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Studies on Synthesis of Some New Chalcone and Pyrimidines and their Antibacterial Activity

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Abstract: Pyrimidine-2-one derivatives, 2-[2-{1'-(p-nitrophenyl)-6'-(substituted-phenyl)-pyrimidine-2'-one-4'-yl}-hydrazinomethyl]-3-(p-methoxy phenyl)-quinazoline-4(3H)-one [4a-j] have been synthesised by the condensation of p-nitro phenylurea and various chalcones, 2-(substituted phenylchalconylhydrazinomethyl)-3-(p-methoxyphenyl)-quinazoline-4(3H)-one [3a-j] in the presence of catalytic amount of conc. HCl. And this series of chalcones have been synthesised by the reaction of 2-acetylhydrazinomethyl-3-(substitutedphenyl)-quinazoline-4(3H)-one [2] with different substituted aldehydes in presence of a 2% NaOH solution. These products have been characterized by means of elemental analysis, IR and NMR spectral studies and tested for antibacterial activities against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Salmonella typhi*.

Key words: Synthesis, Quinazoline, Chalcone, Pyrimidine, Antibacterial activity.

Introduction

The chemistry and pharmacology of quinazolinone have been of great interest to medicinal chemistry because quinazolinone derivatives possessed various biological activities, such as anti-inflammatory¹, antibacterial², CVS³ and anticonvulsant⁴. Chalcones and their derivatives possess some interesting biological properties such as antibacterial⁵, antifungal⁶, insecticidal⁷, analgesic, anti-inflammatory and ulcerogenic⁸ etc.

Pyrimidines and their derivatives are considered to be important for drugs and agricultural chemicals. Pyrimidine derivatives possess several interesting biological activities such as antimicrobial⁹, antitumour¹⁰ and antifungal activities¹¹. Many Pyrimidine derivatives are used for thyroid drugs and leukemia. The starting compound 3-(p-methoxy phenyl)-2-hydrazinomethyl-quinazoline-4(3H)-one [1] can be synthesised according to literature method¹².

Experimental

All the melting points were determined in open capillaries and are uncorrected. The purity of compounds was checked by TLC on silica gel 'G' coated glass plates. IR spectra were recorded with KBr on Shimadzu FT-IR 8300 spectrophotometer, ^1H NMR spectra on a Bruker DRX - 300 in CDCl_3 at 200 MHz using TMS as an internal standard.

Scheme

Preparation of 2-acetylhydrazinemethyl-3-(p-methoxy phenyl)-quinazoline-4(3H)-one. [2]

In a 250 ml conical flask take 2-hydrazino methyl-3-(p-methoxy phenyl)-quinazoline-4(3H)-one **[1]** (0.01 mole) in chloroform (dry, 50 ml), acetyl chloride (0.01 mole) was added drop wise with constant stirring at 0 - 5 $^{\circ}\text{C}$. The reaction mixture was stirred for 8 hours, the excess solvent was distilled off and the separated solid thus obtained was poured into ice water. The resulting solid was filtered, washed with water, dried and recrystallised from ether. m.p. - 156 $^{\circ}\text{C}$. yield - 60 %.

Preparation of 2-(4-chloro phenylchalconylhydrazinomethyl)-3-(p-methoxy phenyl)-quinazoline-4(3H)-one. [3j]

In a R.B.F. take 2-acetylhydrazinomethyl-3-(p-methoxy phenyl)-quinazoline-4(3H)-one [2] (0.01 mole) in methanol. Then add p-chloro benzaldehyde (0.01 mole) and 5 ml of 2% NaOH solution. The reaction mixture was refluxed for 5 hours and then poured into ice water. The resulting mass thus separated was filtered and washed with water, dried and recrystallised from ethanol.

IR (KBr): 3362 (-NH), 1687 (-NHCO), 1637 (-CH=CH), 1675 (-C=N), 1706 (-C=O), 850 (-C-Cl); **¹H NMR:** δ 4.66 (s, 2H, -CH₂), 5.46 (s, 1H, -NH), 5.98 (d, 1H, -COCH), 6.58 (s, 1H, -NHCO), 7.18-7.64 (m, 12H, Ar-H), 8.40 (d, 1H, =CH-Ar), 3.42 (s, 3H, Ar-OCH₃).

Other chalcone derivatives of this series were prepared in a similar manner. Data of the various chalcone derivatives are given in **Table-I**.

Preparation of 2-[2-{1'-(p-nitrophenyl)-6'-(p-chloro phenyl)-pyrimidine-2'-one-4'-yl}-hydrazinomethyl]-3-(p-methoxy phenyl)-quinazoline-4(3H)-one. [4j]

In a R.B.F. take 2-(4-chloro phenylchalconylhydrazino methyl)-3-(p-methoxy phenyl)-quinazoline-4(3H)-one [3j] (0.01 mole) in methanol. Then add p-Nitro phenylurea (0.01 mole) and catalytic amount of conc. HCl. The reaction mixture was refluxed for about 6 hours and poured into ice water. The solid product obtained was filtered and washed with water, recrystallised from absolute alcohol.

IR (KBr): 3360 (-NH), 1675 (-C=N), 1706 (-C=O), 850 (-C-Cl), 1512 (-NO₂); **¹H NMR:** δ 4.61 (s, 4H, -CH₂), 5.41 (s, 2H, -NH), 7.18-7.64 (m, 16H, Ar-H), 3.45 (s, 3H, Ar-OCH₃).

Other pyrimidine-2-one derivatives of this series were prepared in a similar manner. Data of the various pyrimidine-2-one derivatives are given in **Table-II**.

Table – I Analytical Data of Chalcone Derivatives

No.	R	M.F. (M.W.)	Yield (%)	M.P. (°C)	% Analysis Found (Calc.)		
					C	H	N
3a	3'-OCH ₃ , 4'-OH	C ₂₆ H ₂₄ N ₄ O ₅ (472.49)	63	125	66.11 (66.09)	5.15 (5.12)	11.84 (11.86)
3b	4'-CH ₃	C ₂₆ H ₂₄ N ₄ O ₃ (440.49)	60	105	70.92 (70.89)	5.46 (5.49)	12.76 (12.72)
3c	2'-OH	C ₂₅ H ₂₂ N ₄ O ₄ (442.46)	63	114	67.89 (67.86)	5.03 (5.01)	12.65 (12.66)
3d	4'-OCH ₃	C ₂₆ H ₂₄ N ₄ O ₄ (456.49)	65	122	68.40 (68.41)	5.32 (5.30)	12.29 (12.27)
3e	3'-NO ₂	C ₂₅ H ₂₁ N ₅ O ₅ (471.46)	62	119	63.68 (63.69)	4.46 (4.49)	14.88 (14.85)
3f	4'-N(CH ₃) ₂	C ₂₇ H ₂₇ N ₅ O ₃ (469.53)	65	128	69.05 (69.07)	5.82 (5.80)	14.95 (14.92)
3g	2'-NO ₂	C ₂₅ H ₂₁ N ₅ O ₅ (471.46)	60	113	63.66 (63.69)	4.45 (4.49)	14.88 (14.85)
3h	4'-F	C ₂₅ H ₂₁ N ₄ O ₃ F (444.45)	62	130	67.52 (67.56)	4.79 (4.76)	12.64 (12.61)
3i	2'-OCH ₃	C ₂₆ H ₂₄ N ₄ O ₄ (456.49)	65	117	68.45 (68.41)	5.26 (5.30)	12.26 (12.27)
3j	4'-Cl	C ₂₅ H ₂₁ N ₄ O ₃ Cl (460.91)	55	112	65.13 (65.15)	4.57 (4.59)	12.19 (12.16)

Table – II Analytical Data of Pyrimidine Derivatives

No.	R	M.F. (M.W.)	Yield (%)	M.P. (°C)	% Analysis Found (Calc.)		
					C	H	N
4a	3'-OCH ₃ , 4'-OH	C ₃₃ H ₂₉ N ₇ O ₇ (635.62)	52	140	62.38 (62.36)	4.62 (4.60)	15.41 (15.43)
4b	4'-CH ₃	C ₃₃ H ₂₉ N ₇ O ₅ (603.62)	50	123	65.69 (65.66)	4.87 (4.84)	16.21 (16.24)
4c	2'-OH	C ₃₂ H ₂₇ N ₇ O ₆ (605.60)	56	131	63.43 (63.46)	4.45 (4.49)	16.15 (16.19)
4d	4'-OCH ₃	C ₃₃ H ₂₉ N ₇ O ₆ (619.62)	60	138	63.99 (63.97)	4.74 (4.72)	15.81 (15.82)
4e	3'-NO ₂	C ₃₂ H ₂₆ N ₈ O ₇ (634.59)	58	135	60.53 (60.56)	4.11 (4.13)	17.63 (17.66)
4f	4'-N(CH ₃) ₂	C ₃₄ H ₃₂ N ₈ O ₅ (632.66)	59	141	64.57 (64.55)	5.13 (5.10)	17.75 (17.71)
4g	2'-NO ₂	C ₃₂ H ₂₆ N ₈ O ₇ (634.59)	60	132	60.52 (60.56)	4.12 (4.13)	17.65 (17.66)
4h	4'-F	C ₃₂ H ₂₆ N ₇ O ₅ F (607.59)	58	145	63.29 (63.26)	4.30 (4.31)	16.11 (16.14)
4i	2'-OCH ₃	C ₃₃ H ₂₉ N ₇ O ₆ (619.62)	57	142	63.95 (63.97)	4.70 (4.72)	15.81 (15.82)
4j	4'-Cl	C ₃₂ H ₂₆ N ₇ O ₅ Cl (624.04)	51	129	61.58 (61.59)	4.23 (4.20)	15.70 (15.71)

Antimicrobial activity

The synthesized compounds were tested for their antibacterial activity by measuring the zone of inhibition on agar plates (diffusimetric method) with *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Salmonella typhi* as test organisms. (**Table-III**)

Table – III Antibacterial Activity of Newly Synthesised Compounds, Zone of Inhibition (mm)

Compd	R	<i>S.aureus</i>	<i>B.subtilis</i>	<i>E.coli</i>	<i>S.typhi</i>
3a	3'-OCH ₃ ,4'-OH	13.0	11.0	12.0	9.0
3b	4'-CH ₃	10.0	8.0	8.0	10.0
3c	2'-OH	11.0	12.0	8.0	10.0
3d	4'-OCH ₃	12.0	10.0	9.0	12.0
3e	3'-NO ₂	11.0	7.0	9.0	8.0
3f	4'-N(CH ₃) ₂	9.0	10.0	11.0	11.0
3g	2'-NO ₂	8.0	9.0	7.0	7.0
3h	4'-F	13.0	12.0	10.0	10.0
3i	2'-OCH ₃	8.0	10.0	10.0	12.0
3j	4'-Cl	11.0	8.0	8.0	7.0
4a	3'-OCH ₃ ,4'-OH	12.0	7.0	11.0	9.0
4b	4'-CH ₃	10.0	8.0	12.0	7.0
4c	2'-OH	7.0	11.0	8.0	12.0
4d	4'-OCH ₃	9.0	8.0	7.0	11.0
4e	3'-NO ₂	7.0	10.0	9.0	8.0
4f	4'-N(CH ₃) ₂	11.0	12.0	12.0	10.0
4g	2'-NO ₂	8.0	10.0	9.0	12.0

4h	4'-F	13.0	9.0	10.0	7.0
4i	2'-OCH ₃	10.0	12.0	7.0	10.0
4j	4'-Cl	9.0	7.0	10.0	9.0

Studies on Synthesis of Some New Chalcone 156

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