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**SYNTHESIS OF 4-HYDROXY-3-SUBSTITUTED COUMARINS OF EXPECTED BIOLOGICAL ACTIVITY AND THEIR REACTIONS WITH SOME NUCLEOPHILES**

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**Abstract**

3-Acetyl-4-hydroxy substituted coumarins (**II<sub>a-c</sub>**) were prepared. Their reactions with hydrazines in DMF gave the corresponding 4-hydroxy -(3-substituted pyrazolin-3-yl)coumarins (**IV<sub>a-f</sub>**) via the intermediate hydrazone (**III**). Their reaction with hydroxylamine hydrochloride gave the corresponding isoxazol-3-yl coumarin (**VI<sub>a-c</sub>**) and (**VII<sub>a,b</sub>**) via the oxime intermediate (**V**). Reaction of **II** with aromatic aldehydes gave the corresponding chalcone derivatives (**VIII<sub>a-k</sub>**) which were reacted with hydrazines and hydroxyl amine hydrochloride and gave (**IX<sub>a</sub>**) and (**X<sub>a-c</sub>**). Condensation of (**II<sub>a-c</sub>**) with aromatic aldehydes, malononitrile in the presence ammonium acetate yielded the corresponding 3-cyano-4-aryl nictoinamido-6-yl-coumarin (**XI<sub>a-f</sub>**).

4-Hydroxy coumarin (**I<sub>a-c</sub>**) on treatment with POCl<sub>3</sub> in DMF give the corresponding 4-Chloro-3-formyl coumarin (**XII<sub>a-c</sub>**) which on treatment with sod azide gave the corresponding 4-azido-3-formyl coumarin (**XIII<sub>a-c</sub>**). 4-chloro-3-formyl coumarine (**XII**) on treatment with hydrazine gave pyrazolo coumarin derivatives (**XIV<sub>a-d</sub>**) and on treatment with hydroxylamine hydrochloride gave 4-chloro-3-aldo oxime coumarin derivatives (**XV<sub>a,b</sub>**). On treatment of 4-azido-3-formyl coumarin with active methylene compounds such as malononitrile and ethyl cyanacetate derivatives gave (**XVI<sub>a-d</sub>**) respectively.

The antibacterial and antifungal activities of some compounds have been described.

**Results and Discussion :**

Coumarins are versatile reagents and their utility in heterocyclic synthesis has recently received a considerable attention. They possess significant biological activities<sup>(1-3)</sup>, anti-bacterial<sup>(4)</sup>, anti-tumoral<sup>(5)</sup>, and anti-HIV<sup>(6-9)</sup>. Due to those varied biological activities, we have synthesized several 4-substituted, 4,3-substituted-2H-1-benzopyran-2-one derivatives in order to investigate the structure activity relationships of coumarin derivatives. In the present investigation, we report here the synthetic procedures for compounds (**I-IV**) and the anti-microbial activity of the products. Thus 4-hydroxycoumarins (**I<sub>a-c</sub>**) under suitable procedures yielded 3-

acetyl-4-hydroxycoumarin (**II**<sub>a-c</sub>), which reacted with hydrazines, namely hydrazines hydrate, phenyl hydrazine and 4-nitrophenyl hydrazine in boiling DMF containing few drops of piperidine to give the pyrazole derivative (**IV**<sub>a-f</sub>). The reaction of (**II**) with hydroxylamine hydrochloride in boiling ethanol containing sodium acetate yielded the oximes (**V**) which on reaction with DMF/piperidine in boiling xylene gave the corresponding isoxazol-3-yl coumarins (**VI**<sub>a-c</sub>) and (**VII**<sub>a,b</sub>) respectively. It is believed that compounds (**VI**<sub>a-c</sub>) are formed via nucleophilic attack of nitrogen of the hydroxylamine moiety the carbonyl of compounds (**II**) and the formyl groups of DMF affected cyclization to the desired isoxazole derivatives (**VI**) and may be a little of (**VII**<sub>a,b</sub>).

Structure (**VI**) was established on the basis of <sup>1</sup>H-NMR spectrum as the 4-hydroxy proton was observed at δ 12.8 ppm and the absence of the methyl protons.

The base catalyzed reaction of (**II**) with aromatic aldehydes<sup>(10,11)</sup> in chloroform in the presence of piperidine with azeotropic removal of water afforded the corresponding 4-hydroxy-3-cinnamoyl coumarin derivatives (**VIII**<sub>a-k</sub>)<sup>(12)</sup>. The <sup>1</sup>H-NMR spectrum of (**VIII**<sub>a</sub>) showed the coupling of the olefinic protons at δ 5.95 and δ 8.55 ppm (J=15Hz, AB system). The reaction of **VIII** with malononitrile in refluxing ethanol containing ammonium acetate yielded the corresponding 4-hydroxy-3-(3-cyano-4-aryl-2(1H)-pyridine)-yl coumarins (**XI**<sub>a-f</sub>). The formation of **XI** might proceed via an intermediate reaction between β-aminoenones and malononitrile to give 2(1H)-pyridone (**XI**) and considered to begin with a conjugated addition of the nitrile to the enone followed by elimination of water and cyclization to (**XI**). This was further proved by the reaction of (**II**) with aromatic aldehydes namely 4-nitrobenzaldehyde, 2,4-dimethylamino benzaldehyde, furfural and/or isonicotinaldehyde to give **XI**. This was in agreement with the previous findings<sup>(13)</sup>.

The reaction of 3-cinnamoyl coumarins **VIII** with hydrazines namely, hydrazine hydrate, phenyl hydrazine and/or 4-nitro phenyl-hydrazone in boiling ethanol afforded the corresponding pyrazoline derivatives **IX**<sub>a-h</sub>; while the reaction of compounds **VIII** with hydrazine hydrate in refluxing glacial acetic acid, it affected acetylation of NH of the pyrazoline ring and gave the corresponding 4-hydroxy-3-[(N-acetyl)pyrazoline]-3-yl coumarin **IX**<sub>i,j</sub>. Similarly, the reaction of **VIII** with hydroxylamine hydrochloride in boiling pyridine gave the corresponding 3-(isoxazol)-5-yl coumarin (**X**<sub>a-c</sub>).

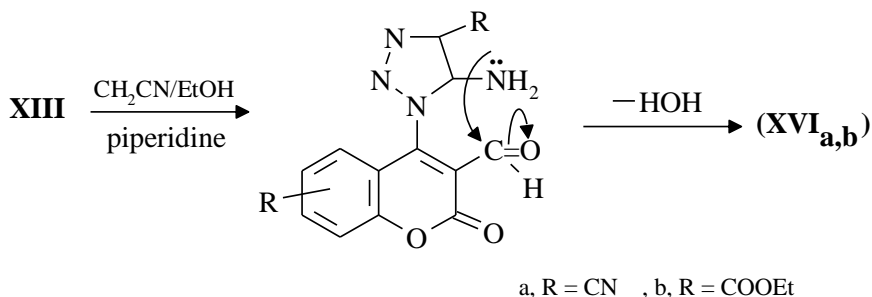
The formation of **IX** and **X** were assumed to proceed via initial nucleophilic attack of the amino group to the carbonyl of the cinnamoyl moiety without attack at the carbonyl of the  $\alpha$ -pyrone ring followed by cyclization.

The present investigation also deals with the action of halogen nucleophiles on the  $\alpha,\beta$ -unsaturated  $\alpha$ -pyrone ring in coumarin derivatives. Thus, the reaction of (**I**) with phosphoryl chloride in DMF afforded 4-chloro-3-formyl-(2-H)-1-benzopyran-2-one derivatives (**XII<sub>a-c</sub>**). The hydroxyl group at position-4-in the  $\alpha$ -pyrone ring seemed to be a good leaving group towards the halogen nucleophile and the behavior of the  $\alpha$ -pyrone ring as a nucleophile was established by the reaction with DMF afforded the corresponding 4-chloro-3-formyl coumarin (**XII<sub>a-c</sub>**). It has been reported<sup>(14)</sup> that ammonia causes ring opening of the  $\alpha$ -pyrone moiety in coumarin.

Similarly, the reaction of 4-azidocoumarins with nitrogen nucleophiles affected  $\alpha$ -pyrone ring fission<sup>(15)</sup>. Thus, the reaction of 4-chloro-3-formyl coumarin (**XII<sub>a-c</sub>**) with sodium azide in DMF afforded the corresponding 4-azido-3-formyl-1-benzopyran-2-one (**XIII**).

The reaction of **XIII** with active methylene compounds such as, malononitrile and/or ethylcyanoacetate in boiling ethanol containing a few drops of piperidine afforded nitrogen bridge head derivatives, which were defined as 3-cyano-6-oxo-[1] benzopyrano[4,3-d] pyrimidino [3,2-c] triazole (**XVI<sub>a-d</sub>**)

The reaction was believed to proceed via the formation of 3-formyl-4-aminotriazolyl coumarin intermediate which underwent intramolecular cyclo condensation gave the desired products.



Hydrazinolysis of compound (**XII**) with hydrazine hydrate in boiling ethanol afforded 1-aryl-4-oxo-[1] benzopyrano[4,3-c] pyrazole (**XIV<sub>a-d</sub>**).

On the other hand the reaction of hydroxylamine hydrochloride with (XII) in boiling ethanol containing few drops of piperidine yielded the corresponding oxime via a nucleophilic attack at the position-3 (XV<sub>a,b</sub>).

### Experimental

All melting points were measured in capillary tubes on a GK apparatus and are uncorrected. The IR spectra were recorded in KBr disks (Wafer technique) on a Shimadzu IR-740 spectrophotometer. The <sup>1</sup>H-NMR spectra were measured on a Perkin-Elmer 360L 60 MHz spectrometer with DMSO-d<sub>6</sub> as a solvent, TMS as internal standard and chemical shifts expressed in δ ppm. The mass spectra were measured on a Finnigan GC/MS INCOS XL spectrometer at 70eV.

### Synthesis of 3-Acetyl-4-hydroxy coumarin (II<sub>a-c</sub>).

They were prepared according to a previous publication<sup>(16,17)</sup>, c.f. Table 1.

### Synthesis of 4-Hydroxy-3-(coumarin-3-yl) pyrazoles (IV<sub>a-f</sub>)

To a solution of II<sub>a-c</sub> (0.01 mol) in 15 ml of DMF hydrazine hydrate, phenyl hydrazine and/or 4-nitrophenylhydrazine (0.01 mol) in 10 ml of absolute ethanol containing a few drops of piperidine was added. The reaction mixture was kept at room temperature overnight, then filtered off, washed with ethanol and dried to give the hydrazone (III<sub>a-f</sub>). Compounds (III<sub>a-f</sub>) each was taken in 15 ml of DMF and 15 ml of ethanol containing few drops of piperidine was heated under reflux for 6 hours, then left to cool. The product was collected and recrystallised from the ethanol as IV<sub>a-f</sub>, c.f. Table 1.

### Synthesis of 4-Hydroxy-3-(coumarin-3-yl) isoxazol (VI<sub>a-c</sub>), (VII<sub>a,b</sub>)

A mixture of II<sub>a-c</sub> (0.01 mol) and hydroxylamine hydrochloride (0.01 mol) in 30 ml of absolute ethanol containing anhydrous sodium acetate (0.01 mol, 0.82g) was refluxed for 6 hours, then filtered while hot and left to cool. The product that obtained was collected, washed well with water and recrystallized from the proper solvent to give (V<sub>a-c</sub>). A mixture of (V<sub>a-c</sub>) (0.01 mol) in 20 ml of DMF and 10 ml of ethanol containing few drops of piperidine was heated under reflux for 6 hours, then left to cool. The products VI<sub>a-c</sub> were separated by filtration recrystallised from the proper solvent in a yield 45-60%, while the filtrate contained VII<sub>a,b</sub> recrystallised from the proper solvent recrystallised from the proper solvent in yield 20-25% c.f. Table 1.

**Synthesis of 3- Cinnamoyl-4-Hydroxycoumarin (VIII<sub>a-k</sub>)**

To a solution **II<sub>a-c</sub>** (0.01 mol) in 30 ml of absolute ethanol containing few drops of piperidine add a solution of the aromatic aldehyde namely, 4-nitrobenzaldehyde, 4-dimethylamineobenzaldehyde, 2-furaldehyde, isonicotinaldehyde, 4-chlorobenzaldehyde, 4-methoxy benzaldehyde, and/or 4-methylbenzaldehyde (0.01 mol) in 10 ml of absolute ethanol while stirring. Stirring was continued for 2 hours and the solution was rendered alkaline to litmus, then left to cool overnight. It was then acidified with dil. HCl and the precipitate was collected, washed well with light petrol, dried and recrystallised from the proper solvents **VIII<sub>a-k</sub>** c.f. Table 1.

**Synthesis of 3- (1-Substituted)-5'-arylpirazo-3'yl-4-hydroxycoumarin (IX<sub>a-h</sub>).**

To a solution of **VIII<sub>a-k</sub>** (0.01 mol) in 50 ml of ethanol-butanol (1:1 involume), add hydrazines namely hydrazine hydrate and/or phenyl hydrazine (0.01 mol). The mixture was heated under reflux for 6 hours, then cooled and the product was collected and washed well with light petrol and recrystallized from the proper solvent as **(IX<sub>a-h</sub>)** c.f. Table 1.

**Synthesis of 3-(1'-acetyl)-5'-arylpirazol-3'-yl-4-hydrazol-3'yl-4-hydroxycoumarin (IX<sub>i,j</sub>).**

To a solution of **VIII<sub>a</sub>**, **VIII<sub>c</sub>**, (0.01 mol) in 25 of glacial acetic acid add hydrazine hydrate (0.01 mol) and the reaction mixture was heated under reflux for 6 hours, then cooled and the product was collected washed with little ethanol, dried and recrystallized from the proper solvent as **IX<sub>i,j</sub>**; c.f. Table 1.

**Synthesis of 6-(4'-hydroxy substituted coumarin-3'yl)-1,2-dihydro-2-oxo-4-aryl nicotinonitrile (XI<sub>a-f</sub>).**

To a solution of **VIII<sub>a-f</sub>** (0.01 mol) in 20 ml of ethanol add a solution of malononitrile (0.01 mol) in 20 ml of ethanol and ammonium acetate (0.04 mol) and the mixture was heated under reflux for 4 hours. After cooling, the product was poured into H<sub>2</sub>O(50 ml), stirred well and the solid obtained was collected, dried and recrystallized from the proper solvent as **XI<sub>a-f</sub>**; c.f. Table 1.

**Reaction of VIII with hydroxyl amine hydrochloride. Formation of 3-(isoxazole-5'yl) coumarine (X<sub>a-c</sub>).**

To a solution of (0.01mol of **VIII a,g,j**) in 50 ml pyridine, add 0.01mol of hydroxyl amine hydrochloride. the mixture was Refluxed for 3 hrs. Cool the mixture

, then add cold dil Hcl. The solid obtained was collected, dried and recrystallized from the proper solvent as (**Xa-c**); c.f. table 1.

**Reaction of (**I<sub>a-c</sub>**) with phosphoryl chloride . Formation of 4-chloro-3-formyl coumarin (**XII<sub>a-c</sub>**).**

To 0.01, mole of **I** in 50 ml DMF added 5ml of phosphoryl chloride then refluxed the mixture for 3 hours on water bath. Cool the mixture and add 1:1 mixture of ice a conc. Hcl. The solid obtained was collected, dried and crystallized from the proper solvent as (**XII<sub>a-c</sub>**); c.f. table (1).

**Reaction of 4-chloro-3-formyl coumarine (**XII<sub>a-c</sub>**) with sodium azide. Formation of 4-azido-3-formyl-2H-1benzopyran-2-one (**XIII<sub>a-c</sub>**).**

To (0.01 mole) of **XII** in 50 ml of DMF add (0.01 mole) of sod azide. the mixture was refluxed for 3 hrs. The solid obtained was collected after cooling dried and recrystallized from the proper solvent as (**XII<sub>a-c</sub>**); c.f. table 1.

**Reaction of **XIII** with active methylene compounds . Formation of 3-cyano-6-oxo [1] benzopyrano [4,3-d] pyrimidino [3,2-c] triazole (**XVI<sub>a-d</sub>**).**

To (0.01 mole) of **XIII** in 50 ml EtOH added (0.01 mole) of active methylene compounds such as, malononitrile and/ or ethylcyanoacetate in the presence of a few drops of piperidine. the mixture was refluxed for 6 hours. The solid obtained was collected after cooling and recrystallized from the proper solvent as (**XVI<sub>a-d</sub>**); c.f. table (1).

**Reaction of 4-chloro-3-formyl coumarin **XII** with hydrazine hydrate. Formation of 1-aryl-4-oxo-[1] benzopyrano [4,3-c] pyrazole (**XIV<sub>a-d</sub>**)**

To (0.01 mol) of **XII** in 50 ml dioxan add (0.01 mole) of hydrazines namely hydrazine hydrate, phenyl hydrazine and/or 4-nitrophenylhydrazine. the mixture was Refluxed for 6 hours. The solid obtained was collected after cooling and recrystallized from the proper solvent as (**XIV<sub>a-d</sub>**) c.f. table (1).

**Reaction of 4-chloro-3-formyl coumarin **XII** with hydroxyl amine. Formation of 4-chloro-3-oximo coumarin **XV<sub>a,b</sub>**.**

To (0.01 mole) of **XII** in 50 ml ethanol in presence of sodium ethoxide add (0.01 mol) of hydroxylamine hydrochloride. the mixture was Refluxed for 6 hours. The solid obtained was collected and recrystallized from the proper solvent as **XV<sub>a,b</sub>**; c.f. table (1).

Table I. Physical data of the prepared compounds

Compd No.	M.P. °C solvent of crystallization	Molecular formula (Mol. wt.)	Analysis calcd./Found %			
			C	H	N	X
I <sub>a</sub>	101	C <sub>10</sub> H <sub>8</sub> O <sub>3</sub> (176)	68.19	4.55	--	--
	E		68.45	4.57	--	--
I <sub>b</sub>	112	C <sub>10</sub> H <sub>8</sub> O <sub>4</sub> (192)	62.50	4.17	--	
	E		62.72	4.25	--	
I <sub>c</sub>	132	C <sub>9</sub> H <sub>5</sub> O <sub>3</sub> Br (240)	45.00	2.08	--	32.92
	E		45.23	2.22	--	33.19
II <sub>a</sub>	152	C <sub>12</sub> H <sub>10</sub> O <sub>4</sub> (218)	66.06	4.59	--	--
	E		66.24	4.75	--	--
II <sub>b</sub>	161	C <sub>12</sub> H <sub>10</sub> O <sub>5</sub> (234)	61.54	4.27	--	
	E		61.75	4.35	--	
II <sub>c</sub>	168	C <sub>11</sub> H <sub>7</sub> O <sub>4</sub> Br (274)	48.18	2.55	--	28.83
	E		48.44	2.60	--	28.95
III <sub>a</sub>	138	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub> (308)	70.13	5.19	9.09	--
	P.E.		70.35	5.35	9.33	--
III <sub>b</sub>	149	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> O <sub>5</sub> (353)	61.19	4.25	11.89	--
	P.F.		61.20	4.12	11.98	--
III <sub>c</sub>	115	C <sub>18</sub> H <sub>14</sub> N <sub>4</sub> O <sub>7</sub> (398)	54.27	3.52	14.07	--
	P.E.		54.45	3.50	14.25	--
III <sub>d</sub>	162	C <sub>12</sub> H <sub>12</sub> N <sub>2</sub> O <sub>4</sub> (248)	58.06	4.83	11.29	--
	E		58.28	4.95	11.43	--
III <sub>e</sub>	157	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>4</sub> (324)	66.67	4.94	8.64	
	E		66.75	4.73	8.60	
III <sub>f</sub>	168	C <sub>18</sub> H <sub>14</sub> N <sub>4</sub> O <sub>8</sub> (414)	52.17	3.38	13.53	
	E		52.36	3.42	13.62	
III <sub>g</sub>	111	C <sub>11</sub> H <sub>9</sub> N <sub>2</sub> O <sub>3</sub> Br (296)	44.59	3.04	9.46	26.69
	P.E.		44.68	3.20	9.50	26.70
III <sub>h</sub>	139	C <sub>17</sub> H <sub>13</sub> N <sub>2</sub> O <sub>3</sub> Br (372)	54.84	3.49	7.53	21.24
	E		55.13	3.30	7.57	21.20
IV <sub>a</sub>	163	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O (318)	71.70	4.40	8.81	--
	E		71.88	4.42	8.79	--
IV <sub>b</sub>	172	C <sub>19</sub> H <sub>13</sub> N <sub>3</sub> O <sub>5</sub> (363)	62.81	3.58	11.57	--
	E		62.89	3.60	11.60	--
IV <sub>c</sub>	159	C <sub>13</sub> H <sub>10</sub> N <sub>2</sub> O <sub>4</sub> (258)	60.47	3.88	10.85	--
	E		60.65	3.67	10.90	--
IV <sub>d</sub>	168	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O <sub>4</sub> (334)	68.26	4.20	8.40	--
	E		68.34	4.21	8.38	--
IV <sub>e</sub>	131	C <sub>12</sub> H <sub>7</sub> N <sub>2</sub> O <sub>3</sub> Br (306)	47.06	2.29	9.15	25.81
	E		47.31	2.38	9.13	25.82
IV <sub>f</sub>	188	C <sub>18</sub> H <sub>11</sub> N <sub>2</sub> O <sub>3</sub> Br (382)	56.54	2.88	7.33	20.68
	E		56.62	2.95	7.32	20.70
VI <sub>a</sub>	128	C <sub>13</sub> H <sub>9</sub> NO <sub>4</sub> (243)	64.20	3.70	5.76	--
	P.E.		64.38	3.68	5.73	--
VI <sub>b</sub>	159	C <sub>13</sub> H <sub>9</sub> NO <sub>5</sub> (259)	60.23	3.50	5.41	--
	E		60.40	3.37	5.40	--
VI <sub>c</sub>	83	C <sub>12</sub> H <sub>6</sub> NO <sub>4</sub> Br (307)	46.91	2.93	4.56	25.73
	P.E.		47.06	2.90	4.58	25.70
VII <sub>a</sub>	67	C <sub>12</sub> H <sub>6</sub> NO <sub>3</sub> (215)	66.98	4.19	6.51	--
	P.E.		67.17	4.37	6.50	--
VII <sub>b</sub>	101	C <sub>12</sub> H <sub>6</sub> NO <sub>4</sub> (231)	62.34	3.90	6.06	--
	P.E.		62.56	4.18	6.10	--
IX <sub>a</sub>	154	C <sub>19</sub> H <sub>13</sub> N <sub>3</sub> O <sub>5</sub> (363)	62.81	3.58	11.57	
	E		63.18	3.60	11.54	
IX <sub>b</sub>	162	C <sub>25</sub> H <sub>17</sub> N <sub>3</sub> O <sub>5</sub> (439)	68.34	3.87	9.57	--
	E		68.53	3.93	9.60	--
		C <sub>21</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub>	69.81	5.26	11.63	--

Compd No.	M.P. °C solvent of crystallization	Molecular formula (Mol. wt.)	Analysis calcd./Found %			
			C	H	N	X
IX <sub>c</sub>	157 E	(361)	69.98	5.33	11.65	--
IX <sub>d</sub>	169 E	C <sub>29</sub> H <sub>23</sub> N <sub>3</sub> O <sub>3</sub> (461)	75.49	4.50	9.11	--
			75.60	4.42	9.00	--
IX <sub>e</sub>	170 E	C <sub>19</sub> H <sub>13</sub> N <sub>3</sub> O <sub>6</sub> (379)	60.16	3.43	11.08	--
			60.35	3.40	11.21	--
IX <sub>f</sub>	162 E	C <sub>25</sub> H <sub>17</sub> N <sub>3</sub> O <sub>6</sub> (455)	65.93	3.74	9.23	--
			66.12	3.70	9.33	--
IX <sub>g</sub>	144 E	C <sub>19</sub> H <sub>13</sub> N <sub>2</sub> O <sub>4</sub> Br (412)	55.34	3.16	6.80	19.17
			55.53	3.21	6.99	19.20
IX <sub>h</sub>	150 E	C <sub>14</sub> H <sub>14</sub> N <sub>3</sub> O <sub>3</sub> Br (503)	57.26	3.70	8.35	12.71
			57.45	3.78	8.34	12.70
IX <sub>i</sub>	203 E	C <sub>21</sub> H <sub>13</sub> N <sub>3</sub> O <sub>6</sub> (405)	62.22	3.70	10.37	--
			62.49	3.73	10.40	--
IX <sub>j</sub>	222 E	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O <sub>5</sub> (350)	65.14	4.00	8.00	--
			64.85	4.11	8.11	--
X <sub>a</sub>	115 P.E.	C <sub>17</sub> H <sub>13</sub> NO <sub>5</sub> (309)	66.02	3.56	4.53	--
			66.21	3.55	4.50	--
X <sub>b</sub>	124 P.E.	C <sub>19</sub> H <sub>12</sub> N <sub>2</sub> O <sub>7</sub> (380)	60.00	3.20	7.37	--
			60.22	3.15	7.35	--
X <sub>c</sub>	136 E	C <sub>19</sub> H <sub>12</sub> NO <sub>3</sub> Br (413)	55.21	2.91	3.39	19.13
			54.95	2.90	3.40	19.12
XI <sub>a</sub>	187 E	C <sub>22</sub> H <sub>13</sub> N <sub>3</sub> O <sub>6</sub> (415)	63.61	3.13	10.12	--
			63.78	3.10	10.00	--
XI <sub>b</sub>	189 E	C <sub>24</sub> H <sub>18</sub> N <sub>3</sub> O <sub>4</sub> (412)	69.91	4.37	10.19	--
			70.4	4.36	10.17	--
XI <sub>c</sub>	192 E	C <sub>22</sub> H <sub>13</sub> N <sub>3</sub> O <sub>7</sub> (431)	61.25	3.02	9.74	--
			61.17	3.01	9.76	--
XI <sub>d</sub>	193 E	C <sub>24</sub> H <sub>19</sub> N <sub>3</sub> O <sub>5</sub> (429)	67.13	4.43	9.79	--
			67.30	4.42	9.80	--
XI <sub>e</sub>	201 E	C <sub>19</sub> H <sub>9</sub> N <sub>2</sub> O <sub>5</sub> (345)	66.17	2.61	8.12	--
			66.08	2.60	8.10	--
XI <sub>f</sub>	202 E	C <sub>20</sub> H <sub>10</sub> N <sub>3</sub> O <sub>4</sub> Br (435)	55.17	2.30	9.66	18.16
			54.95	2.29	9.70	18.20
XII <sub>a</sub>	221 E	C <sub>11</sub> H <sub>7</sub> O <sub>3</sub> Cl (222.5)	59.33	3.15	--	15.96
			59.52	3.14	--	15.95
XII <sub>b</sub>	176 E	C <sub>11</sub> H <sub>7</sub> O <sub>4</sub> Cl (238.5)	55.35	2.94	--	14.88
			55.54	2.93	--	14.86
XII <sub>c</sub>	174 E	C <sub>10</sub> H <sub>7</sub> O <sub>3</sub> BrCl (286.5)	41.88	1.39	--	27.57Br
			42.13	1.40	--	27.60Br 12.39Cl



Compd No.	M.P.°C solvent of crystallization	Molecular formula (Mol. wt.)	Analysis calcd./Found %			
			C	H	N	X
						12.40 Cl
<b>XIII<sub>a</sub></b>	182 E	C <sub>11</sub> H <sub>7</sub> N <sub>3</sub> O <sub>3</sub> (229)	57.64 57.88	3.06 3.05	18.34 18.32	-- --
<b>XIII<sub>b</sub></b>	179 E	C <sub>11</sub> H <sub>7</sub> N <sub>3</sub> O <sub>4</sub> (245)	53.88 54.17	2.86 2.85	17.14 17.12	-- --
<b>XIII<sub>c</sub></b>	180 E	C <sub>16</sub> H <sub>4</sub> N <sub>3</sub> O <sub>3</sub> Br (309)	38.83 39.09	1.29 1.30	13.59 13.60	25.57 25.60
<b>XIV<sub>a</sub></b>	133 P.E.	C <sub>11</sub> H <sub>8</sub> O <sub>2</sub> N <sub>2</sub> (200)	66.00 66.23	4.00 4.02	14.00 14.03	-- --
<b>XIV<sub>b</sub></b>	129 E	C <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub> (264)	77.27 77.35	4.55 4.53	10.61 10.63	-- --
<b>XIV<sub>c</sub></b>	130 E	C <sub>17</sub> H <sub>11</sub> N <sub>3</sub> O <sub>4</sub> (321)	63.55 63.60	3.43 3.42	13.08 13.20	-- --
<b>XIV<sub>d</sub></b>	121 P.E.	C <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> (292)	69.86 70.09	4.11 4.10	9.59 9.60	-- --
<b>XV<sub>a</sub></b>	111 P.E.	C <sub>11</sub> H <sub>8</sub> NO <sub>3</sub> Cl (237.5)	55.58 55.57	3.37 3.36	5.89 5.90	14.95 14.97
<b>XV<sub>b</sub></b>	122 P.E.	C <sub>11</sub> H <sub>8</sub> NO <sub>4</sub> Cl (253.5)	52.07 52.22	3.20 3.16	5.52 5.50	14.00 14.03
<b>XVI<sub>a</sub></b>	66 P.E.	C <sub>14</sub> H <sub>7</sub> N <sub>5</sub> O <sub>2</sub> (277)	60.65 60.84	2.53 2.50	25.27 25.30	-- --
<b>XVI<sub>b</sub></b>	89 P.E.	C <sub>16</sub> H <sub>11</sub> N <sub>4</sub> O <sub>4</sub> (323)	59.44 59.63	3.41 3.40	17.34 17.33	-- --
<b>XVI<sub>c</sub></b>	78 P.E.	C <sub>14</sub> H <sub>7</sub> N <sub>5</sub> O <sub>3</sub> (293)	57.34 57.38	2.39 2.38	23.89 23.90	-- --
<b>XVI<sub>d</sub></b>	80 P.E.	C <sub>16</sub> H <sub>11</sub> N <sub>4</sub> O <sub>5</sub> (339)	56.64 56.43	3.24 3.22	16.52 16.50	-- --

### Pharmacological activity

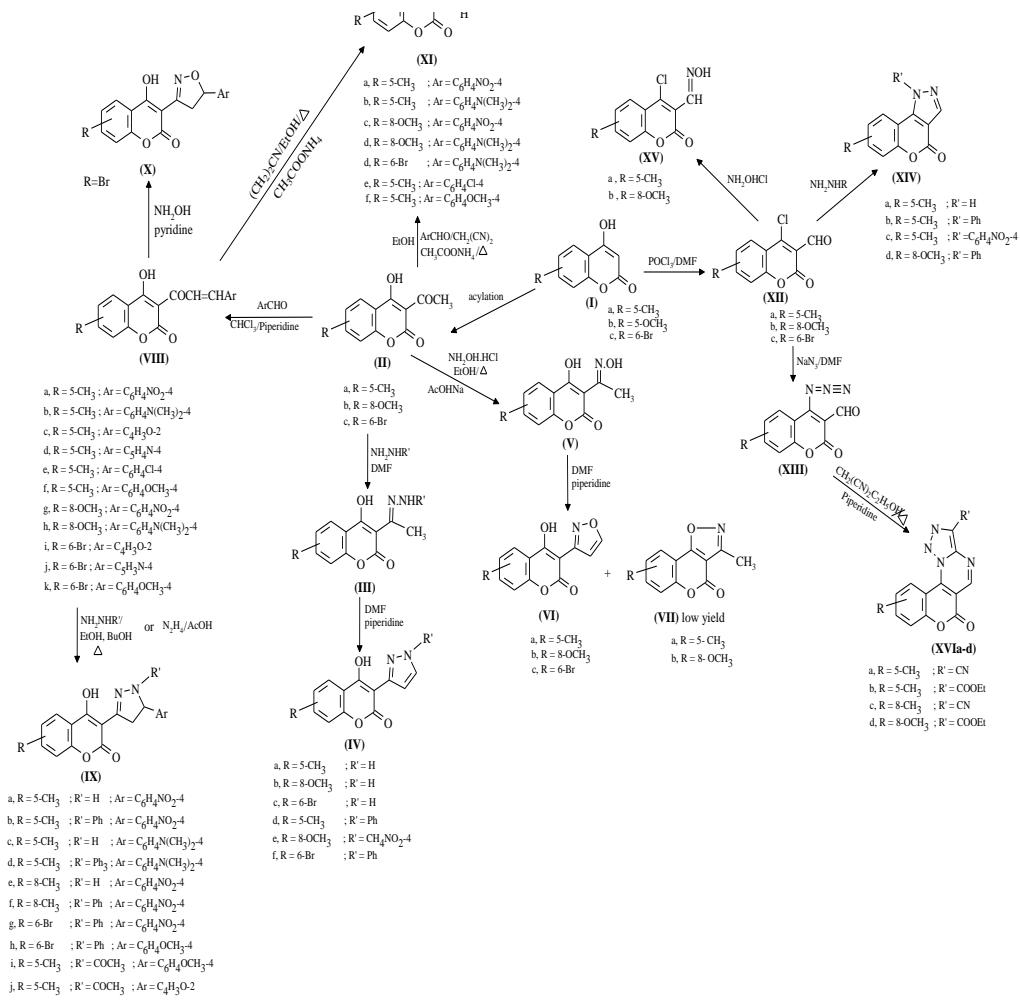
All the compounds **III<sub>b</sub>**, **IV<sub>a-c,e</sub>**, **VI<sub>b</sub>**, **VII<sub>b</sub>**, **VIII<sub>a,b,e,f,h</sub>**, **IX<sub>e</sub>** and **XIV<sub>c,d</sub>** were screened for their *in vitro* antibacterial activity against *E.coli* and *Xanthomonas citri* by cup plate method<sup>(15)</sup>, Summarized in table II. Nutrient agar was melted in a water bath and cooled to 45°C with gentle shaking to bring about uniform cooling. It was with 0.5-0.6 ml of culture and mixed well by pouring gentle shaking before onto the sterilized Petri dishes. The poured materials were allowed to set and thereafter the "CUPS" were made by punching into the agar surface with sterile cork borer and scooping out the punched part of the agar. Into these cups were added 0.1 ml. portion of the tested compound in the solvent with the help of sterile syringe. The drug solution was allowed to diffuse for about an hour into the medium. The plates were incubated at 37°C and the results noted. The standard is (streptomycin)

**Table II. Antibacterial activity data of the tested compounds**

<b>Comp. No.</b>	<i>E.coli</i> * (Zone in mm)	<i>X.Citri</i> * (zone in mm)
<b>III<sub>b</sub></b>	8	13
<b>IV<sub>a</sub></b>	12	15
<b>IV<sub>b</sub></b>	10	11
<b>IV<sub>c</sub></b>	8	10
<b>IV<sub>e</sub></b>	11	8
<b>VI<sub>b</sub></b>	9	10
<b>VII<sub>b</sub></b>	13	12
<b>VIII<sub>a</sub></b>	10	13
<b>VIII<sub>b</sub></b>	12	14
<b>VIII<sub>e</sub></b>	9	9
<b>VIII<sub>f</sub></b>	12	8
<b>VIII<sub>h</sub></b>	7	13
<b>IX<sub>e</sub></b>	10	11
<b>XIV<sub>c</sub></b>	11	10
<b>XIV<sub>d</sub></b>	12	14

\* Standard (Streptomycin)

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