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SYNTHESIS, CHARACTERIZATION AND ANTI MICROBIAL ACTIVITY OF NOVEL CHALCONES AND ITS DI HYDRO PYRIMIDINENONES

CH.M.M.PRASADA RAO*, D.DHACHINAMOORTHI, M.MOUNIKA, M.PAVANI, SK. SHIREENNAAZ, CH. SRAVANI REDDY AND M. SRI ANNAPURNA

Dept. Of Pharm. Chemistry, QIS College of Pharmacy, Vengamukka Palem, Ongole-523272.

ABSTRACT

Novel chalcones were synthesized by condensing 1-(2-chlorophenyl) ethanone with aromatic aldehydes derivatives in dilute ethanolic sodium hydroxide solution at room temperature according to Clasein-Schmidt condensation reaction. The synthesized chalcones compounds were reacted with urea and ethanol upon cyclisation gives pyrimidone derivatives .All these compounds were characterized by means of their IR, ^{1}H NMR spectroscopic data and microanalyses. The antimicrobial activity of these compounds was evaluated by the cup plate method.

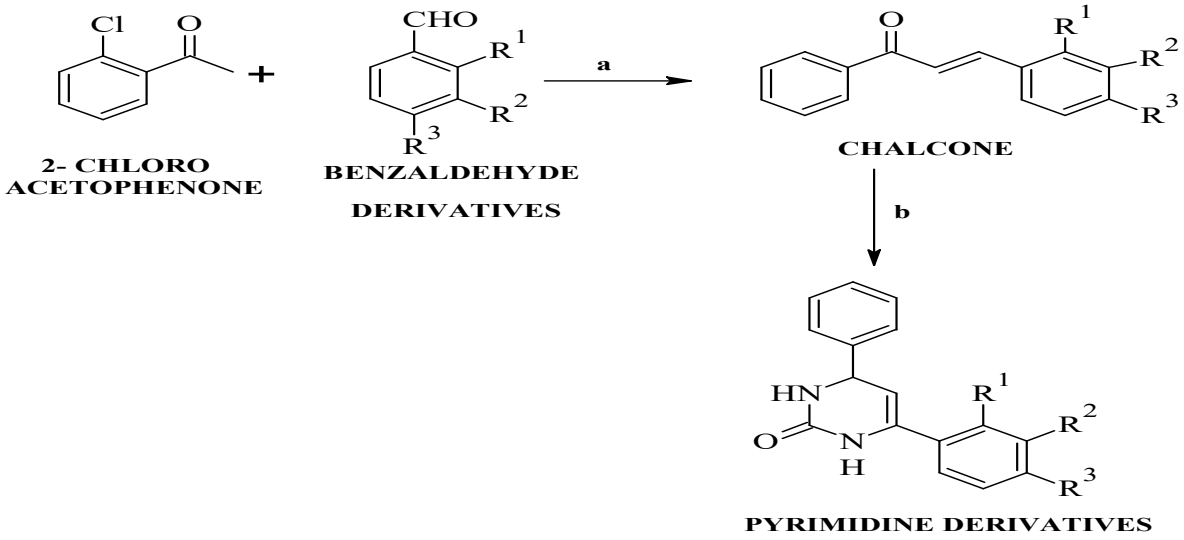
Keywords: Chalcones, Pyrimidone, Antimicrobial activity, Clasein-Schmidt condensation

INTRODUCTION

Discovery of novel synthetic heterocyclic compounds are the target for organic scientists to cure the diseases. Hence, novel chalcones were synthesized because it is known to exhibit various biological activities. Chalcones have been reported to possess antioxidant antiulcer, antimalarial , antileishmanial, anti-inflammatory , antitumor , antitubercular , antibacterial activity and antifungal activity [1]. The presence of a reactive α,β- unsaturated keto functional group in chalcones is found to be responsible for their antimicrobial and other activities, which may be altered depending on the nature and position of substituent on the aromatic rings of aldehydes and 2-Chloro Acetophenone derivative . In the present communication we report the reaction of 1-(2-chlorophenyl)ethanone with different aromatic aldehydes to afford novel chalcones and the synthesized chalcones compounds were reacted with urea and ethanol upon cyclisation gives Pyrimidone derivatives. The structures of the various synthesized compounds were assigned on the basis of elemental analysis, IR and ^{1}H NMR spectral data. These compounds were also screened for their antibacterial activities.

EXPERIMENTAL WORK

Melting points were determined on a capillary melting point apparatus and are uncorrected. 1H NMR spectra was recorded in the indicated solvent on Bruker AV 400 MHz spectrometer using TMS as internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer AC-1 spectrophotometer.
Scheme -I [2-6]



a) Ethanol , 40% KOH at room temperature
b) Urea and ethanol and NaOH, reflex 3-4 hrs

i) R^1:R^2:R^3- H , ii) R^1:R^2 - H, R3: OH, iii) R^1:R^2 - H, R3: Cl, iv) R^1:R^2 - H, R3: SCH_3
v) R^1:R^2 - H, R3: CH_3 ,VI) R^1:R^2 - OCH_3, R3: H

Chalcone Procedure

A mixture of 2- Chloro Acetophenone (0.001moles) and aryl aldehydes (0.001 moles) was stirred in methanol (20ml) and to it 3 mill moles of 40% Potassium hydroxide was added. The mixture was kept stirred continuously for 6 hrs and kept in a dark place for overnight and it was acidified with 1:1 hydrochloric acid and water then it was filtered through vacuum by washing with water.

Pyrimidone Procedure

Chalcones(1eq),urea(1eq), To this mixture 10ml of ethanolic NaoH (1eq) was added at room temperature, reflux for 3-4 hr. The mixture was concentrated by distilling out the solvent under reduced pressure and poured into crushed ice. The obtained solid was purified and recrystallised using a mixture of ethanol.

Spectral Data: [7-8]

(2*E*)-1-(2-chlorophenyl)-3-phenylprop-2-en-1-one (CH-1)
IR(cm-1) 1715 (C=O), 3035 (H of Ar), 750 (C-Cl), 1580 (C=C); 9 (1H, s), 7.8 (1H, s) 7.5 (1H, s), 7.3(1H, s),7 (4H, s)

(2*E*)-1-(2-chlorophenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (CH-2)
IR(cm-1) 1715 (C=O), 3035 (H of Ar), 750 (C-Cl), 1580 (C=C), 2800 (OH); 7.4 (2H, d),7.6 (2H, d), 7.8 (1H, d),7.5 (2H, d), 7.9 (2H, d), 7.6 (2H, d).

(2*E*)-1-(2-chlorophenyl)-3-(4-chlorophenyl)prop-2-en-1-one (CH-3)
IR(cm-1) 1710 (C=O), 3060.39 (H of Ar), 696.55 (C-Cl), 1598.51 (C=C), 8.18 (1H, s),7.95 (1H, s), 7.42 (4H, t),7.17 (3H, d), 3.3 (1H, s).

(2*E*)-1-(2-chlorophenyl)-3-[4-(methylsulfanyl)phenyl]prop-2-en-1-one (CH-4)
IR(cm-1) 1695 (C=O), 3019 (H of Ar), 688.39 (C-Cl), 2590.29 (C-S), 8.5 (1H, s), 8.2 (2H, d), 8 (2H, t), 7.6 (2H, d), 7.4 (3H, t)

(2*E*)-1-(2-chlorophenyl)-3-(4-methylphenyl)prop-2-en-1-one (CH-5)
IR(cm-1) 1695.31 (C=O), 688.39 (C-Cl), 1600 (C=C), 3019 (H of Ar), 8.5 (1H, s),8.2 (2 H, d), 8 (2H, t),7.6 (2H, d), 7.4 (3H, t).

(2*E*)-1-(2-chlorophenyl)-3-(2,3-dimethoxyphenyl)prop-2-en-1-one (CH-6)
IR(cm-1) 1719.60 (C=O), 758 (C-Cl), 1743.1 (C=C), 2840 (C-O-CH_3), 7.4 (2H, d),8.42 (4 H, d), 7.8 (1H, d),7.5 (2H, d), 7.9 (2H, d).

4-(2-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (PY-1)
IR(cm-1) 1794.24 (C=O), 3035 (N-H), 667.07 (C-Cl), 1450 (C=C); 3.366 (1H, s, -C-Cl)
6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH)

4-(2-chlorophenyl)-6-(4-hydroxyphenyl)-3,4-dihydropyrimidin-2(1*H*)- one (PY-2)
IR(cm-1) 1794.24 (C=O), 3515 (N-H), 667.07 (C-Cl), 1450 (C=C), 3400 (Ar-OH),

3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH)

4-(2-chlorophenyl)-6-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)- one (PY-3)

IR(cm-1) 1794.24 (C=O), 3515 (N-H), 667.07 (C-Cl), 1450 (C=C), 3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH)

4-(2-chlorophenyl)-6-(4-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)- one (PY-4)

IR(cm-1) 1794.24 (C=O), 3515 (N-H), 667.07 (C-Cl), 1450 (C=C), 3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH)

4-(2-chlorophenyl)-6-(2,3-dimethoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (PY-5)

IR(cm-1) 1794.24 (C=O), 3515 (N-H), 667.07 (C-Cl), 1450 (C=C), 2860 (C-O-CH_3),3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH)

4-(2-chlorophenyl)-6-[4-(methylsulfanyl)phenyl]-3,4-dihydropyrimidin-2(1*H*)-one(PY-6)

IR(cm-1) 2568.21 (C-S), 147 (S-CH_3), 674.39 (C-Cl), 1614.81 (C=C), 3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH), 2.5-2.55 (1H, s, C-S)

Antibacterial Activity Of Synthesized Compounds [9-10]

The antimicrobial activity was tested by serial dilution method using nutrient broth medium was employed to study the preliminary antibacterial activity of novel chalcones and pyramidinones against *Staphylococcus aureus MTCC 3160,Pseudomonas aeruginosa MTCC 40,Escherichia coli MTCC 1652*

Preparation Of Nutrient Broth Medium

38 g of the nutrient broth medium was suspended in one liter of purified water. Heated with frequent agitation and boiled for one minute to completely dissolve the medium. The medium was finally adjusted to required pH. Autoclaved at 121°C for 15 minutes. Cooled to room temperature.

Procedure

Take 10 test tubes and label it with number from 1 to 10 serially. Then test tubes 1-10 are kept as control ,test tube 1 contains test culture and streptomycin solution. Test tube 10 contains test culture and medium only. In 2nd test tube streptomycin solution and nutrient broth medium was added ,mixed well then serially diluted upto 9. Add 2ml of test tube culture in each test tube. Keep it in incubate for 24hrs ,incubator at 37^0C.The results were tabulated.

Table 1

Anti Microbial Studies Of Novel Chalcones And dihydro Pyrimidone Derivatives

COMPOUNDS	*P.aeruginosa*		*S. aureus*		*E.coli*	
	Zone of inhibition in mm					
	50µg/ml	100µg/ml	50µg/ml	100µg/ml	50µg/ml	100µg/ml
CHB	10	14	10	20	10	20
CHH	12	22	11	23	12	24
CHCl	18	28	16	30	16	32
CHMT	16	26	14	28	14	26
CHMB	14	24	16	30	14	24
CHDMB	12	24	11	20	13	23
DPB	11	22	12	24	14	22
DPH	16	30	18	32	20	32
DPCl	14	28	16	30	14	26
DPMT	13	26	13	28	15	30
DPMB	12	24	13	25	14	26
DPDMB	14	26	13	26	12	24
Streptomycin	16	28	18	26	16	28

RESULTS AND DISCUSSION

Six novel 1,3-diphenyl-2-propene-1-one chalcones and pyrimidone were designed and synthesized by the condensation 1,3-diphenyl-2-propene-1-one with various aromatic aldehydes in dilute ethanolic potassium hydroxide solution at room temperature. and synthesized chalcones upon reaction with urea and sodium hydroxide forms pyrimidone compounds. The obtained compound structures were characterized by its IR and ^{1}H NMR spectral data. The obtained Compounds were screened for antibacterial activities at the concentrations of 50, 100 μg/ml. Among all tested compounds chalcones contains electron with drawing group and electron releasing group and in case of pyrimidone groups contains fluorine and chlorine when comparable with standard antibacterial agent Streptomycin as shown in Table 1.

CONCLUSION

From the above results it is evident that synthesized chalcone derivatives and di hydro Pyrimidone derivatives showed significant in vitro anti microbial studies reveals that broad spectrum antibacterial activity at minimum inhibitory concentration levels when compared with standard drug Streptomycin respectively. In particularly , compounds containing the electron withdrawing groups (halogens) show the maximal antimicrobial activity. the presence of electron releasing groups like methyl and methoxy groups shows moderate activity compare with standard drug.

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