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Research Article

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

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ABSTRACT

In the recent century, chalcones are found to be fundamental constituents of heterocyclic compounds viz., pyrazolines, pyrimidines, pyridines, isoxazolines, flavones, flavonols, benzodiazepines, benzothiazepines. In the present work, a series of chalcones were synthesized by Claisen-Schmidt base catalysed condensation of suitable halogen 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 recrystalization, further confirmed by IR, MASS, ^{1}H-NMR spectroscopic analysis.

KEYWORDS

Chalcones, Claisen -Schmidt Condensation, antioxidant Activity.

1. INTRODUCTION

The first aldol condensation [1] product reported by Kostaneki S.V. and gave the name "chalcone". Chalcones are prepared by claisen-schimdt condensation of aryl ketone and aryl aldehyde in presence of base or acid catalyst followed by dehydration. The chalcones are basic part of various edible plant[2] and heterocyclic compounds viz., pyrazolines, pyrimidines, pyridines, isoxazolines, flavones, flavonols, benzodiazepines, benzothiazepines. chalcone contain two aromatic part are connected by three carbon with α, β unsaturated carbonyl system due to which they shows prominent reactivity towards biological activities such as analgesic[3], antitubercular[4], antimicrobial[5] antitumor[6], antibacterial[7], antiinflamatory[8], antioxidant[9], anticancer[10], insecticidal[11], antiulcer[12], antifungal[13], 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 shows antiinflammatory effects in mice[14] Chalcones have been used as median for the synthesis of compounds having remedial value [15-16]. The most usual chalcones like phloretin and its glucoside phloridzin (phloretin 2′-0-βglucopyranoside), and chalconaringenin are found in foods. Chalcones and their derivatives find application as unnatural sweeteners, polymerization catalyst, scintillator, organic brightening agent, fluorescent whitening agent, stabilizer against heat, visible light, ultraviolet light and aging [17]. Chalcone compound 'Butein' has also been used for cure of pain, stomach cancer, thrombotic disease, and parasitic infection as well as a food additive. Based upon the literature survey we are going to synthesize the various novel halogen substituted hydroxy chalcones (1a-i) starting from bromine substituted hydroxy acetophenone and p-bromo, p-chloro benzaldehyde and thiophene-2-aldehyde so as to increase its therapeutic value. Reaction progress was monitored by TLC and synthesized compounds were purified by recrystalization, further confirmed by IR, MASS, ^{1}HNMR spectroscopic analysis. The synthesized chalcones are tested for their antioxidant activity.

2. MATERIALS AND METHODS

2.1. Chemistry

The synthesis of chalcones (1a-f) was synthesized by Claisen-Schmidt base catalyzed condensation of bromine substituted hydroxy acetophenones with different aromatic aldehydes in presence of 10% alco. NaOH in 95% ethanol .All synthesized compound was monitored by TLC and purified by recrystalization, further characterized by spectral data IR, ^{1}HNMR and MASS. The stereochemistry around the olefinic double bond was confirmed by using ^{1}HNMR coupling constant.

Scheme 1. Synthesis of chalcones (1a-f).

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

Comp. Code	M F	MW	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. RESULTS AND DISCUSSION

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. IR spectra were recorded on Shimadzu FT-IR Spectrometer using

KBr pellets 1HNMR spectra were determined in deuterated (CDCl3) on an Bruker 300 MHZ NMR spectrophotometer. The MASS was recorded on pexciex API2000 MS Spectrophotometer. Reaction progress was monitored by (TLC), using silica gel plate and pet ether ethyl acetate (7:3) as eluent system. The spot were visualized in a short ultraviolet light at δ λ=254-266nm.

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

A mixture of the bromine substituted hydroxy acetophenone (0.001mol) and aryl aldehyde (0.001mol) were dissolved in ethanol (15 ml), under stirring and aqueous 10 % KOH (10 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 15 to 16 hr, the reaction mixture were poured in 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.

3.2. 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 (OH), 1627 (C=O), 1558(CH=CH), 1442 (Ar C=C), 725(C-S-C) 694(C-Br),(^{1}H-NMR(DMSO-d_6): δ 13.65 (s, 1H, OH), 8.14(d, *J*=16 Hz, H_α), 7.94(d, *J*=12Hz, 1H, H_β), 7.30-7.93 (m, 6H, Ar-H); Mass: (M^+): m/z 388.

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

IR (KBr, cm^{-1}): 3438 (OH), 1649 (C=O), 1582 (CH=CH), 1442 (Ar C=C), 813(C-Br), ^{1}H-NMR(DMSO-d_6): δ 13.0 (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), 7.39-7.55(m, 6H, Ar-H), Mass: (M^+): *m/z* 460.

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

IR (KBr, cm^{-1}): 3460 (OH), 1631 (C=O), 1566(Ar C=C), 1492(CH=CH) , ^{1}H-NMR(DMSO-d_6): δ 14.0(s, 1H, OH), δ 13.60(s, 1H, OH),7.93-7.94 (d, 1H, *J* =16 Hz, H_α), 7.42-7.45 (d,1H, *J*=12Hz, 1H, H_β), 7.45-7.63 (m, 5H, Ar-H), Mass: (M^+): *m/z* 432.

3.3. Evaluation of Antioxidant activity

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

3.3.1. DPPH radical scavenging 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.

3.3.2. 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	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 novel chalcones using halogen substituted hydroxyl acetophenone with different aromatic aldehydes with better yield. The newly synthesized chalcone were confirmed by spectral analysis and further evaluated for their antioxidant activity. The compound (1c, 1f, 1i) with two electron withdrawing bromine, electron donating one or two hydroxyl group and thiophene group showed good antioxidant activity. All other compound also showed moderate antioxidant activity.

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