

## Synthesis of novel triazole, quinoline, oxazole and imidazole annulated carbostyrils by microwave irradiation

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3-Bromo carbostyryl **1** on condensation with triazoles **2**, amidinothiocarbamides **4**, amidinocarbamides **6** and guanidines **8** affords the respective title compounds **3**, **5**, **7** and **9**. The rapid microwave irradiation of the reaction mixture gives excellent yield of the product compared to the conventional method. The structures of synthesized compounds are confirmed by IR, <sup>1</sup>H and <sup>13</sup>C NMR data.

**Keywords:** Monobromo carbostyryl, triazole, amidinothiocarbamide, amidinocarbamide, guanidine

**IPC: Int.Cl.<sup>8</sup> C07D**

Heterocyclic compounds containing triazole, quinoline, oxazole and imidazole have been shown to possess significant pharmacological activity such as anti-inflammatory<sup>1</sup>, antifungal<sup>2</sup>, antidepressant<sup>3</sup> and anti HIV infection<sup>4</sup>. In addition, they also found application as dye stuffs, auxiliaries in fiber finishes. Their potential biological activity encouraged us to prepare some new heterocyclic derivatives for them. The compounds **3**, **5**, **7** and **9** were synthesized under microwave irradiation (MWI) using base as a catalyst. Same of them have been also prepared by conventional method for comparison. Their chemical structures have been established by IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectral data and by *co*-TLC, superimposable IR and mixed melting points.

The required starting material **8** were obtained by reported procedure<sup>9-13</sup>. Fused triazoles **3** were obtained by treating 3-bromocarbostyryl **1** with substituted 4-amino-3-mercaptoptriazole **2** in presence of piperidine, using ethanol as solvent in an Erlenmeyer flask under MWI condition. Compound **1** when fused with amidinothiocarbamides **4** in presence of NaOAc as a base and DMSO as a solvent under MWI, the thiazole derivatives **5** were obtained. Amidinocarbamides **6** on treatment with **1** under similar condition gave fused oxazole **7**. Similarly, condensation of **1** with guanidines **8** in presence of piperidine, using DMSO as a solvent, new imidazole derivative **9** was obtained under MWI. The products

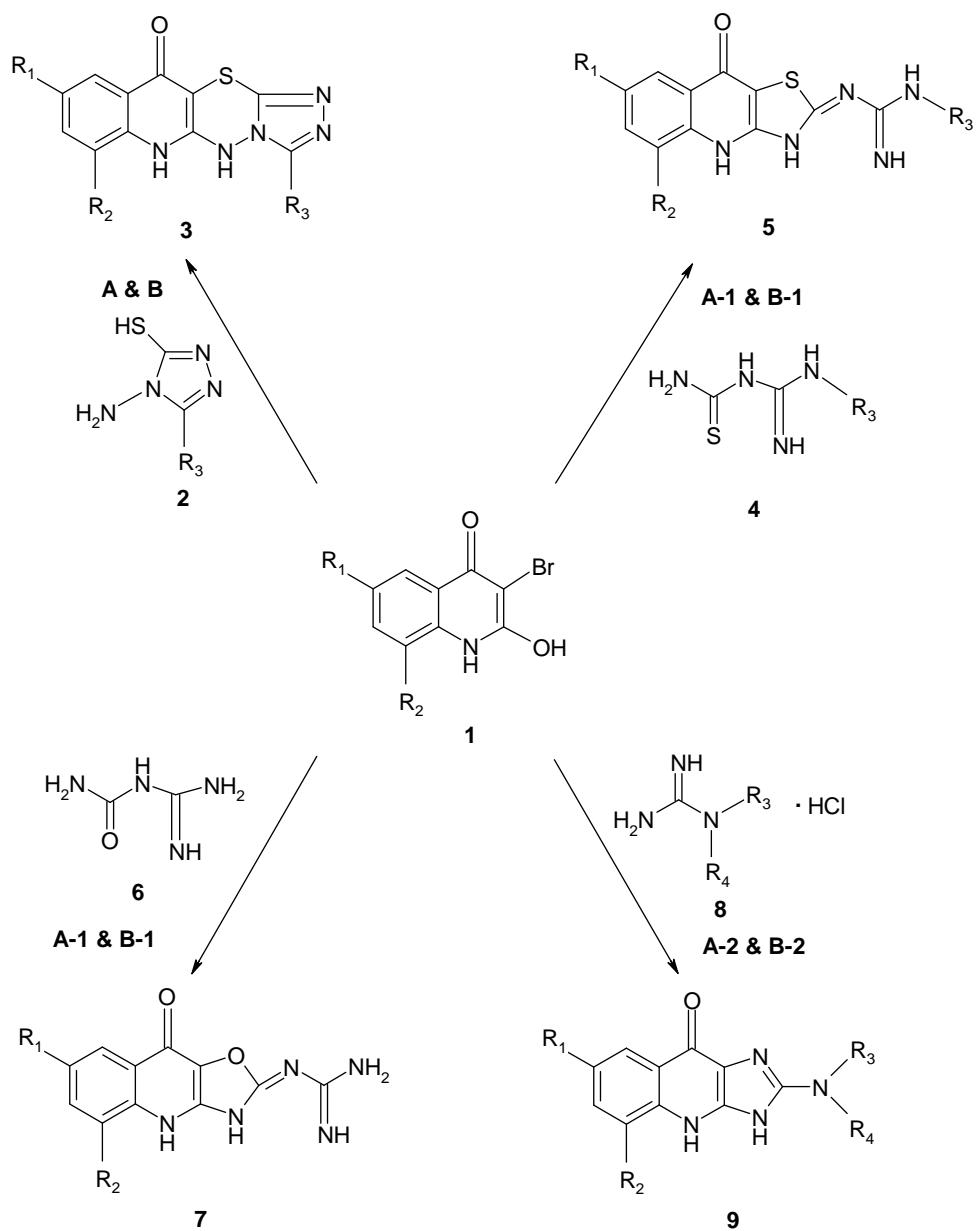
**3**, **5**, **7** and **9** were also prepared by classical procedure (**Scheme I**) and their characterization data is given in the **Table I**.

### Experimental Section

Melting points of all compounds were determined in soft glass open capillaries in an electro thermal apparatus and are uncorrected. IR (KBr) spectra were recorded on a Perkin-Elmer spectrophotometer. <sup>1</sup>H NMR spectra were recorded on a Brucker AMX 500 MHz in DMSO-*d*<sub>6</sub> using TMS as internal standard (chemical shifts in  $\delta$ , ppm). The progress of the reaction was monitored and purity of the compounds were checked by TLC on silica gel coated Al plates (Merck) in the solvent and UV light accomplished visualization. Samsung microwave oven (Model No. M1630N, 2450 MHz) was used for irradiation.

### General procedure

(MWI) A. **3,4,6-Trisubstituted-9,10-dihydro-11-oxo-quinolino[2,3-*b*]-1,3,4-thiadiazino [2, 3-*d*] -1, 2, 4-triazole** **3**. 3-Bromocarbostyryl **1** (0.01 mmole), 4-amino-5-methyl-3-mercaptop-1,2,4-triazole **2** (0.01 mmole), piperidine (0.02 mmole) and 4 mL of alcohol were taken in an Erlenmeyer flask and irradiated for 5 min. Upon completion of the reaction, the mixture was then poured onto crushed ice. The product obtained was filtered, washed with water and dried.



**A)** MWI/ Piperidine/ Alcohol; **A-1)** MWI/ NaOAc/ DMSO; **A-2)** MWI/ Piperidine/ DMSO

**B)** Conventional Method; Piperidine/ Alcohol; **B-1)** NaOAc/ DMSO; **B-2)** Piperidine/ DMSO

Scheme I

**Method B. 2-Guanidino/substituted guanidino-1,3-thiazolo [4,5-*b*]-1-*H*-6,8-disubstituted-4-oxo-quinoline 5.** Compound **1** (0.01 mmole) was allowed to interact with amidinothiocarbamide **4** (0.01 mmole) in presence of fused sodium acetate (0.02 mmole) and DMSO (3 mL) under MWI for 5 min. The contents were poured onto crushed ice and solid obtained was filtered, washed with water and dried.

**Method C. 2-Guanidino/substituted guanidino-1, 3-oxazolo[4, 5-*b*]-1-*H*-6, 8-disubstituted-4-oxo-**

**quinoline 7.** Compound **1** (0.01 mmole), amidino-carbamide **6** (0.01 mmole), fused sodium acetate (0.02 mmole) and DMSO (3 mL) were mixed and subjected to MWI in an Erlenmeyer flask for 5 min at 100 W and the mixture was poured onto crushed ice. The solid obtained was filtered, washed with water and dried.

**Method D. 2-Amino/substituted amino-3,8-dihydro-9-oxo-4,6-disubstituted quinolino [2,3-*d*] imidazole 9.** Compound **1** (0.01 mmole), guanidine

Table I—(Characterization data for 3, 5, 7 and 9 and their derivatives)

Compd	Mol. Formula	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	m.p.	Yield(%)	Spectral data, NMR ( $\delta$ , ppm) in DMSO- $d_6$		
								<sup>1</sup> H	<sup>13</sup> C	
3a	C <sub>12</sub> H <sub>9</sub> N <sub>5</sub> OS	H	H	CH <sub>3</sub>	-	225	68	56	2.47 (s, 3H, CH <sub>3</sub> ), 7.18-7.91 (m, 4H, Ar), 12.43 (s, ring NH), 12.72 (s, ring NH)	
3b	C <sub>13</sub> H <sub>11</sub> N <sub>5</sub> OS	H	CH <sub>3</sub>	CH <sub>3</sub>	-	293	61	2.43 (s, 3H, CH <sub>3</sub> ), 7.1-7.89 (m, 4H, =CH, Ar), 12.28 (s, ring NH), 12.92 (s, ring NH)	25.1 (-CH <sub>3</sub> ), 115.9 (-C=C), 122.2-139.0 (aromatic C atoms), 157.5 & 159.0 (2x C=N), 164.7 (-C=O)	
3c	C <sub>12</sub> H <sub>9</sub> N <sub>5</sub> OS	CH <sub>3</sub>	H	H	-	290	78	61	-	-
3d	C <sub>14</sub> H <sub>13</sub> N <sub>5</sub> OS	CH <sub>3</sub>	H	C <sub>2</sub> H <sub>5</sub>	-	248	75	59	-	-
3e	C <sub>13</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub> S	OCH <sub>3</sub>	H	CH <sub>3</sub>	-	236	63	37	2.43 (s, 3H, CH <sub>3</sub> ), 3.82 (s, 3H, -OCH <sub>3</sub> ), 7.0-7.9 (m, 3H, Ar), 12.39 (s, ring NH), 12.75 (s, ring NH)	-
3f	C <sub>12</sub> H <sub>8</sub> N <sub>5</sub> OSBr	Br	H	CH <sub>3</sub>	-	290	66	57	-	-
3g	C <sub>11</sub> H <sub>6</sub> N <sub>5</sub> OSCl	Cl	H	H	-	318	65	38	-	-
5a	C <sub>11</sub> H <sub>9</sub> N <sub>5</sub> OS	H	H	H	-	274	69	42	2.12 (s, 2H, NH <sub>2</sub> ), 7.06-8.0 (m, 4H, Ar), 9.76 (s, 1H, NH), 12.18 (s, ring NH), 12.72 (s, ring NH)	-
5b	C <sub>18</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub> S	H	H	<i>p</i> -CH <sub>3</sub> -O-C <sub>6</sub> H <sub>4</sub>	-	320	67	57	-	-
5c	C <sub>18</sub> H <sub>15</sub> N <sub>5</sub> OS	H	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	-	312	76	65	-	-
5d	C <sub>19</sub> H <sub>17</sub> N <sub>5</sub> OS	H	CH <sub>3</sub>	<i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	-	315	70	50	2.21 (s, 3H, CH <sub>3</sub> ), 2.24 (s, 3H, CH <sub>3</sub> ), 6.85 (s, 1H, NH), 7.1-7.89 (m, 7H, Ar), 9.20 (s, 1H, NH), 11.19 (s, ring NH), 11.35 (s, ring NH)	-
5e	C <sub>19</sub> H <sub>17</sub> N <sub>5</sub> OS	CH <sub>3</sub>	H	<i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	-	318	63	45	-	-
5f	C <sub>18</sub> H <sub>14</sub> N <sub>5</sub> OSBr	CH <sub>3</sub>	H	<i>p</i> -Br-C <sub>6</sub> H <sub>4</sub>	-	309	60	52	2.31 (s, 3H, CH <sub>3</sub> ), 6.29 (s, 1H, NH), 7.2-7.8 (m, 7H, Ar), 9.21 (s, 1H, NH), 12.11 (s, ring NH), 12.77 (s, ring NH)	-
5g	C <sub>18</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub> S	OCH <sub>3</sub>	H	C <sub>6</sub> H <sub>5</sub>	-	220	68	39	-	-
5h	C <sub>19</sub> H <sub>17</sub> N <sub>5</sub> OS	OCH <sub>3</sub>	H	<i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	-	319	61	41	-	-
5i	C <sub>18</sub> H <sub>14</sub> N <sub>5</sub> O <sub>2</sub> SCl	H	Cl	<i>p</i> -CH <sub>3</sub> -O-C <sub>6</sub> H <sub>4</sub>	-	321	64	52	3.80 (s, 3H, -OCH <sub>3</sub> ), 6.24 (s, 1H, NH), 7.0-8.0 (m, 7H, Ar), 9.75 (s, 1H, NH), 12.10 (s, ring NH), 12.95 (s, ring NH)	-

*—Contd*

Table I—(Characterization data for 3, 5, 7 and 9 and their derivatives)—*Contd*

Compd	Mol. Formula	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	m.p.	Yield (%)	Spectral data, NMR ( $\delta$ , ppm) in DMSO- $d_6$	
								<sup>1</sup> H	<sup>13</sup> C
<b>5j</b>	C <sub>17</sub> H <sub>11</sub> N <sub>5</sub> OSBr <sub>2</sub>	Br	H	<i>p</i> -Br-C <sub>6</sub> H <sub>4</sub>	-	322	60	51	-
<b>5k</b>	C <sub>17</sub> H <sub>12</sub> N <sub>5</sub> OSBr	Br	H	C <sub>6</sub> H <sub>5</sub>	-	318	70	59	6.84 (s, 1H, NH), 7.0-7.9 (m, 8H, Ar), 9.32 (s, 1H, NH), 12.37 (s, ring NH), 12.72 (s, ring NH)
<b>5l</b>	C <sub>11</sub> H <sub>8</sub> N <sub>5</sub> OS	Cl	H	H	-	312	66	55	-
<b>5m</b>	C <sub>17</sub> H <sub>11</sub> N <sub>5</sub> OSBrCl	Cl	H	<i>p</i> -Br-C <sub>6</sub> H <sub>4</sub>	-	250	61	53	-
<b>7a</b>	C <sub>11</sub> H <sub>9</sub> N <sub>5</sub> O <sub>2</sub>	H	H	-	-	330	65	49	-
<b>7b</b>	C <sub>12</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>	H	CH <sub>3</sub>	-	-	272	60	33	2.12 (s, 2H, NH <sub>2</sub> ), 2.23 (s, 3H, CH <sub>3</sub> ), 7.0-7.85 (m, 3H, Ar), 9.55 (s, 1H, NH), 11.48 (s, ring NH), 12.10 (s, ring NH)
<b>7c</b>	C <sub>12</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>	CH <sub>3</sub>	H	-	-	276	67	45	-
<b>7d</b>	C <sub>12</sub> H <sub>11</sub> N <sub>5</sub> O <sub>3</sub>	OCH <sub>3</sub>	H	-	-	247	63	52	2.15 (s, 2H, NH <sub>2</sub> ), 3.84 (s, 3H, -OCH <sub>3</sub> ), 7.0-7.9 (m, 3H, Ar), 9.70 (s, 1H, NH), 12.10 (s, ring NH), 12.94 (s, ring NH)
<b>7e</b>	C <sub>11</sub> H <sub>8</sub> N <sub>5</sub> O <sub>2</sub> Cl	H	Cl	-	-	306	59	31	-
<b>7f</b>	C <sub>11</sub> H <sub>8</sub> N <sub>5</sub> O <sub>2</sub> Br	Br	H	-	-	319	64	54	-
<b>7g</b>	C <sub>11</sub> H <sub>8</sub> N <sub>5</sub> O <sub>2</sub> Cl	Cl	H	-	-	322	61	37	-
<b>9a</b>	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> O	H	H	H	H	325	67	44	3.78 (s, 2H, NH <sub>2</sub> ), 7.1-7.9 (m, 4H, Ar), 12.18 (s, ring NH), 12.73 (s, ring NH)
<b>9b</b>	C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> O	H	CH <sub>3</sub>	H	H	287	60	36	-
<b>9c</b>	C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O	CH <sub>3</sub>	H	CH <sub>3</sub>	CH <sub>3</sub>	291	70	48	2.40 (s, 3H, CH <sub>3</sub> ), 3.82 (s, 3H, -OCH <sub>3</sub> ), 7.5 (s, 1H, NH), 7.0-7.87 (m, 3H, Ar), 12.37 (s, ring NH), 12.89 (s, ring NH)
<b>9d</b>	C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub>	OCH <sub>3</sub>	H	CH <sub>3</sub>	H	280	73	57	-
<b>9e</b>	C <sub>11</sub> H <sub>9</sub> N <sub>4</sub> OCl	H	Cl	CH <sub>3</sub>	H	312	64	42	-
<b>9f</b>	C <sub>11</sub> H <sub>9</sub> N <sub>4</sub> OCl	Cl	H	H	CH <sub>3</sub>	318	69	38	-
<b>9g</b>	C <sub>11</sub> H <sub>9</sub> N <sub>4</sub> OBr	Br	H	CH <sub>3</sub>	H	306	71	55	-

Method A: MWI Time- 5 to 6 min

Method B: Conventional Time- 6 to 7 hr.

All compounds were recrystallized from ethyl alcohol.

C, H, N and S analysis was found satisfactory.

Peaks obtained due to NH, NH<sub>2</sub> are D<sub>2</sub>O exchangeable

hydrochloride **8** (0.01 mmole), piperidine (0.03 mmole) and DMSO (3 mL) underwent cyclisation under MWI condition (3 min). The mixture was poured onto crushed ice. The solid was filtered, washed with water and dried.

### General procedure

#### Conventional method

**Synthesis of compound 3.** Compound **3** was obtained by refluxing equal mmoles (0.01) of **1**, **2** and piperidine (0.02 mmole) in alcohol (10 mL) for 6 hr. The contents were poured onto crushed ice. The solid thus obtained was filtered, washed with water and dried.

**Synthesis of compound 5.** Equimolar mixture of compounds **1** and **4** were refluxed for 6 hr in presence of fused sodium acetate (0.02 mmole) and DMSO (3 mL) and poured onto crushed ice. The solid obtained was filtered, washed with water and dried.

**Synthesis of compound 7.** Compounds **1** (0.01 mmole), **6** (0.01 mmole), fused sodium acetate (0.02 mmole) and DMSO (3 mL) were refluxed for 6 hr and worked-up as mentioned above.

**Synthesis of compound 9.** Compounds **1** (0.01 mmole), **8** (0.01 mmole), piperidine (0.03 mmole) and DMSO (3 mL) were refluxed for 4 hr and the mixture

was poured onto crushed ice. The solid mass separated was filtered, washed with water and dried.

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