

PREPARATION OF *s*-TRIAZOLO[4,3-*c*]QUINAZOLINES

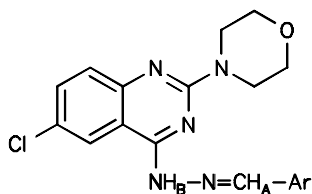
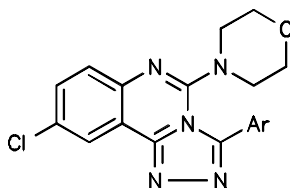
Katarina SPIRKOVA, Stefan STANKOVSKY and Jakub HORNACEK

*Department of Organic Chemistry,**Slovak Technical University, 812 37 Bratislava, The Slovak Republic*

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Several biological activities have been attributed to the quinazoline and triazole derivatives<sup>1-3</sup>. Combining two known active heterocyclic moieties, we prepared a series of 3-aryl-5-morpholino-9-chloro-*s*-triazolo[4,3-*c*]quinazolines by an oxidative cyclization of the corresponding arylhydrazones, with the hope, that the known activities might result in a novel type of activity.

*I**II*

<i>I, II</i>	Ar
<i>a</i>	2-Cl-C <sub>6</sub> H <sub>4</sub>
<i>b</i>	4-CH <sub>3</sub> CONH-C <sub>6</sub> H <sub>4</sub>
<i>c</i>	2-furyl

<i>I, II</i>	Ar
<i>d</i>	5-bromo-2-furyl
<i>e</i>	2-thienyl
<i>f</i>	3-indolyl

TABLE I  
Characteristic data of prepared compounds

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found		
			% C	% H	% N
<i>Ia</i>	C <sub>19</sub> H <sub>17</sub> Cl <sub>2</sub> N <sub>5</sub> O	221 – 223	56.70	4.62	17.40
	(402.0)	92	56.15	4.38	17.28
<i>Ib</i>	C <sub>21</sub> H <sub>21</sub> ClN <sub>6</sub> O <sub>3</sub>	255 – 257	59.40	4.90	19.80
	(424.5)	95	58.77	4.96	19.66
<i>Ic</i>	C <sub>17</sub> H <sub>16</sub> ClN <sub>5</sub> O <sub>2</sub>	160 – 162	57.10	4.50	19.60
	(357.5)	93	57.50	4.43	19.41
<i>Id</i>	C <sub>17</sub> H <sub>15</sub> BrClN <sub>5</sub> O <sub>2</sub>	183 – 185	46.75	3.43	16.04
	(436.4)	94	46.48	3.32	16.28
<i>Ie</i>	C <sub>17</sub> H <sub>16</sub> ClN <sub>5</sub> OS	232 – 234	54.46	4.31	18.73
	(373.8)	85	54.76	4.25	18.61
<i>If</i>	C <sub>21</sub> H <sub>19</sub> ClN <sub>6</sub> O	235 – 238	61.98	4.70	20.65
	(406.8)	56	62.15	4.58	20.49
<i>Ila</i>	C <sub>19</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>5</sub> O	218 – 220	57.00	3.80	17.50
	(400.0)	98	57.26	3.85	17.69
<i>Ilb</i>	C <sub>21</sub> H <sub>19</sub> ClN <sub>6</sub> O <sub>2</sub>	255 – 257	59.60	4.50	19.90
	(422.5)	95	59.51	4.39	19.67
<i>Ilc</i>	C <sub>17</sub> H <sub>14</sub> ClN <sub>5</sub> O <sub>2</sub>	240 – 242	57.40	3.90	19.70
	(355.5)	55	57.29	3.83	19.51
<i>Ild</i>	C <sub>17</sub> H <sub>13</sub> BrClN <sub>6</sub> O	191 – 193	47.00	2.99	19.35
	(434.5)	82	47.32	3.03	19.56
<i>Ile</i>	C <sub>17</sub> H <sub>14</sub> ClN <sub>5</sub> OS	339 – 340	54.90	3.79	18.83
	(371.8)	85	54.78	3.86	18.78
<i>Ilf</i>	C <sub>21</sub> H <sub>17</sub> ClN <sub>6</sub> O	227 – 230	62.29	4.23	20.75
	(404.8)	91	62.37	4.32	20.58

TABLE II  
Spectral data of compounds *I* and *II*

Compound	IR spectrum			<sup>1</sup> H NMR				
	$\nu(\text{C}=\text{N})$	$\nu(\text{NH})$	other	H <sub>A</sub> , s	H <sub>B</sub> , s	H <sub>Ar</sub> , m	H <sub>Mo</sub> , m	H <sub>3</sub> /H <sub>4</sub> , d
<i>Ia</i>	1 624	3 296	–	8.78	11.63	8.42 – 7.25	3.73 3.67	
<i>Ib<sup>a</sup></i>	1 640	3 296	1 672 <sup>b</sup>	8.46	11.34	8.32 – 7.35	3.74 3.38	
<i>Ic<sup>c</sup></i>	1 616	3 216	–	8.53	11.45	8.29 – 7.34	3.78 3.68	7.57 7.35
<i>Id</i>	1 626	3 364	–	8.59	11.67	8.24 – 7.35	3.74 3.51	7.00 6.78
<i>Ie<sup>d</sup></i>	1 612	3 281	–	7.99	10.12	8.61 – 7.20	3.85 3.62	7.65 7.68
<i>If<sup>e</sup></i>	1 614	3 316	–	8.65	11.59	8.57 – 7.16	3.88 3.79	
<i>IIa</i>	1 624	–	–	–	9.09 <sup>f</sup>	8.42 – 7.49	3.73 3.57	
<i>IIb<sup>g</sup></i>	1 612	3 512	1 672 <sup>b</sup>	–	8.53 <sup>f</sup>	8.36 – 7.70	3.89 3.58	
<i>IIc<sup>h</sup></i>	1 636	–	–	–	8.60 <sup>f</sup>	8.45 – 6.70	3.75 3.16	7.40 7.03
<i>IId</i>	1 616	–	–	–	8.43 <sup>f</sup>	8.00 – 7.72	3.67 3.45	7.18 6.84
<i>IIe<sup>i</sup></i>	1 614	–	–	–	7.64 <sup>f</sup>	7.63 – 7.18	3.87 3.59	7.35 7.21
<i>IIj<sup>j</sup></i>	1 631	3 376	–	–	8.83 <sup>f</sup>	8.82 – 7.17	3.81 3.57	

<sup>a</sup> 10.08 s, 2.05 s (CH<sub>3</sub>CONH); <sup>b</sup> CO (CH<sub>3</sub>CONH); <sup>c</sup> 6.93 dd (H-5, furyl); <sup>d</sup> 7.60 d (H-5, thiophene); <sup>e</sup> 11.32 s (NH, indole); <sup>f</sup> H<sub>10</sub>; <sup>g</sup> 10.18 s, 2.11 s (CH<sub>3</sub>CONH); <sup>h</sup> 6.70 dd (H-5, furyl); <sup>i</sup> 7.60 d (H-5, thiophene); <sup>j</sup> 11.48 s (NH, indole).

## EXPERIMENTAL

The IR spectra (given in  $\text{cm}^{-1}$ ) were measured in KBr pellets with a Philips PU 9800 FTIR spectrometer.  $^1\text{H}$  NMR spectra of hexadeuteriodimethyl sulfoxide solution containing tetramethylsilane as an internal standard were recorded with VARIAN-300 (300 MHz) spectrometer and are given in  $\delta$ .

Preparation of the starting 6-chloro-2-morpholino-4-hydrazinoquinazoline was reported in ref.<sup>4</sup>.

### 6-Chloro-2-morpholino-4-quinazolylarylhyazones (*Ia* – *If*)

6-Chloro-2-morpholino-4-hydrazinoquinazoline (1.7 g; 5 mmol) and arylaldehyde (5 mmol) in ethanol (20 ml) were refluxed for 1 h. The solution was then cooled, cold water was added (20 ml) and the separated precipitate was filtered off and crystallized from dimethylformamide.

### 3-Aryl-5-morpholino-9-chloro-*s*-triazolo[4,3-*c*]quinazolines (*Ila* – *Ilf*)

Sodium acetate (0.5 g) was added to the stirred solution of the substituted hydrazone *I* (2 mmol) in acetic acid (20 ml) at room temperature. Bromine (0.32 g; 2 mmol) in acetic acid (10 ml) was then introduced dropwise. The reaction went through during 1 h, the mixture was then poured on crushed ice (100 g). The separated precipitate was filtered off and crystallized from ethanol–dimethylformamide.

## REFERENCES

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