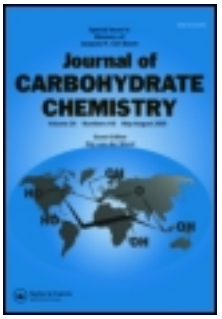

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First Synthesis of Thiophene Thioglycosides

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First Synthesis of Thiophene Thioglycosides

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A new method for the preparation of a new class of thiophene thioglycosides via one-pot reaction of the sodium thiophenethiolate salts with 2,3,4,6-tetra-*O*-acetyl-α-*D*-gluco- and galacto-pyranosyl bromides has been studied. The sodium thiophenethiolate salts are prepared using cyano-di-thioic analogs and their corresponding mono- and dithiolate salts.

Keywords Thiophene thioglycosides, Sodium thiophenethiolate, Galacto-pyranosyl bromides

INTRODUCTION

Thio sugars revealed recently biological interest as potential new therapeutics.[1] Thus, the 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 communication we had already reported the use of dihydropyridine thioglycosides as substrates or inhibitors of protein glycosylation.[6] These common features encouraged us to develop a new, straightforward route for the synthesis of heterocyclic thioglycosides. Here we describe the synthesis of thiophene thioglycosides by the reaction of sodium thiophenethiolates with α-halogeno sugars. As far as we know, this is the first report of a thiophene thioglycoside.

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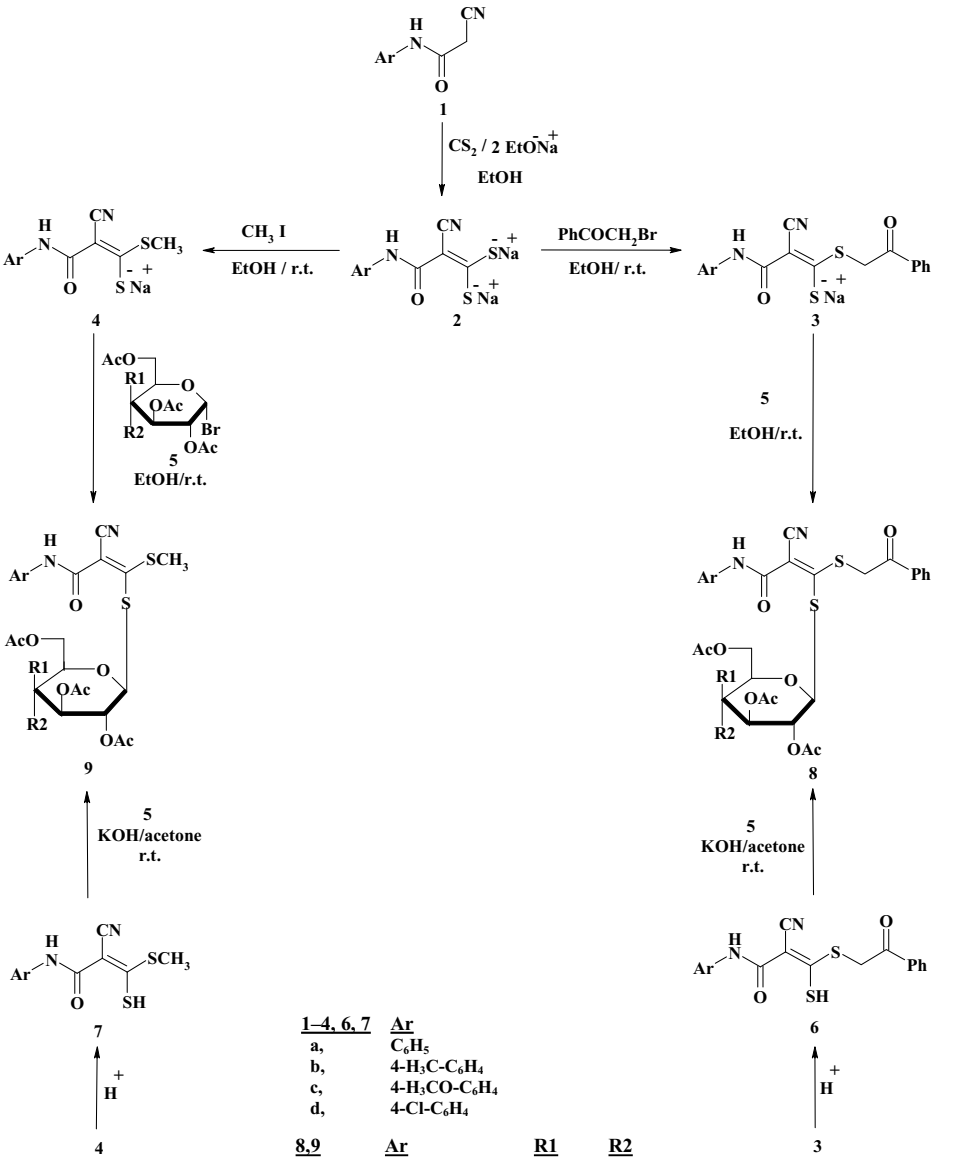
RESULTS AND DISCUSSION

It has been found that reaction of substituted acetanilide derivatives **1** with carbon disulfide in the presence of sodium ethoxide gives the sodium dithiolate salts **2**. Compounds **2** are readily monoalkylated with one equivalent of phenacyl bromide or methyl iodide to give the corresponding sodium salts of monoalkylated products **3** and **4** in good yields. Upon acidification with hydrochloric acid, compounds **3** and**4** gave the novel mercapto products **6** and **7**, respectively. Compounds **3** and **4** reacted with 2,3,4,6-tetra-*O*-acetyl-$\alpha - D$-gluco- and galacto-pyranosyl bromides **5a,b** in ethanol at rt to give in high yield the corresponding *S*-glycosides **8a–h** and **9a–h**. Compounds **8** and **9** could also be prepared by the reaction of the thiols **6** and **7** with **5a,b** in KOH-acetone at rt for 15 h (Sch. 1). It is hypothesized that the cis-(α) sugars react by a simple SN2 reaction to give the β-glycoside products.[7] Structure **8 h** is supported by its mass spectrum, its IR spectrum revealing the presence of a CN band at 2198 cm^{-1} and CO band at 1751 cm^{-1} and its ^1H NMR spectrum showing the anomeric proton as a doublet at δ 5.80 ppm with a spin-spin coupling constant of 10.1 Hz indicating the β-configuration, as confirmed by the ^{13}C NMR spectrum showing C-1′ at δ 85.2 ppm. The ^{13}C NMR spectrum of **8 h** contained a signal at δ 85.2 ppm corresponding to the C-1′ atom of the β-configuration. When compounds **2** were subjected to glycosylation with **5a,b** followed by neutralization to pH 7, the glycoside thiols **12** were obtained. Compounds **12** could also be prepared by alkylation of the dithiol derivatives **11** with one equivalent of **5a,b** (Sch. 2). Indeed, the IR spectrum of **12b** revealed the presence of a CN band at 2198 cm^{-1} and a CO band at 1751 cm^{-1}. The ^1H NMR spectrum showed the anomeric proton as a doublet at δ 6.00 ppm. The ^{13}C NMR spectrum contained a signal at δ 83.6 ppm corresponding to the C-1′ atom of the β-configuration. The sodium α-cyanoketene thiolates **3** were cyclized by refluxing in sodium ethoxide to give the corresponding sodium thiophenethiolates **13**, and subsequently the novel 2-mercaptothiophenes **14**. Upon alkylation with halogenosugars **5**, compounds **13** yielded the corresponding 2-(glycopyranosylthio)thiophene derivative **15**. Attempted preparation of **15** through the reaction of thiophene-2-thiols **14** with halogenosugars **5** in KOH-acetone was also successful in our hands (Sch. 3). The mass spectrum of **15d** revealed a molecular formula $C_{32}H_{31}ClN_2S_2O_{11}$ ($M^+ = 719$); in addition, the ^1H NMR spectrum showed the anomeric proton as a doublet at δ 5.40 ppm ($J_{1',2'} = 9.8$ Hz) indicating the β-configuration, as confirmed by the ^{13}C NMR spectrum showing a signal at δ 85.2 corresponding to C-1′.

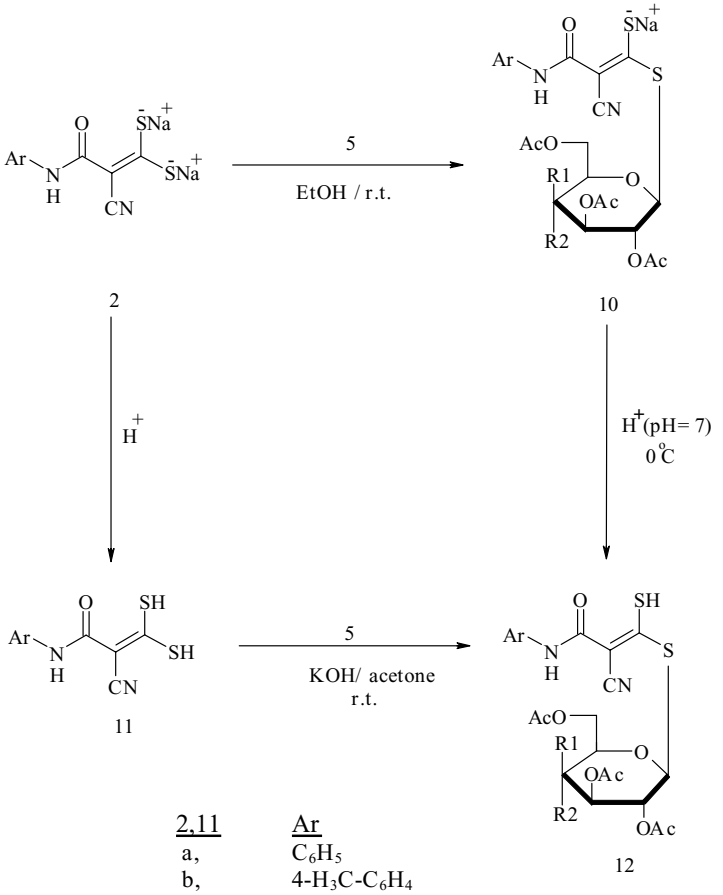
In summary, we have achieved a novel synthesis of thiophene thioglycosides by the reaction of the sodium thiophenethiolates with α-glycosyl halides. These glycosides are excellent starting materials for the synthesis of other carbohydrate derivatives and are evaluated for biological activity.



1–4, 6, 7	Ar
a,	C_6H_5
b,	4-H_3C-C_6H_4
c,	4-H_3CO-C_6H_4
d,	4-Cl-C_6H_4

8,9	Ar	R1	R2
a,	C_6H_5	H	OAc
b,	4-H_3C-C_6H_4	H	OAc
c,	4-H_3CO-C_6H_4	H	OAc
d,	4-Cl-C_6H_4	H	OAc
e,	C_6H_5	OAc	H
f,	4-H_3C-C_6H_4	OAc	H
g,	4-H_3CO-C_6H_4	OAc	H
h,	4-Cl-C_6H_4	OAc	H

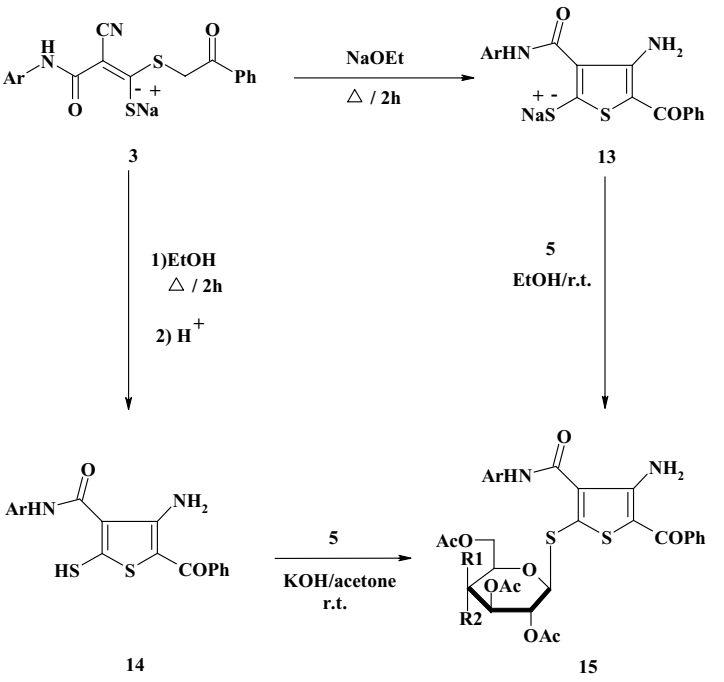
Scheme 1.



2,11	Ar
a,	C_6H_5
b,	4-H_3C-C_6H_4
c,	4-H_3CO-C_6H_4
d,	4-Cl-C_6H_4

10,12	Ar	R1	R2
a,	C_6H_5	H	OAc
b,	4-H_3C-C_6H_4	H	OAc
c,	4-H_3CO-C_6H_4	H	OAc
d,	4-Cl-C_6H_4	H	OAc
e,	C_6H_5	OAc	H
f,	4-H_3C-C_6H_4	OAc	H
g,	4-H_3CO-C_6H_4	OAc	H
h,	4-Cl-C_6H_4	OAc	H

Scheme 2.



13,14	Ar
a,	C_6H_5
b,	4-H_3C-C_6H_4
c,	4-H_3CO-C_6H_4
d,	4-Cl-C_6H_4

15	Ar	R1	R2
a,	C_6H_5	H	OAc
b,	4-H_3C-C_6H_4	H	OAc
c,	4-H_3CO-C_6H_4	H	OAc
d,	4-Cl-C_6H_4	H	OAc
e,	C_6H_5	OAc	H
f,	4-H_3C-C_6H_4	OAc	H
g,	4-H_3CO-C_6H_4	OAc	H
h,	4-Cl-C_6H_4	OAc	H

Scheme 3.

EXPERIMENTAL

All melting points were measured 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 solutions 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 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 (2*Z*)-2-cyano-3-[(2-oxo-2-phenylethyl)thio]-*N*-arylacryl-amide-3-thiolates (3a–d)

General procedure

A solution of compounds **2** (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 by filtration.

Sodium 2-cyano-3-(methylthio)-*N*-arylacrylamide-3-thiolates (4a–d)

General procedure

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

(2*E*)-2-Cyano-3-mercapto-3-[(2-oxo-2-phenylethyl)thio]-*N*-arylacryl-amides (6a–d) and 2-cyano-3-mercapto-3-(methylthio)-*N*-arylacryl-amides (7a–d)

General procedure

A solution of compounds **3** or**4** in ethanol (20 mL) was poured onto cold water and treated with hydrochloric acid until just acidic and the formed solid products **6** or **7** were collected by filtration and recrystallized from ethanol.

(2*Z*)-*N*-Aryl-2-cyano-3-[(2-oxo-2-phenylethyl)thio]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-gluco- or galactopyranosylthio)acrylamides (8a–h)

General procedures

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.

(2*Z*)-2-Cyano-3-[(2-oxo-2-phenylethyl)thio]-*N*-phenyl-3-(2′,3′,4′, 6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(8a):** yellow crystals, m.p. 180°C, 80% method A, 75% method B, $[\alpha]_D$+22.5, IR (KBr) ν_{max}/cm^{-1} 3317 (NH), 2198 (CN), 1751 (CO), 1635 (CO). ^{1}H NMR δ 1.70–2.00 (4s, 12H, 4 × CH_3CO), 3.50 (s, 2H, CH_2), 3.90 (s, 2H, H-6a′, H-6b′), 3.95 (m, 1H, H-5′), 4.10 (t, 1H, H-4′), 4.90 (t, 1H, H-3′), 5.20–5.40 (m, 2H, H-2′, H-1′), 7.00–7.80 (m, 10H, 2C_6H_5), 9.80 (s, 1H, NH). ^{13}C NMR δ 20.4–20.7 (4 × CH_3), 52.8 (CH_2), 62.2 (CH_2, C-6′), 68.2 (C-4′), 69.8 (C-2′), 73.0 (C-3′), 74.8 (C-5′), 85.2 (C-1′), 116.8 (CN), 120.2–141.4 (2C_6H_5), 154.8 (C-2), 160.8 (C-3), 169.7–187.0 (6 × CO). Anal. Calcd for $C_{32}H_{32}N_2O_{11}S_2$ (684.732): C, 56.1; H, 4.7; N, 4.1%. Found: C, 56.0; H, 4.6; N, 4.7%.

(2*Z*)-2-Cyano-*N*-(4-methylphenyl)-3-[(2-oxo-2-phenylethyl)thio]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(8b):** yellow crystals, m.p. 188°C, 84% method A, 77% method B, $[\alpha]_D$+30.5, IR (KBr) ν_{max}/cm^{-1} 3301 (NH), 2206 (CN), 1751 (CO), 1674 (CO). ^{1}H NMR δ 1.70–1.95 (4s, 12H, 4 × CH_3CO), 2.40 (s, 3H, CH_3), 3.50 (s, 2H, CH_2), 3.80 (s, 2H, H-6a′, H-6b′), 3.95 (m, 1H, H-5′), 4.10 (t, 1H, H-4′), 4.90 (t, 1H, H-3′), 5.20–5.40 (m, 2H, H-2′, H-1′), 7.00–7.80 (m, 9H, C_6H_5, C_6H_4), 9.80 (s, 1H, NH). Anal. Calcd for $C_{33}H_{34}N_2O_{11}S_2$ (698.758): C, 56.7; H, 4.9; N, 4.0%. Found: C, 56.8; H, 4.7; N, 4.6%.

(2*Z*)-2-Cyano-*N*-(4-methoxyphenyl)-3-[(2-oxo-2-phenylethyl)thio]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(8c):** yellow crystals, m.p. 155°C, 81% method A, 75% method B, $[\alpha]_D$+27.5, IR (KBr) ν_{max}/cm^{-1} 3348 (NH), 2198 (CN), 1751 (CO), 1650 (CO). Anal. Calcd for $C_{33}H_{34}N_2O_{12}S_2$ (714.758): C, 55.4; H, 4.8; N, 3.9%. Found: C, 55.3; H, 5.1; N, 4.3%.

(2*Z*)-*N*-(4-Bromophenyl)-2-cyano-3-[(2-oxo-2-phenylethyl)thio]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(8d):** yellow crystals, m.p. 206°C, 86% method A, 80% method B, $[\alpha]_D$+29.5, IR (KBr) ν_{max}/cm^{-1} 3325 (NH), 2198 (CN), 1751 (CO), 1643 (CO). ^{1}H NMR δ 1.70–2.00 (4s, 12H,

4 × CH_3CO), 3.40–4.10 (m, 5H, CH_2, H-6a′, H-6b′, H-5′), 4.90 (m, 2H, H-4′, H-3′), 5.30 (m, 2H, H-2′, H-1′), 7.40–7.80 (m, 9H, C_6H_5, C_6H_4), 10.40 (s, 1H, NH). Anal. Calcd for $C_{32}H_{31}BrN_2O_{11}S_2$ (673.628): C, 50.4; H, 4.1; N, 3.7%. Found: C, 49.9; H, 4.5; N, 3.4%.

(2*Z*)-2-Cyano-3-[(2-oxo-2-phenylethyl)thio]-*N*-phenyl-3-(2′,3′,4′, 6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(8e):** yellow crystals, m.p. 177°C, 79% method A, 73% method B, $[\alpha]_D$+34.5, IR (KBr) ν_{max}/cm^{-1}3286 (NH), 2214 (CN), 1744 (CO), 1628 (CO). ^{1}H NMR δ 1.70–2.00 (4s, 12H, 4 × CH_3CO), 3.50 (s, 2H, CH_2), 3.95 (m, 2H, H-6a′, H-6b′), 4.30 (m, 1H, H-5′), 5.00 (t, 1H, H-4′), 5.20–5.30 (m, 3H, H-3′, H-2′, H-1′), 7.10–7.80 (m, 9H, C_6H_5, C_6H_4), 10.30 (s, 1H, NH). Anal. Calcd for $C_{32}H_{32}N_2O_{11}S_2$ (684.732): C, 56.1; H, 4.7; N, 4.0%. Found: C, 55.9; H, 4.9; N, 4.2%.

(2*Z*)-2-Cyano-*N*-(4-methylphenyl)-3-[(2-oxo-2-phenylethyl)thio]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(8f):** yellow crystals, m.p. 170°C, 84% method A, 78% method B, $[\alpha]_D$+24.5, IR (KBr) ν_{max}/cm^{-1}3325 (NH), 2198 (CN), 1751 (CO), 1627 (CO). ^{13}C NMR δ 20.4–20.9 (5 × CH_3), 52.8 (CH_2), 61.9 (CH_2, C-6′), 67.2 (C-4′), 67.8 (C-2′), 71.0 (C-3′), 74.2 (C-5′), 85.5 (C-1′), 116.8 (CN), 120.2–141.3 ($C_6H_5$and C_6H_4), 154.8 (C-2), 160.8 (C-3), 169.7–187.0 (6 × CO). Anal. Calcd for $C_{33}H_{34}N_2O_{11}S_2$ (698.758): C, 56.7; H, 4.9; N, 4.0%. Found: C, 57.1; H, 4.9; N, 3.3%.

(2*Z*)-2-Cyano-*N*-(4-methoxyphenyl)-3-[(2-oxo-2-phenylethyl)thio]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(8g):** yellow crystals, m.p. 170°C, 80% method A, 74% method B, $[\alpha]_D$+32.5, IR (KBr) ν_{max}/cm^{-1}3325 (NH), 2198 (CN), 1751 (CO), 1635 (CO). ^{1}H NMR δ 1.70–2.00 (4s, 12H, 4 × CH_3CO), 3.50 (s, 2H, CH_2), 3.75 (s, 3H, OCH_3), 3.80 (s, 2H, H-6a′, H-6b′), 3.95 (m, 1H, H-5′), 4.30 (t, 1H, H-4′), 5.00 (t, 1H, H-3′), 5.15–5.35 (m, 2H, H-2′, H-1′), 7.30–7.80 (m, 9H, C_6H_5, C_6H_4), 10.40 (s, 1H, NH). Anal. Calcd for $C_{33}H_{34}N_2O_{12}S_2$ (714.758): C, 55.4; H, 4.8; N, 3.9%. Found: C, 55.2; H, 5.0; N, 3.3%.

(2*Z*) – *N*-(4-Chlorophenyl)-2-cyano-3-[(2-oxo-2-phenylethyl)thio]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(8h):** yellow crystals, m.p. 190°C, 85% method A, 82% method B, $[\alpha]_D$+40.5, IR (KBr) ν_{max}/cm^{-1}3317 (NH), 2198 (CN), 1751 (CO), 1635 (CO). ^{1}H NMR δ 1.70–2.00 (4s, 12H, 4 × CH_3CO), 3.45 (s, 2H, CH_2), 3.90 (s, 2H, H-6a′, H-6b′), 3.95 (m, 1H, H-5′), 4.25 (t, 1H, H-4′), 5.00 (t, 1H, H-3′), 5.25 (t, 1H, H-2′), 5.80 (d, $J_{1'-2'}$ = 9.77, 1H, H-1′), 7.30–7.80 (m, 9H, C_6H_5, C_6H_4), 10.40 (s, 1H, NH). Anal. Calcd for $C_{33}H_{31}ClN_2O_{11}S_2$ (731.188): C, 53.4; H, 4.3; N, 3.9%. Found: C, 54.1; H, 4.9; N, 4.5%.

(2*Z*)–*N*-Aryl-2-cyano-3-(methylthio)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-gluco or galactopyranosylthio)acrylamides (9a–h)

General procedures

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

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

(2*Z*)-2-Cyano-3-(methylthio)-*N*–phenyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(9a):** orange crystals, m.p. 156°C, 68% method A, 75% method B, $[\alpha]_D$+28.0, IR (KBr) ν_{max}/cm^{-1} 3332 (NH), 2198 (CN), 1751 (CO of ester), 1666 (CO of amide). ^{1}H NMR δ 1.90–2.10 (4s, 12H, 4 × CH_3CO), 2.60 (s, 3H, SCH_3), 3.60 (s, 2H, H-6a′, H-6b′), 4.05 (m, 1H, H-5′), 4.15 (t, 1H, H-4′), 4.95 (t, 1H, H-3′), 5.05 (t, 1H, H-2′), 5.45 (d, $J_{1',2'}$ = 9.60, 1H, H-1′), 7.10–7.50 (m, 5H, C_6H_5), 10.50 (s, 1H, NH). Anal. Calcd for $C_{25}H_{28}N_2O_{10}S_2$ (580.624): C, 51.7; H, 4.9; N, 4.9%. Found: C, 51.3; H, 5.3; N, 4.2%.

(2*Z*)-2-Cyano-*N*–(4-methylphenyl)-3-(methylthio)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(9b):** yellow crystals, m.p. 175°C, 70% method A, 87% method B, $[\alpha]_D$+35.0, IR (KBr) ν_{max}/cm^{-1} 3355 (NH), 2206 (CN), 1743 (CO of ester), 1658 (CO of amide). ^{1}H NMR δ 2.00–2.10 (4s, 12H, 4 × CH_3CO), 2.30 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 4.05 (s, 2H, H-6a′, H-6b′), 4.20 (m, 2H, H-5′, H-4′), 5.00 (m, 1H, H-3′), 5.50 (m, 2H, H-2′, H-1′), 7.15–7.50 (d.d, 4H, C_6H_4), 10.50 (s, 1H, NH). ^{13}C NMR δ 18.6 (SCH_3), 20.6–20.8 (5 × CH_3), 62.3 (CH_2, C-6′), 68.2 (C-4′), 69.9 (C-2′), 73.1 (C-3′), 75.2 (C-5′), 85.2 (C-1′), 111.9 (C-1 enol form), 115.7 (CN), 120.2–135.8 (C_6H_4), 156.5 (C-2), 161.1 (C-3), 169.5–170.3 (4 × CO). Anal. Calcd for $C_{26}H_{30}N_2O_{10}S_2$ (594.650): C, 52.5; H, 5.1; N, 4.7%. Found: C, 52.5; H, 4.9; N, 4.8%.

(2*Z*)-2-Cyano-*N*–(4-methoxyphenyl)-3-(methylthio)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(9c):** yellow crystals, m.p. 170°C, 75% method A, 82% method B, $[\alpha]_D$+37.5, IR (KBr) ν_{max}/cm^{-1} 3363 (NH), 2206 (CN), 1751 (CO of ester), 1658 (CO of amide). ^{1}H NMR δ 1.90–2.10 (4s, 12H, 4 × CH_3CO), 2.60 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 4.10 (m, 3H, H-6a′, H-6b′, H-5′), 5.05 (m, 2H, H-4′, H-3′), 5.40 (m, 2H, H-2′, H-1′), 7.00–7.50 (d.d, 4H, C_6H_4), 10.45 (s, 1H, NH). ^{13}C NMR (DMSO) δ 18.6 (SCH_3), 20.6–20.8 (4 × CH_3), 55.6 (OCH_3), 62.3 (CH_2, C-6′), 68.20 (C-4′), 69.9 (C-2′), 73.1 (C-3′), 75.2 (C-5′), 85.2 (C-1′), 112.0 (CN), 114.4–131.3

(C_6H_4), 156.5 (C-2), 158.5 (C-3), 161.1 (C-1), 169.5–170.3 (4 × CO). Anal. Calcd for $C_{26}H_{30}N_2O_{11}S_2$ (610.650): C, 51.1; H, 5.0; N, 4.6%. Found: C, 51.2; H, 5.6; N, 4.7%.

(2*Z*) – *N*–(4-Bromophenyl)-2-cyano-3-(methylthio)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(9d):** yellow crystals, m.p. 186°C, 72% method A, 79% method B, $[\alpha]_D$+39.5, IR (KBr) ν_{max}/cm^{-1}3340 (NH), 2206 (CN), 1751 (CO of ester), 1674 (CO of amide). ^{1}H NMR δ 1.90–2.05 (4s, 12H, 4 × CH_3CO), 2.60 (s, 3H, CH_3), 4.10–4.20 (m, 4H, H-6a′, H-6b′, H-5′, H-4′), 4.95–5.10 (m, 2H, H-3′, H-2′), 5.45 (d, $J_{1'-2'}$ = 9.98, 1H, H-1′), 7.40–7.50 (dd, 4H, C_6H_4), 10.70 (s, 1H, NH). ^{13}C NMR δ 18.3 (SCH_3), 20.2–20.4 (4 × CH_3), 61.7 (CH_2, C-6′), 67.7 (C-4′), 69.4 (C-2′), 72.6 (C-3′), 74.7 (C-5′), 84.8 (C-1′), 110.9 (C-1 enol form), 116.2 (CN), 120.1–137.2 (C_6H_4), 158.5 (C-2), 161.1 (C-3), 169.0–169.4 (4 × CO). Anal. Calcd for $C_{25}H_{27}BrN_2O_{10}S_2$ (659.520): C, 45.5; H, 4.2; N, 4.2%. Found: C, 45.2; H, 4.6; N, 4.1%.

(2*Z*)-2-Cyano-3-(methylthio)-*N*–phenyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(9e):** yellow crystals, m.p. 160°C, 65% method A, $[\alpha]_D$+30.0, 75% method B. IR (KBr) ν_{max}/cm^{-1} 3332 (NH), 2198 (CN), 1751 (CO of ester), 1666 (CO of amide). ^{1}H NMR δ 1.90–2.20 (4s, 12H, 4 × CH_3CO), 2.60 (s, 3H, CH_3), 3.60 (s, 2H, H-6a′, H-6b′), 4.10 (m, 1H, H-5′), 4.15 (t, 1H, H-4′), 5.00 (t, 1H, H-3′), 5.05 (t, 1H, H-2′), 5.50 (d, $J_{1',2'}$ = 9.90, 1H, H-1′), 7.10–7.70 (m, 5H, C_6H_5), 10.50 (s, 1H, NH). Anal. Calcd for $C_{25}H_{28}N_2O_{10}S_2$ (580.624): C, 51.7; H, 4.9; N, 4.8%. Found: C, 51.2; H, 5.3; N, 4.2%.

(2*Z*)-2-Cyano-*N*–(4-methylphenyl)-3-(methylthio)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(9f):** yellow crystals, m.p. 175°C, 68% method A, 74% method B, $[\alpha]_D$+25.0, IR (KBr) ν_{max}/cm^{-1}3440 (NH), 2198 (CN), 1751 (CO of ester), 1635 (CO of amide).^{1}H NMR δ 1.90–2.20 (4s, 12H, 4 × CH_3CO), 2.30 (s, 3H, CH_3), 2.60 (s, 3H, SCH_3), 4.10 (s, 2H, H-6a′, H-6b′), 4.40 (t, 2H, H-5′,H-4′), 5.10 (t, 1H, H-3′), 5.40 (m, 2H, H-2′, H-1′), 7.10–7.70 (m, 4H, C_6H_4), 10.50 (s, 1H, NH). ^{13}C NMR δ 18.1 (SCH_3), 20.2 (Ar-CH_3), 20.3–20.4 (4 × CH_3), 61.5 (CH_2, C-6′), 67.3 (C-4′), 67.5 (C-2′), 70.6 (C-3′), 74.1 (C-5′), 85.3 (C-1′), 114.0 (CN), 119.2–135.0 (C_6H_4), 156.5 (C-2), 158.5 (C-3), 161.1 (C-1), 169.0–170.3 (4 × CO). Anal. Calcd for $C_{26}H_{30}N_2O_{10}S_2$ (594.650): C, 52.5; H, 5.1; N, 4.7%. Found: C, 52.1; H, 5.2; N, 5.2%.

(2*Z*)-2-Cyano-*N*–(4-methoxyphenyl)-3-(methylthio)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(9g):** yellow crystals, m.p. 162°C, 72% method A, 79% method B, $[\alpha]_D$+40.0, IR (KBr) ν_{max}/cm^{-1}3363 (NH), 2206 (CN), 1751 (CO of ester), 1658 (CO of amide).^{1}H NMR δ 1.90–2.10 (4s, 12H, 4 × CH_3CO), 2.60 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 4.05–4.20 (m, 3H, H-6a′, H-6b′,H-5′), 5.00–5.10 (m, 2H, H-4′, H-3′), 5.50 (m, 2H, H-2′, H-1′), 6.90–7.50 (dd, 4H, C_6H_4), 10.40 (s, 1H, NH).^{13}C NMR δ 18.2

(SCH_3), 20.2–20.4 (4 × CH_3), 55.1 (OCH_3), 61.7 (CH_2, C-6′), 67.7 (C-4′), 69.5 (C-2′), 72.6 (C-3′), 75.0 (C-5′), 84.7 (C-1′), 114.0 (CN), 115.3–130.9 (C_6H_4), 156.5 (C-2), 158.5 (C-3), 161.1 (C-1), 169.0–169.9 (4 × CO). Anal. Calcd for $C_{26}H_{30}N_2O_{11}S_2$ (610.650): C, 51.1; H, 5.0; N, 4.6%. Found: C, 50.6; H, 5.2; N, 4.6%.

(2*Z*) – *N*–(4-Chlorophenyl)-2-cyano-3-(methylthio)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide**(9h):** yellow crystals, m.p. 193°C, 70% method A, 78% method B, $[\alpha]_D$+36.5, IR (KBr) ν_{max}/cm^{-1}3271 (NH), 2206 (CN), 1751 (CO of ester), 1674 (CO of amide).^{1}H NMR δ 2.00–2.10 (4s, 12H, 4 × CH_3CO), 2.60 (s, 3H, CH_3), 4.00–4.10 (m, 3H, H-6a′, H-6b′, H-5′), 4.20 (t, 1H, H-4′), 5.00 (t, 1H, H-3′), 5.10 (t, 1H, H-2′), 5.50 (d, $J_{1'-2'} = 9.88$, 1H,1′-H), 7.40–7.70 (dd, 4H, C_6H_4), 10.80 (s, 1H, NH). ^{13}C NMR δ 18.3 (SCH_3), 20.2–26.7 (4 × CH_3), 61.8 (CH_2, C-6′), 67.7 (C-4′), 69.4 (C-2′), 72.6 (C-3′), 74.7 (C-5′), 84.8 (C-1′), 115.1 (CN), 119.7–136.8 (C_6H_4), 156.5 (C-2), 158.5 (C-3), 161.1 (C-1), 169.0–169.9 (4 × CO). Anal. Calcd for $C_{25}H_{27}ClN_2O_{10}S_2$ (615.069): C, 48.8; H, 4.4; N, 4.6%. Found: C, 48.1; H, 4.2; N, 4.1%.

Sodium *N*-aryl-2-cyano-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-gluco or galactopyranosylthio)acrylamide-3-thiolates (10a–h)

General procedure

Compounds **2** (0.01 mol) were treated as described for the preparation of **8a–h**. The reaction was completed within 9 h (TLC, $CHCl_3$:CH_3OH, 9:1).

Sodium 2-cyano-*N*-phenyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-gluco-pyranosylthio) acrylamide-3-thiolate **(10a):** yellow crystals, m.p. <300°C, 78%, $[\alpha]_D$+19.5, IR (KBr) ν_{max}/cm^{-1}3440 (NH), 2098 (CN), 1751 (CO). $C_{24}H_{25}N_2O_{10}S_2Na$ (588.579).

Sodium 2-cyano-*N*-(4-methylphenyl)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide-3-thiolate **(10b):** yellow crystals, m.p. <300°C, 80%, $[\alpha]_D$+25.5, IR (KBr) ν_{max}/cm^{-1} 3448 (NH), 2183 (CN), 1751 (CO). $C_{25}H_{27}N_2O_{10}S_2Na$ (602.606).

Sodium 2-cyano-*N*-(4-methoxyphenyl)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide-3-thiolate **(10c):** yellow crystals, m.p. <300°C, 76%, $[\alpha]_D$+27.0, IR (KBr) ν_{max}/cm^{-1}3417 (NH), 2191 (CN), 1751 (CO). $C_{25}H_{27}N_2O_{11}S_2Na$ (618.605).

Sodium *N*-(4-chlorophenyl)-2-cyano-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide-3-thiolate **(10d):** yellow crystals, m.p. <300°C, 85%, $[\alpha]_D$+20.5, IR (KBr) ν_{max}/cm^{-1}3446 (NH), 2186 (CN), 1751 (CO). $C_{24}H_{24}ClN_2O_{10}S_2Na$ (623.024).

Sodium 2-cyano-*N*-phenyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galacto-pyranosylthio)acrylamide-3-thiolate **(10e):** yellow crystals, m.p. <300°C, 77%, $[\alpha]_D$+36.0, IR (KBr) ν_{max}/cm^{-1}3479 (NH), 2113 (CN), 1750 (CO). $C_{24}H_{25}N_2O_{10}S_2Na5$ (88.579).

Sodium 2-cyano-*N*-(4-methylphenyl)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide-3-thiolate **(10f):** yellow crystals, m.p. <300°C, 79%, $[\alpha]_D$+30.0, IR (KBr) ν_{max}/cm^{-1}3217 (NH), 2191 (CN), 1751 (CO). $C_{25}H_{27}N_2O_{10}S_2Na$ (602.606).

Sodium 2-cyano-*N*-(4-methoxyphenyl)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide-3-thiolate **(10g):** yellow crystals, m.p. <300°C, 75%, $[\alpha]_D$+20.5, IR (KBr) ν_{max}/cm^{-1}3417 (NH), 2183 (CN), 1751 (CO). $C_{25}H_{27}N_2O_{11}S_2Na$ (618.605).

Sodium *N*-(4-chlorophenyl)-2-cyano-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide-3-thiolate **(10h)**: yellow crystals, m.p. <300°C, 85%, $[\alpha]_D$+29.5, IR (KBr) ν_{max}/cm^{-1}3417 (NH), 2183 (CN), 1743 (CO). $C_{24}H_{24}ClN_2O_{10}S_2Na$ (623.024).

2-Cyano-3,3-dimercapto-*N*-arylacrylamides (11a–d)

General procedure

A solution of compounds **2** (0.01 mol) in ethanol (20 mL) was poured onto cold water and treated with hydrochloric acid until just acidic and the formed solid products were collected by filtration and recrystallized from ethanol.

N-Aryl-2-cyano-3-mercapto-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-gluco or galactopyranosylthio)acrylamides (12a–h)

General procedures

Method A. A solution of compounds **10** (0.01 mol) in ethanol (30 mL) was poured onto cold water and the medium was adjusted to pH 7 using dilute acetic acid. The formed solid products were collected by filtration and recrystallized from ethanol.

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

2-Cyano-3-mercapto-*N*-phenyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(12a):** yellow crystals, m.p. 231°C, 73% method A, 80% method B, $[\alpha]_D$+47.5, IR (KBr) ν_{max}/cm^{-1}3286 (NH), 2507 (SH), 2183 (CN), 1751 (CO). ^{1}H NMR δ 1.95–2.05 (4s, 12H, 4 × CH_3CO), 3.95–4.10 (m, 3H, H-6a′, H-6b′, H-5′), 4.95 (t, 1H, H-4′), 5.30–5.40 (m, 2H, H-3′, H-2′), 5.90 (d, $J_{1'-2'}$ = 9.80, 1H, H-1′), 7.00–7.70 (m, 5H, C_6H_5), 9.60 (s, 1H, NH), 10.40 (s, 1H, SH).Anal. Calcd for $C_{24}H_{26}N_2O_{10}S_2$ (566.597): C, 50.9; H, 4.6; N, 4.9%. Found: C, 51.0; H, 5.1; N, 4.7%.

2-Cyano-3-mercapto-*N*-(4-methylphenyl)-3-(2′,3′,4′,6′-tetra-*O*-ace-tyl-*β*-*D*-glucopyranosylthio)acrylamide **(12b):** yellow crystals, m.p. 179°C, 78% method A, 85% method B, $[\alpha]_D$+19.5, IR (KBr) ν_{max}/cm^{-1}3294 (NH), 2499 (SH), 2198 (CN), 1751 (CO). ^{1}H NMR δ 1.95–2.00 (4s, 12H, 4 × CH_3CO), 2.30 (s, 3H, CH_3), 3.95 (s, 2H, H-6a′, H-6b′), 4.15 (m, 1H, H-5′), 4.95 (t, 1H, H-4′), 5.10 (t, 1H, H-3′), 5.35 (t, 1H, H-2′), 6.00 (d, $J_{1'-2'}$ = 9.65, 1H, H-1′), 7.10–7.40 (dd, 4H, C_6H_4), 9.80 (s, 1H, NH), 10.70 (s, 1H, SH). ^{13}C NMR δ 17.0 (Ar-CH_3), 18.0–20.9 (4 × CH_3), 62.0 (CH_2, C-6′), 68.4 (C-4′), 68.8 (C-2′), 74.1 (C-3′), 75.1 (C-5′), 83.6 (C-1′), 119.5 (CN), 125.0–137.0 (C_6H_4), 159.8 (C-2), 160.0 (C-3), 162.2 (C-1), 169.5–170.1 (4 × CO). Anal. Calcd for $C_{25}H_{28}N_2O_{10}S_2$ (580.624): C, 51.7; H, 4.9; N, 4.8%. Found: C, 51.2; H, 4.7; N, 4.8%.

2-Cyano-3-mercapto-*N*-(4-methoxyphenyl)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)acrylamide **(12c):** yellow crystals, m.p. 155°C, 74% method A, 79% method B, $[\alpha]_D$+37.5, IR (KBr) ν_{max}/cm^{-1}3230 (NH), 2530 (SH), 2206 (CN), 1751 (CO). ^{1}H NMR δ 1.95–2.10 (4s, 12H, 4 × CH_3CO), 3.70 (s, 3H, OCH_3), 3.80 (s, 2H, H-6a′, H-6b′), 4.15 (m, 1H, H-5′), 5.00 (t, 1H, H-4′), 5.10–5.50 (m, 2H, H-3′, H-2′), 6.00 (d, $J_{1'-2'}$ = 10.00, 1H, H-1′), 6.90–7.50 (dd, 4H, C_6H_4).^{13}C NMR δ 13.7–20.9 (4 × CH_3), 55.5 (OCH_3), 61.8 (CH_2, C-6′), 68.4 (C-4′), 68.8 (C-2′), 74.1 (C-3′), 75.1 (C-5′), 83.6 (C-1′), 112.7 (CN), 114.4–128.4 (C_6H_4), 159.8 (C-2), 160.2 (C-3), 162.2 (C-1), 169.5–170.1 (4 × CO). Anal. Calcd for $C_{25}H_{28}N_2O_{11}S_2$ (596.623): C, 50.3; H, 4.7; N, 4.7%. Found: C, 49.7; H, 4.7; N, 4.2%.

N-(4-Chlorophenyl)-2-cyano-3-mercapto-3-(2′,3′,4′,6′-tetra-*O*-ace-tyl-*β*-*D*-glucopyranosylthio)acrylamide **(12d):** yellow crystals, m.p. 183°C, 80% method A, 84% method B, $[\alpha]_D$+32.5, IR (KBr) ν_{max}/cm^{-1}3294 (NH), 2550 (SH), 2198 (CN), 1751 (CO). ^{13}C NMR δ 13.7–20.9 (4 × CH_3), 62.0 (CH_2, C-6′), 68.4 (C-4′), 68.8 (C-2′), 74.1 (C-3′), 75.1 (C-5′), 83.5 (C-1′), 119.6 (CN), 120.7–129.0 (C_6H_4), 159.8 (C-2), 160.2 (C-3), 162.2 (C-1), 169.5–170.1 (4 × CO). Anal. Calcd for $C_{24}H_{25}ClN_2O_{10}S_2$ (601.042): C, 48.0; H, 4.2; N, 4.7%. Found: C, 47.8; H, 4.2; N, 4.2%.

2-Cyano-3-mercapto-*N*-phenyl-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(12e):** yellow crystals, m.p. 246°C, 71% method

A, 77% method B, $[\alpha]_D$+46.5, IR (KBr) ν_{max}/cm^{-1}3340 (NH), 2600 (SH), 2206 (CN), 1743 (CO). ^{1}H NMR δ 1.90–2.15 (4s, 12H, 4 × CH_3CO), 3.30 (s, 2H, H-6a′, H-6b′), 4.00 (m, 1H, H-5′), 4.25 (t, 1H, H-4′), 5.20 (t, 1H, H-3′), 5.35 (t, 1H, H-2′), 5.80 (d, $J_{1'-2'}$ = 9.70, 1H, H-1′), 7.70–7.80 (m, C_6H_5), 10.30 (s, 1H, NH), 10.70 (s, 1H, SH). Anal. Calcd for $C_{24}H_{26}N_2O_{10}S_2$ (566.597): C, 50.9; H, 4.6; N, 4.9%. Found: C, 50.5; H, 4.9; N, 4.7%.

2-Cyano-3-mercapto-*N*-(4-methylphenyl)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(12f):** yellow crystals, m.p. 130°C, 76% method A, 82% method B, $[\alpha]_D$+41.0, IR (KBr) ν_{max}/cm^{-1}3340 (NH), 2580 (SH), 2198 (CN), 1751 (CO). ^{1}H NMR δ 1.90–2.20 (4s, 12H, 4 × CH_3CO), 2.30 (s, 3H, CH_3), 3.95 (s, 2H, H-6a′, H-6b′), 4.25 (m, 1H, H-5′), 5.10 (t, 1H, H-4′), 5.30 (t, 1H, H-3′), 5.60 (t, 1H, H-2′), 5.90 (d, $J_{1'-2'}$ = 9.98, 1H, H-1′), 7.10–7.50 (dd, 4H, C_6H_4), 9.70 (s, 1H, NH), 10.40 (s, 1H, SH). Anal. Calcd for $C_{25}H_{28}N_2O_{10}S_2$ (580.624): C, 51.7; H, 4.9; N, 4.8%. Found: C, 51.2; H, 5.6; N, 5.4%.

2-Cyano-3-mercapto-*N*-(4-methoxyphenyl)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(12g):** yellow crystals, m.p. 120°C, 72% method A, 79% method B, $[\alpha]_D$+19.0, IR (KBr) ν_{max}/cm^{-1}3294 (NH), 2550 (SH), 2198 (CN), 1751 (CO). ^{1}H NMR δ 1.90–2.20 (4s, 12H, 4 × CH_3CO), 3.70 (s, 3H, OCH_3), 3.80 (s, 2H, H-6a′, H-6b′), 4.00 (m, 1H, H-5′), 4.25 (t, 1H, H-4′), 4.95 (t, 1H, H-3′), 5.30 (t, 1H, H-2′), 5.95 (d, $J_{1'-2'}$ = 9.68, 1H, H-1′), 6.90–7.60 (dd, 4H, C_6H_4), 10.00 (s, 1H, NH). Anal. Calcd for $C_{25}H_{28}N_2O_{11}S_2$ (596.623): C, 50.3; H, 4.7; N, 4.7%. Found: C, 49.8; H, 4.9; N, 4.2%.

N-(4-Chlorophenyl)-2-cyano-3-mercapto-3-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)acrylamide **(12h):** yellow crystals, m.p. 120°C, 79% method A, 82% method B, $[\alpha]_D$+28.5, IR (KBr) ν_{max}/cm^{-1}3240 (NH), 2491 (SH), 2198 (CN), 1751 (CO). Anal. Calcd for $C_{24}H_{25}ClN_2O_{10}S_2$ (601.042): C, 48.0; H, 4.2; N, 4.7%. Found: C, 47.6; H, 4.1; N, 4.5%.

Sodium 4-amino-5-benzoyl-*N*-arylthiophene-3-carboxamide-2-thiolates (13a–e)

General procedure

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

4-Amino-5-benzoyl-2-mercapto-*N*-arylthiophene-3-carboxamides (14a–e)

General procedure

A solution of compounds **3** (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 just acidic, and the formed solid products were collected by filtration and recrystallized from ethanol.

4-Amino-*N*–aryl-5-benzoyl-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-gluco or galactopyranosylthio)thiophene-3-carboxamides (15a–h)

General procedures

Method A. To a solution of compounds **13** (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 sodium bromide formed. The resulting product was crystallized from ethanol.

Method B. A solution of compounds **14** (0.01 mol) in aq. potassium hydroxide [0.56g (0.01 mol) in distilled water (6mL)] was added to a solution of **5a,b** (4.10g, 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.

4-Amino-5-benzoyl-*N*-phenyl-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glu-copyranosylthio)thiophene-3-carboxamide **(15a):** brown crystals, m.p. 230°C, 61% method A, 70% method B, $[\alpha]_D$+27.5, IR (KBr) ν_{max}/cm^{-1}3440, 3325 (NH_2), 1751 (CO), 1680 (CO), 1658 (CO). ^{1}H NMR δ 1.70–1.95 (4s, 12H, 4 × CH_3CO), 3.90 (s, 2H, H-6a′, H-6b′), 4.05 (m, 1H, H-5′), 4.85–4.95 (m, 2H, H-4′, H-3′), 5.25–5.35 (m, 2H, H-2′, H-1′), 7.10–7.80 (m, 12H, 2 C_6H_5 and NH_2), 10.30 (s, 1H, NH). ^{13}C NMR δ 20.4–20.7 (4 × CH_3), 62.2 (CH_2, C-6′), 68.2 (C-4′), 69.8 (C-2′), 73.0 (C-3′), 74.8 (C-5′), 85.2 (C-1′), 109.9–154.7 (aromatic carbons), 160.9–187.0 (6 × CO). Anal. Calcd for $C_{32}H_{32}N_2O_{11}S_2$ (684.732): C, 56.1; H, 4.7; N, 4.1%. Found: C, 55.7; H, 5.2; N, 3.8%.

4-Amino-5-benzoyl-*N*-(4-methylphenyl)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)thiophene-3-carboxamide **(15b):** brown crystals, m.p. 216°C, 65% method A, 73% method B, $[\alpha]_D$+30.5, IR (KBr) ν_{max}/cm^{-1}3447,

3325 (NH_2), 1748 (CO), 1685 (CO), 1637 (CO). ^{1}H NMR δ 1.70–2.00 (4s, 12H, 4 × CH_3CO), 2.25 (s, 3H, CH_3), 3.90 (s, 2H, H-6a′, H-6b′), 4.05 (m, 1H, H-5′), 4.85 (m, 2H, H-4′, H-3′), 5.30–5.40 (m, 2H, H-2′, H-1′), 7.10–8.10 (m, 11H, C_6H_5, $C_6H_4$and NH_2), 10.20 (s, 1H, NH). ^{13}C NMR δ 20.1–20.5 (4 × CH_3), 62.0 (CH_2, C-6′), 67.8 (C-4′), 69.80 (C-2′), 73.5 (C-3′), 74.5 (C-5′), 84.9 (C-1′), 110.0–155.0 (aromatic carbons), 159.9–186.0 (6 × CO). Anal. Calcd for $C_{33}H_{34}N_2O_{11}S_2$ (698.758): C, 56.7; H, 4.9; N, 4.0%. Found: C, 57.0; H, 5.2; N, 4.7%.

4-Amino-5-benzoyl-*N*-(4-methoxyphenyl)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)thiophene-3-carboxamide **(15c):** brown crystals, m.p. 204°C, 68% method A, 76% method B, $[\alpha]_D$+40.5, IR (KBr) ν_{max}/cm^{-1}3448, 3325 (NH_2), 1751 (CO), 1675 (CO), 1635 (CO). ^{1}H NMR δ 1.70–1.95 (4s, 12H, 4 × CH_3CO), 3.75 (s, 3H, OCH_3), 3.95 (s, 2H, H-6a′, H-6b′), 4.05 (m, 1H, H-5′), 4.90 (m, 2H, H-4′, H-3′), 5.30–5.40 (m, 2H, H-2′, H-1′), 6.80–7.80 (m, 11H, C_6H_5, C_6H_4 and NH_2), 10.10 (s, 1H, NH). ^{13}C NMR δ 19.7–20.9 (4 × CH_3), 61.7 (CH_2, C-6′), 66.9 (C-4′), 68.6 (C-2′), 74.2 (C-3′), 75.9 (C-5′), 86.0 (C-1′), 108.7–150.0 (aromatic carbons), 161.0–180.0 (6 × CO). Anal. Calcd for $C_{33}H_{34}N_2O_{12}S_2$ (714.758): C, 55.44; H, 4.75; N, 3.91%. Found: C, 55.33; H, 5.17; N, 3.60%.

4-Amino-5-benzoyl-*N*-(4-chlorophenyl)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-glucopyranosylthio)thiophene-3-carboxamide **(15d):** brown crystals, m.p. 250°C, 69% method A, 77% method B, $[\alpha]_D$+40.0, IR (KBr) ν_{max}/cm^{-1}3433, 3332 (NH_2), 1751 (CO), 1670 (CO), 1651 (CO). ^{1}H NMR δ 1.65–1.95 (4s, 12H, 4 × CH_3CO), 3.95 (m, 3H, H-6a′, H-6b′,H-5′), 4.90 (t, 1H, H-4′), 5.00 (t, 1H, H-3′), 5.30–5.35 (m, 2H, H-2′, H-1′), 6.90–7.80 (m, 11H, C_6H_5, C_6H_4 and NH_2), 10.20 (s, 1H, NH).^{13}C NMR δ 20.0–21.6 (4 × CH_3), 62.0 (CH_2, C-6′), 68.0 (C-4′), 69.3 (C-2′), 73.5 (C-3′), 75.8 (C-5′), 85.0 (C-1′), 111.0–155.9 (aromatic carbons), 160.0–185.0 (6 × CO). Anal. Calcd for $C_{32}H_{31}ClN_2O_{11}S_2$ (719.177): C, 53.4; H, 4.3; N, 3.9%. Found: C, 53.8; H, 4.6; N, 3.4%.

4-Amino-5-benzoyl-*N*-phenyl-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)thiophene-3-carboxamide (**15e):** brown crystals, m.p. 195°C, 60% method A, 70% method B, $[\alpha]_D$+32.5, IR (KBr) ν_{max}/cm^{-1}3440, 3348 (NH_2), 1751 (CO), 1680 (CO), 1658 (CO).^{1}H NMR δ 1.60–2.00 (4s, 12H, 4 × CH_3CO), 3.95 (s, 2H, H-6a′, H-6b′), 4.30 (m, 1H, H-5′), 5.00 (t, 1H, H-4′), 5.20–5.30 (m, 3H, H-3′, H-2′, H-1′), 7.10–7.80 (m, 12H, 2 $C_6H_5$and NH_2), 10.30 (s, 1H, NH). ^{13}C NMR δ 20.4–20.6 (4 × CH_3), 61.9 (CH_2, C-6′), 67.2 (C-4′), 67.8 (C-2′), 71.0 (C-3′), 74.2 (C-5′), 85.5 (C-1′), 109.8–154.7 (aromatic and carbons), 160.9–187.0 (6 × CO). Anal. Calcd for $C_{32}H_{32}N_2O_{11}S_2$ (684.732): C, 56.1; H, 4.7; N, 4.1%. Found: C, 56.5; H, 4.5; N, 3.8%.

4-Amino-5-benzoyl-*N*-(4-methylphenyl)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)thiophene-3-carboxamide **(15f):** brown crystals, m.p.

160°C, 64% method A, 72% method B, $[\alpha]_D$+45.0, IR (KBr) ν_{max}/cm^{-1}3440, 3355 (NH_2), 1751 (CO), 1690 (CO), 1658 (CO). ^{1}H NMR δ 1.70–2.00 (4s, 12H, 4 × CH_3CO), 2.15 (s, 2H, NH_2), 2.30 (s, 3H, CH_3), 3.40 (s, 2H, H-6a′, H-6b′), 3.95 (m, 1H, H-5′), 4.20 (t, 1H, H-4′), 4.90 (t, 1H, H-3′), 5.10–5.30 (m, 2H, H-2′, H-1′), 7.00–8.00 (m, 9H, C_6H_5, C_6H_4), 10.20 (s, 1H, NH).^{13}C NMR δ 20.4–20.9 (5 × CH_3), 61.9 (CH_2, C-6′), 67.2 (C-4′), 67.8 (C-2′), 71.0 (C-3′), 74.2 (C-5′), 85.5 (C-1′), 109.8–154.7 (aromatic carbons), 160.8–187.0 (6 × CO). Anal. Calcd for $C_{33}H_{34}N_2O_{11}S_2$ (698.758): C, 56.7; H, 4.9; N, 4.0%. Found: C, 56.8; H, 4.7; N, 4.1%.

4-Amino-5-benzoyl-*N*-(4-methoxyphenyl)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)thiophene-3-carboxamide (**15g):** brown crystals, m.p. 167°C, 68% method A, 78% method B, $[\alpha]_D$+35.5, IR (KBr) ν_{max}/cm^{-1}3440, 3332 (NH_2), 1680 (CO), 1751 (CO), 1643 (CO).^{1}H NMR δ 1.70–2.05 (4s, 12H, 4 × CH_3CO), 3.75 (s, 3H, OCH_3), 3.95 (m, 3H, H-6a′, H-6b′, H-5′), 4.30 (t, 1H, H-4′), 5.00 (t, 1H, H-3′), 5.20–5.30 (m, 2H, H-2′, H-1′), 6.95–7.80 (m, 9H, C_6H_5, C_6H_4), 10.20 (s, 1H, NH). ^{13}C NMR δ 20.4–20.6 (4 × CH_3), 55.6 (OCH_3), 61.9 (CH_2, C-6′), 67.2 (C-4′), 67.8 (C-2′), 71.1 (C-3′), 74.2 (C-5′), 85.5 (C-1′), 109.7–154.7 (aromatic carbons), 160.7–187.0 (6 × CO). Anal. Calcd for $C_{33}H_{34}N_2O_{12}S_2$ (714.758): C, 55.4; H, 4.8; N, 3.9%. Found: C, 55.6; H, 5.2; N, 3.7%.

4-Amino-5-benzoyl−*N*-(4-bromophenyl)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-*D*-galactopyranosylthio)thiophene-3-carboxamide (**15h):** brown crystals, m.p. 210°C, 70% method A, 78% method B, $[\alpha]_D$+31.5, IR (KBr) ν_{max}/cm^{-1}3440, 3348 (NH_2), 1751 (CO), 1665 (CO), 1658 (CO).^{1}H NMR δ 1.64–1.94 (4s, 12H, 4 × CH_3CO), 3.91 (s, 2H, H-6a′, H-6b′), 4.06 (m, 1H, H-5′), 4.80–4.90 (m, 2H, H-4′, H-3′), 5.24–5.35 (m, 2H, H-2′, H-1′), 7.38–7.75 (m, 9H, C_6H_5, C_6H_4), 10.40 (s, 2H, NH_2), 10.67 (s, 1H, NH).^{13}C NMR δ 18.4–19.9 (4 × CH_3), 62.0 (CH_2, C-6′), 68.0 (C-4′), 69.4 (C-2′), 73.2 (C-3′), 74.5 (C-5′), 86.0 (C-1′), 105.0–150.2 (aromatic carbons), 163.0–181.4 (6 × CO). Anal. Calcd for $C_{33}H_{31}BrN_2O_{11}S_2$ (775.639): C, 50.4; H, 4.1; N, 3.7%. Found: C, 49.7; H, 4.6; N, 3.1%.

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