One-pot and solvent-free synthesis of 3-(9-hydroxy-3-methoxy-7-aryl-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-ones and their antibacterial evaluation

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Abstract: A series of 3-(9-hydroxy-3-methoxy-7-aryl-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-ones (5a-j) were synthesized by one-pot multicomponent reaction of 6-methoxy-1-tetralone, aryl aldehydes, and thiourea followed by cyclization with 3-(2-bromoacetyl)-2H-chromen-2-one in the presence of a Brønsted solid acid catalyst, poly(4-vinylpyridinium)hydrogen sulfate [P(4-VPH)HSO₄] (0.015 g), under solvent-free conditions at 120 °C. All the synthesized compounds were characterized by spectral studies and screened for their in vitro antibacterial activity against S. aureus and B. thuringiensis (gram positive), and E. coli and K. pneumoniae (gram negative) bacterial strains. On comparing with the standard drug gentamicin, compounds derived from 4-methoxy and 3,4,5-trimethoxy benzaldehyde, i.e. 5g and 5h, showed broad spectrum antibacterial activity and the remaining compounds showed weak to moderate activity.

Key words: Quinazolinethiones, thiazoloquinazolines, poly(4-vinylpyridinium)hydrogen sulfate, one pot and solvent-free method, antibacterial activity

1. Introduction

Quinazoline and its annulated derivatives represent an important class of heterocyclic compounds. They play an important role in medicinal chemistry due to their wide range of biological activities such as antimicrobial, antiviral, anticancer, anti-inflammatory, anticonvulsant, anti-HIV, pesticidal, and insecticidal properties. They were also reported as inhibitors of enzymes like poly(ADP-ribose)polymerase-1, glycogen synthase kinase-3, and bacterial DNA polymerase III. Similarly, the thiazole nucleus is one of the most notable motifs in medicinal chemistry, possessing several biological activities. It is an integral part of all the available penicillins for controlling bacterial diseases. On the other hand, coumarin derivatives were found to possess various pharmacological activities such as antimicrobial, anticancer, antihepatitis, antidepressant, antioxidant, anticoagulant, and anti-HIV activities. They are also widely used as additives in foods, perfumes, and cosmetics, in the preparation optical brighteners, and in dispersed fluorescent and laser dyes.

In view of the varied biological activities shown by quinazolines, thiazoles, and coumarins, we focused on the design of a novel structural entity that combines these three structural moieties into a single molecular...
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scaffold and to evaluate their potential additive effect on biological activity, especially antibacterial activity. Therefore, in the present communication and in continuation of our earlier studies on annulated quinazolines, we report the synthesis of novel coumarin incorporated benzo[\(h\)]thiazolo[2,3-\(b\)]quinazolines and evaluate their antibacterial activity.\(^{31,32}\)

2. Results and discussion

2.1. Chemistry

Recently, our group reported the synthesis of 8-methoxy-4-aryl-3,4,5,6-tetrahydrobenzo[\(h\)]quinazoline-2(1\(H\))-thiones via a modified Biginelli reaction of 6-methoxy-1-tetralone, aryl aldehyde, and thiourea in the presence of a Brønsted solid acid catalyst, poly(4-vinylpyridinium)hydrogen sulfate [P(4-VPH)HSO\(_4\)] (0.015 g), under solvent-free conditions at 120 °C.\(^{33}\) This method has the advantages of good yields, shorter reaction times, and reusability of the catalyst over five additional times without losing its activity and product yield. At the same time, several methods are reported for the synthesis of thiazolopyrimidines or fused thiazolopyrimidines resulting from the reaction of 3,4-dihydropyrimidin-2(1\(H\))-thiones (Biginelli products) with chloroacetic acid, bromoacetyl chloride, methyl chloroacetate, ethyl bromoacetate, and 2-haloacetanilides.\(^{34-43}\)

Based upon these reports and the efficiency of acid catalyst poly(4-vinylpyridinium)hydrogen sulfate, we developed one-pot synthesis of benzo[\(h\)]thiazolo[2,3-\(b\)]quinazoline derivatives from 6-methoxy-1-tetralone (1), aryl aldehyde (2\(a-j\)), and thiourea (3) followed by cyclization with 3-(2-bromoacetyl)-2\(H\)-chromen-2-one (4) in poly(4-vinylpyridinium)hydrogen sulfate [P(4-VPH)HSO\(_4\)] (0.015 g) as an acid catalyst under solvent-free conditions at 120 °C with good yields (Table 1). The schematic representation is shown in Scheme 1. A plausible mechanism for formation of products is shown in Scheme 2. The catalyst P(4-VPH)HSO\(_4\) was prepared according to the literature procedure.\(^{44}\)

Table 1. Synthesis of 3-(9-hydroxy-3-methoxy-7-aryl-6,7,9,10-tetrahydro-5\(H\)-benzo[\(h\)]thiazolo[2,3-\(b\)]quinazolin-9-yl)-2\(H\)-chromen-2-ones (5\(a-j\)).

<table>
<thead>
<tr>
<th>Entry(^a)</th>
<th>Compound</th>
<th>Time (min)</th>
<th>Yield(^b) (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>5(a)</td>
<td>55</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>5(b)</td>
<td>50</td>
<td>89</td>
</tr>
<tr>
<td>3</td>
<td>5(c)</td>
<td>55</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>5(d)</td>
<td>60</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td>5(e)</td>
<td>50</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>5(f)</td>
<td>60</td>
<td>82</td>
</tr>
<tr>
<td>7</td>
<td>5(g)</td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>5(h)</td>
<td>45</td>
<td>89</td>
</tr>
<tr>
<td>9</td>
<td>5(i)</td>
<td>45</td>
<td>88</td>
</tr>
<tr>
<td>10</td>
<td>5(j)</td>
<td>45</td>
<td>86</td>
</tr>
</tbody>
</table>

Reaction conditions: (a) 6-Methoxy-1-tetralone (1, 1 mmol), aryl aldehyde (2\(a-j\), 1 mmol), thiourea (3, 1 mmol), 3-(2-Bromoacetyl)-2\(H\)-chromen-2-one (4, 1 mmol), P(4-VPH)HSO\(_4\) (0.015 g), 120 °C, neat conditions. \(^b\)Isolated yields.

In this work, we expected formation of the products benzo[\(h\)]thiazolo[2,3-\(b\)]quinazolines (6\(a-j\)) but, from the IR spectra, the appearance of a broad band in the range of 3439–3447 cm\(^{-1}\) for the hydroxy (–OH) group, the presence of two doublets in the range of 3.45–3.50 ppm and 4.05–4.12 ppm for thiazolidine (–CH\(_2\)–) protons and a singlet at 8.23–8.39 ppm for hydroxy (–OH) proton from \(^1\)H NMR, and the presence of signals
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Ar
a: C₆H₅   f: 3-NO₂C₆H₄
b: 4-ClC₆H₄   g: 4-OCH₃C₆H₄
c: 3-BrC₆H₄   h: 3,4,5-(OCH₃)₃C₆H₂
d: 4-FC₆H₄   i: 4-OH-3-OCH₃C₆H₃
e: 4-OHC₆H₄   j: 4-OH-3-OC₂H₅C₆H₃

P(4-VPH)HSO₄ = \[ \begin{array}{c}
\text{H} \\
\text{N} \\
\text{HSO}_4^- \\
\text{n}
\end{array} \]

at 42.2–42.5 ppm and 94.7–95.5 ppm for thiazolidine (–CH₂–) and –OH attached carbons, respectively, from $^{13}$C NMR confirmed the product as benzo[h]thiazolo[2,3-b]quinazolin-ols (5a–j) not the benzo[h]thiazolo[2,3-b]quinazolines (6a–j). The molecular ion peak from the mass spectra and elemental analyses data further confirmed the formation of products 5a–j.

2.2. Antibacterial activity

All the synthesized compounds (5a–j) were screened for their in vitro antibacterial activity against *Staphylococcus aureus* and *Bacillus thuringiensis* (gram positive), and *Escherichia coli* and *Klebsiella pneumoniae* (gram negative) bacterial strains with respect to the standard antibiotic drug gentamicin.

Zone of inhibition (ZOI) (in mm) values for the analogues (5a–j) at 100 μg/mL and the positive control drug gentamicin at 30 μg/mL were determined by agar disk diffusion method. The bacterial strains were grown and maintained on nutrient agar plates. All the compounds (100 μg) were dissolved in DMSO...
and transferred to each disk with the help of a micropipette, simultaneously maintaining the standard drug gentamicin (30 μg/disk). After overnight incubation at 37 °C, the resulting ZOIs were measured and compared with that of the standard drug. Control measurements were carried out with DMSO. All the experiments were performed in triplicate and the average ZOIs were recorded and are depicted in Table 2. The antibacterial activity data revealed that the compounds having electron donating groups like methoxy and ethoxy groups on aryl aldehyde, i.e. 5g, 5h, and 5j, showed good activity against all the tested bacterial strains. Compound 5i also showed good activity against all bacterial strains except *Escherichia coli*. In particular, compound 5g against *Bacillus thuringiensis* and 5h against both the gram-positive bacterial strains (*Staphylococcus aureus* and *Bacillus thuringiensis*) showed maximum ZOIs. Compounds 5b and 5e were inactive against both the gram-positive bacterial strains, and 5c was inactive against *Bacillus thuringiensis*. The remaining compounds were moderately active against all the tested bacterial strains.

In conclusion, we developed an efficient one-pot and solvent-free synthesis of coumarin incorporated fused thiazolylquinazolinol derivatives (5a-j) in shorter reaction times with good yields. All the newly synthesized compounds were screened for their in vitro antibacterial activity. Among all the compounds, those derived from 4-methoxy benzaldehyde (5g) against *Bacillus thuringiensis* and 3,4,5-trimethoxy benzaldehyde (5h) against

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**Scheme 2.** Plausible mechanism.
Table 2. Zone of inhibition values of 3-(9-hydroxy-3-methoxy-7-aryl-6,7,9,10-tetrahydro-5\(^H\)-benzo[\(h\)] thiazolo[2,3-\(b\)]quinazolin-9-yl)-2\(^H\)-chromen-2-ones (5a–j) at 100 \(\mu\)g/mL and positive control drug gentamicin at 30 \(\mu\)g/mL.

<table>
<thead>
<tr>
<th>Analogue</th>
<th>Zone of inhibition (mm)</th>
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<tbody>
<tr>
<td></td>
<td>S. aureus</td>
<td>B. thuringiensis</td>
<td>E. coli</td>
<td>K. pneumoniae</td>
</tr>
<tr>
<td>5a</td>
<td>9</td>
<td>6</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>5b</td>
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<td>6</td>
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<td>5e</td>
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<td>5f</td>
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<td>5i</td>
<td>10</td>
<td>9</td>
<td>4</td>
<td>11</td>
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<td>5j</td>
<td>10</td>
<td>8</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>15</td>
<td>18</td>
<td>16</td>
<td>14</td>
</tr>
</tbody>
</table>

Bacterial strains: Gram positive: S. aureus – Staphylococcus aureus, B. thuringiensis – Bacillus thuringiensis; Gram negative: E. coli – Escherichia coli, K. pneumoniae – Klebsiella pneumoniae ‘-’ Inactive.

Staphylococcus aureus and Bacillus thuringiensis showed good activity in comparison with the standard drug gentamicin. These compounds can be considered lead compounds for further development of potent antibacterial agents.

3. Experimental section

3.1. General

All the reagents and solvents were purchased from Aldrich/Merck and used without further purification. Melting points were determined in open capillaries using a Stuart SMP30 apparatus and are uncorrected. The progress of the reactions as well as purity of compounds was monitored by thin layer chromatography with F\(_{254}\) silica-gel precoated sheets using hexane/ethyl acetate 8/2 as eluent; UV light and iodine vapors were used for detection. IR spectra were recorded on a PerkinElmer 100S spectrometer utilizing KBr pellets. \(^1\)H NMR and \(^{13}\)C NMR spectra were obtained at 400 MHz and 100 MHz, respectively, on a Bruker spectrometer using DMSO-\(d_6\) as solvent and TMS as internal standard. Elemental analyses were performed on a Carlo-Erba model EA1108 analytical unit and the values are ±0.4% of theoretical values. Mass spectra were recorded on a Jeol JMSD-300 spectrometer.

3.2. General procedure for the synthesis of 3-(9-hydroxy-3-methoxy-7-aryl-6,7,9,10-tetrahydro-5\(^H\)-benzo[\(h\)]thiazolo[2,3-b]quinazolin-9-yl)-2\(^H\)-chromen-2-ones (5a–j)

To a mixture of 6-methoxy-1-tetralone (1, 1 mmol), aryl aldehyde (2a–j, 1 mmol), and thiourea (3, 1 mmol), P(4-VPH)HSO\(_4\) (0.015 g) was added and heated at 120 °C under neat conditions for 20 min. After consuming of all reactants (confirmed by TLC), to this mixture 3-(2-bromoacetyl)-2\(^H\)-chromen-2-one (4, 1 mmol) was added and heated at the same temperature for a further 25–40 min. After completion of the reaction as indicated by TLC, 5 mL of ethanol was added and the mixture was stirred at room temperature for an additional 10–15 min. The residue (catalyst) was separated by filtration and the filtrate was concentrated under reduced pressure; the crude product was crystallized from ethanol to afford the pure product.
3.3. Spectral data

3.3.1. 3-(9-Hydroxy-3-methoxy-7-phenyl-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5a)

Pale yellow solid; mp 244–246 °C; IR (KBr, cm⁻¹)νmax: 3443 (OH), 1717 (C=O), 1630 (C=N); ¹H NMR (400 MHz, DMSO-d₆): δ 1.55–1.61 (m, 1H), 2.09 (t, 1H, J = 7.2 Hz), 2.53 (t, 1H, J = 6.8 Hz), 2.55–2.69 (m, 1H), 3.51 (d, 1H, J = 12.8 Hz), 3.77 (s, 3H), 4.10 (d, 1H, J = 12.8), 5.56 (s, 1H), 6.81–6.97 (m, 6H), 7.15 (d, 1H, J = 8.4 Hz), 7.33–7.41 (m, 2H), 7.59–7.63 (m, 2H), 7.82–7.85 (m, 1H), 8.31 (s, 1H), 8.75 (s, 1H); ¹³C NMR (100 MHz, DMSO–d₆): δ 23.1, 27.0, 42.3, 55.2, 59.5, 94.8, 112.2, 114.2, 115.5, 118.0, 119.1, 122.9, 123.9, 124.8, 127.4, 127.7, 128.1, 128.4, 129.4, 132.8, 137.2, 137.8, 142.2, 153.2, 157.5, 159.6, 165.5; MS (ESI) m/z: 509 [M+H]⁺; Anal. Calcd. for C₂₃H₂₄N₂O₄S: C, 70.85; H, 4.76; N, 5.51. Found: C, 71.08; H, 4.92; N, 5.37.

3.3.2. 3-(7-(4-Chlorophenyl)-9-hydroxy-3-methoxy-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5b)

Brown solid; mp 255–257 °C; IR (KBr, cm⁻¹)νmax: 3442 (OH), 1720 (C=O), 1605 (C=N), 759 (C-Cl); ¹H NMR (400 MHz, DMSO-d₆): δ 1.57–1.61 (m, 1H), 2.09 (t, 1H, J = 7.6 Hz), 2.53–2.69 (m, 2H), 3.50 (d, 1H, J = 12.8 Hz), 3.77 (s, 3H), 4.09 (d, 1H, J = 12.8 Hz), 5.62 (s, 1H), 6.82 (s, 1H), 6.92–7.00 (m, 3H), 7.20–7.28 (m, 1H), 7.41 (d, 2H, J = 8.0 Hz), 7.58 (d, 2H, J = 8.4 Hz), 7.66 (d, 1H, J = 7.6 Hz), 7.84 (d, 1H, J = 8.0 Hz), 8.27 (s, 1H), 8.76 (s, 1H); ¹³C NMR (100 MHz, DMSO–d₆): δ 23.0, 27.0, 42.5, 55.27, 58.7, 94.8, 112.4, 114.2, 115.4, 116.0, 117.9, 118.7, 119.1, 122.9, 124.8, 127.7, 128.4, 129.5, 130.5, 133.0, 133.2, 136.7, 137.3, 153.7, 157.6, 158.6, 159.6, 165.6; MS (ESI) m/z: 543 [M⁺]; Anal. Calcd. for C₃₀H₂₄ClN₂O₄S: C, 66.35; H, 4.27; N, 5.16. Found: C, 66.52; H, 4.09; N, 5.34.

3.3.3. 3-(7-(3-Bromophenyl)-9-hydroxy-3-methoxy-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5c)

Pale yellow solid; mp 238–240 °C; IR (KBr, cm⁻¹)νmax: 3447 (OH), 1719 (C=O), 1630 (C=N), 690 (C-Br); ¹H NMR (400 MHz, DMSO-d₆): δ 1.55–1.64 (m, 1H), 2.07–2.13 (m, 1H), 2.54–2.69 (m, 2H), 3.48 (d, 1H, J = 12.4 Hz), 3.77 (s, 3H), 4.12 (d, 1H, J = 12.8 Hz), 5.61 (s, 1H), 6.82 (s, 1H), 6.93 (d, 1H, J = 8.8 Hz), 7.09 (s, 1H), 7.17–7.22 (m, 2H), 7.32 (s, 1H), 7.38–7.45 (m, 1H), 7.52–7.96 (m, 3H), 8.24 (s, 1H), 8.34 (s, 1H), 8.76 (s, 1H); ¹³C NMR (100 MHz, DMSO–d₆): δ 23.2, 27.2, 42.9, 54.3, 59.1, 94.4, 112.5, 114.8, 127.0, 127.2, 127.4, 127.8, 128.0, 128.5, 128.6, 129.2, 129.5, 131.7, 131.9, 132.7, 133.4, 136.5, 141.4, 143.4, 149.0, 152.0, 158.9, 159.1, 164.4; MS (ESI) m/z: 587 [M⁺]; Anal. Calcd. for C₃₀H₂₃BrN₂O₄S: C, 61.33; H, 3.95; N, 4.77. Found: C, 61.58; H, 3.78; N, 4.62.

3.3.4. 3-(7-(4-Florophenyl)-9-hydroxy-3-methoxy-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5d)

Brown solid; mp 259–261 °C; IR (KBr, cm⁻¹)νmax: 3440 (OH), 1716 (C=O), 1628 (C=N), 810 (C-F); ¹H NMR (400 MHz, DMSO-d₆): δ 1.58–1.63 (m, 1H), 2.06–2.12 (m, 1H), 2.53–2.55 (m, 1H), 2.67 (t, 1H, J = 6.4 Hz), 3.50 (d, 1H, J = 12.4 Hz), 3.77 (s, 3H), 4.10 (d, 1H, J = 12.8 Hz), 5.62 (s, 1H), 6.69 (s, 1H), 6.82 (s, 1H), 6.83–6.95 (m, 1H), 7.03 (s, 1H), 7.21 (d, 2H, J = 8.4 Hz), 7.29 (d, 1H, J = 7.2 Hz), 7.42 (d, 1H, J = 7.6 Hz),
3.3.5. 3-(9-Hydroxy-7-(4-hydroxyphenyl)-3-methoxy-6,7,9,10-tetrahydro-5H-benzo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5e)

White solid; mp 254–256 °C; IR (KBr, cm⁻¹)νmax: 3443 (OH), 1717 (C=O), 1632 (C=N); ¹H NMR (400 MHz, DMSO-d₆): δ 1.59–1.66 (m, 1H), 2.06 (t, 1H, J = 7.2 Hz), 2.55 (t, 1H, J = 7.2 Hz), 2.64–2.68 (m, 1H), 2.49 (d, 1H, J = 12.8 Hz), 3.77 (s, 3H), 4.07 (d, 1H, J = 12.8 Hz), 5.43 (s, 1H), 6.22 (s, 1H), 6.70 (d, 2H, J = 8.4 Hz), 6.82 (d, 1H, J = 7.6 Hz), 6.92–6.94 (m, 1H), 7.19 (d, 1H, J = 8.4 Hz), 7.40 (t, 1H, J = 7.6 Hz), 7.58–7.83 (m, 3H), 7.84–8.30 (m, 2H), 8.69 (s, 1H), 9.38 (s, 1H); ¹³C NMR (100 MHz, DMSO-d₆): δ 23.2, 27.1, 42.2, 55.2, 59.2, 94.7, 111.2, 112.6, 114.2, 115.1, 115.5, 118.1, 119.2, 122.8, 123.7, 124.5, 125.1, 127.8, 129.0, 129.3, 130.0, 132.7, 137.2, 141.7, 153.3, 157.4, 159.5, 165.0; MS (ESI) m/z: 525 [M+H]⁺; Anal. Calcd. for C₃₀H₂₃FN₂O₄S: C, 68.43; H, 4.40; N, 5.32. Found: C, 68.28; H, 4.58; N, 5.16.

3.3.6. 3-(9-Hydroxy-3-methoxy-7-(3-nitrophenyl)-6,7,9,10-tetrahydro-5H-benzo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5f)

Yellow solid; mp 241–243 °C; IR (KBr, cm⁻¹)νmax: 3444 (OH), 1717 (C=O), 1631 (C=NO₂); ¹H NMR (400 MHz, DMSO-d₆): δ 1.58–1.65 (m, 1H), 2.12–2.54 (m, 1H), 2.64–2.71 (m, 2H), 3.48 (d, 1H, J = 12.0 Hz), 3.76 (s, 3H), 4.13 (d, 1H, J = 12.4 Hz), 5.87 (s, 1H), 6.82 (s, 1H), 6.94 (d, 1H, J = 8.0 Hz), 7.08 (d, 1H, J = 8.4 Hz), 7.36–7.48 (m, 3H), 7.53–8.25 (m, 5H), 8.39 (s, 1H), 8.82 (s, 1H); ¹³C NMR (100 MHz, DMSO-d₆): δ 23.2, 27.2, 42.4, 55.2, 59.6, 94.7, 115.4, 118.0, 118.6, 118.8, 124.5, 124.7, 125.4, 126.9, 127.1, 128.0, 128.1, 128.4, 128.6, 129.4, 129.6, 132.8, 136.5, 136.7, 137.0, 142.2, 153.2, 157.7, 166.5; MS (ESI) m/z: 554 [M+H]⁺; Anal. Calcd. for C₃₀H₂₃N₃O₆S: C, 65.09; H, 4.19; N, 7.59. Found: C, 64.91; H, 4.32; N, 7.76.

3.3.7. 3-(9-Hydroxy-3-methoxy-7-(4-methoxyphenyl)-6,7,9,10-tetrahydro-5H-benzo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5g)

White solid; mp 237–239 °C; IR (KBr, cm⁻¹)νmax: 3440 (OH), 1720 (C=O), 1628 (C=N), 1155 (C=O–C); ¹H NMR (400 MHz, DMSO-d₆): δ 1.63–2.10 (m, 2H), 2.55 (t, 1H, J = 6.8 Hz), 2.64–2.68 (m, 1H), 3.44 (s, 3H), 3.50 (d, 1H, J = 12.8 Hz), 3.74 (s, 3H), 4.05 (d, 1H, J = 12.8 Hz), 5.54 (s, 1H), 6.37 (s, 1H), 6.82–6.95 (m, 4H), 7.15–7.20 (m, 2H), 7.40 (t, 1H, J = 7.6 Hz), 7.56–7.67 (m, 2H), 7.82–7.84 (m, 1H), 8.23 (s, 1H), 8.72 (s, 1H); MS (ESI) m/z: 539 [M+H]⁺; Anal. Calcd. for C₃₁H₂₆N₂O₅S: C, 65.13; H, 4.87; N, 5.26. Found: C, 65.38; H, 4.67; N, 5.08.

3.3.8. 3-(9-Hydroxy-3-methoxy-7-(3,4,5-trimethoxyphenyl)-6,7,9,10-tetrahydro-5H-benzo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5h)

White solid; mp 226–228 °C; IR (KBr, cm⁻¹)νmax: 3439 (OH), 1720 (C=O), 1627 (C=N), 1142 (C=O–C); ¹H NMR (400 MHz, DMSO-d₆): δ 1.62–1.78 (m, 1H), 2.05–2.15 (m, 1H), 2.55–2.84 (m, 2H), 3.48 (d, 1H, J = 12.4 Hz), 3.63 (s, 3H), 3.72 (s, 3H), 3.74 (s, 3H), 3.76 (s, 3H), 4.16 (d, 1H, J = 12.4 Hz), 5.83 (s, 1H), 6.22 (d, 1H, J = 8.4 Hz), 6.63 (d, 1H, J = 8.8 Hz), 6.79–6.83 (m, 1H), 6.91–6.94 (m, 1H), 7.15–7.87 (m, 4H), 8.27 (s,
1H), 8.35 (s, 1H), 8.64 (s, 1H); MS (ESI) m/z: 599 [M+H]^+; Anal. Calcd. for C_{33}H_{30}N_{2}O_{7}S: C, 66.21; H, 5.05; N, 4.68. Found: C, 66.40; H, 4.84; N, 4.46.

3.3.9. 3-(9-Hydroxy-7-(4-hydroxy-3-methoxyphenyl)-3-methoxy-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5i)
White solid; mp 230–232 °C; IR (KBr, cm\(^{-1}\))\(v_{\text{max}}\): 3440 (OH), 1721 (C=O), 1629 (C=N); \(^{1}\)H NMR (400 MHz, DMSO-\(d_{6}\)): \(\delta\) 1.62–1.66 (m, 1H), 2.07 (t, 1H, \(J = 7.6\) Hz), 2.55 (t, 1H, \(J = 6.8\) Hz), 2.64–2.68 (m, 1H), 3.44 (s, 3H), 3.49 (d, 1H, \(J = 12.4\) Hz), 3.76 (s, 3H), 4.10 (d, 1H, \(J = 12.4\) Hz), 5.42 (s, 1H), 6.38 (s, 1H), 6.82–6.94 (m, 1H), 7.18 (d, 1H, \(J = 8.4\) Hz), 7.38 (t, 1H, \(J = 8.0\) Hz), 7.54–7.65 (m, 4H), 7.83 (d, 2H, \(J = 8.0\) Hz), 8.30 (s, 1H), 8.68 (s, 1H), 8.91 (s, 1H); MS (ESI) m/z: 555 [M+H]^+; Anal. Calcd. for C_{31}H_{26}N_{2}O_{6}S: C, 67.13; H, 4.73; N, 5.05. Found: C, 67.30; H, 4.58; N, 5.22.

3.3.10. 3-(7-(3-Ethoxy-4-hydroxyphenyl)-9-hydroxy-3-methoxy-6,7,9,10-tetrahydro-5H-benzo[h]thiazolo[2,3-b]quinazolin-9-yl)-2H-chromen-2-one (5j)
White solid; mp 233–235 °C; IR (KBr, cm\(^{-1}\))\(v_{\text{max}}\): 3440 (OH), 1723 (C=O), 1630 (C=N), 1139 (C–O–C); \(^{1}\)H NMR (400 MHz, DMSO-\(d_{6}\)): \(\delta\) 1.05 (t, 3H, \(J = 7.2\) Hz), 1.61–1.66 (m, 1H), 2.07 (t, 1H, \(J = 8.0\) Hz), 2.54 (t, 1H, \(J = 7.6\) Hz), 2.63–2.69 (m, 1H), 3.41–3.46 (m, 2H), 3.49 (d, 1H, \(J = 12.4\) Hz), 3.76 (s, 3H), 4.10 (d, 1H, \(J = 12.4\) Hz), 5.39 (s, 1H), 6.71 (s, 1H), 6.83 (d, 1H, \(J = 6.0\) Hz), 6.91–6.94 (m, 1H), 7.18 (d, 1H, \(J = 8.4\) Hz), 7.39 (t, 1H, \(J = 7.6\) Hz), 7.54–7.85 (m, 5H), 8.31 (s, 1H), 8.68 (s, 1H), 8.85 (s, 1H); MS (ESI) m/z: 569 [M+H]^+; Anal. Calcd. for C_{32}H_{28}N_{2}O_{6}S: C, 67.59; H, 4.96; N, 4.93. Found: C, 67.73; H, 4.80; N, 5.12.

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References


