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Note

Synthesis and characterization of new aromatic aldehyde/ketone 4-(β-D-glucopyranosyl)thiosemicarbazones

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Dedicated to the memory of our colleague and distinguished scientist Dr. Nikos G. Oikonomakos

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ABSTRACT

A series of 22 aromatic aldehyde/ketone 4-(β-D-glucopyranosyl)thiosemicarbazones have been synthesized by condensation of 4-(per-O-acetylated-β-D-glucopyranosyl)thiosemicarbazide with an aldehyde or a ketone, and then, deacetylation of the resulting product. The compounds were fully characterized by spectroscopic techniques, elemental analysis, and for two derivatives by X-ray analysis. The data indicate the β configuration, and the *E* configuration pertaining to the stereochemistry of the C=N bond. However, a partial conversion of the *E*-form into the *Z*-form is possible in solution after several hours.

Glucose derivatives are known to be selective and efficient catalytic inhibitors of human liver glycogen phosphorylase, a target for the design of type 2 diabetes therapeutics.[1] In addition, since carbohydrates are readily available, highly functionalized, and have several stereogenic centres, they have widely been used as ligands in transition-metal catalyzed asymmetric reactions.[2] On the other hand, thiosemicarbazone is a class of biochemically important compounds possessing a wide range of biological activities, and is very promising in the treatment of many diseases.[3] Since these molecules can also serve as phosphane-free multidentate ligands for transition-metal catalysis, recently, we found that they are efficient ligands for palladium-catalyzed coupling reactions, in air.[4] Taking into consideration the broad range of applications of glucose as well as of thiosemicarbazone derivatives, we were interested in synthesising new compounds bearing both of these moieties as part of our ongoing research into glycogen phosphorylase inhibitors and tansition metal catalysis. In the past, only some sporadic papers have been published for the synthesis of aldehyde 4-(per-O-acetylated-β-D-glucopyranosyl)thiosemicarbazones and their corresponding deacetylated analogues, but in most of these papers, the products were not fully characterized, and detailed spectral data are not available.[5] Very recently, the synthesis and the spectroscopic characterization of a number of per-O-acetylated analogues were reported, together with their evaluation as antioxidant and anti-dyslipidemic agents.[6] The main synthetic step for the synthesis of these molecules is being the reaction of a glucosyl thiosemicarbazide with a carbonyl compound. Other glucosyl thiosemicarbazones in which the glucose anomeric centre is directly attached to the carbon atom of the C=N double bond of the thiosemicarbazone moiety have also been published, the synthesis of which was achieved by Raney-nickel–NaH_2PO_2 reduction of glucosyl cyanide to the corresponding semicarbazone in the presence of semicarbazide, and subsequent acid catalyzed transimination with thiosemicarbazide.[7] In the present paper, we report a systematic study for the synthesis and characterization of a series of 22 aromatic aldehyde/ketone 4-(β-D-glucopyranosyl)thiosemicarbazones.

The synthesis of the title molecules is outlined in Scheme 1. Condensation of 4-(per-O-acetylated-β-D-glucopyranosyl)thiosemicarbazide **1**[5a,c–f] with a number of aldehydes and ketones, by a known procedure,[5e,6] afforded aldehyde/ketone 4-(per-O-acetylated-β-D-glucopyranosyl)thiosemicarbazones **2**. The acetyl protective groups of **2** were removed by the Zemplén method[8] in absolute methanol in the presence of sodium methoxide, yielding the target molecules **3**. In the FT-IR spectra, the bands corresponding to N–H, C=N and C=S stretching vibration are observed at 3310–3350,

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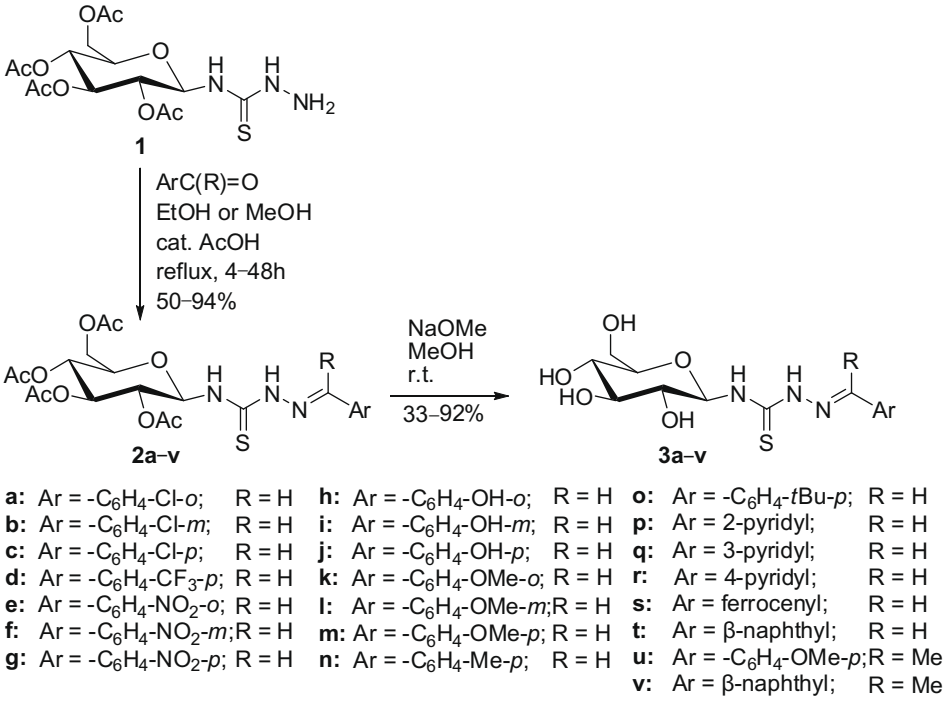

Scheme 1. Synthesis of aldehyde/ketone 4-(β-D-glucopyranosyl)thiosemicarbazones.

1525–1553 and 1031–1049 cm^{-1}, respectively. A band at the region 810–851 cm^{-1} is also contributed to ν(C=S). The characteristic bands at 1725–1753 cm^{-1} due to the C=O stretching vibration of the acetyl groups in compounds **2**, vanish in the IR spectra of **3**, and a broad absorption band of the hydroxyl group appears at 3203–3597 cm^{-1}. The NMR chemical shift range for some characteristic protons (N(2)H, N(4)H, CH=N, anomeric 1-H) in compounds **2** and **3**, and the hydroxy protons of the glucose moiety in compounds **3**, as well as some characteristic carbons (C=S, C=N, 1-C) in compounds **2** and **3** and the acetyl C=O in compounds **2**, is presented in Table 1. The atom numbering used for the NMR data is as shown for **2p** (Fig. 1). In the ^{1}H NMR spectra of **2** and **3**, the anomeric proton 1-H is represented as a doublet of doublets at the range 5.61–5.87 and 5.35–5.44 ppm, respectively, due to the coupling with the N(4)H and the 2-H. The coupling constant $J_{1\text{-H,2-H}}$ (9.0–9.6 Hz) is an evidence which confirms the β configuration in compounds **2** and **3**.[5d,9]

Table 1
NMR chemical shift range (in ppm) for some characteristic proton and carbon atoms in compounds **2** and **3**

	2	**3**
^{1}H NMR		
N(2)H	8.81–11.72 (s)	10.47–12.03 (s)
N(4)H	7.81–8.50 (d)	8.18–8.80 (d)
	$J_{1\text{-H,N(4)H}}$ 8.7–9.3 Hz	$J_{1\text{-H,N(4)H}}$ 8.4–9.3 Hz
CH=N	7.69–8.57 (s)[a]	7.95–8.53 (s)[a]
1-H	5.61–5.87 (dd)	5.35–5.44 (dd)
	$J_{1\text{-H,2-H}}$ 9.0–9.3 Hz	$J_{1\text{-H,2-H}}$ 9.0–9.6 Hz
Glucose OH		4.45–5.13 (br s, m, t)[b]
^{13}C NMR		
C=S	177.0–179.6	177.5–179.6
C=O	169.3–170.0	
C=N	138.8–149.9	138.0–149.1
1-C	81.2–82.5	83.7–84.3

[a] This signal is absent in compounds **2u**,**v** and **3u**,**v**.
[b] An exception: the OH groups in compound **3s** are represented by a broad singlet at 3.90 ppm.

It has previously been published that thiosemicarbazone derivatives pertaining to the stereochemistry of the C=N bond, can exist in the *E*- or *Z*-form or as a mixture of *E*/*Z* isomers, usually with the *E*-form being the major isomer.[10] Variation in isomeric ratios is dependent on the substituents on the thiosemicarbazone moiety and the solvent. The correct configuration can be determined by ^{1}H NMR spectroscopy, as the N(2)H appears at 9–12 ppm for the *E*-form, and 14–15 ppm for the *Z*-form.[10c] In the ^{1}H NMR spectra of freshly prepared solutions of **2** and **3** in $CDCl_3$ or DMSO-d_6, only one signal was observed for each hydrogen, indicating the presence of only one isomer (*E*), since the N(2)H resonance was assigned in the range 8.81–12.03 ppm. However, a partial conversion of the *E*-form into the *Z*-form is possible for some compounds in solution after a while. In Figure 1, we present the ^{1}H NMR spectra of **2p** in $CDCl_3$ at different times. In a freshly prepared solution, only the *E* isomer exists (spectrum (a)), but after 24 h, all signals are duplicated which indicates that both *E* and *Z* isomers coexist in solution, with the *E*-form being the major isomer (spectrum (b)). In the *Z*-form, an intramolecular hydrogen bond should be formed between N(2)H and the pyridine nitrogen.[10b,e] After 48 h, the equilibrium leads to the two forms in a ratio of about 1:1 (spectrum (c)). The most characteristic signals indicating the formation of the two forms are those for N(2)H (10.14 ppm for *E*, 14.63 ppm for *Z*), N(4)H (8.45 ppm for *E*, 8.33 ppm for *Z*), the azomethine hydrogen CH=N (7.96 ppm for *E*, 7.15 ppm for *Z*) and the anomeric proton 1-H (5.72 ppm for *E*, 5.86 ppm for *Z*). ^{13}C NMR spectra could also provide information for the geometry of the molecules.[11] The most significant resonance for the geometry determination is that of the azomethine carbon CH=N, presented as only one signal at 143.5 ppm in a short time ^{13}C NMR experiment (H-decoupling) of a freshly prepared solution of **2p** in $CDCl_3$, indicating the presence of only one isomer. However, in an overnight ^{13}C NMR experiment (H-coupling), the signal is duplicated as an evidence that both *E* and *Z* isomers coexist in solution. In addition to the above-mentioned signal with $^1J_{C,H}$ value of 167.0 Hz, the azomethine carbon resonance of the other isomer appeared at 137.5 ppm ($^1J_{C,H}$ 164.4 Hz). The resonance at lower field is assigned to the *E*-form, and that at the higher field to the *Z*-form.[11b]

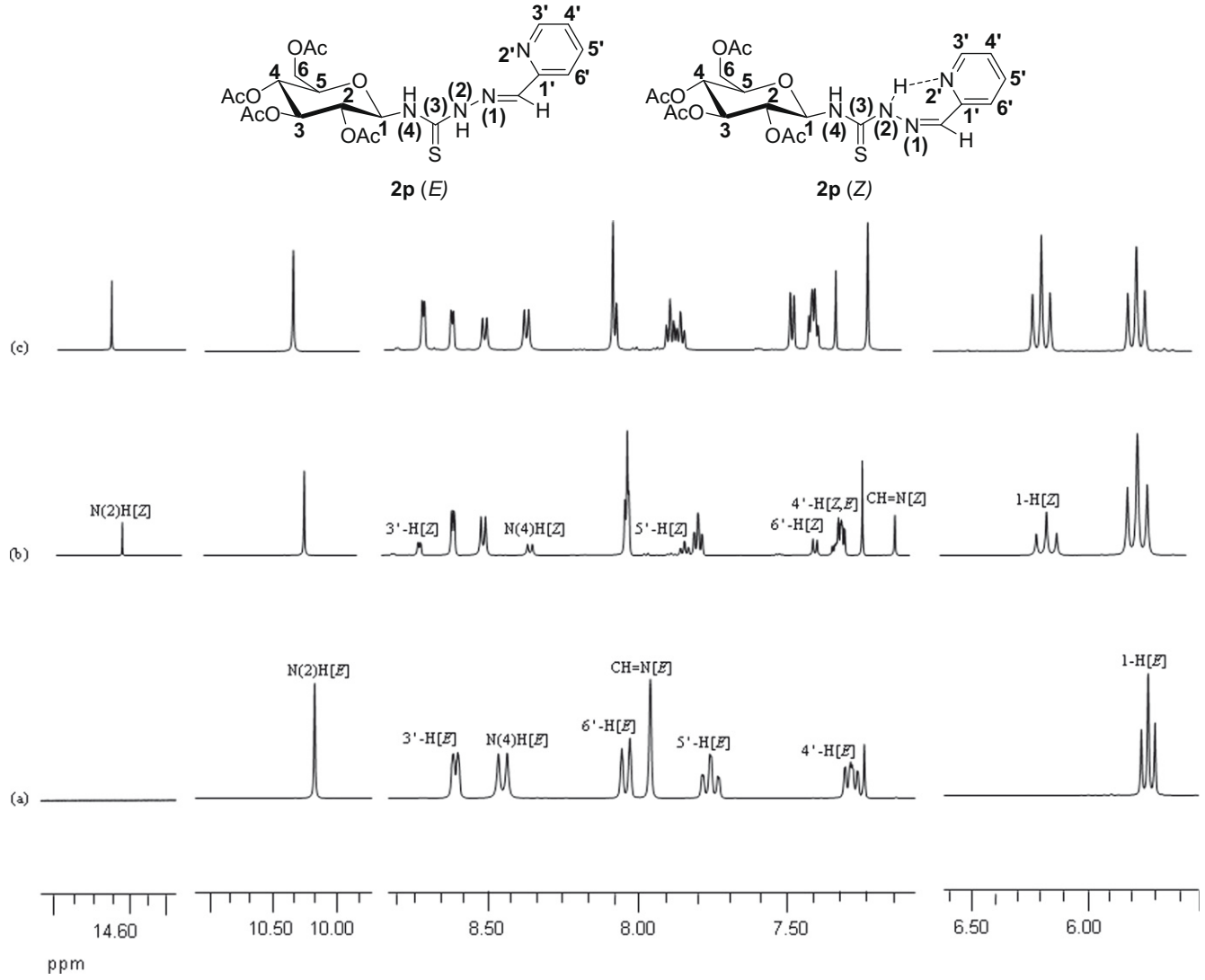

Figure 1. Part of the ^{1}H NMR spectra (600 MHz) for **2p** (*E*/*Z* isomers) in $CDCl_3$ at different times: (a) 5 min; (b) 24 h and (c) 48 h.

Colourless crystals of the acetylated derivative **2d** and the deacetylated product **3j** suitable for X-ray determination were obtained by slow crystallization from ethanol and methanol, respectively. The molecular structures of **2d** and **3j** are given in Figure 2. Selected interatomic distances, bond angles and torsion angles are collected in Table 2. In compound **2d**, the three F atoms are disordered. The pyranosyl ring adopts a chair conformation, with the values of the puckering parameters being $Q = 0.590(3)$ Å, $\theta = 176.6(3)°$, $\varphi = 138(4)°$ (**2d**), and $Q = 0.586(2)$ Å, $\theta = 9.1(2)°$, $\varphi = 42(7)°$ (**3j**). In **2d**, the atoms C(11) and C(14) deviate on opposite sides from the mean plane formed by the other atoms (C(12), C(13), C(15) and O(1)) by 0.232(2) and −0.241(3) Å, respectively. In a similar way in **3j**, the atoms C(9) and C(12) deviate by 0.287(2) and −0.184(1) Å, respectively, from the mean plane through the other atoms (C(10), C(11), C(13) and O(2)). For both compounds, the aglycone occupies an equatorial position (in **2d**, the torsion angle N(2)–C(11)–C(12)–C(13) is −172.8(2)°; in **3j**, the torsion angle N(3)–C(9)–C(10)–C(11) is −180.0(2)°), which is assumed to be the most stable form, and thus indicating the β-configuration. As in other β-pyranoses,[12] the orientation of the primary alcohol group in **3j** is *gauche*, with the torsion angle O(2)–C(13)–C(14)–O(6) being 61.7(2)°. The dihedral angle between the phenyl ring and the pyranosyl ring is 65.5(2) and 67.6(2)° for **2d** and **3j**, respectively. The compound **2d** exhibits *E*, *Z* configuration in relation to the C(8)–N(3) and N(1)–C(10) bond, respectively, and compound **3j** exhibits the same configuration in relation to the C(7)–N(1) and N(2)–C(8) bond, respectively. In both molecules, the thiosemicarbazone moiety is almost planar, due to the C=N double bond. Meanwhile, in **2d**, atoms N(2) and N(3) are involved in an intramolecular N(2)–H···N(3) interaction, and in **3j**, atoms N(3) and N(1) are involved in N(3)–H···N(1) interaction, which also contributes to the planarity of the thiosemicarbazone group. The formation of these hydrogen bonds was favoured by the *Z* configuration in relation to the N(1)–C(10) and N(2)–C(8) bond in **2d** and **3j**, respectively. In both compounds, the S–C and the azomethine C–N bond distances exhibit increased double bond character. The N–N and both thioamide C–N bond distances indicate a considerable double bond character. This is indicative of the greater conjugation and more delocalized electron density of the thiosemicarbazone moiety.[13]

The two molecules are stabilized by intra- and intermolecular interactions. The packing diagrams of **2d** and **3j** are presented in Figure 3, and the intra and inter-molecular contacts are collected in Table 3. The monomers of **2d** are linked by two intermolecular bonds C(8)–H(C8)···O(7) and C(12)–H(C12)···S(1). The monomers of **3j** are connected by strong and weak intermolecular hydrogen

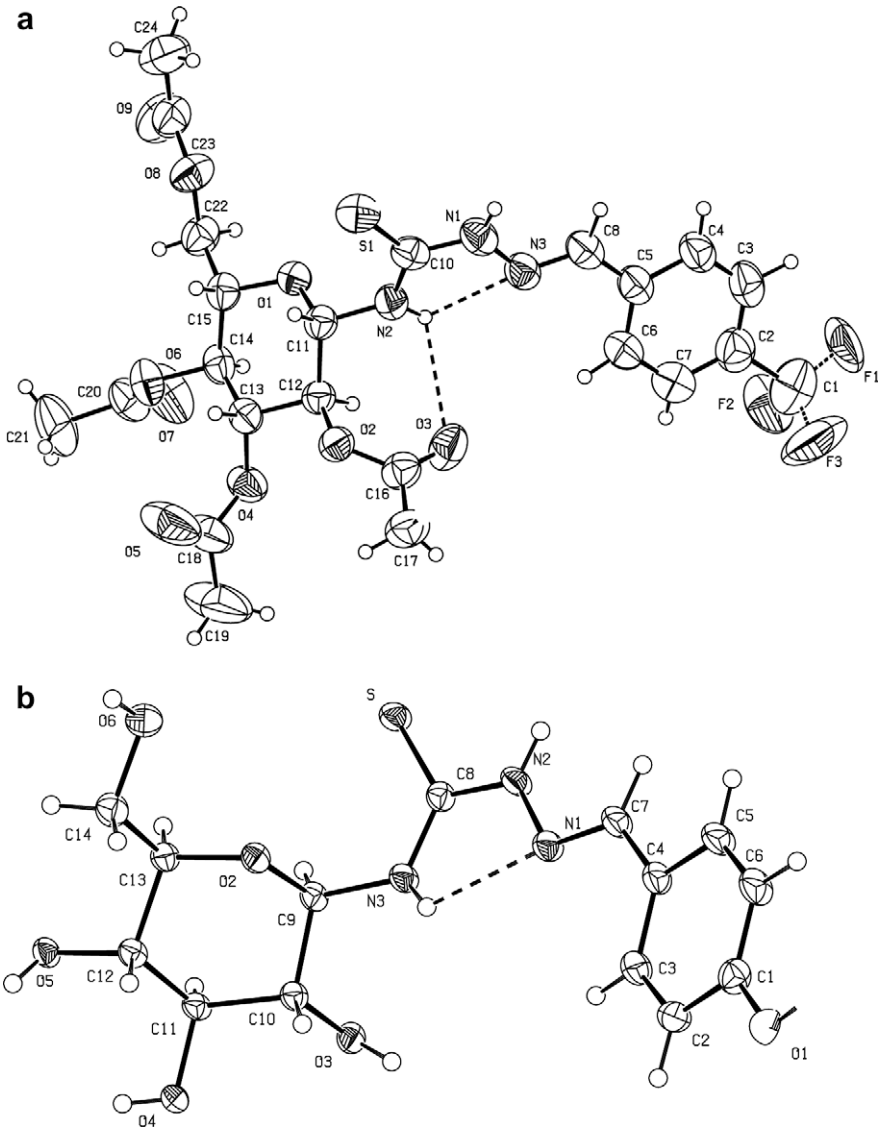

Figure 2. Labelled ORTEP diagram of **2d** ((a), top) and **3j** ((b), bottom) with 40% thermal probability ellipsoids.

bonding interactions O–H···O, N–H···O, O–H···S and C–H···O into a three-dimensional framework.

1. Experimental

1.1. General

4-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazide (**1**) was synthesized in accordance with a known procedure by treatment of (2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)isothiocyanate with dry hydrazine in ethanol.[5e] The only modification in this procedure was the reaction temperature, which was kept at 5–10 °C in order to avoid the formation of a carbohydrate bearing diacylhydrazine framework.[14] The above-mentioned isothiocyanate was prepared by the reaction of (per-O-acetylated-α-D-glucopyranosyl)bromide (prepared from D-glucose pentaacetate)[15] with potassium thiocyanate in the melt.[16] D-Glucose pentaacetate, aldehydes and ketones ArC(R)=O were commercially available. All reactions were carried out under an argon atmosphere with purified and dry reagents and solvents. Column chromatography was performed using silica gel and TLC on Kieselgel 60 F_{254} plates; the plates were visualized under UV light or by gentle heating after spraying with an ethanolic solution (5% H_2SO_4). Melting points were measured on a Nikon 50i Pol microscope equipped with a Linkam THMS600 hot stage and a TMS94 temperature controller or on a Büchi melting point apparatus, and were not corrected. Optical rotations were measured on a Perkin–Elmer polarimeter at room temperature. IR measurements were made using a Bruker Tensor 27 instrument. NMR measurements were made using a Varian 300 (300.13 MHz and 75.47 MHz for ^1H and ^{13}C, respectively) or 600 (599.83 MHz and 150.84 MHz for ^1H and ^{13}C, respectively). The assignment of protons and carbons in the ^1H and ^{13}C NMR spectra was performed by COSY, NOESY, DEPT, GHSQC and GHMBC experiments. Atom numbering used for the NMR spectra is as shown for **2p** in Figure 1. Elemental analyses for C, H and N were carried out on a Perkin–Elmer PE 2400 II instrument. The acetylated derivatives **2a**,[5g,h] **2c**,[5b,g,h] **2g**,[5a,g,h] **2e**,[5g,h] **2h**,[5c] **2i**,[5c] **2j**,[5a,c,e] **2k**[5g,h] and the deacetylated analogues **3c**,[5b] **3g**,[5a] **3h**,[5c] **3i**[5c] and **3j**[5a,c] have been published in the past, but in most cases, without detailed spectral data. In a very recent paper, NMR data were given for compounds **2c**,**g**,**m**,**q**,**r**, and although the data are mainly in accordance with those given below, there are some differences,

Table 2
Selected geometric parameters in compounds **2d** and **3j**

2d		3j	
(a) Bond distances (Å)			
O(1)–C(15)	1.422(3)	O(2)–C(13)	1.425(2)
O(1)–C(11)	1.427(3)	O(2)–C(9)	1.426(2)
N(2)–C(11)	1.435(3)	N(3)–C(9)	1.432(2)
N(2)–C(10)	1.336(4)	N(3)–C(8)	1.346(2)
S(1)–C(10)	1.668(3)	S–C(8)	1.704(2)
N(1)–C(10)	1.359(4)	N(2)–C(8)	1.335(2)
N(1)–N(3)	1.374(4)	N(1)–N(2)	1.389(2)
N(3)–C(8)	1.274(4)	N(1)–C(7)	1.284(2)
F(1)–C(1)	1.278(6)	O(1)–C(1)	1.350(2)
(b) Bond angles (°)			
C(11)–O(1)–C(15)	113.0(2)	C(9)–O(2)–C(13)	112.0(2)
O(1)–C(11)–N(2)	107.2(2)	O(2)–C(9)–N(3)	107.3(2)
N(2)–C(11)–C(12)	109.8(2)	N(3)–C(9)–C(10)	113.0(2)
C(10)–N(2)–C(11)	124.2(2)	C(8)–N(3)–C(9)	121.8(2)
S(1)–C(10)–N(2)	125.8(2)	S–C(8)–N(3)	106.6(2)
S(1)–C(10)–N(1)	120.3(2)	S–C(8)–N(2)	121.2(2)
N(1)–C(10)–N(2)	114.0(3)	N(2)–C(8)–N(3)	116.2(2)
N(3)–N(1)–C(10)	120.2(3)	N(1)–N(2)–C(8)	119.3(2)
N(1)–N(3)–C(8)	117.2(3)	N(2)–N(1)–C(7)	114.1(2)
N(3)–C(8)–C(5)	121.2(3)	N(1)–C(7)–C(4)	122.5(2)
(c) Torsion angles (°)			
O(1)–C(15)–C(22)–O(8)	−74.5(3)	O(2)–C(13)–C(14)–O(6)	61.7(2)
O(1)–C(15)–C(14)–C(13)	−65.2(3)	O(2)–C(13)–C(12)–C(11)	−51.8(2)
C(15)–C(14)–C(13)–C(12)	−56.0(3)	C(13)–C(12)–C(11)–C(10)	48.9(2)
C(14)–C(13)–C(12)–C(11)	53.9(3)	C(12)–C(11)–C(10)–C(9)	−52.8(2)
C(13)–C(12)–C(11)–O(1)	−55.5(3)	C(11)–C(10)–C(9)–O(2)	61.3(2)
C(12)–C(11)–O(1)–C(15)	63.0(3)	C(10)–C(9)–O(2)–C(13)	−69.1(2)
N(2)–C(11)–O(1)–C(15)	−178.1(2)	N(3)–C(9)–O(2)–C(13)	168.6(2)
N(2)–C(11)–C(12)–C(13)	−172.8(2)	N(3)–C(9)–C(10)–C(11)	−180.0(2)
C(11)–N(2)–C(10)–S(1)	7.9(4)	C(9)–N(3)–C(8)–S	−15.1(2)
C(11)–N(2)–C(10)–N(1)	−172.9(3)	C(9)–N(3)–C(8)–N(2)	165.8(2)
N(2)–C(10)–N(1)–N(3)	−2.1(4)	N(3)–C(8)–N(2)–N(1)	−5.2(2)
C(10)–N(1)–N(3)–C(8)	174.2(3)	C(8)–N(2)–N(1)–C(7)	−174.6(20)
N(1)–N(3)–C(8)–C(5)	177.4(3)	N(2)–N(1)–C(7)–C(4)	176.7(20)

in particular the assignment of 1-H and 3-H of the sugar ring in the ^{1}H NMR spectra.[6] The authors assigned 3-H to the lower field resonance compared to that for 1-H,[6] whereas now, based on COSY NMR experiments, we conclude that these assignments should be reversed.

Table 3
Inter- and intramolecular contacts (Å, °) for **2d** and **3j**

Donor (D)	H	Acceptor (A)	D···A[a]	H···A	D–H···A
2d					
C(8)	H(C8)	O(7)^{i}	3.207(4)	2.53(3)	124(2)
C(12)	H(C12)	S(1)^{ii}	3.765(3)	2.78(3)	165(2)
N(2)	H(N2)	O(3)	3.018(3)	2.55(3)	114(2)
N(2)	H(N2)	N(3)	2.592(3)	2.14(3)	111(2)
C(11)	H(C11)	S(1)	3.127(3)	2.69(2)	108(2)
C(12)	H(C12)	O(3)	2.696(3)	2.33(2)	100(2)
C(13)	H(C13)	O(5)	2.683(4)	2.30(2)	105(2)
C(14)	H(C14)	O(7)	2.688(4)	2.24(3)	109(2)
3j					
O(1)	H(O1)	O(6)^{iii}	2.817(2)	2.08(3)	156(3)
N(2)	H(N2)	O(5)^{iv}	3.038(2)	2.23(2)	161(3)
O(3)	H(O3)	S^{v}	3.168(2)	2.32(2)	176(2)
O(4)	H(O4)	O(3)^{vi}	2.730(2)	1.97(2)	160(2)
O(5)	H(O5)	O(4)^{vi}	2.643(2)	1.87(2)	164(2)
O(6)	H(O6)	S^{vii}	3.260(2)	2.48(3)	174(2)
C(6)	H(C6)	O(2)^{iii}	3.203(2)	2.36(2)	152(2)
C(7)	H(C7)	O(5)^{iv}	3.354(2)	2.53(2)	146(2)
C(9)	H(C9)	S	3.043(26)	2.68(2)	103(2)
N(3)	H(N3)	N(1)	2.615(2)	2.20(2)	114(2)
O(4)	H(O4)	O(5)	2.917(2)	2.55(2)	110(2)

[a] Symmetry codes: (i) $1-x, 1/2+y, -7/2-z$; (ii) $1-x, -1/2+y, -7/2-z$; (iii) $1/2+x, 1/2-y, 2-z$; (iv) $3/2-x, 1-y, 1/2+z$; (v) $2-x, -1/2+y, 3/2-z$; (vi) $-1/2+x, 1/2-y, 1-z$; (vii) $-1+x, y, z$.

1.2. General procedure for the synthesis of aldehyde/ketone 4-(per-O-acetylated-β-D-glucopyranosyl)thiosemicarbazones 2

A solution of aldehyde or ketone (2.38 mmol) in ethanol (5 mL) was added dropwise to a solution of 4-(2,3,4,6–tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazide (**1**) (1 g, 2.38 mmol) in ethanol (80 mL). For the synthesis of **2o**, **2p**, **2q** and **2r**, methanol was used as solvent. After the addition of a catalytic amount of AcOH, the reaction mixture was refluxed for 4–48 h. The solution was kept in fridge overnight to form a precipitate; in some cases the solution was concentrated to the half volume at temperature below 40 °C, and then water was added to precipitate a solid. The precipitate

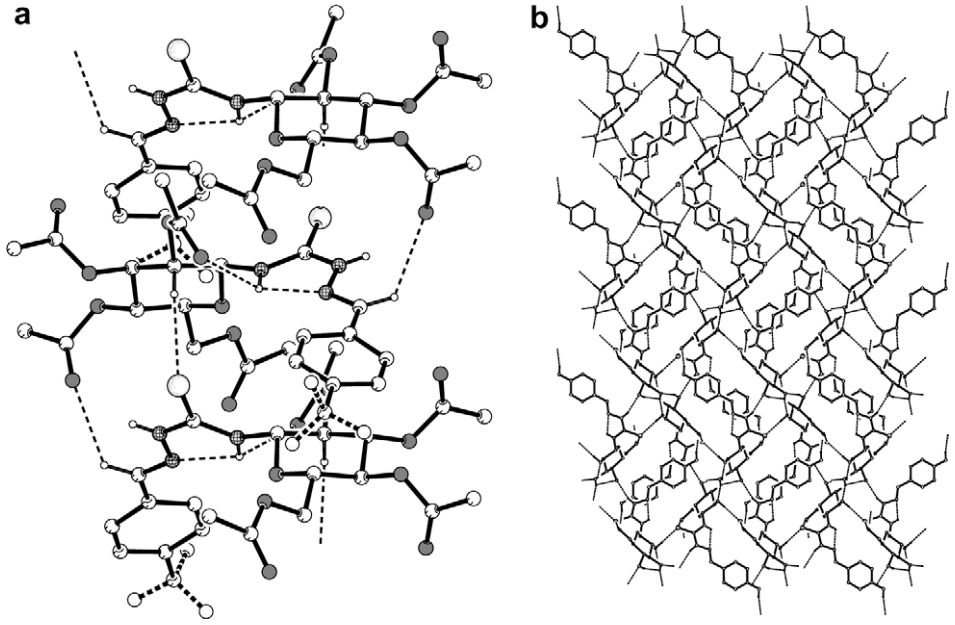

Figure 3. Packing diagram of **2d** ((a), left) and **3j** ((b), right) along the *c*- and *a*-axis, respectively.

was filtered off, washed with cold ethanol and in some cases with ether and recrystallized from methanol (or ethanol for the compounds **2p**, **2q** and **2r**).

1.2.1. 2-Chloro-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2a)

Yield 66%; mp 172–175 °C; R_f (Hex/EtOAc 1:1) 0.43; $[\alpha]_D^{25}$ −103.0 (*c* 1.07, $CHCl_3$); IR (KBr): *ν* 3350 (N–H), 2975 (C–H_{arom}), 1745 (C=O), 1533 (C=N), 1039 (C=S), 920 (1-C–H), 822 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.76 (s, 1H, N(2)H), 8.29 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 8.26 (s, 1H, CH=N), 8.09–8.06 (m, 1H, H_{arom}), 7.37–7.30 (m, 3H, H_{arom}), 5.72 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.41 (t, $^3J_{2\text{-H,3-H}}$ 9.6 Hz, 1H, 3-H), 5.19–5.09 (m, 2H, 2-H, 4-H), 4.37 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.13 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.89 (ddd, $^3J_{4\text{-H,5-H}}$ 9.9 Hz, 1H, 5-H), 2.07, 2.04, 2.03 and 2.02 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.5 (C=S), 170.0, 169.5, 169.4 and 169.3 (C=O), 139.7 (CH=N), 133.4, 131.6, 131.1, 129.8, 127.6 and 127.3 (C_{arom}), 81.5 (1-C), 72.7 (3-C), 72.2 (2-C), 70.9 (5-C) 67.8 (4-C), 61.7 (6-C), 20.5, 20.4, 20.3 and 20.3 (CH_3). Anal. Calcd for $C_{22}H_{26}ClN_3O_9S{\cdot}H_2O$ (561.99): C, 47.02; H, 5.02; N, 7.48. Found: C, 47.54; H, 4.86; N, 7.03.

1.2.2. 3-Chloro-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2b)

Yield 66%; mp 192–196 °C; R_f (Hex/EtOAc 1:1) 0.60; $[\alpha]_D^{25}$ −82.7 (*c* 1, $CHCl_3$); IR (KBr): *ν* 3324 (N–H), 2995 (C–H_{arom}), 1749 (C=O), 1549 (C=N), 1043 (C=S), 908 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.64 (s, 1H, N(2)H), 8.35 (d, 1H, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.77 (s, 1H, H_{arom}), 7.74 (s, 1H, CH=N), 7.58 (d, ^3J 6.9 Hz, 1H, H_{arom}), 7.42–7.33 (m, 2H, H_{arom}), 5.67 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.42 (dd, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.22–5.11 (m, 2H, 2-H, 4-H), 4.38 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.15 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.92 (ddd, $^3J_{4\text{-H,5-H}}$ 9.9 Hz, 1H, 5-H), 2.09 and 2.04 (2 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 179.1 (C=S), 171.2, 170.7, 169.9 and 169.6 (C=O), 141.7 (CH=N), 135.0, 134.7, 130.7, 130.2, 127.3 and 126.0 (C_{arom}), 82.4 (1-C), 73.5 (3-C), 72.5 (2-C), 70.6 (5-C), 68.4 (4-C), 61.6 (6-C), 20.8, 20.7 and 20.6 (CH_3). Anal. Calcd for $C_{22}H_{26}ClN_3O_9S$ (543.97): C, 48.57; H, 4.82; N, 7.72. Found: C, 48.78; H, 5.11; N, 8.04.

1.2.3. 4-Chloro-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2c)

Yield 53%; mp 214–217 °C, lit.[5b] mp 216–218 °C, lit.[6] mp 198–200 °C; R_f (Hex/EtOAc 1:1) 0.58; $[\alpha]_D^{25}$ −78.0 (*c* 1, $CHCl_3$), lit.[5b] $[\alpha]_D^{25}$ −89 (*c* 1, $CHCl_3$); IR (KBr): *ν* 3316 (N–H), 2983 (C–H_{arom}), 1745 (C=O), 1549 (C=N), 1039 (C=S), 912 (1-C–H), 835 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.40 (s, 1H, N(2)H), 8.30 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.72 (s, 1H, CH=N), 7.65 (d, ^3J 8.4 Hz, 2H, H_{arom}), 7.40 (d, ^3J 8.4 Hz, 2H, H_{arom}), 5.69 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.41 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.20–5.10 (m, 2H, 2-H, 4-H), 4.36 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.3 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz; 1H, 6′-H), 3.91 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.09, 2.05, 2.04 and 2.03 and (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 178.9 (C=S), 171.1, 170.7, 169.9 and 169.6 (C=O), 142.7 (CH=N), 137.0, 131.6 129.4 and 129.0 (C_{arom}), 82.3 (1-C), 73.7 (3-C), 72.8 (2-C), 70.7 (5-C), 68.6 (4-C), 61.8 (6-C), 20.7, 20.6, 20.6 and 20.6 (CH_3). Anal. Calcd for $C_{22}H_{26}ClN_3O_9S{\cdot}4H_2O$ (616.04): C, 42.89; H, 5.56; N, 6.82. Found: C, 43.12; H, 5.99; N, 6.44.

1.2.4. 4-Trifluoromethyl-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2d)

Yield 73%; mp 223–225 °C; R_f (Hex/EtOAc 1:1) 0.42; $[\alpha]_D^{25}$ −80.2 (*c* 1.17, $CHCl_3$); IR (KBr): *ν* 3334 (N–H), 2938 (C–H_{arom}), 1749 (C=O), 1529 (C=N), 1031 (C=S), 912 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 10.14 (s, 1H, N(2)H), 8.38 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.84 (s, 1H, CH=N), 7.83 (d, ^3J 8.7 Hz, 2H, H_{arom}), 7.67 (d, ^3J 8.4 Hz, 2H, H_{arom}), 5.67 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.42 (t, $^3J_{2\text{-H,3-H}}$ 9.3 Hz, 1H, 3-H), 5.20–5.10 (m, 2H, 2-H, 4-H), 4.40 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.15 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.90 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.09, 2.05, 2.04 and 2.03 (4 × s, 1H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 179.0 (C=S), 171.1, 170.7, 169.9 and 169.6 (C=O), 141.9 (CH=N), 136.3, 132.3, 131.9, 127.8, 125.8, 125.8 and 121.9 (C_{arom} and CF_3), 82.2 (1-C), 73.5 (3-C), 72.5 (2-C), 70.5 (5-C5), 68.3 (4-C), 61.6 (6-C), 20.7, 20.6 and 20.6 (CH_3). Anal. Calcd for $C_{23}H_{26}F_3N_3O_9S$ (577.53): C, 47.83; H, 4.54; N, 7.28. Found: C, 48.18; H, 4.37; N, 6.99.

1.2.5. 2-Nitro-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2e)

Yield 92%; mp 136–140 °C; R_f (Hex/EtOAc 1:1) 0.46; $[\alpha]_D^{25}$ −49.2 (*c* 1, $CHCl_3$); IR (KBr): *ν* 3320 (N–H), 2946 (C–H_{arom}), 1745 (C=O), 1525 (C=N), 1035 (C=S), 916 (1-C–H), 822 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.69 (s, 1H, N(2)H), 8.43 (s, 1H, CH=N), 8.30 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.21 (dd, *J* 1.5 Hz, *J* 7.8 Hz, 1H, H_{arom}), 8.06 (dd, *J* 1.2 Hz, *J* 8.1 Hz, 1H, H_{arom}), 7.75–7.69 (m, 1H, H_{arom}), 7.61–7.55 (m, 1H, H_{arom}), 5.73 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.42 (dd, $^3J_{2\text{-H,3-H}}$ 9.3 Hz, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.18–5.09 (m, 2H, 2-H, 4-H), 4.38 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.14 (dd, $^3J_{5\text{-H,6′-H}}$ 2.16 Hz, 1H, 6′-H), 3.92 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.09, 2.05, 2.04 and 2.03 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 179.3 (C=S), 171.3, 170.7, 169.9 and 169.7 (C=O), 148.3 (C–NO_2), 138.8 (CH=N), 133.8, 130.8, 128.6 and 125.0 (C_{arom}), 82.3 (1-C), 73.6 (3-C), 72.6 (2-C), 70.7 (5-C), 68.3 (4-C), 61.6 (6-C), 20.8 and 20.6 (CH_3). Anal. Calcd for $C_{22}H_{26}N_4O_{11}S{\cdot}2H_2O$ (590.56): C, 44.74; H, 5.12; N, 9.49. Found: C, 45.01; H, 5.48; N, 9.23.

1.2.6. 3-Nitro-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2f)

Yield 79%; mp 191–195 °C; R_f (Hex/EtOAc 1:1) 0.36; $[\alpha]_D^{25}$ −84.8 (*c* 1, $CHCl_3$); IR (KBr): *ν* 3328 (N–H), 2979 (C–H_{arom}), 1737 (C=O), 1529 (C=N), 1035 (C=S), 920 (1-C–H), 820 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 10.07 (s, 1H, N(2)H), 8.57 (s, 1H, CH=N), 8.43 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.28 (d, *J* 1.28 Hz, 1H, H_{arom}), 8.08 (d, *J* 7.8 Hz, 1H, H_{arom}), 7.91 (s, 1H, H_{arom}), 7.63 (t, *J* 8.1 Hz, 1H, H_{arom}), 5.65 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.43 (t, $^3J_{2\text{-H,3-H}}$ 9.3 Hz, 1H, 3-H), 5.21–5.11 (m, 2H, 2-H, 4-H), 4.39 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H,6′-H}}$ 12.6 Hz, 1H, 6′-H), 3.93 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz,1H, 5-H), 2.09, 2.05, 2.04 and 2.03 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 179.2 (C=S), 171.3, 170.7, 169.9 and 169.6 (C=O), 148.8 (C–NO_2), 140.5 (CH=N), 134.8, 132.8, 130.0, 125.0 and 122.5 (C_{arom}), 82.4 (1-C), 73.6 (3-C), 72.5 (2-C), 70.7 (5-C), 68.4 (4-C), 61.6 (6-C), 21.0 and 20.8 (CH_3). Anal. Calcd for $C_{22}H_{26}N_4O_{11}S{\cdot}3H_2O$ (608.57): C, 43.42; H, 5.30; N, 9.21. Found: C, 43.72; H, 5.68; N, 8.89.

1.2.7. 4-Nitro-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2g)

Yield 64%; mp 218–220 °C, lit.[5a] mp 207 °C, lit.[6] mp 201–203 °C; R_f (Hex/EtOAc 1:1) 0.42; $[\alpha]_D^{25}$ −110.0 (*c* 1, $CHCl_3$), lit.[5a] $[\alpha]_D^{25}$ −114 (*c* 1, $CHCl_3$); IR (KBr): *ν* 3314 (N–H), 2975 (C–H_{arom}), 1741 (C=O), 1525 (C=N), 1031 (C=S), 920 (1-C–H), 826 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 10.11 (s, 1H, N(2)H), 8.42 (d, $^3J_{1\text{-H,N(4)H}}$ 9.3 Hz, 1H, N(4)H), 8.28 (d, *J* 8.7 Hz, 2H, H_{arom}), 7.91 (d, *J* 9.0 Hz, 2H, H_{arom}), 7.90 (s, 1H, CH=N), 5.65 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.43 (dd, $^3J_{2\text{-H,3-H}}$ 9.3 Hz, $^3J_{3\text{-H,4-H}}$ 9.6 Hz,1H, 3-H), 5.20–5.11 (m, 2H, 2-H, 4-H), 4.38 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H,6′-H}}$ 1.8 Hz, 1H, 6′-H), 3.92 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.09, 2.06 and 2.04 (3 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 179.2 (C=S), 171.3, 170.7, 169.9 and 169.6 (C=O), 148.8 (C–NO_2), 140.4 (CH=N), 138.9, 128.2 and 124.2 (C_{arom}), 82.4 (1-C), 73.6 (3-C), 72.4 (2-C), 70.6 (5-C), 68.4 (4-C), 61.6 (6-C), 20.8, 20.7 and 20.6 (CH_3). Anal. Calcd for $C_{22}H_{26}N_4O_{11}S$ (554.53): C, 47.65; H, 4.73; N, 10.10. Found: C, 47.98; H, 5.12; N, 10.76.

1.2.8. 2-Hydroxy-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2h)

Yield 85%; mp 200 °C (decomp.), lit.[5c] mp 158–160 °C; R_f (Hex/EtOAc 1:1) 0.37; $[\alpha]_D^{25}$ −147.0 (*c* 1, $CHCl_3$); IR (KBr): *ν* 3330 (N–H), 2948 (C–H_{arom}), 1745 (C=O), 1533 (C=N), 1022 (C=S), 920 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.81 (s, 1H, N(2)H), 8.90 (s, 1H, CH=N); 7.99 (s, 1H, H_{arom}), 7.81 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.33 (t, *J* 7.8 Hz, 1H, H_{arom}) 7.06 (d, *J* 8.1 Hz, 1H, H_{arom}), 6.69 (t, *J* 7.2 Hz, 1H, H_{arom}), 5.68 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.42 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.15–5.09 (m, 2H, 2-H, 4-H), 4.33 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.90 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.09, 2.08, 2.05 and 2.04 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 177.7 (C=S), 172.1, 170.7, 169.9 and 169.6 (C=O), 157.2 (C–OH), 148.3 (CH=N), 132.8, 132.0, 120.2, 117.4 and 116.6 (C_{arom}), 82.5 (1-C), 73.4 (3-C), 72.3 (2-C), 71.0 (5-C), 68.2 (4-C), 61.5 (6-C), 20.7, 20.6 and 20.5 (CH_3). Anal. Calcd for $C_{22}H_{27}N_3O_{10}S{\cdot}5H_2O$ (615.61): C, 42.92; H, 6.06; N, 6.83. Found: C, 42.88; H, 6.43; N, 7.12.

1.2.9. 3-Hydroxy-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2i)

Yield 50%; mp 201–204 °C, lit.[5c] mp 206–208 °C; R_f (Hex/EtOAc 1:1) 0.22; $[\alpha]_D^{25}$ −115.3 (*c* 1.33, $CHCl_3$); IR (KBr): *ν* 3320 (N–H), 2950 (C–H_{arom}) 1745 (C=O), 1537 (C=N), 1035 (C=S), 920 (1-C–H), 826 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 9.87 (s, 1H, N(2)H), 8.23 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.74 (s, 1H, CH=N), 7.29–7.24 (m, 2H, H_{arom}), 7.07 (d, *J* 7.8 Hz, 1H, H_{arom}), 6.92 (dd, *J* 1.5 Hz, *J* 8.1 Hz, 1H, H_{arom}), 5.71 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.41 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.24–5.11 (m, 2H, 2-H, 4-H), 4.37 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.13 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.92 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.08, 2.06, 2.05 and 2.04 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.3 (C=S), 172.1, 170.1, 169.5 and 169.4 (C=O), 157.7 (C–OH), 144.3 (CH=N), 135.0, 129.7, 118.8, 117.5 and 114.0 (C_{arom}), 81.5 (1-C), 72.8 (3-C), 72.3 (2-C), 71.0 (5-C), 68.0 (4-C), 61.8 (6-C), 21.0, 20.6, 20.4 and 20.3 (CH_3). Anal. Calcd for $C_{22}H_{27}N_3O_{10}S$ (525.53): C, 50.28; H, 5.18; N, 8.00. Found: C, 49.72; H, 5.39; N, 8.02.

1.2.10. 4-Hydroxy-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2j)

Yield 82%; mp 200–202 °C, lit.[5a] mp 210 °C, lit.[5c] mp 216–217 °C; R_f (Hex/EtOAc 1:2) 0.46; $[\alpha]_D^{25}$ −104.8 (*c* 1, $CHCl_3$), lit.[5a] $[\alpha]_D^{25}$ −81 (*c* 0.8, $CHCl_3$); IR (KBr): *ν* 3314 (N–H), 2960 (C–H_{arom}), 1741 (C=O), 1508 (C=N), 1039 (C=S), 920 (1-C–H), 835 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.84 (s, 1H, N(2)H), 8.20 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.69 (s, 1H, CH=N), 7.51 (d, *J* 8.7 Hz, 2H, H_{arom}), 6.68 (d, *J* 8.7 Hz, 2H, H_{arom}), 5.77 (br s, 1H, OH), 5.74 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.41 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.23–5.10 (m, 2H, 2-H, 4-H), 4.36 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.14 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.92 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.08, 2.05, 2.04 and 2.02 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 177.8 (C=S), 170.2, 169.7, 169.7 and 169.5 (C=O), 159.8 (C–OH), 144.3 (CH=N), 129.6, 124.8 and 115.8 (C_{arom}), 81.5 (1-C), 72.9 (3-C), 72.3 (2-C), 71.0 (5-C), 68.1 (4-C), 61.9 (6-C), 20.7, 20.6, 20.6 and 20.5 (CH_3). Anal. Calcd for $C_{22}H_{27}N_3O_{10}S{\cdot}2H_2O$ (561.56): C, 47.05; H, 5.56; N, 7.48. Found: C, 47.46; H, 5.36; N, 7.67.

1.2.11. 2-Methoxy-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2k)

Yield 81%; mp 208 °C (decomp.); R_f (Hex/EtOAc 1:1) 0.32; $[\alpha]_D^{25}$ −83.7 (*c* 0.7, $CHCl_3$); IR (KBr): *ν* 3328 (N–H), 2946 (C–H_{arom}), 1745 (C=O), 1529 (C=N), 1039 (C=S), 910 (1-C–H), 826 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* = 9.43 (s, 1H, N(2)H), 8.25 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 8.21 (s, 1H, CH=N), 7.97 (d, *J* 7.8 Hz, 1H, H_{arom}), 7.39 (t, *J* 7.8 Hz, 1H, H_{arom}), 7.02 (t, *J* 7.5 Hz, 1H, H_{arom}), 6.90 (d, *J* 8.4 Hz, 1H, H_{arom}), 5.78 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.40 (t, $^3J_{2\text{-H,3-H}}$ 9.3 Hz, 1H, 3-H), 5.20–5.09 (m, 2H, 2-H, 4-H), 4.38 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.10 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.88 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 3.86 (s, 3H, OCH_3); 2.09, 2.04, 2.03 and 2.02 (4 × s, 12 H, CH_3CO); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 178.8 (C=S), 170.9, 170.7, 169.9 and 169.6 (C=O), 158.4 (*C*–OMe), 139.8 (CH=N), 132.2, 126.6, 121.2, 121.1 and 111.0 (C_{arom}), 82.3 (1-C), 73.5 (3-C), 72.7 (2-C), 70.5 (5-C), 68.3 (4-C), 61.6 (6-C), 55.6 (OCH_3), 20.8, 20.7 and 20.6 (*C*H_3CO). Anal. Calcd for $C_{23}H_{29}N_3O_{10}S{\cdot}7H_2O$ (665.66): C, 41.50; H, 6.51; N, 6.31. Found: C, 41.89; H, 7.02; N, 6.44.

1.2.12. 3-Methoxy-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2l)

Yield 78%; mp 175–179 °C; R_f (Hex/EtOAc 1:1) 0.47; $[\alpha]_D^{25}$ −102.0 (*c* 1.07, $CHCl_3$); IR (KBr): *ν* 3338 (N–H), 2995 (C–H_{arom}), 1737 (C=O), 1545 (C=N), 1035 (C=S), 912 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 10.22 (s, 1H, N(2)H), 8.30 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.77 (s, 1H, CH=N), 7.36 (s, 1H, H_{arom}), 7.28–7.21 (m, 1H, H_{arom}), 7.11 (d, *J* 7.5 Hz, 1H, H_{arom}), 6.92 (d, *J* 8.1 Hz, 1H, H_{arom}), 5.61 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.36 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.16–5.04 (m, 2H, 2-H, 4-H), 4.31 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.06 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.88 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 3.84 (s, 3H, OCH_3), 2.00, 1.99, 1.97 and 1.94 (4 × s, 12H, CH_3CO); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.4 (C=S), 170.0, 169.6, 169.5 and 169.3 (C=O), 159.6 (*C*–OMe), 143.5 (CH=N), 135.1, 129.8, 120.8, 116.5 and 111.5 (C_{arom}), 81.4 (1-C), 72.6 (3-C), 72.1 (2-C), 70.7 (5-C), 67.9 (4-C), 61.7 (6-C), 20.6, 20.4, 20.4 and 20.3 (*C*H_3CO). Anal. Calcd for $C_{23}H_{29}N_3O_{10}S{\cdot}5H_2O$ (629.63): C, 43.87; H, 6.24; N, 6.67. Found: C, 44.14; H, 6.66; N, 6.93.

1.2.13. 4-Methoxy-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2m)

Yield 88%; mp 213–216 °C, lit.[6] mp 182–183 °C; R_f (Hex/EtOAc 1:1) 0.34; $[\alpha]_D^{25}$ −83.0 (*c* 1, $CHCl_3$); IR (KBr): *ν* 3312 (N–H), 2975 (C–H_{arom}), 1749 (C=O), 1541 (C=N), 1035 (C=S), 920 (1-C–H), 822 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.78 (s, 1H, N(2)H), 8.26 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.70 (s, 1H, CH=N), 7.65 (d, *J* 9.0 Hz, 2H, H_{arom}), 6.95 (d, *J* 8.7 Hz, 2 H, H_{arom}), 5.72 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.40 (dd, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.21–5.10 (m, 2H, 2-H, 4-H), 4.38 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, H, 6-H), 4.14 (dd, $^3J_{5\text{-H,6′-H}}$ 1.8 Hz, 1H, 6′-H), 3.90 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 3.84 (s, 3H, OCH_3), 2.08, 2.04, 2.03 and 2.02 (4 × s, 12H, CH_3CO); ^{13}C NMR (75.47 MHz, $CDCl_3$): *δ* 178.3 (C=S), 170.9, 170.7, 169.9 and 169.5 (C=O), 161.8 (*C*–OMe), 143.9 (CH=N), 129.6, 125.5 and 114.4 (C_{arom}), 82.2 (1-C), 73.5 (3-C), 72.7 (2-C), 70.5 (5-C), 68.3 (4-C), 61.6 (6-C), 20.7, 20.6 and 20.6 (*C*H_3CO). Anal. Calcd for $C_{23}H_{29}N_3O_{10}S$ (539.56): C, 51.20; H, 5.42; N, 7.79. Found: C, 50.94; H, 5.67; N, 8.02.

1.2.14. 4-Methyl-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2n)

Yield 69%; mp 198–201 °C; R_f (Hex/EtOAc 1:1) 0.43; $[\alpha]_D^{25}$ −77.6 (*c* 1.03, $CHCl_3$); IR (KBr): *ν* 3314 (N–H), 2991 (C–H_{arom}), 1741 (C=O), 1553 (C=N), 1043 (C=S), 933 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): *δ* 9.73 (s, 1H, N(2)H), 8.25 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.77 (s, 1H, CH=N), 7.60 (d, *J* 8.1 Hz, 2H, H_{arom}), 7.25 (d, *J* 7.8 Hz, 2H, H_{arom}), 5.72 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.41 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.21–5.10 (m, 2H, 2-H, 4-H), 4.34 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.3 Hz, 1H, 6-H), 4.11 (dd, $^3J_{5\text{-H,6′-H}}$ 1.8 Hz, 1H, 6′-H), 3.89 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.38 (s, 3H, C*H*$_3$–Ar), 2.10, 2.08, 2.04 and 2.03 (4 × s, 12H, CH_3CO); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.1 (C=S), 170.0,

169.5, 169.5 and 169.4 (C=O), 143.9 (CH_3–Ar), 140.2 (CH=N), 131.0, 129.3 and 127.6 (C_{arom}), 81.4 (1-C), 72.7 (3-C), 72.2 (2-C), 69.9 (5-C), 67.9 (4-C), 61.8 (6-C), 20.5, 20.4 20.4 and 20.4 (CH_3CO). Anal. Calcd for $C_{23}H_{29}N_3O_9S{\cdot}2H_2O$ (559.59): C, 49.37; H, 5.94; N, 7.51. Found: C, 48.88; H, 6.24; N, 7.87.

1.2.15. 4-*tert*-Butyl-benzaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2o)

Yield 77%; mp 210–213 °C; R_f (Hex/EtOAc 1:1) 0.64; $[\alpha]_D^{25}$ −77.7 (*c* 1.27, $CHCl_3$). IR (KBr): *v* 3326 (N–H), 2958 (C–H_{arom}) 1749 (C=O), 1533 (C=N), 1047 (C=S), 916 (1-C–H), 826 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ 10.26 (s, 1 H, N(2)H), 8.29 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.85 (s, 1H, CH=N), 7.65 (d, *J* 8.1 Hz, 2H, H_{arom}), 7.44 (d, *J* 8.4 Hz, 2H, H_{arom}), 5.71 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.40 (dd, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.21–5.09 (m, 2H, 2-H, 4-H), 4.37 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.92 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.07, 2.04, 2.03 and 2.01 (4 × s, 12H, CH_3CO), 1.32 (s, 9H, CH_3(*t*Bu)); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 178.7 (C=S), 170.9, 170.7, 169.9 and 169.6 (C=O), 154.4 (C_{arom}–*t*Bu), 143.9 (CH=N), 130.1, 127.5 and 125.9 (C_{arom}), 82.2 (1-C), 73.4 (3-C), 72.7 (2-C), 70.4 (5-C), 68.3 (4-C), 61.6 (6-C), 34.9 (CMe_3), 31.1 (CH_3(*t*Bu)), 20.8, 20.6 and 20.6 (CH_3CO). Anal. Calcd for $C_{26}H_{35}N_3O_9S$ (565.64): C, 55.21; H, 6.24; N, 7.43. Found: C, 55.35; H, 6.66; N, 7.84.

1.2.16. 2-Pyridinecarboxaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2p)

Yield 67%; mp 70–73 °C; R_f (Hex/EtOAc 1:3) 0.17; $[\alpha]_D^{25}$ −66.9 (*c* 1.23, $CHCl_3$); IR (KBr): *v* 3328 (N–H), 2967 (C–H_{arom}), 1741 (C=O), 1529 (C=N), 1035 (C=S), 888 (1-C–H), 839 (C=S) cm^{-1}; ^1H NMR (599.83 MHz, $CDCl_3$): δ 10.14 (s, 1H, N(2)H), 8.60 (d, *J* 4.2 Hz, 1H, 3′-H), 8.45 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 8.04 (d, *J* 7.8 Hz, 1H, 6′-H), 7.96 (s, 1H, CH=N), 7.79–7.74 (m, 1H, 5′-H), 7.33–7.28 (m, 1H, 4′-H), 5.72 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.41 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.21–5.10 (m, 2H, 2-H, 4-H), 4.37 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H,6′-H}}$ 1.8 Hz, 1H, 6′-H), 3.90 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.11, 2.08, 2.04 and 2.03 (4 × s, 12H, CH_3); ^{13}C NMR (150.84 MHz, $CDCl_3$): δ 179.4 (C=S), 171.1, 170.7, 169.9 and 169.6 (C=O), 152.2 and 149.5 (C_{arom}), 143.5 (CH=N), 136.9, 124.6 and 121.1 (C_{arom}), 82.2 (1-C), 73.5 (3-C), 72.7 (2-C), 70.6 (5-C), 68.3 (4-C), 61.6 (6-C), 20.8, 20.7, 20.6 and 20.6 (CH_3). Anal. Calcd for $C_{21}H_{26}N_4O_9S$ (510.52): C, 49.41; H, 5.13; N, 10.97. Found: C, 49.82; H, 5.45; N, 11.12.

1.2.17. 3-Pyridinecarboxaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2q)

Yield 80%; mp 129–131 °C, lit.[6] mp 134–136 °C; R_f (Hex/EtOAc 1:3) 0.16; $[\alpha]_D^{25}$ −82.2 (*c* 1, $CHCl_3$); IR (KBr): *v* 3320 (N–H), 2950 (C–H_{arom}), 1745 (C=O), 1533 (C=N), 1031 (C=S), 928 (1-C–H), 826 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ 10.49 (s, 1H, N(2)H), 8.81 (d, *J* 1.8 Hz, 1H, H_{arom}), 8.64 (dd, *J* 1.5 Hz, *J* 4.8 Hz, 1H, H_{arom}), 8.34 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.16 (dt, *J* 1.8 Hz, *J* 7.8 Hz, 1H, H_{arom}), 7.89 (s, 1H, CH=N), 7.37 (dd, *J* 1.8 Hz, *J* 7.8 Hz, 1H, H_{arom}), 5.68 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.41 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.18–5.09 (m, 2H, 2-H, 4-H), 4.37 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.14 (dd, $^3J_{5\text{-H,6′-H}}$ 1.8 Hz, 1H, 6′-H), 3.90 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.09, 2.07, 2.04 and 2.02 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 179.1 (C=S), 171.1, 170,7, 169.9 and 169.6 (C=O), 151.3 and 149.5 (C_{arom}), 140.3 (CH=N), 133.7, 129.2 and 124.0 (C_{arom}), 82.2 (1-C), 73.5 (3-C), 72.5 (2-C), 70.6 (5-C), 68.3 (4-C), 61.6 (6-C), 20.7, 20.7 and 20.6 (CH_3). Anal. Calcd for $C_{21}H_{26}N_4O_9S$ (510.52): C, 49.41; H, 5.13; N, 10.97. Found: C, 49.86; H, 4.98; N, 11.15.

1.2.18. 4-Pyridinecarboxaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2r)

Yield 64%; mp 196–200 °C, lit.[6] 102–103 °C; R_f (Hex/EtOAc 1:2) 0.14; $[\alpha]_D^{25}$ −93.0 (*c* 1.07, CHCl3); IR (KBr): ϑ3329 (N–H), 2962 (C–H_{arom}), 1737 (C=O), 1525 (C=N), 1031 (C=S), 896 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ 10.56 (s, 1H, N(2)H), 8.69 (d, *J* 5.4 Hz, 2H, H_{arom}), 8.39 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.81 (s, 1H, CH=N), 7.62 (d, *J* 5.4 Hz, 2H, H_{arom}), 5.64. (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.41 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.19–5.09 (m, 2H, 2-H, 4-H) 4.35 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.10 (dd, $^3J_{5\text{-H,6′-H}}$ 2.1 Hz, 1H, 6′-H), 3.90 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.09, 2.08, 2.04 and 2.03 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 179.4 (C=S), 171.3, 170.7, 169.9 and 169.6 (C=O), 150.0 (C_{arom}), 140.7 (CH=N), 140.5 and 121.4 (C_{arom}), 82.2 (1-C), 73.5 (3-C), 72.5 (2-C), 70.6 (5-C), 68.3 (4-C), 61.6 (6-C), 20.8, 20.7, 20.7 and 20.6 (CH_3). Anal. Calcd for $C_{21}H_{26}N_4O_9S{\cdot}3H_2O$ (564.56): C, 44.68; H, 5.71; N, 9.92. Found: C, 45.09; H, 5.83; N, 10.14.

1.2.19. 1-Ferrocenecarboxaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2s)

Yield 90%; mp 212–215 °C; R_f (Hex/EtOAc 1:1) 0.5; IR (KBr): *v* 3322 (N–H), 3073 (C–H_{arom}), 1725 (C=O), 1525 (C=N), 1035 (C=S), 912 (1-C–H), 820 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): δ 11.72 (s, 1H, N(2)H), 8.38 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 7.93 (s, 1H, CH=N), 5.87 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.42 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.26 (t, *J* 9.3 Hz, 1H, 2-H), 4.96 (dd, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, $^3J_{4\text{-H,5-H}}$ 9.9 Hz, 1H, 4-H), 4.84 (s, 1H, Fc), 4.73 (s, 1H, Fc), 4.49–4.45 (m, 2H, Fc), 4.22 (s, 5H, Fc), 4.20 (dd, $^3J_{5\text{-H,6′-H}}$ 4.2 Hz, 1H, 6′-H), 4.06 (ddd, $^3J_{5\text{-H,6-H}}$ 1.8 Hz, 1H, 5-H), 3.97 (dd, $^2J_{6\text{-H,6′-H}}$ 12.3 Hz, 1H, 6-H), 2.01, 2.00, 1.97 and 1.96 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 177.0 (C=S), 170.0, 169.6, 169.5 and 169.3 (C=O), 145.0 (CH=N), 81.2 (1-C), 78.3 (*C*(Fc)–CH=N), 72.5 (3-C), 72.1 (2-C), 70.7 (5-C), 70.3 (Fc), 69.0 (Fc), 68.1 (4-C), 67.9, 67.6 and 64.4 (Fc), 61.7 (6-C), 20.6, 20.4, 20.4 and 20.3 (CH_3). Anal. Calcd for $C_{26}H_{31}FeN_3O_9S$ (617.45): C, 50.58; H, 5.06; N, 6.81. Found: C, 50.78; H, 4.65; N, 7.03.

1.2.20. β-Naphthalenecarboxaldehyde 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2t)

Yield 94%; mp 212–215 °C; R_f (Hex/EtOAc 1:1) 0.4; $[\alpha]_D^{25}$ −116.7 (*c* 1.05, $CHCl_3$); IR (KBr): *v* 3322 (N–H), 2950 (C–H_{arom}) 1753 (C=O), 1533 (C=N), 1035 (C=S), 904 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ 10.41 (s, 1H, N(2)H), 8.38 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 7.98 (d, *J* 5.4 Hz, 3H, H_{naphth}), 7.83 (d, *J* 9.3 Hz, 2H, H_{naphth}), 7.82 (s, 1H, CH=N), 7.49–7.52 (m, 2H, H_{naphth}), 5.72 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.41 (t, $^3J_{2\text{-H,3-H}}$ 9.3 Hz, 1H, 3-H), 5.25–5.10 (m, 2H, 2-H, 4-H), 4.37 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H,6′-H}}$ 1.8 Hz, 1H, 6′-H), 3.91 (ddd, $^3J_{4\text{-H,5-H}}$ 10.2 Hz, 1H, 5-H), 2.08, 2.06 and 2.04 and 2.03 (4 × s, 12H, CH_3); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 178.9 (C=S), 171.0, 170.8, 170.0 and 169.7 (C=O), 144.3 (CH=N), 134.5, 133.0, 130.7, 129.9, 128.8, 128.4, 127.9, 127.4, 126.7 and 122.8 (C_{naphth}), 82.2 (1-C), 73.4 (3-C), 72.7 (2-C), 70.5 (5-C), 68.4 (4-C), 61.7 (6-C), 20.7, 20.7, 20.6 and 20.6 (CH_3). Anal. Calcd for $C_{26}H_{29}N_3O_9S{\cdot}2H_2O$ (595.62): C, 52.43; H, 5.58; N, 7.05. Found: C, 52.12; H, 5.97; N, 6.65.

1.2.21. 4-Methoxy-acetophenone 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2u)

Yield 78%; mp 192–198 °C; R_f (Hex/EtOAc 1:2) 0.64; $[\alpha]_D^{25}$ −48.1 (*c* 1.05, $CHCl_3$); IR (KBr): *v* 3330 (N–H), 2950 (C–H_{arom}), 1741 (C=O), 1529 (C=N), 1035 (C=S), 916 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ 8.81 (s, 1H, N(2)H), 8.38 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 7.78 (d, *J* 9.0 Hz, 2H, H_{arom}), 6.95 (d, *J* 9.0 Hz, 2H, H_{arom}), 5.76 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.40 (t, $^3J_{3\text{-H,4-H}}$ 9.6 Hz, 1H, 3-H), 5.21–5.09 (m, 2H, 2-H, 4-H), 4.36 (dd, $^3J_{5\text{-H,6-H}}$ 4.5 Hz, $^2J_{6\text{-H,6′-H}}$ 12.6 Hz, 1H, 6-H), 4.14 (dd, $^3J_{5\text{-H,6′-H}}$

2.1 Hz, 1H, 6′-H), 3.90 (ddd, $^3J_{4\text{-H},5\text{-H}}$ = 10.2 Hz, 1H, 5-H), 3.85 (s, 3H, OCH_3), 2.23 (s, 3H, CH_3C=N), 2.08, 2.04 and 2.02 (3 × s, 12H, CH_3CO); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 179.1 (C=S), 170.1, 169.9, 169.7 and 169.5 (C=O), 160.7 (C_{arom}–O), 149.9 (C=N), 130.6, 129.8, 128.6, 113.6 and 113.5 (C_{arom}), 81.4 (1-C), 72.6 (3-C), 72.3 (2-C), 71.0 (5-C), 68.2 (4-C), 61.9 (6-C), 55.3 (OCH_3), 20.7, 20.7, 20.6 and 20.5 (CH_3CO), 14.5 (CH_3C=N). Anal. Calcd for $C_{24}H_{31}N_3O_{10}S{\cdot}3H_2O$ (607.63): C, 47.44; H, 6.14; N, 6.92. Found: C, 47.12; H, 5.98; N, 6.55.

1.2.22. 2-Acetonaphthanone 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (2v)

Yield 72%; mp 182–185 °C; R_f (Hex/EtOAc 1:2) 0.42; $[\alpha]_D^{25}$ −61.5 (*c* 1.07, $CHCl_3$); IR (KBr): *ν* 3310 (N–H), 2950 (C–H_{arom}), 1741 (C=O), 1529 (C=N), 1035 (C=S), 916 (1-C–H), 835 (C=S) cm^{-1}; ^{1}H NMR (300.13 MHz, $CDCl_3$, 25 °C): δ 9.18 (s, 1H, N(2)H), 8.50 (d, $^3J_{1\text{-H},N(4)H}$ 8.7 Hz, 1H, N(4)H), 8.17 (s, 1H, H_{naphth}), 8.05 (dd, *J* 1.8 Hz, *J* 8.7 Hz, 1H, H_{naphth}), 7.93–7.83 (m, 3H, H_{naphth}), 7.53–7.50 (m, 2H, H_{naphth}), 5.76 (dd, $^3J_{1\text{-H},2\text{-H}}$ 9.0 Hz, 1H, 1-H), 5.43 (t, $^3J_{2\text{-H},3\text{-H}}$ 9.6 Hz, 1H, 3-H), 5.26–5.11 (m, 2H, 2-H, 4-H), 4.34 (dd, $^3J_{5\text{-H},6\text{-H}}$ 4.5 Hz, $^2J_{6\text{-H},6'\text{-H}}$ 12.6 Hz, 1H, 6-H), 4.12 (dd, $^3J_{5\text{-H},6'\text{-H}}$ 2.1 Hz, 1H, 6′-H), 3.92 (ddd, $^3J_{4\text{-H},5\text{-H}}$ 10.2 Hz, 1H, 5-H), 2.38 (s, 3H, CH_3C=N), 2.08, 2.06 and 2.05 (3 × s, 12H, CH_3CO); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 179.6 (C=S), 171.0, 170.8, 169.9 and 169.6 (C=O), 148.0 (C=N), 134.1, 134.0, 133.0, 128.7, 128.3, 127.6, 127.2, 126.9, 126.5 and 123.4 (C_{naphth}), 82.3 (1-C), 73.5 (3-C), 72.7 (2-C), 70.5 (5-C), 68.4 (4-C), 61.6 (6-C), 20.7, 20.7 and 20.6 (CH_3CO), 13.2 (CH_3C=N). Anal. Calcd for $C_{27}H_{31}N_3O_9S{\cdot}3H_2O$ (627.66): C, 51.67; H, 5.94; N, 6.69. Found: C, 52.01; H, 6.23; N, 6.67.

1.3. General procedure for the deacetylation in compounds 2. Synthesis of aldehyde/ketone 4-(β-D-glucopyranosyl)thiosemicarbazones 3

Sodium methoxide as a powder (7.5 mmol) was added to a solution of **2** (1.5 mmol) in dry methanol (20 mL). The reaction mixture was stirred at room temperature for 3 h and kept in fridge overnight. Then, the solution was neutralized with Amberlist-15 (or acetic acid for the compounds **2c**, **2p**, **2q** and **2r**), it was filtered to remove sodium ions, and the solvent was evaporated by vacuum at a temperature below 40 °C. Purification was carried out by recrystallization. The N–H stretching vibration in the FT-IR spectra of **3** has not been determined as it was obscured by the broad absorption band of the hydroxyl group.

1.3.1. 2-Chloro-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3a)

Yield 50%; mp 204–208 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.40; $[\alpha]_D^{25}$ +41.4 (*c* 1, MeOH); IR (KBr): *ν* 3525 (OH), 2873 (C–H_{arom}), 1537 (C=N), 1039 (C=S), 916 (1-C–H), 830 (C=S) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6): δ 11.93 (s, 1H, N(2)H), 8.66 (d, $^3J_{1\text{-H},N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.53 (s, 1H, CH=N), 8.36 (d, *J* 7.5 Hz, 1H, H_{arom}), 7.52–7.36 (m, 3H, H_{arom}), 5.39 (dd, $^3J_{1\text{-H},2\text{-H}}$ 9.0 Hz, 1H, 1-H), 5.03–5.00 (m, 2H, OH), 4.91 (s, H, OH), 4.50 (t, ^3J 5.6 Hz, 1H, OH), 3.66 (dd, $^3J_{5\text{-H},6\text{-H}}$ 5.4 Hz, $^2J_{6\text{-H},6'\text{-H}}$ 11.4 Hz, 1H, 6-H), 3.55–3.14 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.8 (C=S), 138.9 (CH=N), 133.2, 131.4, 131.2, 129.8, 127.7 and 127.3 (C_{arom}), 84.1 (1-C), 78.7 (3-C), 77.6 (2-C), 71.9 (5-C), 69.8 (4-C), 60.8 (6-C). Anal. Calcd for $C_{14}H_{18}ClN_3O_5S{\cdot}4H_2O$ (447.89): C, 37.54; H, 5.85; N, 9.38. Found: C, 37.68; H, 5.46; N, 9.03.

1.3.2. 3-Chloro-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3b)

Yield 71%; mp 190–193 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.45; $[\alpha]_D^{25}$ +54.8 (*c* 1.33, MeOH); IR (KBr): *ν* 3359 (OH), 2926 (C–H_{arom}), 1537 (C=N), 1035 (C=S), 892 (1-C–H), 830 (C=S) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6): δ 11.82 (s, 1H, N(2)H), 8.75 (d, $^3J_{1\text{-H},N(4)H}$ 8.7 Hz, 1H, N(4)H), 8.08 (s, 2H, CH=N and H_{arom}), 7.71 (s, 1H, H_{arom}), 7.46 (s, 2H, H_{arom}), 5.40 (dd, $^3J_{1\text{-H},2\text{-H}}$ 9.0 Hz, 1H, 1-H), 5.02 (s, 2H, OH), 4.90 (s, 1H, OH), 4.49 (s, 1H, OH), 3.65 (dd, $^3J_{5\text{-H},6\text{-H}}$ 3.9 Hz, $^2J_{6\text{-H},6'\text{-H}}$ 11.4 Hz, 1H, 6-H), 3.56–3.15 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.8 (C=S), 141.4 (CH=N), 136.2, 133.7, 130.5, 129.6, 126.8 and 126.3 (C_{arom}), 84.1 (1-C), 78.7 (3-C), 77.6 (2-C), 71.8 (5-C), 69.9 (4-C), 60.9 (6-C). Anal. Calcd for $C_{14}H_{18}ClN_3O_5S{\cdot}5H_2O$ (465.90): C, 36.09; H, 6.06; N, 9.02. Found: C, 35.78; H, 5.89; N, 8.95.

1.3.3. 4-Chloro-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3c)

Yield 53%; mp 169–171 °C (decomp., MeOH/H_2O 1:1), lit.[5b] mp 166–169 °C; R_f ($CHCl_3$/MeOH 5:1) 0.51; $[\alpha]_D^{25}$ +55.5 (*c* 1, MeOH), lit.[5b] $[\alpha]_D^{25}$ +34.7 (DMF/H_2O); IR (KBr): *ν* 3371 (OH), 2885 (C–H_{arom}), 1537 (C=N), 1031 (C=S), 900 (1-C–H), 830 (C=S) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6): δ 11.78 (s, 1H, N(2)H), 8.62 (d, $^3J_{1\text{-H},N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.09 (s, 1H, CH=N), 7.90 (d, *J* 8.4 Hz, 2H, H_{arom}), 7.48 (d, *J* 8.4 Hz, 2H, H_{arom}), 5.38 (dd, $^3J_{1\text{-H},2\text{-H}}$ 9.3 Hz, 1H, 1-H), 5.01–4.99 (m, 2H, OH), 4.90–4.88 (m, 1H, OH), 4.50–4.46 (m, 1H, OH), 3.65 (dd, $^3J_{5\text{-H},6\text{-H}}$ 5.4 Hz, $^2J_{6\text{-H},6'\text{-H}}$ 11.4 Hz, 1H, 6-H), 3.50–3.14 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.5 (C=S), 142.6 (CH=N), 135.0, 132.7, 129.3 and 129.0 (C_{arom}), 83.9 (1-C), 78.4 (3-C), 77.2 (2-C), 71.8 (5-C), 69.7 (4-C), 60.8 (6-C). Anal. Calcd for $C_{14}H_{18}ClN_3O_5S$ (375.83): C, 44.74; H, 4.83; N, 11.18. Found: C, 44.34; H, 5.12; N, 11.67.

1.3.4. 4-Trifluoromethyl-benzaldehyde 4-(β-D-glucopyranosyl)-thiosemicarbazone (3d)

Yield 76%; mp 160–165 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.44; $[\alpha]_D^{25}$ +48.3 (*c* 1, MeOH); IR (KBr): *ν* 3322 (OH), 2893 (C–H_{arom}), 1541 (C=N), 1035 (C=S), 900 (1-C–H), 826 (C=S) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6): δ 11.92 (s, 1H, N(2)H), 8.73 (d, $^3J_{1\text{-H},N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.16 (s, 1H, CH=N), 8.09 (d, *J* 8.1 Hz, 2H, H_{arom}), 7.76 (d, *J* 8.1 Hz, 2H, H_{arom}), 5.40 (dd, $^3J_{1\text{-H},2\text{-H}}$ 9.0 Hz, 1H, 1-H), 5.08 (br s, 2H, OH), 4.96 (br s, 1H, OH), 4.52 (br s, 1H, OH), 3.66 (dd, $^3J_{5\text{-H},6\text{-H}}$ 5.4 Hz, $^2J_{6\text{-H},6'\text{-H}}$ 11.4 Hz, 1H, 6-H), 3.51–3.17 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.9 (C=S), 141.1 (CH=N), 138.0, 129.7, 129.3, 128.1, 125.5, 125.4 and 125.4 (C_{arom} and CF_3), 84.1 (1-C), 78.7 (3-C), 77.6 (2-C), 71.9 (5-C), 69.8 (4-C), 60.8 (6-C). Anal. Calcd for $C_{15}H_{18}F_3N_3O_5S{\cdot}2H_2O$ (445.41): C, 40.45; H, 4.98; N, 9.43. Found: C, 40.22; H, 4.73; N, 9.83.

1.3.5. 2-Nitro-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3e)

Yield 55%; mp 194–198 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.51; $[\alpha]_D^{25}$ +42.5 (*c* 1.06, MeOH); IR (KBr): *ν* 3355 (OH), 2918 (C–H_{arom}), 1537 (C=N), 1035 (C=S), 896 (1-C–H), 822 (C=S) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6): δ 12.03 (s, 1H, N(2)H), 8.68 (d, $^3J_{1\text{-H},N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.53 (s, 1H, CH=N), 8.47 (dd, *J* 1.5 Hz, *J* 8.1 Hz, 1H, H_{arom}), 7.79–7.74 (m, 1H, H_{arom}), 7.68–7.62 (m, 1H, H_{arom}), 5.39 (dd, $^3J_{1\text{-H},2\text{-H}}$ 9.3 Hz, 1H, 1-H), 5.02–5.00 (m, 2H, OH), 4.90–4.88 (m, 1H, OH), 4.49 (t, ^3J 5.8 Hz, 1H, OH), 3.65 (dd, $^3J_{5\text{-H},6\text{-H}}$ 5.4 Hz, $^2J_{6\text{-H},6'\text{-H}}$ 11.7 Hz, 1H, 6-H), 3.53–3.15 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 179.0 (C=S), 148.3 (C–NO_2), 138.0 (CH=N), 133.3, 130.5, 128.5, 128.2 and 124.5 (C_{arom}), 84.1 (1-C), 78.7 (3-C), 77.5 (2-C), 71.9 (5-C), 69.8 (4-C), 60.8 (6-C). Anal. Calcd for $C_{14}H_{18}N_4O_7S{\cdot}4H_2O$ (458.44): C, 36.68; H, 5.72; N, 12.22. Found: C, 36.42; H, 6.01; N, 11.95.

1.3.6. 3-Nitro-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3f)

Yield 70%; mp 201–205 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.52; $[\alpha]_D^{25}$ +54.0 (*c* 0.75, MeOH/DMF 3:1); IR (KBr): *ν* 3416 (OH), 2987 (C–H_{arom}), 1545 (C=N), 1035 (C=S), 910 (1-C–H), 810 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.91 (br s, 1H, N(2)H), 8.80 (d, $^3J_{1\text{-}H,N(4)H}$ 8.7 Hz, 1H, N(4)H), 8.62 (s, 1H, H_{arom}), 8.34 (d, *J* 7.5 Hz, 1H, H_{arom}), 8.25–8.21 (m, 2H, H_{arom} and CH=N), 7.72 (dd, *J* 7.5 Hz, *J* 8.1 Hz, 1H, H_{arom}), 5.40 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.3 Hz, 1H, 1-H), 5.05 (s, 2H, OH), 4.95 (s, 1H, OH), 4.53 (s, 1H, OH), 3.68 (dd, $^3J_{5\text{-}H,6\text{-}H}$ 5.4 Hz, $^2J_{6\text{-}H,6'\text{-}H}$ 11.7 Hz, 1H, 6-H), 3.53–3.15 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 179.0 (C=S), 148.4 (C–NO_2), 141.0 (CH=N), 136.0, 133.7, 130.3, 124.3 and 121.9 (C_{arom}), 84.3 (1-C), 78.8 (3-C), 77.7 (2-C), 71.9 (5-C), 69.9 (4-C), 60.9 (6-C). Anal. Calcd for $C_{14}H_{18}N_4O_7S{\cdot}5H_2O$ (476.46): C, 35.29; H, 5.92; N, 11.76. Found: C, 34.96; H, 5.34; N, 12.06.

1.3.7. 4-Nitro-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3g)

Yield 39%; mp 213–215 °C (decomp., DMF/MeOH 1:2), lit.[5a] mp 202 °C; R_f ($CHCl_3$/MeOH 5:1) 0.34; $[\alpha]_D^{25}$ +61.3 (*c* 0.75, MeOH/DMF 3:1), lit.[5a] $[\alpha]_D^{25}$ +31 (*c* 0.9, DMF/H_2O); IR (KBr): *ν* 3405 (OH), 2873 (C–H_{arom}), 1537 (C=N), 1035 (C=S), 892 (1-C–H), 822 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.97 (s, 1H, N(2)H), 8.79 (d, $^3J_{1\text{-}H,N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.26–8.14 (m, 5H, H_{arom} and CH=N), 5.40 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.0 Hz, 1H, 1-H), 5.03–5.01 (m, 2H, OH), 4.91–4.90 (m, 1H, OH), 4.50 (t, ^3J 5.7 Hz, 1H, OH), 3.65 (dd, $^3J_{5\text{-}H,6\text{-}H}$ 5.4 Hz, $^2J_{6\text{-}H,6'\text{-}H}$ 11.7 Hz, 1H, 6-H), 3.54–3.15 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 179.0 (C=S), 147.7 (C–NO_2), 140.4 and 140.3 (CH=N and C_{arom}), 128.5 and 123.8 (C_{arom}), 84.1 (1-C), 78.7 (3-C), 77.6 (2-C), 71.9 (5-C), 69.9 (4-C), 60.8 (6-C). Anal. Calcd for $C_{14}H_{18}N_4O_7S{\cdot}4H_2O$ (458.44): C, 36.68; H, 5.72; N, 12.22. Found: C, 36.98; H, 5.58; N, 12.84.

1.3.8. 2-Hydroxy-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3h)

Yield 92%; very hygroscopic, lit.[5c] mp 180–182 °C; R_f ($CHCl_3$/MeOH 5:1) 0.22; $[\alpha]_D^{25}$ +43.0 (*c* 1, MeOH); IR (KBr): *ν* 3203 (OH), 2864 (C–H_{arom}), 1553 (C=N), 1035 (C=S), 910 (1-C–H), 843 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.99 (s, 1H, N(2)H), 8.47 (d, $^3J_{1\text{-}H,N(4)H}$ 8.7 Hz, 1H, N(4)H), 8.43 (s, 1H, CH=N), 7.99 (d, *J* 7.5 Hz, 1H, H_{arom}), 7.26–7.21 (m, 1H, H_{arom}), 6.88–6.80 (m, 2H, H_{arom}), 5.37 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.3 Hz, 1H, 1-H), 5.02–5.01 (m, 2H, OH), 4.91–4.90 (m, 1H, OH), 4.51–4.47 (m, 1H, OH), 3.64 (dd, $^3J_{5\text{-}H,6\text{-}H}$ 5.4 Hz, $^2J_{6\text{-}H,6'\text{-}H}$ 11.7 Hz, 1H, 6-H), 3.48–3.12 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.3 (C=S), 156.6 (C–OH), 140.0 (CH=N), 131.4, 126.7, 120.3, 119.2 and 116.1 (C_{arom}), 83.9 (1-C), 78.6 (3-C), 77.6 (2-C), 72.0 (5-C), 69.8 (4-C), 60.8 (6-C).

1.3.9. 3-Hydroxy-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3i)

Yield 74%; mp 188–194 °C (MeOH/H_2O 1:1), lit.[5c] 170–172 °C; R_f ($CHCl_3$/MeOH 5:1) 0.30; $[\alpha]_D^{25}$ +58.7 (*c* 1, MeOH); IR (KBr): *ν* 3208 (OH), 2950 (C–H_{arom}), 1553 (C=N), 1031 (C=S), 892 (1-C–H), 832 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.69 (s, 1H, N(2)H), 9.61 (s, 1H, OH), 8.44 (d, $^3J_{1\text{-}H,N(4)H}$ 9.3 Hz, 1H, N(4)H), 8.02 (s, 1H, CH=N), 7.22–7.21 (m, 3H, H_{arom}), 6.84–6.81 (m, 1H, H_{arom}), 5.37 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.0 Hz, 1H, 1-H), 5.06–5.02 (m, 2H, OH), 4.92–4.91 (m, 1H, OH), 4.51 (t, ^3J 5.7 Hz, 1H, OH), 3.64 (dd, $^3J_{5\text{-}H,6\text{-}H}$ 5.7 Hz, $^2J_{6\text{-}H,6'\text{-}H}$ 11.4 Hz, 1H, 6-H), 3.48–3.14 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.7 (C=S), 157.8 (C–OH), 144.3 (CH=N), 135.5, 130.4, 119.6, 118.0 and 113.8 (C_{arom}), 84.2 (1-C), 78.8 (3-C), 77.6 (2-C), 72.3 (5-C), 70.1 (4-C), 61.1 (6-C). Anal. Calcd for $C_{14}H_{19}N_3O_6S{\cdot}2H_2O$ (393.41): C, 42.74; H, 5.89;N, 10.68. Found: C, 42.74; H, 5.89; N, 10.98.

1.3.10. 4-Hydroxy-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3j)

Yield 76%; mp 228–230 °C (decomp., MeOH), lit.[5a] mp 218 °C, lit.[5c] mp 224–225 °C; R_f ($CHCl_3$/MeOH 5:1) 0.12; $[\alpha]_D^{25}$ +65.3 (*c* 1, MeOH), lit.[5a] $[\alpha]_D^{25}$ +37 (*c* 0.9, DMF/H_2O); IR (KBr): *ν* 3250 (OH), 2909 (C–H_{arom}), 1521 (C=N), 1018 (C=S), 909 (1-C–H), 839 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.56 (s, 1H, N(2)H), 9.92 (br s, 1H, OH), 8.38 (d, $^3J_{1\text{-}H,N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.00 (s, 1H, CH=N), 7.62 (d, *J* 9.0 Hz, 2H, H_{arom}), 6.78 (d, *J* 9.0 Hz, 2 H, H_{arom}), 5.35 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.6 Hz, 1H, 1-H), 5.00 (s, 2H, OH), 4.88 (s, 1H, OH), 4.45 (s, 1H, OH), 3.64 (dd, $^3J_{5\text{-}H,6\text{-}H}$ 5.7 Hz, $^2J_{6\text{-}H,6'\text{-}H}$ 11.4 Hz, 1H, 6-H), 3.49–3.10 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.0 (C=S), 160.3 (C–OH), 143.6 (CH=N), 129.3, 124.3 and 115.8 (C_{arom}), 83.9 (1-C), 79.2 (3-C), 78.6 (2-C), 72.0 (5-C), 69.8 (4-C), 60.8 (6-C). Anal. Calcd for $C_{14}H_{19}N_3O_6S$ (357.38): C, 47.05; H, 5.36; N, 11.76. Found: C, 46.98; H, 5.64; N, 11.55.

1.3.11. 2-Methoxy-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3k)

Yield 63%; mp172–175 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.42; $[\alpha]_D^{25}$ +37.8 (*c* 1, MeOH); IR (KBr): *ν* 3559 (OH), 2897 (C–H_{arom}), 1537 (C=N), 1026 (C=S), 892 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.73 (s, 1H, N(2)H), 8.51 (d, $^3J_{1\text{-}H,N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.47 (s, 1H, CH=N), 8.14 (dd, *J* 1.8 Hz, *J* 7.8 Hz, 1H, H_{arom}), 7.43–7.37 (m, 1H, H_{arom}), 7.08–6.95 (m, 2H, H_{arom}), 5.37 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.0 Hz, 1H, 1-H), 5.02–4.99 (m, 2H, OH), 4.89–4.88 (m, 1H, OH), 4.47 (t, ^3J 5.8 Hz, 1H, OH), 3.84 (s, 3H, OCH_3), 3.66 (dd, $^3J_{5\text{-}H,6\text{-}H}$ 5.7 Hz, $^2J_{6\text{-}H,6'\text{-}H}$ 11.4 Hz, 1H, 6-H), 3.51–3.43 (m, 2H) and 3.25–3.13 (m, 3H) (2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.4 (C=S), 157.9 (*C*–OMe), 138.6 (CH=N), 131.6, 126.3, 121.9, 120.5 and 111.7 (C_{arom}), 83.9 (1-C), 78.6 (3-C), 77.6 (2-C), 72.0 (5-C), 69.8 (4-C), 60.8 (6-C), 55.7 (OCH_3). Anal. Calcd for $C_{15}H_{21}N_3O_6S{\cdot}3H_2O$ (425.45): C, 42.35; H, 6.40; N, 9.88. Found: C, 41.97; H, 6.67; N, 10.03.

1.3.12. 3-Methoxy-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3l)

Yield 77%; mp 184–187 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.41; $[\alpha]_D^{25}$ +50.7 (*c* 1.14, MeOH); IR (KBr): *ν* 3498 (OH), 2905 (C–H_{arom}), 1557 (C=N), 1031 (C=S), 896 (1-C–H), 851 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.76 (s, 1H, N(2)H), 8.59 (d, $^3J_{1\text{-}H,N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.08 (s, 1H, CH=N), 7.43–7.34 (m, 3H, H_{arom}), 6.99 (d, *J* 7.5 Hz, 1H, H_{arom}), 5.37 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.0 Hz, 1H, 1-H), 5.02 (br s, 2H, OH), 4.91 (br s, 1H, OH), 4.47 (br s, 1H, OH), 3.81 (s, 3H, OCH_3), 3.66 (d, *J* 11.4 Hz, 1H, 6-H), 3.53–3.14 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.6 (C=S), 159.6 (*C*–OMe), 143.0 (CH=N), 135.3, 129.8, 120.4, 115.9 and 112.2 (C_{arom}), 84.0 (1-C), 78.6 (3-C), 77.6 (2-C), 71.9 (5-C), 69.8 (4-C), 60.8 (6-C), 55.3 (OCH_3). Anal. Calcd for $C_{15}H_{21}N_3O_6S{\cdot}4H_2O$ (443.47): C, 40.63; H, 6.59; N, 9.48. Found: C, 40.17; H, 7.01; N, 9.12.

1.3.13. 4-Methoxy-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3m)

Yield 68%; mp 187–190 °C (decomp., MeOH); R_f ($CHCl_3$/MeOH 5:1) 0.33; $[\alpha]_D^{25}$ +68.5 (*c* 1, MeOH); IR (KBr): *ν* 3547 (OH), 2893 (C–H_{arom}), 1549 (C=N), 1031 (C=S), 888 (1-C–H), 839 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): *δ* 11.63 (s, 1H, N(2)H), 8.46 (d, $^3J_{1\text{-}H,N(4)H}$ 9.0 Hz, 1H, N(4)H), 8.06 (s, 1H, CH=N), 7.78 (d, *J* 7.8 Hz, 2H, H_{arom}), 6.98 (d, *J* 7.8 Hz, 2H, H_{arom}), 5.37 (dd, $^3J_{1\text{-}H,2\text{-}H}$ 9.3 Hz, 1H, 1-H), 5.01–4.99 (m, 2H, OH), 4.89–4.88 (m, 1H, OH), 4.47 (t, ^3J 5.8 Hz, 1H, OH), 3.80 (s, 3H, OCH_3), 3.63 (dd, $^3J_{5\text{-}H,6\text{-}H}$ 5.7 Hz, $^2J_{6\text{-}H,6'\text{-}H}$ 11.4 Hz, 1H, 6-H), 3.50–3.44 (m, 2H) and 3.26–3.12 (m, 3H) (2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): *δ* 178.2 (C=S), 160.8 (*C*–OMe), 143.0 (CH=N), 129.2,

126.4 and 114.2 (C_{arom}), 84.0 (1-C), 78.6 (3-C), 77.6 (2-C), 72.0 (5-C), 69.8 (4-C), 60.8 (6-C), 55.3 (OCH_3). Anal. Calcd for $C_{15}H_{21}N_3O_6S{\cdot}5H_2O$ (461.49): C, 39.04; H, 6.77; N, 9.11. Found: C, 38.79; H, 6.34; N, 8.95.

1.3.14. 4-Methyl-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3n)

Yield 60%; mp 182–185 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.40; $[\alpha]_D^{25}$ +63.1 (*c* 1, MeOH); IR (KBr): *v* 3322 (OH), 2979 (C–H_{arom}), 1553 (C=N), 1035 (C=S), 904 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): δ 11.67 (s, 1H, N(2)H), 8.48 (d, $^3J_{1\text{-H,N(4)H}}$ 9.3 Hz, 1H, N(4)H), 8.06(s, 1H, CH=N), 7.72 (d, *J* 8.1 Hz, 2H, H_{arom}), 7.23 (d, *J* 7.8 Hz, 2H, H_{arom}), 5.37 (dd, $^3J_{1\text{-H,2-H}}$ 9.6 Hz, 1H, 1-H), 5.00–4.99 (m, 2H, OH), 4.88–4.87 (m, 1H, OH), 4.46 (t, ^3J 5.7 Hz, 1H, OH), 3.63 (dd, $^3J_{5\text{-H,6-H}}$ 5.7 Hz, $^2J_{6\text{-H,6'-H}}$ 11.4 Hz, 1H, 6-H), 3.50–3.43 (m, 2H) and 3.23–3.12 (m, 3H) (2-H, 3-H, 4-H, 5-H, 6′-H), 2.32 (s, 3H, CH_3); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.4 (C=S), 143.1 (CH=N), 139.9, 131.2, 129.3 and 127.5 (C_{arom}), 83.9 ((1-C), 78.6 (3-C), 77.6 (2-C), 72.0 (5-C), 69.8 (4-C), 60.8 (6-C). Anal. Calcd for $C_{15}H_{21}N_3O_5S{\cdot}2H_2O$ (391.44): C, 46.03; H, 6.44; N, 10.73. Found: C, 46.85; H, 6.29; N, 11.11.

1.3.15. 4-*tert*-Butyl-benzaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3o)

Yield 72%; mp 123–125 °C (decomp., DMF/MeOH 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.53; $[\alpha]_D^{25}$ +66.2 (*c* 1.14, MeOH); IR (KBr): *v* 3324 (OH), 2864 (C–H_{arom}), 1541 (C=N), 1018 (C=S), 900 (1-C–H), 826 (C=S) cm^{-1}; ^1H NMR (599.83 MHz, DMSO-d_6): δ 11.71 (s, 1H, N(2)H), 8.48 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.09 (s, 1H, CH=N), 7.75 (d, *J* 8.4 Hz, 2H, H_{arom}), 7.44 (d, *J* 7.2 Hz, 2H, H_{arom}), 5.38 (dd, *J* 9.0 Hz, 1H, 1-H), 5.03 (br s, 2H, OH), 4.90 (br s, 1H, OH), 4.48 (br s, 1H, OH), 3.65 (d, *J* 11.4 Hz, 1H, 6-H), 3.49–3.10 (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H), 1.30 (s, 9H, CH_3(*t*Bu)); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.5 (C=S), 152.9 (C_{arom}–*t*Bu), 143.1 (CH=N), 131.3, 127.4 and 125.5 (C_{arom}), 84.0 (1-C), 78.7 (3-C), 77.6 (2-C), 72.1 (5-C), 69.9 (4-C), 60.9 (6-C), 34.6 (*C*Me_3), 31.0 (CH_3(*t*Bu)).

1.3.16. 2-Pyridinecarboxaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3p)

Yield 85%; mp 179–182 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 9:1) 0.60; IR (KBr): *v* 3416 (OH), 2832 (C–H_{arom}), 1557 (C=N), 1039 (C=S), 896 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): δ 11.94 (s, 1H, N(2)H), 8.73 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.59–8.56 (m, 1H, H_{arom}), 8.35 (d, *J* 8.1 Hz, 1H, H_{arom}), 8.15 (s, 1H, CH=N), 7.87–7.82 (m, 1H, H_{arom}), 7.41–7.37 (m, 1H, H_{arom}), 5.40 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.05 (br s, 3H, OH), 4.51 (br s, 1H, OH), 3.66 (d, *J* 11.4 HZ, 1H, 6-H), 3.55–3.43 (m, 2H) and 3.27–3.15 (m, 3H) (m, 5H, 2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.9 (C=S), 153.0 and 149.4 (C_{arom}), 143.3 (CH=N), 136.5, 124.3 and 120.6 (C_{arom}), 84.1 (1-C), 78.7 (3-C), 77.6 (2-C), 71.9 (5-C), 69.8 (4-C), 60.8 (6-C). Anal. Calcd for $C_{13}H_{18}N_4O_5S.3H_2O$ (396.42): C, 39.39; H, 6.10; N, 14.13. Found: C, 39.78; H, 6.45; N, 14.15.

1.3.17. 3-Pyridinecarboxaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3q)

Yield 86%; mp 199–201 °C (decomp., MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 9:1) 0.90; IR (KBr): *v* 3399 (OH), 2873 (C–H_{arom}), 1537 (C=N), 1043 (C=S), 904 (1-C–H), 828 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): δ 11.86 (br s, 1H, N(2)H), 8.97 (d, *J* 1.5 Hz, 1H, H_{arom}), 8.69 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.56 (dd, *J* 4.8 Hz, *J* 1.8 Hz, 1H, H_{arom}), 8.29 (dt, *J* 8.1 Hz, *J* 1.8 Hz, 1H, H_{arom}), 8.11 (s, 1H, CH=N), 7.43 (dd, *J* 8.1 Hz, *J* 4.8 Hz, 1H, H_{arom}), 5.37 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.04 (br s, 2H, OH), 4.94 (br s, 1H, OH), 4.53 (t, ^3J 5.6 Hz, 1H, OH), 3.65 (dd, $^3J_{5\text{-H,6-H}}$ 5.7 Hz, $^2J_{6\text{-H,6'-H}}$ 11.4 Hz, 1H, 6-H), 3.56–3.45 (m, 2H) and 3.27–3.14 (m, 3H) (2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.8 (C=S), 150.5 and 149.0 (C_{arom}), 140.1 (CH=N), 134.2, 129.9 and 123.7 (C_{arom}), 84.1 (1-C), 78.7 (3-C), 77.6 (2-C), 71.9 (5-C), 69.9 (4-C), 60.9 (6-C). Anal. Calcd for $C_{13}H_{18}N_4O_5S{\cdot}2H_2O$ (378.40): C, 41.26; H, 5.86; N, 14.81. Found: C, 41.84; H, 5.53; N, 14.74.

1.3.18. 4-Pyridinecarboxaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3r)

Yield 33%; mp 201–205 °C (decomp., DMF/MeOH 3:1); R_f ($CHCl_3$/MeOH 5:1) 0.23; $[\alpha]_D^{25}$ +49.6 (*c* 0.8, MeOH/DMF 3:1); IR (KBr): *v* 3597 (OH), 2848 (C–H_{arom}), 1541 (C=N), 1035 (C=S), 896 (1-C–H), 830 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): δ 11.99 (s, 1H, N(2)H), 8.75 (d, $^3J_{1\text{-H,N(4)H}}$ 8.7 Hz, 1H, N(4)H), 8.61 (dd, *J* 5.7 Hz, 2H, H_{arom}), 8.07 (s, 1H, CH=N), 7.84 (d, *J* 5.7 Hz, 2H, H_{arom}), 5.40 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.03 (br s, 2H, OH), 4.91 (br s, 1H, OH), 4.49 (m, 1H, OH), 3.65 (dd, $^3J_{5\text{-H,6-H}}$ 4.8 Hz, $^2J_{6\text{-H,6'-H}}$ 11.4 Hz, 1H, 6-H), 3.54–3.45 (m, 2H) and 3.27–3.14 (m, 3H) (2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 179.0 (C=S), 150.1 (C_{arom}), 141.4 (CH=N), 140.7 and 121.6 (C_{arom}), 84.1 (1-C), 78.7 (3-C), 77.4 (2-C), 71.8 (5-C), 69.8 (4-C), 60.9 (6-C). Anal. Calcd for $C_{13}H_{18}N_4O_5S$ (342.37): C, 45.61; H, 5.30; N, 16.36. Found: C, 45.02; H, 5.67; N, 16.78.

1.3.19. 1-Ferrocenecarboxaldehyde 4-(β-D-glucopyranosyl)thiosemicarbazone (3s)

Yield 74%; mp 185–191 °C (decomp., MeOH/*i*PrOH 1:1); R_f ($CHCl_3$/MeOH 9:1) 0.90; $[\alpha]_D^{25}$ +40.0 (*c* 1, DMF); IR (KBr): *v* 3326 (OH), 1534 (C=N), 1024 (C=S), 891 (1-C–H), 822 (C=S) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6): δ 11.49 (s, 1H, N(2)H), 8.18 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 7.95 (s, 1H, CH=N), 5.34 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 4.81 (d, *J* 1.8 Hz, 1H, Fc), 4.73 (d, *J* 2.4 Hz, 1H, Fc), 4.44 (m, 2H, Fc), 4.22 (s, 5H, Fc), 3.90 (br s, 4H, OH), 3.65 (d, *J* 11.1 Hz, 1H, 6-H), 3.50–3.38 (m, 3H), and 3.24–3.09 (m, 2H) (2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 177.5 (C=S), 144.3 (CH=N), 83.7 (1-C), 78.6 (*C*(Fc)–CH=N), 78.5 (3-C), 77.6 (2-C), 72.0 (5-C), 70.2 (Fc), 70.1 (Fc), 69.8 (4-C), 68.9 (Fc), 68.2 (Fc), 67.3 (Fc), 60.7 (6-C). Anal. Calcd for $C_{18}H_{23}FeN_3O_5S$ (449.30): C, 48.12; H, 5.16; N, 9.35. Found: C, 48.11; H, 5.68; N, 9.12.

1.3.20. β-Naphthalenecarboxaldehyde 4-(β-D-glucopyranosyl)-thiosemicarbazone (3t)

Yield 67%; mp 218–222 °C (MeOH); R_f ($CHCl_3$/MeOH 5:1) 0.40; $[\alpha]_D^{25}$ +60.5 (*c* 1, MeOH); IR (KBr): *v* 3399 (OH), 1525 (C=N), 1055 (C=S), 900 (1-C–H), 843 (C=S) cm^{-1}; ^1H NMR (599.83 MHz, DMSO-d_6): δ 11.84 (s, 1H, N(2)H), 8.64 (d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.28 (s, 1H, H_{naphth}), 8.24 (d, *J* 8.4 Hz, 1H, H_{naphth}), 8.15 (s, 1H, CH=N), 7.99–7.97 (m, 1H, H_{naphth}), 7.94 (d, *J* 7.8 Hz, 2H, H_{naphth}), 7.56–7.55 (m, 2H, H_{naphth}), 5.42 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.05–5.03 (m, 2H, OH), 4.92–4.91 (m, 1H, OH), 4.50 (t, ^3J 6.0 Hz, 1 H, OH), 3.66 (dd, $^3J_{5\text{-H,6-H}}$ 5.4 Hz, $^2J_{6\text{-H,6'-H}}$ 11.4 Hz, 1H, 6-H), 3.57–3.54 (m, 1H), 3.51–3.47 (m, 1H) and 3.28–3.16 (m, 3H) (2-H, 3-H, 4-H, 5-H, 6′-H); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 178.6 (C=S), 143.2 (CH=N), 133.7, 132.8, 131.7, 129.3, 128.3, 127.8, 127.1, 126.7 and 123.2 8 (C_{naphth}), 84.1 (1-C), 78.7 (3-C), 77.6 (2-C), 71.9 (5-C), 69.9 (4-C), 60.9 (6-C). Anal. Calcd for $C_{18}H_{21}N_3O_5S$ (391.44): C, 55.23; H, 5.41; N, 10.73. Found: C, 55.57; H, 5.12; N, 11.02.

1.3.21. 4-Methoxy-acetophenone 4-(β-D-glucopyranosyl)thiosemicarbazone (3u)

Yield 60%; mp 127–131 °C (MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.60; $[\alpha]_D^{25}$ +45.6 (*c* 1, MeOH); IR (KBr): *v* 3297 (OH), 1510 (C=N), 1018 (C=S), 900 (1-C–H), 835 (C=S) cm^{-1}; ^1H NMR

(599.83 MHz, DMSO-d_6): δ 10.47 (br s, 1H, N(2)H), 8.35 (d, $^3J_{1\text{-H,N(4)H}}$ 8.4 Hz, 1H, N(4)H), 7.85 (d, J 8.4 Hz, 2H, H_{arom}), 6.96 (d, J 8.4 Hz, 2H, H_{arom}), 5.38 (dd, $^3J_{1\text{-H,2-H}}$ 9.0 Hz, 1H, 1-H), 5.01 (br s, 3H, OH), 4.52 (br s, 1H, OH), 3.79 (s, 3H, OCH_3), 3.63 (d, J 11.4 Hz, 1H, 6′-H), 3.48 (dd, J 4.2 Hz, J 12.0 Hz, 1H, 6-H), 3.39 (t, J 9.0 Hz, 1 H), 3.25 (t, J 8.4 Hz, 1 H), 3.17 (dd, J 9.0 Hz, J 9.6 Hz, 1H) and 3.15–3.12 (m, 1H) (2-H, 3-H, 4-H, 5-H), 2.30 (s, 3H, CH_3C=N); ^{13}C NMR (150.84 MHz, DMSO-d_6): δ 179.3 (C=S), 160.4 (C_{arom}–O), 149.1 (C=N), 130.5, 129.9, 128.2, 113.8 and 113.7 (C_{arom}), 83.8 (1-C), 78.6 (3-C), 77.4 (2-C), 72.3 (5-C), 69.8 (4-C), 60.8 (6-C), 55.2 (OCH_3), 14.3 (CH_3C=N). Anal. Calcd for $C_{16}H_{23}N_3O_6S{\cdot}3H_2O$ (439.48): C, 43.73; H, 6.65; N, 9.56. Found: C, 43.57; H, 6.98; N, 10.01.

1.3.22. 2-Acetonaphthanone 4-(β-D-glucopyranosyl)thiosemicarbazone (3v)

Yield 77%; mp 182–185 °C (MeOH/H_2O 1:1); R_f ($CHCl_3$/MeOH 5:1) 0.44; $[\alpha]_D^{25}$ +52.4 (c 1.16, MeOH); IR (KBr): ν 3379 (OH), 1562 (C=N), 1018 (C=S), 892 (1-C–H), 826 (C=S) cm^{-1}; ^{1}H NMR (599.83 MHz, DMSO-d_6): δ 10.65 (s, 1H, N(2)H), 8.51(d, $^3J_{1\text{-H,N(4)H}}$ 9.0 Hz, 1H, N(4)H), 8.34 (s, 1H, H_{naphth}), 8.24 (d, J 9.0 Hz, 1H, H_{naphth}), 8.01 (s, 1H, H_{naphth}), 7.93–7.91 (m, 2H, H_{naphth}), 7.56–7.54 (m, 2H, H_{naphth}), 5.44 (dd, $^3J_{1\text{-H,2-H}}$ 9.3 Hz, 1H, 1-H), 5.13–5.12 (m, 1H, OH), 5.03–5.02 (m, 1H, OH), 4.92–4.91 (m, 1H, OH), 4.49–4.48 (m, 1H, OH), 3.67 (dd, $^3J_{5\text{-H,6-H}}$ 5.4 Hz, $^2J_{6\text{-H,6′-H}}$ 11.4 Hz, 1H, 6-H), 3.52–3.48 (m, 2H) and 3.28–3.19 (m, 3H) (2-H, 3-H, 4-H, 5-H, 6′-H), 2.47 (s, 3H, CH_3C=N); ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 179.6 (C=S), 148.9 (C=N), 134.9, 133.3, 132.7, 128.6, 127.7, 127.5, 126.9, 126.8, 126.4 and 123.9 (C_{naphth}), 84.0 (1-C), 78.6 (3-C), 77.5 (2-C), 72.1 (5-C), 69.8 (4-C), 60.8 (6-C), 14.2 (CH_3). Anal. Calcd for $C_{19}H_{23}N_3O_5S{\cdot}2H_2O$ (441.50): C, 51.69; H, 6.16; N, 9.52. Found: C, 51.12; H, 5.98; N, 9.32.

1.4. X-Ray crystallographic study of 2d and 3j

Slow crystallization from EtOH yielded colourless crystals of **2d** (0.25 × 0.30 × 0.75 mm), which were mounted in air. Diffraction measurements were made on a Crystal Logic Dual Goniometer diffractometer using graphite monochromated Mo radiation. Unit cell dimensions were determined and refined by using the angular settings of 25 automatically centred reflections in the range 11° < 2θ < 23° and they appear in Table 4. Intensity data were recorded using a θ–2θ scan. Three standard reflections monitored every 97 reflections showed less than 3% variation and no decay. Lorentz, polarization and absorption corrections were applied using Crystal Logic software. Slow crystallization from MeOH yielded colourless crystals of **3j** (0.26 × 0.50 × 0.50 mm), which were taken from the mother liquor and immediately cooled to −93 °C. Diffraction measurements were made on a Rigaku R-AXIS SPIDER Image Plate diffractometer using graphite monochromated Cu Kα radiation. Data collection (ω-scans) and processing (cell refinement, data reduction and empirical absorption correction) were performed using the CRYSTALCLEAR program package.[17] The structures were solved by direct methods using SHELXS-97[18] and refined by full-matrix least-squares methods on F^2 with SHELXL-97.[19] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and were refined isotropically (except those of the methyl groups in **2d** which were introduced at calculated positions as riding on bonded atoms).

Table 4
X-ray experimental data of compounds **2d** and **3j**

	2d	3j
Empirical formula	$C_{23}H_{26}F_3N_3O_9S$	$C_{14}H_{19}N_3O_6S$
Formula mass	577.54	357.39
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
α (Å)	17.608(4)	7.5232(1)
b (Å)	9.325(2)	12.6624(2)
c (Å)	17.738(4)	17.4260(3)
V (Å^3)	2912.5(11)	1660.03(4)
Z	4	4
D_{calcd} (gcm^{-3})	1.317	1.430
F(0 0 0)	1200	752
μ (mm^{-1})	0.181	2.068
T (K)	298	180
λ (Å)	0.71073	1.54178
Radiation	Mo Kα	Cu Kα
θ limits	2.3/25.0	6.8/65.0
No. of data with $I > 2\sigma(I)$	3891	2781
No. of variables	440	293
R	0.0418	0.0243
Rw	0.1191	0.0626
Gof	1.01	1.07
Largest difference in final difference map (e Å^{-3})	0.19, −0.14	0.18, −0.20

2. Supplementary data

Supplementary crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC-711876 (**2d**) and 711877 (**3j**). Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

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References

1. Selected reviews: (a) Oikonomakos, N. G. *Curr. Protein Pept. Sci.* **2002**, *3*, 561–586; (b) Oikonomakos, N. G.; Somsák, L. *Curr. Opin. Investig. Drugs* **2008**, *9*, 379–395; (c) Somsák, L.; Czifrák, K.; Tóth, M.; Bokor, É.; Chrysina, E. D.; Alexacou, K.-M.; Hayes, J. M.; Tiraidis, C.; Lazoura, E.; Leonidas, D. D.; Zographos, S. E.; Oikonomakos, N. G. *Curr. Med. Chem.* **2008**, *15*, 2933–2983.
2. Selected reviews: (a) Diéguez, M.; Pàmies, O.; Claver, C. *Chem. Rev.* **2004**, *104*, 3189–3215; (b) Diéguez, M.; Claver, C.; Pàmies, O. *Eur. J. Org. Chem.* **2007**, 4621–4634.
3. Recent selected review and papers: (a) Beraldo, H.; Gambino, D. *Mini-Rev. Med. Chem.* **2004**, *4*, 31–39; (b) Belicchi-Ferrari, M.; Bisceglie, F.; Casoli, C.; Durot, S.; Morgenstern-Badarau, I.; Pelosi, G.; Pilotti, E.; Pinelli, S.; Tarasconi, P. *J. Med. Chem.* **2005**, *48*, 1671–1675; (c) Kovala-Demertzi, D.; Yadav, P. N.; Wiecek, J.; Skoulika, S.; Varadinova, T.; Demertzis, M. A. *J. Inorg. Biochem.* **2006**, *100*, 1558–1567; (d) Kovala-Demertzi, D.; Papageorgiou, A.; Papathanasis, L.; Alexandratos, A.; Dalezis, P.; Miller, J. R.; Demertzis, M. A. *Eur. J. Med. Chem.* **2009**, *44*, 1296–1302. and references cited therein.
4. (a) Kovala-Demertzi, D.; Yadav, P. N.; Demertzis, M. A.; Jasinski, J. P.; Andreadaki, F. J.; Kostas, I. D. *Tetrahedron Lett.* **2004**, *45*, 2923–2926; (b) Kostas, I. D.; Andreadaki, F. J.; Kovala-Demertzi, D.; Prentjas, C.; Demertzis, M. A. *Tetrahedron Lett.* **2005**, *46*, 1967–1970; (c) Kostas, I. D.; Heropoulos, G. A.; Kovala-Demertzi, D.; Yadav, P. N.; Jasinski, J. P.; Demertzis, M. A.; Andreadaki, F. J.; Vo-Thanh, G.; Petit, A.; Loupy, A. *Tetrahedron Lett.* **2006**, *47*, 4403–4407.
5. (a) van de Kamp, F.-P.; Micheel, F. *Chem. Ber.* **1956**, *89*, 133–140; (b) Bognár, R.; Somogyi, L.; Szilágyi, L.; Györgydeák, Z. *Carbohydr. Res.* **1967**, *5*, 320–328; (c) Wójtowicz, M.; Gmernicka-Haftek, C.; Wieniawski, W. *Acta Pol. Pharm.* **1975**, *32*, 49–52; (d) Tashpulatov, A. A.; Afanas'ev, V. A.; Lidak, M. Y.; Sukhova, N. M.; Popelis, Y. Y.; Rakhmatullaev, I. *Chem. Heterocycl. Compd.* **1983**, 137–141; (e) Zhang, S.-S.; Ye, S.-J.; Li, X.-M.; Gu, S.-S.; Liu, Q. *Chem. Res. Chinese U.* **2005**, *21*, 545–548; (f) Tashpulatov, A. A.; Rakhmatullaev, V. A.; Ismailov, N. *Zh. Org. Khim.* **1988**, *24*, 1893–1897; (g) Cao, K.; Wang, Z.; Zhao, X. *Jingxi Shiyou Huagong* **2003**, 42–45; (h) Cao, K.; Wang, Z.; Zhao, X. *Shiyou Daxue Xuebao, Ziran Kexueban* **2004**, *28*, 100–102.
6. Ghosh, S.; Misra, A. K.; Bhatia, G.; Khan, M. M.; Khanna, A. K. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 386–389.
7. Tóth, M.; Somsák, L. *Carbohydr. Res.* **2003**, *338*, 1319–1325.
8. Zemplén, G.; Gerecs, A.; Hadácsy, I. *Chem. Ber.* **1936**, *69*, 1827–1829.
9. Booth, H. *Tetrahedron Lett.* **1965**, *6*, 411–416.
10. Selected papers: (a) Dimmock, J. R.; Jonnalagadda, S. S.; Hussein, S.; Tewari, S.; Quail, J. W.; Reid, R. S.; Delbaere, L. T. J.; Prasad, L. *Eur. J. Med. Chem.* **1990**, *25*,

581–588; (b) West, D. X.; Ives, J. S.; Krejci, J.; Salberg, M. M.; Zumbahlen, T. L.; Bain, G. A.; Liberta, A. E. *Polyhedron* **1995**, *14*, 2189–2200; (c) Pelagatti, P.; Venturini, A.; Leporati, A.; Carcelli, M.; Costa, M.; Bacchi, A.; Pelizzi, G.; Pelizzi, C. *J. Chem. Soc., Dalton Trans.* **1998**, 2715–2721; (d) Martínez, J.; Adrio, L. A.; Antelo, J. M.; Ortigueira, J. M.; Pereira, M. T.; Fernández, J. J.; Fernández, A.; Vila, J. M. *J. Organomet. Chem.* **2006**, *691*, 2721–2733; (e) Graminha, A. E.; Batista, A. A.; Mendes, I. C.; Teixeira, L. R.; Beraldo, H. *Spectrochim. Acta, Part A* **2008**, *69*, 1277–1282.

11. (a) Szilágyi, L.; Györgydeák, Z.; Duddeck, H. *Carbohydr. Res.* **1986**, *158*, 67–79. and references cited therein; (b) Pérez-Rebolledo, A.; Mendes, I. C.; Speziali, N. L.; Bertani, P.; Resende, J. M.; de Carvalho Alcântara, A. F.; Beraldo, H. *Polyhedron* **2007**, *26*, 1449–1458.
12. Sriram, D.; Sreenivasan, H.; Srinivasan, S.; Priya, K.; Thirtha, M. V.; Loganathan, D. *Acta Crystallogr., Sect. C* **1997**, *53*, 1075–1077. and references cited therein.
13. (a) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1–S19; (b) Orpen, A. G.; Brammer, L.; Allen, F. H.; Kennard, O.; Watson, D. G.; Taylor, R. *J. Chem. Soc., Dalton Trans.* **1989**, S1–S83.
14. Yang, B.; Zhang, S.-S.; Li, H.-X.; Li, J.-Z.; Jiao, K. *Chem. Res. Chinese U.* **2005**, *21*, 457–459.
15. Cateni, F.; Bonivento, P.; Procida, G.; Zacchigna, M.; Gabrielli, L.; Scialino, G.; Banfi, E. *Bioorg. Med. Chem.* **2007**, *15*, 815–826.
16. Lindhorst, T. K.; Kieburg, C. *Synthesis* **1995**, 1228–1230.
17. Rigaku/MSC CRYSTALCLEAR; Rigaku/MSC: The Woodlands, TX, USA, 2005.
18. Sheldrick, G. M. SHELS-*97: Structure Solving Program*; University of Göttingen: Göttingen, Germany, 1997.
19. Sheldrick, G. M. SHELXL-*97: Crystal Structure Refinement*; University of Göttingen: Göttingen, Germany, 1997.