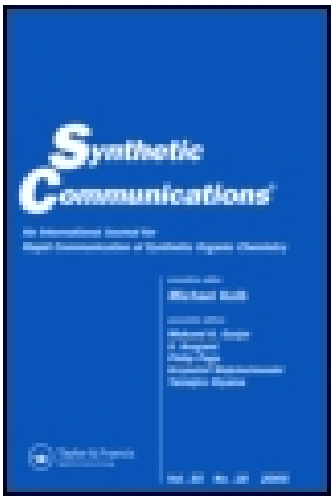

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Design and Synthesis of the First Thiophene Thioglycosides

Galal H. Elgemeie [a], Shahinaz H. Elsayed [a] & Ashraf S. Hassan [a]

[a] Faculty of Science, Chemistry Department, Helwan University, Ain-Helwan, Helwan, Egypt

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Design and Synthesis of the First Thiophene Thioglycosides

Galal H. Elgemeie, Shahinaz H. Elsayed, and Ashraf S. Hassan
Faculty of Science, Chemistry Department, Helwan University, Ain-Helwan, Helwan, Egypt

Abstract: A novel reported method for preparation of the first thiophene thioglycosides via a one-pot reaction of sodium thiophenethiolate salts with 2,3,4,6-tetra-*O*-acetyl-α-*D*-gluco- and galactopyranosyl bromides has been studied. The sodium thiophenethiolate salts were prepared using sodium cyanoethylene thiolate salts.

Keywords: Glycosides, halo sugars, sodium cyanoethylene thiolate salts, thiophene thioglycosides

Thio-sugars have recently received interest as potential new therapeutics.[1] Thus, new developments in the synthetic and medicinal chemistry of thio-sugars are important for carbohydrate drug design.[2,3] In recent reports from our laboratory, we described the preparation of different novel functionalized pyridine thioglycosides, which revealed antagonistic activity.[4,5] In an earlier brief communication, we had already reported the use of dihydropyridine thioglycosides as substrates or inhibitors in the protein glycosylation process.[6] These common features encouraged us to develop a new straightforward route for synthesis of heterocyclic thioglycosides. In the present report, we describe the synthesis of thiophene thioglycosides through reaction of sodium thiophenethiolates with α-halogeno sugars. As far as we know, this is the first thiophene thioglycoside ring system to be reported in the literature.

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Address correspondence to Galal H. Elgemeie, Faculty of Science, Chemistry Department, Helwan University, Ain-Helwan, Helwan, Egypt. E-mail: elgemeie@yahoo.com

It has been found that reaction of malononitrile **1a** or ethyl cyanoacetate **1b** with carbon disulfide in the presence of sodium ethoxide gives the sodium dithiolate salts **2a,b**. Compounds **2** are readily monoalkylated with 1 equivalent of phenacyl bromide or methyl iodide to give the corresponding sodium salts of monoalkylated products **3** and **4** in good yields. On acidification with hydrochloric acid, compounds **3** and **4** gave the novel mercapto products **6** and **7**, respectively. The structure of compounds **6** and **7** were established on the basis of their elemental analysis and spectral data infrared (IR), mass spectra (MS), and ^{1}H NMR). Compounds **3** and **4** reacted with 2,3,4,6-tetra-*O*-acetyl-α-*D*-gluco- and galactopyranosyl bromides **5a,b** in ethanol at room temperature to give the corresponding *S*-glycosides **8a,b** and **9a,b**, respectively, in high yields. Compounds **8** and **9** could also be prepared by the reaction of the thiols **6** and **7** with **5a,b** in potassium hydroxide (KOH)–acetone at room temperature for 15 h. We have hypothesized that the *cis*-(α) sugars react by a simple Sn_2 reaction to give the β-glycoside products.[7] The structure of the reaction products **8** and **9** were established and confirmed by their elemental analysis and spectral data (IR and ^{1}H NMR). Structure **8a** is supported by its mass spectrum, its IR spectrum reveals the presence of a CN band at 2224 cm^{-1} and CO band at 1753 cm^{-1}, and its ^{1}H NMR spectrum shows the anomeric proton as a doublet at δ 5.43 ppm with a spin–spin coupling constant of 11.6 Hz, indicating the β-configuration. The sodium α-cyanoketene thiolates **3** were cyclized by heating under reflux in sodium ethoxide to give the corresponding sodium thiophenethiolates **10** and subsequently the novel 2-mercaptothiophenes **11**. The structures of compounds **11** were established on the basis of their elemental analysis and spectral data (MS, IR, and ^{1}H NMR). Upon alkylation with halogenosugars **5**, compounds **10** yielded the corresponding 2-(glycopyranosylthio)thiophene derivative **12**. Attempted preparation of **12** through the reaction of thiophene-2-thiols **11** with halogenosugars **5** in KOH–acetone was also successful in our hands. The structures of the reaction products **12** were established and confirmed on the basis of their elemental analysis and spectral data (IR and ^{1}H NMR). Thus, the ^{1}H NMR spectrum for **12a** showed the anomeric proton as a double at δ 5.44 ppm with a spin–spin coupling constant of 10.6 Hz, which corresponds to the diaxial orientation of H-1′ and H-2′ protons, indicating the β-configuration, whereas the other six glucose protons resonated at δ 3.87–5.33 ppm. The four-acetyl groups appeared as four singlets at δ 1.92–2.05 ppm.

In summary, we have achieved a novel synthesis of interesting thiophene thioglycosides by the reaction of the sodium thiophenethiolates with α-halogenosugars. These glycosides are excellent starting materials for the synthesis of other carbohydrate derivatives and for biological evaluation studies.

EXPERIMENTAL

All melting points were measured on a Gallenkamp melting-point apparatus. The IR spectra were recorded (KBr disk) on a Perkin-Elmer 1650 Fourier transform (FT)–IR instrument. The ^{1}H NMR spectra were measured on a Varian 400-MHz spectrometer for solutions in dimethyl sulfoxide (DMSO-d_6) 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 thin-layer chromatography (TLC) using aluminum sheets coated with silica gel F254 (Merck). Viewing under a short-wavelength ultraviolet (UV) lamp effected detection. All evaporations were carried out under reduced pressure at 40°C.

Sodium 1-Cyano-2-[(2-oxo-2-phenylethyl)thio]ethylene-2-thiolate (3a,b)

General Procedure

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

Data

Compound **3a**: Yellow, mp > 300°C (EtOH), yield (79%). IR (KBr) ν_{max}/cm^{-1} 2202 (CN), 1641 (CO). $C_{12}H_7N_2S_2ONa$.

Compound **3b**: Yellow, mp > 300°C (EtOH), yield (75%). IR (KBr) ν_{max}/cm^{-1} 2187 (CN), 1670 (CO). $C_{14}H_{12}NS_2O_3Na$.

Sodium 1-Cyano-2-methylthioethylene-2-thiolate (4a,b)

General Procedure

A solution of compounds **2a,b** (0.01 mol) and methyl iodide (1.4 g, 0.01 mol) in methanol (30 ml) was stirred at rt for 2 h. The solution was evaporated, and the formed solid product was collected by filtration.

Data

Compound **4a**: Yellow, mp > 300°C (EtOH), yield (85%). IR (KBr) ν_{max}/cm^{-1} 2220 (CN). $C_5H_3N_2S_2Na$.

Compound **4b**: Yellow, mp > 300°C (EtOH), yield (80%). IR (KBr) ν_{max}/cm^{-1} 2215 (CN), 1730 (CO). $C_7H_8NS_2O_2Na$.

1-Cyano-2-mercapto-2-[(2-oxo-2-phenylethyl)thio]ethylene (6a,b)

General Procedure

A solution of compounds **3a,b** in 20 ml ethanol was acidified with hydrochloric acid until it was neutral, and the formed solid product was collected by filtration.

Data

Compound **6a**: Orange, mp 165°C (EtOH), yield (82%). IR (KBr) ν_{max}/cm^{-1} 2222 (CN), 1627 (CO). ^{1}H NMR (DMSO) δ 4.35 (s, 2H, SCH_2), 7.49–7.73 (m, 5H, C_6H_5), 8.71 (s, 1H, SH). $C_{12}H_8N_2S_2O$ ($M^+ = 260$) calcd.: C, 55.38; H, 3.07; N, 10.76. Found: C, 55.2; H, 3.0; N, 10.4%.

Compound **6b**: Yellow, mp 160°C (EtOH), yield (79%). IR (KBr) ν_{max}/cm^{-1} 2211 (CN), 1720 (CO), 1694 (CO). ^{1}H NMR (DMSO) δ 1.35 (t, 3H, CH_3), 4.00 (q, 2H, CH_2), 4.33 (s, 2H, SCH_2), 7.12–7.65 (m, 5H, C_6H_5), 9.56 (s, 1H, SH). $C_{14}H_{13}NS_2O_3$ ($M^+ = 307$) calcd.: C, 54.70; H, 4.26; N, 4.55. Found: C, 54.5; H, 4.0; N, 4.3%.

1-Cyano-2-mercapto-2-methylthioethylene (7a,b)

General Procedure

A solution of compounds **4a,b** in 20 ml ethanol was acidified with hydrochloric acid until it was neutral, and the formed solid product was collected by filtration.

Data

Compound **7a**: Orange, mp 100°C (EtOH), yield (77%). IR (KBr) ν_{max}/cm^{-1} 2210 (CN). ^{1}H NMR (DMSO) δ 2.65 (s, 3H, SCH_3), 10.71 (s, 1H, SH). $C_5H_4N_2S_2$ ($M^+ = 156$), calcd.: C, 38.44; H, 2.58; N, 17.92. Found: C, 38.1; H, 2.2; N, 17.8%.

Compound **7b**: Orange, mp 80°C (EtOH), yield (82%). IR (KBr) ν_{max}/cm^{-1} 2211 (CN), 1720 (CO). ^{1}H NMR (DMSO) δ 1.22 (t, 3H, CH_3), 2.77 (s, 3H, SCH_3), 4.09 (q, 2H, CH_2), 11.67 (s, 1H, SH). $C_7H_9NS_2O_2$ ($M^+ = 203$), calcd.: C, 41.35; H, 4.46; N, 6.89. Found: C, 41.2; H, 4.1; N, 6.6%.

1-Cyano-2-[(2-oxo-2-phenylethyl)thio]-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco- or Galactopyranosylthio)ethylene (8a–d)

Method A

To a solution of compounds **3** (0.01 mol) in ethanol (30 ml), a solution of **5a,b** (4.10 g, 0.01 mol) in acetone (20 ml) was added. The reaction mixture was stirred at rt until completion (TLC, $CHCl_3$–CH_3OH, 9:1, 15 h) then evaporated under reduced pressure, and the residue was washed with distilled water to remove the formed sodium bromide. The resulting products were crystallized from ethanol.

Method B

A solution of compounds **6** (0.01 mol) in aq. potassium hydroxide [0.56 g (0.01 mol) in distilled water (6 ml)] was added to a solution of **5a,b** (4.10 g, 0.01 mol) in acetone (30 ml). The reaction mixture was stirred at rt until completion (TLC, $CHCl_3$–CH_3OH, 9:1, 15 h) then evaporated under reduced pressure, and the residue was washed with distilled water to remove the formed potassium bromide. The resulting products were crystallized from ethanol.

Data

Compound **8a**: Yellow, mp 100°C (EtOH), yield (84%). IR (KBr) ν_{max}/cm^{-1} 2224 (CN), 1753 (CO), 1635 (CO). ^1H NMR (DMSO) δ 1.91–2.03 (4s, 12H, $4CH_3CO$), 3.90 (s, 2H, SCH_2), 4.06–4.08 (m, 2H, 2H-6′), 4.85 (t, 1H, H-5′), 4.88–4.91 (m, 2H, H-4′ and H-3′), 5.34 (t, 1H, H-2′), 5.43 (d, $J_{1'\text{-}2'}$ 11.6 Hz, 1H, H-1′), 7.48–7.74 (m, 5H, C_6H_5). ^{13}C NMR δ 18.0–20.0 ($4 \times CH_3$), 50.6 (CH_2), 60.9 (CH_2, C-6′), 65.2 (C-4′), 66.8 (C-2′), 73.3 (C-3′), 73.4 (C-5′), 83.9 (C-1′), 110.0 (CN), 115.0 (CN), 120.2–141.9 (C_6H_5), 155.5 (C-2), 160.4 (C-3), 168.3–185.4 ($5 \times CO$). $C_{26}H_{26}N_2S_2O_{10}$ ($M^+ = 590$) calcd.: C, 52.87; H, 4.43; N, 4.74. Found: C, 52.7; H, 4.3; N, 4.6%.

Compound **8b**: Yellow, mp 90°C (EtOH), yield (82%). IR (KBr) ν_{max}/cm^{-1} 2215 (CN), 1735 (CO), 1670 (CO). ^1H NMR (DMSO) δ 1.19 (t, 3H, CH_3), 1.87–2.00 (4s, 12H, $4CH_3CO$), 3.79 (s, 2H, SCH_2), 3.92 (q, 2H, CH_2), 4.12–4.18 (m, 2H, 2H-6′), 4.76 (t, 1H, H-5′), 4.91–4.99 (m, 2H, H-4′ and H-3′), 5.55 (t, 1H, H-2′), 5.87 (d, $J_{1'\text{-}2'}$ 11.6 Hz, 1H, H-1′), 7.39–7.70 (m, 5H, C_6H_5).^{13}C NMR δ 19.7–21.8 ($5 \times CH_3$), 53.0 (SCH_2), 58.3 (OCH_2), 62.3 (CH_2, C-6′), 66.0 (C-4′), 69.1 (C-2′),

71.3 (C-3′), 74.0 (C-5′), 81.7 (C-1′), 111.0 (CN), 119.0–138.5 (C_6H_5), 150.5 (C-2), 163.9 (C-3), 169.0–179.2 ($6 \times CO$). $C_{28}H_{31}NS_2O_{12}$ ($M^+ = 637$) calcd.: C, 52.74; H, 4.90; N, 2.19. Found: C, 52.6; H, 4.8; N, 2.0%.

Compound **8c**: Orange, mp 95°C (EtOH), yield (80%). IR (KBr) ν_{max}/cm^{-1} 2207 (CN), 1743 (CO), 1597 (CO). ^1H NMR (DMSO) δ 1.88–2.00 (4s, 12H, $4CH_3CO$), 3.87 (s, 2H, CH_2), 4.00–4.10 (m, 2H, 2H-6′), 4.66 (t, 1H, H-5′), 4.80–4.95 (m, 2H, H-4′ and H-3′), 5.21 (t, 1H, H-2′), 5.40 (d, $J_{1'-2'}$ 11.0 Hz, 1H, H-1′), 7.22–7.70 (m, 5H, C_6H_5). ^{13}C NMR δ 18.9–20.5 ($4 \times CH_3$), 52.2 (SCH_2), 61.5 (CH_2, C-6′), 67.0 (C-4′), 69.2 (C-2′), 71.6 (C-3′), 75.0 (C-5′), 81.5 (C-1′), 110.8 (CN), 115.9 (CN), 119.0–138.9 (C_6H_5), 153.0 (C-2), 161.0 (C-3), 165.0–183.0 ($5 \times CO$). $C_{26}H_{26}N_2S_2O_{10}$ ($M^+ = 590$) calcd.: C, 52.87; H, 4.43; N, 4.74. Found: C, 52.7; H, 4.4; N, 4.7%.

Compound **8d**: Yellow, mp 100°C (EtOH), yield (78%). IR (KBr) ν_{max}/cm^{-1} 2213 (CN), 1752 (CO), 1668 (CO). ^1H NMR (DMSO) δ 1.15 (t, 3H, CH_3), 1.80–2.08 (4s, 12H, $4CH_3CO$), 3.70 (s, 2H, SCH_2), 3.90 (q, 2H, CH_2), 4.10–4.20 (m, 2H, 2H-6′), 4.66 (t, 1H, H-5′), 4.70–4.96 (m, 2H, H-4′ and H-3′), 5.60 (t, 1H, H-2′), 5.80 (d, $J_{1'-2'}$ 11.2 Hz, 1H, H-1′), 7.49–7.79 (m, 5H, C_6H_5).^{13}C NMR δ 19.0–21.0 ($5 \times CH_3$), 51.9 (CH_2), 56.7 (OCH_2), 61.9 (CH_2, C-6′), 66.7 (C-4′), 69.8 (C-2′), 71.5 (C-3′), 74.9 (C-5′), 80.0 (C-1′), 115.6 (CN), 118.5–139.2 (C_6H_5), 153.4 (C-2), 164.0 (C-3), 167.5–175.7 ($6 \times CO$). $C_{28}H_{31}NS_2O_{12}$ ($M^+ = 637$) calcd.: C, 52.74; H, 4.90; N, 2.19. Found: C, 52.6; H, 4.8; N, 2.1%.

1-Cyano-2-methylthio-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-Gluco- or Galactopyranosylthio)ethylene (9a–d)

Method A

Compounds **4a**–**b** (0.01 mol) were treated as described for the preparation of **8a**–**d**.

Method B

Compounds **7a**–**b** (0.01 mol) were treated as described for the preparation of **8a-d**. The reaction was completed within 12 h (TLC, $CHCl_3$–CH_3OH, 9:1).

Data

Compound **9a**: Orange, mp 98°C (EtOH), yield (76%). IR (KBr) ν_{max}/cm^{-1} 2209 (CN), 1735 (CO). ^1H NMR (DMSO) δ 1.20 (t, 3H, CH_3), 1.97–2.13 (4s, 12H, $4CH_3CO$), 2.62 (s, 3H, SCH_3), 4.00–4.09 (m,

2H, 2H-6′), 4.85 (t, 1H, H-5′), 4.88–4.91 (m, 2H, H-4′ and H-3′), 5.30 (t, 1H, H-2′), 5.49 (d, $J_{1'\text{-}2'}$ 11.2 Hz, 1H, H-1′). ^{13}C NMR δ 18.9–21.0 ($4 \times CH_3$), 22.2 (CH_3), 61.4 (CH_2, C-6′), 64.1 (C-4′), 65.3 (C-2′), 72.8 (C-3′), 74.2 (C-5′), 82.5 (C-1′), 113.0 (CN), 117.0 (CN), 154.3 (C-2), 162.8 (C-3), 166.9–183.0 ($4 \times CO$). $C_{19}H_{22}N_2S_2O_9$ ($M^+ = 486$) calcd.: C, 46.91; H, 4.55; N, 5.76. Found: C, 46.8; H, 4.5; N, 5.7%.

Compound **9b**: White, mp 85°C (EtOH), yield (81%). IR (KBr) ν_{max}/cm^{-1} 2219 (CN), 1753 (CO). ^{1}H NMR (DMSO) δ 1.24 (t, 3H, CH_3), 1.92–2.03 (4s, 12H, $4CH_3CO$), 2.44 (s, 3H, SCH_3), 3.88 (q, 2H, CH_2), 4.01–4.24 (m, 3H, 2H-6′ and H-5′), 4.89–5.13 (m, 2H, H-4′ and H-3′), 5.36–5.39 (d, 1H, H-2′), 6.00–6.02 (d, 1H, H-1′). ^{13}C NMR δ 17.5–20.1 ($5 \times CH_3$), 22.1 (CH_3), 57.0 (OCH_2), 61.9 (CH_2, C-6′), 66.6 (C-4′), 68.9 (C-2′), 73.0 (C-3′), 75.8 (C-5′), 80.5 (C-1′), 112.6 (CN), 153.5 (C-2), 162.4 (C-3), 168.3–176.9 ($5 \times CO$). $C_{21}H_{27}NS_2O_{11}$ ($M^+ = 533$) calcd.: C, 47.27; H, 5.10; N, 2.62. Found: C, 47.0; H, 5.0; N, 2.4%.

Compound **9c**: Yellow, mp 90°C (EtOH), yield (75%). IR (KBr) ν_{max}/cm^{-1} 2218 (CN), 1730 (CO). ^{1}H NMR (DMSO) δ 1.90–2.10 (4s, 12H, $4CH_3CO$), 2.32 (s, 3H, SCH_3), 4.05–4.10 (m, 2H, 2H-6′), 4.80 (t, 1H, H-5′), 4.80–4.90 (m, 2H, H-4′ and H-3′), 5.44 (t, 1H, H-2′), 5.55 (d, $J_{1'\text{-}2'}$ 11.2 Hz, 1H, H-1′). ^{13}C NMR δ 19.2–21.7 ($4 \times CH_3$), 22.9 (CH_3), 61.9 (CH_2, C-6′), 64.8 (C-4′), 65.9 (C-2′), 72.4 (C-3′), 74.9 (C-5′), 82.4 (C-1′), 114.7 (CN), 116.7 (CN), 155.9 (C-2), 163.7 (C-3), 165.9–181.5 ($4 \times CO$). $C_{19}H_{22}N_2S_2O_9$ ($M^+ = 486$) calcd.: C, 46.91; H, 4.55; N, 5.76. Found: C, 46.8; H, 4.5; N, 5.7%.

Compound **9d**: Buff, mp 80°C (EtOH), yield (78%). IR (KBr) ν_{max}/cm^{-1} 2210 (CN), 1753 (CO). ^{1}H NMR (DMSO) δ 1.13 (t, 3H, CH_3), 1.85–2.00 (4s, 12H, $4CH_3CO$), 2.60 (s, 3H, SCH_3), 3.77 (q, 2H, CH_2), 4.11–4.33 (m, 3H, 2H-6′ and H-5′), 4.77–5.10 (m, 2H, H-4′ and H-3′), 5.22–5.40 (d, 1H, H-2′), 6.04–6.09 (d, 1H, H-1′). ^{13}C NMR δ 18.1–21.6 ($5 \times CH_3$), 23.0 (CH_3), 58.2 (OCH_2), 62.5 (CH_2, C-6′), 65.3 (C-4′), 67.5 (C-2′), 72.1 (C-3′), 74.0 (C-5′), 79.5 (C-1′), 111.0 (CN), 154.0 (C-2), 161.5 (C-3), 167.7–179.0 ($5 \times CO$). $C_{21}H_{27}NS_2O_{11}$ ($M^+ = 533$) calcd.: C, 47.27; H, 5.10; N, 2.62. Found: C, 47.2; H, 5.0; N, 2.5%.

Sodium 4-Amino-5-benzoylthiophene-2-thiolate (10a,b)

General Procedure

A solution of compounds **3a,b** (0.01 mol) was refluxed with sodium ethoxide (0.23 g, 0.01 mol) in ethanol (20 ml) for 2 h, the solution was evaporated, and the formed solid product was collected by filtration.

Data

Compound **10a**: Brown, mp > 300°C (EtOH), yield (80%). IR (KBr) ν_{max}/cm^{-1} 3453 (NH_2), 2225 (CN), 1676 (CO). $C_{12}H_7N_2S_2ONa$.

Compound **10b**: Brown, mp > 300°C (EtOH), yield (78%). IR (KBr) ν_{max}/cm^{-1} 3430 (NH_2), 1627 (CO). $C_{14}H_{12}NS_2O_3Na$.

4-Amino-5-benzoyl-2-mercaptothiophene (11a,b)

General Procedure

A solution of compounds **3a,b** (0.01 mol) was refluxed with sodium ethoxide (0.23 g, 0.01 mol) in ethanol (20 ml) for 2 h, then poured on cold water and treated with hydrochloric acid until it was neutral. The formed solid products were collected by filtration and recrystallized from ethanol.

Data

Compound **11a**: Yellow, mp 100°C (EtOH), yield (78%). IR (KBr) ν_{max}/cm^{-1} 3418 (NH_2), 2211 (CN), 1655 (CO). ^1H NMR (DMSO) δ 4.43 (m, 2H, NH_2), 7.41–7.55 (m, 5H, C_6H_5), 8.13 (s, 1H, SH). $C_{12}H_8N_2S_2O$ ($M^+ = 260$) calcd.: C, 55.36; H, 3.09; N, 10.76. Found: C, 55.1; H, 3.0; N, 10.6%.

Compound **11b**: Brown, mp 110°C (EtOH), yield (79%). IR (KBr) ν_{max}/cm^{-1} 3419 (NH_2), 1725 (CO), 1619 (CO). ^1H NMR (DMSO) δ 1.15 (t, 3H, CH_3), 3.97 (q, 2H, CH_2), 4.80 (m, 2H, NH_2), 7.33–7.87 (m, 5H, C_6H_5), 9.15 (s, 1H, SH). $C_{14}H_{13}NS_2O_3$ ($M^+ = 307$) calcd.: C, 54.70; H, 4.26; N, 4.55. Found: C, 54.6; H, 4.1; N, 4.4%.

4-Amino-5-benzoyl-2-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-Gluco- or Galactopyranosylthio)thiophene (12a–d)

Method A

To a solution of compounds **10a,b** (0.01 mol) in ethanol (30 ml), a solution of **5a,b** (4.10 g, 0.01 mol) in acetone (20 ml) was added. The reaction mixture was stirred at rt. until completion (TLC, $CHCl_3$–CH_3OH, 9:1, 14 h) and then evaporated under reduced pressure, and the residue was washed with distilled water to remove the formed sodium bromide. The resulting product was crystallized from ethanol.

Method B

A solution of compounds **11a,b** (0.01 mol) in aq. potassium hydroxide [(0.56 g, 0.01 mol) in distilled water (6 ml)] was added to a solution of **5a,b** (4.10 g, 0.01 mol) in acetone (30 ml). The reaction mixture was stirred at rt until completion (TLC, $CHCl_3$–CH_3OH, 9:1, 14 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 crystallized from ethanol.

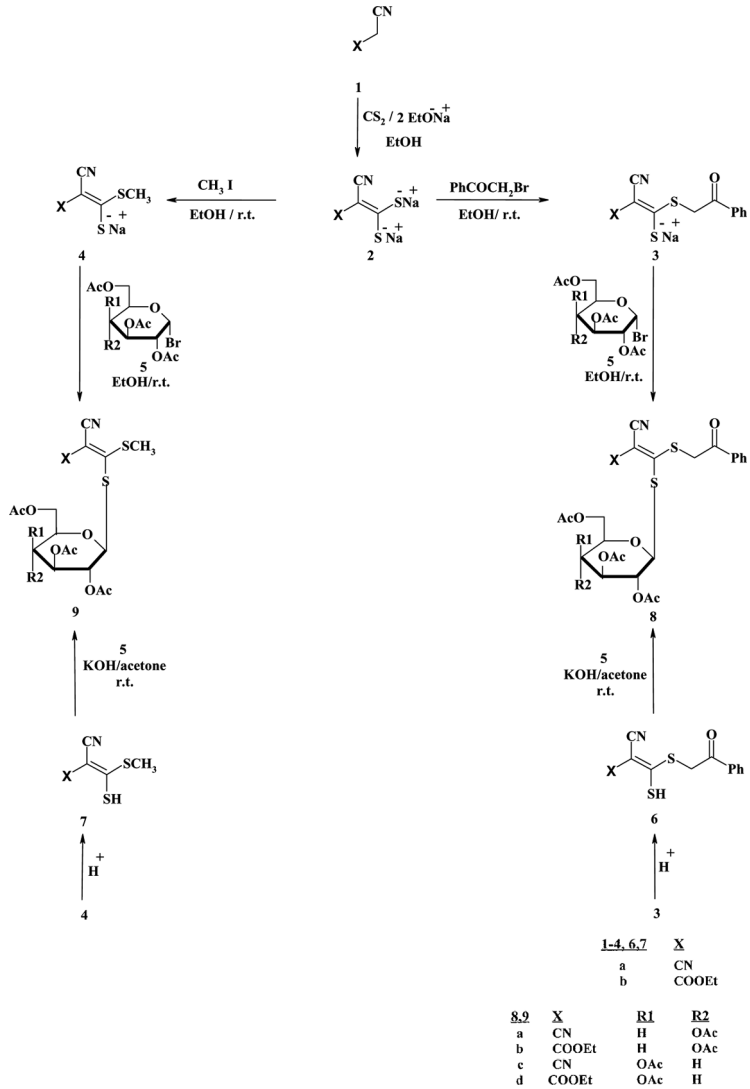
Data

Compound **12a**: Yellow, mp 88°C (EtOH), yield (80%). IR (KBr) ν_{max}/cm^{-1} 3430 (NH_2), 2220 (CN), 1754 (CO), 1650 (CO). ^{1}H NMR (DMSO) δ 1.92–2.05 (4s, 12H, $4CH_3CO$), 3.87–4.29 (m, 3H, 2H-6′ and H-5′), 4.91–5.01 (m, 2H, H-4′ and H-3′), 5.11–5.33 (m, 2H, H-2′), 5.44 (d, $J_{1'\text{-}2'}$ 10.6 Hz, 1H, H-1′), 7.24–7.83 (m, 5H, C_6H_5), 8.42 (s, 2H, NH_2). ^{13}C NMR δ 20.8–21.4 ($4 \times CH_3$), 61.9 (CH_2, C-6′), 68.7 (C-4′), 69.5 (C-2′), 73.7 (C-3′), 74.7 (C-5′), 85.0 (C-1′), 111.0 (CN), 119.4–144.0 (C_6H_5), 160.6–187.9 ($5 \times CO$). $C_{26}H_{26}N_2S_2O_{10}$ ($M^+ = 590$) calcd.: C, 52.88; H, 4.43; N, 4.74. Found: C, 52.8; H, 4.3; N, 4.7%.

Compound **12b**: Brown, mp 85°C (EtOH), yield (84%). IR (KBr) ν_{max}/cm^{-1} 3451 (NH_2), 1754 (CO), 1670 (CO). ^{1}H NMR (DMSO) δ 1.24 (t, 3H, CH_3), 1.94–2.05 (4s, 12H, $4CH_3CO$), 3.88 (q, 2H, CH_2), 4.11–4.24 (m, 3H, 2H-6′ and H-5′), 4.63–4.98 (m, 2H, H-4′ and H-3′), 5.29–5.41 (t, 1H, H-2′), 5.67–5.75 (d, 1H, H-1′), 7.21–7.70 (m, 5H, C_6H_5), 8.22 (m, 2H, NH_2). ^{13}C NMR δ 19.2–20.9 ($4 \times CH_3$), 23.3 (CH_3), 56.0 (OCH_2), 60.5 (CH_2, C-6′), 67.9 (C-4′), 69.9 (C-2′), 74.9 (C-3′), 76.2 (C-5′), 83.2 (C-1′), 118.2–139.0 (C_6H_5), 163.2–185.3 ($6 \times CO$). $C_{28}H_{31}NS_2O_{12}$ ($M^+ = 637$) calcd.: C, 52.74; H, 4.90; N, 2.19. Found: C, 52.7; H, 4.8; N, 2.1%.

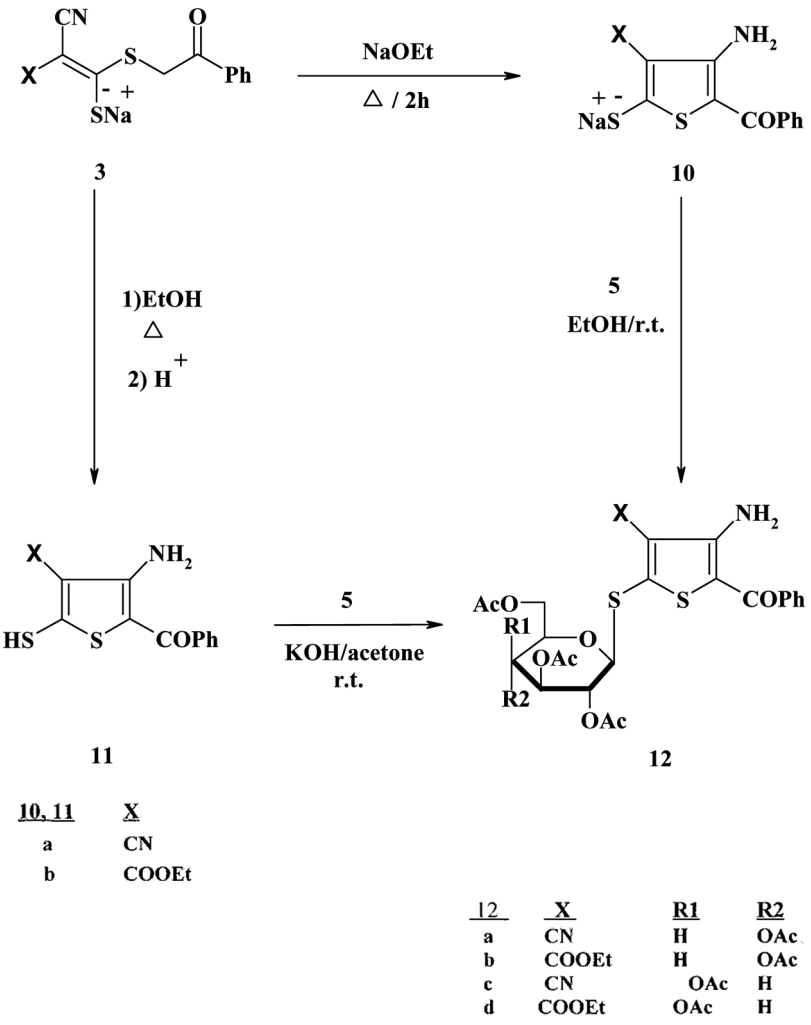
Compound **12c**: Yellow, mp 84°C (EtOH), yield (83%). IR (KBr) ν_{max}/cm^{-1} 3400–3330 (NH_2), 2225 (CN), 1739 (CO), 1670 (CO). ^{1}H NMR (DMSO) δ 1.90–2.00 (4s, 12H, $4CH_3CO$), 3.99–4.20 (m, 3H, 2H-6′ and H-5′), 4.88–5.00 (m, 2H, H-4′ and H-3′), 5.12–5.33 (m, 2H, H-2′), 5.44 (d, 1H, H-1′), 7.24–7.83 (m, 5H, C_6H_5), 8.42 (s, 2H, NH_2). ^{13}C NMR δ 19.6–22.0 ($4 \times CH_3$), 60.5 (CH_2, C-6′), 67.9 (C-4′), 70.3 (C-2′), 72.8 (C-3′), 75.2 (C-5′), 83.4 (C-1′), 114.5 (CN), 119.0–147.0 (C_6H_5), 161.0–186.2 ($5 \times CO$). $C_{26}H_{26}N_2S_2O_{10}$ ($M^+ = 590$) calcd.: C, 52.88; H, 4.43; N, 4.74. Found: C, 52.8; H, 4.4; N, 4.7%.

Compound **12d**: Yellow, mp 86°C (EtOH), yield (78%). IR (KBr) ν_{max}/cm^{-1} 3450, 3370 (NH_2), 1730 (CO), 1650 (CO). ^{1}H NMR (DMSO)



Scheme 1. Reaction of sodium cyanoethylene sodium salts with halo sugars.

δ 1.10 (t, 3H, CH_3), 1.90–2.14 (4s, 12H, $4CH_3CO$), 3.90 (q, 2H, CH_2), 4.08–4.13 (m, 3H, 2H-6′ and H-5′), 4.65–4.90 (m, 2H, H-4′ and H-3′), 5.17–5.38 (t, 1H, H-2′), 5.55–5.87 (d, 1H, H-1′), 7.54–7.90 (m, 5H, C_6H_5), 8.18 (m, 2H, NH_2). ^{13}C NMR δ 18.5–21.3 ($4 \times CH_3$), 22.7 (CH_3), 55.5 (OCH_2), 61.3 (CH_2, C-6′), 66.6 (C-4′), 68.5 (C-2′), 73.5 (C-3′), 75.9 (C-5′), 82.6 (C-1′), 119.9–141.0 (C_6H_5), 162.9–184.9 ($6 \times CO$).



Scheme 2. Synthesis of thiophene thioglycosides.

$C_{28}H_{31}NS_2O_{12}$ ($M^+ = 637$) calcd.: C, 52.74; H, 4.90; N, 2.19. Found: C, 52.7; H, 4.9; N, 2.1%.

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