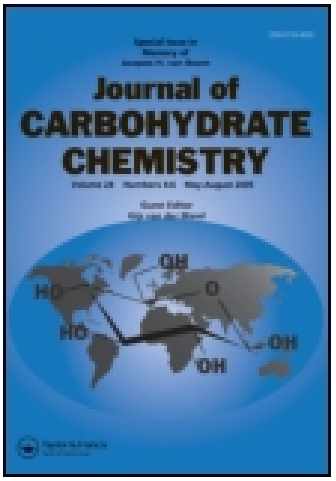


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

Synthesis of 2-(Substituted Benzylideneamino)-4-(4′-hydroxyphenyl) Thiazoles and Their O-Glucosides

V. S. Taile [a] , V. N. Ingle [a] & K. M. Hatzade [a b]
[a] Department of Chemistry , Rashtrasant Tukadoji Maharaj Nagpur University , Nagpur, 440 033, India
[b] Department of Chemistry , Dhote Bandhu Science College , Gondia, 441 614
Published online: 08 Sep 2010.

To cite this article: V. S. Taile , V. N. Ingle & K. M. Hatzade (2010) Synthesis of 2-(Substituted Benzylideneamino)-4-(4′-hydroxyphenyl) Thiazoles and Their O-Glucosides, Journal of Carbohydrate Chemistry, 29:5, 207-221, DOI: 10.1080/07328303.2010.497589

To link to this article: http://dx.doi.org/10.1080/07328303.2010.497589

Journal of Carbohydrate Chemistry, 29:207–221, 2010

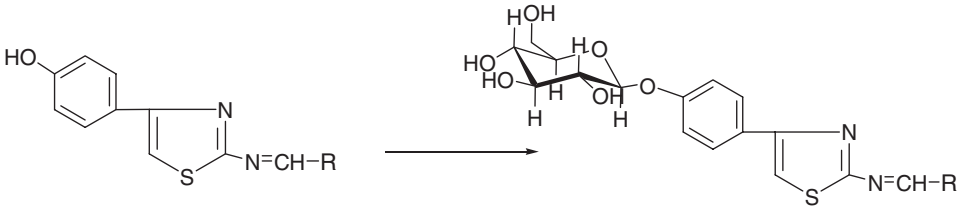
ISSN: 0732-8303 print / 1532-2327 online
DOI: 10.1080/07328303.2010.497589

Synthesis of 2-(Substituted Benzylideneamino)-4-(4′-hydroxyphenyl) Thiazoles and Their *O*-Glucosides

V. S. Taile,[1] V. N. Ingle,[1] and K. M. Hatzade[1,2]

[1]Department of Chemistry, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur-440 033, India
[2]Department of Chemistry, Dhote Bandhu Science College, Gondia-441 614

2-Amino-4-(4′-hydroxyphenyl) thiazole **1a** was prepared from reaction between *p*-hydroxyacetophenone, thiourea, and iodine; compound **1a** was treated with several (aryl/hetro aryl) aldehydes to form 2-(substituted benzylideneamino)-4-(4′-hydroxyphenyl) thiazoles **2a–j**, which were glucosylated by using acetobromoglucose as a glucosyl donor to afford 2-(substituted benzylideneamino)-4-(2, 3, 4, 6-tetera-*o*-acetyl-4′-*o*-*β*-D-glucosidoxyphenyl) thiazoles **3a–j,** which further on during deacetylation produced 2-(substituted benzylideneamino)-4-(4′-*o*-*β*-D-glucosidoxyphenyl) thiazoles **4a–j**. These compounds were evaluated for biological activity, and their structure was confirmed by IR, NMR, mass spectra, elemental, and chemical analysis.



Keywords Thiazole; Azomethine; Acetobromoglucose; *o*-Glucoside; Deacetylation

INTRODUCTION

Thiazole derivatives are of considerable interest from a therapeutic point of view because of their wide spectrum of activity that includes antibacterial,

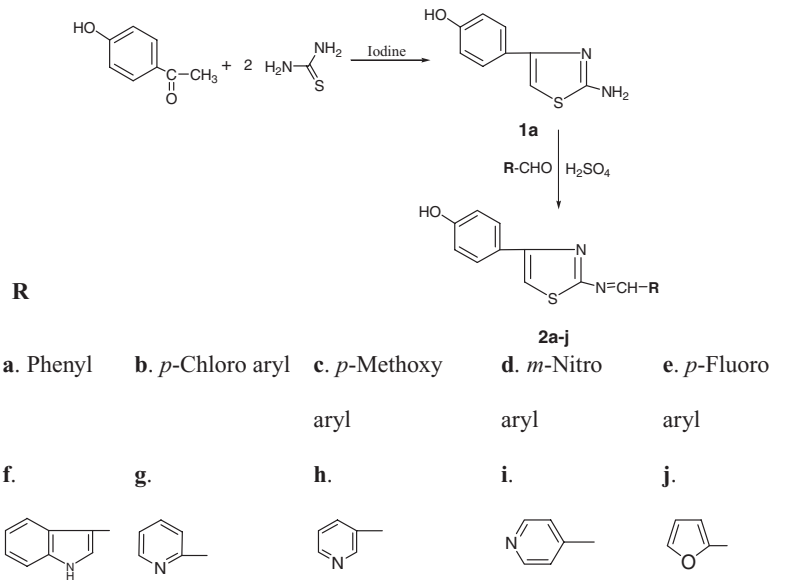
Received March 5, 2010; accepted May 17, 2010.
Address correspondence to V.S. Taile, Department of Chemistry, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur-440 033, India. E-mail: vijaytaile@gmail.com

antifungal, antitumor, anthelmintic, local anesthetic, diuretic, and anti-inflammatory activities.[1–7] The thiazole nucleus forms an important part of the structure of many therapeutic agents of diverse activities. 2-Amino-thiazole possesses potent antiplatelet activity,[8] which is a good antidote for barbiturate poisoning.[9] *o*-Glucosides are widely distributed throughout the plant kingdom, especially in roots, leaves, seeds, and barks of plants, and have good medicinal activity.[10–17] In *O*-glucosides, the carbohydrate residue is termed the glycone, and the compound ROH, from which the carbohydrate residue has been cleaved, is termed the aglycon. One of the most important roles of *o*-glucoside is to increase the water solubility of organic compounds and decrease toxicity of the aglycon portion. For the glucosylation of compounds the mostly preferred method is the Koenigs-Knorr method.[18] We synthesized the *o*-glucosylation by using the modified Michael method.[19] The presence of imino group >C=N is mainly responsible for the potent biological activity of compounds. These azomethines constitute one of the most active classes of compounds possessing diversified biological applications.[20–24] So, in continuation of our research work[25–30] and keeping in mind the various biological activities of thiazole, azomethine, and glucose moiety, we synthesized worthwhile 2-(substituted benzylideneamino)-4-(4′-hydroxyphenyl) thiazoles and their *o*-glucosides; similarly, we studied their biological properties to investigate whether they are associated with therapeutic properties.

RESULTS AND DISCUSSION

The sequence of the reaction, starting from the preparation of the aglycon moiety, which was prepared from condensation between *p*-hydroxyacetophenone, thiourea, and iodine, gives 2-amino-4-(4′-hydroxyphenyl) thiazole **1a**; infrared spectrum of the compound shows the following characteristic bands at 3487.8 (−OH) due to the presence of a free phenolic hydroxyl group, 3379.5 ($-NH_2$), 3127.7 (aromatic compound stretching), and 1600 (C=C), and ^{1}H NMR 6.4 (s, 1H, Thiazole), 6.8–7.8 (m, 4H, Ar−H), 4.8 (bs, 2H, NH_2), and 5.6 (s, 1H, OH). Schiff base was prepared by condensation between **1a** and various substituted aldehydes to form 2-(substituted benzylideneamino)-4-(4′-hydroxyphenyl) thiazoles **2a–j** (Scheme 1).

Acetobromoglucose (ACBG) acts as a glucosyl donor; it was prepared by reaction of glucose pentacetate with brominating agent and extracting the compound in chloroform.[31] 2-(Substituted benzylideneamino)-4-(4′-hydroxyphenyl) thiazoles **2a–j** were glucosylated by using acetobromoglucose to afford 2-(substituted benzylideneamino)-4-(2, 3, 4, 6-tetra-*o*-acetyl-4′-*o*-*β*-D-glucosidoxyphenyl) thiazoles **3a–j**. The compound was obtained in good yield; the deacetylation of 2-(substituted benzylideneamino)-4-(2, 3, 4, 6-tetra-*o*-acetyl-4′-*o*-*β*-D-glucosidoxyphenyl) thiazoles **3a–j** formed 2-(substituted benzylideneamino)-4-(4′-*o*-*β*-D-glucosidoxyphenyl) thiazoles **4a–j**; *o*-Glucoside

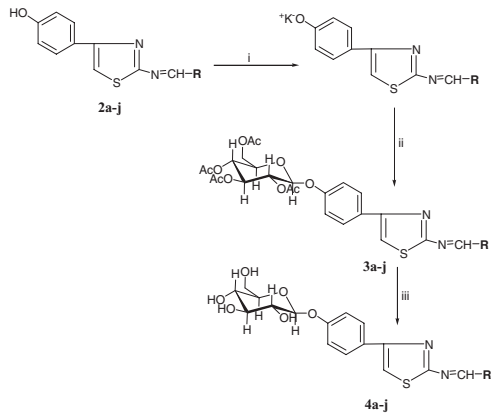


Scheme 1: Synthesis of 2-(substituted benzylideneamino)-4-(4′-hydroxyphenyl) thiazoles.

formation follows an S_N2 mechanism; and the stereochemistry observed is 1,2-trans type in most of the cases reported, as a consequence of neighboring group participation. When the protecting group is acetate at C-2, there is an intramolecular nucleophilic displacement of the leaving group, generating an orthoester,[32] only β-anomer is the preferred product. ^{1}H NMR of the compound displayed the signal due to sugar protons between δ 3.2 and 4.50 ppm and aromatic ring proton between δ 6.8 and 7.75 ppm. The β-glucosidic bond formation was established by the appearance of doublet at δ 5.00–6.00 ppm and coupling constant between 8.0 and 9.0 Hz. Electronic mass spectra also confirmed the molecular weight of the compounds and ^{13}C NMR spectrum; C-1 resonated downfield of the other glucosyl carbon at δ 101–106.0, consistent with the formation of *o*-β-glucosides (Scheme 2).

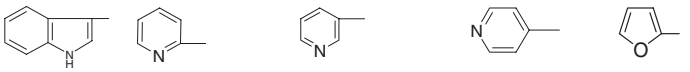
BIOLOGICAL ASSAY

The selected compounds from aglycons and *o*-glucosides were screened for their antibacterial activities against various pathogenic bacteria—*Escherichia coli, Klebsiella aerogens, Staphylococcus aureus,* and *Bacillus subtilis*—by the cup plate diffusion of 100 μg/mL by using standard ciprofloxacin and sulphacetamide (100 μg/mL) for bacteria. Similarly, compounds were screened for antifungal activity tested at 100 μg/mL concentration in methanol against *Aspergillus niger* and *Candida albicans,* which were compared with the standard drugs gentamicin and clotrimazole. The zone of inhibition was after 7 days at



R

a. Phenyl	**b**. *p*-Chloro aryl	**c**. *p*-Methoxy aryl	**d**. *m*-Nitro aryl	**e**. *p*-Fluoro aryl
f.	**g**.	**h**.	**i**.	**j**.



Scheme 2: Synthetic of 2-(substituted benzylideneamino)-4-(4′-*o*-*β*-D-glucosidoxyphenyl) thiazoles: (i) CH_3OH, KOH; (ii) acetone, *α*-acetobromoglucose; (iii) CH_3ONa,CH_3OH.

37°C for antifungal and 24 h of incubation at 37°C for antimicrobial activity. Most of the compounds exhibited mild to moderate antibacterial activity as well as antifungal activity against all the microbes tested. Out of all the tested compounds, the following compounds were found most active against the noted bacteria and fungi: **2a** (*A. niger*), **2e** (*K. aerogens, C. albicans*), **4a** (*C. albicans, A. niger*), **4e** (*K. aerogens, B. subtilis, C. albicans*), **4g** (*C. albicans, A. niger*). A biological activity result revealed that *O*-glucosides showed more pharmaceutical activity than the aglycon (Table 1).

EXPERIMENTAL

The melting points (mp) are taken by using the open capillary method and are uncorrected. The FT-IR spectra were recorded on a Perkin Elmer spectrophotometer using KBr disc. The ^{1}H NMR spectra were recorded on a Bruker DRX-300 (300 MHz FT-NMR) instrument using DMSO-d6 as a solvent and TMS as internal standard, and the chemical shifts are expressed in δ ppm values. EI-MS spectra were recorded by direct insertion technique with a Hitachi Perkin

Table 1: Zone of inhibition[a] (mm) (activity index)[std]

Compd No[b]	Antibacterial Activity				Antifungal Activity	
	Gram positive		Gram negative			
	S. aureus	*B. subtilis*	*E. coli*	*K. aerogens*	*C. albicans*	*A. niger*
2a	12(0.35)* (0.38)#	10(0.34)* (0.38)#	9(0.35)* (0.31)#	15(0.68)* (0.71)#.	18(0.85)* (0.78)#	25(1.00)* (1.04)#
2b	16(0.47)* (0.51)#	12(0.41)* (0.46)#	16(0.45)* (0.55)#	13(0.59)* (0.61)#	14(0.66)* (0.60)#	19(0.76)* (0.79)#
2e	21(0.61)* (0.67)#	21(0.72)* (0.80)#	17(0.48)* (0.58)#	21(0.95)* (1.00)#	20(0.95)* (0.86)#	14(0.56)* (0.58)#
2f	20(0.58)* (0.64)#	25(0.86)* (0.96)#	18(0.51)* (0.62)#	21(0.95)* (1.00)#	12(0.57)* (0.52)#	11(0.44)* (0.45)#
2g	18(0.52)* (0.58)#	19(0.65)* (0.73)#	14(0.40)* (0.48)#	15(0.68)* (0.71)#	18(0.85)* (0.78)#	20(0.80)* (0.83)#
2j	14(0.41)* (0.45)#	10(0.34)* (0.38)#	12(0.34)* (0.41)#	15(0.68)* (0.71)#	12(0.57)* (0.52#	14(0.56)* (0.58)#
4a	15(0.44)* (0.48)#	12(0.41)* (0.46)#	14(0.40)* (0.48)#	16(0.72)* (0.76)#.	21(1.00)* (0.91)#	28(1.12)* (1.16)#
4b	17(0.50)* (0.54)#	15(0.51)* (0.57)#	18(0.51)* (0.62)#	14(0.63)* (0.66)#	18(0.85)* (0.78)#	20(0.80)* (0.83)#
4e	20(0.58)* (0.64)#	25(0.86)* (0.96)#	19(0.54)* (0.65)#	25(1.13)* (1.19)#	23(1.09)* (1.00)#	17(0.68)* (0.70)#
4f	22(0.64)* (0.70)#	29(1.00)* (1.15)#	20(0.57)* (0.68)#	23(1.04)* (1.09)#	16(0.76)* (0.69)#	15(0.60)* (0.62)#
4g	21(0.61)* (0.67)#	20(0.68)* (0.76)#	18(0.51)* (0.62)#	17(0.77)* (0.80)#	20(0.95)* (0.86)#	21(0.84)* (0.87)#
4j	16(0.47)* (0.51)#	13(0.44)* (0.50)#	14(0.40)* (0.48)#	17(0.77)* (0.80)#	14(0.66)* (0.60)#	16(0.64)* (0.66)#
Std.1	34	29	35	22	21	25
Std. 2	31	26	29	21	23	24

[a]Average zone of inhibition in mm.
[b]Concentration of test compounds and standard 100 μg/mL.
Activity index = Inhibition zone of the sample / Inhibition zone of the standard.
*Activity index against std. 1.
#Activity index against std. 2.
For antibacterial activity: Std. 1 = ciprofloxacin and Std. 2 = sulphacetamide; for antifungal activity: Std. 1 = gentamicin and Std. 2 = clotrimazole.

Elmer RMU 6D mass spectrophotometer. Elemental analysis was determined by the FLASH EA 1112 CHN analyzer, Thermo Finigin, Italy.

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 in a water bath for 18 h with occasional stirring and then cooled. The residue was titrated with ether to remove excess of unreacted *p*-hydroxyacetophenone. It was then washed with sodium thiosulfate

to removed iodine impurity. The crude product was dissolved in boiling water and filtered hot. The titled compound was formed after neutralized with aqueous ammonia; the white-colored compound was formed and crystallized from ethanol to get pale yellow needles. Yield 57%; mp 201°C; The infrared 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: δ 6.4 (s, 1H, thiazole), 6.8–7.8 (m, 4H, Ar−H), 4.8 (bs, 2H, NH_2), 5.6 (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-*(Substituted benzylideneamino)-4-(4′-hydroxyphenyl) thiazoles (2a–j)*

A suspension of 2-amino-4-(4′-hydroxyphenyl) thiazole (0.02 mol) and aromatic and heterocyclic aldehyde (0.02 mol) in alcohol was taken in a 250-mL round-bottom flask. To this mixture a few drops of conc. H_2SO_4 were added. The mixture was refluxed for about half an hour. It was cooled and poured in ice-cold water, filtered, and dried. It was crystallized from ethanol.

2-(Benzylideneamino)-4-(4′-hydroxyphenyl) thiazole (2a)

Yield 54%; mp 168°C (ethanol); FT-IR: 3519 (−OH), 3038.0 (aromatic ring, str.), 1610 (C=N) linkage, 1330 (SO_2, asymmetric stretching), 1170.4 (SO_2, symmetric stretching, 1069.3 (C−N,). ^{1}H NMR: δ 6.6–7.6 (m, 9H, Ar−H), 5.3 (s, 1H, OH), 7.8 (s, 1H, thiazole), 8.1 (s, 1H, −CH=N). Anal. Calcd for $C_{16}H_{12}N_2OS$ (280.34): C, 68.55; H, 4.31; N, 9.99; S, 11.44. Found: C, 68.58; H, 4.31; N, 10.02; S, 11.43.

2-(4-Chlorobenzylideneamino)-4-(4′-hydroxyphenyl) thiazole (2b)

Yield 77%; mp 155°C (ethanol); FT-IR: 3438 (−OH), 3088.0 (aromatic ring, str.), 1615 (C=N) linkage, 1334 (SO_2, asymmetric stretching), 1166.2 (SO_2, symmetric stretching, 1070.2 (C−N). ^{1}H NMR: δ 6.2–7.4 (m, 8H, Ar−H), 5.2 (s, 1H, OH), 7.5 (s, 1H, thiazole), 8.5 (s, 1H, −CH=N). Anal. Calcd for $C_{16}H_{11}ClN_2OS$ (314.79): C, 61.05; H, 3.52; Cl, 11.26; N, 8.90; S, 10.19. Found: C, 61.08; H, 3.51; Cl, 11.29; N, 8.92; S, 10.19.

2-(4-Methoxybenzylideneamino)-4-(4′-hydroxyphenyl) thiazole (2c)

Yield 69%; mp 160°C (ethanol); FT-IR: 3518 (−OH), 3175.0 (aromatic ring, str.), 1626 (C=N) linkage, 1330 (SO_2, asymmetric stretching), 1170.3 (SO_2, symmetric stretching), 1073.0 (C−N). ^{1}H NMR: δ 3.76 (s, 3H, OCH_3), 5.4 (s, 1H, OH), 6.4–7.3 (m, 8H, Ar−H), 7.6 (s, 1H, thiazole), 8.2 (s,1H, −CH=N). Anal. Calcd for $C_{17}H_{14}N_2O_2S$ (310.37): C, 65.79; H, 4.55; N, 9.03; S, 10.33. Found: C, 65.77; H, 4.55; N, 9.01; S, 10.29.

2-(3-Nitrobenzylideneamino)-4-(4′-hydroxyphenyl) thiazole (2d)

Yield 65%; mp 120°C (ethanol); FT-IR: 3385 (−OH), 2995.5 (aromatic ring, str.), 1610 (C=N) linkage, 1335 (SO_2, asymmetric stretching), 1164.0 (SO_2, symmetric stretching, 1066.5 (C−N). ^{1}H NMR: δ 6.4–7.3 (m, 8H, Ar−H), 5.3 (s, 1H, OH), 7.9 (s, 1H, thiazole), 8.8 (s, 1H, −CH=N). Anal. Calcd for $C_{16}H_{11}ClN_2OS$ (325.34): C, 59.07; H, 3.41; N, 12.92; S, 9.86. Found: C, 59.06; H, 3.45; N, 12.90; S, 9.89.

2-(4-Fluorobenzylideneamino)-4-(4′-hydroxyphenyl) thiazole (2e)

Yield 62%; mp 161°C (ethanol); FT-IR: 3415 (−OH), 3015.5 (aromatic ring, str.), 1624 (C=N) linkage, 1352 (SO_2, asymmetric stretching), 1158.0 (SO_2, symmetric stretching, 1082.0 (C−N). ^{1}H NMR: δ 6.2–7.5 (m, 8H, Ar−H), 5.7 (s, 1H, OH), 8.2 (s, 1H, thiazole), 8.9 (s, 1H, −CH=N). Anal. Calcd for $C_{16}H_{11}FN_2OS$ (298.33): C, 64.41; H, 3.72; F, 6.37; N, 9.39; S, 10.75. Found: C, 64.42; H, 3.75; F, 6.35; N, 9.41; S, 10.78.

2-(3-Indolylmethylenamino)-4-(4′-hydroxyphenyl) thiazole (2f)

Yield 75%; mp 190°C (ethanol); FT-IR: 3440 (−OH), 3008.2 (aromatic ring, str.), 1638 (C=N) linkage, 1348 (SO_2, asymmetric stretching), 1155.2 (SO_2, symmetric stretching), 1089.2 (C−N). ^{1}H NMR: δ 6.8–7.9 (m, 8H, Ar−H), 5.2 (s, 1H, OH), 8.1 (s, 1H, thiazole), 8.5 (s, 1H, −CH=N); 9.7 (s, 1H, −NH). Anal. Calcd for $C_{18}H_{13}N_3OS$ (319.38): C, 67.69; H, 4.10; N, 13.16; S, 10.04. Found: C, 67.69; H, 4.12; N, 13.17; S, 10.07.

2-(2-Pyridinylmethyleneamino)-4-(4′-hydroxyphenyl) thiazole (2g)

Yield 73%; mp 180°C (ethanol); FT-IR: 3385 (−OH), 3080.2 (aromatic ring, str.), 1634 (C=N) linkage, 1326 (SO_2, asymmetric stretching), 1172.0 (SO_2, symmetric stretching), 1080.5 (C−N). ^{1}H NMR: δ 5.2 (s, 1H, OH), δ 7.0–7.9 (m, 8H, Ar−H), 8.2 (s, 1H, thiazole), 8.5 (s, 1H, −CH=N). Anal. Calcd for $C_{15}H_{11}N_3OS$ (281.33): C, 64.04; H, 3.94; N, 14.94; S, 11.40. Found: C, 64.07; H, 3.96; N, 14.94; S, 11.39.

2-(3-Pyridinylmethyleneamino)-4-(4′-hydroxyphenyl) thiazole (2h)

Yield 68%; mp 174°C (ethanol); FT-IR: 3408 (−OH), 3118.4 (aromatic ring, str.), 1645 (C=N) linkage, 1328 (SO_2, asymmetric stretching), 1166.0 (SO_2, symmetric stretching), 1076.1 (C−N). ^{1}H NMR: δ 5.4 (s, 1H, OH), δ 6.4–7.6 (m, 8H, Ar−H), 7.9 (s, 1H, thiazole), 8.4 (s, 1H, −CH=N). Anal. Calcd for $C_{15}H_{11}N_3OS$ (281.33): C, 64.04; H, 3.94; N, 14.94; S, 11.40. Found: C, 64.10; H, 3.92; N, 14.93; S, 11.41.

2-(4-Pyridinylmethyleneamino)-4-(4′-hydroxyphenyl) thiazole (2i)

Yield 78%; mp 192°C (ethanol); FT-IR: 3467.8 (−OH), 3088.5 (aromatic ring, str.), 1650 (C=N) linkage, 1325 (SO_2, asymmetric stretching), 1158.0 (SO_2, symmetric stretching), 1079.7 (C−N). ^{1}H NMR: δ 5.6 (s, 1H, OH), δ 6.3–7.7 (m, 8H, Ar−H), 7.6 (s, 1H, thiazole), 8.0 (s, 1H, −CH=N). Anal. Calcd for $C_{15}H_{11}N_3OS$ (281.33): C, 64.04; H, 3.94; N, 14.94; S, 11.40. Found: C, 64.00; H, 3.96; N, 13.98; S, 11.42.

2-(2-Furylmethyleneamino)-4-(4′-hydroxyphenyl) thiazole (2j)

Yield 62%; mp 185°C (ethanol); FT-IR: 3515.4 (−OH), 3108.5 (aromatic ring, str.), 1646 (C=N) linkage, 1338 (SO_2, asymmetric stretching), 1152.2 (SO_2, symmetric stretching), 1089.0 (C−N). ^{1}H NMR: δ 5.1 (s, 1H, OH), δ 6.2–7.3 (m, 3H, furan), 7.3–8.5 (m, 4H, Ar−H), 8.8 (s, 1H, thiazole), 9.2 (s, 1H, −CH=N). Anal. Calcd for $C_{14}H_{10}N_2O_2S$ (270.31): C, 62.21; H, 3.73; N, 10.36; S, 11.86. Found: C, 62.20; H, 3.75; N, 10.35; S, 11.85.

General procedure for the preparation of *2-(substituted benzylideneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazoles (3a–j)*

A solution of 3 g potassium salt of 2-(substituted benzylideneamino)-4-(4′-hydroxyphenyl) thiazoles in 10 mL of 5% methanolic KOH was added dropwise to a solution of 5 g of acetobromoglucose in 20 mL of 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 reduced pressure. The reaction was monitored by TLC. A brown syrupy mass of **3a–j** was obtained.

2-(Benzylideneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3a)

Yield 63%; $[\alpha]_D^{30}$ = –11.10 (c, 0.1, DMSO); brown syrup; FT-IR: 1556.4 (C=N), 1077.4 (C−O−C), 625.4 (C−S, bend); ^{1}H NMR: 2.01, 2.05, 1.99, 2.00 (s, 3H) ($COCH_3$), 5.4 (d, 1H, anomeric proton), 6.5–7.9 (m, 9H, Ar−H), 7.5 (s, 1H, thiazole), 7.9 (s, 1H, −CH=N). Anal. Calcd for $C_{30}H_{30}N_2O_{10}S$ (610.63): C, 59.01; H, 4.95; N, 4.59; S, 5.25. Found: C, 59.02; H, 4.96; N, 4.60; S, 5.25.

2-(4-Chlorobenzylideneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3b)

Yield 69%; $[\alpha]_D^{30}$ = –14.12 (c, 0.1, DMSO); brown syrup; FT-IR: 1563.2 (C=N), 1082.0 (C−O−C), 628.2 (C−S, bend); ^{1}H NMR: 2.00, 2.02, 1.99, 1.98 (s, 3H) ($COCH_3$), 5.8 (d, 1H, anomeric proton), 6.2–7.8 (m, 8H, Ar−H), 7.6 (s, 1H, thiazole), 7.8 (s, 1H, −CH=N). Anal. Calcd for $C_{30}H_{29}ClN_2O_{10}S$ (645.08):

C, 55.86; H, 4.53; Cl, 5.50; N, 4.34; S, 4.97. Found: C, 55.90; H, 4.54; Cl, 5.52; N, 4.36; S, 4.99.

2-(4-Methoxybenzylideneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3c)

Yield 65%; $[\alpha]_D^{30}$ = +15.23 (c, 0.1, DMSO); brown syrup; FT-IR: 1551.0 (C=N), 1081.2 (C−O−C), 630.1 (C−S, bend); ^{1}H NMR: 2.02, 2.01, 2.00, 1.97 (s, 3H) ($COCH_3$), δ 3.92 (s, 3H, OCH_3), 5.9 (d, 1H, anomeric proton), 6.2–7.6 (m, 8H, Ar−H), 7.8 (s, 1H, thiazole), 8.4 (s, 1H, −CH=N). Anal. Calcd for $C_{31}H_{32}N_2O_{11}S$ (640.66): C, 58.12; H, 5.03; N, 4.37; S, 5.01. Found: C, 58.12; H, 5.04; N, 4.38; S, 5.05.

2-(3-Nitrobenzylideneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3d)

Yield 64%; $[\alpha]_D^{30}$ = –15.25 (c, 0.1, DMSO); brown syrup; FT-IR: 1562.2 (C=N), 1080.5 (C−O−C), 624.8 (C−S, bend); ^{1}H NMR: 2.01, 2.00, 2.01, 1.99 (s, 3H) ($COCH_3$), 5.7 (d, 1H, anomeric proton), 6.1–7.4 (m, 8H, Ar−H), 7.5 (s, 1H, thiazole), 8.2 (s, 1H, −CH=N). Anal. Calcd for $C_{30}H_{29}N_2O_{12}S$ (655.63): C, 54.96; H, 4.46; N, 6.41; S, 4.89. Found: C, 54.95; H, 4.44; N, 6.39; S, 4.91.

2-(4-Fluorobenzylideneamino)-4–4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3e)

Yield 59%; $[\alpha]_D^{30}$ = –10.12 (c, 0.1, DMSO); brown syrup; FT-IR: 1546.1 (C=N), 1084.0 (C−O−C), 629.2 (C−S, bend); ^{1}H NMR: 2.00, 2.01, 2.03, 1.96 (s, 3H) ($COCH_3$), 5.9 (d, 1H, anomeric proton), 6.3–7.4 (m, 8H, Ar−H), 7.7 (s, 1H, thiazole), 8.4 (s, 1H, −CH=N). Anal. Calcd for $C_{30}H_{29}FN_2O_{10}S$ (628.62): C, 57.32; H, 4.65; F, 3.02; N, 4.46; S, 5.10. Found: C, 57.35; H, 4.66; F, 3.00; N, 4.50; S, 5.10.

2-(3-Indolylmethylenamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3f)

Yield 68%; $[\alpha]_D^{30}$ = +19.18 (c, 0.1, DMSO); brown syrup; FT-IR: 1645.0 (C=N), 1075.5 (C−O−C), 625.5 (C−S, bend); ^{1}H NMR: 1.99, 2.00, 2.01, 2.00 (s, 3H) ($COCH_3$), 6.1 (d, 1H, anomeric proton), 6.4–7.7 (m, 8H, Ar−H), 7.9 (s, 1H, thiazole), 8.5 (s, 1H, −CH=N), 10.3 (s, 1H, −NH). Anal. Calcd for $C_{31}H_{32}N_3O_{10}S$ (649.67): C, 59.16; H, 4.81; N, 6.47; S, 4.94. Found: C, 59.15; H, 4.80; N, 6.48; S, 4.92.

2-(2-Pyridinylmethyleneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3g)

Yield 73%; $[\alpha]_D^{30}$ = –17.45 (c, 0.1, DMSO); brown syrup; FT-IR: 1668.4 (C=N), 1086.2 (C−O−C), 630.2 (C−S, bend); ^{1}H NMR: 2.00, 2.01, 1.99, 2.00 (s, 3H) ($COCH_3$), 5.8 (d, 1H, anomeric proton), 6.1–7.5 (m, 8H, Ar−H), 7.9 (s,

1H, thiazole), 8.4 (s, 1H, −CH=N). Anal. Calcd for $C_{29}H_{29}N_3O_{10}S$ (611.62): C, 56.95; H, 4.78; N, 6.87; S, 5.24. Found: C, 56.98; H, 4.80; N, 6.85; S, 5.25.

2-(3-Pyridinylmethyleneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3h)

Yield 61%; $[\alpha]_D^{30}$ = –12.34 (c, 0.1, DMSO); brown syrup; FT-IR: 1680.0 (C=N), 1090.4 (C−O−C), 635.0 (C−S, bend); ^{1}H NMR: 1.99, 2.01, 2.00, 2.02 (s, 3H) ($COCH_3$), 5.6 (d, 1H, anomeric proton), 6.0–7.6 (m, 8H, Ar−H), 8.5 (s, 1H, thiazole), 8.8 (s, 1H, −CH=N). Anal. Calcd for $C_{29}H_{29}N_3O_{10}S$ (611.62): C, 56.95; H, 4.78; N, 6.87; S, 5.24. Found: C, 56.94; H, 4.77; N, 6.88; S, 5.27.

2-(4-Pyridinylmethyleneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3i)

Yield 59%; $[\alpha]_D^{30}$ = –8.26 (c, 0.1, DMSO); brown syrup; FT-IR: 1677.2 (C=N), 1082.0 (C−O−C), 638.0 (C−S, bend); ^{1}H NMR: 2.00, 2.01, 1.99, 2.03 (s, 3H) ($COCH_3$), 6.1 (d, 1H, anomeric proton), 6.4–7.7 (m, 8H, Ar−H), 8.0 (s, 1H, thiazole), 8.4 (s, 1H, −CH=N). Anal. Calcd for $C_{29}H_{29}N_3O_{10}S$ (611.62): C, 56.95; H, 4.78; N, 6.87; S, 5.24. Found: C, 56.92; H, 4.76; N, 6.87; S, 5.26.

2-(2-Furylmethyleneamino)-4-(2, 3, 4, 6-tetera-O-acetyl-4′-O-β-D-glucosidoxyphenyl) thiazole (3j)

Yield 62%; $[\alpha]_D^{30}$ = +12.11 (c, 0.1, DMSO); brown syrup; FT-IR: 1680.2 (C=N), 1089.5 (C−O−C), 632.0 (C−S, bend); ^{1}H NMR: 1.99, 2.01, 2.04, 2.00 (s, 3H) ($COCH_3$), 6.0 (d, 1H, anomeric proton), 6.2–7.5 (m, 7H, Ar−H), 8.4 (s, 1H, thiazole), 8.8 (s, 1H, −CH=N). Anal. Calcd for $C_{28}H_{28}N_2O_{12}S$ (616.59): C, 55.96; H, 4.70; N, 4.66; S, 5.34. Found: C, 55.95; H, 4.71; N, 4.70; S, 5.35.

General procedure for the preparation of *2-(substituted benzylideneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4a–j)*

To a solution of 2-(substituted benzylideneamino)-4-(2,3,4,6-tetera-O-acetyl-4′-*O*-β-D-glucosidoxyphenyl) thiazoles (2 g) in 25 mL of dry methanol was added 1.5 mL of 5% CH_3ONa solution. The reaction mixture was kept at rt for an additional 24 h. It was neutralized with ion-exchange resin (Amberlite IR 120, s.d. fine, H^+ form), filtered, and concentrated in vacuo to afford viscous, strongly hygroscopic brown-colored syrupy.

2-(Benzylideneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4a)

Yield 71%; $[\alpha]_D^{30}$ = –7.25 (c, 0.1, DMSO); brown syrup; FT-IR: 3365.7 (−OH, broad, stretching), 2158.91 (aromatic str.), 1566 (C=N), 1075.9 (C−O−C), 625.4 (C−S, bend). ^{1}H NMR: 3.4 (1H, 5′H), 3.5 (1H, 4′H), 3.8 (1H, 3′H), 4.0 (1H, 2′H), 5.9 (dd, 1H, $J_{1,2}$ = 8.6 Hz, 1′H, anomeric proton), 6.2–7.9

(m, 9H, Ar—H), 8.5 (s, 1H, thiazole), 9.1 (s, 1H, —CH=N). ^{13}C NMR: δ 175, 165.0, 158.2, 152.4, 140.8, 139.4, 130.8, 130.2, 129.0, 128.8, 128.4, 128.0, 125.6, 120.0, 110.0, 106.2, 99.5, 82.4, 78.2, 75.8, 73.1, 72.5, 65.2. EI-MS: 442.6 (M) (28%), 285 (20%), 190 (100%) base peak, 163 (10%), 117 (14%), 90 (8%), 71 (9%). Anal. Calcd for $C_{22}H_{21}ClN_2O_6S$ (442.48): C, 59.72; H, 5.01; N, 6.33; S, 7.25. Found: C, 59.75; H, 5.02; N, 6.32; S, 7.24.

2-(4-Chlorobenzylideneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4b)

Yield 71%; $[\alpha]_D^{30}$ = –13.25 (c, 0.1, DMSO); brown syrup; FT-IR: 3418.2 (—OH, broad, stretching) 2455.6 (aromatic str.), 1560 (C=N), 1081.2 (C—O—C), 630.4 (C—S, bend). ^{1}H NMR: 3.0 (1H, 5′H), 3.2 (1H, 4′H), 3.5 (1H, 3′H), 3.8 (1H, 2′H), 6.0 (dd, 1H, $J_{1,2}$ = 8.8 Hz, 1′H, anomeric proton), 6.3–7.8 (m, 8H, Ar—H), 7.9 (s, 1H, thiazole), 9.4 (s, 1H, —CH=N). ^{13}C NMR: δ 173, 168.2, 157.2, 153,6, 141.8, 139.0, 131.2, 130.4, 130.2, 129.7, 128.0, 127.0, 126.3, 121.1, 111.4, 105.6, 99.4, 82.6, 77.2, 76.8, 75.6, 73.6, 65.0. EI-MS: 476.6 (M) (12%), 315 (100%) base peak, 203 (14%), 165 (18%), 118 (24%), 94 (14%), 77 (21%). Anal. Calcd for $C_{22}H_{22}N_2O_6S$ (476.93): C, 55.40; H, 4.44; Cl, 7.43; N, 5.87; S, 6.72. Found: C, 55.41; H, 4.43; Cl, 7.43; N, 5.90; S, 6.72.

2-(4-Methoxybenzylideneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4c)

Yield 50%; $[\alpha]_D^{30}$ = +15.10 (c, 0.1, DMSO); brown syrup; FT-IR: 3388.8 (—OH, broad, stretching), 2542.2 (aromatic str.), 1565 (C=N), 1080.5 (C—O—C), 632.5 (C—S, bend). ^{1}H NMR: 3.1 (1H, 5′H), 3.2 (1H, 4′H), 3.3 (1H, 3′H), 3.9 (1H, 2′H), 4.02 (s, 3H, OCH_3), 6.1 (dd, 1H, $J_{1,2}$ = 8.0 Hz, 1′H, anomeric proton) 6.3–7.8 (m, 8H, Ar—H), 8.0 (s, 1H, thiazole), 8.8 (s, 1H, —CH=N). ^{13}C NMR: δ 173.2, 164.2, 160.1, 157.1, 152.3, 135.2, 134.2, 133.2, 129.0, 128.2, 127.4, 127.0, 126.6, 125.0, 112.2, 105.0, 88.6, 78.2, 76.4, 75.2, 74.3, 65.5, 55.6. EI-MS: 473.0 (M) (22%), 280 (20%), 188 (100%) base peak, 165 (18%), 130 (32%), 94 (13%), 78 (16%). Anal. Calcd for $C_{23}H_{24}N_2O_7S$ (472.51): C, 58.46; H, 5.12; N, 5.93; S, 6.79. Found: C, 58.46; H, 5.14; N, 5.93; S, 6.80.

2-(3-Nitrobenzylideneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4d)

Yield 70%; $[\alpha]_D^{30}$ = −11.35 (c, 0.1, DMSO); brown syrup; FT-IR: 3456.2 (—OH, broad, stretching), 2352.0 (aromatic str.), 1560 (C=N), 1084.4 (C—O—C), 628.4 (C—S, bend). ^{1}H NMR: 3.0 (1H, 5′H), 3.2 (1H, 4′H), 3.6 (1H, 3′H), 3.8 (1H, 2′H), 5.8 (dd, 1H, $J_{1,2}$ = 8.2 Hz, 1′H, anomeric proton) 6.0–7.6 (m, 8H, Ar—H), 7.9 (s, 1H, thiazole), 8.2 (s, 1H, —CH=N). ^{13}C NMR: δ 174.0, 165.3, 162.5, 158.0, 155.4, 135.5, 134.2, 134.6, 130.3, 129.2, 128.5, 127.0, 126.0, 125.6, 122.6, 105.2, 92.6, 80.2, 76.4, 75.1, 74.2, 66.5, 65.2. EI-MS: 488.20 (M) (24%), 190 (21%), 164 (12%), 151 (100%) base peak, 135 (18%), 92 (9%), 77 (26%). Anal. Calcd for $C_{22}H_{21}N_3O_8S$ (487.48): C, 54.20; H, 4.34; N, 8.62; S, 6.58. Found: C, 54.21; H, 4.34; N, 8.63; S, 6.56.

2-(4-Fluorobenzylideneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4e).

Yield 62%; $[\alpha]_D^{30}$ = −9.10 (c, 0.1, DMSO); brown syrup; FT-IR: 3510.3 (−OH, broad, stretching), 2456.4 (aromatic str.), 1566 (C=N), 1089.6 (C−O−C), 632.0 (C−S, bend). ^{1}H NMR: 3.1 (1H, 5′H), 3.4 (1H, 4′H), 3.5 (1H, 3′H), 3.7 (1H, 2′H), 6.1 (dd, 1H, $J_{1,2}$ = 8.4 Hz, 1′H, anomeric proton) 6.3–7.9 (m, 8H, Ar−H), 8.3 (s, 1H, thiazole), 8.7 (s, 1H, −CH=N). ^{13}C NMR: δ 176.2, 164.2, 163.2, 160.0, 157.0, 136.4, 135.3, 134.0, 132.8, 130.2, 129.5, 128.0, 127.4, 126.4, 120.2, 105.8, 95.6, 81.2, 76.5, 75.0, 74.6, 65.0, 62.4. EI-MS: 461.14 (M) (26%), 298 (28%), 214 (11%), 190 (100%) base peak, 165 (12%), 150 (19%), 136 (35%), 77 (36%). Anal. Calcd for $C_{22}H_{21}FN_2O_6S$ (460.48): C, 57.38; H, 4.60; F, 4.13; N, 6.08; S, 6.96. Found: C, 57.41; H, 4.61; F, 4.13; N, 6.09; S, 6.95.

2-(3-Indolylmethylenamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4f)

Yield 59%; $[\alpha]_D^{30}$ = −18.18 (c, 0.1, DMSO); brown syrup; FT-IR: 3442.2 (−OH, broad, stretching), 2515.2 (aromatic str.), 1556 (C=N), 1092.5 (C−O−C), 630.2 (C−S, bend). ^{1}H NMR: 3.1 (1H, 5′H), 3.2 (1H, 4′H), 3.4 (1H, 3′H), 3.8 (1H, 2′H), 5.8 (dd, 1H, $J_{1,2}$ = 8.6 Hz, 1′H, anomeric proton) 6.2–7.8 (m, 8H, Ar−H), 8.1 (s, 1H, thiazole), 8.6 (s, 1H, −CH=N), 9.8 (s, 1H, −NH). ^{13}C NMR: δ 174.0, 172.0, 160.2, 157.4, 154.6, 136.3, 135.7, 134.5, 133.8, 130.1, 129.0, 128.2, 128.8, 127.5, 115.2, 114.7, 110.4, 105.2, 103.4, 95.7, 80.2, 75.1, 74.2, 65.6. EI-MS: 483.20 (M) (11%), 318 (31%), 310 (9%), 188 (100%) base peak, 163 (23%), 131 (25%), 118 (12%), 77 (21%). Anal. Calcd for $C_{24}H_{23}N_3O_6S$ (481.52): C, 59.86; H, 4.81; N, 8.73; S, 6.66. Found: C, 59.88; H, 4.80; N, 8.74; S, 6.65.

2-(2-Pyridinylmethyleneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4g)

Yield 68%; $[\alpha]_D^{30}$ = −17.02 (c, 0.1, DMSO); brown syrup; FT-IR: 3312.0 (−OH, broad, stretching), 2310.5 (aromatic str.), 1568.8 (C=N), 1085.2 (C−O−C), 629.6 (C−S, bend). ^{1}H NMR: 3.1 (1H, 5′H), 3.6 (1H, 4′H), 3.8 (1H, 3′H), 3.9 (1H, 2′H), 6.1 (dd, 1H, $J_{1,2}$ = 8.6 Hz, 1′H, anomeric proton) 6.3–7.9 (m, 8H, Ar−H), 8.4 (s, 1H, thiazole), 8.8 (s, 1H, −CH=N), ^{13}C NMR: δ 173.8, 165.4, 160.4, 157.2, 154.8, 149.8, 135.6, 134.0, 133.4, 132.2, 130.0, 129.2, 128.5, 127.3, 118.2, 115.4, 110.2, 106.1, 94.7, 82.4, 75.6, 74.6, 65.1. EI-MS: 444.12 (M) (24%), 311 (28%), 280 (100%) base peak, 201 (34%), 164 (16), 111 (15%), 78 (9%). Anal. Calcd for $C_{21}H_{21}N_3O_6S$ (443.47): C, 56.87; H, 4.77; N, 9.48; S, 7.23. Found: C, 56.89; H, 4.78; N, 9.50; S, 7.24.

2-(3-Pyridinylmethyleneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4h)

Yield 63%; $[\alpha]_D^{30}$ = −11.28 (c, 0.1, DMSO); brown syrup; FT-IR: 3410.2 (−OH, broad, stretching), 2414.2 (aromatic str.), 1570.5 (C=N), 1088.3 (C−O−C), 626.8 (C−S, bend). ^{1}H NMR: 3.1 (1H, 5′H), 3.4 (1H, 4′H), 3.5 (1H, 3′H), 3.6 (1H, 2′H), 5.7 (dd, 1H, $J_{1,2}$ = 8.5 Hz, 1′H, anomeric proton) 6.2–7.5 (m, 8H, Ar−H), 7.9 (s, 1H, thiazole), 8.2 (s, 1H, −CH=N), ^{13}C NMR: δ 173.3, 166.4, 162.1, 158.8, 157.2, 150.6, 135.7, 134.8, 133.7, 132.0, 131.4, 130.2, 129.2,

128.0, 127.2, 120.4, 110.2, 105.6, 95.6, 84.2, 75.2, 74.6, 65.5. EI-MS: 445.10 (M) (34%), 314 (26%), 282 (100%) base peak, 198 (25%), 163 (12%), 110 (10%), 77 (13%). Anal. Calcd for $C_{21}H_{21}N_3O_6S$ (443.47): C, 56.87; H, 4.77; N, 9.48; S, 7.23. Found: C, 56.88; H, 4.77; N, 9.49; S, 7.20.

2-(4-Pyridinylmethyleneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4i)

Yield 57%; $[\alpha]_D^{30} = -7.20$ (c, 0.1, DMSO); brown syrup; FT-IR: 3318.5 (−OH, broad, stretching), 2515.4 (aromatic str.), 1572.6 (C=N), 1064.4 (C−O−C), 630.2 (C−S, bend). ^{1}H NMR: 3.1 (1H, 5′H), 3.2 (1H, 4′H), 3.5 (1H, 3′H), 3.8 (1H, 2′H), 6.2 (dd, 1H, $J_{1,2} = 8.8$ Hz, 1′H, anomeric proton) 6.3–7.9 (m, 8H, Ar−H), 8.1 (s, 1H, thiazole), 8.7 (s, 1H, −CH=N), ^{13}C NMR: δ 173.7, 169.1, 164.2, 160.6, 158.0, 151.2, 145.0, 134.0, 133.2, 132.0, 131.2, 130.2, 129.2, 128.4, 125.2, 121.4, 110.5, 105.0, 96.2, 84.1, 75.0, 74.2, 65.2. EI-MS: 446.10 (M) (41%), 311 (22%), 281 (100%) base peak, 200 (25%), 165 (15%), 112 (12%), 79 (14%). Anal. Calcd for $C_{21}H_{21}N_3O_6S$ (443.47): C, 56.87; H, 4.77; N, 9.48; S, 7.23. Found: C, 56.87; H, 4.75; N, 9.44; S, 7.21.

2-(2-Furylmethyleneamino)-4-(4′-O-β-D-glucosidoxyphenyl) thiazoles (4j)

Yield 60%; $[\alpha]_D^{30} = +6.45$ (c, 0.1, DMSO); brown syrup; FT-IR: 3404.5 (−OH, broad, stretching), 2610.2 (aromatic str.), 1575.2 (C=N), 1080.2 (C−O−C), 625.5 (C−S, bend). ^{1}H NMR: 3.1 (1H, 5′H), 3.4 (1H, 4′H), 3.5 (1H, 3′H), 3.9 (1H, 2′H), 5.9 (dd, 1H, $J_{1,2} = 8.4$ Hz, 1′H, anomeric proton) 6.1–7.8 (m, 8H, Ar−H), 8.6 (s, 1H, thiazole), 8.9 (s, 1H, −CH=N). ^{13}C NMR: δ 173.0, 166.2, 153.1, 151.0, 150.0, 146.4, 145.2, 135.6, 130.2, 129.2, 128.4, 127.2, 110.5, 109.0, 105.1, 95.1, 85.2, 75.4, 73.1, 65.8. EI-MS: 435.10 (M) (8%), 325 (25%), 270 (100%) base peak, 190 (12%), 164 (18%), 92 (30%), 77 (17%). Anal. Calcd for $C_{20}H_{20}N_2O_7S$ (432.45): C, 55.55; H, 4.66; N, 6.48; S, 7.41. Found: C, 55.56; H, 4.65; N, 6.48; S, 7.42.

ACKNOWLEDGEMENT

The authors are thankful to the director of the Sophisticated Analytical Instrument Facility (SAIF), Chandigarh, IIT-Powai Mumbai, for providing necessary spectral analysis; the head of the Department of Chemistry for providing necessary laboratory facilities; and the dead of the Department of Pharmacy for the biological activities.

REFERENCES

1. Werbel, L.; Eslanger, E.; Phillips, A.; Worth, D.; Islip, P.; Neville, M. 2-(Alkyl-and arylamino)-5-nitrothiazole derivatives with antiamebic, antitrichromonal, and antimalerial properties. *J. Med. Chem.* **1969**, *12*, 521.

2. Pattan, S.R.; Dighe, N.S.; Nirmal, S.A.; Merekar, A.N.; Laware, R.B.; Shinde, H.V.; Musmade, D.S. Synthesis and biological evaluation of some substituted amino thiazole derivatives. *Asian J. Res. Chem.* **2009**, *2*, 196–201.

3. Uchikawa, O.; Fukatsu, K.; Suno, M.; Aono, T.; Doi, T. In vivo biological activity of antioxidative aminothiazole derivatives. *Chem. Pharm. Bull.* **1996**, *44*, 2070–2077.

4. Shaharyar, M.; Ansari, Z.H. Synthesis and in vivo diuretic activity of biphenyl bezothiazole-2-carboxamide derivatives. *Acta Poloniae Pharm. Drug Res.* **2009**, *66*, 387–392.

5. Geronikaki, A.; Sotiropoulou, E.; Kourounakis, P. Synthesis of Some thiazole derivatives with prospective local anesthetic activity. *Pharmazie* **1989**, *44*, 349.

6. Geronikaki, A.A.; Hadjipavlou-Litina, D.J. Synthesis of some new aroyl/aroyloxy-2-amino-1, 3-thiazole derivatives with anti-inflammatory activity. *Arzeneimittelforschung* **1998**, *48*, 263.

7. Kumar, Y.; Green, R.; Borysko, K.Z.; Wise, D.S.; Wotring, L.L.; Townsend, L.B. Synthesis of 2,4-disubstituted thiazoles and selenazenol as potential antitumor and antifilarial agents. 1. (Isothiocyanatomethyl)thiazole-2-carbamates, -selenazole-2-carbamates, and related derivatives. *J. Med. Chem.* **1993**, *36*, 3843–3848.

8. Rehse, K.; Baselt, T.; New 2-amino-thiazole-4-acetamides with antiplatlet activity. *Achiv. Pharmazie*. **2008**, *34*, 645–654.

9. Shaw, F.H.; Simon, S.E.; Cass, N.; Shulman, A.; Anstee, J.R.; Nelson, E.R. Barbiturate antagonism. *Nature* **1954**, *174*, 402–403.

10. Zhang, X.; Urbanski, M.; Patel, M.; Zeck, R.E.; Cox, G.G.; Bian, H.; Conway, B.R.; Beavers, M.P.; Rybczynski, J.P.; Demarst, K.T. Hetroaryl O-glucosideas novel sodium glucose co-transporter 2 inhibitors. *Bioorg. Med. Chem.* **2005**, *15*, 5202–5206.

11. Koganty, R.R.; Reddish, M.A.; Longenecker, B.M. In *Glycopeptides and Related Compounds*; Warren, D.G., Ed.; Marcel Dekker: New York, **1997**.

12. Smith, P.; Brown, L.; Boutagy, J.; Thomas, R. Synthesis and biological activity of glucosides 17Cβ-modified derivatives of digitoxigenin. *J. Med. Chem.* **1982**, *25*(10), 1222.

13. Huiying, L.; Yong, C.; Hongxing, Z.; Xinhong, L.; Baorui, L.; Fanbo, Z.; Xiaorui, C.; Synthesis of glucoside compounds of ferrocenyl phenols and their antianeamic activity. *Wuhan Univ. J. Nat. Sci.* **1998**, *3*(1), 81–85.

14. Jose, R.; Marino, A.; Robert, B.; Andrews, P.; Eric, M. Synthesis and growth inhibitory properties of glycosides of 1-*O*-hexadecyl-2-*O*-methyl-sn-glycerol, analogs of the antitumor ether lipid ET-18-OCH_3. *J. Med. Chem.* **1996**, *39*(17), 3241.

15. Pereira, A.P.; Ferreira, I.C.; Marcelino, F.; Valentao, P.; Andrade, P.B.; Seabra, R.; Estevinho, L.; Bento, A.; Pereira, J.A. Phenolic compounds and antimicrobial activity of olive (Olea europea L.Cv.Cobrancosa)leaves. *Molecules* **2007**, *12*, 1153.

16. Ohsumi, K.; Matsueda, H.; Hatanaka, T.; Hirama, R.; Umemura, T.; Oonuki, A.; Ishida, N.; Kageyama, Y.; Maezono, K.; Kondo, N. Pyrazole-O-glucosides as novel Na^+-glucose contransporter (SGLT) inhibitors. *Bioorg. Med. Chem. Lett.* **2003**, *13*(14), 2269–2272.

17. Vogel, A.I. *Text Book of Practical Organic Chemistry*, 4th Ed.; Chapman and Hall: London, **1978**.

18. Koenig, W.; Knorr, E. Ueber einige derivatives des traubenzuckers and der galactose. *Chem. Ber.* **1901**, *34*(1), 957–981.

19. Garazd, Y.L.; Garazd, M.M.; Khilya, V.P. Modified coumarins. 12. Synthesis of 3, 4-cycloannlated coumarin β-D-glucopyranosides. *Chem. Nat. Compds.* **2004**, *40*(1), 6–12.

20. Silverstein, R.M.; Webster, F.X. *Spectrometric Identification of Organic Compounds*, 6th Ed.; John Wiley & Sons, Inc.: New York, **1998**.

21. T'ang, A.; Lien, E.J.; Lai, M.M.C. Optimization of the Schiff bases of N-hydroxy-N'-aminoguanidine as anticancer and antiviral agents. *J. Med. Chem.* **1985**, *28*(8), 1103–1106.

22. Sun, X.; Tao, Y.; Liu-Y.; Chen, B.; Jia, Y.; Yang, J. Synthesis and biological activities of alkyl substituted triazolelethione Schiff base. *Chinese J. Chem.* **2008**, *26*(6), 1133–1136.

23. Bharti, S.K.; Tilak, N.R.; Singh, S.K. Synthesis, antibacterial and anti-fungal activities of some novel Schiff bases containing 2, 4-disubstituted thiazole ring. *Eur. J. Med. Chem.* **2010**, *45*(2), 651–660.

24. Dalloul, H.M.; Al-Abadla, N.S.; El-Nwairy, K.H. Heterocyclic synthesis using nitrile imines. 6*. Synthesis of some new substituted 4, 5-dihydro-1H-1, 2, 4-triazole. *Chem. Hetrocycl. Compd.* **2007**, *43*(3), 314–319.

25. Ingle, V.N.; Hatzade, K.M.; Taile, V.S.; Gaidhane, P.K.; Kharche, S.T. Synthesis of *O*-β-D-glucopyranosides of 7-hydroxy-3-(imidazole-2-yl)-4H-chromen-4-ones. *J. Carbohydr. Chem.* **2007**, *26*, 107–123.

26. Hatzade, K.M.; Taile, V.S.; Gaidhane, P.K.; Haldar, A.G.M.; Ingle, V.N. Synthesis and biological activities of new hydroxy-3-pyrazolyl-4H-chromen-4-ones and their *O*-glucosides. *Ind. J. Chem.* **2008**, *47B*, 1260–1270.

27. Hatzade, K.M.; Taile, V.S.; Gaidhane, P.K.; Haldar, A.G.M; Ingle, V.N. Synthesis and biological activities of new 7-*O*-β-D-glucopyranosyloxy-3-(3-oxo-3-arylprop-1-enyl)-chromones. *Ind. J. Chem.* **2009**, *48B*, 1548.

28. Taile, V.; Hatzade, K.; Gaidhane, P.; Ingle, V. Synthesis and biological activity of 4-(4-hydroxybenzylidine)-2-(substituted styryl) oxazol-5-ones and their *O*-glucosides. *Turk. J. Chem.* **2009**, *33*, 295–305.

29. Taile, V.S.; Hatzade, K.M.; Gaidhane, P.K.; Ingle, V.N. Synthesis and biological evaluation of novel 2-(4-O- β-D-glucisidoxyphenyl)-4,5-disubstituted imidazoles. *J. Hetrocycl. Chem.* **2010**, *47*, 903–907.

30. Ingle, V.N.; Gaidhane, P.K.; Hatzade, K.M.; Umare, V.D.; Taile, V.S. Synthesis and biological activities of glucoconjugated Spiro triones. *Int. J. Pharmtech. Res.* **2009**, *1*(3), 605–612.

31. Furniss, B.S.; Hannaford, A.J.; Smith, P.W.G.; Tatchell, A.R. *Vogel's Text Book of Practical Organic Chemistry*, 5th Ed.; Pearson Education; Singapore **2005**, 644–647.

32. Igarashi, K. The Koenigs-Knorr reaction. *Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 243–283.