Current Pharma Research
ISSN-2230-7842
CODEN-CPRUE6
www.jcpronline.in/

Research Article

Synthesis, Characterization and Antioxidant Activity of New Halogen substituted Chalcones.

S. N. Lakhekar, G. B. Rahatikar, M. A. Baseer*

P.G. Research Centre, Department of Chemistry, Yeshwant Mahavidyalaya, Nanded-431602, Maharashtra, India.

Received 12 February 2019; received in revised form 26 March 2019; accepted 04 April 2019

***Corresponding author E-mail address:** *dr.baseer.nanded@gmail.com*

ABSTRACT
In the recent century, chalcones are found to be fundamental constituents of heterocyclic compounds viz., pyrazolines, pyrimidines, pyridines, isoxazolines, flavones, flavonols, benzodiazepines, benzothiazepines, etc. In the present work, a series of chalcones were synthesized by Claisen-Schmidt base catalysed condensation of suitable halo substituted hydroxy acetophenones with different aromatic aldehydes and assessed for their antioxidant activity. Their synthesis was monitored by TLC and synthesized compounds were purified by recrystallization, further confirmed by IR, MASS, ^{1}HNMR spectroscopic analysis.

KEYWORDS
Chalcones, Claisen -Schmidt Condensation, antioxidant Activity.

1. INTRODUCTION

Kostaneki S.V. [1] has given the name "chalcone" to the first aldol condensation product. Chalcones are prepared by Claisen-Schimdt condensation of aryl ketone and aryl aldehyde in presence of a base followed by dehydration. The chalcones are basic part of various edible plant [2] and they are the precursors of different heterocyclic compounds viz., pyrazolines, pyrimidines, pyridines, isoxazolines, flavones, flavonols, benzodiazepines, benzothiazepines. Chalcone contain two aromatic parts connected by three carbon with α, β-unsaturated carbonyl system due to which they show prominent biological activities such as analgesic [3], antitubercular [4], antimicrobial [5] antitumor [6], antibacterial [7], anti-inflammatory [8], antioxidant [9-10], anticancer [11], insecticidal [12], antiulcer [13], antifungal [14]etc. The manmade and naturally occurring chalcones have been developed as one of the pharmacological important moiety. 2'-hydroxychalcones, 4'-hydroxychalcones and 2',4'-dihydroxychalcones reduce 12-Lipoxygenase and cyclooxygenase enzymes in the mouse epidermis and 2'-hydroxychalcones that show antiinflammatory effects in mice[15]. Chalcones have been used as median for the synthesis of useful heterocyclic compounds having paramount remedial values [16-17].Based upon the literature survey we comprehensively synthesized various new halo substituted hydroxy chalcones (1a-i) in bulb oven having 100 Watt light source starting from the bromine substituted hydroxy acetophenones and *p*-bromo, *p*-chloro benzaldehyde and thiophene-2-aldehyde. Newly formed compounds were obtained in good yield and they were purified by recrystallization, further they were confirmed by IR, MASS, ^{1}HNMR spectroscopic analysis. These chalcones were tested for their antioxidant activity.

2. MATERIALS AND METHODS

All the starting materials were commercially available research grade chemicals and used without purification. Reaction progress was monitored by (TLC), using silica gel plate and pet ether, ethyl acetate (7:3) as eluent system. The spots were visualized in a short ultraviolet light at λ=254-266nm. Melting points were determined in open capillary tube using melting point apparatus and are uncorrected. IR spectra were recorded on Shimadzu FT-IR Spectrometer using KBr pellets.^{1}HNMR spectra were determined in deuterated ($CDCl_3$) on an Bruker 300 MHZ NMR spectrophotometer. The MASS was recorded on pexciex API2000 MS Spectrophotometer.

3. RESULTS AND DISCUSSION

The chalcones (1a-i) were synthesized by Claisen-Schmidt base catalyzed condensation of bromine substituted hydroxy acetophenones with different aromatic aldehydes in presence of 10% aqueous NaOH in 95% ethanol. The progresses of reactions were monitored by TLC and synthesized compounds were purified by recrystallization. Further their structures were

confirmed by IR, ^{1}HNMR and MASS spectroscopy (Scheme-1). The stereochemistry around the olefinic double bond was confirmed by using ^{1}HNMR coupling constant.

3.1. Spectral data of selected compounds

1c: (E)-1-(3,5-dibromo-2-hydroxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one

IR (KBr, cm^{-1}): 3433 (Ar-OH str.), 1627 (C=O str.), 1558(CH=CH str.), 1442 (Ar C=C str.), 725(C-S-C str.) 694(C-Br str.),(^{1}H-NMR(DMSO-d_6): δ 13.65 (s, 1H, OH), 8.14(d, *J*=16 Hz, H_α), 8.09(d, *J*=16Hz, 1H, H_β), 7.27-7.85 (m, 6H, Ar-H); Mass (m/z) 388.88 $[M+1]^+$

1e: ((E)-3-(4-bromophenyl)-1-(3,5-dibromo-4-hydroxyphenyl)prop-2-en-1-one

IR (KBr, cm^{-1}): 3438 (Ar-OH str.), 1649 (C=O str.), 1582 (CH=CH str.), 1442 (Ar C=C str.), 813(C-Br str.), ^{1}H-NMR(DMSO-d_6): δ 6.3 (s, 1H, OH), 7.80-7.74 (d, 1H, *J* =16 Hz, H_α), 7.59-7.56 (d,1H, *J*=16Hz, 1H, H_β), 7.39-7.54(m, 6H, Ar-H), Mass (m/z) 460 $[M]^+$

1g: (E)-3-(4-chlorophenyl)-1-(3,5-dibromo-2,4-dihydroxyphenyl)prop-2-en-1-one

IR (KBr, cm^{-1}): 3460 (Ar-OH str.), 1631 (C=O str.), 1566(Ar C=C Str.), 1492(CH=CH str.) , ^{1}H-NMR(DMSO-d_6): δ 14.04 (s, 1H, OH), δ 6.5 (s, 1H, OH),7.93-7.88 (d, 1H, *J* =16 Hz, H_α), 7.63-7.61 (d,1H, *J*=16Hz, 1H, H_β), 7.42-7.50 (m, 5H, Ar-H), Mass (m/z) 430.9 $[M-1]^+$

Table 1. Substitution pattern and yields for synthesized compounds (1a-i)

Comp. Code	M F	M W	R^1	R^2	R^3	R^4	Ar-CHO	M.P ^{0}C	Yield %
1a	$C_{15}H_9O_2Br_2Cl$	416	OH	Br	H	Br		182-184	77
1b	$C_{15}H_9O_2Br_3$	460	OH	Br	H	Br		143-145	81
1c	$C_{13}H_8O_2Br_2S$	388	OH	Br	H	Br		141-143	74
1d	$C_{15}H_9O_2Br_2Cl$	416	H	Br	OH	Br		157-159	70
1e	$C_{15}H_9O_2Br_3$	460	H	Br	OH	Br		137-139	73
1f	$C_{13}H_8O_2Br_2S$	388	H	Br	OH	Br		230-232	77

1g	$C_{15}H_9O_3Br_2Cl$	432	OH	Br	OH	Br	154-156	82
1h	$C_{15}H_9O_3Br_3$	476	OH	Br	OH	Br	178-180	72
1i	$C_{13}H_8O_3Br_2S$	404	OH	Br	OH	Br	157-159	76

3.2. General procedure for synthesis of chalcone (1a-i)

A mixture of the bromine substituted hydroxy acetophenone (0.001mol) and aryl aldehyde (0.001mol) was dissolved in ethanol (10 ml), then aqueous 10 % NaOH (10 ml) was added dropwise. The reaction mixture was stirred at room temperature and kept overnight in a bulb (100 watt) oven at 50-60^{0}C. After 15 to 16 hr, the reaction mixture was poured in an ice water and acidified by 10 % dil. HCl. The separated solid was filtered, washed with cold water. Then crude product was crystallized from glacial acetic acid.

3.3. Evaluation of Antioxidant activity

Antioxidant activity of synthesized compounds was evaluated by DPPH and OH radical scavenging assay.

3.4. DPPH radical scavenging assay

DPPH (2, 2, diphenyl-1-picrylhydrazyl) radical scavenging assay was carried out as per reported methods [9]. Briefly, 1ml of test solution (Test compound) was added to equal quantity of 0.1mM solution of DPPH in ethanol. After 20 min incubation at room temperature, the DPPH reductions were measured by reading the absorbance at 517 nm. Ascorbic acid was used as reference compound.

3.5. Hydroxyl radical scavenging assay

Hydroxyl radical scavenging activities were determined by the earlier reported method [10]. The reaction cocktail contained 60 µl of 1 mM, $FeCl_3$, 90 µl of 1 mM 1,10-Phenanthroline, 2.4 ml of 0.2 M Phosphate buffer (pH 7.8), 150 µl of 0.17 M H_2O_2, and 1.5 ml of various concentration of individual compound. Reaction mixture was kept at room temperature for 5 min incubation and absorbance was measured at 560 nm using spectrophotometer. α- Tocopherol was used a reference compound.

Table 2. DPPH radical scavenging activity and OH radical scavenging activity

Sr. NO	**Code of compound**	**DPPH radical scavenging activity**	**OH radical scavenging activity**

1	**1a**	28.96±0.25	27.43 ±0.28
2	**1b**	25.15±0.13	23.04 ±0.09
3	**1c**	41.21±0.05	39.07±0.36
4	**1d**	27.89±0.55	24.12±0.65
5	**1e**	23.31±0.45	20.02±0.71
6	**1f**	44.94±0.65	47.56±0.90
7	**1g**	33.69±0.18	29.24±0.77
8	**1h**	55.21±0.85	51.62±0.38
9	**1i**	63.52±0.15	58.52±0.78
10	**STD**	93.11±0.15	90.87±0.98

4. CONCLUSION

In conclusion, here we have reported some new chalcones using bromine substituted hydroxyl acetophenone with different aromatic aldehydes. The newly synthesized chalcones were confirmed by spectral analysis and further evaluated for their antioxidant activity. All synthesized compounds exhibited moderate antioxidant activity in which the compound (1c, 1f, 1i) with two electron withdrawing bromine, electron donating hydroxyl group (one or two) and thiophene group showed good antioxidant activity.

5. ACKNOWLEDGEMENTS

Authors are thankful to the Principal, Yeshwant College Nanded for providing necessary facilities to carry out the research work.

6. REFERENCES

1. Kostaneki S V, Tambor. (1899), *Chem. Ber*. 32,1921.
2. Chetan B P, Mahajan S, Suvarna K, (2009)**.** Chalcone: versatile molecules. *Journal of Pharm. sci.& Res*.1,3,11-22.
3. Srinivasa R, (2011) Synthesis and Analgesic Activity of Some Chalcones. *Asian journal of Chemistry*. 23, 4373-4376.
4. Viral J, Vrajlal K, Viresh H (2015). Characterization and antitubercular activity of synthesised pyrimidines via chalcones. *Indian J. Chemistry*, 54B, 391-398.
5. Thasneem C K, Biju C R, Babu G, (2013). Synthesis and antimicrobial study of chalcone linked 1,3,4-oxadiazole derivatives. *World Journal of Pharmacy and Pharmaceutical Sciences*, 4,1, 643-655.
6. Echeverria C, Santibañez J F, Donoso T O, Escobar C A, Ramirez T R. (2009) Structural antitumoral activity relationships of synthetic chalcones. *Int. J. Mol. Sci*. 10, 221–231.
7. Vibhute Y B, Baseer M A (2003). synthesis and activity of a new series of chalcones as antibacterial agents. *Indian J. of Chemistry***.** 42B, 202-205.

8. Yau H C, Wei H W, Yun H W, Zi-Yu L, Chi-Chung W, Ching-Yuh C,(2013). Evaluation of the Anti-Inflammatory Effect of Chalcone and Chalcone Analogues in a Zebrafish Model *Molecules*, 18 ,2052-2060.

9. Yogesh M, Ashish G, Pradeep M, (2013). Synthesis and antioxidant activity of some chalcones and flavanoids. *Int J PharmTech Res* ,5,811-812.

10. Gacche R N, Dhole N A, Kambale.S G, Bandgar B P,(2008) .in vitro evaluation of selected chalcones for antioxidant activity. *Journal of Enzyme inhibition and Medicinal Chemistry*, 23,1, 28-31.

11. Shah A, Khan A M, Qureshi R., Ansari F.L.,Nazar F.M., and Shah S.S., (2008). Redox Behavior of Anticancer Chalcone on a Glassy Carbon Electrode and Evaluation of its Interaction Parameters with DNA. *Int. J. Mol. Sci. 9,8,*1424-1434.

12. Nidhi G, Chorasia O P, (2010). Synthesis, antimicrobial and insecticidal activity of some new cinnoline based chalcones and cinnolinc based pyrazoline derivatives. *Indian Journal of Chemistry*. 49 (6) 830-835.

13. Lalitha C H, Gopinath C, Kumar K M., Kumar P S, (2012).synthesis charecterisation and antibacterial evaluation of some novel chalcones. *Int. J. of Applied Pattern Recognition.* 3, 8, 1038-1044.

14. Lahtchev K L, Batovska D.I., Parushev P., Ubiyvovk V.M., and Sibirny A.A., (2008).antifungal activity of chalcones: a mechanistic study using various yeast strains. *Eur. J. Med. Chemistry*. 43, 2220-2228.

15. Vishwandham Y, T Kumarswamy, Suman D. (2013). A review on chalcones and its importance. *Pharmatutor Magazine*. 1,2,54-59.

16. Straub T S. (1995). Epoxidation of α, β-unsaturated ketone with sodium perborate. *Tetrahedron Lett.* 36,5,663-664.

17. Sandler S, karo W. (1972) *Organic functional Group preparation*. 3, 372.