



## Synthesis and Antimicrobial Activity of Newer Quinazolinones

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**Abstract:** 2-alkyl-6-bromo-3,1-benzoxazine-4-one (2) is synthesized by treating p-Bromoanthranilic acid and Acetylorchloride or Benzoylchloride. Reaction of 2-alkyl-6-bromo-3,1-benzoxazine-4-one (2) with hydrazinehydrate furnish the corresponding 3-Amino-2-methyl-6-bromoquinazolin-4(3H)-one (3) which on reaction with benzaldehyde afford N,N - arylidene derivative (4). Reaction of 4 with various diazonium salts yields 6-bromo-2-alkyl/aryl-3{[phenyl(phenyldiazenyl)methylene]amino}quinazolin-4(3H)-one .

**Key words:** Synthesis, quinazolidinone, antibacterial activity

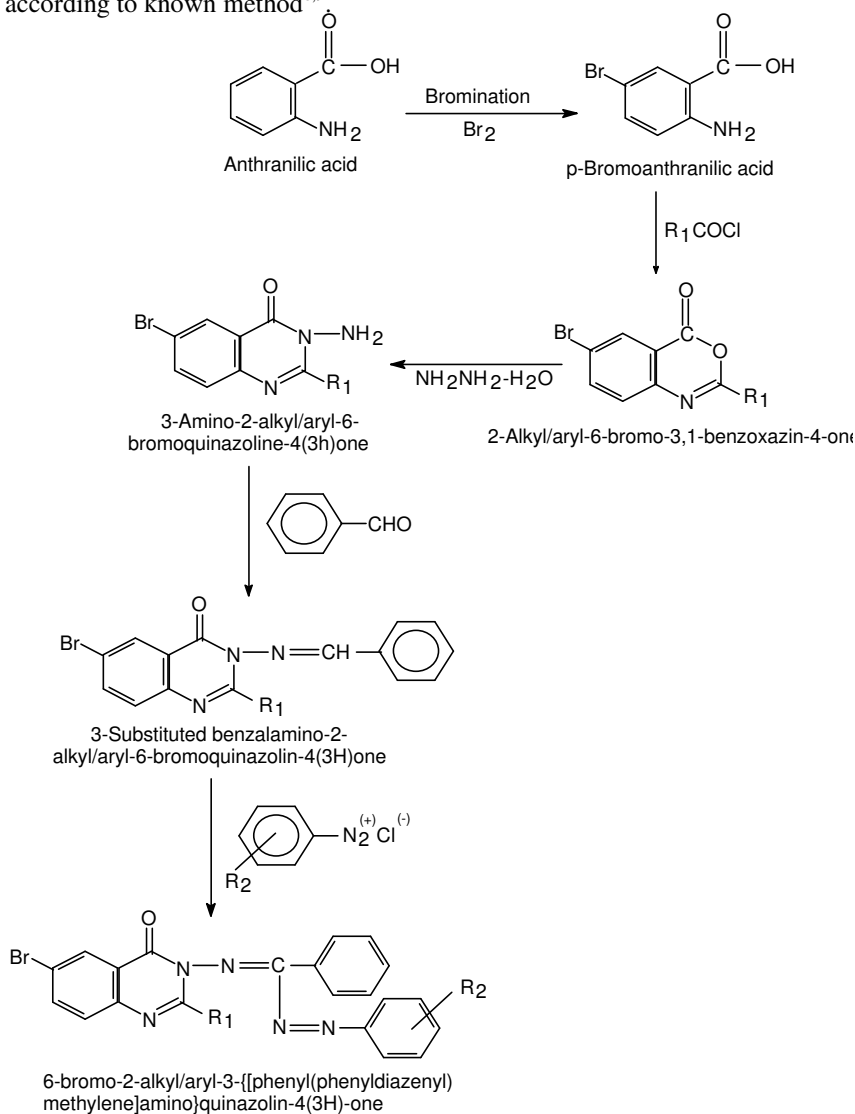
### Introduction

Quinazoline nucleus possessed the potent pharmacodynamic nucleus. In addition several quinazoline derivatives possess diverse biological activities Viz. anticonvulsant<sup>1</sup>, hyponotics<sup>2</sup>, antiinflammatory<sup>3,4</sup>, diuretics antihypertensive<sup>5,6,7</sup>, antitubercular etc. quinazoline system possess variable sites at 2 and 3 positions substituted by various hetrocyclic moieties afford the potent anticonvulsant agent. Furthermore SAR study of different quinazolinone derivatives have revealed that the substitution at 3-position has significant role on hypotensive activity.

### Experimental

All the melting points were determined in open capillary and are uncorrected. The purity is checked by TLC. IR Spectras were recorded in KBr on shimatzu F.T. - IR 8300 spectrophotometer. Analytical data were also confirmed from its H - NMR Spectra.

The starting compound 2-alkyl/aryl-3-amino-6-bromo quinazolinone has been prepared according to known method<sup>8,9</sup>



3-amino-2-alkyl/aryl-6-bromoquinazolin-4(3H)-one **3** has been prepared by known method.<sup>8,9</sup>

*Synthesis of 6-bromo-2-alkyl/aryl-3-[(1E)-phenylmethylene]amino}quinazolin-4(3H)-one **4**:*

3-Amino-2-alkyl/aryl-7-bromoquinazolin-4(3H)-one **3** (0.01 mole) and benzaldehyde (0.01 mole) were refluxed in absolute ethanol (40ml) for 3 hrs. The excess solvent was then distilled off and the resulting solid washed with water, dried and recrystallized from ethanol.

*Synthesis of 6-bromo-2-alkyl/aryl-3-[[phenyl(phenyldiazenyl)methylene]amino]quinazoline-4(3H)-one 5 :*

Appropriate amine (0.02 Mole) in glacial Acetic acid (2ml) & HCl (1.5ml) was diazotised with NaNO<sub>2</sub> (0.2 g in 2 ml H<sub>2</sub>O) at 0–5 °C. The resultant diazonium chloride solution was added with stirring to a solution of (4) (0.02 mole) in pyridine. (3 ml) in the cold. The reaction mixture. was left over night at ambient temperature. There after, it was poured into cold water (250 ml) with stirring when a dark coloured solid separated out. It was filtered, washed, repeatedly with water containing HCl and finally with water and recrystallized from methanol to furnish 5a<sub>1</sub>–a<sub>16</sub>. (Table 1)

**Table 1.** Elemental analysis of synthesized compounds 5a<sub>1</sub>–a<sub>16</sub>

No.	R <sub>1</sub>	R <sub>2</sub>	M.F.	Yield %	M.P. (°C)	%Analysis Calc.(Found)		
						C	H	N
5a <sub>1</sub>	CH <sub>3</sub>	-H	C <sub>27</sub> H <sub>18</sub> N <sub>5</sub> OBr	76	160°C	63.79 (63.20)	3.57 (4.28)	13.78 (12.40)
5a <sub>2</sub>	CH <sub>3</sub>	2-OCH <sub>3</sub>	C <sub>28</sub> H <sub>20</sub> N <sub>5</sub> O <sub>2</sub> Br	55	110– 112°C	62.46 (62.75)	3.74 (3.94)	13.01 (13.50)
5a <sub>3</sub>	CH <sub>3</sub>	3-OCH <sub>3</sub>	C <sub>28</sub> H <sub>20</sub> N <sub>5</sub> O <sub>2</sub> Br	58	113– 115°C	62.46 (62.75)	3.74 (3.94)	13.01 (13.50)
5a <sub>4</sub>	CH <sub>3</sub>	4-OCH <sub>3</sub>	C <sub>28</sub> H <sub>20</sub> N <sub>5</sub> O <sub>2</sub> Br	52	120°C	62.46 (62.75)	3.74 (3.94)	13.01 (13.50)
5a <sub>5</sub>	CH <sub>3</sub>	2-Br	C <sub>27</sub> H <sub>17</sub> N <sub>5</sub> OBr <sub>2</sub>	56	145°C	55.22 (55.50)	2.92 (3.02)	11.93 (12.05)
5a <sub>6</sub>	CH <sub>3</sub>	3-Br	C <sub>27</sub> H <sub>17</sub> N <sub>5</sub> OBr <sub>2</sub>	62	130– 135°C	55.22 (55.50)	2.92 (3.02)	11.93 (12.05)
5a <sub>7</sub>	CH <sub>3</sub>	4-Br	C <sub>27</sub> H <sub>17</sub> N <sub>5</sub> OBr <sub>2</sub>	80	155°C	55.22 (55.50)	2.92 (3.02)	11.93 (12.05)
5a <sub>8</sub>	CH <sub>3</sub>	2-Cl	C <sub>27</sub> H <sub>17</sub> N <sub>5</sub> OBr Cl	66	136– 140°C	59.74 (60.03)	3.16 (3.33)	12.90 (13.15)
5a <sub>9</sub>	CH <sub>3</sub>	3-Cl	C <sub>27</sub> H <sub>17</sub> N <sub>5</sub> OBr Cl	68	148°C	59.74 (60.03)	3.16 (3.33)	12.90 (13.15)
5a <sub>10</sub>	CH <sub>3</sub>	4-Cl	C <sub>27</sub> H <sub>17</sub> N <sub>5</sub> OBr Cl	56	142°C	59.74 (60.03)	3.16 (3.33)	12.90 (13.15)
5a <sub>11</sub>	CH <sub>3</sub>	2-NO <sub>2</sub>	C <sub>27</sub> H <sub>17</sub> N <sub>6</sub> O <sub>3</sub> Br	68	162– 165°C	58.60 (58.61)	3.10 (3.28)	15.19 (15.75)
5a <sub>12</sub>	CH <sub>3</sub>	3-NO <sub>2</sub>	C <sub>27</sub> H <sub>17</sub> N <sub>6</sub> O <sub>3</sub> Br	63	168°C	58.60 (58.61)	3.10 (3.28)	15.19 (15.75)
5a <sub>13</sub>	CH <sub>3</sub>	4-NO <sub>2</sub>	C <sub>27</sub> H <sub>17</sub> N <sub>6</sub> O <sub>3</sub> Br	67	156°C	58.60 (58.61)	3.10 (3.28)	15.19 (15.75)
5a <sub>14</sub>	CH <sub>3</sub>	2-CH <sub>3</sub>	C <sub>28</sub> H <sub>20</sub> N <sub>5</sub> OBr	52	128°C (d)	64.38 (64.81)	3.86 (4.07)	13.41 (13.71)
5a <sub>15</sub>	CH <sub>3</sub>	3-CH <sub>3</sub>	C <sub>28</sub> H <sub>20</sub> N <sub>5</sub> OBr	54	140(d)	64.38 (64.81)	3.86 (4.07)	13.41 (13.71)
5a <sub>16</sub>	CH <sub>3</sub>	4-CH <sub>3</sub>	C <sub>28</sub> H <sub>20</sub> N <sub>5</sub> OBr	55	156(d)	64.38 (64.81)	3.86 (4.07)	13.41 (13.71)

**Table –2.** Elemental analysis of synthesized compounds **5b<sub>1</sub>-b<sub>16</sub>**

No.	R <sub>1</sub>	R <sub>2</sub>	M.F.	Yield %	M.P. (°C)	%Analysis Calc.(Found)		
						C	H	N
5b <sub>1</sub>	C <sub>6</sub> H <sub>5</sub>	-H	C <sub>22</sub> H <sub>16</sub> N <sub>5</sub> OBr	68	179– 180°C	59.21 (59.20)	3.61 (3.59)	15.69 (15.40)
5b <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	2-OCH <sub>3</sub>	C <sub>23</sub> H <sub>18</sub> N <sub>5</sub> O <sub>2</sub> Br	66	120°C	58.00 (58.25)	3.81 (3.94)	14.70 (14.88)
5b <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	3-OCH <sub>3</sub>	C <sub>23</sub> H <sub>18</sub> N <sub>5</sub> O <sub>2</sub> Br	65	124°C	58.00 (58.25)	3.81 (3.94)	14.70 (14.88)
5b <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	4-OCH <sub>3</sub>	C <sub>23</sub> H <sub>18</sub> N <sub>5</sub> O <sub>2</sub> Br	60	130– 132°C	58.00 (58.25)	3.81 (3.94)	14.70 (14.88)
5b <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	2-Br	C <sub>22</sub> H <sub>15</sub> N <sub>5</sub> OBr <sub>2</sub>	78	125– 127°C	50.31 (50.12)	2.88 (2.75)	13.33 (13.55)
5b <sub>6</sub>	C <sub>6</sub> H <sub>5</sub>	3-Br	C <sub>22</sub> H <sub>15</sub> N <sub>5</sub> OBr <sub>2</sub>	73	148°C	50.31 (50.12)	2.88 (2.75)	13.33 (13.55)
5b <sub>7</sub>	C <sub>6</sub> H <sub>5</sub>	4-Br	C <sub>22</sub> H <sub>15</sub> N <sub>5</sub> OBr <sub>2</sub>	74	136– 137°C	50.31 (50.12)	2.88 (2.75)	13.33 (13.55)
5b <sub>8</sub>	C <sub>6</sub> H <sub>5</sub>	2-Cl	C <sub>22</sub> H <sub>15</sub> N <sub>5</sub> OBrCl	56	145°C	54.96 (54.87)	3.14 (3.33)	14.57 (14.76)
5b <sub>9</sub>	C <sub>6</sub> H <sub>5</sub>	3-Cl	C <sub>22</sub> H <sub>15</sub> N <sub>5</sub> OBrCl	52	140– 141°C	54.96 (54.87)	3.14 (3.33)	14.57 (14.76)
5b <sub>10</sub>	C <sub>6</sub> H <sub>5</sub>	4-Cl	C <sub>22</sub> H <sub>15</sub> N <sub>5</sub> OBrCl	58	151°C	54.96 (54.87)	3.14 (3.33)	14.57 (14.76)
5b <sub>11</sub>	C <sub>6</sub> H <sub>5</sub>	2-NO <sub>2</sub>	C <sub>22</sub> H <sub>15</sub> N <sub>6</sub> O <sub>3</sub> Br	82	170– 172°C	53.78 (53.91)	3.08 (3.28)	17.11 (17.35)
5b <sub>12</sub>	C <sub>6</sub> H <sub>5</sub>	3-NO <sub>2</sub>	C <sub>22</sub> H <sub>15</sub> N <sub>6</sub> O <sub>3</sub> Br	76	165°C	53.78 (53.91)	3.08 (3.28)	17.11 (17.35)
5b <sub>13</sub>	C <sub>6</sub> H <sub>5</sub>	4-NO <sub>2</sub>	C <sub>22</sub> H <sub>15</sub> N <sub>6</sub> O <sub>3</sub> Br	78	162°C	53.78 (53.91)	3.08 (3.28)	17.11 (17.35)
5b <sub>14</sub>	C <sub>6</sub> H <sub>5</sub>	2-CH <sub>3</sub>	C <sub>23</sub> H <sub>18</sub> N <sub>5</sub> OBr	62	132– 134°C (d)	60.01 (60.23)	3.94 (4.07)	15.21 (15.43)
5b <sub>15</sub>	C <sub>6</sub> H <sub>5</sub>	3-CH <sub>3</sub>	C <sub>23</sub> H <sub>18</sub> N <sub>5</sub> OBr	56	138°C (d)	60.01 (60.23)	3.94 (4.07)	15.21 (15.43)
5b <sub>16</sub>	C <sub>6</sub> H <sub>5</sub>	4-CH <sub>3</sub>	C <sub>23</sub> H <sub>18</sub> N <sub>5</sub> OBr	58	142 (d)	60.01 (60.23)	3.94 (4.07)	15.21 (15.43)

## Results and Discussion

Synthesized compounds have been confirmed by elemental analysis, IR Spectra and <sup>1</sup>HNMR Spectra.

Compound 5a<sub>1</sub> shows IR absorption bands at 1716–1670 cm<sup>-1</sup> (C=O stretching), 1676–1670 cm<sup>-1</sup> (C=N), 1340 cm<sup>-1</sup> (Ar-CH<sub>3</sub>), 650 cm<sup>-1</sup> (C–Br stretching).

Compound 5b<sub>1</sub> shows IR absorption bands at 1734–1684 cm<sup>-1</sup> (C=O stretching) 1684 – 1654 cm<sup>-1</sup> (C=N), 652 cm<sup>-1</sup> (C–Br stretching).

<sup>1</sup>H NMR of compound 5a<sub>1</sub>: δ 2.45 (s, 3H, Ar-CH<sub>3</sub>), 8.66 (d, 1H, C<sub>5</sub>-H), 8.25 (d, 1H, C<sub>7</sub>-H), 8.12 (d, 1H, C<sub>8</sub>-H), 7.45–7.98 (m, 9H, Ar-H).

<sup>1</sup>H NMR of compound 5b<sub>1</sub>: δ 8.65 (d, 1H, C<sub>5</sub>-H), 8.3 (d, 1H, C<sub>7</sub>-H), 8.265 (d, 1H, C<sub>8</sub>-H), 7.4–8.2 (m, 14H, Ar-H).

### Antibacterial Activity

The synthesized compounds were tested against gram positive bacteria staphylococcus aureus and Bacillus cereus and gram negative bacteria E. coli and Pseudomonas aeruginosa and a yeast candida albicans.

**Table 3.** Antimicrobial Activity of Newly Synthesised Compounds, Zone of Inhibition (Mm)

Sample No.	E.coli	Pseudomonas aeruginosa	S.aureus	Bacilus cereus	Candida	M.I.C. for mycobacterium tuberculosis µg/ml
5a <sub>1</sub>	8	9	8	9	00	>100
5a <sub>2</sub>	6	6	6	6	00	>100
5a <sub>3</sub>	8	9	6	6	00	>100
5a <sub>4</sub>	9	9	6	6	00	>100
5a <sub>5</sub>	10	8	11	6	00	>100
5a <sub>6</sub>	8	7	8	8	00	>100
5a <sub>7</sub>	7	7	8	8	00	>100
5a <sub>8</sub>	6	6	6	6	00	>100
5a <sub>9</sub>	6	6	6	6	00	>100
5a <sub>10</sub>	8	8	8	8	00	>100
5a <sub>11</sub>	6	9	8	8	00	>100
5a <sub>12</sub>	7	8	8	8	00	>100
5a <sub>13</sub>	9	8	8	7	00	>100
5a <sub>14</sub>	9	8	6	6	00	>100
5a <sub>15</sub>	8	9	6	6	00	>100
5a <sub>16</sub>	8	8	6	6	00	>100
5b <sub>1</sub>	9	8	9	9	00	>100
5b <sub>2</sub>	7	9	7	7	00	>100
5b <sub>3</sub>	8	8	6	6	00	>100
5b <sub>4</sub>	11	12	9	9	00	>100
5b <sub>5</sub>	8	7	8	8	00	>100
5b <sub>6</sub>	9	8	8	8	00	>100
5b <sub>7</sub>	8	8	6	6	00	>100
5b <sub>8</sub>	9	9	8	8	00	>100
5b <sub>9</sub>	8	8	9	9	00	>100
5b <sub>10</sub>	11	12	10	10	00	>100
5b <sub>11</sub>	8	8	9	9	00	>100
5b <sub>12</sub>	7	7	7	7	00	>100
5b <sub>13</sub>	9	8	8	9	00	>100
5b <sub>14</sub>	6	6	6	6	00	>100
5b <sub>15</sub>	6	6	6	7	00	>100
5a <sub>16</sub>	6	6	6	8	00	>100

The stock solutions of compounds were prepared at a concentration of 5mg/ml & from stock solution the discs were prepared at a concentration of 100i g/ml. The testing was done on muller hinton agar plates by swabbing the agar plates with respective cultures, and placing the disc on it and incubating at 37°C for 24 hrs. the above results were obtained.

The compounds were also tested against mycobacterium tuberculosis at a concentration of 100i g/ml.

The L.J. medium was prepared from dehydrated powder following the instructions given on the dehydrated medium bottle. The compound were then added into the medium in the desired concentration and then inspissated then the prepared L.J. medium was inoculated with the pure culture of mycobacterium tuberculosis and incubated at 37°C for 7 weeks and then the results were read.

Standard drug tetracycline and Greseofulvin were also screened under similar conditions for comparison. Results are shown in **Table 3**.

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