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Synthesis of some heterocyclic compounds derived from chalcones

Mohamed J Elarfi and Hussniyia A Al-Difar

Department of Chemistry, Faculty of Science, Garyounis University, Benghazi, Libya.

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ABSTRACT

Chalcone derivatives were synthesized by reaction of some benzaldehyde derivatives with acetophenone , 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.

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, and etc.[9, 10].

In the view of the varied biological and pharmacological applications, we have decided to synthesize some heterocyclic derivatives of chalcone and test their antibacterial activity.

Experimental

Melting points were determined on Stuart apparatus and were uncorrected. IR spectra were recorded on FTIR Perkin-Elmer spectrophotometer using KBr disc method. ^{1}H-NMR spectra were recorded on Bruker AMX-300 MHz spectrometer in d_6-DMSO.

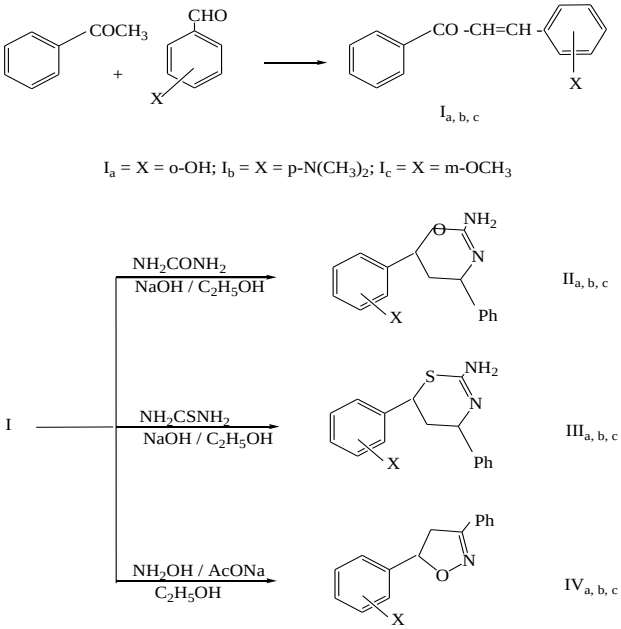
Chemical shifts relative to TMS used as internal standard were obtained in δ unit.

All analysis were carried out at Cairo university, Egypt. Physical and spectral data are shown in tables 1 and 2 below.

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) and were carried out at the botany department, Garyounis university, the results are given in table

The chalcones then the heterocyclic derivatives were prepared as shown in the following scheme:



Reaction scheme

Synthesis of Chalcones (I_{a-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 for4hrs then it was poured into 400 mL of water with constant stirring and left overnight inRefrigerator. 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.

Tele:

E-mail addresses: melarfi@yahoo.com

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.

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 method[11]. All compounds were suspended in aqueous solutions in different concentrations ranged from 10-100mg/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 ^{1}HNMR, and they all gave satisfactory results as shown in tables 1 and 2.

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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Table 1: Physical and elemental analysis of synthesized compounds

Compd. No.	Mol. Formula	Mol. Wt.	M.P. °C	Yield %	Microanalysis Calc. / Found %			
					C	H	N	S
I_a	$C_{15}H_{12}O_2$	224	150-3	50	80.35 (80.66)	5.35 (5.85)	-----	-----
I_b	$C_{17}H_{17}NO$	251	95-9	80	81.27 (81.76)	6.77 (6.04)	5.57 (5.03)	-----
I_c	$C_{16}H_{14}O_2$	238		40	80.67 (80.23)	5.88 (6.24)	------	-----
II_a	$C_{16}H_{14}N_2OS$	282	148-9	40	68.08 (67.86)	4.96 (5.54)	9.92	11.34
II_b	$C_{18}H_{19}N_3S$	309	73-5	60	69.90 (69.45)	6.14 (6.48)	13.59 (13.21)	10.35 (10.68)
II_c	$C_{17}H_{16}N_2OS$	296		40	68.91 (68.34)	5.40 (5.96)	9.45 (9.92)	10.81 (10.36)
III_a	$C_{16}H_{14}N_2O_2$	266	144-5	50	72.18 (72.58)	5.26 (5.68)	10.52 (10.86)	-----
III_b	$C_{18}H_{19}N_3O$	293	65-6	60	73.72 (73.34)	6.48 (6.78)	14.33 (14.84)	-----
III_c	$C_{17}H_{16}N_2O_2$	280		45	72.85 (72.34)	5.71 (6.34)	10.00 (10.56)	-----
IV_a	$C_{15}H_{11}NO_2$	237	140-2	35	75.94 (75.36)	4.64 (4.16)	5.90 (5.23)	-----
IV_b	$C_{17}H_{16}N_2O$	264	76-8	40	77.27 (76.93)	60.60 (60.22)	10.60 (10.16)	-----
IV_c	$C_{16}H_{13}NO_2$	251		30	76.49 (77.01)	5.17 (5.67)	5.57 (6.21)	-----

Table 2: Spectral data of the synthesized compounds

Compd. No.	IR (KBr) υ cm^{-1}	^{1}H NMR (d_6-DMSO) δ ppm
I_a	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)
I_b	3400(Ar-N); 1680(CH=CH-CO); 1635(C=C); 1520(Ar-C=C)	2.47(s,6H,N(CH_3)$_2$); 4.6(d,2H,2CH); 7.1-7.8(m,9H,Ar-H)
I_c	1670(CH=CH-CO); 1645(C=C); 1528(Ar-C=C); 1100(Ar-OC)	3.4(s,3H,OCH_3); 4.5(d,2H,2CH); 6.9-7.8(m,9H,Ar-H)
II_a	3370(Ar-OH); 2370(C-S-C); 1655(C=C); 1624(C=N); 1610(NH_2)	2.1(s,2H,NH_2); 3.5(s,1H); 5.2(s,1H,Ar-OH); 5.7(s,1H); 6.8-7.9(m,9H,Ar-H)
II_b	3430(Ar-N); 2356(C-S-C); 1650(C=C); 1620(C=N); 1590(NH_2)	2.0(s,2H,NH_2); 2.4(s,6H,N(CH_3)$_2$); 3.4(s,1H); 5.6(s,1H); 6.9-8.0(m,9H,Ar-H)
II_c	2368(C-S-C); 1660(C=C); 1625(C=N); 1616(NH_2); 1110(Ar-OC)	2.2(s,2H,NH_2); 3.4(s,3H,OCH_3); 3.5(s,1H); 5.6(s,1H); 7.0-7.9(m,9H,Ar-H)
III_a	3440(Ar-OH); 1640(C=C); 1618(C=N); 1600(NH_2); 1240(C-O-C); 1080(Ar-OC)	2.1(s,2H,NH_2); 3.3(s,1H); 4.8(s,1H,Ar-OH); 5.7(s,1H); 7.0-8.1(m,9H,Ar-H)
III_b	3420(Ar-N); 1656(C=C); 1615(C=N); 1585(NH_2); 1300(C-O-C)	2.2(s,2H,NH_2); 2.4(s,6H,N(CH_3)$_2$); 3.4(s,1H); 5.6(s,1H); 6.9-8.0(m,9H,Ar-H)
III_c	1670(C=C); 1628(C=N); 1600(NH_2); 1360(C-O-C); 1118(Ar-OC)	2.0(s,2H,NH_2); 3.3(s,1H); 3.5(s,3H,OCH_3) 5.7(s,1H); 7.1-8.2(m,9H,Ar-H)
IV_a	3450(Ar-OH); 1680(C=C); 1610(C=N); 1390(C-O-N)	4.6(s,1H); 5.2(s,1H,Ar-OH); 6.8-8.1(m,9H,Ar-H)
IV_b	3460(Ar-N); 1660(C=C); 1618(C=N); 1388(C-O-N)	2.5(s,6H,N(CH_3)$_2$); 3.4(s,1H); 6.9-8.1(m,9H,Ar-H)
IV_c	1680(C=C); 1620(C=N); 1394(C-O-N); 1130(Ar-OC)	3.2(s,1H); 3.6(s,3H,OCH_3); 7.1-8.2(m,9H,Ar-H)

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

Compound	E.coli	S.aureus	P.aregenosa
II_a	18	19	17
II_b	21	18	20
II_c	22	20	18
III_a	18	20	22
III_b	22	21	19
III_c	23	21	20
IV_a	17	19	18
IV_b	20	20	19
IV_c	22	21	18
Antibiotics	-------	-------	------
Ampicillin	23	20	21
Vibromycin	24	22	20