# Synthesis and Antimicrobial Activity of New Substituted 5-(Pyridine-3-yl)-1,3,4-Thiadiazoles and Their Sugar Derivatives

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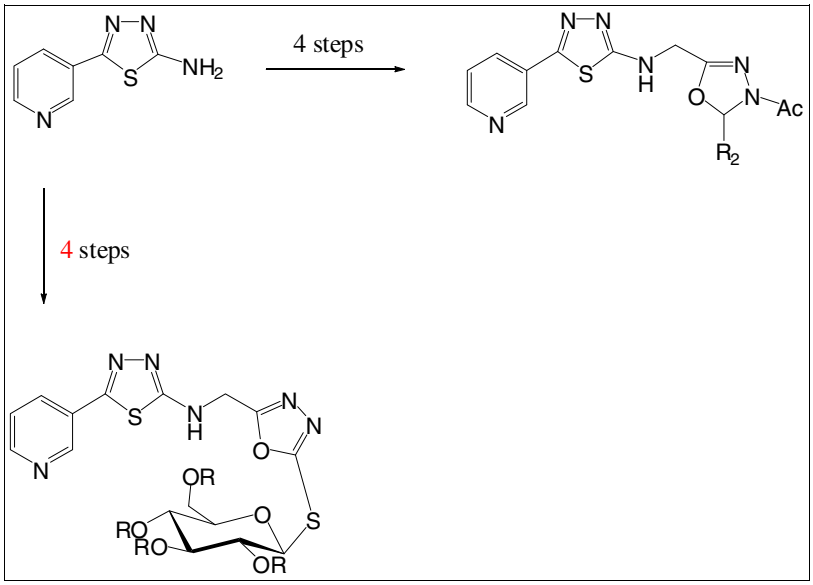
Received November 21, 2010
DOI 10.1002/jhet.901
Published online 29 March 2013 in Wiley Online Library (wileyonlinelibrary.com).




New substituted 5-(pyridine-3-yl)-1,3,4-thiadiazoles, their sugar hydrazones and acyclic *C*-nucleoside analogs as well as the corresponding thioglycoside derivatives were synthesized. The synthesized compounds were tested for their antimicrobial activity against *Escherichia coli*, *Bacillus subtilis*, *Staph aureus*, *Aspergillus niger*, and *Candida albicans* The obtained results indicated that most of tested compounds exhibited moderate to high antimicrobial activity while few compounds were found to exhibit little or no activity against the tested microorganisms.

*J. Heterocyclic Chem.*, **50,** 194 (2013).

## INTRODUCTION

The importance of the pyridine ring in the chemistry of biological system has been greatly realized because of their presence as substructure in many natural products of therapeutic importance, involved in oxidation–reduction process. The potent biological activity of various vitamins and drugs [1–3] is primarily contributed by the presence of pyridine ring in their molecular make-up. The pyridine ring is found in the skeleton of many compounds with potent antibacterial, antifungal, and anticancer properties [4, 5]. Substituted pyridines exhibit a wide range of biological activity among which anti-tumor and cytotoxic activities [6, 7] were described. On the other hand, thiadiazoles exhibit broad spectrum of biological activities, possibly due to the presence of toxophoric NeCe S moiety [8]. They find applications as antibacterial, antitumor, antiinflammatory agents, pesticides, herbicides, dyes, lubricants, and analytical reagents [9–13]. Furthermore, the glycosylthio heterocycles [14, 15] and the acyclic nucleoside [16–18] analogs including modifications of both the glycon and aglycon parts have stimulated extensive research as biological inhibitors [19, 20]. Thioglycosides have received considerable attention, because they are widely employed as ligands [21] for affinity chromatography for carbohydrate processing-enzymes and proteins. In view of the above facts and our interest [19, 22–25] in the attachment of carbohydrate residues to heterocycles to find new biologically active leads, we report here the synthesis and antimicrobial activity of new Substituted 5-(pyridine-3-yl)-1,3,4-thiadiazoles, their sugar hydrazones and acyclic *C*-nucleoside analogs as well as the corresponding glycoside derivatives.

## RESULTS AND DISCUSSION

The starting compounds 2-amino-5-(pyridin-3-yl)-1,3,4-thiadiazole (**2**) was prepared by the reaction of nicotinic acid (**1**) with thiosemicarbazide in polyphosphoric acid (PPA) medium. Reaction of **2** with ethylchloroacetate in ethanol in the presence of sodium acetate trihydrate at reflux temperature gave ethyl 2-[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino]acetate (**3**) in 51.6% yield. The IR spectrum of **3** showed characteristic absorption band at 1737 $cm^{-1}$ for the carbonyl ester group. Reaction of the ester **3** with hydrazine hydrate in ethanol afforded the acid hydrazide **4** in 98% yield. The IR spectrum of **4** showed characteristic absorption bands at v 1676, and 3420–3617 $cm^{-1}$ corresponding to the carbonyl amide, NH, and $NH_2$ groups, respectively and the $^1H$ NMR spectrum showed $CH_2$ signal at δ 3.69 ppm and $NH_2$ signal at δ 4.29 ppm.

When the hydrazide **4** was allowed to react with D-mannose, D-galactose, and D-xylose in presence of catalytic amount of acetic acid gave the corresponding sugar hydrazones **5–7** were obtained. The IR spectra of the latter hydrazones **5–7** showed the presence of characteristic absorption bands corresponding to the hydroxyl groups in the region v 3407–3410 $cm^{-1}$. Their $^1H$ NMR spectra showed signals corresponding to sugar chain protons, hydroxyl protons, NH, and pyridyl protons signals (see Experimental part).

Acetylation of sugar hydrazones **5–7** by acetic anhydride in pyridine at room temperature afforded the corresponding per-*O*-acetyl derivatives **8–10** in good yields. The later structures were established on the basic of their spectral and analytical data which were in full agreement with the assigned structures. Their IR spectra showed characteristic absorption bands at v 1728–1740 $cm^{-1}$ corresponding to the *O*-acetylcarbonyl groups. The $^1H$ NMR spectra of **8-10** showed the signals of *O*-acetyl-methyl protons at δ 1.82–2.18 ppm and the H-1 signal appeared as doublet at δ 7.21–7.34 ppm. Reaction of sugar hydrazones **5-7** with boiling acetic anhydride is well know to give either the respective per-*O,N*-acetyl derivatives or oxadiazoline acyclic *C*-nucleoside analogs depending on the applied conditions [26–28]. Carrying out the reaction with acetic anhydride at the reflux temperature afforded the oxadiazoline acyclic *C*-nucleoside derivatives **11–13** bearing acetylated sugar moieties. The later structures were confirmed by their spectral and analytical data. There IR spectra showed characteristic absorption bands at v 1728–1730 $cm^{-1}$ and 1668–1671 $cm^{-1}$ corresponding to the carbonyl ester and imide groups, respectively indicating the presence of *N*-acetyl group in addition to the *O*-acetyl groups. The $^1H$ NMR spectra of **11–13** showed signals of the *O*-acetyl-methyl protons and *N*-acetyl-methyl protons in the rang δ 1.88–2.29 ppm.

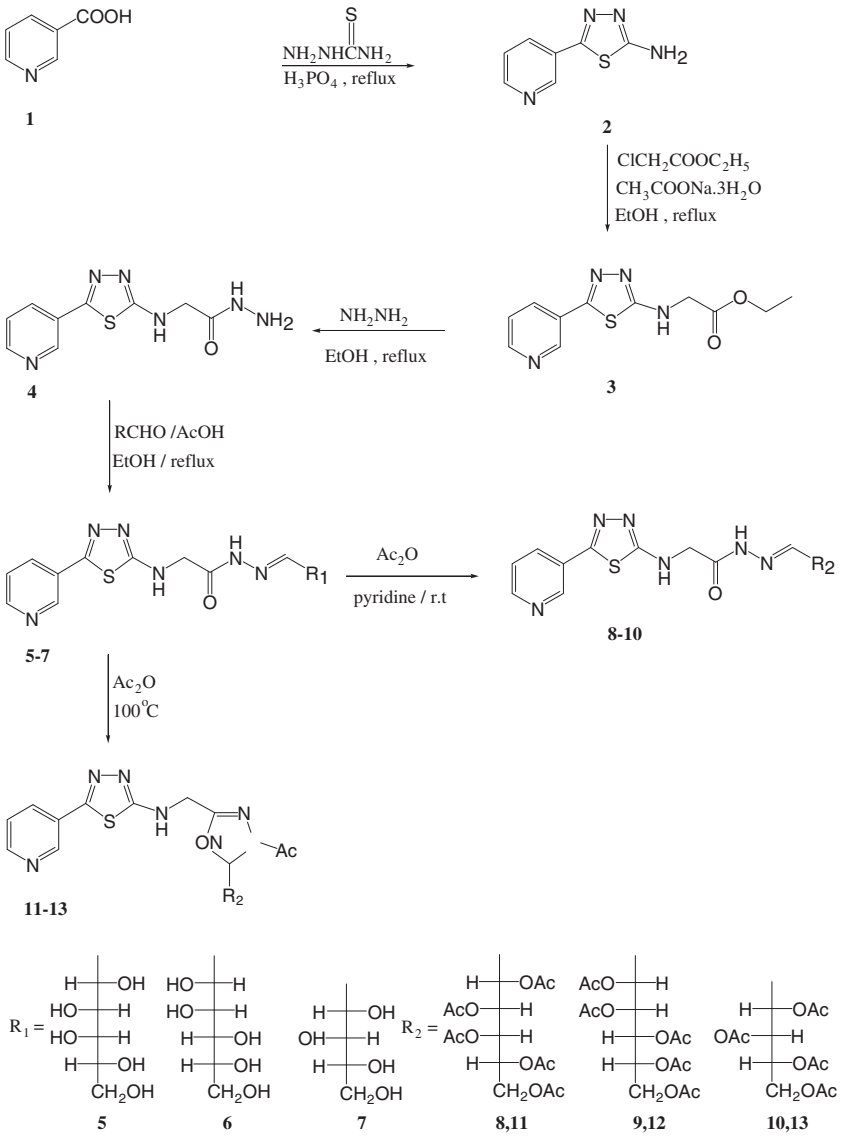
When the hydrazide **4** was allowed to react with carbon disulphide in ethanol in the presence of potassium hydroxide, it afforded the 1,3,4-oxadiazol-2-thiol derivative **14** in 71.4% yield. Reaction of **14** with 1-chloro-2,3-dihydroxypropane, 2′-(2-chloroethoxy)ethanol and chloroethylmethylether gave the corresponding 5-substituted derivatives **15–17**. The structures of these compounds were confirmed on the basis of their spectral and analytical data which were in full agreement with the assigned structures (see Experimental part).

Reaction of the 1,3,4-oxadiazole **14** with acetobromoglucose afforded the thioglucoside derivative **18**. Its IR spectra showed the presence of characteristic absorption band at v 1730 $cm^{-1}$ corresponding to the *O*-acetylcarbonyl groups. Its $^1H$ NMR spectrum revealed the presence of the *O*-acetyl-methyl groups at δ 1.239–2.075 ppm. The anomeric proton signal appeared as doublet at δ 5.77 ppm with a coupling constant 10.2 Hz indicating the β-configuration of the sugar moiety. The anomeric proton of β-*N*-glucosides having adjacent to C S group was reported [29–32] to appear at higher chemical shift due to the anisotropic deshielding effect of the C S. Deacetylation of thioglycoside **18** using methanolic ammonia solution at room temperature afforded the deprotected thioglucoside **19**. Its IR spectrum showed the characteristic absorption bands corresponding to the hydroxyl groups (Schemes 1 and 2).

The 1,3,4-thiadiazol derivative **20** was synthesized by substitution of the amino hydrogen of compound **2** by its reaction with chloroacetyl chloride in DMF and anhydrous potassium carbonate. Reaction of **20** with thiosemicarbazide and thiourea produced 1,2,4-triazin-3-thione derivative **21** and imidazolthione derivative **22**, respectively in 36-43% yields. The mass spectra of **22** revealed the presence of the characteristic signals corresponding to the molecular ion peaks corresponding to their molecular formulas. Reaction of **22** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosylbromide in acetone at room temperature afforded the thioglucoside derivative **23** in 80% yield. Its IR spectra showed the presence of characteristic band at v 1735 $cm^{-1}$ corresponding to the *O*-acetyl carbonyl groups and its $^1H$ NMR spectrum agreed with the assigned structure. Deacetylation of **23** using methanolic ammonia at room temperature afforded the deprotected thioglycoside **24**. Its IR spectrum showed the characteristic absorption bands corresponding to the hydroxyl groups and $^1H$ NMR spectrum agreed with the assigned structure (Scheme 3).

**Antimicrobial activity:.** The newly synthesized compounds were tested for their *in vitro* antimicrobial activity against a panel of standard strains; *Escherichia coli* NRRL B-210 (Gram -ve bacteria), *Bacillus subtilis* NRRL B-543 and *Staphylococcus aureus* (Gram +ve bacteria), *Aspergillus niger* and *Candida albicans* NRRL Y-477 (Fungi) using the agar diffusion method [33]. The results of the preliminary antimicrobial and the antifungal activates are shown in Table 1. The result of the antibacterial activity against *Escherichia coli* (Gram-negative bacteria) and *Bacillus subtilis* (Gram +ve bacteria) showed that compounds **9, 13, 15, 17**, and **24**

**Scheme 1**

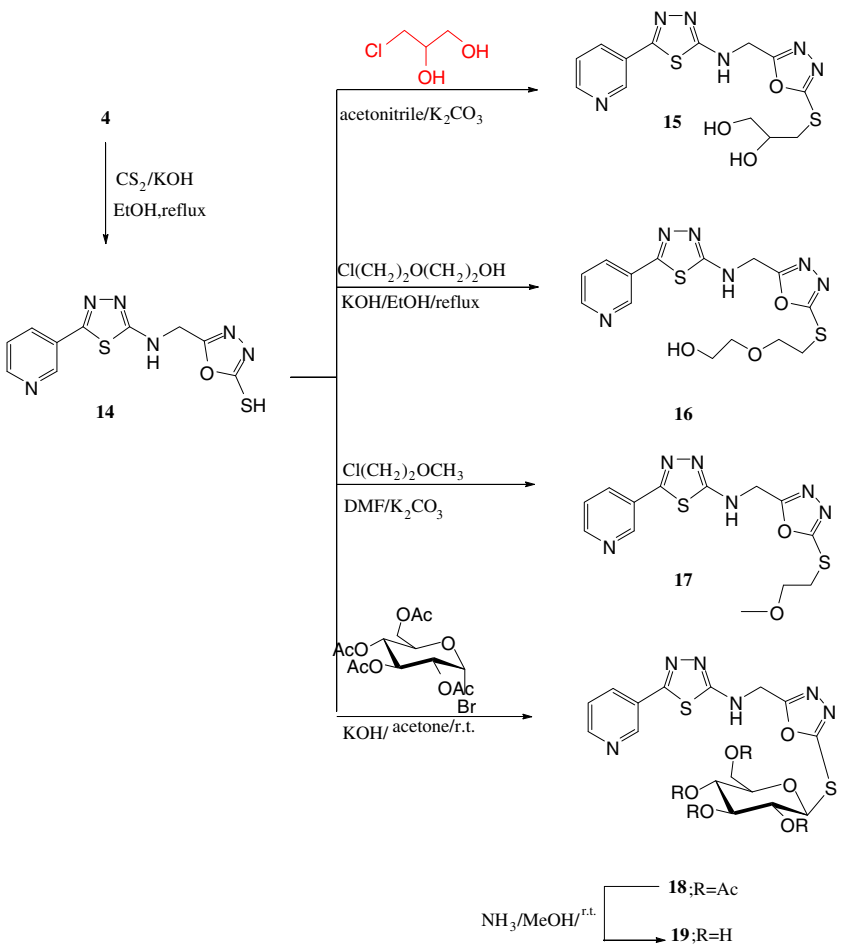



exhibited the highest antibacterial activity while followed by compounds **2**, **8**, **11-14**, and **22**. The results also revealed that compounds **9, 13, 17**, and **23** showed the highest activities against *Staph. aureus*, *aspergillus niger* and *candida albicans* (Table 1).

The antimicrobial activity results and structure activity relationship indicated that the attachment of free hydroxyl glycosyl moiety to the substituted (thiadiazol-2-ylamino)-1*H*-imidazole ring through a thioglucosidic linkage resulted in a marked increase in inhibition activity. Furthermore, the activity observed for the 1,3,4-oxadiazoline acyclic *C*-nucleoside analog with the xylotetritolyl moiety was higher than that of the corresponding manno- or galactopentitolyl analogs or their sugar hydrazone precursors. The results also revealed that the attachment of acyclic oxygenated alkyl chains to the 1,3,4-oxaidazole ring enhanced the inhibition activities. This is clear as the activity was higher for the acyclic nucleoside analogs **15** and **17** in comparison with the starting 1,3,4-oxadiazole. In addition, the free hydroxyle glucoside derivative showed relatively higher activity than the corresponding acetylated derivative as the activity when the glycoside **23** was deacetylated. In addition, the free hydroxyl thioglucoside exhibited high activity against all tested bacteria and fungi strains.

The results also revealed that the imidazolyl thioglucosides exhibited higher activities than the corresponding 1,3,4-oxadiazolyl thioglucosides except for the activity against *candida albicans*. The attachment of glucosyl moiety to 1,3,4-oxadiazolyl ring through thioglucosidic linkage resulted in decrease of inhibition activity except for *candida albicans*.

**Scheme 2**




## EXPERIMENTAL

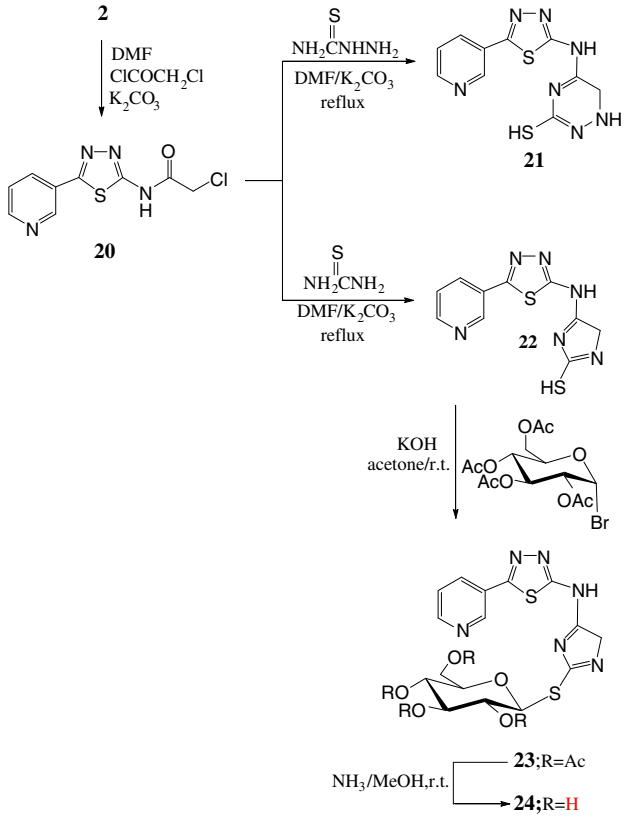
Melting points were determined with a kofler block apparatus and are uncorrected. The IR spectra were recorded on a perkin-Elmer model 1720 FTIR spectrometer for KBr disc. NMR spectra were recorded on a varian Gemini 200 NMR Spectrometer at 300 MHz for $^{1}H$ and 75 MHz for $^{13}C$. Chemical shifts were reported in δ scale (ppm) relative to TMS as a standard and the coupling constants *J* values are given in Hz. The progress of the reactions was monitored by TLC using aluminum silica gel plates 60 $F_{245}$. Elemental analyses were determined on a Perkin Elmer 240 (micro-analysis) at the Microanalytical data centre at Faculty of science, Cairo University, Egypt.

**2-Amino-5-(pyridin-3-yl)-1,3,4-thiadiazole (2).** A 100 mL round bottomed flask was fitted with a reflux condenser, thermometer, mechanical stirrer, and dropping funnel and polyphosphoric acid (25 mL) was poured in. Thiosemicarbazide (0.91 g, 10 mmole) was added and the mixture obtained was heated on an oil bath at 50°C under constant stirring. The flask was then charged with the nicotinic acid **(1)** (1.23 g, 10 mmole) and the product was held strictly at 100–110°C for 3 h. The reaction mixture was then poured into water, cooled to room temperature, and aqueous ammonia (25%) was added to pH 9-10. The precipitate was filtered off and dried at 60°C. The obtained product was recrystallized from a mixture of DMF and ethanol (3:7). Pale yellow crystals, 0.89 g (50%), m.p 202–204° C; ms (ESI): *m/z* = [$M^+$, 178 ($M^+$)]. *Anal.* Calcd. for $C_7H_6N_4S$: C, 47.18; H, 3.39; N, 31.44. Found: C, 47.42; H, 3.47; N, 31.21.

**Ethyl 2-(5-(pyridine-3-yl)-1,3,4-thiadiazol-2-ylamino) acetate (3).** To as solution of 2-amino-5-(pyridin-3-yl)-1,3,4-thiadiazole **(2)** (8.54 g, 48 mmole) in ethanol (15 mL) was added ethyl chloroacetate (6.125 g, 4.3 mL, 50 mmole) and sodium acetate trihydrate (6.0 g). The reaction mixture was refluxed for 6h, then poured into water and extracted by chloroform (50 mL). Calcium chloride was added to the chloroform layer, stirred overnight then filtered and evaporated to afford **3** as a white powder, 1.36 g (51.6%), mp 64–66°C; IR (KBr): υ 3381 (NH), 1737 (C O), 1623 $cm^{-1}$ (C N). $^{1}H$ NMR (DMSO-$d_6$) δ 1.26 (t, *J* = 5.8 Hz, 3H, $CH_3$), 3.92 (s, 2H, $CH_2$), 4.21 (q, *J* = 5.8 Hz, 2H, $CH_2$), 5.20 (s, 1H, NH), 7.53–7.66 (m, 3H, Ar-H), 7.71 (s, 1H, Ar-H). *Anal. Calcd.* for $C_{11}H_{12}N_4O_2S$: C, 49.99; H, 4.58; N, 21.20. Found: C, 49.72; H, 4.49; N, 21.29.

**2-(5-(Pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino)acetohydrazide (4).** A mixture of **3** (2.64 g, 10 mmole), hydrazine hydrate (2.5 g, 50 mmole) and ethanol (30 mL) was refluxed for 30 min. The resulting solution was concentrated, cooled to room temperature and the resulting precipitate was filtered, dried, and recrystallized from ethanol to afford the hydrazide **4**. Pale yellow powder, 2.45 g (98%), mp 142–144°C; IR (KBr): υ 3450–3421 (NH, $NH_2$), 1676 (C O),

**Scheme 3**




1625 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$) δ 3.69 (s, 2H, $CH_2$), 4.29 (s, 2H, $NH_2$), 5.61 (s, 1H, NH), 7.21–7.26 (m, 3H, Ar-H), 7.40 (s, 1H, Ar-H), 9.25 (s, H, NH). *Anal. Calcd.* for $C_9H_{10}N_6OS$: C, 43.19; H, 4.03; N, 33.58. Found: C, 43.41; H, 4.05; N, 33.48.

**General procedure for the synthesis of sugar hydrazone derivatives (5-7).** To a well stirred solution of the hydrazide **4** (2.50 g, 10 mmole) in ethanol (10 mL) was added glacial acetic acid (0.2 mL), the respective monosaccharide (1.8 g, 10 mmole) in water (2 mL)]. The mixture was heated under reflux for 3 h and the resulting solution was concentrated and left to cool to room temperature. The formed precipitate was filtered off, washed with water and ethanol, then dried and recrystallized from ethanol.

**d-Galactose-[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino] acetohydrazone (5).** This compound was obtained as a white powder, 3.5 g (85%), mp 179–180°C; IR (KBr): υ 3469–409 (OH), 3305 (NH), 1669 (C O), 1612 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 3.33–3.42 (m, 2H, H-6,6′), 4.12-4.15 (m, 2H, H-4,5), 4.28 (m, 1H, H-3), 4.40 (dd, *J* = 7.4 Hz, *J* = 7.8 Hz, 1H, H-2), 4.47 (m, 1H, OH), 4.49 (d, *J* = 6.4 Hz, 1H, OH), 4.53 (s, 2H, $CH_2$), 5.24 (m, 1H, OH), 5.55 (t, *J* = 4.6 Hz, 1H, OH), 5.61 (t, *J* = 4.6 Hz, 1H, OH), 6.08 (s, 1H, NH), 7.21–7.69 (m, 4H, Ar-H+H-1), 8.02 (m, 1H, Ar-H), 9.88 (s, 1H, NH). *Anal. Calcd.* for $C_{15}H_{20}N_6O_6S$: C, 43.68; H, 4.89; N, 20.38. Found: C, 43.58; H, 4.81; N, 20.49.

**d-Mannose-[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino] aceto-hydrazone (6).** This compound was obtained as a white solid, 3.7 g (85%), mp 182-183 $^0$C; IR (KBr): υ 3465-3407 (OH), 3315 (NH), 1662 (C O), 1618 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 3.35–3.46 (m, 2H, H-6,6′), 4.11–4.14 (m, 2H, H-4,5), 4.30 (m, 1H, H-3), 4.41 (dd, *J* = 7.4 Hz, *J* = 7.8 Hz, 1H, H-2), 4.46 (m, 1H, OH), 4.50 (d, *J* = 6.4 Hz, 1H, OH), 4.52 (s, 2H, $CH_2$), 5.24 (m, 1H, OH), 5.56 (t, *J* = 4.6 Hz, 1H, OH), 5.62 (t, *J* = 4.6 Hz, 1H, OH), 5.92 (s, 1H, NH), 7.21–7.72 (m, 4H, Ar-H), 7.97 (m, 1H, Ar-H+H-1), 9.94 (s, 1H, NH). *Anal. Calcd.* for $C_{15}H_{20}N_6O_6S$: C, 43.68; H, 4.89; N, 20.38. Found: C, 43.51; H, 4.80; N, 20.22.

**d-Xylose-[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino] aceto-hydrazone (7).** This compound was obtained as a pale yellow powder, 3.3 g (85%), mp 185–186°C; IR (KBr): υ 3469–3409 (OH), 3309 (NH), 1672 (C O), 1624 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300MHz) δ 3.37–3.45 (m, 2H, H-5,5′), 4.14–4.19 (m, 2H, H-3,4), 4.45 (m, 1H, H-2), 4.47 (m, 1H, OH), 4.52 (s, 2H, $CH_2$), 5.25 (m, 1H, OH), 5.57 (t, *J* = 4.6 Hz, 1H, OH), 5.63 (t, *J* = 4.6 Hz, 1H, OH), 6.02 (s, 1H, NH), 7.24–7.82 (m, 4H, Ar-H+H-1), 7.95 (m, 1H, Ar-H), 10.05 (s, 1H, NH). *Anal. Calcd.* for $C_{14}H_{18}N_6O_5S$: C, 43.97; H, 4.74; N, 21.98. Found: C, 43.72; H, 4.71; N, 21.79.

**General procedure for the synthesis of per-*O*-acetyl-sugar hydrazone derivatives (8–10).** To a solution of **5–7** (10 mmole) in pyridine (7 mL) was added acetic anhydride (1.02 g, 10 mmole) and the mixture was stirred at room temperature for 10 h. The resulting solution was poured onto crushed ice and the product was extracted with chloroform (30 mL). Sodium hydrogen carbonate was added and the mixture was stirred for 30 min and filtered. The chloroform layer was dried with calcium chloride and evaporated till dryness to afford the corresponding per-*O*-acetylated product.

**2,3,4,5,6-Penta-*O*-acetyl-D-galactose-[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino]acetohydrazone (8).** This compound was obtained as a white powder, 3.1 g (51.1%), mp 142–143°C; IR (KBr): υ 3349 (NH), 1728 (C O), 1686 (C O), 1635 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 1.85, 1.98, 2.03, 2.10, 2.18 (5s, 15H, 5$CH_3$), 4.16 (dd, *J* = 11.4 Hz, *J* = 2.8 Hz, 1H, H-6), 4.21 (dd, *J* = 11.4 Hz, *J* = 3.2 Hz, 1H, H-6′), 5.14 (m, 2H, H-4,5), 5.26 (dd, *J* = 6.5 Hz, *J* = 7.4 Hz, 1H, H-3), 5.52 (dd, *J* = 7.4 Hz, *J* = 7.2 Hz, 1H, H-2), 5.79 (s, 1H, NH), 7.14 (d, *J* = 7.2 Hz, 1H, H-1), 7.27–7.87 (m, 3H, Ar-H), 7.98 (s, 1H, Ar-H), 9.71 (s, 1H, NH). *Anal. Calcd.* for $C_{25}H_{30}N_6O_{11}S$: C, 48.23; H, 4.86; N, 13.50. Found: C, 48.30; H, 4.82; N, 13.62.

**2,3,4,5,6-Penta-*O*-acetyl-D-mannose-[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino]acetohydrazone (9).** This compound was obtained as a white powder, 3.1 g (51.1%), mp 130–131°C; IR (KBr): υ 3339 (NH), 1739 (C O), 1680 (C O), 1625 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300MHz) δ 1.82, 1.99, 2.04, 2.11, 2.17 (5s, 15H, 5$CH_3$), 4.17 (dd, *J* = 11.4 Hz, *J* = 2.8 Hz, 1H, H-6), 4.22 (dd, *J* = 11.4 Hz, *J* = 3.2 Hz, 1H, H-6′), 5.15 (m, 2H, H-4,5), 5.27 (dd, *J* = 6.5 Hz, *J* = 7.4 Hz, 1H, H-3), 5.51 (dd, *J* = 7.4 Hz, *J* = 7.2 Hz, 1H, H-2), 5.78 (s, 1H, NH), 7.15 (d, *J* = 7.2 Hz, 1H, H-1), 7.31–7.89 (m, 3H, Ar-H), 7.97 (s, 1H, Ar-H), 10.02 (s, 1H, NH). *Anal. Calcd.* for $C_{25}H_{30}N_6O_{11}S$: C, 48.23; H, 4.86; N, 13.50. Found: C, 48.28; H, 4.81; N, 13.59.

**2,3,4,5-Tetra-*O*-acetyl-*D*-xylose-[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino]acetohydrazone (10).** This compound was obtained as a pale yellow powder, 2.8 g (51.1%), mp 133–134°C; IR (KBr): υ 3342 (NH), 1739 (C O), 1666 (C O), 1619 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300MHz) δ 1.82, 1.98, 2.03, 2.12 (4s, 12H, 4$CH_3$), 4.17 (dd, *J* = 11.4 Hz, *J* = 2.8 Hz, 1H, H-5), 4.21 (dd, *J* = 11.4 Hz, *J* = 3.2 Hz, 1H, H-5′), 5.14 (m, 2H, H-3,4), 5.54 (dd, *J* = 7.4 Hz, *J* = 7.2 Hz, 1H, H-2), 5.86 (s, 1H, NH), 7.34 (d, *J* = 7.2 Hz, 1H, H-1), 7.57-7.89 (m, 3H, Ar-H), 8.05 (s, 1H, Ar-H), 10.02 (s, 1H, NH). *Anal. Calcd.* for $C_{22}H_{26}N_6O_9S$ (550.54): C, 48.00; H, 4.76; N, 15.27. Found: C, 48.14; H, 4.70; N, 15.36.

**Table 1**

*In vitro* antimicrobial activity by agar diffusion method of tested compounds.

| Tested compounds | Sample wt. | Microorganisms | | | | |
|---|---|---|---|---|---|---|
| | | *Escherichia coli* | *Bacillus subtilis* | *Staph. aureus* | *Aspergillus niger* | *Candida albicans* |
| **2** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **3** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **4** | 0.1 g | −ve | −ve | −ve | −ve | ++ve |
| **5** | 0.05 g | +ve | −ve | −ve | −ve | +ve |
| **6** | 0.05 g | +ve | −ve | _−ve | −ve | +ve |
| **7** | 0.05 g | ++ve | −ve | −ve | −ve | ++ve |
| **8** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **9** | 0.04g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **10** | 0.1 g | ++ve | −ve | ++ve | ++ve | ++ve |
| **11** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **12** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **13** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **14** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **15** | 0.02 g | ++ve | ++ve | −ve | ++ve | −ve |
| **16** | 0.1 g | −ve | −ve | −ve | −ve | ++ve |
| **17** | 0.02 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **18** | 0.1 g | −ve | −ve | −ve | −ve | ++ve |
| **19** | 0.1 g | −ve | −ve | −ve | −ve | ++ve |
| **20** | 0.1 g | −ve | +−ve | +ve | −ve | +ve |
| **21** | 0.1 g | +ve | ++ve | +e | +ve | ++ve |
| **22** | 0.1 g | ++ve | ++ve | ++ve | ++ve | ++ve |
| **23** | 0.1 g | +ve | ++ve | ++ve | ++ve | +ve |
| **24** | 0.05 g | ++ve | ++ve | ++ve | ++ve | ++ve |

+ve, zone of inhibition 10 mm or less.
++ve, zone of inhibition 20 mm or less.
−ve, no inhibition.

**General procedure of the synthesis of 11–13.** A solution of **5-7** (10 mmole) in acetic anhydride (10 mL) was boiled under reflux for 3-5 h. The resulting solution was poured onto crushed ice and the product was extracted with chloroform (40 mL). Sodium hydrogen carbonate was added and the mixture was stirred for 45 min and filtered. The chloroform layer was dried with calcium chloride and evaporated till dryness to afford the corresponding **11–13**.

**1-{2-(1,2,3,4,5-Penta-*O*-acetyl-D-galactopentitolyl)-5-[[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino]methyl]-1,3,4-oxadiazol-3(2*H*)-yl}ethanone (11).** This compound was obtained as a pale yellow powder, 2.79 g (42%), mp 98–99°C; IR (KBr): υ 3415 (NH), 1730 (C O), 1670 (C O), 1610 $cm^{-1}$ (C N). $^1H$ NMR (DMSO-$d_6$, 300MHz) δ 1.90, 1.94, 2.03, 2.09, 2.11, 2.28 (6s, 18H, $6CH_3$), 3.91 (dd, $J$ = 2.8, $J$ = 11.6 Hz, 1H, H-5′), 4.10 (dd, $J$ = 3.6, $J$ = 11.6 Hz, 1H, H-5′′), 4.32 (m, 1H, H-4′), 4.69 (m, 1H, H-3′), 4.82 (dd, $J$ = 7.6, $J$ = 8.2 Hz, 1H, H-2′), 4.93 (s, 2H, $CH_2$), 5.21 (t, $J$ = 9.4 Hz, 1H, H-1′), 5.70 (d, $J$ = 9.8 Hz, 1H, oxadiazoline-H), 5.88 (s, 1H, NH), 7.30-7.82 (m, 3H, Ar-H), 8.02 (s, 1H, Ar-H). *Anal. Calcd*. for $C_{27}H_{32}N_6O_{12}S$ :C, 48.79; H, 4.85; N, 12.64. Found: C, 48.61; H, 4.82; N, 12.52.

**1-{2-(1,2,3,4,5-Penta-*O*-acetyl-D-mannopentitolyl)-5-[[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino]methyl]-1,3,4-oxadiazol-3(2*H*)-yl}ethanone (12).** This compound was obtained as a pale yellow powder, 3.18 g (48%), mp 103–104°C; IR (KBr): υ 3418 (NH), 1738 (C O), 1668 (C O), 1605 $cm^{-1}$ (C N). $^1H$ NMR (DMSO-$d_6$, 300 MHz) δ 1.88, 1.92, 2.02, 2.09, 2.10, 2.29 (6s, 18H, $6CH_3$), 3.92 (dd, $J$ = 2.8, $J$ = 11.6 Hz, 1H, H-5′), 4.11 (dd, $J$ = 3.6, $J$ = 11.6 Hz, 1H, H-5′′), 4.32 (m, 1H, H-4′), 4.72 (m, 1H, H-3′), 4.82 (dd, $J$ = 7.6, $J$ = 8.2 Hz, 1H, H-2′), 4.96 (s, 2H, $CH_2$), 5.22 (t, $J$ = 9.4 Hz, 1H, H-1′), 5.73 (d, $J$ = 9.8 Hz, 1H, oxadiazoline-H), 5.89 (s, 1H, NH), 7.37-7.85 (m, 3H, Ar-H), 8.01 (s, 1H, Ar-H). *Anal. Calcd*. for $C_{27}H_{32}N_6O_{12}S$: C, 48.79; H, 4.85; N, 12.64. Found: C, 48.71; H, 4.80; N, 12.70.

**1-{2-(1,2,3,4-Tetra-*O*-acetyl-D-xylotetritolyl)-5-[[5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino]methyl]-1,3,4-oxadiazol-3(2*H*)-yl}ethanone (13).** This compound was obtained as a pale yellow powder, 2.84 g (48%), mp 107–108 °C; IR (KBr): υ 3421 (NH), 1739 (C O), 1671 (C O), 1605 $cm^{-1}$ (C N). $^1H$ NMR (DMSO-$d_6$, 300MHz) δ 1.94, 2.02, 2.09, 2.12, 2.29 (5s, 15H, $5CH_3$), 3.92 (dd, $J$ = 2.8, $J$ = 11.6 Hz, 1H, H-4′), 4.11 (dd, $J$ = 3.6, $J$ = 11.6 Hz, 1H, H-4′′), 4.75 (m, 1H, H-3′), 4.88 (dd, $J$ = 7.6, $J$ = 8.2 Hz, 1H, H-2′), 4.98 (s, 2H, $CH_2$), 5.24 (t, $J$ = 9.4 Hz, H-1′), 5.75 (d, $J$ = 9.8 Hz, 1H, oxadiazoline-H), 5.89 (s, 1H, NH), 1H, H-1), 7.37–7.87 (m, 3H, Ar-H), 8.04 (s, 1H, Ar-H). *Anal. Calcd*. for $C_{24}H_{28}N_6O_{10}S$: C, 48.64; H, 4.76; N, 14.18. Found: C, 48.79; H, 4.60; N, 14.00.

**5-{[5-(Pridine-3-yl)-1,3,4-thiadiazol-2-ylamino]methyl}-1,3,4-oxadiazole-2-thiol (14).** To a solution of **4** (5 g, 10 mmole) in ethanol (50 mL) was added a solution of potassium hydroxide (1.12 g, 20 mmole) in water (2 mL) and carbon disulphide (5 mL). The solution was heated under reflux for 7 h. the solvent was evaporated and the residue was dissolved in water, filtered, and acidified with dilute hydrochloric acid. The precipitate was filtered off, washed with water and recrystallized from ethanol to afford **14** as a white powder, 2.08 g (71.4%), mp 132–133°C; IR (KBr): υ 3433 (NH), 1610 $cm^{-1}$ (C N). $^1H$ NMR (DMSO-$d_6$, 300MHz) δ 4.92 (s, 2H,

$CH_2$), 6.04 (s, 1H, NH), 7.17 (d, $J$ = 8.5 Hz, 2H, Ar-H), 7.35 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.72 (d, 1H, $J$ = 8.5 Hz, Ar-H), 8.12 (s, 1H, Ar-H), 14.50 (s, 1H, NH). *Anal. Calcd.* for $C_{10}H_8N_6OS_2$: C, 41.08; H, 2.76; N, 28.75. Found: C, 41.22; H, 2.72; N, 28.84.

**3-{5-[(5-(Pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino)methyl]-1,3,4-oxadiazol-2-ylthio}propane-1,2-diol (15).** To a solution of **14** (2.92 g, 10 mmole) in acetonitrile (15 mL) was added anhydrous potassium carbonate (1.38 g, 10 mmole) and the mixture was stirred at room temperature for 1 h. 1-Chloro 2,3-dihydroxy propane (1.1 g, 10 mmole) was added and stirring was continued for 18 h at room temperature and then filtered, the filtrate was evaporated and recrystallized from ethanol to give **15** as a white powder, 1.54 g (42%), mp 160–162 $^0$C; IR (KBr): υ 3367 (OH), 2933cm$^{-1}$ ($CH_2$); $^1$H NMR (DMSO-$d_6$, 300MHz) δ 3.93 (m, 2H, $CH_2$), 4.25 (d, $J$ = 6.8 Hz, 2H, $CH_2$), 4.98 (s, 2H, $CH_2$), 6.07 (s, 1H, NH), 7.12 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.34 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.52 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.11 (s, 1H, Ar-H). *Anal.* Calcd. for $C_{13}H_{14}N_6O_3S_2$: C, 42.61; H, 3.85; N, 22.94.. Found: C, 42.49; H, 3.77; N, 23.10.

**2-{2-[5-((5-(Pyridine-3-yl)-1,3,4-thiadiazol-2-ylamino)methyl)-1,3,4-oxadiazol-2-ylthio]ethoxy}ethanol (16).** To a solution of **14** (2.92 g, 10 mmole) in absolute EtOH (15 mL) was added potassium hydroxide (0.56 g, 10 mmole) and the mixture was stirred at room temperature for 1 h. 2-(2-Chloroethoxy)ethanol (1.25 g, 10 mmole) was added and the reaction mixture was heated at reflux temperature for 6 h. The solvent was evaporated under reduced pressure and the resulting precipitate was collected and recrystallized from ethanol to give **16** as a pale yellow powder, 1.44 g (38%), mp 155–156 °C; IR (KBr): υ 3350 (OH), 2943 cm$^{-1}$ ($CH_2$). $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 3.93 (t, $J$ = 6.2 Hz, 2H, $CH_2$), 3.93 (m, 2H, $CH_2$), 4.25 (t, $J$ = 6.2 Hz, 2H, $CH_2$), 4.31 (t, $J$ = 6.4 Hz, 2H, $CH_2$), 5.11 (s, 2H, $CH_2$), 6.08 (s, 1H, NH), 7.14 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.33 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.54 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.14 (s, 1H, Ar-H). *Anal. Calcd.* for $C_{14}H_{16}N_6O_3S_2$: C, 44.20; H, 4.24; N, 22.09. Found: C, 44.39; H, 4.28; N, 21.91.

***N*-{[5-(2-Methoxyethylthio)-1,3,4-oxadiazol-2-yl)methyl]-5-(pyridine-3-yl}-1,3,4-thiadiazol-2-amine (17).** To a solution of **14** (2.92 g, 10 mmole) in DMF (15 mL) was added anhydrous potassium carbonate (1.38 g, 10 mmole) and the mixture was stirred at room temrerature for 1 h. Chloromethylethyl ether (0.96 g, 10 mmole) was added and stirring was continued for 8 h at room temperature and then poured on to ice-cold water. The resulting precipitate was filtered off and recrystallized from ethanol to give **17** as a pale yellow powder, 1.75 g (50%), mp 110–112 $^0$C; IR (KBr): υ 3330 cm$^{-1}$ (NH), 1608 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 3.91 (s, 3H, $CH_2$), 3.97 (t, $J$ = 6.2 Hz, 2H, $CH_2$), 4.25 (t, $J$ = 6.2 Hz, 2H, $CH_3$), 5.10 (s, 2H, $CH_2$), 6.02 (s, 1H, NH), 7.15 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.35 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.54 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.08 (s, 1H, Ar-H); *Anal. Calcd.* for $C_{13}H_{14}N_6O_2S_2$ (350.42): C, 44.56; H, 4.03; N, 23.98. Found: C, 44.72; H, 4.00; N, 24.15.

**6-(Acetoxymethyl)-2-{5-[(5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino)methyl]-1,3,4-oxadiazol-2-ylthio}tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate (18).** To a solution of **14** (5.84 g, 20 mmole) in aqueous potassium hydroxide [1.12 g, 20 mmoles in distilled water (3 mL)] was added a solution of 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide (9.38 g, 20 mmole) in acetone (20 mL). The reaction mixture was stirred at room temperature for 5 h. until reaction was judged complete by TLC using chloroform/methanol 99.5:0.5. the solvent was evaporated under reduced pressure at 40°C and the residue was washed with distilled water to remove potassium bromide formed. The product was dried, and crystallized from ethanol as a pale yellow powder, 3.73 g (60%), mp 124–125°C; IR (KBr): υ 3435 (NH), 1730 (C O), 1608 cm$^{-1}$ (C N). $^1$H NMR ($CDCl_3$, 300 MHz) δ 1.92, 2.03, 2.12, 2.14 (45s, 12H, 4 $CH_3$CO), 4.04 (m, 1H, H-5), 4.15 (dd, $J_{6,6'}$ = 11.4 Hz, $J_{5,6}$ = 2.8 Hz, 1H, H-6), 4.21 (m, 1H, H-6′), 5.10 (s, 2H, $CH_2$), 4.97 (t, $J_{3,4}$ = 9.3 Hz, 1H, H-4), 5.28 (dd, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 9.3 Hz, 1H, H-3), 5.37 (t, $J_{2,3}$ = 9.6 Hz, 1H, H-2), 5.39 (s, 2H, $CH_2$), 5.77 (d, $J_{1,2}$ = 10.2 Hz, 1H, H-1), 7.17 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.36 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.59 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.09 (s, 1H, Ar-H); $^{13}$C NMR ($CDCl_3$) δ 19.31, 19.55, 20.20, 20.24 (4$CH_3$CO), 52.27 ($CH_2$), 62.71 (C-6), 64.23 (C-4), 68.73 (C-3), 71.25 (C-2), 71.94 (C-5), 87.18 (C-1), 119.10-150.05 (Ar-6C), 155.92, 156.40, 157.05, 159.41 (4C N), 169.64, 170.30, 171.27, 171.49 (4C O). *Anal. Calcd.* for $C_{24}H_{26}N_6O_{10}S_2$ (622.63): C, 46.30; H, 4.21; N, 13.50. Found: C, 46.18; H, 4.12; N, 13.72.

**2-{5-[(5-(Pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino)methyl]-1,3,4-oxadiazol-2-ylthio}-tetrahydro-6-(hydroxymethyl)-2*H*-pyran-2,3,4,5-tetraol (19).** A solution of **18** (6.81 g, 10 mmole) in methanolic ammonia solution was stirred at room temperature for 8h. The solvent was evaporated under reduced pressure and the residue was dissolved in absolute ethanol (10 mL) and left over night to give compound **19** as a brownish solid as a yellow powder, 3.31 g (73%); mp 162–163°C; IR (KBr): υ 3405 (OH), 1608 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 3.88 (m, 2H, H-6,6′), 4.21 (m, 2H, H-4,5), 4.32 (m, H-2,3), 4.52 (d, 1H, OH), 4.94 (m, 2H, 2 OH), 5.10 (s, 2H, $CH_2$), 5.24 (d, 1H, OH), 5.79 (d, $J_{1,2}$ = 10.2 Hz, 1H, H-1), 7.18 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.35 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.60 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.12 (s, 1H, Ar-H). Anal. Calcd. for $C_{16}H_{18}N_6O_6S_2$ (454.48): C, 42.28; H, 3.99; N, 18.49. Found: C, 42.10; H, 4.05; N, 18.28.

**2-Chloro-*N*-(5-(Pyridin-3-yl)-1,3,4-thiadiazol-2-yl)acetamide (20).** To a solution of **2** (1.78 g, 10 mmole) in DMF (20 mL) was added anhydrous potassium carbonate (1.38 g, 10 mmole) and the mixture was stirred for 2h. The mixture was cooled to 0°C. Chloroacetylchloride (1.13 g, 10 mmole) was added and stirring was continued for 3h at room temperature and then poured onto ice-cold water. The resulting precipitate was filtered off and the product was collected as a white powder, 1.85 g (73%), mp 282–283°C; IR (KBr): υ 3315 (NH), 1690 (C O), 1608 cm$^{-1}$ (C N); $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 5.10 (s, 2H, $CH_2$), 5.79 (s, 1H, NH), 7.19 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.36 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.61 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.15 (s, 1H, Ar-H). *Anal. Calcd.* for $C_9H_7ClN_4OS$ (254.7): C, 42.44; H, 2.77; N, 22.00. Found: C, 42.29; H, 2.70; N, 21.88.

**5-(5-(Pyridine-3-yl)-1,3,4-thiadiazol-2-ylamino)-1,2-dihydro-1,2,4-triazine-3(*6H*)-thione (21).** To a solution of compound **20** (2.55 g, 10 mmole) and potassium carbonate (1.38 g, 10 mmole) in DMF (20 mL), thiosemicarbazide (0.91 g, 10 mmole) was added and the reaction mixture was heated under reflux for 8 h. The reaction mixture was left to cool, poured onto ice water. The precipitate was collected by filtration and recrystallized from appropriate solvent as a pale yellow powder, 1.04 g (36%), mp 279–280 °C; IR (KBr): υ 3325 (NH), 1608 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300MHz) δ 5.28 (s, 1H, $CH_2$), 6.14 (s, 1H, NH), 6.92 (s, 1H, NH), 7.18 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.35 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.61 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.14 (s, 1H, Ar-H), 8.83 (s, 1H, SH). *Anal. Calcd.* for $C_{10}H_9N_7S_2$ (291.36): C, 41.22; H, 3.11; N, 33.65. Found: C, 41.38; H, 3.05; N, 33.39.

**4-(5-(Pyridine-3-yl)-1,3,4-thiadiazol-2-ylamino)-1*H*-imidazole-2(5*H*)-thione (22).** To a solution of compound **20** (2.55 g, 10 mmole) and potassium carbonate (1.38 g, 10 mmole) in DMF (20 mL), thiourea. (0.76 g, 10 mmole) was added and the reaction mixture was heated under reflux for 8 h. The reaction mixture was left to cool,

poured onto ice water. The precipitate was collected by filtration and recrystallized from appropriate solvent as a pale yellow powder, 1.18 g (43%), mp 281–282 $^0$C; IR (KBr): υ 3327 (NH), 1608 cm$^{-1}$ (C N). $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 5.22 (s, 2H, $CH_2$), 6.12 (s, 1H, NH), 7.17 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.34 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.64 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.11 (s, 1H, Ar-H), 8.92 (s, 1H, SH). *Anal*. *Calcd*. for $C_{10}H_8N_6S_2$: C, 43.46; H, 2.92; N, 30.40. Found: C, 43.29; H, 2.85; N, 30.51.

**2-(Hydroxymethyl)-6-{5-[5-(pyridine-3-yl)-1,3,4-thiadiazol-2-ylamino]-4*H*-imidazol-2-ylthio}tetrahydro-2*H*-pyran-3,4,5-triol (23).** To a solution of **22** (5.52 g, 20 mmole) in aqueous potassium hydroxide [1.12 g, 20 mmole) in distilled water (3 mL)] was added a solution of 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide (9.38 g, 20 mmole) in acetone (20 mL). The reaction mixture was stirred at room temperature for 5h. until reaction was judged complete by TLC using chloroform/methanol 99.5:0.5. The solvent was evaporated under reduced pressure at 40°C and the residue was washed with distilled water to remove potassium bromide formed. The product was dried, and crystallized from ethanol as a pale yellow powder, 4.84 g (80%), mp 100–102°C; IR (KBr): υ 3420 (NH), 1735 (C O), 1608 cm$^{-1}$ (C N). $^1$H NMR ($CDCl_3$, 300 MHz) δ 1.91, 1.97, 2.05, 2.12 (4s, 12H, 4 $CH_3$CO), 4.05 (m, 1H, H-5), 4.14 (dd, $J_{6,6'}$ = 11.4 Hz, $J_{5,6}$ = 2.8 Hz, 1H, H-6), 4.24 (m, 1H, H-6′), 4.97 (t, $J_{3,4}$ = 9.3 Hz, 1H, H-4), 5.14 (s, 2H, $CH_2$), 5.27 (dd, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 9.3 Hz, 1H, H-3), 5.33 (t, $J_{2,3}$ = 9.6 Hz, 1H, H-2), 5.36 (s, 1H, $CH_2$), 5.78 (d, $J_{1,2}$ = 10.2 Hz, 1H, H-1), 7.19 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.36 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.62 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.11 (s, 1H, Ar-H); $^{13}$C NMR ($CDCl_3$) δ 19.30, 19.54, 20.22, 20.25 (4$CH_3$CO), 53.12 ($CH_2$), 62.74 (C-6), 64.25 (C-4), 69.70 (C-3), 71.16 (C-2), 71.94 (C-5), 87.19 (C-1), 121.10-149.15 (Ar-6C), 155.90, 156.97, 157.'15, 158.61 (4C N), 169.65, 170.34, 171.29, 171.96 (4C O). *Anal*. *Calcd*. for $C_{24}H_{26}N_6O_9S_2$: C, 47.52; H, 4.32; N, 13.85. Found: C, 47.30; H, 4.58; N, 13.41.

**2-(Hydroxymethyl)-6-(5-(5-(pyridin-3-yl)-1,3,4-thiadiazol-2-ylamino)-4*H*-imidazol-2-ylthio)tetrahydro-2*H*-pyran-3,4,5-triol (24).** A solution of **23** (6.07 g, 10 mmole) in methanolic ammonia solution was stirred at room temperature for 8 h. The solvent was evaporated under reduced pressure and the residue was dissolved in absolute ethanol (10 mL) and left over night to give compound **24** as a brown solid. 3.28 g (75%), mp 172–173°C; IR (KBr): 3450 (OH), 1608 cm$^{-1}$ (C N); $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 3.79 (m, 2H, H-6,6′), 4.23 (m, 2H, H-4,5), 4.30 (m, H-2,3), 4.42 (d, 1H, OH), 4.95 (m, 1H, 2 OH), 5.12 (s, 2H, $CH_2$), 5.25 (d, 1H, OH), 5.65 (d, $J_{1,2}$ = 10.2 Hz, 1H, H-1), 7.15 (d, $J$ = 8.5 Hz, 1H, Ar-H), 7.34 (d, $J$ = 7.2 Hz, 1H, Ar-H), 7.61 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.11 (s, 1H, Ar-H). *Anal*. Calcd. for $C_{16}H_{18}N_6O_5S_2$ (438.48): C, 43.83; H, 4.14; N, 19.17. Found: C, 44.00; H, 4.50; N, 18.99.

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