



## Synthesis and spectral Characterization of $\alpha$ , $\beta$ -Unsaturated Ketones and Their Dibromo Derivatives

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### Abstract :

Reaction of 2-chloro-6-methylquinoline-3-carbaldehyde (1) and 2-hydroxy 5-methyl acetophenone afforded a novel Chalcone (1a). Similarly, some more novel Chalcones (2a-d) were synthesised by condensing benzyloxy benzaldehyde (2) with different substituted 2-hydroxy acetophenones (a-d) by Claisen-Schmidt reaction. Synthesised Chalcones (1a and 2a-d) were then brominated to afford corresponding dibromo chalcone derivatives (3a and 4a-d) respectively. The structures of the newly synthesized chalcones were elucidated by elemental analysis and spectral methods such as IR, <sup>1</sup>H NMR and mass spectra.

Keywords: Chalcone, dibromo chalcones, quinoline-3-carbaldehyde, benzyloxy benzaldehyde

### Introduction:

Chalcones or  $\alpha$ ,  $\beta$ -unsaturated ketones are 1, 3-diaryl-2-propen-1-

ones, consisting of open chain flavonoids in which two aromatic rings are joined by a three carbon bridge having a keto carbonyl moiety and  $\alpha$ ,  $\beta$ -unsaturation. Literature survey [1-3] indicates that one of the popular methods for the preparation of chalcone is Claisen-Schmidt condensation of 2-hydroxy acetophenones with appropriate aromatic aldehydes. However, the search for an efficient synthesis for chalcones is still a challenging task. Chalcones are a diverse group of compounds that can be synthesized or obtained from natural sources [4] and have attracted increasing attention due to their numerous pharmacological activities [5] such as antibacterial, antifungal, anticancer, anti-inflammatory, antitubercular, antihyperglycemic [6] and antimalarial agents [7]. The presence of a reactive and unsaturated keto moiety as well as aryl conjugation in chalcones is found to be responsible for their biological activity. Moreover, chalcones provide an opportunity for chemist to synthesize a wide variety of bioactive heterocycles [8-11] due to the presence of  $\alpha$ ,  $\beta$ -unsaturated carbonyl functionality.

Chalcones can be further brominated by using different brominating agents such as molecular bromine in different organic solvents to get dibromo derivatives [12] having much pharmacological importance.  $\alpha$ ,  $\beta$ -Dibromo chalcones are valuable synthetic building blocks, which are employed for several types of synthetic transformations, in particular for synthesis of heterocyclic compounds such as pyrazoles, hydroxy pyrazoline and isoxazoles [13] derivatives with antibacterial and antifungal activities [14,15].

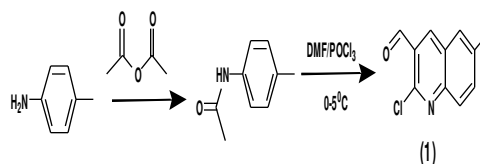
Appreciation of these findings motivated us to synthesize chalcones and extend its reaction by brominating them to prepare its dibromo derivative and characterize them by spectral analysis.

### Experimental:

The preparation of starting material includes following three steps.

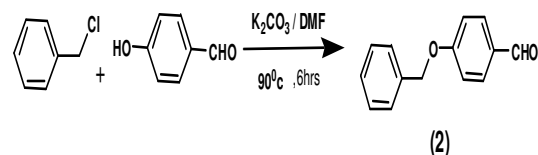
- 1. Preparation of 2-chloro-6-methylquinoline-3-carbaldehyde (1):** p-Toluidine was acetylated to obtain corresponding 4-methyl acetanilide, which were then treated with DMF and POCl<sub>3</sub> at 0-5°C according to Vilsmeier-Haack reaction to afford **1** (Scheme 1).

Reaction Scheme : 1



- 2. Preparation of Benzyloxy benzaldehyde (2):** Benzyloxy benzaldehyde was prepared by treating p-hydroxybenzaldehyde and benzylchloride with K<sub>2</sub>CO<sub>3</sub> in DMF at 80-90°C (Scheme 2).

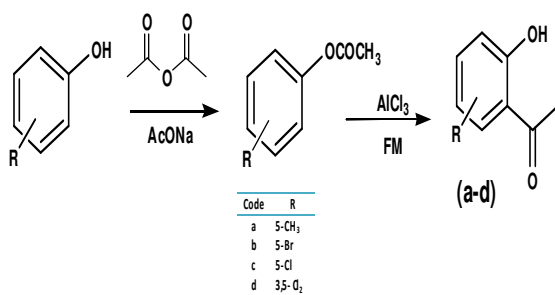
Reaction Scheme : 2



- 3. Preparation of substituted acetophenones (a-d):** Substituted acetophenones such as 2-hydroxy 5-methyl acetophenone (**a**), 2-hydroxy 5-

bromo acetophenone **(b)**, 2-hydroxy 5-chloro acetophenone **(c)**, and 2-hydroxy 3,5-dichloro acetophenone **(d)**, were prepared by refluxing substituted phenols such as p-methyl phenol, p-bromophenol, p-chloro phenol, and 3,5-dichloro phenol respectively with acetic anhydride and anhydrous sodium acetate according to known procedure followed by Fries migration of respective phenyl acetate in presence of anhydrous aluminium chloride.

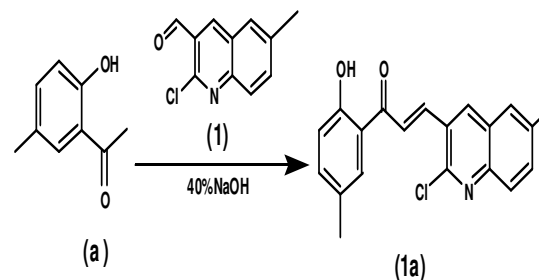
#### Reaction Scheme : 3



**General procedure for Synthesis of Chalcones (1a and 2a-d):** **a** (10mmole) and **1**(10mmole) were dissolved in minimum quantity of ethanol and heated till the solid get dissolved. Aqueous 40% sodium hydroxide

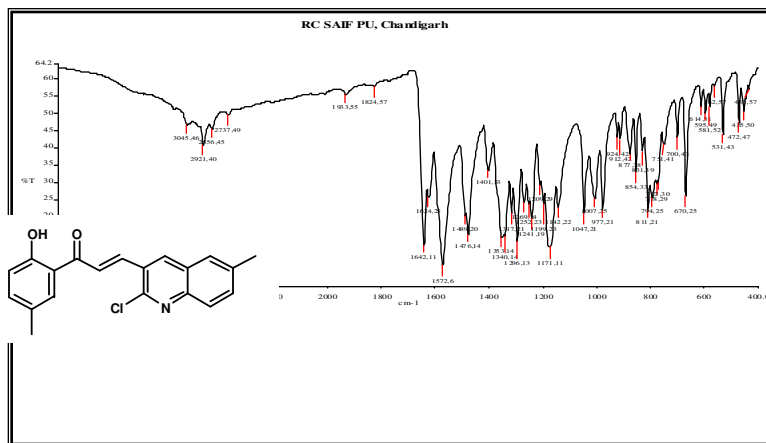
solution (10 mL) was added drop wise with constant stirring. The mixture was further stirred mechanically at room temperature to obtain dark orange mass and kept overnight. Then it was acidified by 1:1 hydrochloric acid. The solid obtained was filtered, washed and recrystallized to get **1a** (Scheme 4).

#### Reaction Scheme : 4

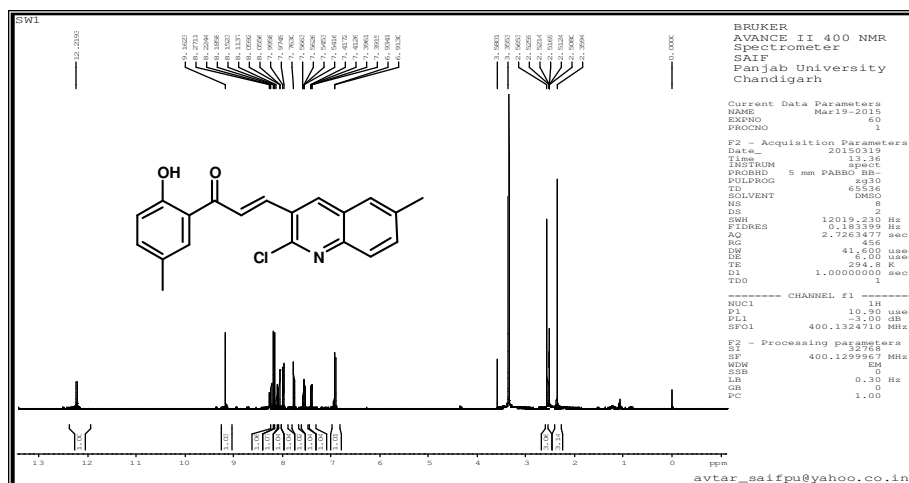


**(E)-3-(2-chloro-6-methylquinolin-3-yl)-1-(2-hydroxy-5-methylphenyl) prop-2-en-1-one (1a):** Yellowish crystals, MP: 210-212°C, Yield: 79%, Recrystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>20</sub>H<sub>16</sub>ClNO<sub>2</sub> IR: 3045 (ArH), 2856, 2921 (CH<sub>3</sub>), 1642 (C=O), 1476, 1489 (C=C), 1572 (C=N) <sup>1</sup>H NMR: 2.3594 (s, 3H, -CH<sub>3</sub>), 2.5653 (s, 3H, -CH<sub>3</sub>), 12.2193 (b, 1H, -OH), 6.9130 - 9.1623 (m, 9H, ArH) MS: 338 [M+H]<sup>+</sup> Calculated: C, 71.11; H, 4.77; N, 4.15 Found: C, 69.82; H, 4.76; N, 3.81.

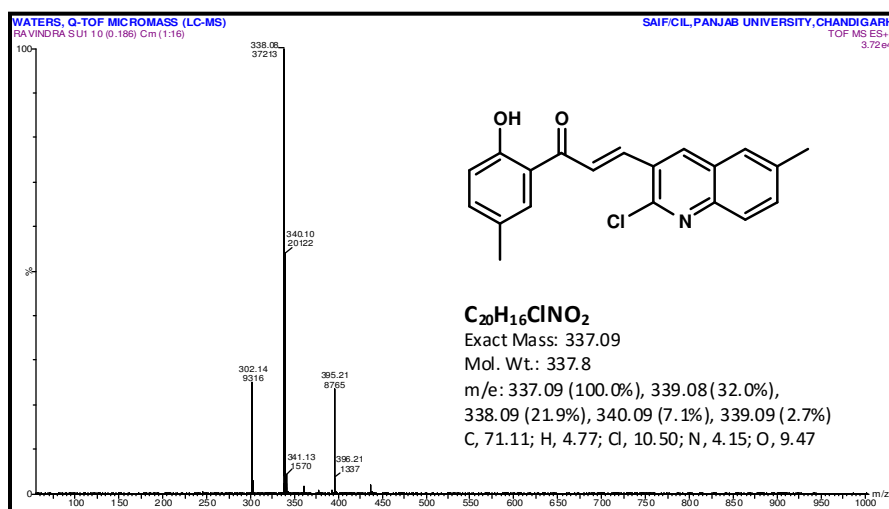
#### IR spectra of 1a



#### <sup>1</sup>H NMR spectra of 1a



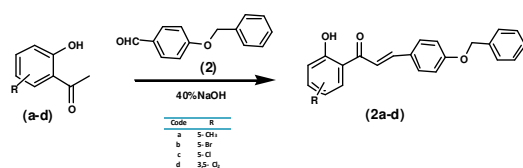
Mass spectra of 1a



Similarly, **2a-d** were synthesised from **a-d** by extending the same procedure followed for **1a** (Scheme

5).

Reaction Scheme : 5



**(2E)-3-[4-(benzyloxy)phenyl]-1-(2-hydroxy-5-methylphenyl)prop-2-en-1-one (2a):** Orange colour, MP:131°-133°C, Yield: 84.00% Recrystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>23</sub>H<sub>20</sub>O<sub>3</sub>, <sup>1</sup>H NMR: 2.3518 (s, 3H, -CH<sub>3</sub>), 2.5232 (s, 2H, -CH<sub>2</sub>), 12.2267 (b, 1H, -OH), 6.8346 – 8.9928 (m, 14H, ArH) MS: 345 [M+H]<sup>+</sup>, Calculated: C, 80.21; H, 5.85; Found: C, 80.43; H, 5.91.

**(2E)-3-[4-(benzyloxy)phenyl]-1-(5-bromo-2-hydroxyphenyl)prop-2-en-1-one (2b):** Orange colour, MP:141°-143° Yield: 91.88% Recrystallizing solvent: CH<sub>3</sub>COOH,

MF: C<sub>22</sub>H<sub>17</sub>O<sub>3</sub>Br. <sup>1</sup>H NMR: 2.5196 (s, 2H, -CH<sub>2</sub>), 12.4001 (b, 1H, -OH), 6.8357– 9.5181 (m, 14H, ArH) MS: 409 [M]<sup>+</sup>, Calculated: C, 64.56; H, 4.19 Found: C, 64.54; H, 4.25.

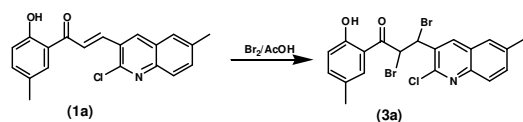
**(2E)-3-[4-(benzyloxy)phenyl]-1-(5-chloro-2-hydroxyphenyl)prop-2-en-1-one (2c):** Orange colour, MP:135°-136°C, Yield: 88.56%, Recrystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>22</sub>H<sub>17</sub>O<sub>3</sub>Cl. <sup>1</sup>H NMR: 2.4999 (s, 2H, -CH<sub>2</sub>), 12.3564 (b, 1H, -OH), 6.8132–9.5012 (m, 14H, ArH) MS: 366 [M+H]<sup>+</sup>, Calculated: C, 72.43; H, 4.70; Found: C, 72.41; H, 4.65.

**(2E)-3-[4-(benzyloxy)phenyl]-1-(3,5-dichloro-2-hydroxyphenyl)prop-2-en-1-one (2d):** Orange colour, MP:163°-165°C, Yield: 71.16%, Recrystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>22</sub>H<sub>16</sub>O<sub>3</sub>Cl<sub>2</sub>, <sup>1</sup>H NMR: 2.5881 (s, 2H, -CH<sub>2</sub>), 12.5144 (b, 1H, -OH), 6.8762 – 9.4357 (m, 13H, ArH) MS: 399 [M]<sup>+</sup>, 422 [M+Na]<sup>+</sup>,

Calculated: C, 66.18; H, 4.04; Found: C, 66.33; H, 4.01.

**Preparation of 2,3-dibromo-3-(2-chloro-6-methylquinolin-3-yl)-1-(2-hydroxy-5-methylphenyl)propan-1-one (3a):** Chalcone (1a, 0.01M) was added to acetic acid (5mL) and then Br<sub>2</sub> solution (25%, 3.4ml) was added drop wise with vigorous stirring. Solid was separated out and reaction mixture was allowed to stand at room temperature for 30 minutes, product so obtained was filtered, washed and re-crystallized to get 3a (Scheme 6).

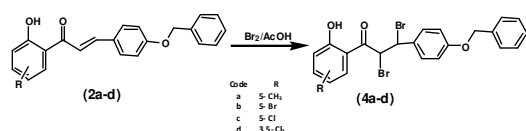
Reaction Scheme : 6



**2,3-dibromo-3-(2-chloro-6-methylquinolin-3-yl)-1-(2-hydroxy-5-methylphenyl)propan-1-one (3a):** Pale yellow colour, MP:148-150°C Yield: 75%, Recrystallizing solvent: Ethanol, MF: C<sub>20</sub>H<sub>16</sub>Br<sub>2</sub>ClNO<sub>2</sub>. <sup>1</sup>H NMR: 2.3475 (s, 3H, -CH<sub>3</sub>), 2.4989 (s, 3H, -CH<sub>3</sub>), 12.1356 (b, 1H, -OH), 5.6523 (d, 1H, H<sub>β</sub>, J=11.24), 6.2084 (d, 1H, H<sub>α</sub>, J=11.24), 6.5695 - 9.8739 (m, 7H, ArH) MS: 498 [M+H]<sup>+</sup>, Calculated: C, 48.47; H, 2.85; N, 2.83; Found: C, 48.54; H, 2.76; N, 2.80.

Similarly, 4a-d were synthesised from 2a-d by extending the same procedure followed for 3a (Scheme 7).

Reaction Scheme : 7



**3-(4-(benzyloxy)phenyl)-2,3-dibromo-1-(2-hydroxy-5-methylphenyl)propan-1-one (4a):** Pale yellow colour, MP:143-145°C, Yield: 51.09%, Re crystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>23</sub>H<sub>20</sub>Br<sub>2</sub>O<sub>3</sub>.

**3-(4-(benzyloxy)phenyl)-2,3-dibromo-1-(2-hydroxy-5-bromophenyl)propan-1-one (4b):** Orange colour, MP:124-126°C, Yield: 61.69%, Re crystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>22</sub>H<sub>17</sub>Br<sub>3</sub>O<sub>3</sub>.

**3-(4-(benzyloxy)phenyl)-2,3-dibromo-1-(2-hydroxy-5-chlorophenyl)propan-1-one (4c):** Yellowish colour, MP:130-132°C, Yield: 54.64%, Re crystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>22</sub>H<sub>17</sub>O<sub>3</sub>ClBr<sub>2</sub>.

**3-(4-(benzyloxy)phenyl)-2,3-dibromo-1-(2-hydroxy-3,5-dichlorophenyl)propan-1-one**

**(4d):** Yellowish colour, MP:168-170°C, Yield: 61.46% Re crystallizing solvent: CH<sub>3</sub>COOH, MF: C<sub>22</sub>H<sub>16</sub>Br<sub>2</sub>Cl<sub>2</sub>O<sub>3</sub>.

### Results and Discussion:

The synthesis of the novel chalcones (1a and 2a-d) and its dibromo derivatives (3a and 4a-d) are described in reaction schemes. The identities of the chalcones have been established on the basis of their elemental analysis and spectral data such as IR, <sup>1</sup>H NMR and Mass spectral studies [16].

The reaction of 2-chloro-6-methylquinoline-3-carbaldehyde (1) with 2-hydroxy 5-methyl acetophenone in presence of 40% NaOH afforded (1a) by Claisen-Schmidt condensation. FeCl<sub>3</sub> test for 1a gave violet colouration showing the presence of phenolic -OH. The IR spectra of 1a showed stretching bands at 1572 cm<sup>-1</sup> due to C=N and at 1642 cm<sup>-1</sup> for C=O. Similarly the <sup>1</sup>H NMR spectrum showed a singlet at δ 12.2193 ppm for one -OH proton, a singlet at δ 2.3594 ppm for three protons of one CH<sub>3</sub> and another singlet at δ 2.5653 ppm for three protons of another CH<sub>3</sub>, a multiplet in the range of δ 6.9130 to 9.1623 ppm due to nine protons confirms the formation of 1a which was further confirmed by mass spectrum with a molecular ion peak at m/z 338 [M+H]<sup>+</sup> and 360 [(M +Na)<sup>+</sup>] is in agreement with the molecular formula C<sub>20</sub>H<sub>15</sub>NO<sub>2</sub>Cl (Scheme 4).

Extending the reaction, Chalcones 1a and 2a-d were further brominated by using molecular bromine in acetic acid to get dibromo derivatives 3a and 4a-d respectively. <sup>1</sup>H NMR spectrum of 3a showed one doublet at δ 5.6523 ppm for H<sub>β</sub> proton while another doublet at δ 6.2084 ppm for H<sub>α</sub> proton confirms the addition of bromine to form 3a. Similarly, its mass spectrum gave a [M+H]<sup>+</sup> peak at m/z 498, confirms the molecular formula C<sub>20</sub>H<sub>16</sub>Br<sub>2</sub>ClNO<sub>2</sub>.

### Conclusion:

In conclusion, we have synthesised Chalcones (1a and 2a-d) in the sufficient quantities by refluxing substituted aldehydes with substituted ketones. Simultaneously, extended their reactions to afford dibromo derivatives (3a and 4a-d) in good yields and confirmed their structures on the basis of spectral and the elemental analysis data.

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