'RESEARCH JOURNEY' International E- Research Journal
Impact Factor - (SJIF) – 6.261, (CIF) - 3.452(2015), (GIF)–0.676 (2013)
Special Issue 110 (B) : Chemistry
UGC Approved Journal
ISSN : 2348-7143
February -2019

Antimicrobial Activity of Chalcone Derivatives and Their Synthesis

Shankesh C. Zyate*, Amardeep R. Jadhao, Nikita V. Awajare**
*Department Of Chemistry, R.L.T. College Akola
Email: zshanky19@gmail.com
** Department Of Chemistry, Savitribai Fule Pune University, Pune
Email:amarviraam@gmail.com

Abstract:

At the past many researches had done on Chalcone derivatives as anticancer and antimicrobial agents. Our prediction is that Chalcone derivatives having reacting α,β-unsaturated keto group is responsible for this biological activity. The derivatives of Chalcones were prepared using Claisen-Schmidt condensation scheme with appropriate Acetophenone and Benzaldehyde derivatives in presence of base and ethanol at room temperature. The antimicrobial activity of the compound was found to be good. 3-Hydroxyacetophenone derivatives shows better antimicrobial activity against both the microbes. The characterizations of the compound have been confirmed by IR spectroscopy, H^1NMR spectroscopy, TLC method and Melting point.

Keywords: *Chalcone derivatives, Claisen-Schmidt condensation, Antimicrobial activity*

Introduction:

The world Age Standardize (AS) mortality rate shown that there are 126 cancer deaths for every 1000,000 man in the world. Cancer mortality is higher among man than woman (207.9 per 100,000 man and 145.4 per 100,000 woman). Chalcones are one of the most important classes of flavonoids. Chalcones (trans-1,3-diaryl-2-propen-1-ones) are α,β-unsaturated ketones consisting of two aromatic rings (ring A and B) having diverse array of substituents. Chalcones have been used as intermediate for the preparations of compounds having therapeutic value. Chalcones have been identified as interesting compounds that are associated with several biological activities. The most common chalcones found in foods are phloretin and its glucosidephloridzin (phloretin 2′-0-β-glucopyranoside), and chalconaringenin. These are naturally occurring compounds exhibiting broad spectrum biological activity including anticancer through multiple mechanism. Lots of derivatives can be synthesised and were biologically screened for antifungal activity. It also possesses wide range of pharmacological activity such as antibacterial, antituberculosis, antigout, anti-inflammatory, antiplasmodic, etc. The presence of reacting α,β unsaturated keto group in chalcones is found to be responsible for their biological activity. The derivatives of chalcone were prepared using Claisen-Schmidt condensation scheme with appropriate acetophenone and aldehyde derivatives. Chalcone bears a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed.

Experimental:

Determining the melting point of a compound is one way to test if the substance is pure. So, melting point of the compound has been taken in an oil bath using thermometer. All antimicrobial activities measured in millimetre as unit. IR spectral data were recorded on FTIR-RX1 spectrophotometer. H^1NMR data were measured using $CDCl_3$ solvent on 300 MHz

frequency. And their chemical shift values (δ) are in (ppm) units using TMS (Tetramethylsilane) as an internal standard. The reaction progress has been monitored by Thin Layer chromatography (TLC) using 3:1,(Hexane : Ethyl acetate solvent system) and spots of the compound was visualised using iodine chamber and $KMnO_4$ spray.

Method Of Preparation:

In a 250 ml conical flask placed in an ice bath KOH (1.2 eq.) was dissolved in ethanol (50ml). Then Acetophenone derivatives (1 eq.) were added slowly to the reaction mixture with continue stirring using magnetic stirrer. After 20 minutes Benzaldehyde (1 eq.) derivative was added slowly to the reaction mixture. Then reaction mixture was kept for 12-16 hrs with constant stirring at room temperature. Finally work up with water recrystallized it by ethanol. The residue obtained was purified by column chromatography (Silica gel with 8 % ethyl acetate in hexane).

1-(2-hydroxyphenyl)-3-(phenyl)-prop-2en-1-one (IA)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml) , 2-hydroxy Acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes Benzaldehyde (0.38 g, 3.58 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1590, 1542 (C=C), 1650 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 12.47 (s, 1H), 8.08 (m, 1H), 8.04 (d, 1H), 7.62 (d, 1H), 7.54 (m, 2H),7.43 (m, 2H), 7.36 (m, 3H), 6.94 (m, 1H)

1-(2-hydroxyphenyl)-3-(4-chloro phenyl)-prop-2en-1-one (IB)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml) , 2-hydroxy Acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 4-chloro Benzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1590, 1542 (C=C), 1650 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 12.47 (s, 1H), 8.08 (m, 1H), 8.06 (d, 1H), 7.68 (d, 2H), 7.62 (d, 2H), 7.60 (d, 1H), 7.46 (m, 2H), 6.96 (m, 1H)

1-(2-hydroxyphenyl)-3-(2-chloro phenyl)-prop-2en-1-one (IC)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml), 2-hydroxy Acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 2-chloro Benzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1590, 1542 (C=C), 1650 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 12.47 (s, 1H), 8.30 (d, 1H), 7.53 (m, 1H), 7.46 (m, 2H), 7.43 (d, 1H), 7.28 (m, 1H), 7.25 (m, 1H), 7.06 (m, 1H), 6.96 (m, 1H)

1-(3-hydroxyphenyl)-3-(phenyl)-prop-2en-1-one (IIA)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml) , 3-hydroxy Acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes Benzaldehyde (0.38 g, 3.58 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}):1590, 1542 (C=C), 1650 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 9.43 (s, 1H), 8.04 (d, 1H), 7.55 (m, 1H), 7.53 (d, 1H), 7.52 (m, 2H), 7.36 (m, 3H), 7.37 (m, 1H), 7.23 (m, 1H), 7.20 (t, 1H)

1-(3-hydroxyphenyl)-3-(4-chloro phenyl)-prop-2en-1-one (IIB)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml) , 3-hydroxy acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 4-chloro Benzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the

method of preparation. IR (cm^{-1}) : 1590, 1542 (C=C), 1650 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 9.43 (s, 1H), 8.03 (d, 1H), 7.68 (d, 2H), 7.62 (d, 2H), 7.60 (d, 1H), 7.55 (m, 1H), 7.37 (m, 1H), 7.23 (m, 1H), 7.20 (t, 1H)

1-(3-hydroxyphenyl)-3-(2-chloro phenyl)-prop-2en-1-one (IIC)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml) , 3-hydroxy acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 2-chloro Benzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1590, 1542 (C=C), 1650 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 9.43 (s, 1H), 8.30 (d, 1H), 7.53 (m, 1H), 7.55 (m, 1H), 7.43 (d, 1H), 7.37 (m, 1H), 7.28 (m, 1H), 7.25 (m, 1H), 7.23 (m, 1H), 7.20 (t, 1H), 7.06 (m, 1H)

1-(4-Bromophenyl)-3-phenyl-prop-2en-1-one (IIIA)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml), 4-Bromoacetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes benzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1556 (C=C), 1660 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 7.9 (d, 2H), 7.8 (d, 2H), 7.5 (m, 5H), 7.6 (d, 2H), 7.7 (d, 2H)

1-(4-Bromophenyl)-3-(4-Chlorophenyl)-prop-2en-1-one (IIIB)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml), 4-Bromoacetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 4-Chlorobenzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1581 (C=C), 1662 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 7.9 (d, 2H), 7.8 (d, 2H), 7.6 (m, 4H), 7.7 (d, 2H), 7.6 (d, 2H)

1-(4-Bromophenyl)-3-(2-Chlorophenyl)-prop-2en-1-one (IIIC)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml) , 4-Bromoacetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 2-Chlorobenzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1583 (C=C), 1678 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 7.8 (d, 2H), 7.7 (d, 2H), 7.9 (m, 1H), 7.8 (m, 1H), 7.7 (m, 1H), 7.6 (m, 1H), 7.9 (d, 1H), 7.8 (d, 1H)

1-(4-hydroxyphenyl)-3-(phenyl)-prop-2en-1-one (IVA)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml) , 4-hydroxy Acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes Benzaldehyde (0.38 g, 3.58 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}):1556 (C=C), 1656 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 7.8 (d, 2H), 7.7 (d, 2H), 7.5 (m, 5H), 7.6 (d, 2H), 7.4 (d, 2H)

1-(4-hydroxyphenyl)-3-(4-chloro phenyl)-prop-2en-1-one (IVB)

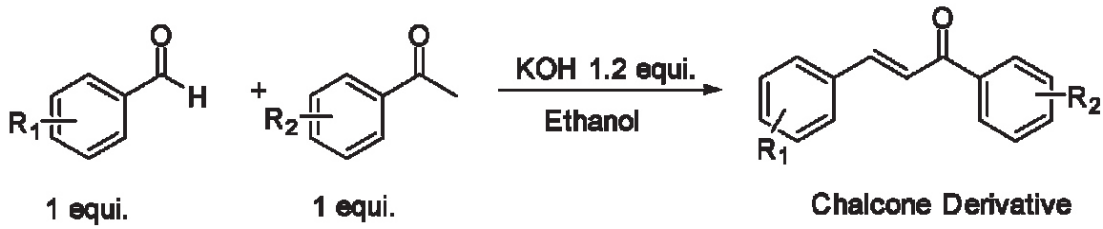
In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml), 4-hydroxy acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 4-chloro benzaldehyde (0.51 g, 3.67 mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1542 (C=C), 1650 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 7.7 (d, 2H), 7.6 (d, 2H), 7.7 (m, 4H), 7.3 (d, 2H), 7.5 (d, 2H)

1-(4-hydroxyphenyl)-3-(2-chloro phenyl)-prop-2en-1-one (IVC)

In a mixture of KOH (0.24 g, 4.27 mmol) and ethanol (50 ml), 4-hydroxy acetophenone (0.5 g, 3.67 mmol) was added slowly. After 15-20 minutes 2-chloro benzaldehyde (0.51 g, 3.67

mmol) was added drop wise with continue stirring. Further steps will be according to the method of preparation. IR (cm^{-1}) : 1590 (C=C), 1660 (>C=O conjugated), H^1NMR (300 MHz, $CDCl_3$) δ(ppm) : 7.6 (d, 2H), 7.5 (d, 2H), 7.7 (m, 1H), 7.9 (m, 1H), 7.6 (m, 1H), 7.5 (m, 1H), 7.7 (d, 1H), 7.4 (d, 1H)

Scheme :



Result And Discussion:

Code of Compound	R1	R2	Percent Yield (%)	Rf value	Antimicrobial Activity		Melting point (°C)
					S.aureus. (mm)	E.Coli. (mm)	
IA	H	2-OH	75.80	0.4	20	14	87-89
IB	4-chloro	2-OH	84.22	0.7	Not shown	16	136-138
IC	2-chloro	2-OH	78.00	0.3	14	Not shown	101
IIA	H	3-OH	77.20	0.2	20	12	125
IIB	4-chloro	3-OH	83.00	0.5	14	19	---
IIC	2-chloro	3-OH	76.88	0.3	12	16	115-117
IIIA	H	4-Br	78.80	0.6	22	Not shown	85
IIIB	4-chloro	4-Br	80.22	0.6	17	16	182
IIIC	2-chloro	4-Br	78.00	0.5	Not shown	12	82-88
IVA	H	4-OH	62.35	0.5	14	16	---
IVB	4-chloro	4-OH	58.90	0.4	13	14	---
IVC	2-chloro	4-OH	54.75	0.6	13	Not shown	---

The characterizations of the compound have been confirmed by IR spectroscopy, H^1NMR spectroscopy, TLC method and Melting point. IR data shows that there is a sharp band observed between 1650-1654 cm^{-1} due to presence of conjugated carbonyl group and second peak 1590, 1542 cm^{-1} due to presence of >C=C< in conjugation with carbonyl group. This is a single step and easy method for the preparation of Chalcone derivatives obtained in good yield.

Conclusion:

The synthesised product has good antimicrobial activity against S.aureus and E.coli bacteria. Among these 3-Hydroxyacetophenone derivatives show better antimicrobial activity. Easy work up and good yield will make our methodology valuable contribution to the existing process for synthesis. Preparation of chalcones is beneficial for the medicinal purposes like anti-cancer agents, anti-tuberculosis, anti-hepatic, and has many other pharmacological applications. This will encourage further research related to chalcones.

References:

1. Prasad Y R, Rao A L and Rambabu R. (2008); Synthesis and antimicrobial activity of Chalcone derivatives , E. Journal of Chemistry,; 5(3): 461-466
2. Wong, B.(1968). The role of Chalcones and Flavonones in Flavonoid biosynthesis. Phytochemistry; 7, 1751-1758
3. Baradia R. and Rao J T. (2004); Asian J. Chem.:, 16, 1194
4. Dhar D. N.(1981), The chemistry of Chalcones and related compounds. Wiley, New york pp. 213
5. Ni, L; Meng, C. Q.; Sikorski, J.A.(2004). Recent advances in therapaticchalcones. Expert Opin. Ther. Pat., 14, 1669-1691
6. Choudhary A. N. and Juyal V. (2011); Synthesis of Chalcone and their Derivatives as antimicrobial agents , International Journal of Pharmacy And Pharmaceutical Sciences, , 3 (11) : 0975-1491
7. Dwey W , Tivey D. . (1958); J. Chem. Soc, P. 1320