Studies on quinazolines: Part II—Synthesis and antimicrobial evaluation of some 2,2-disubstituted-3,3-biquinazolin-4(3H)-ones

A A F Wasfy
Chemistry Department, Faculty of Science, Benha University, Benha, Egypt

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N-(2-Styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-4-oxo-3H-quinazolin-3-yl)-2-aminobenzamides 6a-c react with triethyl orthoesters to furnish some new 2-styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-2-substituted-3,3-biquinazolin-4(3H)-ones (7a-c—9a-c). An alternative synthesis of (7-9)b has been accomplished by reaction of acetylanthranil with 2-amino-2-styryl-2-p-chlorostyryl- or 2-p-nitrostyryl-quinazolin-4(3H)-ones 4a-c. The synthesised products are tested for antimicrobial activities using methaqualone as reference standard.

Quinazolin-4(3H)-ones substituted in the 3-position with a heterocyclic system are attracting the attention of various types of chemists. Compounds of this type appear to be important because of their sedative, hypnotic and anticonvulsive effects. An examination of the current literature shows that a series of 2-aryl-3-(1,3,4-thiadiazol-2-yl)quinazolin-4(3H)-ones had little hypothermic activity, and that some patented pyridylsubstituted quinazolinones have shown antinflammatory activity. In previous communications, we reported the synthesis of several 3-(2-phenyl-1,3,4-thiadiazolin-3-yl)-2-methyl-5-substituted-quinazolin-4(3H)-ones, and 4-(thiazol- or oxazol-2-ylidenehydrazinocarbonylmethoxy)-2-methylquinazolin-4(3H)-ones which in a preliminary biological screening, showed interesting antibacterial activities. These observations prompted us to incorporate the 2-alkylquinazolin-4(3H)-one moiety into the quinazolin-4(3H)-one ring with a view to testing the novel 2,2-disubstituted-3,3-biquinazolin-4(3H)-ones for antimicrobial activity against several strains of bacteria and fungi and for recording the influence of different substituents at C-2,2 of the biquinazolinone molecule on their biological properties. Methaqualone was included in all tests for comparison purposes. The syntheses of the hitherto unknown 2,2-disubstituted-3,3-biquinazolin-4(3H)-ones (7a-c—9a-c) were carried out according to the route given in the Scheme I. The required compound 3-amino-2-methylquinazolin-4(3H)-one 1 was prepared by reacting 2-methyl-3,1-benzoazin-4-one with hydrazine hydrate in pyridine. Thus, the N-amino group in 1 was quantitatively protected with phthalic anhydride to afford the 3-phthalimido-2-methylquinazolin-4(3H)-one 2. Compound 2 on treatment with aromatic aldehydes, namely, benzoaldehyde, p-chlorobenzaldehyde and p-nitrobenzaldehyde in the presence of p-toluene sulfonic acid as catalyst to furnish 3-phthalimido-2-styryl-, 2-p-chlorostyryl- or 2-p-nitrostyrylquinazolin-4(3H)-ones 3a-c. Dephtthaloylation of 3a-c with 0.5M methanolic hydrazine at room temperature gave 3-amino-2-styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-quinazolin-4(3H)-ones 4a-c with the released phthalazin-1,4-dione (Scheme II). We have now prepared the title compounds 7a-c—9a-c using N-(2-styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-4-oxo-3H-quinazolin-3-yl)-2-nitrobenzamides 5a-c as the starting material. Thus, action of α-nitrobenzoyl chloride on 2-aminoquinazolin-4(3H)-ones 4a-c in acetonitrile solution gave the expected 5a-c in 80–85% yield. When compounds 5a-c were treated with stannous chloride in aqueous concentrated hydrochloric acid, the N-(2-styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-4-oxo-3H-quinazolin-3-yl)-2-nitrobenzamides 6a-c were obtained. From these products 6a-c and the appropriate orthoesters the 2,2-disubstituted-3,3-biquinazolin-4(3H)-ones (7a-c—9a-c) were formed in very good yield (Scheme II). Moreover, the synthesis of this heterocyclic ring system, i.e., (7-9)b, was achieved in high yield, by a facile one-step alternative route starting from the readily available acetylanthranil which was allowed to react with 2-amino-2-styryl-, 2-p-chlorostyryl- or 2-p-nitrostyrylquinazolin-4(3H)-ones 4a-c in boiling xylene by eliminating water azeotropically. The structure of these new products were supported by elemental analyses, IR and 1H NMR spectra (Table I).
WASFY: STUDIES ON QUINAZOLINES: PART II

Scheme I

1. 

2. 

3. 

4. 

5. 

6. 

Scheme II

1. 

2. 

3. 

4.
<table>
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<tr>
<th>Compd</th>
<th>R¹</th>
<th>R²</th>
<th>m.p. °C</th>
<th>Yield (%)</th>
<th>Mol. formula</th>
<th>Calc. (%)</th>
<th>Found (%)</th>
<th>lH NMR (DMSO-d₆) (δ, ppm)</th>
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<tr>
<td>1</td>
<td>-</td>
<td>-</td>
<td>143-44</td>
<td>17.2(82)</td>
<td>C₅H₈NO₂</td>
<td>61.70</td>
<td>5.17</td>
<td>23.98</td>
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<tr>
<td>3a</td>
<td>A</td>
<td>-</td>
<td>230-32</td>
<td>6.3(67)</td>
<td>C₂₄H₁₄NO₃</td>
<td>73.27</td>
<td>3.84</td>
<td>10.68</td>
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<tr>
<td>3b</td>
<td>B</td>
<td>-</td>
<td>201-03</td>
<td>6.5(63)</td>
<td>C₁₇H₁₄NO₃</td>
<td>66.88</td>
<td>3.63</td>
<td>13.76</td>
</tr>
<tr>
<td>3c</td>
<td>C</td>
<td>-</td>
<td>260-62</td>
<td>7.3(69)</td>
<td>C₂₄H₁₄NO₃</td>
<td>73.27</td>
<td>3.84</td>
<td>10.68</td>
</tr>
<tr>
<td>4a</td>
<td>A</td>
<td>-</td>
<td>210-12</td>
<td>2.9(78)</td>
<td>C₁₇H₁₄NO₃</td>
<td>66.88</td>
<td>3.63</td>
<td>13.76</td>
</tr>
<tr>
<td>5c</td>
<td>C</td>
<td>-</td>
<td>271-73</td>
<td>3.5(85)</td>
<td>C₁₇H₁₄NO₃</td>
<td>66.88</td>
<td>3.63</td>
<td>13.76</td>
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<tr>
<td>6a</td>
<td>A</td>
<td>-</td>
<td>162-64</td>
<td>1.6(66)</td>
<td>C₁₇H₁₄NO₃</td>
<td>66.88</td>
<td>3.63</td>
<td>13.76</td>
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<tr>
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<td>-</td>
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<td>13.76</td>
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<tr>
<td>C</td>
<td>CH₂CH₃</td>
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<td>C₂₆H₁₉NO₄</td>
<td>67.09</td>
<td>4.11</td>
<td>15.04</td>
</tr>
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Table 1 — Characterization data of various compounds synthesized
Table I — Characterization data of various compounds synthesized — Contd

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<tr>
<th>Compd</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>m.p.</th>
<th>Yield</th>
<th>Mol. formula</th>
<th>Calc. (%) (Found)</th>
<th>&lt;sup&gt;1&lt;/sup&gt;H NMR (DMSO-d&lt;sub&gt;6&lt;/sub&gt;) (δ, ppm)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>°C</td>
<td>g (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>6c</td>
<td>C</td>
<td>-</td>
<td>180-82&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.8(68)</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;7&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;4&lt;/sub&gt; (427.41)</td>
<td>64.63 4.00 16.38</td>
<td>5.55 (broad, 2H, NH&lt;sub&gt;2&lt;/sub&gt;, D&lt;sub&gt;2&lt;/sub&gt;O exchangeable), 6.45(d, 1H, J = 15 Hz, β-olefinic-H), 7.23-8.46 (a set of signals, 13H, Ar-H and α-olefinic-H), 10.50 (broad, 1H, NH, D&lt;sub&gt;2&lt;/sub&gt;O exchangeable).</td>
</tr>
<tr>
<td>7a</td>
<td>A</td>
<td>H</td>
<td>202-04&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.36(92)</td>
<td>C&lt;sub&gt;24&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt; (392.41)</td>
<td>73.45 4.10 14.27</td>
<td>6.30(d, 1H, J = 15 Hz, β-olefinic-H), 7.10-8.32 (a set of signals, 15H, Ar-H and α-olefinic-H and quinazolone H-2).</td>
</tr>
<tr>
<td>7b</td>
<td>A</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>183-85&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.36(90)</td>
<td>C&lt;sub&gt;24&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt; (406.44)</td>
<td>73.87 4.46 13.78</td>
<td>2.42 (s, 3H, CH&lt;sub&gt;3&lt;/sub&gt;), 6.36 (d, 1H, J = 15Hz, β-olefinic-H), 7.14-8.38 (a set of signals, 14H, Ar-H and α-olefinic-H).</td>
</tr>
<tr>
<td>7c</td>
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<td>CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>222-24&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.36(87)</td>
<td>C&lt;sub&gt;25&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt; (420.47)</td>
<td>74.27 4.79 13.32</td>
<td>1.10 (t, 3H, CH&lt;sub&gt;3&lt;/sub&gt;), 2.58 (q, 2H, CH&lt;sub&gt;2&lt;/sub&gt;), 6.32 (d, 1H, J = 15Hz, β-olefinic-H), 7.14-8.33 (a set of signals, 14H, Ar-H and α-olefinic-H).</td>
</tr>
<tr>
<td>8a</td>
<td>B</td>
<td>H</td>
<td>194-96&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.38(90)</td>
<td>C&lt;sub&gt;25&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;CIN&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt; (426.86)</td>
<td>67.53 3.54 13.12</td>
<td>6.22(d, 1H, J = 15 Hz, β-olefinic-H), 7.08-8.34 (a set of signals, 14H, Ar-H and α-olefinic-H and quinazolone H-2).</td>
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<td>B</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>173.75&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.40(91)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;CIN&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt; (440.89)</td>
<td>68.10 3.88 12.70</td>
<td>2.36 (s, 3H, CH&lt;sub&gt;3&lt;/sub&gt;), 6.26 (d, 1H, J = 15Hz, β-olefinic-H), 7.09-8.38 (a set of signals, 13H, Ar-H and α-olefinic-H).</td>
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<tr>
<td>8c</td>
<td>B</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>218-20&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.38(85)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;CIN&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt; (454.91)</td>
<td>68.64 4.21 12.31</td>
<td>1.08 (t, 3H, CH&lt;sub&gt;3&lt;/sub&gt;), 2.62 (q, 2H, CH&lt;sub&gt;2&lt;/sub&gt;), 6.26 (d, 1H, J = 15Hz, β-olefinic-H), 7.15-8.44 (a set of signals, 13H, Ar-H and α-olefinic-H).</td>
</tr>
<tr>
<td>9a</td>
<td>C</td>
<td>H</td>
<td>215-17&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.40(92)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;4&lt;/sub&gt; (437.41)</td>
<td>65.90 3.45 16.01</td>
<td>6.40 (d, 1H, J = 15 Hz, β-olefinic-H), 7.20-8.41 (a set of signals, 14H, Ar-H and α-olefinic-H and quinazolone H-2).</td>
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<tr>
<td>9b</td>
<td>C</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>192-94&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.41(93)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;4&lt;/sub&gt; (451.44)</td>
<td>66.51 3.79 15.51</td>
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</tr>
<tr>
<td>9c</td>
<td>C</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>230-32&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.40(88)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;4&lt;/sub&gt; (465.46)</td>
<td>67.09 4.11 15.04</td>
<td>1.08 (t, 3H, CH&lt;sub&gt;3&lt;/sub&gt;), 2.66 (q, 2H, CH&lt;sub&gt;2&lt;/sub&gt;), 6.48 (d, 1H, J = 15Hz, β-olefinic-H), 7.27-8.49 (a set of signals, 13H, Ar-H and α-olefinic-H).</td>
</tr>
</tbody>
</table>

<sup>1</sup>A = styryl; B = p-chlorostyryl; C = p-nitrostyryl.
<sup>2</sup>Solvent for crystallization: *Ethanol; *Methanol + benzene; *(Ethanol + dimethyl formamide); *Methanol; *(Dioxane); *Benzene; *(Acetic acid); *(Methanol + chloroform); *(Ethyl acetate); *(Toluene).

**Antimicrobial activity**

The antimicrobial activity of synthesized derivatives was examined in vitro by filter-paper disc method<sup>3</sup>. All compounds were tested for activity against several strains of Gram-positive and Gram-negative bacteria and selected fungi using methaqualone as a reference standard. The culture medium was normal nutrient agar supplemented with 1g of yeast per ml. According to the solubility of the tested compounds, different polar and nonpolar solvents were used; good solubility was found in 8 % (V/V) acetone for all the tested compounds. Based on the previous preliminary test, closely spaced test con-
centrations were selected; they are 500, 250, 125 μg/L. Methaqualone was dissolved in filter sterilized 10 mL of 8% acetone (VIV) and employed in similar concentration as control. A qualitative screen was performed on all compounds while quantitative assays were done on active compounds only. The results are summarized in Table II. The data indicate that antimicrobial activity is affected by the substitution at 2,2-positions of the biquinazolinone compound. The results showed that most of the compounds were moderately active against different strains of bacteria and fungi as compared to standard. Regarding the structure-activity relationships, it is clear that compounds having R = 4-chlorostyryl or 4-nitrostyryl in combination with R1 = ethyl group at 2,2-position of the biquinazolinonyl moiety were found to show higher activity over those having R1 = hydrogen or methyl group.

**Experimental Section**

All melting points were taken in open capillary tubes and are uncorrected. IR spectra in KBr were recorded on a shimadzu 470 spectrophotometer; and 1H NMR spectra in DMSO on a Joel Fx 90 Q9 MHz (Fourier transform NMR spectrometer) using TMS as internal reference (chemical shifts in δ, ppm).

3-Amino-2-methylquinazolin-4(3H)-one 1. A mixture of anthranilic acid (26g, 0.19 mole) and acetic anhydride (142 mL, 98%, 1.5 mole) was heated under reflux for 4hr. The excess of acetic anhydride was then distilled off under reduced pressure. On chilling the flask the residue solidified, the crude benzoxazole was dissolved in hot, dry ethyl acetate, the solution was decolourized by charcoal, and the filtrate was treated with n-hexane just to remove turbidity and was chilled in an ice-bath. A second crop was obtained by concentration of the mother liquor, the product was washed sparingly with cold ethyl acetate-n-hexane and was dried in vacuo over calcium chloride. The intermediate benzoxazin-4-one obtained as a pure solid, was used up immediately for the next step, because of its unstable and highly reactive nature, yield 20.2g (66 %), mp 79-81 °C (lit. yield 66.7 %, m.p. 80-81 °C).

A mixture of benzoxazin-4-one (19.3 g, 0.12 mole) and hydrazine hydrate (7.3 mL, 99 %, 0.15 mole) in dried pyridine (60 mL) was refluxed for 5hr. It was allowed to cool, then poured with stirring in ice-cold distilled water and kept overnight in a refrigerator. The resulting solid was washed with cold water, dried and recrystallised from a suitable solvent to furnish 1. 3-Phthalimido-2-methylquinazolin-4(3H)-one 2. A mixture of 1 (16.5g, 0.094 mole) and phthalic anhydride (17.8g, 0.12 mole) in chloroform (150 mL) was heated under reflux for 5hr. The solvent was distilled and the residual solid filtered with a small volume of methanol. Recrystallization from a suitable solvent gave 2.

<table>
<thead>
<tr>
<th>Compd</th>
<th>Bacillus subtilis A MIC</th>
<th>Bacillus cereus A MIC</th>
<th>Escherichia coli A MIC</th>
<th>Aspergillus niger A MIC</th>
<th>Penicillium notatum A MIC</th>
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<tbody>
<tr>
<td>7a</td>
<td>+</td>
<td>1.27</td>
<td>+</td>
<td>0.64</td>
<td>+</td>
</tr>
<tr>
<td>7b</td>
<td>++</td>
<td>1.23</td>
<td>+</td>
<td>0.62</td>
<td>+</td>
</tr>
<tr>
<td>7c</td>
<td>++</td>
<td>0.59</td>
<td>++</td>
<td>1.19</td>
<td>+</td>
</tr>
<tr>
<td>8a</td>
<td>++</td>
<td>1.17</td>
<td>+</td>
<td>0.58</td>
<td>++</td>
</tr>
<tr>
<td>8b</td>
<td>++</td>
<td>0.57</td>
<td>++</td>
<td>0.58</td>
<td>++</td>
</tr>
<tr>
<td>8c</td>
<td>++</td>
<td>0.55</td>
<td>++</td>
<td>0.57</td>
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<tr>
<td>9a</td>
<td>++</td>
<td>1.14</td>
<td>++</td>
<td>0.57</td>
<td>++</td>
</tr>
<tr>
<td>9b</td>
<td>++</td>
<td>0.55</td>
<td>++</td>
<td>0.55</td>
<td>++</td>
</tr>
<tr>
<td>9c</td>
<td>++</td>
<td>0.54</td>
<td>++</td>
<td>0.54</td>
<td>++</td>
</tr>
<tr>
<td>M*</td>
<td>++</td>
<td>0.50</td>
<td>++</td>
<td>0.50</td>
<td>++</td>
</tr>
</tbody>
</table>

1 The width of the inhibition zone indicates the potency of activity (diameter of the zone, mm):
   + mild (1-7)
   ++ moderate (8-13)
   +++ marked (14-17)

2 The results of control samples (showing negative response) are not included.

3 Origin of cultures: Botany Department, Faculty of Science, Benha University, Benha (Egypt).

4 Methaqualone
Reaction of 2 with benzaldehydes. General procedure. To a solution of 2 (7.3 g, 0.024 mole) in anhydrous toluene (100 mL) were added 0.03 mole of aldehydes, namely, benzaldehyde (3.0 g), p-chlorobenzaldehyde (4.2 g) or p-nitrobenzaldehyde (4.5 g) and a few crystals of p-toluene sulfonic acid. The mixture was refluxed with a water knockout trap for 6 hr, the solvent was distilled and the residue crystallized from an appropriate solvent to furnish 3a-c.

3-Amino-2-styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-quinazolin-4(3H)-ones 4a-c. Compounds 3a-c (0.014 mole), namely, 3-phthalimido-2-styryl-(5.5 g), 2-p-chlorostyryl- (6 g) or 2-p-nitrostyrylquinazolin-4(3H)-ones (6.1 g) were dissolved in 0.5 M methanolic hydrazine by slight warming and the solution was left at room temperature overnight. The solvent and excess hydrazine were removed under reduced pressure and the residue repeatedly washed with 2 N HCl to remove the insoluble phthalyl hydrazine so formed and the soluble hydrochlorides of 4a-c were obtained by distillation of the solvent in vacuo. The hydrochlorides were dissolved in ethyl acetate containing triethylamine (3.7 mL, 0.04 mole) and stirred for 30 min. at room temperature and cooled to 0°C. The triethylamine hydrochlorides were filtered off and the free amino-heterocyclic compounds 4a-c were obtained by distillation of the solvent in vacuo. Recrystallization of the solid from a proper solvent gave 4a-c.

N-(2-Styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-4-oxo-3H-quinazolin-3-yl)-2-nitrobenzamides 5a-c. Equimolar amounts (0.009 mole) of compounds 4a-c, namely, 2-amino-2-styryl- (2.4 g), 2-p-chlorostyryl- (2.7 g) or 2-p-nitrostyryl-quinazolin-4(3H)-ones (2.8 g) and 2-nitrobenzoyl chloride (1.2 mL, 97 %) in acetonitrile (25 mL) were refluxed for 7-8 hr. Excess solvent was distilled off in vacuo. The solid separated on cooling was recrystallized from an appropriate solvent to give 5a-c.

N-(2-Styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-4-oxo-3H-quinazolin-3-yl)-2-aminobenzenamides 6a-c. Compounds 5a-c (0.0063 mole), namely, N-2-styryl-(2.6 g), 2-p-chlorostyryl-(2.8 g) or 2-p-nitrostyryl-4-oxo-3H-quinazolin-3-yl) -2-aminobenzamides (2.9 g) were added to a stirred suspension of finely powdered stannous chloride (3.4 g, 0.018 mole) in conc. HCl (8.4 mL, 37 %, 0.1 mole) at such a rate so that the temperature of the slurry was maintained below 10 °C. After the complete addition of the nitro compound, the resulting mixture was stirred for an additional 24 hr at 20 °C. White slurry thus obtained was diluted with cold water and sodium hydroxide (40 %) was added till the salts of tin were dissolved. The solution was extracted with ethyl acetate (3x100 mL), the extracts were dried (Na2SO4) and evaporated in vacuo to give an oil, which on standing, solidified. The solid products formed were crystallized from an appropriate solvent to give 6a-c.

2-Styryl-, 2-p-chlorostyryl- or 2-p-nitrostyryl-2-unsubstituted-, 2-methyl- or 2-ethyl-3,3-biquinazolin-4(3H)-ones (7a-c-9a-c). Compounds 6a-c (0.001 mole), namely, N-(2-styryl- (0.4 g), 2-p-chlorostyryl- (0.42 g) or 2-p-nitrostyryl-4-oxo-3H-quinazolin-3-yl)-2-aminobenzamides (0.43 g) and appropriate orthoester (0.02 mole), namely, triethyl orthoformate (3.3 mL), triethyl orthoacetate (3.6 mL) or triethyl orthopropionate (4 mL) were heated under reflux for 5 hr. After cooling, the crystalline solid which separated out, was recrystallized from an appropriate solvent to furnish 2,2-R1,3, 3-biquinazolin-4(3H)-one derivatives (7a-c-9a-c).

Reaction of acetylanthranil with 4a-c to give (7-9)b. Equimolar amounts (0.001 mole) of acetylanthranil (0.16 g) and 2-amino-2-styryl- (0.26 g), 2-p-chlorostyryl- (0.29 g) or 2-p-nitrostyryl-quinazolin-4(3H)-ones (0.3 g) 4a-c in xylene (10 mL) were refluxed for 24 hr. The products separated were identified by comparison (mp and mixed mp, NMR, IR) with an authentic samples prepared by the above method.

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