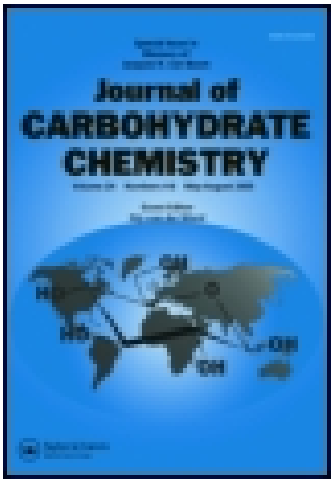

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First Synthesis of Thienopyrazole Thioglycosides

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First Synthesis of Thienopyrazole Thioglycosides

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Reported is the first method to prepare a new class of thienopyrazole thioglycosides via a one-pot reaction of the sodium thienopyrazolthiolate salts with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and galactopyranosyl bromides. The sodium thienopyrazolthiolate salts are prepared using pyrazoldithioic acids and their corresponding mono- and dithiolate salts.

Keywords Thienopyrazole thioglycosides, Sodium thienopyrazolthiolate salts, Pyrazoldithioic acids

There is a great interest in the synthesis of nucleosides due to their incorporation into DNA, RNA, protein, and all intracellular essential nucleotides. Chemical modification of nucleosides is an important approach to fight various infections and cancer. In recent reports from our laboratory, we described the preparation of different novel functionalized pyrimidine and pyridine thioglycosides, which revealed antagonistic activity against human carcinoma cells and HIV.[1–3] Earlier, we had reported the use of dihydropyridinethione glycosides as P-glycoprotein (Pgp) substrates or inhibitors of protein glycosylation.[4] These common features encouraged us to develop a new straightforward route for the synthesis of these compounds. Here, we describe the synthesis of thienopyrazole thioglycosides through reaction of sodium thienopyrazolthiolates with α-halogeno sugars. To our knowledge, this is the first thienopyrazole thioglycoside ring system to be reported. The

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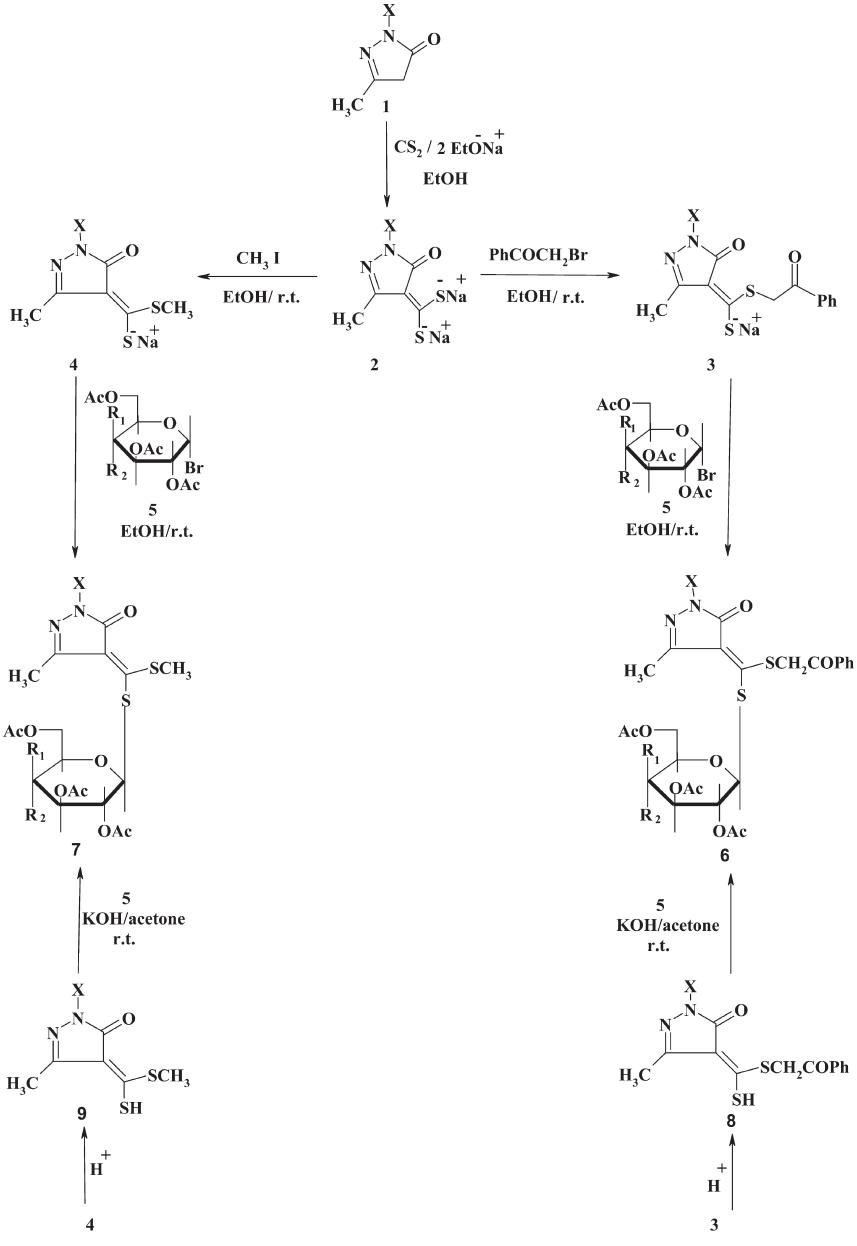
sequence of reactions followed in the preparation of the compounds is summarized in Charts 1 through 3. Thus, it has been found that pyrazolin-5-one **1** reacted with carbon disulfide in the presence of sodium ethoxide to afford the sodium dithiolate salts **2**. Compounds **2** were readily monoalkylated to give the stable sodium salts of monoalkylthio derivatives. Thus, one equivalent of phenacyl bromide or methyl iodide gave the corresponding sodium salts of monoalkylated products **3** or **4**, respectively. When neutralized with hydrochloric acid **3** and **4** gave the novel thiol products **8** and **9**. Compounds **3** and **4** reacted with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or galactopyranosyl bromides **5a**,**b** in ethanol at rt to give the corresponding *S*-glycosides **6** and **7** in high yields. These compounds were also prepared by the reaction of the thiols **8** and **9** with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or galacto-pyranosyl bromides **5** in KOH-acetone at rt for 12 h. The IR spectrum of **6a** revealed the presence of NH band at 3300 cm^{-1}, the mass spectrum showed a molecular formula $C_{27}H_{30}N_2O_{11}S_2$ ($M^+ = 622$), and the ^1H NMR spectrum indicated the anomeric proton as a doublet at δ 6.05 ppm with spin-spin coupling constant of 10.11 Hz, while the other six glucose protons resonated at δ 3.95 to 5.50 ppm. The four acetyl groups appeared as four singlets at δ 1.95 to 2.00 ppm. Furthermore, the ^{13}C NMR spectrum of **6a** represented a signal at δ 80.00 ppm corresponding to the C-1′ atom of the β-configuration.

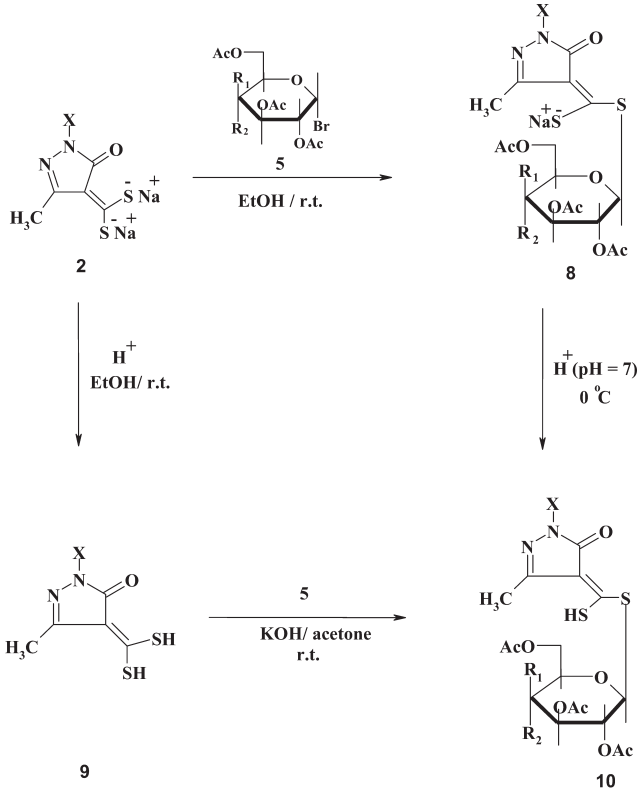
When compounds **2a**,**b** (Chart 2) were subjected to monoalkylation with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and galactopyranosyl bromides **5** they yielded compounds **8** that, upon neutralization to ph 7, yielded the glycoside thiols **10**. These compounds could also be prepared by alkylation of the dithiol derivatives **9** (obtained by neutralization of compound 2) with one equivalent of **5**. The structures of compounds **10** were established on the basis of their elemental analyses, MS, IR, and ^1H NMR spectroscopies. The mass spectrum of **10b** was compatible with the molecular formula $C_{19}H_{24}N_2O_{10}S_2$ ($M^+ = 580$). The ^1H NMR spectrum indicated the anomeric proton as a doublet at $\delta = 5.95$ ppm with spin-spin coupling constant of 10.11 Hz, while the other six galactose protons resonated at $\delta = 4.00$ to 5.40 ppm. The acetyl groups appeared as four singlets at $\delta = 1.90$ to 2.15 ppm. The synthetic pathways adopted for the preparation of our target thienopyrazole thioglycosides are illustrated in Chart 3. Compound **3** was cyclized in refluxing sodium ethoxide to give the corresponding sodium thieno[3,4-c]pyrazole-thiolate **11** that upon alkylation with halosugars **5** yielded the corresponding 2-(glycopyranosylthio)thienopyrazole derivatives **12**. When compound **3** was cyclized in refluxing sodium ethoxide followed by acidification it afforded the thienopyrazole-4-thiol **13**, which was coupled with halosugars **5** in KOH-acetone to yield also compounds **12**. The structures of the reaction products **12** were established and confirmed on the basis of their elemental analyses and spectral data (MS, IR, ^{1}HNMR, ^{13}CNMR). Thus, the mass spectrum of **12a** revealed a molecular formula of $C_{27}H_{28}N_2O_{10}S_2$ ($M^+ = 604$). The



1-9 X = H

6,7	X	R_1	R_2
a,	H	H	OAc
b,	H	OAc	H

Chart 1

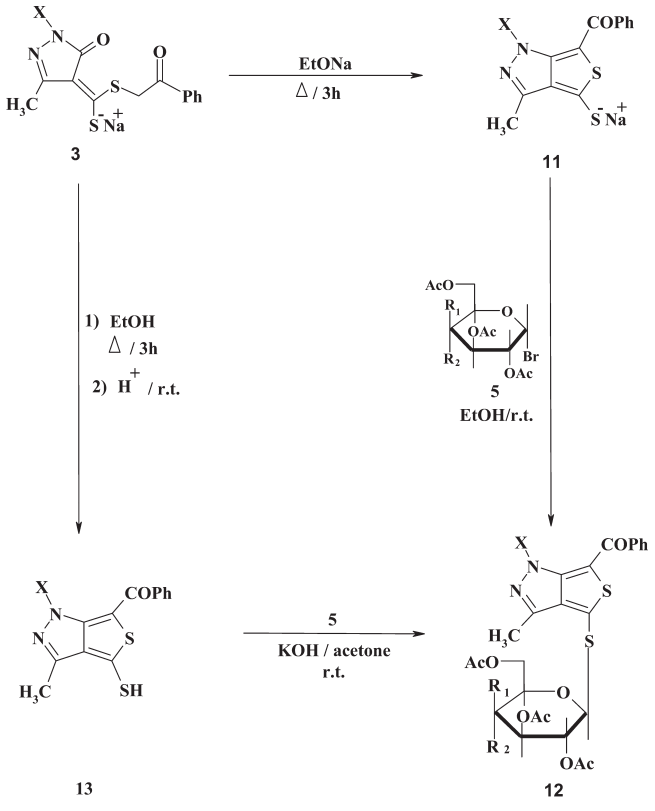


2,9	X
a,	H
b,	Ph

8,10	X	R_1	R_2
a,	H	H	OAc
b,	H	OAc	H
c,	Ph	H	OAc
d,	Ph	OAc	H

Chart 2

^{1}H NMR spectrum for **12b** showed the anomeric proton as a doublet at δ 5.90 ppm with a spin-spin coupling constant of 9.8 Hz, while the other six galactose protons resonated at δ 4.05 to 5.40 ppm and the four acetyl groups appeared as four singlets at δ 1.80 to 2.00 ppm.



11,13 X = H

12	X	R_1	R_2
a,	H	H	OAc
b,	H	OAc	H

Chart 3

EXPERIMENTAL

All melting points were uncorrected on a Gallenkamp melting point apparatus. The IR spectra were recorded (KBr disk) on a Perkin Elmer 1650 FT-IR instrument. The ^{1}H NMR spectra were measured on a Varian 400 MHz spectrometer for solution $(CD_3)_2SO$ using $Si(CH_3)_4$ as an internal standard. Mass spectra were recorded on a Varian MAT 112 spectrometer. Elemental analyses were obtained from the Microanalytical Data Center at Cairo University, Egypt.

Progress of the reactions was monitored by TLC using aluminum sheets coated with silica gel F254 (Merck). Viewing under a short-wavelength UV lamp effected detection. All evaporations were carried out under reduced pressure at 40°C.

Sodium 5-methylpyrazol-3-one-4-methylenedithiolates (2a,b)

General Procedure

A solution of pyrazolones **1a**,**b** (0.01 mol) and sodium ethoxide (0.46 g, 0.02 mol) in absolute ethanol (20 mL) was refluxed for 20 min. The reaction mixture was cooled to rt; carbon disulphide (0.01 mol) was added. The reaction mixture was stirred at rt for 30 min, and then the solution was evaporated and the formed solid product was collected by filtration.

Sodium 5-methylpyrazol-3-one-4-((2-oxo-2-phenylethyl)thio)methyl-enethiolates (3a,b)

General Procedure

A solution of compounds **2a**,**b** (0.01 mol) and phenacyl bromide (1.98 g, 0.01 mol) in ethanol (20 mL) was stirred at rt for 2 h, the solution was evaporated, and the formed solid product was collected and recrystallized from methanol.

Sodium 5-methylpyrazol-3-one-4-(methylthio) methylenethiolates (4a,b)

General Procedure

A solution of compounds **2a**,**b** (0.01 mol) and methyl iodide (0.01 mol) in ethanol (20 mL) was stirred at rt for 2 h, the solution was evaporated, and the formed solid product was collected by filtration.

(4Z)-4-{mercapto((2-oxo-2-phenylethyl)thio)methylene}-5-methyl-pyrazol-3-ones (8a,b)

General Procedure

A solution of compounds **3a**,**b** in ethanol (20 mL) was poured on cold water and treated with hydrochloric acid until just acidic and the formed solid products **8a**,**b** were collected by filtration and recrystallized from ethanol.

4-[Mercapto(methylthio)methylene]-5-methylpyrazol-3-ones (8a,b)

General Procedure

A solution of compounds **4a**,**b** in ethanol (20 mL) was poured on cold water and treated with hydrochloric acid until just acidic and the formed solid products **9a**,**b** were collected by filtration and recrystallized from ethanol.

(4*E*)-5-methyl-4-{[(2-oxo-2-phenylethyl)thio](2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco or galactopyranosylthio)methylene}-2,4-dihydro-3*H*-pyrazol-3-ones (6a,b)

General Procedure

Method A

To a solution of compound **3a** (3.14 g, 0.01 mol) in ethanol (30 mL), a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco or galactopyranosyl bromide **5a**,**b** (4.10 g, 0.01 mol) in acetone (20 mL) was added. The reaction mixture was stirred at rt until completion (TLC, 16 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the sodium bromide formed. The resulting product was recrystallized from ethanol.

Method B

A solution of compound **8a** (2.92 g, 0.01 mol) in aqueous potassium hydroxide [0.56 g (0.01 mol) in distilled water (6 mL)] was added to a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or galactopyranosyl bromide **5a**,**b** (4.10 g, 0.01 mol) in acetone (30 mL). The reaction mixture was stirred at rt until completion (TLC, 16 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the formed potassium bromide salt. The resulting product was recrystallized from ethanol.

6a: brown, m.p. 213°C (from EtOH), yield (65% method A, 75% method B). IR (KBr) ν_{max}/cm^{-1} 3300 (NH), 1750 (CO), 1690 (CO). ^{1}H NMR (DMSO) δ 1.95–2.00 (4s, 12H, 4 × CH_3CO), 2.40 (s, 3H, CH_3), 2.90 (s, 1H, OH), 3.95–4.15 (m, 3H, 6′-H_2, 5′-H), 4.25 (t, 1H, 4′-H), 4.90 (s, 2H, CH_2), 5.10 (t, 1H, 3′-H), 5.50 (t, 1H, 2′-H), 6.05 (d, 1H, 1′-H), 7.50–8.10 (m, 5H, C_6H_5). ^{13}C NMR (DMSO) δ 14.93 (Ar-CH_3), 20.72–20.87 (4 × CH_3), 42.35 (SCH_2), 61.83 (CH_2, C-6′), 66.42 (C-4′), 68.26 (C-2′), 71.05 (C-3′), 71.52 (C-5′), 72.47 (C-1′), 129.00–156.00 (aromatic carbons), 160.00 (=C-S), 165.00–185.00 (6 × CO). $C_{27}H_{30}N_2O_{11}S_2$, Calcd: C, 52.07; H, 4.86; N, 4.50. Found: C, 52.29; H, 4.83; N, 4.85%.

6b: Brown, m.p. 230°C (from EtOH), yield (68% method A, 76% method B). IR (KBr) ν_{max}/cm^{-1} 3200 (NH), 1751 (CO), 1681 (CO). ^{1}H NMR (DMSO) δ 1.90–2.20 (4s, 12H, 4 × CH_3CO), 2.45 (s, 3H, CH_3), 4.00–4.10 (m, 3H,

6′-H_2, 5′-H), 4.45 (t, 1H, 4′-H), 4.95 (s, 2H, CH_2), 5.25–5.45 (m, 2H, 3′-H, 2′-H), 6.00 (d, 1H, 1′-H), 7.40–8.10 (m, 5H, C_6H_5). ^{13}C NMR (DMSO) δ 14.93 (Ar-CH_3), 20.70–20.87 (4 × CH_3), 42.36 (SCH_2), 61.41 (CH_2, C-6′), 67.65 (C-4′), 68.60 (C-2′), 70.63 (C-3′), 70.81 (C-5′), 80.00 (C-1′), 128.00–146.00 (aromatic carbons), 160.15 (=C-S), 165.21–183.00 (6 × CO). $C_{27}H_{30}N_2O_{11}S_2$, Calcd: C, 52.07; H, 4.86; N, 4.50. Found: C, 51.85; H, 5.03; N, 4.51%.

5-Methyl-4-[(methylthio)(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco or gala-ctopyranosylthio)methylene]-2,4-dihydro-3*H*-pyrazol-3-ones (7a,b)

General Procedure

Method A

To a solution of compound **4a** (2.10 g, 0.01 mol) in ethanol (30 mL), a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco or galactopyranosyl bromide **5a**,**b** (4.10 g, 0.01 mol) in acetone (20 mL) was added. The reaction mixture was stirred at rt until completion (TLC, 13 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the sodium bromide formed. The resulting product was recrystallized from ethanol.

Method B

A solution of compounds **9a** (1.88 g, 0.01 mol) in aqueous potassium hydroxide [0.56 g (0.01 mol) in distilled water (6 mL)] was added to a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or galactopyranosyl bromide **5a**,**b** (4.10 g, 0.01 mol) in acetone (30 mL). The reaction mixture was stirred at rt until completion (TLC, 13 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the formed potassium bromide. The resulting product was recrystallized from ethanol.

7a: yellow, m.p. 192°C (from EtOH), yield (70% method A, 78% method B). IR (KBr) ν_{max}/cm^{-1} 3371 (NH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.90–2.10 (4s, 12H, 4 × CH_3CO), 2.45 (s, 1H, OH), 2.60 (s, 3H, CH_3), 2.65 (s, 3H, SCH_3), 3.90–4.05 (m, 3H, 6′-H_2, 5′-H), 4.20 (t, 1H, 4′-H), 5.05 (t, 1H, 3′-H), 5.45 (t, 1H, 2′-H), 6.00 (d, 1H, 1′-H). ^{13}C NMR (DMSO) δ 13.92 (Ar-CH_3), 15.66 (S-CH_3), 18.83–20.84 (4 × CH_3), 59.91 (CH_2, C-6′), 68.48 (C-4′), 71.10 (C-2′), 71.48 (C-3′), 73.01 (C-5′), 74.53 (C-1′), 113.00 (C-4), 143.74 (C-5), 144.68 (C-3 enol form), 160.15 (=C-S), 169.21–169.52 (4 × CO). $C_{20}H_{26}N_2O_{10}S_2$, Calcd: C, 46.31; H, 5.06; N, 5.40. Found: C, 46.70; H, 5.14; N, 5.42%.

7b: Yellow, m.p. 145°C (from EtOH), yield (69% method A, 77% method B). IR (KBr) ν_{max}/cm^{-1} 3340 (NH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.90–2.15 (4s, 12H, 4 × CH_3CO), 2.45 (s, 1H, OH), 2.60 (s, 3H, CH_3), 2.65 (s, 3H, SCH_3), 4.05–4.15 (m, 3H, 6′-H_2, 5′-H), 4.45 (t, 1H, 4′-H), 5.30–5.45 (m, 2H, 3′ - H -2′-H), 5.90 (d, 1H, 1′-H). ^{13}C NMR (DMSO) δ 14.52 (Ar-CH_3), 18.05 (S-CH_3), 18.87–

20.85 (4 × CH_3), 61.39 (CH_2, C-6′), 64.89 (C-4′), 67.42 (C-2′), 68.87 (C-3′), 70.97 (C-5′), 71.08 (C-1′), 113.81 (C-4), 144.63 (C-5), 160.00 (=C-S), 165.00 (NHCO), 169.24–170.32 (4 × CO). $C_{20}H_{26}N_2O_{10}S_2$, Calcd: C, 46.31; H, 5.06; N, 5.40. Found: C, 46.38; H, 5.31; N, 5.85%.

Sodium 5-methyl-3-one-pyrazole-4-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco or galactopyranosylthio)methylenethiolates (8a–d)

General Procedure

To a solution of compounds **2a**,**b** (0.01 mol) in ethanol (30 mL), a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco or galactopyranosyl bromide **5a**,**b** (4.10 g, 0.01 mol) in acetone (20 mL) was added. The reaction mixture was stirred at rt until completion (TLC, 12 h) and then evaporated under reduced pressure, and the product was separated by filtration.

8a: yellow, m.p. >300°C (from EtOH), yield (74%). IR (KBr) ν_{max}/cm^{-1} 3417 (NH), 1751 (CO), 1596 (C=C). $C_{19}H_{23}N_2O_{10}S_2Na$.

8b: yellow, m.p. >300°C (from EtOH), yield (73%). IR (KBr) ν_{max}/cm^{-1} 3417 (NH), 1743 (CO), 1596 (C=C). $C_{19}H_{23}N_2O_{10}S_2Na$.

8c: yellow, m.p. >300°C (from EtOH), yield (82%). IR (KBr) ν_{max}/cm^{-1} 1751 (CO), 1612 (C=C). $C_{25}H_{27}N_2O_{10}S_2Na$.

8d: yellow, m.p. >300°C (from EtOH), yield (81%). IR (KBr) ν_{max}/cm^{-1} 1743 (CO), 1620 (C=C). $C_{25}H_{27}N_2O_{10}S_2Na$.

4-(Dimercaptomethylene)-5-methyl-pyrazol-3-ones (9a,b)

General Procedure

A solution of compound **2a**,**b** in ethanol(20 mL) was poured on cold water and treated with hydrochloric acid until just acidic and the formed solid product **9a**,**b** was collected by filtration and recrystallized from ethanol.

4-[Mercapto(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco or galactopyrano-sylthio)methylene]-5-methyl-pyrazol-3-ones (10a–d)

General procedures

Method A

A solution of compounds **8a**–**d** (0.01 mol) in ethanol (30 mL) was poured on ice-cooled water and the medium was adjusted to pH 7 using dilute acetic acid,

and the formed solid product **10a–d** was collected by filtration and recrystallized from ethanol.

Method B

A solution of compounds **9a**,**b** (0.01 mol) in aqueous potassium hydroxide [0.56 g (0.01 mol) in distilled water (6 mL)] was added to a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or galactopyranosyl bromide **5a**,**b** (4.10 g, 0.01 mol) in acetone (30 mL). The reaction mixture was stirred at rt until completion (TLC, 15 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the formed potassium bromide. The resulting product was recrystallized from ethanol.

10a: yellow, m.p. 110°C (from EtOH), yield (70% method A, 77% method B). IR (KBr) ν_{max}/cm^{-1} 3200 (NH), 2507 (SH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.95–2.00 (4s, 12H, 4 × CH_3CO), 2.45 (s, 3H, CH_3), 4.00–4.20 (m, 3H, 6′-H_2, 5′-H), 4.95 (t, 1H, 4′-H), 5.20 (t, 1H, 3′-H), 5.40 (t, 1H, 2′-H), 5.95 (d, 1H, 1′-H). ^{13}C NMR (DMSO) δ 15.92 (Ar-CH_3), 20.65–20.87 (4 × CH_3), 61.97 (CH_2, C-6′), 68.37 (C-4′), 68.81 (C-2′), 73.92 (C-3′), 75.25 (C-5′), 81.91 (C-1′), 116.00 (C-4), 147.00 (C-5), 160.10 (C-S), 165.00 (NHCO), 169.45–170.29 (4 × CO). $C_{19}H_{24}N_2O_{10}S_2$, Calcd: C, 45.22; H, 4.80; N, 5.55. Found: C, 45.00; H, 4.76; N, 5.35%.

10b: Yellow, m.p. 155°C (from EtOH), yield (73% method A, 80% method B). IR (KBr) ν_{max}/cm^{-1} 3209 (NH), 2550 (SH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.90–2.15 (4s, 12H, 4 × CH_3CO), 2.45 (s, 3H, CH_3), 4.00–4.10 (m, 3H, 6′-H_2, 5′-H), 4.30 (t, 1H, 4′-H), 5.30–5.40 (m, 2H, 3′-H, 2′-H), 5.95 (d, 1H, 1′-H). ^{13}C NMR (DMSO) δ 15.91 (Ar-CH_3), 20.69–20.89 (4 × CH_3), 61.94 (CH_2, C-6′), 66.22 (C-4′), 68.01 (C-2′), 71.73 (C-3′), 74.33 (C-5′), 82.28 (C-1′), 115.00 (C-4), 145.00 (C-5), 160.15 (C-S), 165.00 (NHCO), 169.66–170.33 (4 × CO). $C_{19}H_{24}N_2O_{10}S_2$, Calcd: C, 45.22; H, 4.80; N, 5.55. Found: C, 45.21; H, 4.59; N, 5.51%.

10c: Yellow, m.p. 165°C (from EtOH), yield (82% method A, 88% method B). IR (KBr) ν_{max}/cm^{-1} 3020 (CH, aromatic), 2939 (CH, aliphatic), 2507 (SH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.90–2.00 (4s, 12H, 4 × CH_3CO), 2.55 (s, 3H, CH_3), 4.00 (s, 2H, 6′-H), 4.15 (m, 1H, 5′-H), 4.95 (t, 1H, 4′-H), 5.20 (t, 1H, 3′-H), 5.35 (t, 1H, 2′-H), 6.10 (d, 1H, 1′-H), 7.20–7.80 (m, 5H, C_6H_5). ^{13}C NMR (DMSO) δ 18.21 (Ar-CH_3), 20.67–20.89 (4 × CH_3), 62.04 (CH_2, C-6′), 68.49 (C-4′), 68.92 (C-2′), 74.27 (C-3′), 75.14 (C-5′), 81.30 (C-1′), 120.12–150.00 (aromatic and heteroaromatic carbons), 159.00 (C-S), 162.00 (NHCO), 169.38–169.65 (4 × CO). $C_{25}H_{28}N_2O_{10}S_2$, Calcd: C, 51.70; H, 4.82; N, 4.87. Found: C, 51.99; H, 5.26; N, 4.47%.

10d: Yellow, m.p. 108°C (from EtOH), yield (81% method A, 87% method B). IR (KBr) ν_{max}/cm^{-1} 3020 (CH, aromatic), 2962 (CH, aliphatic), 2507 (SH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.90–2.10 (4s, 12H, 4 × CH_3CO), 2.60 (s, 3H, CH_3),

4.00 (s, 2H, 6′-H), 4.30 (m, 1H, 5′-H), 5.00 (t, 1H, 4′-H), 5.35 (m, 2H, 3′-H, 2′-H), 6.05 (d, 1H, 1′-H), 7.20–7.80 (m, 5H, C_6H_5). $C_{25}H_{28}N_2O_{10}S_2$, Calcd: C, 51.70; H, 4.82; N, 4.87. Found: C, 51.08; H, 5.46; N, 4.85%.

Sodium 3-methyl-1*H*-thieno(3,4-c)pyrazol-6-yl-(phenyl)methanone-4-thiolate (11)

General Procedure

A solution of compound **3** (0.01 mol) and sodium ethoxide (0.01 mol) in ethanol (20 mL) was refluxed for 3 h, the solution was evaporated, and the formed solid product was collected by filtration.

(4-Mercapto-3-methyl-1*H*-thieno(3,4-c)pyrazol-6-yl) (phenyl)methan-one (13)

General Procedure

A solution of compound **3** in (20 mL) ethanol was poured on cooled water acidified with hydrochloric acid, and the formed solid product **13** was collected by filtration and recrystallized from ethanol.

(3-Methyl-4-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco- and galacto-pyranosyl-thio)-1*H*-thieno(3,4-c)pyrazol-6-yl) (phenyl)methanones (12a,b)

General Procedures

Method A

To a solution of compound **1** (0.01 mol) in ethanol (30 mL), a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco or galactopyranosyl bromide **5a,b** (4.10 g, 0.01 mol) in acetone 20 mL was added. The reaction mixture was stirred at rt until completion (TLC, 14 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the sodium bromide formed. The resulting product was recrystallized from ethanol.

Method B

A solution of compounds **13** (0.01 mol) in aqueous potassium hydroxide [0.56 g (0.01 mol) in distilled water (6 mL)] was added to a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- or galactopyranosyl bromide **5a**,**b** (4.10 g, 0.01 mol) in acetone (30 mL). The reaction mixture was stirred at rt until completion (TLC, 14 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the formed potassium bromide. The resulting product was crystallized from ethanol.

12a: brown, m.p. 160°C (from EtOH), yield (75% method A, 80% method B). IR (KBr) ν_{max}/cm^{-1} 3201 (NH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.90–2.00 (4s, 12H, 4 × CH_3CO), 2.10 (s, 3H, CH_3), 3.90 (m, 3H, 6′-H_2, 5′-H), 4.20 (t, 1H, 4′-H), 4.95 (t, 1H, 3′-H), 5.50 (t, 1H, 2′-H), 5.90 (d, 1H, 1′-H), 7.10–8.10 (m, 5H, C_5H_4). $C_{27}H_{28}N_2O_{10}S_2$, Calcd: C, 53.62; H, 4.67; N, 4.63. Found: C, 53.12; H, 4.84; N, 4.95%.

12b: Brown, m.p. 205°C (from EtOH), yield (77% method A, 85% method B). IR (KBr) ν_{max}/cm^{-1} 3193 (NH), 1751 (CO). ^{1}H NMR (DMSO) δ 1.80–2.00 (4s, 12H, 4 × CH_3CO), 2.10 (s, 3H, CH_3), 4.05 (s, 2H, 6′-H), 4.60 (m, 1H, 5′-H), 4.95 (t, 1H, 4′-H), 5.20–5.40 (m, 2H, 3′-H, 2′-H), 5.95 (d, 1H, 1′-H), 7.00–8.10 (m, 5H, C_6H_5). $C_{27}H_{28}N_2O_{10}S_2$, Calcd: C, 53.62; H, 4.67; N, 4.63. Found: C, 53.57; H, 4.22; N, 4.70%.

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