Synthesis of 2-(Sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-hydroxyphenyl)-thiazoles and Their *O*-Glucosides

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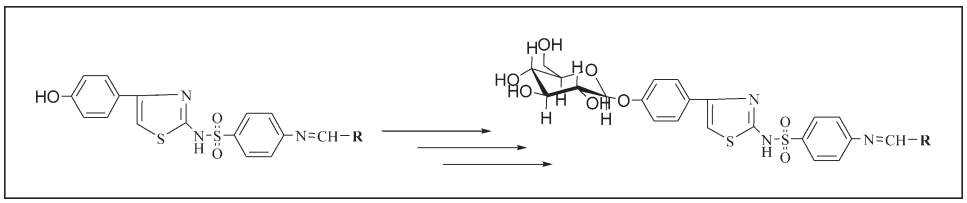

In continuation of our work, we synthesized 2-(sulfamoylphenyl)-4′-amino-4-(4″-hydroxyphenyl)-thiazole (**3a**), which were reacted with various (aryl/hetroaryl) aldehyde to form 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-hydroxyphenyl)-thiazoles (**4a–f**). Glucosylation of compounds (**4a–f**) have been done by using acetobromoglucose as a glucosyl donor to afford 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(2,3,4,6-tetra-*O*-acetyl-4″-*O*-β-D-glucosidoxyphenyl)-thiazoles (**5a–f**), further on deacetylation to produce 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-*O*-β-D-glucosidoxyphenyl)-thiazoles (**6a–f**). The compounds are confirmed by FTIR, ^{1}H-NMR, ^{13}C-NMR, and ES-Mass spectral analysis.

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INTRODUCTION

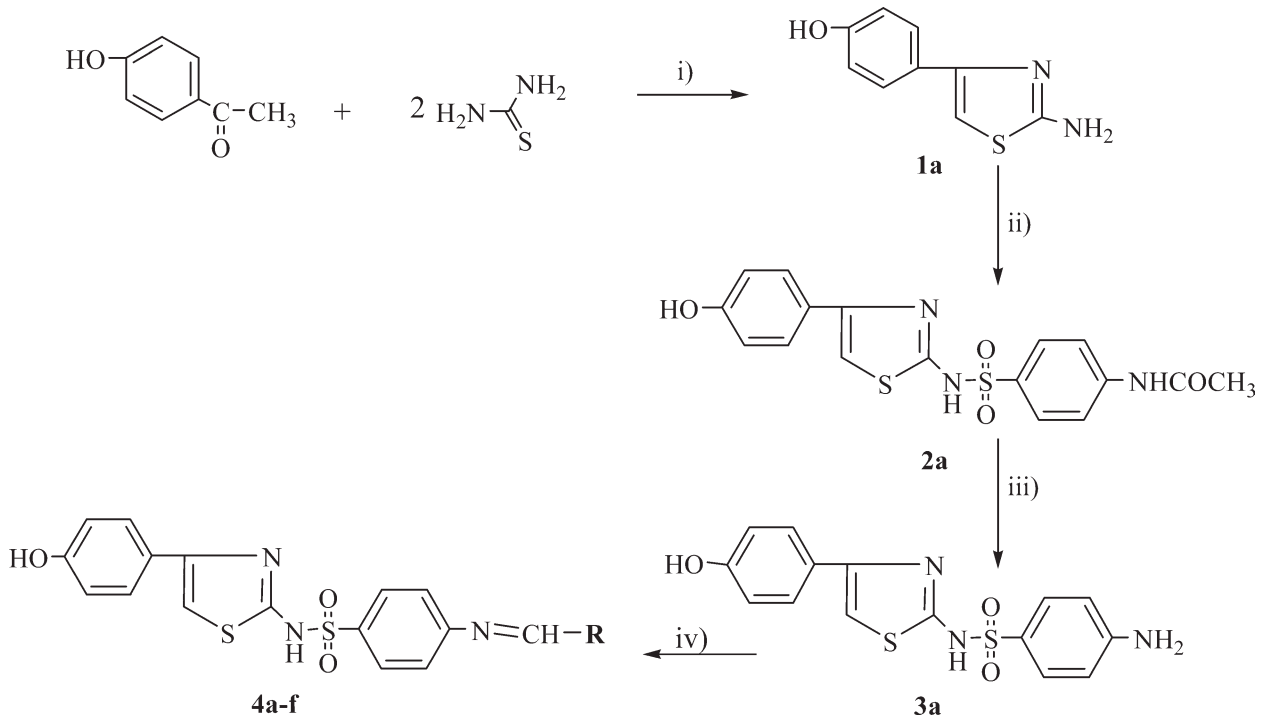
Thiazoles are important heterocycles with great applicability in medicinal chemistry, and this core structure can be found in various biological/medicinal applications like antimicrobial, anti-inflammatory, antitubercular, anthelmintic, sedative hypnotics, and antiretroviral activity [1–10]. The presence of imino group is mainly responsible for the potent biological activity of many compounds. These imines constitute one of the most active classes of compounds possessing diversified biological applications [11–15]. The sulfonamide drugs were the first effective chemotherapeutic agents to be used systematically for the prevention and cure of bacterial infections in man. The main feature of these compounds lies in the high therapeutics index and low toxicity. Sulfonamide posses various biological activity such as antifungal, antimalerial, antidiabetic, and anti-ischemic [16–20]. *O*-glucosides play important role in the carbohydrate chemistry, mainly it used as carrier of aglycon. *o*-Glycosides have various biological activities like anti-inflammatory, antifungal, anticancer, antiviral, and antitumor activity [21–31].

So, continuation of our work [32–38] and keeping view of the various biological activities, it was proposed to synthesize new molecules containing thiazole, azomethine, *O*-glucoside, and sulfonamide moiety in one frame-work.

RESULTS AND DISCUSSION

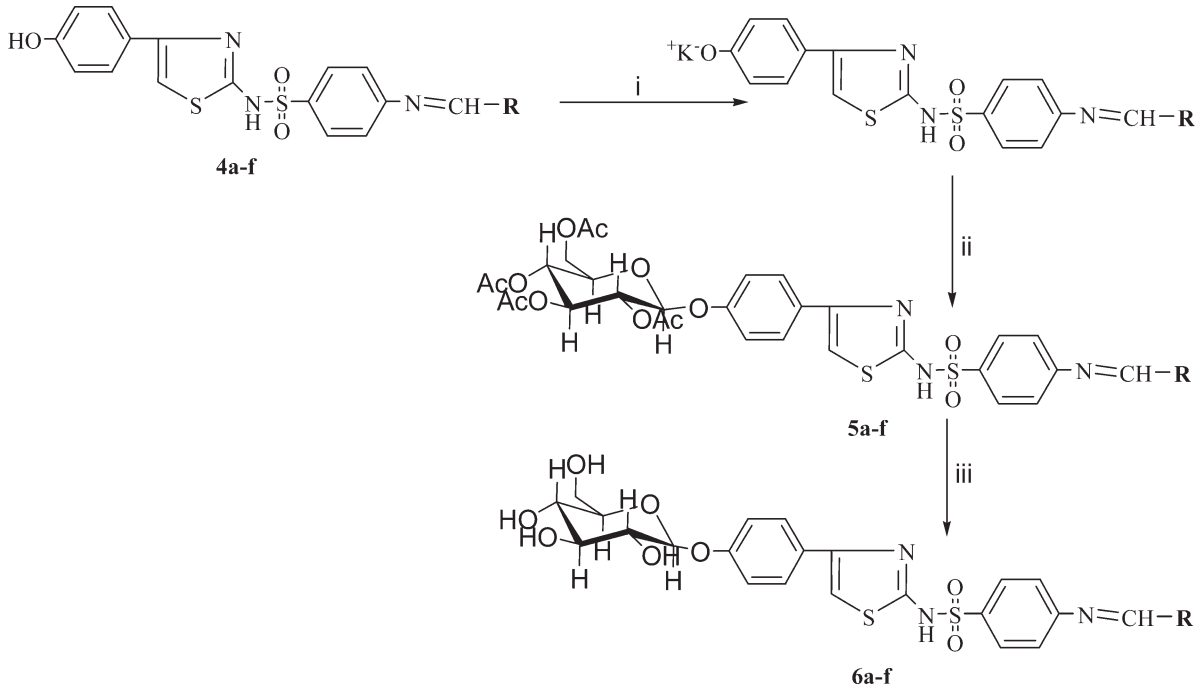
Our research envisage starts with the synthesis of 2-amino-4-(4′-hydroxyphenyl)-thiazole (**1a**); it was prepared from 4-hydroxyacetophenone, iodine, and thiourea [39,40]. Infra-red spectrum of this compound shows characteristic bands at 3487.8 (—OH), 3379.5 (—NH_2), 3127.7 (aromatic compound stretching), 1600 (C=C), ^{1}H NMR 6.44 (s, 1H, Thiazole), 6.80–7.82 (m, 4H, Ar-H), 4.82 (bs, 2H, NH_2), 5.66 (s, 1H, OH), which confirmed the 2-amino-4-(4′-hydroxyphenyl)-thiazole. By using these starting material, we synthesized 2-(sulfamoylphenyl)-4′-acetamido-4-(4″-hydroxyphenyl)-thiazole (**2a**) from reaction between *p*-acetamidobenzenesulfonyl chloride and 2-amino-4-(4′-hydroxyphenyl)-thiazole in aqueous medium. These on further acid hydrolysis form 2-(sulfamoylphenyl)-4′-amino-4-(4″-hydroxyphenyl)-thiazole (**3a**), which shows the following characteristic bands 3441.0 (—OH, str.), 3340 (—NH_2), 1643 (C=N), 3126.4 (Aromatic, str.), 1362.1 (SO_2 str. asymmetric), 1112.2 (SO_2 str. symmetric), 689.3 (C—S, str.), 771.1 (C—S—C, str.). ^{1}H-NMR 3.81 (s, 1H,—NH), 4.65 (bs, 2H, NH_2), 5.22 (s, 1H, OH), 6.56 (s, 1H, Thiazole), 6.76–7.74 (m, 8H, Ar-H) confirmed the formation of (**3a**). Schiff base was prepared by using 2-(sulfamoylphenyl)-4′-amino-4-(4″-hydroxyphenyl)-thiazole (**3a**) to react with various substituted (aryl/hetroaryl) aldehyde to afford our aglycon moiety, *i.e.*, 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-hydroxyphenyl)-thiazoles

Scheme 1. Synthetic route of 2-(sulfamoylphenyl)-4′-((iminoaryl/hetroaryl))-4-(4″-hydroxyphenyl)-thiazole (**4a–f**). (i) iodine, (ii) *p*-acetamidosulofonylchloride, (iii) acid hydrolysis, (iv) (aryl/hetroaryl) aldehyde.



(**4a–f**) (Scheme 1). The infra-red spectrum of the compound (**4a**) showed following characteristic bands at 3367.1(—OH), 3105.1 (—NH), aromatic stretching observed at 3043.1, and 1634 (C=N), 1335 (SO_2 str. asymmetric), 1126 (SO_2 str. symmetric), 640 (C—S, str.), 759.1 (C—S—C, str), and there is absence of secondary amine group peak; ^{1}H-NMR spectrum showed chemical shift values and displayed signal due to aromatic protons

Scheme 2. Synthetic route of 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-*O*-β-D-glucosidoxyphenyl)-thiazoles (**6a–f**). (i) CH_3OH, KOH, (ii) acetone, α-acetobromoglucose, (iii) CH_3ONa,CH_3OH.



multiplet at δ = 7.24–8.20 Hz (m, 13H, Ar-H), hydroxyl group proton at δ =4.88 Hz and δ = 3.2063 Hz (1H, —NH, D_2O exchangeable).

Glucosylation of 2-(sulfamoylphenyl)-4′-((iminoaryl/hetroaryl))-4-(4″-hydroxyphenyl)-thiazole (**4a–f**) with acetobromoglucose (ACBG) followed by deacetylation leads to the desired *O*-glucoside with distereoselectivity in favor of β-anomer. An ester protecting group on the 2-hydroxyl group of the donor will lead to the neighboring group participation during *O*-glucosylation reaction, only β-anomer is obtained. The glucosylation carried out by using Koeing-Knorr method [41] started with the preparation of acetobromoglucose from glucose pentacetate and red phosphorous, which is then reacted with potassium salt of compounds (**4a–f**) to produce 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(2,3,4,6-tetra-*O*-acetyl-4″-*O*-β-D-glucosidoxyphenyl)-thiazoles (**5a–f**). The infra-red spectrum of the compound (**5a**) shows following characteristic bands at ν_{max}. The secondary amine group observed at 3330.5 cm^{-1}, and the aromatic ring stretching at 3120.5–2980.6, 1620.5(C=N), 628 (C—S), 740 (C—S—C, str.), 1310 (SO_2 str. asymmetric), 1115.4 (SO_2 str. symmetric); the band due to C—O—C that appears at 1180 cm^{-1} confirms the formation of *O*-glucoside. ^{1}H-NMR also confirmed the **5a**. Further deacetylation of compound (**5a–g**) produces our title molecules *i.e.* 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-*O*-β-D-glucosidoxyphenyl)-thiazoles (**6a–f**) (Scheme 2). Infra-red spectrum shows that 3405 (—OH, broad, stretching) was observed due to carbohydrate hydroxyl groups. In the spectrum, 1411.5 (SO_2 asymmetric, str.), 924.3 (SO_2 asymmetric, str.), and the presence of band at 1050.3 (C—O—C) indicate the formation of glucosidic linkage, and the band at 1635.9 (C=N) cm^{-1} was also observed which confirmed the (**6a**); ^{1}H-NMR of the compound displayed the signal due to sugar protons between δ 3.25–3.54 ppm and aromatic ring proton between δ 7.28–8.24 ppm. The β-glucosidic bond formation was established by the appearance of doublet at δ = 5.85 ppm. ES-spectra of (**6a**) show *m/z* (% abundance): 627.5 (M, 10), 434 (base peak, 100), 313 (12), 237 (49), 160 (09), 91 (02). ^{13}C-NMR spectrum, C-1 resonated downfield of the other glucosyl carbon at δ 101–105.0 consistent with the formation of *o*-β-glucosides.

EXPERIMENTAL RESULT

General remarks. The melting points (m.p.) are taken by using open capillary method and are uncorrected. The FTIR spectra were recorded by using the Perkin-Elmer spectrophotometer with KBr disc. The ^{1}H-NMR spectra recorded on Bruker DRX-300 (300MHz FT-NMR) instrument using DMSO-d_6 as a solvent and TMS as internal standard, and the chemical shift is expressed in δ ppm values. ES-MS were recorded on Micromass: Q-T of micro (YA-105). Elemental analyses were determined by the FLASH EA 1112 CHN analyzer, Thermo Finigin, Italy.

General procedure for the preparation of 2-amino-4-(4′-hydroxyphenyl)-thiazole (1a). A mixture of *p*-hydroxyacetophenone (0.1 mol), thiourea (0.2 mol), and iodine (0.2 mol) was heated on water bath for 18 h with occasional stirring and then cooled. The residue titurated with ether to remove excess of unreacted *p*-hydroxyacetophenone. It was then washed with sodium thiosulfate to removed iodine impurity. The crude product is dissolved in boiling water and filter hot. The titled compound formed after neutralized with aqueous ammonia; the white colored compound was formed which was crystallized from ethanol to get pale yellow needles, Yield (57%), m.p. 201°C; The infra-red spectrum of the compound showed 3487.8 (—OH), 3379.5 (—NH_2), 3127.7 (Ar-H), 1600 (C=C),1273 (C—N). ^{1}H-NMR 6.44 (s, 1H, Thiazole), 6.80–7.82 (m, 4H, Ar-H), 4.82 (bs, 2H, NH_2), 5.66 (s, 1H, OH). Anal. Calcd. for $C_9H_8N_2OS$ (192.24): C, 56.23; H, 4.19; N, 14.97; S, 16.68; Found: C, 56.24; H, 4.17; N, 14.97; S, 16.69.

General procedure for the preparation of 2-(sulfamoylphenyl)-4′-acetamido-4-(4″-hydroxyphenyl)-thiazole (2a). A mixture of the crude *p*-acetamidobenzenesulfonyl chloride (0.064 mol), 2-amino-4-(4′-hydroxyphenyl)-thiazole (0.40 mol), and water (30 mL) was heated with shaking on water bath for 30 min. The reaction mixture was cooled at room temperature, and the solid suspension of sulfonamide was obtained. The reaction mixture was acidified with dil. H_2SO_4. A yellow-colored solid separated out. It was washed several times with water, filtered and dried, yield 66%, m.p. 240°C, The infra-red spectrum of the compound showed 3440.2 (—OH), 3385.0 (—NH_2), 3115.5 (Ar-H), 1622 (C=C), 1270 (C—N); ^{1}H-NMR 3.80 (s, 1H, —NH), 4.35 (bs, 2H, NH_2), 5.46 (s, 1H, OH), 6.68 (s, 1H, Thiazole), 6.90–7.92 (m, 4H, Ar-H), 9.10 (s, 1H, NH); Anal. Calcd. for $C_{17}H_{15}N_3O_4S_2$ (389.45): C, 52.43; H, 3.88; N, 10.79; S, 16.47; Found: C, 52.44; H, 3.88; N, 10.80; S, 16.47.

General procedure for the preparation of 2-(sulfamoylphenyl)-4′-amino-4-(4″-hydroxyphenyl)-thiazole (3a). A mixture of 2-(sulfamoyl phenyl)-4′-acetamido-4-(4″-hydroxyphenyl)-thiazole (10 g), conc. HCl (10 mL), and water (50 mL) was refluxed until a clear solution was obtained (for about 1h). The clear solution was then cooled at room temperature. It was made alkaline with $NaHCO_3$ (10 g) and cooled in ice bath. A yellow solid was obtained. It was washed with water, filtered, and dried yield 6 g (67%). The compound was crystallized with aqueous ethanol, m.p.110°C. Infra-red shows the following characteristic bands 3441.0 (—OH, str.) due to the presence of free phenolic hydroxyl group, 3340 (—NH_2), 1643 (C=N), 3126.4 (Aromatic, str.), 1362.1 (SO_2 str. asymmetric), 1112.2 (SO_2 str. symmetric), 689.3 (C—S, str.), 771.1 (C—S—C, str.); ^{1}H-NMR: 3.81 (s, 1H,—NH), 4.65 (bs, 2H, NH_2), 5.22 (s, 1H, OH), 6.56 (s, 1H, Thiazole), 6.76–7.74 (m, 8H, Ar-H). Anal. Calcd. for $C_{15}H_{13}N_3O_3S_2$ (347.41): C, 51.86; H, 3.77; N, 12.10; S, 18.46; Found: C, 51.86; H, 3.78; N, 12.09; S, 18.48.

General procedure for the preparation of 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-hydroxyphenyl)-thiazoles (4a–f). The condensation of 2-(sulfamoyl phenyl)-4′-(amino phenyl)-4-(4″-hydroxyphenyl)-thiazole (0.01 mol) and substituted aldehyde (0.01 mol) in 250-mL round-bottom flask

with alcohol as solvent. To this mixture, few drops of conc. H_2SO_4 were added. The mixture was refluxed about 3–4 h or up to TLC passed. It was cooled to obtain the solid, filtered and dried. It was crystallized from ethanol. Similarly, the entire compounds **(4a–f)** were prepared.

2-(Sulfamoylphenyl)-4′-(iminobenzal)-4-(4″-hydroxyphenyl)-thiazole (4a) Yield (62%); m.p. 120°C; FTIR spectra 3367.1 (—OH), 3105.1 (—NH), 3043.1 (aromatic str.), 1634 (C=N), 1335 (SO_2 str. asymmetric), 1126 (SO_2 str. symmetric), 640 (C—S, str.), 759.1 (C—S—C, str); ^{1}H-NMR δ: 4.88 (s, 1H, OH), 3.20 (1H, —NH, D_2O exchangeable), 6.66 (s, 1H, Thiazole), 7.24–8.20 (m, 13H, Ar-H), 9.2 (s, 1H ,imines); Anal. Calcd. for $C_{22}H_{17}N_3O_3S_2$ (435.52): C, 60.67; H, 3.93; N, 9.65; S, 14.72; Found: C, 60.66; H, 3.93; N, 9.66; S, 14.71.

2-(Sulfamoylphenyl)-4′-(imino-4-methoxybenzal)-4-(4″-hydroxyphenyl)-thiazole (4b) Yield (73%); m.p.105°C; FTIR spectrum shows 3330.4 (—OH), 3138.5 (—NH), 3010.4 (aromatic str.), 1624 (C=N), 1334 (SO_2 str. asymmetric), 1121 (SO_2 str. symmetric), 640 (C—S, str.), 762.4 (C—S—C, str); ^{1}H-NMR δ: 3.42 (s, 3H, OCH_3), 3.73 (1H, —NH, D_2O exchangeable), 4.28 (s, 1H, OH), 6.51 (s, 1H, Thiazole), 6.70–7.52 (m, 12H, Ar-H), 8.85 (s, 1H, imines); Anal. Calcd. for $C_{22}H_{16}ClN_3O_3S_2$ (465.54): C, 59.34; H, 4.11; N, 9.03; S, 13.78; Found: C, 59.32; H, 4.10; N, 9.08; S, 13.79.

2-(Sulfamoylphenyl)-4′-(imino-4-fluorobenzal)-4-(4″-hydroxyphenyl)-thiazole (4c) Yield (72%); m.p. 170°C; FTIR spectrum shows 3342.0 (—OH), 3125.4 (—NH), 3008.2 (aromatic str.), 1630 (C=N), 1338 (SO_2 str. asymmetric), 1122 (SO_2 str. symmetric), 642 (C—S, str.), 761.0 (C—S—C, str); ^{1}H-NMR δ: 4.62 (s, 1H, OH), 3.50 (1H, —NH, D_2O exchangeable), 6.83 (s, 1H, Thiazole), 7.0–8.44 (m, 12H, Ar-H), 9.4 (s, 1H, imines); Anal. Calcd. for $C_{22}H_{16}FN_3O_3S_2$ (453.51): C, 58.26; H, 3.56; F, 4.19; N, 9.27; S, 14.14; Found: C, 58.28; H, 3.56; F,4.20; N, 9.26; S, 14.15.

2-(Sulfamoylphenyl)-4′-(imino-3-indolyl)-4-(4″-hydroxyphenyl)-thiazole (4d) Yield (70%); m.p.156°C; FTIR spectrum shows 3415.0 (—OH), 3345.7 (—NH), 3014.2 (aromatic str.), 1635 (C=N), 1332 (SO_2 str. asymmetric), 1124 (SO_2 str. symmetric), 640.6 (C—S, str.), 758.0 (C—S—C, str); ^{1}H-NMR δ : 4.84 (s, 1H, OH), 3.83 (1H, —NH, D_2O exchangeable), 6.67 (s, 1H, Thiazole), 7.0–8.84 (m, 13H, Ar-H), 9.17 (s, 1H, imines), 10.55 (s, NH, indole); Anal. Calcd. for $C_{24}H_{18}N_4O_3S_2$ (474.55): C, 60.74; H, 3.82; N, 11.81; S, 13.51; Found: C, 60.75; H, 3.84; N, 11.80; S, 13.51.

2-(Sulfamoylphenyl)-4′-(imino-4-pyridyl)-4-(4″-hydroxyphenyl)-thiazole (4e) Yield (75%); m.p.178°C; FTIR spectrum shows 3440.3 (—OH), 3375.0 (—NH), 3025.1 (aromatic str.), 1632 (C=N), 1330 (SO_2 str. asymmetric), 1126 (SO_2 str. symmetric), 635.8 (C—S, str.), 759.2 (C—S—C, str); ^{1}H-NMR δ: 3.94 (1H, —NH, D_2O exchangeable), 4.42 (s, 1H, OH), 6.82 (s, 1H, Thiazole), 7.22–8.56 (m, 12H, Ar-H), 8.8 (s, 1H, imines); Anal. Calcd. for $C_{21}H_{16}N_4O_3S_2$ (436.51): C, 57.78; H, 3.69; N, 12.84; S, 14.69; Found: C, 57.77; H, 3.69; N, 12.83; S, 14.69.

2-(Sulfamoylphenyl)-4′-(imino-2-furyl)-4-(4″-hydroxyphenyl)-thiazole (4f) Yield (64%); m.p.165°C; FTIR spectrum shows 3408.5 (—OH), 3342.2 (—NH), 3038.2 (aromatic str.), 1634 (C=N), 1333 (SO_2 str. asymmetric), 1129 (SO_2 str. symmetric), 637.2 (C—S, str.), 762.3 (C—S—C, str); ^{1}H-NMR δ: 3.85 (1H, —NH, D_2O exchangeable), 4.8 (s, 1H, OH), 6.72 (s, 1H, Thiazole), 6.92–7.41 (m, 11H, Ar-H), 7.95 (s, 1H, imines); Anal. Calcd. for $C_{20}H_{15}N_3O_4S_2$ (425.48): C, 56.46; H, 3.55; N, 9.88; S, 15.07; Found: C, 56.47; H, 3.56; N, 9.85; S, 15.09.

General procedure for the preparation of 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(2,3,4,6-tetra-*O*-acetyl-4″-*O*-β-D-glucosidoxyphenyl)-thiazoles (5a–f). A mixture of 3 g of potassium salt of 2-(sulfamoyl phenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-hydroxyphenyl)-thiazole (**4a–f**) in 10 mL of 5% methanolic KOH was added drop wise to a solution of 5 g of acetobromoglucose in 20-mL dry acetone. The resulting mixture was stirred at 0°C for 2 h. The reaction was allowed to proceed for an additional 24 h, and the solvent removed under pressure. The resulting brown syrup was dissolved in CH_3OH-CH_2Cl_2 (8:2) and chromatogram on 60–120 cm silica gel. The reaction was monitored by TLC. The solvent was evaporated to obtained a brown syrupy, 2-(sulfamoyl phenyl)-4′-(iminoaryl/hetroaryl)-4-(2,3,4,6-tetra-*O*-acetyl-4″-*O*-β-D-glucosidoxyphenyl)-thiazole (**5a–f**). Similarly, using this procedure all the compound 2-(sulfamoyl phenyl)-4′-(iminoaryl/hetroaryl)-4-(2,3,4,6-tetra-*O*-acetyl-4″-*O*-β-D-glucosidoxyphenyl)-thiazole (**5a–f**) were prepared.

2-(Sulfamoylphenyl)-4′-(iminobenzal)-4-(2,3,4,6-tetra-O-acetyl-4″-O-β-D-glucosidoxyphenyl)-thiazole (5a) Yield 72%; $[\alpha]_D^{30} = -14.18$ (c, 0.1, DMSO); brown syrup; FTIR: 1310 (SO_2 str. asymmetric), 1115.4 (SO_2 str. Symmetric), 1180.0 (C—O—C), 1620.5 (C=N), 740 (C—S—C), 628.0 (C—S, bend); ^{1}H-NMR: 2.02, 2.04, 1.99, 2.03 (s, 3H) ($COCH_3$), 3.98 (s, 1H, NH), 5.95 (d, 1H, anomeric proton), 6.44 (s, 1H, Thiazole), 6.53–7.62 (m, 13H, Ar-H), 8.85 (s, 1H, —CH=N); Anal. Calcd. for $C_{36}H_{35}N_3O_{12}S$ (765.81): C, 56.46; H, 4.61; N, 5.49; S, 8.37; Found: C, 56.47; H, 4.60; N, 5.50; S, 8.37.

2-(Sulfamoylphenyl)-4′-(imino-4-methoxybenzal)-4-(2,3,4,6-tetra-O-acetyl-4″-O-β-D-glucosidoxyphenyl)-thiazole (5b) Yield 66%; $[\alpha]_D^{30} = -11.56$ (c, 0.1, DMSO); brown syrup; FTIR: 1312 (SO_2 str. asymmetric), 1118.0 (SO_2 str. Symmetric), 1178.5 (C—O—C), 1622.4 (C=N), 742 (C—S—C), 630.5 (C—S, bend); ^{1}H-NMR: 2.01, 2.02, 1.99, 2.04 (s, 3H) ($COCH_3$), 3.6 (s, 3H, OCH_3), 3.9 (s, 1H, NH), 6.2 (d, 1H, anomeric proton), 6.8 (s, 1H, Thiazole), 6.9–7.8 (m, 12H, Ar-H), 8.2 (s, 1H, —CH=N); Anal. Calcd. for $C_{37}H_{37}N_3O_{13}S_2$ (795.83): C, 55.84; H, 4.69; N, 5.28; S, 8.06; Found: C, 55.85; H, 4.69; N, 5.30; S, 8.07.

2-(Sulfamoylphenyl)-4′-(imino-4-fluorobenzal)-4-(2,3,4,6-tetra-O-acetyl-4″-O-β-D-glucosidoxyphenyl)-thiazole (5c) Yield 74%; $[\alpha]_D^{30} = -35.25$ (c, 0.1, DMSO); brown syrup; FTIR: 1312 (SO_2 str. asymmetric), 1118.0 (SO_2 str. Symmetric), 1177.7 (C—O—C), 1622.2 (C=N), 742 (C—S—C), 629.5 (C—S, bend); ^{1}H-NMR: 2.02, 1.99, 1.98, 2.05 (s, 3H) ($COCH_3$), 3.66 (s, 1H, NH), 6.20 (d, 1H, anomeric proton), 6.85 (s, 1H, Thiazole), 6.93–7.91 (m, 12H, Ar-H), 8.52 (s, 1H, —CH=N); Anal. Calcd. for $C_{36}H_{34}FN_3O_{12}S$ (783.8): C, 55.17; H, 4.37; F, 2.42; N, 5.36; S, 8.18; Found: C, 55.17; H, 4.36; F, 2.41; N, 5.35; S, 8.17.

2-(Sulfamoylphenyl)-4′-(imino-3-indolyl)-4-(2,3,4,6-tetra-O-acetyl-4″-O-β-D-glucosidoxyphenyl)-thiazole (5d) Yield 64%; $[\alpha]_D^{30} = -9.18$ (c, 0.1, DMSO); brown syrup; FTIR: 1318 (SO_2 str. asymmetric), 1116.0 (SO_2 str. Symmetric), 1172.4 (C—O—C), 1624.1 (C=N), 738.8 (C—S—C), 627 (C—S, bend); ^{1}H-NMR: 1.98, 1.99, 2.06, 2.07 (s, 3H) ($COCH_3$), 3.85 (s, 1H, NH), 6.06 (d, 1H, anomeric proton), 6.60 (s, 1H, Thiazole), 6.80–7.75 (m, 13H, Ar-H), 7.92 (s, 1H, —CH=N); 8.94 (s, 1H, NH); Anal. Calcd. for $C_{38}H_{34}N_4O_{12}S_2$ (804.84): C,

56.71; H, 4.51; N, 6.96; S, 7.97; Found: C, 56.70; H, 4.50; N, 6.96; S, 7.97.

2-(Sulfamoylphenyl)-4′-(imino-4-pyridyl)-4-(2,3,4,6-tetra-O-acetyl-4″-O-β-D-glucosidoxyphenyl)-thiazole (5e) Yield 60%; $[\alpha]_D^{30} = -16.46$ (c, 0.1, DMSO); brown syrup; FTIR: 1312 (SO_2 str. asymmetric), 1112.4 (SO_2 str. Symmetric), 1175.6 (C—O—C), 1625.2 (C=N), 731.2 (C—S—C), 626.8 (C—S, bend); ^{1}H-NMR: 1.99, 2.06, 1.99, 2.05 (s, 3H) ($COCH_3$), 4.04 (s, 1H, NH), 6.33 (d, 1H, anomeric proton), 6.82 (s, 1H, Thiazole), 7.10–8.25 (m, 12H, Ar-H), 8.77 (s, 1H, —CH=N); Anal. Calcd. for $C_{35}H_{34}N_4O_{12}S_2$ (766.79): C, 54.82; H, 4.47; N, 7.31; S, 8.36; Found: C, 54.80; H, 4.47; N, 7.30; S, 8.37.

2-(Sulfamoylphenyl)-4′-(imino-2-furyl)-4-(2,3,4,6-tetra-O-acetyl-4″-O-β-D-glucosidoxyphenyl)-thiazole (5f) Yield 62%; $[\alpha]_D^{30} = -18.77$ (c, 0.1, DMSO); brown syrup; FTIR: 1322 (SO_2 str. asymmetric), 1110.7 (SO_2 str. Symmetric), 1177.8 (C—O—C), 1621.3 (C=N), 728.6 (C—S—C), 625.3 (C—S, bend); ^{1}H-NMR: 2.01, 1.98, 1.99, 2.06 (s, 3H) ($COCH_3$), 3.99 (s, 1H, NH), 6.52 (d, 1H, anomeric proton), 6.70 (s, 1H, Thiazole), 7.02–8.30 (m, 11H, Ar-H), 8.52 (s, 1H, —CH=N); Anal Calcd. for $C_{34}H_{33}N_3O_{13}S_2$ (755.77): C, 54.03; H, 4.40; N, 5.56; S, 8.49; Found: C, 54.03; H, 4.41; N, 5.55; S, 8.50.

General procedure for the preparation of 2-(sulfamoylphenyl)-4′-(iminoaryl/hetroaryl)-4-(4″-*O*-β-D-glucosidoxyphenyl)-thiazoles (6a–f). To the compound 2-(sulfamoyl phenyl)-4′-(iminoaryl/hetroaryl)-4-(2, 3, 4, 6-tetra-*O*-acetyl-4″-*O*-β-D-glucosidoxyphenyl)-thiazole (**5a**) 2 g in 25 mL of dry methanol was added 1.5 mL of 5% CH_3ONa solution. The reaction mixture was kept at room temperature for additional 24 h. It was neutralized with ion-exchanged resin (Amberlite IR-120, sd fine, H^+ form), filtered and concentrated in vacuum to afford viscous, strongly hygroscopic, brown colored syrupy compounds. By similar way compounds (**6a–f**) were prepared.

2-(Sulfamoylphenyl)-4′-(iminobenzal)-4-(4″-O-β-D-glucosidoxyphenyl)-thiazole (6a) Yield 77%; $[\alpha]_D^{30} = -13.21$ (c, 0.1, DMSO); brown syrup; FTIR: 3405 (—OH, broad, stretching), 2980.0 (aromatic str.), 1635.9 (C=N), 1050.3 (C—O—C), 1411.5 (SO_2 asymmetric, str.), 924.3 (SO_2 asymmetric, str.), 628.4 (C—S, bend); ^{1}H-NMR: 3.0 (1H, 5′H), 3.1 (1H, 4′H), 3.5 (1H, 3′H), 3.2 (1H, 2′H), 5.85 (dd, 1H, $J_{1,2}$ =8.4 Hz, 1′H) anomeric proton, 7.28–8.24 (m, 13H, Ar-H), 7.70 (s, 1H, Thiazole), 8.60 (s, 1H,—CH=N); ^{13}C-NMR: δ 175.0, 163.3, 157.5,156,0, 148.4, 145.5, 138.2, 133.6, 131.3, 129.4, 128.9, 128.6, 128.5, 127.0, 126.6, 125.6, 124.9, 122.9, 122.0, 121.0, 118.0, 105.4, 100.1, 90.6, 80.5, 76.1, 75.0, 65.4. EI-MS: 627.5 (M, 10), 434 (base peak, 100), 313 (12), 237(49), 160 (09), 91 (02); Anal.Calcd. for $C_{28}H_{27}N_3O_8S$ (627.59): C, 55.49; H, 4.66; N, 6.69, S, 10.22; Found: C, 55.47; H, 4.66; N, 6.69; S, 10.23.

2-(Sulfamoylphenyl)-4′-(imino-4-methoxybenzal)-4-(4″-O-β-D-glucosidoxyphenyl)-thiazole (6b) Yield 69%; $[\alpha]_D^{30} = -10.24$ (c, 0.1, DMSO); brown syrup; FTIR: 3484.6 (—OH, broad, stretching), 3008.2 (aromatic str.), 1640.1 (C=N), 1052.3 (C—O—C), 1414.0 (SO_2 asymmetric, str.), 926.1 (SO_2 asymmetric, str.), 631.2 (C—S, bend); ^{1}H-NMR: 3.1 (1H, 5′H), 3.3 (1H, 4′H), 3.4 (1H, 3′H), 3.5 (1H, 2′H), 3.8 (s, 3H, OCH_3), 6.11 (dd, 1H, $J_{1,2} = 8.0$ Hz, 1′H) anomeric proton, 6.6 (s, 1H, Thiazole), 6.88–8.72 (m, 12H, Ar-H), 8.8 (s, 1H, —CH=N); ^{13}C-NMR: δ 173.0, 164.3, 160.5, 156.0, 153.0, 146.4, 145.3, 132.6, 131.4, 129.1, 128.4, 128.1, 127.2, 127.0, 126.7, 125.1, 124.4, 123.2, 122.4, 121.8, 119.5, 104.2, 100.5, 81.2, 76.4, 75.3, 65.1. 56.4; EI-MS: 627 (M, base peak, 100), 465 (20), 310 (06), 275 (31), 244 (14), 175 (14), 145 (21), 95 (12), 78 (16); Anal.-Calcd. for $C_{29}H_{29}N_3O_9S_2$ (627.69): C, 55.49; H, 4.66; N, 6.69, S, 10.22; Found: C, 55.47; H, 4.68; N, 6.70; S, 10.23.

2-(Sulfamoylphenyl)-4′-(imino-4-fluorobenzal)-4-(4″-O-β-D-glucosidoxyphenyl)-thiazole (6c) Yield 66%; $[\alpha]_D^{30} = -30.80$ (c, 0.1, DMSO); brown syrup; FTIR: 3406.2 (—OH, broad, stretching), 3020.1 (aromatic str.), 1642.8 (C=N), 1055.1 (C—O—C), 1415.2 (SO_2 asymmetric, str.), 924.8 (SO_2 asymmetric, str.), 630.3 (C—S, bend); ^{1}H-NMR: 3.0 (1H, 5′H), 3.1 (1H, 4′H), 3.5 (1H, 3′H), 3.3 (1H, 2′H), 5.98 (dd, 1H, $J_{1,2} = 8.1$ Hz, 1′H) anomeric proton, 6.48 (s, 1H, Thiazole), 6.52–7.96 (m, 12H, Ar-H), 8.44 (s, 1H, —CH=N); ^{13}C-NMR: δ 174.0, 163.1, 161.2, 156,3, 154.1, 146.3, 145.0, 142.3, 140.2, 133.9, 129.1, 128.4, 128.0, 127.7, 126.6, 126.3, 125.6, 124.6, 123.0, 122.9, 120.8, 118.5, 103.5, 100.1, 83.1, 76.5, 75.5, 65.7; EI-MS: 615.6 (M, base peak, 100), 455 (28), 358 (34), 185 (22), 176 (21), 165 (12), 117 (18), 104 (12), 77 (15); Anal.-Calcd. for $C_{28}H_{26}FN_3O_8S_2$ (615.65): C, 54.63; H, 4.26; F, 3.06; N, 6.83, S, 10.42; Found: C, 54.64; H, 4.26; F, 3.08; N, 6.82; S, 10.43.

2-(Sulfamoylphenyl)-4′-(imino-3-indolyl)-4-(4″-O-β-D-glucosidoxyphenyl)-thiazole (6d) Yield 56%; $[\alpha]_D^{30} = -8.12$ (c, 0.1, DMSO); brown syrup; FTIR: 3422.4 (—OH, broad, stretching), 3028.4 (aromatic str.), 1636.2 (C=N), 1058.2 (C—O—C), 1420.0 (SO_2 asymmetric, str.), 920.2 (SO_2 asymmetric, str.), 634.1 (C—S, bend); ^{1}H-NMR: 3.2 (1H, 5′H), 3.0 (1H, 4′H), 3.0 (1H, 3′H), 3.4 (1H, 2′H), 3.88 (1H, —NH, D_2O exchangeable), 6.02 (dd, 1H, $J_{1,2} = 8.9$ Hz, 1′H) anomeric proton, 6.76 (s, 1H, Thiazole), 6.83–7.97 (m, 13H, Ar-H), 8.85 (s, 1H, —CH=N), 9.95 (s, NH, indole); ^{13}C-NMR: δ 173.4, 161.0, 157.6, 153.2, 148.2, 143.0, 139.2, 138.4, 135.5, 130.4, 128.8, 128.6, 128.1, 127.5, 126.0, 125.2, 124.2, 123.5, 122.7, 122.4, 122.0, 120.6, 118.8, 104.2, 102.8, 100.7, 82.1, 77.4, 75.2, 65.2; EI-MS: 636.0 (M, base peak, 100), 475 (16), 357 (25), 190 (40), 170 (20), 163 (18), 117 (13), 75 (10); Anal.-Calcd. for $C_{30}H_{28}N_4O_8S_2$ (636.7): C, 56.59; H, 4.43; N, 8.80, S, 10.07; Found: C, 56.62; H, 4.42; N, 8.82; S, 10.06.

2-(Sulfamoylphenyl)-4′-(imino-4-pyridyl)-4-(4″-O-β-D-glucosidoxyphenyl)-thiazole (6e) Yield 65%; $[\alpha]_D^{30} = -11.24$ (c, 0.1, DMSO); brown syrup; FTIR: 3402.6 (—OH, broad, stretching), 3015.5 (aromatic str.), 1633.1 (C=N), 1055.0 (C—O—C), 1418.0 (SO_2 asymmetric, str.), 922.8 (SO_2 asymmetric, str.), 636.0 (C—S, bend); ^{1}H-NMR: 3.0 (1H, 5′H), 3.1 (1H, 4′H), 3.2 (1H, 3′H), 3.4 (1H, 2′H), 3.92 (1H,—NH, D_2O exchangeable), 5.92 (dd, 1H, $J_{1,2} = 8.0$ Hz, 1′H) anomeric proton, 6.60 (s, 1H, Thiazole), 6.72–7.82 (m, 12H, Ar-H), 7.95 (s, 1H,—CH=N); ^{13}C-NMR: δ 174.5, 162.2, 157.3, 154.6, 148.0, 144.2, 138.3, 130.4, 128.2, 128.1, 127.6, 126.4, 125.3, 124.1, 121.3, 115.2, 114.5, 110.6, 103.1, 101.4, 100.8, 81.5, 77.7, 76.8, 75.5, 71.6, 65.0; EI-MS: 598.0 (M, 12), 435 (base peak, 100 %), 330 (16), 240 (34), 162 (16), 136 (23), 77 (18); Anal.Calcd. for $C_{27}H_{26}N_4O_8S_2$ (598.65): C, 54.17; H, 4.38; N, 9.36, S, 10.71; Found: C, 54.16; H, 4.40; N, 9.38; S, 10.72.

2-(Sulfamoylphenyl)-4′-(imino-2-furyl)-4-(4″-O-β-D-glucosidoxyphenyl)-thiazole (6f) Yield 58%; $[\alpha]_D^{30} = -17.14$ (c, 0.1, DMSO); brown syrup; FTIR: 3388.8 (—OH, broad, stretching), 3081.0 (aromatic str.), 1631.0 (C=N), 1055.3 (C—O—C), 1412.6 (SO_2 asymmetric, str.), 932.5 (SO_2 asymmetric, str.), 631.2 (C—S, bend); ^{1}H-NMR: 3.0 (1H, 5′H), 3.4 (1H, 4′H), 3.2 (1H, 3′H), 3.4 (1H, 2′H), 6.05 (dd, 1H, $J_{1,2}$ =8.9 Hz, 1′H)

anomeric proton, 6.65 (s, 1H, Thiazole), 7.10–8.34 (m, 11H, Ar-H), 8.42 (s, 1H,-CH=N). ^{13}C-NMR: δ 173.2, 158.2, 153,2, 149.3, 148.3, 146.2, 143.2, 140.4, 138.9, 131.4, 129.6, 128.3, 127.1, 126.2, 125.7, 124.6, 122.6, 122.2, 115.2, 114.2, 103.3, 100.5, 98.4, 83.5, 78.3, 75.4, 66.2. EI-MS: 587.2 (M, base peak 100), 425 (28), 345 (30), 254 (24), 176 (11), 163 (21), 92 (08), 77 (14); Anal.Calcd. for $C_{26}H_{25}N_3O_9S_2$ (587.62): C, 53.14; H, 4.29; N, 7.15, S, 10.91; Found: C, 53.16; H, 4.26; N, 7.14; S, 10.93.

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