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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SOME NEW CHALCONES

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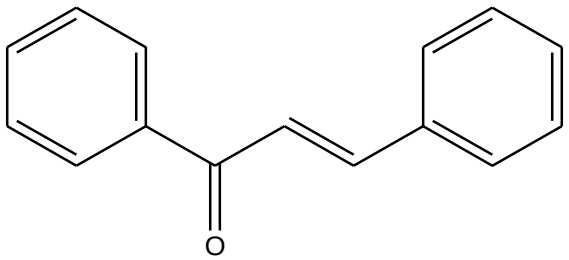
ABSTRACT

In this work, new substituted chalcones (1-6) were prepared by reacting 4-Methoxy acetophenone with the corresponding substituted aromatic aldehydes in the presence of methanolic potassium hydroxide solution at room temperature.Some of the compounds synthesized from methoxy, chloro, Dimethlyamino derivatives showed moderate antibacterial activity at 0.2% concentration. These compounds may show more antibacterial activity at higher concentrations.

Keywords: Chalcones, synthesis, activity

INTRODUCTION

Chalcones are 1,3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a threecarbon α, β-unsaturated carbonyl system as,



chalcone

These are abundant in edible plants and are considered to be precursors of flavonoids and isoflavonoids.

Chalcones possess conjugated double bond and acompletly delocalized π-electron system on both benzene rings. Molecules possessing such system have relatively low redox potentials and have a greater probability of undergoing electron transfer reactions

All the chalcones give pink coloration with concentrated H_2SO_4 (positive Wilson test) and violet coloration with alcoholic ferric chloride solution.

Chalcones on heating with traces of iodine in dimethyl sulfoxide (DMSO) for 2hrs give the corresponding flavones.

Chalcones were converted to the corresponding flavonols by their oxidation using hydrogen peroxide in methanolic sodium hydroxide solution and these flavonols showed characteristic greenish yellow fluorescence in ethanolic solution as well as with concentrated sulphuric acid[2].

Literature review revealed that substituted chalcones and its derivatives showed different pharmacologiocal activities like antimicrobial, anticancer, anti-inflammatory, antioxidant activity etc.

In the present study, we planned to synthesize substituted novel chalcones associated with antibacterial activity.

MATERIALS AND METHODS:

CHEMICALS USED:

Methoxy acetophenone, Benzaldehyde, Dimethyl amino benzaldehyde, Chloro benzaldehyde, 4-Fluoro benzaldehyde, Anisaldehyde, Salicylaldehyde, Potassium hydroxide, Methanol, Hydrochloric acid, Chloroform, Ethylacetae, Benzene, Silica gel, Distilled water.

APPARATUS USED:

Beakers(100 ml, 250 ml and 500 ml), Conical flask, Dessicator, thermometer, funnel, flat bottomed flask, glass slides test tubes, pipettes, glass rods, measuring cylinder, magnetic beads, magnetic stirrer, weighing machine

ANALYTICAL WORK:

Reactions were monitored by thin layer chromatography(TLC) on a coated silica gel G Plate using benzene and ethyl acetate in the 3:1 ratio. NMR and MASS were recorded on PLANTEX from Lailaimplex,Vijayawada using TMS as standard. IR spectra were also recorded from RVR Labs, Guntur. Melting points were determined by using open capillary method.

General procedure for the synthesis of (E)-3-(4^1-Methoxy phenyl)-1-(substituted phenyl) prop-2-ene-1ones(compounds, 1-6)

Equimolar concentrations of 4-methoxy acetophenone (412 mg, 0.01mol) and substituted benzaldehydes (350 mg, 0.01 mol) were dissolved in 20ml of methanol. Methanolic Potassium hydroxide solution (0.05 mol) was added slowly and the mixture was stirred for two hours or till the completion of the reaction (progress of the reaction checked by TLC). The mixture was acidified with 0.1 N HCl. Then it was filtered, washed with water, dried and recrystallised from methanol.

Antibacterial Activity:

The antibacterial activity was tested by *cup-plate method*. The antimicrobial activity of chalcones were tested and compared with the standard (Ciprofloxacin) solution at concentration of 100mg/ml. DMSO (Dimethyl sulphoxide) was used as a solvent and control. The following organisms were used.

Test organisms:

Gram positive bacteria: *Bacillus subtilis*

Gram negative bacteria: *Pseudomonas aeruginosa*

Experimental procedure:

Nutrient agar (Hi-media) was dissolved and distributed in 25 ml quantities in 100ml conical flasks and were sterilized in an autoclave at 121^0c(15lbs/sq.in)for 20 minutes .

The medium was inoculated at one percent level using 18hrs old cultures of the test organism mentioned above aseptically in to sterile petri dishes and allowed to set at room temperature for about 30 minutes.

In a size of 4 inches petri dishes, four cups of 8mm diameter at equal distance were made in each plate. In each plate, one cup was used for control i.e. DMSO (Dimethyl sulphoxide), other for standard ciprofloxacin with 100mg/ml. Other two cups with concentrations of test compound i.e. 50µl and 100µl solutions[72].

The plates thus prepared were left for 90 minutes in refrigerator for diffusion. After incubation for 24 hours at 37^0c ± 1^0c, the plates were examined for inhibition zones .The experiments were performed in duplicate and the average diameter of the zones of inhibition measured were recorded. There is no zone of inhibition for control.

RESULTS AND DISCUSSION:

The chalcones prepared were:

1. 1-(4'-Methoxyphenyl)-3-(4-dimethylaminophenyl)-2-propene-1-one
2. 1-(4'-Methoxyphenyl)-3-(-4-chloroPhenyl)-2- propene-1-one
3. 1-(4'-Methoxyphenyl)-3-(4-methoxyPhenyl)-2- propene-1-one
4. 1-(4'-Methoxyphenyl)-3-(2-hydroxyPhenyl)-2-propene-1-one
5. 1-(4'-Methoxyphenyl)-3- phenyl -2-propene-1-one
6. 1-(4'-Methoxyphenyl)-3-(4-fluro phenyl)-2-propene-1-one

The physical data such as melting points and yields are given in the table 1.

The chalcone derivatives of the present study were characterized by IR, ^{1}H NMR & MASS analysis.

The IR spectra of compounds (1,2,3) displayed bands at2962.54 -3005.46 cm^{-1} due to C-H (Ar-H) stretching, 1650.79 – 1667.74 cm^{-1} due to C=O stretching, 1503.66 – 1596.20 cm^{-1} due to C=C stretching.

^{1}HNMR spectra were taken for compounds (1,2 and 3) which also supported the structures assigned. These

compounds displayed a doublet at δ 6.913- – 6.979 (d, CO-CH=CH) of the α,β- unsaturated carbonyl group and singlet in the range of δ 7.649 – 8.064 and doublet in the range of δ 6.957-8.039due to aromatic hydrogens (Ar-H). Compounds displayed a doublet at 3.824 – 3.859 due to methoxy substitution on the ring.

The structure of the compounds was also assigned by Mass spectral analysis which showed (M^++1) peaks of the compounds. The mass spectra of the compound1 showed a characteristic of molecular ion peaks (M^++1) at 282.2 and the compound-2 showed a characteristic molecular ion peaks (M^++1) at 273.2.

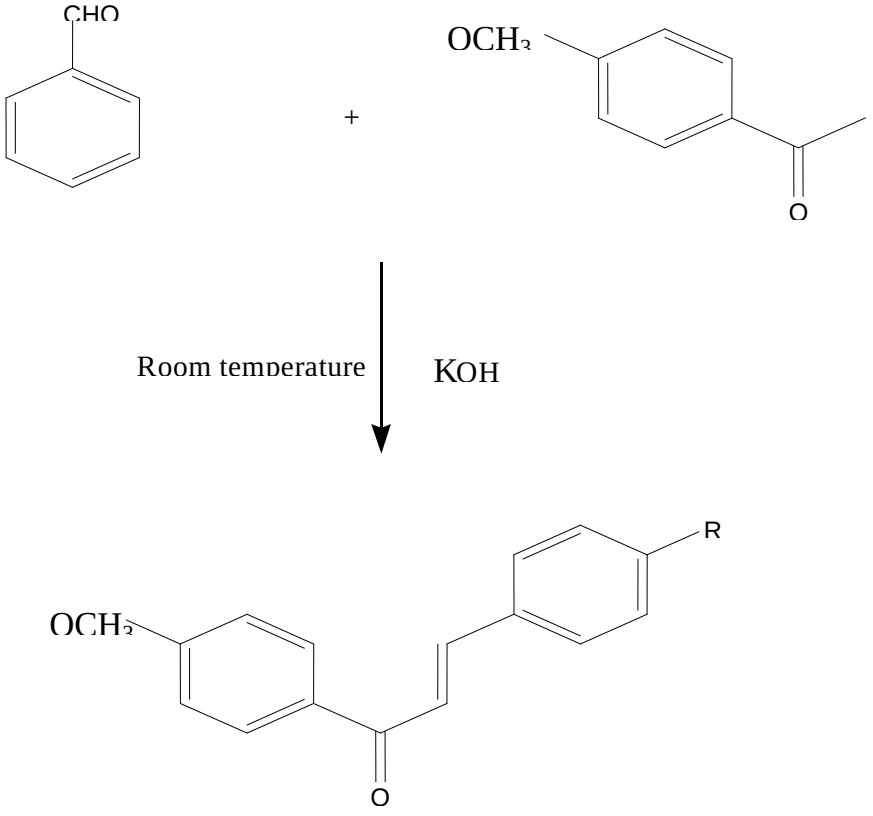
SUMMARY AND CONCLUSION

A great deal of interest has been developed in the synthesis of 4^1-methoxy chalcones and their derivatives.

The chalcones were synthesized by a base catalysed claisen- Schmidt reaction between a substituted benzaldehyde and a methoxyacetophenone. Mechanistically, the reaction involves formation of a carbanion from the acetophenone in the presence of the base KOH, followed by nucleophillic attack by the carbanion on the carbonyl carbon of the benzaldehyde and subsequent loss of water to give the chalcone.

Substituted chalcones (1-6) were prepared by reacting 4-methoxy acetophenone with the corresponding substituted aromatic aldehydes in the presence of methanolic potassium hydroxide at room temperature.Some substitutions such as 4-methoxy, Dimethlyamino and chloro derivative took longer reaction time (8-11 hr). Majority of the compounds were obtained in less than two hours. All the compounds were purified by recrystallization using methanol as solvents.

Synthesized compound were evaluated for antibacterial activities. Among these compounds, chloro and methoxy derives showed better activity against gram +ve bacteria whereas Dimethlyamino and chloro derivatives showed activity against gram – ve bacteria.



SCHEME: 1 Synthesis of chalcones

Table 1: Physical data and yields of substituted- 1- (4-methoxyphenyl)-3-phenylpropan-1-one:

COMPOUND NO.	R	R^1	M.P.^{0}C	Yield %	Formula
1	4-N$(CH_3)_2$	OCH_3	110	55	$C_{18}H_{19}O_2N$
2	4-Cl	OCH_3	112	25	$C_{16}H_{14}O_3$
3	4-OCH3	OCH_3	98	37	$C_{16}H_{13}O_2Cl$
4	2-OH	OCH_3	94	21	$C_{17}H_{16}O_3$
5	H	OCH_3	123	25	$C_{16}H_{14}O_2$
6	4-F	OCH_3	130	60	$C_{16}H_{14}O_2F$

Table 2: Microbial activity

S.No	**ZONE OF INHIBITION (in cm)**			
	B.subtilis		**P.aeruginosa**	
	0.1%	**0.2%**	**0.1%**	**0.2%**
Standard	**4**	**8.1**	**4.8**	**9.7**
Control	**-**	**-**	**-**	**-**
1	**3.4**	**6.8**	**3.5**	**7.2**
2	**3.5**	**5.4**	**2.6**	**7.1**
3	**1.5**	**3.5**	**2.6**	**5.2**
4	**2.2**	**3.1**	**2.5**	**4.9**
5	**1.5**	**2.3**	**3.3**	**3.2**
6	**2**	**4.1**	**3.1**	**5.6**

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