OPEN ACCESS INTERNATIONAL JOURNAL OF SCIENCE & ENGINEERING

IN-VITRO EVALUATION OF ANTIOXIDANT ACTIVITY OF 2'-HYDROXY CHALCONE

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Abstract: **Chalcone are important class of natural product, they are found to be much in use for their therapeutic properties. They are also used as precursors for the synthesis of different heterocyclic derivatives. In the present work 2'-hydroxy chalcone are synthesized by halogen substituted 2'-hydroxy acetophenone and orthofluorobenzaldehydes. Chalcone are synthesized by Claisen-Schmidt condensation in the presence of aqueous 50% sodium hydroxide at room temperature and assessed for their antioxidant activity. The structure of these chalcone have been determined by physical and spectral method such as melting point, IR, MASS ,[1] H-NMR spectroscopy.**

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I INTRODUCTION

The chalcone are naturally occurring compound belonging to the flavonoid family. Specificity of chalcone is specific ring system linked by an aliphatic three carbon chain in which carbonyl group is linked with double bond[1]. So that variety of novel heterocyclic compound with good pharmaceutical profile can be designed. Kostaneki S.V. and Tambor [2] gave the name "chalcone" are an important class of compound which are good intermediate for the synthesis of various heterocyclic compound like pyridine , pyrimidine, pyrazoline, Iso-oxazole.[3] Chalcone exhibit high reactivity due to α, β-unsaturation present in the compound. Chalcone have been revised for their wide biological activities such as anticancer[4], antitubercular[5], anti HIV[6], antibacterial[7], antitumor[8], antiinflamatory[9], antioxidant [10]. In the recent year, chalcone and its substituted derivatives play a significant role in pharmaceutical chemistry. Chalcone have been proved to be having promising therapeutic efficacy in the management of many human cancer.[11]

Chalcones continue to attract considerable scientific attention because of their diverse biological activities. Venkadari Srinivasrao *et al* synthesized a series of brominated chalcone[12] and Saiharish Ragvan *et al* synthesized vanilline chalcone[13] evaluate and their biological activity and found that the potencies' of these compounds were comparable or better than that of the well known drugs. Similarly as part of our continuous research interest in the chemistry of 2'-hydroxy chalcone which is core system in various synthetic pharmaceutical with broad spectrum of biological activities, we report here in the convenient synthesis of some novel 2'-hydroxy chalcone (1a-e) starting from halogen substituted 2'-hydroxy acetophenone and 2-fluoro benzaldehyde. The antioxidant activities of synthesized chalcone are described.

II METHOD AND RESULT

2.1 Chemistry

The synthesis of chalcone (1a-f) was accomplished by Claisen –Schmidt condensation[14], in 95% ethanol between the substituted acetophenone and vanilline, ortho bromo benzaldehyde. In the synthesized chalcone, only *trans* double bond was obtained.The purity was established by TLC. The stereochemistry around the olefinic double bond was established using corresponding, [1]H-NMR coupling constant.

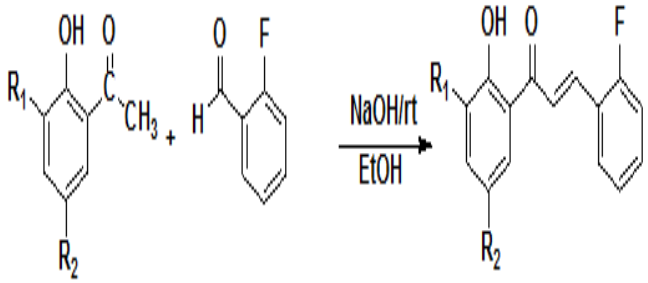


Table 1 Substitution pattern and yields for compounds (1a-1e)

Sl. No.	R^1	R^2	Melting Point ^{0}C	Yield %	Colour
1a	I	Cl	147	60	yellow
1b	I	I	152	62	Pale yellow
1c	Br	Cl	123	60	yellow
1d	Br	CH_3	148	70	yellow
1e	Br	Br	127	68	yellow

III EXPERIMENTAL SECTIONS

3.1 Chemistry

All the starting materials are commercially available research grade chemical and used without purification. Melting points were determined in open capillary tube using melting point apparatus and are uncorrected.

Reaction progress was monitored by (TLC), using silicagel plate and pet ether ethyl acetate (7:3) as eluent system. The spot were visualized in an ultraviolet light at δ λ=254-266nm.

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

A mixture of the corresponding acetophenone (0.001mol) and aldehyde (0.001mol) were dissolved in ethanol (15 ml), under stirring and aqueous KOH (50% 12 ml) was added drop wise. The reaction mixture was stirred at room temperature and kept overnight in a bulb oven at 50-60^{0}C. After 14 to 16 hr, the reaction mixture was diluted with H_2O and acidified with HCl (10%). The separated solid was filtered and crystallized from glacial acetic acid afforded crystalline chalcone.[15]

1a:(E)-1-(5-chloro-2-hydroxy-3-iodophenyl)-3-(2-fluorophenyl) prop-2-en-1-one

IR (KBr, cm^{-1}): 3442 (OH), 1647 (C=O), 1574 (CH=CH); ^{1}H-NMR(DMSO-d_6): δ 13.52 (s, 1H, OH), 8.31-8.34 (d, *J*=16 Hz, H_α), 7.66-7.69 (d, *J*=12Hz, 1H, H_β), 7.30-7.97 (m, 6H, Ar-H); Mass: (M^+): m/z 402.6.

1c:(E)-1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-(2-fluorophenyl)prop-2-en-1-one

IR (KBr, cm^{-1}): 3438 (OH), 1649 (C=O), 1582 (CH=CH); ^{1}H-NMR(DMSO-d_6): δ 13.62 (s, 1H, OH), 7.91-7.95 (d, 1H, *J* =16 Hz, H_α), 7.50-7.58 (d,1H, *J*=12Hz, 1H, H_β), 7.00-7.60 (m, 5H, Ar-H); Mass: (M^+): *m/z* 355.49.

1d: (E)-1-(3-bromo-2-hydroxy-5-methylphenyl)-3-(2-fluorophenyl)prop-2-en-1-one

IR (KBr, cm^{-1}): 3427 (OH), 1643 (C=O), 1567(CH=CH); ^{1}H-NMR(DMSO-d_6): δ 13.60 (s, 1H, OH), 7.91-7.94 (d, 1H, *J* =16 Hz, H_α), 7.31-7.35 (d,1H, *J*=12Hz, 1H, H_β), 7.00-7.79 (m, 5H, Ar-H);Mass: (M^+): *m/z* 335.17.

IV EVALUATION OF ANTIOXIDANT ACTIVITY

Antioxidant activity of synthesized compound was evaluated by DPPH and OH radical

DPPH assay:

DPPH (2, 2, diphenyl-1-picrylhydrazyl) radical scavenging assay was carried out as per reported methods with slight modification (Kato *et al*., 1998). Briefly, 1ml of test solution (Test compound) 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 used as reference compound.

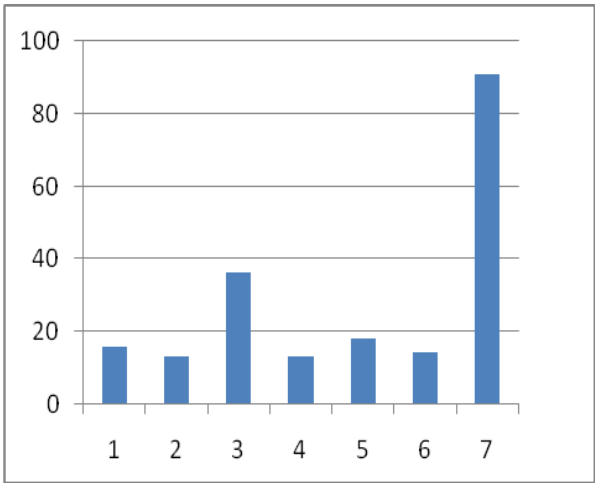
Hydroxyl radical scavenging assay:

Hydroxyl radical scavenging activities were determined by the earlier reported method (Yu *et al.*, 2004). 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 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.	Name of compound	DPPH	OH
1	1a	14.30±0.67	25.65±0.88
2	1b	19.79±0.34	13.27±0.92
3	1c	31.19±0.02	36.45±0.17
4	1d	3.70±0.63	13.35±0.06
5	1e	13.50±0.96	18.37±0.52
7	STD	93.11±0.15	90.87±0.98

DPPH radical



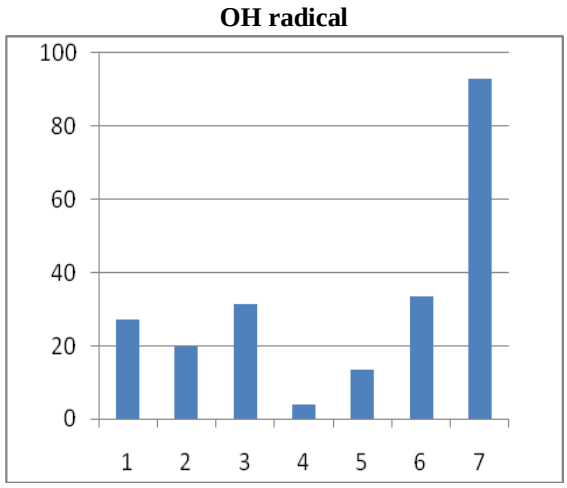


Figure 1 Antioxidant activity DPPH and OH radical scavenging activity of synthesized compounds.

V CONCLUSION

In conclusion, here we have reported some novel chalcones using halogen substituted ortho hydroxyl acetophenone with two different aromatic aldehydes with better yield. The newly synthesized chalcone were confirmed by spectral analysis and further evaluated for their antioxidant activity. The above result we concluding the compound 1c was showing the good antioxidant activity. The reason is due to that compound contain two different halogen group. We concluding the compound 1c is may be best fit molecule having the antioxidant activity. All other compound showed good activity.

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