

# Synthesis of Benzopyran-4-one and Phloroglucinol Monomethyl Ether Derivatives from the Naturally Occurring Compound (Visnagin)

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The reaction of 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one with dimethyl acetylenedicarboxylate and benzil gave the respective 4*H*,6*H*-pyrano[3,2-*g*]chromene and imidazolylbenzopyran derivatives. Treatment of the imidazolylbenzopyran with hydrazine hydrate or hydroxylammonium chloride yielded imidazolylpyrazolyl- or imidazolylisoxazolylbenzenes, while the alkaline hydrolysis of imidazolylbenzopyran afforded imidazolylacetophenone that reacted with some aromatic aldehydes to give the corresponding chalcones. Oxidation of the chalcone with hydrogen peroxide led to the formation of 6-hydroxy-4-methoxy-5-[4,5-diphenylimidazol-2-yl]-2-(4-methoxybenzylidene)coumaran-3-one, while the reaction with hydrazine hydrate gave the corresponding imidazolylpyrazolylbenzene. Also, the imidazolylacetophenone was reacted with phenylhydrazine and hydroxylammonium chloride to give the respective hydrazone and oxime products. Fischer indolization of the above hydrazone yielded the corresponding indole derivative.

Numerous imidazole derivatives have been prepared and investigated for therapeutic and prophylactic application [1–3].

Also benzopyran derivatives possess coronary vasodilating [4], spasmolytic [5], and antiatherogenic and antiatherosclerotic activity [6]. In the light of this report, compounds having a combination of benzopyran and imidazole moieties can be expected to exhibit marked biological activity. Thus this investigation deals with the synthesis of such type of compounds.

The naturally occurring furobenzopyran "visnagin" (*I*) yields 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one (*II*) upon oxidation with potassium dichromate and sulfuric acid by rupture of furan ring [7]. The reaction of *II* with dimethyl acetylenedicarboxylate (DMAD) in the presence of anhydrous potassium carbonate gave 7,8-bis(methoxycarbonyl)-6-hydroxy-5-methoxy-2-methyl-4*H*,6*H*-pyrano[3,2-*g*]chromen-4-one (*III*). The <sup>1</sup>H NMR spectrum of compound *III* showed the presence of two singlets for two methyl ester groups at  $\delta = 3.90$  and  $3.99$ , the IR spectrum showed the absence of aldehyde absorption ( $\bar{\nu} = 1710 \text{ cm}^{-1}$ ), also the mass spectrum revealed a molecular ion [ $M^+$ ] at  $m/z = 376$ , which was in agreement with its molecular mass.

When the aldehyde *II* was refluxed with benzil in the presence of ammonium acetate in glacial acetic acid, it gave 7-hydroxy-5-methoxy-2-methyl-6-[4,5-diphenylimidazol-2-yl]benzopyran-4-one (*IV*). The <sup>1</sup>H

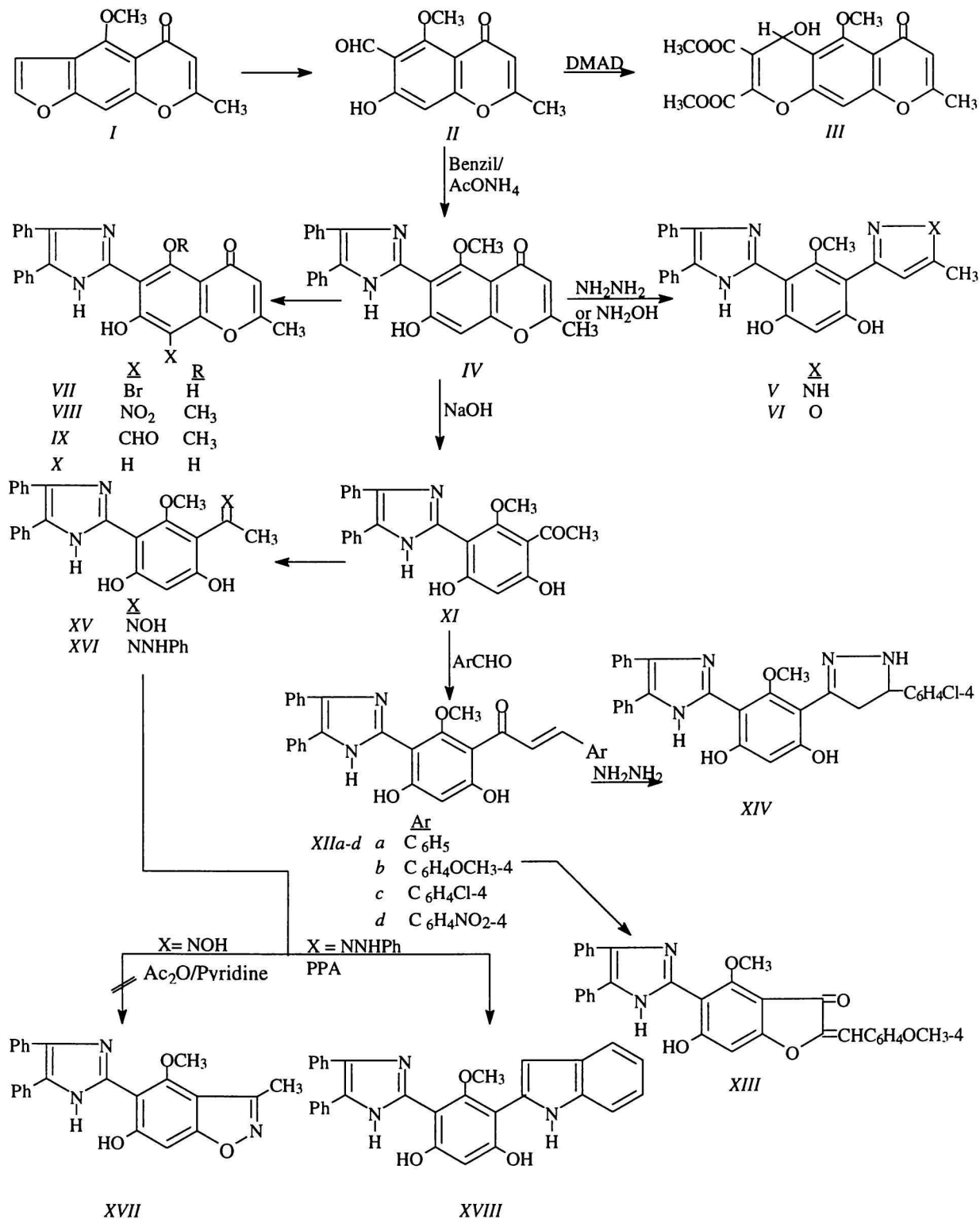
NMR spectrum showed the presence of 10 aromatic protons at  $\delta = 7.5$ – $8.0$  of imidazole moiety, and the IR spectrum revealed the presence of NH group at  $\bar{\nu} = 3250 \text{ cm}^{-1}$ .

Treatment of *IV* with hydrazine hydrate or hydroxylammonium chloride led to the formation of the only regioisomers: 1,3-dihydroxy-5-methoxy-6-[4,5-diphenylimidazol-2-yl]-4-[5-methyl-3-pyrazolyl or isoxazolyl]benzene (*V*) and (*VI*), respectively, *via* the opening of the chromone ring followed by reaction with the above reagents.

The mass spectrum of *V* revealed molecular ion peak [ $M^+$ ] at  $m/z = 439$  as the base peak, which was in agreement with its molecular mass, also two daughter peaks at  $m/z = 220$  and  $140$  from the rupture of the diphenylimidazole and methylpyrazole rings, respectively.

Bromination of *IV* using an excess of bromine led to the formation of 8-bromo-5,7-dihydroxy-2-methyl-6-[4,5-diphenylimidazol-2-yl]benzopyran-4-one (*VII*). Demethylation of 5-methoxy group was accomplished from the effect of the hydrogen bromide formed during the reaction as reported in the case of khellin and visnagin with several reagents such as dilute hydrogen halides [8, 9].

On the other hand, nitration of compound *IV* gave 8-nitrobenzopyranone derivative *VIII*. IR spectrum revealed the vibrations  $\bar{\nu}_{\text{as}}(\text{NO}_2) = 1350 \text{ cm}^{-1}$  and  $\bar{\nu}_{\text{s}}(\text{NO}_2) = 1530 \text{ cm}^{-1}$ . The mass spectrum of *VIII* revealed molecular ion [ $M^+$ ] at  $m/z = 470$  which cor-



Scheme 1

responded with its molecular mass.

The Vilsmeier—Haack formylation of IV failed to give the corresponding 8-formyl derivative IX but demethylation of 5-methoxy group occurred affording 5,7-dihydroxy-2-methyl-6-[4,5-diphenylimidazol-2-yl]benzopyran-4-one (X).

Alkaline hydrolysis of IV gave a quantitative yield of imidazolylacetophenone derivative XI which was reacted with some aromatic aldehydes, namely benzaldehyde, *p*-anisaldehyde, *p*-chloro- and *p*-nitrobenzaldehyde to give the corresponding chalcones XIIIa—XIII d. The IR spectra of XIIIa—XIII d showed a charac-

teristic  $\alpha,\beta$ -unsaturated ketone band at  $\tilde{\nu} = 1630$ — $1640\text{ cm}^{-1}$ , also  $^1\text{H NMR}$  spectra of *XIIa* showed a doublet signal of  $-\text{CH}=\text{CH}-\text{Ar}$  at  $\delta = 5.67$  ( $J = 10\text{ Hz}$ ).

Oxidation of the chalcone *XIIb* with hydrogen peroxide in sodium hydroxide led to the formation of 6-hydroxy-4-methoxy-5-[4,5-diphenylimidazol-2-yl]-2-(4-methoxybenzylidene)coumaran-3-one (*XIII*). The assigned structure of *XIII* was established on the basis of the correct analytical and spectral data. Mass spectrum showed a molecular ion peak  $[\text{M}^+]$  at  $m/z = 516$  as the base peak which corresponded to its molecular mass. Also, when the chalcone *XIIc* was reacted with hydrazine hydrate, it gave the corresponding imidazolylpyrazolanylbenzene derivative *XIV*. The oxime derivative *XV* which was obtained from condensation of compound *XI* with hydroxylammonium chloride failed to give the isoxazole derivative *XVII* on treatment with acetic anhydride/pyridine mixture. On the other hand, on boiling phenyl hydrazone derivative *XVI* that was obtained from condensation of compound *XI* with phenyl hydrazine with polyphosphoric acid gave according to Fischer indole synthesis the corresponding indole product *XVIII*.

## EXPERIMENTAL

Melting points were uncorrected. Elemental analysis was carried out in the Microanalytical Unit at the Faculty of Science, Mansoura and Cairo Universities. IR spectra were recorded on Mattson 5000 FTIR spectrometer using KBr wafer technique.  $^1\text{H NMR}$  spectra were determined on Varian-Gemini 200 MHz and Jeol-Ex-270 MHz NMR spectrometers using TMS as an internal standard with  $\delta = 0$ . Electron impact (EI) mass spectra were determined on a GC-MS QP-100 EX spectrometer Shimadzu (Japan). The purity of the synthesized compounds was tested by TLC.

Compound *II* was prepared adopting the published [7] procedure with the same m.p. =  $189^\circ\text{C}$ .

### 7,8-Bis(methoxycarbonyl)-6-hydroxy-5-methoxy-2-methyl-4*H*,6*H*-pyrano[3,2-*g*]-chromen-4-one (*III*)

A mixture of aldehyde *II* (1.0 g; 4 mmol), dimethyl acetylenedicarboxylate (0.6 g; 4 mmol), and anhydrous potassium carbonate (0.5 g; 4 mmol) in dry benzene ( $50\text{ cm}^3$ ) was refluxed for 6 h. The reaction mixture was cooled, then diethyl ether ( $50\text{ cm}^3$ ) was added. The organic layer was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave a yellow viscous material, which was triturated with petroleum ether (b.p. =  $60$ — $80^\circ\text{C}$ ) and crystallized from diluted ethanol (60 %) to give *III*, m.p. =  $80$ — $81^\circ\text{C}$ ; yield = 20 %. For  $\text{C}_{18}\text{H}_{16}\text{O}_9$  ( $M_r = 376.32$ )  $w_i$ (found): 56.98 % C, 3.93 % H;  $w_i$ (calc.): 57.45 %

C, 4.28 % H. IR spectrum:  $\tilde{\nu}(\text{C}=\text{O chromone})/\text{cm}^{-1}$ : 1658,  $\tilde{\nu}(\text{C}=\text{O ester})/\text{cm}^{-1}$ : 1723, 1750,  $\tilde{\nu}(\text{OH})/\text{cm}^{-1}$ : 3450.  $^1\text{H NMR}$  spectrum ( $\text{CDCl}_3$ ),  $\delta$ : 2.3 (s, 3H,  $\text{CH}_3$ ), 3.8 (s, 3H,  $\text{OCH}_3$ ), 3.9 (s, 3H,  $\text{COOCH}_3$ ), 3.99 (s, 3H,  $\text{COOCH}_3$ ), 5.3 (s, 1H, H-4), 6.1 (s, 1H, H-7), 6.7 (s, 1H, OH), 8.1 (s, 1H, H-10). EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 376 (3,  $[\text{M}^+]$ ).

### 7-Hydroxy-5-methoxy-2-methyl-6-[4,5-diphenylimidazol-2-yl]benzopyran-4-one (*IV*)

A mixture of aldehyde *II* (1.0 g; 4 mmol), benzil (0.9 g; 4 mmol), and ammonium acetate (3 g; 4 mmol) in glacial acetic acid ( $20\text{ cm}^3$ ) was refluxed for 2 h. The precipitate that formed was filtered off and washed several times with hot acetone to give *IV*, m.p. =  $256$ — $257^\circ\text{C}$ ; yield = 70 %. For  $\text{C}_{26}\text{H}_{20}\text{O}_4\text{N}_2$  ( $M_r = 424.45$ )  $w_i$ (found): 73.80 % C, 5.00 % H, 6.6 % N;  $w_i$ (calc.): 73.57 % C, 4.75 % H, 6.6 % N. IR spectrum,  $\tilde{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1620,  $\tilde{\nu}(\text{C}=\text{O chromone})/\text{cm}^{-1}$ : 1658,  $\tilde{\nu}(\text{NH})/\text{cm}^{-1}$ : 3250,  $\tilde{\nu}(\text{OH})/\text{cm}^{-1}$ : 3500.  $^1\text{H NMR}$  spectrum ( $\text{DMSO}-d_6$ ),  $\delta$ : 2.4 (s, 3H,  $\text{CH}_3$ ), 3.9 (s, 3H,  $\text{OCH}_3$ ), 6.1 (s, 1H, H-3), 7.1 (s, 1H, H-8), 7.5—8.0 (m, 12H, 10Ar—H, OH and NH). EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 424 (74.4,  $[\text{M}^+]$ ).

### 1,3-Dihydroxy-5-methoxy-6-[4,5-diphenylimidazol-2-yl]-4-[5-methylpyrazol-3-yl]benzene (*V*)

A mixture of *IV* (1.0 g; 4 mmol) and hydrazine hydrate (0.4  $\text{cm}^3$ , 8 mmol) in absolute ethanol ( $30\text{ cm}^3$ ) was refluxed for 8 h. The solid so obtained was filtered off, then washed several times with hot acetone to give compound *V*, m.p. =  $299$ — $300^\circ\text{C}$ ; yield = 97 %. For  $\text{C}_{26}\text{H}_{22}\text{O}_3\text{N}_4$  ( $M_r = 438.5$ )  $w_i$ (found): 71.50 % C, 5.00 % H, 12.5 % N;  $w_i$ (calc.): 71.22 % C, 5.05 % H, 12.78 % N. IR spectrum:  $\tilde{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1630,  $\tilde{\nu}(\text{NH, OH})/\text{cm}^{-1}$ : 3200—3450. EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 439 (100,  $[\text{M}^+]$ ).

### 1,3-Dihydroxy-5-methoxy-6-[4,5-diphenylimidazol-2-yl]-4-[5-methylisoxazol-3-yl]benzene (*VI*)

A solution of hydroxylammonium chloride (0.8 g) in water ( $5\text{ cm}^3$ ) was added to a solution of *IV* (1.0 g) in pyridine ( $10\text{ cm}^3$ ) and refluxed for 4 h, the mixture was cooled, then acidified with diluted acetic acid. The precipitate that formed was filtered off and crystallized from ethanol to give compound *VI*, m.p. =  $120$ — $121^\circ\text{C}$ ; yield = 93 %. For  $\text{C}_{26}\text{H}_{21}\text{O}_4\text{N}_3$  ( $M_r = 439.47$ )  $w_i$ (found): 71.20 % C, 4.9 % H, 9.6 % N;  $w_i$ (calc.): 71.06 % C, 4.82 % H, 9.56 % N. IR spectrum:  $\tilde{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1630,  $\tilde{\nu}(\text{NH, OH})/\text{cm}^{-1}$ : 3200—3500.  $^1\text{H NMR}$  spectrum ( $\text{CDCl}_3$ ),  $\delta$ : 2.4 (s, 3H,  $\text{CH}_3$ ), 3.7 (s, 3H,  $\text{OCH}_3$ ), 6.55 (s, 1H, isoxazolyl H), 6.56 (s, 1H, H-2), 7.3—7.6 (m, 12H, Ar—H, NH, OH), 10.4 (s, 1H, OH). EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 439 (100,  $[\text{M}^+]$ ).

**8-Bromo-5,7-dihydroxy-2-methyl-6-[4,5-diphenylimidazol-2-yl]benzopyran-4-one (VII)**

To a solution of *IV* (1 g; 2 mmol) in chloroform (8 cm<sup>3</sup>) was added bromine (1.88 g; 10 mmol) in chloroform (25 cm<sup>3</sup>). The reaction mixture was shaken and left to stand for 24 h. The precipitate that formed was filtered off, dried, then crystallized from chloroform to give *VII*, m.p. = 262–263 °C; yield = 87 %. For C<sub>25</sub>H<sub>17</sub>O<sub>4</sub>N<sub>2</sub>Br (*M<sub>r</sub>* = 489) *w<sub>i</sub>*(found): 60.93 % C, 3.62 % H, 16.2 % Br; *w<sub>i</sub>*(calc.): 61.37 % C, 3.5 % H, 16.33 % Br. IR spectrum:  $\bar{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1614,  $\bar{\nu}(\text{C}=\text{O chromone})/\text{cm}^{-1}$ : 1655,  $\bar{\nu}(\text{NH, OH})/\text{cm}^{-1}$ : 3200–3500. EI mass spectrum, *m/z* (*I<sub>r</sub>*/%) : 489 (78.1, [M<sup>+</sup>]).

**7-Hydroxy-5-methoxy-2-methyl-8-nitro-6-[4,5-diphenylimidazol-2-yl]benzopyran-4-one (VIII)**

To a suspension of *IV* (1 g) in glacial acetic acid (2.5 cm<sup>3</sup>) was added a mixture of concentrated nitric acid (1 cm<sup>3</sup>) and glacial acetic acid (0.5 cm<sup>3</sup>). The reaction mixture was left at room temperature for 30 min, then poured onto water (50 cm<sup>3</sup>). The precipitate that formed was filtered off, dried and crystallized from ethanol to give compound *VIII*, m.p. = 145–146 °C; yield = 60 %. For C<sub>26</sub>H<sub>19</sub>O<sub>6</sub>N<sub>3</sub> (*M<sub>r</sub>* = 469.45) *w<sub>i</sub>*(found): 66.14 % C, 3.80 % H; *w<sub>i</sub>*(calc.): 66.52 % C, 4.08 % H. IR spectrum:  $\bar{\nu}(\text{NO}_2)/\text{cm}^{-1}$ : 1350, 1530,  $\bar{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1620,  $\bar{\nu}(\text{C}=\text{O chromone})/\text{cm}^{-1}$ : 1660,  $\bar{\nu}(\text{NH, OH})/\text{cm}^{-1}$ : 3200–3600. EI mass spectrum, *m/z* (*I<sub>r</sub>*/%) : 470 (31.8, [M<sup>+</sup>]).

**5,7-Dihydroxy-2-methyl-6-[4,5-diphenylimidazol-2-yl]benzopyran-4-one (X)**

To a cold solution of *IV* (1 g) in *N,N*-dimethylformamide (6 cm<sup>3</sup>) phosphorous oxychloride (0.5 cm<sup>3</sup>) was added dropwise in the course of 30 min with shaking. The reaction mixture was then refluxed on water bath for 5 h and then left to cool. After pouring on crushed ice and decomposition with sodium acetate solution, the solid that separated was filtered off, dried, then crystallized from a mixture of ethanol–acetone (1 : 1) to give compound *X*, m.p. = 265 °C; yield = 80 %. For C<sub>25</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub> (*M<sub>r</sub>* = 410.43) *w<sub>i</sub>*(found): 73.14 % C, 4.15 % H; *w<sub>i</sub>*(calc.): 73.16 % C, 4.42 % H. IR spectrum:  $\bar{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1620,  $\bar{\nu}(\text{C}=\text{O chromone})/\text{cm}^{-1}$ : 1658,  $\bar{\nu}(\text{NH})/\text{cm}^{-1}$ : 3250,  $\bar{\nu}(\text{OH})/\text{cm}^{-1}$ : 3500. EI mass spectrum, *m/z* (*I<sub>r</sub>*/%) : 410 (100, [M<sup>+</sup>]).

**4,6-Dihydroxy-2-methoxy-3-[4,5-diphenylimidazol-2-yl]acetophenone (XI)**

A mixture of *IV* (2.0 g) and sodium hydroxide

(30 cm<sup>3</sup> of 50 % aqueous solution) in ethanol (20 cm<sup>3</sup>) was refluxed for 3 h. Then the reaction mixture was cooled, poured onto crushed ice (50 g) and acidified with concentrated hydrochloric acid. The precipitate that formed was filtered off, dried and crystallized from ethanol to give compound *XI*, m.p. = 200–202 °C; yield = 50 %. For C<sub>24</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub> (*M<sub>r</sub>* = 400.43) *w<sub>i</sub>*(found): 72.40 % C, 5.1 % H, 7.00 % N; *w<sub>i</sub>*(calc.): 72.00 % C, 5.03 % H, 7.00 % N. IR spectrum:  $\bar{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1610,  $\bar{\nu}(\text{C}=\text{O})/\text{cm}^{-1}$ : 1630,  $\bar{\nu}(\text{NH, OH})/\text{cm}^{-1}$ : 3300–3450. <sup>1</sup>H NMR spectrum (DMSO-*d*<sub>6</sub>),  $\delta$ : 2.58 (s, 3H, COCH<sub>3</sub>), 3.6 (s, 3H, OCH<sub>3</sub>), 6.67 (s, 1H, H-2), 7.5 (m, 12H, Ar–H, OH, NH), 12.3 (s, 1H, OH). EI mass spectrum, *m/z* (*I<sub>r</sub>*/%) : 400 (70.2, [M<sup>+</sup>]).

**Chalcones XIIa–XIIId**

To a mixture of *XI* (2.0 g; 0.005 mol) and aqueous potassium hydroxide (10 g in 10 cm<sup>3</sup> of water) was added a solution of aromatic aldehydes (0.005 mol), namely: benzaldehyde, *p*-anisaldehyde, *p*-chlorobenzaldehyde, and *p*-nitrobenzaldehyde in 10 cm<sup>3</sup> of ethanol with stirring. The reaction mixture was allowed to stand for 24 h at room temperature and was then diluted with water and acidified. The orange precipitate was filtered off, dried and crystallized from the proper solvent to give chalcones *XIIa–XIIId*. Characterization data are listed in Table 1. IR spectrum:  $\bar{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1610,  $\bar{\nu}(\alpha,\beta\text{-unsaturated ketone})/\text{cm}^{-1}$ : 1627,  $\bar{\nu}(\text{NH, OH})/\text{cm}^{-1}$ : 3300–3450. <sup>1</sup>H NMR spectrum of *XIIa* (DMSO-*d*<sub>6</sub>),  $\delta$ : 3.95 (s, 1H, OCH<sub>3</sub>), 5.67 (d, *J* = 10 Hz, 1H, CO–CH=CH–Ar), 6.45 (s, 1H, H-2), 7.5 (m, 18H, Ar–H, CO–CH=CH–Ar, NH, OH), 13.7 (br, 1H, OH). EI mass spectrum, *m/z* (*I<sub>r</sub>*/%) : 488 (100, [M<sup>+</sup>]), 523 (100, [M<sup>+</sup>]) of *XIIa* and *XIIc*, respectively.

**6-Hydroxy-4-methoxy-5-[4,5-diphenylimidazol-2-yl]-2-(4-methoxybenzylidene)-coumaran-3-one (XIII)**

To an ice-cooled mixture of *XIIb* (15.5 g; 0.03 mol), sodium hydroxide (5.2 g; 0.13 mol), ethanol (200 cm<sup>3</sup>), and water (100 cm<sup>3</sup>) was added 30 % hydrogen peroxide (11.4 cm<sup>3</sup>, 0.1 mol). The reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 16 h. The crude product which separated on acidification with 2 M hydrochloric acid, was filtered off, washed with water, dried and crystallized from acetone to give compound *XIII*, m.p. = 240–241 °C; yield = 80 %. For C<sub>32</sub>H<sub>24</sub>O<sub>5</sub>N<sub>2</sub> (*M<sub>r</sub>* = 516.5) *w<sub>i</sub>*(found): 74.40 % C, 4.60 % H; *w<sub>i</sub>*(calc.): 74.0 % C, 4.68 % H. IR spectrum:  $\bar{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ : 1610,  $\bar{\nu}(\text{C}=\text{O})/\text{cm}^{-1}$ : 1650,  $\bar{\nu}(\text{NH, OH})/\text{cm}^{-1}$ : 3300–3500. EI mass spectrum, *m/z* (*I<sub>r</sub>*/%) : 516 (100, [M<sup>+</sup>]).

Table 1. Characterization Data of Chalcones *XIIa*—*XIIId*

Compound	Formula	$M_r$	$w_i(\text{found})/\%$ $w_i(\text{calc.})/\%$			Yield %	M.p. °C	Solvent of crystallization
			C	H	N			
<i>XIIa</i>	$C_{31}H_{24}O_4N_2$	488.54	76.38	5.00	5.67	85	238—239	Ethanol—acetone (1 1)
			76.20	4.95	5.73			
<i>XIIb</i>	$C_{32}H_{26}O_5N_2$	518.57	73.90	5.30	5.40	84	170—171	Ethanol—H <sub>2</sub> O (2 1)
			74.12	5.05	5.40			
<i>XIIc</i>	$C_{31}H_{23}O_4N_2Cl$	523	70.90	4.80	5.30	87	139—140	Ethanol—H <sub>2</sub> O (2 1)
			71.20	4.43	5.36			
<i>XIIId</i>	$C_{31}H_{23}O_6N_3$	533.54	70.00	4.73	7.80	80	259—260	Acetone
			69.79	4.34	7.88			

### 1,3-Dihydroxy-5-methoxy-6-[4,5-diphenylimidazol-2-yl]-4-[5-chlorophenylpyrazolin-3-yl]benzene (*XIV*)

A mixture of *XIIc* (1.0 g; 2 mmol) and hydrazine hydrate (0.1 cm<sup>3</sup>, 2 mmol) in absolute ethanol (20 cm<sup>3</sup>) was refluxed for 2 h. The solid so obtained was filtered off and washed several times with hot acetone to give compound *XIV*, m.p. = 134—135; yield = 90 %. For  $C_{31}H_{24}O_3N_4Cl$  ( $M_r = 536.01$ )  $w_i(\text{found})$ : 69.70 % C, 4.9 % H, 10.2 % N;  $w_i(\text{calc.})$ : 69.47 % C, 4.5 % H, 10.45 % N. IR spectrum:  $\tilde{\nu}(Cl)/\text{cm}^{-1}$ : 760,  $\tilde{\nu}(C=N)/\text{cm}^{-1}$ : 1620,  $\tilde{\nu}(NH, OH)/\text{cm}^{-1}$ : 3300—3500. <sup>1</sup>H NMR spectrum (DMSO-*d*<sub>6</sub>),  $\delta$ : 2.2 (s, 1H, NH), 3.8 (s, 3H, OCH<sub>3</sub>), 3.3 (dd, 2H, pyrazolinyl H-4), 4.8—4.9 (t, 1H, pyrazolinyl H-5), 6.3 (s, 1H, H-2), 7.5 (m, 16H, Ar—H, NH, OH), 12.2 (s, 1H, OH). EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 536 (100, [M<sup>+</sup>]).

### 4,6-Dihydroxy-2-methoxy-3-[4,5-diphenylimidazol-2-yl]acetophenone Oxime (*XV*)

A mixture of *XI* (2.0 g; 5 mmol), hydroxylammonium chloride (0.35 g; 5 mmol), and few drops of pyridine in absolute ethanol (30 cm<sup>3</sup>) was refluxed for 5 h. The precipitate that formed was filtered off, dried and crystallized from ethanol to give *XV*, m.p. = 242°C; yield = 91 %. For  $C_{24}H_{21}O_4N_3$  ( $M_r = 415.45$ )  $w_i(\text{found})$ : 69.55 % C, 5.00 % H;  $w_i(\text{calc.})$ : 69.39 % C, 5.09 % H. IR spectrum:  $\tilde{\nu}(C=N)/\text{cm}^{-1}$ : 1620,  $\tilde{\nu}(NH, OH)/\text{cm}^{-1}$ : 3300—3450. EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 415 (87.9, [M<sup>+</sup>]).

### Phenylhydrazone Derivative *XVI*

A mixture of *XI* (2.0 g; 5 mmol) and phenylhydrazine (0.54 cm<sup>3</sup>, 5 mmol) in absolute ethanol (30 cm<sup>3</sup>) was refluxed for 2 h. The precipitate that formed was filtered off and crystallized from chloroform to give *XVI*, m.p. = 275—276°C; yield = 90 %. For  $C_{30}H_{26}O_3N_4$  ( $M_r = 490.56$ )  $w_i(\text{found})$ : 73.00 % C, 5.1 % H;  $w_i(\text{calc.})$ : 73.45 % C, 5.34 % H. IR spectrum:

$\tilde{\nu}(C=N)/\text{cm}^{-1}$ : 1620,  $\tilde{\nu}(NH, OH)/\text{cm}^{-1}$ : 3300—3500. EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 490 (21.3, [M<sup>+</sup>]).

### 1,5-Dihydroxy-3-methoxy-2-(4,5-diphenylimidazol-2-yl)-4-(indol-2-yl)benzene (*XVIII*)

Compound *XVI* (1.0 g) was added portionwise to a polyphosphoric acid (30 cm<sup>3</sup>). The reaction mixture was stirred at 120°C in an oil bath for 2 h. The reaction mixture was cooled and poured onto crushed ice, then basified with 10 % aqueous sodium hydrogencarbonate. The precipitate that formed was filtered off, washed with water, dried and crystallized from methanol to give *XVIII*, m.p. = 209—210; yield = 95 %. For  $C_{30}H_{23}O_3N_3$  ( $M_r = 473.53$ )  $w_i(\text{found})$ : 76.40 % C, 5.1 % H, 8.8 % N;  $w_i(\text{calc.})$ : 76.09 % C, 4.9 % H, 8.87 % N. IR spectrum:  $\tilde{\nu}(NH, OH)/\text{cm}^{-1}$ : 3200—3500. EI mass spectrum,  $m/z$  ( $I_r/\%$ ): 474 (100, [M<sup>+</sup>]).

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