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Synthesis and Antibacterial Activity of Chalcones and Pyrimidine-2-ones

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Abstract: Some new chalcones have been prepared by Claisen-schmidt condensation of ketone and different aromatic aldehydes. These chalcones on condensation with urea in presence of acid gave Pyrimidine-2-ones. The synthesized compounds have been characterized by elemental analysis, IR and ^1H NMR spectral data. They have been screened for their antibacterial activity against Gram positive bacteria *B. subtilis* & *S. aureus* and Gram negative bacteria *E. coli* & *S. typhi*.

Key words: Chalcones, Pyrimidine-2-ones, Antibacterial activity.

Introduction

The chemistry of chalcones have been recognized as a significant field of study. The chalcones and their derivatives possess good antibacterial activity.¹⁻³ Besides this they show antifungal⁴, insecticidal⁵, anaesthetic⁶, anti-inflammatory, analgesic and ulcerogenics⁷ properties. Pyrimidines and their derivatives are considered to be important as drugs and agricultural chemicals. Some substituted pyrimidines and their derivatives have been reported to possess interesting biological activities such as hypnotic properties⁸, antifungal⁹, antitumour¹⁰, activities. Many pyrimidines are used as thyroid drugs.¹¹

Experimental

Melting points of synthesized compounds have been taken in open capillaries and are uncorrected. Purity of compounds were checked by TLC on silica gel coated glass plates. IR spectra were recorded by preparing pallets in KBr on Shimatzu FT-IR 8300 spectrophotometer. ^1H NMR spectra recorded on "Perkin Elmer Model -32 NMR spectrometer" of 300 MHz using TMS as an internal standard. All the synthesized compounds have been screened for their antibacterial activity.

Scheme

Preparation of chalcones

2-Hydroxy-4-isopropoxy-5-nitroacetophenone (0.01mole) dissolved in ethanol and various substituted aromatic aldehydes (0.01mole) dissolved in ethanol were mixed and potassium hydroxide solution (40%, 25ml) was added to it drop wise with stirring and kept overnight at room temperature. The content was then poured over crushed ice and acidified with cold dilute HCl (10%). The solid thus separated was filtered, washed with water, dried and crystallised from acetic acid.

Preparation of 4-[2'-hydroxy-4'-isopropoxy-5'-nitrophen-1'-yl]-6-[substituted aryl]-tetrahydropyrimidine-2-one.

A mixture of different 2'-hydroxy-4'-isopropoxy-5'-nitro substituted chalcones (0.01 mole) and urea (0.01 mole) in ethanol (40 ml) and concentrated HCl (10 ml) were refluxed at 70-80°C for 16 hours. The reaction mixture was then cooled and poured into ice water with stirring. The product thus separated was filtered, washed with water and crystallised from ethanol.

Results and Discussion

Structures of the compounds synthesized have been confirmed by elemental analysis, IR spectra and ¹H NMR spectra.

2'-Hydroxy-4'-isopropoxy-5'-nitrosubstituted chalcones show IR absorption bands at 3438-3466cm⁻¹(-OHstr.), 3050-3062 cm⁻¹(Aromatic C-H str.), 1093 cm⁻¹(C-O-C str.), 1540-1555 cm⁻¹(N=O str.), 1633-1640 cm⁻¹(C=O str.), 1583-1600 cm⁻¹ (C=C str.) and 1380-1390 cm⁻¹(C-H ben.) and NMR signals at δ=1.25 (6H, (d), -CH[CH₃]₂), δ=2.32 (1H, (m), -CH[CH₃]₂), δ=7.05 (αH, (d), -COCH=CH), δ=7.79 (βH, (d), -COCH=CH), δ=9.17 (1H, (s), Ar-OH), δ=6.70-8.23 (6H, (m), Ar-H).

Pyrimidine-2-ones show IR absorption bands at 3422-3475 cm⁻¹ (-OH str.), 3225-3260 cm⁻¹ (N-H str.) 3067-3090 cm⁻¹(Aromatic C-H str.), 1075-1108 cm⁻¹(C-O-C str.), 1540-1550 cm⁻¹(N=O str.), 1650-1670 cm⁻¹ (C=O str.), 1593cm⁻¹ (C=N str.) and 1380-1390 cm⁻¹(C-H ben.) and NMR Signals at δ=1.29 (6H, (d), -CH[CH₃]₂), δ=2.17 (1H, (m), -CH[CH₃]₂), δ=2.73(1H, (t), -CH of pyrimidine ring),

$\delta=3.11$ (1H, (d), -CH of pyrimidine ring), $\delta=4.05$ (1H, (d), -NH), $\delta=9.01$ (1H, (s), Ar-OH), $\delta=6.75$ -7.40 (6H, (m), Ar-H).

Table-1 Characterization Data of Compounds 3a-3h

No.	R	M.F.	M.W.	Yield (%)	M.P. ($^{\circ}$ C)	% Analysis Calc.(Found)		
						C	H	N
3a	H	C ₁₈ H ₁₇ O ₅ N	327	69	182	66.05 (66.01)	5.19 (5.07)	4.28 (4.19)
3b	2-Cl	C ₁₈ H ₁₆ O ₅ NCl	361.5	67	191	59.75 (59.69)	4.42 (4.34)	3.87 (3.80)
3c	4-Cl	C ₁₈ H ₁₆ O ₅ NCl	361.5	74	207	59.75 (59.70)	4.42 (4.31)	3.87 (3.78)
3d	2,4-(Cl) ₂	C ₁₈ H ₁₅ O ₅ NCl ₂	396	76	223	54.54 (54.48)	3.78 (3.66)	3.53 (3.45)
3e	2-OCH ₃	C ₁₉ H ₁₉ O ₆ N	357	65	216	63.86 (63.72)	5.32 (5.27)	3.92 (3.83)
3f	4-OCH ₃	C ₁₉ H ₁₉ O ₆ N	357	68	228	63.86 (63.74)	5.32 (5.26)	3.92 (3.81)
3g	3-OC ₆ H ₅	C ₂₄ H ₂₁ O ₆ N	419	72	252	68.73 (68.59)	5.01 (4.93)	3.34 (3.25)
3h	4[N(CH ₃) ₂]	C ₂₀ H ₂₂ O ₅ N ₂	419	75	232	64.88 (64.72)	5.94 (5.86)	7.56 (7.44)

Table-2 Characterization data of compounds 4a-4h

No.	R	M.F.	M.W.	Yield (%)	M.P. ($^{\circ}$ C)	% Analysis Calc.(Found)		
						C	H	N
4a	H	C ₁₉ H ₁₉ O ₅ N ₃	369	67	133	61.78 (61.72)	5.14 (5.13)	11.38 (11.35)
4b	2-Cl	C ₁₉ H ₁₈ O ₅ N ₃ Cl	303.5	69	139	56.50 (56.44)	4.46 (4.41)	10.40 (10.36)
4c	4-Cl	C ₁₉ H ₁₈ O ₅ N ₃ Cl	303.5	73	144	56.50 (56.48)	4.46 (4.40)	10.40 (10.32)
4d	2,4-(Cl) ₂	C ₁₉ H ₁₇ O ₅ N ₃ Cl ₂	438	76	157	52.05 (52.01)	3.88 (3.84)	9.58 (9.51)
4e	2-OCH ₃	C ₂₀ H ₂₁ O ₆ N ₃	399	71	152	60.15 (60.09)	5.26 (5.23)	10.52 (10.44)
4f	4-OCH ₃	C ₂₀ H ₂₁ O ₆ N ₃	399	74	163	60.15 (60.07)	5.26 (5.21)	10.52 (10.48)
4g	3-OC ₆ H ₅	C ₂₅ H ₂₃ O ₆ N ₃	461	73	179	65.07 (65.04)	4.98 (4.95)	9.11 (9.07)
4h	4-[N(CH ₃) ₂]	C ₂₁ H ₂₄ O ₅ N ₄	412	76	168	61.16 (61.12)	5.82 (5.77)	13.59 (13.54)

Antibacterial activity

The synthesized compounds were tested for their antibacterial activity by measuring the inhibition area on agar plates (diffusimetric method)¹² with Gram positive bacteria *B. subtilis* & *S. aureus* and Gram negative bacteria *E. coli* & *S. typhi* as test germs.

The results of antibacterial screening indicated that very good activity was shown by compound 3d against all four organisms while compound 3g was found to possess moderate activity against Gram negative bacteria but poor activity against Gram positive bacteria. Compounds 4d, 4f and 4h exhibited

very good activity. Other compounds showed moderate activity against both Gram positive and Gram negative bacteria.

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Table-3 Antibacterial Activity of Newly Synthesized Compounds, Zone of Inhibition (mm).

No.	Gram positive		Gram negative	
	B. Subtilis	S. aureus	E. coli	S. typhi
3a	6	8	9	4
3b	8	7	9	7
3c	12	10	10	11
3d	15	17	16	14
3e	6	8	7	8
3f	8	7	8	6
3g	8	7	12	12
3h	8	14	12	7
4a	7	6	6	4
4b	8	6	8	7
4c	9	11	-	-
4d	14	16	12	8
4e	-	11	13	7
4f	15	16	12	7
4g	9	8	8	6
4h	17	18	18	14

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