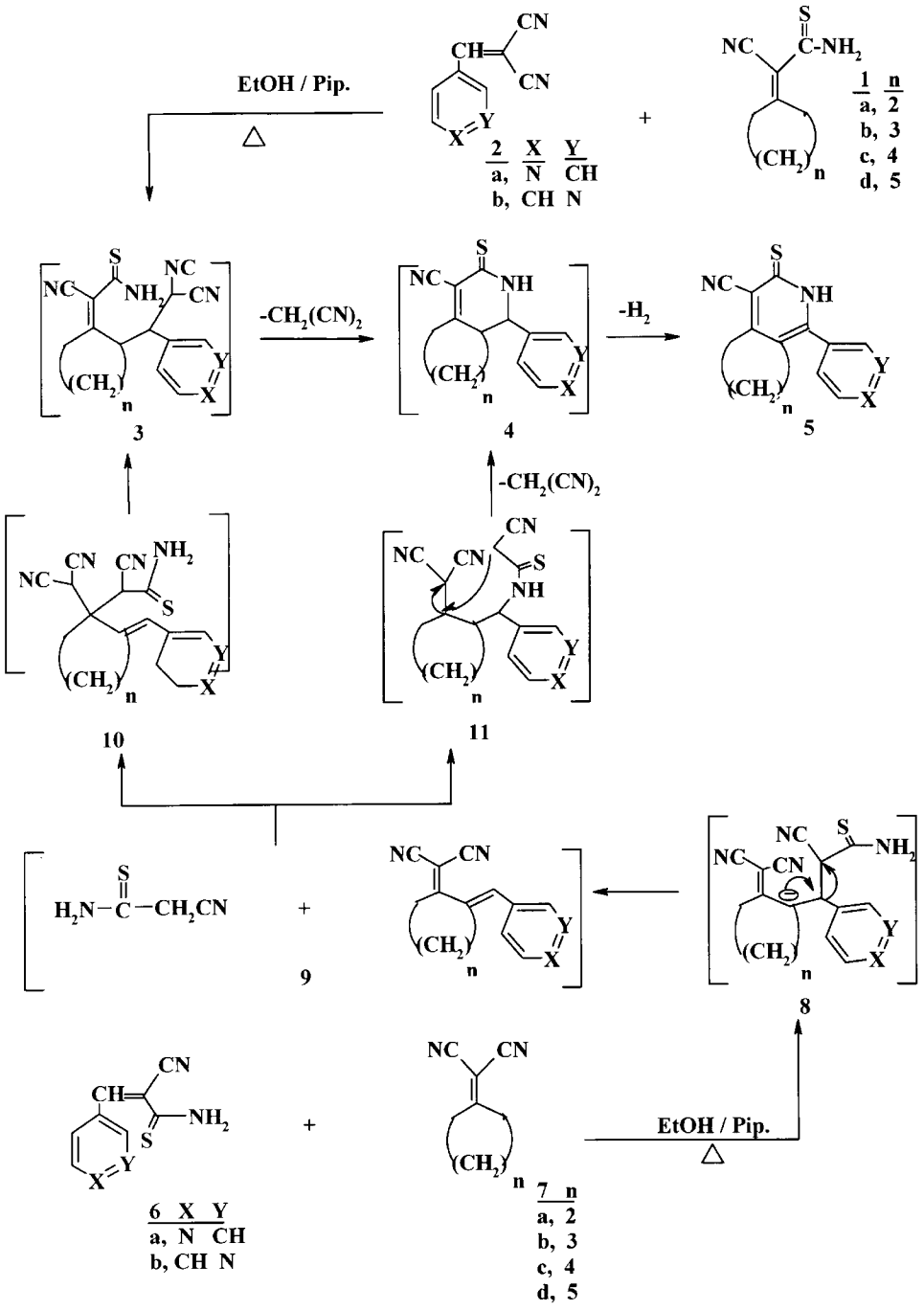

Chart 1.

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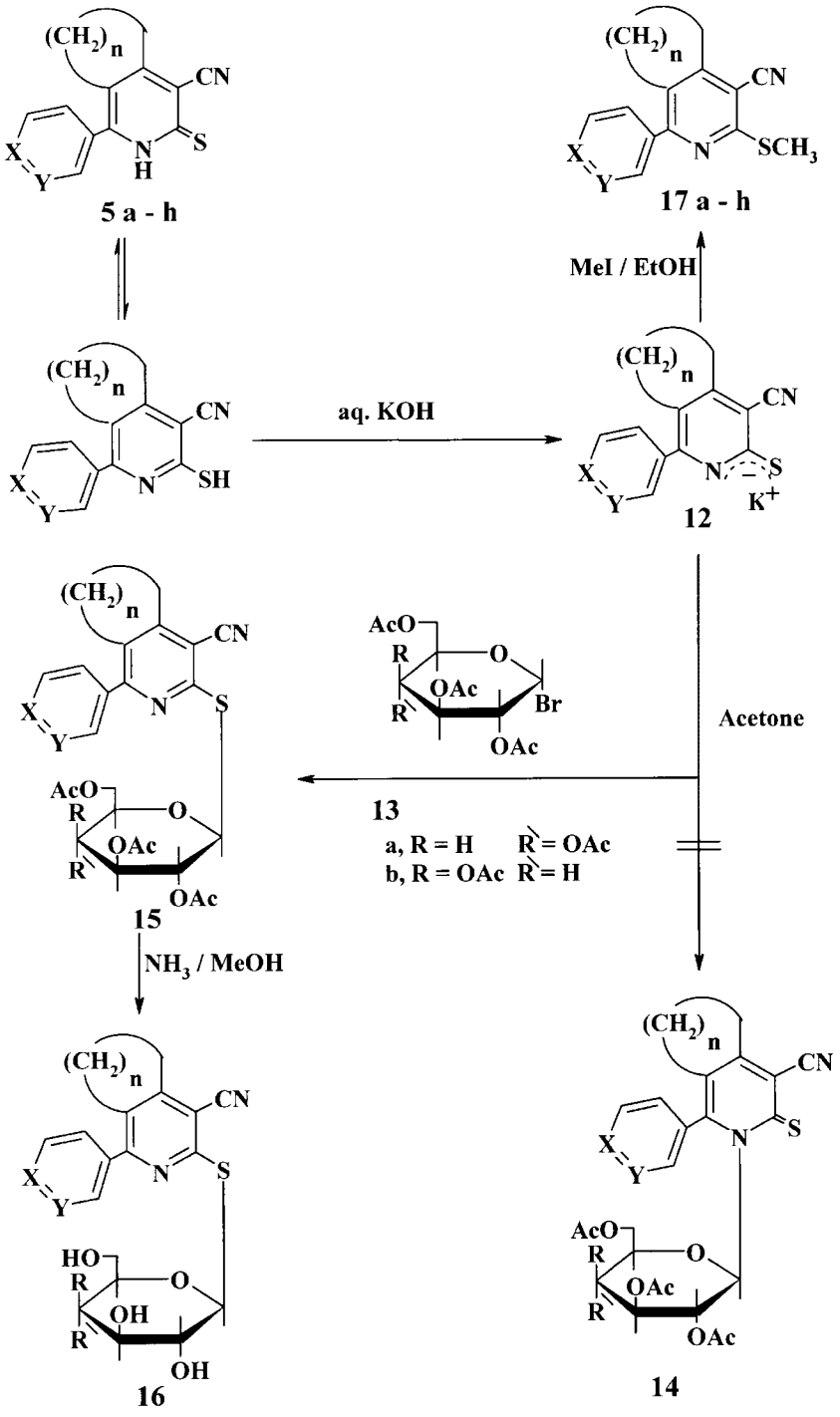

Chart 2.

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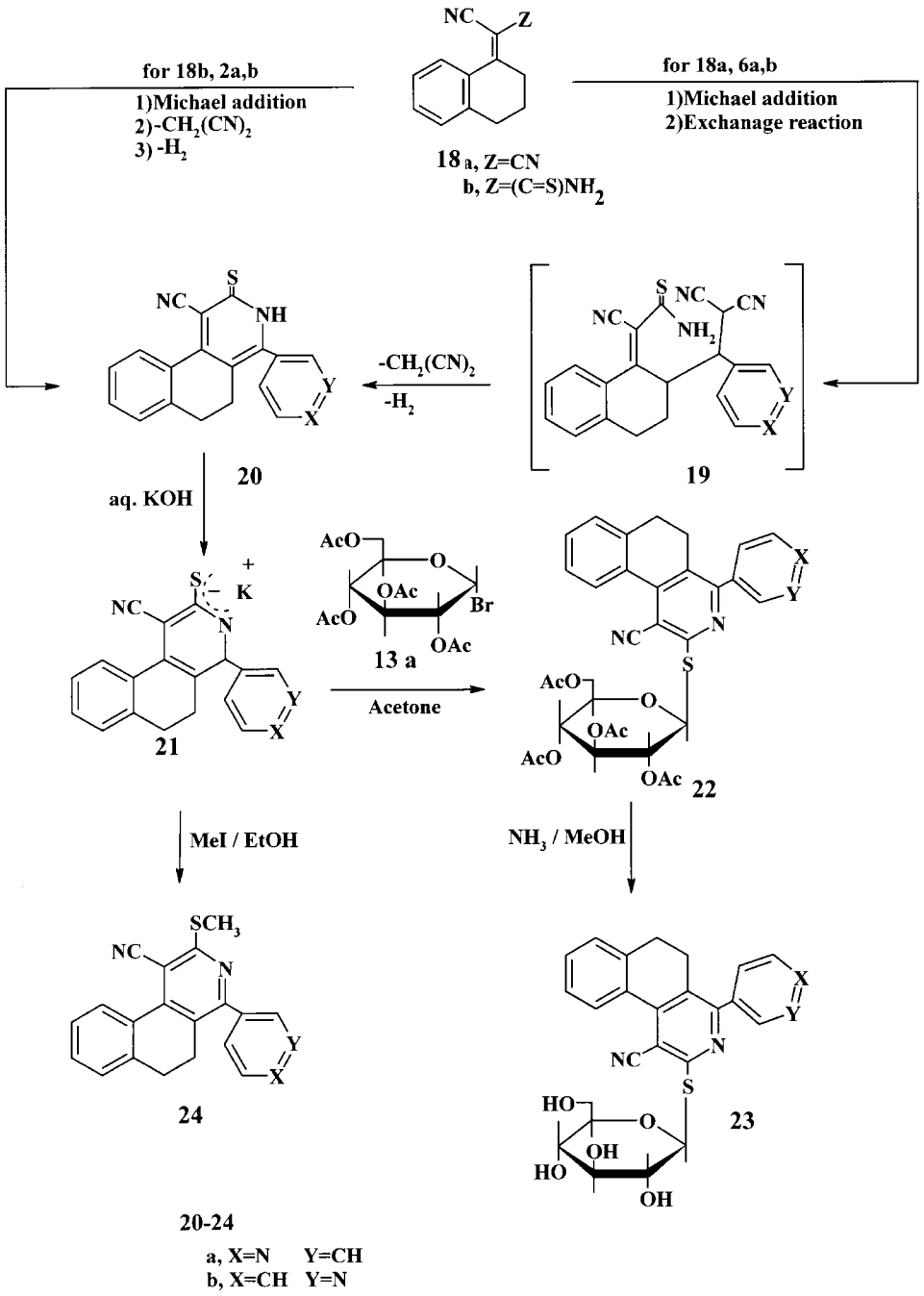

Chart 3.

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5	n	X	Y	5	n	X	Y
a	2	N	CH	e	4	N	CH
b	2	CH	N	f	4	CH	N
c	3	N	CH	g	5	N	CH
d	3	CH	N	h	5	CH	N

15	n	X	Y	R	R\
a,	2	N	CH	H	OAc
b,	2	CH	N	H	OAc
c,	3	N	CH	H	OAc
d,	3	CH	N	H	OAc
e,	4	N	CH	H	OAc
f,	4	CH	N	H	OAc
g,	5	N	CH	H	OAc
h,	5	CH	N	H	OAc
i,	2	N	CH	OAc	H
j,	2	CH	N	OAc	H
k,	3	N	CH	OAc	H
l,	3	CH	N	OAc	H
m,	4	N	CH	OAc	H
n,	4	CH	N	OAc	H
o,	5	N	CH	OAc	H
p,	5	CH	N	OAc	H

16	n	X	Y	R	R\
a,	2	N	CH	H	OH
b,	2	CH	N	H	OH
c,	3	N	CH	H	OH
d,	3	CH	N	H	OH
e,	4	N	CH	H	OH
f,	4	CH	N	H	OH
g,	5	N	CH	H	OH
h,	5	CH	N	H	OH
i,	2	N	CH	OH	H
j,	2	CH	N	OH	H
k,	3	N	CH	OH	H
l,	3	CH	N	OH	H
m,	4	N	CH	OH	H
n,	4	CH	N	OH	H
o,	5	N	CH	OH	H
p,	5	CH	N	OH	H

Chart 4.

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four acetoxy groups appeared as four singlets at δ 1.80–2.03 ppm and the four methylene protons of the agylcon resonated at δ 1.65, 1.78, 2.15 and 3.02 ppm. The ^{13}C NMR spectrum was characterized by a signal at δ_c 80.08 corresponding to the C-1′ atom of the β-D-glucopyranose. The four signals appearing at δ_c 169.01–170.08 ppm were due to the four acetoxy carbonyl carbon atoms, while the four signals at δ_c 20.00–20.20 were attributed to the acetate methyl carbons. The five methylene carbon atoms of the aglycone resonated at δ_c 25.00, 26.05, 27.00, 28.30, 33.30 ppm. Another five signals at δ_c 61.80, 68.00, 69.01, 73.20 and 75.00 were assigned to C-6′, -4′, -2′, -3′ and -5′, respectively. The IR spectrum of compound **15c** was characterized by the presence of acetoxy carbonyl groups at 1755 cm^{-1}. It could have been argued that the coupling reaction of **5** with **13** happened on the nitrogen atom to give the corresponding N-glycosides **14**. However, the formation of the S-glycosides **15** was proved using ^{13}C NMR which revealed the absence of the thione carbon at δ_c 178 ppm[6] and appearance of C-2 at δ_c 161 ppm,[7] nearly the same value as the corresponding S-methyl derivatives **17**. Also, the UV spectra of compounds **15** proved that the reaction had led selectively to the formation of S-glycosyl derivatives since the corresponding S-methyl derivatives **17** gave the same UV absorption maxima. For example, the S-methyl derivative **17c** showed two maxima at 277 and 362 nm and its corresponding glucosyl derivative also exhibited two maximum absorption bands at 272.2 and 317.6 nm. The protected nucleosides **15a–p** were deblocked through treatment with methanolic ammonia to give the free glycosides **16a–p** after chromatographic purification. TLC of compounds **16a–p** showed that a single unique compound was produced, and their structures were confirmed by their elemental analysis and spectral data. The analytical data for compound **16j** revealed a molecular formula $C_{20}H_{21}N_3O_5S$ (m/z = 415). The IR absorption spectrum of this compound showed a characteristic band at 3200–3600 cm^{-1} due to the hydroxy groups of the galactose moiety. The ^{1}H NMR spectrum of compound **16j** revealed the presence of a doublet at δ 5.62 ($J_{1'-2'} = 10.75$ Hz), indicating the presence of only the β-D galactopyranose. The other six-galactose protons appeared as a multiplet at δ 3.10–3.80 ppm, while the four hydroxy protons of the galactose moiety resonated at δ 4.55, 4.95 and 5.30 ppm (exchangeable by D_2O). The ^{13}C NMR spectrum was characterized by a signal at δ_c 83.50 corresponding to the C-1′ atom of β-D galactopyranose. Another five signals at δ_c 60.00, 69.50, 69.10, 75.10, and 80.00 were assigned to C-6′, -4′, -2′, -3′, and -5′ of the galactose part, respectively. In order to explore the synthetic potential of this exchange reaction for producing not readily accessible condensed pyridinethiones and their corresponding nucleosides, we investigated this reaction with other class of cycloalkylidene ring system. So, it was been found that tetralinylidenecyanothioacetamide **18b** reacted with pyridylmethylidene-malononitrile **2a,b** in refluxing ethanol containing catalytic amounts of piperidine for 3 h to give the interesting phenanthridine analogues **20a,b**. The formation of

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20 from **18b** and **2a,b** is assumed to proceed via addition of the active methylene group of **1** to the double bond of **2a,b**, giving Michael intermediates which then cyclize via malononitrile elimination and oxidation under the reaction conditions to yield compounds **20**. The obtained products **20** were shown to be the same as those resulted from the reaction of **18a** with **6a,b** by TLC, melting point and spectral data. The mechanism of the reaction of **18a** and **6a,b** is assumed to proceed through Michael addition followed by the exchange reaction between the cycloalkylidene group of **18a** and the pyridylmethylidene group of **6a,b**, which leads to the intermediates **19** and hence to the final product **20**. The analytical data for compound **20a** revealed a molecular formula $C_{19}H_{13}N_3S$ (m/z = 315). The IR spectrum showed a broad band at 3250–3650 cm^{-1} indicating the NH group. The ^1H NMR of **20a** also illustrated the presence of NH proton as a broad band at δ 14.02 ppm. Compounds **20a,b** were then reacted with 2,3,4,6-tetra-O-acetyl-α-D-glycopyranosyl bromide **13a** in the presence of aqueous potassium hydroxide to give the corresponding glycosides **22a,b.** The structures of the reaction products **22a,b** were established by their elemental analyses and spectral data (MS, IR, UV, ^1H NMR and ^{13}C NMR). The analytical data for **22a** revealed a molecular formula $C_{33}H_{32}N_3SO_9$ (m/z = 645). The ^1H NMR spectrum showed the anomeric proton as a doublet at δ 6.10 ppm with a spin-spin coupling constant of 8.7 Hz, which corresponds to the diaxial orientation of 1′-H and 2′-H protons, indicating the presence of only the β-configuration. The other six protons of the glucopyranosyl ring resonated in the δ 3.95–5.45 ppm region, while the four acetoxy groups appeared as four singlets at δ 1.78–2.18 ppm. The formation of the S-glycosides **22** was proved using the UV spectra, which gave the same UV absorption maxima as the corresponding S-methyl derivatives **24**. The *S*-methyl derivative **24a** showed two maxima at 280 and 360 nm and its glucosyl derivative **22a** also exhibited two absorption maxima at 271 and 355 nm. Moreover, the ^{13}C NMR of **22a** revealed the absence of the thione carbon at δ_c 178 ppm[6] and the appearance of the C-2 at δ_c 159 ppm,[7] the same value of the corresponding S-methyl derivative **24a**. Upon deprotection of compounds **22** with methanolic ammonia the free nucleosides **23** were obtained in almost quantitative yields, the structures of the latter were established on the basis of elemental analyses and spectral data. The analytical data for compound **23a** revealed a molecular formula $C_{25}H_{24}N_3O_5S$ (m/z = 482). The IR absorption spectra of this compound showed a characteristic band at 3200–3600 cm^{-1} due to the hydroxy groups of the glucose moiety. ^1H NMR spectrum revealed the presence of a doublet at δ 5.69 ($J_{1'-2'} = 9.8$ Hz), indicating the presence of only the β-D-glucopyranose. The other six-galactose protons appeared as a multiplet at δ 3.18–3.70 ppm, while the four hydroxy groups of glucose moiety resonated at δ 4.55, 5.14, 5.28 and 5.58 ppm (exchangeable by D_2O). ^{13}C NMR spectrum were characterized by a signal at δ_c 84.01 corresponding to the C-1′ atom of β-D-glucopyranose. Another five signals, at δ_c 60.00,

69.76, 71.86, 78.68 and 81.68, were assigned to C-6′, -4′, -2′, -3′, and -5′ of the glucose moiety, respectively.

In summary, we have achieved the synthesis of interesting nonclassical bipyridyl and biheterocyclic-nitrogen thioglycosides by the reaction of substituted pyridinethiones with α-halosugars. These glycosides can be utilized as an excellent starting material for the synthesis of other carbohydrate derivatives and for biological evaluation studies.

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EXPERIMENTAL

All evaporations were carried out under reduced pressure at 40°C. M.p.s are uncorrected. Aluminum sheets coated with silica gel F254 (Merck) were used for TLC. Detection was effected by viewing under a short-wavelength UV lamp. IR spectra were obtained (KBr disk) on a Pye Unicam Spectra 1000. ^{1}H NMR and ^{13}C NMR spectra were measured on a Wilmad 270 MHz or on a Varian 400 MHz spectrometer for solution in $CDCl_3$ or $(CD_3)_2SO$ with $SiMe_4$ as the internal standard. *J* values are given in Hz. Mass spectra were recorded on a Varian MAT 112 spectrometer. Analytical data were obtained from the Microanalytical Data Center at Cairo University.

Cycloalkane Ring-Fused 6-Pyridyl-3-cyanopyridine-2-(1*H*)-thiones (5a–h)

General Procedure

To a mixture of **2a,b** and **1a–d** or **6a,b** and **7a–d** (0.01 mol of each) in ethanol (50 mL), piperidine (1 mL) was added. The mixture was heated under reflux for 2 h, and then set aside overnight. The resultant precipitate filtered off and crystallized from the appropriate solvent.

5a: orange, from EtOH-DMF, m.p. 275°C, yield 80%. IR: ν_{max}/cm^{-1} (KBr): 3240 (NH); 2225 (CN). $C_{14}H_{11}N_3S$ Calcd: C, 66.42; H, 4.35; N, 16.60, S, 12.64%. Found: C, 66.23; H, 4.23; N, 16.34, S, 12.83%, **5b**: orange, from EtOH-DMF, m.p. 275°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 3240 (NH); 2225 (CN), $C_{14}H_{11}N_3S$, Calcd: C, 66.42; H, 4.35; N, 16.60, S, 12.64%. Found: C, 66.23; H, 4.25; N, 16.38, S, 12.85%, **5c**: yellow, from EtOH-DMF, m.p. 265°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3330 (NH); 2225 (CN), ^{1}H NMR: δ ppm: 1.60 (m, 2H, CH_2); 1.65 (m, 2H, CH_2); 2.10 (m, 2H, CH_2); 2.80 (m, 2H, CH_2); 7.42 (d, 2H, pyridyl-H); 8.78 (d, 2H, pyridyl-H); 14.12 (br s, 1H, NH), ^{13}C NMR: δ ppm: 20.85 (CH_2); 21.55 (CH_2); 24.85 (CH_2); 27.85 (CH_2); 113.10 (C-5); 116.00 (CN); 119.85 (C-3); 123.00 (2CH, pyridyl-C); 142.30 (C-4′, pyridyl-C); 149.85 (2CH, pyridyl-C); 152.80 (C-4); 155.30 (C-6); 176.00 (C=S) $C_{15}H_{13}N_3S$ ($M^+ = 267$), Calcd: C, 67.40; H, 4.87; N, 15.73; S, 11.99%. Found: C, 67.63; H, 4.64; N, 15.92; S, 11.70%, **5d**: yellow, from EtOH-

DMF, m.p. 265°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 3330 (NH); 2225 (CN), $C_{15}H_{13}N_3S$, Calcd: C, 67.40; H, 4.87; N, 15.73; S, 11.99%. Found: C, 67.28; H, 4.94; N, 15.95; S, 12.14%, **5e**: yellow, from EtOH-DMF, m.p. 280°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3330 (NH); 2225 (CN), $C_{16}H_{15}N_3S$, Calcd: C, 68.32; H, 5.34; N, 14.95; S, 11.39%. Found: C, 68.12; H, 5.54; N, 14.72; S, 11.20%, **5f**: yellow, from EtOH-DMF, m.p. 280°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3330 (NH); 2225 (CN), $C_{16}H_{15}N_3S$, Calcd: C, 68.32; H, 5.34; N, 14.95; S, 11.39%. Found: C, 68.24; H, 5.65; N, 14.73; S, 11.57%, **5g**: yellow, from EtOH-DMF, m.p. 285°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3400 (NH); 2225 (CN), $C_{17}H_{17}N_3S$, Calcd: C, 69.15; H, 5.76; N, 14.23; S, 10.85%. Found: C, 69.35; H, 5.45; N, 14.41; S, 10.73%, **5h**: yellow, from EtOH-DMF, m.p. 220°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 3400 (NH); 2225 (CN), ^{1}H NMR: δ ppm: 1.20–1.55 (m, 6H, $3 \times CH_2$); 1.65 (m, 2H, CH_2); 2.28 (m, 2H, CH_2); 2.88 (m, 2H, CH_2); 7.55 (d, 1H, pyridyl-H); 7.87 (d, 1H, pyridyl-H); 8.55 (d, 1H, pyridyl-H); 8.65 (d, 1H, pyridyl-H); 14.18 (br s, 1H, NH), ^{13}C NMR: δ ppm: 24.00 (CH_2); 25.5 (CH_2); 26.8 (CH_2); 27.8 (CH_2); 29.85 (CH_2); 31.2 (CH_2); 114.60 (C-5); 115.50 (CN); 123.50 (CH, pyridyl-C); 124.20 (C-3); 132.30 (C-3′, pyridyl-C); 135.00 (CH, pyridyl-C); 138.40 (CH, pyridyl-C); 151.50 (CH, pyridyl-C); 155.80 (C-4); 156.70 (C-6); 176.70 (=C=S), $C_{17}H_{17}N_3S$ ($M^+ = 295$), Calcd: C, 69.15; H, 5.76; N, 14.23; S, 10.85%. Found: C, 69.05; H, 5.58; N, 14.43; S, 10.96%.

2-(2′,3′,4′,6′-Tetra-o-acetyl-β-D-gluco- and galacto-pyranosylthio)-4-pyridyl-pyridine-3-carbonitriles (15a–p)

General Procedures

To a solution of pyridine-2-(1*H*)-thiones **5a–h** (0.01mol) in aqueous potassium hydroxide [0.56 g, 0.01 mol, in distilled water (6 mL)] was added a solution of 2,3,4,6-tetra-O-acetyl-α-D-gluco- or -galacto-pyranosyl bromide **12a,b** (4.521 g, 0.011 mol) in acetone (30 mL). The reaction mixture was stirred at room temperature until reaction judged complete by TLC (30 min to 2 h). The mixture was evaporated under reduced pressure at 40°C, and the residue was washed with distilled water to remove the formed potassium bromide. The product was dried, and crystallized from the appropriate solvent.

15a: yellow, from EtOH, m. p. 195°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN); 1750 (C=O), $C_{28}H_{29}N_3O_9S$, Calcd: C, 57.63; H, 4.97; N, 7.2; S, 5.49%. Found: C, 57.43; H, 4.75; N, 7.43; S, 5.62%, **15b**: white, from EtOH, m.p. 125°C, yield 65%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN); 1750 (C=O), ^{1}H NMR: δ ppm: 1.58 (t, 2H, CH_2); 1.7–2.2 (4 s, 12H, $4 \times OAc$); 2.56 (t, 2H, CH_2); 3.13 (t, 2H, CH_2); 3.85–4.23 (m, 3H, 6′-H_2, 5′-H); 5.18–5.39 (m, 3H, 4′-H, 3′-H, 2′-H); 6.01 (d, $J_{1'-2'}$ 10.2 Hz, 1H, 1′-H); 7.45 (m, 1H, pyridyl-H); 7.80

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(m, 1 H, pyridyl-H); 8.47 (d, 1H, pyridyl-H); 8.72 (d, 1H, pyridyl-H), $C_{28}H_{29}N_3O_9S$, Calcd: C, 57.63; H, 4.97; N, 7.2; S, 5.49%, Found: C, 57.80; H, 4.70; N, 7.00; S, 5.6%. **15c**: yellow, from EtOH, m.p. 215°C, yield 60%. IR: ν_{max}/cm^{-1} (KBr): 2200 (CN); 1720 (C=O), UV: λ_{max}: 317.6, 272.2; ^1H NMR: δ ppm: 1.65 (m, 2H, CH_2); 1.78 (m, 2H, CH_2); 1.90–2.03 (4s, 12H, $4 \times OAc$); 2.15 (t, 2H, CH_2); 3.02 (t, 2H, CH_2); 3.99–4.20 (m, 3H, 6′-H_2, 5′-H); 4.98–5.22 (m, 2H, 4′-H, 3′-H); 5.53 (t, 1H, 2′-H); 6.15 (d, $J_{1'-2'}$ 11.28 Hz 1H, 1′-H); 7.47 (d, 2H, pyridyl-H); 8.79 (d, 2H, pyridyl-H), ^{13}C NMR: δ ppm: 20–20.10 ($4 \times CH_3$); 21.10 (CH_2); 25.5 (CH_2); 27.8 (CH_2); 33.30 (CH_2); 61.80 (CH_2, C-6′); 68.00 (CH, C-4′); 69.01 (CH, C-2′); 73.20 (CH, C-3′); 75.00 (CH, C-5′); 80.50 (CH, C-1′); 103.50 (C-5); 114.50 (CN); 123.40 (2CH, pyridyl-C); 127.06 (C-3); 129.08 (C-4″, pyridyl-C); 150.00 (2CH, pyridyl-C); 151.50 (C-4); 154.00 (C-6); 162 (=C-S); 169.01–170.08 ($4 \times C=O$), $C_{29}H_{31}N_3O_9S$ ($M^+ = 597$) Calcd: C, 58.29; H, 5.19; N, 7.03; S, 5.36%. Found: C, 58.03; H, 5.42; N, 6.93; S, 5.34%, **15d**: white, from EtOH, m.p. 135°C, yield 70%, IR: ν_{max}/cm^{-1} (KBr): 2225 (CN); 1720 (C=O), ^1H NMR: δ ppm: 1.64 (m, 2H, CH_2); 1.85 (m, 2H, CH_2); 1.95–2.18 (4 s, 12H, $4 \times OAc$); 2.46 (m, 2H, CH_2); 3.00 (m, 2H, CH_2); 4.05 (m, 2H, 6′-H_2); 4.20 (t, 1H, 5′-H); 5.05 (m, 1H, 4′-H); 5.20 (m, 1H, 3′-H); 5.50 (t, 1H, 2′-H); 6.10 (d, $J_{1'-2'}$ 10.5 Hz, 1H, 1′-H); 7.60 (t, 1H, pyridyl-H); 7.90 (t, 1H, pyridyl-H); 8.60 (t, 1H, pyridyl-H); 8.70 (d, 1H, pyridyl-H), ^{13}C NMR: δ ppm: 20.00–20.10 ($4 \times CH_3$); 20.20 (CH_2); 26.20 (CH_2); 29.8 (CH_2); 33.50 (CH_2); 61.30 (CH_2, C-6′); 67.50 (CH, C-4′); 68.50 (CH, C-2′); 73.00 (CH, C-3′); 75.00 (CH, C-5′); 80.10 (CH, C-1′); 105.50 (C-5); 114.50 (CN); 123.20 (CH, pyridyl-C); 129.00 (C-3); 131.00 (C-4″ pyridyl-C); 136.00 (CH, pyridyl-C); 146.70 (CH, pyridyl-C); 150.10 (CH, pyridyl-C); 151.20 (C-4); 152.10 (C-6); 161.02 (=C-S-); 169.01–170.08 ($4 \times C=O$), $C_{29}H_{31}N_3O_9S$ ($M^+ = 598$), Calcd: C, 58.29; H, 5.19; N, 7.03; S, 5.36%. Found: C, 58.05; H, 5.14; N, 6.95; S, 5.40%, **15e**: yellow, from EtOH, m.p. 203°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 2222 (CN); 1750 (C=O), UV: λ_{max}: 315.6, 271.2, ^1H NMR: δ ppm: 1.56 (m, 2H, CH_2); 1.75 (m, 2H, CH_2); 1.95–2.15 (4s, 12H, $4 \times OAc$); 2.45 (m, 4H, CH_2); 3.16 (m, 4H, $2CH_2$); 4.00 (m, 2H, 6′-H_2); 4.15 (m, 1H, 5′-H); 5.05 (m, 1H, 4′-H); 5.15 (m, 1H, 3′-H); 5.5 (t, 1H, 2′-H); 6.20 (d, $J_{1'-2'}$ 9.9 Hz, 1H, 1′-H); 7.45 (m, 2H, pyridyl-H); 8.78 (d, 2H, pyridyl-H), ^{13}C NMR: δ ppm: 20.10 ($4 \times CH_3$); 24.30 (CH_2); 26.20 (CH_2); 29.00 (CH_2); 32.8 (CH_2), 39.40 (CH_2); 61.5 (CH_2, C-6′); 66.50 (CH, C-4′); 67.30 (CH, C-2′); 73.00 (CH, C-3′); 75.00 (CH, C-5′); 80.10 (CH, C-1′); 104.00 (C-5); 114.50 (CN); 124.10 (2CH, pyridyl-C); 124.10 (C-3); 132.00 (C-4″, pyridyl-C); 144.10 (C-4); 150.00 (2 CH, pyridyl-C); 150.02 (C-6) 154.04 (=C-S-); 168.10–170.10 ($4 \times C=O$), $C_{30}H_{33}N_3O_9S$, Calcd: C, 58.91; H, 5.44; N, 6.87, S 5.24%. Found: C, 60.12, H, 5.34; N, 6.62, S, 5.18%, **15f**: white, from EtOH, m.p. 135°C, yield 70%, IR: ν_{max}/cm^{-1} (KBr): 2222 (CN); 1750 (C=O), UV: λ_{max}: 317.6, 273.2, $C_{30}H_{33}N_3O_9S$, Calcd: C, 58.91; H, 5.44; N, 6.87, S, 5.24%, Found: C, 60.23, H, 5.53; N, 6.92, S 5.12%, **15g**: yellow, from EtOH, m.p. 155°C, yield 60%,

IR: ν_{max}/cm^{-1} (KBr): 2225 (CN); 1720 (C=O), UV: λ_{max}: 314.6, 269.8, Calcd: C, 59.52; H, 5.60; N, 6.72, S, 5.12%. Found: C, 59.42, H, 5.54; N, 6.60, S, 5.30%, **15h**: white, from EtOH, m.p. 125°C, yield 65%. IR: ν_{max}/cm^{-1} (KBr): 2225 (CN); 1720 (C=O), ^{1}H NMR: δ ppm: 0.84 (m, 2H, CH_2); 1.37 (m, 2H, CH_2); 1.73–1.83 (m, 2H, CH_2); 1.95–2.15 (4s, 12H, $4 \times$ OAc); 2.56 (m, 2H, CH_2); 3.12 (m, 2H, CH_2); 3.46 (m, 2H, CH_2); 3.95–4.25 (m, 3H, 6′-H_2, 5′-H); 4.98–5.24 (m, 2H, 4′-H, 3′-H); 5.61 (t, 1H, 2′-H); 6.20 (d, $J_{1'-2'}$ 10.0 Hz, 1H, 1′-H); 7.57 (m, 1H, pyridyl-H); 7.89 (m, 1H, pyridyl-H); 8.64 (d, 1H, pyridyl-HH); 8.75 (d, 1H, pyridyl-H), $C_{31}H_{35}N_3O_9S$, Calcd: C, 59.52; H, 5.60; N, 6.72, S, 5.12%. Found: C, 59.34, H, 5.42; N, 6.85, S, 5.23%, **15i**: white, from EtOH, m.p. 185°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN); 1750 (C=O), $C_{28}H_{29}N_3O_9S$, Calcd: C, 57.63; H, 4.97; N, 7.2; S, 5.49%. Found: C, 57.83; H, 4.74; N, 7.43; S, 5.20%, **15j**: white, from EtOH, m.p. 125°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN); 1750 (C=O), $C_{28}H_{29}N_3O_9S$, Calcd: C, 57.63; H, 4.97; N, 7.2; S, 5.49%. Found: C, 57.72; H, 4.69; N, 7.32; S, 5.65%, **15k**: yellow, from EtOH, m.p. 195°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 2200 (CN); 1720 (C=O), $C_{29}H_{31}N_3O_9S$, Calcd: C, 58.29; H, 5.19; N, 7.03; S, 5.36%. Found: C, 58.43; H, 5.44; N, 6.80; S, 5.30%, **15l**: white, from EtOH, m.p. 125°C, yield 75%, IR: ν_{max}/cm^{-1} (KBr): 2225 (CN); 1720 (C=O), $C_{29}H_{31}N_3O_9S$, Calcd: C, 58.29; H, 5.19; N, 7.03; S, 5.36%. Found: C, 58.15; H, 5.36; N, 6.87; S, 5.42%, **15m**: yellow, from EtOH, m.p. 207°C, yield 75%, IR: ν_{max}/cm^{-1} (KBr): 2222 (CN); 1750 (C=O), $C_{30}H_{33}N_3O_9S$, Calcd: C, 58.91; H, 5.44; N, 6.87, S, 5.24%. Found: C, 58.85, H, 5.34; N, 7.15, S, 5.18%, **15n**: white, from EtOH, m.p. 135°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 2222 (CN); 1750 (C=O), $C_{30}H_{33}N_3O_9S$, Calcd: C, 58.91; H, 5.44; N, 6.87, S, 5.24%. Found: C, 60.25, H, 5.53; N, 6.90, S, 5.10% .**15o**: buff, from EtOH, m.p. 204°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2225 (CN); 1720 (C=O), $C_{31}H_{35}N_3O_9S$, Calcd: C, 59.52; H, 5.60; N, 6.72, S, 5.12%. Found: C, 59.55, H, 5.43; N, 6.50, S 5.30%. **15p**: white, from EtOH, m.p. 125°C, yield 65%, IR: ν_{max}/cm^{-1} (KBr): 2225 (CN); 1720 (C=O), $C_{31}H_{35}N_3O_9S$, Calcd: C, 59.52; H, 5.60; N, 6.72, S, 5.12%. Found: C, 59.45, H, 5.43; N, 6.82, S, 5.00%.

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2-(β-D-gluco- and galacto-pyranosylthio)-6-pyridyl-pyridine-3-carbonitriles (16a–p)

General Procedure

Dry gaseous ammonia was passed through a solution of a protected nucleoside **15a–p** (0.5 gm) in dry methanol (20 mL) at 0°C for 0.5 h, then the mixture was stirred at 0°C until reaction was judged to be complete by TLC (2–6 h). The mixture was evaporated at 40°C to a solid residue, which was

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purified by chromatography or by crystallization from the appropriate solvent.

16a: white, from MeOH, m.p. 245°C, yield 55%, IR: ν_{max}/cm^{-1} (KBr): 3000–3600 (OH); 2225 (CN), ^{1}H NMR: δ ppm: 2.41–2.51 (m, 2H, CH_2); 2.68 (m, 2H, CH_2); 2.78 (m, 2H, CH_2), 3.18–3.66 (m, 6H, 6′-H_2, 5-H′, 4-H′, 3′-H); 4.51 (t, 1H, H-2′); 5.11–5.23 (m, 2H, 3′-OH, 4′-OH); 5.50 (m, 1H, 6′-OH); 5.73 (d, $J_{1'-2'}$ 10.1 Hz, H, 1′-H); 8.33 (d, 2H, pyridyl-H); 8.80 (d, 2H, pyridyl-H), $C_{20}H_{21}N_3O_5S$, Calcd: C, 57.83; H, 5.06; N, 10.12; S, 7.72%. Found: C, 57.60; H, 4.90; N, 10.30; S, 7.80%, **16b**: yellow, from MeOH, m.p. 245°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 3050–3600 (OH); 2225 (CN), $C_{20}H_{21}N_3O_5S$, Calcd: C, 57.83; H, 5.06; N, 10.12; S, 7.72%. Found: C, 57.74; H, 4.82; N, 10.00; S, 7.83%, **16c**: white, from MeOH, m.p. 235°C, yield 65%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), UV: λ_{max}: 322.2, 276.2, ^{1}H NMR: δ ppm: 1.26 (m, 4H, $2CH_2$); 1.73 (m, 2H, CH_2); 1.82 (m, 2H, CH_2), 2.02–2.34 (m, 2H, CH_2), 3.39–3.99 (m, 6H, 6′-H_2, 5′-H, 4′-H, 3′-H, 2′-H);; 4.16 (t, 2H, 2′-OH, 3′-OH); 5.17 (m, 1H, 4′-OH); 5.55 (m, 1H, 6′-OH); 6.15 (d, $J_{1',-2'}$ 9.7 Hz, H, 1′-H); 7.42 (t, 2H, pyridyl-H); 8.79 (d, 2H, pyridyl-H), $C_{21}H_{23}N_3O_5S$, Calcd: C, 58.74; H, 5.36; N, 9.79; S, 7.46%. Found: C, 58.62; H, 5.63; N, 10.00; S, 7.62%, **16d**: white, from MeOH, m.p. 175°C, yield 70%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), $C_{21}H_{23}N_3O_5S$, Calcd: C, 58.74; H, 5.36; N, 9.79; S, 7.46%. Found: C, 58.80; H, 5.40; N, 10.00; S, 7.30%, **16e**: white, from MeOH, m.p. 225°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), UV: λ_{max}: 324.6, 276.2, $C_{22}H_{25}N_3O_5S$, Calcd: C, 59.59; H, 5.64; N, 9.48; S, 7.22%. Found: C, 59.80; H, 5.40; N, 9.20; S, 7.30%, **16f**: white, from MeOH, m.p. 170°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), UV: λ_{max}: 324.6, 275.2, $C_{22}H_{25}N_3O_5S$, Calcd: C, 59.59; H, 5.64; N, 9.48; S, 7.22%. Found: C, 59.70; H, 5.40; N, 9.30; S, 7.00%, **16g**: white, from MeOH, m.p. 211°C, yield 70%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN),^{1}H NMR: δ ppm: 1.26 (m, 6H, $3CH_2$); 1.73 (m, 4H, $2CH_2$); 3.04 (m, 2H, CH_2); 3.14–3.64 (m, 6H, 6′-H_2, 5′-H, 4′-H, 3′-H, 2′-H); 4.48 (t, 1H, 2′-OH); 5.05 (m, 1H, 3′-OH); 5.25 (m, 1H, 4′-OH); 5.63 (d, $J_{1'-2'}$ 10.3 Hz, 1H, 1′-H); 7.46 (t, 2H, pyridyl-H); 8.78 (d, 2H, pyridyl-H), $C_{23}H_{27}N_3O_5S$, Calcd: C, 60.39; H, 5.90; N, 9.19; S, 7.02%. Found: C, 60.40; H, 5.60; N, 9.30; S, 7.00%, **16h**: white, from MeOH, m.p. 185°C, yield 75%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), $C_{23}H_{27}N_3O_5S$, Calcd: C, 60.39; H, 5.90; N, 9.19; S, 7.02%. Found: C, 60.50; H, 5.80; N, 9.30; S, 7.20%, **16i**: white, from MeOH, m.p. 174°C, yield 77%, IR: ν_{max}/cm^{-1} (KBr): 3050–3550 (OH); 2225 (CN), $C_{20}H_{21}N_3O_5S$, Calcd: C, 57.83; H, 5.06; N, 10.12; S, 7.72%. Found: C, 57.60; H, 5.20; N, 10.20; S, 7.80%, **16j**: yellow, from MeOH, m.p. 245°C, yield 80%. IR: ν_{max}/cm^{-1} (KBr): 3050–3600 (OH); 2225 (CN), ^{1}H NMR: δ ppm: 2.06 (t, 2H, CH_2); 2.80 (m, 2H, CH_2); 3.00 (m, 2H, CH_2); 3.1–3.80 (m, 6H, 6′-H_2, 5′-H, 4′-H, 3′-H, 2′-H); 4.55 (t, 2H, 2′-OH, 3′-OH); 4.95 (m, 1H, 4′-OH); 5.35 (m, 1H, 6′-OH); 5.62 (d, $J_{1'-2'}$ 10.75 Hz, 1H, 1′-H); 7.64 (t, 1H, pyridyl-H); 8.02 (m, 1H,

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pyridyl-H); 8.7 (m, 2H, pyridyl-H), ^{13}C NMR: δ ppm: 22.02–33.01 ($3CH_2$); 60.00 (CH_2, 6′-H_2); 69.50 (CH, C-4′); 69.10 (CH, C-2′); 75.10 (CH, C-3′); 80.00 (CH, C-5′); 83.50 (CH, C-1′); 103.3 (C-5); 115.03 (CN); 123.01 (CH, pyridyl-C); 126.50 (C-3); 127.01 (C-5″, pyridyl-C); 147.01 (C-4); 148.00 (CH, pyridyl-C); 151.01 (CH, pyridyl-C); 160.00 (C-6); 168 (=C-S), $C_{20}H_{21}N_3O_5S$, Calcd: C, 57.83; H, 5.06; N, 10.12; S, 7.72%. Found: C, 57.70; H, 4.80; N, 10.00; S, 7.80%, **15k**: white, from MeOH, m.p. 235°C, yield 50%. IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), $C_{21}H_{23}N_3O_5S$, Calcd: C, 58.74; H, 5.36; N, 9.79; S, 7.46%. Found: C, 58.60; H, 5.60; N, 10.00; S, 7.60%, **16l**: white, from MeOH, m.p. 175°C, yield 65%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), $C_{21}H_{23}N_3O_5S$, Calcd: C, 58.74; H, 5.36; N, 9.79; S, 7.46%. Found: C, 58.80; H, 5.40; N, 10.00; S, 7.30, **16m**: white, from MeOH, m.p. 225°C, yield 60%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), $C_{22}H_{25}N_3O_5S$, Calcd: C, 59.59; H, 5.64; N, 9.48; S, 7.22%. Found: C, 59.80; H, 5.40; N, 9.20; S, 7.30%, **16n**: white, from MeOH, m.p. 170°C, yield 75%. IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), ^{1}H NMR: δ ppm: 1.50–1.90 (m, 6H, 3 CH_2); 3.01 (m, 4H, $2CH_2$); 3.21–3.80 (m, 6H, 6′-H_2, 5′-H, 4′-H, 3′-H, 2′-H); 4.50 (t, 2H, 2′-OH, 3′-OH); 4.95 (t, 1H, 4′-OH); 5.35 (d, 1H, 6′-OH); 5.67 (d, $J_{1'-2'}$ 9.8 Hz, 1H, 1′-H); 7.64 (t, 1H, pyridyl-H); 7.83 (m, 1H, pyridyl-H); 8.55 (m, 1H, pyridyl-H); 8.72 (m, 1H, pyridyl-H), ^{13}C NMR: δ ppm: 22.02 (CH_2), 27.6 (CH_2), 33.01 (CH_2); 60.00 (CH_2, 6′-H_2); 69.10 (CH, C-4′); 69.20 (CH, C-2′); 75.50 (CH, C-3′); 80.00 (CH, C-5′); 89.01 (CH, C-1′); 103.50 (C-5); 115.50 (CN); 123.10 (CH, pyridyl-C); 131.50 (C-3); 132.50 (C-5″, pyridyl-C); 139.001 (C-3); 139.50 (CH, pyridyl-C); 150.01 (CH, pyridyl-C); 156 (C-6); 167.50 (=C-S), $C_{22}H_{25}N_3O_5S$, Calcd: C, 59.59; H, 5.64; N, 9.48; S, 7.22%. Found: C, 59.70; H, 5.40; N, 9.30; S, 7.00, **16o**: white, from MeOH, m.p. 211°C, yield 70%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), ^{1}H NMR: δ ppm: 1.35 (m, 8H, 4 CH_2); 1.76 (m, 2H, CH_2); 3.23–3.574 (m, 6H, 6′-H_2, 5′-H, 4′-H, 3′-H, 2′-H); 4.46 (t, 1H, 2′-OH); 5.03 (m, 1H, 3′-OH); 5.25 (m, 1H, 4′-OH); 5.60 (d, 1H, 6′-OH); 5.69 (d, $J_{1'-2'}$ 9.9 Hz, 1H, 1′-H); 7.46 (t, 2H, pyridyl-H); 8.78 (d, 2H, pyridyl-H), $C_{23}H_{27}N_3O_5S$, Calcd: C, 60.39; H, 5.90; N, 9.19; S, 7.02%. Found: C, 60.40; H, 5.60; N, 9.30; S, 7.00%, **16p**: white, from MeOH, m.p. 185°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), $C_{23}H_{27}N_3O_5S$, Calcd: C, 60.39; H, 5.90; N, 9.19; S, 7.02%. Found: C, 60.50; H, 5.80; N, 9.30; S, 7.20%.

4-Cyano-1-pyridyl-7,8-dihydrobenzo[f]isoquinoline-3(2*H*)-thiones (20a,b)

The above procedure for preparation of compounds **5** were followed.

20a: red, from EtOH/DMF, m.p. 275°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3250–3750 (NH); 2225 (CN), ^{1}H NMR: δ ppm: 2.31–2.40 (m, 2H, CH_2); 2.58 (m, 2H, CH_2); 7.32–7.68 (m, 4H, phenyl); 8.13 (d, 2H, pyridyl-H);

8.78 (t, 2H, pyridyl-H); 14.2 (bs, 1H, NH), $C_{19}H_{13}N_3S$ ($M^+ = 315$), Calcd: C, 72.38; H, 4.13; N, 13.33; S, 10.15%. Found: C, 72.60; H, 4.00; N, 13.20; S, 10.10%, **20b**: orange, from EtOH/DMF, m.p. 280°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 3250–3750 (NH); 2225 (CN), ^1H NMR: δ ppm: 2.37 (m, 2H, CH_2); 2.75 (m, 2H, CH_2); 7.36–7.60 (m, 4H, phenyl); 7.96 (d, 1H, pyridyl-H); 8.12 (d, 1H, pyridyl-H); 8 .70 (d, 1H, pyridyl-H); 8.76 (d, 1H, pyridyl-H); 14.20 (s, bs, 1H, NH), $C_{19}H_{13}N_3S$ ($M^+ =$ 315), Calcd: C, 72.38; H, 4.13; N, 13.33; S, 10.15%. Found: C, 72.50; H, 4.30; N, 13.10; S, 10.00%.

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4-Cyano-1-pyridyl-3-(2′,3′,4′,6′-tetra-o-acetyl-β-d-glucopyranosylthio)-7,8-dihydrobenzo[f]isoquinolines (22a,b)

The above procedure for preparation of compounds **15** were followed. **22a**: white, from EtOH, m.p. 190°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN); 1750 (C=O), UV: λ_{max}: 355.0, 271.2 ,^1H NMR: δ ppm: 1.78–2.18 (4 s 12H, $4CH_3$); 2.67 (m, 2H, CH_2); 2.85 (m, 2H, CH_2); 3.95 (t, 1H, 6′-H_2); 4.17 (t, 1H, 5′-H); 5.18–5.45 (m, 3H, 4′-H, 3′-H, 2′-H); 6.1 (d, $J_{1'-2'}$ 8.7 Hz, 1H, 1′-H); 7.24–7.48 (m, 4H, phenyl-H); 8.26–8.31 (m, 2H, pyridyl-H); 8.87 (d, 2H, pyridyl-H), ^{13}C NMR: δ ppm: 20.20–20.40 ($4 \times CH_3$); 24.60 (CH_2), 25.8 (CH_2), 26.5 (CH_2), 27.11 (CH_2); 62.05 (CH_2, C-6′); 68.16 (C-4′); 68.70 (C-2′); 74.07 (C-3′); 76.30 (C-5′); 81.07 (C-1′); 105.60 (C-5); 114.80 (CN); 123.14–157.55 (aromatic-C, pyridyl-C), 169.4–170.00 (4 C=O), $C_{33}H_{32}N_3O_9S$ ($M^+ =$ 646) Calcd: C, 61.40; H, 4.96; N, 6.51; S, 4.96%. Found: C, 61.23; H, 4.64; N, 6.51; S, 4.75%, **21b**: white, from EtOH, m.p. 219°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN); 1750 (C=O), ^1H NMR δ ppm: 1.62–2.08 (s, 12H, 4 CH_3); 2.70–2.83 (m, 4H, 2 CH_2); 3.90 (m, 2H, 6′-H_2); 4.17 (t, 1H, 5′-H); 5.14–5.45 (m, 3H, 4′-H, 3′-H, 2′-H) 6.1 (d, $J_{1'-2'}$ 9.8 Hz, 1H, 1′-H); 7.24–7.48 (m, 4H, phenyl); 7.69 (d, 1H, pyridyl-H); 8.30 (d, 1H, pyridyl-H); 8.58 (s, 1H, pyridyl-C); 8.87 (d, 1H, pyridyl-H), $C_{33}H_{32}N_3O_9S$, Calcd: C, 61.40; H, 4.96; N, 6.51; S, 4. 96%. Found: C, 61.50; H, 4.75; N, 6.33; S, 4.80%.

3-(β-D-glucopyranosylthio)-4-cyano-1-pyridyl-7,8-dihydro-benzo[f]-isoquinolines (23a,b)

The above procedure for preparation of compounds **16** were followed. **23a**: white, from MeOH, m.p. 260°C, yield 70%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), UV: λ_{max}: 363.6, 275.2, ^1H NMR: δ ppm: 2.52–2.65 (m, 2H, CH_2); 2.83 (t, 2H, CH_2); 3.18–3.70 (m, 6H, 6′-H_2, 5′-H, 4′-H, 3′-H, 2′-H); 4.55 (d, 1H, 2′-OH); 5.14 (d, 1H, 3′-OH); 5.28 (d, 1H, 4′-OH); 5.28 (d, 1H, 6′-OH); 5.69 (d, $J_{1'-2'}$ 9.8 Hz 1H, 1′-H); 7.20–7.68 (m, 4H, phenyl-H); 8.30 (d, 2H, pyridyl-H); 8.82 (d, 2H, pyridyl-H), ^{13}C NMR: δ ppm: 24.40 (CH_2); 26.7 (CH_2); 60 (CH, C-6′); 69.76 (CH, C-4′); 71.86 (CH, C-2′); 78.68 (C-3′); 81.68 (C-5′); 84.01(C-1′); 104.49 (C-b); 115.16 (CN); 123.45–158.40 (aromatic-C, pyridyl-C), $C_{25}H_{24}N_3O_5S$, Calcd: C, 62.24; H, 4.98; N, 8.71; S,

6.64%. Found: C, 62.50; H, 4.60; N, 8.91; S, 6.85%, **23b**: white, from MeOH, m. p. 250°C, yield 75%, IR: ν_{max}/cm^{-1} (KBr): 3200–3600 (OH); 2225 (CN), $C_{25}H_{24}N_3O_5S$, Calcd: C, 62.24; H, 4.98; N, 8.71; S, 6.64%. Found: C, 62.50; H, 4.60; N, 8.91; S, 6.85%.

2-Methylthio-6-pyridyl-3-cyano-pyridine-2-(1*H*)-thiones (17a-h) and 4-Cyano-1-pyridyl-3-(methylthio)-7,8-dihydrobenzo[f] isoquinolines (24a,b)

General Procedure

A solution of compounds **5a–h** and **20a,b** (0.01 mol), methyl iodide (0.01 mol) and NaOH (0.01 mol), water (16 mL) and ethanol (20 mL) was stirred at 60°C, and a white solid began to precipitate almost immediately. Stirring was continued for 30 min and the mixture was allowed to cool, the solid was collected, washed with water, dried and recrystalized from ethanol.

17a: white, from EtOH, m.p. 215°C, yield 80%, $C_{15}H_{13}N_3S$, Calcd: C, 67.40; H, 4.87; N, 15.73; S, 11.9%. Found: C, 67.67; H, 4.66; N, 15.82; S, 11.78%, **17b**: white, from EtOH, m.p. 202°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN), $C_{15}H_{13}N_3S$, Calcd: C, 67.40; H, 4.87; N, 15.73; S, 11.9%. Found: C, 67.67; H, 4.66; N, 15.82; S, 11.78%, **17c**: white, from EtOH, m.p. 300°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN). UV: λ_{max}: 362, 277, $C_{16}H_{15}N_3S$, Calcd: C, 68.32; H, 5.34; N, 14.95; S, 11.39%. Found: C, 68.25; H, 5.58; N, 14.60; S, 10.96%, **17d**: white, from EtOH, m.p. 201, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2220 (CN), $C_{16}H_{15}N_3S$, Calcd: C, 68.32; H, 5.34; N, 14.95; S, 11.39%. Found: C, 68.25; H, 5.58; N, 14.60; S, 10.96%, **17e:** white, from EtOH, m.p. 219°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2225 (CN), UV: λ_{max}: 328.6, 278.2,^{1}H NMR: δ ppm: 1.53 (m, 2H, CH_2); 1.70 (m, 2H, CH_2); 1.81 (m, 2H, CH_2); 2.46 (m, 2H, CH_2); 2.61 (s, 3H, CH_3); 3.16 (m, 2H, CH_2); 7.55 (d, 2H, pyridyl-H); 8.76 (d, 2H, pyridyl-H), ^{13}C NMR: δ ppm: 12.93 (CH_3); 25.33–31.37 ($5CH_2$); 108.07 (C-5); 118.92 (CN); 123.32 (2CH, pyridyl-C); 128.01 (C-3); 131.19 (C-4″); 143.70 (C-4); 149.58 (2CH, pyridyl-C); 154.09 (C-6); 161.70 (=C-S-), $C_{17}H_{17}N_3S$ ($M^+ = 295$), Calcd: C, 69.15; H, 5.76; N, 14.23; S, 10.85%. Found: C, 68.87; H, 5.66; N, 14.52; S, 10.78%, **17f**: white, from EtOH, m.p. 203°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2225 (CN), UV: λ_{max}: 330.6, 280.2, $C_{17}H_{17}N_3S$, Calcd: C, 69.15; H, 5.76; N, 14.23; S, 10.85%. Found: C, 68.97; H, 5.59; N, 14.00; S, 10.75%, **17g**: white, from EtOH, m.p. 197°C, yield 85%, $C_{18}H_{19}N_3S$, Calcd: C, 69.90; H, 6.14; N, 13.59; S, 10.35%. Found: C, 69.55; H, 5.88; N, 13.91; S, 10.66%, **17h**: white, from EtOH, m.p. 201°C, yield 80%, $C_{18}H_{19}N_3S$, Calcd: C, 69.90; H, 6.14; N, 13.59; S, 10.35%, Found: C, 69.75; H, 5.78; N, 13.40; S, 10.45%, **24a**: white, from EtOH, m.p. 201°C, yield 70%, IR: ν_{max}/cm^{-1} (KBr): 2225, UV: λ_{max}: 360.6, 281.2,^{1}H NMR: δ ppm: 2.58 (m, 2H, CH_2); 2.61 (s, 3H, CH_3); 2.86 (m, 2H, CH_2); 7.33–7.52 (m, 4H, phenyl-H); 8.34 (d, 2H, pyridyl-H); 8.79 (d, 2H, pyridyl-H), ^{13}C NMR: δ ppm: 13.23 (CH_3); 24.28 (CH_2); 26.64 (CH_2); 104.094–154.29 (aromatic-C, CN, pyridyl-C); 159.0 (=C-S-), $C_{20}H_{15}N_3S$

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($M^+ = 329$), Calcd: C, 69.95; H, 6.10; N, 14.23; S, 10.85%. Found: C, 69.25; H, 5.68; N, 14.40; S, 10.96%, **24b**: white, from EtOH, m.p. 230°C, yield 80%, IR: ν_{max}/cm^{-1} (KBr): 2225 (CN), $C_{20}H_{15}N_3S$, Calcd: C, 69.95; H, 6.10; N, 14.23; S, 10.85%. Found: C, 69.25; H, 5.68; N, 14.40; S, 10.96%.

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