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**REACTION OF MERCAPTOACETIC ACID AND CHLOROACETYL CHLORIDE WITH BENZALAMINO THIAZOLYL COUMARINS\***

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Received February 16, 1989

Accepted May 22, 1989

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2-Aryl-3-[4-(2-oxo-2*H*-1-benzopyran-3-yl)-2-thiazolyl]-4-thiazolidinones (*III*), have been synthesized by the reaction of Schiff's bases (*II*) derived from 3-(2-amino-4-thiazolyl)-2*H*-1-benzopyran-2-ones (*I*) with mercaptoacetic acid. The Schiff's bases on reaction with chloroacetyl chloride in the presence of triethylamine in dioxane gave chloroacetamido derivative (*IV*) instead of expected compound *V*.

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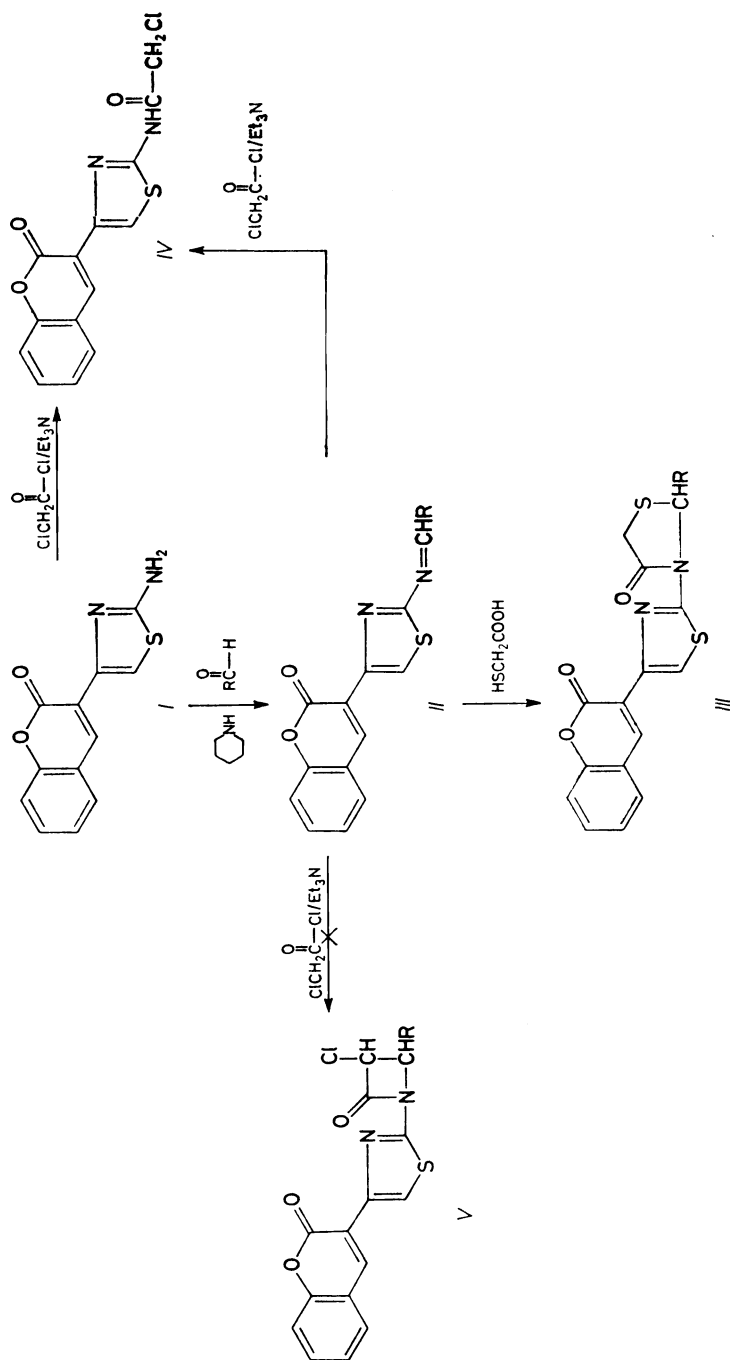
In continuation of earlier work on the heterocyclic systems derived from coumarin<sup>1-4</sup> we report here the reaction of mercaptoacetic acid and chloroacetyl chloride with the C=N functionality of 2-benzalaminothiazolyl coumarin *II* giving thiazolidinone *III* and chloroacetamido derivative of *I*. Though the literature contains sporadic reports<sup>5-7</sup> concerning the utilization of various Schiff's bases in this dipolar additions, thiazolyl anils have not been used so far.

3-(2-Amino-4-thiazolyl)coumarins (*I*) were obtained<sup>8</sup> by the reaction of 3-( $\omega$ -bromoacetyl)coumarins with thiourea in the presence of dry methanol and sodium acetate. Condensation of *I* with aromatic aldehydes in hot ethanol containing catalytic amount of piperidine led to the Schiff's bases *II*. These Schiff's bases on reaction with mercaptoacetic acid in dry benzene under reflux gave the thiazolidinones *III* (Scheme 1).

The interaction of Schiff's bases (*II*) with chloroacetyl chloride leads to 4-chloroacetamido derivatives of thiazolyl coumarins *IV* instead of the expected  $\beta$ -lactams *V*. Compound *IV* has been prepared through an unambiguous route. The 2-amino-3-(4-thiazolyl)coumarin (*I*) on treatment with chloroacetyl chloride under similar conditions, i.e. in the presence of triethylamine in refluxing benzene or dioxane, gave product identical with *IV* in all respects, i.e. mixed m.p., TLC and IR spectrum. All the Schiff's bases used in the reaction gave one and the same compound *IV* instead of the expected cyclo adduct *V*. The structures of the products have been confirmed

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\* Part IX in the series Studies on Coumarin Derivatives; Part VIII see ref.<sup>9</sup>.



*IIa, IIIa*, R = 2-hydroxyphenyl

*IIb, IIIb*, R = 2-hydroxy-3-methoxyphenyl

*IIc, IIIc*, R = 2-hydroxy-3-bromophenyl

*IId, IIId*, R = 2-hydroxy-3,5-dibromophenyl

*IIe, IIIe*, R = *p*-methoxyphenyl

*IIf, IIIf*, R = *p*-(*N,N*-dimethylamino)phenyl

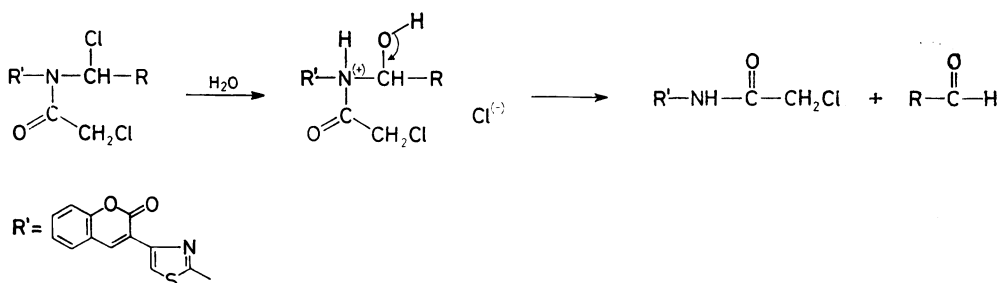
*IIg, IIIg*, R = 2-hydroxy-1-naphthyl

TABLE I  
Melting points and elemental analyses of compounds II, III, and IV

Compd. <sup>a</sup>	Formula (M.w.)	M.p. °C	Calculated/Found			
			% C	% H	% N	% S
<i>IIa</i>	C <sub>19</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> S (348.0)	194—196	65.52	3.45	8.05	9.20
			65.47	3.42	8.00	9.10
<i>IIb</i>	C <sub>20</sub> H <sub>14</sub> N <sub>2</sub> O <sub>4</sub> S (378.0)	196—197	63.49	3.70	7.41	8.47
			63.41	3.66	7.36	8.42
<i>IIc</i>	C <sub>19</sub> H <sub>11</sub> BrN <sub>2</sub> O <sub>3</sub> S (426.9)	275—277	53.41	2.58	6.56	7.50
			53.37	2.55	6.60	7.42
<i>IId</i>	C <sub>19</sub> H <sub>10</sub> Br <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S (505.8)	254—256	45.08	1.98	5.54	6.33
			45.01	1.94	5.52	6.30
<i>IIf</i>	C <sub>20</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub> S (362.0)	191—192	66.30	3.87	7.74	8.84
			63.26	3.86	7.60	8.75
<i>IIg</i>	C <sub>21</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S (375.0)	166—167	67.20	4.53	11.20	8.53
			67.16	4.51	11.00	8.50
<i>IIIa</i>	C <sub>23</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub> S (398.0)	277—279	69.35	3.52	7.04	8.04
			69.28	3.49	7.00	8.10
<i>IIIb</i>	C <sub>21</sub> H <sub>14</sub> N <sub>2</sub> O <sub>4</sub> S <sub>2</sub> (422.0)	282—284	59.72	3.32	6.64	15.17
			59.67	3.29	6.61	15.10
<i>IIIc</i>	C <sub>22</sub> H <sub>16</sub> N <sub>2</sub> O <sub>5</sub> S <sub>2</sub> (452.0)	200—201	58.41	3.54	6.20	14.16
			58.32	3.50	6.16	14.00
<i>IIId</i>	C <sub>21</sub> H <sub>13</sub> BrN <sub>2</sub> O <sub>4</sub> S <sub>2</sub> (500.9)	210—212	50.31	2.69	5.59	12.76
					5.50	12.80
<i>IIIe</i>	C <sub>21</sub> H <sub>12</sub> Br <sub>2</sub> N <sub>2</sub> O <sub>4</sub> S <sub>2</sub> (579.8)	218—220	43.46	2.07	4.83	11.04
			43.31	2.02	4.80	11.10
<i>IIIe</i>	C <sub>22</sub> H <sub>16</sub> N <sub>2</sub> O <sub>4</sub> S <sub>2</sub> (436.0)	172—173	60.55	3.67	6.42	14.68
			60.50	3.62	6.36	14.60
<i>IIIg</i>	C <sub>23</sub> H <sub>19</sub> N <sub>2</sub> O <sub>3</sub> S <sub>2</sub> (449.0)	228—230	61.47	4.23	9.35	14.25
			61.42	4.20	9.30	14.30
<i>IIIg</i>	C <sub>25</sub> H <sub>16</sub> N <sub>2</sub> O <sub>4</sub> S <sub>2</sub> (472.0)	242—244	63.56	3.39	5.93	13.56
			63.43	3.36	5.90	13.50
<i>IV</i>	C <sub>14</sub> H <sub>9</sub> ClN <sub>2</sub> O <sub>3</sub> S (320.0)	262—264	52.50	2.81	8.75	10.00
			52.45	2.79	9.00	10.23

<sup>a</sup> All the compounds were obtained in 70—80% yields.

on the basis of analytical and spectral data (Table I). A plausible mechanism has been proposed for the formation of *IV* in Scheme 2. The Schiff's base undergoes



SCHEME 2

1,2-addition with chloroacetyl chloride (positive<sup>10</sup> Tollen's test) giving the dichloro-compound which might be hydrolyzed with a trace of water to the product and benzaldehyde.

### EXPERIMENTAL

All the melting points are uncorrected. IR spectra ( $\tilde{\nu}_{\text{max}}$  in  $\text{cm}^{-1}$ ) were recorded in Nujol on a Perkin-Elmer 282 instrument. <sup>1</sup>H NMR spectra were scanned on 90 MHz NMR spectrometer using tetramethylsilane as internal standard. Mass spectrum was scanned on Jeol JMS-D 300 mass spectrometer at 70 eV. The substituted 3-( $\omega$ -bromoacetyl)coumarins and 2-aminothiazolyl coumarins have been prepared by known<sup>8</sup> procedures.

#### 3-(2-((Arylmethylene)amino)-4-thiazolyl)-2H-1-benzopyran-2-one (*II*)

A mixture of 2-amino-4-thiazolyl coumarin (1 mmol) and the appropriate aromatic aldehyde (1 mmol) was refluxed in ethanol (15 ml) containing catalytic amount of piperidine for 4 hours. The reaction mixture was cooled and the separated solid was filtered and crystallized from benzene. IR spectrum of *Ila*: 1 600 ( $\text{C}=\text{N}$ ), 1 720 (lactone carbonyl). <sup>1</sup>H NMR spectrum ( $\text{CDCl}_3$ ) of *Ila*:  $\delta$  6.9 s, 1 H ( $\text{CH}=\text{}$ ); 7.0–7.6 m, 8 H (aromatic); 8.3 s, 1 H (thiazole); 8.6 s, 1 H (coumarin H-4); 9.1 s, 1 H (phenolic OH). Mass spectrum of *Ila* ( $m/z$ ): 348 ( $\text{M}^+$ , 30%), 315(15), 286(20), 245(5), 244(34), 216(5), 211(7), 58(40), 43(100).

#### 2-Aryl-3-(4-(2-oxo-2H-1-benzopyran-3-yl)-2-thiazolyl)-4-thiazolidinones (*III*)

To a well stirred solution of Schiff's base *II* (1 mmol) in dry benzene (50 ml) mercaptoacetic acid (1 mmol) was added. The contents were refluxed for 6 hours. The reaction mixture was cooled. The separated solid was washed with  $\text{NaHCO}_3$  and crystallized from dimethylformamide. IR spectrum of *IIIa*: 1 600 ( $\text{C}=\text{N}$ ), 1 675 ( $\text{N}-\text{C}=\text{O}$ ), 3 300–3 600 (phenolic OH). <sup>1</sup>H NMR spectrum (TFA) of *IIIa*:  $\delta$  3.9 s, 2 H ( $\text{CH}_2$ ); 7.2 s, 1 H (tertiary H of thiazolidine ring); 7.3–7.7 m, 8 H (aromatic); 8.4 s, 1 H (thiazole); 9.5 s, 1 H (coumarin H-4); 10.0 s, 1 H (phenolic OH). Mass spectrum of *IIIa* ( $m/z$ ): 422 ( $\text{M}^+$ , 83%), 350(25), 349(100), 271(20), 244(20), 137(37), 102(10).

## Chloroacetamido Derivative of I

A mixture of Schiff's base (II) (1 mmol) and chloroacetyl chloride (1 mmol) was refluxed in dioxane containing catalytic amount of triethylamine for 6 hours. The reaction mixture was cooled, the solid separated was washed with water and recrystallized from dimethylformamide.

When the reaction is carried out with I and chloroacetyl chloride under similar conditions it gives IV.

IR spectrum of IVa: 660 (C—Cl), 1 610 (C=N), 1 685 (NH—C=O), 1 720 (lactone carbonyl). Due to poor solubility of the compound IVa the NMR could not be run. Mass spectrum of IVa ( $m/z$ ): 320 ( $M^+$ , 50%), 245(20), 244(100), 216(12), 211(20), 170(22), 101(12).

The authors are thankful to Professor P. S. Rao, Head of the Department of Chemistry for providing facilities, one of us (U.V.) is grateful to CSIR, New Delhi, India for the award of senior research fellowship.

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