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Synthesis and Characterization of Some Chalcone Derivatives as Antibacterial and Antifungal Agent

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Abstract
In a wide search program towards new and efficient antimicrobial agents, substituted chalcones have been synthesized by condensing benzaldehyde derivatives with acetophenone derivatives in dilute ethanolic sodium hydroxide solution at room temperature according to Claisen – Schmidt condensation. . The structures of these compounds have been investigated by infrared spectroscopy, nuclear magnetic resonance spectroscopy and mass spectrometry.Chalcone and their derivatives are so useful nowadays because of their anti-inflammatory activities. Chalcone and their derivatives are so many use in so many drugs and medicine, chalcone and their derivatives have so many properties against many bacterial and microbial diseases therefore grab attention of hygiene department, chalcone are forms by using aldehyde and ketone with use of base as a catalyst and then use as part of a broad search for new and effective antibacterial agents.

Keywords: *Chalcone, phenyl hydrazine, NaOH, Claisen- Schmidt condensation, Benzaldehyde, Acetophenone, IR,1H NMR*

Introduction

The chemistry of chalcone has generated extensive scientific studies throughout the world. The name chalcone was introduced by Kostanecki and Tambor. Chalcone are 1,3-diphynyl-2-propene-1-one, in which two aromatic rings are linked by a three-carbon α-β unsaturated carbonyl system Alpha-beta unsaturated ketones or commonly referred as chalcones are one of the important classes of organic compounds frequently encountered in synthetic chemistry. Chalcones were synthesized by base catalyzed Claisen-Schmidt condensation reaction of appropriately substituted acetophenones and aldehydes1. They are important intermediates not only as key building blocks for the synthesis of core heterocycles such as pyrazole, isoxazole, triazole, flavone, benzodiazepine and pyrimidine in medicinal chemistry, but also as an invaluable chelating ligand for various lanthanide and transition metals in material chemistry. Chalcones, α, β-unsaturated carbonyls, play a crucial role in many biological processes as well as are well-known intermediates for synthesizing various heterocycles2 and bear a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed3. Presence of enone functionality in chlcone shows the antibiotic activity. Chalcone were also synthesized by non-conventional green techniques such as ultrasound (sonochemistry), microwave irradiations, grinding and by using ionic liquied4,5 Chalcones are popular intermediates for synthesizing various heterocyclic compounds. The compounds with the backbone of chalcones have been reported to possess various biological activities as antioxident6, Antibacterial7-9, Anthelmintic activity10, Antifungal11-12, Antimicrobial13, Anticancer Activity14 Chalcone and its derivatives form an important group of natural products. chalcones acts as well-known key intermediate for various heterocyclic compounds. In present studies, we synthesized and characterized three chalcone derivatives derived from variously substituted acetophenones with differently substituted benzaldehyde.

Experimental

The melting points were recorded in open sulphuric acid or oil bath using thermometer and were uncorrected. IR spectra were recorded using Perkin-Elmer FTIR-RX1 spectrophotometer. A ^{1}HNMR spectrum was recorded using CDCl3 on Bruker Avance (400 MHz) and their chemical shifts are recorded in δ (parts per million) units with respect to tetramethyl silane (TMS) as internal standard. Mass spectra were recorded on a Waters Q-T of micro MS. All the reagents and solvents used were of analytical grade and were used as supplied unless otherwise stated.

Progress of the reactions was monitored using TLC, performed on aluminium plates precoated with silica gel-G, using chloroform: methanol (92:8) as the solvent systems and the spots were visualized by exposure to iodine vapors.

General Procedure

Chalcones were synthesized by base catalyzed Claisen-Schmidt condensation reaction of appropriately substituted acetophenones and aldehydes by known literature method.A mixture of benzaldehyde derivatives (0.01 mol) and acetophenone derivatives (0.01 mol) was dissolved in 10 ml rectified spirit in a 250 ml round-bottomed flask equipped with a magnetic stirrer. Then 10 ml NaOH solution (1g in 10ml H2O) was added drop wise to the reaction mixture on vigorous stirring for 30 minutes when solution became turbid. The reaction temperature was maintained between 20-25˚ C using a cold water bath on the magnetic stirrer. After vigorous stirring for 4-5 hours the reaction mixture was neutralized by 0.1-0.2N HCl whereby the precipitation occurred. On filtering off, the crude chalcones were dried in air and recrystallized by rectified spirit. The residue was purified on column chromatography (silica gel with 10% ethyl acetate in hexane) to afford pure chalcones

Compound (a)

(E) -3-(2- chlorophenyl)-1-phenylprop-2-en-1-one

IR: 3048 (C-H aromatic), 1664 (C=O), 1608 (C=C), 829 (Ar-Cl) ; 1H-NMR: 7.9 (d,1Hα), 8.2(d,1Hβ), 7.93 (m, 9H, Ar-H).

Compound (b)

(E) -3-(2- chlorophenyl)-1-(4-hydroxyphenyl1) prop-2-en-1-one

IR: 3452(OH), 1664 (C=O), 1615 (C=C), 829 (Ar-Cl) ; 1H-NMR: 7.5 (d,1Hα), 8.19(d,1Hβ), 6.4-8 (m, 8H, Ar-H), 12.7(s, 1H,OH).

Compound (c)

(E) -3-(2- chlorophenyl)-1-(p-tolyl) prop-2-en-1-one

IR: 3054 (C-H aromatic), 1664 (C=O), 1598 (C=C), 829 (Ar-Cl) ; 1H-NMR: 7.9 (d,1Hα), 8.19(d,1Hβ), 7.5-8.1 (m, 8H, Ar-H), 2.3(s,3H,- CH3).

Compound (d)

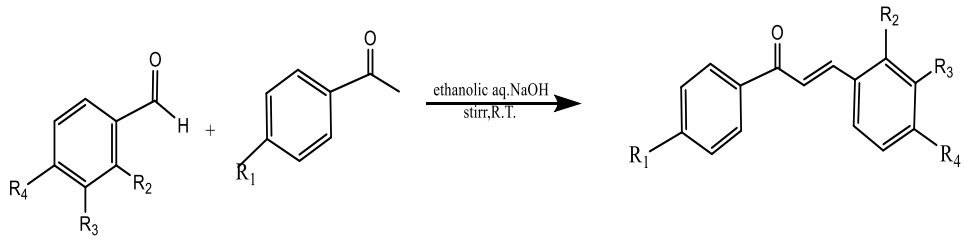
(E) -3-(2- chlorophenyl)-1-(4-methoxyphenyl) prop-2-en-1-one

IR: 3034 (C-H aromatic),1664 (C=O), 1590 (C=C),1132(-O CH3), 828 (Ar-Cl) ; 1H-NMR: 7(d,1Hα), 7.8 (d,1Hβ), 6.9-8.1 (m, 8H, Ar-H), 3.78 (s,3H,- CH3).

Table:1 Physical data of chalcone

Sr.no	Compound	R1	R2	R3	R4	% Yield	Melting point (0C)
1	a	H	Cl	H	H	68	54-55
2	b	OH	Cl	H	H	56	193-194
3	c	CH3	Cl	H	H	73	52-53
4	d	OCH3	Cl	H	H	62	125-126

Scheme 1: Scheme of synthesis of compounds



Antibacterial activity of the synthesized compounds

The newly synthesized compound were screened for theirantibacterial activity against Escherichia coli, Staphylococcus aureus, Pseudomonas aeuroginosa and (reculteured) bacterial

strains by disc diffusion method 17, 18. Discs measuring 6.25 mm in diameter were in diameter were punched from Whatman no.1 filter paper. The The test compounds were prepared with different concentrations using dimethylformamide. One millilitre containing 100 times the the amount of chemical in each disc Was added to each bottle which contains 100 dish the dish of each concentration were placed in duplicate in the nutrient Agar medium seeded with fresh bacteria separately.The incubation was carried out at 37°C for 24 hour ciprofloxacin was used as a standard drug. Solvent and growth controls were prepared and kept. Zones of inhibition and minimum inhibition concentrations (MICs) were noted. The results of antibacterial studies are given in Table 2

Antifungal activity of the synthesized compounds

Newly prepared compounds were were screened for their antifungal activity against Aspergillus flavus, Aspergillus fumigants, Candila albicans and penicillium marneffei in DMSO by serial plate dilution method 19,20. Sabourands agar media were prepared by dissolving (1g), D-glucose (4g) and agar (2g) in distilled water (100mL) and adusting Ph to 5.7. Normal saline used to makae a suspension of spore of fungal stain for lowning. A loopful of particular fungal strain was transferred to 3 ml saline to get a suspension of corresponding species. Agar media (20ml) were poured into each petri dish. Excess of suspension was decanded and the the plates were dried by placing in an anticubator at 370C for 1 h using an agar punch. A control was also prepared in triplicate and maintened at 370C for 3-4 days. The activity of each compound was compaired with fluconazole as the standard drug. The result of antifungal studies are given in Table 3.

Table 2 : Antibacterial activity of chalcone

Compound No.	Escherichia coli	Staphylococcus aureus	Pseudomonas aeuroginosa	Streptococcus pyogenes
a	18	12	22	16
b	22	13	14	17
c	17	12	17	12
d	16	10	13	11

Table 3 : Antifungal activity of chalcone

Compound No.	Aspergillus flavus	Aspergillus fumigants	Candila albicans	Penicillium Marneffei
a	11	08	10	10
b	10	13	07	08
c	12	09	13	11
d	13	11	11	12

Conclusion

The current study reveals the synthesis of some substituted chalcone derivatives were successfully synthesized in satisfactory yield by employing Claisen-Schmidt condensation and their structure were elucidated by chemical by elemental analysis and IR, IH NMR spectroscopic techniques. The result of antibacterial studies posses antibacterial activity against all tested micro organisms.

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