Pharmaceutical Chemistry Journal, Vol. 48, No. 4, July, 2014 (Russian Original Vol. 48, No. 4, April, 2014)

SYDNONE SULFONAMIDE DERIVATIVES AS ANTIBACTERIAL, ANTIFUNGAL, ANTIPROLIFERATIVE AND ANTI-HIV AGENTS

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Original article submitted May 5, 2014.

Three series of substituted sydnone sulfonamide derivatives were synthesized wherein 3-(4-methylphenyl)-4-(chlorosulfonyl)sydnone **(5)** was linked by a sulfonamide linkage with various thiazole, benzothiazole and quinazoline groups. The structures of the compounds were confirmed by IR and NMR spectroscopy and elemental analysis. The synthesized compounds were evaluated for their antibacterial, antifungal, antiproliferative and anti-HIV activities. Anti-HIV activity was determined against human immunodeficiency virus HIV-1 (III-B) and HIV-2 (ROD) in MT-4 cells. Inhibition of cytomegalovirus and varicella-zoster virus (VZV) replication was measured in human embryonic lung (HEL) cells.

Keywords: anti-HIV, antiprolioferative, sydnone, sulfonamides

INTRODUCTION

Thiazole, benzothiazole and quinazoline are among the most versatile heterocyclic groups which play an important role in synthetic and pharmaceutical chemistry [1 – 5]. Sydnones are interesting series of mesoionic heterocycles having vast range of various biological and synthetic applications [6 – 8]. The hydrogen atom at C4 of sydnone ring underwent substitution with a variety of electrophiles [9]. Consequently, the synthesis of these sydnones comprising sulfonamide linkage is of continuing interest and a prerequisite for the development of new drugs in the field. Combination of sydnone ring with thiazole, benzothiazole and quinazolines by sulfonamide linkage at C4 might lead to the creation of further efficient compounds. The present article reports the synthesis of new sydnone sulfonamides and determination of their antibacterial, antifungal, antiproliferative, and anti-HIV activity.

EXPERIMENTAL CHEMICAL PART

Melting points were determined by the open capillary method and are uncorrected. Elemental analyses were carried out on a Heraeus Carlo Erba 1180 CHN analyzer. All compounds were analyzed satisfactorily for C, H, and Ncontent. The infrared (IR) spectra were scanned on a Thermo Scientific Nicolet *i*S10 FT-IR spectrometer. NMR spectra were recorded on Brucker Avance II NMR spectrometer. Chemical shifts (δ) refer to internal tetramethylsilane (TMS). Thin layer chromatography (TLC) was performed on E-Merck pre-coated 60 F_{254} plates and the spots were rendered visible by exposing the plates to UV light.

RESULTS AND DISCUSSION

In our previous work, we have synthesized several sydnone derivatives and evaluated their antibacterial activity [10]. To continue our efforts in this area, the present article describes the synthesis of sydnone sulfonamide derivatives and their antibacterial, antifungal, anti-HIV, and anticancer activity against some important species.

3-(4-Methylphenyl)sydnone **(4)** has been synthesized using a four-step procedure starting from 4-methylaniline according to Fig. 1 by undergoing esterification, hydrolysis, nitrosation and cyclization [11]. The mechanism of sydnone ring formation is depicted in Fig. 1.

Compound **4** undergoes chlorosulfonation to get sulfonylchloride derivative which, when treated with different thiazole, benzothiazole and quinazoline derivatives, yields the corresponding sulfonamide derivatives **(13 – 15)**.

The structures of newly synthesized compounds were confirmed by IR and NMR spectroscopy. The IR spectra of the newly synthesized compounds show bands near 1750 cm^{-1} for C=O group of sydnone ring. The absorption bands between 1392 – 1349 and 1177 – 1170 cm^{-1} represent the characteristic SO_{2asym} and SO_{2sym} vibrations, respec-

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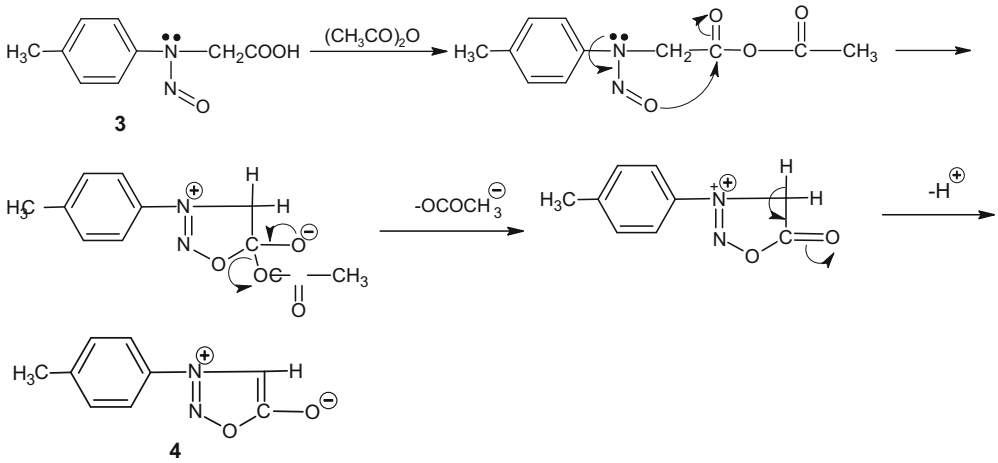

Fig. 1. Mechanism of formation of a sydnone ring.

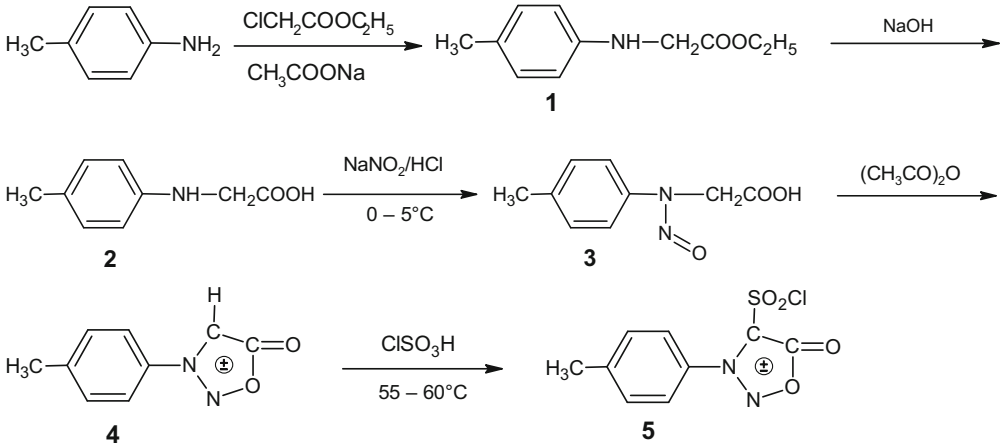

Fig. 2. Synthesis of 3-(4-methylphenyl)-4-(chlorosulfonyl)sydnone.

tively. The C-S-C and C-N bonds of thiazole and benzothiazole show bands near 690 – 734 and 1628 – 1663 cm^{-1}, respectively, whereas C-N and C=O bonds of quinazoline show absorption between 1590 – 1612 and 1660 – 1674 cm^{-1}, respectively. Furthermore, ^{1}H NMR spectra of compounds **13 – 15** show confirmatory signals near δ = 10.00 ppm for sulfonamide linkage, and ^{13}C NMR spectra show verification signals for carbonyl carbon of sydnone ring near δ = 168 ppm. The compounds showed modest activity against bacteria and fungi and no specific activity against CMV, VZV or HIV.

*General Procedure for the Synthesis of 3-(4-Methylphenyl)-4-(chlorosulfonyl)sydnones (**5**)*

Chlorosulfonic acid (0.66 mL, 0.01 mol) was added dropwise into the mixture of 3-(4-methylphenyl)sydnone (1.76 g, 0.01 mol) and catalytic amount of phosphorous pentoxide (P_2O_5) over 30 min with constant stirring at 0 – 5 °C. The temperature of the well-stirred mixture did not rise above 5 °C. When all the chlorosulfonic acid had been added, the mixture was refluxed at about 60 °C for about 1 h. Then, the solution was poured into a mixture of crushed ice and water with vigorous stirring. The precipitate was collected by filtration, washed with water, dried, and recrystallized from ethanol (Fig. 2). Yield, 3.94 g (74 %); m.p., 122 – 124°C.

Synthesis of 4-(substituted phenyl)-1,3-thiazol-2-amines (8). Bromine (0.025 mol) in chloroform (20 mL) was added dropwise to a solution of substituted phenylethanone (0.01 mol) in chloroform (20 mL) at room temperature and the solution was then stirred for about 12 hours util complete disappearance of bromine in the solution. Precipitates of 2,2-dibromo-1-(substituted phenyl)ethanone **(6)** were formed. The precipitates were washed with 10 % sodium bisulfite solution and recrystallized from methanol. To a solution of 2,2-dibromo-1-(substituted phenyl)ethanone in ethanol (0.01 mol) was added thiourea (0.76 g, 0.01 mol) in ethanol and the reaction mixture was stirred for about 1 h. The

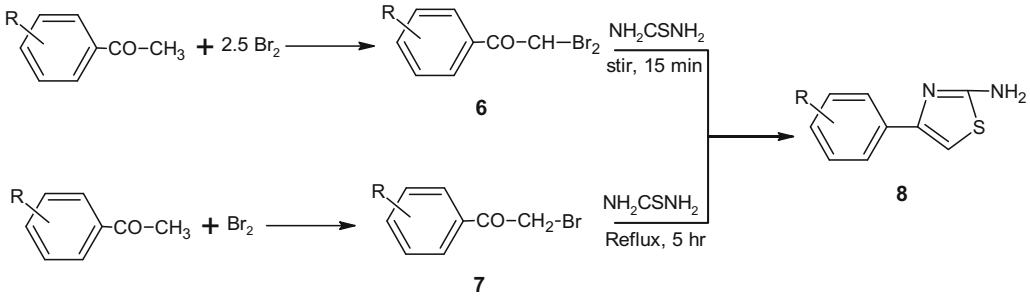

Fig. 3. Synthesis of 4-(substituted phenyl)-1,3-thiazol-2-amines **6a** – **6j**.

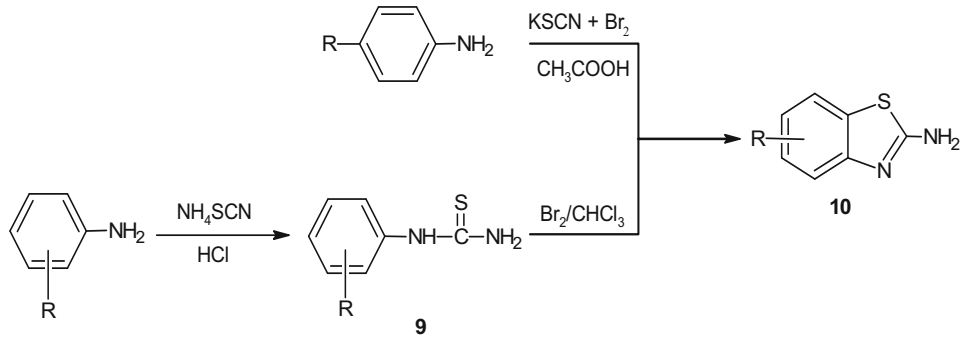

Fig. 4. Synthesis of 2-amino-substituted benzothiazoles **10**.

solid product was separated and recrystallized from ethanol (Fig. 3).

2-Amino-(6-substituted)benzothiazoles (10a – 10g)

To a well stirred solution of 4-substituted aniline (0.01 mol) and potassium thiocyanate (3.88 g, 0.04 mol) in glacial acetic acid (30 mL), a solution of bromine (0.52 mL, 0.01 mol) dissolved in glacial acetic acid (25 mL) was added dropwise over a period of 5 h. The temperature of the reacting mixture was kept below 35 °C. After all bromine had been added, the reaction mixture was stirred for 12 hour at this temperature and filtered. The filtrate was neutralized with ammonium hydroxide. The precipitate was collected and filtered. The product was washed with cold water.

2-Amino-(4/5-substituted)benzothiazoles (10h – 10j).

Compounds **10h – 10j** were synthesized according to a two-step procedure described below. First, 1-(2/3-substituted phenyl)thioureas (**9**) were synthesized from a

mixture of 2/3-substituted aniline (0.01 mol), ammonium thiocyanate (0.91 g, 0.012 mol) and sodium hydrogen sulfite (0.07 g) was dissolved in 20 % hydrochloric acid (3.0 mL) and heated at 90 °C for 14 hours. The cooled mixture was filtered, washed with water till neutral and dried to give 1-(2/3-substituted phenyl)thiourea.

Then, a solution of bromine (7 mL, 0.136 mol) in chloroform (10 mL) was added dropwise to a stirred suspension of 1-(2/3-substituted phenyl)thiourea (0.068 mol) in chloroform (130 mL). The reaction mixture was refluxed for 2.5 hours and allowed to stand at room temperature for 12 hours. The residue was treated with dilute ammonium hydroxide solution. Finally, the solid product was filtered and recrystallized from chloroform to yield 2-amino-(4/5-substituted)benzothiazoles **10h** – **10j** (Fig. 4).

Synthesis of 3-(4-aminophenyl)-2-(substituted phenyl)quinazolin-4(3H)-ones (12). To a stirred solution of 2-aminobenzoic acid (1.37 g, 0.01 mol) in pyridine (15 mL), a solution of substituted acid chloride (0.015 mol) in pyridine (15 mL) was added dropwise, while the temperature was maintained at 0 – 5 °C for 2 hour. Then, the reaction mixture was stirred for another 2 hours at room temperature. The whole reaction mixture was neutralized with 10% sodiumbicarbonate solution. The solid product was separated and filtered off, washed with water, and recrystallized from benzene.

A solution of 2-(substituted phenyl)-4H-3,1-benzoxazin-4-one (0.01 mol) and 4-phenylenediamine (1.08 g, 0.01 mol) in pyridine (20 mL) was refluxed for 6 hours. After cooling, the solution was poured over ice to obtain compounds **12a – 12j,** which were recrystallized from ethanol (Fig. 5).

*General Procedure for the Synthesis of Compounds **13 – 15***

A solution of appropriate thiazole, benzothiazole and quinazoline derivatives (0.01 mol) in acetone was added dropwise to 3-(4-methylphenyl)-4-(chlorosulfonyl)sydnone (3.02 g, 0.011 mol) in acetone over a period of 5 hours with constant stirring. Pyridine (1 mL) was added to the well

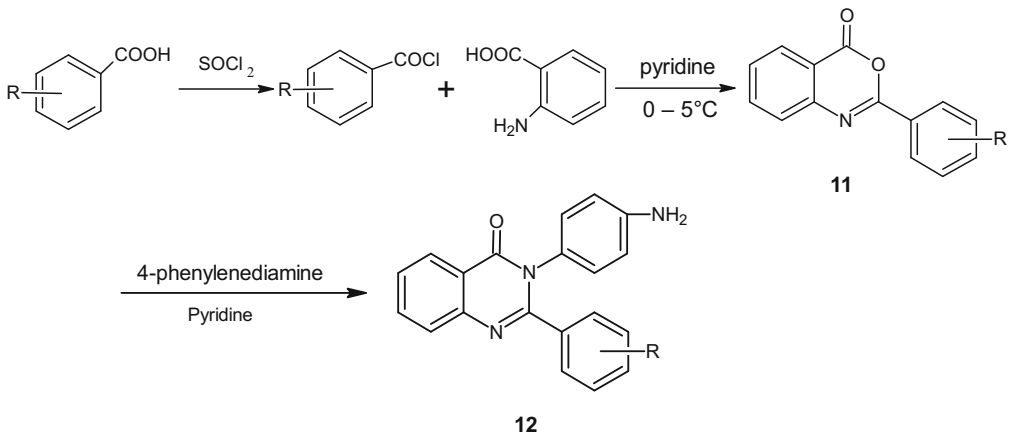

Fig. 5. Synthesis of 3-(4-aminophenyl)-2-(substitutedphenyl)quinazolin-4(3*H*)-ones **12**.

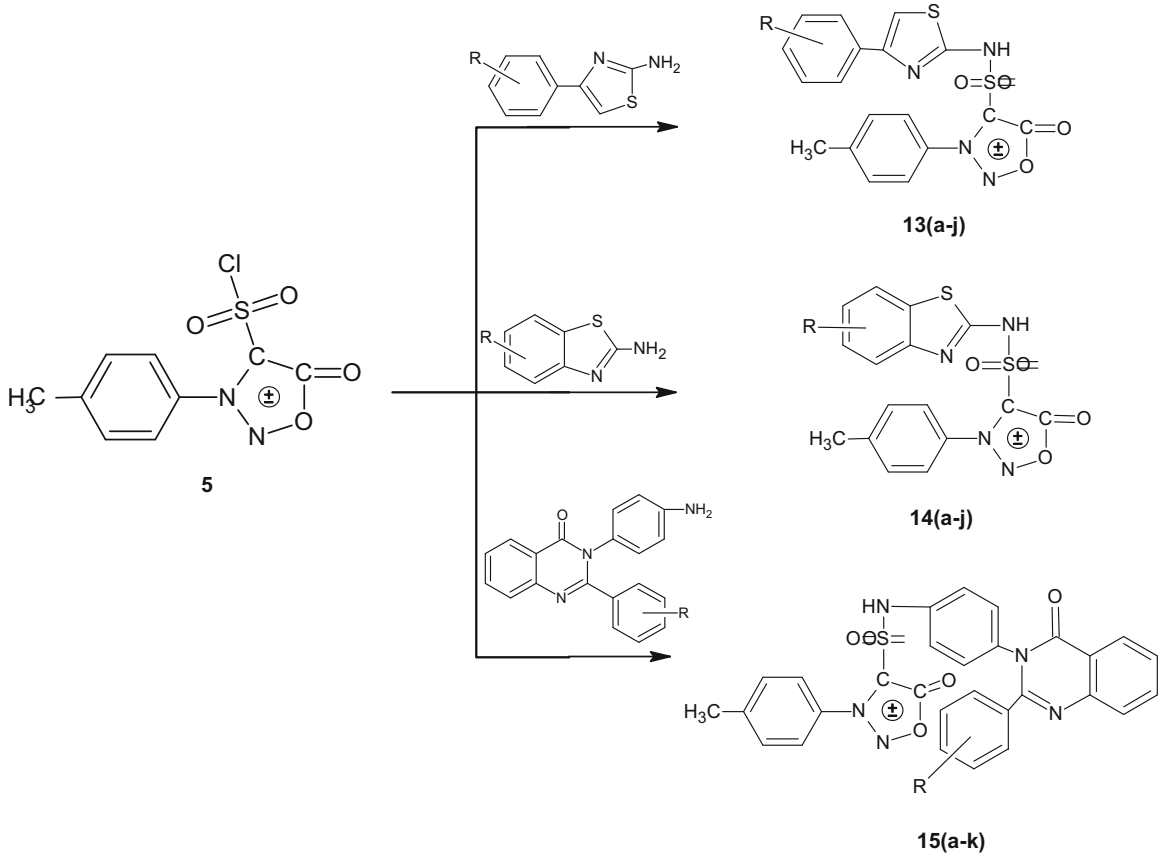

Fig. 6. Synthesis of thiazole, benzothiazole and quinazoline substituted sydnone sulfonamides**: (13a)** R = 4-Br; **(13b)** R = 4-Cl**; (13c)** R = 4-OCH_3**; (13d)** R = 4-CH_3**;** (13e) R = 4-NO_2 ;(13f) R = 4-$O(CH_2)_3CH_3$; (13g) R = 2,4-F; (13h) R = 2,4-Cl; (13i) R = 2,4-Cl-6-F; (13j) R = 2,6-Cl; (14a) R = 6-CH_3; (14b) R = 6-OCH_3; (14c) R = 6-Cl; (14d) R = 6-Br; (14e) R = 6-NO_2; (14f) R = 6-F; (14g) R = 6-OCH_2CH_3; (14h) R = 5-Cl; (14i) R = 5-CH_3; (14j) R = 4-NO_2; (15a) R = H; (15b) R = 4-NO_2; (15c) R = 4-OCH_3; (15d) R = 4-Cl; (15e) R = 3-NO_2; (15f) R = 3-Cl; (15g) R = 3-Br; (15h) R = 2-NO_2; (15i) R = 2-Cl; (15j) R = 2-Cl-6-NO_2; (15k) R = 3-NO_2 _ 4-OCH_3.

stirred solution after 1 and 2 h. Finally, the solution was poured onto ice with stirring. The precipitate was collected by filtration, washed with water, dried, and recrystallized from ethanol (Figure 6).

Physicochemical characteristics of compounds **13 – 15** are as follows:

4-{[4-(4-Bromophenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13a): IR (KBr; ν, cm^{-1}): 3285

(N-H), 2980 (CH_3), 1738 (CO sydnone), 1634 (C-N thiazole), 1392 (SO_2), 1177 (SO_2), 713 (C-S-C thiazole), 596 (Br); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.47 (s, 3H, CH_3), 7.36 – 8.00 (m, 9H, Ar-H), 9.73 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.59, 108.73, 121.74, 124.53, 127.66, 132.40, 132.66, 133.85, 136.73, 139.06, 142.66, 153.00, 175.20, 168.54

4-{[4-(4-Chlorophenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13b): IR (KBr; δ, cm^{-1}): 3266 (N-H), 2960 (CH_3 stretching), 1751 (C=O sydnone), 1607 (C-N thiazole), 1346 (SO_2), 1175 (SO_2), 817 (Cl), 705 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.60 (s, 3H, CH_3), 7.10 – 7.90 (m, 9H, Ar-H), 9.80 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.69, 108.64, 123.64, 127.86, 130.11, 132.67, 135.53, 135.84, 136.38, 139.54, 141.70, 153.10, 175.27, 168.33

4-{[4-(4-Methoxyphenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13c): IR (KBr; ν, cm^{-1}): 3244 (N-H), 2964 (CH_3 stretching), 1746 (C=O sydnone), 1615 (C-N thiazole), 1347 (SO_2), 1253 (COC), 1170 (SO_2), 1045 (COC), 707 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.48 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 9.77 (s, 1H, SO_2NH), 7.28 – 8.15 (m, 9H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.63, 56.25, 108.42, 112.78, 123.83, 130.00, 132.62, 135.73, 136.78, 138.78., 140.93, 153.84, 161.11, 175.23, 168.49

4-{[4-(4-Methylphenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13d): IR (KBr; ν, cm^{-1}): 3258 (N-H), 2960 (CH_3 stretching), 1755 (C=O sydnone), 1607 (C-N thiazole), 1349 (SO_2), 1175 (SO_2), 712 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.67 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 7.18 – 8.60 (m, 9H, Ar-H), 9.76 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.59, 21.86, 108.76, 121.90, 128.19, 130.73, 132.64,133.63, 134.73, 139.12, 140.52, 142.84, 151.69, 175.10, 169.06

4-{[4-(4-Nitrophenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13e):

IR (KBr; ν, cm^{-1}): 3245 (NH), 2960 (CH_3), 1751 (CO sydnone), 1629 (C-N thiazole), 1591 (NO_2), 1359 (SO_2), 1325 (NO_2), 1174 (SO_2), 693 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.20 (s, 3H, CH_3), 7.25 – 7.95 (m, 9H, Ar-H), 8.90 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.43, 106.55, 123.31, 123.50, 126.88, 130.64, 136.58, 138.64, 140.00, 142.90, 148.37, 152.80, 175.70, 167.27

4-{[4-(4-Butoxyphenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13f): IR (KBr; ν, cm^{-1}): 3250 (N-H), 2964 (CH_3 stretching), 2925 (CH2), 1747 (C=O sydnone), 1610 (C-N thiazole), 1255 (COC), 1345 (SO_2), 1174 (SO_2), 1047 (COC), 710 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 1.20 (t, 3H, $\underline{CH_3}CH_2CH_2CH_2O$), 1.30 – 1.74 (m, 4H, $CH_3\underline{CH_2}\underline{CH_2}CH_2O$), 2.45 (s, 3H, CH_3), 4.13 (t, 2H, $CH_3CH_2CH_2\underline{CH_2}O$), 7.00 – 7.78 (m, 9H, Ar-H), 9.95 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 14.25, 20.55, 21.44, 30.74, 68.90, 109.07, 113.74, 123.95, 130.00, 130.73, 135.60, 136.47, 139.53, 142.75, 162.79, 153.08, 175.39, 168.96

4-{[4-(2,4-Difluorophenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13g): IR (KBr; ν, cm^{-1}): 3290 (N-H), 2963 (CH_3), 1749 (CO sydnone), 1638 (C-N thiazole), 1338 (SO_2), 1261 (F), 1164 (SO_2), 729 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.30 (s, 3H, CH_3), 7.31 – 8.12 (m, 8H, Ar-H), 10.00 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.52, 102.47, 108.22, 114.78, 117.73, 126.36, 123.70, 132.38, 136.37, 138.60, 140.53, 154.60, 159.83, 162.63, 175.10, 167.90

4-{[4-(2,4-Dichlorophenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13h): IR (KBr; ν, cm^{-1}): 3270 (N-H), 2964 (CH_3 stretching), 1746 (C=O sydnone), 1610 (C-N thiazole), 1343 (SO_2), 1170 (SO_2), 812 (Cl), 712 (C-S-C thiazole) cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.46 (s, 3H, CH_3), 7.16 – 7.92 (m, 8H, Ar-H), 9.90 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.48, 108.42, 121.57, 127.38, 128.06, 128.74, 129.64, 132.50, 134.20, 136.63, 135.00, 139.66, 142.37,154.68, 173.90, 168.47

4-{[4-(2,4-Dichloro-6-fluorophenyl)-1,3-thiazol-2-yl]-sulfamoyl}-3-(4-methylphenyl) sydnone (13i): IR (KBr; ν, cm^{-1}): 3275 (N-H), 2960 (CH_3 stretching), 1748 (C=O sydnone), 1614 (C-N thiazole), 1353 (SO_2), 1255 (F), 1164 (SO_2), 800 (Cl), 730 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.44 (s, 3H, CH_3), 6.80 – 7.75 (m, 8H, Ar-H), 9.88 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.85, 108.70, 118.72, 121.96, 129.85, 131.30, 131.85, 132.61, 132.84, 136.38, 139.32, 141.68, 154.15, 161.68, 175.40, 168.73

4-{[4-(2,6-Dichlorophenyl)-1,3-thiazol-2-yl]sulfamoyl}-3-(4-methylphenyl)sydnone (13j): IR (KBr; ν, cm^{-1}): 3263 (N-H), 2957 (CH_3 stretching), 1745 (C=O sydnone), 1614 (C-N thiazole), 1350 (SO_2), 1174 (SO_2), 810 (Cl), 717 (C-S-C thiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.50 (s, 3H, CH_3), 7.46 – 7.96 (m, 8H, Ar-H), 10.12 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.69, 108.47, 121.16, 130.18, 131.48, 132.10, 132.86, 133.46, 136.65, 139.55, 140.78, 154.74, 175.00, 169.36

4-[(6-Methyl-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14a): IR (KBr; ν, cm^{-1}): 3280 (N-H), 2956 (CH_3), 1746 (CO sydnone), 1360 (SO_2), 1183 (SO_2), 690 (C-S-C thiazole), 1636 (C-N benzothiazole) ; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.50 (s, 3H, CH_3), 2.79 (s, 3H, CH_3), 6.76 – 7.80 (m, 7H, Ar-H), 9.53 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.68, 22.18, 119.45, 122.74, 123.20, 128.53, 131.00, 132.56, 134.64, 136.63, 139.63, 142.79, 153.33, 175.83, 168.05

4-[(6-Methoxy-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14b):

IR (KBr; ν, cm^{-1}): 3274 (N-H), 2961 (CH_3), 1750 (CO sydnone), 1356 (SO_2), 1235 (COC), 1180 (SO_2), 694 (C-S-C

thiazole), 1632 (C-N benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.39 (s, 3H, CH_3), 4.16 (s, 3H, OCH_3), 6.82 – 7.49 (m, 7H, Ar-H), 9.57 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.60, 57.48, 107.55, 112.96, 119.48, 123.82, 132.50, 132.66, 136.74, 139.33, 140.17, 151.38, 156.62, 175.28, 168.75

4-[(6-Chloro-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14c): IR (KBr; ν, cm^{-1}): 3283 (N-H), 2960 (CH_3), 1751 (CO sydnone), 1362 (SO_2), 1174 (SO_2), 812 (Cl), 695 (C-S-C thiazole), 1640 (C-N benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.30 (s, 3H, CH_3), 6.90 – 7.80 (m, 7H, Ar-H), 9.00 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.48, 121.52, 121.63, 123.66, 123.80, 124.97, 132.47, 133.65, 136.59, 138.86, 140.19, 153.58, 175.46, 168.42

4-[(6-Bromo-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14d): IR (KBr; ν, cm^{-1}): 3266 (N-H), 2995 (CH_3), 1751 (C=O sydnone), 1647 (C-N benzothiazole), 1327 (SO_2), 1175 (SO_2), 726 (C-S-C benzothiazole), 553 (Br); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.48 (s, 3H, CH_3), 7.00 – 7.73 (m, 7H, Ar-H), 9.63 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.50, 113.69, 121.38, 121.67, 122.74, 129.85, 132.10, 132.31, 136.33, 139.34, 142.56, 153.41, 175.52, 168.04

4-[(6-Nitro-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)-sydnone (14e): IR (KBr; ν, cm^{-1}): 3271 (N-H), 2983 (CH_3), 1745 (C=O sydnone), 1640 (C-N benzothiazole), 1550 (NO_2), 1376 (NO_2), 1336 (SO_2), 1172 (SO_2), 733 (C-S-C benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.20 (s, 3H, CH_3), 7.25 – 7.95 (m, 7H, Ar-H), 8.90 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.60, 118.13, 119.63, 120.78, 123.84, 132.37, 132.69, 136.70, 138.53, 140.96, 142.63, 154.00, 175.83, 168.64

4-[(6-Fluoro-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14f): IR (KBr; ν, cm^{-1}): 3278 (N-H), 2983 (CH_3), 1745 (C=O sydnone), 1640 (C-N benzothiazole), 1336 (SO_2), 1172 (SO_2), 1100 (F), 733 (C-S-C benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.40 (s, 3H, CH_3), 7.33 – 7.75 (m, 7H, Ar-H), 10.24 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.38, 108.20, 113.66, 122.89, 123.84, 130.47, 132.85, 135.11, 138.57, 142.83, 153.13, 161.40, 175.34, 168.41

4-[(6-Ethoxy-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14g): IR (KBr; ν, cm^{-1}): 3273 (N-H), 2974 (CH_3), 2932 (CH_2), 1751 (C=O sydnone), 1663 (C-N benzothiazole), 1345 (SO_2), 1267 (C-O-C), 1175 (SO_2), 1038 (C-O-C), 726 (C-S-C benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 1.40 (t, 3H, $OCH_2\underline{CH_3}$), 2.45 (s, 3H, CH_3), 4.36 (s, 3H, $OC\underline{H_2}CH_3$), 6.95 – 7.54 (m, 7H, Ar-H), 9.55 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 15.43, 21.60, 65.23, 106.55, 112.96, 118.48, 123.82, 132.50, 132.66, 136.74, 138.33, 140.17, 151.38, 154.62, 175.28, 168.51

4-[(5-Chloro-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14h): IR (KBr; ν, cm^{-1}): 3268 (N-H), 2980 (CH_3), 2936 (CH_2), 1745 (C=O sydnone), 1643 (C-N benzothiazole), 1347 (SO_2), 1260 (C-O-C), 1172 (SO_2), 1047 (C-O-C), 827 (Cl), 729 (C-S-C benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.40 (s, 3H, CH_3), 7.13 – 7.79 (m, 7H, Ar-H), 10.05 (s, 1H, SO_2NH) ; ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.72, 120.74, 121.37, 123.84, 125.70, 130.00, 130.70, 131.49, 136.21, 139.00, 140.00, 150.90, 175.82, 168.83

4-[(5-Methyl-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14i): IR (KBr; ν, cm^{-1}): 3270 (N-H), 2977 (CH_3), 2942 (CH_2), 1750 (C=O sydnone), 1637 (C-N benzothiazole), 1340 (SO_2), 1267 (C-O-C), 1177 (SO_2), 1030 (C-O-C), 734 (C-S-C benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.48 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 7.32 – 7.85 (m, 7H, Ar-H), 10.26 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.29, 21.68, 120.38, 122.35, 123.73, 124.73, 131.37, 132.68, 136.80, 136.88, 139.32, 142.73, 151.63, 175.21, 168.53

4-[(4-Nitro-1,3-benzothiazol-2-yl)sulfamoyl]-3-(4-methylphenyl)sydnone (14j): IR (KBr; ν, cm^{-1}): 3250 (N-H), 2962 (CH_3), 1750 (CO sydnone), 1628 (C-N benzothiazole), 1554 (NO_2), 1341 (SO_2), 1390 (NO_2), 1174 (SO_2), 727 (C-S-C benzothiazole); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.20 (s, 3H, CH_3), 6.70 – 7.65 (m, 7H, Ar-H), 8.70 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.62, 121.44, 123.63, 123.80, 126.55, 130.48, 134.72, 136.39, 139.21, 142.74, 143.00, 150.53, 175.84, 168.55

4-{[4-(2-phenyl-4-oxoquinazolin-3(4*H*)-yl)phenyl]sulfamoyl}-3-(4-methylphenyl)-sydnone (15a): IR (KBr; ν, cm^{-1}): 3275 (N-H), 2990 (CH_3), 1748 (C=O sydnone), 1666 (C=O quinazoline), 1593 (C-N quinazoline), 1309 (SO_2), 1174 (SO_2) ;^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.47 (s, 3H, CH_3), 6.85 – 8.56 (m, 17H, Ar-H), 9.36 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.86, 111.79, 122.33, 123.48, 125.87, 126.62, 127.16, 127.22, 127.39, 128.94, 129.00, 132.63, 135.33, 135.70, 136.48, 136.70, 137.58, 139.64, 142.63, 149.53, 151.47, 163.17, 169.12

4-({4-[2-(4-Nitrophenyl)-4-oxoquinazolin-3(4*H*)-yl]-phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15b): IR (KBr; ν, cm^{-1}): 3270 (N-H), 2986 (CH_3), 1754 (C=O sydnone), 1661 (C=O quinazoline), 1590 (C-N quinazoline), 1530 (NO2), 1323 (SO_2), 1178 (SO_2), 1357 (NO2); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.42 (s, 3H, CH_3), 7.03 – 7.66 (m, 16H, Ar-H), 9.47 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.75, 142.53, 130.85, 121.49, 136.52, 133.70, 111.67, 126.47, 136.21, 163.70, 122.10, 126.38, 127.80, 135.16, 127.10, 139.34, 149.38, 153.75, 135.74, 128.63, 124.58, 150.80, 168.86

4-({4-[2-(4-Methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl]phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15c): IR (KBr; ν, cm^{-1}): 1267 (C-O-C), 1034 (C-O-C), 3276 (N-H), 2980 (CH_3), 1746 (C=O sydnone), 1660 (C=O

quinazoline), 1594 (C-N quinazoline), 1320 (SO_2), 1170 (SO_2); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.38 (s, 3H, CH_3), 4.00 (s, 3H, OCH_3), 6.87 – 7.53 (m, 16H, Ar-H), 9.53 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.33, 57.39, 111.59, 112.96, 120.63, 123.73, 125.00, 126.81, 127.20, 128.51, 130.38, 131.46, 133.60, 134.81, 135.10, 136.80, 139.52, 137.84, 140.48, 149.52, 151.85, 163.28, 163.78, 168.30

4-({4-[2-(4-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]-phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15d): IR (KBr; ν, cm^{-1}): 3248 (N-H), 2980 (CH_3), 1748 (C=O sydnone), 1667 (C=O quinazoline), 1595 (C-N quinazoline), 1318 (SO_2), 1174 (SO_2), 819 (Cl); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.46 (s, 3H, CH_3), 6.96 – 7.62 (m, 16H, Ar-H), 9.77 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.62, 113.63, 127.00, 122.54, 123.41, 126.73, 128.10, 128.95, 129.47, 131.59, 132.52, 134.94, 135.63, 135.84, 136.28, 137.36, 137.57, 139.11, 142.47, 149.46, 152.98, 163.67, 168.68

4-({4-[2-(3-Nitrophenyl)-4-oxoquinazolin-3(4*H*)-yl]-phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15e): IR (KBr; ν, cm^{-1}): 3250 (N-H), 2980 (CH_3), 1749 (C=O sydnone), 1674 (C=O quinazoline), 1600 (C-N quinazoline), 1528 (NO2), 1328 (SO_2), 1183 (SO_2), 1360 (NO2); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.16 – 7.87 (m, 16H, Ar-H), 2.37 (s, 3H, CH_3), 9.55 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.37, 112.64, 122.64, 123.64, 125.37, 125.73, 126.95, 128.16, 128.58, 129.00, 129.43, 130.37, 131.78, 133.26, 135.10, 135.39, 135.93, 136.25, 138.48, 141.74, 146.48, 149.47, 153.39, 162.75, 168.10

4-({4-[2-(3-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]-phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15f): IR (KBr; ν, cm^{-1}): 3278 (N-H), 2985 (CH_3), 1754 (C=O sydnone), 1666 (C=O quinazoline), 1599 (C-N quinazoline), 1310 (SO_2), 1175 (SO_2), 817 (Cl); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.30 (s, 3H, CH_3), 6.80 – 8.30 (m, 16H, Ar-H), 9.75 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.57, 122.57, 112.64, 122.63, 126.94, 127.64, 128.47, 129.12, 129.54, 130.67, 131.43, 131.26, 132.38, 133.50, 135.00, 136.00, 135.46, 136.74, 138.17,142.48, 147.57, 152.63, 163.48, 168.08

4-({4-[2-(3-Bromophenyl)-4-oxoquinazolin-3(4*H*)-yl]-phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15g): IR (KBr; ν, cm^{-1}): 3268 (N-H), 2970 (CH_3), 1750 (C=O sydnone), 1673 (C=O quinazoline), 1607 (C-N quinazoline), 1327 (SO_2), 1170 (SO_2), 570 (Br); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.53 (s, 3H, CH_3), 9.73 (s, 1H, SO_2NH), 6.74 – 7.50 (m, 16H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.47, 112.80, 121.63, 122.58, 122.86, 126.85, 127.00, 127.24, 128.48, 128.75, 129.53, 131.69, 132.85, 133.10, 133.45, 135.36, 135.73, 136.37, 136.63, 138.75, 142.04, 149.58, 153.42, 162.69, 168.72

4-({4-[2-(2-Nitrophenyl)-4-oxoquinazolin-3(4*H*)-yl]-phenyl}-3-(4-methylphenyl)sulfamoyl)sydnone (15h): IR (KBr; ν, cm^{-1}): 3255 (N-H), 2980 (CH_3), 1751 (C=O sydnone), 1665 (C=O quinazoline), 1610 (C-N quinazoline), 1511 (NO_2), 1370 (NO_2), 1325 (SO_2), 1175 (SO_2) ;^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.58 (s, 3H, CH_3), 6.70 – 8.80 (m, 16H, Ar-H), 9.50 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.47, 112.85, 122.42, 122.84, 125.58, 126.50, 128.00, 128.48, 128.53, 128.90, 129.47, 131.68, 132.37, 133.46, 134.25, 135.33, 135.85, 136.39, 138.84, 141.74, 149.38, 163.10, 150.76, 153.47, 168.33

4-({4-[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]-phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15i): IR (KBr; ν, cm^{-1}): 3267 (N-H), 2987 (CH_3), 1752 (C=O sydnone), 1664 (C=O quinazoline), 1602 (C-N quinazoline), 1325 (SO_2), 1170 (SO_2), 830 (Cl); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.35 (s, 3H, CH_3), 6.88 – 7.95 (m, 16H, Ar-H), 9.70 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.37, 112.68, 122.53, 123.10, 126.85, 127.44, 128.37, 128.48, 128.89, 129.47, 131.36, 131.90, 132.00, 132.58, 133.50, 135.35, 135.54, 135.73, 136.00, 139.36, 141.82, 149.27, 153.74, 163.35, 168.58

4-({4-[2-(2-Chloro-6-nitrophenyl)-4-oxoquinazolin-3(4*H*)-yl]phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15j): IR (KBr; ν, cm^{-1}): 3281 (N-H), 2987 (CH_3), 1745 (C=O sydnone), 1668 (C=O quinazoline), 1605 (C-N quinazoline), 1522 (NO_2), 1373 (NO_2), 1335 (SO_2), 1178 (SO_2), 823 (Cl); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.38 (s, 3H, CH_3), 7.10 – 7.66 (m, 15H, Ar-H), 9.68 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.57, 111.74, 122.48, 122.82, 124.42, 125.48, 125.75, 126.85, 128.62, 128.80, 129.35, 131.56, 133.78, 134.10, 134.23, 135.52, 135.60, 136.32, 139.38, 141.47, 147.68, 150.37, 153.00, 163.74, 168.46

4-({4-[2-(4-Methoxy-3-nitrophenyl)-4-oxoquinazolin-3(4*H*)-yl]phenyl}sulfamoyl)-3-(4-methylphenyl)sydnone (15k): IR (KBr; ν, cm^{-1}): 3280 (N-H), 2975 (CH_3), 1748 (C=O sydnone), 1664 (C=O quinazoline), 1612 (C-N quinazoline), 1520 (NO_2), 1373 (NO_2), 1336 (SO_2), 1230 (COC), 1175 (SO_2), 1053 (COC); ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 2.40 (s, 3H, CH_3), 4.32 (s, 3H, OCH_3), 6.88 – 7.79 (m, 15H, Ar-H), 9.64 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 21.47, 58.25, 112.74, 113.64, 120.89, 122.58, 125.83, 126.73, 127.73, 128.57, 129.14, 129.74, 131.37, 131.90, 132.48, 135.38, 135.51, 135.63, 136.72, 138.56, 141.74, 149.28, 153.53, 153.81, 162.37, 168.53

EXPERIMENTAL BIOLOGICAL PART

Antibacterial Activity

Most of the synthesized compounds exhibited moderate to good antibacterial activity against the tested organisms. *S. aureus* MTCC 96 and *S. pyogenes* MTCC 442 were taken as Gram-positive bacteria species while *E. coli* MTCC 443 and *P. aeruginosa* MTCC 424 were taken as Gram-negative bac-

teria species. Ampicillin, chloramphenicol, ciprofloxacin, and norfloxacin were used as standard drugs.

Minimum inhibitory concentration (MIC) was determined by the broth dilution method [12]. DMSO was used as solvent to get desired concentration of the compounds. In primary screening, different concentrations (e.g. 1000, 500, 250, 125, and 62.5 μg/mL) of synthesized compounds were prepared. The active compounds found in the primary screening were chosen for secondary screening and further diluted to obtain 200, 100, 50, 25, 12.5, and 6.250 μg/mL concentrations. Mueller Hinton broth was used as nutrient medium to grow and dilute the drug suspension for the test bacteria. The lowest concentration inhibiting growth of the organism was recorded as the MIC.

Zone of inhibition was determined by the Kirby – Bauer technique [13]. Aliquot of 0.01 mL of 250 μg/mL concentration for each test compound was used for to determine the zone of inhibition. The incubation was carried out at 37 °C for 24 h. The antibacterial activity of compounds is shown in Table **1**. From these data, it seems that compound **13h** containing a 2,4-dichlorophenyl thiazole linkage showed highest activity besides compounds; **13c** possessing a 4-methoxyphenyl thiazole linkage, **13f** containing a 4-butoxyphenylthiazole linkage, **14a** having a 6-methylbenzothiazole linkage, and compound **15g** having a 3-bromophenyl quinazolinone linkage exhibited higher activity against *S. aureus MTCC 96*. Compounds **13b** having a 4-chlorophenyl thiazole, **14a** having a 6-methylbenzothiazole substituent, **13j** containing a 2,6-dichlorophenyl thiazole, **15c** having a 4-methoxyphenyl quinazolinone linkage were found to possess higher activity against *S. pyogenes MTCC 442*. Compound **14i** containing a 5-methylbenzothiazole, compound **13i** containing a 2,4-dichloro-6-florophenyl thiazole, **14c** having a 6-chlorobenzothiazole, and **15i** having a 2-chloroquinazolinone group were found to show good activity against *E. coli MTCC 443*. Compounds **14i** containing 5-methylbenzothiazole was found to possess highest activity, whereas Compounds **13c** having 4-methoxyphenyl thiazole, **14g** having a 6-ethoxybenzothiazole linkage and **14h** possessing 5-chlorobenzothiazole, **15h** having a 2-nitroquinazolinone were found to possess good activity against *P. aeruginosa MTCC 424*.

Antifungal Activity

The antifungal activity was evaluated against *C. albicans MTCC 227*, *A. niger MTCC 282* and *A. clavatus MTCC 323*. Griseofulvin and nystatin were used as standard drugs. Seborane dextrose broth was used for fungal nutrition. The incubation was carried out at 22 °C for 74 hours.

The antifungal activity of the compounds is depicted in Table 2. Compound **14e** having a 6-nitro benzothiazole linkage was the most active. Compound **13b** having a 4-chloro phenylthiazole, **14e** having a 6-nitro benzothiazole were found to possess good antifungal activity against *C. albicans MTCC 227*. Compound **13f** having a 4-butoxyphenyl thiazole, **13g** containing a 2,4-diflorophenyl thiazole, **14c** having 6-chloro benzothiazole, **14e** 6-nitro benzothiazole were found to possess highest activity against *A. niger MTCC 282*. Compound **13g** having a 2,4-difluro phenyl thiazole, **14d** having a 6-bromobenzothiazole linkage, **15d** having a 4-chloroquinazolinone, **15f** having a 3-chloroquinazolinone

TABLE 1. Antibacterial Activity of Compounds **13 – 15**

Compound	Gram Positive				Gram Negative			
	S. aureus MTCC 96		*S. pyogenes MTCC 442*		*E. coli MTCC 443*		*P. aeruginosa MTCC 424*	
	ZI	MIC	ZI	MIC	ZI	MIC	ZI	MIC
13a	20	100	17	500	18	250	16	500
13b	17	500	22	62.5	20	200	20	250
13c	21	200	17	500	19	250	22	100
13d	16	500	19	250	18	250	17	500
13e	20	200	18	250	16	500	17	500
13f	21	125	18	500	20	200	20	250
13g	19	200	17	500	19	200	19	250
13h	22	100	17	500	19	250	18	500
13i	17	500	19	200	21	100	19	200
13j	18	250	22	100	18	250	20	200
14a	21	100	23	100	16	500	20	100
14b	18	250	19	250	19	250	20	125
14c	20	100	17	500	21	125	19	250
14d	19	200	20	200	20	100	18	200
14e	18	200	19	200	19	250	17	250
14f	19	250	17	500	20	100	19	250
14g	18	250	17	250	20	200	21	100
14h	17	500	20	100	19	250	23	100
14i	19	200	19	125	24	50	24	100
14j	19	250	16	500	18	250	17	500
15a	20	200	17	500	18	250	17	500
15b	19	200	19	250	20	200	19	250
15c	19	250	22	100	18	200	20	100
15d	16	500	18	200	18	250	17	500
15e	17	500	19	200	20	200	22	50
15f	16	500	17	500	19	250	20	200
15g	21	100	19	200	17	500	18	250
15h	20	200	17	500	16	500	22	125
15i	17	500	19	200	21	100	18	250
15j	18	500	16	500	18	250	20	200
15k	17	125	16	250	19	200	20	200
Ampicillin	18	250	19	100	20	100	20	100
Chloramphenicol	21	50	20	50	23	50	21	50
Ciprofloxacin	22	50	22	50	28	25	27	25
Norfloxacin	28	10	21	10	29	10	23	10

ZI = zone of inhibition (diameter of growth inhibition zone in millimeters after 24 h); MIC = minimum inhibitory concentration (μg/mL).

TABLE 2. Antifungal Activity of Compounds **13 – 15**

Compound	*C. albicans MTCC 227*		*A. niger MTCC 282*		*A. clavatus MTCC 323*	
	ZI	MIC	ZI	MIC	ZI	MIC
13a	21	250	21	250	21	250
13b	24	125	23	250	20	500
13c	20	500	18	1000	21	500
13d	17	1000	23	250	17	1000
13e	17	1000	21	250	18	1000
13f	23	200	24	200	23	250
13g	21	250	22	200	25	200
13h	18	1000	20	500	22	500
13i	21	250	17	1000	17	1000
13j	18	1000	21	250	20	500
14a	23	250	19	1000	21	500
14b	21	500	19	1000	24	250
14c	20	1000	24	200	22	500
14d	18	>1000	21	500	24	200
14e	25	100	25	200	24	250
14f	23	250	21	500	19	1000
14g	19	1000	23	500	23	250
14h	21	500	19	1000	23	250
14i	22	500	24	500	24	500
14j	21	500	19	1000	21	500
15a	20	1000	20	1000	24	250
15b	24	250	24	500	23	500
15c	22	500	20	1000	23	250
15d	24	250	24	250	25	200
15e	23	500	23	500	24	250
15f	25	1000	25	250	24	200
15g	22	500	18	1000	23	500
15h	23	500	24	250	20	1000
15i	19	1000	22	500	20	1000
15j	21	1000	18	1000	23	250
15k	22	250	22	1000	22	>1000
Griseofulvin	24	500	28	100	24	100
Nystatin	22	100	29	100	26	100

ZI = zone of inhibition (diameter of growth inhibition zone in millimeters after 24 h); MIC = minimum inhibitory concentration (μg/mL).

were found to possess potent activity, while the other compounds were found to possess moderate to poor activity against *A. clavatus MTCC 1323*.

Anti-HIV Activity

Antiviral activity and cytotoxicity of synthesized compounds was tested according to the MTT method [14]. The compounds were tested for antiviral activity and cytotoxicity against cytomegalovirus (CMV) and varicella-zoster virus (VZV) in human embryonic lung (HEL) cells and evaluated for their anti-HIV activity against HIV-1 and HIV-2 in MT-4 cells. None of the compounds exhibited a specific antiviral activity against either CMV, VZV or HIV.

Antiproliferative Activity

Compounds **3b**, **3h** and **4a** were tested against 60 human tumor cell lines derived from nine different cancer types (leukemia, non-small cell lung cancer, colon cancer, CNS cancer, melanoma, ovarian cancer, renal cancer, prostate cancer and breast cancer) by the National Cancer Institute (NCI). The compounds did not display anticancer activity having GI50 values (the concentration required to achieve 50 % growth inhibition) at a high concentration. Therefore, these compounds were not selected for further testing.

ACKNOWLEDGEMENTS

One of the authors (STA) thanks the University Grants Commission (New Delhi) for providing a Research Fellowship. He is also thankful to Atul Limited, Valsad and Ami Organics, Sachin for providing some useful chemicals.

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