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Synthesis of some new chalcones, flavones and screening for their antimicrobial activity

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ABSTRACT

New chalcones (3a-k) were synthesized from substituted 2-hydroxy acetophenones and 2-benzyloxy, 3-benzyloxy-4-methoxy, 4-benzyloxy-3-methoxy benzaldehyde via claisen-schmidt condensation. Further these chalcones converted into corresponding flavones (4a-k) by oxidative cyclization of chalcones using DMSO-I_2. The structure of synthesized compound was confirmed by elemental analysis and spectral data. The newly synthesized compounds were screened for antimicrobial activity against E-coli, S. Typhi, Staph. aureus, and Aspergillus niger

Keywords: Hydroxyacetophenones, Aldehydes, 2-Hydroxychalcones, Flavones and antimicrobial activity**.**

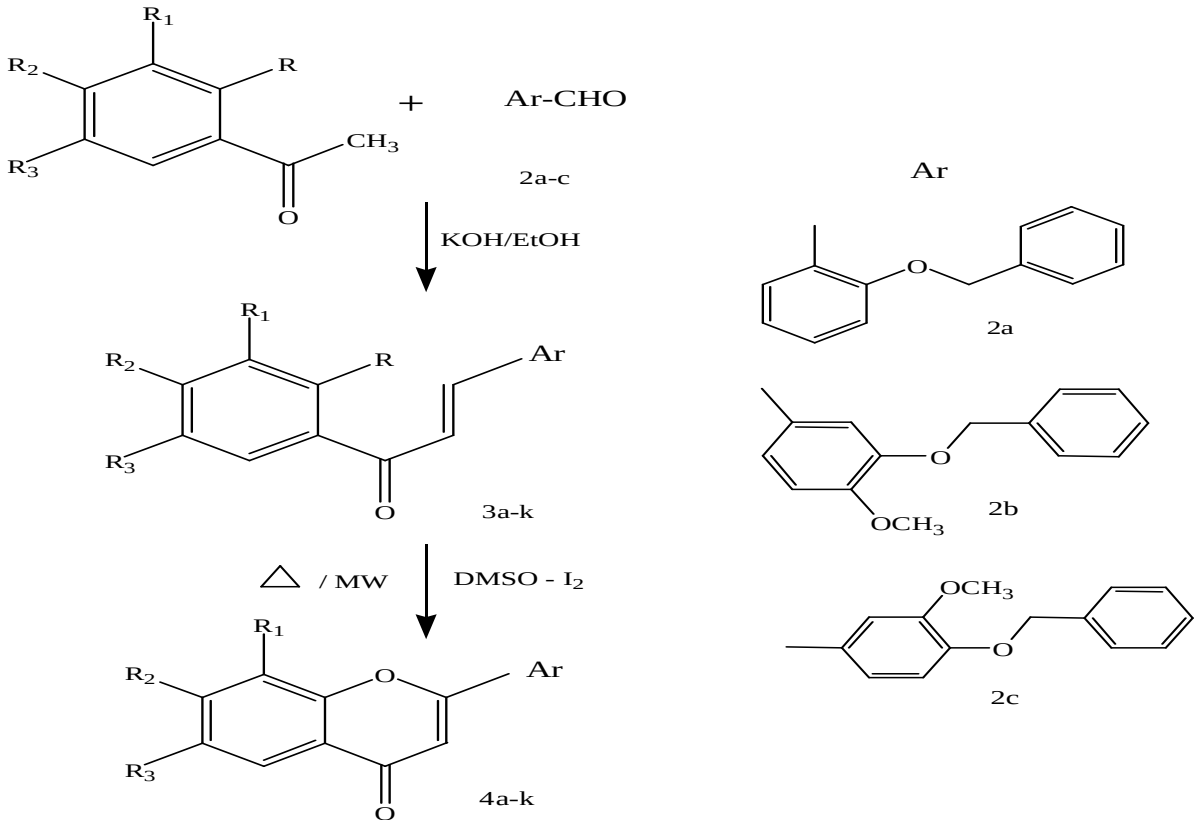
INTRODUCTION

The presence of α, β – unsaturated carbonyl compounds is one main structural components in various naturally occurring biologically active substances chalcones, analogs of 1,3-diaryl prop-2-ene-1-one form a wide class of compounds containing two aromatic rings bound with vinyl ketone fragment. It is well known that most natural or synthetic chalcones are highly active with extensive pharmaceutical and medicinal application. Chalcones are found to be effective as analgesic [1], antimalerial [2], antiviral [3], antibacterial [4], antifungal [5], antimitotic [6], cytotoxic [7], antifeedant [8], anti-inflammatory [9], antileishamanial [10], antitumor [11], anticancer [12], antimicrobial [13], antinociceptive [14], insecticidal [15] and antiinvasive [16] activities.

In view of these observations and in continuation of our research work on biologically active chalcones and their heterocycles [17] we have synthesized some new chalcones, flavones and screened for their antimicrobial activity.

MATERIAL AND METHODS

Melting points were determined in open glass capillaries and are uncorrected. The purity of compounds was checked by TLC. The IR spectra of all compounds were recorded on perkin-Elmer-1420 spectrometer and ^{1}H NMR spectra ($CDCl_3$) on a Varian 300 MHz spectrometer using TMS as internal standard (δ ppm).



Scheme-I

3a,4a: R= OH, R_1,R_3= Cl, R_2= H, Ar = 2a
3b,4b: R= OH, R_1= Br, R_2= H, R_3= CH_3, Ar= 2b
3c,4c: R= OH, R_1,R_3= Cl , R_2= H, Ar= 2b
3d,4d: R= OH, R_1,R_3= Br, R_2= H, Ar= 2b
3e,4e: R= OH, R_1= Br, R_2= H, R_3= Cl, Ar= 2b
3f,4f: R= OH, R_1,R_3= I, R_2= H, Ar= 2b
3g,4g: R= OH, R_1= I, R_2=H, R_3= CH_3, Ar= 2b
3h,4h: R,R_2= OH, R_1,R_3= Br, Ar= 2b
3i,4i: R= OH, R_1=Br, R_2= CH_3,R_3= Cl,Ar=2b
3j,4j: R,R_2= OH, R_1,R_3= I, Ar= 2b
3k,4k: R= OH,R_1,R_3= Cl, R_2= H, Ar= 2c

General procedure for synthesis of chalcones

Equimolar quantities of halosubtituted 2-hydroxy acetophenone (0.01 mole) and 2-benyloxy, 3-benzyloxy-4-methoxy, 4-benyloxy-3-methoxy benzaldehyde (0.01mole) were dissolved in ethanol (15ml) with stirring aqueous KOH (50% 10 ml) was added dropwise. The reaction mixture was diluted with water and acidified with 10% HCl. The separated solid was filtered and recrystallised from DMF to give compounds (3a-k). The physical and analytical data is given in table-I.

Spectral data of some chalcones (3a-l).

(1) 3-(2-benzyloxy-phenyl)-1-(3,5-dichloro-2-hydroxy phenyl) propenone (3a):- IR ν max (KBr) Cm^{-1}: 3424 (OH), 1631 (C=O), 1559 (CH=CH), 1288 (Ar-O), 1046 (O-CH_2), 748 (O-disubstituted benzene). **^{1}H NMR (300 MHz, $CDCl_3$):** δ 13.6 (s, 1H, OH), 5.2 (s, 2H, OCH_2),

6.8 (d, 1H, =CH_α), 7.6 (d, 1H, =CH_β), 7.3-8.3 (m, 11H, Ar-H). **MS (m/z):** 399 (M^+), 398, 380, 307, 290, 189, 154, 136, 123, 109, 91.

(2) 3-(3-Benyloxy-4-methoxy-phenyl)-1-(3,5-dichloro-2-hydroxy-phenyl)-propenone (3c):- IR ν max (KBr) Cm^{-1}: 3422 (OH), 1632 (C=O), 1564 (CH=CH), 1261 (Ar-O), 1010 (OCH_3). ^{1}H NMR (300 MHz, $CDCl_3$): δ 13.6 (s, 1H, OH), 5.50 (s, 2H, OCH_2), 4.0 (s, 3H, OCH_3), 6.9 (d, 1H, =CH_α), 7.4 (d, 1H, =CH_β), 7.2-8.0 (m, 10, Ar-H). **MS (m/z):** 429 (M^+), 428, 399, 307, 189, 154, 136, 107, 91.

(3) 3-(3-Benzyloxy-4-methoxy-phenyl)-1-(8-bromo-6-chloro-2-hydroxy-phenyl)-propenone (3e):- IR ν max (KBr) Cm^{-1}: 3446 (OH), 1631 (C=O), 1563 (CH=CH), 1261 (Ar-O), 1047 (OCH_3), 699, 770 (monosubstituted benzene). **^{1}H NMR (300 MHz, $CDCl_3$):** δ 13.7(s, 1H, OH), 5.25 (s, 2H, OCH_2), 4.0 (s, 3H, OCH_3), 6.9 (d, 1H, =CH_α), 7.2 (d, 1H, =CH_β), 7.2-7.9 (m, 10H, Ar-H). **MS (m/z):** 474 (M^+), 475, 460, 391, 307, 289, 155, 154, 136, 123, 107, 91.

(4) 3-(3-Benzyloxy-4-methoxy-phenyl)-1-(3,5-dichloro-2-hydroxy phenyl)-propenone (3k):- IR ν max (KBr) Cm^{-1}: 3421 (OH), 1636 (C=O), 1570 (CH=CH), 1260 (Ar-O), 1051 (OCH_3), 770, 745 (monosubstitued benzene). **^{1}H NMR (300 MHz, $CDCl_3$):** δ 13.6, (s, 1H, OH), 5.25 (s, 2H, OCH_2), 4.0 (s, 3H, OCH_3), 6.9 (d, 1H, =CH_α), 7.2 (d, =CH_β), 7.2-7.9 (m, 10H, Ar-H). **MS (m/z):** 429 (M^+), 428, 307, 391, 289, 240, 154, 136, 123, 107, 91.

Analytical and physical data of compounds (3a-l) are recorded in table-I.

Table:-I Analytical and physical data of chalcones

Entry	Molecular formula	M.p (^{0}C)	Yield	Elemental analysis (%) Found (calculated)		
				C	H	X(Cl, Br,I)
3a	$C_{24}H_{16}O_3Cl_2$	124	86	66.61 (66.11)	4.01 (4.00)	18.13 (17.79)
3b	$C_{24}H_{21}O_3Br$	171	82	63.57 (63.53)	4.63 (4.61)	17.97 (17.66)
3c	$C_{23}H_{18}O_4Cl_2$	182	87	64.33 (64.31)	4.19 (4.17)	16.20 (16.55)
3d	$C_{23}H_{18}O_4Br_2$	194	84	53.28 (53.24)	3.47 (3.45)	30.50 (30.88)
3e	$C_{23}H_{18}O_4BrCl$	175	80	58.28 (58.26)	3.80 (3.77)	24.70 (24.39)
3f	$C_{23}H_{18}O_4I_2$	120	65	45.09 (45.11)	2.94 (2.96)	40.80 (41.50)
3g	$C_{24}H_{21}O_4I$	165	83	57.6 (57.63)	4.2 (4.12)	25.75 (25.40)
3h	$C_{23}H_{18}O_5Br_2$	145	78	52.07 (52.1)	3.39 (3.37)	29.63 (29.96)
3i	$C_{24}H_{20}O_4Cl_{Br}$	164	82	59.07 (59.2)	4.10 (4.12)	23.35 (23.69)
3j	$C_{23}H_{18}O_5I_2$	60	62	43.94 (43.91)	2.86 (2.84)	40.12 (40.44)
3k	$C_{23}H_{18}O_4Cl_2$	165	85	64.33 (64.32)	4.19 (4.18)	16.22 (16.55)

General procedure for synthesis of flavones (4a-k):-

Chalcones (0.01 mole) was suspended in DMSO (10 ml) and a crystal of iodine was added to it. The reaction mixture was refluxed for 30 min and diluted with water. The solid obtained was filtered off washed with 20% sodium thiosulphate and recrystallised from aqueous ethyl alcohol to give compounds (4a-k). It gave a positive mg/HCl.

Spectral data of some flavones:-

(1) 2-(2-Benzyloxy-phenyl)-6,8-dichloro chromen-4-one(4a): IR ν max (KBr) Cm^{-1}: 3051 (CH- stretch), 2950 (CH- stretch), 1641 (C=O), 1575,1498,1446 (ring C=C), 1249 (Ar-O), 1008 (-O-CH_2), 791,755 (monosubstituted benzene). **^{1}H NMR (300 MHz, $CDCl_3$):** δ 5.25 (s, 2H, OCH_2), δ 6.8 (s, 1H, 3-CH of pyrone),δ 7.1-8.2 (m, 11H, Ar-H). **MS (m/z) :** 398 (M^+), 379, 305, 249, 186, 179, 150, 132, 92, 75, 65.

(2) 2-(3-Benzyloxy-4-methoxy-phenyl)-6,8-dichloro-chromen-4-one(4c): IR ν max (KBr) Cm^{-1}: 3055 (CH-stretch), 2850 (CH-stretch), 1639 (C=O), 1597,1560,1456 (ring C=C), 1257 (Ar-O), 1024 (O-CH_3), 700,756 (monosubstituted benzene). **^{1}H NMR (300 MHz, $CDCl_3$):** δ 3.95 (s, 3H, O-CH_3), δ 5.25 (s, 2H, O-CH_2), 6.8 (s, 1H, 3-CH of pyrone), 7.0-8.1 (m, 10H, Ar-H). **MS (m/z) :** 428 (M^+), 391, 337, 335, 307, 236, 189, 173, 153, 119, 91, 76, 65, 51.

(3) 2-(3-Benzyloxy-4-methoxy-phenyl)-8-bromo-6-chloro-chromen-4-one(4e): IR ν max (KBr) Cm^{-1}: 3064 (CH-stretch), 2931 (CH-stretch), 1647 (C=O), 1599,1454 (ring C=C), 1271 (Ar-O), 1020 (O-CH_3), 758,702 (monosubstituted benzene). **^{1}H NMR (300 MHz, $CDCl_3$):** δ 4.0 (s, 3H, OCH_3), 5.25 (s, 2H, OCH_2), 6.8 (s, 1H, 3-CH of pyrone), 7.0-8.2 (m, 10H, Ar-H). **MS (m/z):** 472 (M^+), 413, 381, 353, 235, 206, 153, 138, 91, 76, 65, 51.

(4) 2-(4-Benzyloxy-3-methoxy-phenyl)-6,8-dichloro-chromen-4-one(4f): IR ν max (KBr) Cm^{-1}: 3061 (CH-stretch), 2951,2876 (CH-stretch), 1647 (C=O), 1595,1562,1510,1458 (ring C=C), 1234 (Ar-O), 1053 (O-CH_3), 748, 698 (monosubstituted benzene). **^{1}H NMR (300 MHz, $CDCl_3$):** δ 4.0 (s, 3H, OCH_3), δ 5.25 (s, 2H, OCH_2), 6.85 (s, 1H, 3-CH of pyrone), 7.0-8.1 (m, 10H, Ar-H). **MS (m/z) :** 428 (M^+), 411, 335, 264, 236, 189, 160, 119, 98, 91, 76, 65.
Analytical and physical data of flavones (4a-l) are recorded in table-II

Table-II: Analytical and physical data of flavones

Entry	Molecular formula	M.p(^{0}C)	Yield	Elemental analysis (%) Found (calculated)		
				C	H	X (Cl,Br,I)
4a	$C_{22}H_{15}O_3Cl_2$	155	82	66.33 (66.31)	3.76 (3.73)	18.44 (18.11)
4b	$C_{24}H_{20}O_4Br$	200	84	63.71 (63.69)	4.42 (4.40)	17.32 (12.69)
4c	$C_{23}H_{17}O_4Cl_2$	217	80	64.48 (64.46)	3.97 (3.96)	16.24 (16.58)
4d	$C_{23}H_{17}O_4Br_2$	204	79	53.38 (53.36)	3.28 (3.26)	30.54 (30.94)
4e	$C_{23}H_{17}O_4BrCl$	198	75	58.41 (58.39)	3.59 (3.57)	24.82 (24.44)
4f	$C_{23}H_{17}O_4I$	174	85	45.17 (47.15)	2.78 (2.80)	41.23 (41.57)
4g	$C_{24}H_{20}O_4I$	182	80	57.71 (57.73)	4.00 (4.02)	25.78 (25.45)
4h	$C_{23}H_{17}O_5Br_2$	227	60	51.78 (51.76)	3.18 (3.20)	29.61 (30.01)
4i	$C_{24}H_{19}O_4ClBr$	192	72	59.19 (59.31)	3.90 (3.94)	23.43 (23.74)
4j	$C_{23}H_{17}O_5I_2$	170	61	44.01 (44.19)	2.71 (2.73)	40.16 (40.51)
4k	$C_{23}H_{17}O_4Cl_2$	212	86	64.48 (64.46)	3.97 (3.95)	16.24 (16.580

RESULT AND DISCUSSION

In present work chalcones were prepared by claisen-schmidt condensation of halogenosubtituted 2-hydroxy acetophenone and 2-benyloxy, 3-benzyloxy-4-methoxy, 4-benyloxy-3-methoxy benzaldehyde in presence of base using ethanol as a solvent. Chalcones showed pink colouration with Conc.H_2SO_4 and positive Wilson test[18]. Structures were confirmed on the basis of elemental and spectral data. All the chalcones showed absorption band in region 1632-1631 Cm^{-1} due to C=O. ^1H NMR showed doublet in the region δ 6.9-7.5 due to olefinic protons (CH=CH) and also showed singlet in region δ 13.6-13.7 due to ortho hydroxyl group, multiplet in the region δ 7.3-8.3 due to aromatic protons and singlet at δ 4.0 due to methoxy group.

Oxidative cyclization of chacolens (3a-l) was carried out by refluxing with dimethyl sulfoxide and iodine. Structrure were confirmed by negative Wilson test and no pink colouration with conc. H_2SO_4. All the flavones showed IR absorption at 1639, 1647 cm^{-1} due to C=O, ^1H NMR showed a peak at δ 6.85 due to 3H of pyrone ring.

The antimicrobial activity reveals that none of the compounds is founds more active than standard antibiotic tetracycline which is used for comparision.

Antimicrobial activity

The newly synthesized compounds were screened for their antimicrobial activity against various microorganisms via *E-coli, S. Typhi, Staph. aureus, and Aspergillus niger*. The antimicrobial activity was checked by paper disc diffusion method using different concentration via 100 ppm, 150 ppm, 200 ppm dissolved in 10% aqueous DMF. Tetracycline was used as a standard antibiotic for comparision. All the tested compounds are not inhibitor to the growth of bacteria.

CONCLUSION

We have synthesized new chalcones and flavones containing benzyloxy moiety in their structured excepting enhanced bioactivity. None of the compounds have shown good antimicrobial activity.

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