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Synthesis of Some Heterocyclic Compounds Derived From Chalcones

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ABSTRACT
Chalcone derivatives were synthesized by reaction of some **substituted** benzaldehyde derivatives with acetophenone, and then the products obtained were allowed to react with urea, thiourea and hydroxylamine, to give the heterocyclic derivatives of oxazine, thiazine and isoxazole, respectively. The final products have been characterized by elemental analysis, IR and proton NMR spectra. These compounds were also screened for their antibacterial activities.
Key words: Synthesis, Heterocyclic compounds, Chalcone, Antibacterial.

INTRODUCTION

Chalcones were prepared by condensation of acetophenone with aromatic aldehydes in presence of suitable condensing agent [1, 2]. They undergo a variety of chemical reactions that leads to many heterocyclic compounds [3-6]. Chalcones have been used as intermediates for the preparation of compounds having therapeutic value [7,8]. Many reviews reveal that chalcone derivatives exhibit diverse pharmacological activities, such as potential cytotoxic agents, antimicrobial agents, antiviral, anti-inflammatory, anesthetic, etc. [9,10]. In the view of the varied biological and pharmacological applications, we have planned to synthesize some heterocyclic derivatives of chalcone and test their antibacterial activity.

EXPERIMENTAL

Melting points were determined open capillary tube and were uncorrected. IR spectra were recorded on FT IR Perkin-Elmer spectrophotometer using KBr disc method. 1H NMR spectra were recorded on Bruker AMX-300 MHz spectrometer in DMSO. Chemical shifts relative to TMS used as internal standard were obtained in δ unit. The heterocyclic derivatives of chalcone were subjected to antimicrobial screening using nutrient agar medium by well diffusion method [8]. The antibacterial activity was tested against various types of bacteria and compared with standard drugs (Ampicillin and Vibromycin). The chalcones then the heterocyclic derivatives were prepared as shown in the following scheme:

Reaction scheme

Synthesis of chalcones (Ia-c)

Benzaldehyde derivative (0.01 mol) and acetophenone (0.01 mol) were dissolved in ethanol (25 mL).Sodium hydroxide solution, 10% (25 ml) was added slowly and the mixture stirred for 4 hrs then it was poured into 400 ml of water with constant stirring and left overnight in Refrigerator. The precipitate obtained was filtered, washed and recrystallized from ethanol.

Preparation of Thiazine/Oxazine derivatives (II a-c; III a-c)

A mixture of chalcone (0.02 mol), thiourea/urea (0.02 mol) were dissolved in ethanolic sodium hydroxide solution (10 ml) was stirred for 3 hrs, then it was poured into 400 ml of cold water with continuous stirring for 1 hr then left overnight. The precipitate formed was filtered, washed and recrystallized from ethanol.

Preparation of Isoxazole derivatives (IV a-c)

A mixture of chalcone (0.02 mol), hydroxylamine hydrochloride (0.02 mol) and sodium acetate in ethanol (25 ml) was refluxed for 6 hrs, and then the reaction mixture was poured into ice water (50 ml). The precipitate obtained was filtered, washed and recrystallized from ethanol.

Table 1: Physical and elemental analysis of synthesized compounds Compd. Microanalysis Calc. / Found %

No.	Mol. Formula	Mol. Wt.	M.P. (oC)	Yield (%) C H I S
Ia	$C_{15}H_{12}O_2$	224	150-350	80.35 (8 .66) 5.35 (5.85) ----- -----
Ib	$C_{17}H_{17}NO$	251	95-980	81.27 (81.76) 6.77 (6.04) 5.57 (5.03) -----
Ic	$C_{16}H_{14}O_2$	238	40	80.67 (80.23) 5.88 (6.24) ------ -----
IIa	$C_{16}H_{14}N_2OS$	282	148-9	40 68.08 (67.86) 4.96 (5.54) 9.92 11.34
IIb	C18H19N3S	309	73-5	60 69.90 (69.45) 6.14 (6.48) 13.59 (13.21) 10.35 (10.68)
IIc	C17H16N2OS	296	40	68.91 (68.34) 5.40 (5.96) 9.45 (9.92) 10.81 (10.36)
IIIa	C16H14N2O2	266	144-5	50 72.18 (72.58) 5.26 (5.68) 10.52 (10.86)-----
IIIb	C18H19N3O	293	65-6	60 73.72 (73.34) 6.48 (6.78) 14.33 (14.84) -----
IIIc	C17H16N2O2	280	45	72.85 (72.34) 5.71 (6.34) 10.00 (10.56) -----
Iva	C15H11NO2	237	140-2	35 75.94 (75.36) 4.64 (4.16) 5.90 (5.23) -----
IVb	C17H16N2O	264	76-8	40 77.27 (76.93) 60.60 (60.22) 10.60 (10.16) -----
IVc	C16H13NO2	251	30	76.49 (77.01) 5.17 (5.67) 5.57 (6.21) -----

Table 2: Spectral data of the synthesized compounds

Compd. IR (KBr) ν cm-1 1H NMR (d6-DMSO) δ ppm

Ia 3350 (Ar-OH); 1675 (CH = CH-CO); 1640 (C = C); 1480 (Ar-C = C) 4.4 (d,2H,2CH); 5.0 (s,1H,Ar-OH); 7.0-7.8 (m,9H, Ar-H)

Ib 3400 (Ar-I); 1680(CH = CH-CO); 1635 (C = C); 1520 (Ar-C = C) 2.47 (s,6H,I(CH3)2); 4.6 (d,2H,2CH); 7.1-7.8 (m,9H,Ar-H)

Ic 1670 (CH = CH-CO); 1645 (C = C); 1528 (Ar-C = C); 1100 (Ar-OC) 3.4 (s,3H,OCH3); 4.5 (d,2H,2CH); 6.9-7.8 (m,9H,Ar-H)

IIa 3370 (Ar-OH); 2370 (C-S-C); 1655 (C = C); 1624 (C = N); 1610 (NH2) 2.1 (s,2H,NH2); 3.5 (s,1H); 5.2 (s,1H,Ar-OH); 5.7 (s,1H); 6.8-7.9 (m,9H,Ar-H)

IIb 3430 (Ar-N); 2356 (C-S-C); 1650 (C = C); 1620 (C = N); 1590 (NH2) 2.0 (s,2H,NH2); 2.4 (s,6H,N(CH3)2); 3.4 (s,1H); 5.6 (s,1H); 6.9-8.0 (m,9H,Ar-H)

Table 3: Antibacterial activity data of the heterocyclic derivatives of chalcone

Compound	***E. coli***	***S. aureus***	***P. aregenosa***
IIa	18	19	17
IIb	21	18	20
IIc	22	20	18
IIIa	18	20	22
IIIb	22	21	19
IIIc	23	21	20
IVa	17	19	18
IVb	20	20	19
IVc	22	21	18
Ampicillin	23	20	21
Vibromycin	24	22	20

Biological assay of the synthesized products

Antibacterial activity of the heterocyclic derivatives of chalcone have been carried out against several types of bacteria such as, *E. coli*; *S. aureus*; and *P. aregenosa*, using nutrient agar medium by well diffusion method11. All compounds were suspended in aqueous solutions in different concentrations ranged from 10-100 mg/mL, the results are expressed on MIC (minimal inhibitory concentration), solvent blanks were run against each test organism in all assays and the experimental biological data is given in Table 3.

RESULTS AND DISCUSSION

All synthesized compounds as well as the reactions that carried out were characterized and monitored by TLC, melting points, elemental analysis, IR and 1H NMR, and they all gave satisfactory results.

The compounds were evaluated for their antibacterial activities against various types of bacteria, and they showed comparable activity with that of standard drugs.

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