

## Design, synthesis and characterization of new azoflavone derivatives through diazotisation - coupling reactions of aromatic amines (sulfanilic acid, 2-amino pyridine)

Hadi Aqel Khdera<sup>a\*</sup>

<sup>a</sup>Chemistry Department, Faculty of Sciences, Tishreen University, Lattakia, Syria

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### ABSTRACT

In this research, new azochalcone derivatives (6, 7) were synthesized by using three methods: the first one is diazotization - coupling method of different aromatic amines (sulfanilic acid, 2-aminopyridine) with chalcone (5), the second, aldol condensation method of azoaryl hydroxyacetophenone compounds with 4-dimethylamino benzaldehyde in presence of sodium hydroxide as a catalyst, the last one is method of aldol condensation of azoaryl hydroxyacetophenone compounds with 4-dimethylaminobenzaldehyde in presence of piperidine as an organic catalyst. The yield was the best by using the aldol condensation method with sodium hydroxide as a catalyst. New azoflavone derivatives (8, 9) with good yields (78-84 %) were also synthesized by performing cyclization reactions of azochalcone derivatives using iodine in dimethyl sulfoxide. The identity of the new compounds was determined using spectroscopic methods (FT-IR, <sup>13</sup>C-NMR, <sup>1</sup>H-NMR).

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## 1. Introduction

Azo compounds are of great importance in various fields. They are highly colored synthetic dyes that are widely used in the textile and dyeing industries, chromatography analysis of drugs, in the food industry, and in cosmetics. They possess high optical and photoelectric properties.<sup>1-5</sup> Azo dyes are used in the medical field as they are antibacterial and antifungal.<sup>6-9</sup> Flavonoids are low molecular weight polyphenolic compounds found in the plant kingdom.<sup>10,11</sup> They have biological activity and play an important role in vital cells. Scientific name: 2-phenylbenzo- $\gamma$ -pyrone (C<sub>15</sub>H<sub>10</sub>O<sub>2</sub>).<sup>12,13</sup> It has biological activity: antioxidant,<sup>14</sup> anti-inflammatory,<sup>15</sup> anti-malarial,<sup>16</sup> anti-bacterial,<sup>17</sup> and anti-cancer.<sup>18</sup> In our previous study, we synthesized flavonoid derivatives containing heterocyclic rings (oxadiazole, thiazole) via diazotization and coupling reactions of two aromatic amines (aminophenyl oxadiazole thiol, aminothiazole) with hydroxychalcone.<sup>19</sup>

The present study indicates the synthesis of two chalcone derivatives and two flavonoid derivatives that include an azo group in its structure, through aldol condensation reactions, diazotisation-coupling and cyclization reactions. The new compounds were characterized using spectroscopic methods (FT-IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR).

## 2. Results and Discussion

Chalcone compound (5) was prepared by aldol condensation using o-hydroxyacetophenone and 4-dimethylaminobenzaldehyde in presence of NaOH as a catalyst which gave (85 %) of the yield.

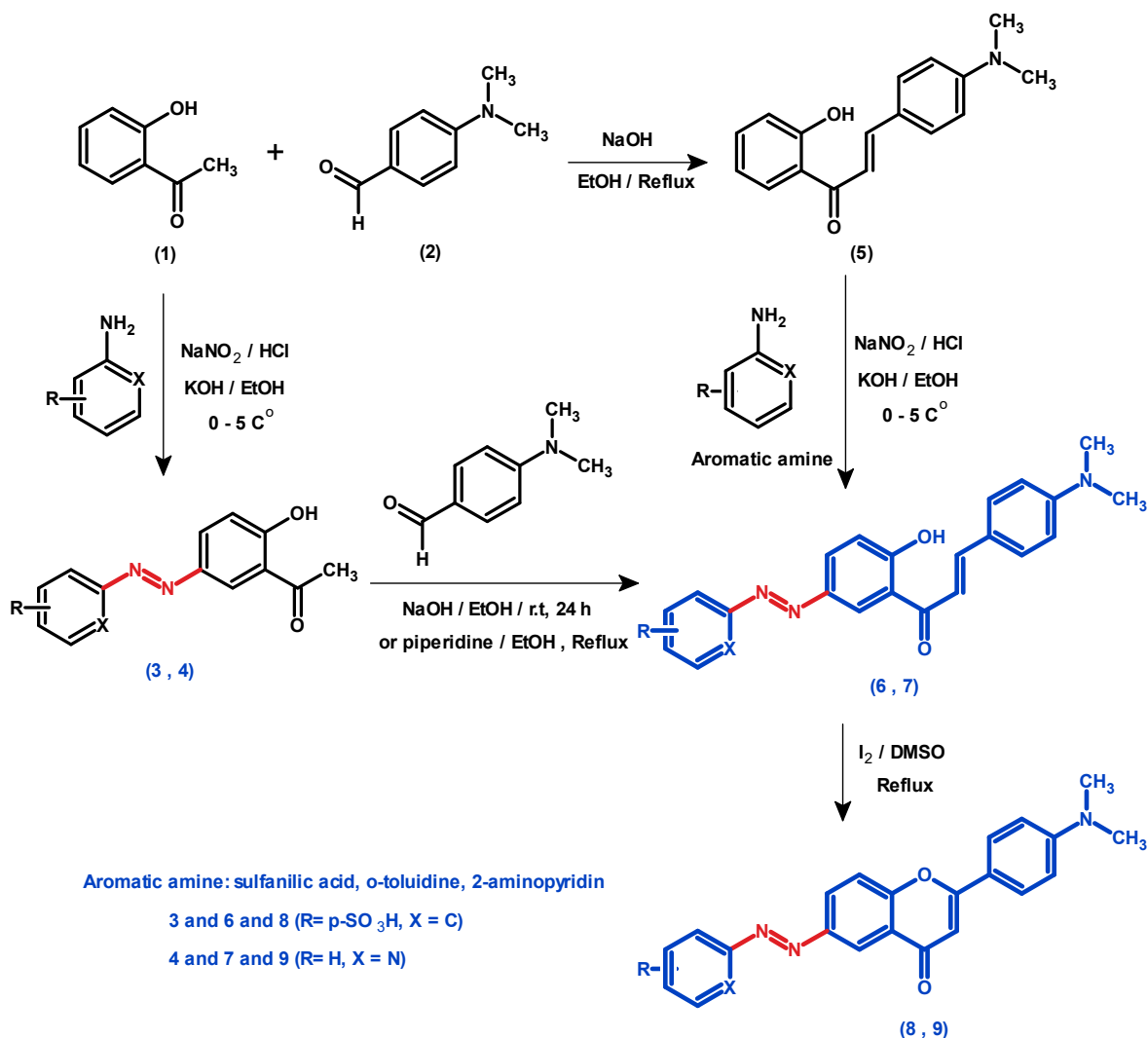
\* Corresponding author

E-mail address [hadiaqelkhdera@gmail.com](mailto:hadiaqelkhdera@gmail.com) (H. A. Khdera)

Intermediate compounds (3, 4) were also prepared by performing diazotisation and coupling reactions of different aromatic amines (sulfanilic acid, 2-amino pyridine) with *o*-hydroxyacetophenone, with yields ranging between (85.5 - 88 %).

New chalcone derivatives (6, 7) containing an azo group in its structure were prepared in three methods. The first method included conducting diazotisation and coupling reactions for three aromatic amines with the chalcone compound (5), and the second method included conducting an aldol condensation reaction between azophenyl hydroxyacetophenone derivatives (3, 4) With 4-dimethylaminobenzaldehyde in presence of sodium hydroxide and ethanol. The third method included performing the aldol condensation reaction in the presence of ethanol and piperidine as an organic catalyst. The results showed that the yield was better using the aldol condensation method using sodium hydroxide as a catalyst. New azoflavone derivatives (8, 9) with yields (78 - 84 %) were also prepared by carrying out cyclization reactions of azochalcone derivatives using iodine in dimethyl sulfoxide. Melting points of the synthetic compounds ranged from (169 - 273) °C, and were highest for the compounds 6 and 8 as they contain the highly polar -SO<sub>3</sub>H group. **Fig. 1** shows a reaction scheme for the synthesis of azochalcone (6, 7) and azoflavone derivatives (8, 9).

Infrared spectroscopy of azochalcone compounds (6, 7) showed the presence of absorption bands at the frequency (3415-3420 cm<sup>-1</sup>) belonging to the (-OH) group, and an absorption band at the frequency (1620-1640 cm<sup>-1</sup>) belonging to the carbonyl group (C=O). The absorption band at (1381 cm<sup>-1</sup>) belongs to the azo group (-N=N-), which indicates the occurrence of the diazotisation-coupling reaction and the formation of new derivatives. Spectral analysis of the flavonoid compound (8) showed the presence of an absorption band at frequency (3416 cm<sup>-1</sup>) which belongs to the sulfonic (-OH) group. Spectroscopic analysis of the flavonoid (9) showed the disappearance of the absorption band of the (-OH) group, indicating the occurrence of the cyclization reaction of chalcone compounds with iodine in dimethyl sulfoxide and the formation of new derivatives.



**Fig. 1.** Reaction scheme of the synthesis of azo chalcone (6, 7) and azo flavone derivatives (8, 9)

<sup>1</sup>H-NMR spectroscopy of the chalcone compounds (6, 7) showed binary signals at chemical shift values ( $\delta = 7.65, 7.60$  ppm) belonging to the CH <sub>$\alpha$</sub>  proton, binary signals at ( $\delta = 8.11, 8.06$  ppm) belonging to the CH <sub>$\beta$</sub>  proton, and single signals at ( $\delta = 11.23, 11.32$  ppm) belongs to the -OH group in the mentioned compounds. While the proton NMR spectroscopy of the flavonoids (8, 9) showed distinct single signals at chemical shift values ( $\delta = 6.71, 6.71$ ) ppm belonging to the proton attached to carbon C<sub>3</sub> in the pyrane ring, in addition to the presence of other signals common to all compounds.

<sup>13</sup>C-NMR spectroscopy of the chalcone compounds (6, 7) showed signals at chemical shift values ( $\delta = 118.75, 118.66$  ppm) belonging to the C <sub>$\alpha$</sub>  carbon and signals at chemical shift values ( $\delta = 145.54, 145.74$  ppm) belonging to the C <sub>$\beta$</sub>  carbon. While the <sup>13</sup>C-NMR spectroscopy of the flavonoid compounds (8, 9) showed distinct signals at chemical shift values ( $\delta = 104.64, 104.85$  ppm) belonging to the C<sub>3</sub> carbon in the pyranic ring, in addition to the presence of other signals common to all compounds.

### 3. Conclusions

Using the aldol condensation reaction in the presence of piperidine or sodium hydroxide as a catalyst and the diazotisation - coupling reaction, three new azochalcone derivatives were synthesized with good yields, the best of which was the aldol condensation method in the presence of sodium hydroxide. Three new azoflavone derivatives were synthesized via cyclization reactions of chalcone derivatives using iodine in DMSO. The chemical structures of the synthetic compounds were confirmed by spectroscopic methods (FT-IR, <sup>13</sup>C-NMR, <sup>1</sup>H-NMR) and elemental analysis. Chalcones, flavonoids and their derivatives are of great interest to chemical researchers and their design can lead to pharmaceutical compounds with important biological activity.

### 4. Experimental

#### 4.1. Materials and Methods

All compounds were purified by recrystallization and separated by preparative thin-layer chromatography. The progress of the reactions was observed by thin-layer chromatography (TLC) on silica gel-coated aluminium plates using a DESAGA-UVIS/254/366 nm UV lamp. Melting points were measured with Stuart Electrothermal Engineering LTD 9100 (measurements up to 400 °C). Infrared spectra were recorded with a Jasco 460 Plus spectrophotometer using the KBr disc method. <sup>13</sup>C and <sup>1</sup>H-NMR spectra were recorded with a Bruker Avance II 400 (model 400 MHz AVANCE SPECTROMETER) at 100 and 400 MHz, DMSO-*d*<sub>6</sub> was used as solvent.

Chemical and Materials: absolute ethanol, diethylether, dry acetone, hexane, dimethylsulfoxide (Sigma Aldrich, Merck, Fluka). The materials used are o-hydroxyacetophenone, 4-dimethylamino benzaldehyde, piperidine 2-aminopyridin, sulfanilic acid, sodium hydroxide, potassium hydroxide, iodine, sodium nitrite, sodium thiosulfate, concentrated hydrochloric acid from different companies (Merck, Fluka, BDH, Sigma Aldrich).

#### 4.2. General procedure

##### 4.2.1 Synthesis of Chalcone: (2E)-3-[4-(dimethylamino)phenyl]-1-(2-hydroxyphenyl)prop-2-en-1-one (5)

Compound (5) which was used in this study was prepared following procedures previously described in the literature.<sup>20</sup> Bright pink solid; Yield: 80 %; mp 178-180 °C; R<sub>f</sub> = 0.44 (acetone : hexane 1:3); IR (KBr, cm<sup>-1</sup>)  $\nu$ : 3650 (OH), 2890 (C-H<sub>aliphatic</sub>), 1596 (C=O pyrone), 1432-1485 (C=C), 1202 (C-O).

##### 4.2.2 Synthesis azoaryl hydroxyacetophenone compounds (3, 4)

###### 4.2.2.a. Synthesis of 4-[(E)-(3-acetyl-4-hydroxyphenyl) diazenyl]benzene-1-sulfonic acid (3)

Sulfanilic acid (0.008 mol) is taken and dissolved in (40 ml) aqueous solution with potassium hydroxide (0.008 mol). After cooling the solution to (0-5 °C), slowly added 5 ml of concentrated hydrochloric acid and then (10 ml) of sodium nitrite solution (0.008 mol) and stirred the mixture well in an ice bath for 20 minutes to form the 4-sulfobenzenediazonium salt. (0.008 mol) of o-hydroxy acetophenone (1) is taken and dissolved in (40 ml) of ethanol containing potassium hydroxide (0.016 mol) and cooled in an ice bath, then the diazonium solution is added to the hydroxyacetophenone solution in batches for 4 hours with good stirring. The reaction medium is neutralized with dilute hydrochloric acid, the resulting precipitate is filtered, washed with water and recrystallized with ethanol. Brown solid; Yield (85.5 %); m.p. 218-220 °C; R<sub>f</sub> = 0.34 (mobile phase acetone : hexane 1:3).

###### 4.2.2.b. Synthesis of 1-{2-hydroxy-5-[(E)-(pyridin-2-yl) diazenyl]phenyl}ethan-1-one (4)

(0.008 mol) 2-aminopyridine was taken and dissolved in (20 ml) water and (8 ml) concentrated hydrochloric acid. After cooling the solution to (0-5 °C), (10 ml) of sodium nitrite solution (0.008 mol) was added. The mixture was stirred well in an ice bath for 20 minutes to form the pyridine-2-diazonium salt. (0.008 mol) of o-hydroxyacetophenone (1) was dissolved in (40 ml) ethanol containing (0.016 mol) potassium hydroxide and cooled in an ice bath. The diazonium solution was then added in batches to the hydroxyacetophenone solution and stirred well for 4 hours. The reaction medium was neutralized with dilute hydrochloric acid, the resulting precipitate is filtered, washed with water, and recrystallized with ethanol. Dark yellow solid; Yield (88 %); m.p. 158-160 °C; R<sub>f</sub> = 0.42 (mobile phase acetone: hexane 1:3).

### 4.2.3 Synthesis of azo chalcone derivatives (6, 7)

#### 4.2.3.a Method (A) Diazotisation-Coupling Reaction

##### 4.2.3.a.1. Synthesis of 4-[(E)-(4-hydroxy-3-((2E)-3-[4-(dimethylamino)phenyl]prop-2-enoyl)phenyl) diazenyl]benzene-1-sulfonic acid (6)

(0.005 mol) sulfanilic acid was dissolved in (40 ml) aqueous solution with potassium hydroxide (0.005 mol). After cooling the solution to (0-5 °C), slowly (3 ml) of concentrated hydrochloric acid was added and then (10 ml) of sodium nitrite solution (0.005 mol) and the mixture stirred well in an ice bath for 20 minutes to form the aryldiazonium salt. (0.005 mol) of chalcone (5) was taken and dissolved in (40 ml) of ethanol containing potassium hydroxide (0.03 mol) and cooled in an ice bath, then the diazonium solution was added to the chalcone solution in batches for 4 hours with good stirring. The reaction medium was neutralized with dilute hydrochloric acid, the resulting precipitate is filtered, washed with water and recrystallized with ethanol.

##### 4.2.3.a.2 Synthesis of (2E)-3-[4-(dimethylamino)phenyl]-1-{2-hydroxy-5-[(E)-(pyridin-2-yl)diazenyl]phenyl} prop-2-en-1-one (7)

(0.005 mol) of 2-aminopyridine in was dissolved (20 ml) water and (5 ml) of concentrated hydrochloric acid. After cooling the solution to (0-5 °C), 10 ml of sodium nitrite solution (0.005 mol) was added. The mixture was stirred well in an ice bath for 20 minutes to form the aryl diazonium salt. (0.005 mol) of chalcone (5) was dissolved in (40 ml) ethanol containing potassium hydroxide (0.03 mol) and cooled in an ice bath. The diazonium solution was then added to the chalcone solution in batches and stirred well for 4 hours. The reaction medium is neutralized with dilute hydrochloric acid, the resulting precipitate is filtered, washed with water and recrystallized with ethanol.

#### 4.2.3.b. Method (B) Aldol condensation reaction using NaOH as catalyst

(0.00156 mol) of compound (3 or 4) and (0.00156 mol) of 4-dimethylaminobenzaldehyde (2) were added in (50 ml) of absolute ethanol, 5 ml (20%) of alcoholic NaOH solution was added to the previous solution. The mixture for was stirred for 24 hours at room temperature and the reaction was observed with TLC (mobile phase acetone : hexane 1:3). The mixture was poured into a beaker with crushed ice, the medium was neutralized by adding a dilute hydrochloric acid solution, the precipitate was filtered, washed with water and recrystallized with absolute ethanol to obtain the compounds (6, 7).

#### 4.2.3.c. Method (C) Aldol condensation reaction using piperidine as catalyst

(0.00156 mol) of compound (3 or 4) and (0.00156 mol) of 4-dimethylaminobenzaldehyde (2) were added in (50 ml) of absolute ethanol, (2 ml) of piperidine were added to the previous solution. The mixture was refluxed for 15 hours and the reaction was observed with TLC (mobile phase acetone : hexane 1:3). The mixture was poured into a beaker containing crushed ice, the medium was neutralized by adding a dilute hydrochloric acid solution, and the precipitate was filtered, washed with water and recrystallized with absolute ethanol to give the compounds (6, 7).

### 4.2.4. Synthesis of azoflavone derivatives (8, 9)

Azochalcone (6 or 7) (1.2 mmol) was dissolved in DMSO (30 ml), and iodine (0.22 mmol) was added to the previous solution. The reaction mixture was refluxed for 3 h. After completion of the reaction, the mixture was added to another mixture consisting of crushed ice and a saturated solution of sodium thiosulfate and stirred for 20 minutes. The precipitate was filtered, washed with water and ethanol and finally recrystallized with ethanol. Preparative thin layer chromatography was used to further purify the flavonoid compounds using the mobile phase (acetone : hexane 2:3) to give compound 8 and the mobile phase (acetone : hexane 1:3) to give compounds 9.

## 4.3 Physical and Spectral Data

### 4.3.1. 4-[(E)-(4-hydroxy-3-((2E)-3-[4-(dimethylamino) phenyl]prop-2-enoyl)phenyl)diazenyl]benzene-1-sulfonic acid (6)

Brown solid; Yield (76<sup>a</sup>, 87<sup>b</sup>, 56<sup>c</sup> %); m.p. 271-273 °C; R<sub>f</sub> = 0.28 (mobile phase acetone : hexane 1:3); IR (KBr, cm<sup>-1</sup>) ν<sub>max</sub>: 3420 (OH), 2856-2911 (C-H<sub>aliphatic</sub>), 1627 (C=O), 1412-1487 (C=C), 1366 (N=N), 1179 (S=O) 1122-1229 (C-O). <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 3.02 (s, 6H, 2 CH<sub>3</sub>), 6.82 (d, 2H, *J* = 8.2 Hz, H<sub>3',5'</sub>), 7.25 (d, 1H, *J* = 7.9 Hz, H<sub>3</sub>), 7.59 (d, 2H, *J* = 8.2 Hz, H<sub>2',6'</sub>), 7.65 (d, 1H, *J* = 14.2 Hz, H<sub>a</sub>), 8.02 (d, 1H, *J* = 2 Hz, H<sub>6</sub>), 8.1 (dd, 1H, *J* = 7.9 Hz, *J* = 2 Hz, H<sub>4</sub>), 8.11 (d, 1H, *J* = 14.2 Hz, H<sub>β</sub>), 8.08 (d, 2H, *J* = 7.8 Hz, H<sub>3'',5''</sub>), 8.55 (d, 2H, *J* = 7.8 Hz, H<sub>2'',6''</sub>), 8.78 (s, 1H, OH), 11.23 (s, 1H, OH). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 40.42 (CH<sub>3</sub>, 2 CH<sub>3</sub>), 111.68 (C<sub>3',5'</sub>), 118.75 (CH<sub>a</sub>), 116.76 (C<sub>3</sub>), 123.28 (C<sub>3'',5''</sub>), 122.86 (C<sub>1</sub>), 123.96 (C<sub>1'</sub>), 124.14 (C<sub>6</sub>), 124.42 (C<sub>2'',6''</sub>), 156.45 (C<sub>1''</sub>), 130.14 (C<sub>4</sub>), 129.25 (C<sub>2',6'</sub>), 147.54 (C<sub>4''</sub>), 145.67 (C<sub>5</sub>), 145.54 (CH<sub>β</sub>), 151.16 (C<sub>4'</sub>), 164.98 (C<sub>2</sub>), 192.85 (C=O). Anal Calcd for C<sub>23</sub>H<sub>21</sub>N<sub>3</sub>O<sub>5</sub>S, C, 61.17; H, 4.68; N, 9.32; S, 7.10; found C, 61.12; H, 4.74; N, 9.27; S, 7.04 %.

### 4.3.2. (2E)-3-[4-(dimethylamino)phenyl]-1-{2-hydroxy-5-[(E)-(pyridin-2-yl)diazenyl]phenyl}prop-2-en-1-one (7)

Red solid; Yield (78<sup>a</sup>, 84<sup>b</sup>, 44<sup>c</sup> %); m.p. 169-170 °C; R<sub>f</sub> = 0.31 (mobile phase acetone : hexane 1:3); IR (KBr, cm<sup>-1</sup>) ν<sub>max</sub>: 3415 (OH), 2909 (C-H<sub>aliphatic</sub>), 1620 (C=O), 1520 (C=N), 1408-1487 (C=C), 1381 (N=N), 1124-1231 (C-O). <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 3.02 (s, 6H, 2 CH<sub>3</sub>), 6.77 (d, 2H, *J* = 8.6 Hz, H<sub>3',5'</sub>), 7.01 (d, 1H, *J* = 7.8 Hz, H<sub>3</sub>), 7.32 (d, 1H, *J* = 2 Hz, H<sub>6</sub>), 7.37 (d, 1H, *J* = 7.8 Hz, *J* = 2 Hz, H<sub>4</sub>), 7.38 (td, 1H, *J* = 7.9 Hz, *J* = 2.1 Hz, H<sub>5''</sub>), 7.54 (d, 2H, *J* = 8.6 Hz, H<sub>2',6'</sub>), 7.60 (d, 1H, *J* = 14.3 Hz, H<sub>a</sub>), 7.64 (dd, 1H, *J* = 7.9 Hz, *J* = 2.1 Hz, H<sub>3''</sub>), 7.75 (td, 1H, *J* = 7.9 Hz, *J* = 2.1 Hz, H<sub>4''</sub>), 8.06 (d, 1H, *J* = 14.3

Hz, H<sub>β</sub>), 8.70 (dd, 1H, J= 7.9 Hz, J= 2.1 Hz, H<sub>6''</sub>), 11.32 (s, 1H, OH). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 40.43 (CH<sub>3</sub>, 2 CH<sub>3</sub>), 111.66 (C<sub>3',5'</sub>), 118.66 (CH<sub>α</sub>), 116.77 (C<sub>3</sub>), 114.23 (C<sub>3''</sub>), 123.15 (C<sub>5''</sub>), 122.67 (C<sub>1</sub>), 123.24 (C<sub>1'</sub>), 129.59 (C<sub>6</sub>), 149.76 (C<sub>6''</sub>), 136.04 (C<sub>4</sub>), 129.22 (C<sub>2',6'</sub>), 139.53 (C<sub>4''</sub>), 121.84 (C<sub>5</sub>), 145.74 (CH<sub>β</sub>), 151.24 (C<sub>4</sub>), 164.23 (C<sub>2''</sub>), 163.95 (C<sub>2</sub>), 192.75 (C=O). Anal Calcd for C<sub>22</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>, C, 70.93; H, 5.43; N, 15.02; found C, 70.90; H, 5.48; N, 15.06 %.

4.3.3. 4-[(*E*)-{2-[4-(dimethylamino)phenyl]-4-oxo-4*H*-1-benzopyran-6-yl}diazonyl]benzene-1-sulfonic acid (**8**) Dark yellow solid; Yield (84 %); m.p. 195-197 °C; R<sub>f</sub> = 0.31 (mobile phase acetone : hexane 1:3); IR (KBr, cm<sup>-1</sup>) ν<sub>max</sub>: 3416 (OH), 1634 (C=O), 1435-1566 (C=C), 1382 (N=N), 1119-1251 (C-O). <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 3.02 (s, 6H, 2 CH<sub>3</sub>), 6.71 (s, 1H, CH), 6.78 (d, 2H, J= 8.2 Hz, H<sub>3',5'</sub>), 7.17 (d, 2H, J= 7.8 Hz, H<sub>2',6'</sub>), 7.20 (d, 1H, J= 7.8 Hz, H<sub>8</sub>), 7.96 (d, 1H, J= 2 Hz, H<sub>5</sub>), 7.99 (dd, 1H, J= 7.8 Hz, J= 2 Hz, H<sub>7</sub>), 8.01 (d, 2H, J= 7.9 Hz, H<sub>3'',5''</sub>), 8.45 (d, 2H, J= 7.9 Hz, H<sub>2'',6''</sub>), 8.61 (s, 1H, OH). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 40.14 (CH<sub>3</sub>, 2 CH<sub>3</sub>), 104.64 (C<sub>3</sub>), 111.76 (C<sub>3',5'</sub>), 114.21 (C<sub>8</sub>), 123.19 (C<sub>3'',5''</sub>), 118.98 (C<sub>1'</sub>), 123.35 (C<sub>5</sub>), 124.24 (C<sub>10</sub>), 124.14 (C<sub>2'',6''</sub>), 156.45 (C<sub>1''</sub>), 127.53 (C<sub>2',6'</sub>), 129.49 (C<sub>7</sub>), 147.75 (C<sub>4''</sub>), 147.35 (C<sub>6</sub>), 150.84 (C<sub>4</sub>), 158.23 (C<sub>9</sub>), 163.63 (C<sub>2</sub>), 178.10 (C=O pyron). Anal Calcd for C<sub>23</sub>H<sub>19</sub>N<sub>3</sub>O<sub>5</sub>S, C, 61.47; H, 4.25; N, 9.37; S, 7.14; found C, 61.42; H, 4.29; N, 9.31; S, 7.10 %.

4.3.4. 2-[4-(dimethylamino)phenyl]-6-[(*E*)-(pyridin-2-yl)diazonyl]-4*H*-1-benzopyran-4-one (**9**) Yellow solid; Yield (78 %); m.p. 181-183 °C; R<sub>f</sub> = 0.19 (mobile phase acetone : hexane 1:3); IR (KBr, cm<sup>-1</sup>) ν<sub>max</sub>: 1630 (C=O), 1434-1464 (C=C), 1368 (N=N), 1171-1261 (C-O). <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 3.02 (s, 6H, 2 CH<sub>3</sub>), 6.71 (s, 1H, CH), 6.77 (d, 2H, J= 8.6 Hz, H<sub>3',5'</sub>), 7.01 (d, 1H, J= 7.8 Hz, H<sub>8</sub>), 7.18 (d, 2H, J= 8.6 Hz, H<sub>2',6'</sub>), 7.33 (d, 1H, J= 2 Hz, H<sub>5</sub>), 7.34 (d, 1H, J= 7.8 Hz, J= 2 Hz, H<sub>7</sub>), 7.40 (td, 1H, J= 7.8 Hz, J= 2 Hz, H<sub>5''</sub>), 7.71 (dd, 1H, J= 7.8 Hz, J= 2 Hz, H<sub>3''</sub>), 7.82 (td, 1H, J= 7.8 Hz, J= 2 Hz, H<sub>4''</sub>), 8.82 (dd, 1H, J= 7.8 Hz, J= 2 Hz, H<sub>6''</sub>). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>, δ ppm): 40.15 (CH<sub>3</sub>, 2 CH<sub>3</sub>), 104.85 (C<sub>3</sub>), 111.75 (C<sub>3',5'</sub>), 113.64 (C<sub>8</sub>), 114.17 (C<sub>3''</sub>), 123.14 (C<sub>5''</sub>), 118.86 (C<sub>1'</sub>), 129.14 (C<sub>5</sub>), 124.15 (C<sub>10</sub>), 149.76 (C<sub>6''</sub>), 127.45 (C<sub>2',6'</sub>), 135.53 (C<sub>7</sub>), 139.53 (C<sub>4''</sub>), 123.64 (C<sub>6</sub>), 150.45 (C<sub>4</sub>), 163.95 (C<sub>2''</sub>), 156.42 (C<sub>9</sub>), 163.64 (C<sub>2</sub>), 178.13 (C=O pyron). Anal Calcd for C<sub>22</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>, C, 71.34; H, 4.92; N, 15.10; found C, 71.29; H, 4.98; N, 15.14 %.

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