

## SOME REACTIONS WITH 3-AMINOCOUMARIN

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3-Aminocoumarin was reacted with the diazonium salts of aromatic amines to obtain the azo compounds (Ia-e), which cyclized to as triazines (VI) upon treatment with benzaldehyde. Further, 3-aminocoumarin was reacted with chloroacetyl chloride to give the chloroacetylated derivative (II) which reacted with aromatic and aliphatic amines to afford its amide derivatives (IIIa-f), and with ammonium thiocyanate to afford the thiocyanate derivative (IV) which underwent cyclization by reaction with benzaldehyde to obtain the thiazolidone derivative (V) in good yields.

On the other hand, treating of 3-aminocoumarin with 4-(2-quinoline)-2-phenyl-2-oxazolin-5-one [10] in alcohol gave the quinoline coumarin acrylic acid derivative (IX) which undergoes cyclization to the 2-coumarin-4-quinoline imidazolone derivative X by refluxing in acetic acid.

*Key words:* 3-Aminocoumarin, Azo-compounds; Diazonium salts.

## INTRODUCTION

In view of the considerable biological and medicinal activities of coumarin ring [1-3] it was thought of interest of synthesize some new coumarin derivatives fused and substituted with biologically active heterocycles. We report here the syntheses of some new azo dyes derived from 3-aminocoumarin, and their cyclization to triazines upon treatment with aldehydes, the reactivity of the 3-chloroacetylamine-coumarin towards aromatic amines and ammonium thiocyanate, and the condensation reactions of 3-amino coumarin with 4-(2-quinolyl)-2-oxazolin-5-one.[3]

3-Aminocoumarin was coupled with different diazonium salts in cold ethanol containing sodium acetate to give the corresponding 4-arylaazo-3-aminocoumarin (Ia-e) in good yield [4-8]. Treatment of Ia with benzaldehyde in acetic anhydride acetic acid mixture containing anhydrous sodium acetate gave the corresponding coumarin [1,2-b]-as-triazine-2, 3-diphenyl (IV). Coumarin ring transformation reaction to pyridone derivative was achieved via the reaction of compound (IV) with *p*-chloroaniline in ethanol afford *N*-(*p*-chlorophenyl)- $\alpha$ -pyridone-[1, 2-b] as triazino-2, 3-diphenyl (VII).

3-Aminocoumarin was readily acylated upon warming with chloroacetyl chloride to give the corresponding 3-( $\alpha$ -chloroacetamido)-coumarin (II).

Fusion of 3-( $\alpha$ -chloroacetamido)-coumarin (II) with primary aromatic amines at 150-170<sup>o</sup>, was found to give

3-( $\alpha$ -arylaminoacetamido) coumarin (IIIa-b). Similarly, the reaction of 3-chloroacetamido coumarin with piperidine, and phenylhydrazine under the same conditions gave 3-( $\alpha$ -piperidinoacetamido)-coumarin (IIIe), and 3-( $\alpha$ -phenylhydrazinoacetamido)-coumarin (IIIf), respectively. These results are in agreement with the previously reported reactions of aromatic amines, secondary amines and phenylhydrazine with 3-carbethoxy coumarin [4-5].

The reaction of 3-( $\alpha$ -chloroacetamido)-coumarin with potassium thiocyanate in ethanol was found to give the corresponding 3-( $\alpha$ -thiocyanateacetamido)-coumarin (IV). Treatment of (IV) with dil. hydrochloric acid ethanol mixture was found to give 3-aminocoumarin by hydrolysis.

Reaction of (IV) with benzaldehyde in the presence of acetic anhydride/acetic acid mixture containing fused sodium acetate was found to give the corresponding thiazolidinone derivative (V).

Similarly, the 3-amino coumarin was reacted with 4-(2-quinolyl)-2-oxazolin-5-one [6], to give the (2-amino-coumarin) carboxamido of *N*-phenyl carboxy- $\alpha$ -quinolyl glycine (IX).

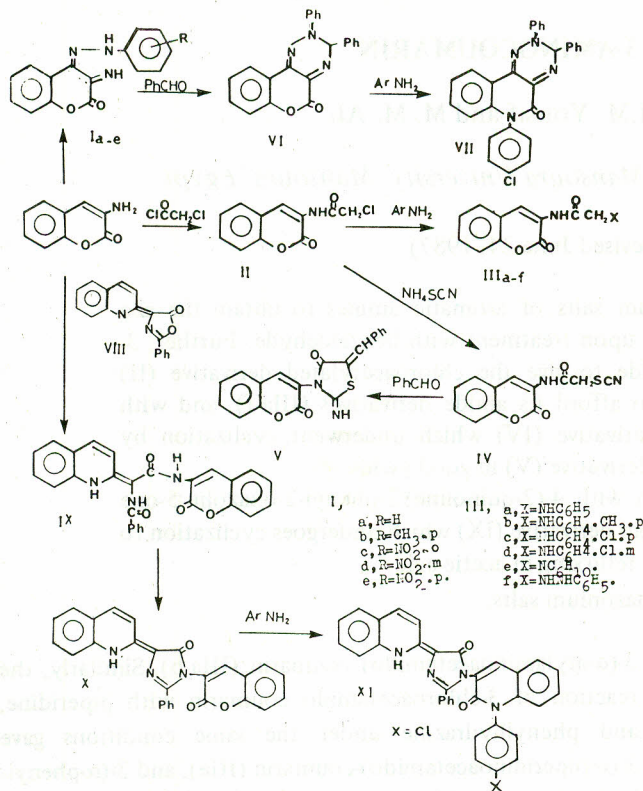
Refluxing of (IX) in acetic acid containing sodium acetate gave the 1-(3-coumarin)-2-phenyl-4-(2-quinolyl)-2-imidazolin-5-one X. [9].

On the other hand the treatment of X with *p*-chloroaniline in ethanol gave the 1-(3-*N*-aryl- $\alpha$ -pyridone)-2-phenyl-4-(2-quinolyl)-2-imidazolin-5-one (XI).

The given scheme shows the structures and reactions.

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## EXPERIMENTAL

Analytical data were determined at the Microanalytical Unit, Cairo University. Infrared spectra were recorded on a SP 1000 Pye Unicam Spectrophotometer. All melting points are uncorrected.

**4-Arylazo-3-aminocoumarin (Ia-e):** The appropriate diazonium solution was added (0.1 mole) in ethanol (100 ml) containing sodium acetate (2 g) in an ice-salt bath. Stirring was continued for 15 min. at 0°. The stirred mixture was then allowed to attain room temperature.

The crude product was almost completely precipitated within 1 hr. It was filtered, dried by suction and recrystallized from acetic acid to give 4-arylazo-3-aminocoumarin (Ia-e) (Table I).

Structure of (Ia-e) was established by elemental analyses and by IR measurements which showed stretching frequencies at 1730, 3300  $cm^{-1}$  characteristic for C=O ( $\alpha$ -lactone) and NH groups, respectively. IR spectra did not reveal any -N=N- group around 1540  $cm^{-1}$ . This suggests that the tautomeric iminohydrazone structure (Ia-e) predominates over the amino azo structure.

**3-( $\alpha$ -Chloroacetamido)-coumarin II:** A mixture of 3-aminocoumarin (0.1 mole) and chloroacetyl chloride

(11 ml) in (50 ml) ether was heated under reflux for 2 hr. The reaction mixture was cooled, and the crude product was collected. Recrystallization from ethanol gave 3-( $\alpha$ -chloroacetamido)-coumarin (II) as pale yellow crystals, m.p. 195°; yield 84%. IR spectra showed two carbonyl stretching bands at 1730 and 1680  $cm^{-1}$  for C=O ( $\alpha$ -lactone and amide group, respectively).

Calculated for  $C_{11}H_8NO_3Cl$ : C, 55.5; H, 3.3; N, 5.9; Cl, 14.9  
Found: C, 55.49; H, 3.26; N, 5.87; Cl, 14.95

**3-( $\alpha$ -Arylaminoacetamido)-coumarins (IIIa-d):** A mixture of (II) (0.01 mol) and appropriate primary aromatic amine (0.01 mol) was heated at 150-170° in an oil bath for 1 hr. The reaction mixture was cooled, and the crude product was collected and washed with petroleum ether (60-80°).

Recrystallization from ethanol gave 3-( $\alpha$ -arylaminoacetamido)-coumarins (IIIa-d) as white crystals (Table 2).

The assigned structure for products (IIIa-f) was based on elemental analysis and IR measurements. In the later absorption bands were noted at 1730, 1680, and 3300  $cm^{-1}$  which are characteristic of stretching frequencies for carbonyl ( $\gamma$ -lactone), carbonyl of amide, and NH groups, respectively.

**3-( $\alpha$ -Piperidinoacetamido)-coumarin (IIIe):** A mixture of (II) (2.49g) and piperidine (1 ml) was heated as described above to give 3-( $\alpha$ -piperidinoacetamido)-coumarin (IIIe) as white crystals, m.p. 150°, yield 90%.

Calculated for  $C_{16}H_{18}N_2O_3$ : C, 67.1; H, 6.3; N, 9.8%  
Found: C, 67.15; H, 6.35; N, 9.81%

**3-( $\alpha$ -Phenylhydrazinoacetamido)-coumarin (IIIf):** A mixture of (II) (2.4 g) and phenylhydrazine (1.1 ml) was treated as described above to give 3-( $\alpha$ -phenylhydrazinoacetamido)-coumarin (IIIf) as white crystals, m.p. 170°; yield 82%.

Calculated for  $C_{17}H_{15}N_3O_3$ : C, 66.0; H, 4.9; N, 13.6%  
Found: C, 66.0; H, 5.01; N, 13.6%

**3-( $\alpha$ -Thiocyanoacetamido)-coumarin (IV):** A mixture of (II) (2.4 g) in 30 ml ethanol, and potassium thiocyanate (1g) in 10 ml water was heated under reflux for 4 hr. The crude product was collected from the cooled mixture. Recrystallization from acetic acid gave 3-( $\alpha$ -thiocyanoacetamido)-coumarin (IV) as pale yellow crystals, m.p. 240°, yield 87%.

Calculated for  $C_{12}H_8N_2O_3S$ : C, 55.4; H, 3.1; N, 10.8; S, 12.3%  
Found: C, 55.37; H, 3.13; N, 1.82; S, 12.33%



Table 1. 4-Arylazo-3-aminocoumarins (Ia-c)

Compound	Colour	M.p. (°C)	Yield (%)	Molecular formula	Found (%)			Calcd. (%)		
					C	H	N	C	H	N
Ia	Red	199	85	C <sub>15</sub> H <sub>11</sub> O <sub>2</sub> N <sub>3</sub>	67.88	4.15	15.85	67.9	4.1	15.8
Ib	Red	195	87	C <sub>16</sub> H <sub>13</sub> O <sub>2</sub> N <sub>3</sub>	68.79	4.60	15.77	68.8	4.6	15.8
Ic	Brown	210	85	C <sub>15</sub> H <sub>10</sub> O <sub>4</sub> N <sub>4</sub>	58.13	3.18	18.13	58.1	3.2	18.1
Id	Red	238	85	C <sub>15</sub> H <sub>10</sub> O <sub>4</sub> N <sub>4</sub>	58.10	3.24	18.10	58.1	3.2	18.1
Ie	Violet	245	90	C <sub>15</sub> H <sub>10</sub> O <sub>4</sub> N <sub>4</sub>	58.12	3.20	17.96	58.1	3.2	18.1

Table 2. 3-( $\alpha$ -Arylaminoacetamido)-coumarins (IIIa-d).

Compound	M.p. °C	Yield %	Molecular formula	Found (%)			Calcd. (%)		
				C	H	N	C	H	N
IIIa	215	83	C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub>	69.45	4.68	9.48	69.4	4.7	9.5
IIIb	205	85	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub>	70.16	5.19	9.05	70.1	5.2	9.1
IIIc	205	80	C <sub>17</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>3</sub>	62.15	3.86	8.19	62.1	3.9	8.5
IIId	220	81	C <sub>17</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>3</sub>	62.15	3.87	8.55	62.1	3.9	8.5

*Action of ethanol-hydrochloric acid mixture on (IV):* Compound (IV) (2.6 g) was heated under reflux with 50 ml ethanol di. hydrochloric acid (1:1) for 3 hr. The reaction mixture was cooled and the precipitated solid was collected. Crystallization of the product from ethanol gave 3-aminocoumarin (m.p. and mixed m.p. 133°).

*5-Benzylidene-2-imino-3-coumarin-(3-yl)-Thiazolidinone (V):* A mixture of 3-( $\alpha$ -thiocyanatoacetamido)-coumarin (IV) (2.6 g) (0.1 mol) and benzaldehyde (0.9 ml., 0.1 mol) in 20 ml acetic anhydride and 20 ml acetic acid containing freshly fused sodium acetate (0.5 g) was heated on a water bath at 100° for 3 hr. The reaction mixture was cooled and the precipitated product was collected. Recrystallization from acetic acid gave 5-benzyliden-2-imino-3-coumarin-(3-yl)-4-thiazolidinone (V) as yellow crystals, m.p. 272°, yield 79%.

The structure of (V) was confirmed by correct analytical result and IR measurements which show stretching frequencies at 1730, 1700, and 3300cm<sup>-1</sup> attributable to C=O of  $\gamma$ -lactone, C=O of thiazolidinone ring, NH groups, respectively.

Calculated for C<sub>19</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>S: C, 65.5, H, 3.1, N, 8.0, S, 9.2%

Found: C, 65.53, H, 3.12; N, 8.02; S, 9.3%.

*Preparation of coumarin [1,2-b-triazine-2, diphenyl (VI):* Ia (0.01 mol) was refluxed with 0.01 mole) of ben-

zaldehyde in the presence of 50 ml of glacial acetic acid and 5 g of freshly fused sodium acetate for three hours on a hot plate, the reaction mixture was cooled, and the collected precipitate recrystallized from benzene to give yellow crystals of VI with m.p. 249°, with an yield of 55%. IR spectra showed stretching frequencies at 1730, and 1640 cm<sup>-1</sup>, characteristic for the  $\gamma$ -lactone and C=N groups, respectively. (molecular formula : C<sub>22</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>)

Found : C, 75.0 H, 3.95 N, 11.90%

Requires: C, 75.00 H, 4.00 N, 11.95%

*N-p-chlorophenyl- $\alpha$ -pyridone [1, 2-b] triazine-2, 3-diphenyl VII.* Triazine derivative (VI) (0.01 mole) was refluxed with (0.01 mole) of *p*-chloroaniline in 100 ml ethanol for 2 hr. The reaction mixture was cooled, and the collected precipitate was recrystallized from ethanol to give orange crystals of VII with m.p. 198°, and yield 85%; It shows stretching frequencies at 1640, and 1680 cm<sup>-1</sup> for C=N and C<sup>o</sup>-N groups respectively.

Calcd. C, 72.57, H, 4.10, N, 12.10%

Found C, 72.54, H, 4.08, N, 12.07%

*2-Aminocoumarin) carboxamido of N-phenyl carboxy- $\alpha$ -quinolyl-glycine (IX):* 0.01 mole of the 2-phenyl-4-(2-quinoline)-2-oxazolin-5-one VIII [10], was refluxed with (0.01 mole) of 2-amino coumarin in 100ml ethanol on a water bath for 2 hr. The reaction mixture, was cooled

and the collected precipitate was recrystallized from ethanol to give a red crystals of IX with m.p.  $320^{\circ}$ , and yield 75% IR spectra showed bands at 3300, 1680,  $1730\text{ cm}^{-1}$  for NH,  $\text{C}''\text{O}-\text{N}$ - and  $-\text{C}''\text{O}$ -groups respectively.

Calcd. C, 72.16, H, 4.45, N, 9.36%

Found C, 72.12, H, 4.43, N, 9.33%

*1-(3-Coumarin)-2-pheynl-4-(2-quinoline)-2-oxazolin-5-one X*: 0.01 mole of the glycine derivative IX was refluxed in 100 ml glacial acetic acid contained 1 g of freshly fused sodium acetate, on a hot plate for 2 hr. After cooling the reaction mixture the collected precipitate was recrystallized from acetic acid to give yellowish crystals of X with m.p.  $167^{\circ}$ , and yield 85%, IR spectra, 3300, 1680, 1640,  $1730\text{ cm}^{-1}$  for NH,  $-\text{C}''\text{O}-\text{N}$ -, C=N and  $-\text{C}''\text{O}$  groups respectively.

Calcd. C, 73.55, H, 94 and N, 9.73%

Found C, 73.52, H, 91 and N, 9.72%

*1-(3-N-aryl- $\alpha$ -pyridone)-2-phenyl-4-(2-quinoline)-2-oxazolin-5-one XI*: 0.01 mole of the imidazolone derivative (X) was refluxed with 0.01 mole of *p*-chloroaniline in 100ml ethanol containing 1 g of fused sodium acetate for 2 hr. The reaction mixture was cooled and the collected precipitate washed with water and recrystallized from ethanol to give brownish crystals of XI with m.p.  $250^{\circ}$ , and yield 86% IR spectra showed bands at 3300, 1640,  $1680\text{ cm}^{-1}$  for NH, C=N and C=O-N groups resectively.

Calcd. C, 73.19 H, 3.88 and N, 10.35%

Found C, 73.17 H, 3.84 and N, 10.32%

#### REFERENCES

1. A.M. El-Nagar, F.S.M. Ahmed, A.M. Abdel-Salam, M.A. Radi and M.S.A. Latif, J. Heterocyclic Chem., 18 1203, (1981).
2. K. Okumura, K. Ashino and T. Okuda, Yakugaku Zasshi, 81 1482, (1961) Chem. Abstr., 56 7938 (1962)
3. R.B. Moppett, J. Med. Chem, 7 446 (1964).
4. A. Sammour, A. Marei, and S. El-Ashry, J. Chem. U.A.R. 21 464 (1970).
5. A. Sammour, M.I.B. Selim, and M. El-Kady, J. Chem. U.A.R., 14, 261 (1971).
6. I. Hisashi, I. Mastaka, and S. Nobuhiro, Yakagaku Zasshi, 88, 755 (1968), Chem-Abstr., 70, 3751 (1969).
7. J. Cottam, and R. Livingstone, J. Chem. Soc., 6646 (1965).
8. J. D. Hepworth, and R. Livingstone, J. Chem., Soc., 2013 (1966).
9. H.M. Hassan, M.S. El-Housseni, and O.M.O. Habib, J. Prakt. Chemie, Band 325, 4, 685 (1963).
10. M.M. Yousif, S. Saeki and M. Hamava, J. Heterocyclic Chem., 17, 1029 (1980).