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Research Article

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Synthesis, Characterization, Mass Spectral Investigation and Antibacterial Activity Studies of Some Arylfuranylpropenones

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ABSTRACT

Keeping in view of the varied biological activities of chalcones and their heterocyclic analogues, various arylfurylpropenones were prepared by the condensation of substituted arylfurfuraldehydes with various suitably substituted acetophenones by Claisen-Schmidt condensation reaction. All the newly synthesized compounds were characterized by elemental analysis and spectral studies. The common mass spectral fragmentation patterns are presented here. These compounds were also tested for their antibacterial activities.

Keywords: Chalcones; Claisen-Schmidt condensation; Antibacterial properties

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INTRODUCTION

Medicinal chemistry deals with the design, synthesis and production of molecules having therapeutic value. During the past few decades, significant growth in areas like heterocyclic and pharmaceutical chemistry has lead to the development of many privileged structure with proven utility in medicinal chemistry [1,2]. The chemistry of chalcones has been recognized as one of the significant fields of study for a long time. Various methods of synthesis of substituted chalcones and their reactions are described by Dhar [3] in a recent monograph. Some of the chalcones are reported to inhibit the growth of several pathogenic micro-organisms and fungi and are also reported to possess important therapeutic properties such as hypertensive, antipeptic-ulcer activity etc. Heterocyclic analogues of chalcones are reported to possess bactericidal, bacteriostatic, cholerostatic activities [4-8].

Some substituted chalcones and their derivatives including some of their heterocyclic analogues are reported to possess some interesting biological properties, which are detrimental to the growth of microbes, tubercle bacilli, malarial parasites and intestinal worms. Some of the compounds are claimed to be toxic to animals and insects and are also reported to exhibit inhibitory action on several enzymes, fungi and herbaceous plants. The compounds of the chalcone series also show a profound influence on the cardiovascular, cerebrovascular and neuromuscular systems including the vital organs of the experimental animals. It is reported that chalcones and some furan analogues of chalcones exhibit acaricidal activity. They also inhibit the activity of papain. Furan analogues of chalcones have marked ability to inhibit the activity of enzyme dihydroxyphenylalanine decarboxylase. The antibacterial action is associated with α,β-unsaturated carbonyl group of the molecule.

Many patents have appeared in literature describing the usefulness of chalcones and their derivatives. These find applications as artificial sweeteners, stabilizers against heat, visible light, ultraviolet light, aging, colour photography, scintillators, polymerization catalysts, fluorescent whitening agents and organic brightening additives [3]. The chalcones are natural biocides [6] and are well known intermediates in the synthesis of heterocyclic compounds exhibiting various biological activities [7,8]. The introduction of halogen substituents in the benzenoid part of α,β-unsaturated ketones has been reported to appreciably increase the biological activity [9].

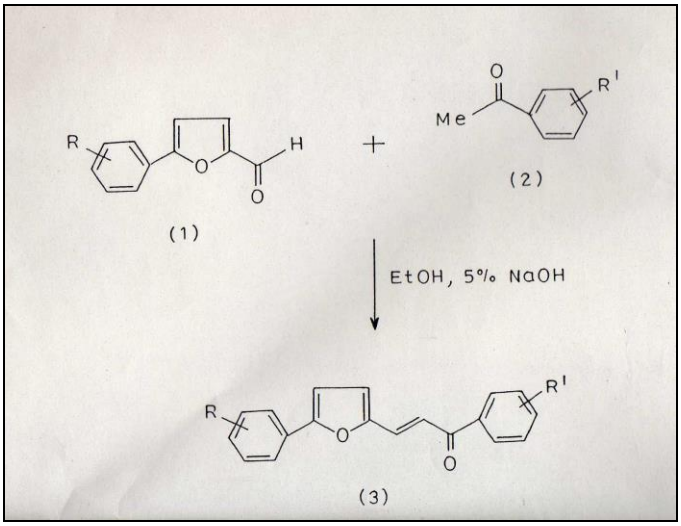
Prompted by the varied biological activities of chalcones and their heterocyclic analogues and in continuation of our work on the synthesis of antimicrobial compounds [10-13], it was contemplated to synthesize and to study their antibacterial activities.

EXPERIMENTAL SECTION

All the chemicals and reagents were obtained from CDH (India) and Ranbaxy (India) and were recrystallized/ redistilled as necessary. Melting points were determined by open capillary method and are uncorrected. Purity of the compounds was checked on thin layer chromatography (TLC) plates precoated. With silica gel G using solvent system benzene:methanol (2:1). The spots were located under iodine vapors. The IR spectra (in KBr pellets) were recorded on a Shimadzu FT-IR 157 spectrophotometer. ^{1}H-NMR spectra were recorded on a Perkin-Elmer EM-300 MHz spectrometer with DMSO-d_6 as solvent and TMS as an internal standard. Chemical shift values are expressed in ppm. The mass spectra were recorded on a JEOL JMS-D 300 spectrometer operating at 70 eV. Elemental analyses were carried out with a Perkin-Elmer Model 240-C apparatus (CDRI, Lucknow). The results of the elemental analysis (C, H, and N) were within ± 0.4% of the calculated amounts.

General Procedure for the Synthesis of 1-aryl-3-(5-aryl-2-furyl)-2-propen-1-ones 3

To a mixture of suitably substituted acetophenones 2 (10 mmol) and substituted arylfurfurals 1 (10 mmol) in ethanol, a solution of sodium hydroxide (5 ml, 5%) was added with continuous stirring. The clear solution so obtained was allowed to stand overnight. The solid which separated on standing, was filtered off, dried and recrystallized from a mixture of ethanol and dimethylformamide.



Scheme 1: Condensation of arylfurfuraldehydes 1 with substituted acetophenones 2 by Claisen-Schmidt condensation

The physical characterization data of all the compounds has been summarized in Table 1.

Table 1: Physical characterization data of compounds

Compd	R	R^1	m.p (˚C)	Yield (%)	Mol. Formula	Halochro-mism with conc. H_2SO_4	Analysis (%) Found (calcd.)		
							C	H	N
3a	4-NO_2	2,4-Cl_2-5-F	198-200	78	$C_{19}H_{10}Cl_2FNO_4$	Reddish pink colour	56.78	2.52	3.5
							-56.29	-2.5	-3.5
3b	4-Br	2,4-Cl_2-5-F	176-178	73	$C_{19}H_{10}BrCl_2FO_2$	Violet colour	52.66	2.05	-
							-52.05	-2.3	
3c	4-Cl	2,4-Cl_2-5-F	114-116	90	$C_{19}H_{10}Cl_3FO_2$	Violet colour	57.13	2.42	-
							-57.86	-2.5	
3d	3-NO_2	2,4-Cl_2-5-F	169-171	61	$C_{19}H_{10}Cl_2FNO_4$	Blood red colour	56.88	2.34	3.39
							-56.29	-2.5	-3.5
3e	2-Cl	2,4-Cl_2-5-F	119-121	89	$C_{19}H_{10}Cl_3FO_2$	Violet colour	57.59	2.38	-
							-57.86	-2.5	
3f	2-NO_2	2,4-Cl_2-5-F	105-106	60	$C_{19}H_{10}Cl_2FNO_4$	Red colour	56.42	2.31	3.46
							-56.29	-2.5	-3.5

The significant mass spectral data of these arylfurylpropenones are given in Table 2.

Table 2: Mass spectral data of arylfuranylpropenones

Compd. No.	R	m/z values (Rel. abundance)		
		M^+/M+2/M+4/M+6 (%)	A/A+2/A+4 (%)	B (%)
3a	4-NO_2	405/407/409/- (11)/(8.4)/(3.6)	191/193/195 (12.4)(7.0)(2.5)	283 (4.3)
3b	4-Br	438/440/442/444 (64)/(8.4)/(3.6)	191/193/195 (100)/(64.8)/(11.3)	283 (2.9)
3c	4-Cl	394/396/398/400 (100)/(92.6)/(37.7)/(4.6)	191/193/195 (33.9)/(20.5)/(4.4)	283 **(12.7)**
3d	3-NO_2	405/407/409/- (100)/(67.9)/(11.8)	191/193/195 (35.8)/(24.6)/(2.8)	283 (32.4)
3e	2-Cl	394/396/398/400 (100)/(86.8)/(33.6)/(5.3)	191/193/195 (19.9)/(10.3)/(2.2)	283 (25)

Antibacterial Activity

All the newly synthesized arylfuranylpropenones 3 were screened for their antibacterial activity against *E.coli, S.aureus, P.aeruginosa and B.subtilis*. Their minimum inhibitory concentrations (MIC values) were determined according to serial dilution method [14]. Furacin was used as a standard drug for comparison. The results of such studies are given in Table 3.

Table 3: Antibacterial screening data of compounds

Compd	*Minimum Inhibitory Concentration (µg/ml)*			
	E.coli	***S.aureus***	***P.aeruginosa***	***B.subtilis***
3a	*6*	*6*	*6*	*6*
3b	*6*	*1.5*	*6*	*6*
3c	*6*	*6*	*6*	*6*
3d	*3*	*6*	*3*	*6*
3e	*12.5*	*6*	*6*	*6*
3f	*12.5*	*6*	*6*	*6*
Furacin (Standard)	*6*	*12.5*	*12.5*	*12.5*

RESULTS AND DISCUSSION

For the present work, the various substituted arylfurylpropenones 3 were obtained by condensation of arylfurfuraldehydes 1 with substituted acetophenones 2 by Claisen-Schmidt condensation (Scheme 1). The required arylfurfuraldehydes 1 were synthesized by Meerwein reaction. The structures of these chalcones were confirmed on the basis of elemental analysis, IR, ^{1}H NMR and mass spectral data.

The UV spectrum of compound 3a showed absorption bands at λmax=270 nm (€=950) and 400 nm (€=4000). Similarly, the UV spectrum of compound 3b also showed absorption peaks at λmax=270 nm (€=946) and 390 nm (€=3042) along with an additional peak at λmax 315 nm (€=845). It is worthwhile to note that all compounds showed absorption peaks around 400 nm or beyond visible region. This can be attributed to the resonance participation arising out of conjugation with arylfuran moieties.

The IR spectrum of compound 3b showed an absorption band at 1682 cm^{-1}, typical of α,β-unsaturated carbonyl functional group. The absorption band corresponding to the olefinic group was seen at 1600 cm^{-1}.

The 500 MHz ^{1}H-NMR spectrum of compound 3e showed a doublet in the range δ, 7.0-7.04 with a coupling constant of 16 Hz corresponding to olefinic proton of the propenone moiety. The other olefinic proton appeared as a doublet in the range δ, 7.35-7.37 (J=16 Hz). The two β-protons of furan ring were seen as two closely spaced doublets in the range δ, 7.24-7.25 (J=3.5 Hz) and 7.33-7.34 (J=3.5 Hz) respectively. A complex multiplet was observed in the region δ, 7.44-7.50 which corresponds to o-chlorophenyl protons. A doublet was seen in the range δ, 7.59-7.61 which accounts for one of the protons of 2,4-dichloro-5-fluorophenyl ring. This can be explained due to ortho coupling of proton with the neighboring fluorine atom. However, the meta coupling of proton with fluorine atom produced a doublet in the range δ, 7.98-7.99 (J=6 Hz). The para coupling of two aromatic protons of 2,4-dichloro-5-fluorophenyl ring resulted in two doublets at δ, 7.76-7.77($J_{H\text{-}H\ para}$= 9 Hz) and 8.04-8.06 ($J_{H\text{-}H\ para}$= 9.5 Hz) respectively. As a part of structural investigation, mass spectra of five arylfurylpropenones were recorded and all the spectra showed characteristic common fragmentation pathways. In most cases, intense molecular ion peaks were observed. The important mass spectral fragmentation pathways are discussed. The mass spectra of compounds 3a, 3b, 3c, 3d and 3e showed molecular ion peaks at m/z at 405, 438, 394, 405 and 394 which correspond to their

molecular formulae $C_{19}H_{10}Cl_2FNO_4$, $C_{19}H_{10}BrCl_2FO_2$, $C_{19}H_{10}Cl_3FO_2$, $C_{19}H_{10}Cl_2FNO_4$ and $C_{19}H_{10}Cl_3FO_2$ respectively. The formation of M+2 and M+4 peaks was also observed due to the presence of two chlorine atoms, thereby confirming the presence of dichlorofluorophenyl moiety. In the mass spectra of all these compounds, a common ion was observed at m/z 191/193/195 which was explained due to the fragment ion viz., 2,4-dichloro-5-fluorobenzoyl cation ((A/A+2/A+4). The peaks observed at m/z 359 and 283(B) in the mass spectra of 6a and 6d were accounted for the formation of ions due to the loss of nitro and nitrophenyl radials from the respective molecular ion. However, the peaks appeared in the mass spectra of 6b, 6c and 6e were due to the loss of bromine, chlorine and chlorine radicals respectively from the corresponding molecular ions. The significant mass spectral data of these arylfurylpropenones are given in Table 2. The synthesized compounds were screened for their antibacterial activity. The activity was compared with that of the standard drug Furacin. The screening data indicate that all the compounds are found to possess a greater degree of antibacterial activities compared to Furacin. In particular, arylfuryl propenones carrying 4-bromo, 3-nitro and 2-nitro substituents showed excellent antibacterial activity against *S.aureus*, *P.aeruginosa and B.subtilis* respectively. Thus, compounds 3b, 3d and 3f turned out to be promising antibacterial agents and hence it is worth pursuing these compounds for further pharmacological investigations.

CONCLUSION

The present work describes a simple and convenient approach for the synthesis of chalcones carrying arylfuran substituents. The pharmacological profile of the synthesized compounds revealed that the antibacterial activity of some of the arylfuranylpropenones was greater than that of the standard drug and hence deserve further in depth pharmacological investigations. The analysis of mass spectral fragmentation patterns of chalcones revealed that there was appearance of a common peak at m/z 191/192/194 and 283 in their mass spectra.

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